Global public and philanthropic investment in childhood cancer research: systematic analysis of research funding, 2008–16

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Childhood cancers caused an estimated 75 000 deaths in children aged 0–14 years in 2018, of which 90% were in low-income and middle-income countries, and yet this group is missing from global health agendas. We examined global patterns in public and philanthropic funding for childhood cancer research—a proxy for global research activity—to address the critical gaps in knowledge. We used data from the Dimensions database to systematically search for and analyse 3414 grants from 115 funders across 35 countries between 2008 and 2016, organised by funding source, recipient, tumour type, research focus, and pipeline categories, to investigate trends over time. During this period, global funding for childhood cancer research was US$2 billion, of which $772 million (37·9%) was for general childhood cancer, $449 million (22·0%) was for leukaemias, and $330 million (16·2%) was for CNS tumours. $1·6 billion (77·7%) of funding was awarded from, and to, institutions based in the USA. Preclinical research received $1·2 billion (59·3%), and around $525 million (25·7%) included support for clinical trials, but only $113 million (5·5%) supported health-care delivery research. Overall, funding was inadequate and geographically inequitable, and new commitments to funding have declined since 2011.

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Introduction

Childhood cancers have long been missing from the global child health agenda, erroneously considered to occur predominantly in high-income countries where other causes of childhood mortality and morbidity have diminished. Estimated age-standardised incidence of cancers in children aged 0–14 years (per million person-years) varies from around 50 in sub-Saharan Africa to 100 in south Asia and 150 in North America and northern Europe, although cancer registry coverage in Africa and south Asia is very low.[1,2] Worryingly, the incidence of childhood cancers appears to be increasing in all settings.[1,3] Cancer is already the leading cause of non-injury related childhood deaths in the USA and Europe, and in 2018, it was estimated that 75 000 children under the age of 15 would die from cancer in 2018.[4–6] More recent estimates put the worldwide incidence at almost 400 000 new cases per year, with one in two cases undiagnosed in Africa and southeast Asia.[7] Globally, more than 90% of childhood deaths from cancer are estimated to occur in low-income and middle-income countries.[8]

During the past decade, the integration of clinical trials and better routine clinical care has led to substantial improvements in survival of children with cancer in high-income settings, where the mean 5-year survival has reached 80%.[9] Progress has been most marked in research for therapies for acute lymphoblastic leukaemia, and yet the disparity in childhood 5-year survival across the world for this condition is stark, ranging from less than 60% in China, Ecuador, and Mexico to over 95% in Scandinavia.[9] Furthermore, improvements in survival have varied enormously between childhood cancer types and across age groups, with improvements in teenage and young adult survival lagging behind.[10,11] Improved organisation, resourcing, and capability of childhood cancer services also play a major part in producing better outcomes, with current models of care for childhood cancers ranging from multidisciplinary specialist care, coordinated by tertiary health centres in well resourced settings, to single-handed general paediatric care by physicians with limited oncological experience in district hospital settings in low-income countries.[12] Global disparities in access to and quality of care for children with cancer are a major driver of the unacceptable variation in outcomes worldwide, and addressing these disparities by improving the infrastructure of health-care systems is crucial. However, development assistance alone is unlikely to be sufficient to combat the growing global impact of childhood cancer, and new research will be a key tool for making progress, as shown by major sociotechnical and economic analyses of the association between research (and its funding) and better outcomes in cancer.[8,13,14]

Childhood cancer must be understood as its own entity, rather than as being on a continuum with adult oncology. Mismatches between funding, research activity, and the most important knowledge gaps—either in terms of burden or potential for impact—are key emerging issues in many areas of health research, including oncology.[15–19] Hence, assessing the current research landscape is essential to address gaps in the understanding of the epidemiology, causation, management, and outcomes of childhood cancer. Judicious investment in research is particularly urgent given that the burden and mortality of childhood cancer is growing in the same places where challenges to data quality and availability are the greatest, as many countries do not have national vital registration data, and rely on verbal autopsy for childhood deaths.[2,7,20]

Reviews of the state of childhood cancer research have been conducted previously, including the SIOPE European strategic cancer plan for children and

Panel 1: **The Dimensions database**

- Dimensions is an interlinked research information system provided by Digital Science
- It uses automated methods to collate funding data from open-access, web-based sources and manually sourced information directly from funders, and is updated on a monthly basis
- It is not actively restricted to English, and gives automatic translation of abstracts when provided in another language
- The database allows the use of keywords and Boolean search terms to identify relevant grants, similar to online databases of scientific publications
- At the time of data collection, the database included more than 3·5 million research projects with aggregate funding of US$1·2 trillion, covering 173 countries and 597 funders
- Available grant information includes the title, abstract, funding amount, start and end dates, and the name and location of funders and recipients
- Grant funding amounts are obtained in their original currencies as well as converted to US dollars, on the basis of 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 (eg, US National Institutes of Health projects), the funding amount is converted for each year's exchange rate

adolescents, and the 2013 *Lancet Oncology* Series on childhood cancer.[19,21–24] Beyond the need for new therapies, common themes that have been voiced relate to creating equitable access to care, addressing late and missed diagnosis and the specific needs of adolescent cancer patients, improving the quality of life of childhood cancer survivors, and developing preventive strategies specific to childhood cancer types.[19,21–24] However, knowledge about the landscape of funding for childhood cancer research has so far been limited to geographical regions, specific funding organisations, or bibliometric analyses.[18,25,26] In order to provide both comprehensive input and a more up-to-date analysis of worldwide research activity, we analysed the global research funding landscape for childhood cancer, categorised funding amounts, number of awards, funders, and recipients, and identified trends spanning a 9-year period.

Methods

Search strategy and selection criteria

For the **Dimensions database** see https://www.dimensions.ai/

See **Online** for appendix

We searched the Dimensions database (panel 1; appendix p 1) for all grants awarded for research on childhood cancers, using keywords relating to childhood, specific age groups (up to and including 18 years), and all relevant tumour types, including those listed under the International Classification of Childhood Cancer (ICCC-3; appendix pp 2–3).[27] We did not use any language or geographical restrictions. The final search was on March 20, 2017, and we included grants active in the 10 years preceding this date (ie, active in 2008–17).

Blinded to funding amount and funding organisation, EML (with input from EJAF) manually screened the titles and abstracts of 7418 resulting grants 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 excluded basic science research that did not demonstrate a genuine paediatric focus in the grant abstract.[28,29] Some grants did not provide the monetary value of the award, in which case we made direct requests to individual funders, thus reducing the number of grants with missing data from 714 (21%) of 3414 included grants to 204 (6%; figure 1).

To aid interpretation of our analysis of the funding data captured in the Dimensions database, we also conducted a supplementary analysis (appendix p 12), in which we aimed to identify major sources of funding of childhood cancer research that were not included in the Dimensions database at the time of data collection. We used several complementary strategies as detailed in the appendix (pp 12–25) and in 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 from a 2016 analysis by Viergever and Hendriks;[30] direct communication with the International Cancer Research Partnership (ICRP) funding network; and additional online searches for any state funders from the USA with open access grant data.[30] 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 generally not publicly available. However, we included grants made to industry as recipients of public or philanthropic funding.

Grant categorisation

We categorised 3414 relevant grants from 115 different funders in 35 countries (appendix pp 4–7), according to three sets of criteria, which are further detailed in panel 2: (1) tumour type (according to ICCC-3) or general paediatric oncology, (2) research focus, describing the core subject a research project addresses with categories aligned to the Common Scientific Outline codes used by the ICRP, and (3) research pipeline, a term aligned with previous studies on research funding, which describes research activity in terms of the so-called bench to bedside categorisation.[15,18,31–34] Additional tags were assigned for research grants with substantial adult oncology overlap or with an explicit focus on teenaged children aged 13–17 years.

We based our categorisation on grant summaries, seeking further information online from institutional websites where required. In an initial pilot analysis, a second researcher (EJAF or EML) categorised 500 randomly sampled grants (using computer-generated, unique random numbers), after which minor clarifications were made to the categorisation criteria to ensure consistency and mutual exclusivity. In any further instances of ambiguity, grants were discussed and categorisation agreed with a second researcher.

Funding analyses

We analysed the data using Stata v14.2. All monetary values were analysed and are presented as US$. A small number of grants in the database only provided monetary values in pounds sterling, which we manually converted to US$ using the first January exchange rate of the year the grant started. All grants were then adjusted for inflation using the Consumer Price Index at the beginning of each year of the grant, thus equating all funding to the value of US$ in 2010 to ensure comparability across years (appendix p 3).[35]

Although the search returned all grants that were active at some point between 2008 and 2017, the period of analysis was subsequently restricted to 2008–16 because data were incomplete for 2017. Some active grants during 2008–16 were initiated before 2008, and large grants usually span multiple years. To attempt to demonstrate the real, annual funding available to researchers, we assumed that multi-year grants were spread equally across their duration, rather than analysing awards by their start date, which would reflect only new commitments and be skewed by large grants of long duration. Therefore, grants with end dates after 2016 or start dates before 2008 were restricted to the portion of funding assumed to be available annually during the 2008–16 period. The grants with no available data on funding could not be included in monetary analyses, but we included them in the analysis of number of grants by topic.

Descriptive analyses included the number of grants, median grant size (because mean values were highly skewed by large outliers), IQR, and total funding in US$. These values were categorised by funder, country and WHO global region of funder (appendix p 7), and country of primary recipient, in addition to the research categories already described. Where grants had been assigned to multiple tumour types or research focus categories, we assumed that funding amounts were divided equally across categories. To illustrate funding for research by tumour type relative to global burden, we sourced age-standardised incidence from Steliarova-Foucher and colleagues.[1] Details of our approach to the estimation of financial contributions from additional funders identified

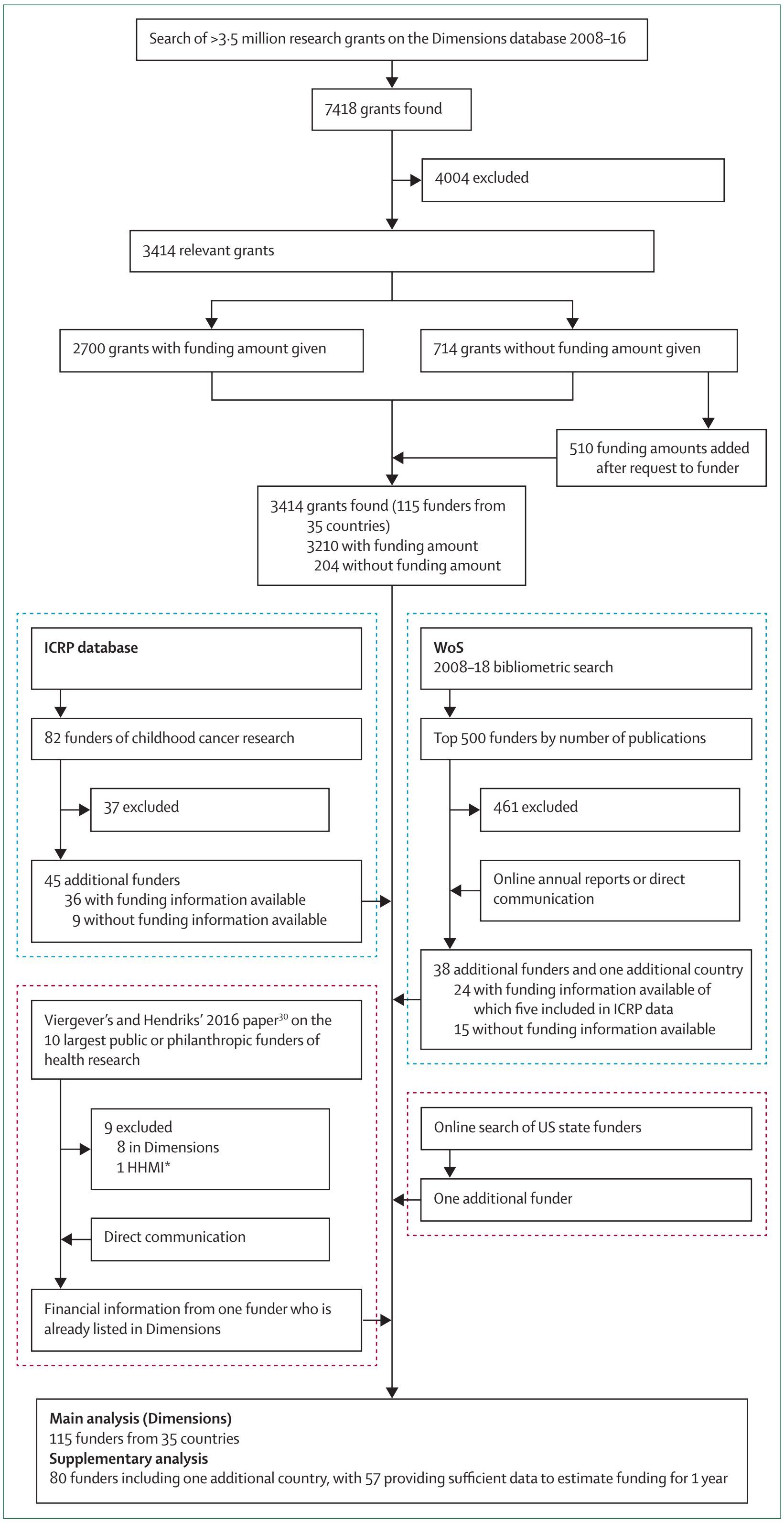

Figure 1: **Flowchart of data collection**
Funding information=any funding data (ie, a monetary amount for at least a year) that allowed estimation of annual contribution to childhood cancer research. ICRP= International Cancer Research Partnership. WoS=Web of Science. HHMI=Howard Hughes Medical Institute. *HHMI grants cannot be categorised by research topic.

Panel 2: Categorisation of grants

Tumour type, according to the International Classification of Childhood Cancer, 3rd edition

- Leukaemias, myeloproliferative diseases, and myelodysplastic diseases
- Lymphomas and reticuloendothelial neoplasms
- CNS and miscellaneous intracranial and intraspinal neoplasms
- Neuroblastoma and other peripheral nervous cell tumours
- Retinoblastoma
- Renal tumours
- Hepatic tumours
- Malignant bone tumours
- Soft tissue and other extraosseous sarcomas
- Germ cell tumours, trophoblastic tumours, and neoplasms of gonads
- Other malignant epithelial neoplasms and malignant melanomas
- Other and unspecified malignant neoplasms
- General paediatric oncology (funding that was specific to childhood cancer but not specific to any particular tumour type)

Research focus, broadly in line with the Common Scientific Outline categories used by the International Cancer Research Partnership

- Biology and causation: basic sciences, cancer biology, studies into the origin and progression of cancers, and studies into causal factors, including epidemiological risk factor studies
- Prevention: research aiming to identify interventions that reduce cancer risk, such as lifestyle, drugs, and vaccines
- Diagnosis or prognosis: research to identify or test cancer markers and imaging methods that are helpful in detecting and diagnosing cancer and predicting the outcome or chance of recurrence
- Model systems: research to develop new animal models, cell cultures, or computer simulations
- Treatment: research identifying and testing locally or systemically administered treatments, the immediate complications of cancer treatments (such as infections, neuropathy, and hearing loss), and treatment resistance
- Survivorship: research into patient care and pain management, beliefs and attitudes that affect behaviour regarding cancer control, supportive and end-of-life care, quality of health-care delivery, long-term side-effects of cancer treatment (such as infertility or cardiovascular disease), and ethics, education, and communication

Research pipeline

- Preclinical research: basic science and public health research, such as surveillance, modelling, and bioinformatics
- Clinical trials: phase 1, 2, or 3
- Health-care delivery: including survivorship, outcomes, health-care apps and products, tissue banks, and developing a health-care intervention
- Crossdisciplinary research: awards containing significant components across any two distinct areas along the above research pipeline
- Infrastructure grants: funding for research centres or research staff dedicated to childhood cancer research

in the supplementary analysis are in the appendix (pp 12–25).

Findings

Funding for childhood cancer research

A summary of total funding, median award size, and number of grants is outlined in table 1. On the basis of data from the Dimensions database, we found the total funding for childhood cancer research from 2008 to 2016 to be roughly $2·0 billion. The mean funding available per year was therefore $226·8 million during this time, with a median award size of $149 620 (IQR $49 800–432 300; table 1).

Between 2008 and 2011, the annual funding available from all active grants increased, but between 2011 and 2013, there was an overall decrease in funds (table 1). Funding appeared to increase in 2015, but this change was due to a small number of large research infrastructure grants, which increased research infrastructure investment by $24 million. Excluding research infrastructure investment, the overall direct funding of childhood cancer 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 amount equates to a mean of $166·0 million in new awards each year, but with considerable year-to-year variability. In one case, for example, $256·0 million was awarded in 2014 but only $160·0 million was awarded the following year (figure 2).

As we describe in detail in the appendix (pp 12–25), we identified 80 additional potentially important funders of childhood cancer research that were 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 (appendix p 12). Sufficient data to estimate funding for one year of childhood cancer research were available from 57 of these funders (figure 1; appendix p 16). After adjustment for inflation, the total additional funding we estimated for one year of childhood cancer research was $80·29 million, including $32·06 million estimated by the ICRP to account for support from additional ICRP partners and $48·23 million identified through our analyses. In addition to our estimates from the Dimensions database, we therefore estimate the annual active funding for 2016 to be $307·1 million, although this estimate cannot be extrapolated to before 2016.

Funding by tumour type

We found that $771·8 million (37·9% of the total active funding for 2008–16) was spent on what we termed general paediatric oncology research, without a focus on specific tumour types, $181·6 million (23·5%) of which was investment in research infrastructure (eg, supporting new research centres and networks). Analysed by tumour type, research in leukaemia (and other myeloproliferative and myelodysplastic diseases) was the most highly funded ($448·8 million [22·0%]), followed by research into CNS tumours ($329.6 million [16·2%]), and neuroblastoma and peripheral nerve cell tumours ($181·2 million [8·9%]). The remaining 15·2% ($309·0 million) of the total funding was dedicated to research in all other tumour types. For germ cell and

	Total active funding*, 2008–16, US$ (n=2 040 816 028)	Number of active grants†, 2008–16 (n=3414)	Median award size, US$ (IQR)	Number of grants with monetary value unavailable (n=204)
Totals	2 040 816 028	3414	149 620 (49 829–432 311)	204
Tumour type, as per ICCC-3				
General paediatric oncology	771 837 100 (37·82%)	908 (26·6%)	81 500 (41 600–334 200)	30
Leukaemia, myeloproliferative diseases, and myelodysplastic diseases	448 754 400 (21·99%)	1001 (29·3%)	170 400 (50 800–457 700)	96
CNS and miscellaneous intracranial and intraspinal neoplasms	329 561 100 (16·15%)	618 (18·1%)	185 300 (642 200–488 900)	19
Neuroblastoma and peripheral nerve cell tumours	181 231 400 (8·88%)	385 (11·3%)	196 700 (60 000–533 900)	31
Malignant bone tumours	86 368 400 (4·23%)	186 (5·4%)	116 300 (51 600–334 100)	10
Soft tissue and extraosseous sarcomas	86 385 700 (4·23%)	134 (3·9%)	120 200 (50 400–435 900)	7
Lymphomas and reticuloendothelial neoplasms	47 931 000 (2·35%)	110 (3·2%)	149 300 (51 100–332 400)	6
Renal tumours	40 334 100 (1·98%)	76 (2·2%)	170 400 (51 800–399 500)	5
Retinoblastoma	16 944 300 (0·83%)	42 (1·2%)	155 500 (43 500–394 500)	1
Other malignant epithelial neoplasms and malignant melanomas	11 334 400 (0·56%)	37 (1·1%)	83 600 (29 400–284 800)	2
Germ cell tumours, trophoblastic tumours, and neoplasms of gonads	10 294 000 (0·50%)	28 (0·8%)	178 100 (90 300–381 700)	1
Hepatic tumours	7 139 000 (0·35%)	42 (1·2%)	77 900 (43 300–155 500)	4
Other or unspecified malignant neoplasms	2 701 000 (0·13%)	10 (0·3%)	55 600 (21 200–993 600)	3
Research focus				
Biology and causation, including basic science, cancer biology, and epidemiology or risk factors	806 424 100 (39·51%)	1536 (45·0%)	153 800 (52 200–428 700)	101
Treatment, including therapies for cancer, complications, and treatment resistance	645 795 600 (31·64%)	1018 (29·8%)	154 100 (52 400–430 100)	62
Survivorship, including symptom management, end-of-life care, quality of health-care delivery, long-term side-effects of treatment, beliefs, and attitudes to care	236 765 900 (11·60%)	555 (16·3%)	100 000 (31 200–387 300)	21
Diagnosis and prognosis, including cancer biomarkers, imaging, and predicting outcomes	111 359 500 (5·46%)	295 (8·6%)	138 600 (49 100–359 400)	31
Model systems, including new animal models, cell cultures, and computer simulations	28 854 000 (1·41%)	118 (3·5%)	114 000 (33 300–294 200)	5
Prevention, including interventions to reduce cancer risk, such as lifestyle, drugs, and vaccines	18 144 400 (0·89%)	35 (1·0%)	172 300 (104 000–355 300)	1
Pipeline				
Preclinical, including basic science, public health research, surveillance, modelling, and bioinformatics	1 209 570 700 (59·27%)	2621 (76·8%)	165 800 (56 300–434 300)	172
Crossdisciplinary, including significant components across more than two areas	409 655 900 (20·07%)	49 (1·4%)	926 300 (859 800–4 185 600)	1
Infrastructure, including research centres and staff dedicated to childhood cancer research	192 943 500 (9·45%)	246 (7·2%)	48 400 (45 700–207 400)	2
Clinical trials (ie, phase 1, 2, or 3)	115 615 200 (5·67%)	141 (4·1%)	279 000 (92 100–859 800)	13
Health-care delivery, including survivorship, outcomes, health-care apps and products, tissue banks, and health-care interventions	113 009 500 (5·54%)	355 (10·4%)	77 100 (22 700–301 800)	15
Year				
2008	190 463 300 (9·33%)	823 (24·1%)	101 900 (30 100–230 300)	41
2009	203 924 500 (9·99%)	906 (26·5%)	99 500 (33 500–230 300)	45
2010	222 759 300 (10·92%)	1069 (31·3%)	94 200 (29 700–222 600)	60
2011	237 022 300 (11·61%)	1199 (35·1%)	89 700 (29 400–212 300)	74
2012	239 153 200 (11·72%)	1263 (37·0%)	88 800 (31 700–212 000)	84
2013	235 831 000 (11·56%)	1274 (37·3%)	85 700 (31 800–206 700)	94
2014	253 072 400 (12·40%)	1352 (39·6%)	79 500 (31 200–199 000)	100
2015	255 349 700 (12·51%)	1379 (40·4%)	78 400 (31 200–184 400)	91
2016	203 240 300 (9·96%)	1373 (40·2%)	62 800 (27 600–159 600)	79

Apart from the initial totals, all values are in US$, rounded to the nearest $100. ICCC-3=International Classification of Childhood Cancer, 3rd edn. *Funding estimates for childhood cancer research from active grants between 2008 and 2016 (Dimensions database data). †Includes grants where the monetary value of the award was not available.

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

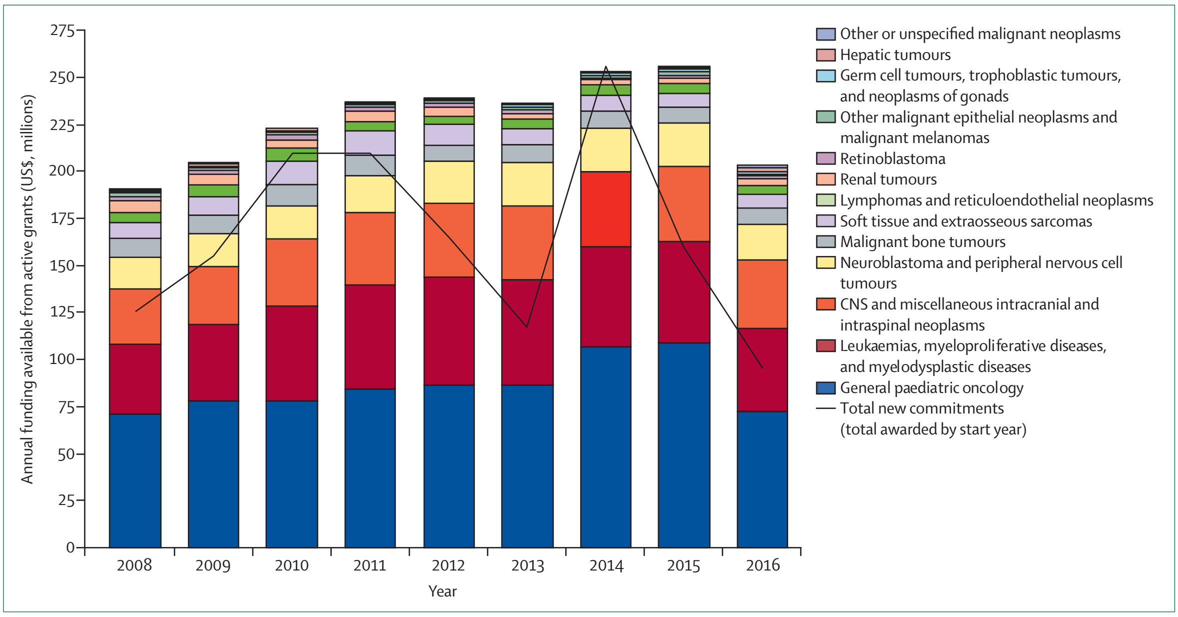

***Figure 2:* Annual active funding and total new commitments available for childhood cancer research, by cancer type, 2008–16**
Annual active funding categorised by tumour type and adjusted for inflation (equating all figures to the value of US$ in 2010). Total funding from new grants (adjusted for inflation) starting each year are also shown (line).

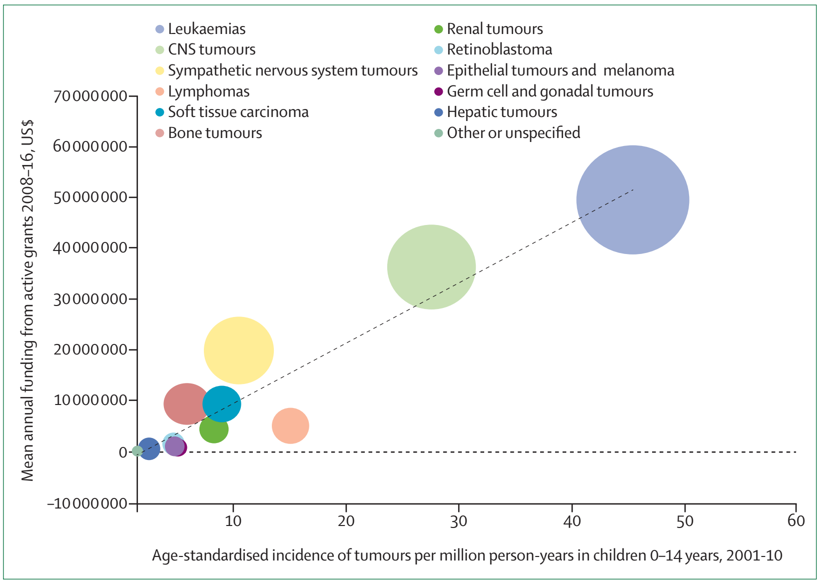

***Figure 3:* Relationship between mean annual funding, number of active grants, and incidence, by tumour type, 2008–16**
Overall mean annual research funding estimated from active grants between 2008 and 2016 (Dimensions data), categorised by tumour type and plotted by estimated age-standardised incidence, where the size of the bubble is proportional to the mean number of active grants from this period. Incidence data sourced from Steliarova-Foucher and colleagues.[1]

hepatic tumours, we only identified 28 and 42 grants each, respectively, with total minimal budgets of $10·3 million and $7·1 million, respectively, over the 9-year period (table 1).

Figure 2 illustrates the investments by tumour type over 9 years in the context of the overall number of new grant commitments each year. Although 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 10–11). The distribution of investment across tumour types has remained relatively static (figure 2).

The relationship between burden of disease (age-standardised incidence for 2001–10) by tumour type, and investment in research (mean annual funding and number of grants) is illustrated in figure 3. In general, funding by tumour type appears to be aligned with the estimated number of new cases, except for lymphomas (and reticulo-endothelial 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 causation, diagnosis and prognosis, treatment, model systems, and survivorship), which cross-tabulates these categories by tumour type and pipeline. Although investigation of the biology and causation of childhood cancers was awarded $806·4 million (39·5% of the $2·0 billion total active funding for 2008–16) during the 9-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%) awarded to research with any focus on prevention of childhood cancers (table 1).

	Biology and causation	Treatment	Survivorship	Diagnosis and prognosis	Model systems	Prevention
General paediatric oncology	166 333 000	227 630 000	178 581 000	13 322 000	1 242 000	3 178 000
Leukaemias, myeloproliferative and myelodysplastic diseases	209 504 000	163 621 000	25 706 000	37 174 000	5 744 000	1 735 000
CNS and miscellaneous intracranial and intraspinal neoplasms	174 823 000	103 749 000	20 870 000	18 075 000	6 593 000	2 946 000
Neuroblastoma and peripheral nerve cell tumours	81 812 000	84 973 000	985 000	8 127 000	2 491 000	1 599 000
Malignant bone tumours	38 804 000	22 869 000	113 000	17 235 000	7 130 000	174 000
Soft tissue and extraosseous sarcomas	43 564 000	23 822 000	0	8 665 000	3 095 000	6 767 000
Lymphomas and reticuloendothelial neoplasms	29 762 000	10 111 000	2 156 000	2 635 000	211 000	732 000
Renal tumours	28 479 000	2 024 000	7 327 000	1 889 000	618 000	0
Retinoblastoma	10 004 000	4 237 000	117 000	805 000	1 522 000	262 000
Other malignant epithelial neoplasms and malignant melanomas	10 392 000	26 000	82 000	212 000	0	625 000
Germ cell tumours, trophoblastic tumours, and gonad neoplasms	7 900 000	364 000	834 000	862 000	207 000	130 000
Hepatic tumours	3 870 000	1 479 000	0	1 266 000	8 000	0
Other or unspecified malignant neoplasms	1 115 000	667 000	0	921 000	0	0
Pre-clinical	643 780 000	326 433 000	90 637 000	101 820 000	28 855 000	17 520 000
Cross-disciplinary	161 193 000	214 167 000	27 236 000	7 020 000	0	42 000
Clinical trials	60 000	102 193 000	10 565 000	2 217 000	0	584 000
Health-care delivery	1 394 000	3 005 000	108 309 000	304 000	0	0

≤200 000; 200 001 to ≤1 000 000; 1 000 001 to ≤5 000 000; 5 000 001 to ≤25 000 000; 25 000 001 to ≤125 000 000; >125 000 000

Figure 4: **Total active funding (US$) for 2008–16, by research focus and tumour type**
Intersection of funding across categories available from active grants between 2008 and 2016, rounded to the nearest $100. Where multiple categories were assigned for tumour type and research focus, funding was assumed to be split equally across categories (panel 2).

The majority of funding ($1·2 billion; 59·3% of the $2·0 billion total active funding for 2008–16) was for preclinical research, including all types of surveillance, $643·8 million of which was to investigate the biology and causation of childhood cancers (figure 4). We categorised $525·3 million (25·7%) as being clinical trials or so-called crossdisciplinary research (ie, studies that included multiple elements of the research pipeline, of which 43 out of 48 studies included clinical trials), and $115·6 million (5·7%) of this amount was for 141 grants solely awarded for phase 1, 2, or 3 clinical trials (table 1). Crossdisciplinary grants were much larger awards (median $926 300; IQR 926 300–4 185 600) than those solely for clinical trials (median $279 000; IQR 92 100–859 800). However, despite more funding being awarded for preclinical studies overall, the median award per study was $165 800 (IQR 56 300–434 300; table 1). Research on improving health-care delivery for children with cancer received a relatively small proportion of the total research funding, amounting to $113·0 million (5·5%) over the 9 years, with a median award size of $77 100 (IQR 22 700–301 800; table 1).

Only 82 (2·4%) of 3414 grants, allocating $19·4 million (1·0%), had an explicit focus on cancers in what they termed adolescent patients, most of which ($15·7 million [80·9%]) was for general oncology research rather than for specific tumour types that are more common in this age group. Research for this age group also related particularly to issues around survivorship ($16·0 million [83·0%]). By comparison, 209 (6·1%) grants funded research with a substantial focus on adult oncology, amounting to $197·6 million (9·7%). The median size of grants for those with and without overlap with adult cancer were $251 700 (IQR 99 300–897 600) and $142 000 (IQR 48 400–421 200), respectively.

Funding by country

Funders from North America awarded most of the funding (table 2), and most funding originating from funders in the USA. The National Cancer Institute (NCI; USA) alone awarded $1·2 billion (59·9%), with the next most substantial funder from our data being the European Commission, which gave $135·2 million (6·6%) in the same period. Less than 2% of funding was awarded from funders in Australia and New Zealand, Asia, and Latin America and the Caribbean (table 2).

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 organisations, 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, which received fewer grants (261) but more funding overall ($105·4 million; 5·2%).

	Total active funding*, 2008–16, US$† (n=2 040 816 028)	Number of active grants‡, 2008–16 (n=3414)	Median award size, US$ (IQR)	Number of grants with monetary value unavailable (n=204)
Global region of funders§				
North America	1 685 398 100 (82·58%)	2238 (65·6%)	184 399 (61 136–549 617)	29
Europe	292 198 900 (14·32%)	633 (18·5%)	206 265 (84 032–417 319)	153
Australia and New Zealand	37 685 900 (1·85%)	86 (2·5%)	356 214 (118 858–549 244)	0
Asia	21 014 400 (1·03%)	388 (11·4%)	33 556 (18 616–51 261)	3
Latin America and the Caribbean	4 518 700 (0·22%)	67 (2·0%)	62 260 (20 548–145 812)	17
Africa	0	0		
Top funding countries¶‖				
USA	1 586 042 200 (77·72%)	1803 (52·8%)	230 613 (72 498–732 223)	26
EU member states	144 920 800 (7·10%)	57 (1·7%)	1 049 009 (210 114–3 791 585)	0
UK	100 061 300 (4·90%)	264 (7·7%)	178 988 (63 459–386 888)	14
Canada	99 355 900 (4·87%)	435 (12·7%)	98 001 (39 714–242 544)	3
Australia	37 262 500 (1·83%)	84 (2·5%)	356 214 (122 888–554 335)	0
Top recipient countries‖**				
USA	1 576 330 800 (77·24%)	1773 (51·9%)	234 404 (72 683–744 432)	32
UK	105 398 800 (5·16%)	261 (7·6%)	178 327 (63 459–404 596)	14
Canada	98 117 800 (4·81%)	435 (12·7%)	98 477 (43 191–242 544)	3
Australia	37 815 600 (1·85%)	89 (2·6%)	321 614 (116 521–542 470)	0
France	31 546 600 (1·55%)	16 (0·5%)	244 367 (119 522–3 124 454)	1
Germany	24 315 900 (1·19%)	72 (2·1%)	2 098 976 (212 297–3 947 584)	61
Sweden	23 892 100 (1·17%)	39 (1·1%)	352 971 (212 191–613 103)	0

*Data shown are estimates of funding for childhood cancer research, from active grants between 2008 and 2016 (Dimensions database data). †All monetary values are rounded to the nearest $100. ‡Includes grants where the monetary value of the award was not available. §Analysed according to global region of funder country (appendix p 7). ¶Defined as the countries of funders collectively providing >1% of the total active funding from 2008 to 2016. ‖The German Research Foundation (Germany) had 69 active grants between 2008 and 2016, but the funding amount was unavailable so is not included here. **Defined as the countries of institutions collectively receiving >1% of the total active funding 2008 to 2016.

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**

The vast majority of grants (3257; 97% of the 3374 with recipient countries listed) could be labelled as internal, meaning that funding was awarded and received by organisations in the same country, amounting to at least $1·9 billion (92%). Overall, only $65·6 million (3·2%) of funding was awarded directly to organisations 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 southeast Asia. We provide in the appendix (pp 6–8) additional figures with a breakdown of total active funding by pipeline category, global region of funders, and research focus.

Implications of current patterns and future directions

To our knowledge, this is the first comprehensive global analysis of major public and philanthropic funding for childhood cancer research, incorporating the extensive data sourced from the Dimensions database with supplementary analyses. Research and innovation for cost-effective diagnostics, treatment, and methods of service delivery is one of five key action points to drive the global fight to stop cancer, identified by the World Oncology Forum in 2017.[17,36,37] Yet our analysis revealed little investment in cancer research that is primarily focused on children, with only $307·1 million per year (including our supplementary analysis estimate) available to researchers, most of whom are in high-income settings. This finding is in the context of $4·8 billion new investments in cancer research for all ages, reported by just 54 funding organisations in 2008.[29] In the same year, HIV/AIDS and malaria, which are also neglected diseases with high mortality burdens predominantly in low-income and middle-income countries, received $1·3 billion and $611 million for research and development, respectively.[38]

There is a dearth of estimates with which to compare our results. However, our findings are consistent with data on UK cancer research funding in 2000–13, which showed that 293 (3·8%) of 7583 awards contained paediatrics as a cross-cutting theme, and that the investment sum of these grants represented 2·6% of the total funding.[18] Similarly, a bibliometric analysis estimated that 5% of papers published by the global oncology research community relate to childhood

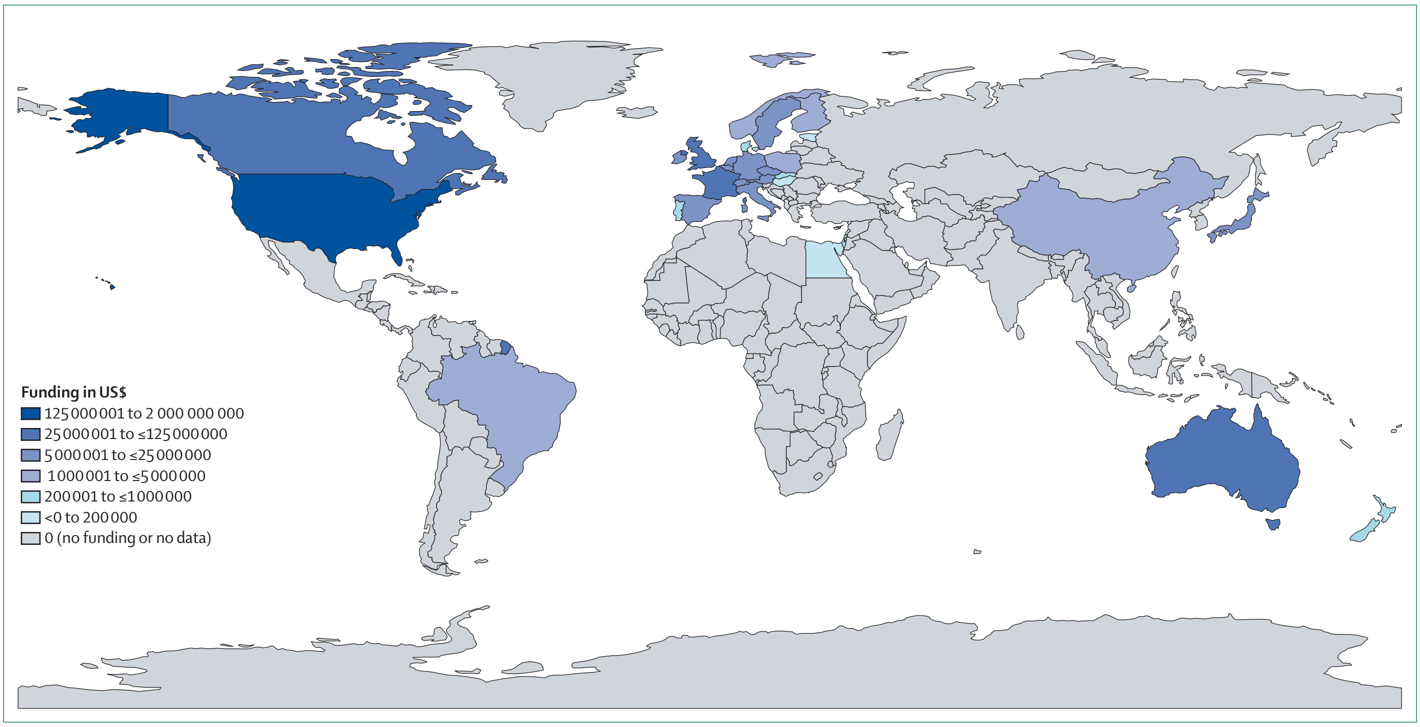

Figure 5: **Countries where funding for childhood cancer research is received, showing the main recipient institutions for active grants, 2008–16**

cancer.[25] An analysis of 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 (in which only grants with at least 25% relevance to paediatric cancer were included in analysis), including those predominantly supporting adult research.[28] Our analysis demonstrates that grants that include adult cancer receive substantially 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 period of our 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, apart from a small number of large USA-based infrastructure grants. Although research infrastructure is essential, particularly in facilitating the interaction between research and clinical care, it is important that infrastructure funding is in addition to, rather than a detraction from, the active funding available to researchers. We took grant duration into account, estimating the active funds during 2008–16 (including relevant portions of ongoing grants from previous years), rather than assessing all funding commitments by start date, which allowed us to demonstrate the real availability of funding to researchers during the time period of analysis.

The Dimensions database provides a unique source of funding data, allowing objective and comparable analysis of trends and categories of funding, albeit limited to those funders included. The key advantage is access to standardised grant data, including details of grant duration, which allows the spread of funding across multi-year grants to be more accurately assessed than if data were obtained from 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 EU and Cancer Research UK (CRUK) were represented in our data through personal communication with both organisations.

However, as other funding analyses have identified, monetary data is not available from many funders, and some well known, important funders of childhood cancer research were missing from the Dimensions database.[39] This is a key limitation of our analysis, which is based on a data source reliant on transparent declaration of finances from research funders. Although a myriad of diverse, smaller funders exist, the primary focus of our analysis was to highlight key patterns of funding over time, across different countries and research categories, none of which are likely to be influenced by small contributions from minor funders. Despite this limitation, we have demonstrated that a handful of major public and philanthropic funders drive the overall direction of funding, and missing such funders would risk creating bias in our estimates. Our supplementary search for major funders missing from the Dimensions database, and our estimation of their annual additional contribution to funding of childhood cancer research gives some context to our main estimates (appendix p 12). Our estimate of $80·29 million of additional support for one year of childhood cancer research is relatively small for 57 different funders (ie, those who had available funding data out of the 80 additional funders identified), and suggests our analysis captured up to 70% of global public and philanthropic funding. It also supports our claim that most of the largest contributors were already included in the database and our analysis, and that the addition of other funders adds diminishing increments to the overall estimate. Importantly, the independently conducted ICRP analyses of funding distribution across categories (of research focus and tumour types) for funding partners that were not included in the Dimensions analysis showed a very similar pattern of investment to what we have reported (appendix p 17).

Almost half of the total funding for childhood cancer research was focused on just three tumour types: leukaemia, CNS tumours, and neuroblastoma. This finding is consistent with investments reported from ICRP funders (including the supplementary analysis of ICRP funders missing from the Dimensions database; appendix p 17) and prior analyses of NCI funding.[26,28] Funding by tumour type is broadly aligned with the estimated number of new cases, but a notable exception is funding for childhood lymphoma research, which is underfunded relative to its global burden (figure 3). The incidence of endemic Burkitt's 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 cancers in equatorial Africa.[40,41] This large difference in prevalence represents an unmet need for prevention and improved care for a malignancy that predominantly occurs in countries other than those funding and carrying out childhood cancer research.[41,42]

For the **India–UK Cancer Research Initiative** see http://www.dbtindia.nic.in/india-uk-cancer-research-initiative/

For the **WHO Global Initiative for Childhood Cancer** see http://www.who.int/cancer/childhood-cancer/en/

Funding for germ cell and gonadal tumours is also low relative to tumour burden (figure 3). This finding supports earlier calls to address the specific challenges and unmet needs of adolescent patients with cancer, with less than 1% of the total funding specifically focused on adolescents in our analysis.[10,23] Incidence is only one lens through which to consider the allocation of research investments. Analyses of funding specific to tumour type against other measures of disease burden—such as survival, mortality, or morbidity—would provide additional perspectives. Currently, however, comparable mortality data is available for only a few types of childhood tumour.[1,9]

Our analysis indicates that the majority of childhood cancer research is preclinical, with the most common research focus category being the biology and causation of childhood cancers (figure 4). There is very limited investment into the translation of basic science research on childhood cancer into new medicines, technologies, diagnostics, and prevention strategies (although understanding causation feeds into prevention research in the case of childhood cancer), with little evidence of any changes in this trend over time (appendix p 9). Known bottlenecks affect clinical trials for individually rare diseases (despite their large collective burden), in both study design and the financial incentives for innovation.[19,43] It is odd that this is still the picture despite Europe's Innovative Therapies for Children with Cancer, European Network for Cancer Research in Children and Adolescents, and other translational initiatives that have been mirrored by the US Children's Oncology Group. Our findings suggest that research funding organisation strategies are not necessarily aligned with needs, or that these initiatives were insufficient to move the research domains. Priorities for new investment would include improving surveillance and data collection (eg, cancer registries) to understand the true burden of childhood cancer in all regions, addressing failures in early diagnosis and high rates of treatment abandonment, and supporting the development of health systems for childhood cancer care. In this context, the low spending of $111·4 million on diagnostics and $113·0 million on health-care delivery over the 9 years of analysis warrant urgent action. Some collaborations show promising steps forward, such as the 5-year India–UK Cancer Research Initiative between CRUK and India's Department of Biotechnology and the WHO Global Initiative for Childhood Cancer supported by St Jude Children's Research Hospital.

Particularly striking is the near absence of funders and recipients in South America, southeast Asia, and Africa in our data, despite the vast majority of childhood cancer deaths occurring in low-income and middle-income settings.[19,44] Funding data from these regions might not have been automatically picked up by the database, which could introduce an element of bias if organisations from some countries are less likely to provide open-access data. Some monetary or technological research is probably channelled via US-based or Europe-based institutions, as occurs in other areas of expertise in global health. The simple binary nature of the Dimensions database data, representing only one recipient and one funder for each grant, oversimplifies funding into a linear transaction, and does not allow more complex modelling of funding flows between institutions in different regions. Further limitations on the data could be missing funders and a selection bias towards English language funders. However, given our extensive supplementary analyses to identify major funders not included in the Dimensions database, the number of funders missed is likely to be small relative to overall research funding, and the trends described are unlikely to be influenced by these potential omissions. A genuine paucity of support for childhood cancer research clearly affects low-income and middle-income countries, and most existing research not captured here is probably directly or indirectly led by principal investigators employed in high-income countries.

The predominance of funding for childhood cancer given and received by organisations within the USA (78% and 77%, respectively) is consistent with the USA's top global position in supporting health research and development in most domains,[45] and suggests that global childhood cancer research is vulnerable to changes in the USA's overall national spending on research. The estimates of funding from missing ICRP partners also indicated a similar pattern of North American funders being the highest contributors to the field. The ten-fold difference in contributions between the USA and Europe in our data is noteworthy, and concerns have been voiced previously regarding the growing gap between the USA and Europe in the funding of non-commercial cancer research.[46,47] A larger number of funders from Europe were missing from the Dimensions database than from other areas, and the mean estimated 1-year contributions from European funders in our supplementary analysis were considerably less than those from US funders ($1·9 million *vs* $4·0 million; appendix p 12). We only identified one additional funder's country in our supplementary search (Italy), and no additional funders in South America, southeast Asia, or Africa. 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.

Around two thirds of the additional funders in our supplementary analysis were non-governmental organisations, in contrast with the predominance of public funders in the Dimensions database. This is probably because open-access funding data is more commonly a feature of governmental funders that are subject to a greater degree of public scrutiny. The fact that half of non-commercial funding in the EU is provided by the charitable sector might explain why more European than North American major funders were identified as missing from the Dimensions database (appendix pp 18, 22).[46,47] By contrast, the US National Institutes of Health provides an online platform (NIH RePORT) for access to information on all grants made through its branches, which was previously used in isolation for a number of funding analyses.[28,48–50]

The funding amounts reported here are certainly underestimates of the true values to some extent, since total funding cannot be fully captured while the majority of funding organisations continue to be opaque in their financial reporting. We found that most organisations providing data only report their total spending on childhood cancer research, usually in one recent annual report, without clarifying whether this figure reflects new commitments that year or overall active funding (including previous and ongoing grants), let alone specific topics of research, focus, or grant duration. These details are crucial for analyses of funding, and it is essential that organisations aim to publish this information in conjunction with overall spending amount, ideally presenting grant data as part of the move towards full transparency. This practice would allow assessment of national and global trends, which could highlight neglected areas, guide future funding priorities, and provide insight into the efficiency of current funding strategies.

Our analysis covered only public and philanthropic grants, excluding potential investments from biotechnology, pharmaceutical, and other industries. Industry has been reported to account for 57% of all biomedical research in the USA,[45] but the extent to which for-profit companies are specifically supporting research for children with cancer is unknown. A previous bibliometric analysis detected limited commercial funding of published childhood cancer research and clinical trials for rare diseases such as childhood cancers.[25] However, industry-funded studies are less likely to be published than publicly funded studies and might also be conducted in partnership with academic institutions who are listed as the main sponsors.[51] Despite these considerations, mapping public and philanthropic funding is essential, because industry funding cannot be relied on as a sustainable force for driving improved outcomes for children with cancer globally.

Conclusions

Childhood cancers represent one of the greatest future opportunities for reducing avoidable deaths and suffering in children. Even after identifying additional funding not included in the Dimensions database, we have demonstrated a relatively low level of investment for childhood cancer research from major funders, with no evidence of recent acceleration in investment. Through this descriptive analysis, which attempts to review the appropriateness of funding, we have shown that available funding is limited in scope by tumour types, that it is highly concentrated in the USA and Europe, and that it mirrors the known bottleneck in translating preclinical findings into clinical trials and health-care delivery research. Future funding should be made more balanced by increasing funding for preclinical research, health systems, and health-care delivery research on methods and mechanisms to improve diagnostic capabilities, registries, training, and education. A key challenge will be unifying researchers and funders in a coordinated approach to childhood cancer as a major and increasing burden, while meeting the resource needs particular to the unique challenges posed by individually rare tumour types.

Research funding activity should be underpinned by aligning research strategies to address need in all regions, including priorities expressed by patients and their families, and minimising so-called wasteful research.[52] The momentum for universal health coverage for children must be met with major new public and philanthropic commitments in global childhood cancer research, to better understand the distribution and causes of childhood cancer, develop innovative diagnostic and treatment strategies, and support new models of care for all settings. Crucially, if funding is to support a global strategy on childhood cancer, full transparency of all funders and their contributions to childhood cancer research is of paramount importance.

Contributors

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 categorise grants, and reviewed categorisation parameters with EJAF and RA. EML categorised 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, and RS and RA reviewed and edited the manuscript.

Declaration of interests

We declare no competing interests.

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