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Correlation Between National Institutes of Health Funding for Pediatric Research and Pediatric Disease Burden in the US

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IMPORTANCE The US National Institutes of Health (NIH) is the largest government funding source for biomedical research globally. Burden of disease is one of the factors considered by the NIH in making funding allocations, though it is not known how funding patterns are associated with disease burden for pediatric conditions.

OBJECTIVE To determine the correlation between NIH funding and disease burden across pediatric conditions.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study evaluates NIH grants funding pediatric research from 2015 to 2018 in the US. Pediatric grants were classified according to disease categories studied. Disease burden for each category was determined using measures from the Institute of Health Metrics and Evaluation and hospitalization data from the 2016 Kids' Inpatient Database.

MAIN OUTCOME AND MEASURE Correlation between NIH funding and pediatric disease burden using Spearman rank order coefficients and predicted amounts of disease-specific funding based on disease burden estimated from linear regression models.

RESULTS This study analyzed 14 060 disease-specific pediatric grants awarded by the NIH from 2015 to 2018 in the US. Annual funding for disease categories ranged from $0 to $382 849 631. Funding for pediatric research was correlated with pediatric disability-adjusted life-years (DALYs), deaths, years lived with disability, and years of life lost (r, 0.56-0.63; $P < 0.001$ for all measures). There was also a correlation between funding and hospital-based metrics, including hospital days, number of hospital admissions, and hospital charges (r, 0.67-0.69; $P < .001$ for all measures). Eight disease categories received greater than $500 million more than predicted levels relative to DALYs, while 5 disease categories were funded more than $50 million less than predicted levels. Based on predicted levels of funding, congenital birth defects; endocrine, metabolic, blood, and immune disorders; and HIV/AIDS were the most overfunded categories relative to DALYs and hospital days. Conditions identified as most underfunded differed depending on use of DALYs or hospital days in estimating predicted funding levels.

CONCLUSIONS AND RELEVANCE NIH funding for pediatric research was correlated with pediatric disease burden in the US with variable correlation based on the disease metric applied. There was substantial overfunding and underfunding of certain conditions. Ongoing evaluation of pediatric funding patterns using a complementary set of disease measures may help inform and prioritize pediatric research funding.

Editorial

Supplemental content

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The US National Institutes of Health (NIH) is the largest government funding source for biomedical research globally with a budget of more than $40 billion in 2020.[1,2] Each year, more than 60 000 grants are awarded by the NIH, funding approximately 300 000 researchers in every state in the US.[3] NIH-funded research programs have made substantial contributions to scientific discovery and translational research, with one analysis indicating that NIH funding supported the basic research underlying every one of the 210 new drugs approved by the FDA from 2010 to 2016.[4] While only a small proportion of the NIH's annual budget is allocated to pediatric research, NIH-funded research has been instrumental in improving pediatric health outcomes, with large contributions toward reductions in infant and childhood mortality, declines in serious pediatric infections, and improved neonatal outcomes.[1]

There are a number of factors influencing investment in pediatric research.[5] Conducting clinical studies in children is associated with unique challenges, including ethical considerations for research involving minors, logistical and technical factors in administering pediatric-specific interventions (eg, drugs with liquid formulations), and financial disincentives related to small market shares for pediatric drugs compared with adult drugs.[5-8] As a result, fewer studies are conducted in children even for diseases and conditions that are common in pediatrics, and children tend to be underrepresented in randomized clinical trials.[9-11] While as much as 65% of funding for studies in adult populations is provided by the pharmaceutical industry, nearly 60% of pediatric clinical trials are sponsored primarily by government and nonprofit organizations.[12]

The NIH considers public health needs in funding prioritization and reports mortality and prevalence data alongside yearly funding amounts for disease categories.[13] Given the more limited resources available for pediatric research, it is critical that funding allocations appropriately target pediatric diseases representing the greatest burden in children. Our objective was to assess the correlation between NIH funding and disease burden across pediatric conditions and to identify diseases with relative underfunding and overfunding.

Key Points

Question Is National Institutes of Health (NIH) funding allocated to pediatric diseases correlated with disease burden for these conditions in the US?

Findings In this cross-sectional analysis of 14 060 pediatric grants in the US, funding for pediatric research was correlated with a number of measures of disease burden, including measures of health care use. Certain conditions were substantially overfunded or underfunded relative to predicted funding levels based on disease burden.

Meaning Ongoing assessment of pediatric funding patterns using a complementary set of disease measures may help inform and prioritize pediatric research funding.

Methods

Study Design

We conducted a cross-sectional analysis of NIH grants awarded for pediatric research between January 1, 2015, and December 31, 2018. Data were analyzed from November 1, 2019, to October 15, 2020. The study period was selected to capture the first year the NIH added a pediatric category to its research classification system. Data on disease burden were available from the Institute of Health Metrics and Evaluation (IHME) through 2018 at the time of our analysis.[14] The study was deemed exempt from review by the Institutional Review Board at Boston Children's Hospital because it did not involve human subjects.

Disease Categories

The NIH uses the Research, Condition, and Disease Categories (RCDC) system to report on research funding for study topics and populations.[13] We used the NIH RCDC data to identify all pediatric grants and funding allocated to each. For grants that extended to years beyond 2015 or 2018, we only included the amount awarded in years during the study period.

Measures of Disease Burden

Metrics of disease burden were obtained from the IHME for 2015 to 2018. We extracted annual numbers of disability-adjusted life-years (DALYs), deaths, years lived with disability, and years of life lost for children in the US. DALYs combine years of life lost and years lived with disability for an individual, taking into account both acute and chronic components of a disease,[15] and have been used to assess the association between disease burden and research activity for a variety of conditions and diseases.[16-18]

The IHME uses prespecified age groups of birth to 1 year, 1 to 4 years, 5 to 9 years, 10 to 14 years, and 15 to 19 years. To obtain data for youth aged 0 to 17 years, we summed values for youth 0 to 14 years and three-fifths of values for youth aged 15 to 19 years.[16,19] The IHME disease classification comprises of 4 hierarchical, nested categories with increasing specificity at each level. Categorizations are mutually exclusive and comprehensive at each level. We selected the 168 level causes reported in the IHME. This level provides categories such as asthma, depressive disorders, and leukemia, with each cause mapped to diagnoses codes in the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*) coding system. We excluded 11 disease categories pertaining to nonpediatric conditions (eg, Alzheimer disease and other forms of dementia, breast cancer, and cervical cancer), leaving 157 disease categories for our analysis.

For children in the US, death may not adequately capture the impact of many diseases, requiring the use of additional measures to address chronic burden and health care use.[20] To complement the IHME-based metrics, we queried the Kids' Inpatient Database (KID) and extracted data on hospitalizations for children aged 0 to 17 years.[21] The KID is an administrative data set and represents the largest publicly available, all-payer pediatric inpatient database in the US. The design of the data set allows extrapolation to national estimates of health care metrics. Data are made available every 3 years, with the latest data set released in 2016. We extracted data on number

of hospital days, number of hospitalizations, and hospital charges along with corresponding diagnoses reported using *ICD-10* codes.

Definitions and Data Characterization

Two investigators (C.A.R., V.H.) reviewed grant titles and abstracts in the NIH Research Portfolio Online Reporting Tools (NIH Reporter)[22] and assigned disease categories to each grant according to the IHME disease classification. An additional investigator (F.T.B.) provided input as needed. The investigators underwent a rigorous classification development process in which 400 grants were reviewed to establish consistency in disease category assignment. The process was piloted on a random selection of 100 grants, which indicated a high degree of interrater reliability (Cohen κ, 0.89). All subsequent disease category assignments were performed by a single reviewer.

Grants studying more than 1 disease (eg, the impact of respiratory syncytial virus immunoprophylaxis on respiratory syncytial virus morbidity and asthma) were classified according to each disease studied and the total funding amount divided equally between diseases. In cases where a grant abstract described conditions representing risk factors for a disease, we categorized grants by the disease studied and not the risk factor.

We excluded institutional and training grants that were not disease specific, grants to non–disease-specific research centers, and grants for non–disease-specific registries. We also excluded grants related to maternal health if the study population was not adolescent and grants studying precursors to adult disease in children (eg, risk factors for multiple myeloma, prostate cancer, or breast cancer in children and adolescents). We included only grants for research that was focused on diseases in the US and excluded grants from the Fogarty International Center and grants for work conducted outside the US.

Statistical Analyses

We performed descriptive statistics for pediatric grants and determined total funding by disease category. We calculated Spearman rank order coefficients to compare the summed amounts of disease-specific NIH funding and metrics of pediatric disease burden over the study period. As hospital data from the KID were only available in 2016, we restricted our comparison of hospital-based metrics to NIH pediatric funding allocated in 2016.

To determine predicted amounts of funding as a function of DALYs and hospital days, we summed funding amounts and disease burden metrics over the study period for each disease category and estimated linear regression models with funding amount as the dependent variable and disease burden metric as the independent variable. Both measures were log transformed. We confirmed that the assumptions of the linear model were satisfied vis-à-vis the residuals, which were normally distributed by the Shapiro-Wilk and kurtosis tests for normality. We also compared the fit of the linear model to one with a higher-order term (ie, quadratic), which did not provide additional predictive value. Disease categories that did not receive NIH funding were not included in the model as the log of zero is undefined. From this model, we derived the predicted funding levels and residual values (ie, the difference between the observed funding level and predicted funding level) among funded conditions and ranked diseases according to relative underfunding and overfunding. All analyses were conducted using Stata SE version 16.1 (Stata Corp). All tests were 2-tailed, and a P value of <.05 was considered significant.

Results

There were 16 042 pediatric grants awarded by the NIH from 2015 to 2018, with 14 060 meeting our inclusion criteria (1437 were excluded for non–disease-specific research, 529 for non-US-based research, and 16 for studying adult diseases). The total NIH funding allocated for these grants was $13 027 850 240, corresponding to approximately $3 256 962 560 per year. This pediatric research funding represented a yearly average of 10.7% of the total NIH budget.

The amount of funding allocated to each disease category varied widely, with funding across disease categories ranging from $0 to $382 849 631 (eTable in the Supplement). Among the 157 disease categories, those that received the most NIH funding were congenital birth defects ($382 849 631 per year), the category endocrine, metabolic, blood, and immune disorders ($265 596 923 per year), and HIV/AIDS ($209 745 599 per year). There were 27 disease categories that did not receive funding. Overall, 9 disease categories received 55.6% of all funding during the study period, with the remaining 121 receiving 44.4%. The disease categories that received the least NIH pediatric funding were esophageal cancer ($36 091 per year), ovarian cancer (annual mean, $27 562), and falls ($18 670 per year).

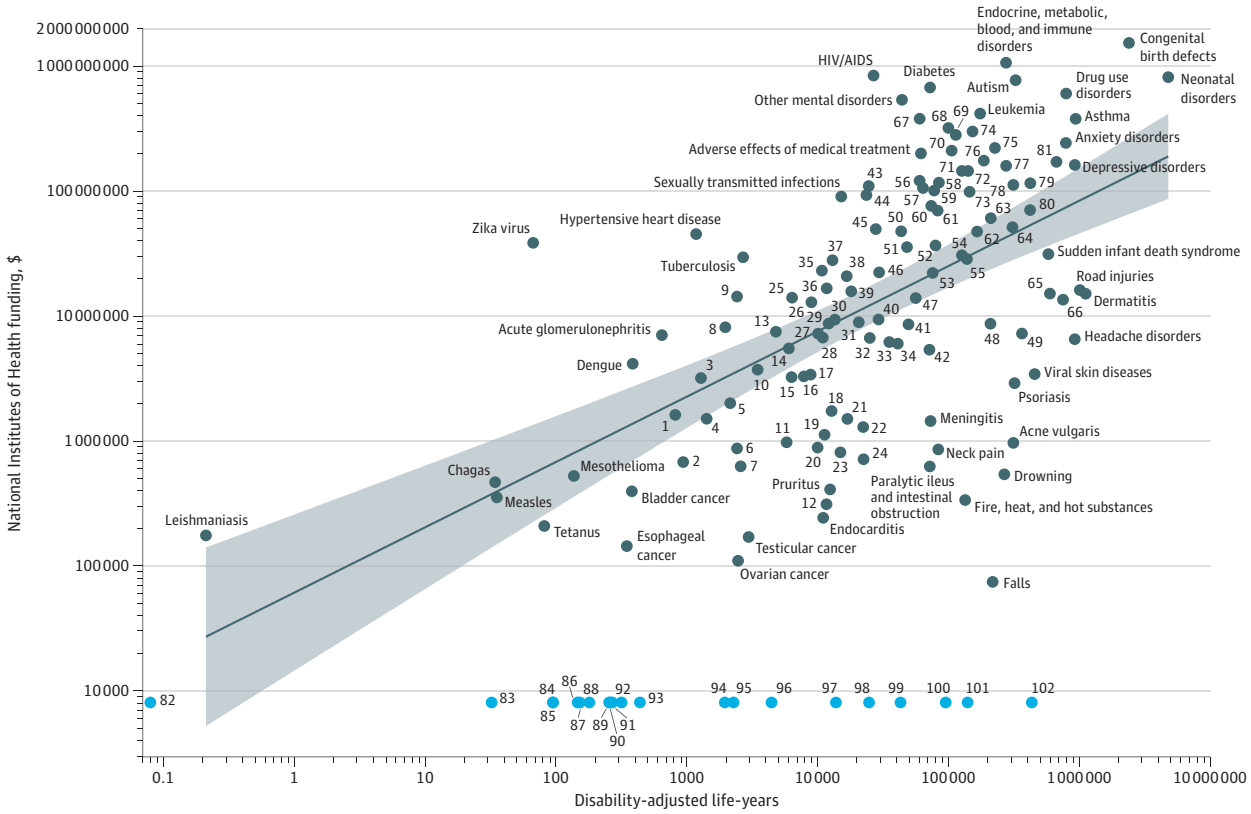
NIH Funding and Pediatric Disease Burden

Disease burden varied widely for pediatric conditions, with a range of 0 to 1 281 916 DALYs per year. The median (interquartile range) yearly number of DALYs per disease category was 5422 (1670-33 525). Similarly, the hospital-based disease metrics indicated a wide range of disease burden, with an annual sum of hospital days in 2016 ranging from 1 to 1 581 082 (median [interquartile range], 4287 [262-41 538]) across funded disease categories.

Funding for pediatric research was correlated with pediatric disease burden as measured by DALYs (**Figure 1**), deaths, years of life lost, and years lived with disability, with Spearman correlation coefficients ranging from 0.56 to 0.63 (**Table**). Among the 27 unfunded conditions, the yearly range of DALYs was 0 to 115 157. Unfunded conditions in the top 30% of disease burden by DALYs included foreign body ingestion or inhalation, exposure to mechanical forces (eg, unintentional firearm injuries), and other transport injuries.

Based on predicted levels of funding, the most overfunded conditions relative to DALYs were congenital birth defects; endocrine, metabolic, blood, and immune disorders; and HIV/AIDS (**Figure 2**). Eight disease categories received greater than $500 million more than predicted levels relative to DALYs. Conversely, 5 disease categories were

Figure 1. Association Between National Institutes of Health Funding for Pediatric Diseases and Disability-Adjusted Life-Years Among Children Aged 0 to 17 Years in the US From 2015-2018



Additional pediatric diseases are listed in the eAppendix in the Supplement.

Table. Correlation Between Measures of Disease Burden and National Institutes of Health Funding for Pediatric Conditions in the US, 2015-2018

Measure	Spearman rank order coefficient	*P* value
IHME-based disease metrics		
Disability-adjusted life-years	0.63	<.001
Deaths	0.56	<.001
Years lived with disability	0.59	<.001
Years of life lost	0.56	<.001
Hospital-based disease metrics[a]		
Hospital days	0.68	<.001
Hospital admissions, No.	0.67	<.001
Hospital charges	0.69	<.001

Abbreviation: IHME, Institute of Health Metrics and Evaluation.

[a] Limited to 2016 as the Kids' Inpatient Database only provided data for 2016.

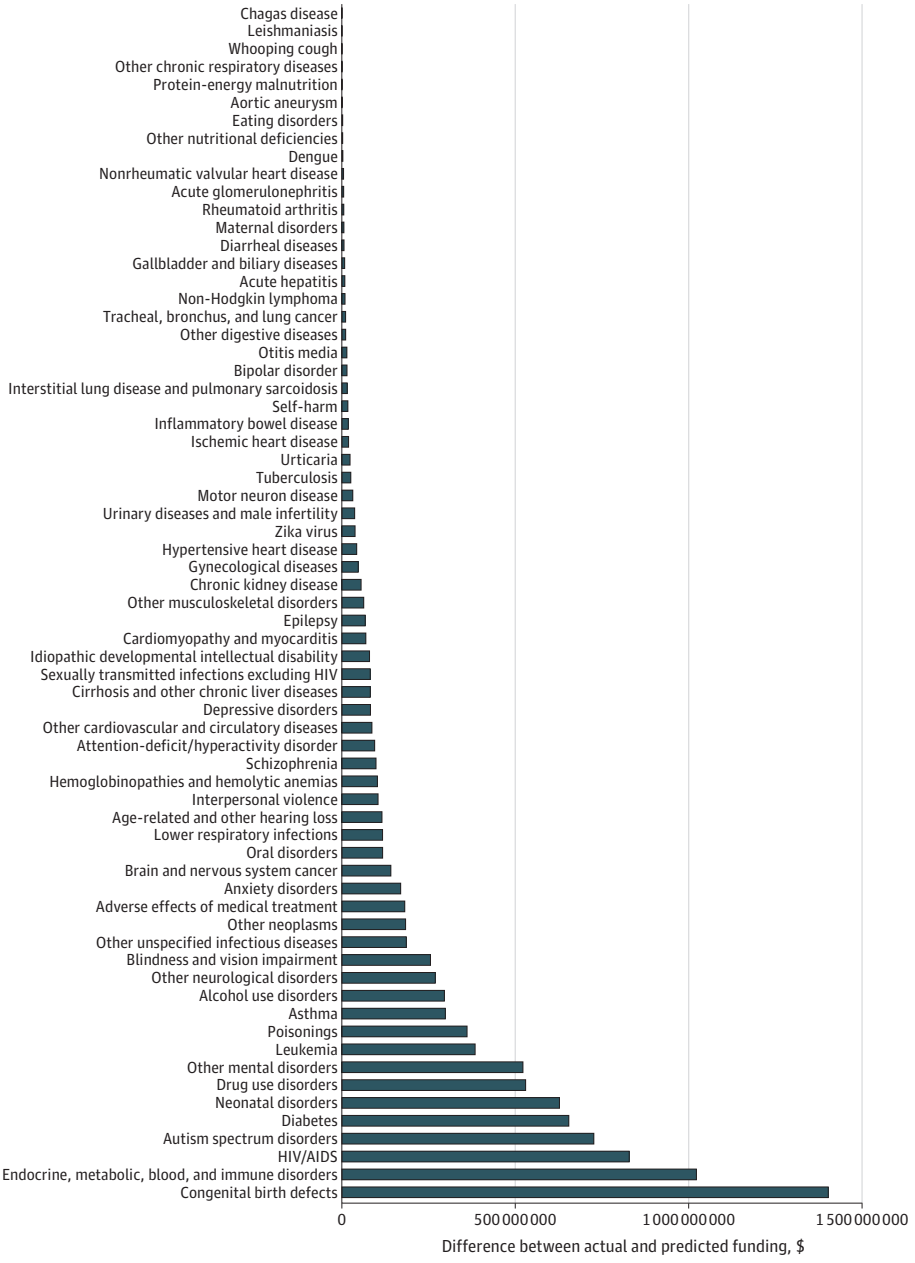
funded more than $50 million less than predicted levels. The most underfunded conditions relative to DALYs were headaches, dermatitis, and road injuries (**Figure 3**). In addition to road injuries, several other underfunded conditions were also trauma-related, including drowning, falls, and the category fire, heat, and hot substances, which encompasses burn-related injuries.

NIH pediatric funding and hospital-based metrics of disease burden demonstrated correlation, with Spearman correlation coefficients ranging from 0.67 to 0.69 (Table). Similar to what we observed for DALYs, the conditions that received the most funding relative to the number of pediatric hospital days were congenital birth defects; endocrine, metabolic, blood, and immune disorders; and HIV/AIDS (eFigure 1 in the Supplement). The most underfunded conditions relative to the number of hospital days differed from those observed using DALYs, and consisted of appendicitis, maternal disorders (among adolescents), other chronic respiratory diseases (eg, sleep apnea and sleep-disordered breathing), and other digestive diseases (eg, gastroparesis and eosinophilic esophagitis) (eFigure 2 in the Supplement). Pediatric bacterial skin diseases did not receive NIH funding during the study period but were in the top 30% of diseases by hospital days.

Discussion

The NIH determines funding allocations using a variety of factors, including maintenance of a diverse research portfolio, scientific advances and available infrastructure, number and quality of investigators and research proposals submitted, and public health needs for specific conditions and diseases.[23] Our analysis of more than 14 000 pediatric research grants

Figure 2. Differences Between Actual and Predicted National Institutes of Health Pediatric Funding Based on Disease Burden in Disability-Adjusted Life-Years Among Conditions That Received Funding Above Predicted Levels



indicated alignment between NIH funding patterns and pediatric disease burden in the US, although the degree of correlation varied based on disease metrics used. DALYs, which account for the age of a person and both the years of life lost and years affected by a disease, revealed a correlation. Though most disease categories were funded commensurate to their disease burden, several conditions were relatively overfunded across disease measures, while others were underfunded. Our findings highlight the need for the NIH and other funding organizations to consider various metrics of disease burden in the allocation of research funds, including consideration of specific measures that may be most appropriate in the assessment of pediatric disease.

The NIH has been gradually increasing its capacity to incorporate and report on disease burden relative to funding allocations. In response to concerns regarding NIH procedures in allocating research funds,[24,25] the NIH convened a working group in 1997 to delineate the criteria used in the process of priority setting and to increase transparency around their assessment of health needs and scientific opportunities.[26] The following year, the Institute of Medicine was charged with conducting a comprehensive study to assess the NIH's policies and

Figure 3. Differences Between Actual and Predicted National Institutes of Health Pediatric Funding Based on Disease Burden in Disability-Adjusted Life-Years Among Conditions That Received Funding Below Predicted Levels

processes in funding allocation, recommending that the NIH strengthen its analysis and use of health data, such as disease burden and cost of diseases, and improve reporting on disease-specific funding allocations.[27] This led to the implementation of the RCDC system[13] to readily monitor funding patterns and alignment with public health needs. In 2016, mortality and prevalence data were added for certain disease categories alongside funding information to further guide understanding of the NIH's research portfolio.

Several studies have assessed the correlation between NIH funding and disease burden in adult populations.[28-30] These studies used a number of disease metrics, with several demonstrating good correlation between NIH funding and DALYs.[28,29] There have been conflicting findings regarding the association between NIH funding and years of life lost and deaths.[28,29] The number of hospitalizations in the US also correlated with NIH funding in 2 analyses,[29,30] but not another.[28] This difference may relate to the inclusion of only 29 diseases in the former 2 compared with 107 diseases in the latter study. None of these studies focused on pediatric populations or considered pediatric-specific diseases and metrics of pediatric disease burden.

Given the different impact of diseases and distribution of disease burden among children, pediatric-specific consideration of NIH funding allocation is needed. Because children in the US experience generally low mortality rates for most conditions, measures capturing disease chronicity, such as health care use, should be included in funding decisions. Underscoring this notion, a recent analysis of pediatric health care expenditures found that among Medicaid beneficiaries in the US, children with complex chronic conditions accounted for 11% of pediatric beneficiaries but 47% of pediatric health care expenditures.[31] Another consideration is the impact of certain rare diseases, such as genetic disorders, that occur pre-

dominantly in children and have low disease prevalence but substantial disease burden and large expenditures for medical care.[32] Measuring disease prevalence alone would not appropriately account for the societal burden associated with these pediatric conditions.

Several pediatric conditions were relatively overfunded based on disease burden. Congenital birth defects received the most funding relative to predicted levels based on both DALYs and hospital days. This relative overinvestment may be owing to reductions in DALYs for congenital birth defects over time without decreases in historic funding levels.[33] The disease category endocrine, metabolic, blood, and immune disorders was also particularly well funded compared with other categories. This is a heterogeneous category used to capture a range of conditions, including obesity, glycogen storage diseases, and cystic fibrosis. As the disease category encompasses obesity, our findings may reflect the NIH's substantial investment in addressing the growing childhood obesity epidemic in the US.[34] Another relatively overfunded disease category was HIV/AIDS. In 1992, at the peak of the HIV epidemic in the US, there were more than 2000 infants with HIV at birth.[35] However, owing to advances in research and preventive measures, fewer than 150 infants are now born with HIV in the US each year. The relative overfunding of HIV/AIDS may be because of ongoing advocacy efforts or the extension of ongoing adult needs to pediatric populations.

Disease categories identified as relatively underfunded differed based on use of DALYs vs hospital days. When assessed using DALYs, a variety of unintentional injuries, including road injuries, falls, drowning, and burns, were underfunded. Underfunding of firearm injuries has been well documented since the passage of the Dickey Amendment in 1996, which essentially banned federal funding for firearm-related research despite the significant loss of life and ongoing morbidity associated with these injuries.[36] Use of hospital days as a disease metric identified a number of respiratory and gastrointestinal disorders as underfunded. These differences do not necessarily imply contradictory findings, but do highlight the need to consider complementary metrics across diseases with different mortality rates and short-term and long-term health care requirements.

Limitations

Our analysis had several limitations. Pediatric grants were identified using the NIH RCDC, which uses an automated algorithm to label grants as pediatric and may lead to misclassification. However, the process uses a robust methodology[37] and our manual review did not identify misclassifications. Another limitation relates to the use of IHME level 3 causes. While these provide a comprehensive representation with relatively detailed descriptions of disease categories, certain categories did not necessarily provide the granularity needed to fully understand funding for individual conditions. A more specific pediatric health disorder taxonomy, focused on disease categories relevant to the US, could improve the capacity to assess pediatric research funding in the US. We also did not examine funding by nonfederal sources, such as foundations and other private entities, or funding initiatives, such as NIH Notices of Special Interest, which may have impacted funding decisions.[38] Moreover, prior studies have documented changes in funding patterns over time,[39,40] and ongoing assessments are needed to measure correlation of NIH funding and pediatric disease burden over time.

Conclusions

NIH funding for children is correlated with pediatric disease burden in the US, with variable correlation based on the disease metric applied. Our findings demonstrate the value of considering various metrics of disease burden in the allocation of research funds, including consideration of specific measures that may be most appropriate in the assessment of pediatric disease. Ongoing evaluation of pediatric funding patterns using a complementary set of disease measures may help inform and prioritize research funding for pediatric conditions.

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Concept and design: Rees, Bourgeois.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Rees, Monuteaux.
Critical revision of the manuscript for important intellectual content: Rees, Herdell, Fleegler, Bourgeois.
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