

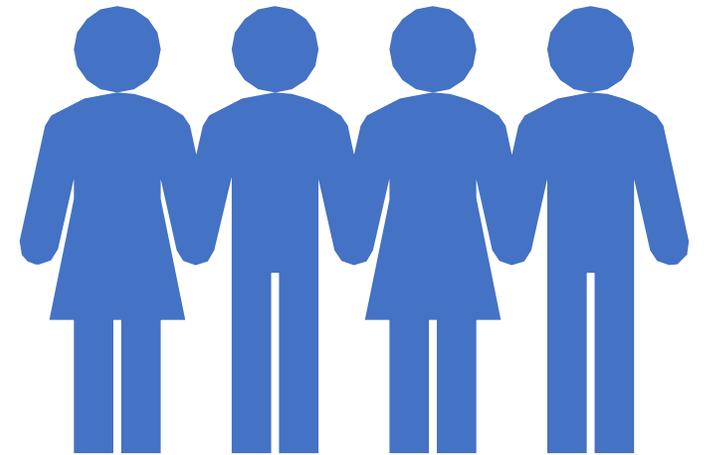
Childhood Cancer Data Initiative (CCDI) Working Group Report

Board of Scientific Advisors

Ad Hoc Working Group in Support of the
Childhood Cancer Data Initiative

Co-Chairs: Drs. Otis Brawley & Kevin Shannon

June 15, 2020



CCDI Working Group Members



Kevin Shannon
(Co-Chair)
UCSF



Otis Brawley
(Co-Chair)
John Hopkins



Peter Adamson
Sanofi



Tom Curran
Children's Mercy



James Downing
St. Jude's



Julie Guillot
*Leukemia &
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Amanda Haddock
*Dragon Master
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Douglas Hawkins
Seattle Children's



Andrea Hayes-
Jordan
UNC



Katherine Janeway
DFCI



Warren Kibbe
Duke



Andrew Kung
MSKCC



John Maris
CHOP



Samuel
Volchenbom
U Chicago

Charge to the Working Group

The NCI Board of Scientific Advisors will convene a Working Group to provide general guidance related to the development and implementation of the Childhood Cancer Data Initiative (CCDI), an effort to establish more efficient ways to share and use childhood cancer data to help identify novel therapeutic targets and approaches, underpin new drug development, and enable new research pursuits to better understand the biology of childhood cancers. In addition, the Working Group will consider how to best advance the themes proposed for the Initiative and may recommend other research activities to enhance this effort.

The Childhood Cancer Data Initiative (CCDI)

$$\begin{array}{ccccccc} \$50 & + & 10 & = & \$500 \\ \text{million} & & \text{years} & & \text{million} \\ \text{Per year} & & \text{Starting FY20} & & \text{Total} \end{array}$$

Purpose: To support the wider pediatric cancer community's goal of maximizing the benefit of data to learn from every patient so that ultimately those patients, survivors and their families can benefit from what we learn.

A composite image featuring two scenes. On the left, a woman and a man in white lab coats are looking through a microscope. On the right, a man with a beard is smiling as a young child uses a stethoscope on a brown teddy bear. A large yellow circle with a white center is overlaid in the middle, containing the text.

**WE WILL LEARN
FROM EVERY CHILD
AND EVERY CHILD
WILL BENEFIT FROM
WHAT WE LEARN**

NCI Childhood Cancer Data Initiative Goals

- **Maximize** every opportunity to improve treatments and outcomes for children with cancer
- **Build** a connected data infrastructure to enable sharing of childhood cancer data from multiple sources
- **Identify** opportunities to make data work better for patients, clinicians, and researchers
- **Develop** and enhance tools and methods to extract knowledge from data



CCDI complements other NCI childhood & AYA cancer initiatives by optimizing data sharing

Connect data from:

- Basic Research



- Population Studies



- Real-world Patient Data



- Pre-clinical Models



- Biospecimen Repositories

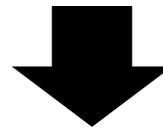


- Clinical Trials





Pediatric/AYA data from multiple sources



Improved understanding of why some cancers develop resistance or don't respond to treatment

Generation of new ideas for intervention

Development of new research and analytical tools

Identification of less toxic treatments and strategies for management

Culture change towards improved collaboration and data sharing

New therapies for childhood/AYA cancers

Timeline of Working Group Activities

Co-Chairs Identified
Members Confirmed

New WG formed by
Dr. Sharpless (NCAB)

- Discuss key focus areas for CCDI guidance
- Identification of priority topics & goals for March F2F

- Working Meetings to:
- develop & finalize recommendations
 - Write final report



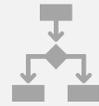
- CCDI WG Kick-Off Meeting – Introductions
- CCDI Background
- Charge to WG
- Discuss priority areas for childhood/AYA cancer data

- Virtual F2F (Due to **COVID-19**)
- Overview of NCI Ped/AYA Efforts; relationship to CCDI
- Brainstorming
- Consensus on priority areas for recommendations
- Roadmap for compiling report

Key Areas of Focus & Consensus



Types of Data for Collection and Aggregation



Landscape of Pediatric/AYA Cancer Research Data & Needs Analysis



Potential Barriers to Progress



Generating New Data



Distinction Between Research & Clinical Data



Engaging Diverse Array of Stakeholders for Input



Potential Opportunities for Transformative Discoveries

Types of Data for Collection & Aggregation

Recommendations

1. We recommend that the CCDI aggregate six broad categories of data:

- **Clinical, treatment, and outcome data** from clinical trials & the electronic health record (EHR)
- **Molecular data** including research sequencing (i.e. **genomic, epigenetic & proteomic data**) and clinical molecular profiling
- Information regarding **the availability & location of archived biospecimens, including germline and tumor DNA**
- **Longitudinal population data** from patients and survivors of pediatric and AYA cancers
- Characteristics of cell line, **patient derived xenograft (PDX) & genetically engineered mouse (GEM) models** of pediatric and AYA cancers
- Any **existing preclinical data generated** from studies performed in these models



Types of Data for Collection & Aggregation

Recommendations

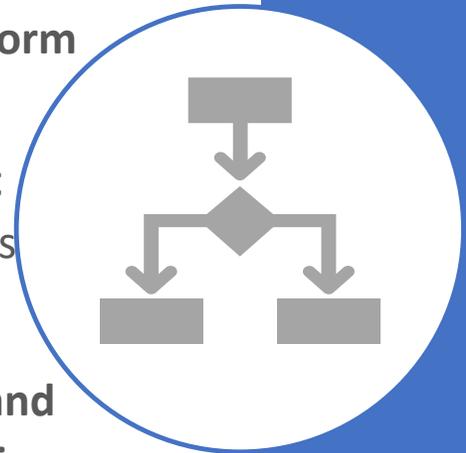
2. We recommend **that the CCDI aggregate data from previous molecular analyses of pediatric/AYA cancers irrespective of whether these studies were performed for diagnostic or research purposes and/or as part of a clinical trial.**
3. We recommend **that the NCI implement strategies to make all CCDI data as representative as possible of the full spectrum of pediatric/AYA cancer patients in the United States (U.S.).** Recruitment targets should reflect the percentage of minorities in the U.S. population and to achieve this, we recommend the NCI include resources for persons obtaining consent to communicate and educate in a racially and ethnically sensitive manner.
4. We recommend **that the 10-year CCDI effort includes plans to evolve;** to include new data and adapt treatments, diagnostics and prevention strategies to the knowledge gained as methods advance.



Landscape of Pediatric/AYA Cancer Research Data & Needs Analysis

Recommendations

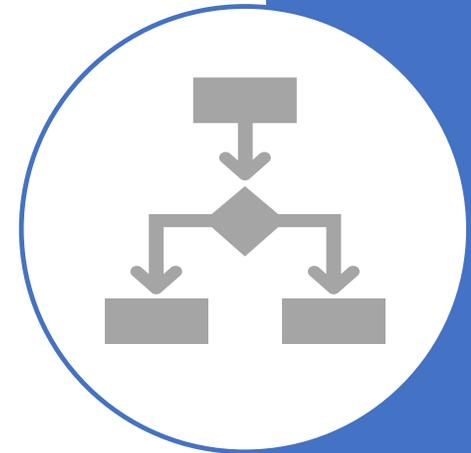
1. We recommend **convening experts to develop consensus guidelines addressing what clinical and molecular characterization and sample archiving should be performed and when they should be performed for each pediatric and AYA cancer diagnosis.**
 - The WG suggests that this group consider **both clinically actionable sequencing to inform diagnosis and therapy and discovery analysis for research purposes.**
 - Finally, **NCI should consider potential ways of paying for molecular testing that is not currently funded by insurance or other sources.** Addressing these challenging issues is central to the achieving the CCDI's mission of learning from every child with cancer.
2. We recommend **that the NCI perform a comprehensive inventory of data, databases and shared research infrastructures with each assessed for quality, relevance and integration feasibility** to better understand the landscape of pediatric and AYA cancer and survivorship data.
3. We recommend **that CCDI efforts include collection and integration of new "ideal" data types prospectively, on every newly diagnosed patient -- offering standardized biomarker/omics testing (biology panel) to every child and seamlessly linking their biology, clinical, and other critical data.**



Landscape of Pediatric/AYA Cancer Research Data & Needs Analysis

Recommendations

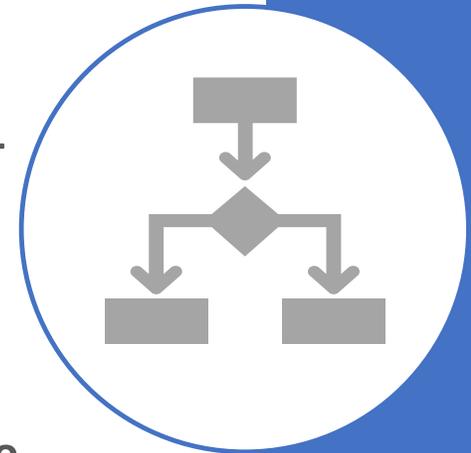
4. We recommend that **the NCI consider how to collect off-trial patient clinical data**, as well as data to enable synthetic control arms to support precision match trials.
5. We recommend that **the NCI review current practices for collecting and cataloging biospecimens** from pediatric/AYA cancer patients **and assigning unique and privacy-preserving identifiers** and consider implementing strategies for enhancing these key activities, particularly in the context of clinical trials.
6. We recommend **developing the National Childhood Cancer Registry (NCCR) as a national resource for aggregating and accessing high-quality curated clinical information, molecular data, and other associated critical patient information** and make every effort to avoid costly redundancies.



Landscape of Pediatric/AYA Cancer Research Data & Needs Analysis

Recommendations

7. We recommend that the **NCI convene a broad spectrum of subject matter experts and stakeholders with expertise in technology, data science and disease biology and clinical care to assist with architecture design and road-mapping** of the NCCR and overall CCDI data infrastructure.
8. We recommend that **the CCDI include activities focused on generating and aggregating preclinical data and the development of infrastructure and tools that will enhance clinical translation. These efforts would ideally focus on the FDA's Relevant Molecular Targets List and on fulfilling the mandates of the RACE for Children Act.** The NCI should also consider providing resources to validate potential targets in pediatric and AYA cancers to expand the reach of precision oncology.



Potential Barriers to Progress

Recommendations

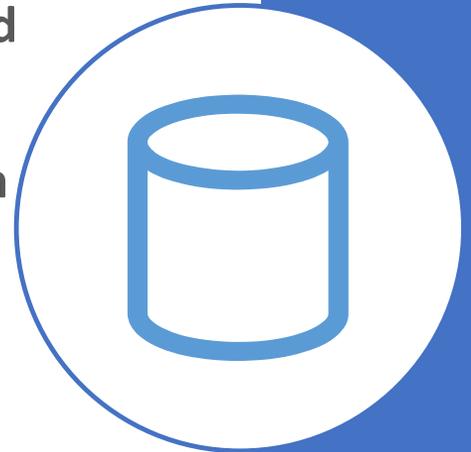
1. We recommend that **the NCI commit to support ongoing data sharing over time through policy and funding**. The WG identified a lack of dedicated financial support to personnel, time and other resources needed to implement effective data sharing as a substantial barrier to achieving the overall goals of CCDI.
2. We recommend that **the NCI consider multiple, creative ways to engage with & utilize expertise from a wide variety of stakeholders in the pediatric and AYA cancer and survivor communities**. NCI should explore **public-private partnerships with other entities including large pediatric care centers, foundations, and industry** for interoperability and sustainability models for data and infrastructure. NCI could also consider, in addition to a panel of scientific advisors, creating a panel of technology advisors to bring valuable outside perspectives to the CCDI.
3. We recommend that **the NCI consider committing resources to consent, sequence samples from, and retain diverse populations** in the CCDI database to proactively ensure that this resource accurately reflects the diversity of the population.



Generating New Data

Recommendations

1. We recommend that the **NCI seek ways to support the generation of evidence** needed to change outcomes for pediatric cancer. This will require an investment in generating data through **new or existing NCI initiatives, aligned with the NCAB *ad Hoc* Data Science WG report.**
2. We recommend that **the CCDI harmonize terminologies and coding between cancer research and clinical care data** as recommended in the NCAB *ad Hoc* Data Science WG report.
3. **We concur with applying of AI and machine learning approaches to analyze pediatric/AYA cancer datasets from EHR** as recommended in the NCAB *ad Hoc* Data Science WG report.
4. We recommend **that the CCDI remove barriers to data access for the broader community by supporting the creation of data resources that simplify data access, such as limited data sets, safe harbor data sets, and synthetic data sets that can be broadly accessed.**



Distinction Between Research & Clinical Data

Recommendations

1. We recommend **that the NIH/NCI set clear expectations regarding the need for broad data sharing policies governing all CCDI activities.** An embargo period on data sharing is reasonable, but expectation should be that data collected using NCI funds will be made available to research community within 6 – 12 months of collection.
2. We recommend that **the NCI explore barcoding approaches to data & metadata from individual patient data so that uniqueness can be assured,** and further evaluate this by funding one or more pilot projects using existing data sets.
3. We recommend **that the NCI develop a long-term strategy for tracking pediatric and AYA cancer patients over many decades across their lifespan.** During this time, they will become independent adults and transition their lives (and care) many times. Assigning a universal, anonymized and privacy-protected unique patient identifier to link clinical information, biospecimens, and any molecular data over time is a particularly appealing solution to this problem that should be strongly considered.



Engaging Diverse Stakeholders for Input

Recommendations

1. We recommend that **the NCI consider multiple, creative ways to engage with and utilize expertise from a wide variety of stakeholders in the pediatric and AYA cancer and survivor communities**. NCI should explore public-private partnerships with other entities including large pediatric care centers, foundations & industry for interoperability and sustainability models for data and infrastructure.
 - NCI could also consider, in addition to a panel of scientific advisors, creating a panel of technology advisors to bring valuable outside perspectives to CCDI.
2. We recommend that **the NCI explore creative ways for parents to “opt-in” to share (de-identified) data collected on their child (versus institutional or organizational ownership of data)**, especially genomic data.
3. We recommend **that the NCI consider developing the CCDI’s infrastructure in a way that could allow patients and families to see their data and allow them to share it with other families, clinicians, and/or researchers**.
 - **There should also ideally be a mechanism for switching control of that consenting process from parent to child when the child comes of age.**

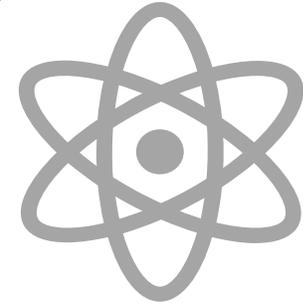


Opportunities for Transformative Discoveries

- **Developing a national strategy to offer appropriate biospecimen collection and genomic testing to every pediatric/AYA patient with cancer within two years.**

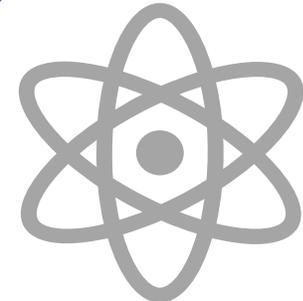
While this is a large and complex topic, specific priorities include:

1. Developing a comprehensive plan for collecting and archiving diagnostic germline and tumor samples from all pediatric/AYA cancer patients irrespective of whether they are enrolled on a clinical trial & for linking this to treatment data & outcome
 2. Implementing a national standard for performing deep sequencing of ~15% of pediatric/AYA cancers that relapse after an initial response to front-line therapies (germline, diagnostic, relapse triads); and,
 3. Consider what type(s) of molecular profiling should be performed at diagnosis in different pediatric/AYA cancers to guide care and enhance discovery.
- **Aggregate data from existing cell line, patient derived xenografts (PDX), and genetically engineered mouse (GEM) models of pediatric or AYA cancers) that might inform rapid pediatric clinical translation in accordance with the RACE for Children Act.** Consider funding focused efforts to test promising new agents in the most relevant pediatric cancer models.



Opportunities for Transformative Discoveries

- **Identify patients who have a remarkable initial response to conventional chemotherapy and/or targeted therapies.** Deep molecular profiling of these “outliers” have provided mechanistic insights and identified key dependencies in adult cancers. Systematically pursuing this approach will likely also be informative in pediatric/AYA cancers.
- The COG Biorepository includes multiple rare childhood cancer specimens. **A focused biologic effort to delineating the molecular landscapes (and potential therapeutic vulnerabilities) of specific rare cancers should leverage the COG Biorepository and other archived specimens.** Strategies to increase submission of high value tissues could increase the number of cases available.
- The COG Biorepository has a large number of **germline samples that could be used for predisposition gene discovery, especially for histologies for which large germline analysis has not been done (e.g. liver tumors, germ cell tumors, etc.)**
- **Improve biobanking efforts at intake by adding quality control, digital image generation, and nucleic acid extraction for all children diagnosed with specific solid tumors.**



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A special thanks to:

Malcolm Smith, MD

Stephen J. Chanock, MD

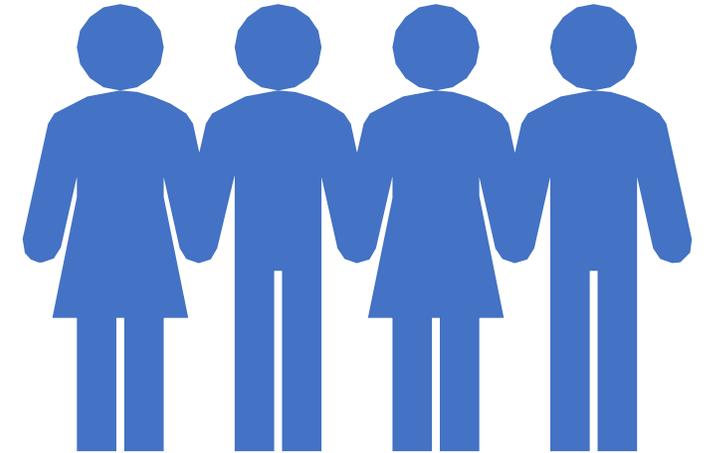
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