CCDI Community Forum

CCDI Webinar Series

NIH NATIONAL CANCER INSTITUTE

September 11, 2023

1. *Introductions*
2. *Introduction to CCDI*
3. *Workshops and Symposium Summaries*
4. *Program Updates by Priority*
5. *Upcoming Meetings and Plans*
6. *Working Group Priorities – Recap*

Introductions

Dr. Gregory Reaman

CCDI
Scientific Director, NCI

Dr. Subhashini Jagu

Chief, Scientific Policy and Program Branch, NCI

Dr. Malcolm Smith

Associate Branch Chief, Pediatrics, NCI

Dr. Mary Frances Wedekind

Staff Clinician, Research Assistant, Pediatric Oncology Branch, NCI

Dr. Emily Boja

Chief, Scientific Policy and Program Branch, Office of Data Sharing, NCI

Dr. Lynne Penberthy

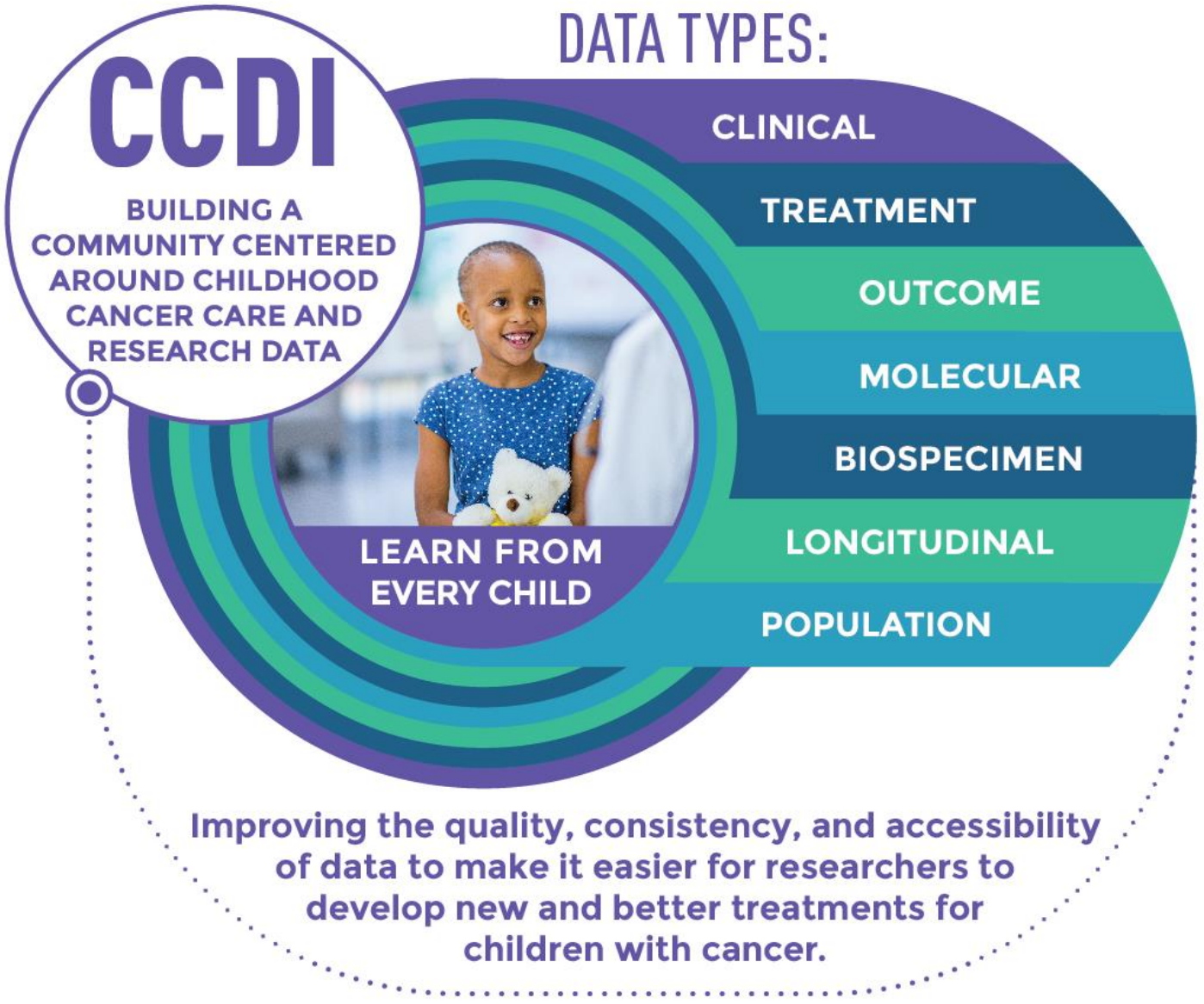
Associate Director, Surveillance Research Program, NCI

Rules of Engagement

- During Q&A, we welcome you to use Slido to ask any questions. We'll do our best to answer as many questions as possible before the session ends.
- For technical questions throughout this presentation, please use the chat function and a member of our team will assist.

Introduction to CCDI

Gregory Reaman



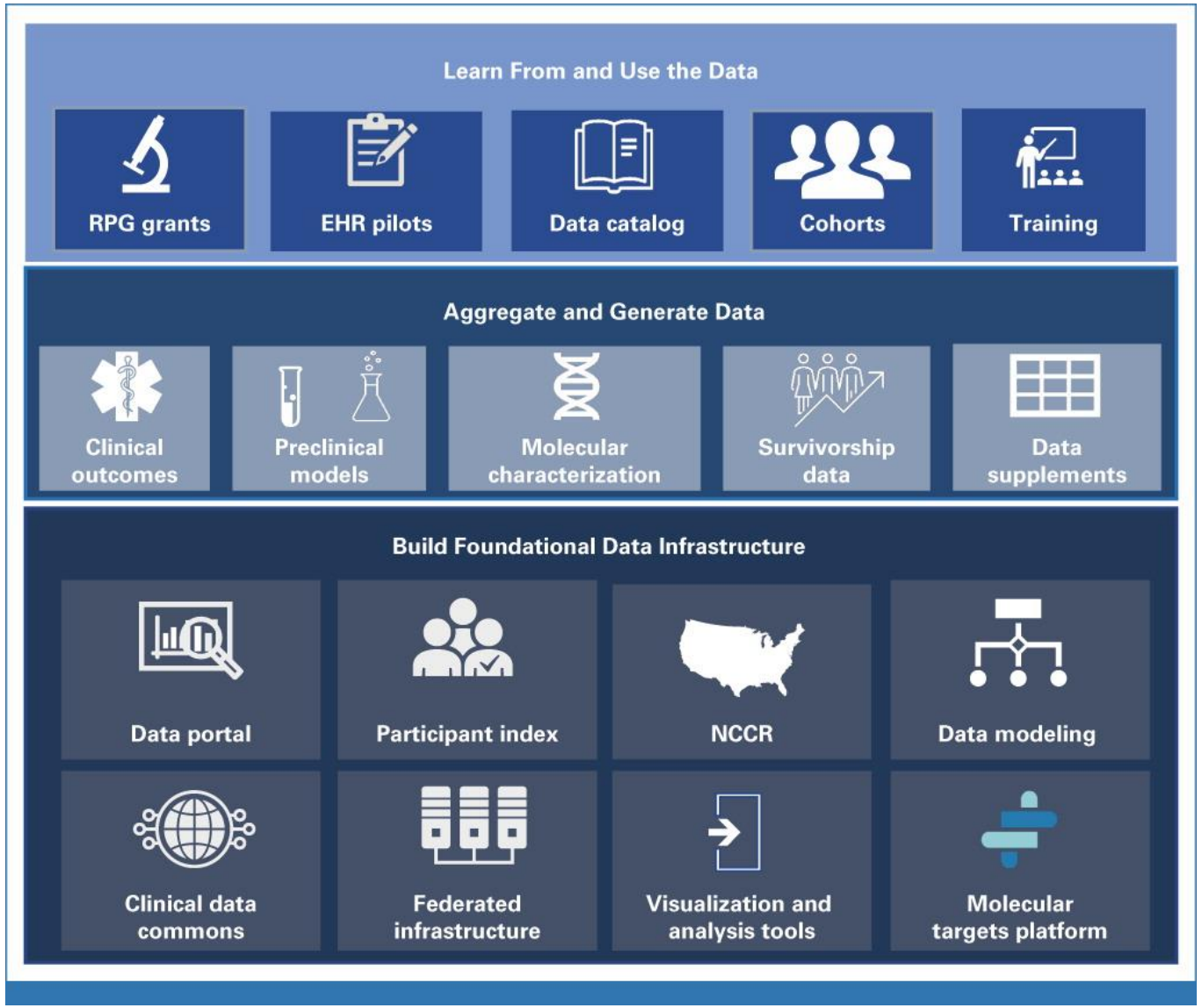
Build a strong base: Progress requires data from many sources that is connected and easy to access.

Assemble better data: Complete data sets are needed to understand each type of cancer.

Make data easy to use: More thoughtful tools for analyzing data will help answer important questions.

Improve treatments and outcomes: Data is the foundation that informs new treatments and improves lives faster.

The Three Pillars of CCDI



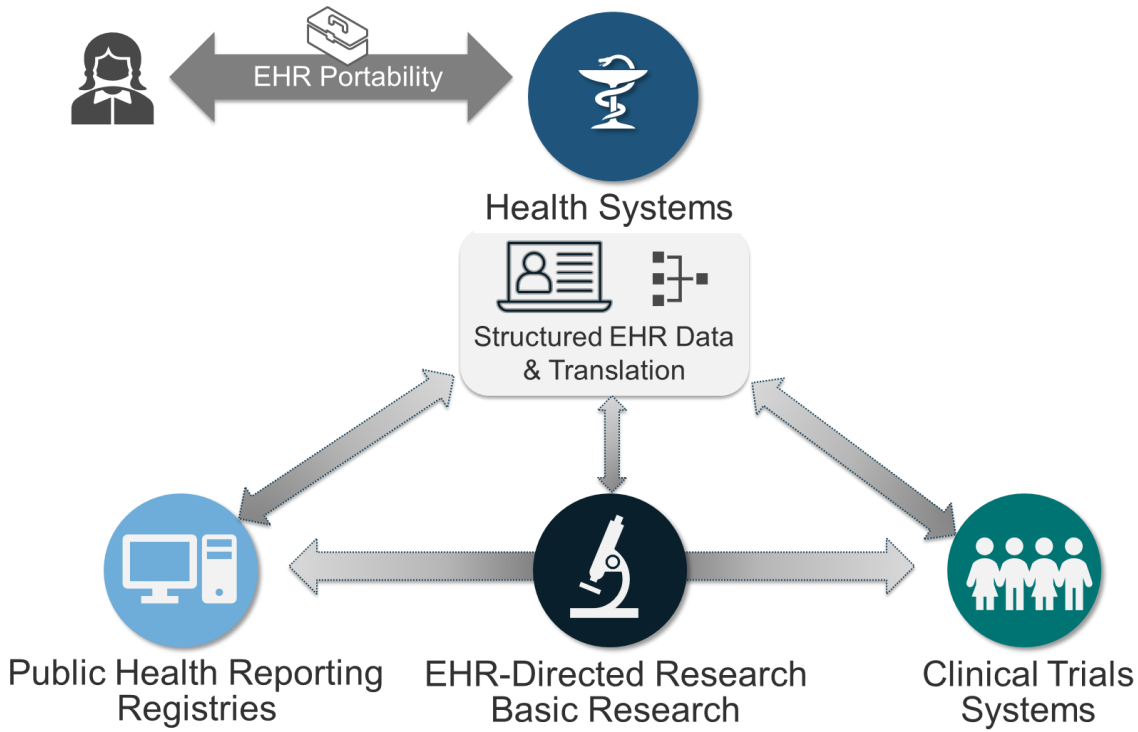
Workshops and Symposium

Gregory Reaman

Workshop: The Importance of Electronic Health Record (EHR) Data in Clinical Care and Research – Nov. 2, 2022

Key points:

- Empower patients to provide informed consent for use of health care data in research.
- Ensure equal access to health care data for patients and providers.
- Highlight the necessity for developing data standards and harmonization and the critical importance of obtaining patient treatment and other data from EHRs.
- Stress the importance of structured eligibility criteria.
- Encourage exploration options for validation and discovery in research and public health reporting.



Workshop: Advancing a National Initiative for Rare Cancers in Children, Adolescents, and Young Adults – Nov. 18, 2022

Key points:

- Broad endorsement for NCI-sponsored, national strategy for investigational-observational/interventional trials.
- Emphasize addressing the lack of a standard of care, limited clinical trials, and the prevalence of isolated, institutional-focused programs.
- Recognize the need for patient support and partnership with foundations and advocacy groups to navigate all aspects of the healthcare system.
- Establish sustainable infrastructure to facilitate support collaborative efforts.
- Utilize the opportunity to implement computable consent and to collect high-priority data elements.

CCDI Symposium – March 24-25, 2023

- Well-attended: 85 in-person, 749 virtual.
- Very positive feedback on progress, especially for Data Ecosystem.
- Feedback on six breakout sessions confirmed CCDI priorities and provided new insights and recommendations for next steps:
  - MCI and future cohort studies
  - Computable consent and the CCDI Participant Index
  - EHR extraction challenges and opportunities
  - External controls for pediatric cancer clinical trials
  - Research opportunities using data in the CCDI Data Ecosystem
  - Studies and new treatment approaches for rare pediatric cancers

CCDI Updates

Ecosystem Updates

Subhashini Jagu

CCDI Data Ecosystem Components: Connecting the Data

Primary databases

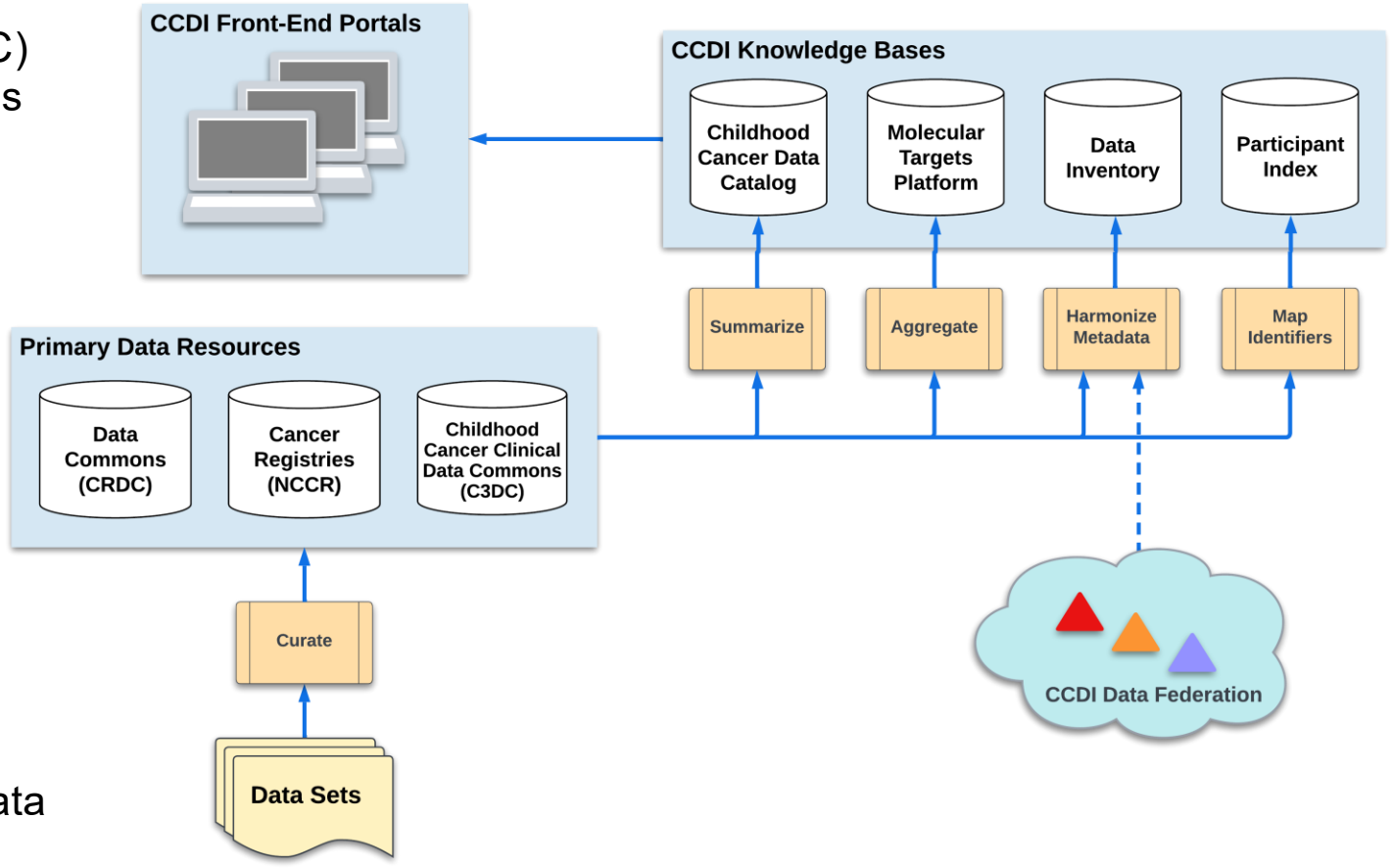
- Cancer Research Data Commons (CRDC)
- Childhood Cancer Clinical Data Commons (C3DC)
- National Childhood Cancer Registry (NCCR)

Knowledge Bases

- Childhood Cancer Data Catalog
- Molecular Targets Platform
- Data Inventory
- Participant Index

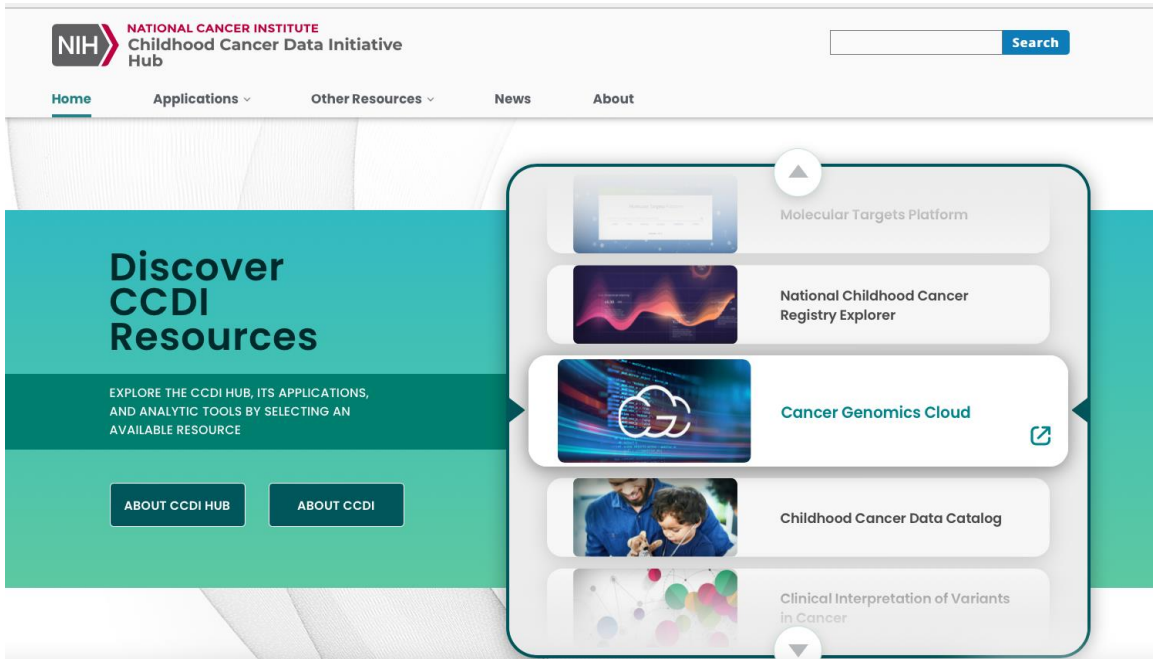
Curation & Harmonization

- Data Coordination Center – assist with data submission and harmonization



Access to CCDI Data & Tools

- The CCDI Hub is an entry point for researchers, data scientists, and citizen scientists looking to use and connect with CCDI-related data.
- It provides information and direct links to CCDI platforms, tools, and resources, along with additional technical information.
- CCDI Hub 2.0 tentatively planned for October 2023.
  - Integrate with CCDI Data Inventory; leverage existing Bento design, customized for CCDI.
    - e.g., https://dataservice.datacommons.cancer.gov/#/data
  - Sharing CCDI clinical metadata and linkages to sample data.



ccdi.cancer.gov

CCDI Data Sets

- phs002790.v1.p1 (CNS, STS, rare tumors - MCI)
  - Case count: 1,552; Sample count: 4,377
- phs002599.v1.p1 (Acute myeloid leukemia - OHSU)
  - Case count: 129; Sample count: 1347
- phs002504.v1.p1 (Juvenile myelomonocytic leukemia - UCSF)
  - Case count: 188; Sample count: 388
- phs002620.v1.p1 (Solid tumors - MSK)
  - Case count: 114; Sample count: 326
- phs003111.v1.p1 (High-risk neuroblastoma - MSK)
  - Case count: 130, sample count: 488
- phs002518.v1.p1 (All cancer types - USC)

- phs002518.v1.p1 (All cancer types - USC)

  - Case count: 1036 Sample count: 2240
- phs002529.v1.p1 (Solid tumors & leukemias - CMRI/KUCC)
  - Case count: 194; sample count: 373
- phs002517.v1.p1 (Brain & other solid, hematologic malignancies - CHOP)
  - Case count: 1031; sample count: 3,225
- phs000720.v4.p1 (Rhabdomyosarcomas whole-slide hematoxylin and eosin-stained images from COG trials ARST0331, ARST0431, D9602, D9803, and D9902)
  - Will be available through NCI's Imaging Data Commons and listed in the Childhood Cancer Data Catalog

CCDI Data Access

- For the CCDI studies, genomic data is hosted in the Cancer Data Service (CDS), which is a data repository under the Cancer Research Data Commons infrastructure.
- dbGaP maintains a list of the subject IDs, sample IDs, and consents.
- Accessing controlled-access data and clinical/phenotypic files requires authorization through dbGaP.
- Users can analyze CCDI data on the Cancer Genomics Cloud through the Cancer Data Service Explorer.
- Here is a tutorial on how to import CDS data: docs.cancergenomicscloud.org/docs/import-cds-data

CCDI_CGC_Data_Access_Instructions: datacatalog.ccdi.cancer.gov/CCDI_CGC_Data_Access_Instructions_1.0.pdf

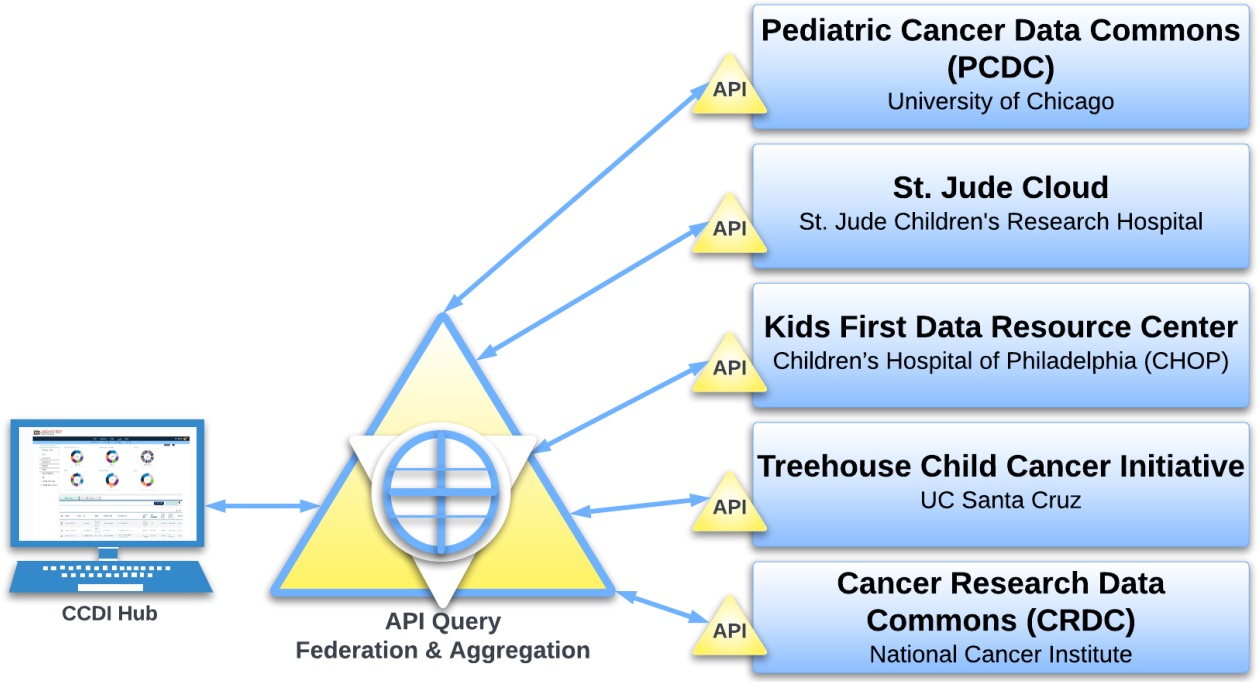
Data Federation Demonstration Project

Goal: Facilitate large-scale analytic research through heterogeneous data aggregation.

- Make deidentified participant-level data (non-PHI/PII) findable across the sources, enabling the creation of a virtual cohort (without moving or warehousing data).

Status Update:

- Developed scientific use cases to drive requirements for data and an API.
- Defining a minimal set of demographic and clinical phenotype data to allow queries across the CCDI Federation data resources.
- Drafting API requirements for the CCDI Federation.



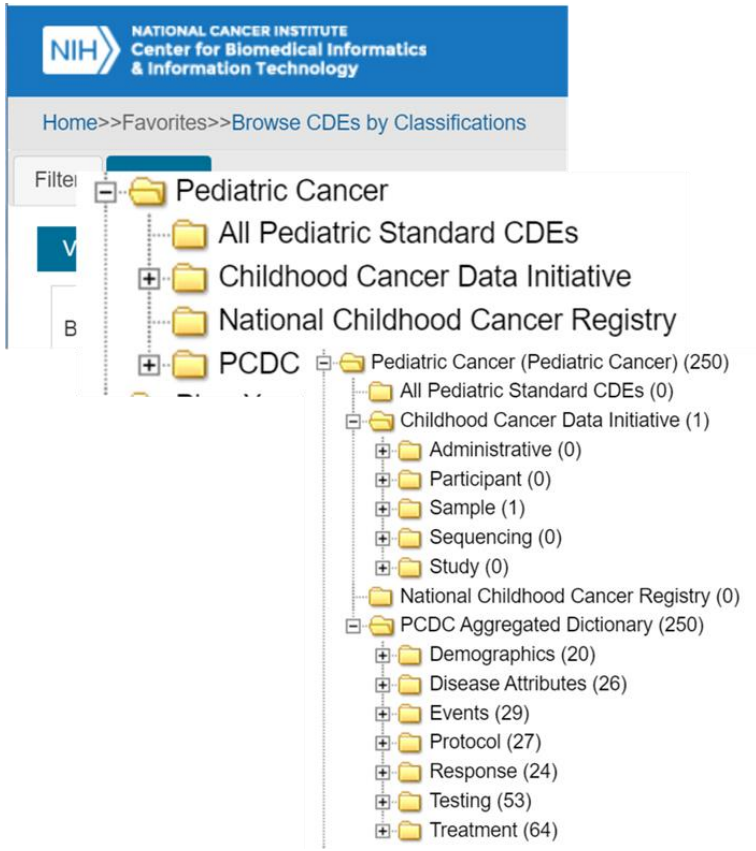
Childhood Cancer Clinical Data Commons (C3DC)

Goal: Allows researchers to search for participant-level data collected from multiple studies to create synthetic cohorts.

Status Update

- Working on establishing the reference set of Common Data Elements (CDEs) that will constitute a pediatric cancer clinical data standard.
- Created C3DC data model in GitHub.
- Tentative MVP release Q4 of 2023.

How do I find the CDEs?



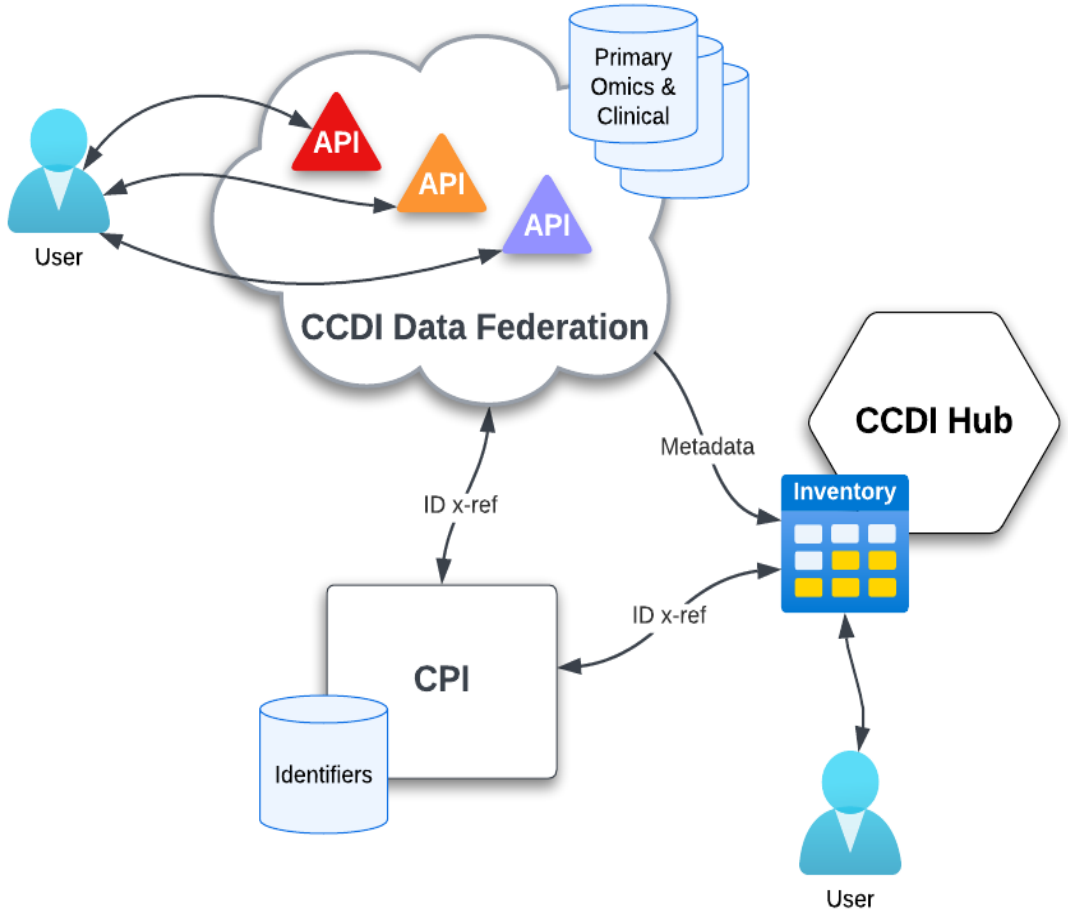
cadsr.cancer.gov/onedata/Home.jsp

Childhood Cancer Data Initiative Participant Index (CPI)

Goal: Link participants' data from the Federation and the CCDI projects.

Status Update

- COG has provided an endorsement that authorizes institutes to share the COG IDs with NCI.
- Received COG ID - USI pairs for MCI participants.
  - Will facilitate crosswalk of CBTN data to overlapping MCI participants
- Received Kids First Study IDs mapped to USIs.
  - Working with other institutions to acquire mapped IDs
- Identifying institutions to participate in PPRL process.
  - Working with NCCR
- Defining the technical architecture for the database.



Molecular Characterization Initiative (MCI) Update

Malcolm Smith

MCI Updates

- As of August 2023 – cumulative enrollment surpassed **2,000**
  - **1,965** patients from **~180** institutions have a sample shipped to the Biopathology Center
    - CNS: 1,397; soft tissue sarcoma: 429; rare tumors: 139
  - Phs002790: Monthly molecular characterization data releases are going as planned (1,552 participants).
    - Deidentified clinical reports will be available in JSON format (converted from PDF) in October.
- COG has submitted the second batch (delivery occurs every 6 months) of clinical data and will be made available by end of October.
- Clinical reports currently support **5** clinical trials:
  - Timely return of results has enabled trial enrollment in short windows.

MCI Updates Continued

- Validation and CLIA certification of a lower input exome assay is underway.
- BioPathology Core (BPC) is currently in the process of submitting pathology-reviewed H&E slides to NCI.
- COG Central Nervous System and Soft Tissue Sarcoma committees are preparing abstracts describing the first year of experience using the MCI.
- Working on developing an MCI page on the CCDI Hub, which will incorporate the assay specific details.

Coordinated National Initiative for Rare Cancers in Children and Young Adults

Mary Frances Wedekind

Coordinated National Initiative for Rare Cancers in Children and Young Adults

- Rare tumor: Less than 150 cases per million per year
  - Very rare pediatric cancer: less than 2 cases per million per year (11% of all pediatric cancers)

- Challenges:
  - Accurate and timely diagnosis
  - Poor understanding of natural history and biology
  - Lack of standard therapy & treatment trials

- Substantial progress for select cancers, but:
  - Siloed, focused on few tumors
  - Insufficient patient numbers for most tumors
  - Data collection not standardized/structured

- A national effort will allow enrolling adequate numbers of participants so researchers can more rapidly, efficiently, and consistently study multiple rare cancers

Initiative Objectives

Feasibility of a national observational protocol for very rare childhood and AYA solid cancers and hematologic malignancies

Longitudinally evaluate the disease course of participants with rare cancers

- Structured and real-world data
- External control for interventional trials
- Meaningful comparison across multiple cancer types

Collect clinical and research molecular characterization

- Identification of therapeutic targets and inform clinical trials

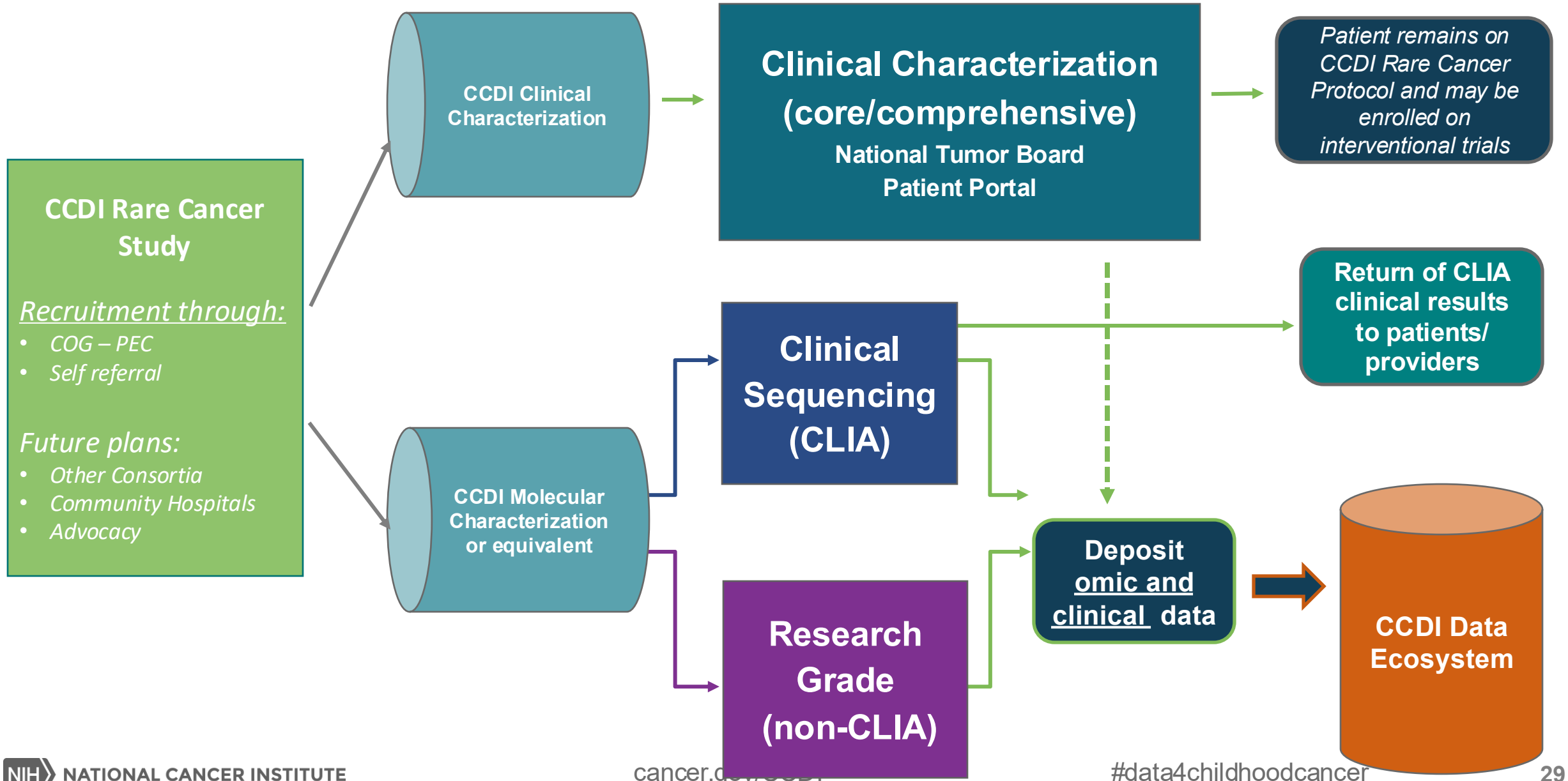
Feasibility of national molecular/clinical tumor boards for rare cancers

- Facilitation of patient navigation and treatment recommendations

Status Update

- Presented to CCDI and COG leadership
- Discussed framework and sought support during CCDI rare cancers workshop
- Discussed rare cancer effort during CCDI Symposium meeting and breakout sessions; overwhelming support for this initiative
- Held internal CCDI meetings to compile data elements and mapping from various efforts: COG APEC, CCSS, AT/RT, MyPART

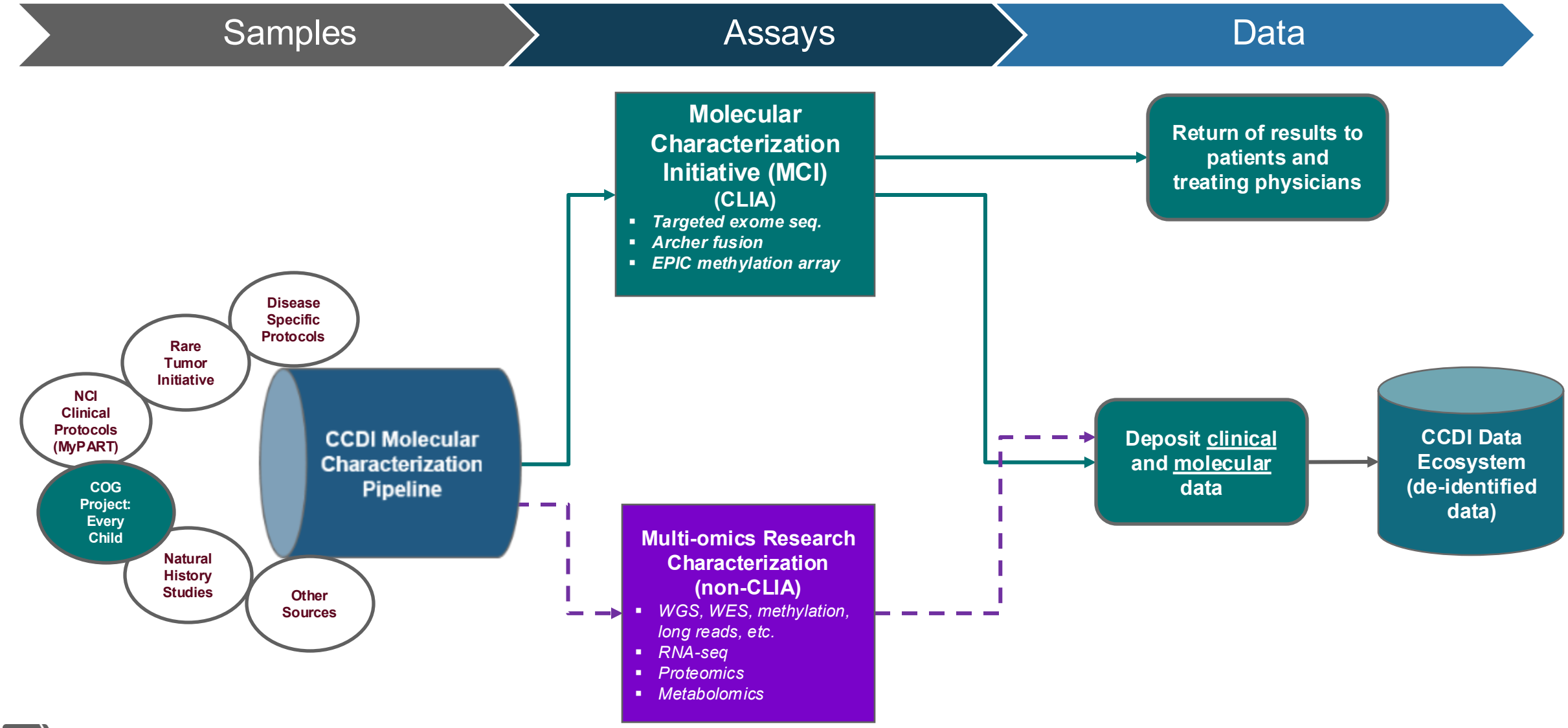
Data Flow


CCDI Rare Cancer Study
Recruitment through:
COG – PEC
Self referral
Future plans:
Other Consortia
Community Hospitals
Advocacy
CCDI Clinical Characterization
CCDI Molecular Characterization or equivalent
Clinical Characterization (core/comprehensive)
National Tumor Board
Patient Portal
Patient remains on CCDI Rare Cancer Protocol and may be enrolled on interventional trials
Clinical Sequencing (CLIA)
Research Grade (non-CLIA)
Return of CLIA clinical results to patients/ providers
Deposit omic and clinical data
CCDI Data Ecosystem

Research Characterization Request For Information (RFI)

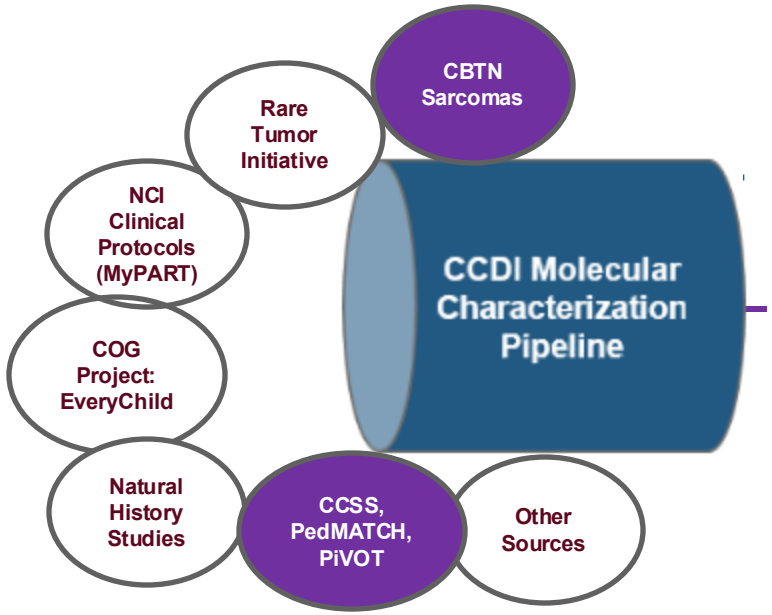
Emily Boja

A National Strategy for Comprehensive Molecular Characterization



What *Is* A Comprehensive Patient Molecular Profile?

- Scientific questions to address to fill our knowledge gaps
- Pediatric cancer community needs
- Available samples and data for new data generation
- Research characterization methodologies



Multi-omics Research Characterization (non-CLIA)

- WGS, WES, methylation arrays, long reads, etc.
- RNA-seq
- Proteomics
- Metabolomics

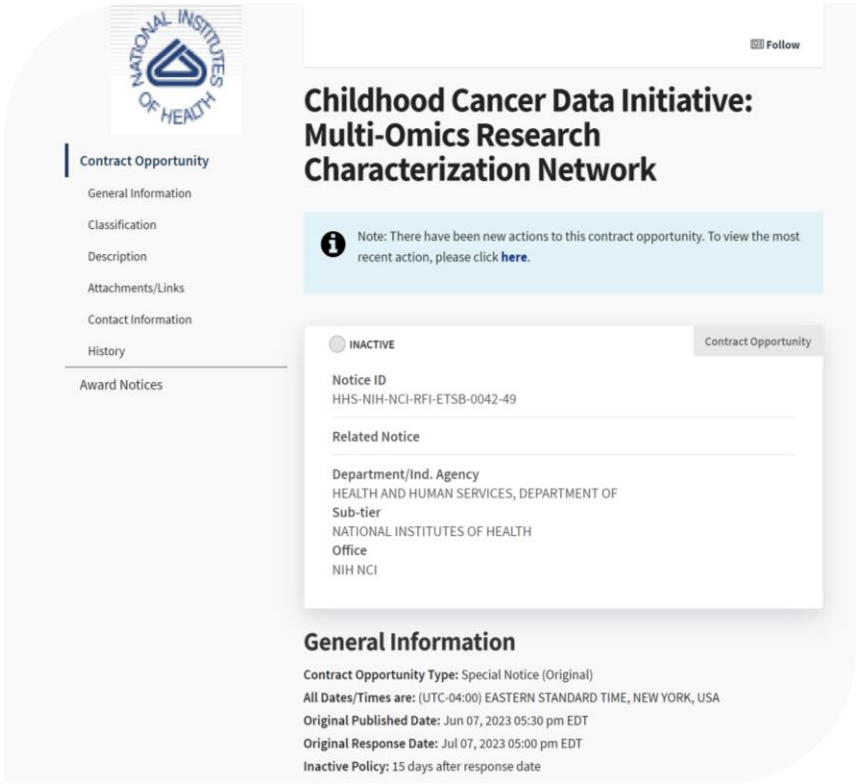
Deposit clinical and molecular data

CCDI Data Ecosystem (de-identified data)

Genomics	Transcriptomics	Epigenetics	Proteomics	Metabolomics
Targeted Exome Seq. (MCI)	Archer Fusion (MCI)	EPIC methylation array (MCI)		
WGS/WES (Kids First)	Total RNA-seq (Kids First)		Global Proteome Phosphoproteome Surface-omes (Kids First)	Metabolite Profiling
Long reads DNA sequencing	Total RNA-seq mRNA-seq miRNA-seq	WG Bisulfate-seq WG ATAC-seq	Glycoproteomics, Acetylomics	

Request for Information (Research Characterization Network)

- **Purposes:**
  - Perform market research to help refine research characterization scope and technical requirements in 3 main areas:
    - Genomics, Transcriptomics, Epigenomics
    - Proteomics
    - Metabolomics
  - Help inform key decision points for the pipeline
- **Summary:**
  - In coordination with NCI's Office of Acquisition (OA), we published the CCDI Research Molecular Characterization RFI.
  - RFI comprised of 13 questions ranging from sample processing, analytical capability and throughput, to data analysis and delivery.
  - Statistics: 15 responses received [8 commercial vendors (2 small business); 7 academic institutions]



Summary of RFI Responses

- All omics vendors have sample processing and analytical capability in genomics to generate data from a variety of specimens (e.g., FFPE tissue slides, blood), *with the flexibility to switch from one platform to another* (e.g., WGS to RNA-seq).
- 8/15 vendors possess analytical capabilities in more than one omics areas. As expected, there is a range of analytical capabilities amongst vendors.
- Some vendors possess extensive experience with pediatric samples and data analysis pipelines that could be leveraged to deliver analysis results such as structural variants and fusion calling.
- Vendors provided valuable input on the (un)suitability of assays for certain specimen types: e.g., phosphoproteomics on FFPE samples will yield little benefits.

What's Next?

- Continue to work with NCI OA to refine CCDI research characterization network scope, technical requirements and acquisition strategies.
- Engage the pediatric cancer community on key questions such as what are the unmet scientific needs, cohort availability, "must-have" assays.
  - Consider a 2nd RFI to identify opportunities to generate research molecular data on available samples and data.
  - Hold additional workshops.
  - Leverage outcomes from previous workshops and symposiums.

National Childhood Cancer Registry (NCCR)

Lynne Penberthy

Expanding the NCCR

- NCCR*Explorer – updated version released Sept 7, 2023
  - Predesigned tables, figures with limited customization
  - New features: US prevalence estimates for people diagnosed with a childhood cancer
- SEER*Stat for NCCR (new) – released Sept 7, 2023
  - Offers broader capacity for custom analyses
- NCCR Data Platform – anticipated release in 2024
  - Key unique data sets that will be linked at the patient level with registry data:
    - Proton/Photon Consortium Registry https://www.pediatricradiationregistry.org/
    - COG-reported clinical trials participation
    - Pharmacy and medical claims (treatment, comorbid conditions, adverse events)
    - Detailed diagnostic, prognostic, and treatment information from NCI-supported Cancer Centers
    - Social determinants of health
- NCCR is adding 2 new registries this fall to increase the population coverage of the US (from 66% to 71%) and more in 2024

NCCR: Coming Soon

- CDC's National Center on Birth Defects and Developmental Disabilities has funded a collaborative of Centers for Birth Defects Research and Prevention (CBDRP) and Birth Defects Study to Evaluate Pregnancy exposureS (BD-STEPS): https://www.cdc.gov/birth-defects/research/?CDC_AAref_Val=https://www.cdc.gov/ncbddd/birthdefects/cbdrp.html

- ExtractEHR scaling: supports children's hospitals in rapid reporting of detailed diagnostic, prognostic, genomic treatment information to Central Cancer Registries for public health surveillance https://www.cancer.gov/research/areas/childhood/childhood-cancer-data-initiative/events-webinars/past-symposiums/electronic-health-record-data-extraction.pdf

Upcoming Plans

Gregory Reaman

Coming Soon to CCDI Events

WEBINAR

Using NCCR*Explorer and NCCR Data in SEER*Stat

Tuesday, October 24, 2023, 2:00pm – 3:00pm

CCDI Task Forces

- Forming small task forces to focus on making progress in CCDI priority areas:
  - Computable consent
  - Longitudinal follow-up of MCI participants
  - Molecular pipeline harmonization
  - CCDI Rare Pediatric Cancer Initiative
  - Industry forum
  - Research molecular characterization
- Each task force will have a set of goals and objectives, which we will work to accomplish using consistent approaches and with the resources available to CCDI.
- Interested in task force participation? Please contact Greg Reaman at gregory.reaman@nih.gov and Eve Shalley at eve.shalley@nih.gov.

How You Can Help Communicate About CCDI

Use our hashtag.
#Data4ChildhoodCancer

Subscribe to our monthly newsletter.
cancer.gov/CCDI

Questions? Email us.
NCIChildhoodCancerDataInitiative@mail.nih.gov

Thank you for attending!

U.S. Department of Health & Human Services

National Institutes of Health | National Cancer Institute

cancer.gov

1-800-4-CANCER