# Childhood Leukemia and Down Syndrome: What Research Is Teaching Us About Learning, Behavior, and Daily Life

**DS-Connect Webinar**

**October 27, 2026**

**Lisa Jacola, PhD, ABPP-CN**

**Psychology and Biobehavioral Sciences**

**St. Jude Children's Research Hospital**

# About Me

St. Jude Children's Research Hospital
Finding cures. Saving children.

- Neuropsychologist
- Optimizing quality of life for children and families
- Childhood cancer and neurodevelopmental populations





Childhood Leukemia

Childhood Leukemia in Down Syndrome

Summary and Future Directions



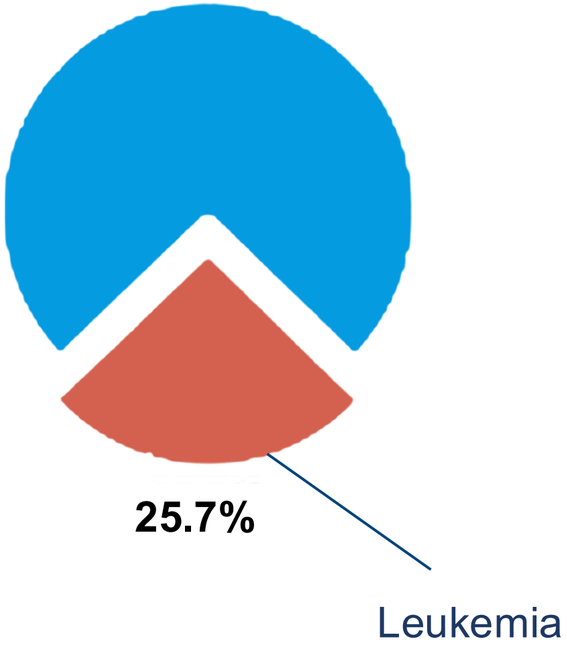
**Childhood Leukemia**

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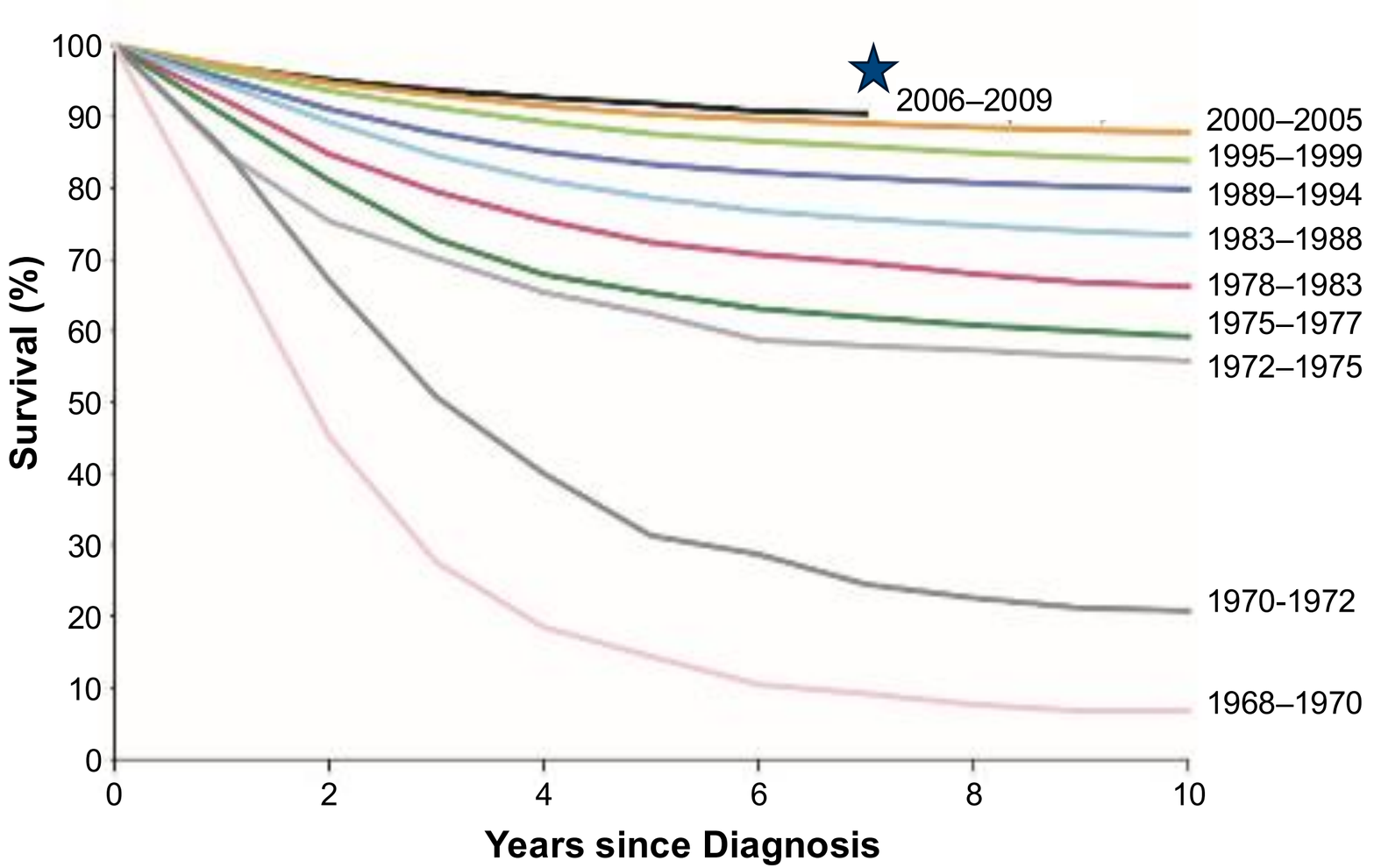
# Childhood Leukemia

- Cancer of the blood and bone marrow
  - Acute lymphoblastic leukemia (ALL)
  - Acute myeloid leukemia (AML)
- Most common childhood cancer diagnosis
  - 3500 to 4000 new cases each year in the US
  - Majority of cases are ALL




https://seer.cancer.gov/statfacts

# Improved Survival for Childhood Leukemia




- Childhood ALL: Overall survival ~90%

Hunger & Mullighan 2015. NEJM

# Late Effects in Childhood Leukemia

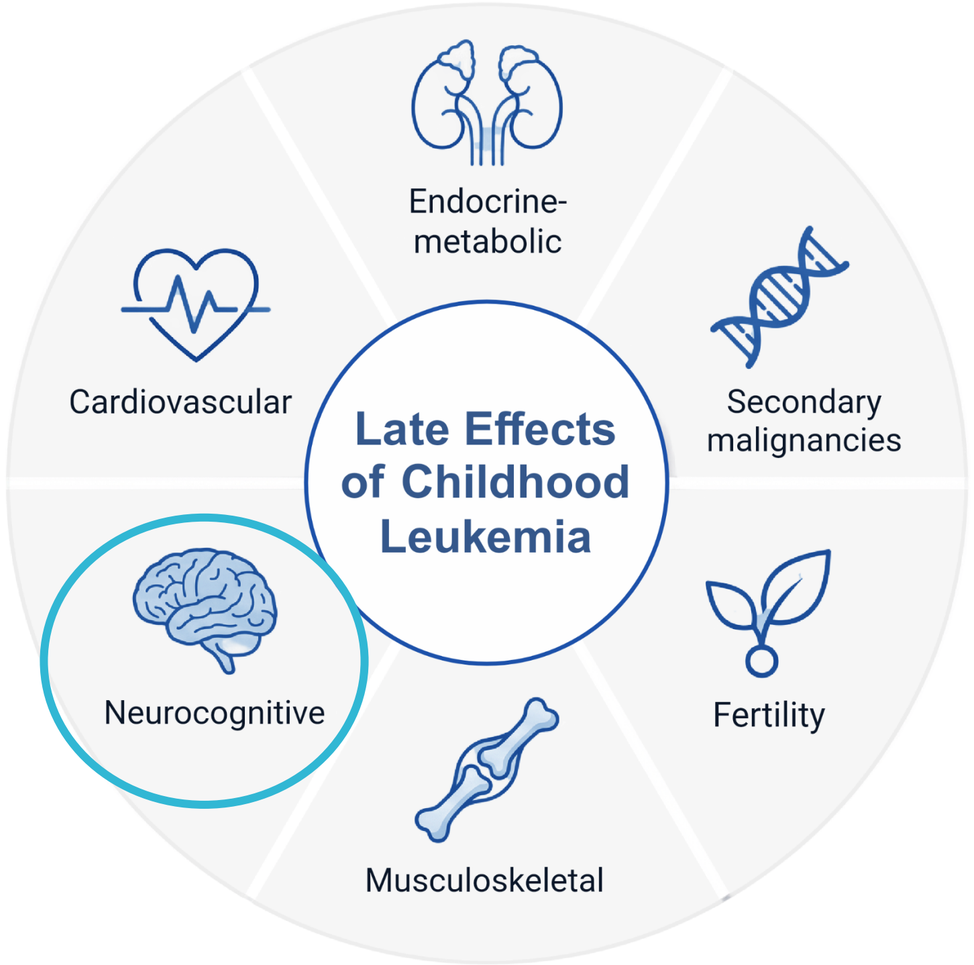



Figure created in Biorender

- Late effects → poorer quality of life
  - Reduced independence
  - Lower educational and social attainment
- Individual, clinical, and environmental factors contribute to risk
  - Age at diagnosis
  - Treatment experience
  - Family and social context

Bhakta et al. 2017, Lancet; cancer.gov/types/childhood-cancers/late-effects-pdq

# Late Effects in Childhood Leukemia

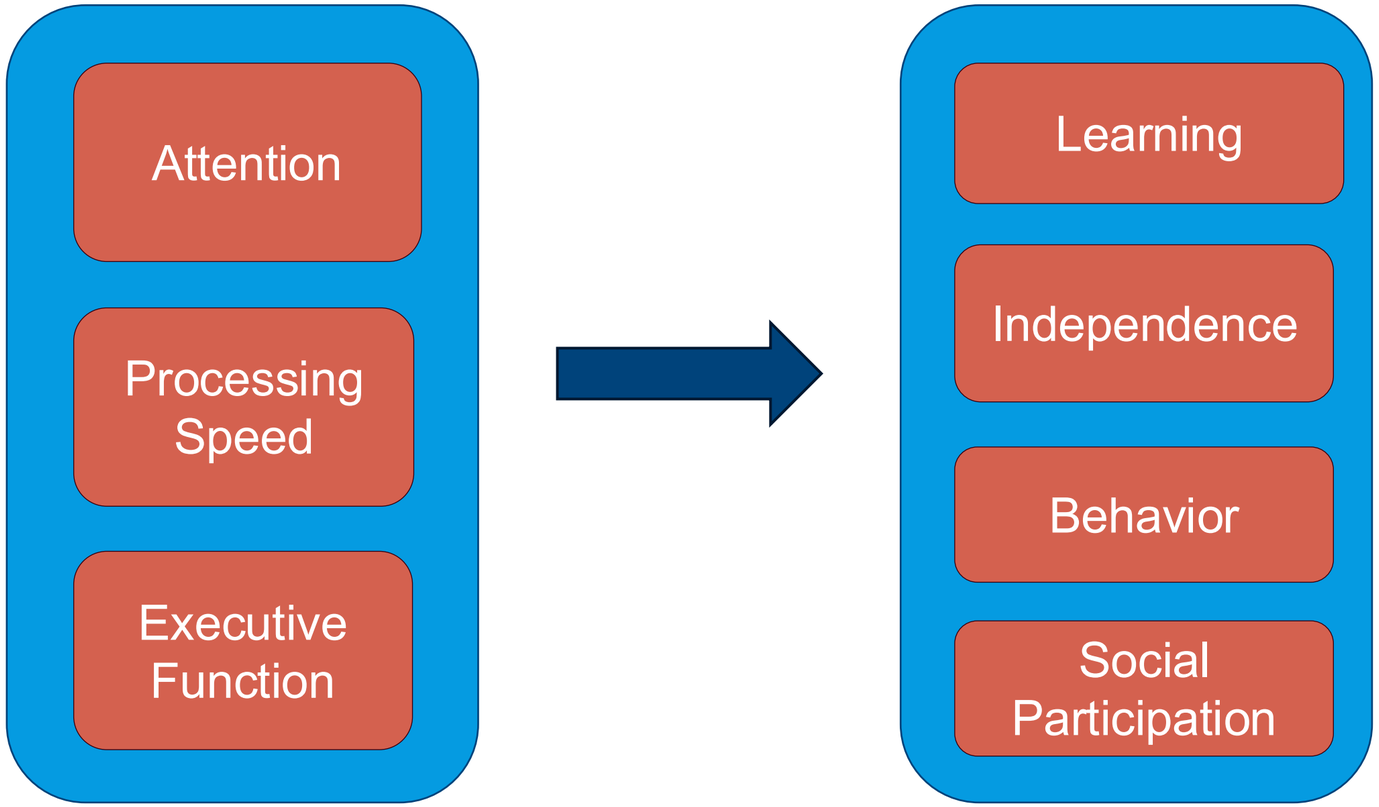
- Cognitive late effects = difficulties with thinking and learning
  - Present in up to 40% of long-term survivors
  - Start during therapy and continue into survivorship
  - Predict lower functional and quality of life outcomes



Van der plas et al. 2021, J Clin Oncol; Jacola et al. 2021, J Clin Oncol, Jacola 2025, J Clin Exp Neuropsych

# Late Effects in Childhood Leukemia

- Cognitive late effects → real world difficulties






Van der plas et al. 2021, J Clin Oncol; Jacola et al. 2021, J Clin Oncol, Jacola 2025, J Clin Exp Neuropsych

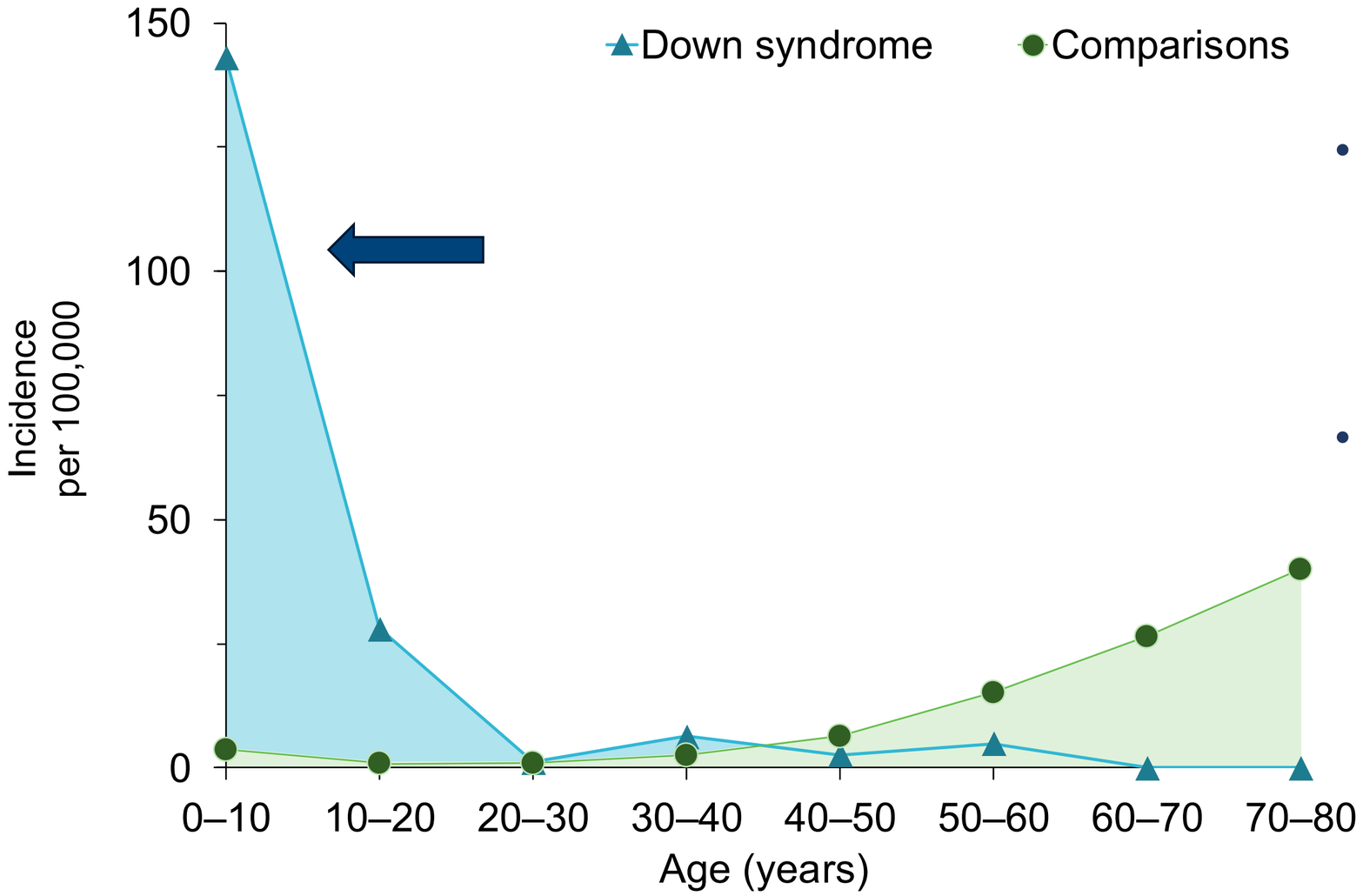


Childhood Leukemia

**Childhood Leukemia in Down Syndrome**

Summary and Future Directions

# Childhood Leukemia and Down Syndrome



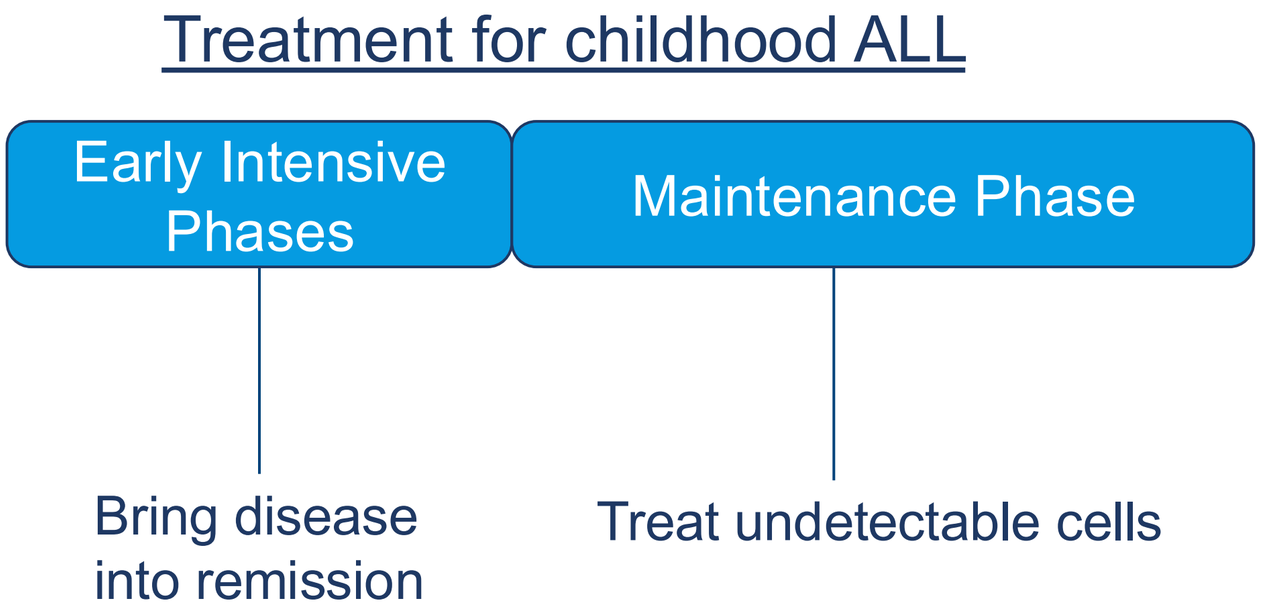

- Absolute risk for leukemia diagnosis:
  - Down syndrome: 2.49%
  - Age comparison: 0.07%

- Individuals with Down syndrome:
  - 20-fold increased risk for ALL
  - 500-fold increased risk for AML

Wachtmeister et al. 2026, Brit J Cancer

# Childhood Leukemia and Down Syndrome

- Duration of therapy: 2 to 3 years
  - Chemotherapy
  - Central nervous system directed therapy
  - Immunotherapy
- Increased acute toxicity for individuals with Down syndrome
- Reduced community participation
  - Early intervention, rehab, school



# Late Effects are Understudied

- Few studies have described treatment effects in survivors of childhood leukemia with Down syndrome
- Lack of tailored guidelines for supportive care and survivorship
- Need to identify targets for interventions to optimize quality of life

We have an opportunity to shift the paradigm from exclusion to inclusion

# Research Questions

- What do cognitive, behavior, and quality of life outcomes look like in survivors of childhood leukemia with Down syndrome?
- How do outcomes change over time?
- What are risk and resiliency factors?
- How do we design and implement intervention to support quality of life for patients and families?

# Cognitive Outcomes in Long-Term Survivors

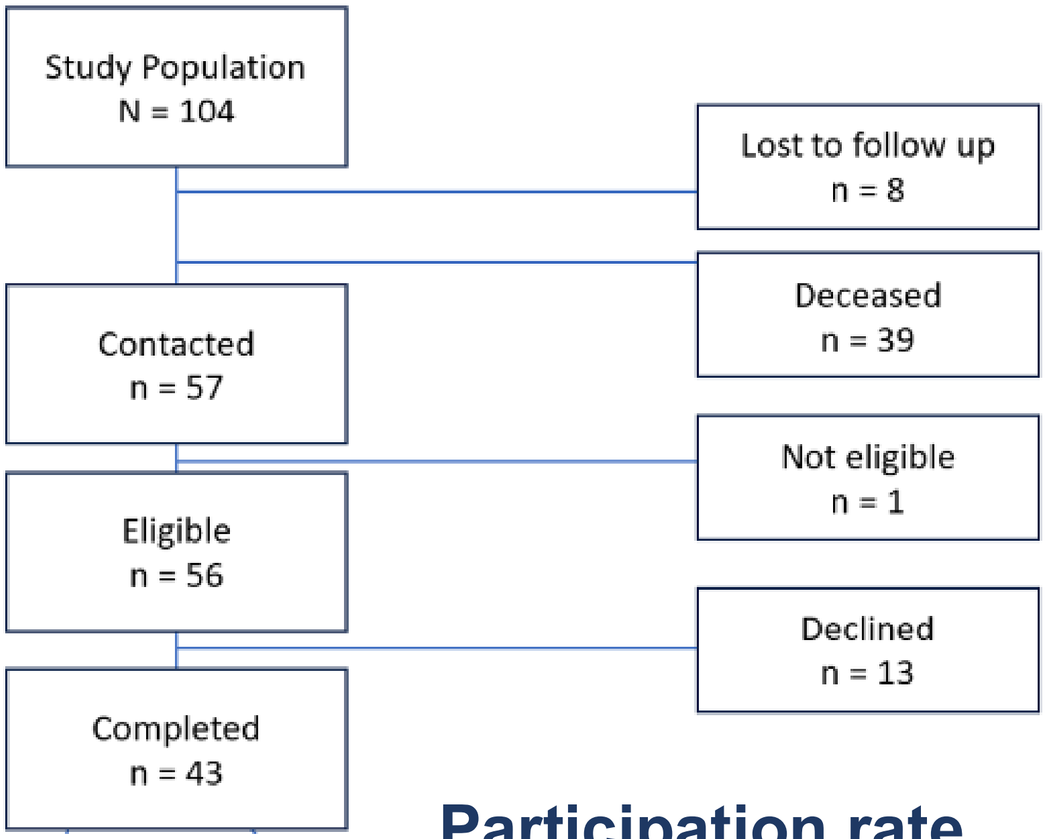
- Study population:
  - Survivors of childhood leukemia with Down Syndrome treated at St. Jude
- Historical comparison group:
  - Individuals with Down syndrome and no cancer history
- Approach:
  - Single time point
  - Direct assessment and caregiver ratings

Gandy et al. 2024, Cancer Medicine

Psychosocial Launch Grant (PI: Jacola)

# Study Participants

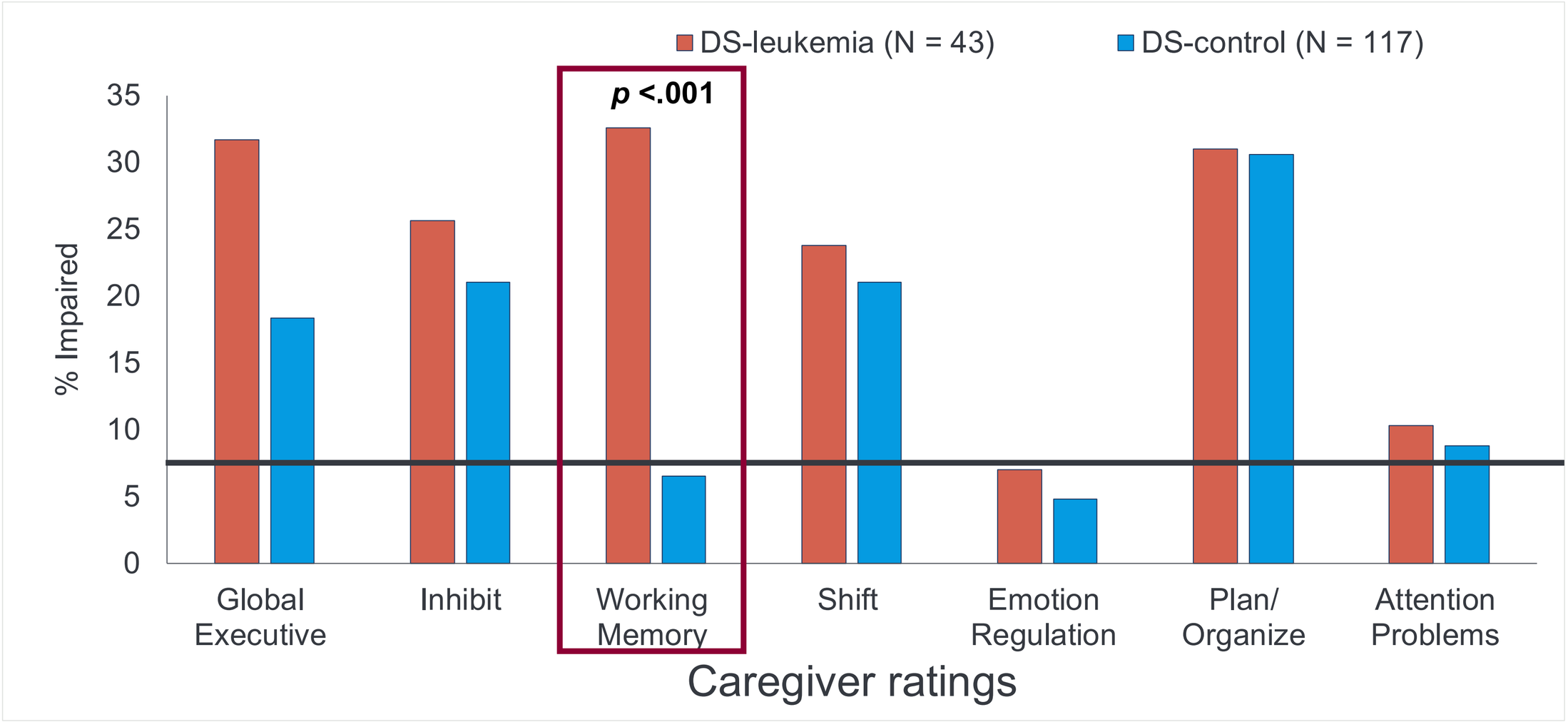
- Survivors of DS-leukemia treated at St. Jude
  - ≥ 6 months off treatment
  - Primary language of English
- Exclusion Criteria
  - Current age  >30 years old
  - CNS injury or disease post-treatment
  - Prior or current substance abuse




**Participation rate**
**77%**

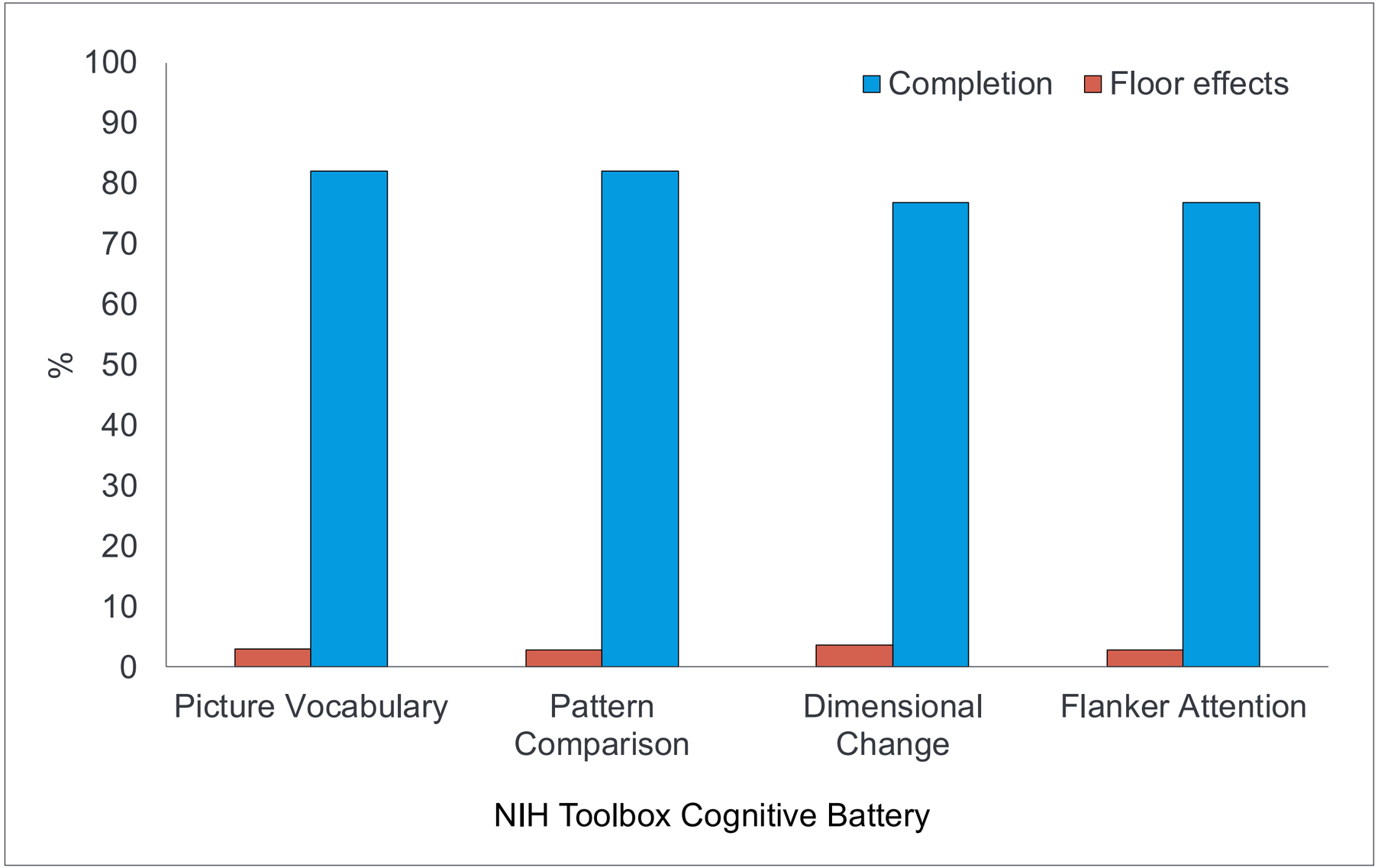
Gandy et al. 2024, Cancer Medicine

# Group Differences in Attention and Executive Function




Gandy et al. 2024, Cancer Medicine

# Feasibility of Direct Assessment

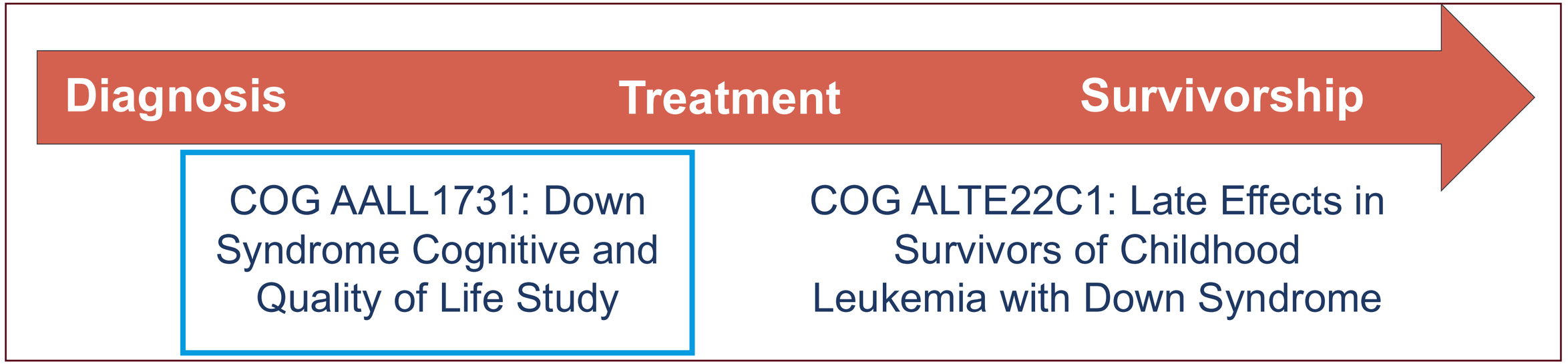



Gandy et al. 2024, Cancer Medicine

# Summary

- What did we learn?
  - Strong interest from families
  - Study measures ‘work’
  - Specific areas of vulnerability
- Next steps
  - Multiple sites
  - Multiple time points
  - Risk and resiliency factors

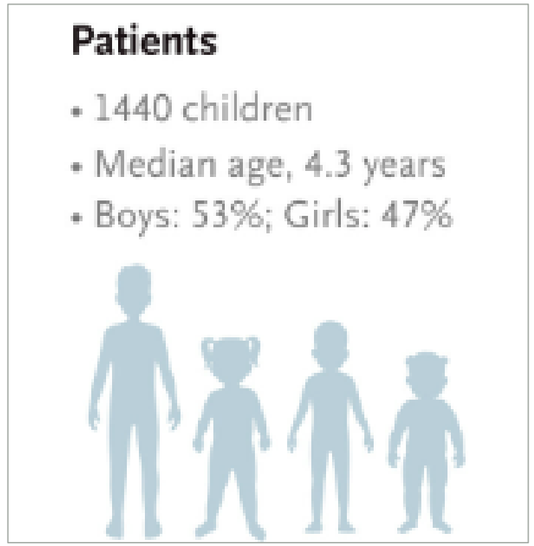
# Ongoing Studies



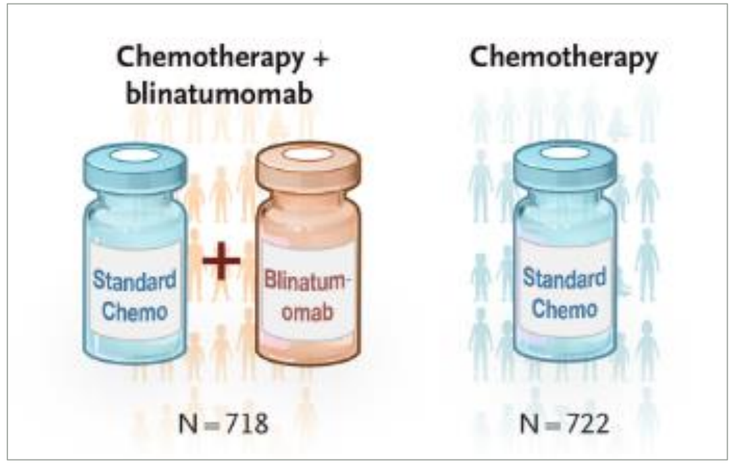

CHILDREN'S ONCOLOGY GROUP

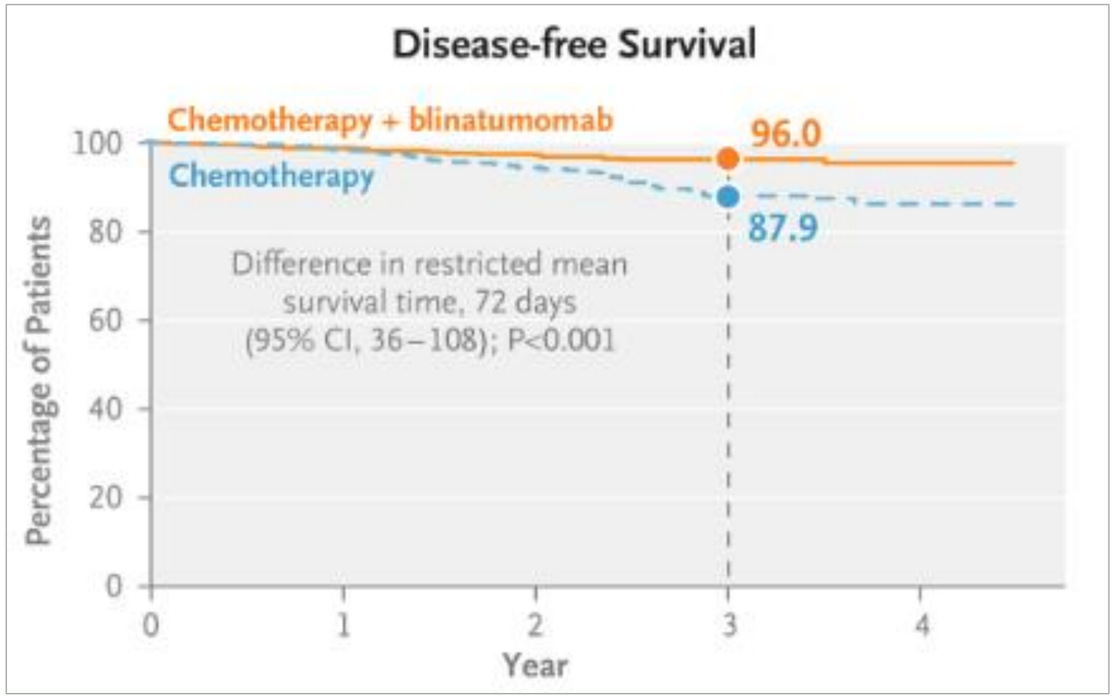
# COG AALL1731 Clinical Treatment Trial

- Newly diagnosed standard-risk or Down syndrome B-ALL




- Down syndrome = 3.8% of randomized patients




Gupta et al. 2025, NEJM

# AALL1731: Down Syndrome Neurocognitive Study

- Study Population: Individuals with childhood B-ALL and Down syndrome
- Comparison group: Individuals with Down syndrome and no cancer
- Research Questions:
  - Investigate cognition, behavior, and adaptive skills during therapy and early survivorship
  - Identify risk and resiliency factors

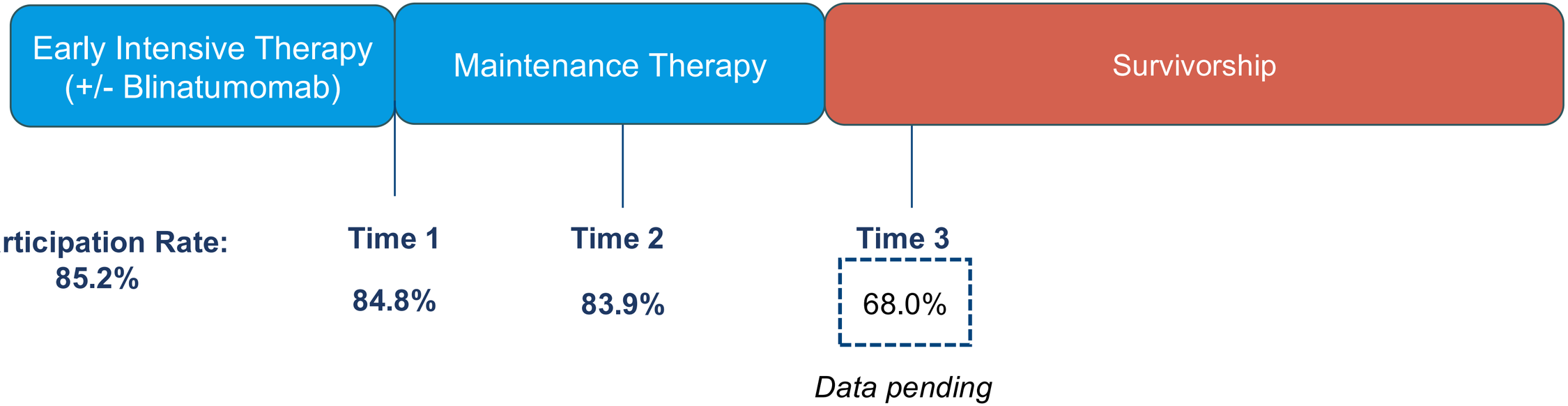


**Understanding Differences in Thinking, Learning, and Behavior for Individuals with Down Syndrome With and Without Childhood Cancer**

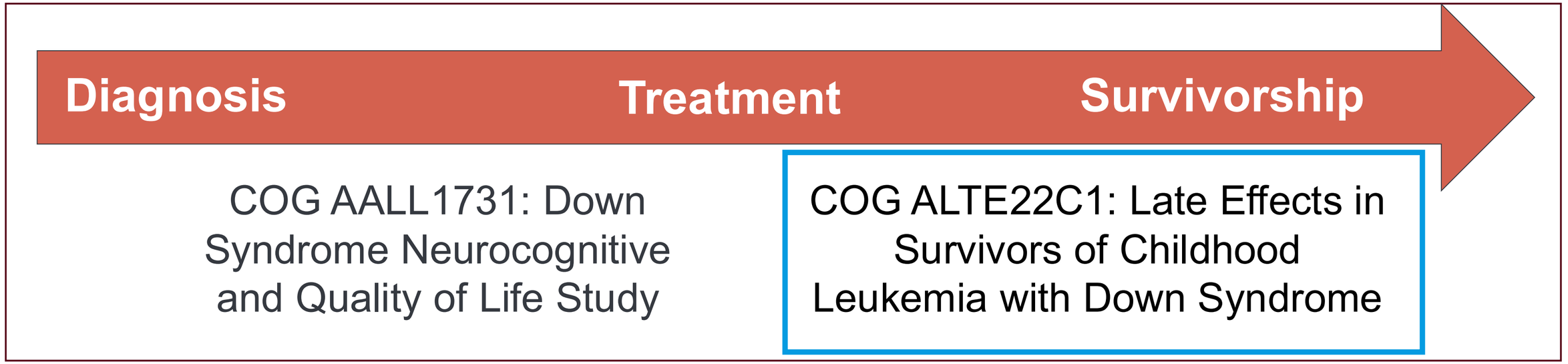
PI: Jacola

# AALL1731 Down Syndrome Neurocognitive Study

- Centralized study model
- Caregiver ratings
  - Attention, executive function, adaptive skills, quality of life
  - Community participation questionnaire (early intervention, school, rehab)



# Ongoing Studies




CHILDREN'S ONCOLOGY GROUP

# COG ALTE22C1: Late Effects in Survivors of Childhood Leukemia with Down syndrome

- Study Population: Long-term survivors of childhood leukemia (AML and ALL)
- Comparison Group: Individuals with Down syndrome without cancer
- Research Questions:
  - Investigate chronic health conditions and cognitive, functional, and quality of life outcomes
  - Identify biomarkers of outcomes

DS Cognition Project



Tracie Rosser, PhD

NIH NATIONAL CANCER INSTITUTE

Multiple PIs: Gramatges, Lupo, Jacola, Rabin, Rosser

# COG ALTE22C1: Late Effects in Survivors of Childhood Leukemia with Down syndrome

| Centralized activities | Site-based activities |
| --- | --- |
| • Registry-based recruitment<br>• Chronic health conditions survey<br>• Medical record abstraction<br>• Neurobehavioral surveys (proxy)<br>• Saliva DNA | • Site-based recruitment<br>• Long-term survivor clinic visit (routine labs & tests)<br>• DS-ALL: direct cognitive assessment & blood sample |

Return of Results

- 164 of 300 survivors enrolled

# INCLUDE Collaboration for Down Syndrome

- Develop a cohort of individuals with Down syndrome across the lifespan
- Goal is to improve understanding of:
  - Natural history
  - Frequency and variability of co-occurring conditions
  - Demographic, socioenvironmental, and experiential factors
  - Currently used therapies and interventions

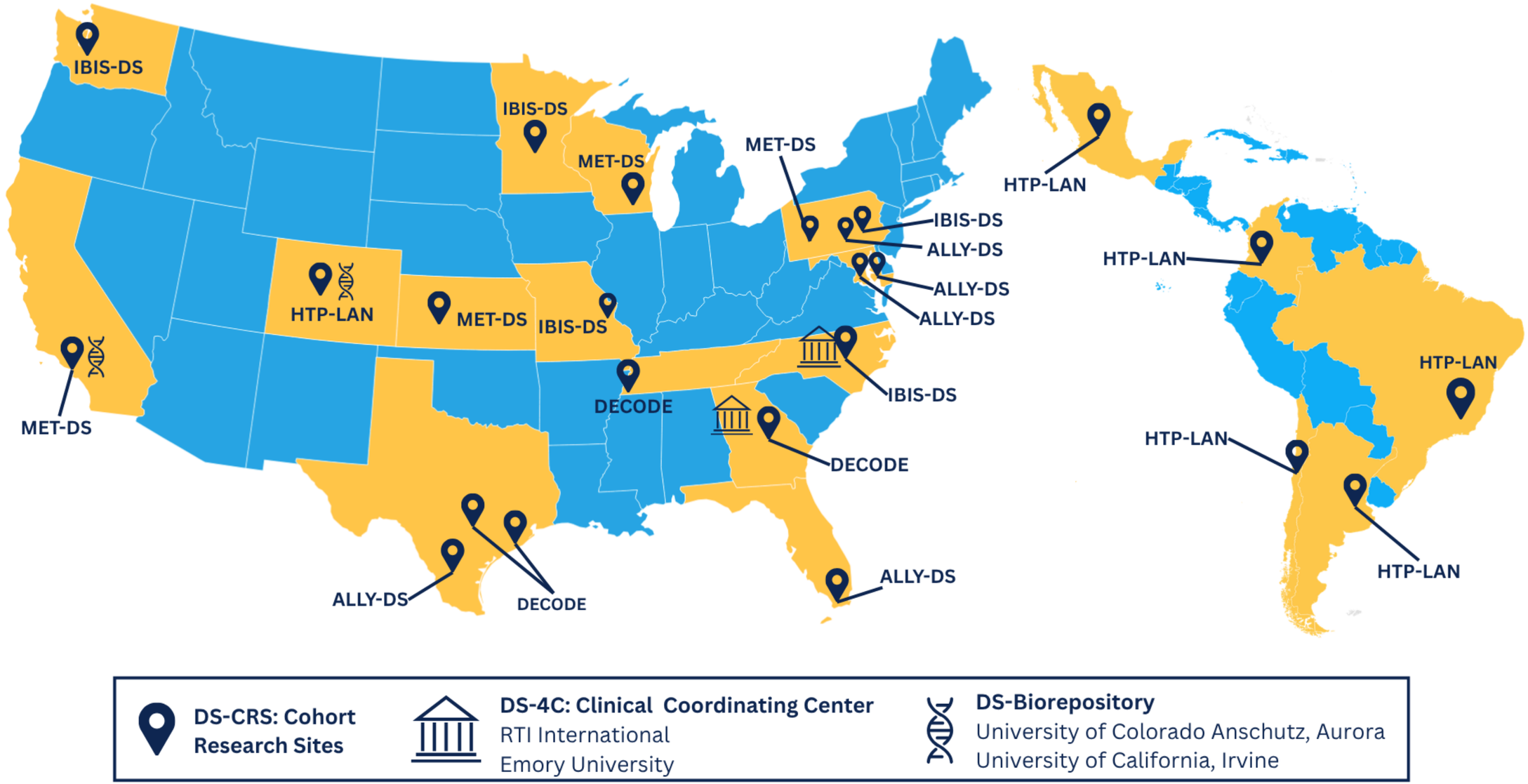
NIH NICHD

NIH INCLUDE Down Syndrome Research Plan

INCLUDE Collaboration for Down Syndrome Progress

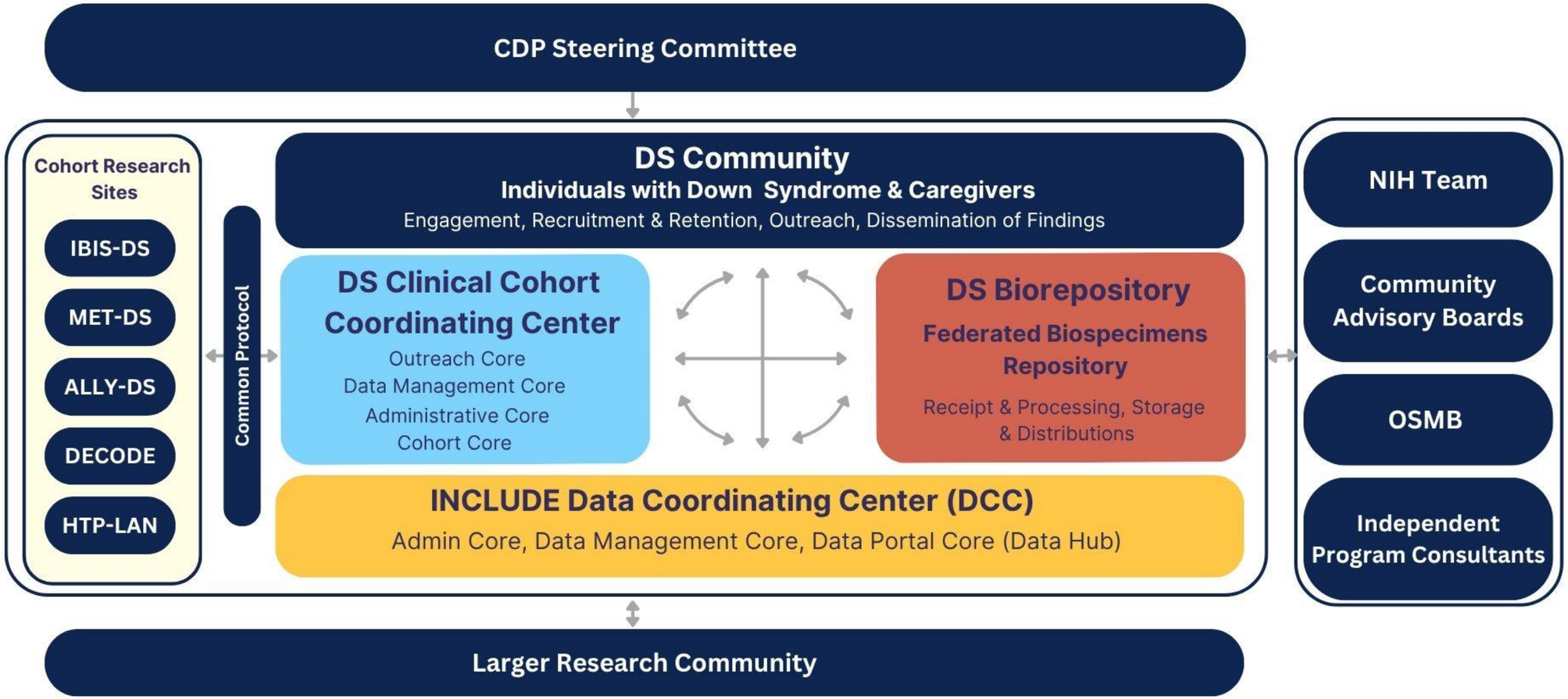
https://includecdp.org/

# INCLUDE Collaboration for Down Syndrome




https://includecdp.org/

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https://includecdp.org/

# INCLUDE Collaboration for Down Syndrome

## COMMUNITY ADVISORY BOARD (CAB) COMPOSITION

| | | |
|---|---|---|
| **DS-4C CAB** | **Total Members:** 15<br>**Composition:** 11 family members/advocates, 3 self-advocates, 1 professional; (note: a few individuals overlap with DS-CRS CABs) | **Age Range Represented:** 23 months-adult |
| **DECODE CAB** | **Total Members:** 8<br>**Composition:** 5 family members/advocates, 1 self-advocate, 2 professionals | **Age Range Represented:** adolescent - adult |
| **IBIS-DS CAB** | **Total Members:** 13<br>**Composition:** 12 family members/advocates, 1 professional | **Age Range Represented:** 18 months - 23 years old |
| **MET-DS CAB** | **Total Members:** 8<br>**Composition:** 7 family members/advocates, 1 self-advocate | **Age Range Represented:** 4-20 years old |
| **ALLY-DS CAB** | **Total Members:** 6<br>**Composition:** all self-advocates (with support partners), functioning levels: college graduate to nonverbal | **Age Range Represented:** 8 - 41 years old |
| **HTP-LAN CAB** | **Total Members:** 6<br>**Composition:** 4 family members, 2 professionals | **Age Range Represented:** child - adult ages |

We are recruiting!

https://includecdp.org/



Childhood Leukemia

Childhood Leukemia in Down Syndrome

**Summary and Future Directions**

# Summary & Future Directions

- Individuals with Down syndrome and childhood leukemia have been excluded from survivorship outcome studies
- Gap in understanding of how to optimize quality of life for patients and families
- Ongoing work aims to address this gap

# Summary and Future Directions

- Move from identifying difficulties to developing solutions
  - Survivorship and supportive care guidelines
  - Interventions to support cognition, behavior, and quality of life
- Engage the community throughout the research process
  - Patients/families, clinicians, researchers, advocates



# Thank you!

- Self-advocates and families
- Colleagues and study teams
  - St. Jude Children's Research Hospital
  - Children's Oncology Group
  - INCLUDE CDP
- Funding

Alex's Lemonade Stand Foundation for Childhood Cancer
Andrew McDonough B+ Foundation
NIH National Cancer Institute
American Cancer Society
NIH NICHD

# Questions?

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