

PROACTIVE NYS:
Preliminary Results and Lessons Learned from a
Longitudinal Study of Children with
Congenital CMV in New York State

ANDREW S. HANDEL, MD, FAAP

CO-PI, PROACTIVE NYS
ASSOCIATE PROFESSOR OF PEDIATRICS
DIVISION OF INFECTIOUS DISEASES
STONY BROOK CHILDREN'S HOSPITAL

Disclosures

ASHA DISCLOSURE

- *Financial* - Receives grants for other activities from *Eunice Kennedy Shriver* National Institute of Child Health and Human Development
- *Nonfinancial* - No relevant nonfinancial relationship exists

AAA DISCLOSURE

- *Financial* - Receives support from *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) for Research funding (75N94021D00018 / 75N94022F0000)

Learning Objectives

- To characterize the preliminary findings of a longitudinal study of infants with congenital CMV **identified through a universal screening program**
- To describe the challenges of conducting a multicenter longitudinal study of infants with congenital CMV
- To discuss potential solutions for maximizing participant enrollment and retention

The PROACTIVE NYS Team

PROACTIVE Co-PIs:

- Denise M. Kay, PhD
- Sharon Nachman, MD

NYS CMV Newborn Screening Team

- Denise Kay, PhD
- Norma Tavakoli, PhD
- Virginia Sack, MS, CGC
- And many others

Neurodevelopmental Consultant

- Kathleen Malee, PhD

Frontier Science Team

- Statistical and Data Management Support

PROACTIVE Study Sites

Albany Medical Center	Gillian Taormina, DO Jency Daniel, MD Saul Hymes, MD
New York Presbyterian - Brooklyn Methodist	Minnie John, MD
SUNY Upstate	Danielle Daniels, MD Leonard Weiner, MD
NYP - Weill Cornell	Christine Salvatore, MD
Stony Brook Children's	Andrew Handel, MD Sharon Nachman, MD
BCH/NY Medical College / Westchester Medical Center	Sheila Nolan, MD Patricia De La Mora, MD
NYU School of Medicine Children's Hospital at Montefiore	Stephanie Ungar, MD Julia Piwoz, MD
URMC/Strong Memorial	Michael C. Quinn, MD, PhD Jennifer Nayak, MD Geoffrey A. Weinberg, MD
Cohen Children's Medical Center / Northwell Health	Sunil Sood, MD
SUNY Buffalo	Mark Hicar, MD, PhD Gitanjali Rebello, MD Karl Yu, MD, PhD

Study Overview

- Long-term follow-up study of cCMV screen-positive newborns
- Goal: Systematically follow all children through 2 years of life
- Periodic assessments of:
 - Exam & growth features
 - Antiviral treatment status
 - Neurodevelopmental outcomes
 - Audiological outcomes
 - Ophthalmological outcomes



Study Objectives

Among a cohort of infants identified with cCMV by universal newborn screen:

- Describe the **distribution of neonatal features** of cCMV
- Describe trends in **antiviral** and **non-pharmaceutical treatments, adverse effects**, and impact on **long-term outcomes**
- Assess the long-term **audiologic, neurologic, and developmental** outcomes
- Describe the impact of a positive cCMV screen on the **quality of life** of infants and families

Inclusion Criteria

- Neonates born in NYS State during the 1-year cCMV NBS Pilot Program
 - 10/2023 – 10/2024
- Evaluated for cCMV by a designated Peds ID referral center
- Family willing and able to complete all study procedures



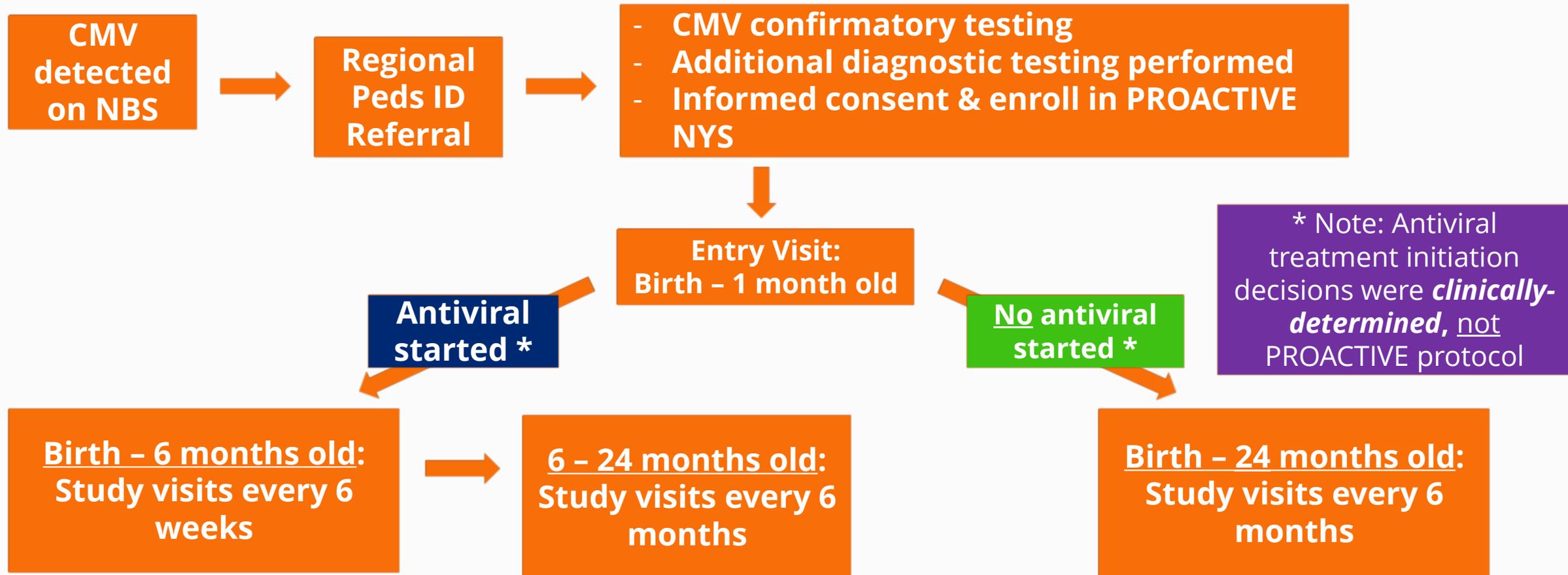
Inclusion Criteria

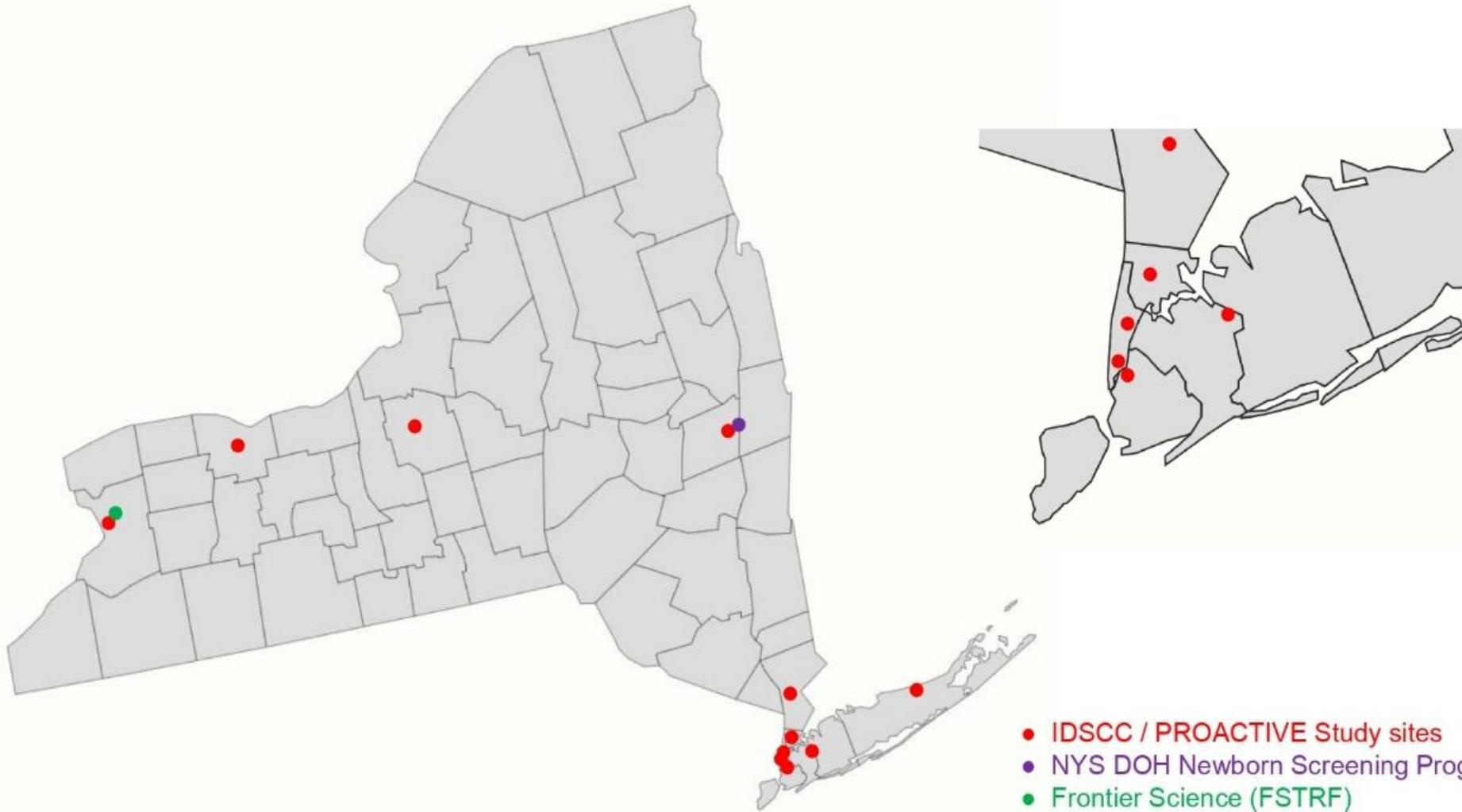
- Study participants meet criteria for one of the four following categories:
 - **Category 1:** Confirmed cCMV identified by NBS
 - **Category 2:** Confirmed cCMV **not** identified by NBS (False-negative cCMV screen)
 - **Category 3:** False-positive cCMV screen
 - **Category 4:** Premature infants with confirmed CMV on late positive NBS

Exclusion Criteria

- Neonate whose parents refuse participation in the long-term follow-up study

Study Visit Procedures





Study Entry Visit (Birth – 1 month old)

Newborn evaluation

- Confirmatory CMV testing results
- Maternal CMV history
- Neonatal medical diagnoses
- Physical exam findings
 - Growth parameters

Diagnostic results

- Laboratory testing
- Imaging
- Neonatal hearing tests
- Ophthalmology exam

Treatment decisions

- Treatment provided (if any)

Long-Term Outcomes: Neurodevelopment

Neurodevelopmental assessments

- ASQ-3
- ASQ:SE-2
 - Every 6 months
- MCHAT-R/F
 - 18, 24 months

Children with developmental delays identified

- Early Intervention referral
- Neuropsychology assessment
- Bayley-III
- Vineland Adaptive Behavior Scales

Long-Term Outcomes: Hearing and Vision

Audiological monitoring

- Every 3-6 months (or more frequent)
- Interventions provided



Ophthalmologic monitoring

- High-risk infants & site preference
- Per Ophtho recommendations



Quality of Life (QoL)

- Standardized assessments:
 - PedsQL (Child QoL)
 - Parental Stress Scale (Parent/Caretaker QoL)
- Time points:
 - 1 year from study start date (Oct 2024)
 - 2 years of life

Prospective Observational study of Asymptomatic cCMV Transmission to Infants for Virological Evaluation in New York State

Working **Together** to Improve Outcomes

While cytomegalovirus (CMV) is the most common congenital infection, the vast majority of newborns show minimal or no symptoms at birth and go undiagnosed.

www.proactivenys.org

Project Home and Design

[Project Home](#) · [Codebook](#)

Project status: **Production**

Data Collection — 99 - Training Site

[Record Status Dashboard](#)

[View / Edit Records](#)

Patid: 100001 [Select other record](#)

Applications

[Data Exports, Reports, and Stats](#)

[Resolve Issues](#)

Help & Information

[Help & FAQ](#)

[Video Tutorials](#)

[Suggest a New Feature](#)

[Contact REDCap administrator](#)

Record Home Page

The grid below displays the form-by-form progress of data entered for the currently selected record. You may click on the colored status icons to access that form/event.

[Choose action for record](#)

Legend for status icons:

- Incomplete
- Incomplete (no data saved) ?
- Unverified
- Complete
- ● ● Many statuses (all same)
- Many statuses (mixed)

Patid: **100001**

Data Collection Instrument	Entry 11-08-2023	6 Weeks (+/- 3 weeks) 11-02-2023	12 Weeks (+/- 3 weeks) 11-02-2023	18 Weeks (+/- 3 weeks)	6 Months (+/- 3 months)	12 Months (+/- 3 months)	18 Months (+/- 3 months)	24 Months (+/- 3 months)	+ Add new Extra Visit	Antiviral Treatment	Final Contact
Enrollment Category	●										
Entry CMV Screening and Maternal History	●										
Visit Tracking		●	●	●	●	●	●	●	●		
Antiviral Treatment										●	
Neonatal Data and Medical Problems	●										
Physical Measurements	●	●	●	●	●	●	●	●	●		
Physical Exam and Medical Diagnoses	●	●	●	●	●	●	●	●	●		
Laboratory Testing	●	●	●	●	●	●	●	●	●		
CSF Analysis	●	●	●	●	●	●	●	●	●		
Ophthalmology Assessment	●	●	●	●	●	●	●	●	●		
Abdominal Ultrasound	●	●	●	●	●	●	●	●	●		
Head Ultrasound	●	●	●	●	●	●	●	●	●		
MRI Brain	●	●	●	●	●	●	●	●	●		
Final Contact											●

PROACTIVE Study Dashboard

PROACTIVE NYS Summary Dashboard

Reset Filters

V1.0.0.1

Site

- (All)
- Albany Medical Center
- BCH/NY Medical College/Westchester Medical Center
- Children's Hospital at Montefiore
- Cohen Children's Medical Center/Northwell Health
- New York Presbyterian - Brooklyn Methodist Hospital
- New York Presbyterian - Weill Cornell
- Stony Brook Children's Hospital
- SUNY Buffalo Olshai Children's Hospital
- SUNY Upstate Golisano Children's Hospital
- University of Rochester Strong Memorial Hospital

Sex at Birth

- (All)
- Male
- Female

Race

- (All)
- Asian
- Black or African American
- White
- More than one race
- Unknown

Ethnicity

- (All)
- Hispanic or Latino
- Not Hispanic or Latino
- Unknown

Sex at Birth

Male: 52

Female: 46

Race

Asian: 3

Black or African American: 11

White: 51

More than one race: 3

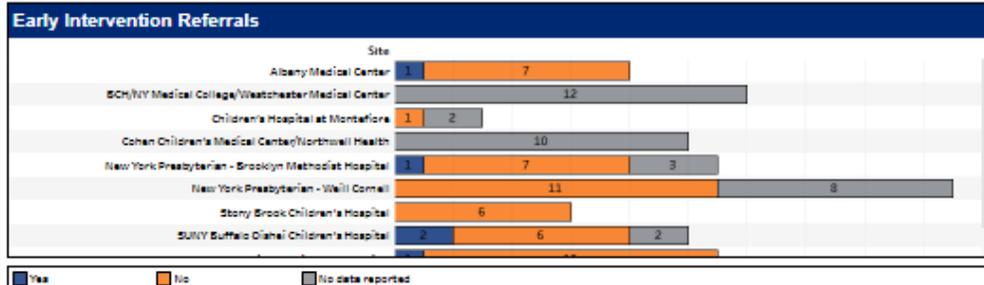
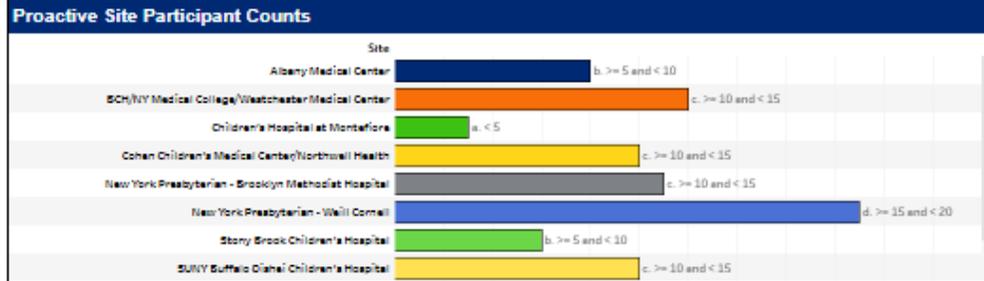
Unknown: 30

Ethnicity

Hispanic or Latino: 13

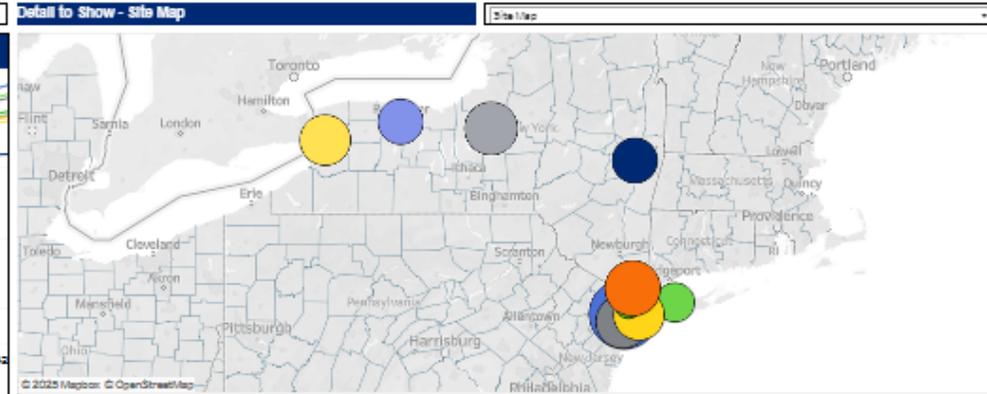
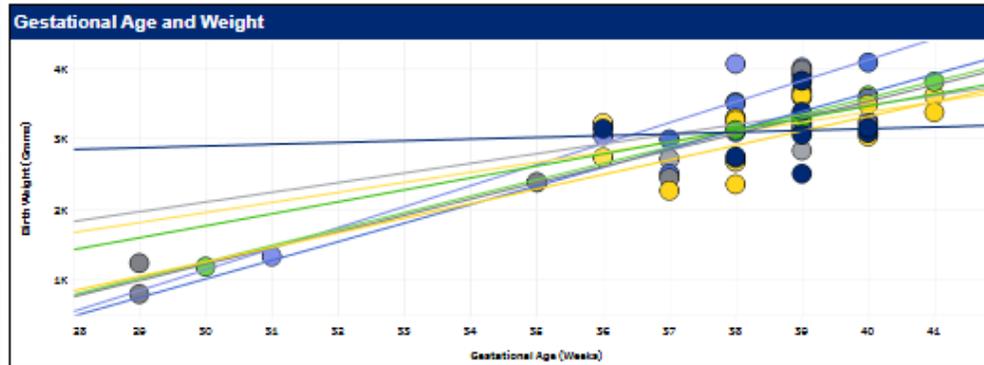
Not Hispanic or Latino: 46

Unknown: 29

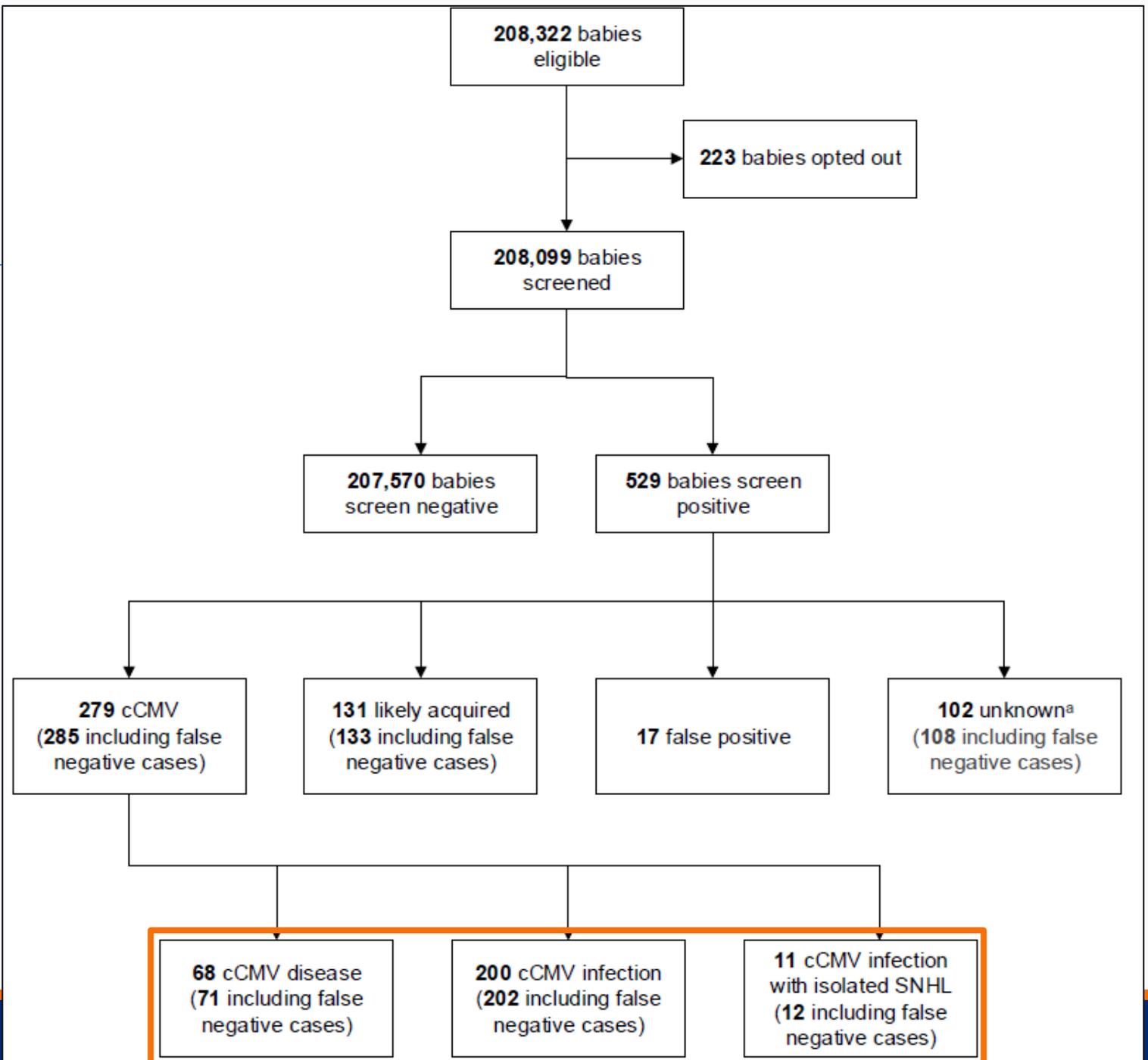


Antiviral Detail

Site	Abnormal Examination Findings	Abnormal Hearing Assessment	Abnormal Laboratory Findings	Abnormal Ophthalmologic Assessment	Abnormal Radiographic Findings
Albany Medical Center	0	0	0	0	1
BCH/NY Medical College/Westchester Medical Center	0	0	0	0	0
Children's Hospital at Montefiore	1	0	1	0	0
Cohen Children's Medical Center/Northwell Health	0	1	0	0	2
New York Presbyterian - Brooklyn Methodist Hospital	2	2	1	0	4
New York Presbyterian - Weill Cornell	0	0	1	0	6



Potential Study Participants



Expected Study Accrual

- Expected number of children with cCMV in NYS greatly over-estimated:
 - Original **estimate**: 0.25% – 0.5% of births
 - 500 – 1,000 infants expected in NYS
- **Actual** rate of congenital CMV: **0.13%**
 - 279 identified with cCMV in NYS
 - Ontario cCMV rate: **0.13%** (Dunne, 2025)

PROACTIVE Study Accrual

Total Accrual	Confirmed cCMV (identified by NBS)	Confirmed cCMV with a <u>false negative</u> CMV NBS	<u>False positive</u> CMV NBS	Premature infant with postnatal CMV (<44 weeks gest)
111	102	4	1	4

Current Study Accrual

- Successes
 - > 100 enrolled children
 - Inclusion of children with clinically inapparent cCMV
 - Approaching 2 years follow up every 6 months
- Challenges with enrolling referred infants
 - Loss to follow-up
 - Family uninterested in research involvement
 - Time to site activation

Confirmed cCMV: Participant Characteristics

Characteristic		Total (N=106)
Sex	Male	56 (53%)
	Female	50 (47%)
Gestational age at birth (Weeks)	Mean (s.d.)	38.2 (2.4)
Age (months)	Mean (s.d.)	17.3 (3.5)
Race	Asian	4 (4%)
	Black or African American	12 (11%)
	White	57 (54%)
	More than one race	2 (2%)
	Unknown	31 (29%)

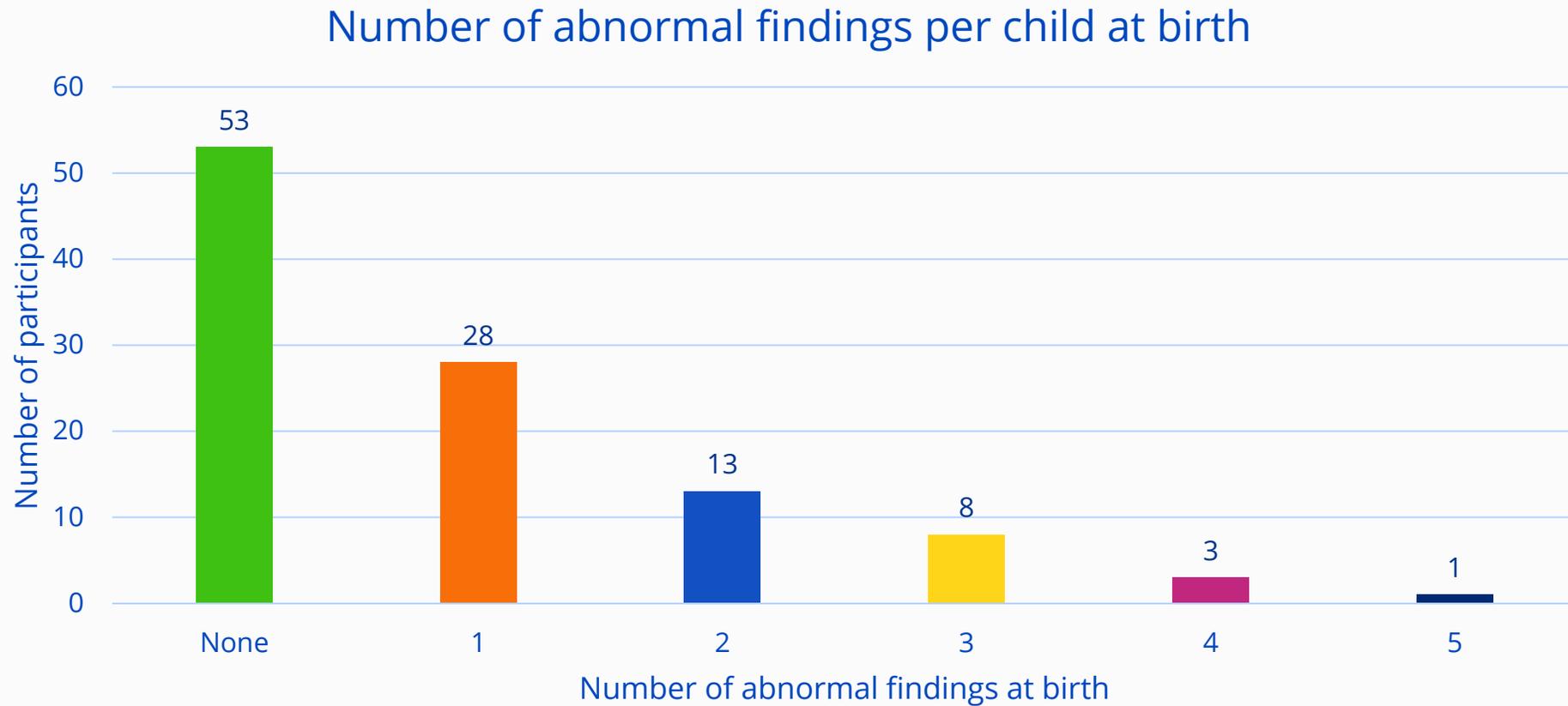
Characteristic		Total (N=106)
Ethnicity	Hispanic or Latino	11 (10%)
	Not Hispanic or Latino	62 (58%)
	Unknown	33 (31%)
Birth Weight (kg)	Mean (s.d.)	3.1 (0.6)
Category	Confirmed cCMV identified by NBS program	102 (96%)
	Confirmed cCMV not identified by NBS	4 (4%)

Cohort Description: Abnormal findings at Birth

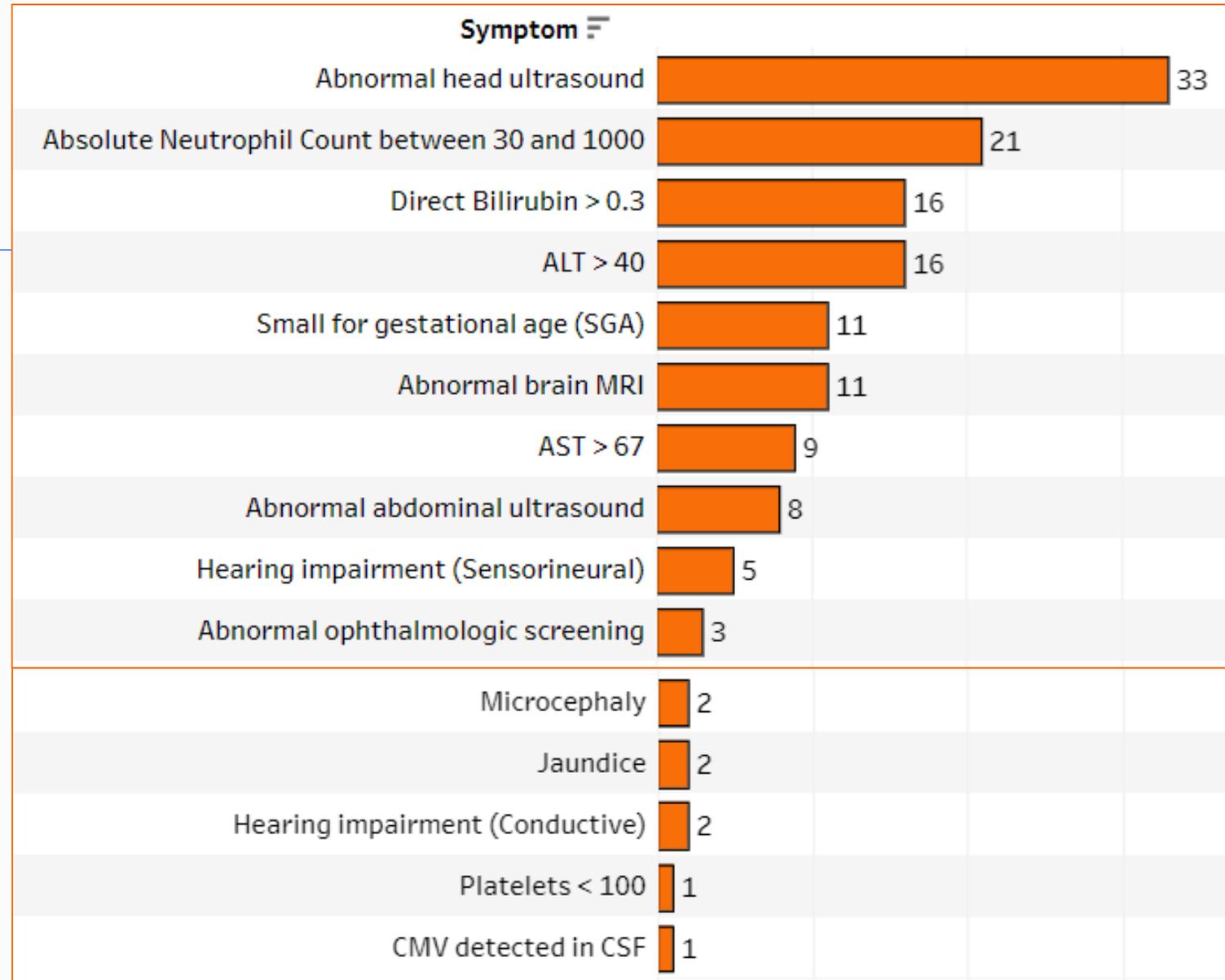
Diagnostic abnormalities at birth		Total (N=106)
	None	53 (50%)
	≥ 1	53 (50%)

* **Diagnostic abnormality:** At least 1 abnormal exam, laboratory, or imaging result based on the AAP Red Book 2024 case definitions *

Cohort Description: Abnormal findings at Birth



Cohort Description: Abnormal findings at Birth



Cohort Description: Antiviral treatment

Antiviral treatment		Total (N=106)
	Untreated	75 (71%)
	Treated	31 (29%)

Cohort Description: Hearing Loss

Hearing loss detected		Total (N=106)
	Among entire cohort	13 (12.3%)
	Hearing Loss <u>prior to reaching 3 months old</u>	5 (38%)
	Hearing Loss at <u>3 months old or older</u>	8 (62%)

Cohort Description: Brain Imaging Utilization

Characteristic		Total (N=89)
Head Ultrasound Performed?		
	No	16 (18%)
	Yes	73 (82%)
MRI Brain Performed?		
	No	69 (78%)
	Yes	20 (22%)
Both Head Ultrasound and MRI Brain Performed?		
	No	69 (78%)
	Yes	20 (22%)

Cohort Description: Ophthalmology Evaluations

Characteristic		Total (N=89)
Ophthalmology evaluation performed		
	Yes	48 (54%)
	No	41 (46%)
Age at Ophtho eval	< 3 months old	41 (85%)
	>= 3 months old	7 (15%)
Findings among infants tested <3 months old		
	No cCMV-related abnormality	39 (95%)
	cCMV-related abnormality	2 (5%)

Challenges Faced

- Maximizing participant enrollment and retention
 - Less interest in following up among clinically inapparent cases
 - Initial enthusiasm wanes over time
 - Concerns about data entry into a large database
- Solutions
 - Simplifying study design
 - Minimizing time required of families
 - Encouraging remote/virtual study visits
 - Emphasis on developing strong rapport and trust

Challenges Faced

- Diagnostic harmonization across study sites
 - Differences in
 - Clinical practice
 - Guidelines used
 - Evaluations performed
 - MRI brain, lumbar punctures, ophtho exam
 - Catchment areas and driving distances
 - Patient populations

Challenges Faced

- Solutions for diagnostic harmonization
 - Recommended schedule of events
 - Submit raw data (not clinical interpretation)
 - E.g.: Microcephaly definition
 - Analyses based on a single guideline document (AAP Red Book)
 - Monthly calls to discuss challenges, share approach
 - Allow for flexibility in logistical approach
 - In-person vs virtual visits, telephone follow-ups, etc.

Challenges Faced

- Study definitions
 - Abnormal findings: cCMV-related or coincidence?
 - Head ultrasound abnormalities
 - Lab abnormalities at diagnosis
- Solutions
 - Consistent approach to data analysis
 - Report on findings (i.e. exact platelet count), not interpretation

Take-away

- Universal cCMV screening is essential for understanding the full spectrum of short- & long-term outcomes
- Must facilitate child & family participation
- Long-term cCMV studies are possible, but require careful planning & implementation
 - >100 infants enrolled - most without overt cCMV symptoms
 - Granular data obtained through prospective study
 - More *late-onset* hearing loss detected than at birth

Next Steps

- Complete 2-year follow-up
 - Data analysis and dissemination
 - Working to extend follow-up to 3 years - and beyond
- Additional studies
 - Retrospective study of children NOT enrolled in PROACTIVE
 - Leveraging PROACTIVE NYS network for additional observational and interventional studies

The PROACTIVE NYS Team

PROACTIVE Co-PIs:

- Denise M. Kay, PhD
- Sharon Nachman, MD

NYS CMV Newborn Screening Team

- Denise Kay, PhD
- Norma Tavakoli, PhD
- Virginia Sack, MS, CGC
- And many others

Neurodevelopmental Consultant

- Kathleen Malee, PhD

Frontier Science Team

- Statistical and Data Management Support

PROACTIVE Study Sites

Albany Medical Center	Gillian Taormina, DO Jency Daniel, MD Saul Hymes, MD
New York Presbyterian - Brooklyn Methodist	Minnie John, MD
SUNY Upstate	Danielle Daniels, MD Leonard Weiner, MD
NYP - Weill Cornell	Christine Salvatore, MD
Stony Brook Children's	Andrew Handel, MD Sharon Nachman, MD
BCH/NY Medical College / Westchester Medical Center	Sheila Nolan, MD Patricia De La Mora, MD
NYU School of Medicine Children's Hospital at Montefiore	Stephanie Ungar, MD Julia Piwoz, MD
URMC/Strong Memorial	Michael C. Quinn, MD, PhD Jennifer Nayak, MD Geoffrey A. Weinberg, MD
Cohen Children's Medical Center / Northwell Health	Sunil Sood, MD
SUNY Buffalo	Mark Hicar, MD, PhD Gitanjali Rebello, MD Karl Yu, MD, PhD

Questions?

[Andrew.Handel@
stonybrookmedicine.edu](mailto:Andrew.Handel@stonybrookmedicine.edu)

Visit us:

ProactiveNYS.org/



PROACTIVE
New York State

