Congenital Cytomegalovirus: Knowledge is Power

2023 Annual Family Medicine CME Weekend / Melanie Morris, Au.D., CCC-A / November, 10, 2023

Financial Disclosures

I have no **relevant financial or nonfinancial relationships** in the products or services described, reviewed, evaluated or compared in this presentation.

Learning Objectives

At the end of this presentation, participants should be able to describe the following:

1) The connection between congenital cytomegalovirus (cCMV) and hearing loss in infants

2) The current methods of cCMV testing and their benefits/limitations

3) The role of the medical home in timely cCMV detection and follow-up

4) How early diagnosis and early intervention can impact children's auditory development and overall quality of life

"Cytomegalovirus: The Elephant in our living room."

Cytomegalovirus

(sy-toe-MEG-a-low-vy-rus)

cCMV Transmission

What is Cytomegalovirus?

- A common virus that is typically harmless to healthy children and adults
- Part of the herpes family – Once infected, CMV stays in your body in an inactive state that can reactivate
- Common in children 1-3 years of age, particularly if they attend daycare
- In the US, 1 in 3 children have been infected by 5 years of age; 50% of adults have been infected by 40 years of age

What is *Congenital* Cytomegalovirus?

- CMV that is acquired by the fetus in utero
- Infants can be asymptotic or symptomatic
- The "most common infectious disease cause of birth defects in the United States," impacting 1 of every 200 births
- Leading cause of non-genetic, childhood-onset sensorineural hearing loss

Transmission: Spread by *direct and indirect* close contact with bodily fluids (e.g. saliva, urine, mucous, tears, etc)

(*National Center for Immunization and Respiratory Diseases*, *Division of Viral Diseases*)

Congenital Cytomegalovirus (cCMV)

CMV is common, serious, and preventable.

1 out of 3

pregnant women who become infected with CMV will pass the virus to their unborn child

1 Child

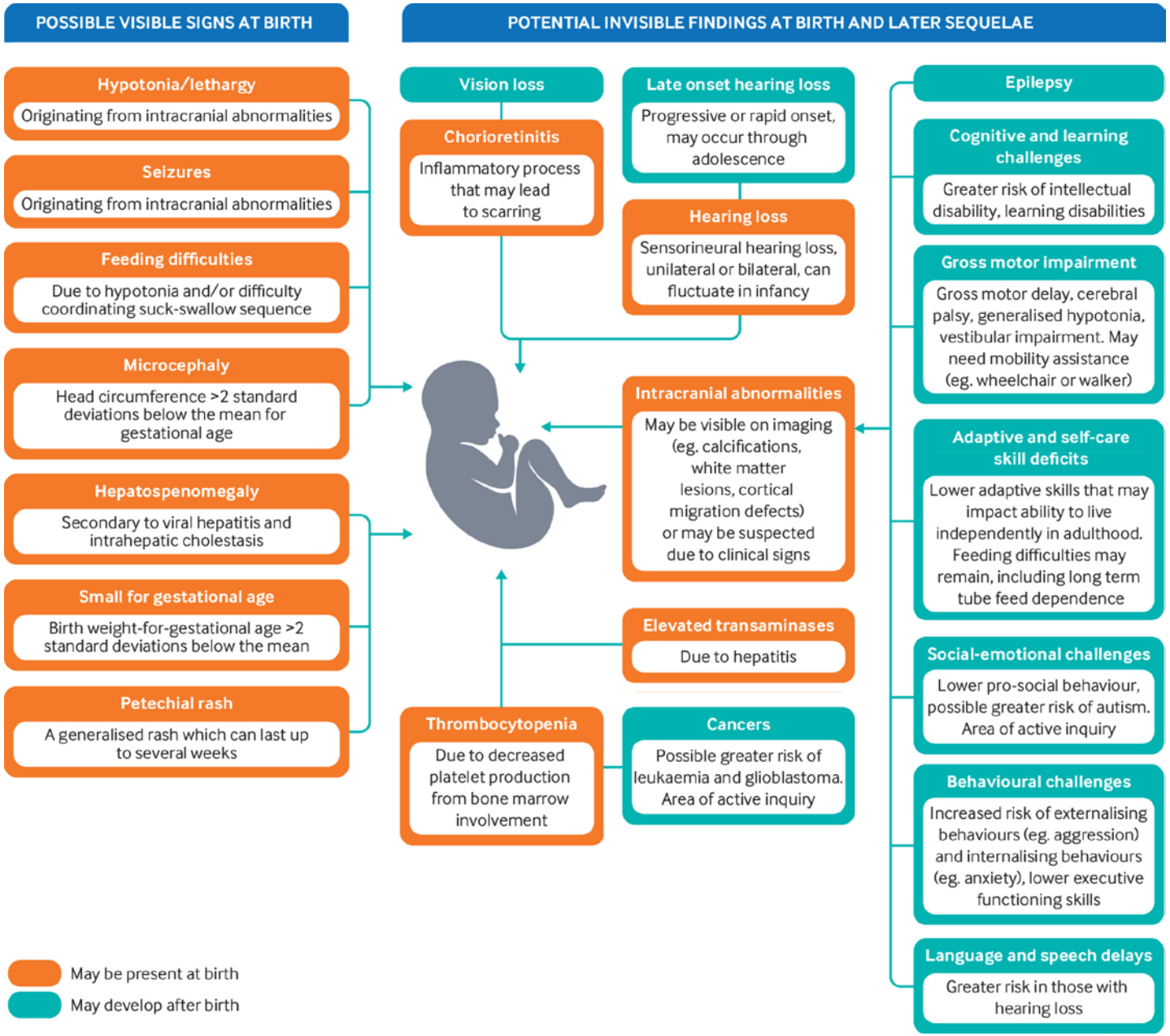
is permanently disabled by congenital CMV every hour

1 in 200

children are born with congenital CMV each year

(National CMV Foundation)

Potential clinically visible and invisible signs and sequelae of cCMV at birth and later in life



(Pesch, et al 2021)

How Common is *Primary* cCMV Infection?

- All pregnancies: ≈2%
- Minority populations are at higher risk
  - Non-Hispanic white = 1.4%
  - Non-Hispanic black = 5.7%
  - Mexican American = 5.1%
- Healthcare workers: ≈2%
- Childcare workers ≈ 10-20%
- Parents with another child in daycare ≈ 24%

(Hyde, et al. 2010)

cCMV Prevention Strategies:

Parents/Caregivers:

- Avoid contact with saliva when kissing a child
- Do not put their pacifier in your mouth
- Do not share food, utensils, drinks, or straws
- Do not share a toothbrush
- Wash your hands after changing a diaper

Early Childcare and Healthcare Providers:

- Use gloves when changing diapers
- Wipe down surfaces
- Clean toys routinely

cCMV Testing and Treatment

cCMV Screening Methods

cCMV screening must occur prior to 21 days of life

Specimen	Advantages	Disadvantages
Dried Blood Spot	NBS Program already in place	CMV viral load lower in blood (50-85% Sensitivity), less available specimen
Saliva*	CMV viral load higher (88% Sensitivity)	Not part of existing NBS Program; Possible contamination with breastmilk
Urine	CMV viral load higher (79% Sensitivity)	Not part of existing NBS Program; Challenges with collection

Universal Screening=Test all infants for cCMV

Targeted Screening=Test for cCMV after 1-2 failed hearing screenings

*Current standard diagnostic tool

Dollard (2010); Schleiss, et al (2023)

Treatment: Antiviral Therapy

- Ganciclovir and Valganciclovir

- Not currently recommended for asymptomatic cases of cCMV
  - Risk of neutropenia
  - After cessation of antiviral therapy, viral replication may rebound with hearing loss

- Ongoing ValEAR Study: To determine if valganciclovir improves hearing thresholds and language scores

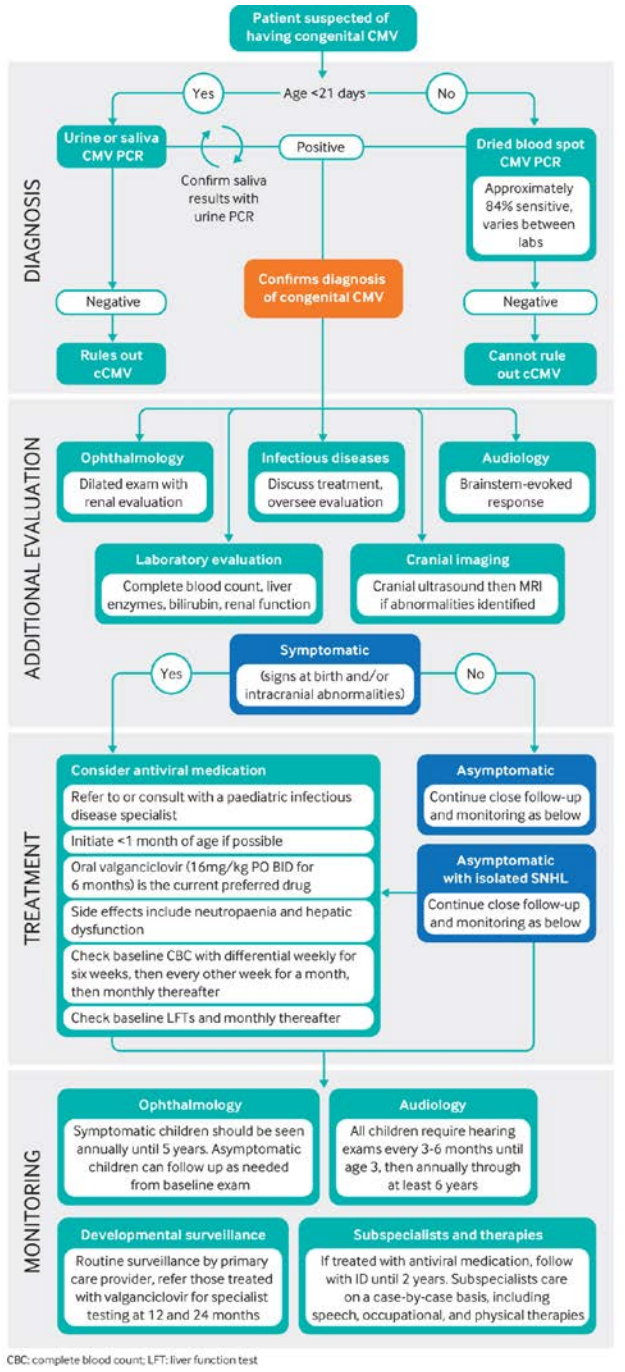
Hearing, Vision, and Developmental Surveillance

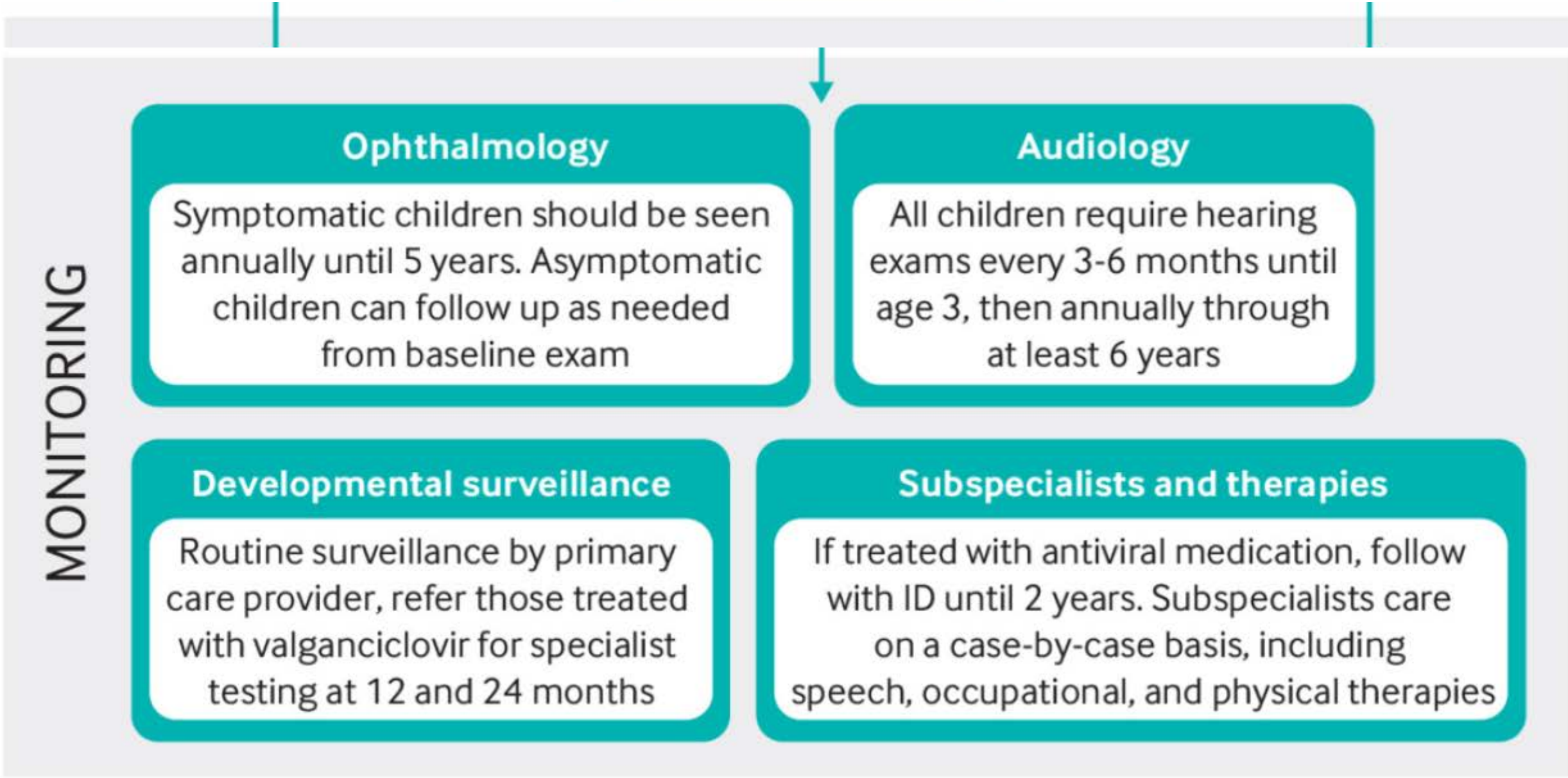
- Hearing Surveillance:
  - Routine and frequency hearing tests
  - Amplification
  - Early intervention
    - Auditory Verbal therapy
    - American Sign Language services
    - Speech-language therapy
    - Parent education resources
- Vision Surveillance:
  - Ophthalmologic evaluation at diagnosis; Annual thereafter

- Developmental Surveillance

Overview of the diagnosis, evaluation, treatment, and follow-up of infants with congenital cytomegalovirus

(Pesch, et al 2021)





CBC: complete blood count; LFT: liver function test

cCMV and Hearing

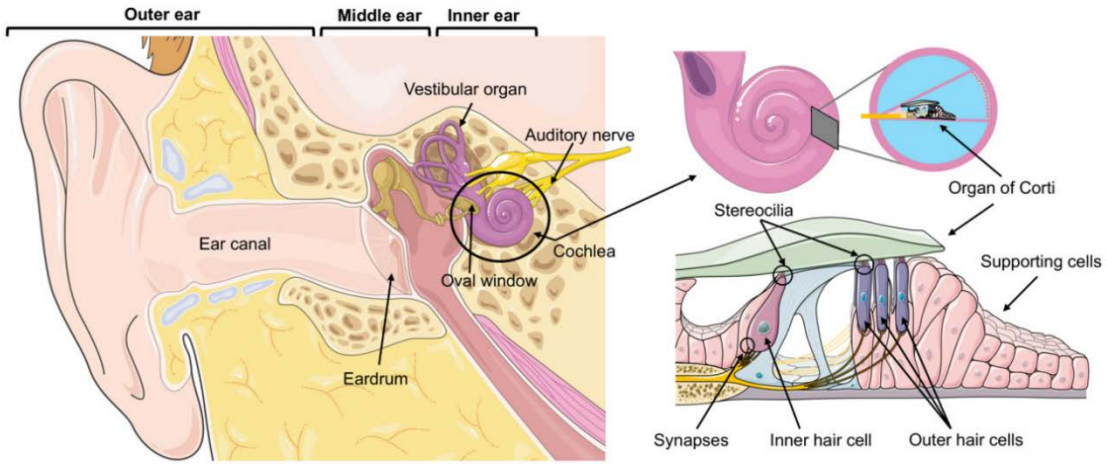
cCMV and Hearing Loss

- 10–15% of asymptomatic cCMV+ infants will have hearing loss at birth or experience delayed-onset hearing loss.
- In the United States, 15–20% of all cases of bilateral moderate to profound sensorineural hearing loss (SNHL) in children are due to cCMV
- cCMV is the leading environmental cause of hearing loss among children, affecting 4:1000 newborns.

Lanzieri, et al (2018); Philips, et al (2023); Fowler, et al (2018)

Pathophysiology: Possible Mechanisms

- Inflammation may damage the spiral ganglion neurons (SGN) of the inner ear
- Inner ear development disruption
- Disruption of inner ear homeostasis



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cCMV and Hearing Loss-Related Position Statements

American Academy of Audiology Position Statement (March 2023)
"The American Academy of Audiology recommends early identification of cCMV through screening to allow for appropriate early diagnosis, intervention, and monitoring for congenital, progressive, and delayed-onset hearing loss in infants with cCMV."

Joint Commission on Infant Hearing (JCIH) Position Statement (2019)
"Additional laboratory testing to be considered in the process of evaluating a newborn or infant diagnosed with sensorineural hearing loss and to rule out the most common etiologies that impact intervention plans include (a) connexin gene, (b) electrocardiogram, and (c) urine and saliva swabs for congenital cytomegalovirus (cCMV)."

Kettler, M., Shoup, A., Moats, S., Steuerwald, W., Jones, S., Stiell, S. C., & Chappetto, J. (2023). American Academy of Audiology Position Statement on early identification of cytomegalovirus in newborns. Journal of the American Academy of Audiology. https://doi.org/10.1055/s-0043-1768036

Hearing Loss and cCMV Summary

- Symptomatic children are more likely to have hearing loss compared with asymptomatic children
  - 22-65% of symptomatic cases have hearing loss
  - 6-23% asymptomatic cases have hearing loss
- Hearing loss can be unilateral or bilateral
  - "Poorer hearing ear" is more likely to progress
  - Majority of patients born with unilateral hearing loss (normal hearing in one ear), developed hearing loss in the "normal" hearing ear
- Progressive and late-onset hearing loss is common

(Lanzieri, et al. 2018)

cCMV Audiologic Management Considerations

- cCMV can impact vision
  - Can influence communication plan
  - Can influence type of assessment used
- cCMV can impact vestibular function
  - Children with normal hearing can still have balance issues
  - Consider vestibular evaluations for cCMV+ patients
- cCMV can cause progressive hearing loss and risk of contralateral hearing deterioration
  - Routine hearing and speech development is imperative
  - Can influence hearing aid selection
  - Consideration of unilateral cochlear implantation

National cCMV Trends

States with **Universal** cCMV Screening (Bloodspot Panel)

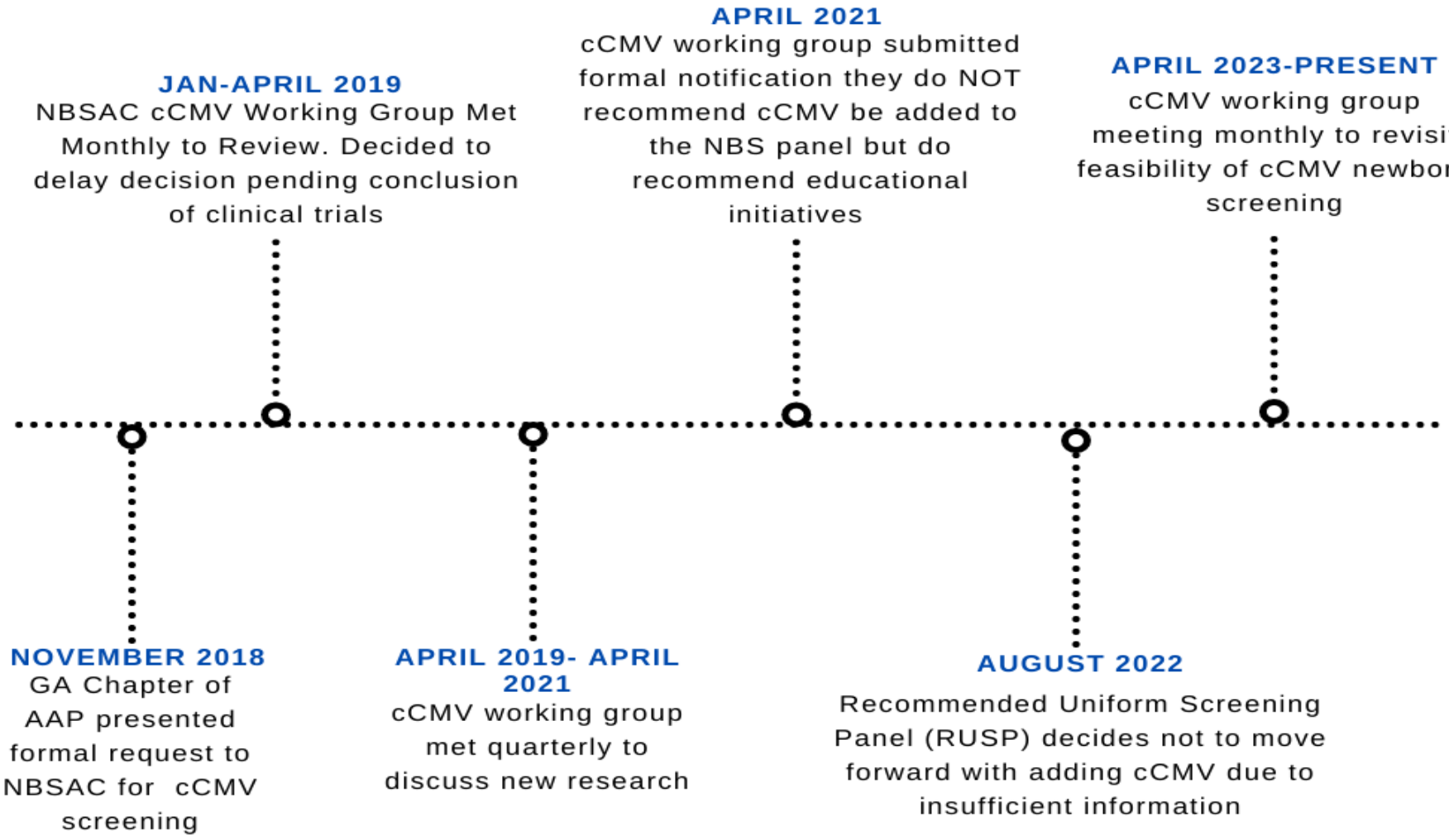
- Minnesota (February 2023)
- Connecticut (To begin 2025)
- New York (NICHD Grant, 2023-2024)

States with **Hearing-Targeted** cCMV Screening (Point of Care)

- Florida
- Virginia
- Illinois (to be offered*)
- Iowa
- Kentucky
- Louisiana
- Maine
- New York
- Pennsylvania
- Utah

Georgia's Current cCMV Recommendations

Georgia's Newborn Screening and Genetics Advisory Committee (NBSAC) cCMV Working Group Efforts Timeline



NBSAC cCMV Working Group Continued Efforts

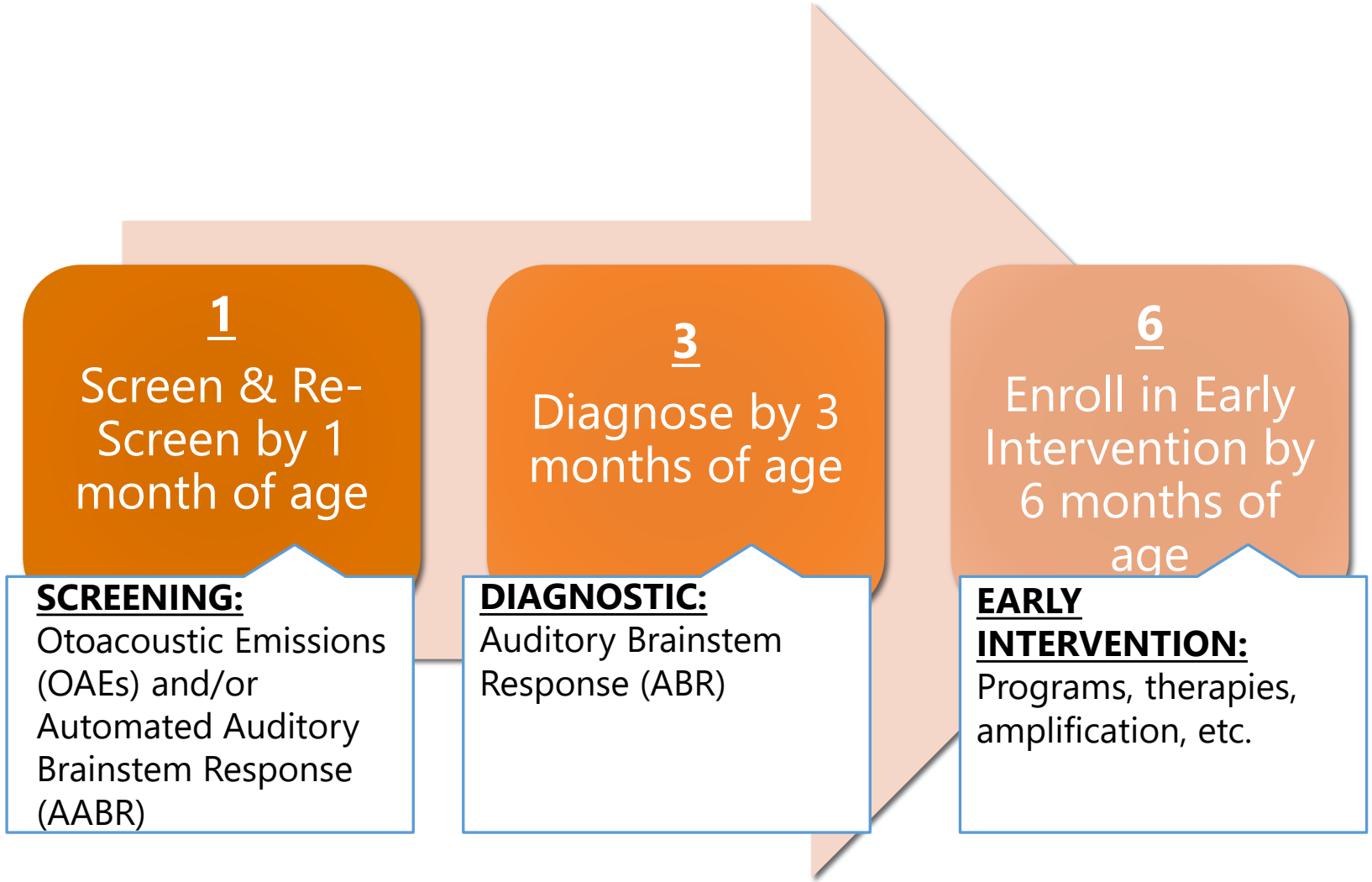
Newborn Screening Advisory Committee (NBSAC), cCMV Working Group:

- Comprised of 13 members
- Multidisciplinary team with ENT, Neurology, Early Hearing Detection and Intervention (EHDI), Lab Directors, Infectious Disease, Geneticists

October 2023: Submitted a request to DPH to add *hearing-targeted* cCMV screening at the birthing facility

Let’s pause to discuss Newborn Hearing Screening

Joint Committee on Infant Hearing (JCIH) 1:3:6 Benchmarks:



Why Screen for All Babies for Hearing Loss?

- 2-3 out of every 1,000 babies are born with some degree of hearing loss

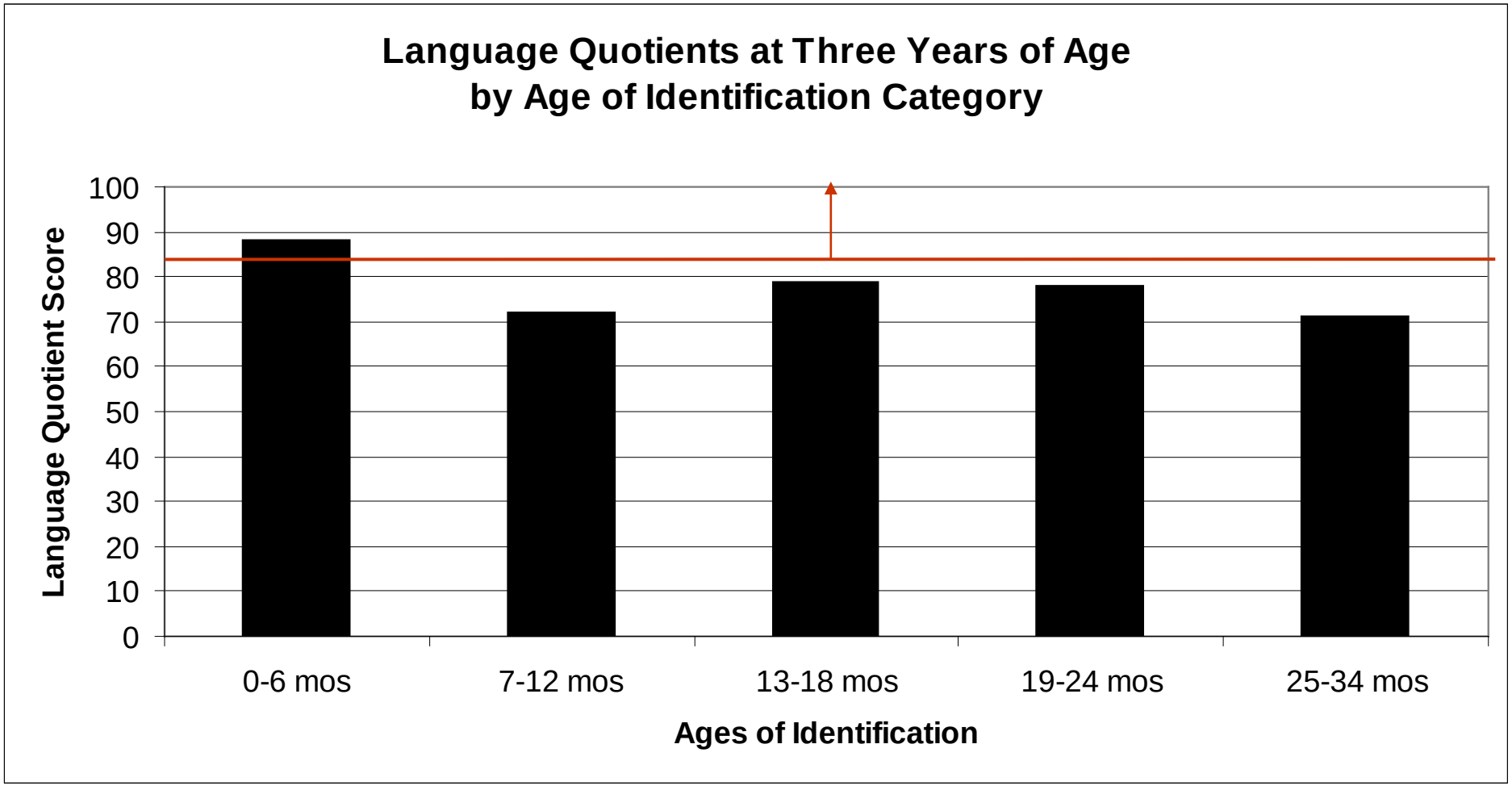
- If a child has *undiagnosed* hearing loss, it can impact the child's communication and language skills, academic achievement, and social-emotional development.

- Most children with hearing loss who receive ***timely services** from trained staff progress at age-appropriate rates.

***Meet 1:3:6 benchmarks**

(National Institute on Deafness and Other Communication Disorders [NIDCD], 2010)

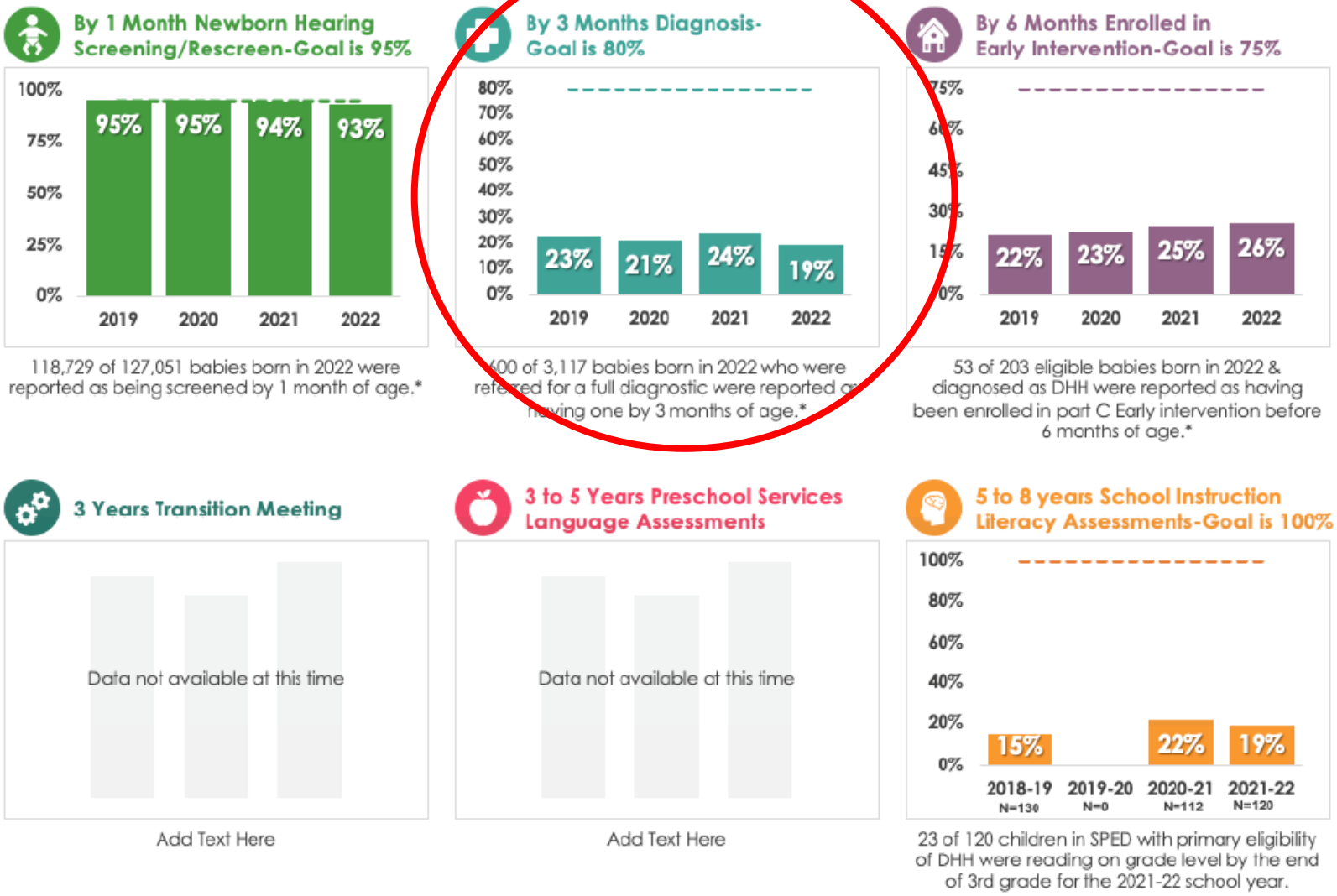
Effects of Age of Identification on Language Development



Average language score

(Yoshinaga-Itano, et al. 1998)

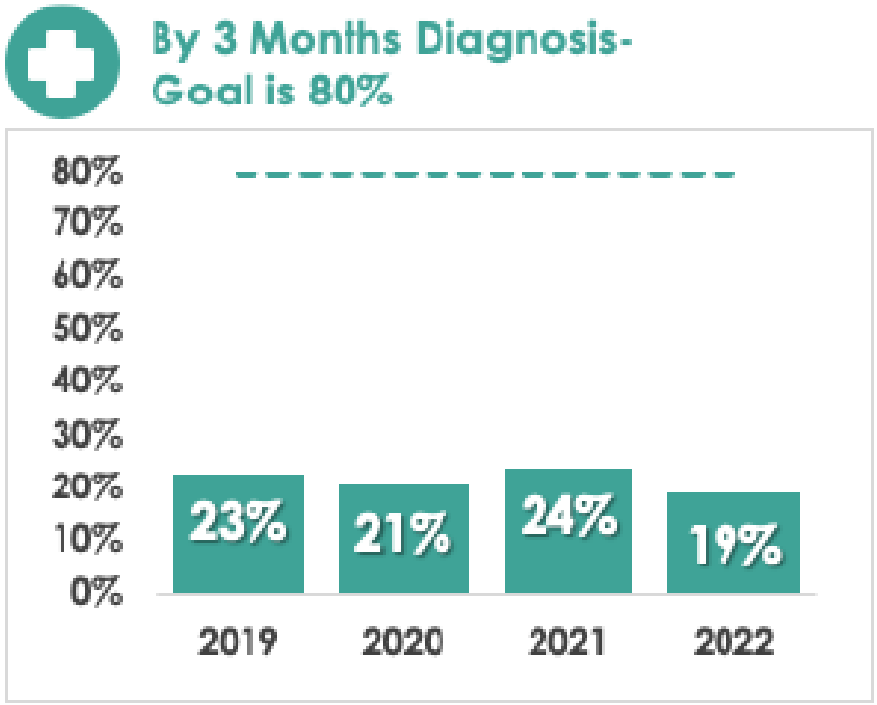
2023 DHH Language and Literacy Dashboard



* Sources: Georgia DPH, 2019-2022 HSFS Data for GaDOE PHIP Request as of 8-292023 (2022 data are preliminary and subject to change); GaDOE 2018-22 School Year End of Grade Assessments, Grade 3 Milestones English Language Arts Assessment for children in Special Education with a primary eligibility of DHH. Data unavailable for 2019-20 school year due to lack of testing during the COVID-19 pandemic.

O.C.G.A. 30-1-5 Year 4 (2022): Annual Report on Language and Literacy Outcomes for Children who are Deaf and Hard of Hearing

Why so low?



600 of 3,117 babies born in 2022 who were referred for a full diagnostic were reported as having one by 3 months of age.*

- The "system" is confusing and challenging for families
- Family must find an audiologist who does ABR testing *and* who takes their insurance (very few free options)
- Facilities that do ABR testing often have wait lists
- Health Insurance is an obstacle to getting these services in a timely manner (waiting on prior authorization; waiting on insurance to become active)
- Audiologist MUST enter results into Georgia's mandatory reporting system, SENDSS
- Potential misinformation at screening: "it's probably just fluid"
- Too many babies are referred for additional testing, clogging up the system

O.C.G.A. 30-1-5 Year 4 (2022): Annual Report on Language and Literacy Outcomes for Children who are Deaf and Hard of Hearing

The Role of the Medical Home

cCMV Prevention:

- Education about signs and symptoms of cCMV
- Education about prevention, particularly to the following high-risk populations:
  - Childcare workers = 10-20%
  - Parents with another child in daycare = 24%
  - Minority populations
    - Non-Hispanic white = 1.4%
    - Non-Hispanic black = 5.7%
    - Mexican American = 5.1%

(Hyde, et al. 2010)

cCMV Testing and Referral Management

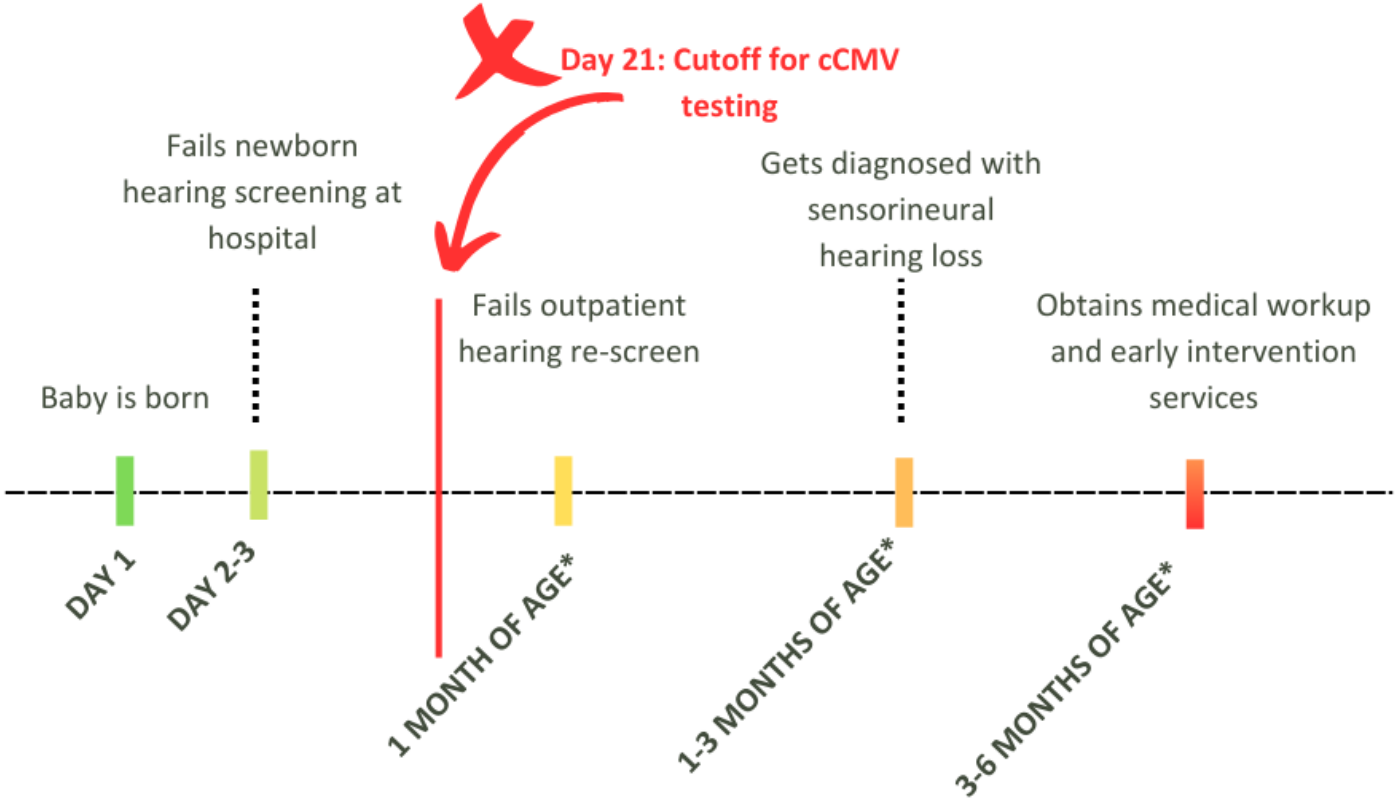
No confirmed cCMV diagnosis:

- If infant has symptoms of cCMV and/or failed the newborn hearing screening and is <21 days of age – Order and coordinate cCMV testing
- Educate families on the importance of cCMV and hearing testing and the urgency behind both

Confirmed cCMV diagnosis:

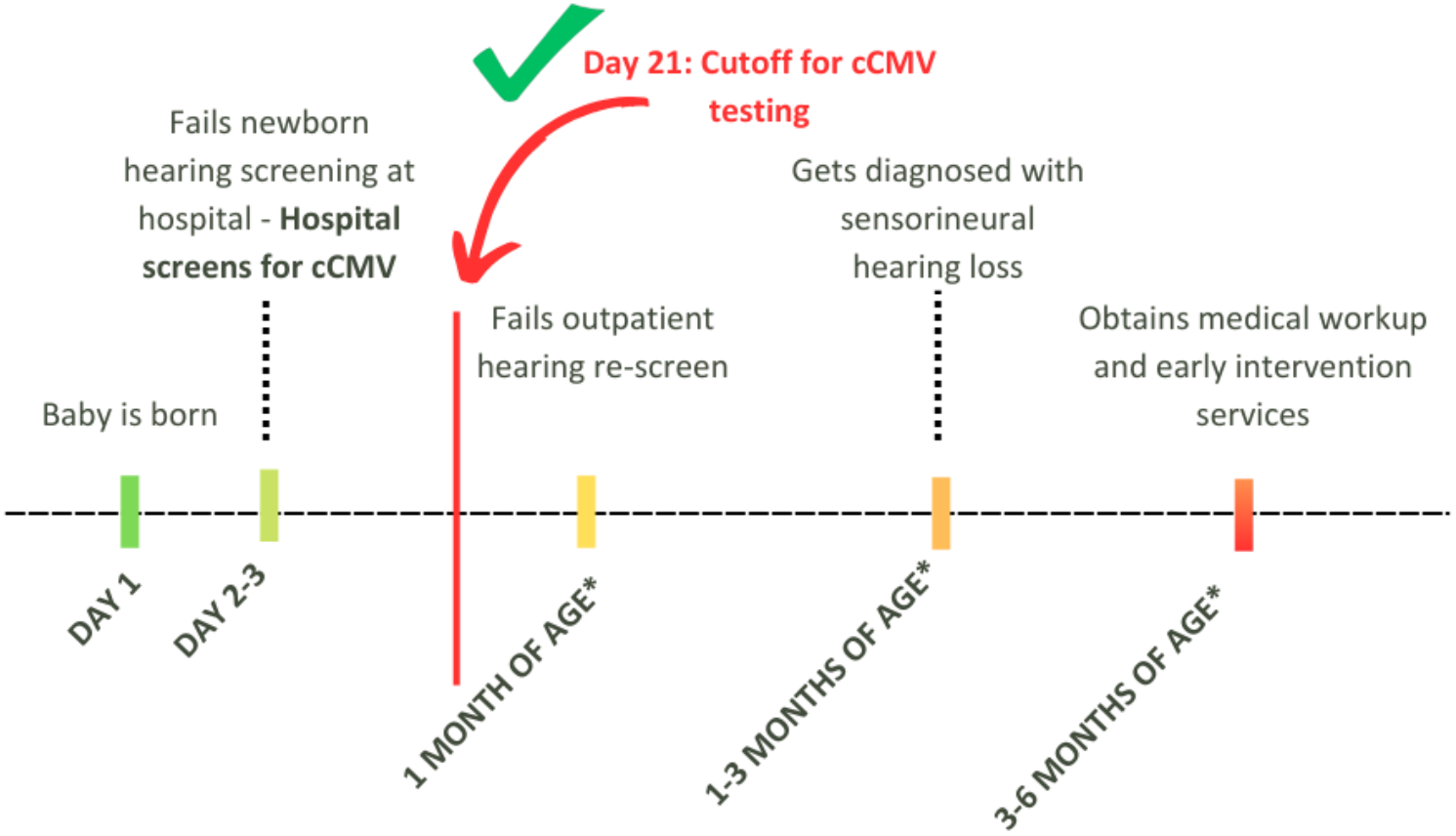
- Refer to infectious disease, ophthalmology, audiology
- Connect families to support resources
- Routine hearing, vision, and developmental surveillance
- Refer to Children 1st DPH for triage into Child Health programs

Newborn Hearing Testing Timeline – *No Targeted cCMV Screening Program*



* Indicates the Joint Committee on Infant Hearing (JCIH) Guidelines, but these tests can and should be completed earlier when feasible

Newborn Hearing Testing Timeline – *Targeted cCMV Screening Program*



* Indicates the Joint Committee on Infant Hearing (JCIH) Guidelines, but these tests can and should be completed earlier when feasible

Case Study #1

- Baby girl born at 39 weeks gestation
- Weighed 5 lbs 5 oz
- Inpatient newborn hearing screening:
  - Right Ear: Passed
  - Left Ear: Referred/Failed
- Hospital provided a list of providers to complete follow-up testing
- Mom scheduled a re-screen with Georgia Mobile Audiology

Case Study #1, Continued.

- Seen for re-screen at 5 days of age (turned into a diagnostic evaluation):
  - Right ear: Normal hearing
  - Left ear: Severe-to-profound sensorineural hearing loss
- Audiologist spoke with primary care physician regarding concern of cCMV
- Physician ordered urinalysis, showed positive cCMV result
- Referred to ophthalmology, otolaryngology, and infectious disease
- Established care with managing audiologist

Case Study #1, Audiological Considerations

- Communication options:
  - Auditory-Verbal
  - Visual (American Sign Language)
  - Total communication
- Amplification options:
  - Consideration of cochlear implant earlier due to risk of progression of “good ear”
- Hearing monitoring:
  - Test “good ear” every 3 months until age 3, annual until adolescence

Case Study #2 – CMV Diagnosis In Utero

- 28-year-old female
- Works in childcare
- Pregnant with first child
- Ultrasound at 20 weeks showed fetal anomalies (IUGR and microcephaly)
- Amniocentesis completed - positive for CMV

Case Study #2 Continued

- Infant born at 35 weeks gestation
- 4-week NICU stay
- Microcephaly, recessed jaw, feeding issues
- Passed hearing screening at hospital discharge
- Referred for diagnostic hearing evaluation due to cCMV

Case Study #3 – Hearing Surveillance

- September 2022:
  - Right Ear: Normal Auditory Brainstem Response (ABR) but absent Otoacoustic Emissions (OAEs) with normal tympanogram – concerning for progressive loss
  - Left Ear: Normal ABR and Present OAEs
- December 2022:
  - Right Ear: Mild conductive hearing loss; flat tympanogram
  - Left Ear: Normal hearing, present OAEs
- January 2023:
  - Right Ear: Normal hearing; absent OAEs; normal tympanogram
  - Left Ear: Normal hearing, present OAEs

Case Study #3 – Hearing Surveillance

- April 2023:
  - Right Ear: Mild to moderate sensorineural hearing loss
  - Left Ear: Normal hearing, present OAEs
- July 2023:
  - Right Ear: Moderate sensorineural hearing loss
  - Left Ear: Mild sensorineural hearing loss

Fit with bilateral hearing aids at 1 year of age, enrolled in GA PINES, Babies Can't Wait, and private auditory-verbal therapy

Resources

Maternal-Fetal Medicine Units Network cCMV Calculator - https://mfmunetwork.bsc.gwu.edu/web/mfmunetwork/cmv-calculator

National CMV Foundation - https://www.nationalcmv.org/

- Free resources to download or request shipped

Flowcharts referenced in this presentation, Pesch, et al 2021 - https://renaissance.stonybrookmedicine.edu/system/files/CMV.pdf

Questions

For more information, please contact:

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