Hearing outcomes in children aیٔected by congenital cytomegalovirus (cCMV) in Utah

Stephanie Browning McVicar, Au.D., M.S., CCC-A
Early Hearing Detection and Intervention (EHDI) programs manager

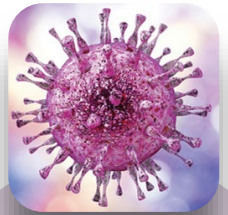
Utah Department of Health & Human Services

Learning objectives

- Describe the three cCMV surveillance case classifications
- Identify hearing outcomes by cCMV case severity
- Predict timing of hearing changes that can be seen with cCMV

Utah EHDI programs

Early Hearing Detection and Intervention (EHDI)



CMV public health initiative

Children's Hearing Aid Program (CHAP)

Utah EHDI Team

Stephanie B. McVicar, AuD
EHDI Programs Director
smcvicar@utah.gov

Krysta Badger, BS
Data Coordinator
kbehring@utah.gov

Ashleigh Sorenson, BA
UPC* Parent Consultant
ashleighsorenson@utah.gov

Aubri Ogden, BS
UPC* Parent Consultant
aubrianneogden@utah.gov

*Utah Parent Center

Shannon Wnek, AuD
Audiology &
Compliance Coordinator
swnek@utah.gov

Holley Ezzell, BA
Follow-up Coordinator
hezzell@utah.gov

Jenny Pedersen, AuD
CHAP Coordinator
jpedersen@utah.gov

Jacinda Merrill, MPH
CMV Epidemiologist
jamerrill@utah.gov

Max Sidesinger, MPH
CMV Data Coordinator
Epidemiologist
msidesinger@utah.gov

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What is cytomegalovirus (CMV)?

- **Cytomegalovirus is a very common virus of the *herpes* family** - Roughly 50% of Americans will be infected with it by child-bearing / middle age.
- A vast majority of cases are **asymptomatic** or result in **mild flu or mono like symptoms**.
- When a mother contracts CMV **during pregnancy** and passes it to her baby in utero, this is a case of **congenital cytomegalovirus (cCMV)**.

What is cytomegalovirus (CMV)?

- **1 in every 200** babies is born with cCMV in the US.
- cCMV is the most common infectious cause of birth defects
- **1 in 5** cCMV babies will have long-term health concerns such as **developmental disabilities,** vision loss, or **sensorineural hearing loss (SNHL)**.
- cCMV is the leading non-genetic cause of SNHL in children
    - About 25% of childhood hearing loss (HL) by age 4 years

26-10-10 UCA, “Cytomegalovirus (CMV) **Public Education** and Testing”

- **DHHS establish and conduct a public education program** to inform *pregnant women and women who may become pregnant* about CMV (incidence, transmission, birth defects, diagnostic methods, preventative measures)

26-10-10 UCA, “Cytomegalovirus (CMV) Public Education and **Testing**”

If a newborn infant fails the newborn hearing screening test(s)…

- **Medical Practitioner** shall: ***Test the newborn infant for CMV before 21 days of age***… unless the parent objects;

Utah CMV Rule

R398-4-3. Clarification of when a newborn fails a hearing screen.

- The newborn **must fail both hearing screens**, the initial hearing screen routinely done at birth **and** the subsequent follow up screen, **OR**
- **Initial failed hearing screen is obtained after 14 days of age**, OR
- **Follow-up screening isn't complete by 14 days of age**

Utah CMV Rule

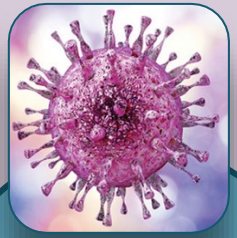
R398-4-4. Special populations of newborns.

- In special populations of newborns where newborn hearing screening(s) cannot be accomplished prior to 21 days of age, **testing for CMV is left to the discretion of the medical practitioner(s) caring for the newborn.**

- Special populations of newborns may include, but are not limited to, premature or medically fragile newborns or newborns receiving ongoing medical care.

Utah EHDI goals: T - 3 - 6Y

Screen
< 10 days of age



CMV testing
< 21 days of age

Diagnose
< 3 months of age

Early intervention
< 6 months of age

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Two-stage newborn hearing screening

1st stage

< 24-48 hours

Initial screening

PASS

FAIL

Medical home monitoring

2nd stage

< 10 DAYS

Rescreening

PASS

FAIL

Medical home monitoring

Schedule with Pediatric audiologist

Auditory Brainstem Response (ABR) testing

< 21 DAYS

LAB

CMV PCR testing

** **>2 hours** after feeding*

High-risk targeted CMV testing

- Intermountain Health birthing hospitals + 2 others adopted high-risk testing protocol in late 2019 (represent about half the birthing hospitals in Utah)

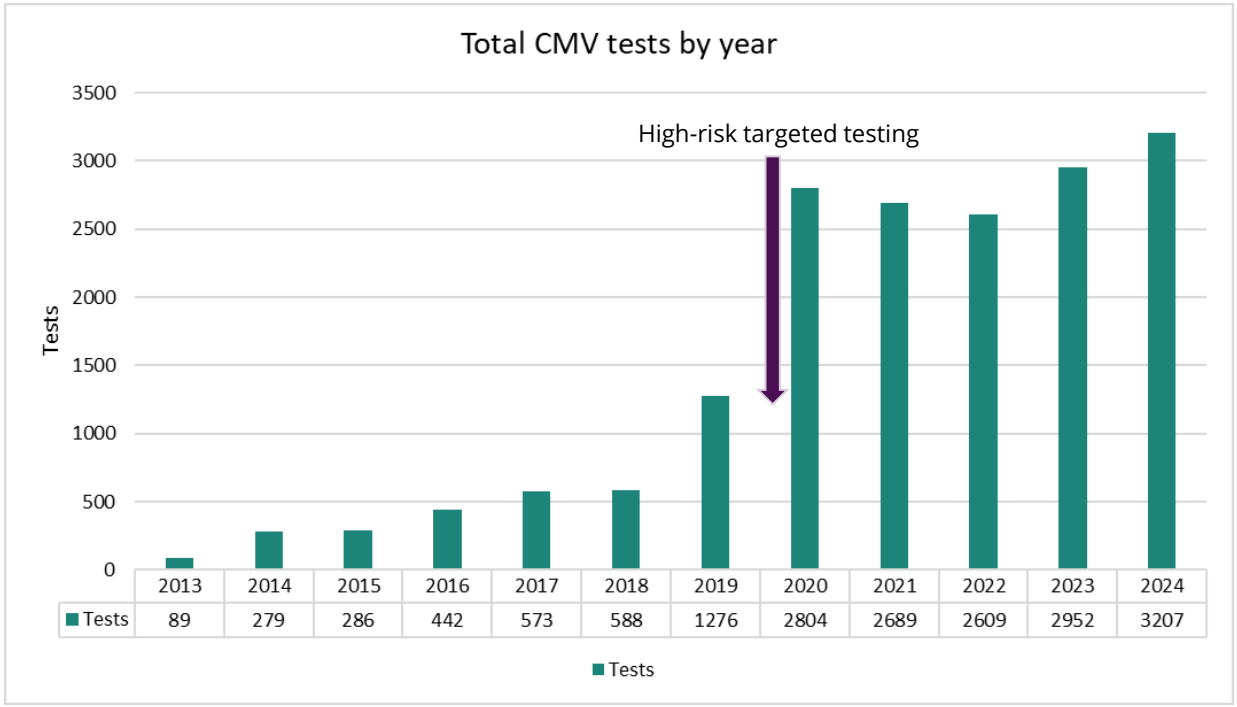
If any of the following present:

1) Mother positive for CMV infection during pregnancy
2) Abnormal head size (OFC <10th %ile OR >90th %ile at birth)
3) Intrauterine growth restriction (weight <10th %ile for gestational age)
4) Unexplained hydrops
5) Intracranial OR intraabdominal calcifications on first imaging exam
6) Unexplained hepatomegaly OR splenomegaly (>1 cm below the right or left costal margin)
7) AST or ALT >100 U/L OR unexplained direct bilirubin >1.0 mg/dL
8) Petechial rash or blueberry muffin rash at any time
9) Leukomalacia, polymicrogyria, lissencephaly, pachygyria, schizencephaly
10) Unexplained persistent thrombocytopenia (platelets < 100k/mm^3)
11) Failed hearing screen

Send urine CMV PCR

(obtain by 21 days of life when possible)

Increase in CMV testing in Utah over time



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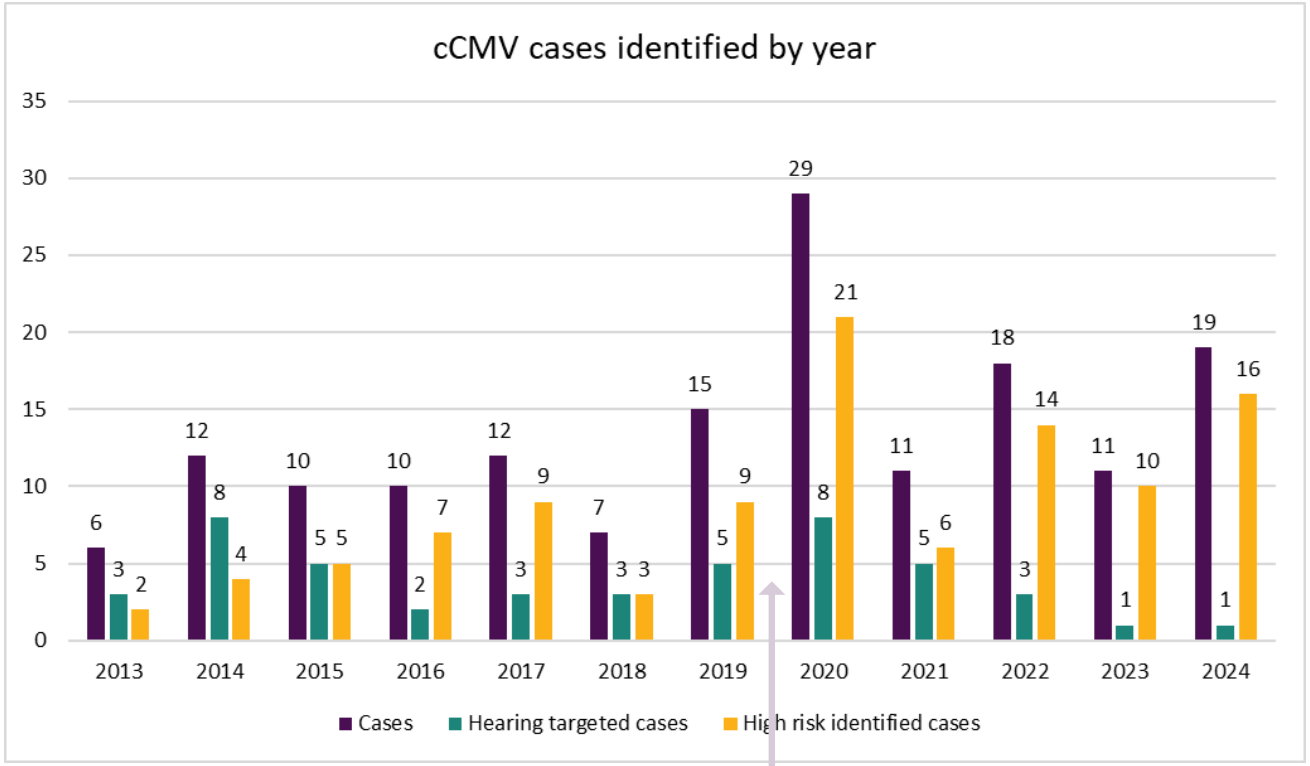
Confirmed cases

Note:
The difference in numbers are because of the small #s of "inpatient r/o" tests that aren't hearing or high risk targeted.



High-risk targeted testing

n=160

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- Confirmed cCMV infection
  - Confirmatory laboratory evidence **without** clinical evidence
- Confirmed cCMV disease
  - Confirmatory laboratory evidence **with** clinical evidence
- Probable cCMV disease
  - Presumptive laboratory evidence **with** clinical evidence

Laboratory results:

  - Urine, whole blood, CSF, DBS within 21 days are **confirmed**
  - 22-42 days are **presumptive**
  - Saliva at any point up to 42 days is presumptive

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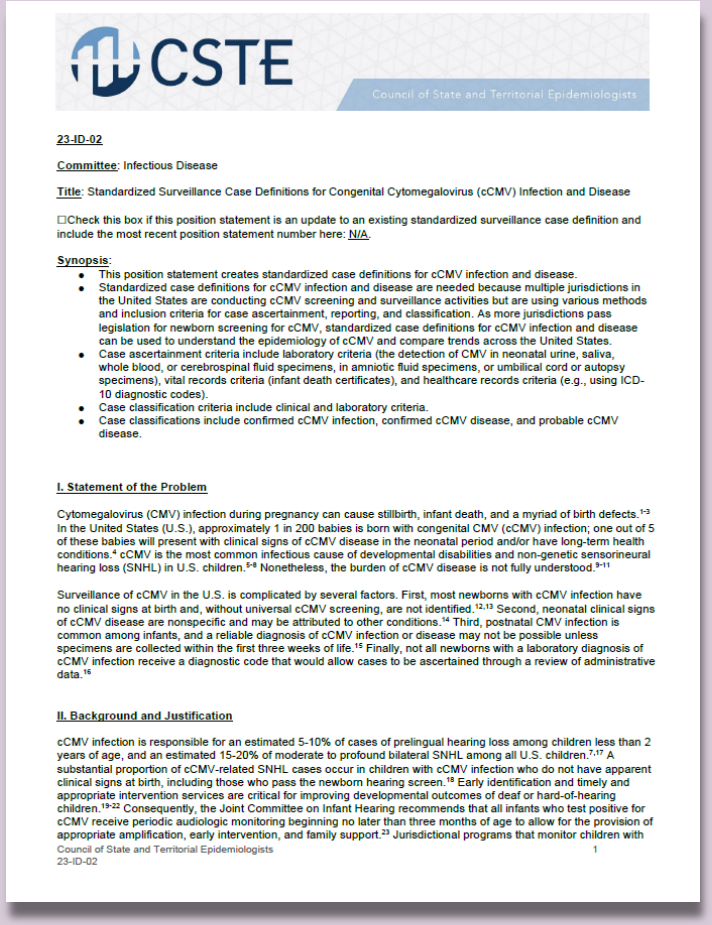

CSTE
Council of State and Territorial Epidemiologists

23-ID-02

Committee: Infectious Disease

Title: Standardized Surveillance Case Definitions for Congenital Cytomegalovirus (cCMV) Infection and Disease

☐Check this box if this position statement is an update to an existing standardized surveillance case definition and include the most recent position statement number here: N/A.

Synopsis:

- This position statement creates standardized case definitions for cCMV infection and disease.
- Standardized case definitions for cCMV infection and disease are needed because multiple jurisdictions in the United States are conducting cCMV screening and surveillance activities but are using various methods and inclusion criteria for case ascertainment, reporting, and classification. As more jurisdictions pass legislation for newborn screening for cCMV, standardized case definitions for cCMV infection and disease can be used to understand the epidemiology of cCMV and compare trends across the United States.
- Case ascertainment criteria include laboratory criteria (the detection of CMV in neonatal urine, saliva, whole blood, or cerebrospinal fluid specimens, in amniotic fluid specimens, or umbilical cord or autopsy specimens), vital records criteria (infant death certificates), and healthcare records criteria (e.g., using ICD-10 diagnostic codes).
- Case classification criteria include clinical and laboratory criteria.
- Case classifications include confirmed cCMV infection, confirmed cCMV disease, and probable cCMV disease.

I. Statement of the Problem

Cytomegalovirus (CMV) infection during pregnancy can cause stillbirth, infant death, and a myriad of birth defects.[1-3] In the United States (U.S.), approximately 1 in 200 babies is born with congenital CMV (cCMV) infection; one out of 5 of these babies will present with clinical signs of cCMV disease in the neonatal period and/or have long-term health conditions.[4] cCMV is the most common infectious cause of developmental disabilities and non-genetic sensorineural hearing loss (SNHL) in U.S. children.[5-8] Nonetheless, the burden of cCMV disease is not fully understood.[9-11]

Surveillance of cCMV in the U.S. is complicated by several factors. First, most newborns with cCMV infection have no clinical signs at birth and, without universal cCMV screening, are not identified.[12,13] Second, neonatal clinical signs of cCMV disease are nonspecific and may be attributed to other conditions.[14] Third, postnatal CMV infection is common among infants, and a reliable diagnosis of cCMV infection or disease may not be possible unless specimens are collected within the first three weeks of life.[15] Finally, not all newborns with a laboratory diagnosis of cCMV infection receive a diagnostic code that would allow cases to be ascertained through a review of administrative data.[16]

II. Background and Justification

cCMV infection is responsible for an estimated 5-10% of cases of prelingual hearing loss among children less than 2 years of age, and an estimated 15-20% of moderate to profound bilateral SNHL among all U.S. children.[7,17] A substantial proportion of cCMV-related SNHL cases occur in children with cCMV infection who do not have apparent clinical signs at birth, including those who pass the newborn hearing screen.[18] Early identification and timely and appropriate intervention services are critical for improving developmental outcomes of deaf or hard-of-hearing children.[19-22] Consequently, the Joint Committee on Infant Hearing recommends that all infants who test positive for cCMV receive periodic audiologic monitoring beginning no later than three months of age to allow for the provision of appropriate amplification, early intervention, and family support.[23] Jurisdictional programs that monitor children with

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23-ID-02

Standardized Surveillance Case Definition for cCMV Infection and Disease (2023)

Clinical criteria

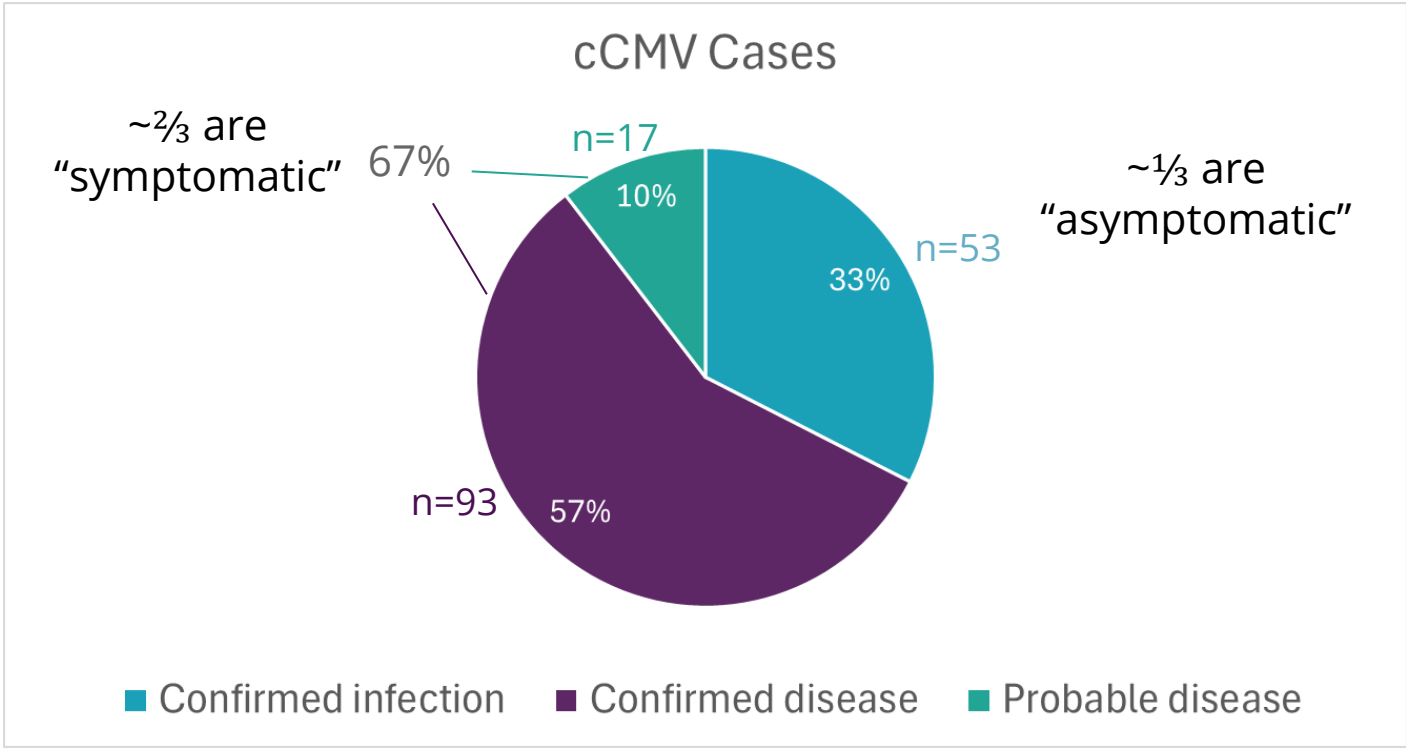
In the absence of a more likely alternative etiology:

- An infant with at least one of the following clinical signs during the neonatal period:[28,29]
  - Hepatomegaly
  - Splenomegaly
  - Petechial rash or purpura ("blueberry muffin rash"),

OR

- A child aged 6 years or younger with one or more of the following permanent conditions:[28,29,30]
  - Microcephaly (defined as head circumference measurement >2 standard deviations below the average (or <3rd percentile) for the same age and sex, notation in the medical record, or diagnostic code of microcephaly (e.g., ICD-10 code Q02),
  - Brain imaging abnormalities consistent with cCMV, such as intracranial calcifications, periventricular calcifications, leukomalacia, polymicrogyria, lissencephaly, pachygyria, schizencephaly, or ventriculomegaly
  - Sensorineural hearing loss
  - Seizures
  - Cerebral palsy
  - Chorioretinitis
  - Vision impairment, resulting from conditions consistent with cCMV, such as retinitis, retinal scarring, optic neuritis, optic atrophy, or brain damage resulting in cortical vision impairment

Case classi cations: July 2013-June 2025



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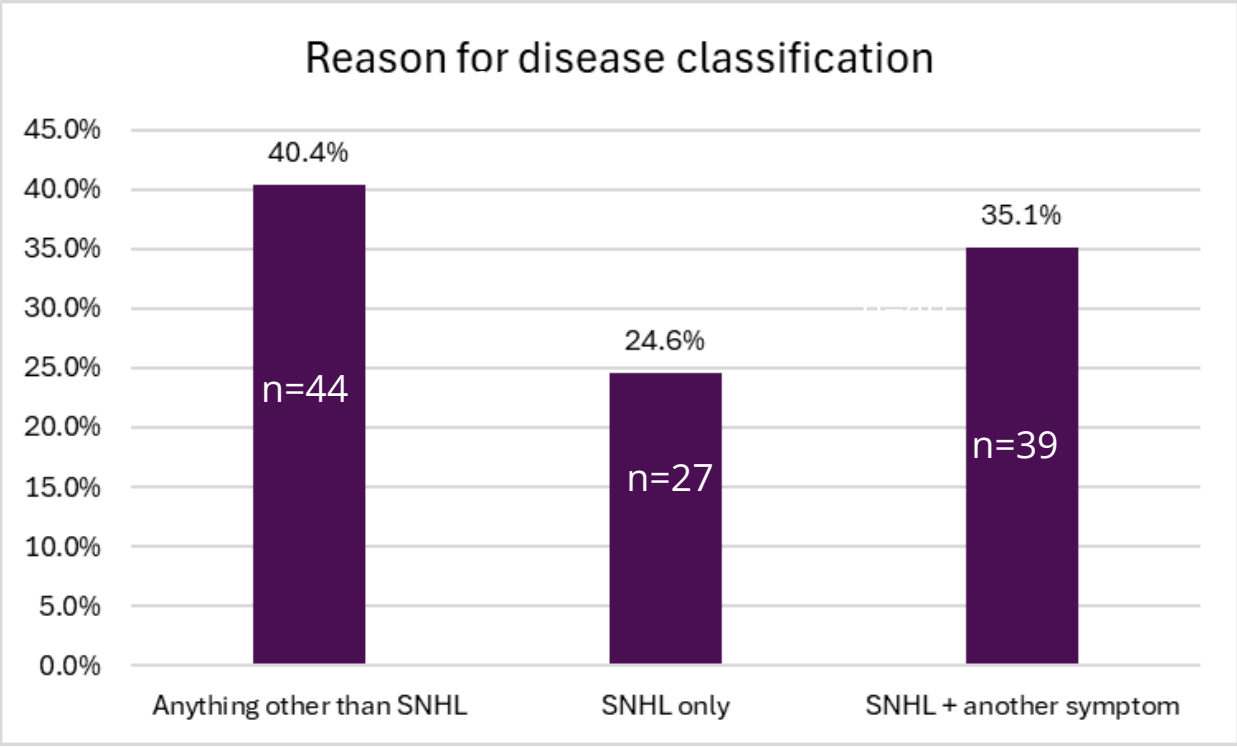
n=163

cCMV and hearing loss (HL)

- Can be delayed in onset
- Can progress
- Can fluctuate
- “Symptomatic” (Sx) cCMV typically affected earlier, more often, more severely
- Vos et al review *(Ear Hear. 2021 Nov-Dec;42(6):1447-1461)*
  - >33% in Sx cCMV
  - <15% in Asymptomatic (Asx) cCMV
- Sx: ~ 33-65% develop SNHL
- Asx: ~ 7-15% develop SNHL

- *PubMed (2021) - "Cytomegalovirus-A Risk Factor for Childhood Hearing Loss: A Systematic Review"*
- *PMC (2022) - "A Review of Sensorineural Hearing Loss in Congenital Cytomegalovirus"*
- *PMC (2023) - "Congenital Cytomegalovirus and Hearing Loss: The State of the Art"*
- *PubMed (2014) - "Hearing loss and congenital CMV infection: a systematic review"*

Case classi cations: July 2013-June 2025



n=110

Overall cases:

~⅓ are “asymptomatic”
~⅔ are “symptomatic”

~ 33% are “asymptomatic”
~ 16.5% have “isolated SNHL”
~ 24% have SNHL +
~ 27% are affected but w/o SNHL

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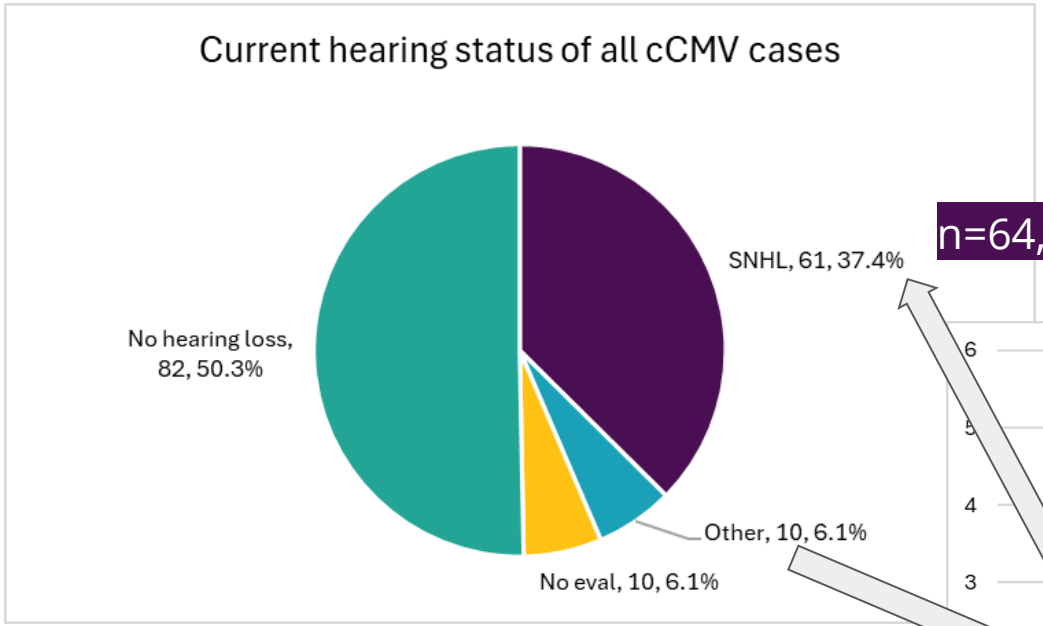
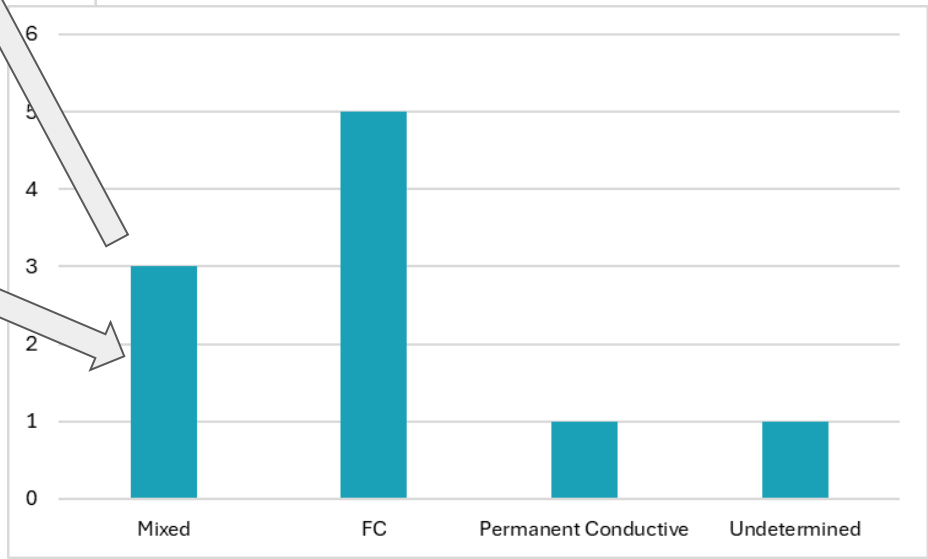
cCMV and hearing loss



39% of all of our cases have SNHL!!

n=64, 39.3%



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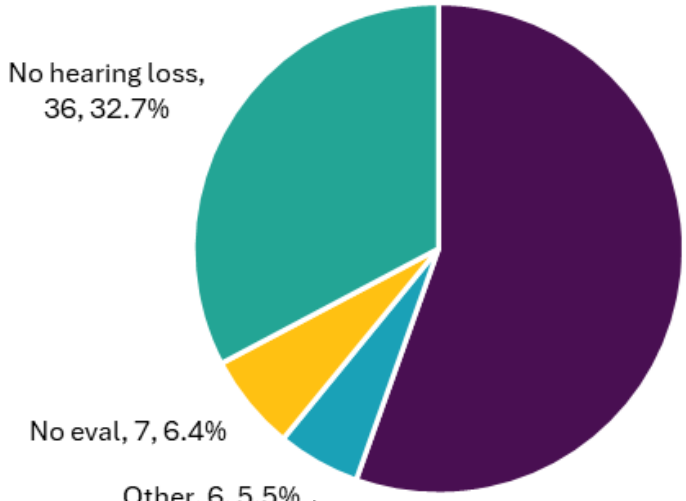
FC=fluctuating conductive

cCMV and hearing loss

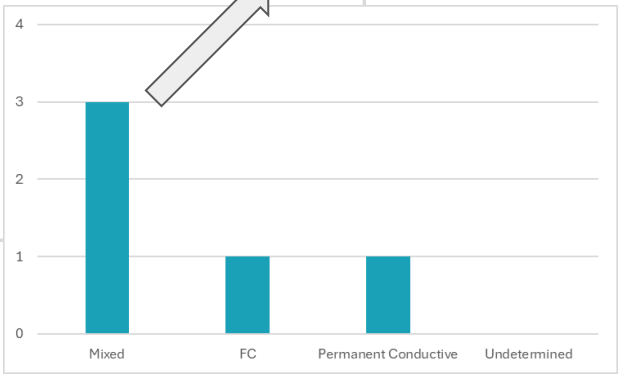
Current hearing status of cCMV disease cases

n=110

- 93 confirmed disease
- 17 probable disease



n=64, 58.2%



58% of our disease cases have SNHL!!

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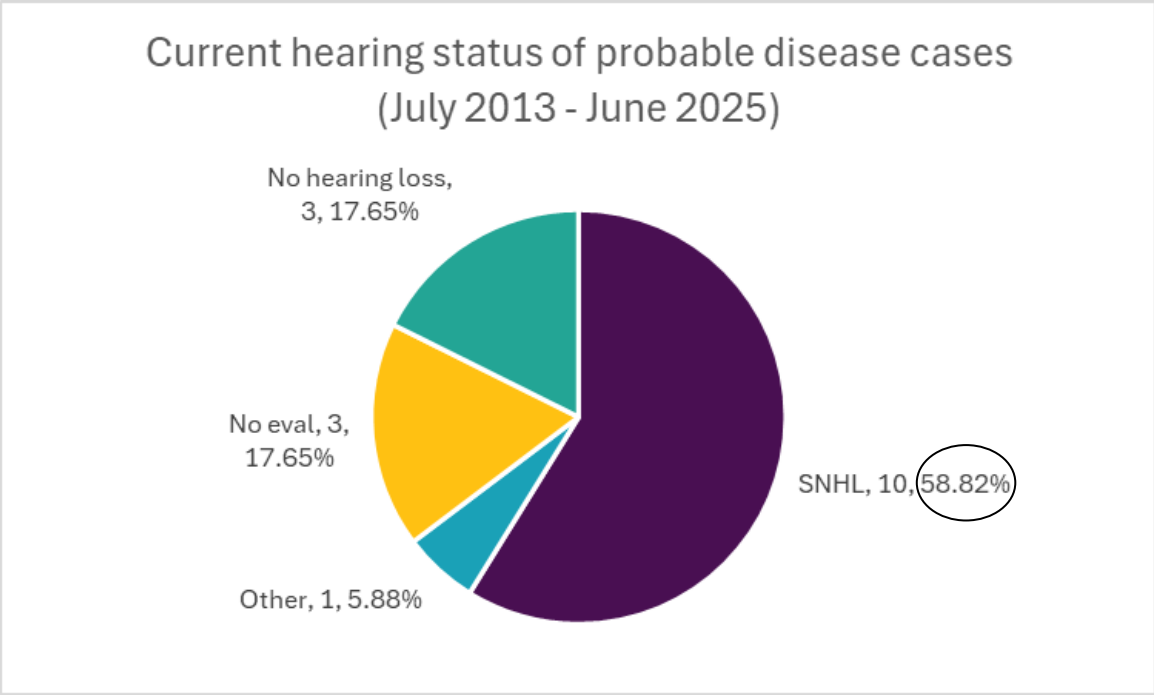
cCMV and hearing loss



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Audiological follow-up for cCMV

Regular and long-term monitoring is KEY.

Every 3 months for the first 3 years of life then every 6 months up to 6 years; annually thereafter. Always sooner if concerns or changes are noted.

Hearing loss onset

Average age of onset of all cases with SNHL (64 cases) = **6.62 months**

- Min: 0.10 months, Max: 54 months

Average age of onset of all **confirmed disease** cases with SNHL (54 cases) = **7.6 months**

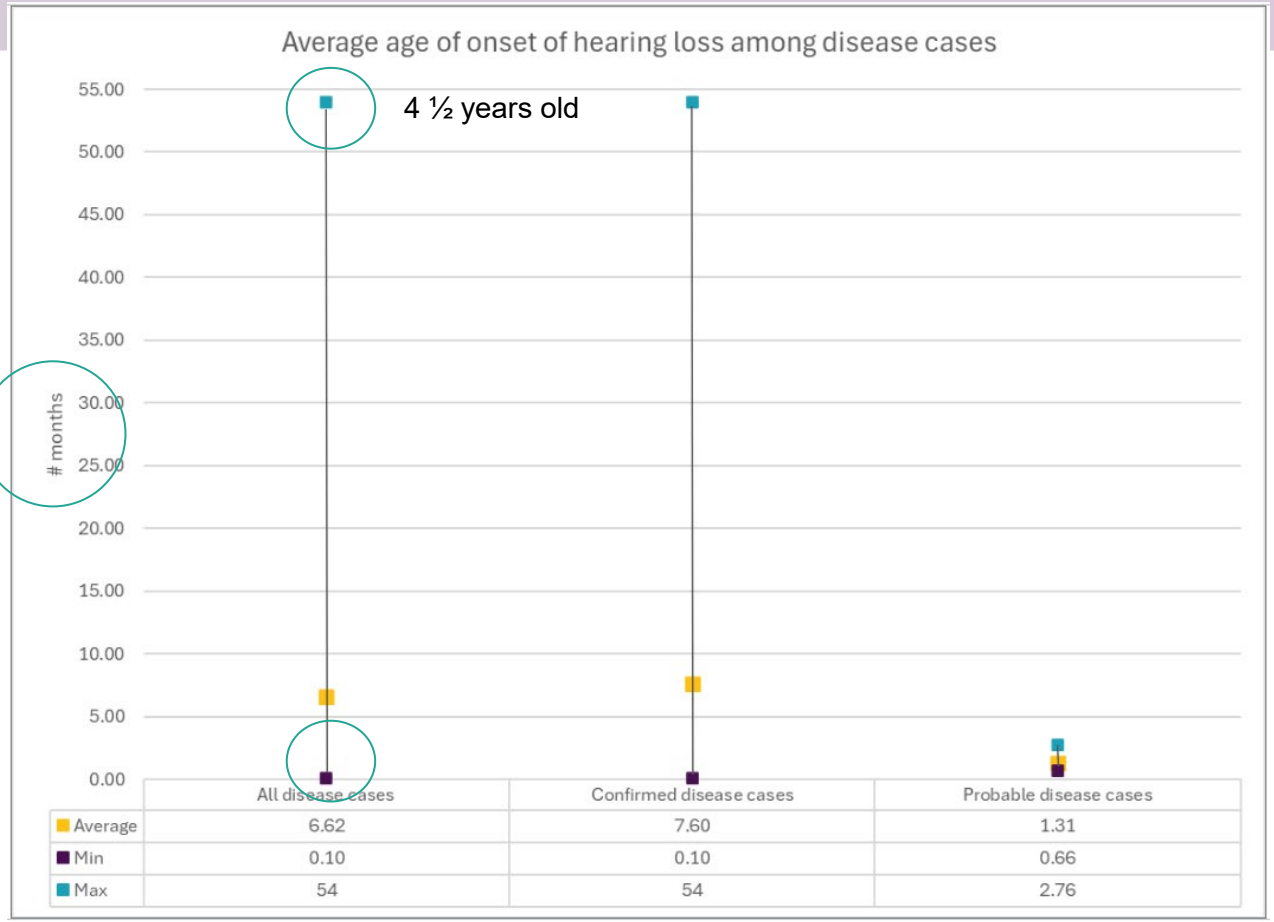
- Min: 0.10 months, Max: 54 months

Average age of onset of all **probable disease** cases with SNHL (10 cases) = **1.31 months**

- Min: 0.66 months, Max: 2.76 months

*Age of onset was calculated by date of first Dx Auditory Brainstem Response (ABR) showing signs of HL

Hearing loss onset



	All disease cases	Confirmed disease cases	Probable disease cases
Average	6.62	7.60	1.31
Min	0.10	0.10	0.66
Max	54	54	2.76

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Hearing loss onset among cases with classification changes

Average age of onset of disease cases with **no symptoms at birth** (could be classified as infection at birth but are now disease) = **31.43 months**

- N=**9**, Min: **8 months**, Max: **54 months**

15% "asx" developed SNHL

Average age of onset of disease cases with **symptoms at birth but no hearing loss present at first DxABR** (classified as disease at birth because of other symptoms, but had late onset hearing loss) = **18.82 months**

- N= **5**, Min: **4 months**, Max: **24 months**

*Age of onset was calculated by date of first Dx audiology eval showing signs of HL

This is why continued monitoring is important!!

Hearing loss progression (Note: 7/1/13-6/30/23)

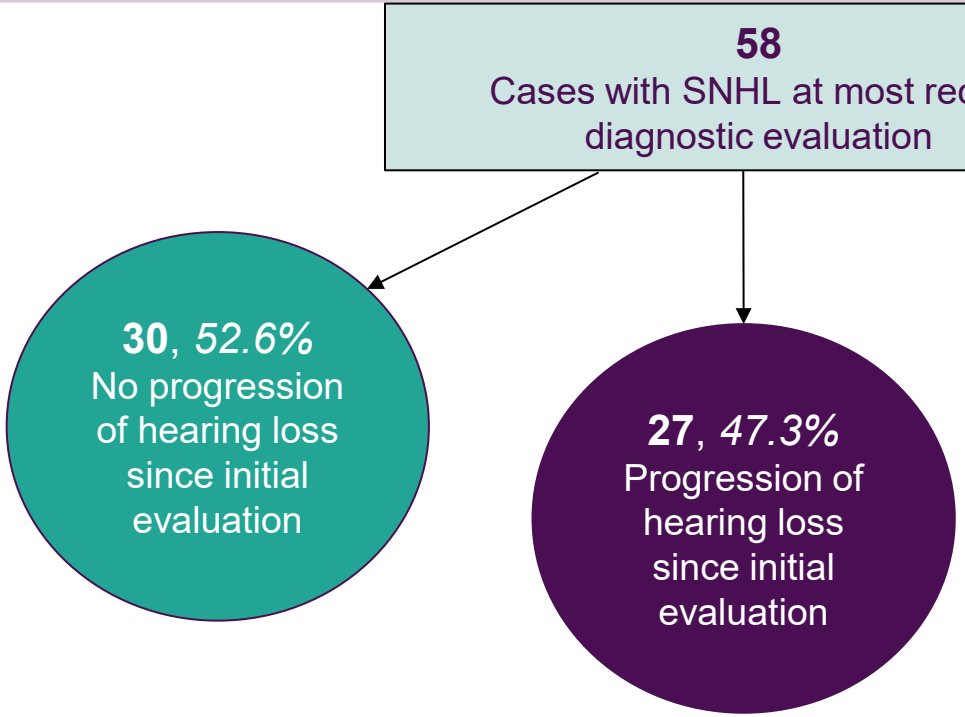

Table represents degree of loss in poorer hearing ear

Severity	Initial evaluation	Most recent evaluation
No loss	10	0
Mild	4	1
Moderate	5	7
Severe	7	4
Profound	1	15

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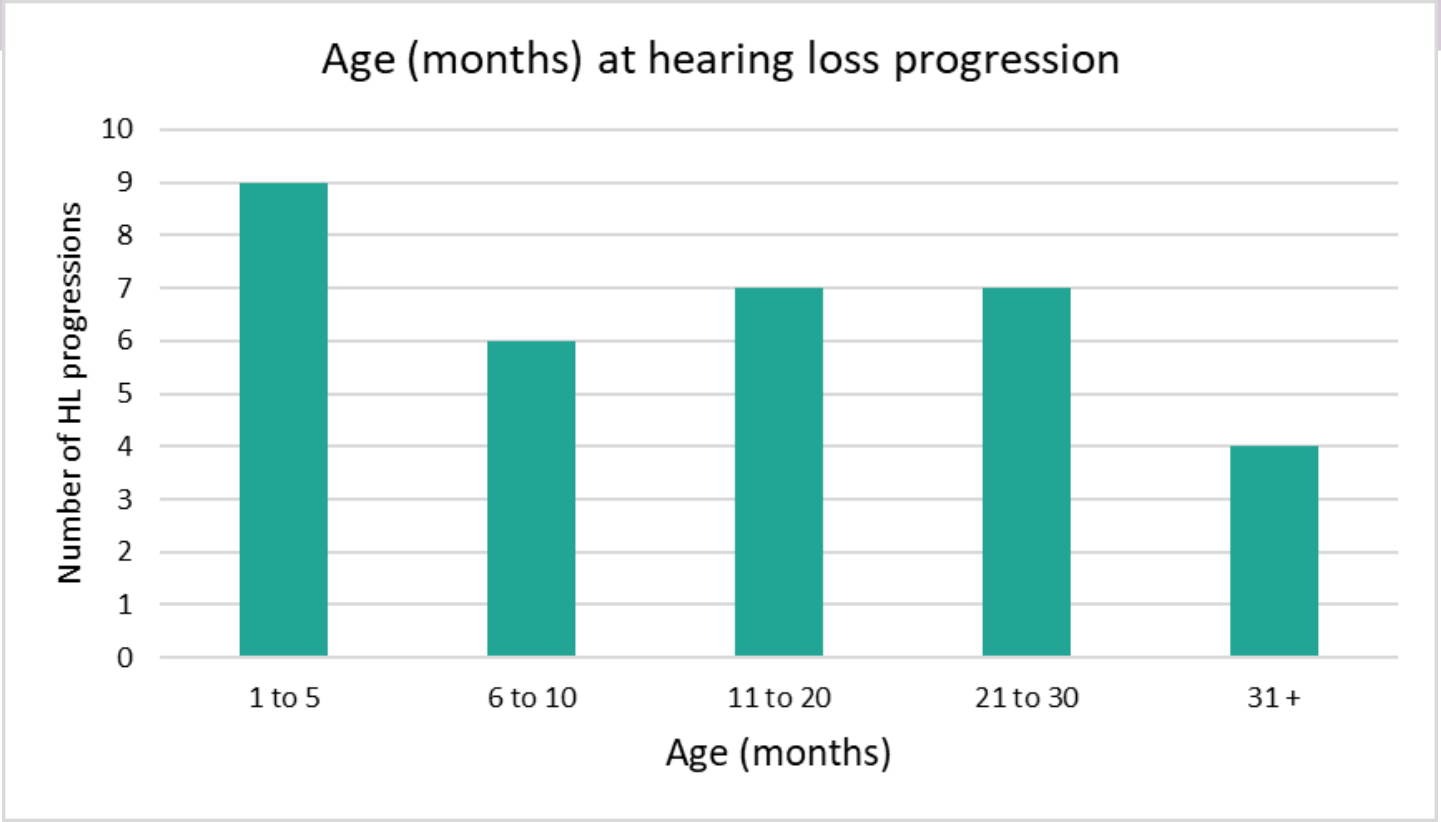
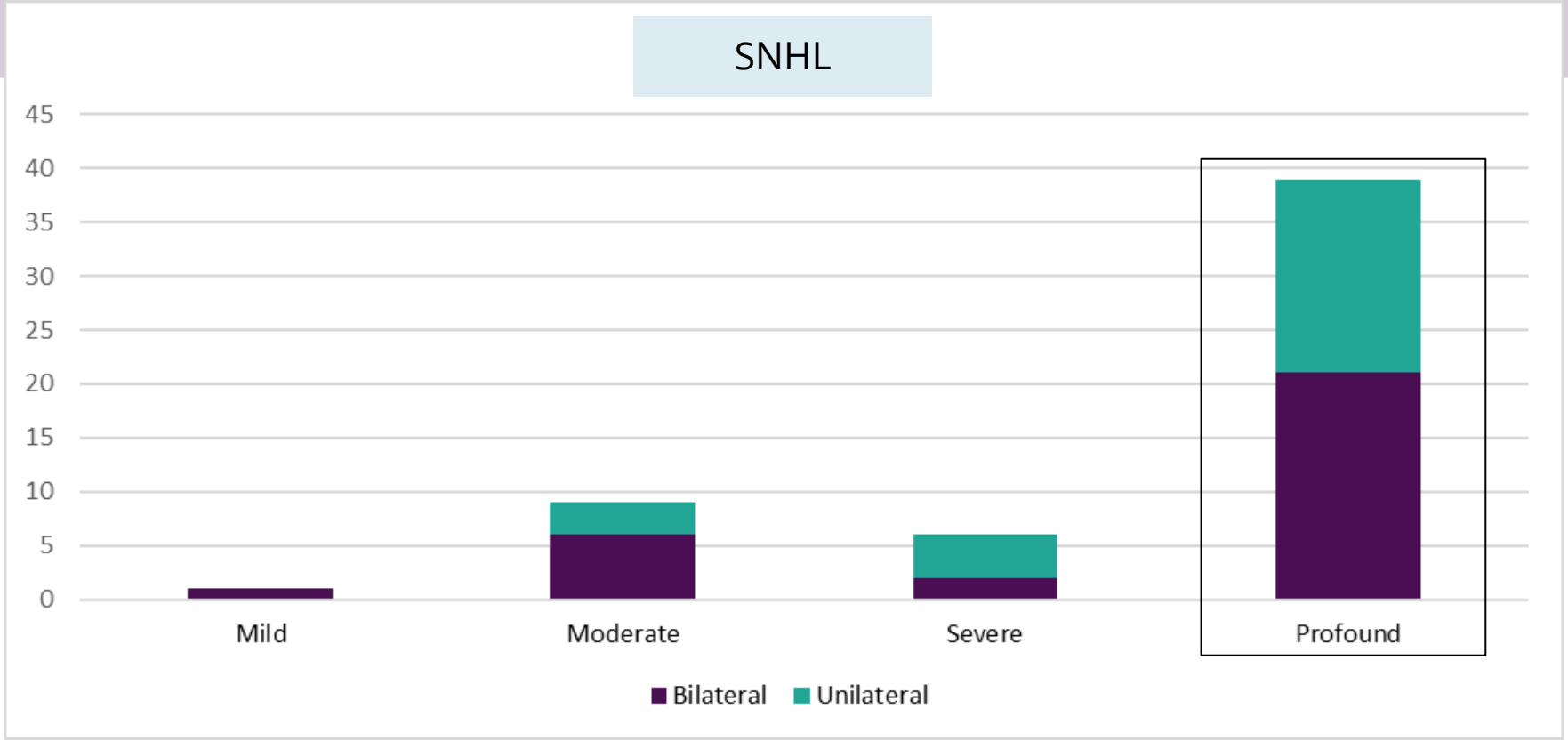
Hearing loss progression (Note: 7/1/13-6/30/23)



Hearing loss severity and laterality



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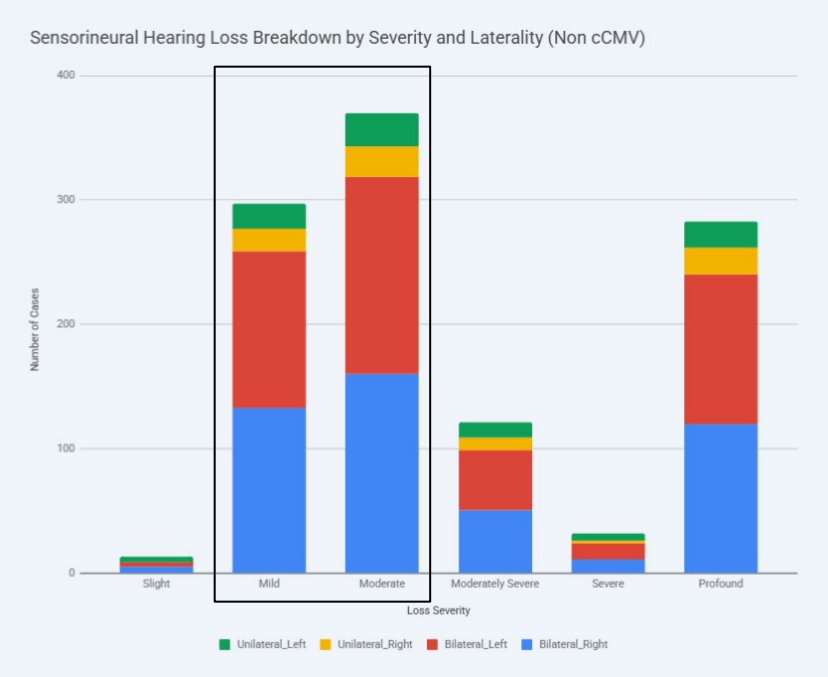
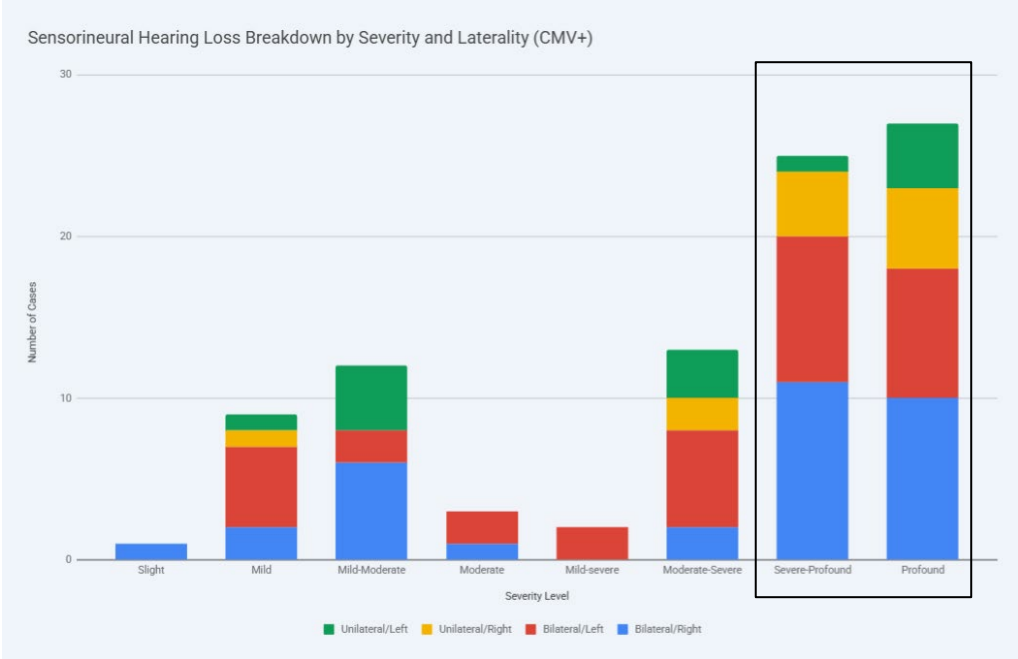
17.5% of unilateral losses became bilateral

Hearing loss severity (7/1/2013 - 6/30/25)



Non-cCMV SNHL



All cCMV SNHL

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Infection cases that became disease cases

Example of 10 cases:

1. No apparent signs at birth, passed NBHS - later identified via dried blood spot (DBS) (no SNHL, but has cerebral palsy (CP))

2-7. Six cases passed NBHS, no apparent signs at birth - later identified via DBS (all have SNHL, and one also has CP)

8-9. Both failed NBHS, had normal initial Dx ABR, then later developed SNHL (one identified by urine <21 days, the other by DBS)

10. Failed NBHS, had normal initial Dx ABR. Brain imaging in late infancy was abnormal. DBS came back positive (now has SNHL and CP)

Infection cases that became disease cases

Case 2:

- Passed inpatient NBHS
- Later referred to audiology by early intervention due to motor skills and speech delay
- Evaluation at 18 months found moderate to severe SNHL in one ear and mild to moderately-severe SNHL in the other
- DBS was tested and positive for cCMV

Infection cases that became disease cases

Case 3:

- Passed NBHS
- Sudden SNHL in one ear at age 4 yrs. Received cochlear implant; other ear still hearing well
- DBS was tested and positive for cCMV

Infection cases that became disease cases

Case 4:

- Passed NBHS
- Evaluated at 39 months for suspected hearing loss: Unilateral severe/profound SNHL
- DBS was tested and positive for cCMV

Infection cases that became disease cases

Case 5:

- Passed NBHS
- Diagnosed with unilateral SNHL at age 2 years
- DBS was tested and positive for cCMV
- Vestibular testing at 2 ½ yrs found bilateral loss of vestibular function
- Diagnosed with CP and developmental delays

Infection cases that became disease cases

Case 6:

- Passed NBHS
- Referred for ABR at 23 months d/t speech and developmental delays, lack of response to sounds at home
- Bilateral profound SNHL; received cochlear implants at 30 months
- DBS was tested after ABR and cCMV positive

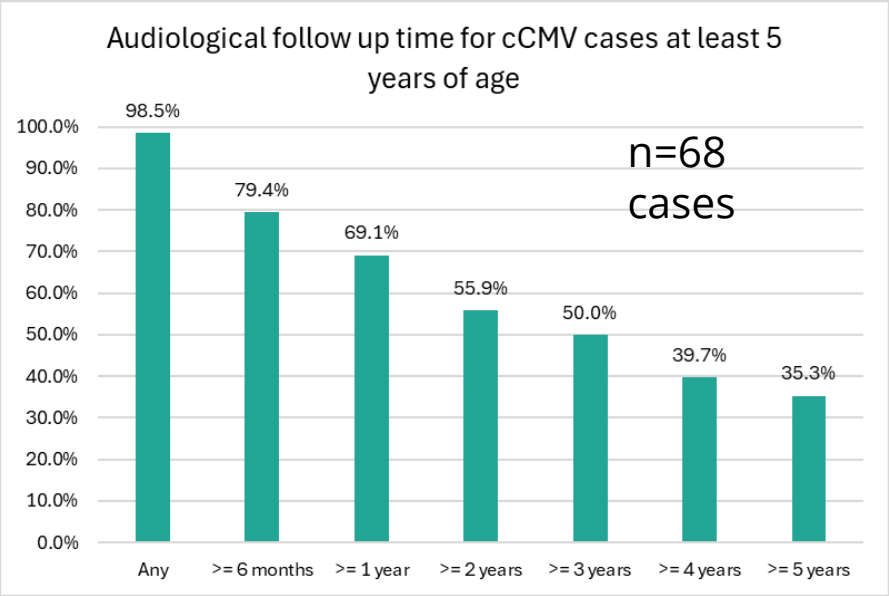
Audiological follow-up for cCMV

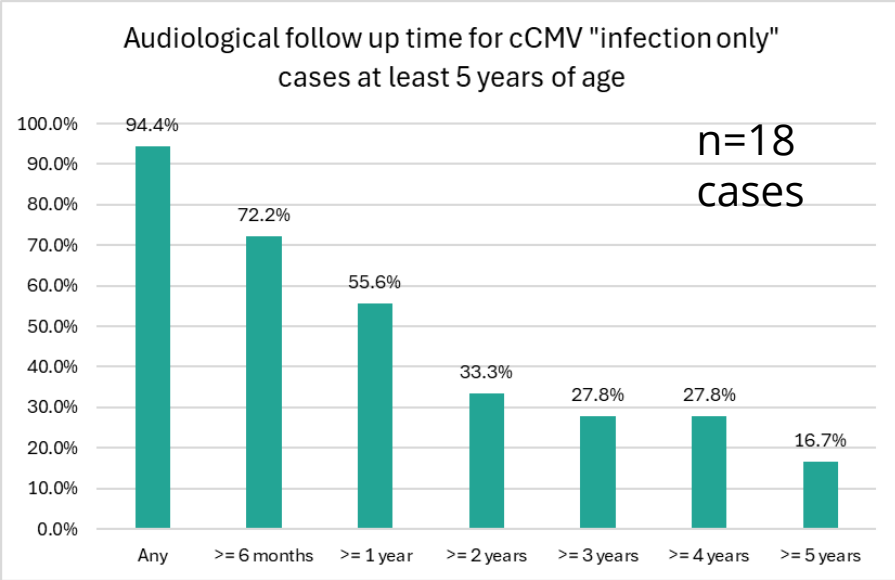
Regular and long-term monitoring is KEY.

Every 3 months for the first 3 years of life then every 6 months up to 6 years; annually thereafter. Always sooner PRN - if concerns or changes are noted.

Audiological follow up - TIME

(7/1/13-12/31/19)





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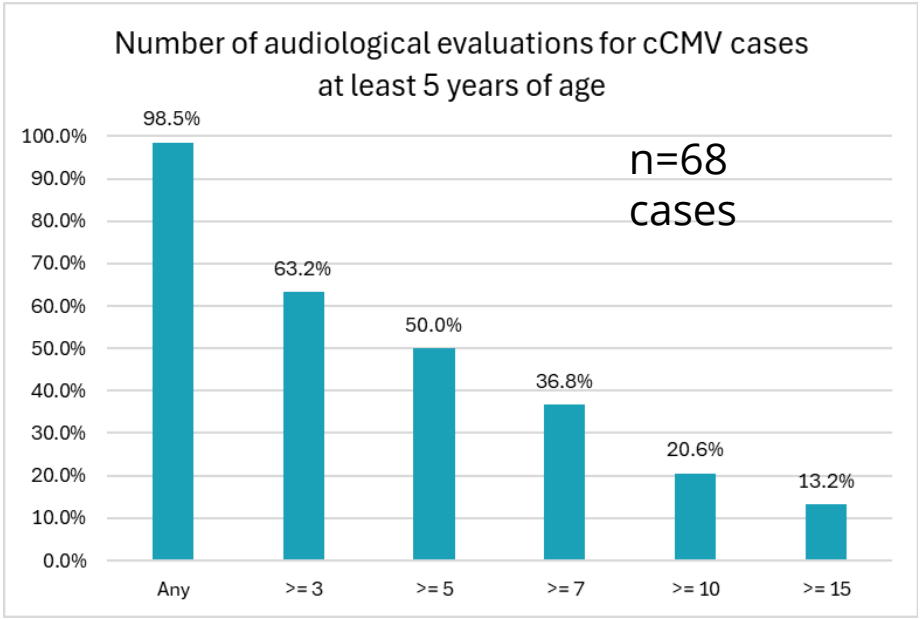
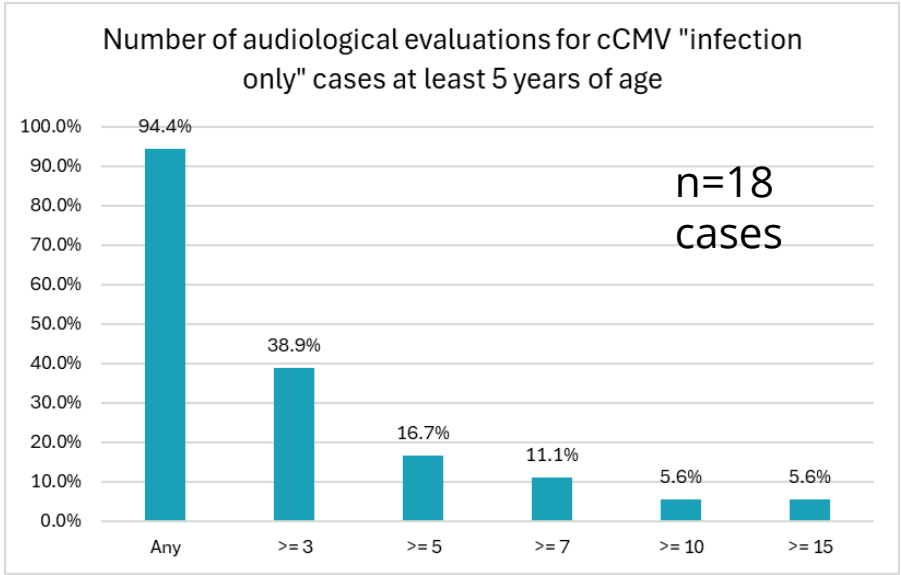
Audiological follow up - NUMBER

(7/1/13-12/31/19)



Recommendation is 16 evaluations in first 5 yrs



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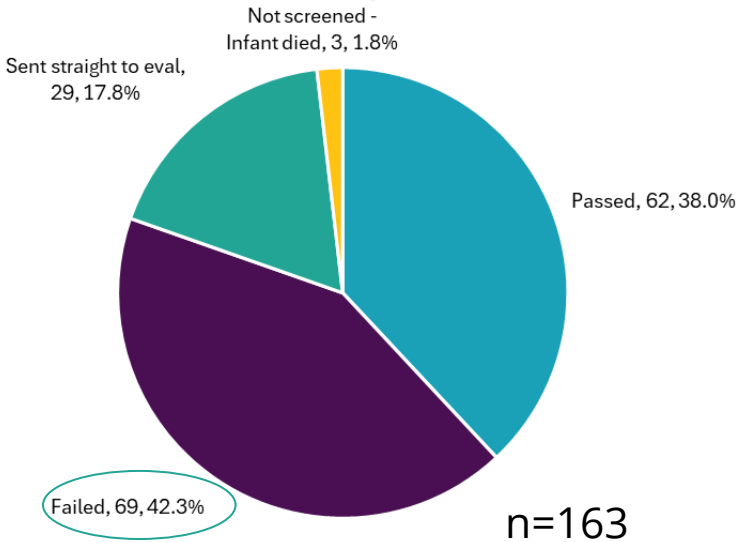
Newborn hearing screening (NBHS) Note: 7/1/13 - 6/30/25



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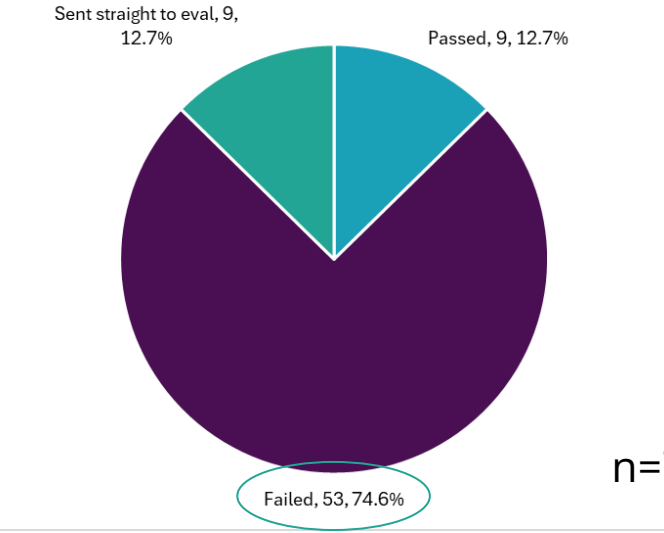
Overall UT births NBHS failure (most conclusive result) = 1%



n=71

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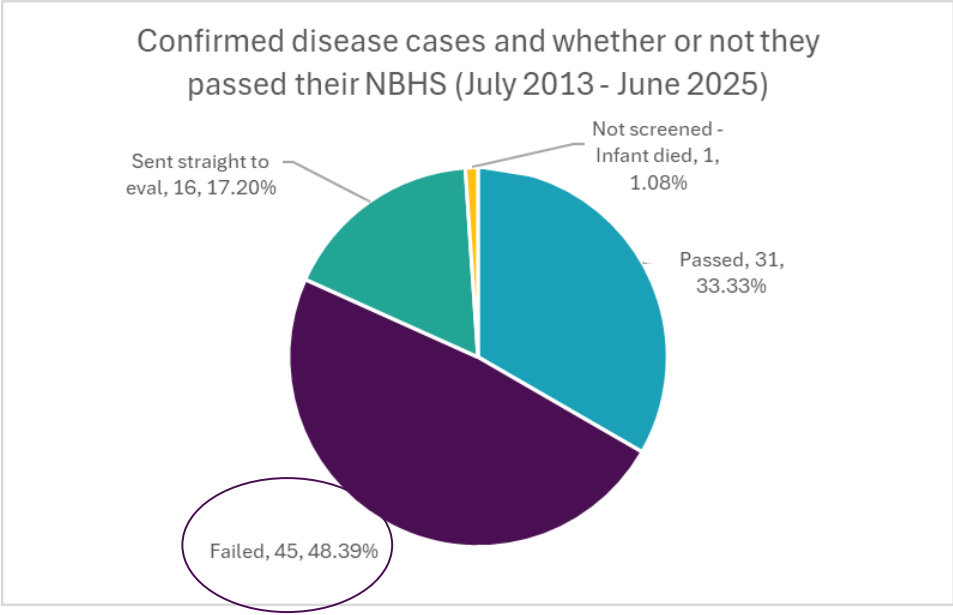
Newborn hearing screening (NBHS) by classification



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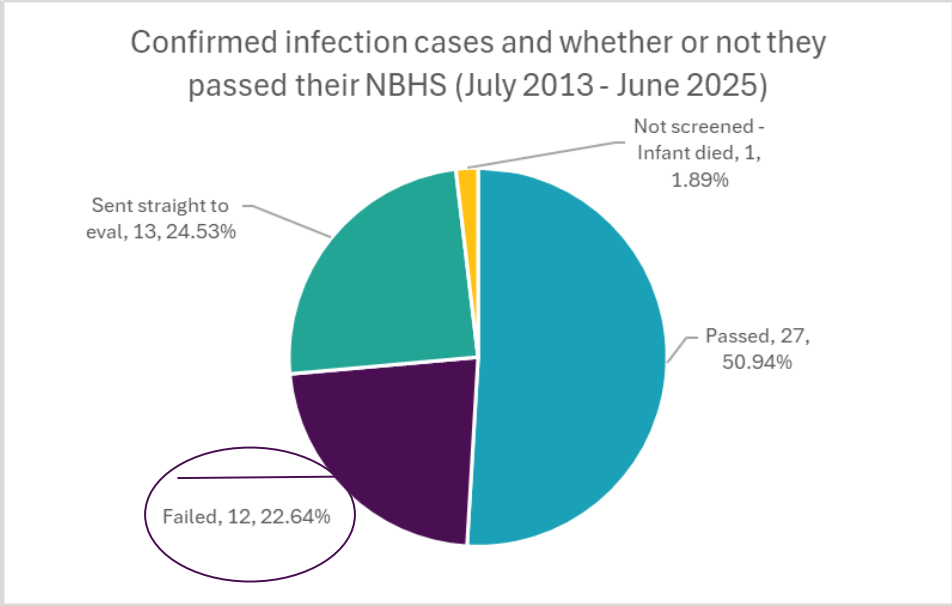

n=53

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Takeaways

- If a child has cCMV, there is ~39% chance they'll have hearing loss
- Those with clinical signs have a high likelihood of SNHL
- Regular audiology follow-up is **essential** due to the late onset and/or progressive nature of cCMV-induced hearing loss
- Almost 1/5th of unilateral hearing losses became bilateral
- Hearing changes occur throughout infancy and early childhood
- Newborns with cCMV have a much greater risk of failing NBHS than the general population
- Testing stored DBS useful in confirming cCMV in late-onset sequelae

Thank you!

smcvicar@utah.gov
cmv@utah.gov
ehdi@utah.gov
chap@utah.gov

Krysta Badger, BS
EHDI Data Coordinator

Max Sidesinger, MS
EHDI Epidemiologist
CMV Data Coordinator

Jacinda Merrill, MPH
CMV Epidemiologist

cCMV surveillance position statement

Utah Department of Health & Human Services
Family Health