An overview of the CSTE cCMV position statement's impact on Utah's case classification

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Utah Department of Health & Human Services

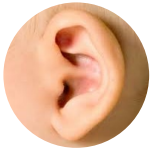
Learning objectives

1. Describe how Utah's cCMV case classification has changed since participating in the CSTE cCMV case definition process.

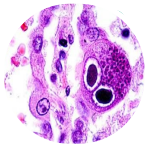
2. Provide a breakdown of how Utah's cases align with the new CSTE cCMV position statement.

3. Compare CMV disease/infection vs. CMV symptomatic/ asymptomatic case classifications.

Overview: Utah EHDI programs



Early Hearing Detection and Intervention (EHDI)



Congenital Cytomegalovirus (CMV) Public Health Initiative

Children’s Hearing Aid Program (CHAP)

Utah's CMV screening

- Hearing targeted

- High-risk targeted

Hearing targeted

Utah CMV legislation

- 26-10-10 UCA, “Cytomegalovirus (CMV) Public Education and Testing” (Into effect 7/1/2013)
  - If a newborn **fails the newborn hearing screening test(s)**... Medical practitioner shall test the infant for **CMV before 21 days of age**

- R398-4, “Cytomegalovirus Public Health Initiative”
  - CMV testing if... infant fails **both** initial and follow-up hearing screen
  - Or, initial screen is failed after **14 days** of age
  - Practitioners must report results to DHHS within **10 days** of receiving them

- R386-702, “Communicable Disease Rule” (Into effect in 2015)
  - **All laboratory results** for... CMV in infants less than or equal to **12 months of age**

High-risk targeted

- Intermountain Health birthing hospitals adopted high-risk testing protocol in 2019

If any of the following present:

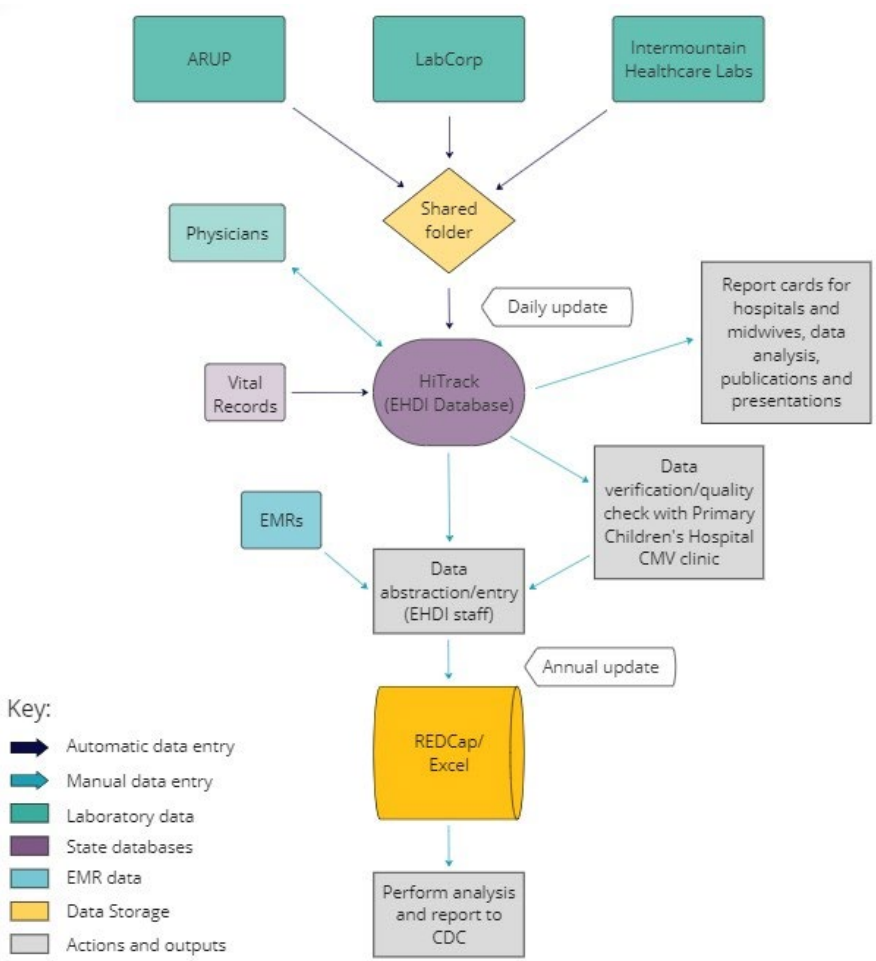
1) Mother positive for CMV infection during pregnancy
2) Abnormal head size (OFC <10th %ile OR >90th %ile at birth)
3) Intrauterine growth restriction (weight <10th %ile for gestational age)
4) Unexplained hydrops
5) Intracranial OR intraabdominal calcifications on first imaging exam
6) Unexplained hepatomegaly 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

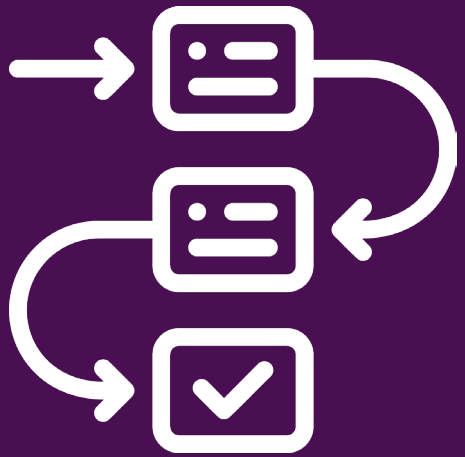
(obtain by 21 days of life when possible)

cCMV cases

Case ascertainment/ abstraction process



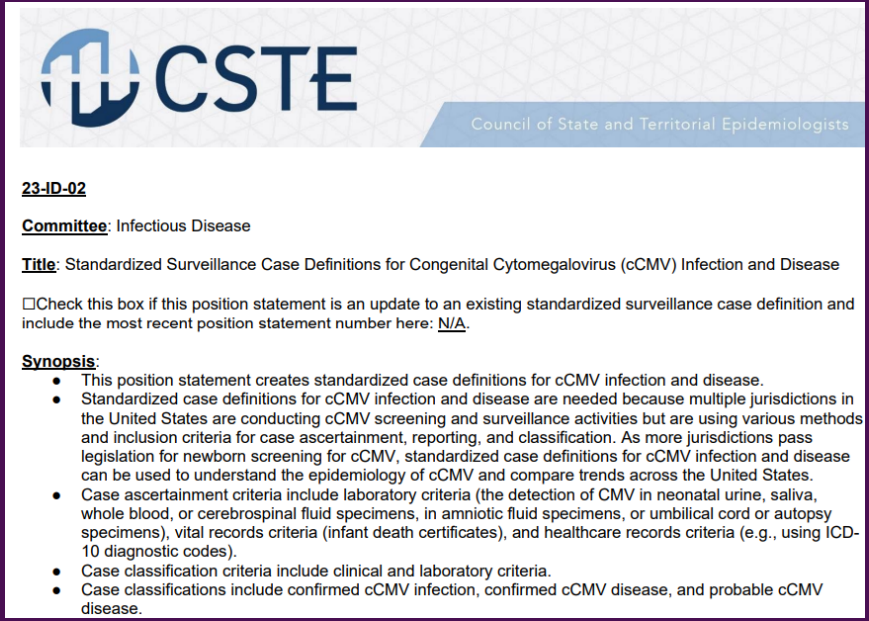
Changes in classification



Previous classification

- Confirmed congenital infection
  - Confirmatory test **within** 21 days
- Probable infection (symptomatic)
  - Confirmatory test **after** 21 days with clinical symptoms of disease
- Suspect infection (asymptomatic)
  - Confirmatory test **after** 21 days without clinical symptoms of disease

CSTE position statement



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.

- Establish standardized classifications for surveillance purposes
- Worked together with authors and Subject Matter Experts
- Passed June 2023

CSTE cCMV classification

- Confirmed congenital infection
  - Confirmatory test **within** 21 days
- Probable infection (symptomatic)
  - Confirmatory test **after** 21 days with clinical symptoms of disease
- Suspect infection (asymptomatic)
  - Confirmatory test **after** 21 days without clinical symptoms of disease
- 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

Comparing classifications

Comparing classifications

- Clinical evidence in new classification is more specific to cCMV

Evidence in previous vs. CSTE classification

Symptoms:

- Hepatomegaly
- Splenomegaly
- Microcephaly
- Brain imaging abnormalities
- Petechiae
- Sensorineural hearing loss
- Seizures
- Cerebral palsy
- Chorioretinitis
- Vision impairment
- SGA/IUGR
- Unexplained persistent thrombocytopenia
- Unexplained hyperbilirubinemia
- Hydrops

Clinical evidence:

- Hepatomegaly
- Splenomegaly
- Microcephaly
- Brain imaging abnormalities
- Petechiae
- Sensorineural hearing loss
- Seizures
- Cerebral palsy
- Chorioretinitis
- Vision impairment

Comparing classifications

- Clinical evidence in new classification is more specific to cCMV

- Clarification on testing time frame

Old classification:

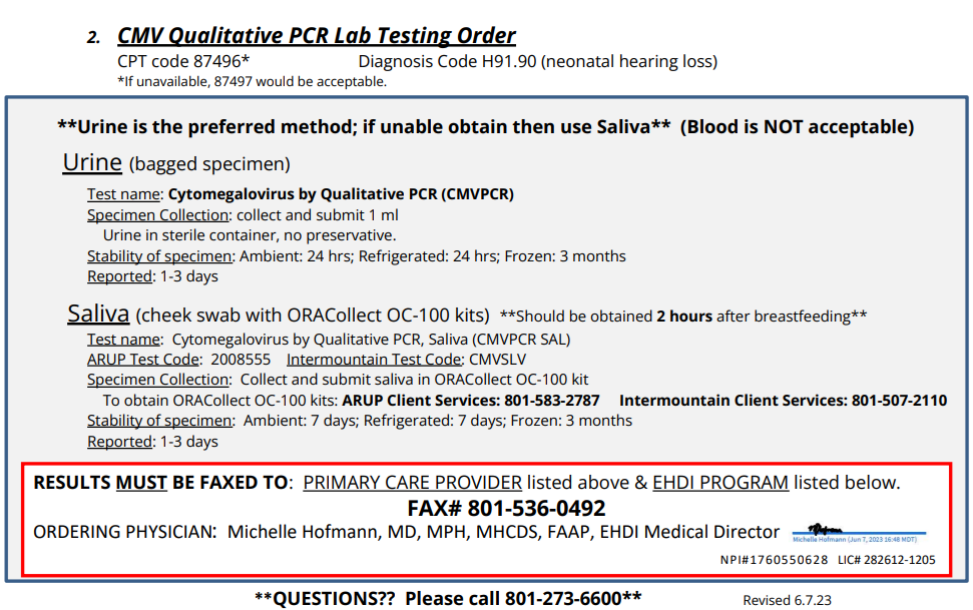
- Confirmed congenital infection: within 21 days
- Probable/suspect infection: after 21 days

CSTE classification:

- Confirmed disease/infection: within 21 days
- Probable disease: 22-42 days

Comparing classifications

- Clinical evidence in new classification is more specific to cCMV
- Clarification on testing time frame
- Types of tests



2. ***CMV Qualitative PCR Lab Testing Order***

CPT code 87496* Diagnosis Code H91.90 (neonatal hearing loss)

*If unavailable, 87497 would be acceptable.

****Urine is the preferred method; if unable obtain then use Saliva** (Blood is NOT acceptable)**

Urine (bagged specimen)

Test name: **Cytomegalovirus by Qualitative PCR (CMVPCR)**
Specimen Collection: collect and submit 1 ml
Urine in sterile container, no preservative.
Stability of specimen: Ambient: 24 hrs; Refrigerated: 24 hrs; Frozen: 3 months
Reported: 1-3 days

Saliva (cheek swab with ORACollect OC-100 kits) **Should be obtained **2 hours** after breastfeeding**

Test name: Cytomegalovirus by Qualitative PCR, Saliva (CMVPCR SAL)
ARUP Test Code: 2008555 Intermountain Test Code: CMVSLV
Specimen Collection: Collect and submit saliva in ORACollect OC-100 kit
To obtain ORACollect OC-100 kits: **ARUP Client Services: 801-583-2787** **Intermountain Client Services: 801-507-2110**
Stability of specimen: Ambient: 7 days; Refrigerated: 7 days; Frozen: 3 months
Reported: 1-3 days

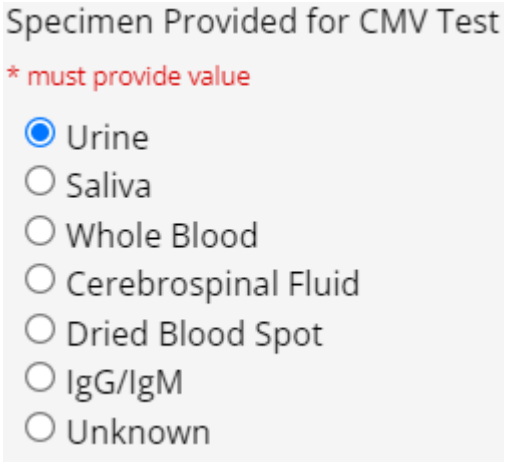
RESULTS MUST BE FAXED TO: PRIMARY CARE PROVIDER listed above & EHDI PROGRAM listed below.
FAX# 801-536-0492
ORDERING PHYSICIAN: Michelle Hofmann, MD, MPH, MHCDS, FAAP, EHDI Medical Director
NPI#1760550628 LIC# 282612-1205

****QUESTIONS?? Please call 801-273-6600****

Revised 6.7.23

Old classification:

- Subjectivity in how to classify different test types due to differing specificities and sensitivities



CSTE classification:

- Provides guidance on classifying various test types:
  - 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

Comparing classifications

- Clinical evidence in new classification is more specific to cCMV
- Clarification on testing time frame
- Types of tests
- Symptomatic/asymptomatic vs. disease/infection

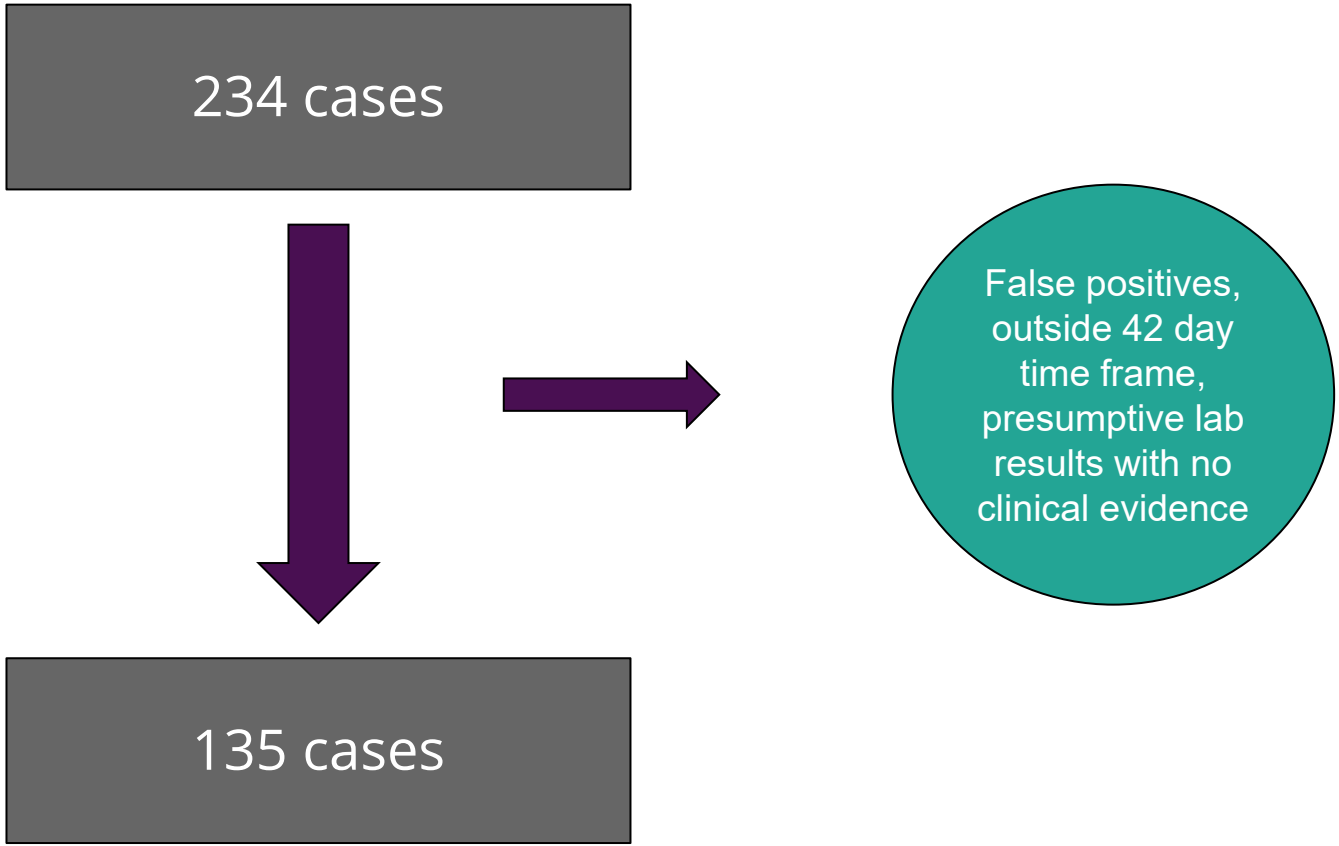
Old classification:

- Asymptomatic vs. symptomatic
  - Differing opinions on if hearing loss was symptom or not

CSTE classification:

- Disease vs. infection
  - Simplifies classification process
  - Provides consistency among jurisdictions

Utah's cCMV cases


234 cases
False positives, outside 42 day time frame, presumptive lab results with no clinical evidence
135 cases

53.3%

72 cases

Confirmed disease

- Confirmatory laboratory evidence
- Clinical evidence

31.9%

43 cases

Confirmed infection

- Confirmatory laboratory evidence

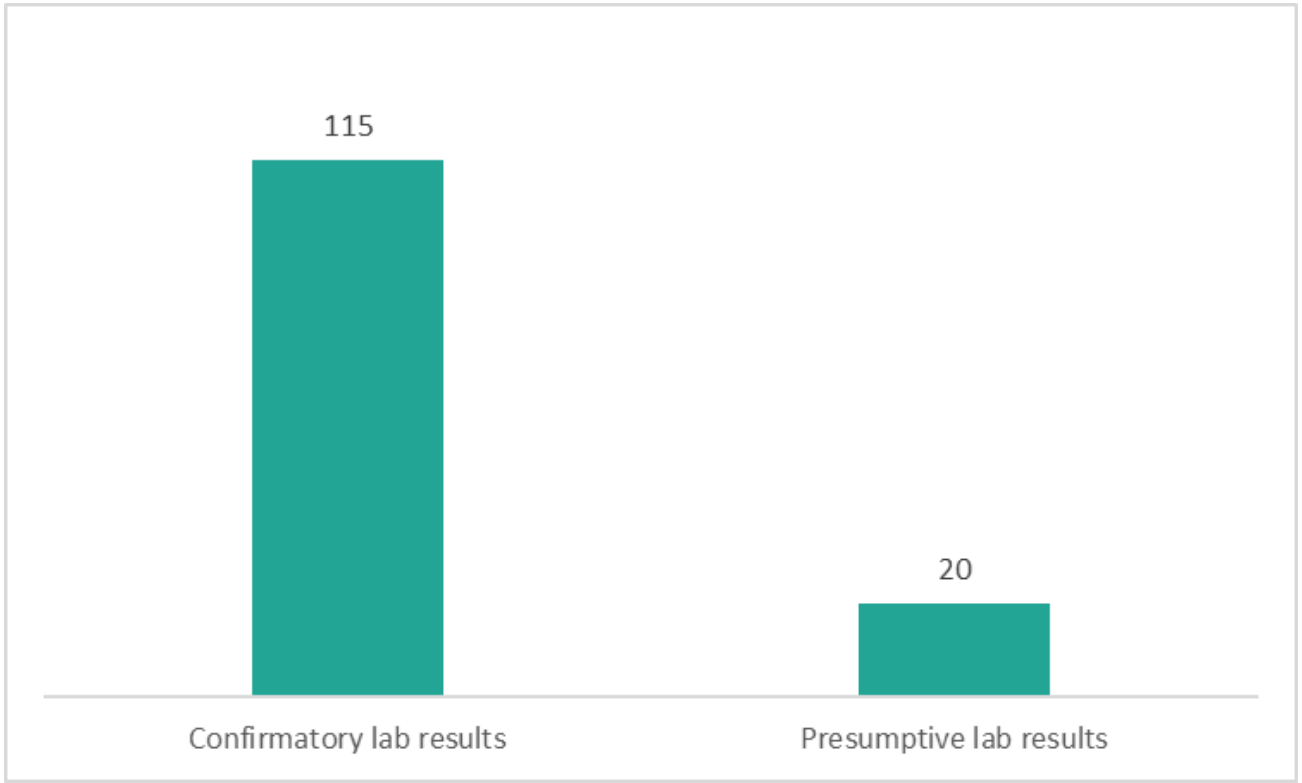
14.8%

20 cases

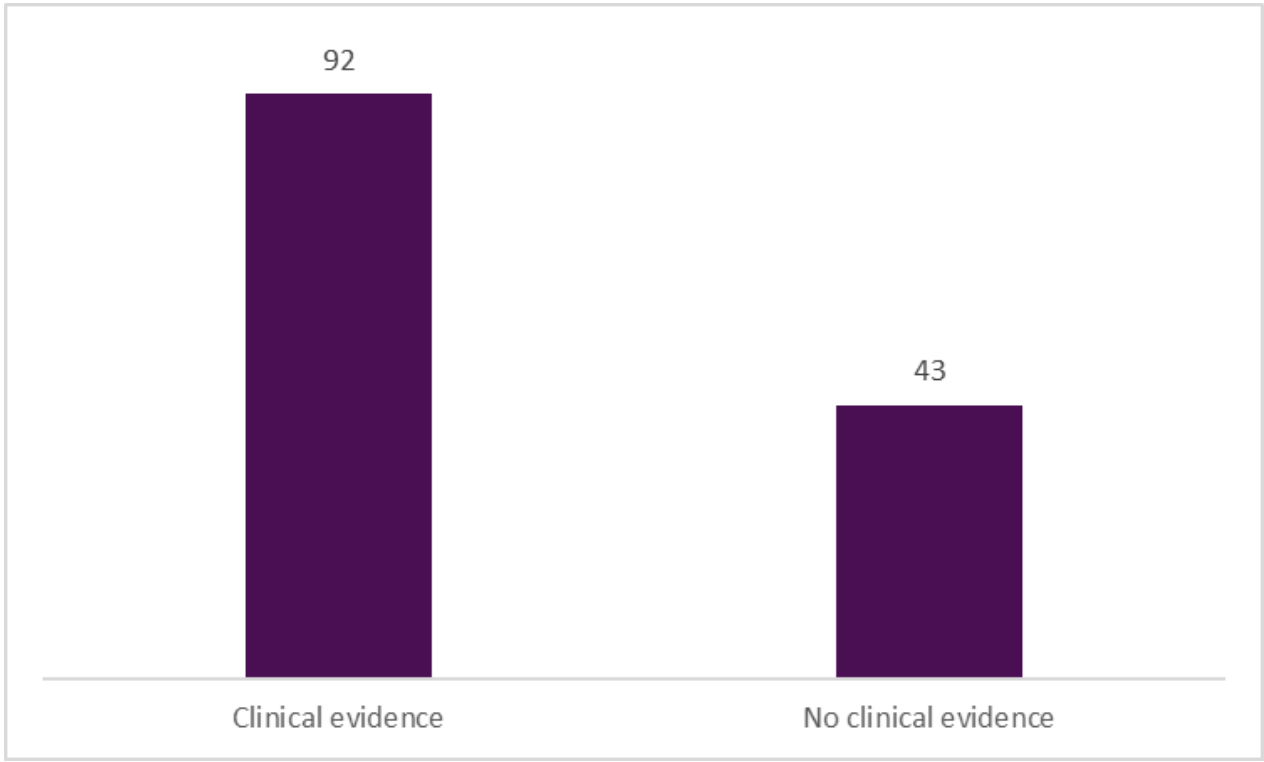
Probable disease

- Presumptive laboratory evidence
- Clinical evidence

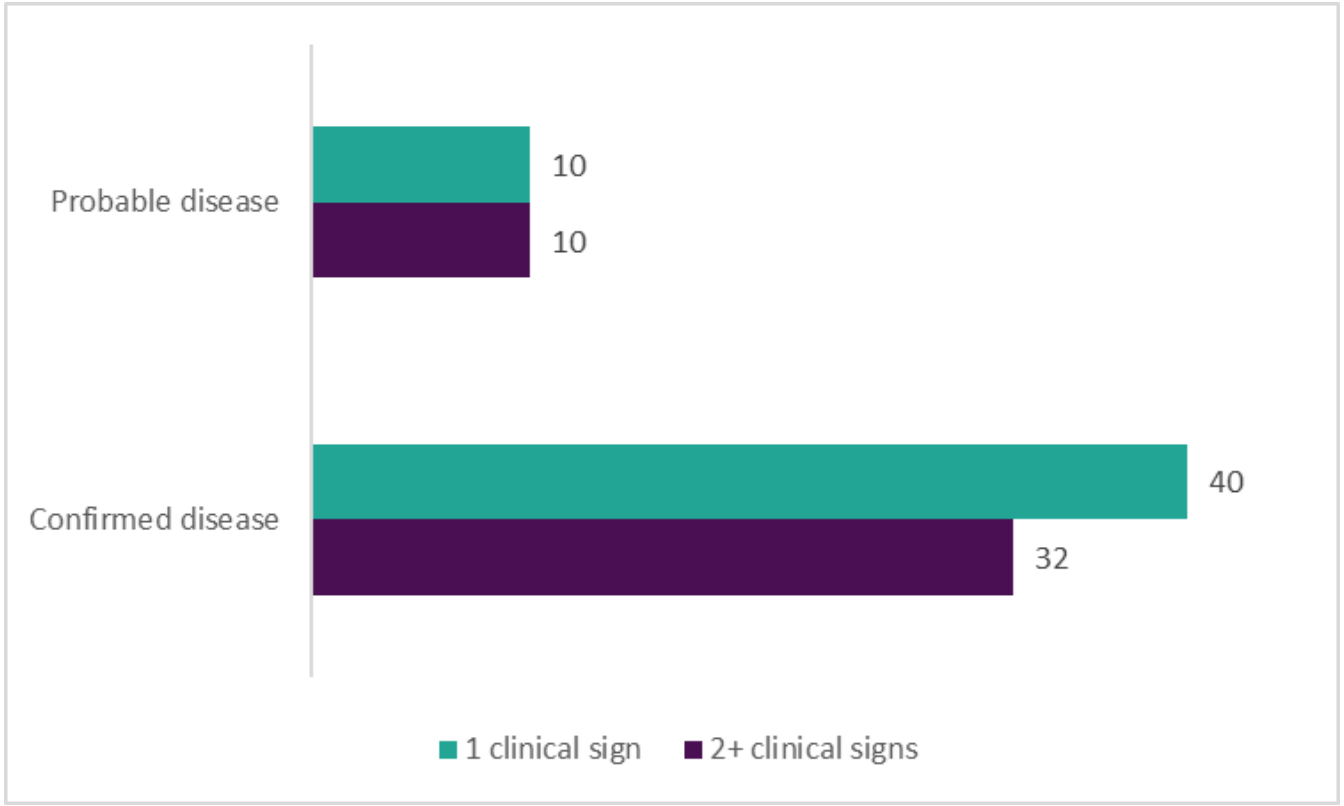
cCMV cases with confirmed vs. presumptive laboratory evidence



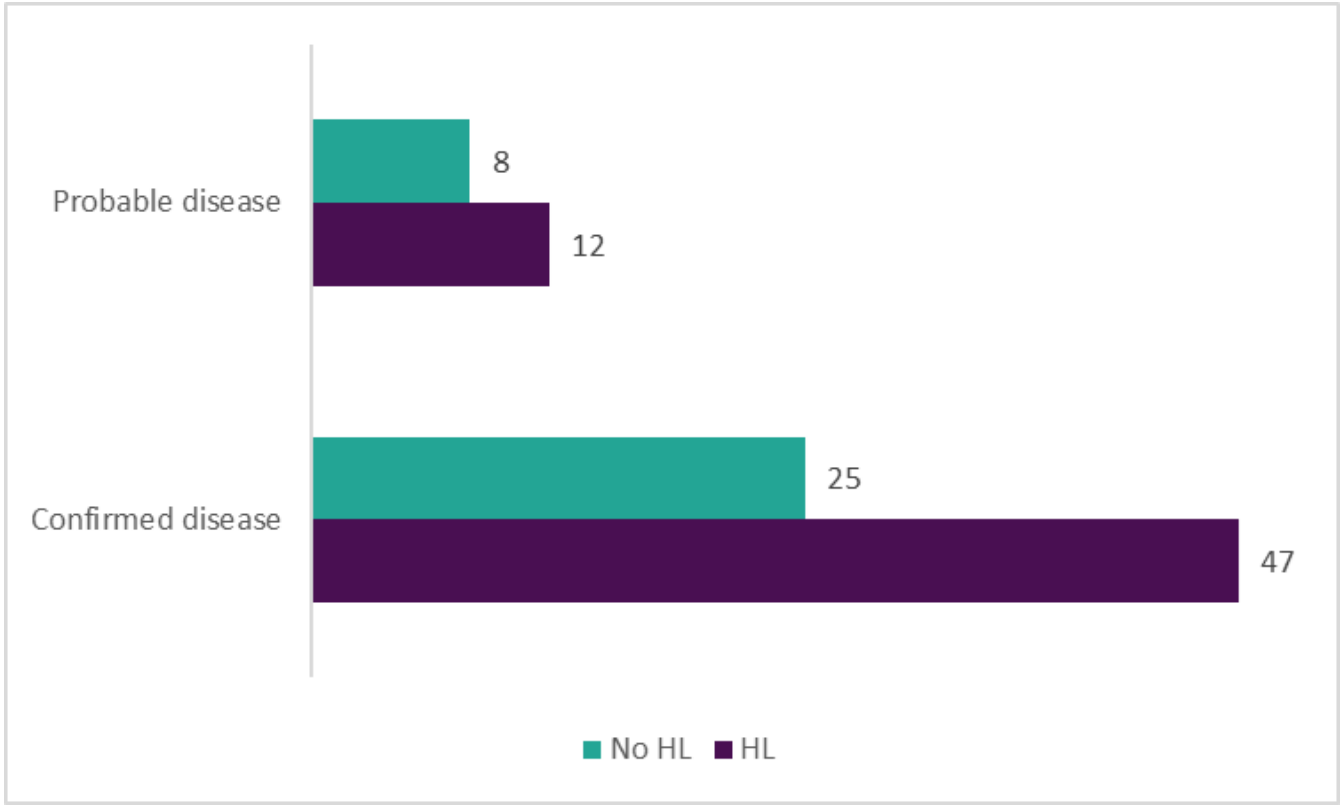
cCMV cases with clinical evidence vs. cases without clinical evidence



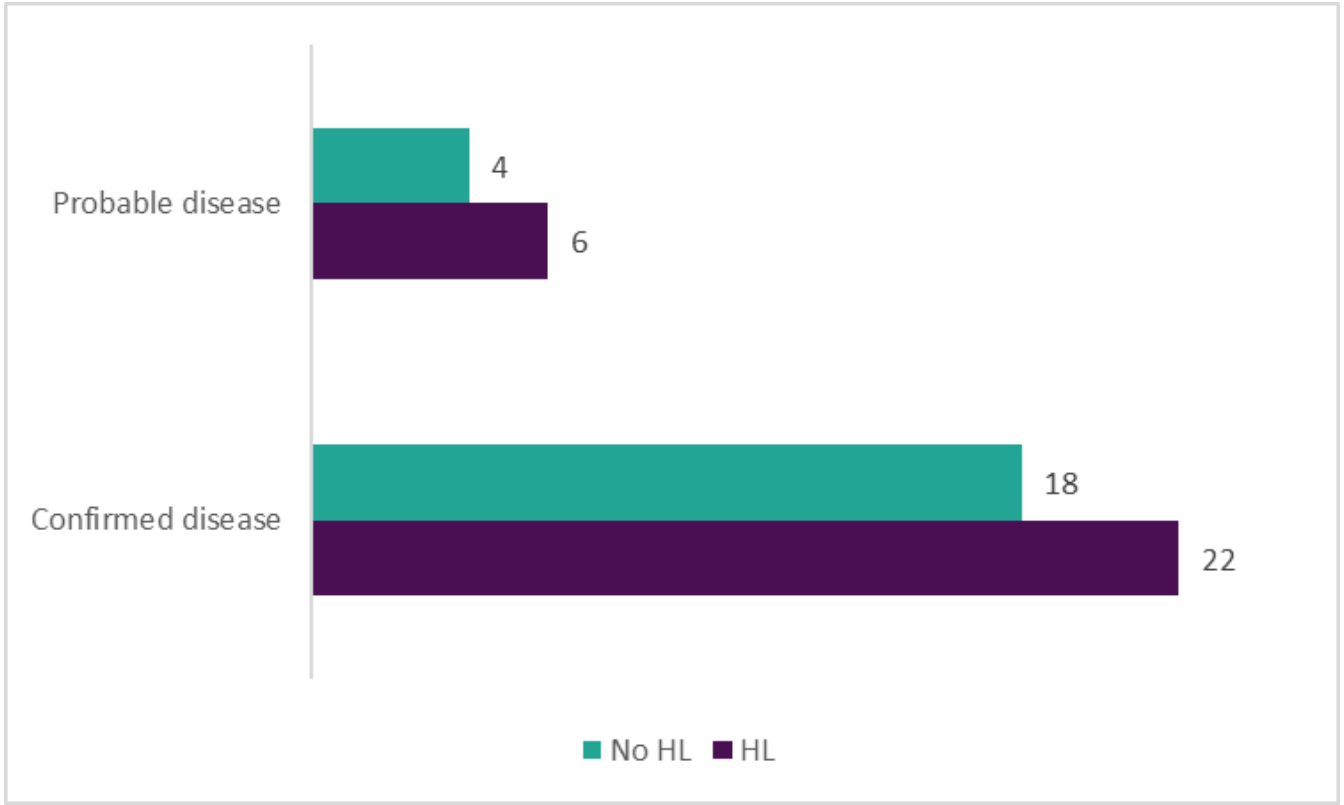
Number of clinical signs among confirmed and probable disease cases



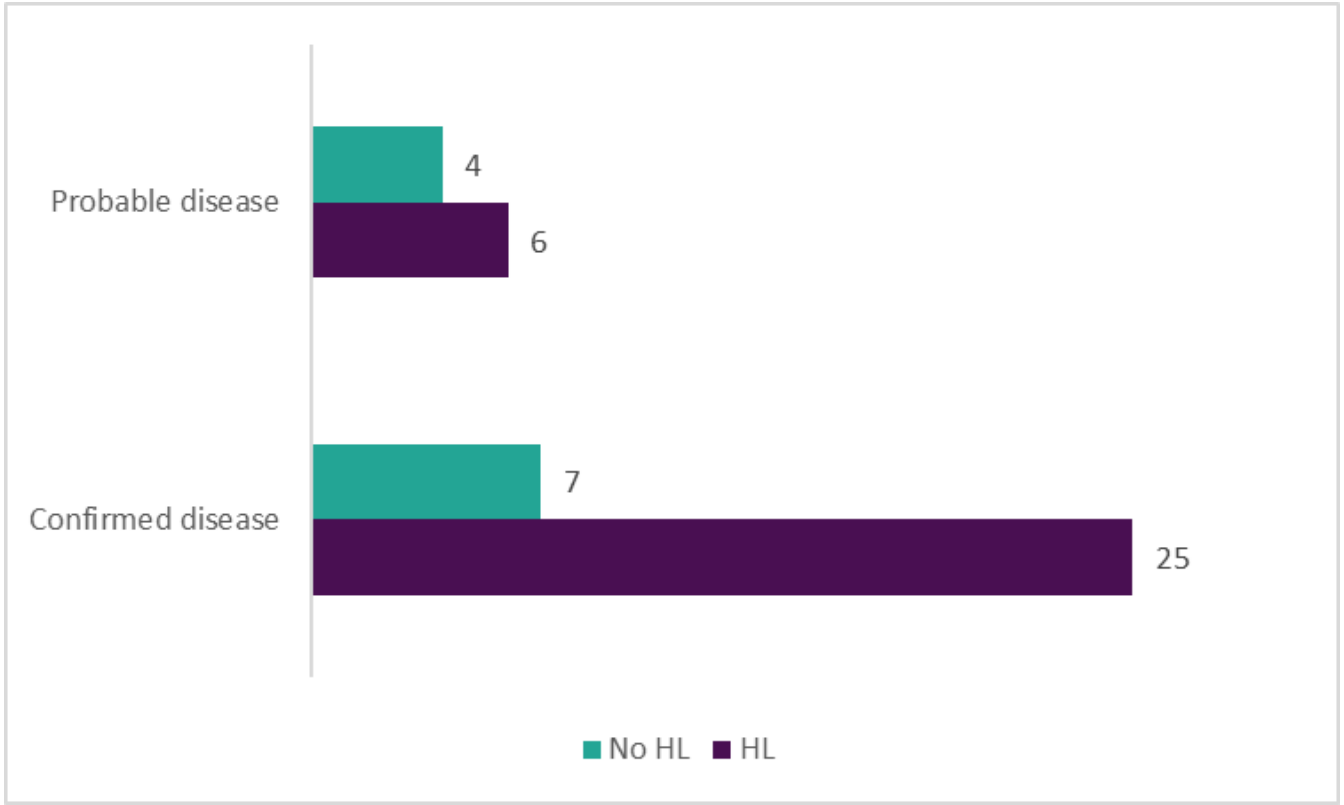
Hearing loss among confirmed and probable disease cases



Hearing loss present in cases as the only clinical sign



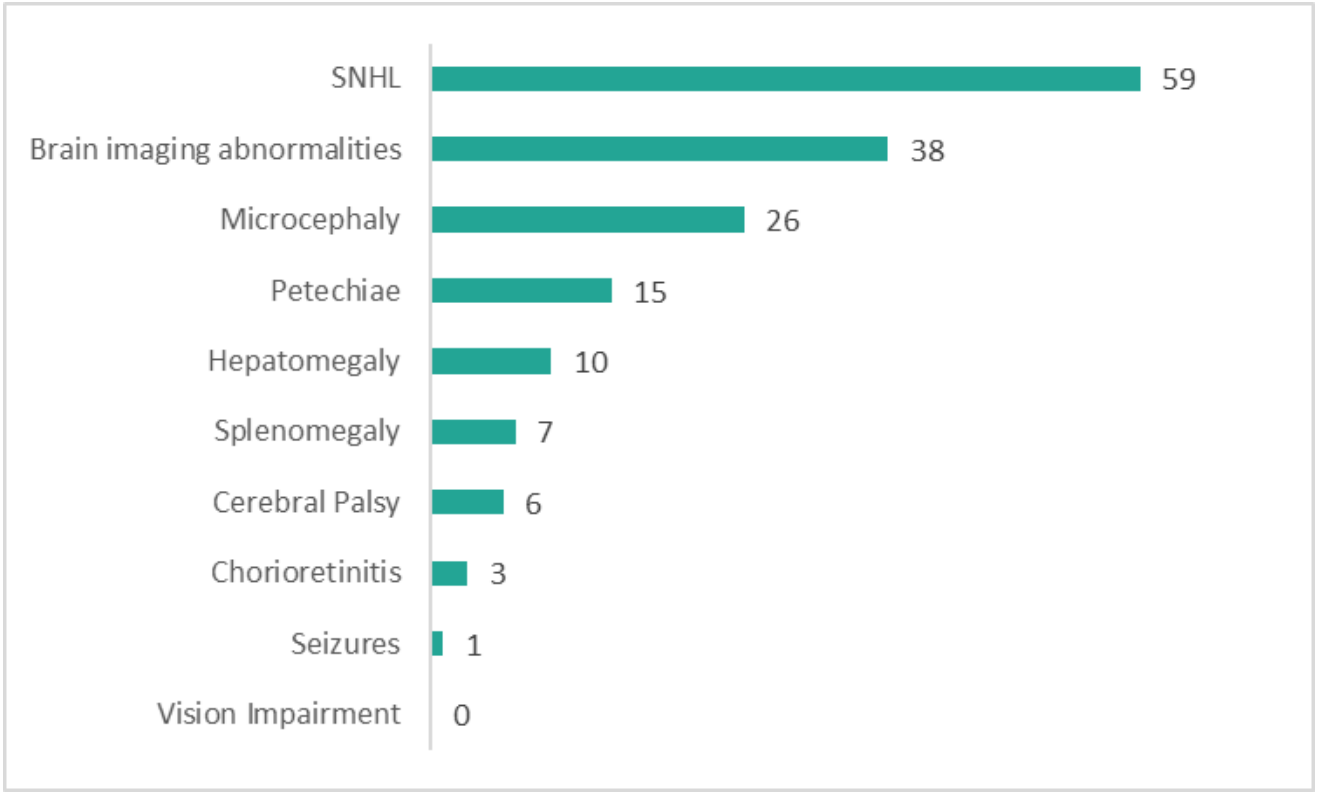
Hearing loss present in cases with two or more clinical signs



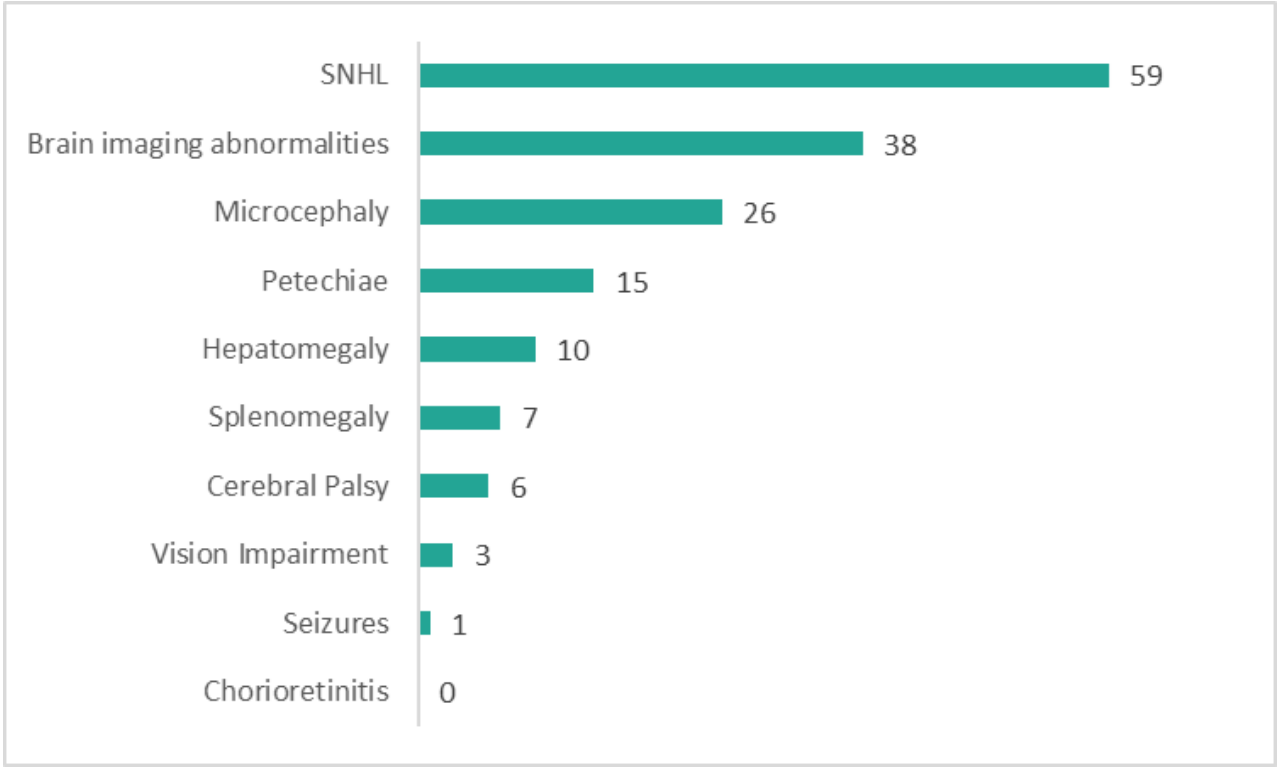
Hearing loss among confirmed and probable disease cases as the only clinical sign vs cases with 2+ clinical signs

	Confirmed disease	Probable disease
1 sign + HL	55% (22/40)	60% (6/10)
1 sign + no HL	45% (18/40)	40% (4/10)
2+ signs + HL	78% (25/32)	60% (6/10)
2+ signs + no HL	22% (7/32)	40% (4/10)

Clinical evidence present in disease cases



Clinical evidence present in disease cases after clarification of vision impairment



Lessons learned

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- Ongoing nature of manual data abstraction and the development of the position statement

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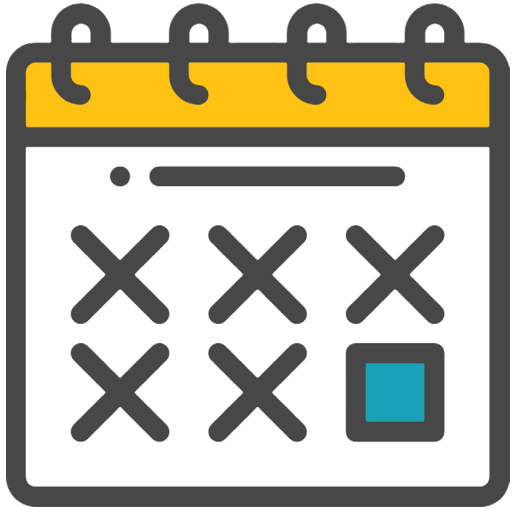
- Ongoing nature of manual data abstraction and the development of the position statement
- CSTE classifications are less subjective
    - Probable category is easier to define due to 42 day cutoff



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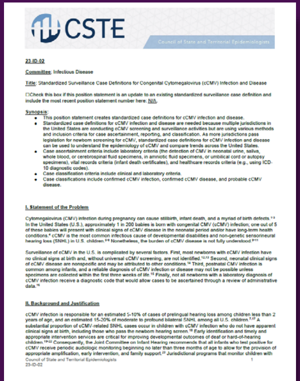

CSTE

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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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