An analysis of cCMV cases identified in Utah, 2013-2023

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Utah Early Hearing Detection and Intervention Program

Utah Department of Health & Human Services

Learning objectives

1. Describe Utah's current methods and capacities for cCMV case ascertainment and how they've evolved over the past 10 years

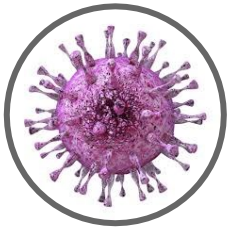
2. List a breakdown of the clinical symptoms associated with cCMV cases from Utah

3. Explain the demographic and geographic patterns that exist in Utah's cCMV cases

Utah EHDI programs

- Early Hearing Detection and Intervention (EHDI)

- Congenital Cytomegalovirus (cCMV) Public Health Initiative



- Children’s Hearing Aid Program (CHAP)

Case ascertainment

Relevant legislation

- 26B-7-105, “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”
  - **All laboratory results** for... CMV in infants less than or equal to **12 months of age**

Early Hearing Detection &
NEWBORN HEARING SCREENI

Rating pe

		SCREENING	
	Births	% receiving initial screen (IP)	% failed init screen
2021	50	100%	8% (4/50)
2022	51	100%	7.8% (4/51

IP = Inpatient/1st screen OP = Outpatient/2nd screen

	% eligible tested	
2021	100%	2/2
2022	100%	1/1

	UTAH HOSPITAL BIRTH 1-3-6 MILESTONES		
	% Screened	% Screened < 1 month (of total births)	% Diagnosed < 3 months (of not passing)
2022	98.9%	97.5%	79.5%

CMV mandate starts

Utah Department of
Health & Human Services
Family Health

Cytomegalovirus & Auditory

**NOTE: NO ACTION REQUIRE

Parent: Your baby failed their newborn hearing sc completed for a common virus, **Cytomegalovirus (CI** painless, requiring a urine sample (preferred) or a sal *after breastfeeding*. * It is vital that this CMV lab test is **requires a more detailed hearing test known as A| scheduled as soon as possible.** Results of both the (provider (PCP) and the State Early Hearing Detection newborn hearing screening and CMV test mandates.

Infant's Full Name: _____
Mother's Full Name: _____
Primary Care Provider (PCP): _____
PCP Phone #: _____
NBHS Facility: _____

**For patient-specific q

1. ***Diagnostic ABR Testing***
   CPT code 92652 Diagnosis Cod
   Diagnostic ABR testing should include BOTH click and fre
   *ABR test date: _____ Lo

2. ***CMV Qualitative PCR Lab Testing O***
   CPT code 87496* Diagnosis Cod
   *If unavailable, 87497 would be acceptable.

**Urine is the preferred method; if unable ob

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

Saliva (cheek swab with ORACollect OC-100 ki
Test name: Cytomegalovirus by Qualitative PCR, Saliva
ARUP Test Code: 2008555 Intermountain Test Code:
Specimen Collection: Collect and submit saliva in ORAC
To obtain ORACollect OC-100 kits: **ARUP Client Servi**
Stability of specimen: Ambient: 7 days; Refrigerated: 7
Reported: 1-3 days

RESULTS MUST BE FAXED TO: PRIMARY CARE PRO
FAX#
ORDERING PHYSICIAN: Michelle Hofmann, MD, MPH,

**QUESTIONS?? Please

Evaluation of Suspected Congenital Cytomegalovirus Infection (cCMV)

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/mm³)
11) Failed hearing screen

Send urine CMV PCR
(obtain by 21 days of life when possible)

If CMV + , perform the following tests:
(If in WBN/SCN, consider neonatology consult)
- CBC with differential
- CMP
- Ophthalmology (inpatient or outpatient) within 2 weeks of + test
- Head Ultrasound
- Hearing: Diagnostic ABR, OAE (Tympanometry and Bone if indicated)
- Refer to Early Intervention
- EMAIL Utah Dept Health CMV@Utah.gov

ASYMPTOMATIC if all of the following:
- Normal Ophthalmology Exam
- Normal ABR *
- Normal Head US
- Normal Platelet Count
- No hepatosplenomegaly
- Normal Liver Function

* Normal ABR = 25 dBeHL or less at all test frequencies (500, 1k, 2k, and 4k whenever possible) with present OAE

Isolated Sensorineural Hearing Loss

SYMPTOMATIC if one or more of the following:
- Thrombocytopenia
- Hepatomegaly
- Splenomegaly
- IUGR/SGA
- Sensorineural hearing loss (if also one or more of the above)
- Microcephaly
- Abnormal HUS
- Hepatitis

At 3mos of age:
- Follow up with **Audiology & ENT**

By 4 weeks of age:
- Consult **Pediatric ID** to discuss antiviral treatment
- Consult **Pediatric Neurology** if abnormal HUS or microcephaly

Evaluation in Multidisciplinary Congenital CMV Clinic
Call (801) 662-1740 to schedule:
- Infectious Disease
- ENT
- Neurology

Approved by University of Utah Divisions of Neonatology, Pediatric Infectious Disease, Pediatric Neurology, Pediatric Otolaryngology and the Utah Department of Health in January 2020.

2022

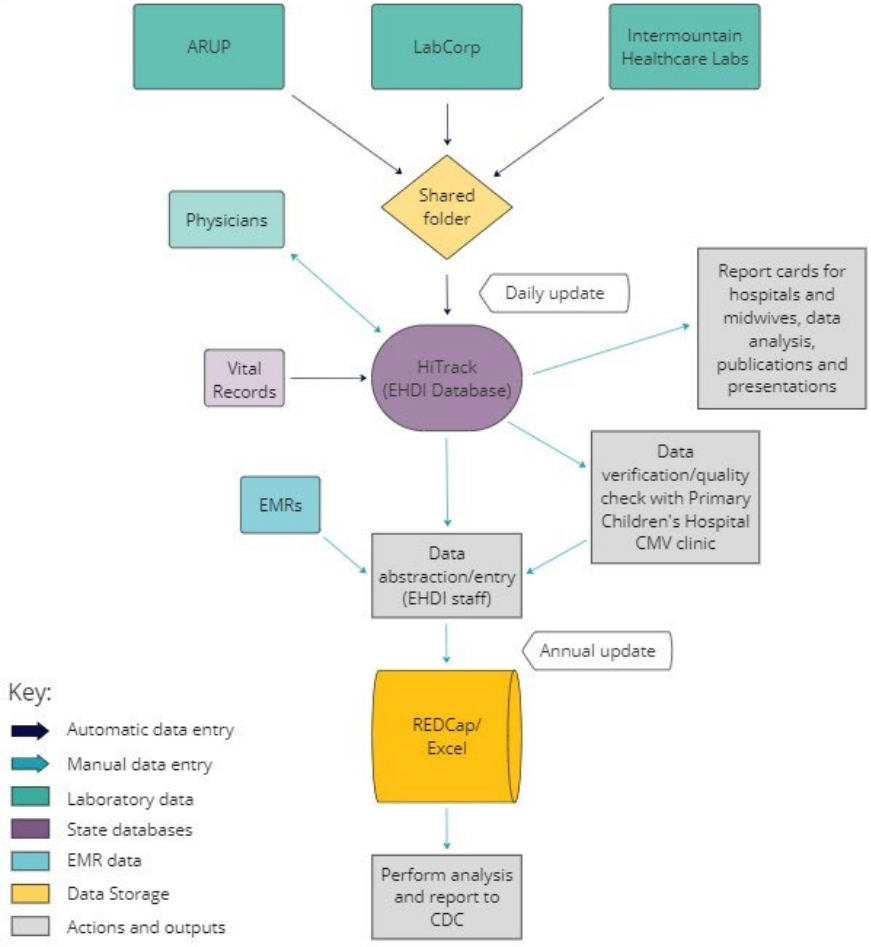
Automation of lab reporting

CMV epidemiologist hired with SET-NET funding

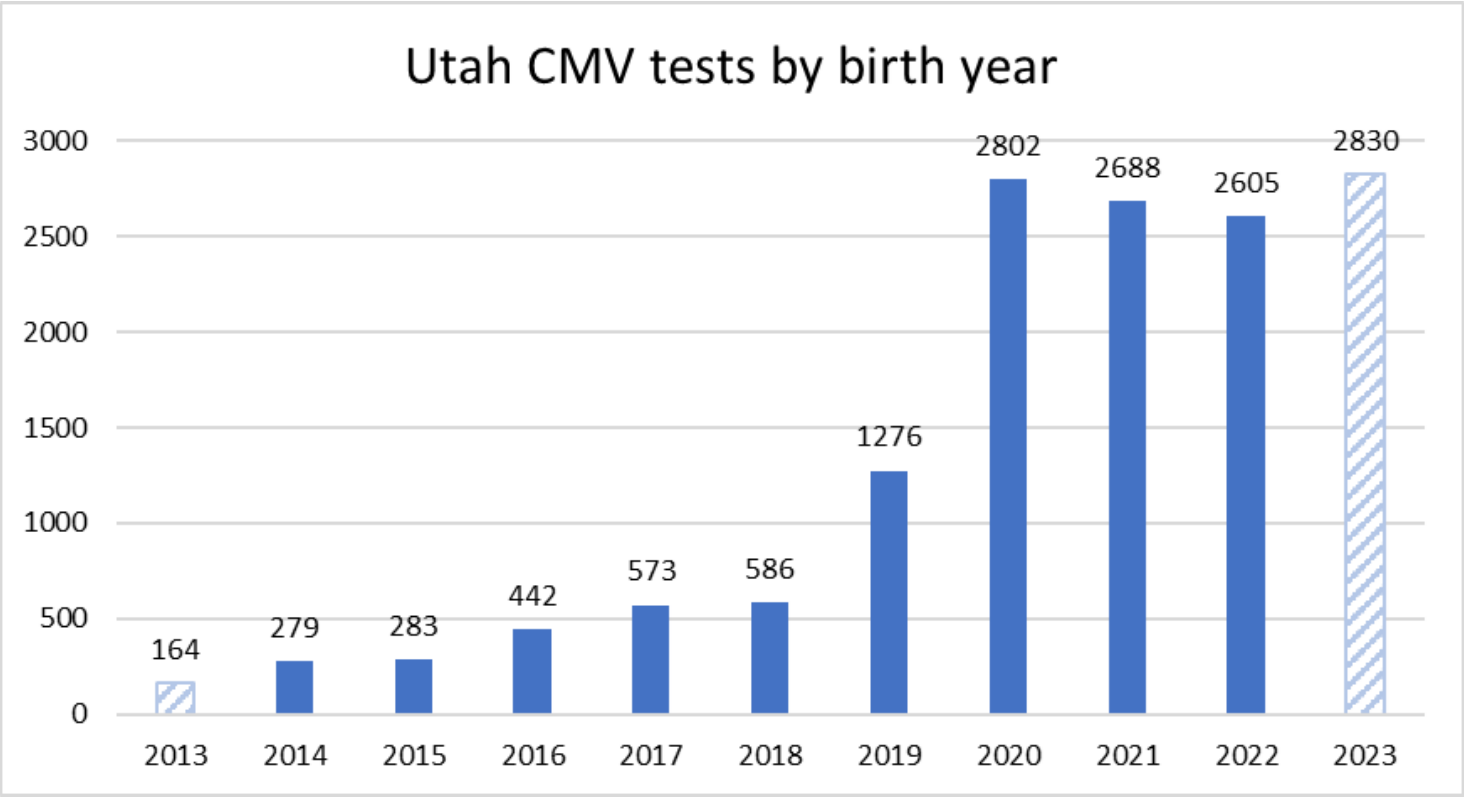
Case ascertainment currently

- Reporting
  - Lab reports
  - Provider communications
- Data sources and storage
  - EMR
  - CMV working group meetings
  - Data abstraction
  - REDCap

- Future goals
  - Further automation
  - System evaluation
    - ICD-10 code access
  - Access to additional health systems



Lab reporting increase



*2013 (July - Dec) and 2023 (Jan - June) are projections based data from half of the year

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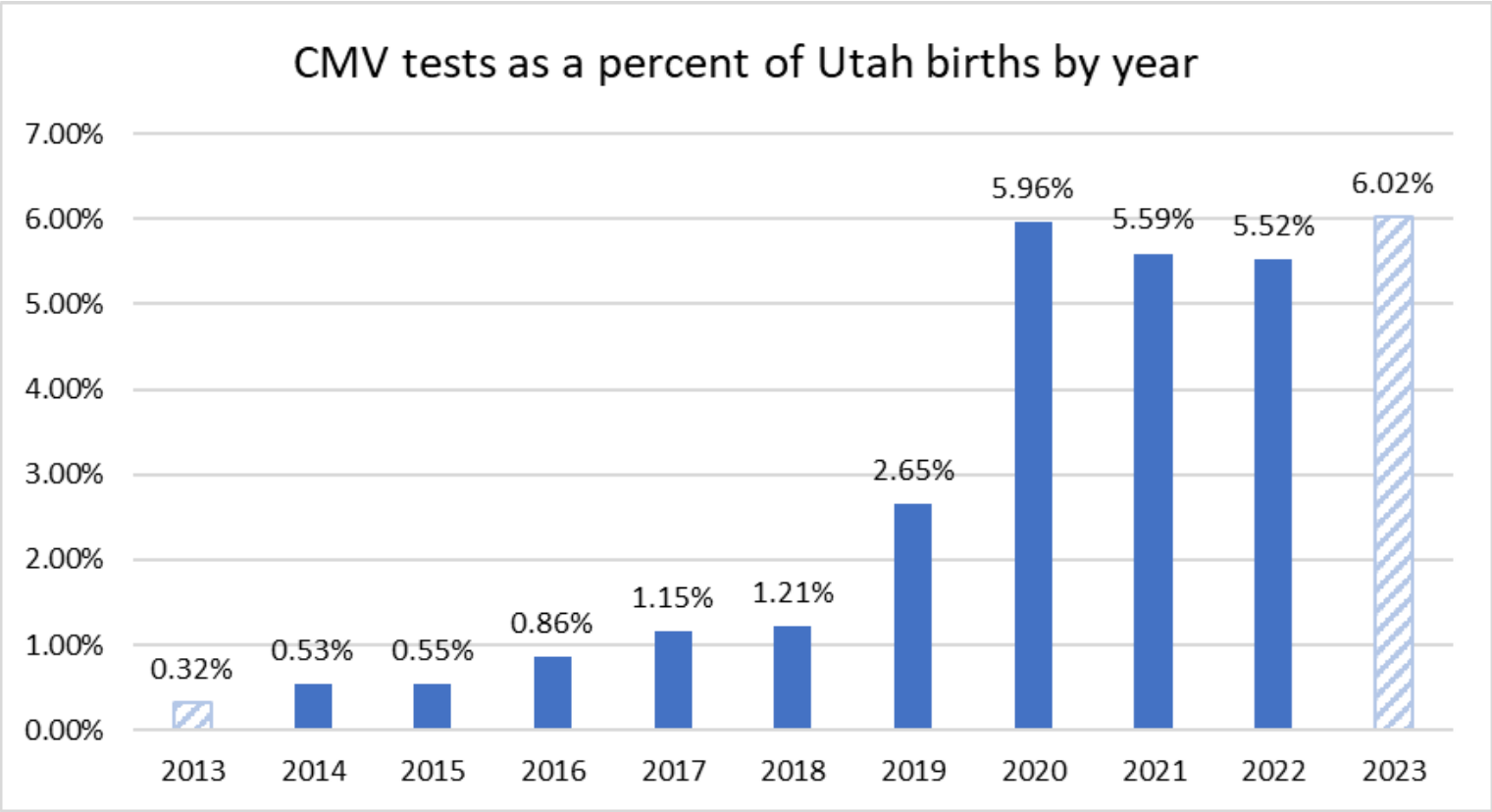

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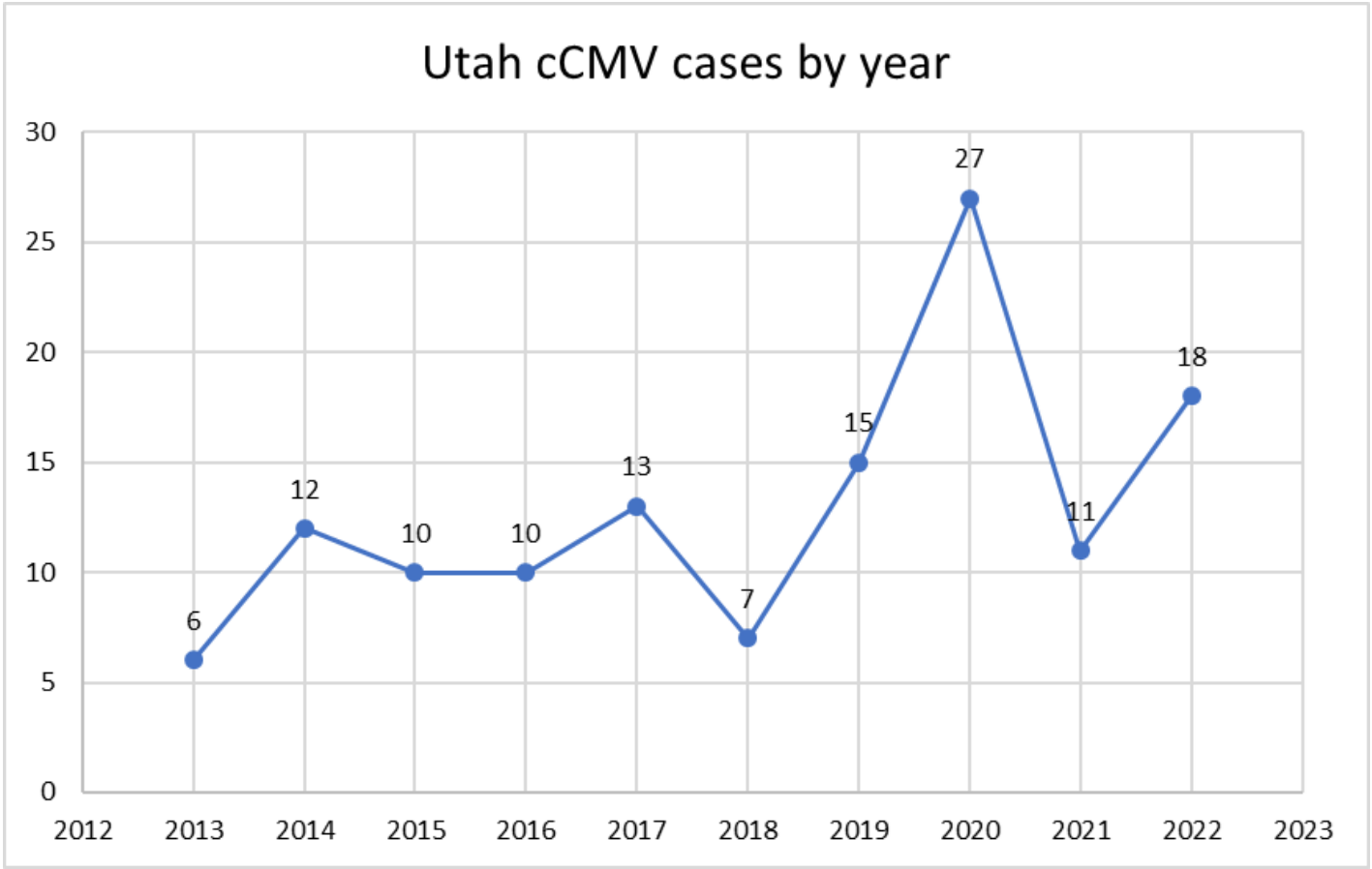
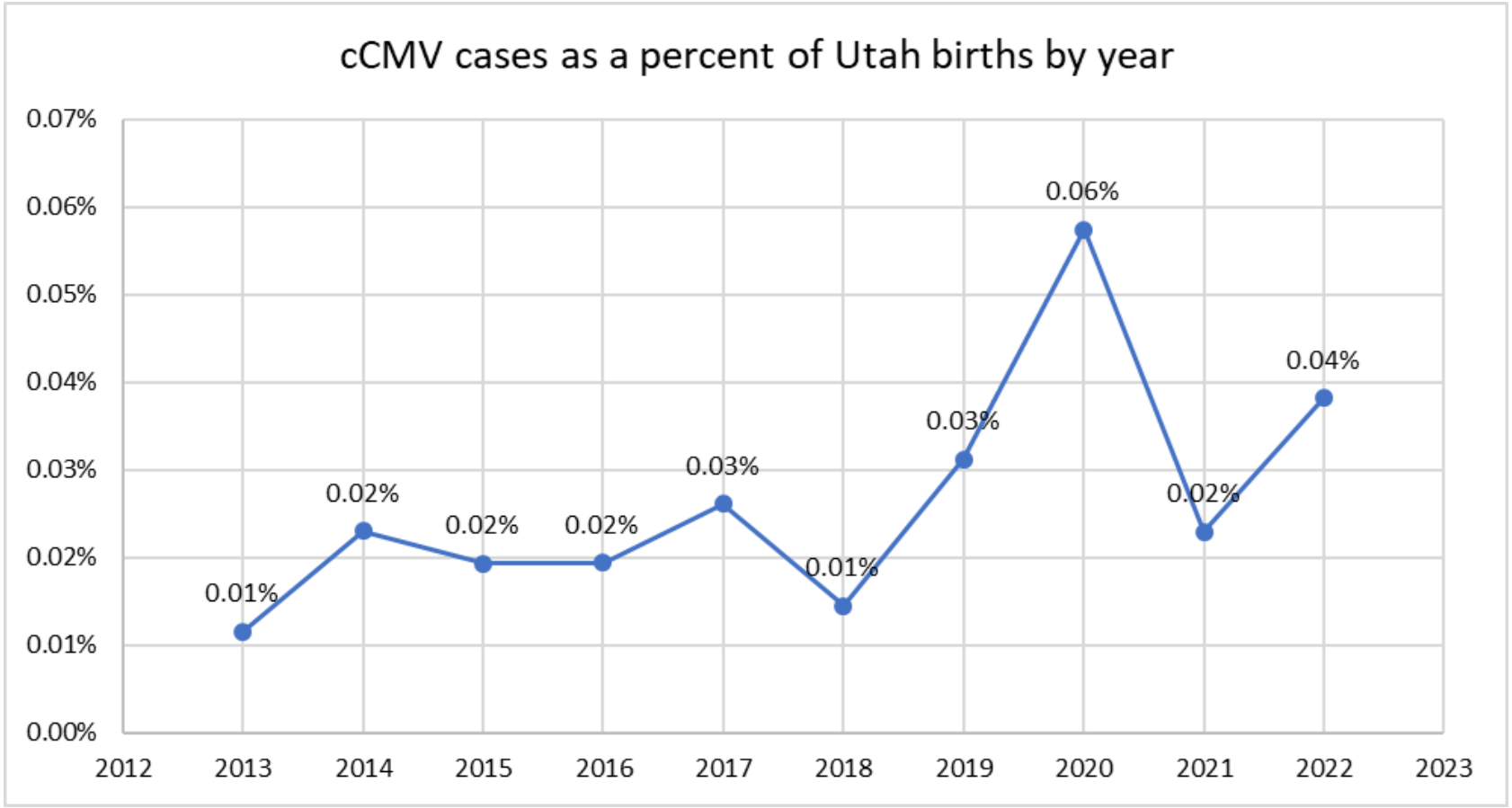
Cases by year



Cases by year



Important events in improving case ascertainment

2013	2015	2016	2019	2022
CMV mandate starts	CMV data coordinator position created CMV added to communicable disease rule CMV report cards started	CMV standing order form created	High risk testing protocol for CMV adopted by Intermountain Healthcare birthing hospitals	Automation of lab reporting CMV epidemiologist hired with SET-NET funding

Case characteristics

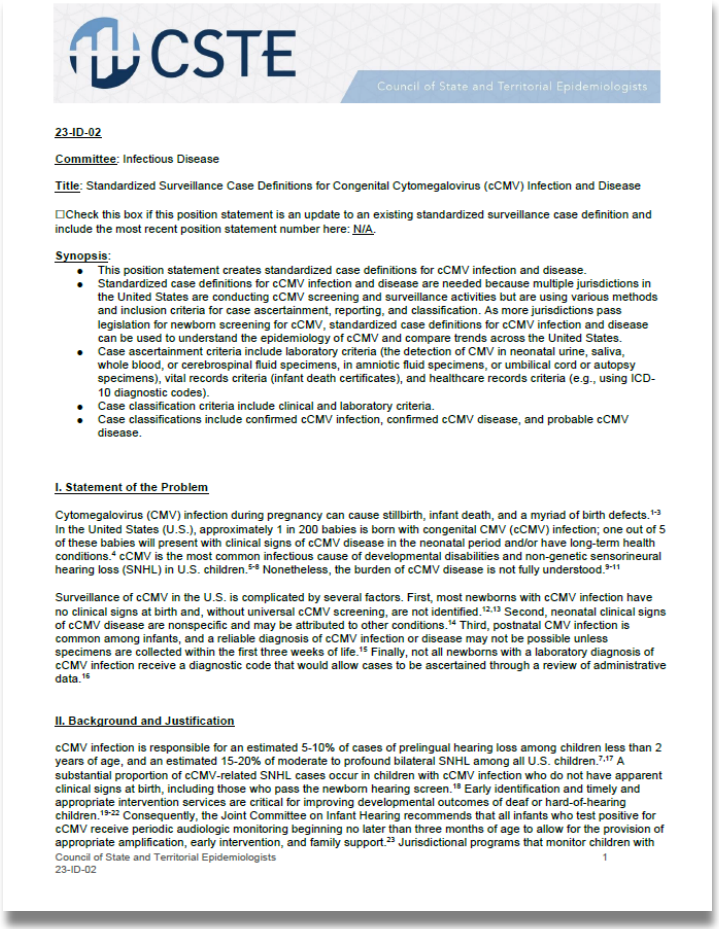
CSTE standardized case definition for cCMV

Confirmed:

- **cCMV infection**: meets confirmatory laboratory evidence
- **cCMV disease**: meets clinical criteria AND confirmatory laboratory evidence

Probable:

- **cCMV disease**: meets clinical criteria AND presumptive laboratory evidence



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

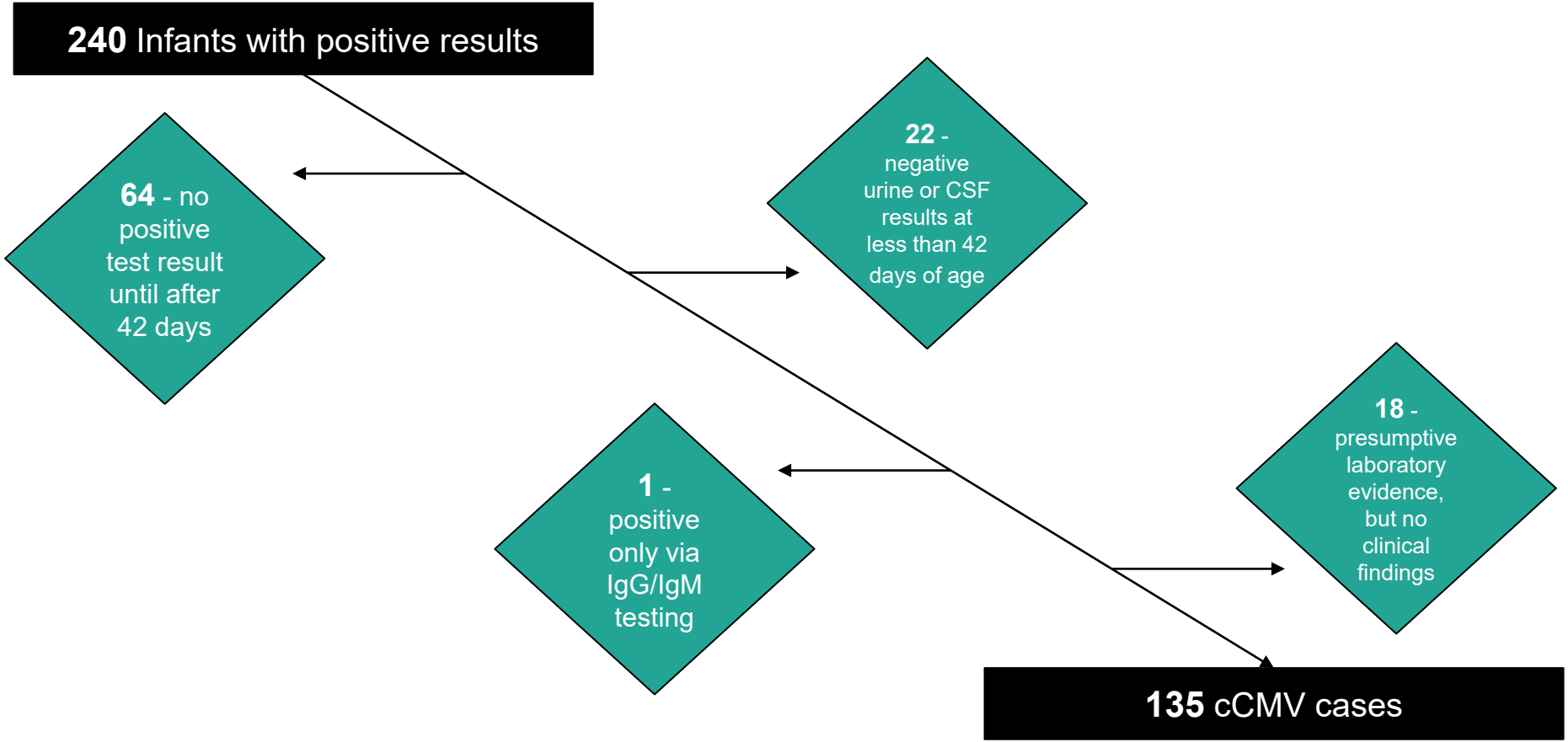
Cytomegalovirus (CMV) infection during pregnancy can cause stillbirth, infant death, and a myriad of birth defects.[1-3] In the United States (U.S.), approximately 1 in 200 babies is born with congenital CMV (cCMV) infection; one out of 5 of these babies will present with clinical signs of cCMV disease 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]

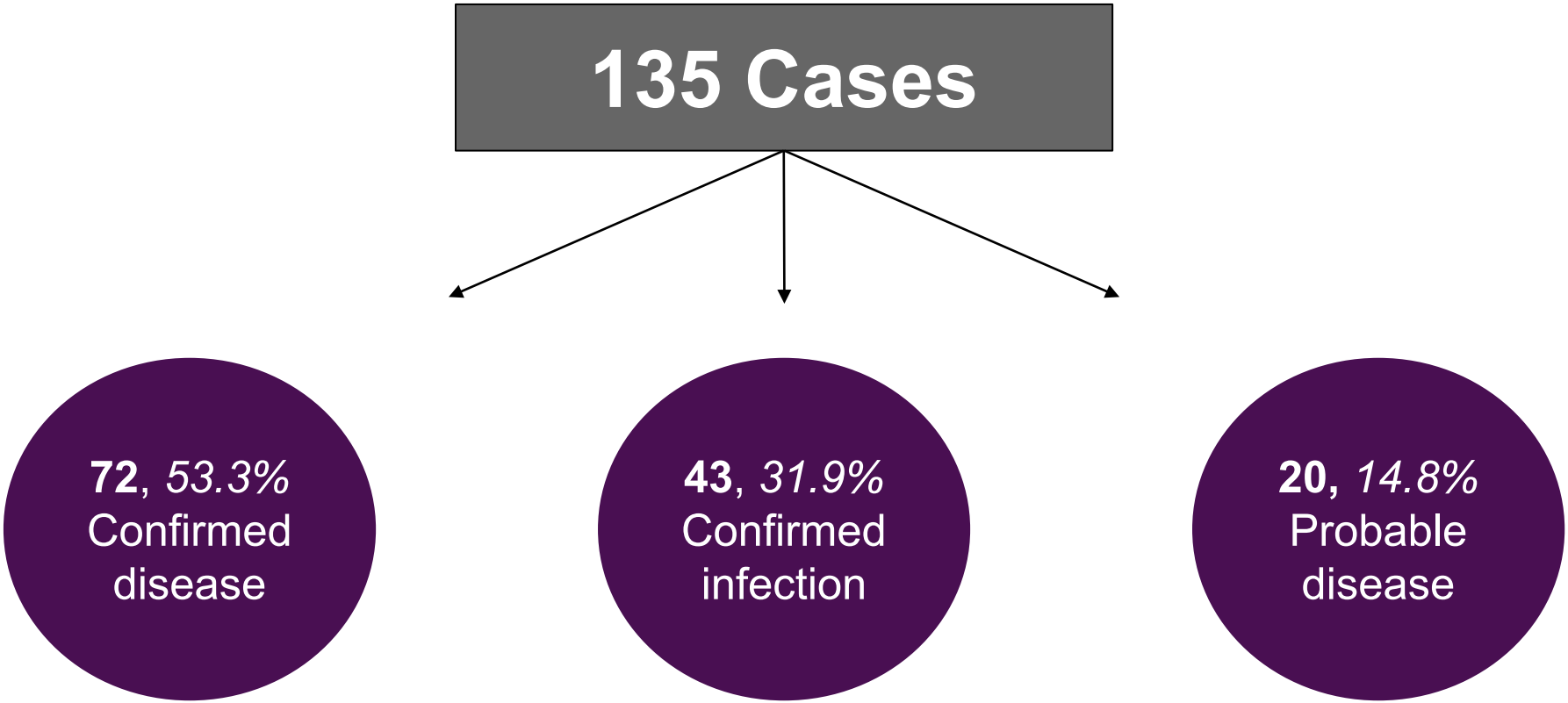
II. Background and Justification

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

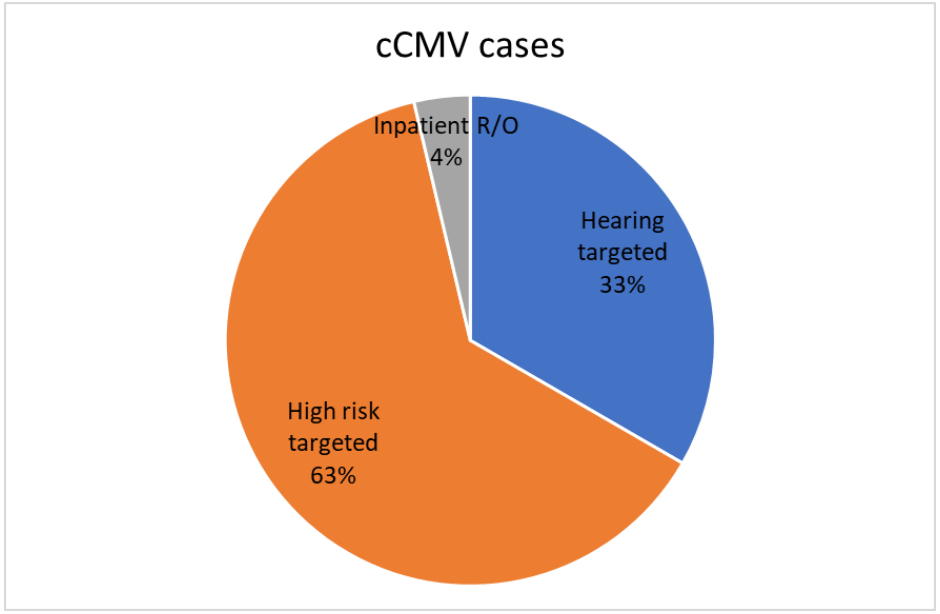
10 years of cCMV cases

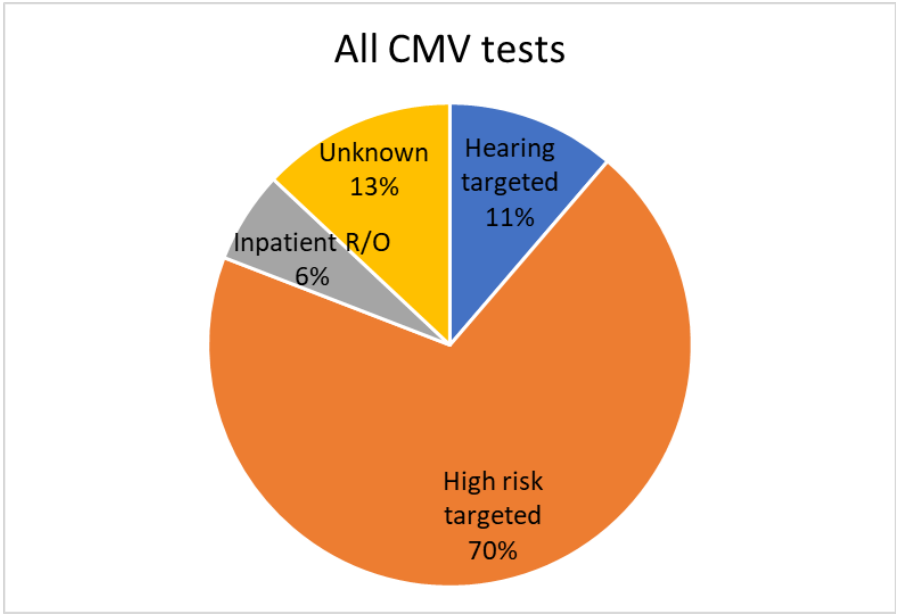


Confirmed and probable cases



Reasons for testing





Hit rate by testing type

Since September, 2019

Hearing targeted = **1.39%**

High risk targeted = **0.69%**

- *Petechiae = 38.5%*
- *Maternal infection = 12.9%*
- *Hepato/splenomegaly = 11.8%*
- *Microcephaly = 7.4%*
- *Hyperbilirubinemia = 0.84%*
- *SGA/IUGR = 0.5%*

Inpatient R/O = **0.16%**

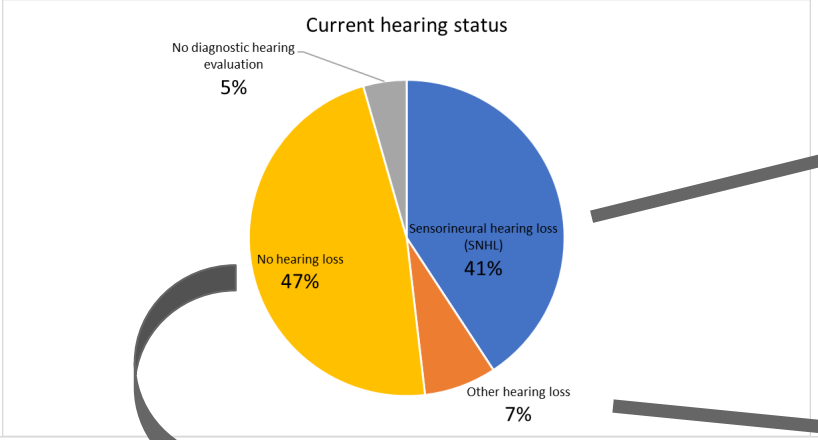
Clinical characteristics

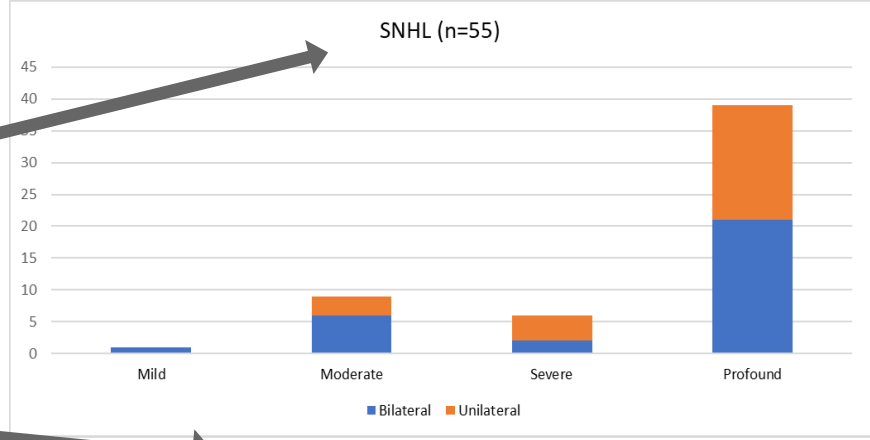
cCMV cases	All 2022 Utah births
Nursery • NICU - 49 (***36.3%***) • Well baby - 81 (***60%***) • Unknown - 5 (***3.7%***)	Nursery • NICU - ***10.4%*** • Well baby - ***74.7%*** • Unknown - ***14.9%***
Birth weight • Average = ***2.67 kg***	Birth weight • Average = ***3.26 kg****
Birth length • Average = 45.6 cm	
Head circumference • Average = 32.4 cm	
Gestational age • Average = *37 weeks, 3 days*	Gestational age • Average = *37 weeks, 5 days**
Maternal age • Average = ***26.9 years***	Maternal age • Average = ***29.5 years***

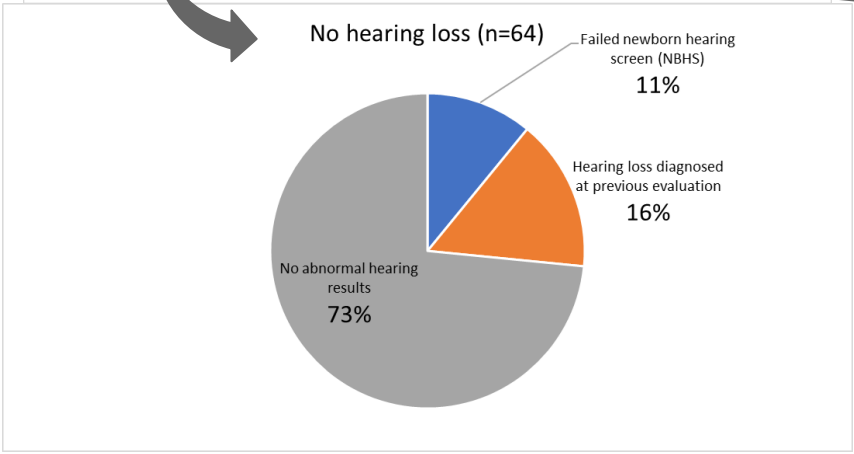
*Importance of data abstraction:

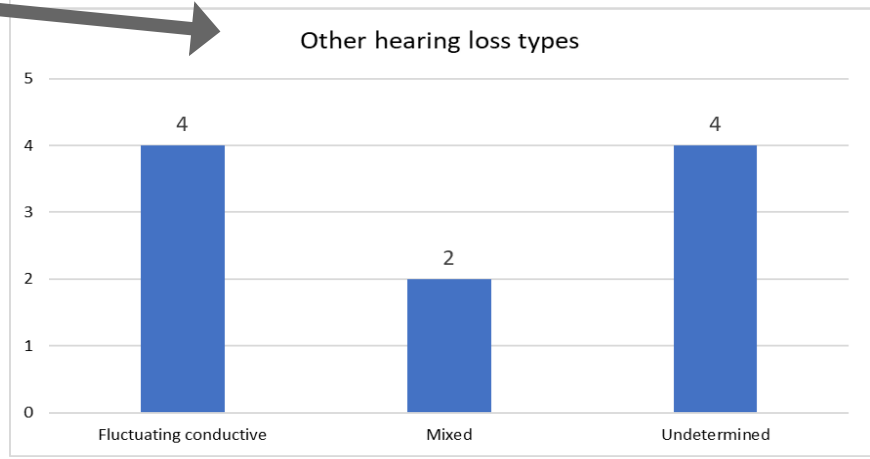
- Birth weight available for only ~20% of all Utah births
- Gestational age available for only ~5% of all Utah births
- Both over 90% for cCMV cases

Birth information

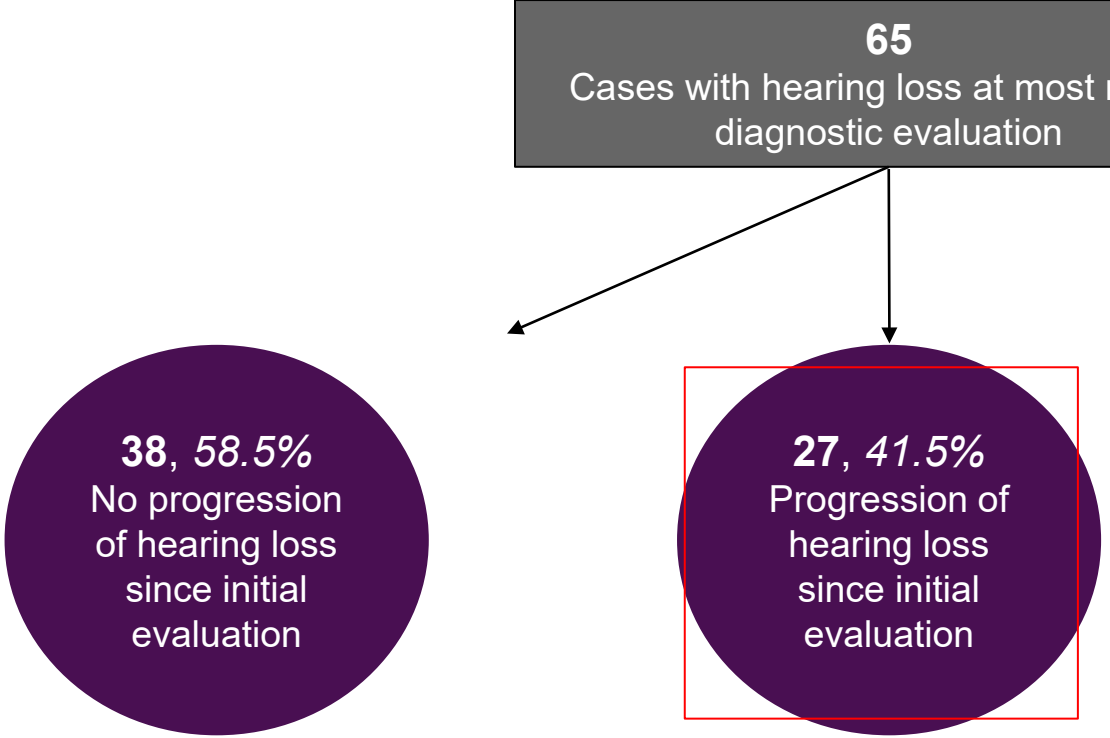






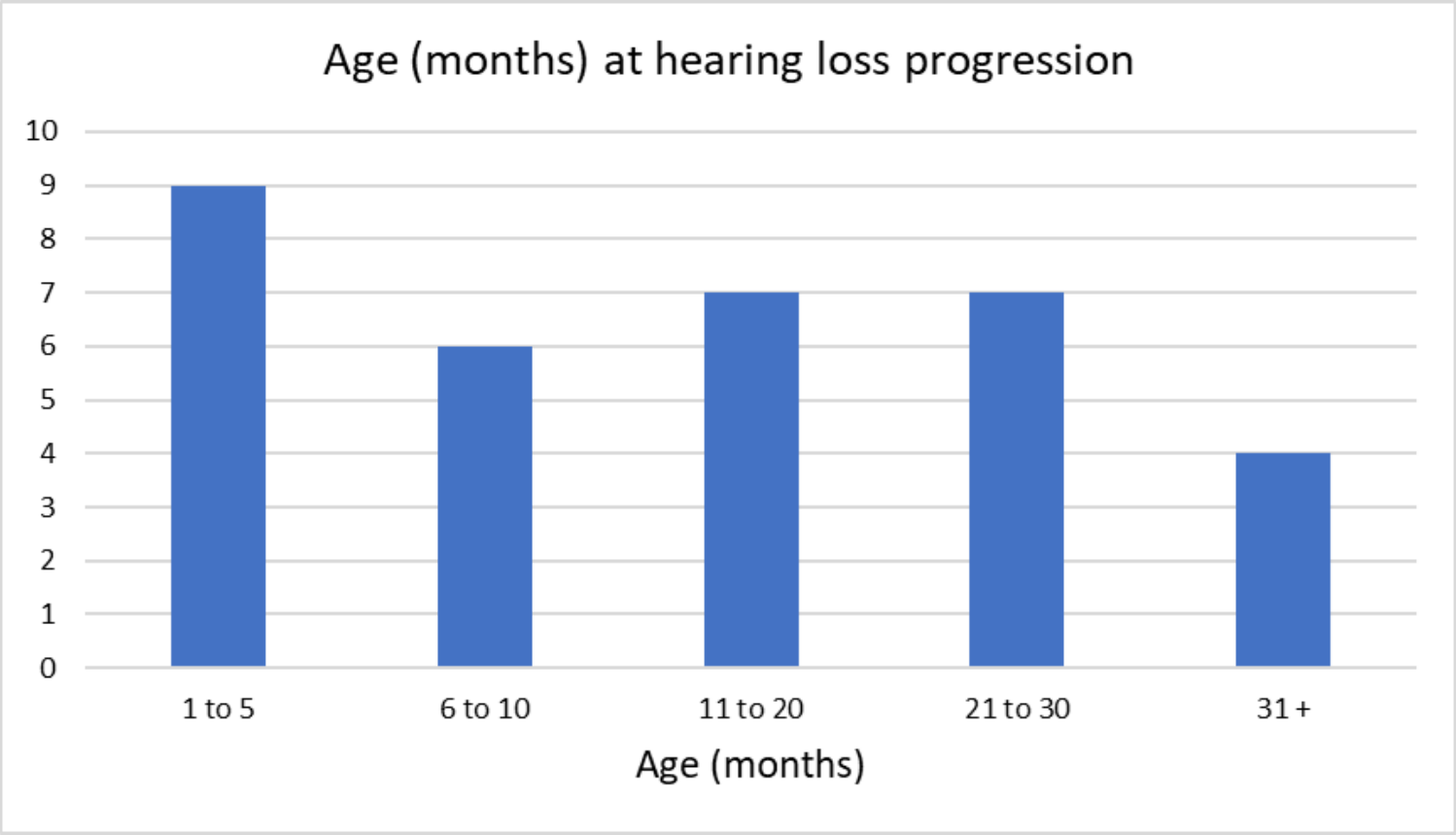


Hearing information



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

Hearing loss progression



Age at hearing loss progression

Clinical criteria

A1. Clinical Criteria

Cases should be assessed according to absence or presence of clinical evidence as defined below and the clinical data should be included in the case investigation.

In the absence of a more likely alternative etiology:

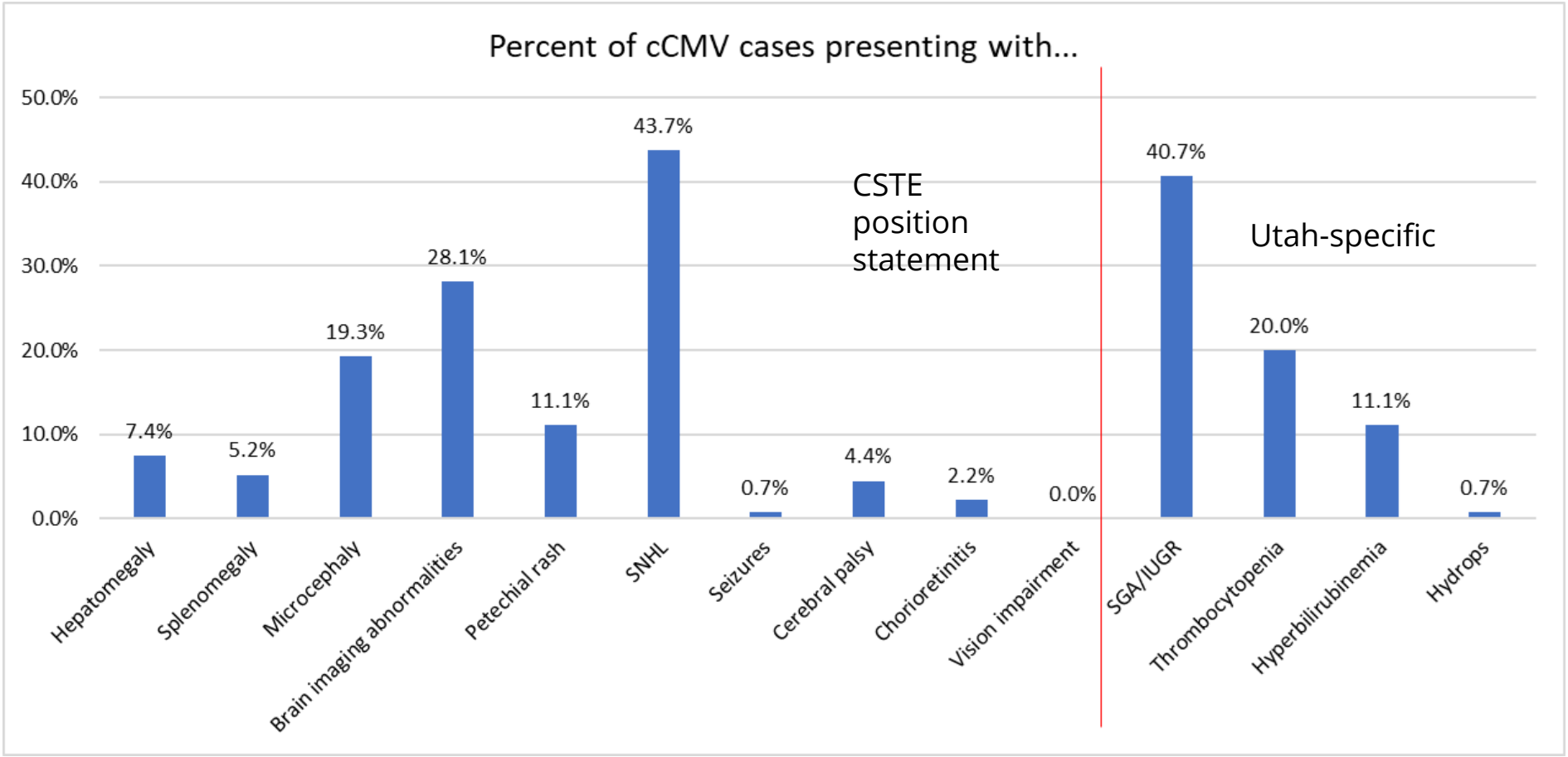
- An infant with at least one of the following clinical signs during the neonatal period:[28,29]
  - Hepatomegaly
  - Splenomegaly
  - Petechial rash or purpura ("blueberry muffin rash"),

OR

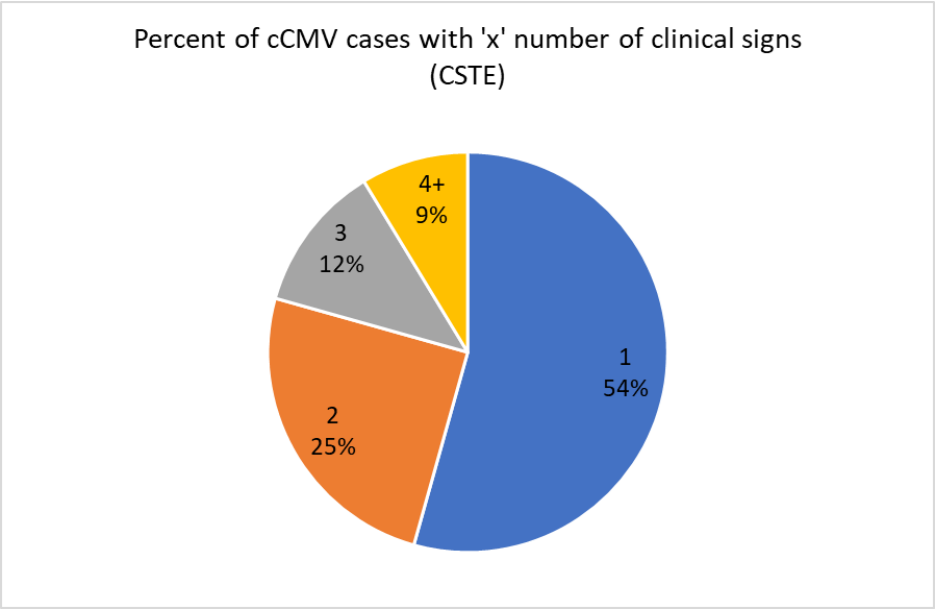
- A child aged 6 years or younger with one or more of the following permanent conditions:[28,29,30]
  - Microcephaly (defined as head circumference measurement >2 standard deviations below the average (or <3rd percentile) for the same age and sex, notation in the medical record, or diagnostic code of 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

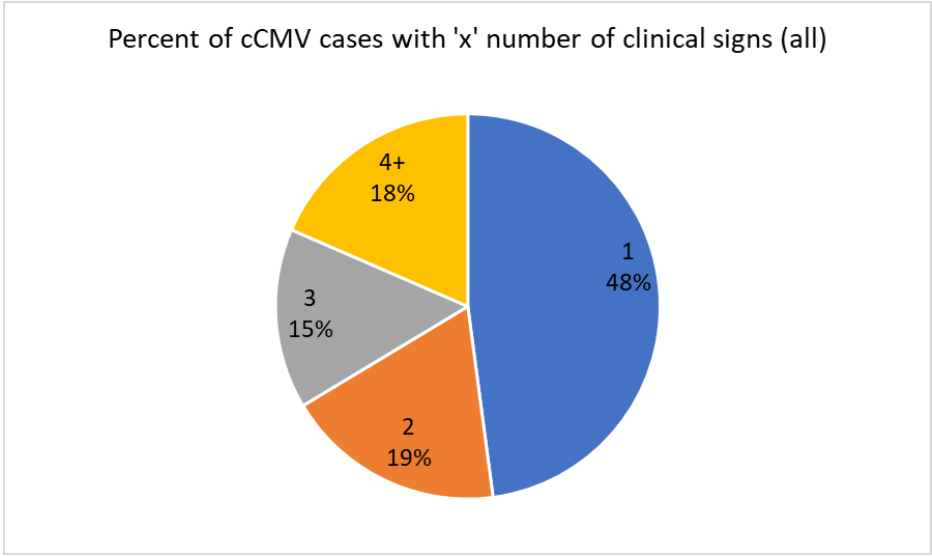
CSTE

Clinical signs summary

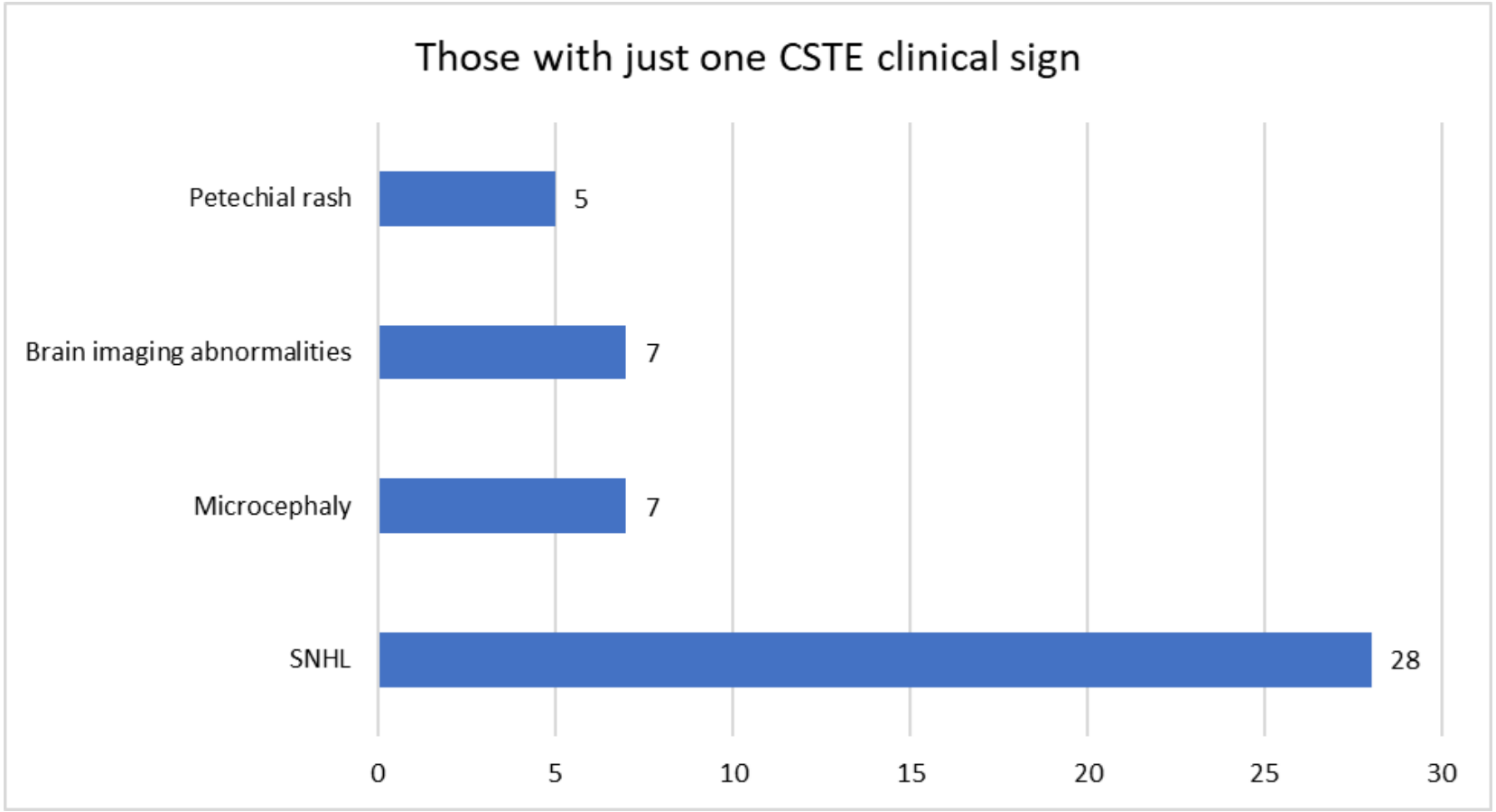


Clinical signs



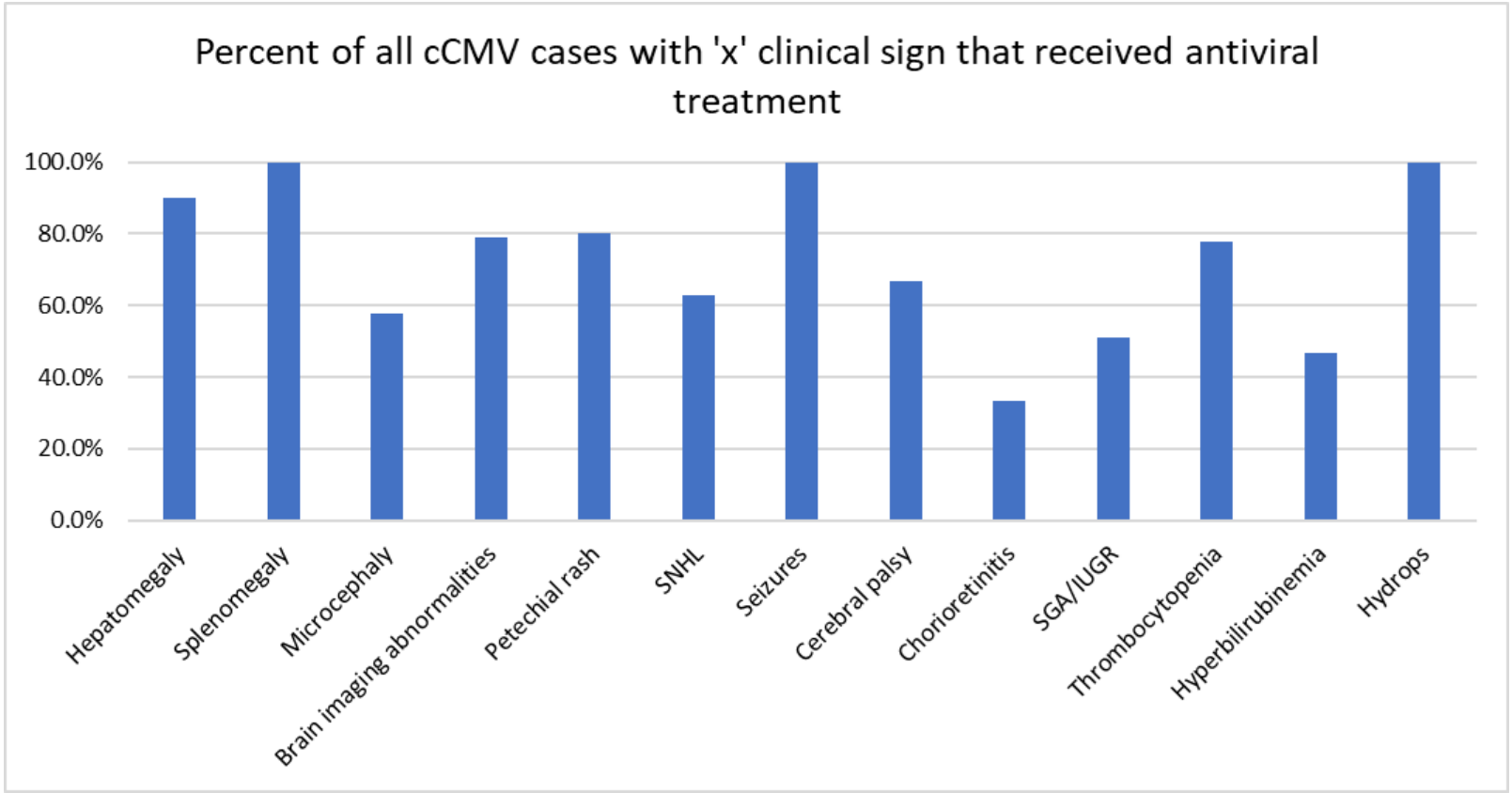


Clinical signs



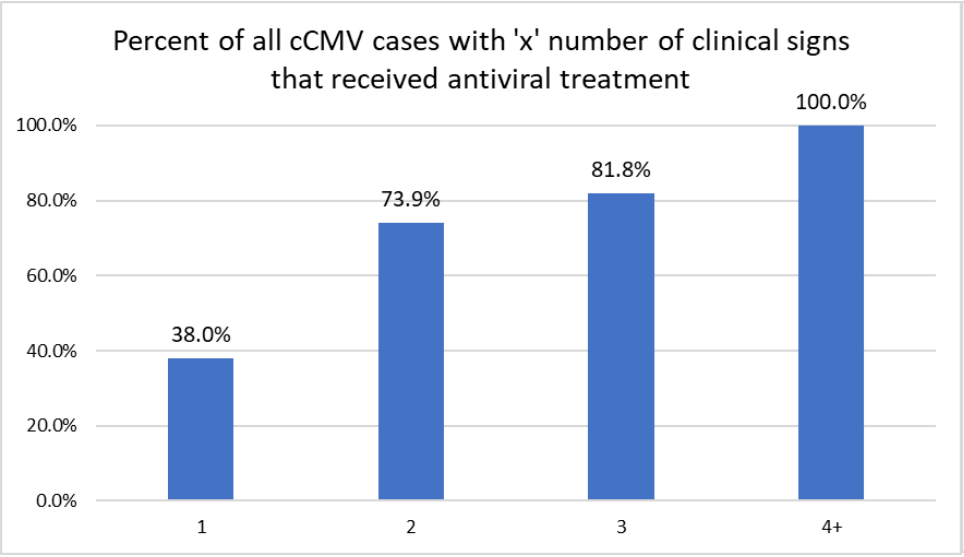
Treatment

59 cases with antiviral treatment

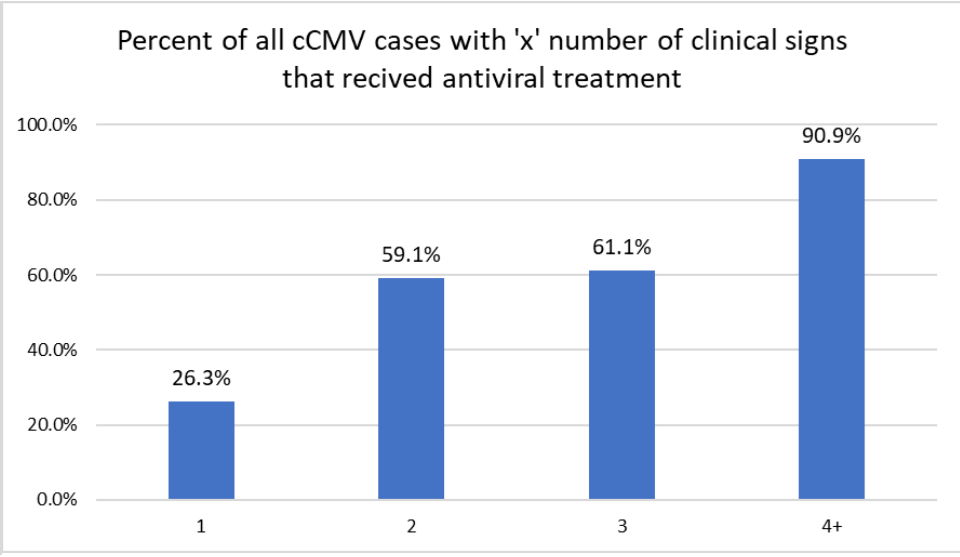


Treatment

CSTE case definition clinical signs



All clinical signs tracked in Utah



*There were 6 cases with no CSTE case definition clinical signs that received treatment

Additional treatment information

- Drug
  - Valganciclovir - **79.7%**
  - Ganciclovir - **20.3%**
- Treatment-induced neutropenia - **30.5%**
  - Of these, at least 44% still completed 6-month course of treatment
- Average treatment length - **143 days**

Case demographics

Demographics

cCMV cases	All of Utah
• Sex	• Sex
53% Female	**49.2%** Female
• Maternal ethnicity	• Ethnicity
13.3% Hispanic	**15.1%** Hispanic/Latino
• Maternal race	• Race
83% White	**90%** White
3% American Indian/Alaska Native	**1.5%** American Indian/Alaska Native
3% Asian	**2.8%** Asian
2.2% Black	**1.6%** Black
2.2% Native Hawaiian/Pacific Islander	**1.2%** Native Hawaiian/Pacific Islander

Demographics

cCMV cases	All of Utah
• Maternal education	• Education
26.7% College graduate	**24.1%** College graduate
29.6% Some college	**34.2%** Some college/Associate's
22.2% High school graduate/GED	**22.1%** High school graduate/GED
7.4% Less than high school	**6.8%** Less than high school
• Maternal language spoken at home	• Language spoken at home
88.1% English	**84.6%** English
• Home county	• Home county
79.3% Urban	**81.5%** Urban
18.5% Rural/frontier	**18.5%** Rural/frontier

Cases by county

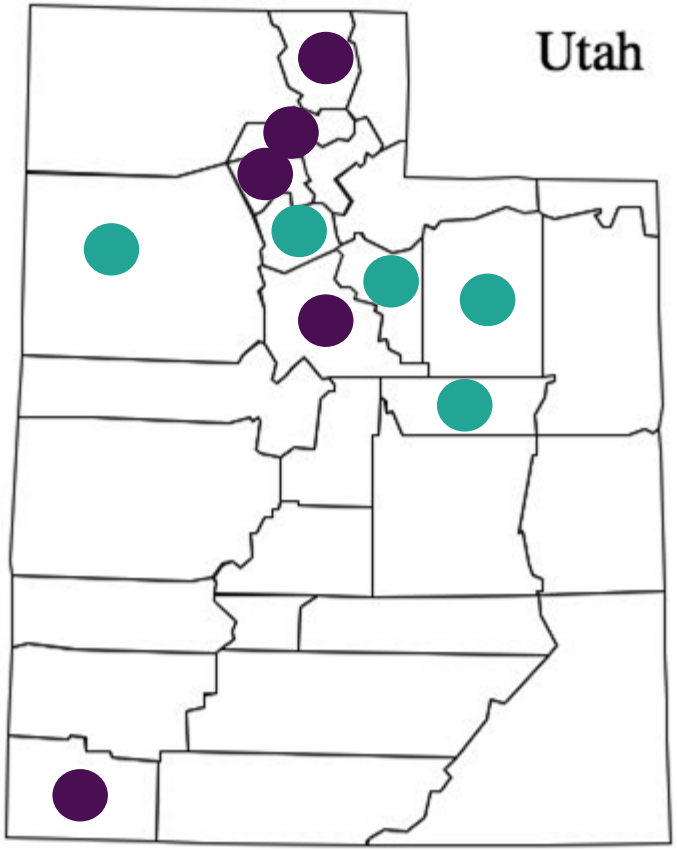
County number	Percent of cCMV cases	Percent of Utah's population
1	45.9%	36.3%
2	17.8%	21.5%
3	6.7%	11.3%
4	6.7%	8.2%
5	3.7%	2.4%
6	3%	1.1%
7	3%	6%
8	2.2%	4.3%

County number	Percent of cCMV cases	Percent of Utah's population
9	1.5%	0.6%
10	1.5%	0.6%
11	1.5%	1.9%
12	1.5%	1.1%
13	0.7%	0.2%
14	0.7%	0.4%
15	0.7%	0.9%
16	0.7%	1.3%

Any geographic patterns?

More cases than expected

Fewer cases than expected



Takeaways

- No demographic/geographic patterns
    - Difficult to identify key areas for intervention
    - Confident we are capturing cases that represent the overall affected population of Utah

Thank you!

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