Congenital cytomegalovirus (cCMV) surveillance: a recently added threat in the Surveillance for Emerging Threats to Pregnant People and Infants Network (SET-NET)

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DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

DEPARTMENT OF HEALTH

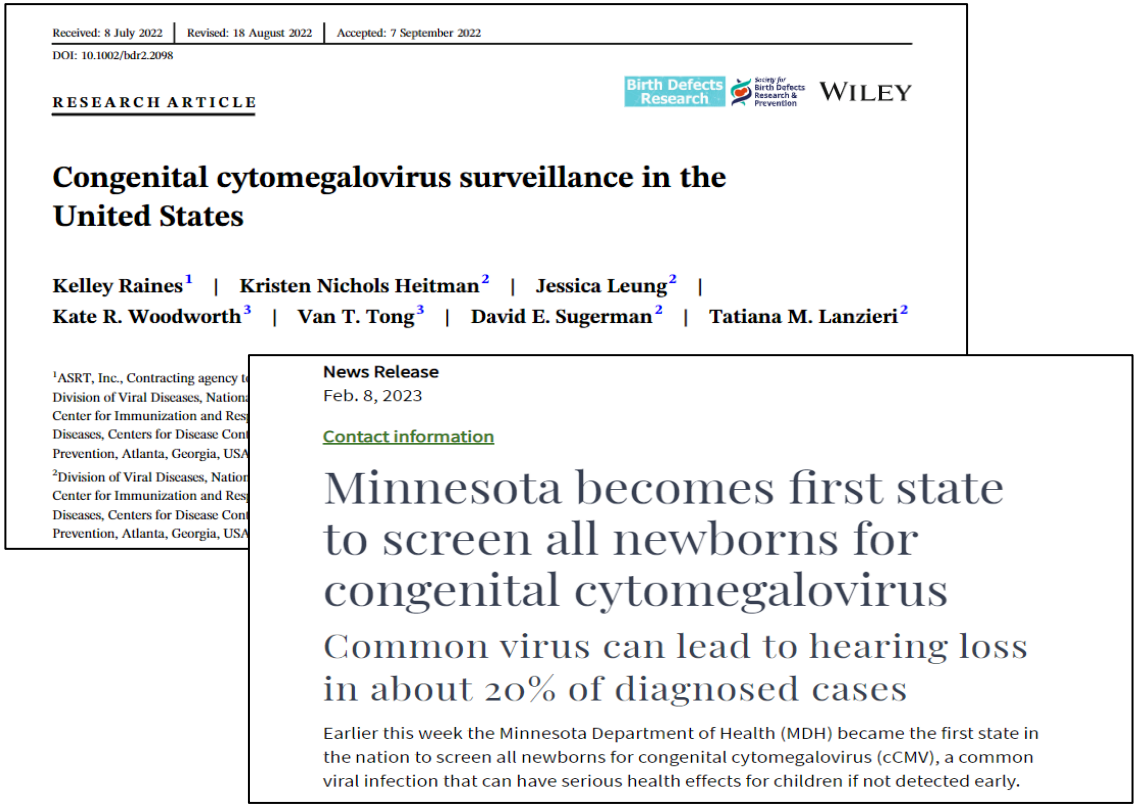
Agenda

- Summarize the status of state-level cCMV surveillance in the United States
- Describe the goals and cross-jurisdictional outcomes of the cCMV surveillance pilot within SET-NET
- Report findings from the first year of the SET-NET pilot
  - Across all participating jurisdictions
  - In-Depth report from Minnesota
- Questions and answers

Status of state-level cCMV surveillance in the United States

Status of state-level cCMV surveillance in the U.S.

Eleven* states systematically collect cCMV surveillance data:
New Jersey (1985), Colorado (1987), Illinois (1989), Oklahoma (1994), Delaware (2003), Michigan (2011), Utah (2013), Connecticut (2016), New York (2016), Virginia (2020), Minnesota (2023)



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RESEARCH ARTICLE

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Congenital cytomegalovirus surveillance in the United States

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News Release
Feb. 8, 2023

Contact information

Minnesota becomes first state to screen all newborns for congenital cytomegalovirus

Common virus can lead to hearing loss in about 20% of diagnosed cases

Earlier this week the Minnesota Department of Health (MDH) became the first state in the nation to screen all newborns for congenital cytomegalovirus (cCMV), a common viral infection that can have serious health effects for children if not detected early.

*Since 2022, legislation for targeted hearing screening for cCMV has been enacted in Florida, Kentucky, Louisiana, and Maine with cCMV surveillance practices unknown

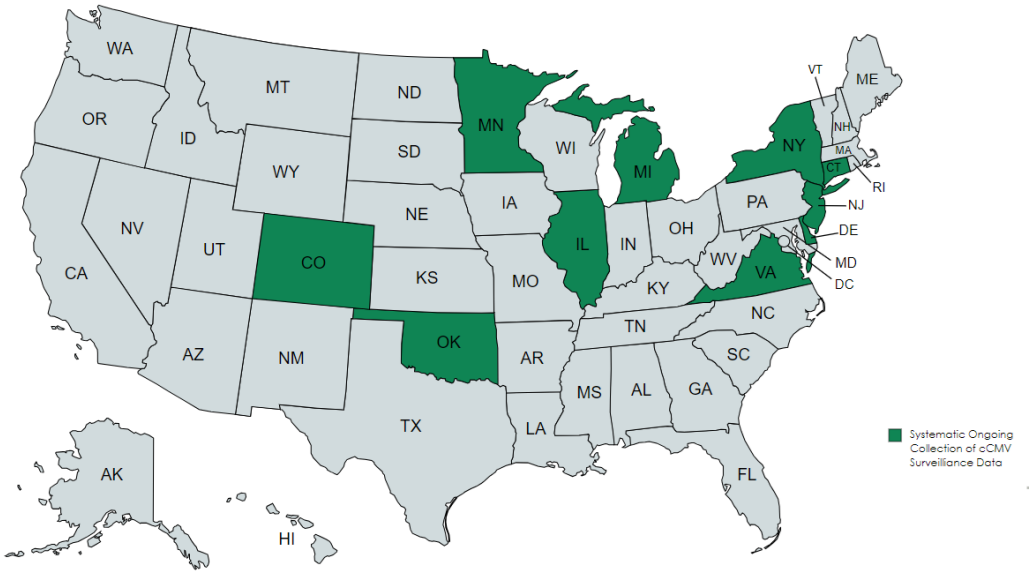
Status cCMV Surveillance: Methods of Surveillance

Method of Ascertainment/Reporting:

- Laboratory results (DE, UT, CT, VA, MN)
- Diagnostic codes (NJ, CO, IL, OK, NY)
- Reported diagnosis (NJ, CO, IL, NY)

cCMV Screening Practices:

- Targeted hearing screening (UT, CT, NY, VA)
- Universal screening (MN)
- High-risk symptom screening (UT)



Status of cCMV Surveillance: Data Elements Collected

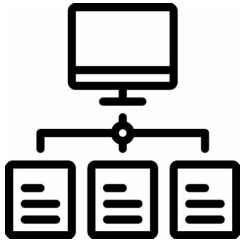
State	Data Elements Collected						Data Analysis Capacity¶	Data Disseminated††
	Demographics	Clinical Signs	Laboratory	Treatment	Long-term Outcomes	Maternal		
New Jersey	X	X					X	
Colorado	X					X	X	
Illinois	X	X		X		X§	X	X
Oklahoma	X	X				X§	X	
Delaware	X	X	X			X§	X	
Michigan	X	X				X	X	X
Utah	X	X	X	X	X	X§	X	X
Connecticut	X	X	X	X		X	X	
New York	X					X	X	
Virginia	X	X	X	X		X	X	X
Minnesota	X	X	X	X	X	X	X	X
Total	**11**	**9**	**5**	**5**	**2**	**10**	**11**	**5**

§ Maternal infection data collected along with maternal demographics
¶ Includes states who showed the capacity to analyze birth prevalence
††Includes states who developed summaries, reports, or visualizations that they reported sharing

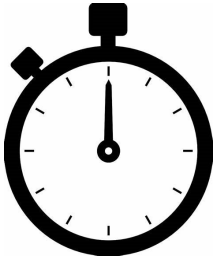
Status of cCMV Surveillance: Challenges Reported

Limited Personnel

Limited Funding



Complex and Siloed Data Systems



Delays in Case Data Submission

Incomplete Reporting

CSTE

Lack of Standardized Case Definition

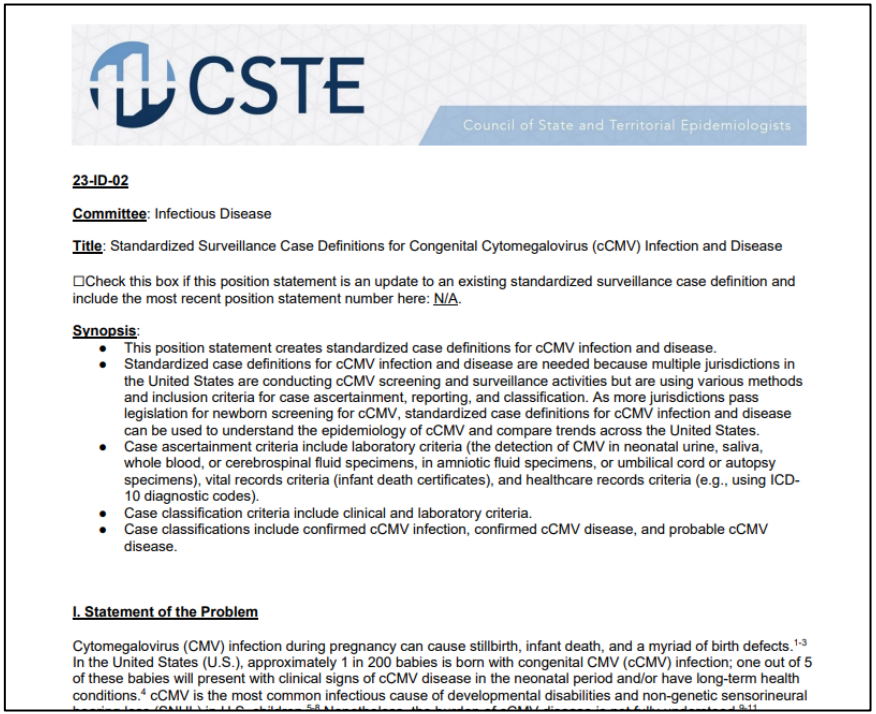
CSTE: Council of State and Territorial Epidemiologists

Status of cCMV Surveillance: Standardized Case Definition

What was approved by CSTE at the annual June meeting (effective Jan 2024):

1. Reporting criteria
2. Case classifications based on clinical and laboratory evidence:

Case Classification	Laboratory Evidence	Clinical Evidence
Confirmed cCMV infection	Confirmatory	No
Confirmed cCMV Disease	Confirmatory	Yes
Probable cCMV disease	Presumptive	Yes



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

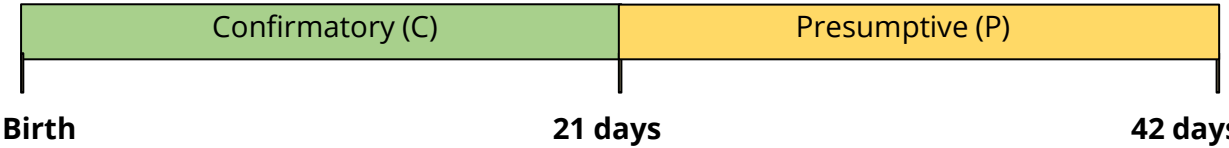
Status of cCMV Surveillance: Standardized Case Definition

Reporting Criteria

- Laboratory
  - CMV-positive PCR or culture of urine, saliva, whole blood, dried blood spot, CSF **or**
  - detection of CMV antigen in other specimens (umbilical cord, autopsy specimen, whole blood)
- Vital Records
  - An infant aged one year or less whose death certificate lists cCMV or CMV as an underlying cause of, or significant condition contributing to, death
- Healthcare Record
  - A child aged 6 years or younger with a diagnosis of cCMV infection (P35.1) **or**
  - An infant aged 45 days or younger with a diagnosis of CMV disease (B25.x)

Status of cCMV Surveillance: Standardized Case Definition

Laboratory Evidence



Specimens	NAAT	Culture	Antigen Test	Specimens	NAAT	Culture	Antigen Test
Urine	C	C		Urine	P	P	
Whole blood	C	C	C	Whole blood	P	P	P
Dried blood spot	C						
CSF	C	C		CSF	P	P	
Saliva*	P	P		Saliva*	P	P	

*Presumptive in absence of negative urine test; requires confirmation with urine test <21 days to become "confirmatory"

Status of cCMV Surveillance: Standardized Case Definition

Clinical Evidence

- An infant with at least one of the following clinical signs **during the neonatal period**:
  - Hepatomegaly
  - Splenomegaly
  - Petechial rash or purpura

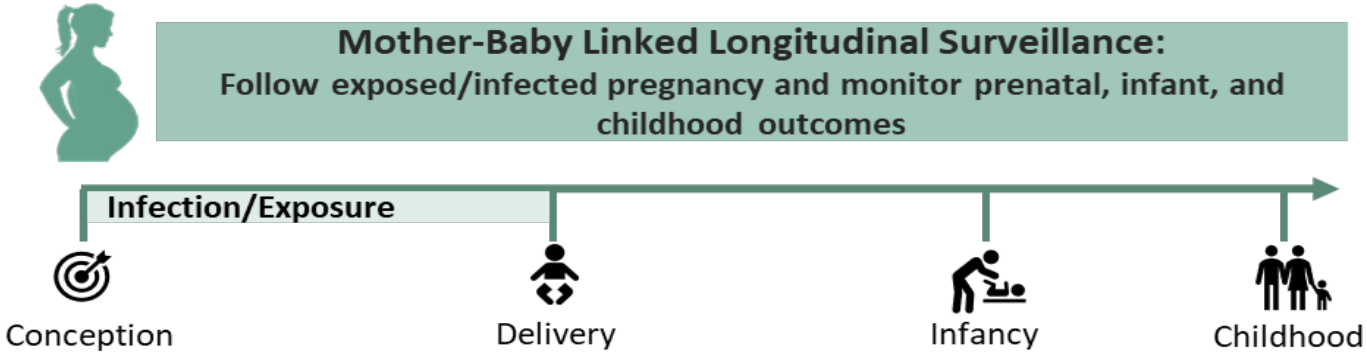
- A child aged **6 years or younger** with one or more of the following permanent conditions:
  - Microcephaly
  - Brain imaging abnormalities consistent with cCMV
  - Sensorineural hearing loss
  - Seizures
  - Cerebral palsy
  - Chorioretinitis
  - Vision impairment, resulting from conditions consistent with cCMV

Goals and outcomes of the cCMV surveillance pilot within SET-NET

cCMV SET-NET Surveillance Pilot: What is SET-NET?

Surveillance for Emerging Threats to Pregnant People and Infants Network

- State, local, and territorial health departments work with CDC to identify the impact of emerging health threats on pregnant people & infants
- Collects information on five infectious diseases, including cCMV



Used to inform **clinical and public health guidance**

cCMV SET-NET Surveillance Pilot: Participants and Activities

Eight jurisdictions participating in the cCMV SET-NET Pilot:

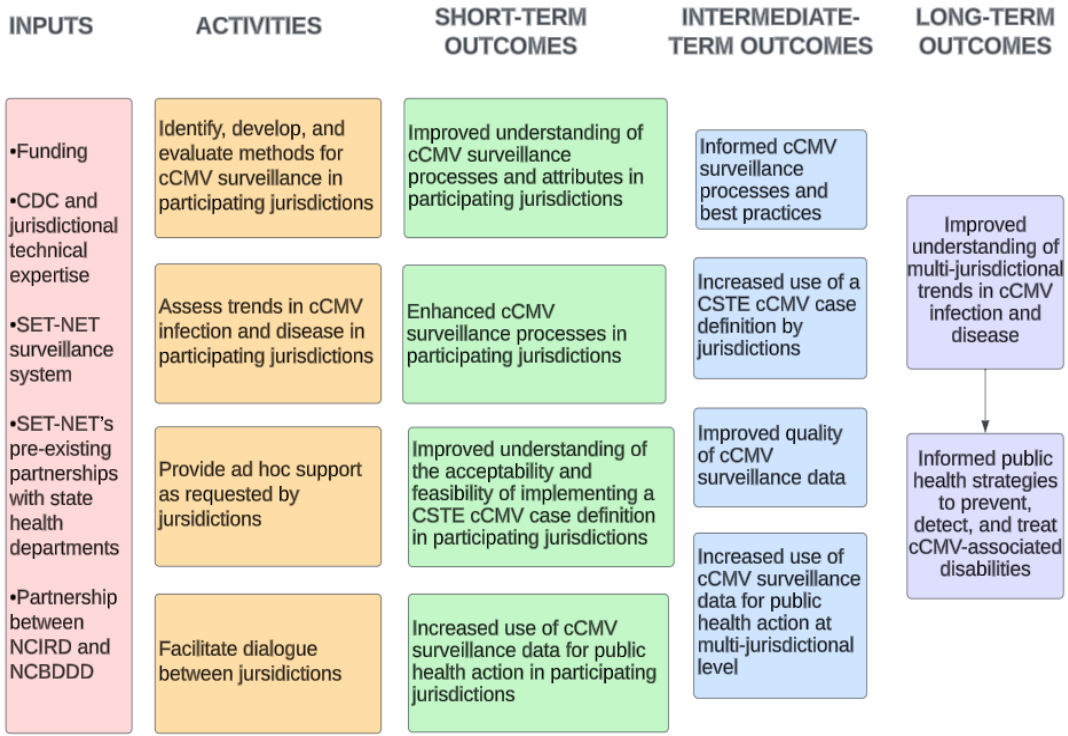
- Year 1 (2022-2024): Minnesota, Utah, New York, New Jersey & Iowa
- Year 2 (2023-2024): **Plus,** LA County, Virginia, Illinois

Year 1 (2022-2023) Objectives:

- Identify, develop, and evaluate surveillance methods for cCMV
- Assess trends in cCMV infection and disease (**aggregate data** submitted)

Year 2 (2023-2024) Objectives:

- Identify, develop, and evaluate surveillance methods for cCMV
- Assess trends in cCMV infection and disease (**case-level data** submitted)



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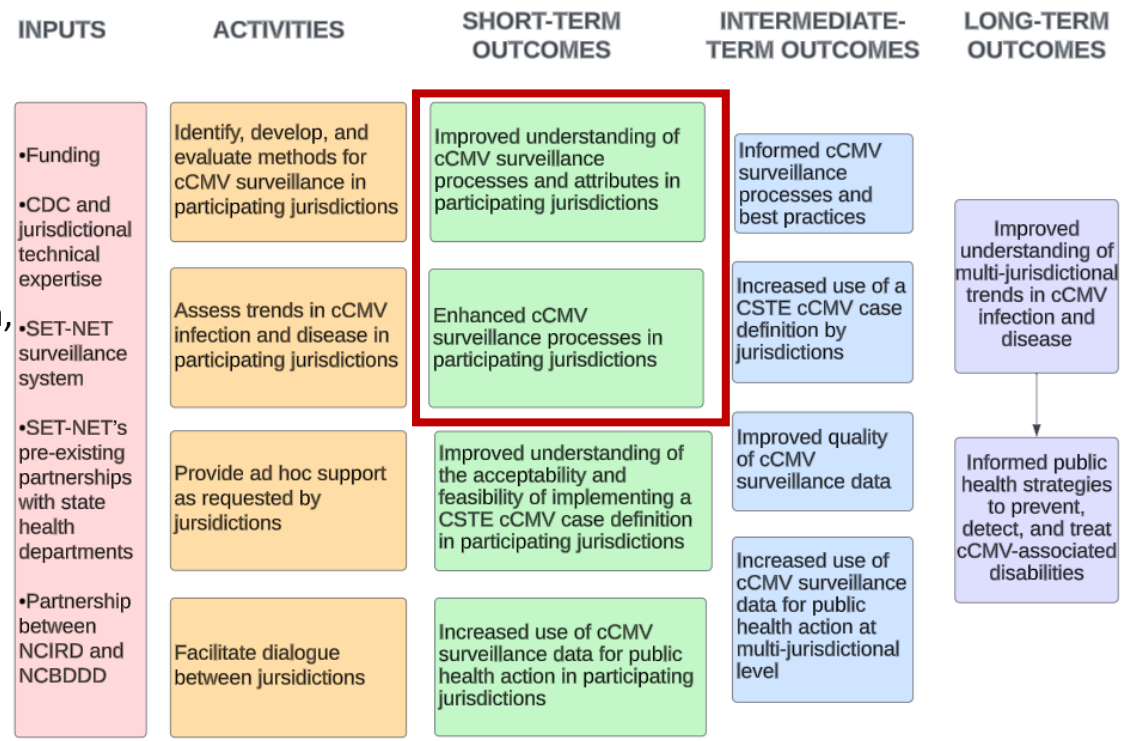
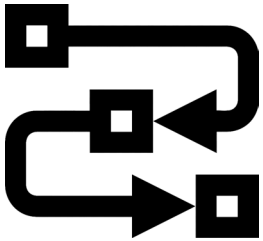


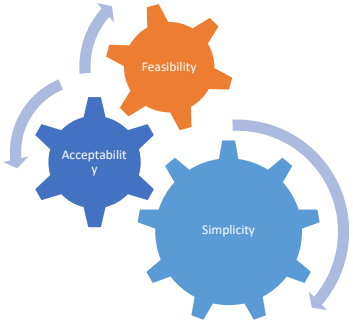
cCMV SET-NET Surveillance Pilot: Preliminary Findings (Year 1)

Outcome #1: Improved understanding of cCMV surveillance methods and attributes

Identify and **evaluate** jurisdictions' cCMV surveillance methods by collecting information on:



Surveillance Processes



Acceptability and Simplicity of Surveillance

Data Completeness

Surveillance Data (Aggregate)

cCMV SET-NET Surveillance Pilot: Preliminary Findings (Year 1)

Surveillance Processes as of July 2023:

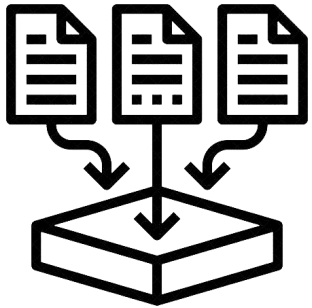
Surveillance Criteria	Utah	Minnesota	New Jersey	New York*	Iowa*
Conducting cCMV Surveillance	Yes	Yes	Yes	Yes	No
Method of Ascertainment/ Reporting	Laboratory Results	Laboratory Results or Diagnostic Code	Laboratory Results, Diagnostic Code, or Clinical Report	Diagnostic Code	N/A
cCMV Case Classification	Confirmed: Positive PCR or viral culture test (Urine, Saliva, Blood, CSF) before 21 days of of life	Confirmed: Positive NAAT from urine, urine, whole blood, or CSF within 21 21 days of life. Probable: Positive NAAT from saliva saliva within 42 days and NAAT from from urine, whole blood, or CSF within 22 – 42 days of life with clinical signs. (CSTE Case Definition) Definition)	Confirmed: Clinical report, Diagnostic code, or Positive PCR PCR test (Urine, Saliva, Blood) before before 21 days of life life	Confirmed: Diagnostic Diagnostic Code	N/A

* After July 2023, New York began a pilot for universal screening of cCMV with corresponding surveillance; Iowa added CMV to the Communicable Disease Rule to begin cCMV surveillance

cCMV SET-NET Surveillance Pilot: Preliminary Findings (Year 1)

Reports on Simplicity of cCMV surveillance:

Data Collection



Multiple data sources and complex/unstandardized abstraction processes make data collection challenging

Data Management

System maintenance was reported as fairly simple and can be easily streamlined and/or outsourced

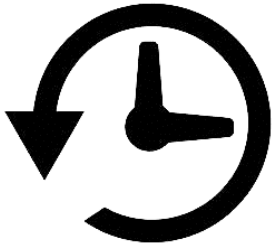
cCMV SET-NET Surveillance Pilot: Preliminary Findings (Year 1)

Reports on Acceptability of cCMV surveillance:

Case Ascertainment/Reporting

Statutes are key for reporting compliance and case ascertainment

Timeliness of Reporting



ELR are received in 1-2 days by MN and UT. Timeliness of non-automated systems is dependent on clinician awareness.

cCMV Awareness

cCMV awareness has been low early in screening/surveillance, leading to the need for consistent training

cCMV SET-NET Surveillance Pilot: Preliminary Findings (Year 1)

Data Collected for cCMV Surveillance (MN and UT)*:

Category of Data	Data Sources	Data Elements	Status of Data Collection^
Laboratory Records	Electronic lab records, newborn screening reports, clinician reports	Infants Testing Results	Systematically collected (MN and UT mandate reporting via lab confirmation)
		Prenatal Testing Results	Not systematically collected
Maternal Information	Infant medical records, vital records	Demographics	Systematically Collected
		Obstetrics Information	Not Systematically Collected
		Ultrasound Results	Not Systematically Collected
Pregnancy and Birth Outcomes	Medical records, vital records, early hearing and detection intervention system, birth defects system	cCMV Clinical Signs	Systematically Collected
		Hearing Screening Results	Systematically Collected
		Adverse Outcomes	Systematically Collected
		Treatment Data	Systematically Collected
Long-Term Follow-Up (MN collected > 1 year; UT on-going follow-up)	Infant medical records, vital records, early hearing and detection intervention system	Referrals (i.e., Ophthalmology and audiology)	Systematically Collected
		Ophthalmologic Evaluation Data	Systematically Collected
		Audiologic Evaluation Data	Systematically Collected
		Brain Imaging Data	Systematically Collected
		Treatment Outcomes	Systematically Collected
		Developmental Screening Data	Not Systematically Collected

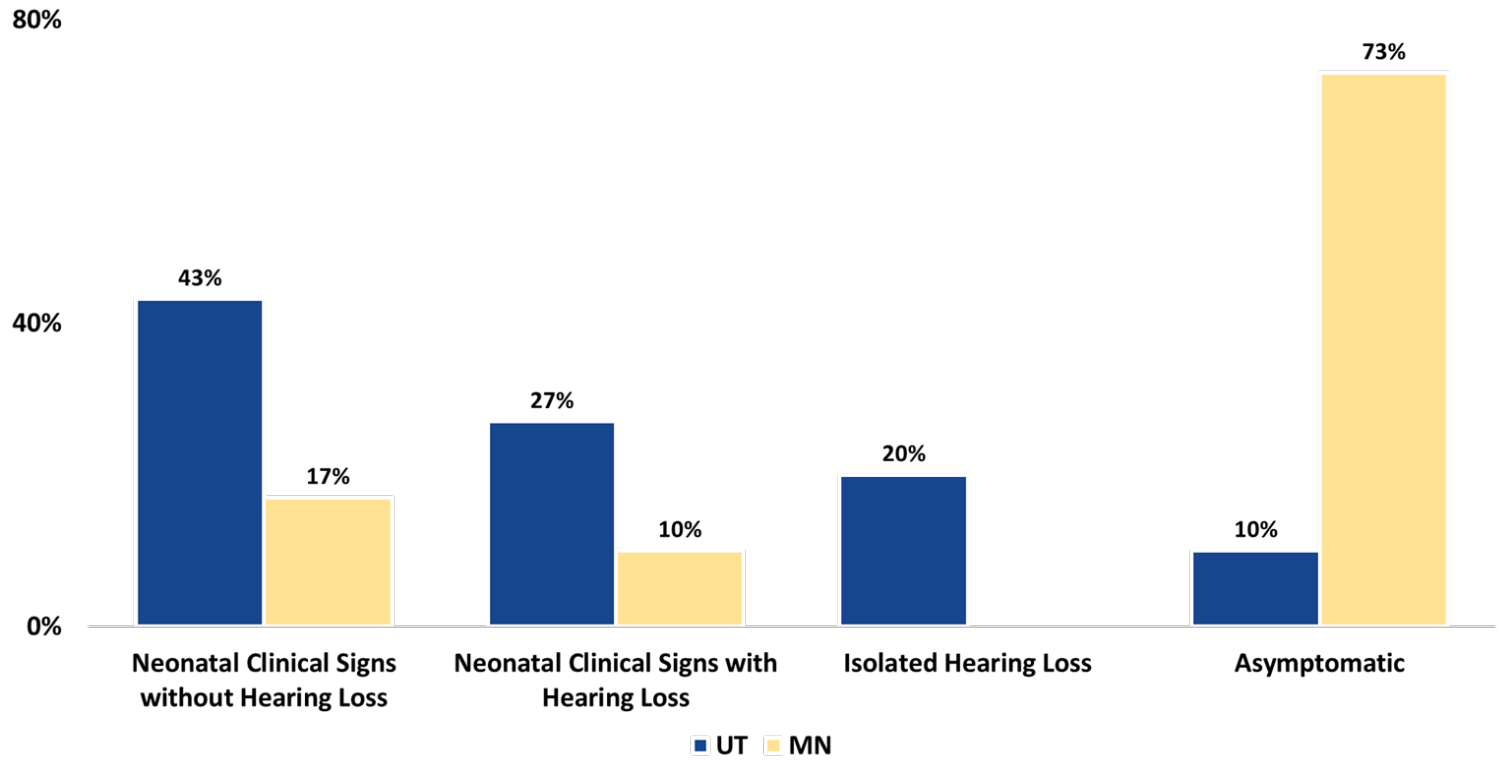
*Summary for MN and UT only as only predictive estimated reported by other participating jurisdictions

^Systematically collected was defined as completeness >80% for variables collected within each data element

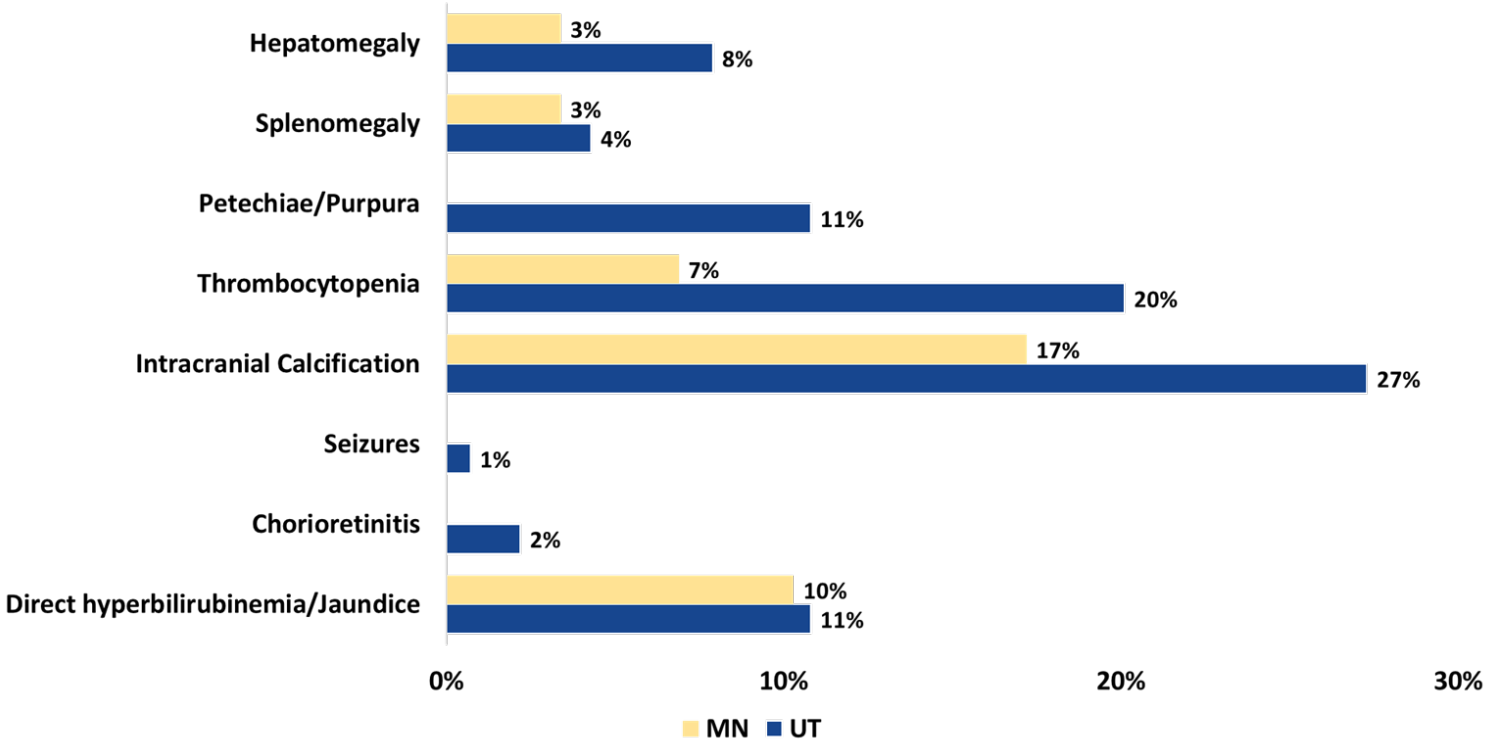
cCMV SET-NET Surveillance Pilot: Preliminary Findings (Year 1)

Jurisdiction	Case Ascertainment	Period for Reported cCMV Cases	Annual Number of Reported cCMV Cases	Annual Prevalence per 1,000 Live Births
Utah	Targeted Hearing and High-Risk Screening	2013 - 2023	4 - 28	0.12 – 0.60
New Jersey	Diagnostic Codes, Clinical Reports	2018 - 2022	16 - 26	0.16 – 0.26
Minnesota	Universal Screening	2023	29	1.96

cCMV SET-NET Surveillance Pilot: Preliminary Findings (Year 1)



cCMV SET-NET Surveillance Pilot: Preliminary Findings (Year 1)



cCMV SET-NET Surveillance Pilot: Key Activities (Year 1)

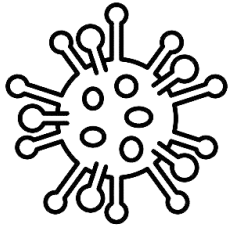
Outcome #2: Enhanced cCMV surveillance processes in participating jurisdictions

Two jurisdictions started cCMV surveillance

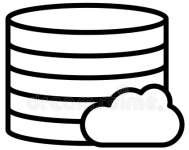
Jurisdictions established data use agreements

One jurisdictions evaluated and backfilled missing cCMV surveillance

One jurisdiction surveyed the processes of targeted screening hospitals



Two jurisdictions added/in the process of adding cCMV to the communicable disease rule



Jurisdictions developed cCMV specific databases

Jurisdictions collaborated with programs across the HD for cCMV surveillance

Jurisdictions shared surveillance best practices with each other

cCMV SET-NET Surveillance Pilot: Participants and Activities

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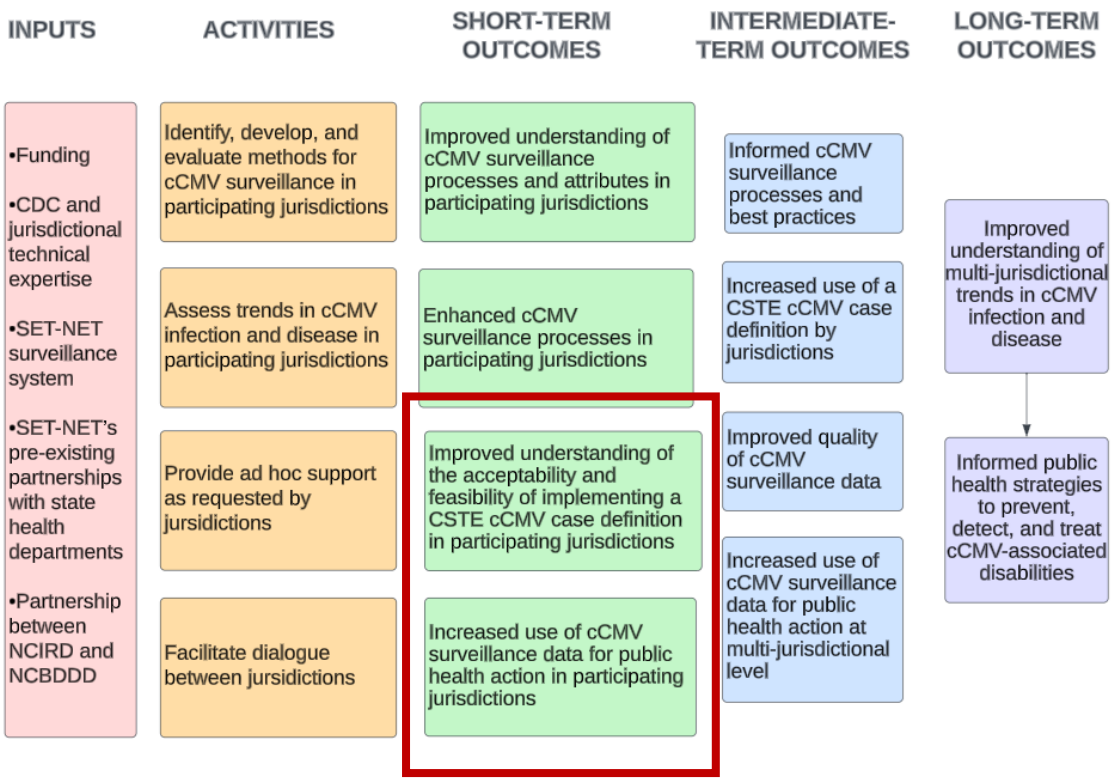
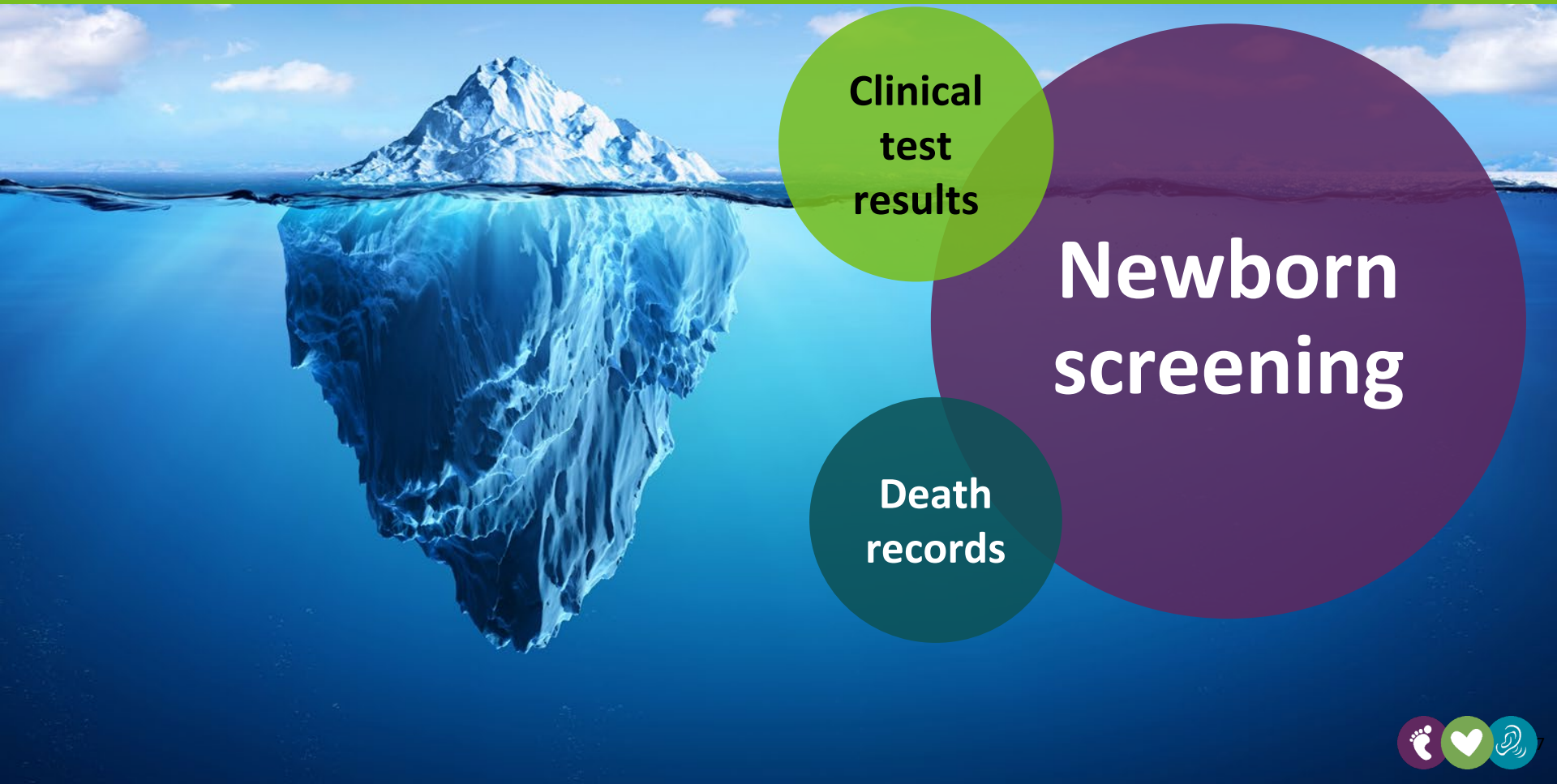
- Assess trends in cCMV infection and disease (**aggregate data** submitted)

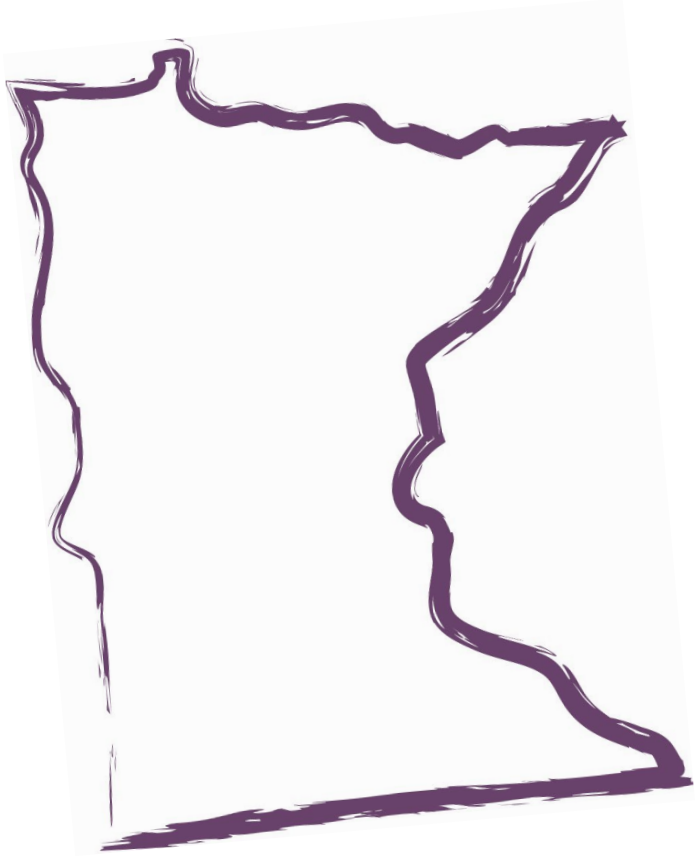


Minnesota Surveillance Process & Attributes

Case ascertainment in Minnesota



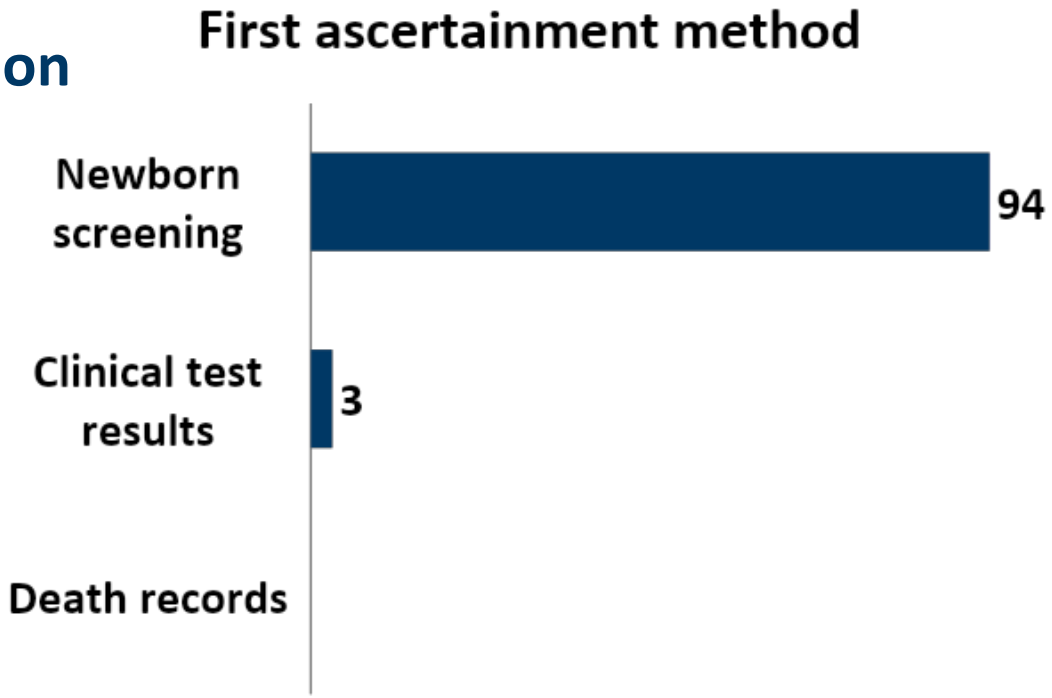
cCMV surveillance in Minnesota



- Statewide, population-based
- Reporting criteria
  - cCMV/CMV listed as cause of death
  - Positive laboratory test ≤ 90 days of life
- Case definition:
  - Resident of MN at birth
  - Born on/after February 6, 2023
  - Meets CSTE case definition for cCMV
  - Initial data collection complete

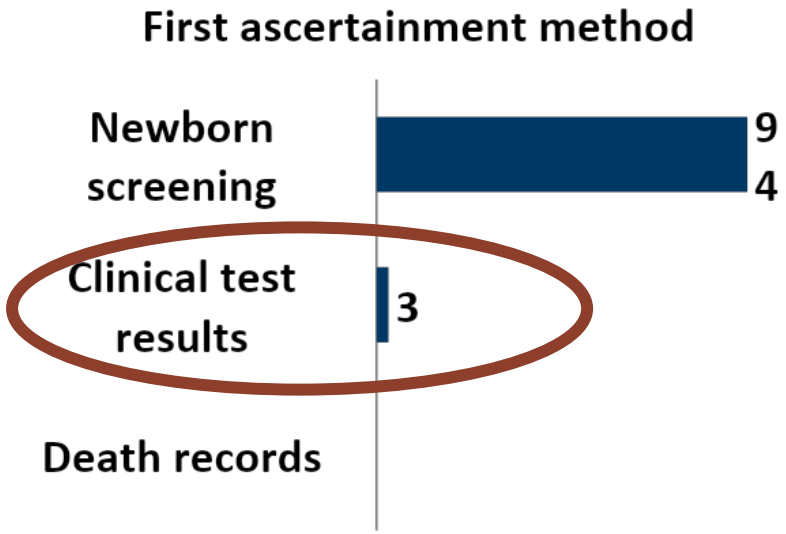
Preliminary surveillance data in Minnesota
February 6–August 5, 2023

- **97 infants meeting inclusion criteria reported**
- **78 with initial data collection complete**

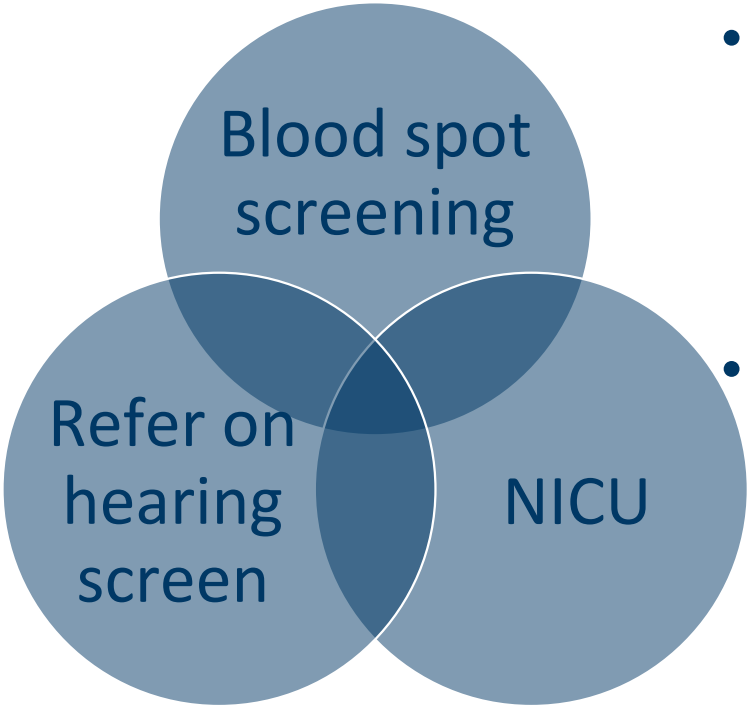


We only know what we know

- cCMV is not a reportable disease (yet)
  - Cannot mandate clinical reporting
  - 3 of 6 clinical labs voluntarily reporting positive results
- With universal screening, will providers assume we already know about the case?



Targeted screening still useful



- **Even after mandated reporting, asymptomatic babies are unlikely to be tested and reported**
- **Targeted screening can pick up more**

Feasibility & Acceptability of Applying a Case Definition

Applying the CSTE surveillance case definition

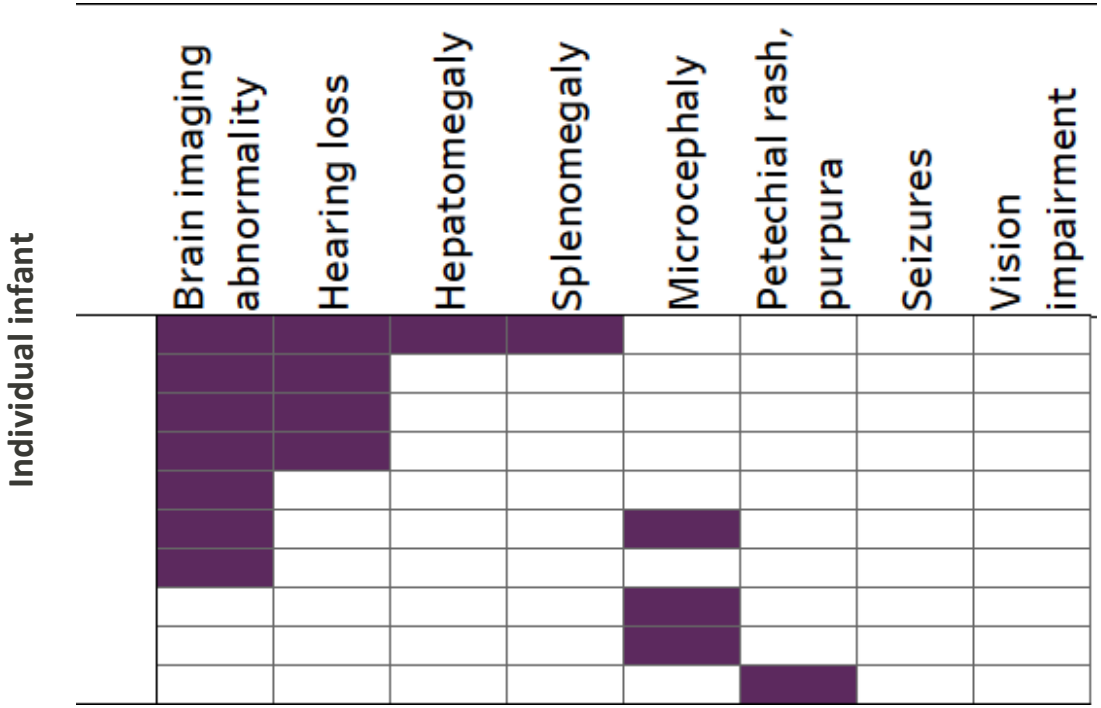
- **Laboratory criteria**
  - **Confirmatory: 72 (92%)**

    - Dried blood spot (DBS) collected ≤ 21 days, no negative urine
  - **Presumptive: 2 (3%)**

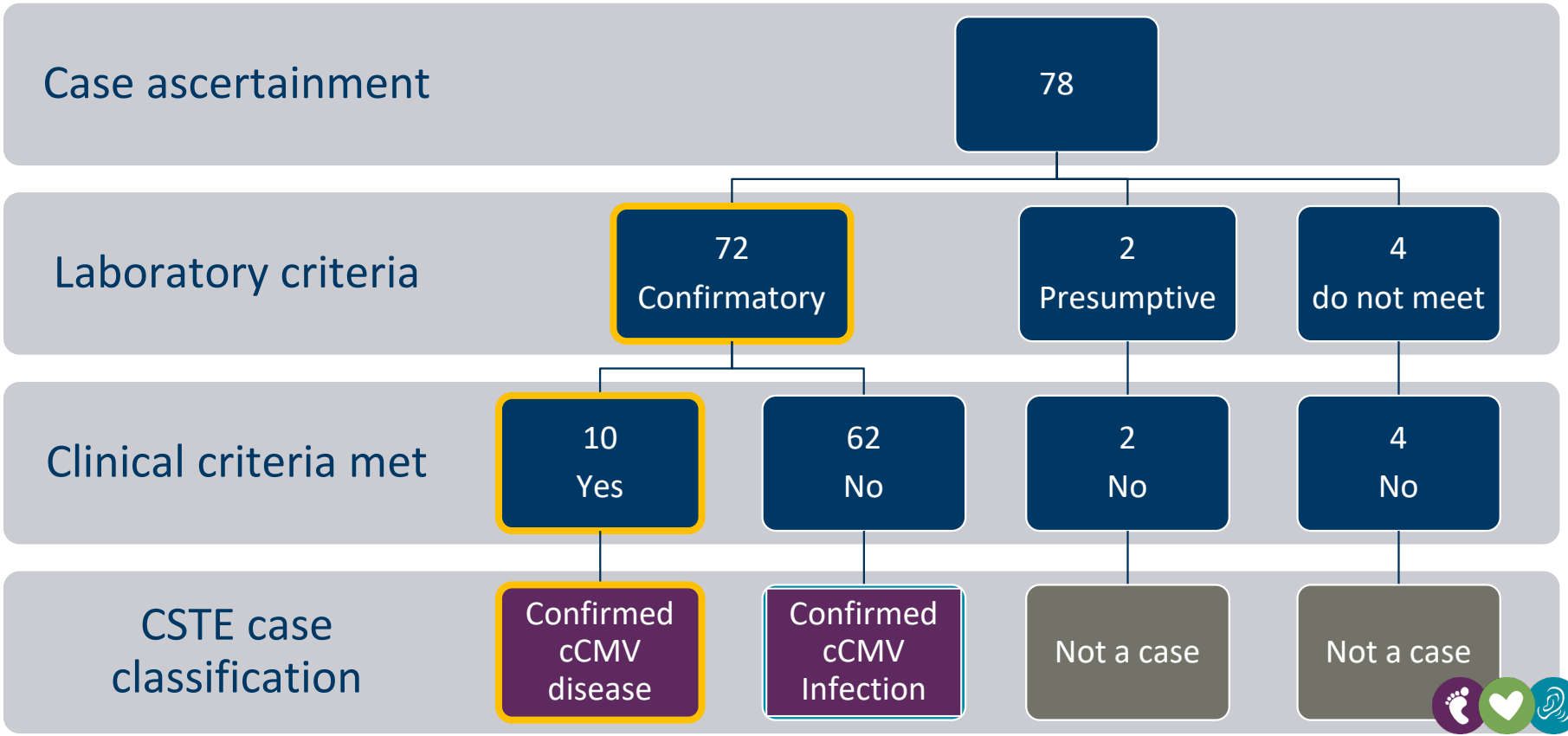
    - Dried blood spot collected 21 ≤ 42 days, no negative urine
  - **Does not meet: 4 (5%)**
    - Positive blood or saliva with a negative urine (and negative DBS)
    - Positive urine with prior negative urine, whole blood, DBS
    - Positive DBS with negative confirmatory urine

Applying the CSTE surveillance case definition

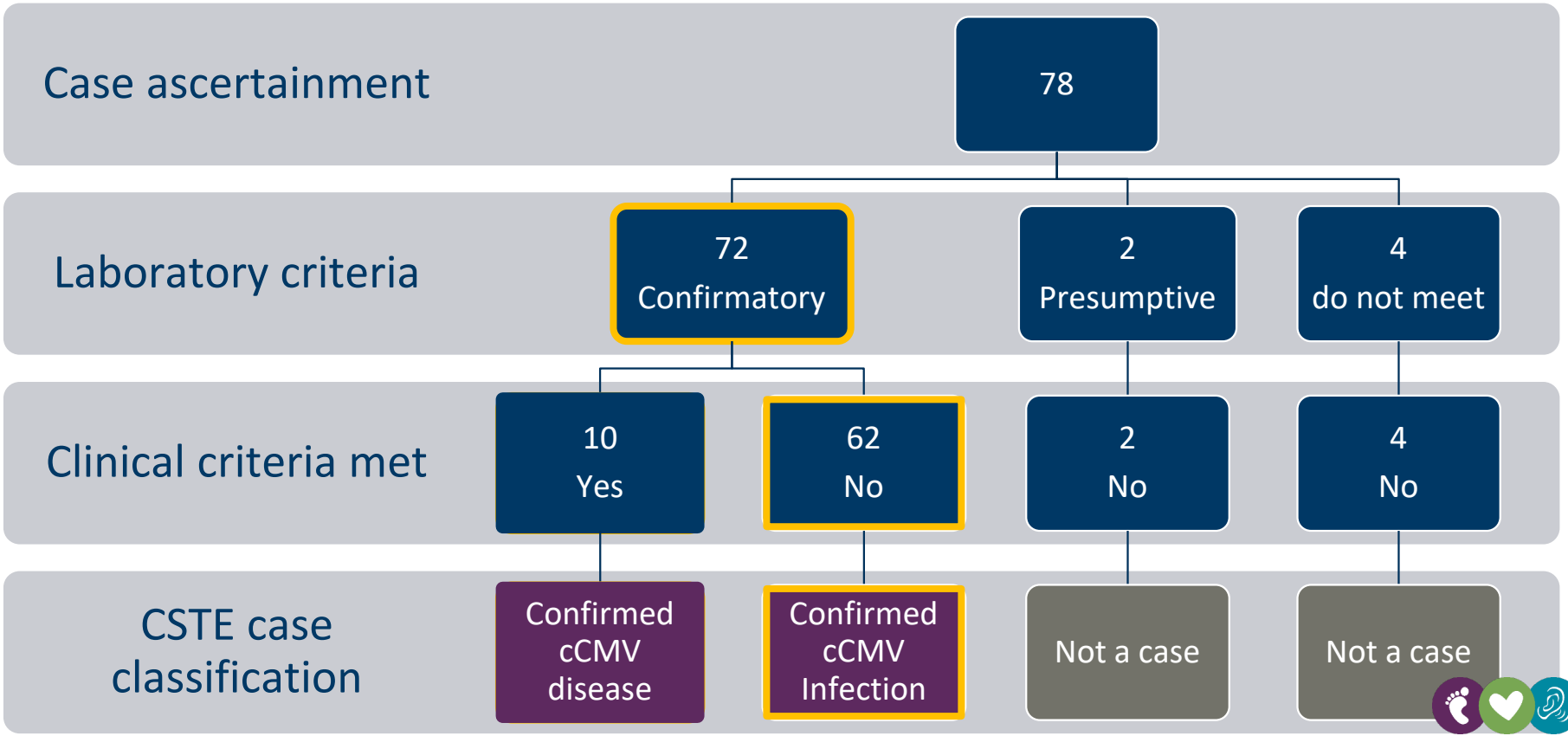
- **Clinical criteria**
  - **Yes, 10 (13%)**
  - **No, 68 (87%)**



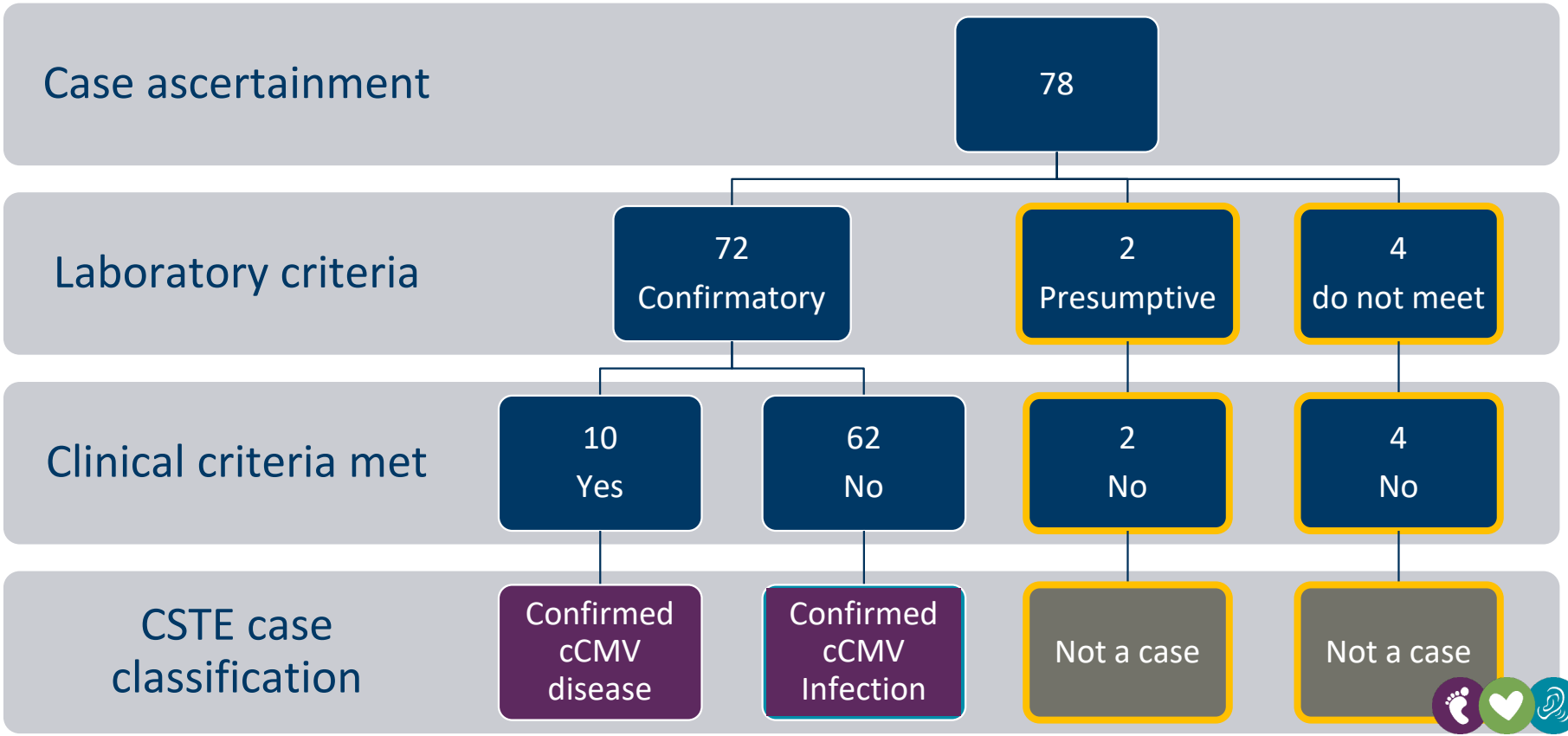
Applying the CSTE surveillance case definition



Applying the CSTE surveillance case definition

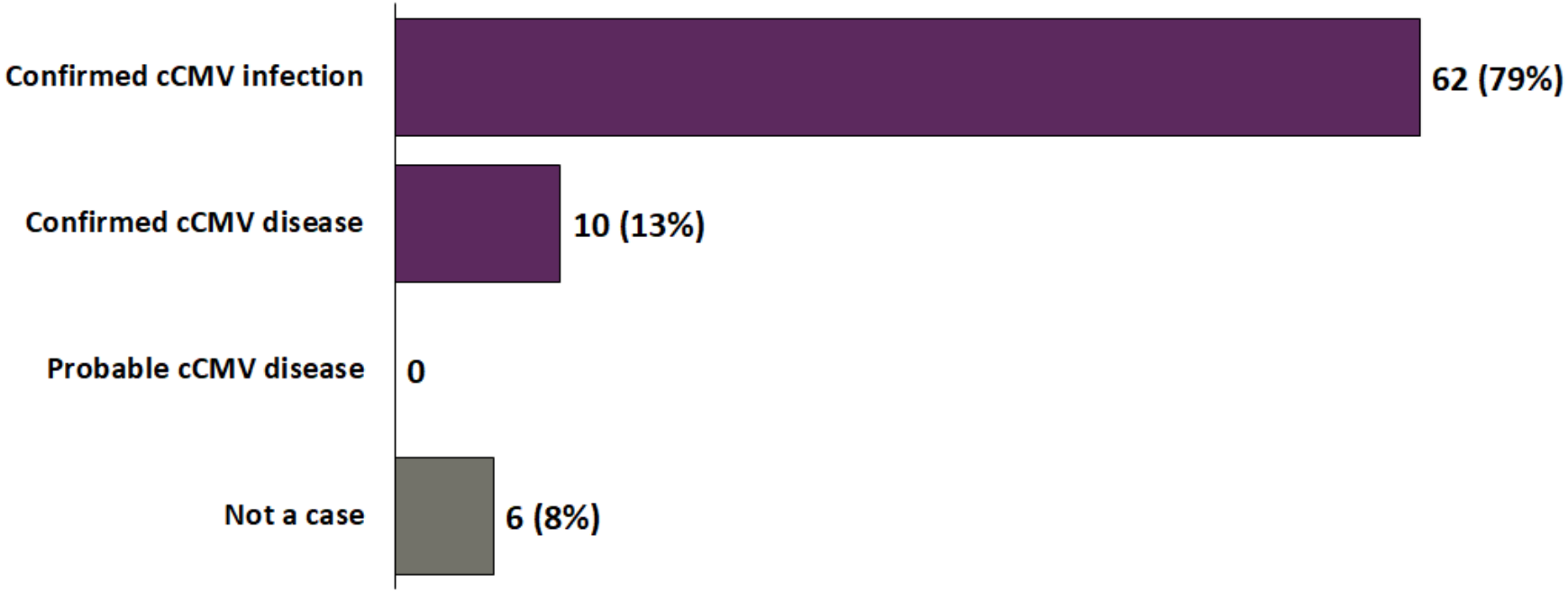


Applying the CSTE surveillance case definition



Applying the CSTE surveillance case definition

72 (92%) of ascertained cases **meet the CSTE standardized surveillance case definition**



Feasibility of standardized case definition

- **Feasible from an epidemiological/surveillance standpoint**
  - **Acceptance that public health data are messy**
  - **All information collected by newborn screening follow-up**

- **Resource intensive**
  - **Medical record abstraction takes 1-3 hours per infant**

Feasibility of standardized case definition

- **Brain imaging data collection**
  - **Complex medical information**
  - **“Brain imaging abnormalities consistent with cCMV, such as intracranial calcifications,…”**
- **Hard to tell whether something was due to cCMV or alternative diagnosis**
  - **“In the absence of a more likely alternative etiology:”**

Acceptability of standardized case definition

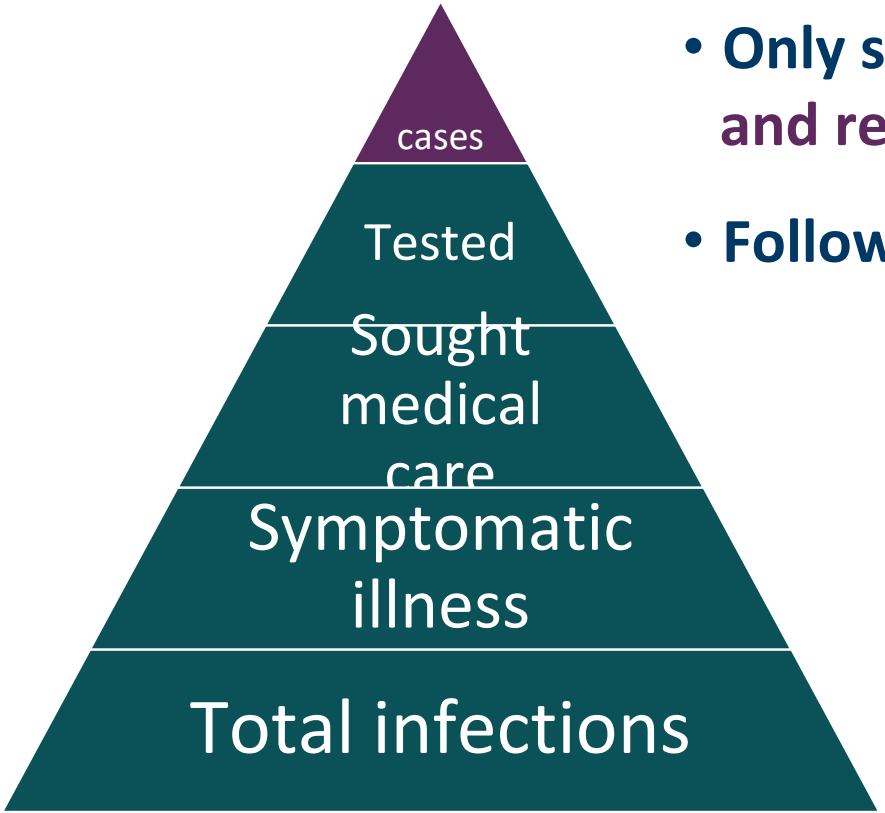
- **Difficult from newborn screening which has a more clinical perspective**
  - **Asymptomatic, mildly symptomatic, moderate/severely symptomatic do not align well with case definition**
  - **Dried blood spot positive without confirmatory specimen**
    - **Confirmed surveillance case**
    - **“No follow-up” for screening- not useful for performance metrics**

Acceptability of standardized case definition

- **Separate screening and surveillance**
  - **Newborn screening would be a data source and aid in defining cohort**

Use of Surveillance Data for Public Health Action

Typical infectious disease case ascertainment

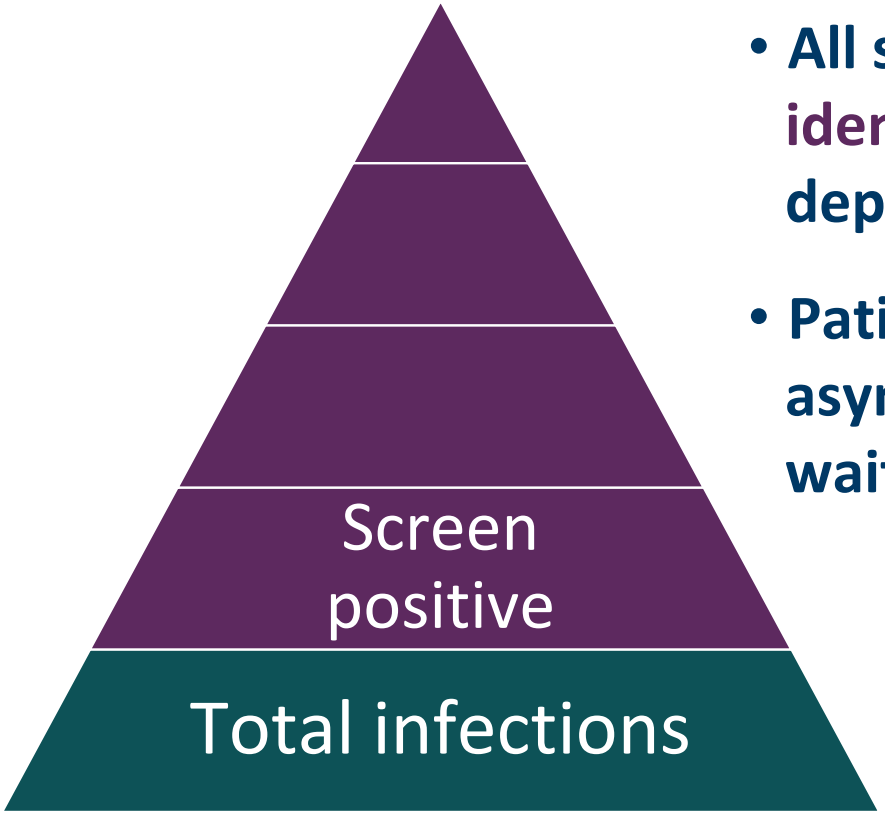


- **Only symptomatic cases are identified and reported to health departments**
- **Follow-up is defined**

Use of infectious disease surveillance

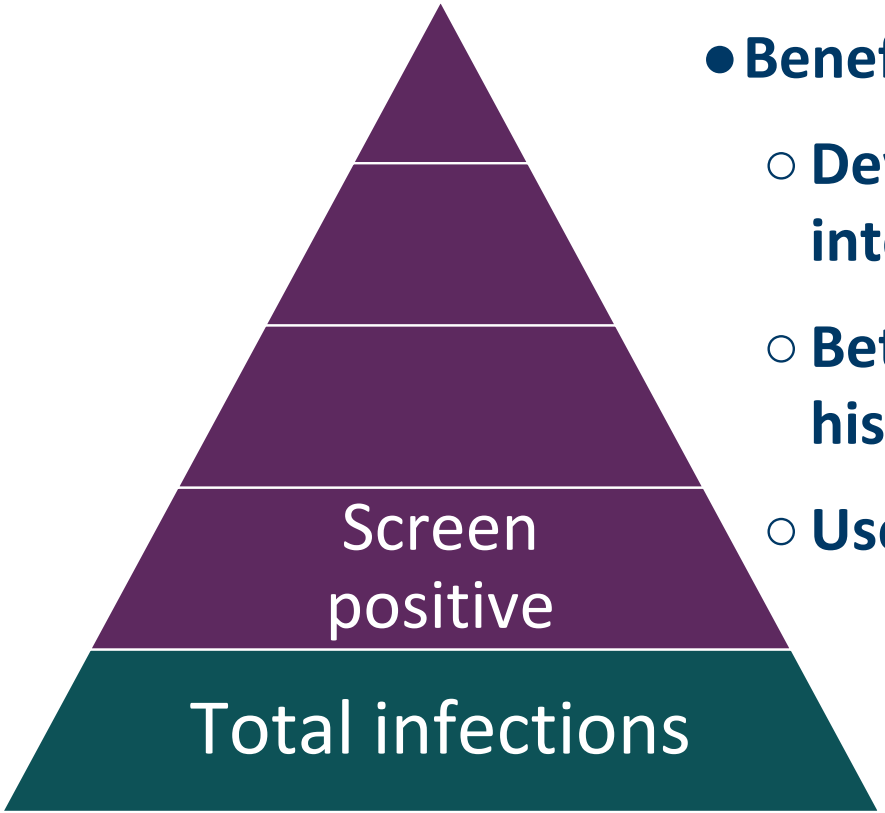
- Surveillance data support public health action
- Most well known for outbreak detection
  - Mostly acute diseases
- Identify at-risk groups
- Estimate burden
- Public health action is quick
  - -Remove the implicated source = stop the outbreak
  - -Protect against additional illness

cCMV with universal screening case ascertainment



- **All screen-positive cases are identified and reported to health department**
- **Patients without hearing loss and asymptomatic are now “patients in waiting”**

cCMV with universal screening



- **Benefits to identifying all infections**
  - **Developmental monitoring, early intervention**
  - **Better understanding of natural history**
  - **Useful for prevention**

Comparison of surveillance purposes

Typical Infectious Disease Surveillance	cCMV Surveillance
Most well known for outbreak detection	CMV is ubiquitous, does not occur in outbreaks
Mostly acute diseases	
Public health action is quick	
Remove the implicated source = stop the outbreak	
Protect people from getting sick	
Identify at-risk groups; estimate disease burden	

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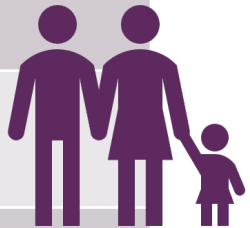

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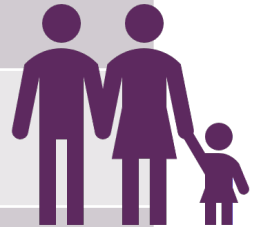

Comparison to petting zoos

Comparison of surveillance purposes

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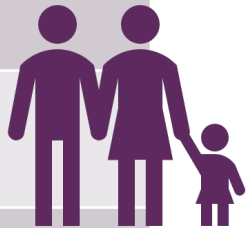

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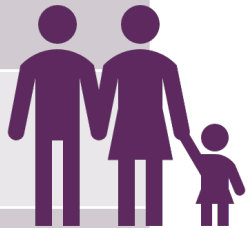

Using surveillance data in Minnesota

- **cCMV consortium, hear from families and providers**
- **Congenital community of practice at MDH**

Using multistate surveillance data

- **How can multistate surveillance help situations like these?**
  - **Increase conversation about inherent risks**
  - **Pool data collected to increase knowledge**
  - **Lead to new or improved public health action**

cCMV Surveillance: What's Next?

- Develop cCMV surveillance best practices
- Enhance awareness, implementation, and evaluation of the CSTE cCMV case definition
- Evaluate and improve cCMV surveillance data quality
- Increase use of cCMV surveillance data for public health action