Uncovering the Iceberg: Describing the Epidemiology of Congenital Cytomegalovirus through Universal Newborn Screening

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Congenital Cytomegalovirus Public Health & Policy Conference

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Key objectives

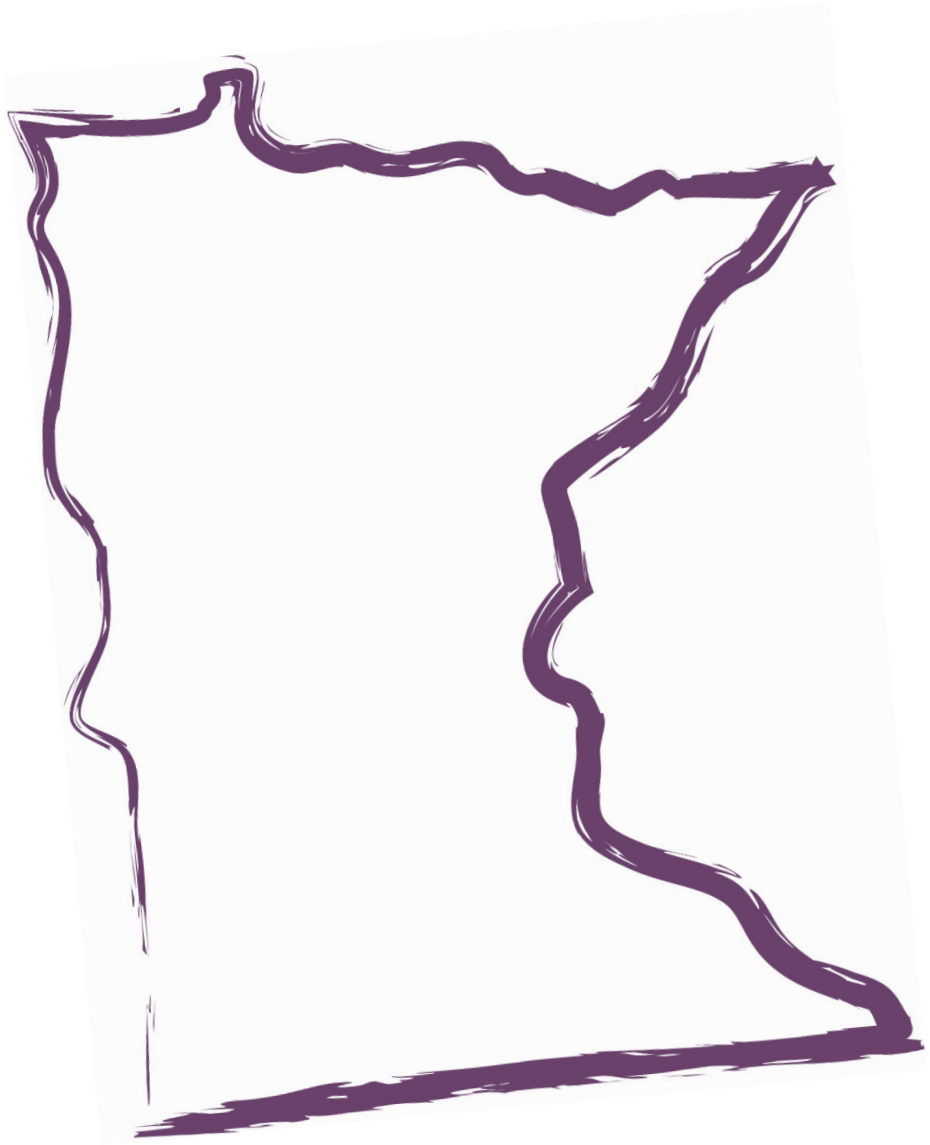
- **Describe the epidemiology of cCMV in MN**
- **Identify populations disproportionately burdened by cCMV**
- **Review findings that can be used to improve public health**

Setting the stage

- **Minnesota added congenital CMV (cCMV) to the universal newborn screening panel**
- **Screening began February 6, 2023**
- **Surveillance for cCMV began at the same time**

Case ascertainment in Minnesota

cCMV surveillance



- **Part of CDC's Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET)**
- **Statewide, population-based**
- **Electronic laboratory reporting and death record review**
- **Case definition:**
  - **Resident of MN at birth**
  - **Meets CSTE case definition for cCMV**
  - **Born February 6, 2023–August 5, 2023**
  - **Initial data collection complete**

Methods: data sources

- **Child's birth certificate**
  - Mother's and father's race and ethnicity
  - Mother's address (city, state, county, zip code) at time of birth
  - Mother's age
  - Mother's education
  - Mother's country of birth*
  - Number of living children*
  - Whether mother received WIC support
  - Payor for delivery
  - When prenatal care began*
  - Plurality
- **Newborn Screening Data**
  - Sex
  - Gestational age, birthweight
  - Signs/symptoms (medical record abstraction)
    - Head ultrasound, audiology, and ophthalmology evaluation results
  - Treatment
- **Death certificates**
  - Match quarterly to assess mortality

**currently available for infants with cCMV born Feb-June*

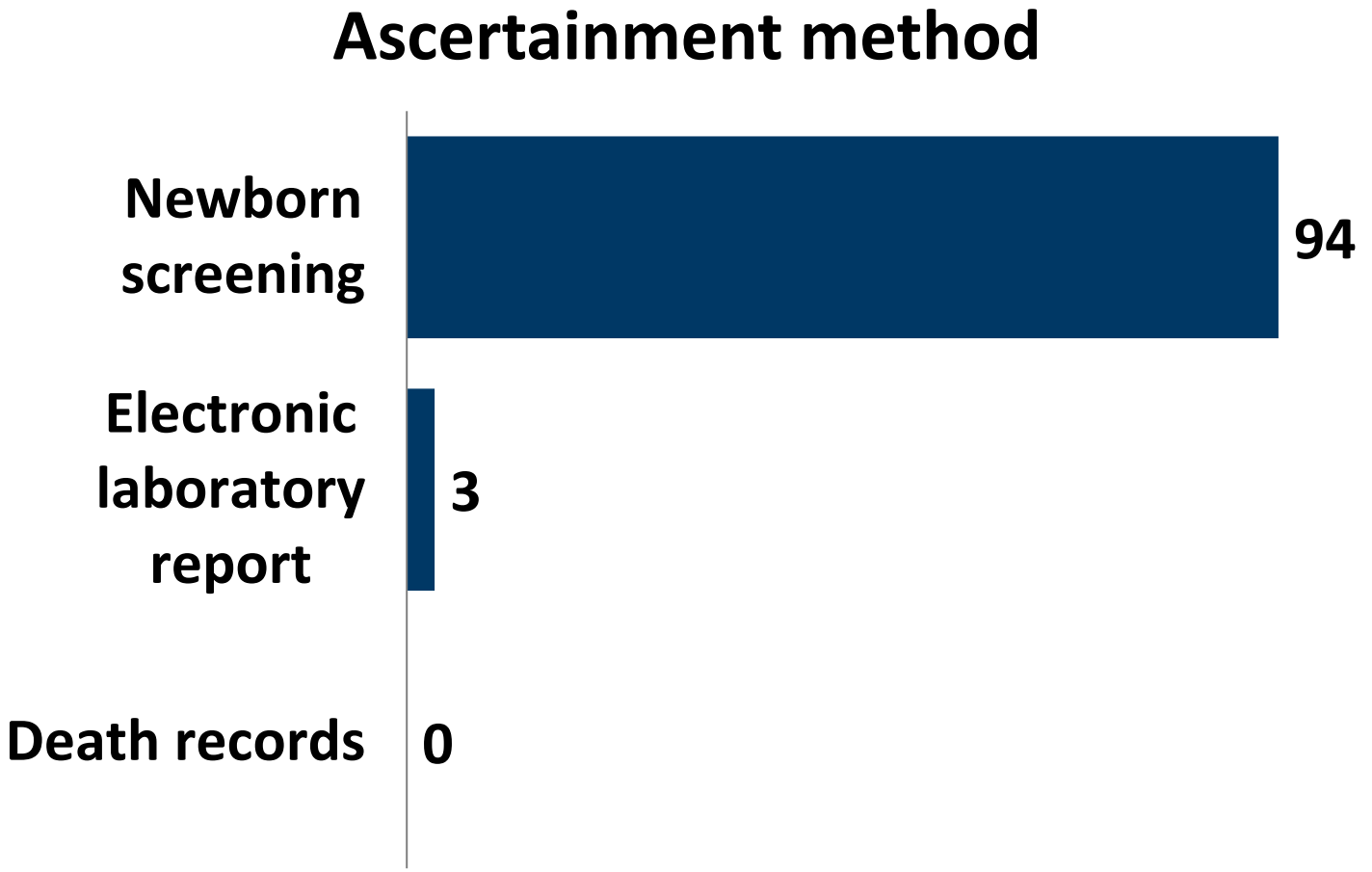
Methods: demographics

- **Race and ethnicity were grouped into broad categories**
  - **Mother's and father's data were combined to represent the newborn**
  - **Used to describe demographics, not as a risk factor for infection or outcome**

- **American Indian (non-Hispanic)**
- **Asian (non-Hispanic)**
  - Asian Indian, Cambodian, Chinese, Filipino, Hmong, Japanese, Korean, Laotian, Vietnamese, Other Asian
- **Black (non-Hispanic)**
  - African American, Ethiopian, Ghanian, Kenyan, Liberian, Nigerian, Somali, Sudanese, Other African
- **Native Hawaiian, Pacific Islander (non-Hispanic)**
  - Hawaiian, Guamanian, Samoan, Other Pacific Island
- **Hispanic (any race)**
  - Cuban, Hispanic, Mexican,, Puerto Rican, Other Spanish
- **White (non-Hispanic)**
- **Multiracial, any combination of the above (non-Hispanic)**

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

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

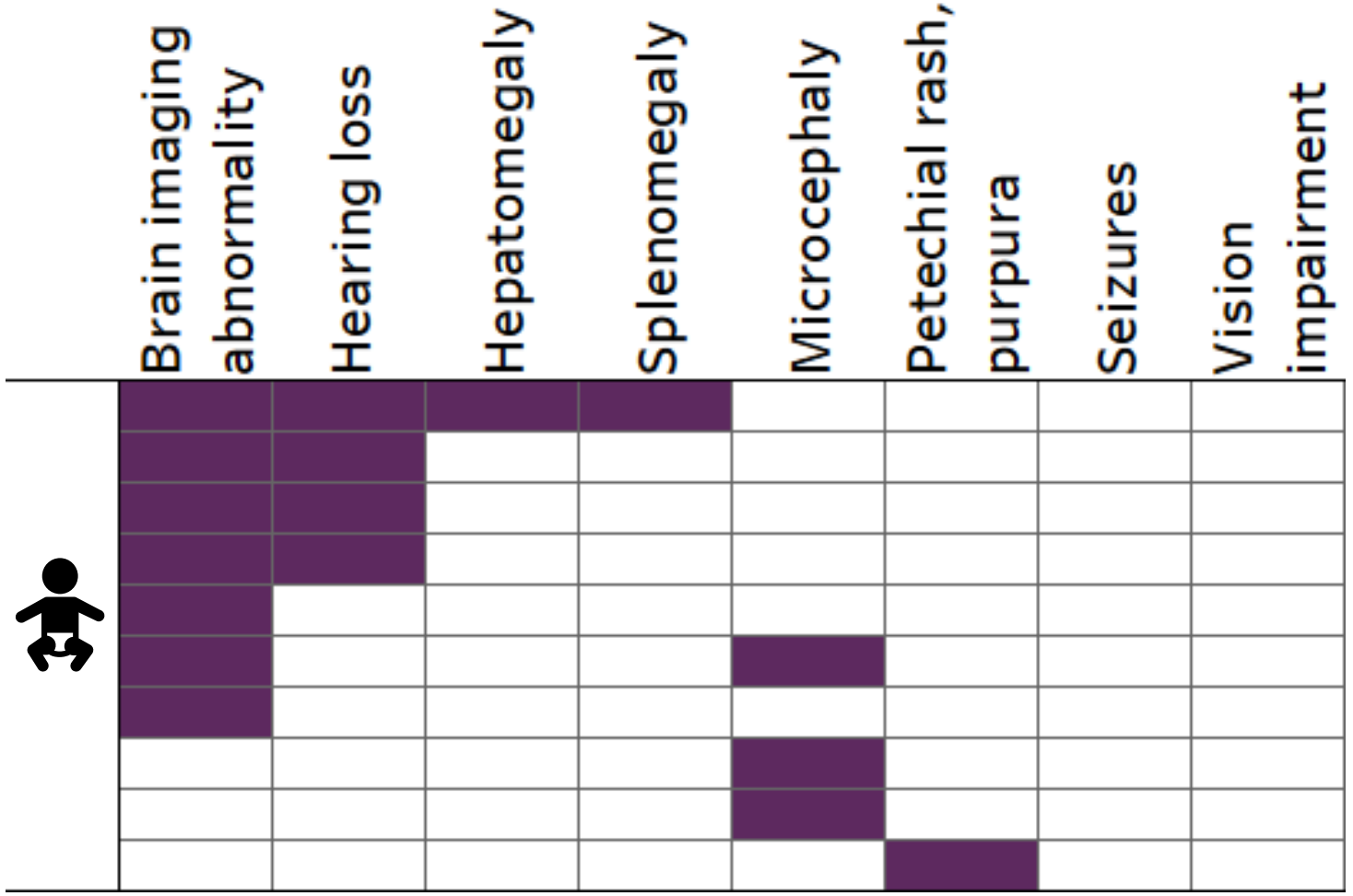


Applying the CSTE surveillance case definition

- **Laboratory criteria**
  - **Confirmatory: 72 (92%)**
    - Dried blood spot collected ≤ 21 days, no negative urine
  - **Presumptive: 2 (3%)**
    - Dried blood spot collected 22–42 days, no negative urine
  - **Does not meet: 4 (5%)**
    - Positive result with negative urine result

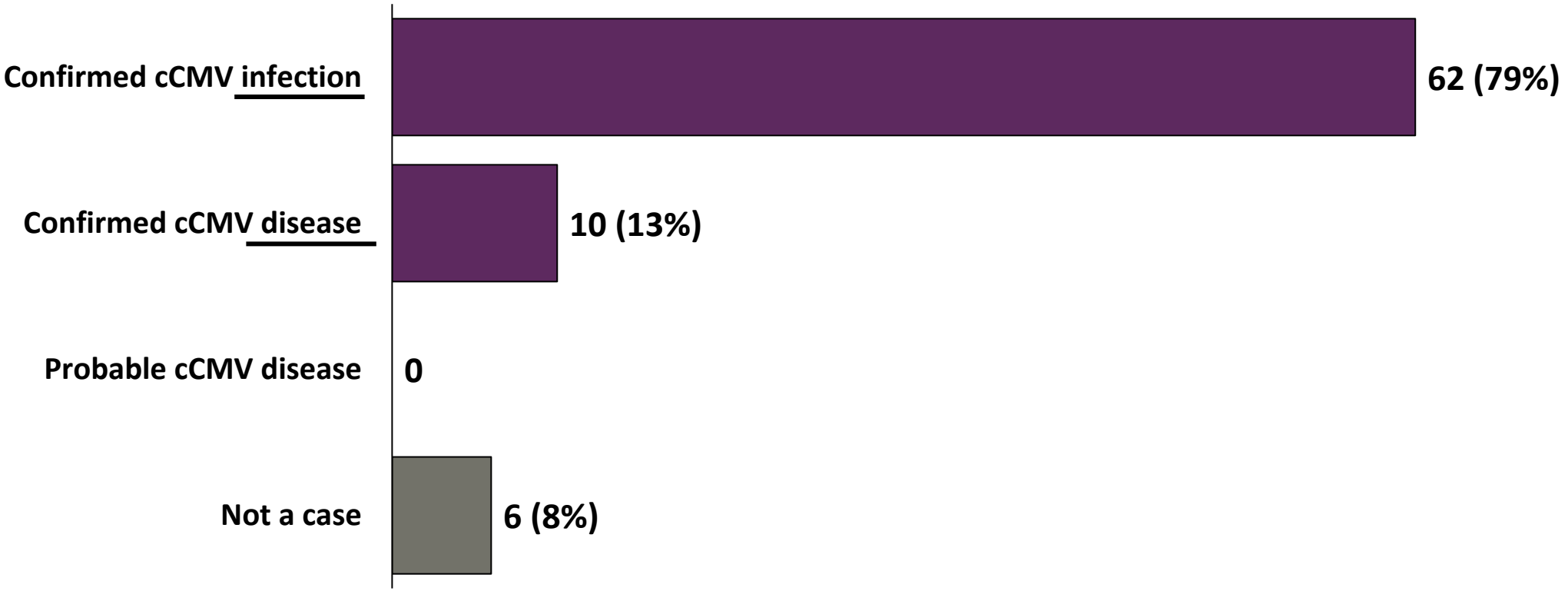
Applying the CSTE surveillance case definition

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



Applying the CSTE surveillance case definition

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



72

Infants with cCMV (cases)

Estimated prevalence of cCMV in Minnesota

1:350 newborns

or

0.28% of births

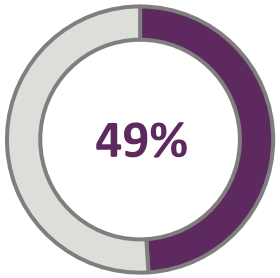
Proceed with caution

- Our dataset is still a newborn
  - Limited number of cases
  - Limited variables/data to assess disadvantage/disparity
- Know proportions are unstable
- All data presented should be considered preliminary and subject to change

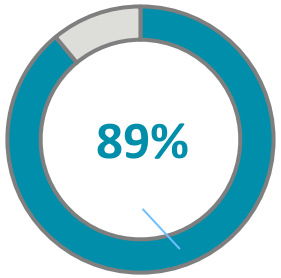
Let’s describe our cohort

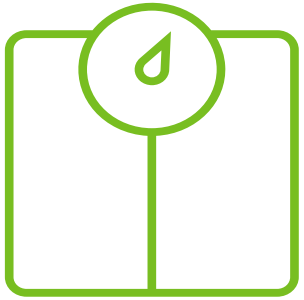
Infants with cCMV birth stats

Half were female



Most were not in the NICU





Birthweight

Median, 3,251 grams

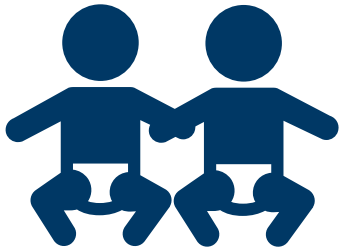
range, 1,620 – 4,289

(that's about 7 pounds)

Gestational age

Median, 39 weeks

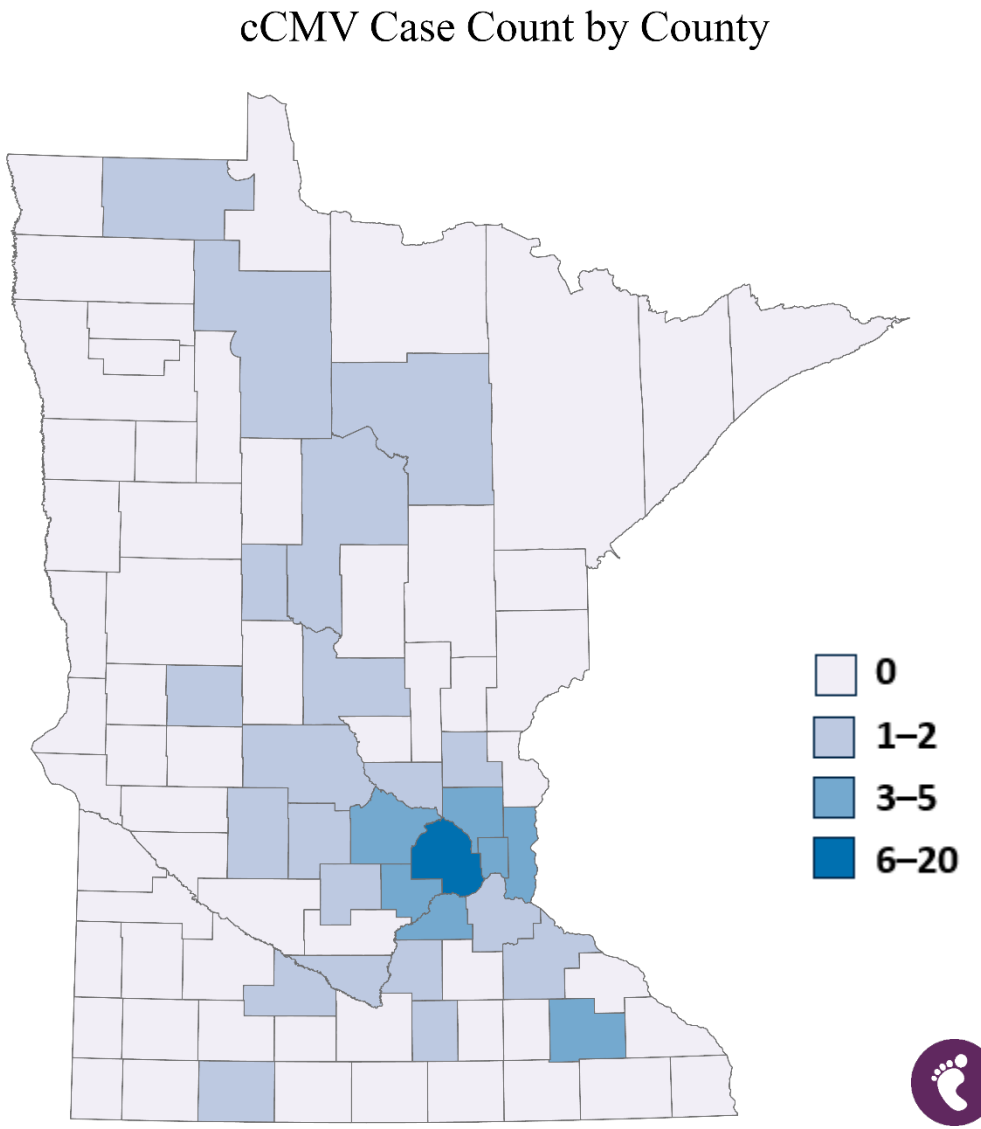
range, 33-40



1 was a twin

Where do infants with cCMV live?

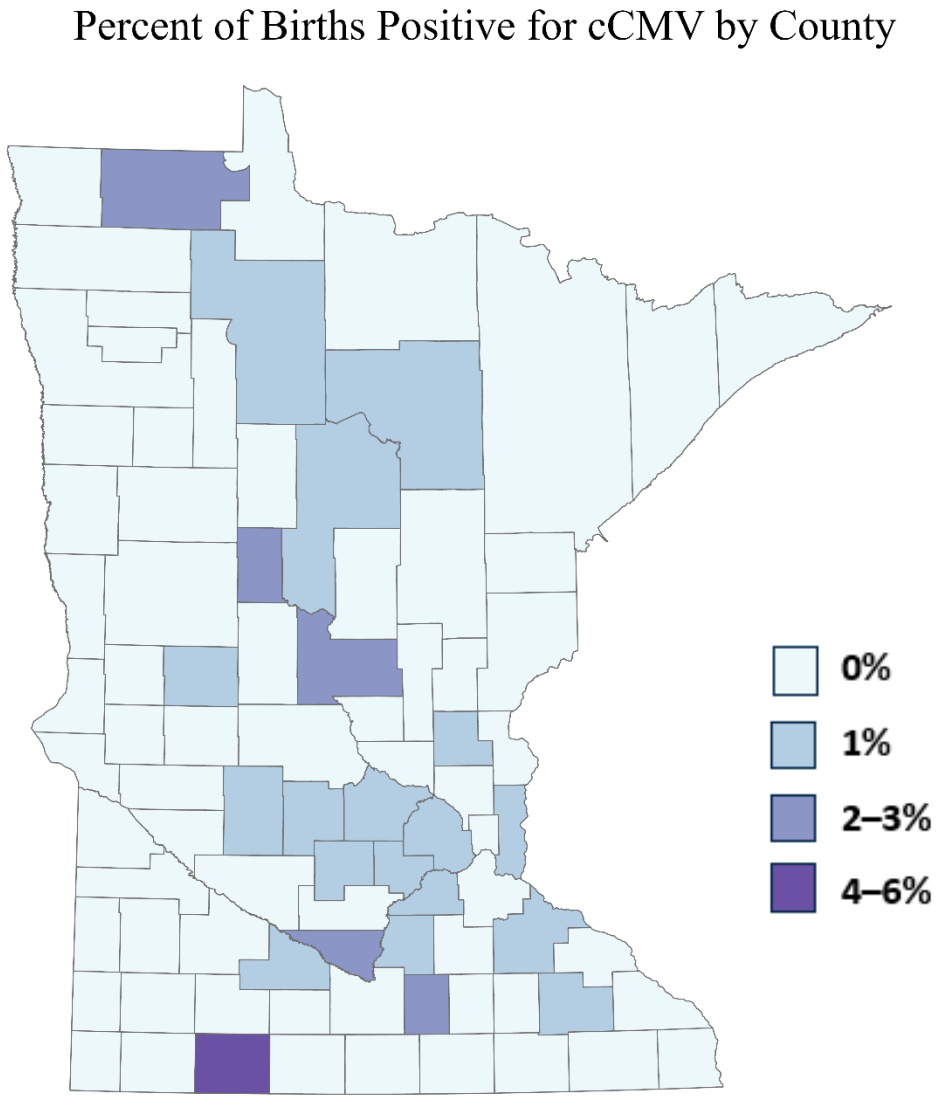
- **Infants with cCMV concentrate in Minnesota's most populous area**
- **56% live in the Twin Cities metro area**
  - **similar to the birth population**



Where do infants with cCMV live?

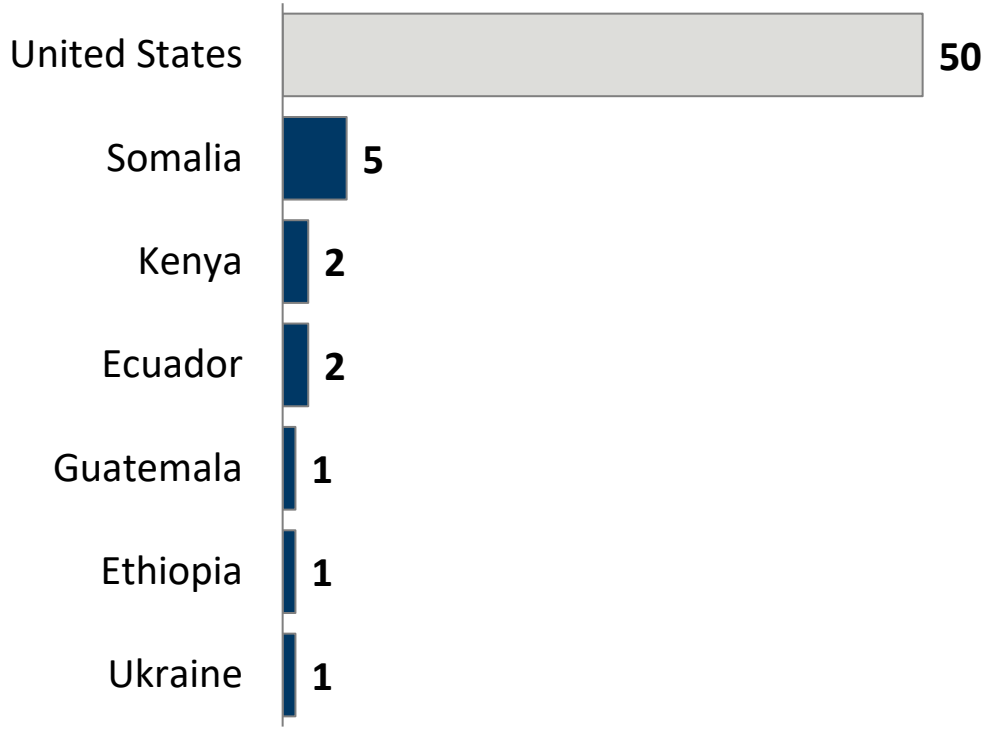
- **As a share of the births in each county, the spread evens out**

! Birth populations in some counties can be very small



Nativity status

19% of infants with cCMV had **foreign-born** mothers



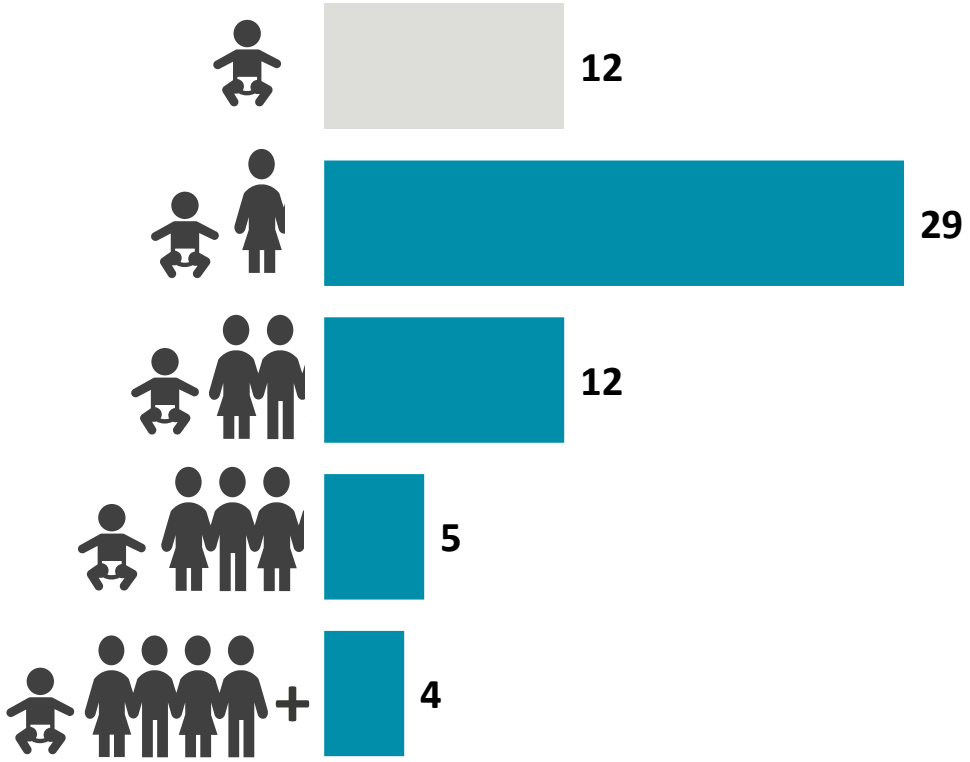
- **Similar to 20% of all births**
- **Does not tell us how long the mother has lived in the United States**

https://www.health.state.mn.us/data/mchs/genstats/annsum/index.html

Most mothers of infants with cCMV have other children

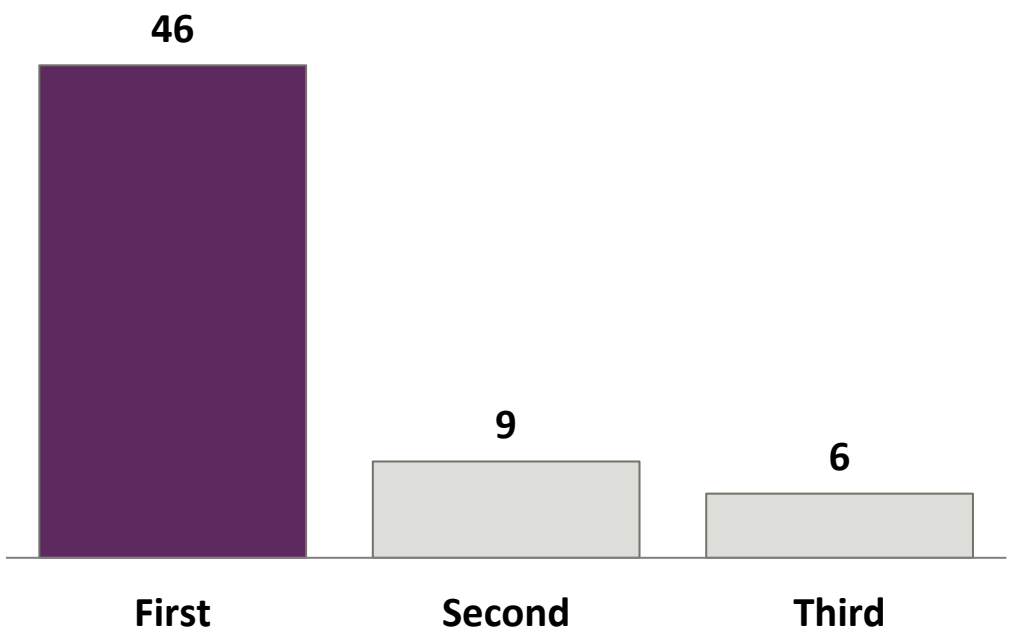
- **Proxy for exposure risk to CMV at home**
- **Does not tell us whether those children live at home or if there are other (e.g., occupational) exposures**

81% of mothers had **other children**



Most mothers begin prenatal care on time

Prenatal care began in the **first trimester** for **75%** of mothers

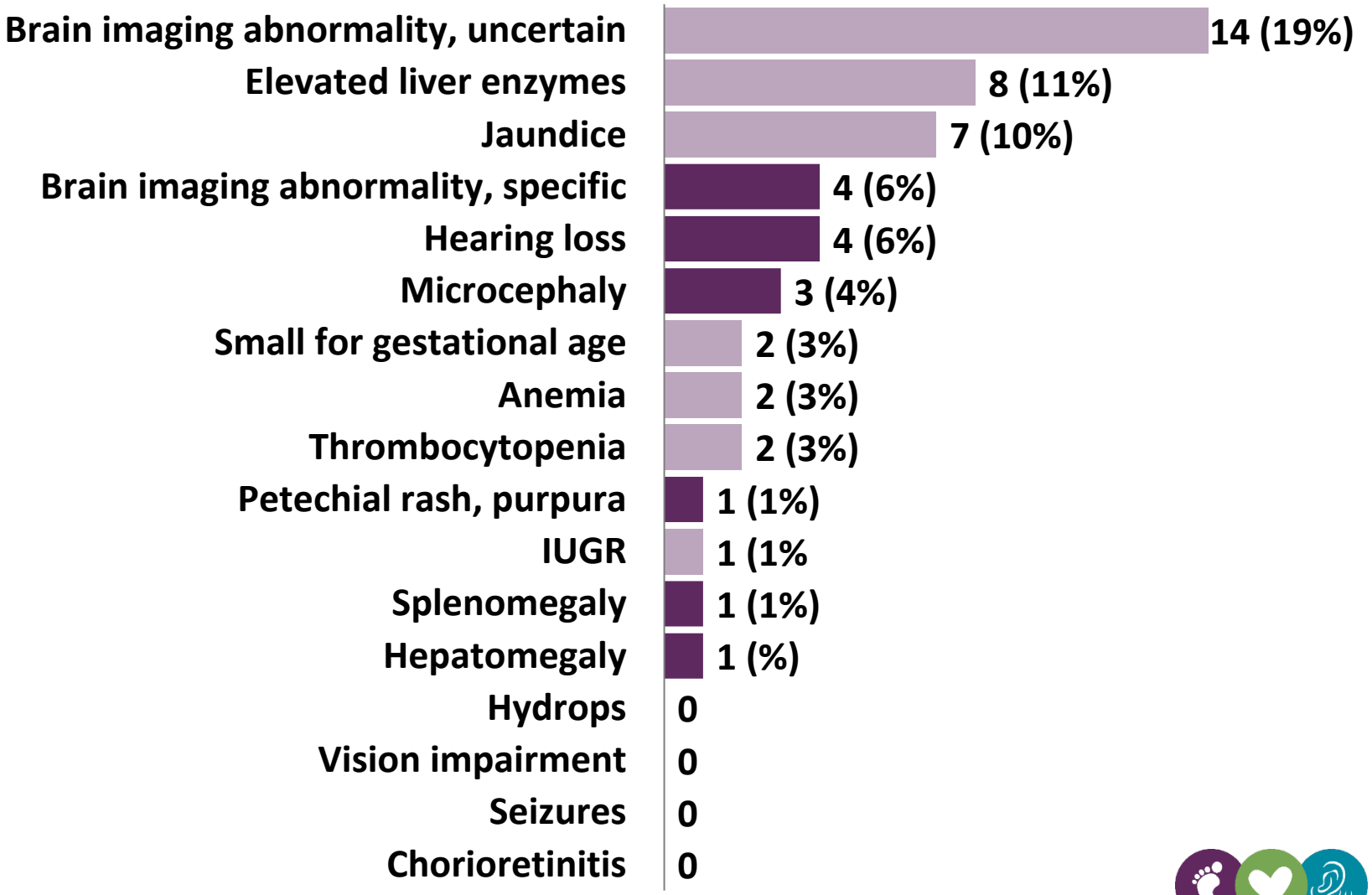


- **Similar to 79% of all births**
- **Cannot determine adequacy of prenatal care**
- **Indicates most mothers are available for multiple education/prevention touch points**

https://www.health.state.mn.us/data/mchs/genstats/annsum/index.html

cCMV disease and clinical spectrum

- **10 (13%) of cCMV cases meet the case definition for cCMV disease**
- **A total of 23 (32%) infants with cCMV have clinical findings that may be related to their infection**

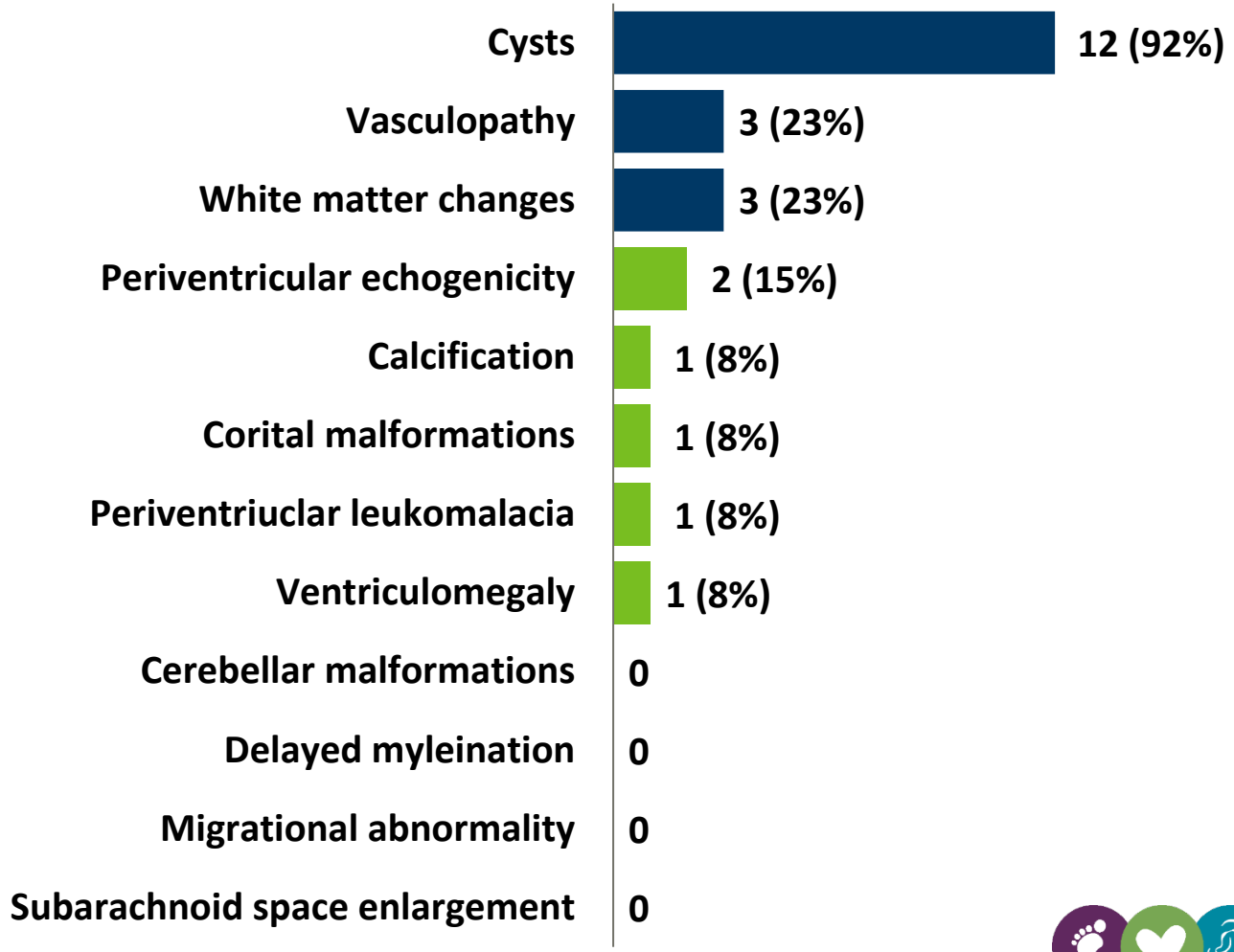


cCMV clinical spectrum

- **10 (14%) had only brain imaging or elevated liver enzymes**
- **8 (11%) had only one sign or symptom (6 of which were non-specific brain imaging abnormalities)**
- **None with classic blueberry muffin rash**
- **No deaths**

Head ultrasound findings

- **Cerebral cysts were the most commonly noted abnormality**
- **Few (4) infants have abnormalities that are cited in the Rawlinson et al. consensus paper or included as examples in the CSTE case definition**



Rawlinson, W., *et al*. doi: 10.1016/S1473-3099(17)30143-3

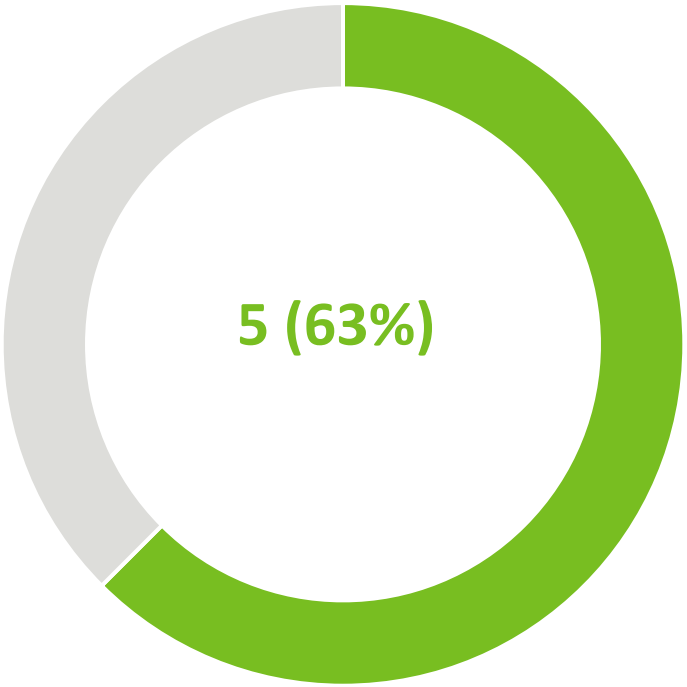
Hearing loss

- 4 infants known to have hearing loss
  - 10 infants with cCMV have not completed an initial audiologic evaluation
- All affected unilaterally
- 1 passed their birth hearing screen
- Follow-up monitoring underway to identify later onset hearing loss in additional infants

Treatment for cCMV

- 8 (12%) were started on antiviral therapy
  - 7 with clinical findings
    - 5 meeting clinical criteria for cCMV disease
  - 1 w/o clinical findings
  - Median of 22 days from birth (range 11 to 43 days)

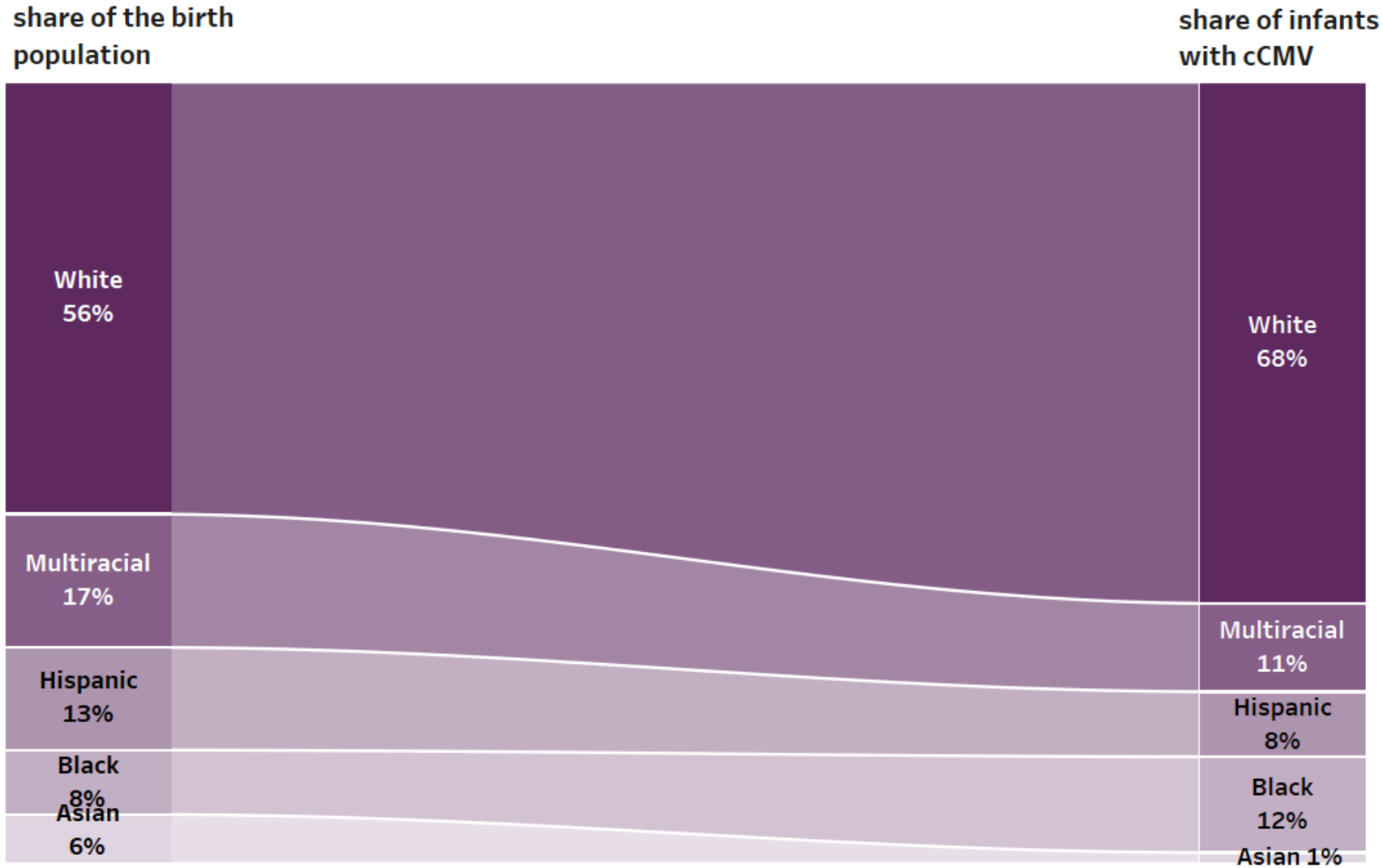
63% treated **within 30 days**



How does our cohort compare to the Minnesota birth population?

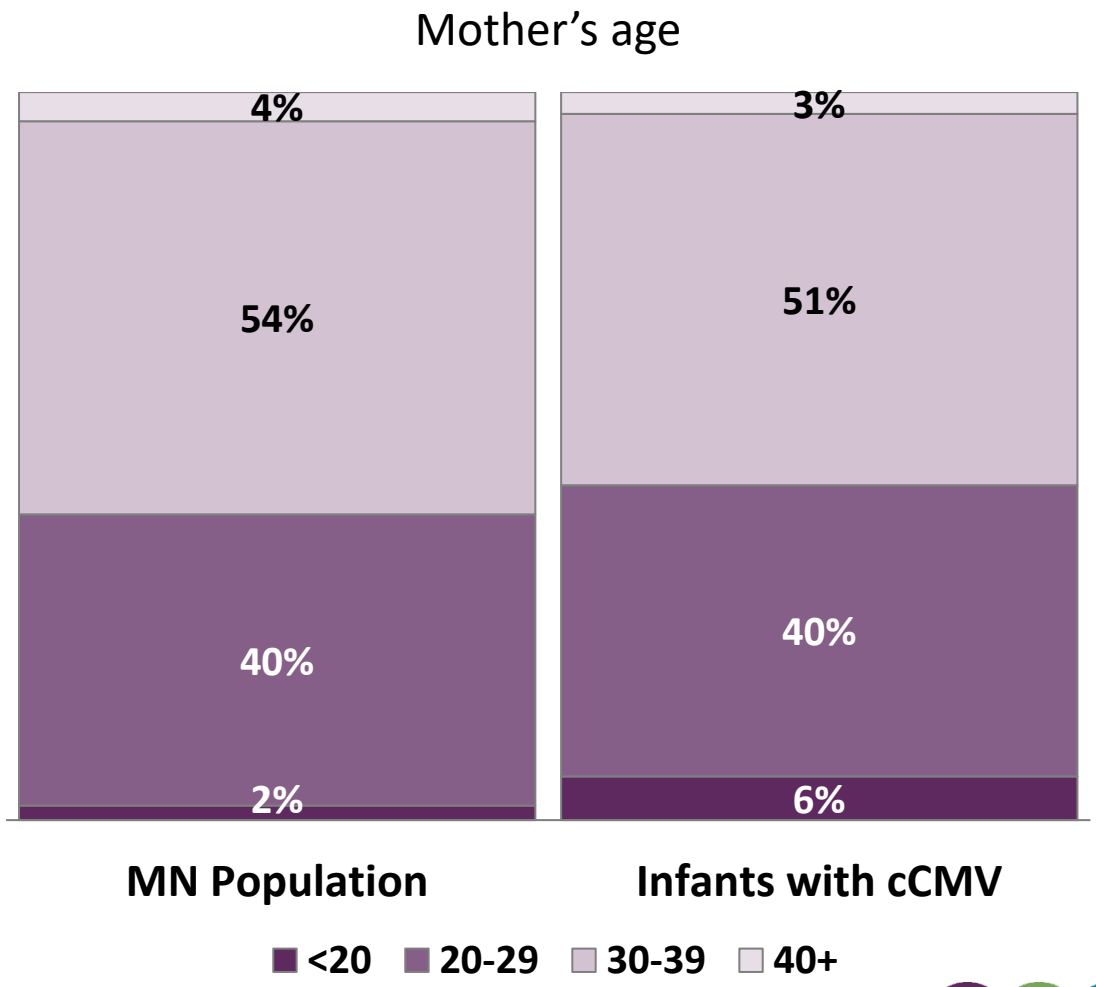
Demographics: race and ethnicity

- **Compared to the Minnesota birth population, there is a higher proportion of White and Black infants with cCMV**



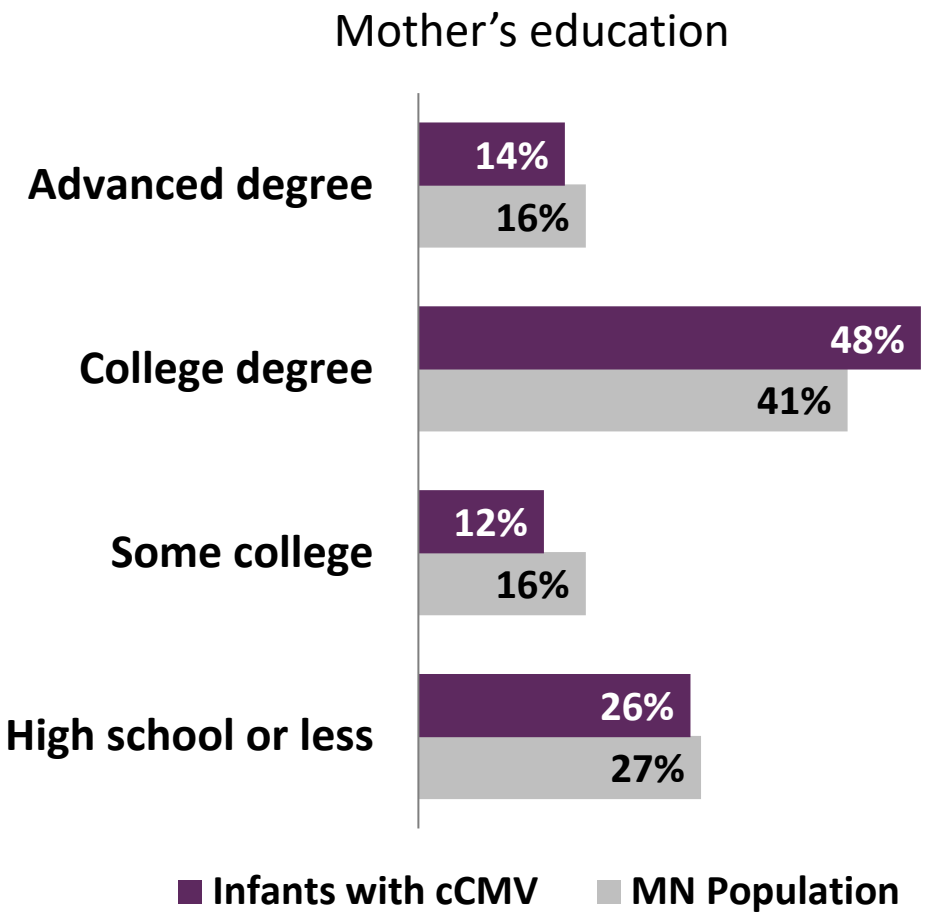
Demographics: mother's age

- **Compared to the Minnesota birth population, infants with cCMV have slightly younger mothers**
  - **Median, 30 years vs 31 years**



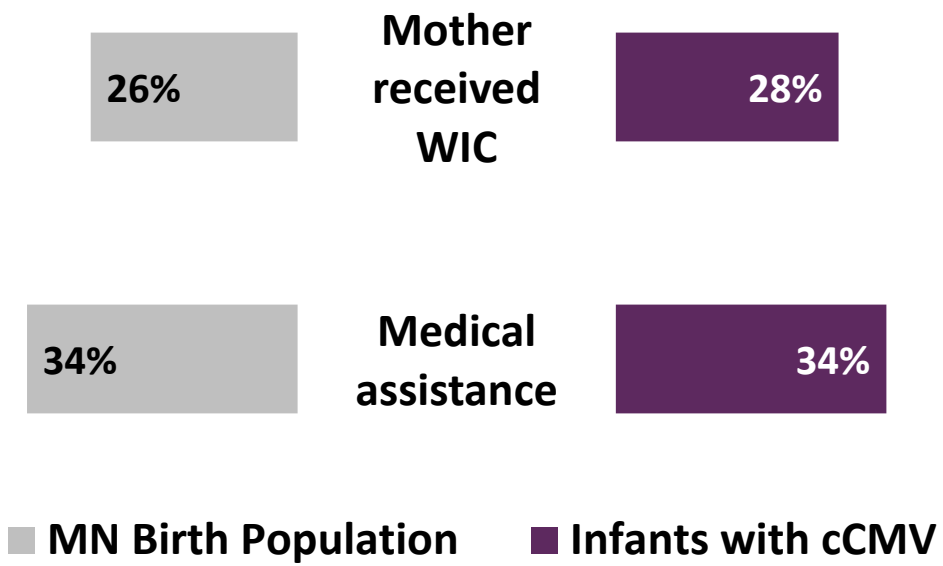
Demographics: mother's education

- **Compared to the Minnesota birth population, mothers of infants with cCMV have higher educations**



Demographics: economic indicators

- The proportion of infants with cCMV whose mothers received WIC or were on medical assistance for delivery were similar to the birth population
- Other indicators of economic, social, and other disadvantages remain to be investigated



Let’s discuss

Limitations

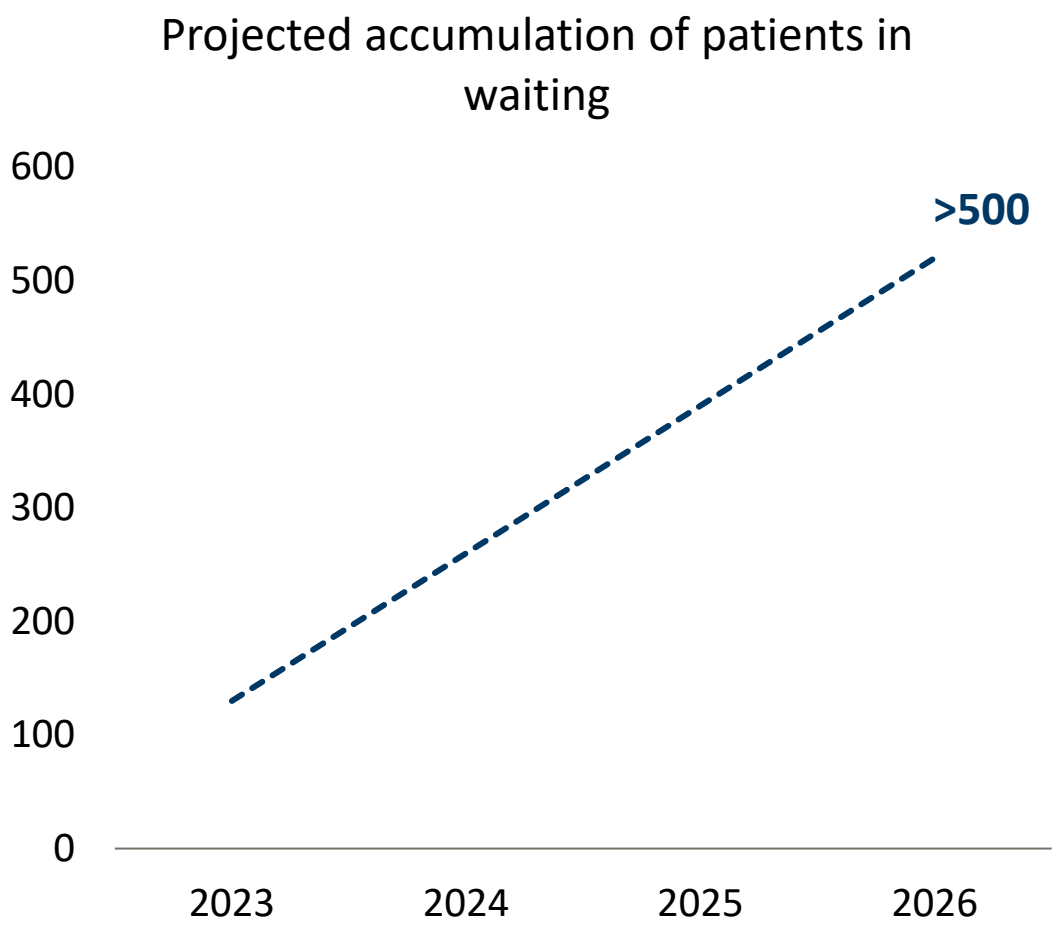
- **This cohort of evaluated infants may be biased**
  - **More likely to include families willing and able to complete evaluations**
- **No retrospective data to compare to (i.e. no previous statewide surveillance)**
  - **What was clinically identified previously? Is it odd that we haven't identified any "classic" cCMV infections?**

Discussion: is MN's prevalence lower than expected

- **1:200 or 0.2–2.0% (average 0.64%) cited in literature**
  - **Usually, newborn screening finds more than reported in the literature**
  - **Possible explanations for lower prevalence:**
    - **Low viremia early in life**
    - **Reduced sensitivity of dried blood spot testing**
    - **Minnesota's population is different than population used for estimates**

Discussion: potential patients in waiting

- **71% of cases have no initial signs/symptoms related to CMV infection**
- **~130 Minnesota infants each year become patients in waiting**
- **What is the toll on families?**
- **Are we over-medicalizing kids?**
- **What is the public health impact, are there enough public health resources?**



Discussion: potential patients in waiting

- **Benefits to identification of all infected infants:**
  - **Monitoring leads to early intervention**
  - **Better understanding of the true burden and natural history of cCMV**
  - **Informative for prevention measures**
- **Necessary to learn more about how these infants do after identification**
  - **Longitudinal surveillance**
  - **Survey to learn from families**

How can this improve public health?

- **Surveillance data based on universal screening gives truly population level data**
- **Collecting these data can direct us to where public health resources can be applied**
  - **Resources needed toward navigating health system, health literacy**
  - **Inform what languages you should provide materials in**
  - **Are people in care throughout their pregnancy and available for prevention interventions**
  - **Are certain populations over-burdened**

Conclusion

- **We have a lot to learn about cCMV in Minnesota**
- **Surveillance data will help us get there**
  - **Multistate data will accelerate the knowledge gain**

Acknowledgments

- **Parents and advocates**
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Thank you

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