Congenital Cytomegalovirus (cCMV) Screening and Follow-up in Minnesota: Process and Lessons Learned to Date

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Learning Objectives

- Understand the Vivian Act legislation that instructed the Minnesota Department of Health to establish a CMV awareness and education program
- Understand the Minnesota Newborn Screening new condition approval and implementation process
- Learn about the cCMV implementation planning and coordination efforts between newborn screening and the EHDI program in Minnesota, including lessons learned so far

MN Statute 144.064 – The Vivian Act

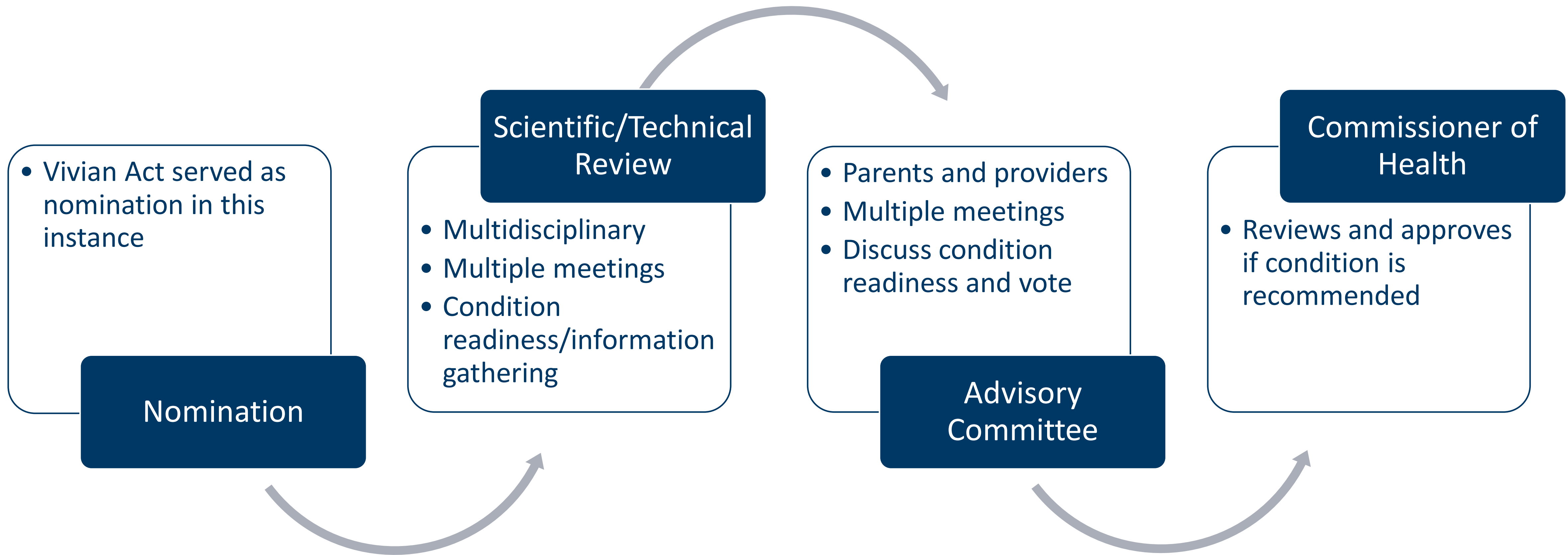
- Recent legislation passed requiring the following from the MN Dept of Health:
  - Education, resource provision, and outreach about congenital CMV – this will be led by MDH's Child and Family Health Division
  - Review by the Advisory Committee on Heritable and Congenital Disorders for possible inclusion on Minnesota's newborn screening panel
    - If added, a fee increase of $43 per specimen automatically goes into effect

SF1698

VIVIAN ♥ ACT

STOP CytoMegaloVirus from devastating 400+ MN families a year

Advisory Committee Process (for conditions not on RUSP)



CMV Readiness Determination

- Number of Required Criteria Met (6 max): **6**
- Number of Supporting Factors Met:
  - Clinical Characteristics of the Condition (6 max): **2**
  - The Screening Test (8 max): **5**
  - Diagnosis, Follow-up, Treatment and Management (10 max): **8**

Advisory Committee Outcome

- Committee voted to recommend its addition to Minnesota’s newborn screening panel on January 11, 2022
- Commissioner of Health approved recommendation
- After fee increase per Vivian Act, Newborn screening card fee now $235

Program Wide Planning

- Weekly internal implementation planning, dedicated Teams channel, & shared project timeline.
  - Ops, lab, bloodspot follow-up, point of care follow-up, longitudinal follow-up, communications
- Screening Method determined (DBS)
  - Qualitative Real-Time PCR
  - Assay detects CMV DNA extracted from dried blood spots
  - Specimen card update to collect 6 blood spot circles instead of 5
  - Screening is performed M-F; not on weekends or most holidays
- Changes to laboratory information management systems (4 units and 3 systems)
- Space accommodations for new testing & instrumentation
- Assay development & validation

Program Wide Planning

- Hiring and training more staff
- Hosting implementation work group meetings with providers and parents to finalize follow-up algorithms
- Updating materials to include CMV and creating new cCMV materials
  - Internal materials: SOP’s, job aids, fax back forms, etc
  - External materials: Parent materials, Audiology guideline, provider materials
- Communicating to providers and public
- Working to add congenital CMV to Communicable Disease Rule to help identify false negatives

MDH cCMV

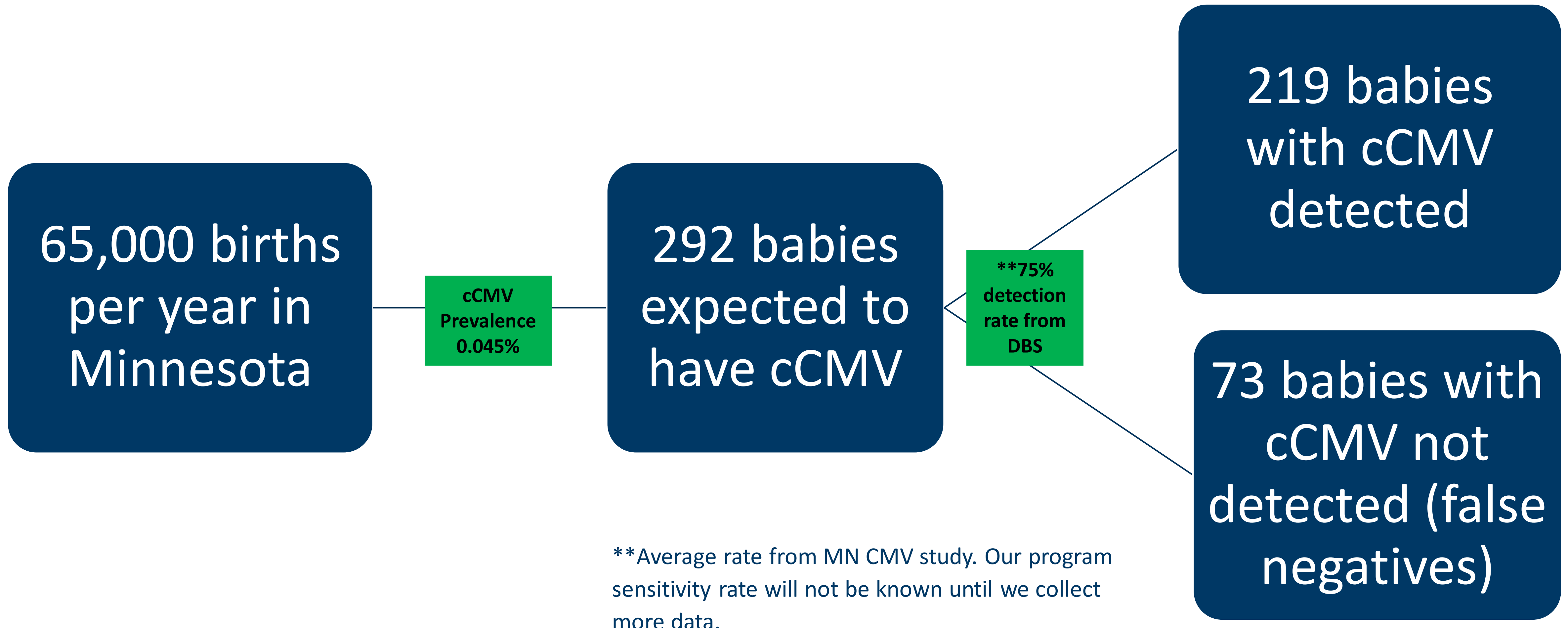
Blood Spot screening, result notification, ‘Just in Time’ education, confirmation results

Connect families to information, resources, and support

Complete ongoing data collection, integration, and analysis for public health surveillance and program improvement

Build NBS system capacity and ensure equitable access and interventions

Projected Numbers for Universal NBS for cCMV In Minnesota



CMV Screening Results

- CMV Not Detected
  - "Normal" result
  - False negatives expected
- CMV Detected
  - MDH actively follows up
  - False positives expected
    - Age
    - Contamination

Minnesota Newborn Screening
601 Robert Street North, St. Paul, MN 55155-2531
Phone: 1-800-664-7772 or 651-201-5466 Fax: 651-215-6285
Email: newbornscreening@health.state.mn.us

Final Newborn Screening Report

LABORATORY REPORT
Submitter:
Address:

Card Barcode:
Physician/Clinic:

Patient Information:
Infant Name:
Date of Birth:
MRN:
Mother's Name:

Specimen Information:
Date Collected:
Date Received:
Date Reported:
Copy Printed:

Cytomegalovirus (CMV) Screening Results

Result	Expected Result
CMV Not Detected*	CMV Not Detected

There is decreased sensitivity in screening for CMV in dried blood spots, so not all infants with congenital CMV will be identified. Of those who are identified by newborn screening, up to 80% will be unaffected.

Comments

Resources: An MDH genetic counselor is available for consultation regarding screening results at 651-201-3548. Disorder fact sheets and specialist contact list can be found here: https://www.health.state.mn.us/people/newbornscreening/materials/factsheets/bloodspotdisorders.html

The purpose of newborn screening is to identify at risk infants in need of diagnostic testing. As with any screening test, false positive or false negative results are possible. Newborn screening is insufficient information on which to base, or rule out, diagnosis or treatment.CF variant analysis is completed using the Luminex® xTAG® Cystic Fibrosis (CFTR) 39 Kit.
*This real-time PCR assay was developed and its performance characteristics were determined by the MDH Public Health Laboratory. It has not been cleared or approved by the U.S. Food and Drug Administration: 21 CFR 809.30(e).
**The performance characteristics of these tests were determined by the MDH Public Health Laboratory. It has not been cleared or approved by the U.S. Food and Drug Administration.
***Testing is performed by Mayo Clinic Laboratories-Rochester Main Campus; 200 First Street SW, Rochester, MN 55905

CMV Screening - Notification

- Abnormal screen result notifications made to primary care clinic/provider, midwife, or NICU if baby is admitted by newborn screening genetic counselors by phone
- Provide “just-in-time” education
- Recommend urine CMV PCR for confirmation by 21 days of age
  - Saliva will not be encouraged
- Fax MDH Newborn Screening report and informational fact sheets for both provider and the family
- Obtaining diagnostic results:
  - Utilize electronic medical records if access exists
  - Request from PCP via fax and phone

CMV Screening Follow-up – Outcomes

- Bloodspot Screening Outcomes:
  - False positives – expected to be minimal, no further follow-up needed unless clinical concerns exist
  - True positives – additional evaluations recommended
    - Symptomatic at birth – ID consult encouraged
    - Asymptomatic at birth
- Confirmed cases receive additional tracking and longitudinal follow-up

cCMV Follow-up – Confirmed Cases

Laboratory testing: liver function tests (AST/ALT) and complete blood count (CBC) with differential

Pediatric diagnostic audiologic evaluation (even if baby passed their newborn hearing screen) with continued regular audiologic monitoring

Pediatric ophthalmology examination; follow-up as recommended

Cranial ultrasound; a brain MRI may be recommended to clarify nonspecific findings

Developmental assessments and referral to Early Intervention

Longitudinal Follow-up: Information and Resources

- Connect families to information, resources, and support after confirmation of diagnosis
  - Parent/guardian receives a letter and print materials by mail from MDH
    - Content was developed in partnership with the National CMV Foundation and a workgroup of 7 parents of children with cCMV from MN and 1 parent from North Dakota
    - Packet includes information about cCMV, recommended short-term and long-term follow-up, and community resources/supports

Longitudinal Follow-up: Information and Resources

- MDH will make a referral to the Local Public Health (LPH) department in the county of residence for each infant
  - Family is contacted and offered a nursing assessment at no cost (funded by MDH)
  - Goal: Identify child and family needs and to ensure connection with appropriate community resources and services, including Early Intervention services

Births per year in County	Estimated number of LPH referrals for cCMV per year
500	1-2
1000	3-4
5000	15-17

Longitudinal Follow-up: Parent Support and Networking

- Pilot program for parent-to-parent support in partnership with Minnesota Hands and Voices
  - Families with kids who are symptomatic
  - Will receive 1:1 support from a parent guide
  - Direct referral from MDH
- Promoting connection to the National CMV Foundation

Longitudinal Follow-up: Growth and Development

- Congenital CMV is a condition known to hinder growth and development
  - Automatic qualification for connection to Early Intervention for all kids
  - Will refer all children through Help Me Grow MN unless they are already connected with these services

Longitudinal Follow-up: Follow Along Program

- Offer and encourage enrollment in the MDH Follow Along Program
  - Empowers parents and helps them track their child's development and lets them know if their child is meeting milestones
  - Offers professional support and resources to address any concerns
  - No cost for participation

Longitudinal Follow-up: Hearing Monitoring

- Hearing loss is the most common sequalae of congenital CMV
- Sensorineural hearing loss related to cCMV may
  - Impact one or both ears
  - Have a delayed onset
  - Be unstable with fluctuations and progression
- All children will need hearing monitoring at regular intervals throughout childhood

Suggested Clinical Protocol for Hearing*

Initial Diagnostic Audiology Assessment	• Test ABR by 1 month of age or no later than 1 month after cCMV confirmed with urine test
2nd Diagnostic Audiology Assessment	• Test ABR by 4-5 months of age (can be done under natural sleep) • Vestibular function screening – CDC Milestone Checklists
Monitoring Audiology Visits up to age 2 years	• Test every 3 months until age 2 years, using typical test battery with ear-specific procedures for child's age/skills • Vestibular function screening – review motor milestones
Monitoring Audiology Visits age 2 to 6 years	• Test every 6 months until age 6, using typical test battery with ear-specific procedures for child's age/skills • Vestibular function screening – one leg standing screen
Monitoring Audiology Visits age 6-10 years	• Test every 12 months from age 6-10 year, using typical test battery with ear-specific procedures for child's age/skills • Vestibular screening by Pediatric Dizziness Handicap Inventory

*Decisions on timing and type of evaluations (for example, how often children receive sedated testing) may need to be adjusted based on clinical judgement or to accommodate needs of individual families. These decisions should be made jointly between family and child's care teams.

Surveillance

- Describe the epidemiology of cCMV in Minnesota
  - Prevalence (adding cCMV to reportable disease rule)
  - Spectrum of disease
  - Identify at-risk groups and disparities
- Evaluate newborn screening for cCMV
  - Test performance (sensitivity, specificity, PPV)
  - Determine if newborn screening improves outcomes
  - Equity in confirmation and follow-up
- Inform education and prevention efforts

Lessons Learned

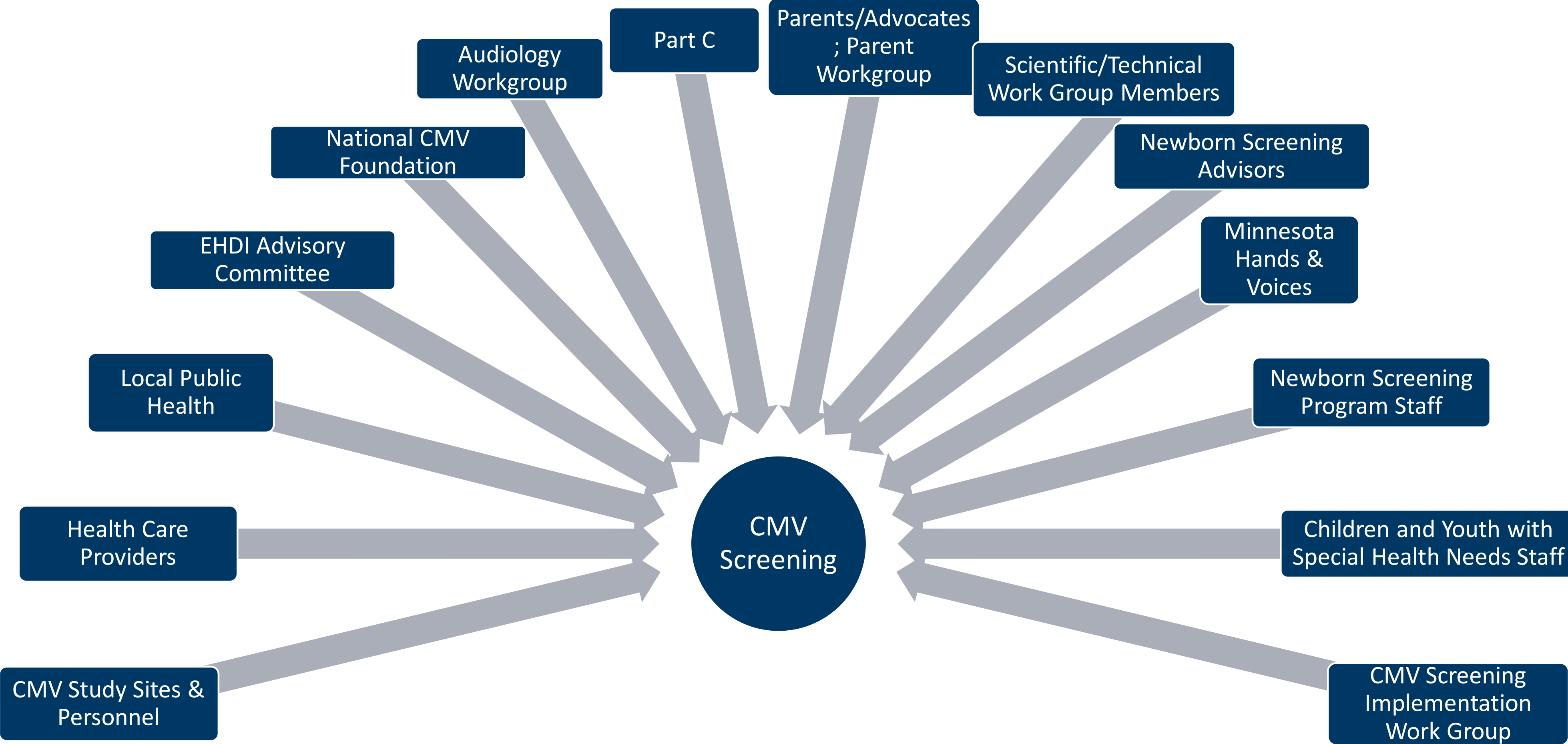
- **Unique Challenges**
  - Being first to implement statewide universal cCMV screening
  - CMV is the first infectious disease on the NBS panel
  - Most infants (75%) confirmed to have cCMV will not manifest symptoms
  - Bloodspot card printing error
- **Communications with Stakeholders (listen to/use your experts)**
  - Implementation work group
  - Audiology work group
  - MN EHDI Advisory Committee
  - MN Dept of Education, Part C, MN Low incidence projects
- **Patience!** -- internally and externally as specific processes were created, published, and communicated

Lessons Learned

Possible Audiology Scheduling Challenges

- A few early cases were scheduled for outpatient rescreens instead of diagnostic testing. We are monitoring the situation and working on the following:
  - Help PCPs and families navigate (i.e. PCP orders should include “CMV”, families will need to register as new audiology patients at some clinics before the correct appointment can be scheduled)
  - Increase audiology clinic scheduler awareness of urgency, recommending other clinics if can’t accommodate within 1 month

Many Contributors



MN Universal cCMV Screening

- **Successful GO LIVE February 6, 2023**
- **Press Release & Media Coverage Feb 8, 2023**

Minnesota becomes first state to screen all newborns for congenital cytomegalovirus

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

DEPARTMENT OF HEALTH

Thank You!

MN CMV Team

www.health.state.mn.us/CMV