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AUGUST 22ND  AUGUST 24TH

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Parent Story

William Jones





Universal Screening: The Ontario Story

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Objective



July 2018

- *Ontario starts hearing-targeted CMV screening using newborn dried blood spots*

July 2019

- *Ontario starts universal screening for cCMV*

How did we get here?

Objective



July 2018

- Ontario starts hearing-targeted CMV screening using newborn dried blood spots

July 2019

- Ontario starts universally offering testing dried blood spots for hearing loss risk factors (CMV and genetic)

How did we get here?

What is Screening?

Screening is the systematic, population-based application of a test or inquiry to individuals who do not have symptoms of a specific disease or condition in order to identify those who warrant further investigation and/or intervention to achieve better outcomes.

Definition of Screening Task Force, 2012

Screening tests are about:

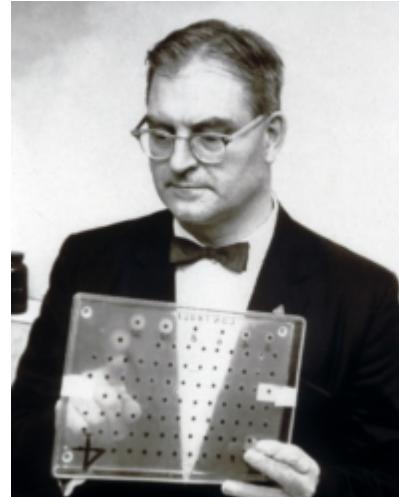
- an asymptomatic/minimally symptomatic population
- risk estimation – increased or decreased risk
- Outcomes



Screening = Better outcomes from starting **treatment early** in the course of disease

The Advent of Newborn Screening

- What is PKU? **Folling (1934)**
- Is there a treatment to prevent mental retardation? **Bickel (1953)**
- Is there a reliable, simple and sensitive test? **Guthrie (1961)**

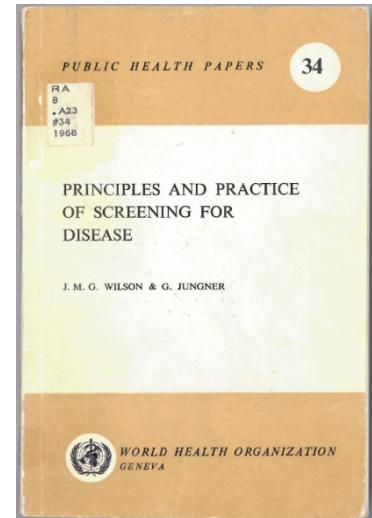


- Public Health emergency
 - ~2% of severely cognitively disabled and institutionalized people had PKU
 - Treatment before the onset of symptoms results in normal IQ

Screening “Principles”

Wilson and Jungner 1968

1. The condition sought should be an important public health problem.
2. There should be an accepted treatment for patients with recognized disease.
3. Facilities for further diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a “once and for all” project.



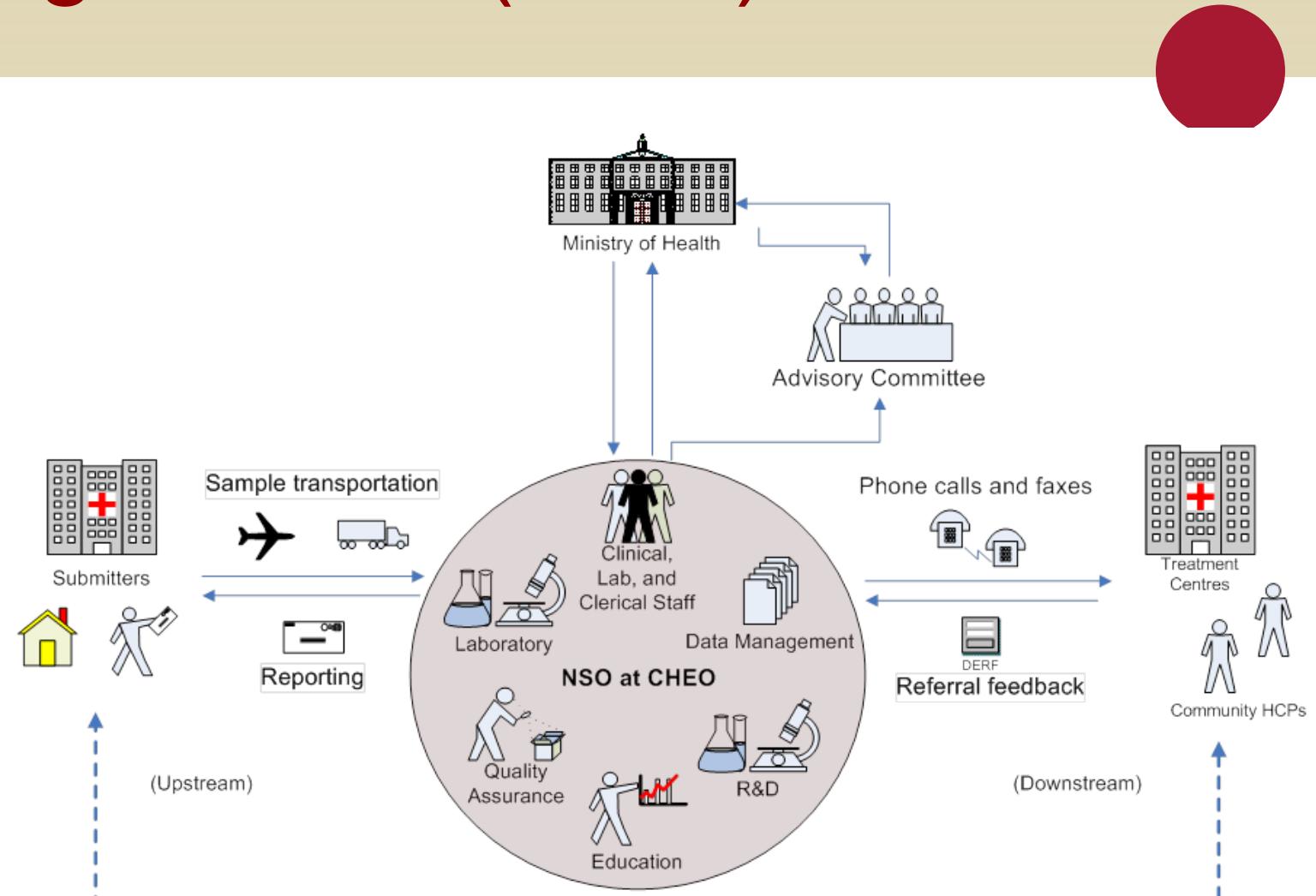
Elements of a system of care



- Education, enrolment, consent
- Screening test and interpretation
- Retrieval, diagnosis, treatment
- Data management and performance measurement
- Policy setting and governance

Newborn Screening Ontario (NSO)

- Provincial program based at CHEO in Ottawa
- NSO offers **Dried blood spot** and Critical Congenital Heart Disease screening to all babies born in Ontario
- Since NSO established in 2006
 - >2 million babies screened
 - ~2,750 babies diagnosed and treated early



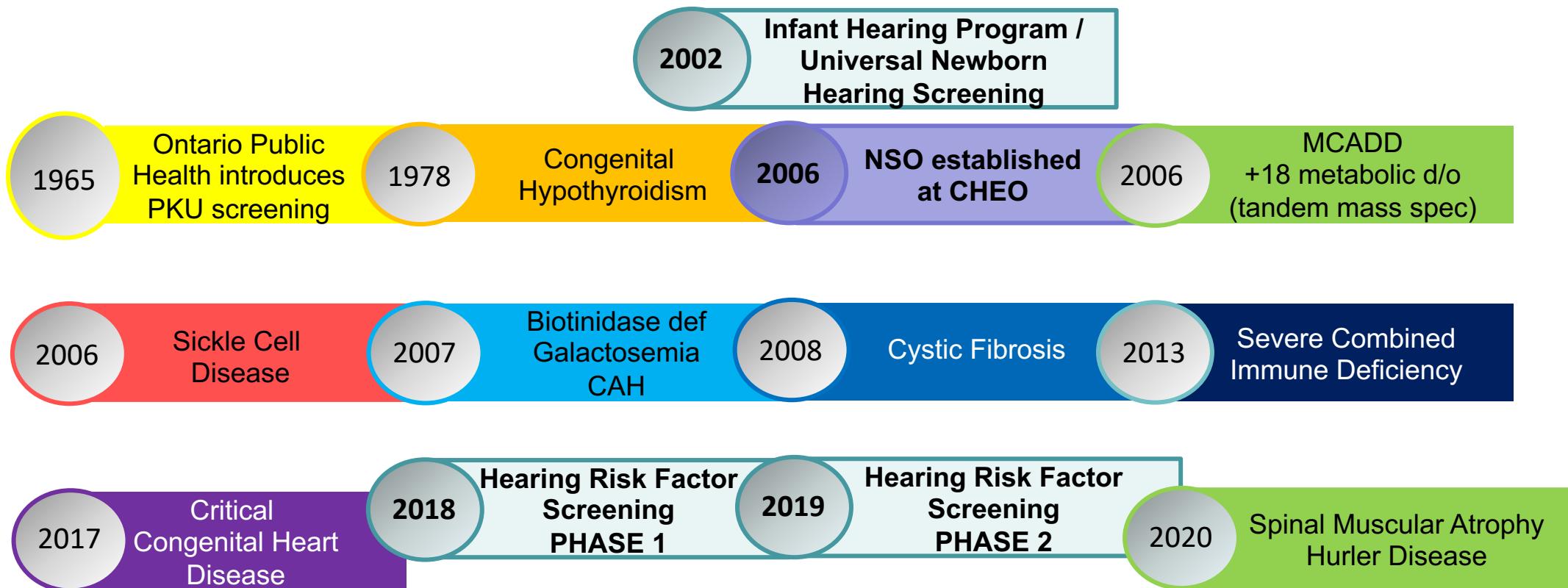
Ontario Infant Hearing Program

- A comprehensive program to identify infants with permanent hearing loss (PHL) or at risk for late-onset or progressive PHL and provide them with the supports and services required for communication and language development, so they are as ready to learn as possible when they reach school.
- IHP provides universal newborn hearing screening, audiology assessment, hearing aid selection, follow-up audiology visits, family support services and communication/language development services for children until school entry.
- The program targets are:
 - screening of newborns by *1 month of age*,
 - identify those born deaf or hard of hearing by *3 months of age*, and
 - start intervention by *6 months of age*.
- Children who meet these targets can develop language comparable to their hearing peers by the time they enter school.
- Delivered through **12 regional lead agencies** across the province:
 - responsible for delivering the program in accordance with **provincial guidelines**
 - in a manner which reflects regional and **local needs**.

Program Components

- **Universal newborn hearing screening** in all birthing hospitals, birthing centres, by midwives, and at community locations for newborns who were missed in hospital.
- **Surveillance screening** is provided for all infants born at risk of developing hearing loss in early childhood
- **Hearing assessment** by pediatric audiologists to confirm the presence of a PHL, and referral for medical evaluation.
- **Hearing aid evaluation**, and/or referral to Cochlear Implant Programs as required or chosen by the family.
- Family support and a range of communication development services including **spoken and/or sign language services**.

History of Newborn Screening in Ontario



Newborn Screening



Condition: NBS Barcode: A 861340

NBS Barcode: A 861340

NBS Barcode: A 861340

NBS Barcode: A 861340

INFANT: [Redacted]
Name: [Redacted] Date: [Redacted]

MOTHER/GUARDIAN: [Redacted]
Name: [Redacted] Date: [Redacted]

Address: [Redacted]
Phone: [Redacted]

Other Health Care Provider: [Redacted]

Report: Screen Positive Screen Negative

Comments: [Redacted]

Un résultat négatif signifie que l'échantillon est normal.
Si l'échantillon de votre sage-femme, infirmière ou décharge des inconvénients, demandez à votre bébé de rentrer à la maison.

Demandez à votre sage-femme, infirmière ou décharge des inconvénients d'avoir une des maladies nécessaires.

Time of Collection: [Redacted]

Date of Collection: [Redacted]

Time of Birth: [Redacted]

Date of Birth: [Redacted]

Photo Number: [Redacted]

Photo Date: [Redacted]

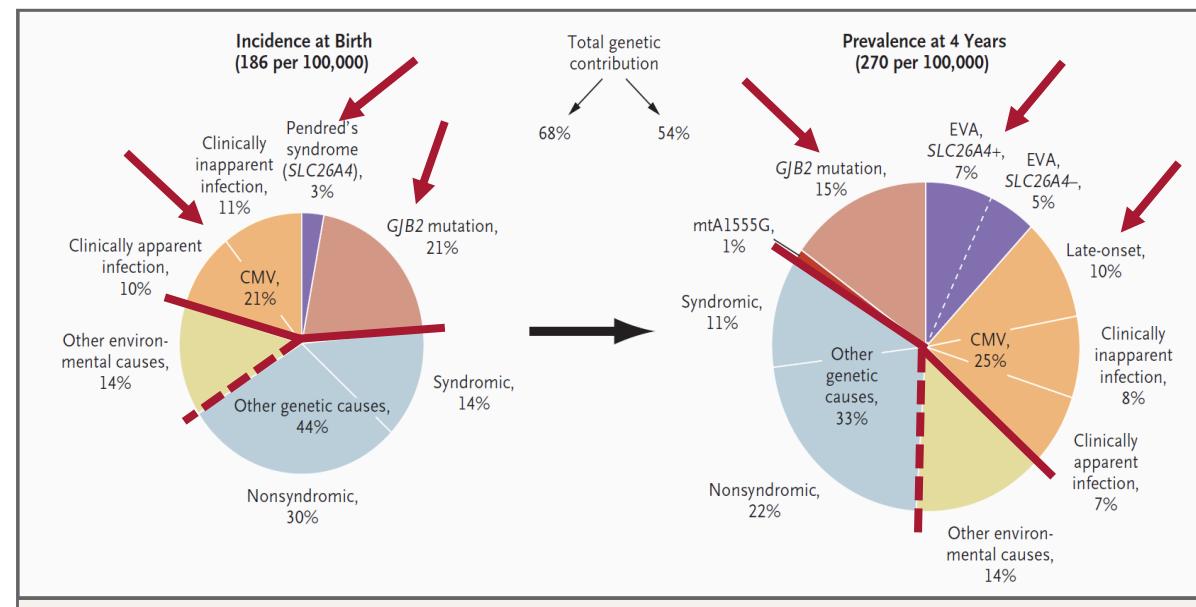
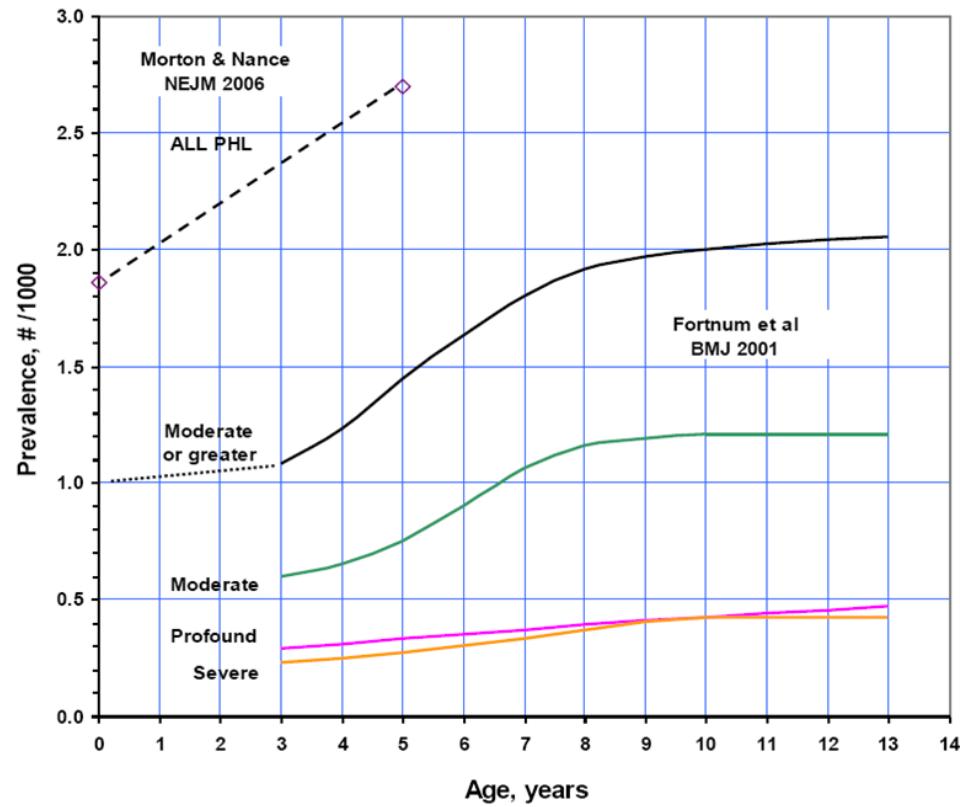


Universal newborn hearing screening

Challenges

- **Identification of infants at risk for non-congenital hearing loss**
 - Risk assessment difficult: chart, family interview
 - Surveillance – who, how often, until when
- **Identification of infants with congenital hearing loss who pass the audiometric screening (i.e. false negatives)**
- **Etiology of hearing loss is often unknown, uncertain or presumed on the basis of risk indicators**
 - Additional/recurring audiological assessment
 - Prognostic value re: treatment decisions
 - Other medical follow-up

Morton and Nance (N Engl J Med 2006;354:2151-2164)

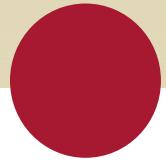


Morton and Nance (N Engl J Med 2006;354:2151-2164)

If screening for these ***three causes**** of late-onset hearing loss was performed, together with a test for the presence of ***cytomegalovirus***, we estimate that the follow-up of at-risk infants should result in the presymptomatic detection of nearly 60 percent of all infants in whom late-onset prelingual hearing loss develops, as well as an immediate etiologic diagnosis for at least 40 percent of those with congenital loss.

**DFNB1 (GJB2/6), DFNB4 (SLC26A4-Pendred/EVA), mt15553A>G*

The policy process in Ontario



Should we screen for congenital CMV infection?

vs

Should we enhance screening for early Permanent Hearing Loss Risk?

The policy process in Ontario



Should we screen for congenital CMV infection?

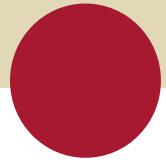
vs

Should we enhance screening for early Permanent Hearing Loss Risk?

i.e. The policy context was a desire to

- *Improve and enhance the IHP (primarily the UNHS component)*
- *Bring together the two newborn screening programs (IHP and NSO) to achieve this*

NSO and IHP – expected enhancements



The current method of audiotric screening, even together with risk assessment:

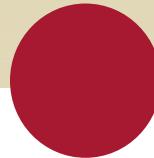
1. Limited in detection of non-congenital PHL
2. Lack of focus on etiology
3. Cases not identified through screening (false negatives)
4. Not all babies are screened (missed screens)



1. Early detection of non-congenital hearing loss
2. Etiological focus
3. Improved sensitivity (fewer false negatives)
4. Improved access (fewer missed screens)

cCMV vs PHL risk factor screening

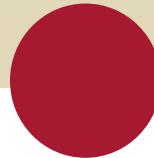
Wilson and Jungner principles



Principle	cCMV screening	PHL risk factor screening
Important public health problem	cCMV is the leading cause of non-genetic sensorineural hearing loss and the 2nd leading cause of intellectual disability after Down syndrome. It involves ~6/1000 babies born in industrialized countries. There is a wide range of health outcomes with some babies being severely affected and most who will have no symptoms or sequelae.	Early permanent hearing loss affects ~3/1000 children, and is associated with permanent developmental sequelae which can be prevented with hearing/communication services and treatment. About 40% of children with PHL by 5 years of age will have intact hearing at birth.
Accepted treatment for patients	Modest benefit of valganciclovir on hearing and developmental outcomes in symptomatic patients. Treatment of asymptomatic children or those with isolated SNHL? Duration of treatment? Possible harms of treatment with wider-spread use?	Early communication and language services and/or hearing interventions (e.g. hearing aids, cochlear implants) lead to improved cognitive and communication outcomes
Facilities for diagnosis and treatment	New medical care network coordinating with tertiary care audiology/ENT or established Infant Hearing program	New medical care network in the context of established Infant Hearing Program (screening and surveillance system).
Recognizable latent or early symptomatic stage	Majority of infants (85-90%) with cCMV will be asymptomatic - Risk of harm with identification of healthy babies? - Ability to predict which 10% of asymptomatic cCMV babies will develop sequelae?	There is a 10% risk of PHL with asymptomatic cCMV infection, and a >30% risk with symptomatic infection. Recognizing this risk provides the opportunity for early intervention (if already deaf) or surveillance in the existing risk factor UNHS system

cCMV vs PHL risk factor screening

Wilson and Jungner principles



Principle	cCMV screening	PHL risk factor screening
Suitable test or examination	Concerns re sensitivity of DBS testing. Specificity?	Overall improvement in sensitivity of ascertainment of PHL risk due to cCMV vs status quo. Specificity?
Test acceptable to the population	DBS accepted. Possible maternal guilt, concern re prenatal care/education, stigmatization (e.g. day-care)	DBS accepted and same concerns. Opportunity to consent for testing when hearing screen offered
Natural history, including from latent to declared disease, adequately understood	Natural history of asymptomatic cCMV unclear with poor predictors of risk for later onset sequelae	Early onset PHL has well described patterns of natural history (e.g. stable, progressive, fluctuating) with established protocols for surveillance.
Cost of case-finding economically balanced in relation to expenditure on medical care as a whole.	Cost effectiveness unproven	Cost effectiveness unproven
Case-finding should be a continuing process	Intended to be a continuing process	Intended to be a continuing process

The policy process in Ontario



- Policy process and decision making
 - Led by the MCCSS (child services) with support from MOH (health)
 - Screening principles primarily considered from the perspective of the Infant Hearing Program with risk of permanent hearing loss by age 5 as the target of screening
- Decision
 - Augment the IHP led UNHS program with secondary testing of the NSO DBS for CMV DNA and DFNB1/DFNB4 mutation panel
 - enrollment and consent as part of hearing and not DBS screening
 - data sharing between programs
 - education and training shared
 - referral of screen positive infants
 - CMV: medical referral by NSO physician, audiology care and surveillance fully integrated into IHP
 - Genetic: joint IHP/NSO retrieval with back up of medical referral by NSO

The policy process in Ontario



Conception (2010-12)

Development

- Phase 1 (2013-14)
 - Test development: qPCR for CMV DNA / MassArray for DFNB1 (GJB2/6) and DFNB4 (SLC26A4)
 - Anonymized testing of 10,000 stored residual DBS sample
- Phase 2 (2014-16)
 - Test refinement including consideration of saliva sampling and DNA extraction optimization
 - Define options for enrolment and consent, pre and post screening care pathways, and integration of DBS and UNHS systems
- Phase 3 (2016-18)
 - Policy submission and consideration
 - Identification of budget and development of implementation plan

Implementation

- Phase 1 (2018)
 - Hearing-targeted cCMV screening
- Phase 2 (2019)
 - Universal cCMV and genetic risk factor screening

Expanded Hearing Screening



Newborn Blood Spot Screening

Testing for rare, treatable diseases:

- Metabolic Diseases
- Endocrine Diseases
- Sickle Cell Disease
- Cystic Fibrosis
- Severe Combined Immune Deficiency



Hearing Screening Audiometric screening



PASS



REFER

No further follow-up unless risk factors identified and/or dried blood spot tests positive

Specialized audiology testing and/or surveillance



Parental consent obtained by IHP to test dried blood spot

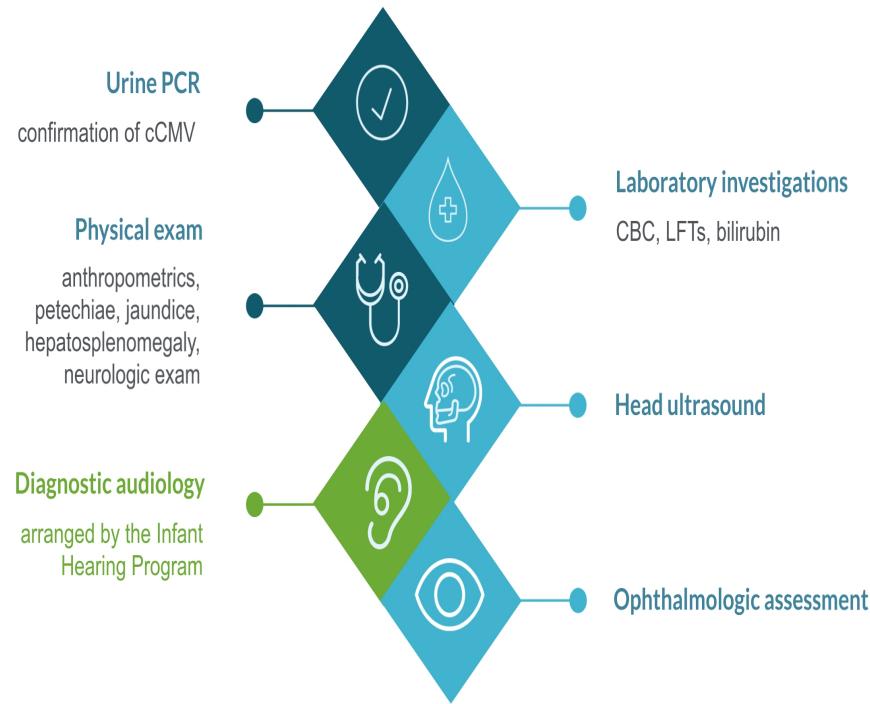
NSO tests for hearing loss risk factors (July 2019)



1. Cytomegalovirus (CMV)

2. Genetic factors

Initial Evaluation of Screen Positive infants



Indications for ID referral

- Symptoms of cCMV (regardless of age)
 - Microcephaly, cerebral calcifications, retinitis (clear cut)
 - IUGR, thrombocytopenia (non-specific)
 - **Isolated SNHL**
- Uncertainty of whether symptomatic disease
- Need for further counseling/parental request
- Babies admitted to NICU (*generally*)



Hearing Loss Risk Factor Screening

Home Hearing Loss Risk Factor Screening Overview

Explore

Overview

- > Risk Factor Screening Process
- > Congenital Cytomegalovirus
- > Genetic Risk Factors
- > Risk Factor Screening FAQ
- > Hearing Screening Resources
- > Screening Results
- > For Health Care Providers

Overview

The Ontario Infant Hearing Program (IHP) provides universal newborn hearing screening in hospital or community settings to identify newborns with permanent hearing loss (PHL) and support their language development so they will be ready to start school.

The IHP also offers monitoring for children who are at increased risk of developing hearing loss, in the following ways:

- Babies with certain risks for PHL recognized at the time of hearing screening are offered monitoring for hearing loss through the IHP.
- All babies who have hearing screening are offered risk factor screening for PHL using the sample already collected by the hospital or midwife for routine newborn screening (the heel prick test).
 - This screening is performed by Newborn Screening Ontario (NSO) and specifically looks for [Cytomegalovirus \(CMV\)](#) infection and some common [genetic risk factors](#) for PHL.
 - Babies with these risk factors have a higher chance of having PHL at birth or of developing it in early childhood and, when found through screening, can be connected with the appropriate audiology and medical follow-up.

Babies and children who are identified with hearing loss as early as possible can have access to support and services sooner and have better outcomes.

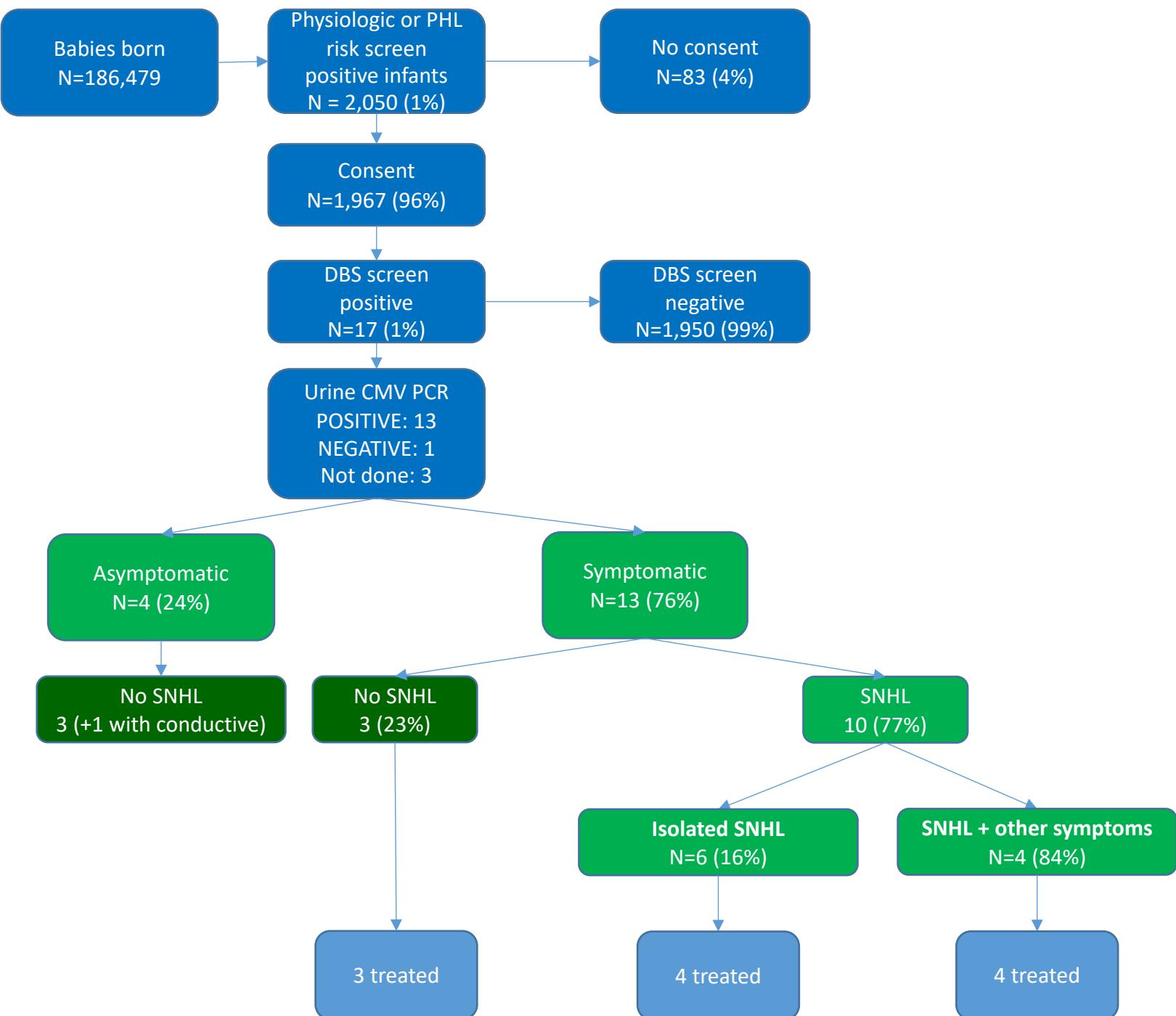
Risk factor screening for PHL started in Ontario for babies born on or after July 29, 2019. This screening is offered to parents/guardians at the time the infant hearing screening is done, or when the hearing screening appointment is booked.

From May 2018 until July 29, 2019, screening for CMV infection was offered for babies who had a refer result to an audiologist because they did not pass their hearing screening or because a strong risk factor for PHL was recognized at birth. Babies who screen positive for CMV on this targeted screen are referred directly to an Infectious Diseases Clinic for further evaluation.

IMPORTANT NOTIFICATION (March 2020)

Phase 1 (May 2018 - July 2019)

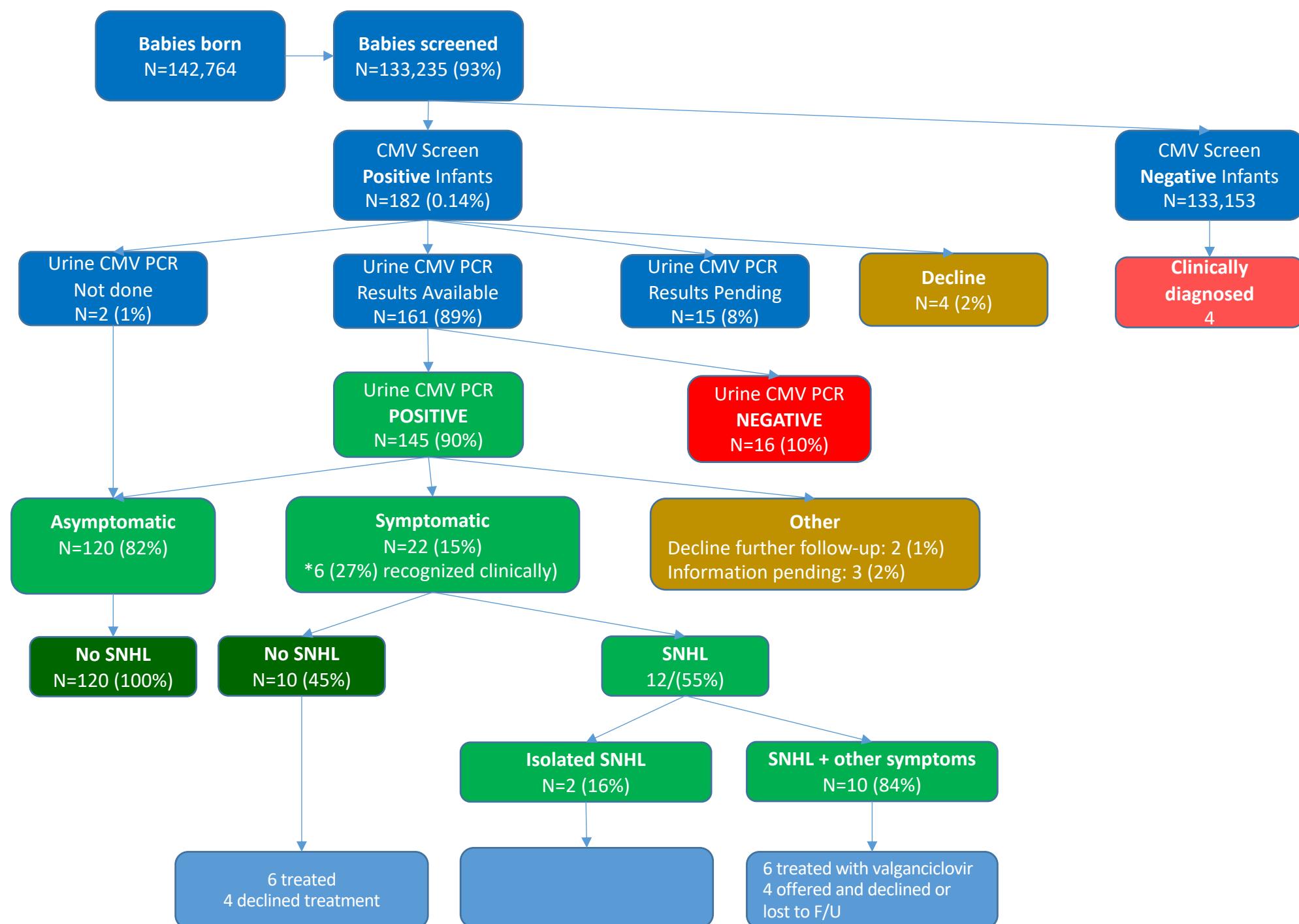
Hearing- targeted CMV screening



Phase 2

(July 28, 2019-July 29, 2020)

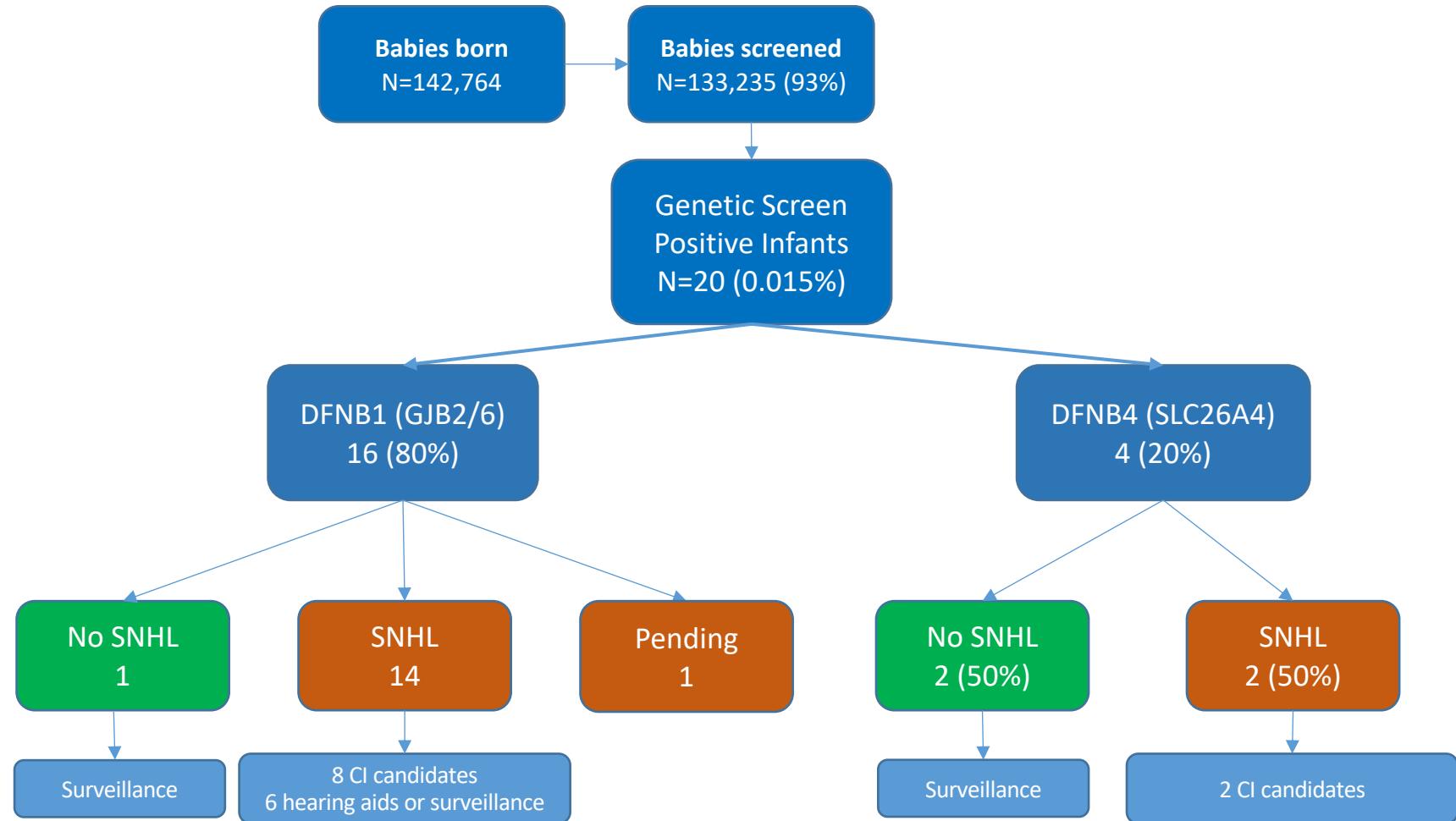
Universal offer CMV / Genetic screening



Phase 2

(July 28, 2019-
July 29, 2020)

Universal offer
CMV / Genetic
screening



Conclusions and Next Steps

- Ontario considered and implemented newborn DBS CMV screening as an improvement to existing PHL risk factor screening in the IHP
- We are picking up both asymptomatic and symptomatic kids with cCMV who would otherwise be missed
- Focus on education and ensuring awareness of the program and acceptability of testing
- Evaluation and next steps
 - Acceptability – parents, providers, public
 - Consent rate, decline/lost to follow up rate
 - Performance
 - Sensitivity – most likely lower than projected
 - Specificity/Discrepant results
 - Timing
 - Earlier care for many infants but may need to speed up process
 - Health economics

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