

Results of a Targeted Screening Program for Congenital Cytomegalovirus (cCMV) Infection in Montréal, Québec

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CHU Sainte-Justine

Le centre hospitalier
universitaire mère-enfant

Université 
de Montréal

Targeted Screening

- Universal vs. targeted screening for cCMV infection is a subject of considerable debate
- Identifying risk factors that allow for targeted screening cCMV patients would diminish the costs and potentials risk associated with universal screening – identifying those who need treatment
- A number of centers have started targeted CMV screening of infants who fail newborn hearing screen
- **Other targeted groups considered:** Infants of HIV infected mothers, infants admitted to NICU

Targeted Screening

The objective of this study to describe the experience with targeted CMV screening through infant newborn hearing program, at CHU Sainte-Justine, Montreal, Quebec

❖ Phase I: 2008-2011

❖ Phase II: 2014-2018

CHU Sainte-Justine

3500 births/year
65 bed NICU
Tertiary care for
premature
babies and
neonatal surgery



450 bed
Maternal-Child Health Center
Montréal, Québec

Universal newborn hearing screening

Programme québécois de dépistage de la surdité chez les nouveau-nés (PQDSN)

- Beginning in 2008, the PQDSN program was meant to diagnose and manage:
 - **Moderate or profound bilateral hearing loss:**
 - ≥ 40 dBHL
 - Average thresholds at frequencies :
500-1000-2000-4000 Hz
 - **Bilateral ANSD (auditory neuropathy spectrum disorder) in babies presenting at least one hearing risk factor**

CHU Sainte-Justine UNHS

- As part of the UNHS program, all infants were tested using a combined protocol of
 - Automated distortion product otoacoustic emissions (DPOAE-A) and
 - Automated auditory brainstem response (A-ABR)

**Programme québécois
de dépistage de la surdité
chez les nouveau-nés**

CADRE DE RÉFÉRENCE



Québec 

Le centre hospitalier
universitaire mère-enfant

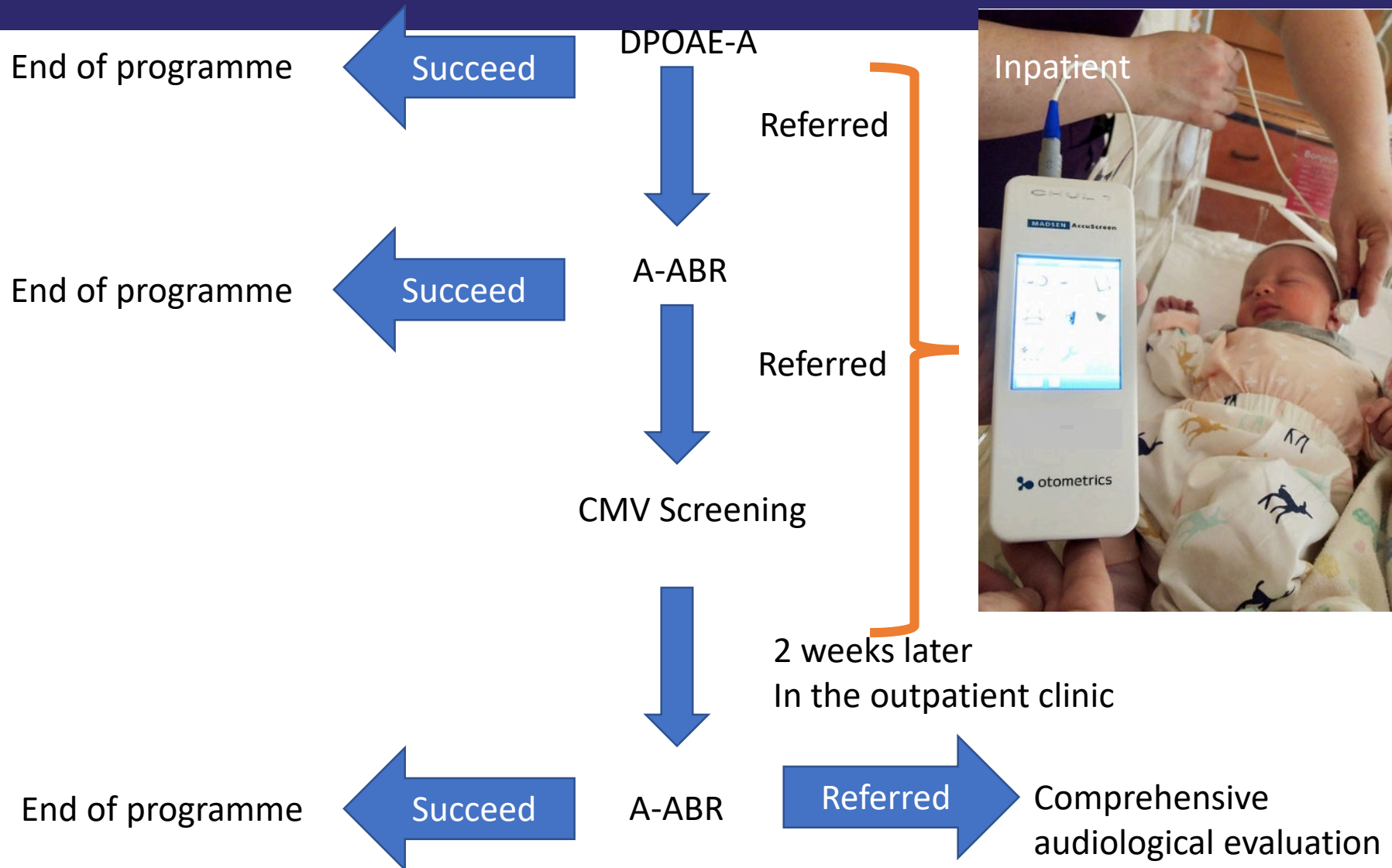
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Risk factors for hearing loss

- Family history of hearing loss
- Congenital infection suspected or confirmed
- Craniofacial anomaly
- Genetic syndrome associated with hearing loss
- Hyperbilirubinemia
- Very low birth weight (VLBW) less than 1500g
- Prematurity (less than 29 weeks of gestation)
- Respiratory disorders
- Neurology disorders
- Excessive doses of ototoxic drugs
- Confirmed bacterial or viral meningitis
- Anotia, microtia, atresi (one or both ears)
- Extended stay in NICU (reached the corrected age of 3 months)

UNHS protocol

Newborn WITHOUT risk factors



UNHS protocol Newborn WITH risk factors

NICU
20% of Births
at CHUSJ

End of programme

Succeed

A-ABR

Referred

CMV screening

2 weeks later
In the outpatient clinic

End of programme

Succeed

A-ABR

Referred

Comprehensive
audiological evaluation



METHODS

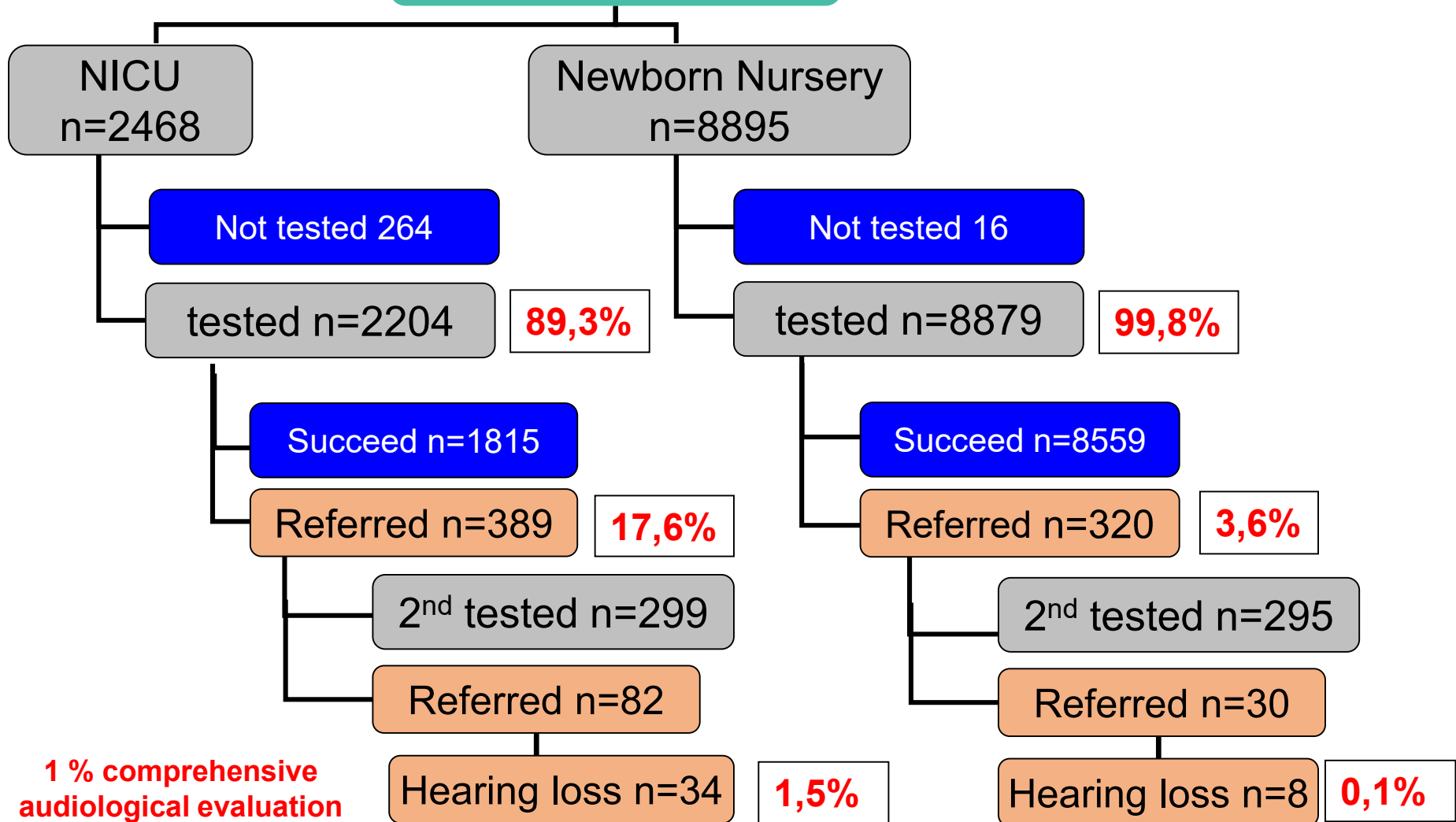
- Retrospective analysis of UNHS results related to CMV screening results
- The data for the current study were drawn from 3 sources
 - CHU Ste-Justine UNHS database
 - CHU Ste-Justine Virology Laboratory
 - CHU Ste-Justine CMIS HIV database

Phase 1: 2008-2011, Urine PCR

Phase 2: 2013-2018, Saliva PCR

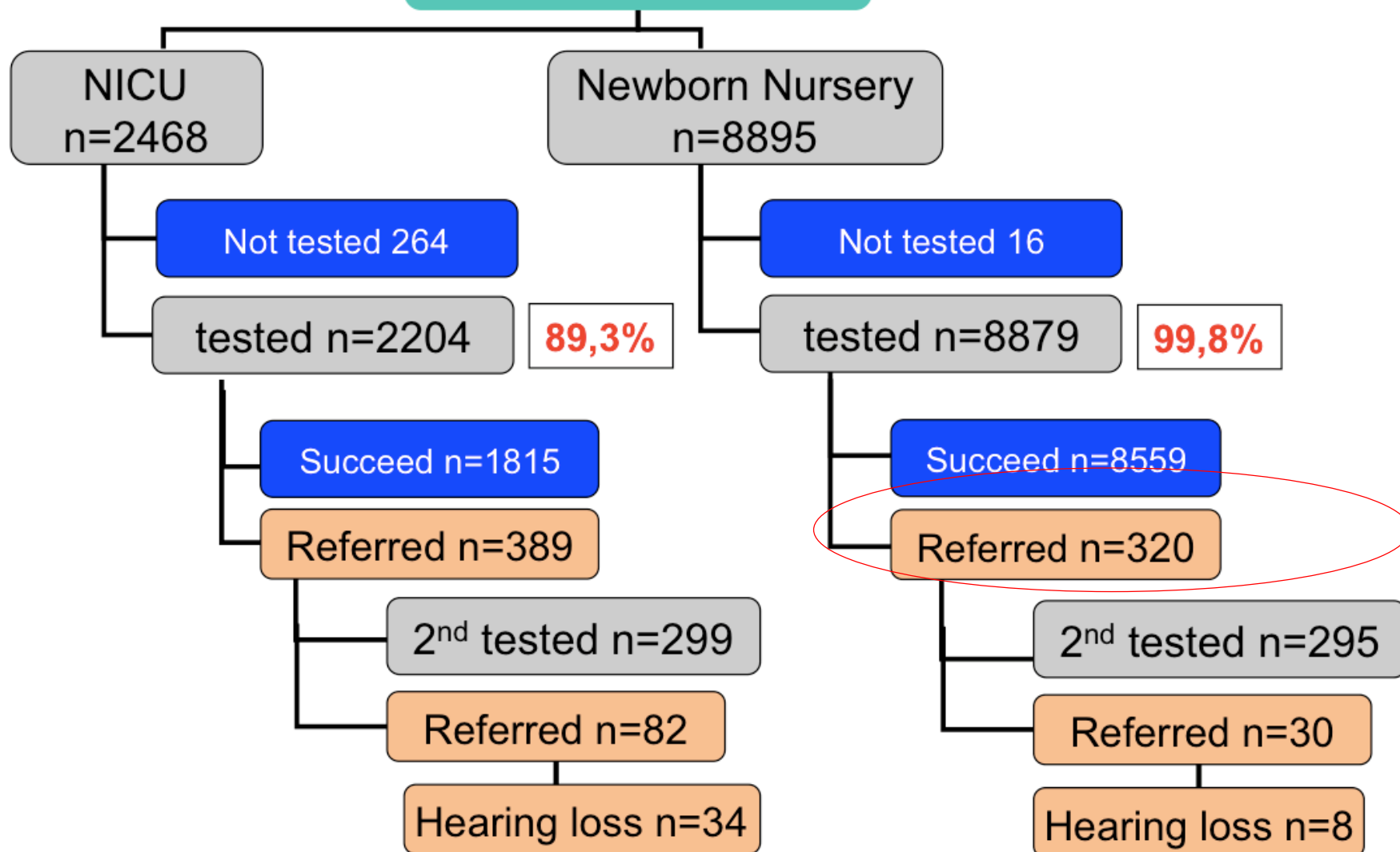
UNHS from 2008 to 2011

11363 Newborns



UNHS from 2008 to 2011

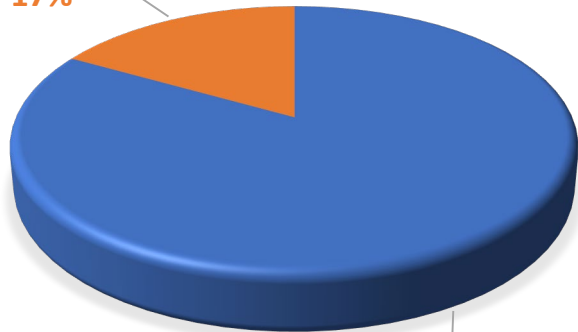
11363 Newborns



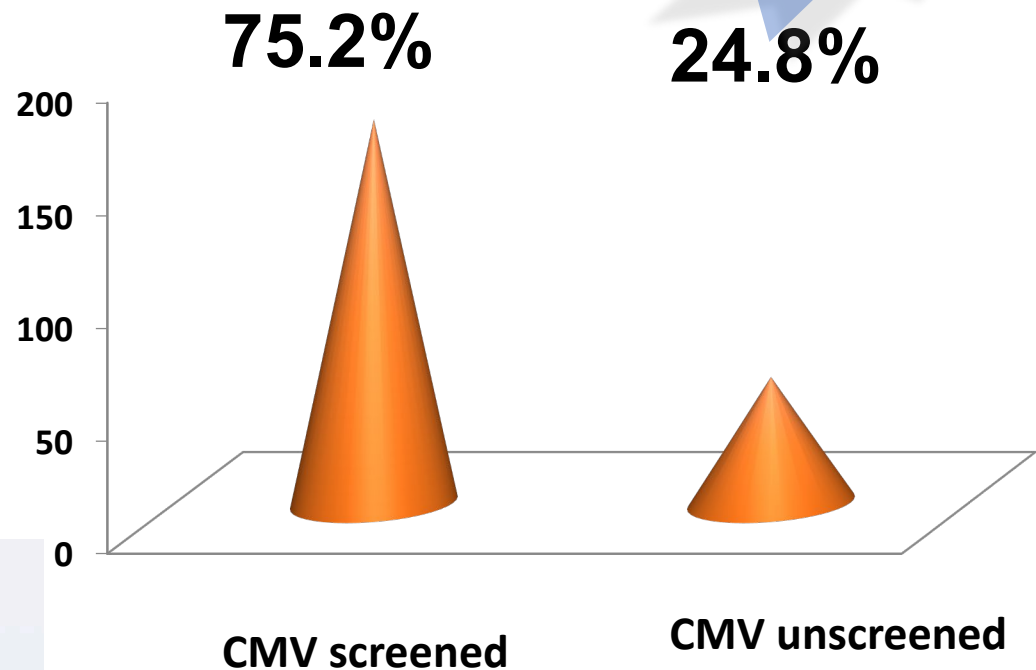
CMV urine testing (shell vial) in the nursery

n=226 tested for CMV
(320 Referred)

Bilatérale
17%

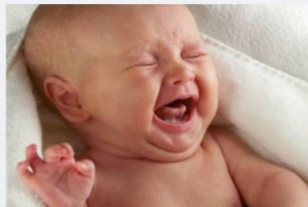


Unilatérale
83%



Difficult to
screen with
URINE

Newborn urine bag collection



CMV testing in children with hearing loss (n=42)

PHASE I 2008-2011

- **Newborn nursery n=8:**

- CMV positive = 0
- CMV negative = 3
- CMV unscreened = 5

- **NICU n=34:**

- CMV positive = 3 (8,8%)
- CMV negative = 11
- CMV unscreened = 20

Many cases
unscreened...

Directly related to the fact that
most hearing screen is
performed after 21 days of age
because of mechanical
ventilation

Medoro et al. "Targeted" Screening for Cytomegalovirus (CMV)-Related Hearing Loss: It's Time for Universal CMV Screening in the NICU!, Abstract 2326, ID Week 2017

Validation of CMV Screening from Saliva with in house CMV PCR

Comparison of 56 patients tested by CMV urine culture and CMV PCR on saliva (2012)

	Urine +	Urine -
saliva +	9	4
Saliva -	0	43

Sensitivity: 100%
Specificity: 91.5%

**Decision to screen with CMV PCR on saliva but
confirm with CMV PCR on urine**



Revised and upgraded targeted screening Program for cCMV in the Newborn Nursery

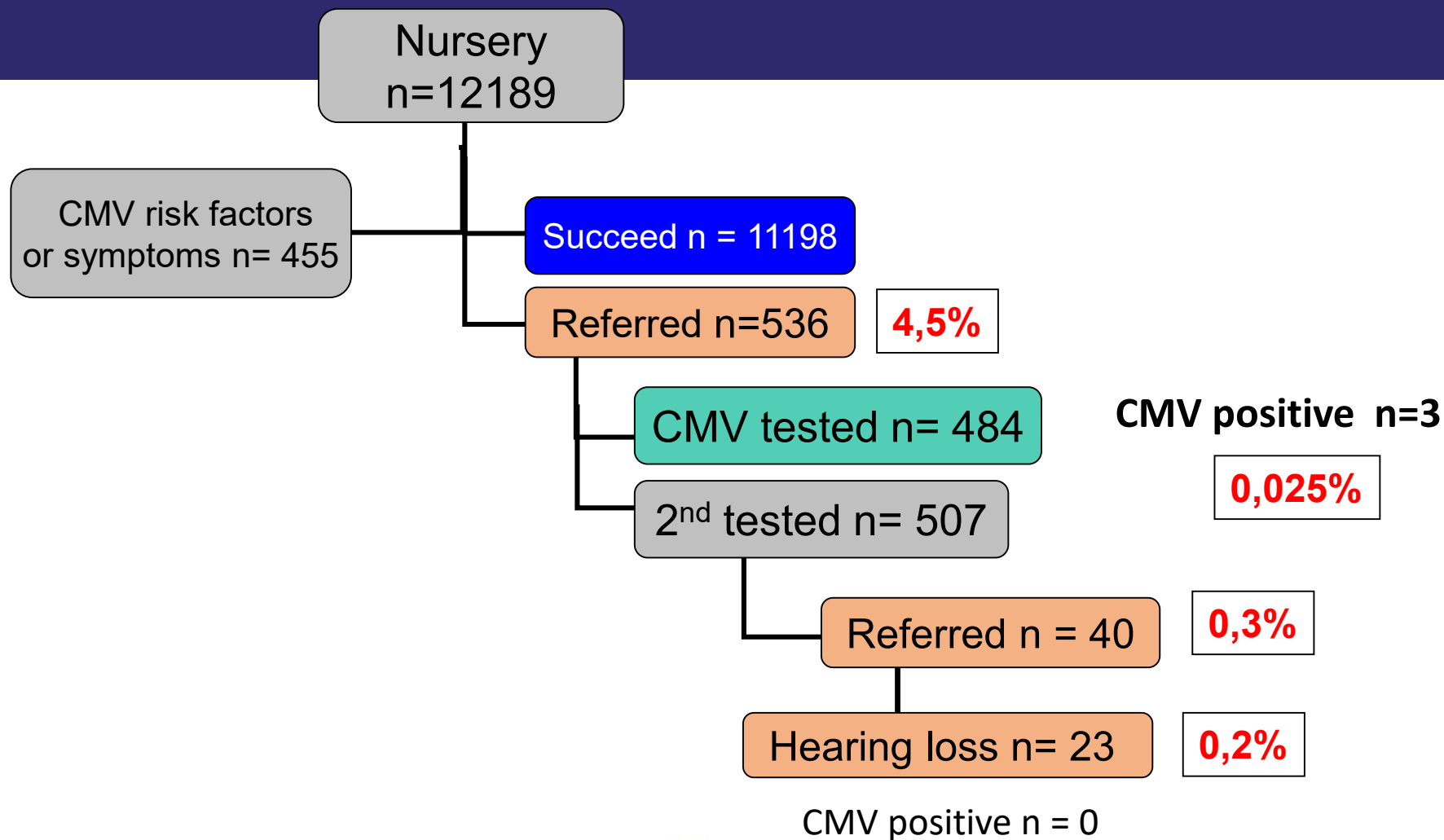
2014-2018: Phase II, Saliva testing by PCR for

All newborns who did not pass their hearing test

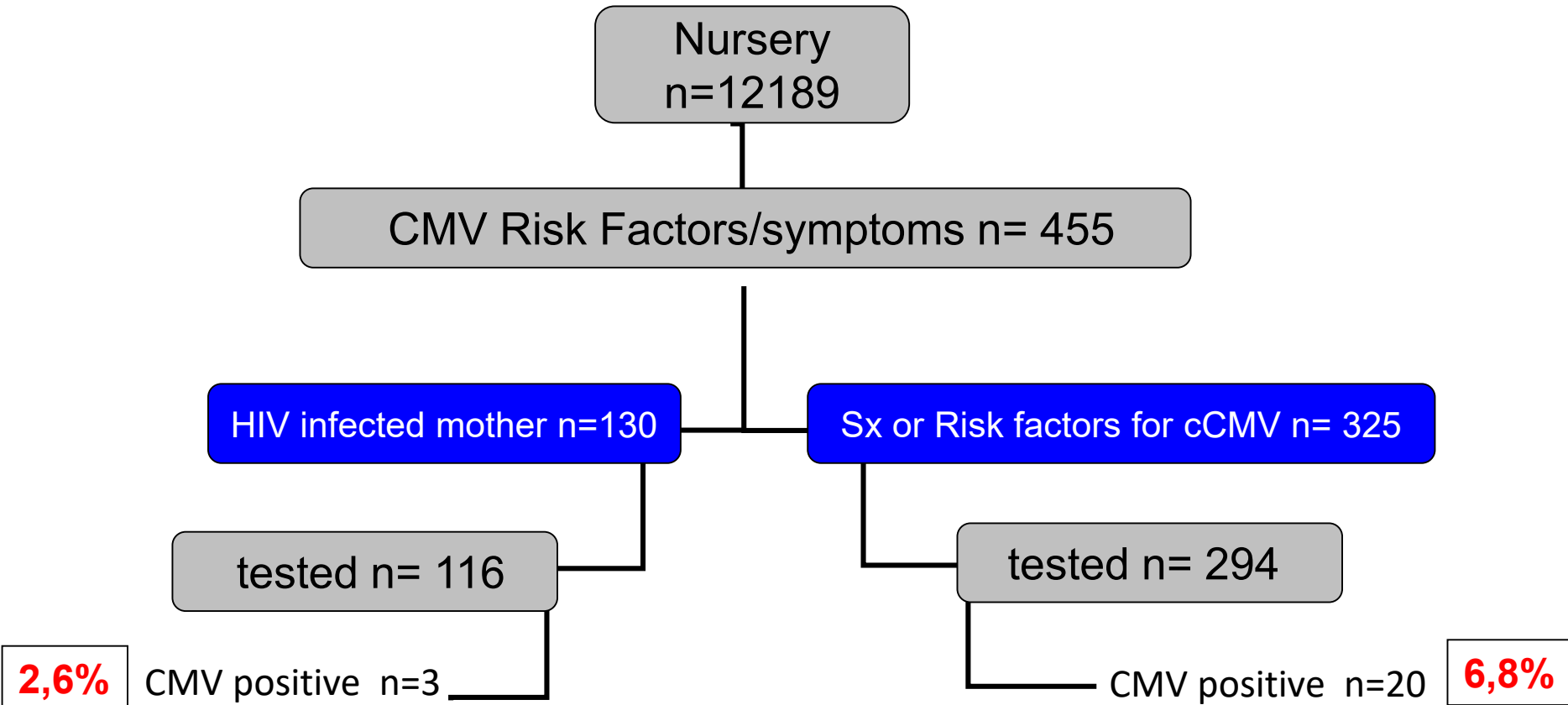
All newborns of HIV infected mothers

All newborns symptoms suggestive of cCMV (paediatrician's judgement) ex: IUGR, thrombocytopenia, hepatitis, cholestasis, hepatosplenomegaly) or of mothers with confirmed or suspected primary CMV infection in pregnancy

UNHS Targeted cCMV Screening from 2014 to 2018



cCMV Screening (newborns with identified with risk factors) 2014 to 2018



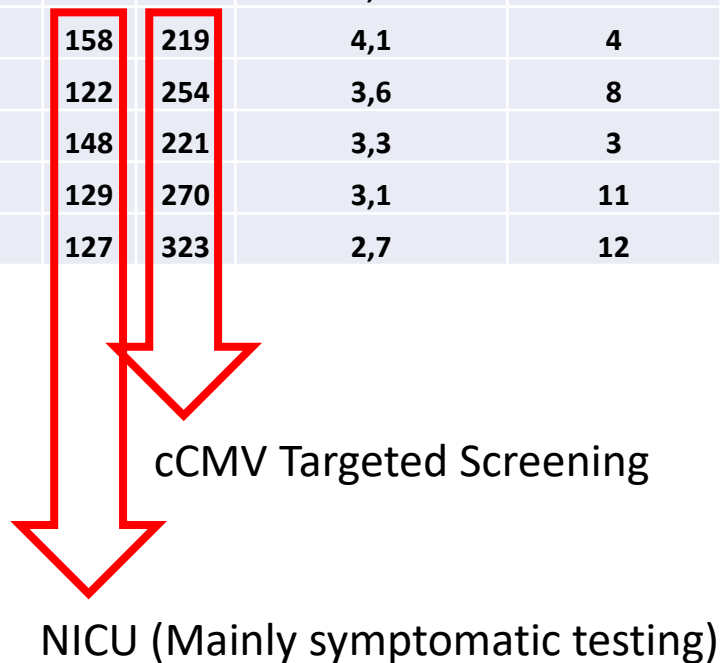
RESULTS

- Using these combined methods, a total of 0.21% of newborns enrolled in the targeted screening program tested positive for cCMV infection
- Incidence of cCMV is unknown in our population but we expect 0,5 to 1% as other North American metropolitan populations...

	Symptomatic or risk factor	HIV exposed	UNHS only
% Positive for CMV among those screened	6.8%	2.6%	0.62%
% of overall cohort	0.17%	0.025%	0.017%

From the laboratory perspective...

	patients	urine	saliva	patient age (average in days)	Positive patients	shell vial	PCR	Tube culture	Low positive CMV PCR in saliva
2012	194	137	30	5,6	4	212	13	183	0
2013	297	158	219	4,1	4	340	140	215	1
2014	340	122	254	3,6	8	350	180	212	1
2015	334	148	221	3,3	3	25	352	340	0
2016	375	129	270	3,1	11	2	391	381	0
2017	423	127	323	2,7	12	0	446	443	3



- More patients are tested every year in the targeted screening program
- Same number of patients are tested in the NICU every year
- Patient age at testing has gone down annually
- Approximately 13% false positive in saliva

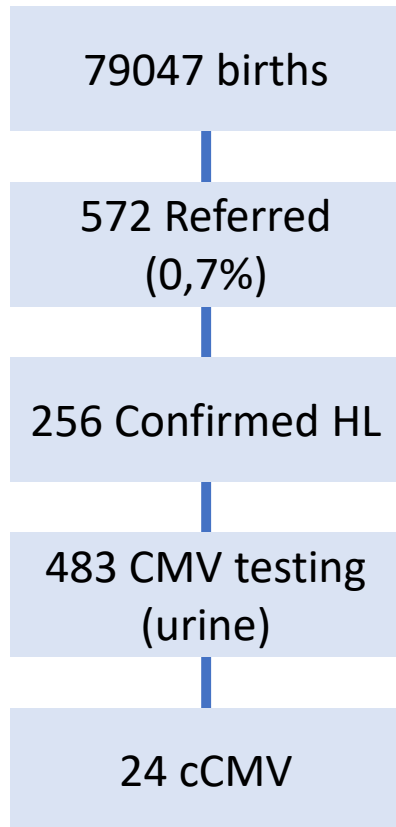
DISCUSSION

Renaud et al. 2018 Québec	Diener et al. 2017 Utah	Roth et al. 2017 Israel	Vancor et al. 2018 Connecticut	Stehel et al. 2008 Texas	Kadambari et al. 2015 UK
11734 births (excluding NICU + CMV RF)	103868 births (NICU?)	19830 births (including NICU)	10964 births (NICU?)	79047 births	10385 births (NICU?)
536 Referred (1st) (4,6%)	509 Referred (2 nd) (0,4%)	200 Referred (1%)	171 Referred (1,6%)	572 Referred (0,7%)	349 Referred (1st) (3,4%)
23 Confirmed HL	104 Confirmed HL (SNHL and mixte)	36 Confirmed HL (SNHL)	22 Confirmed HL (uni and bilateral)	256 Confirmed HL	
484 CMV testing (saliva)	314 CMV testing (mixte)	178 CMV testing (saliva)	171 CMV testing (saliva)	483 CMV testing (urine)	203 CMV testing (saliva)
2 cCMV	14 cCMV	4 cCMV	3 cCMV	24 cCMV	2 cCMV
0% of Confirmed 0,37% of Referred 0,017% of cohort 2 normal hearing	5,7% of Confirmed 2,75% of Referred 0,013% of cohort 8/14 normal hearing	8,3% of Confirmed 2% of Referred 0,020% of cohort 1/4 normal hearing	4,5% of Confirmed 1,8% of Referred 0,027% of cohort 2/3 normal hearing	6,3% of Confirmed 4,2% of Referred 0,034% of cohort 8/24 normal hearing	0,6% of Referred 0,019% of cohort 1/2 normal hearing

Multicriteria targeted screening

Stehel et al. 2008

Texas



6,3% of Confirmed
4,2% of Referred
0,034% of cohort
8/24 normal hearing

Using these same criteria:

- HIV infected mothers
- UNHS
- Clinical

Identified 50 cCMV cases
= 0,06% of the cohort

CIME cohort: We identified 0,21% of the cohort with cCMV

Difference in criteria (clinical thresholds? Or difference in incidence?

Future directions

Is the UNHS a good targeted population for cCMV screening?

	Symptomatic or risk factor	HIV exposed	UNHS only
% Positive for CMV among those screened	6.8%	2.6%	0.62%
% of overall cohort	0.17%	0.025%	0.017%

Improving targeted screening – beyond the hearing program

- Define additional risk factors for cCMV infection (other infants to target):
 - All infants of immunocompromised mothers
 - With data from local epidemiology
- Enhance nursery identification/physician awareness of symptoms for screening
- Consider other at risk groups to targeted (NICU)

Acknowledgements

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- ENT team
- CHU Sainte-Justine Virology Laboratory

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