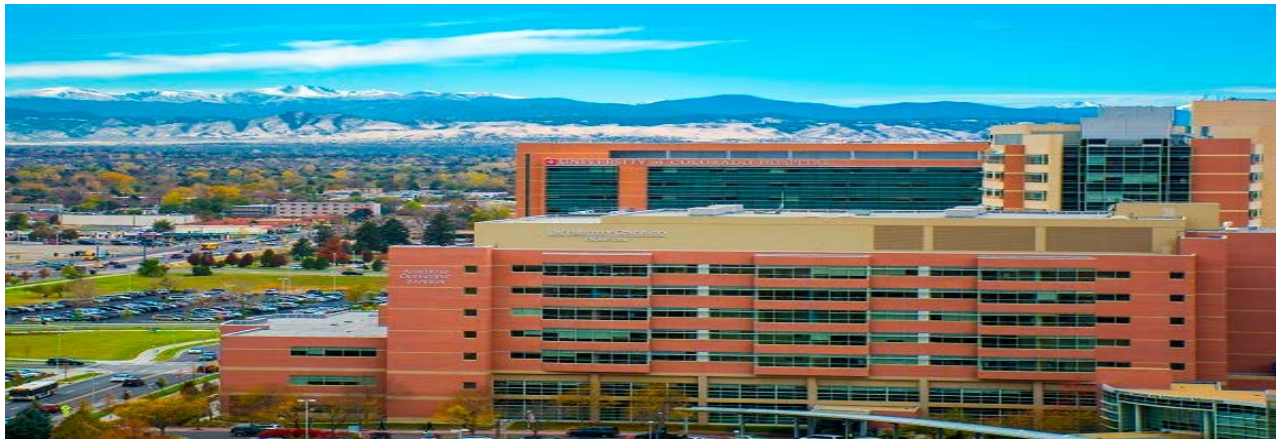


Evaluation of Modified Newborn Screening Algorithms for Critical Congenital Heart Disease at Moderate Altitude



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Background

- Critical Congenital Heart Disease (CCHD) was added to the RUSP in September 2011
 - Call for more data from high and moderate altitude areas
- American Academy of Pediatrics (AAP) algorithm based on studies conducted near sea-level

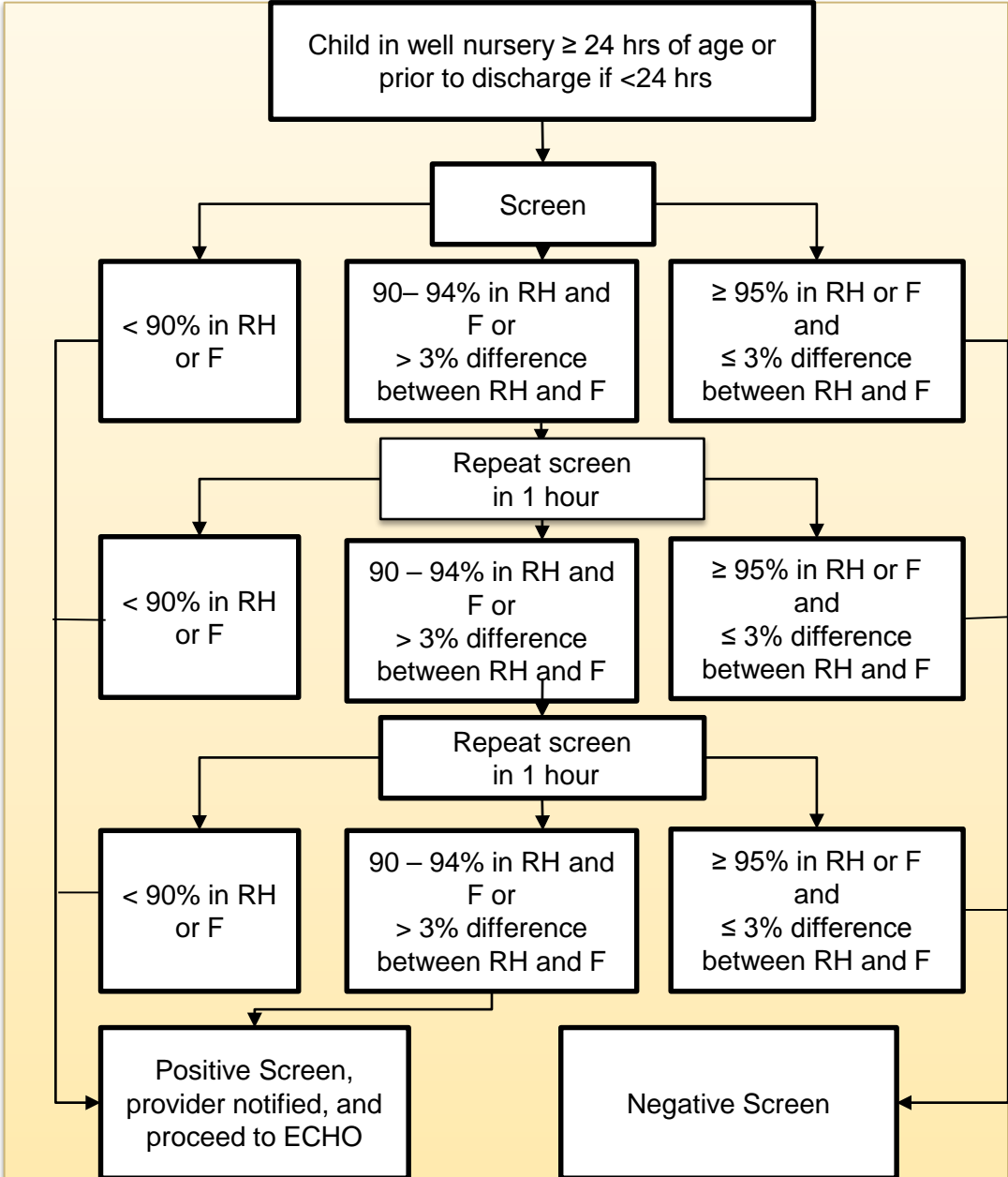
CCHD in Colorado

- As altitude increases the partial pressure of oxygen decreases resulting in lower oxygen saturations
- Expected delay in transition from fetal to neonatal circulatory system for some newborns at altitude
- Increased screen failures lead to increased cost and stress for families and facilities

American Academy of Pediatrics Algorithm:



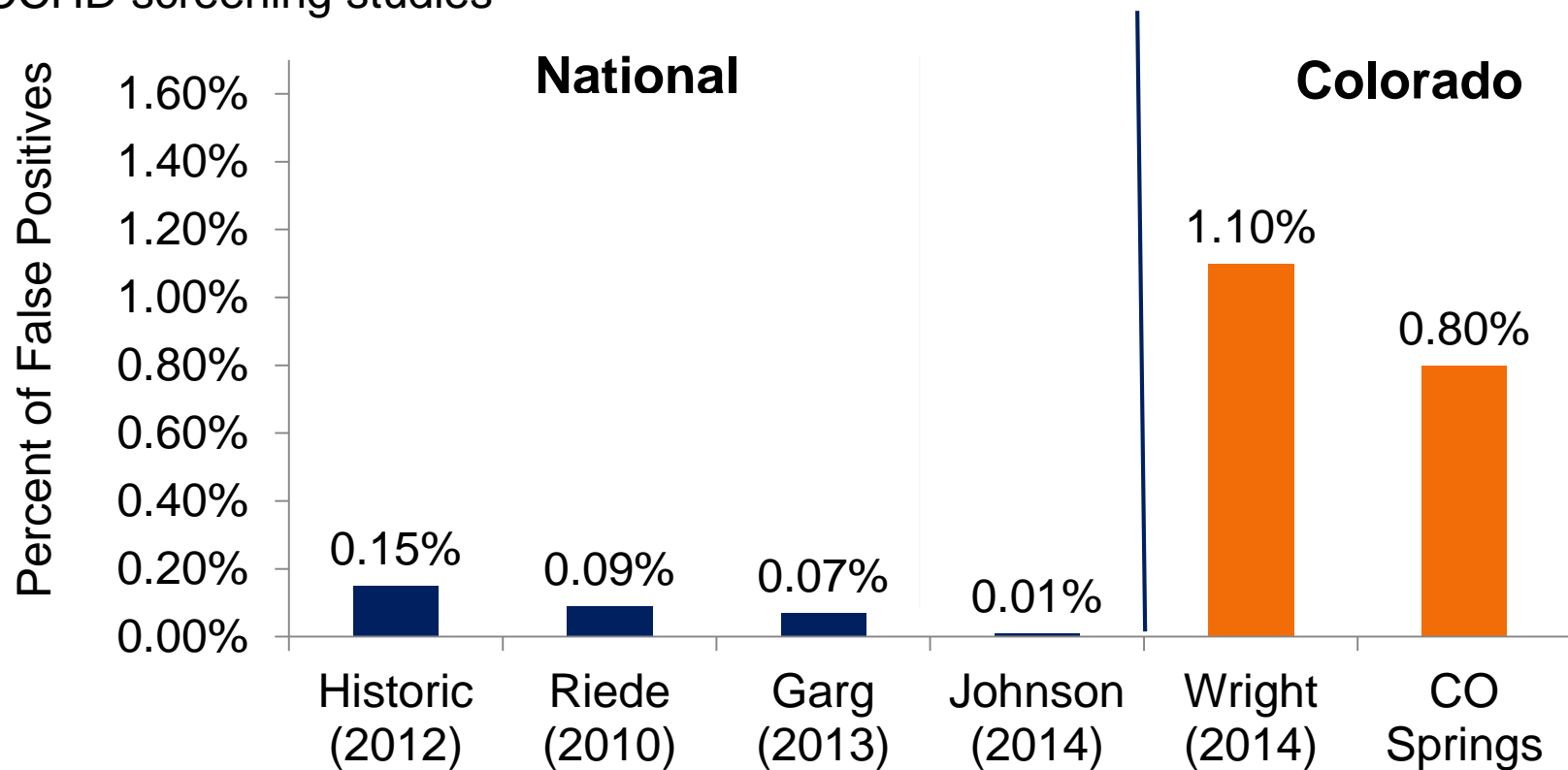
RH = right hand
F = either foot



Credit: Pictures-<http://www.masimo.fr/Eve/index.htm>, Figure-Lueth et al., 2015 (submitted for publication)

Previous Research on CCHD Newborn Screening

Proportions of CCHD newborn screening false positives in National and Colorado CCHD screening studies



Thangaratinam, et al Lancet 2012. Riede et al Eur.J.Pediatr. 2010. Garg, et al Pediatrics 2013. Johnson, et al Pediatrics, 2014.

Research Objective

Identify modified algorithms that lower the percentage of CCHD newborn screening false positives in Colorado while maintaining screening sensitivity.

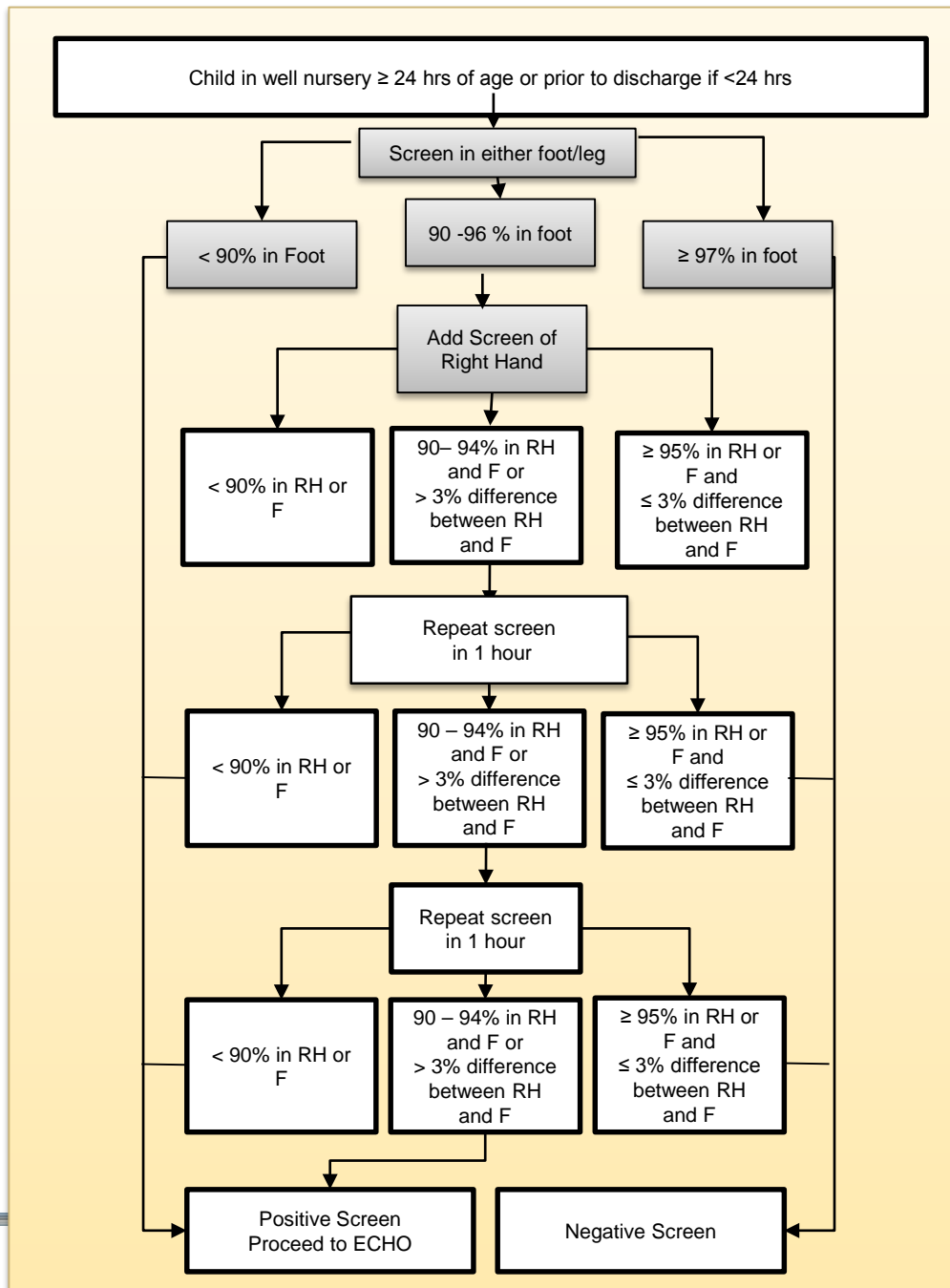
Methods

- Retrospective cross-sectional study
- Newborns born at the University of Colorado Hospital between October 2012- December 2013
- Recommended algorithm (AAP) compared to 3 modified algorithms: Tennessee, Kohn, and Tennessee+Kohn
- Collaboration with the Colorado Department of Public Health and Environment's (CDPHE) Birth Defects Registry to identify CCHD screening false negatives in the study population

Tennessee Algorithm:

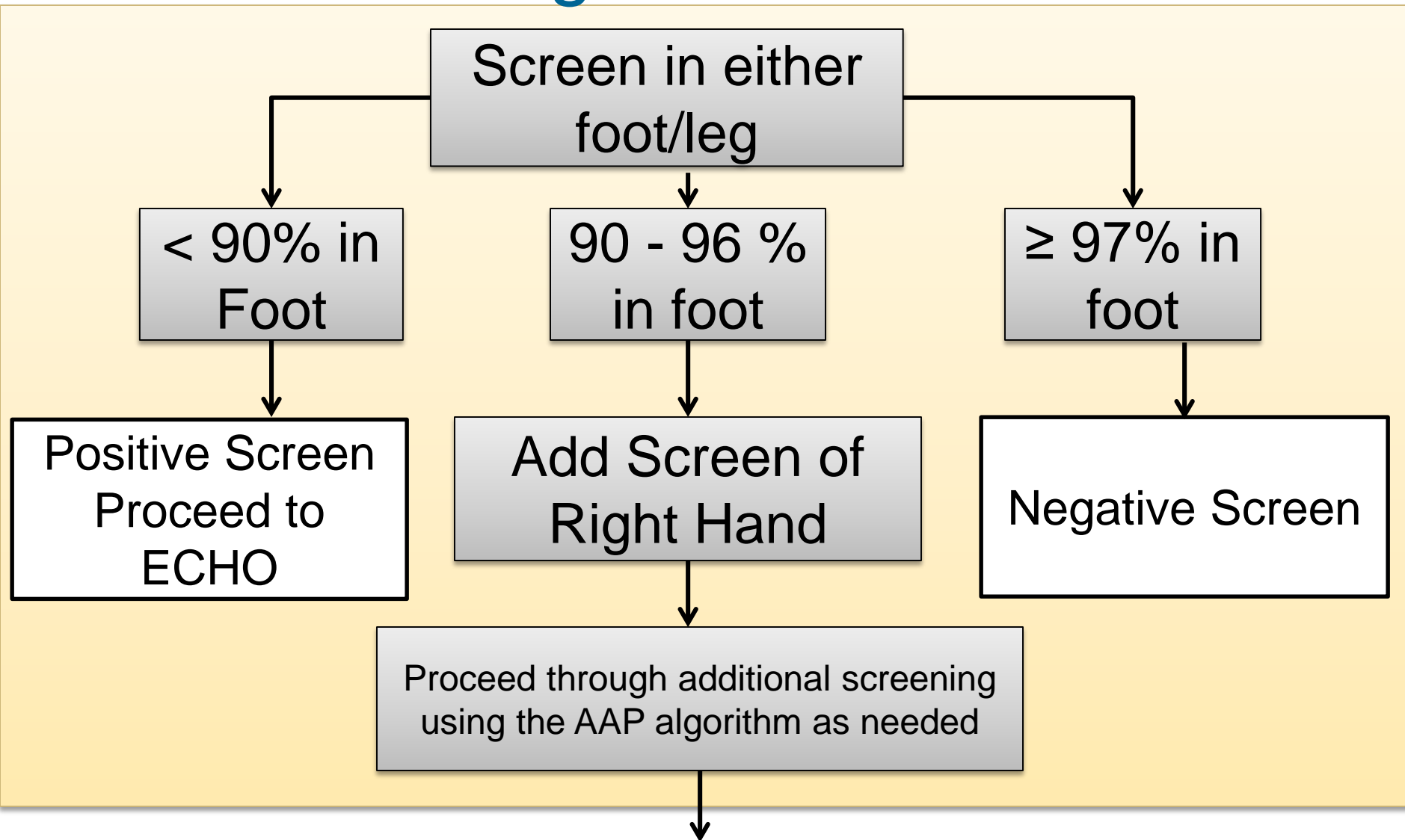
Modifications are highlighted in gray

RH = right hand
F = either foot



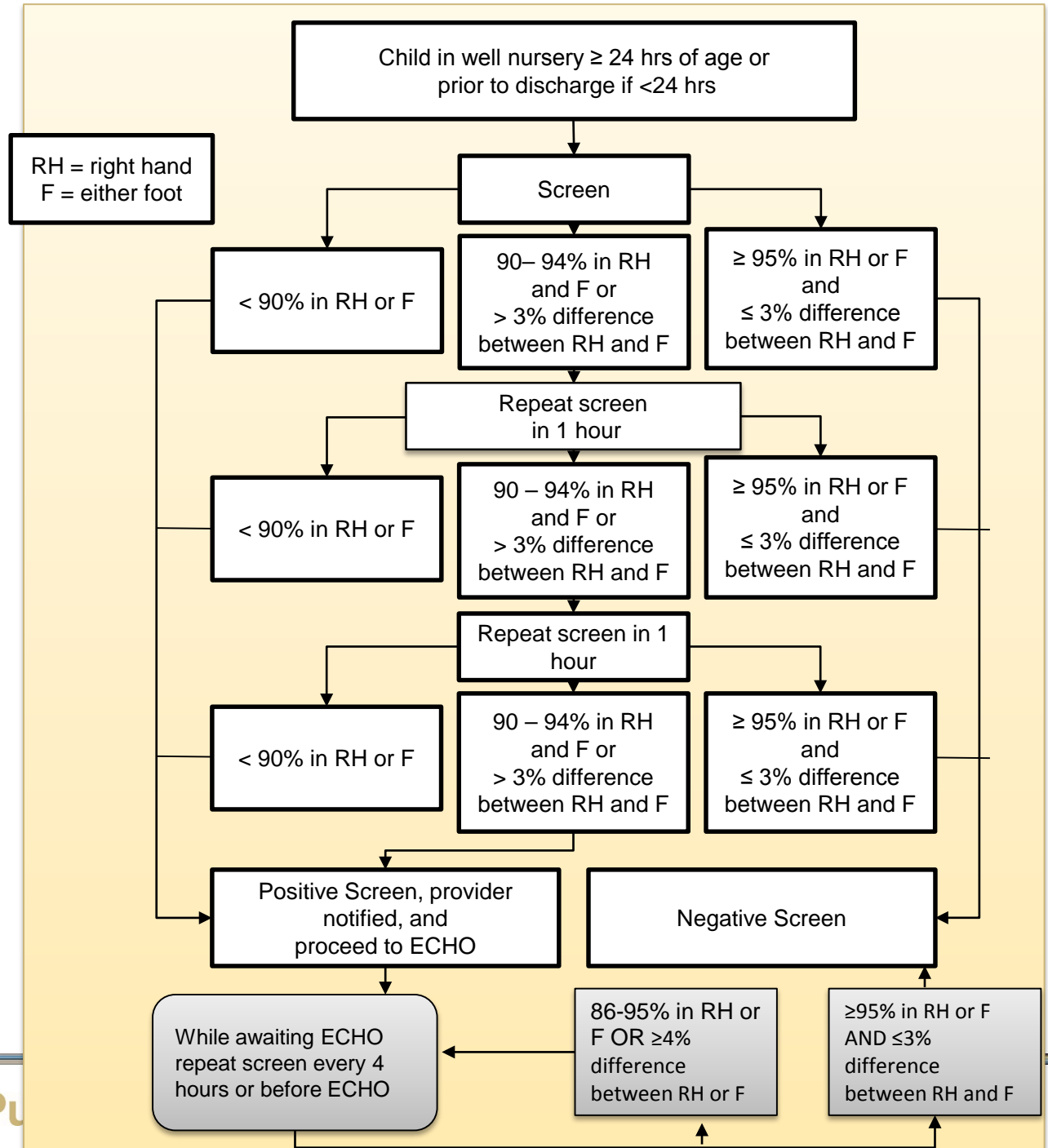
Algorithm Credit: Tennessee Department of Health
https://tn.gov/assets/entities/health/attachments/CCHD_Screening_Protocol_Algorithm.pdf

Tennessee Algorithm



Kohn Algorithm

Modifications are highlighted in gray



Kohn Algorithm

Positive screen, provider notified,
and proceed to ECHO

While awaiting ECHO repeat screen
every 4 hours or before ECHO

86-95% in RH or F OR
 $\geq 4\%$ difference between
RH or F

Repeat or perform
ECHO

$\geq 95\%$ in RH or F AND $\leq 3\%$
difference between RH and
F

Negative screen

Exclusion Criteria

Excluded:

- < 35 weeks EGA
- <1800 gms
- Pulse Ox values before 20 hours of life
- NICU admission
- Newborns prenatally diagnosed with 1 or more CCHD lesions (4 newborns)
- Missing either preductal or postductal values

Included:

- 2,435 medically stable newborns asymptomatic for CCHD

Analysis

- Data validation completed with clinical experts
- Overall failure percentages of the CCHD screen were Calculated for 4 algorithms
 - AAP
 - Kohn
 - Tennessee
 - Tennessee + Kohn
- Compare rates using Fischer's Exact test and Chi square
- Collaboration with the Colorado Department of Public Health and Environment's Birth Defects Registry
- SAS version 9.4

Demographic Characteristics of newborns screened for CCHD

Characteristics:	N= 2,435 (%)
Gender	
Male	1243 (51.1)
Gestational Age (weeks)	
35-37	359 (14.7)
≥ 38	2076 (85.3)
Birth weight (grams)	
1,800-2,000	5 (0.2)
2,001-3,000	683 (28.0)
3,001-4,000	1609 (66.1)
≥ 4,001	138 (5.7)
Median age at time of 1st screen (hours)	24.1 IQR (23.83-24.37)

Characteristics:	N= 2,435 (%)
Race	
White	1162 (47.7)
Black	432 (17.7)
Asian	104 (4.3)
Native Hawaiian / Other Pacific Islander	11 (0.5)
American Indian or Alaskan	8(0.3)
Other	675 (27.7)
Missing	43 (1.8)
Ethnicity	
Hispanic	747(30.7)
Non-Hispanic	1659 (68.1)
Missing	29 (1.2)
Median maternal age (years)	28 (IQR 23 -33)

False Positives of Well Newborns Screened for CCHD at UCH using Different Screening Algorithms

Algorithm	N	Percent of false positives (95% CI)	Specificity (%)
AAP	29	1.11 (0.70, 1.54)	98.1

** None of the false positive rates from the modified algorithms are statistically different from that of the AAP algorithm

False Positive Rate of Well Newborns Screened for CCHD at UCH using Different Screening Algorithms

Algorithm	N	Percent of false positives (95% CI)	Specificity (%)
AAP	29	1.11 (0.70, 1.54)	98.1
Tennessee	26	1.07 (0.66, 1.48)	98.9

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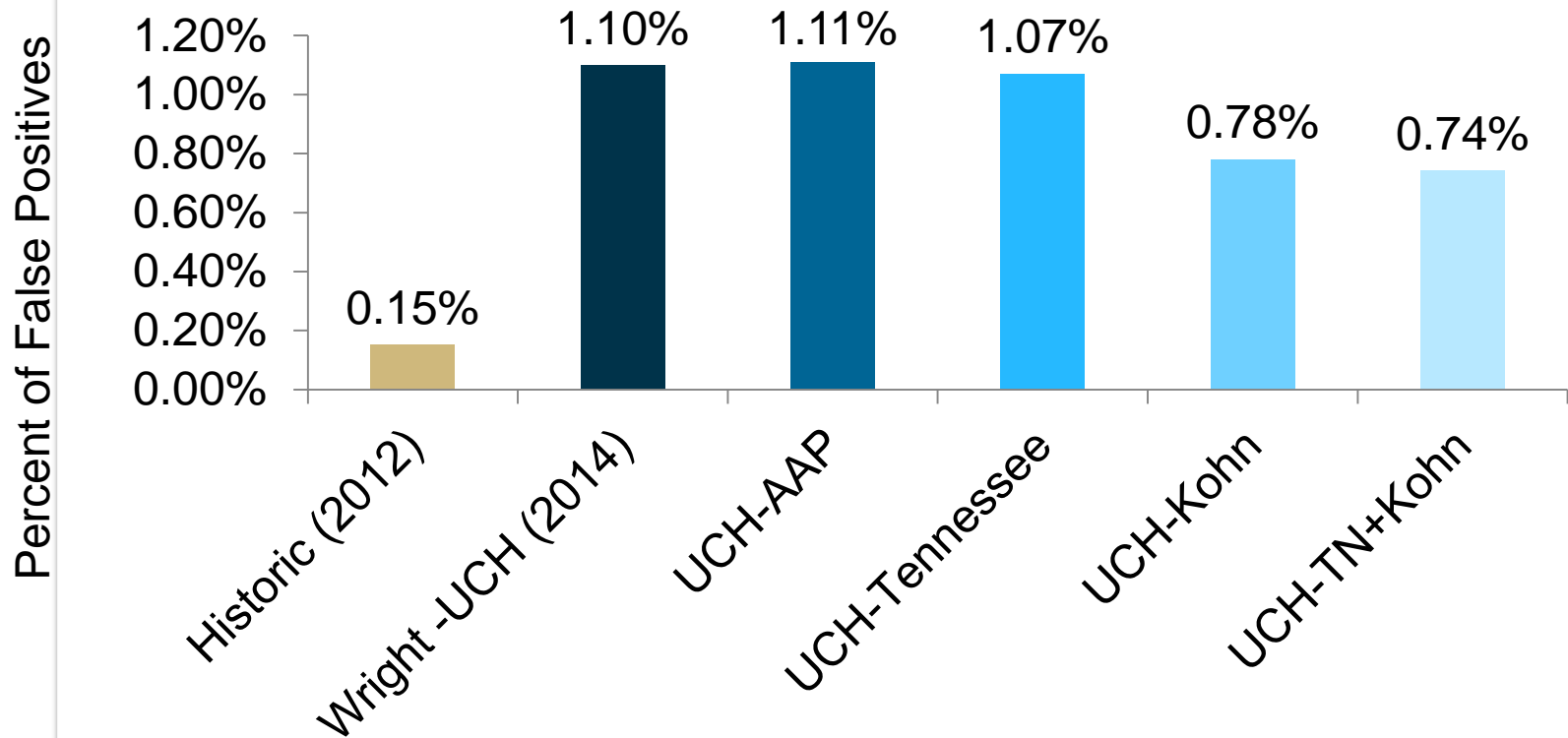
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Kohn	19	0.78 (0.44, 1.14)	99.2
Tennessee+ Kohn	18	0.74 (0.40, 1.09)	99.3

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How does this compare to previous research?



Thangaratinam, et al Lancet 2012. Wright et al Pediatrics 2014.

Incomplete screens

- Newborn is flagged as having an indeterminate screen or requiring an ECHO but did not receive either a rescreen nor an ECHO.

	Percentages of Incompletes (N)	95% CI (%)
AAP	1.72% (42)	(1.21, 2.24)
Tennessee	1.03% (25)	(0.63, 1.43)
Kohn	1.19% (29)	(0.76, 1.62)
Tennessee+Kohn	0.49% (12)	(0.21, 0.77)

Limitations

- Incomplete data
- Incomplete screens
- No newborns with CCHD were detected using newborn screening during the study
- Unable to determine positive predictive value or sensitivity

Moving Forward

- Evaluate modified CCHD screen use in NICUs
- Recommend changes to EMRs to ease analysis
- Evaluation of population based data
- Studies of CCHD screening above 7,000 ft
 - Evaluation of modified screening algorithms at various altitudes



Conclusions

- While still higher than studies conducted near sea-level the Tennessee + Kohn algorithm has the lowest percentage of false positives and incomplete screens
- Improving the screen algorithm is possible at moderate altitude
- Modified algorithms should be considered for implementation in Colorado below 7,000 ft


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- Staff at the Well-baby nursery of the University of Colorado Hospital
- Families and newborns involved with the study

THANK YOU



Credit: Marci Sontag, PhD



CCHD lesions likely (or not) to be detected with pulse oximetry newborn screening

Most likely to be detected:	Less likely to be detected:
Hypoplastic left heart syndrome	Coarctation of the aorta
Pulmonary atresia (with intact septum)	Double-outlet right ventricle
Tetralogy of Fallot	Ebstein anomaly
Total anomalous pulmonary venous return	Interrupted aortic arch
D-Transposition of the great arteries	Singe ventricle
Tricuspid atresia	
Truncus arteriosus	