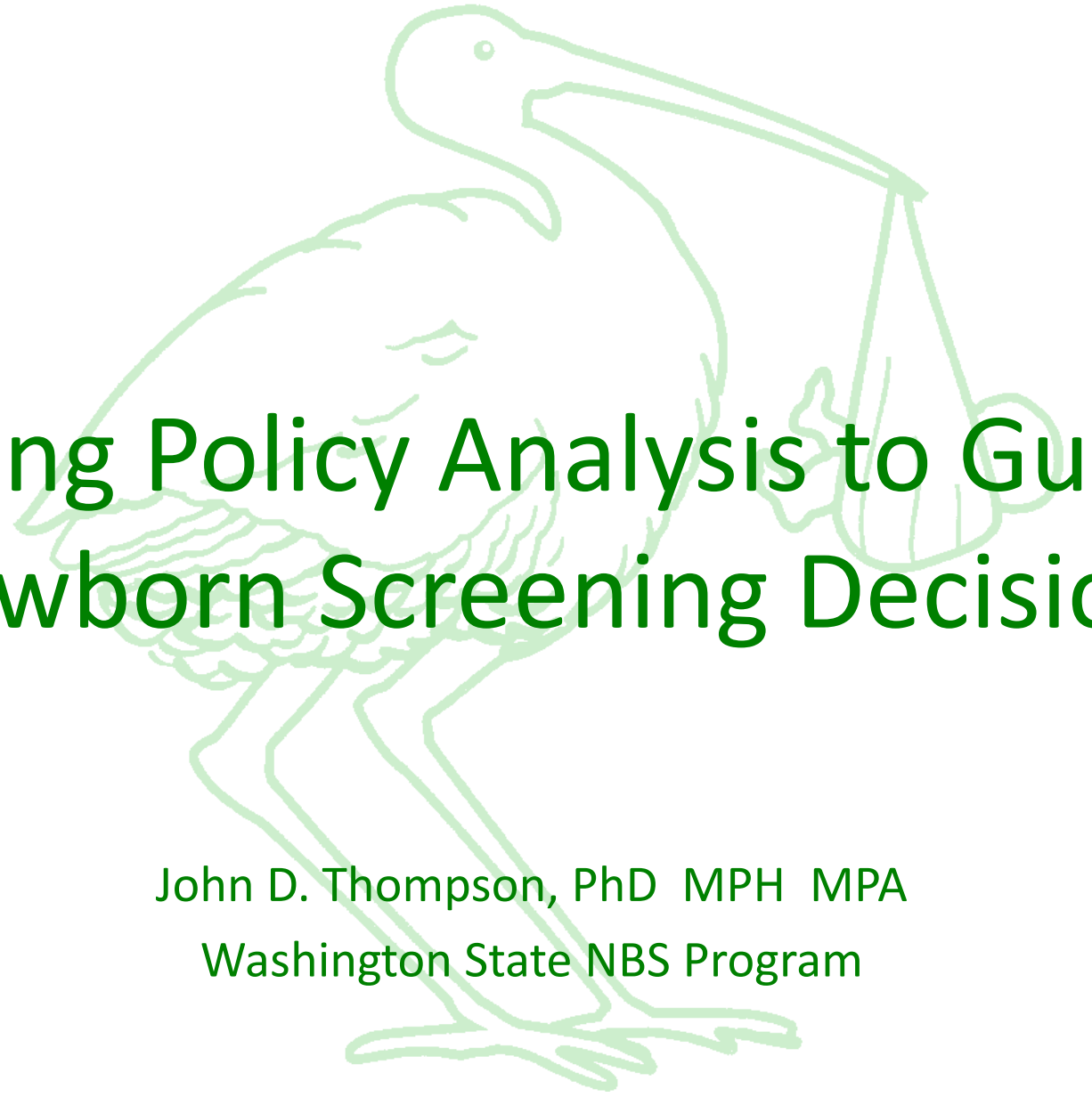


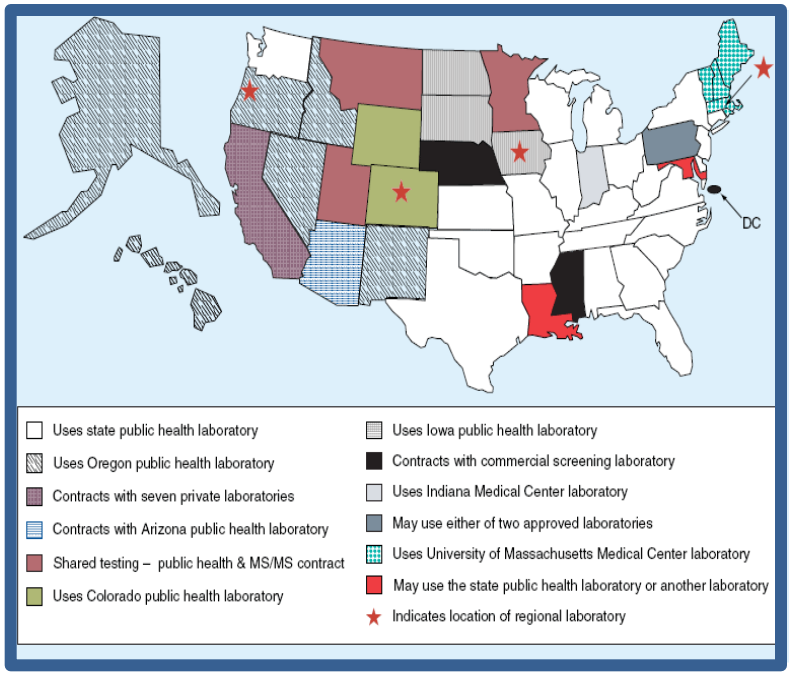
Using Policy Analysis to Guide Newborn Screening Decisions

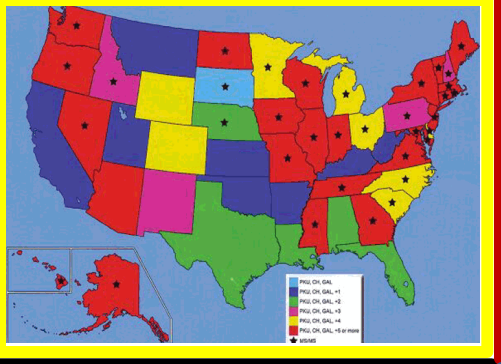
John D. Thompson, PhD MPH MPA

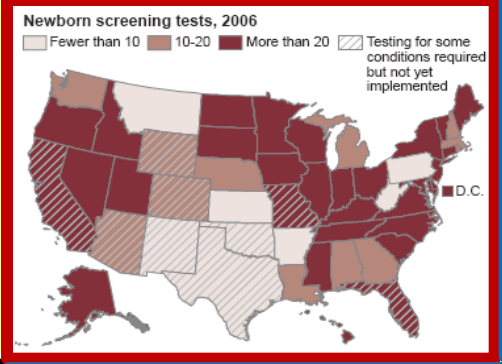
Washington State NBS Program

10th Amendment to the United States Constitution:

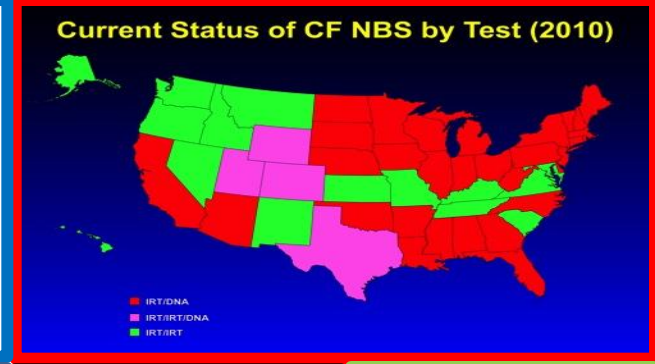
"The powers not delegated to the United States by the Constitution, nor prohibited by it to the States, are reserved to the States respectively, or to the people."

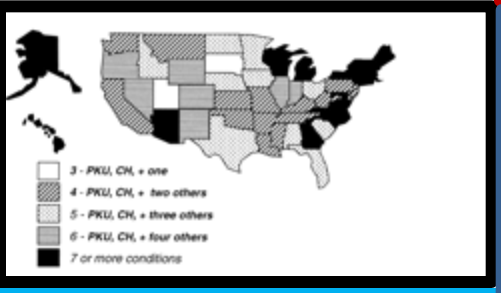

DC
Uses state public health laboratory
Uses Oregon public health laboratory
Contracts with seven private laboratories
Contracts with Arizona public health laboratory
Shared testing – public health & MS/MS contract
Uses Colorado public health laboratory
Uses Iowa public health laboratory
Contracts with commercial screening laboratory
Uses Indiana Medical Center laboratory
May use either of two approved laboratories
Uses University of Massachusetts Medical Center laboratory
May use the state public health laboratory or another laboratory
Indicates location of regional laboratory

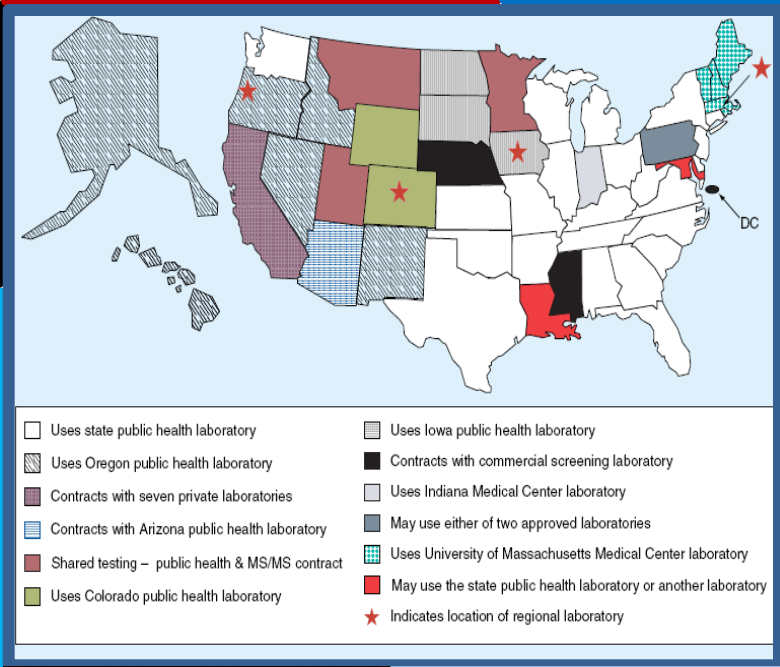



Newborn screening tests, 2006
Fewer than 10
10-20
More than 20
Testing for some conditions required but not yet implemented
D.C.


less than 10 disorders
10 - 19 disorders
20 - 29 disorders
30 - 39 disorders
40 - 49 disorders
more than 50 disorders
tests for Krabbe Disease


Current Status of CF NBS by Test (2010)
IRT/DNA
IRT/IRT/DNA
IRT/IRT


3 - PKU, CH, + one
4 - PKU, CH, + two others
5 - PKU, CH, + three others
6 - PKU, CH, + four others
7 or more conditions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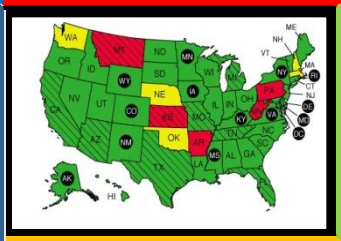
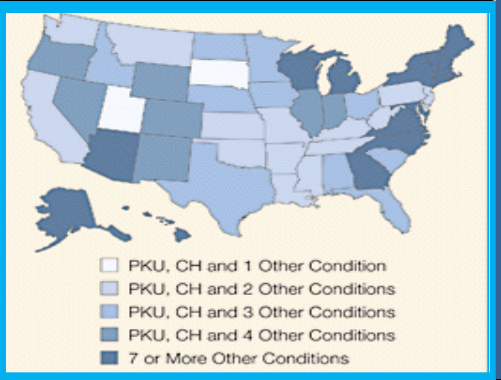
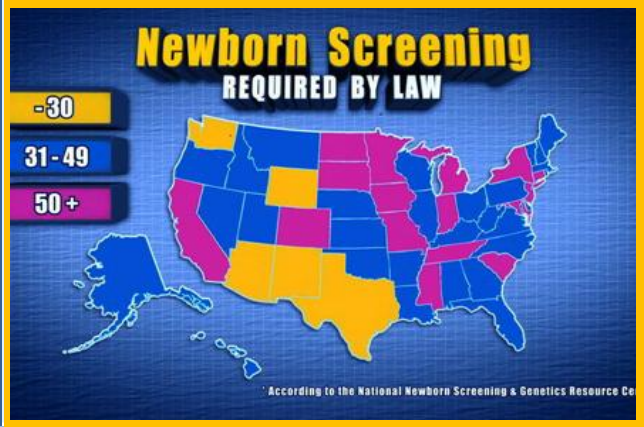
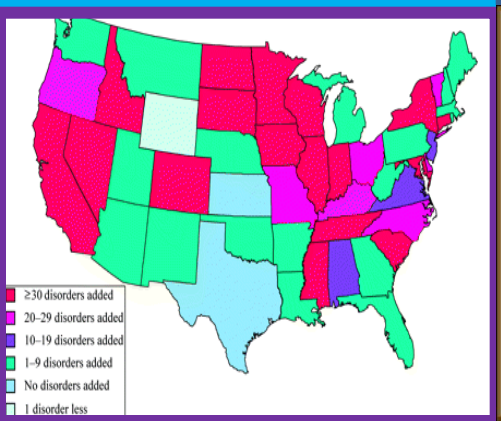
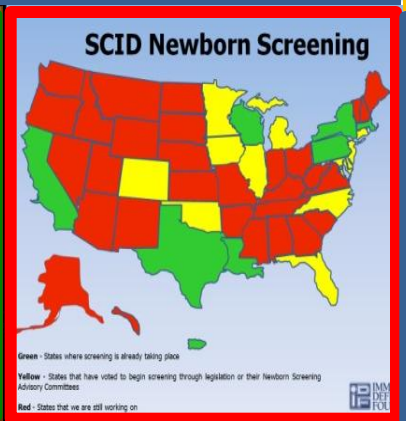


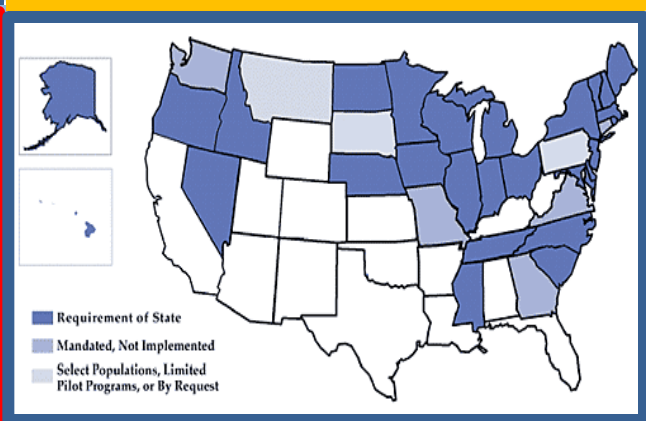

PKU, CH and 1 Other Condition
PKU, CH and 2 Other Conditions
PKU, CH and 3 Other Conditions
PKU, CH and 4 Other Conditions
7 or More Other Conditions


Newborn Screening
REQUIRED BY LAW
-30
31 - 49
50 +
According to the National Newborn Screening & Genetics Resource Ce


≥30 disorders added
20–29 disorders added
10–19 disorders added
1–9 disorders added
No disorders added
1 disorder less

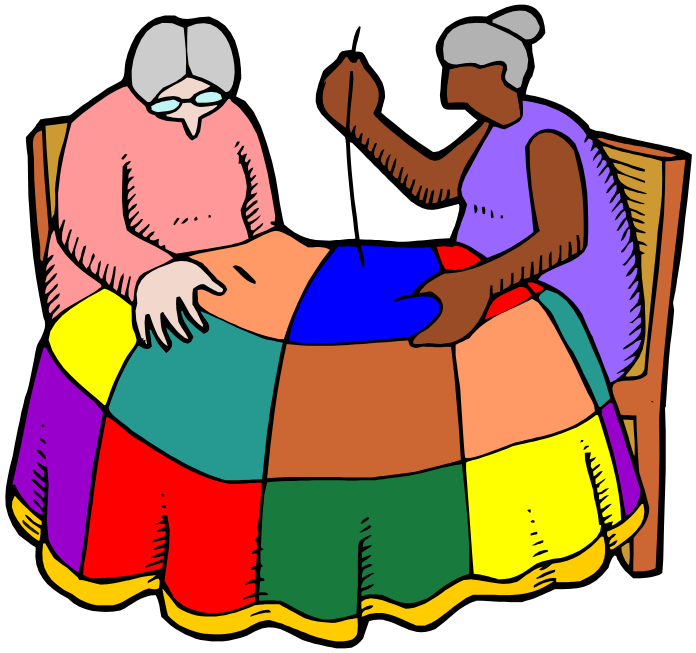

K
*2010
*2012
K - Krabbe
*Law to add Krabbe, Pompe, Niemann-Pick, Gaucher, and Fabry
States that test for
less than 29 disorders
more than 29 disorders (but less than 54)
more than 54 disorders
Source: National Newborn Screening & Genetics Resource Center (12/17/09)


SCID Newborn Screening
Green - States where screening is already taking place
Yellow - States that have voted to begin screening through legislation or their Newborn Screening Advisory Committees
Red - States that we are still working on


Requirement of State
Mandated, Not Implemented
Select Populations, Limited Pilot Programs, or By Request

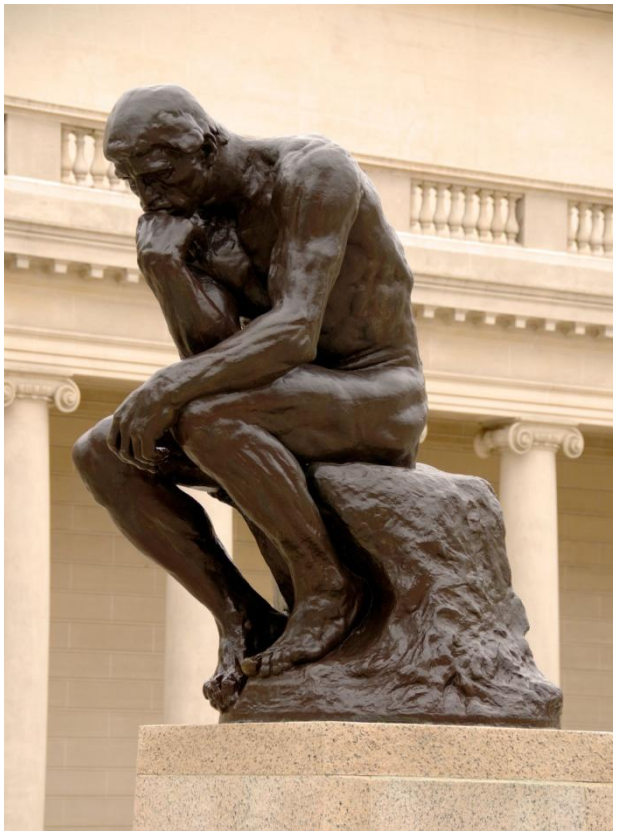
NBS Patchwork

- Screening Panels
- Laws and Regulations
- Fee Structure
- Screening Algorithms
- Follow-up Strategies
- Policy Making Process



Policy Analysis 101

1. Carefully define the problem
2. Gather the data
3. Analyze the data
4. Identify policy options
5. Refine the analysis
6. Make a decision
7. Evaluate changes



Historical Context

- Steps 1-6 of policy analysis were done as we considered CF screening algorithms
- Pressure because of IRT/IRT choice
- We've attempted to make improvements to standard IRT/IRT

⑦ Evaluate changes (IRT/IRT)

- Yearly review of NBS screening data
- False(-) ascertainment efforts
- New proposed screening method: IRT/IRT/DNA

189★

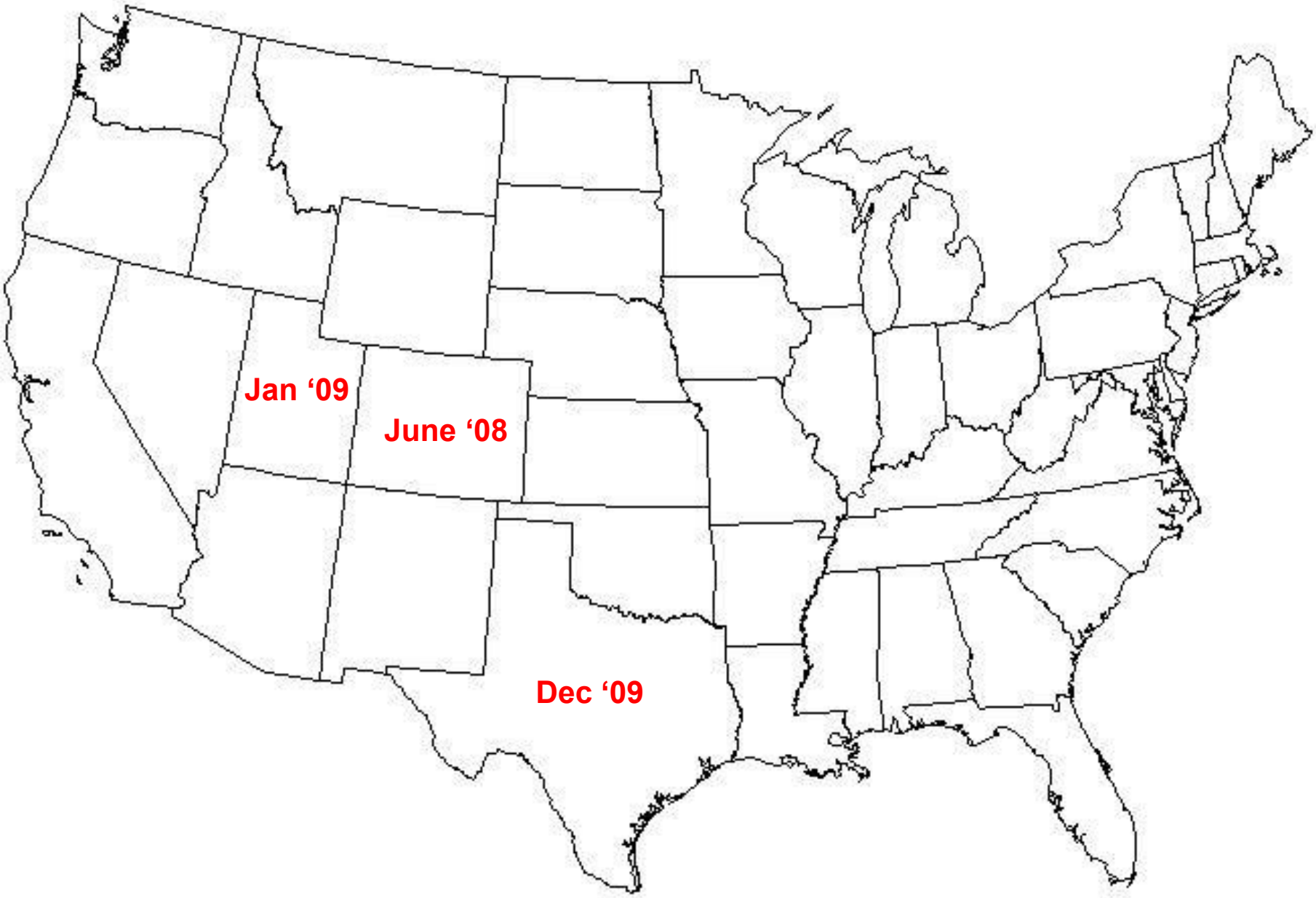
AN IMPROVED NEWBORN SCREENING ALGORITHM IN COLORADO: IRT/IRT/DNA

Sontag, M.K.[1]; Wright, D.G.[2]; Taylor, L.[3]; Beebe, J.L.[2]; Sagel, S.D.[4]; Spector, E.[4] *1. Preventive Medicine and Biometrics, University of Colorado at Denver and Health Sciences Center, Denver, CO, USA; 2. Laboratory Services Division, Colorado Department of Public Health and Environment, Denver, CO, USA; 3. Prevention Services Division, Colorado Department of Public Health and Environment, Denver, CO, USA; 4. Pediatrics, University of Colorado at Denver and Health Sciences Center, Denver, CO, USA*

In Colorado, 318 infants with CF (non-meconium ileus) have been diagnosed with CF by a two tiered immunoreactive trypsinogen (IRT/IRT) based newborn screening approach. The IRT/IRT algorithm has been recently adopted by other screening programs with two mandatory screening tests. While most infants in Colorado have been successfully identified, the program has had a missed case rate of approximately 5%. The more common approach to CF newborn screening is the IRT/DNA method in which the blood spot of infants with an initial elevated IRT is tested for the most common CF mutations. The initial IRT cutoff is lower in the IRT/DNA programs than in the IRT/IRT programs, resulting in a lower missed case rate. The considerable number of carriers identified through the IRT/DNA approach puts a significant burden on the genetic counseling community, as carriers are identified at a rate of 1/20-1/25 of positive IRTs We propose an IRT/IRT/DNA newborn screening algorithm that will maximize sensitivity and specificity while minimizing the number of identified carriers. Using new database technologies in the newborn screening lab we will be able to identify those infants with an elevated first IRT (>60ng/ml, approximately 97th percentile). All infants with an IRT >60ng/ml will have a

(Poster at 2007 NACFC)

IRT/IRT/DNA



② Gather the data

- Roundtable at last symposium
- Fantastic collaboration with CO, UT and TX
- Data shared on common spreadsheet

③ Analyze the data

- Reviewed the data and asked questions
- Examined birth demographics for each state
- Calculated rates based on CO, UT and TX experience – applied those to WA birthrate
- Added a new column for WA data to compare screening performance

④ Identify policy options

Policy Options

- Status quo
- Hybrid method (limited DNA)
- IRT/IRT/contract DNA (UT)
- IRT/IRT/in house DNA (CO & TX)

④ Identify policy options

Policy Options

- Status quo
- Hybrid method (limited DNA)
- IRT/IRT/contract DNA (UT)
- IRT/IRT/in house DNA (CO & TX)

Considerations

- NBS performance
- Impact to NBS lab ($)
- Impact to NBS follow-up
- Impact to CF clinics
- Impact to individual families

④ Identify policy options - matrix

IRT/IRT/DNA matrix

Per 83,000 births	NBS performance	Impact of NBS lab	Impact to NBS follow-up	Impact to CF clinics	Impact to individual families	Miscellaneous
Status quo	Sensitivity=97.85% Specificity=99.96% PPV (referral)=30.7%	Equipment: no Δ Staff time (FTE): no Δ	Initial elevated IRT=361 Subs. elevated IRT=531 SwCl referrals=52	SwCl referrals=52	Need 2nd NBS=361 SwCl referrals=52	*Pressure to incorporate DNA
Hybrid method? -IRT/IRT/ΔF508 -equivocal IRT/IRT/DNA		Equipment: ? Staff time (FTE):?				
IRT/IRT/contract DNA (Utah/Ambry)	Sensitivity=100% (so far) Specificity=99.98% PPV (DNA)=13.9% PPV (referral)=57.6%	Equipment: TBD # DNA tests: 168-1713* Staff time (FTE): TBD	Initial elevated IRT=1628 SwCl referrals=41	SwCl referrals=59 Genetic counseling referrals (carriers)=16	SwCl referrals=59 Carriers identified=16	*Ambry turn-around=7-10 days
IRT/IRT/in house DNA (Colorado/Luminex)	Sensitivity=96.30% Specificity=99.97% PPV (DNA)=6.4% PPV (referral)=40.0%	Equipment: TBD # DNA tests: 322-588 Staff time (FTE): TBD	Initial elevated IRT=2404 SwCl referrals=52	SwCl referrals=125 Genetic counseling referrals (carriers)=25	SwCl referrals=125 Carriers identified=25	
IRT/IRT/in house DNA (Texas/Hologic)	Sensitivity=96.83% Specificity=99.92% PPV (DNA)=1.3% PPV (referral)=14.8%	Equipment: in cost/test # DNA tests: 874-953 Staff time (FTE): TBD	Initial elevated IRT=1946 SwCl referrals=78	SwCl referrals=399 Genetic counseling referrals (carriers)=39	SwCl referrals=399 Carriers identified=39	Failsafe protocols: high number of carriers and false(+) SwCl tests

TBD= to be determined

DNA options – cost estimates for DNA testing (does not include staff time)

Cutoff Scheme/Method	ΔF508 only – in house	Hologic – in house (42 mutations)	Luminex – in house (39 mutations)	Ambry - contract (33 mutations)
Utah (168-1713*/year)	~$2,800	~$7,000	~$10,000	~$13,700
Colorado (322-588/year)	$5,500-$10,000	$13,500-$24,700	$19,300-$35,300	$26,400-$48,200
Texas (874-953/year)	$14,800-$16,200	$36,700-$40,000	$52,400-$57,200	$71,600-$78,100

* effect of floating cutoff – our estimate is biased high because we took the median cutoff value and applied it to the WA population.

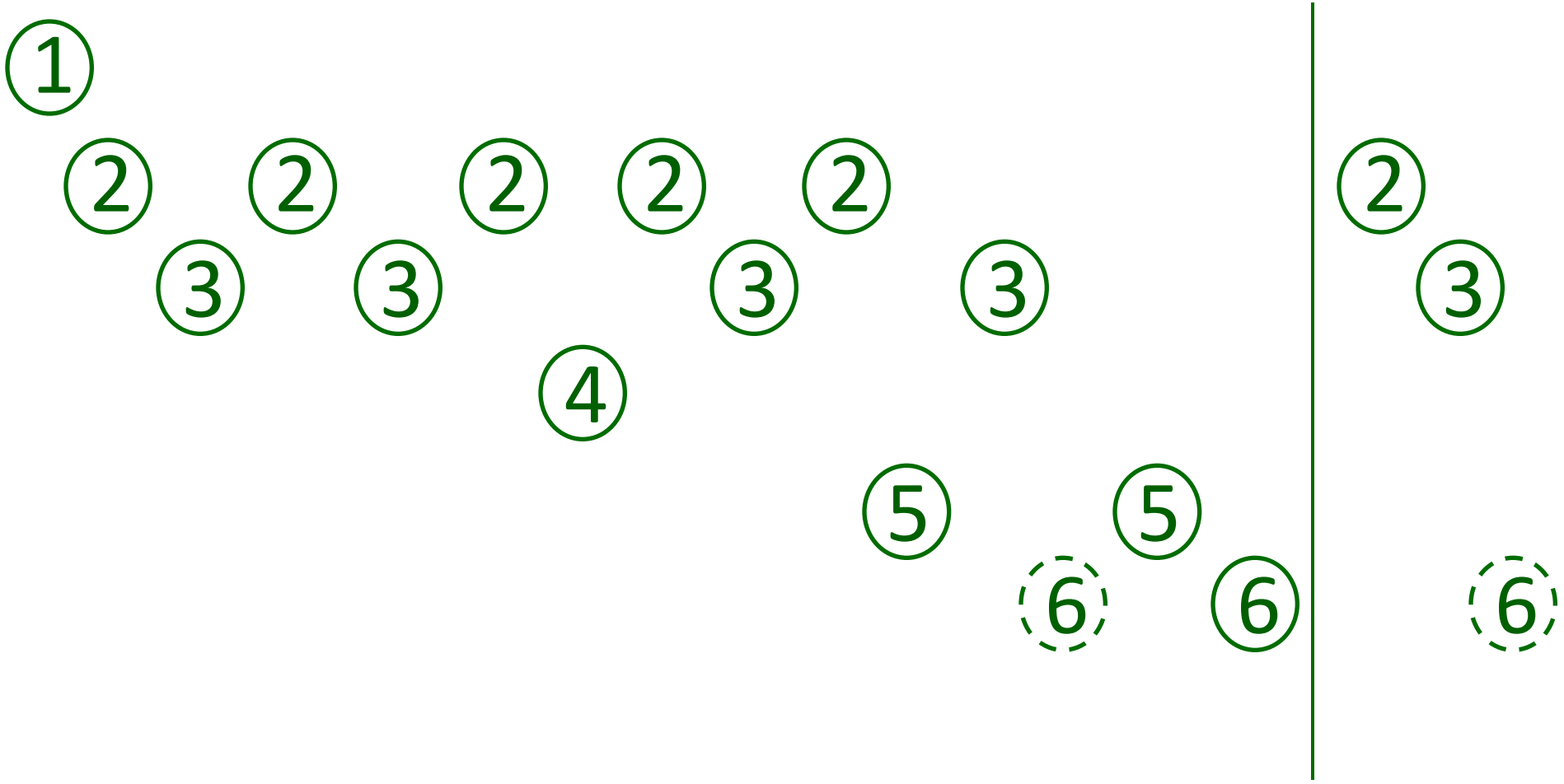
⑤ Refine the analysis

- Preliminary presentation during summer conference to all CF providers in region
- Internal DOH meeting
- External meeting with CF specialists
  - CF center director
  - NBS consultant – pediatric pulmonologist
  - CF nurse coordinator
  - Genetic counselor

⑥ Make a decision

- Recommendation to NBS program director:
  - Maintain status quo
  - Continue to monitor IRT/IRT/DNA
  - Reevaluate in 2 years time
    - ~2 million screened
    - kinks in algorithms should be worked out
- CF specialists were less comfortable
  - Intersect of clinical and public health realms

Policy Analysis:
simple idea/complex reality

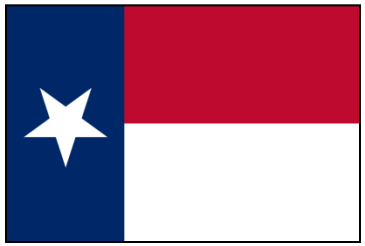


Special thanks to:

Marci Sontag

Laura Taylor

Norm Brown



Rachel Lee

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Special thanks to:

Washington State Department of Health

Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

Sheila Weiss

Amber LaBounty

Charleen Adams

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Ron Gibson

Margaret Rosenfeld

Janine Cassidy

Darcy Sternen