# Routine Second Testing in Newborn Screening Project

Harry Hannon, PhD

Jelili Ojodu, MPH

APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES

# Background

- Only 22.3 % of the newborns in the US receive the possible benefit of a routine second screen.
- Scientific literature indicates that cases of CH and CAH are missed on the initial screen that are detected by a routine second screen.
- To achieve greater uniformity in NBS services, the justification for a routine second screen needs a thorough examination with comprehensive data for an evidence–based decision.

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# Project Timeline

- Draft Protocol Developed – 2006
- Work Group Meeting – Dec 4-5, 2006
  - 41 participants/ 14 States represented, HRSA, CDC, NNSGRC, APHL, Parent Advocates, Endocrinologists, SACHDNC, Private Lab
- Unanimous support from States and stakeholders to proceed with project
- Project split into a 5-Year Retrospective Project and a 1-Year Prospective Project by Work Group

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# Study Hypothesis

"Additional cases of congenital hypothyroidism and congenital adrenal hyperplasia are captured by the practice of a routine second screen algorithm."

# Study Questions to Address

- (Are there biochemical or laboratory-based practices that cause non-detected cases on the first screen)?
- (Is the second screen effective in detecting treatable cases and preventing negative outcomes)?
- (If better analytical and post-analytical steps were taken with first specimen screen, would there be a need for a routine second screen)?
- (Is routine second screen a reasonable cost-effective public policy)?

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# Study Questions

The questions can best be answered by evaluating and validating laboratory and medical results of cases detected in States that perform both first and second routine screens.

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# Project Protocol: General Content for Laboratory Data For Each Analyte and Screen

- Age of newborn at specimen collection
Gestational age
- Birth weight of newborn
- Weight of newborn at specimen collection
- Neonatal intensive care unit (NICU) status
- Sex
- Race/Ethnicity
- Feeding Status
- Transfusion status
- Medication/Drugs
- Valid specimen by lab criteria
- Time: (from collection to lab)
- Filter paper (source and lot)
- Assay method
- Time (from lab receipt to assay)
- Final assay value
- Assay in control at all levels
- Cutoff value
- Cutoff algorithm
- Population median value (including case)

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# Project Protocol: General Content of Medical Data Form

**Congenital Hypothyroidism**

- Confirmatory test results
- Hypothyroidism type
- Treatment for hypothyroidism
- Neonatal history
- Family history

**Congenital Adrenal Hyperplasia**

- Prenatal history
- Sex
- CAH type
- Clinical manifestations when came to medical attention
- Degree of virilization
- Imaging studies
- Genetic studies
- Confirmatory serum tests
- Initial medications
- Family history

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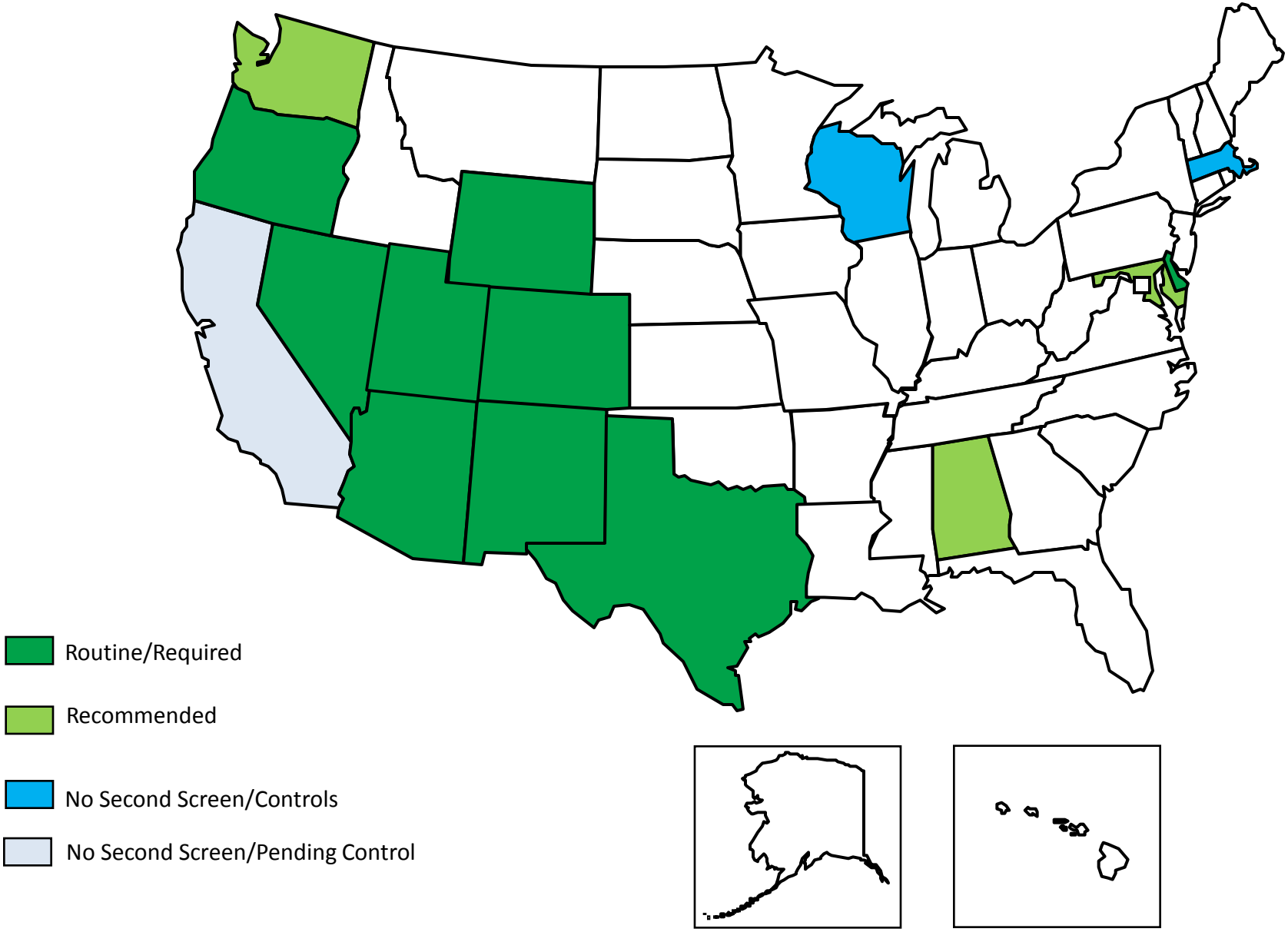
# States with Routine Second Screening



# CUTOFF VALUES 2008

| States | T4 µg/dL serum | TSH µIU/mL serum | 17-OHP ng/mL serum |
|---|---|---|---|
| Alabama | 5.1 | 25.0 | 25.0 |
| Arizona | 6.0 | 60.0 | 70.0 |
| Colorado | 6.0 | 20.0 | 55.0 |
| Delaware | 3.5 | 20.0 | 35.0 |
| Maryland | 6.5 | 20.0 | 58.0 |
| Nevada | 5.0 | 35.0 | 75.0 |
| New Mexico | 5.0 | 35.0 | 75.0 |
| Oregon | 5.0 | 35.0 | 75.0 |
| Texas | 5.9 | 20.0 | 67.0 |
| Utah | 4.0 | 25.0 | 45.0 |
| Wyoming | 6.0 | 20.0 | 55.0 |
| Washington | - | 45.0 | 90.0 |
| Massachusetts | 5.0 | 20.0 | 50.0 |
| Wisconsin | - | 37.0 | 86.0 |

# Status of Routine Second Screen Study 2010

| States | IRB Status - Retrospective 5-year (date) | IRB Status – Prospective 1-year |
|---|---|---|
| Alabama | Jan 2008 | Pending |
| Arizona | Pending | Pending |
| Colorado | Declined (11/2009) | Pending |
| Delaware | Dec 2007 | Pending |
| Maryland | July 2008 | Pending |
| Nevada | Pending | Pending |
| New Mexico | Pending | Pending |
| Oregon | March 2009 | Pending |
| Texas | Nov 2008 | Pending |
| Utah | Jan 2008 | Pending |
| Wyoming | Pending | Pending |
| Washington | Pending | Pending |
| Massachusetts | Pending | Pending |
| Wisconsin | March 2010 | Pending |

| States | Number of newborns screened in 2008 | Presently covered by IRBs for 5-year study |
|---|---|---|
| Alabama | 64,830 | 64,830/yr |
| Arizona | 115,371 | |
| Colorado | 72,396 | |
| Delaware | 13,040 | 13,040/yr |
| Maryland | 77,753 | 77,753/yr |
| Nevada | 18,225 | |
| New Mexico | 30,986 | |
| Oregon | 50,595 | 50,595/yr |
| Texas | 424,937 | 424,937/yr |
| Utah | 58,011 | 58,011/yr |
| Wyoming | 8,030 | |
| Washington | 93,083 | |
| Massachusetts | 73,828 | |
| Wisconsin | 74,383 | 74,383/yr |

# Newborns Covered by the Study (To Date)

- 2008 US Births = 4,505,255
- 2008 Newborns with Second Screen = 1,027,257
  - 22.3% of 2008 Births

IRB Approved to Date

- 2008 Second Screen Newborns for Database = 689,116
  - 15.3% of 2008 Births / 67% of Second Screens
- Second Screen Newborns for 5-Year Study = 3,445,580*

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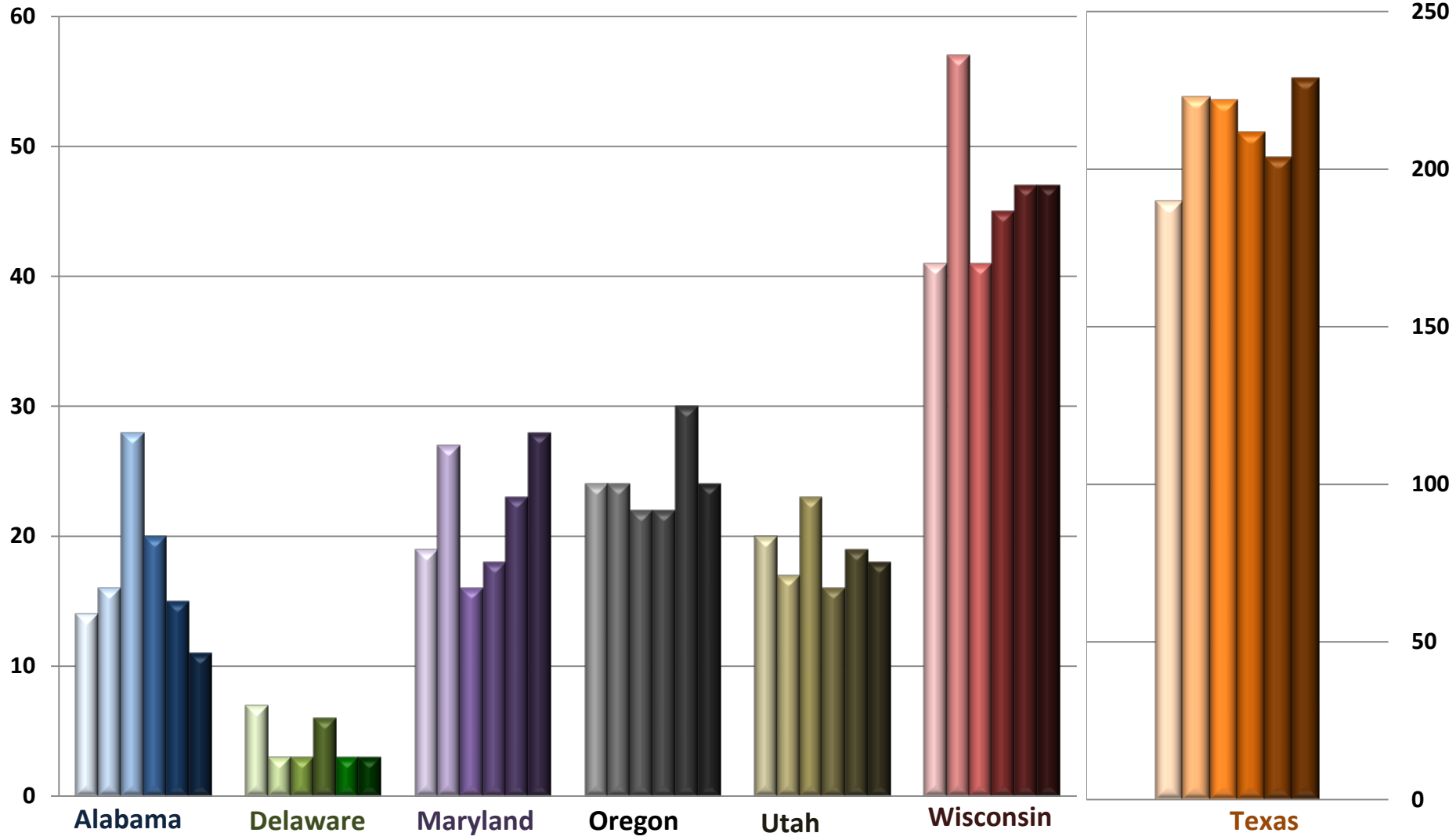
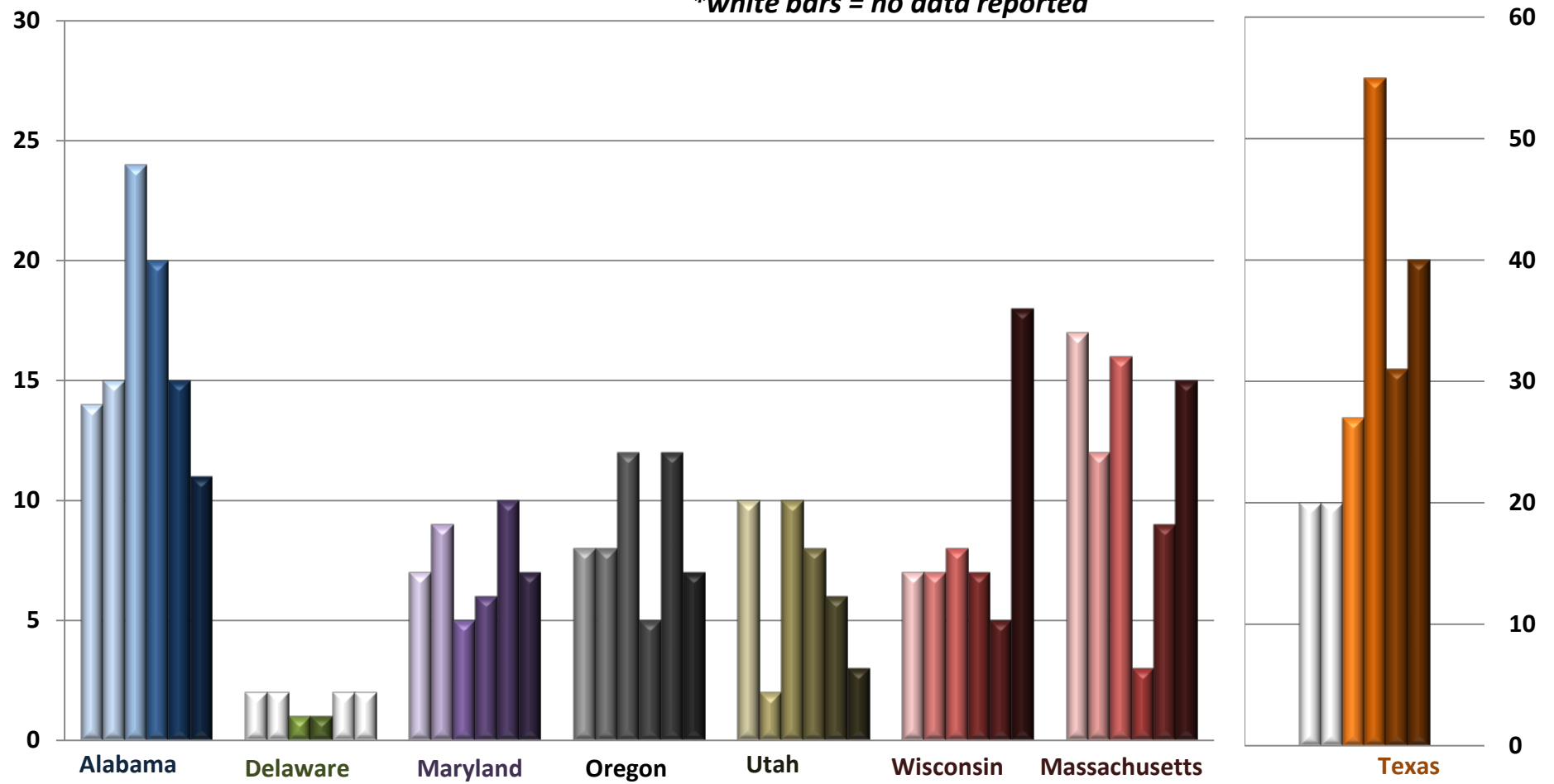
# Congenital Hypothyroidism
# Confirmed Cases
# 2003 - 2008




National Newborn Screening and Genetics Resource Center
Austin, Texas USA
NNSGRC

# Congenital Hypothyroidism
# Confirmed by Second Screen
# 2003 - 2008

**white bars = no data reported*

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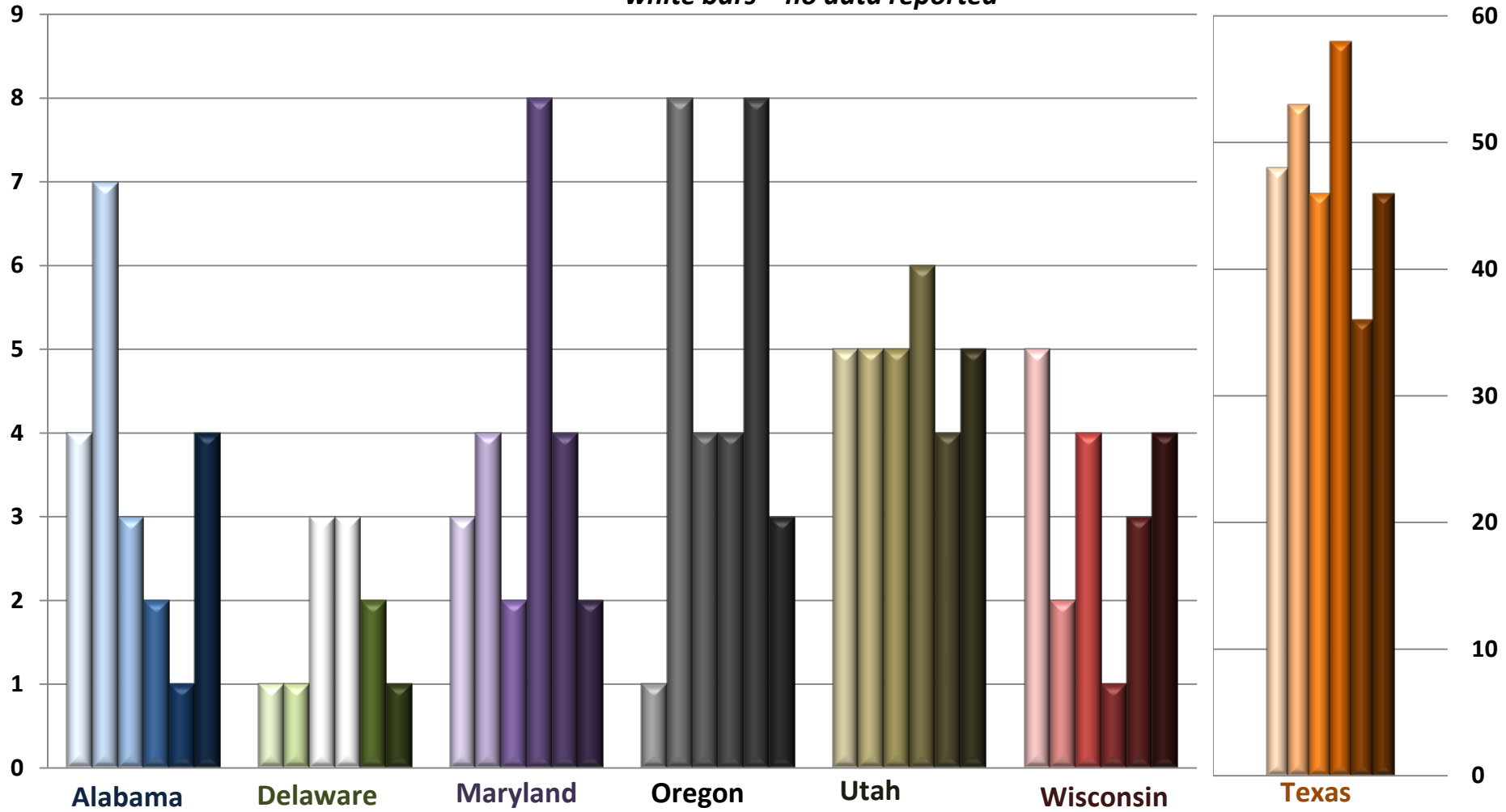
Austin, Texas USA
NNSGRC

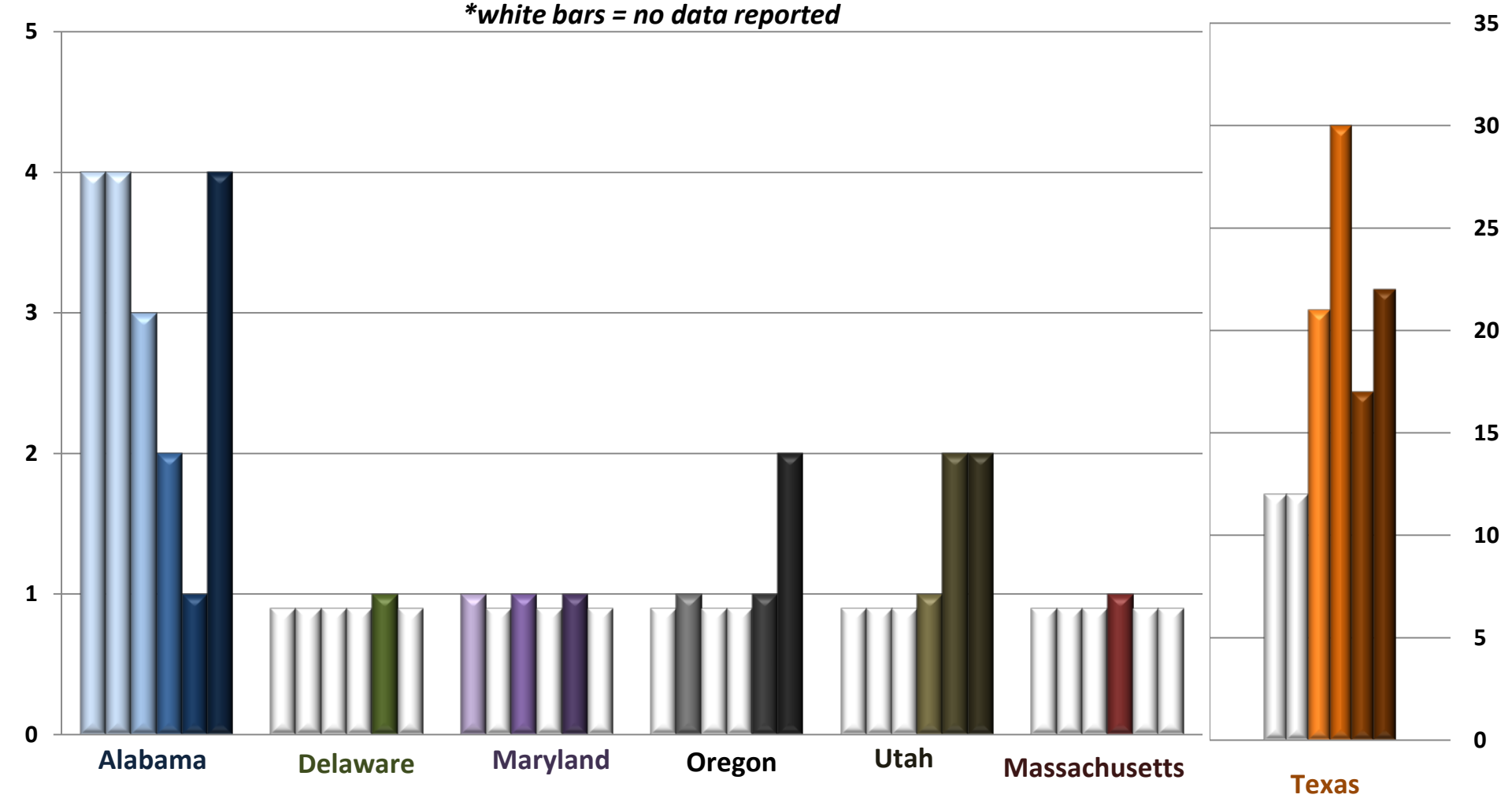
# Congenital Adrenal Hyperplasia
# Confirmed Cases
# 2003 – 2008

**white bars = no data reported*

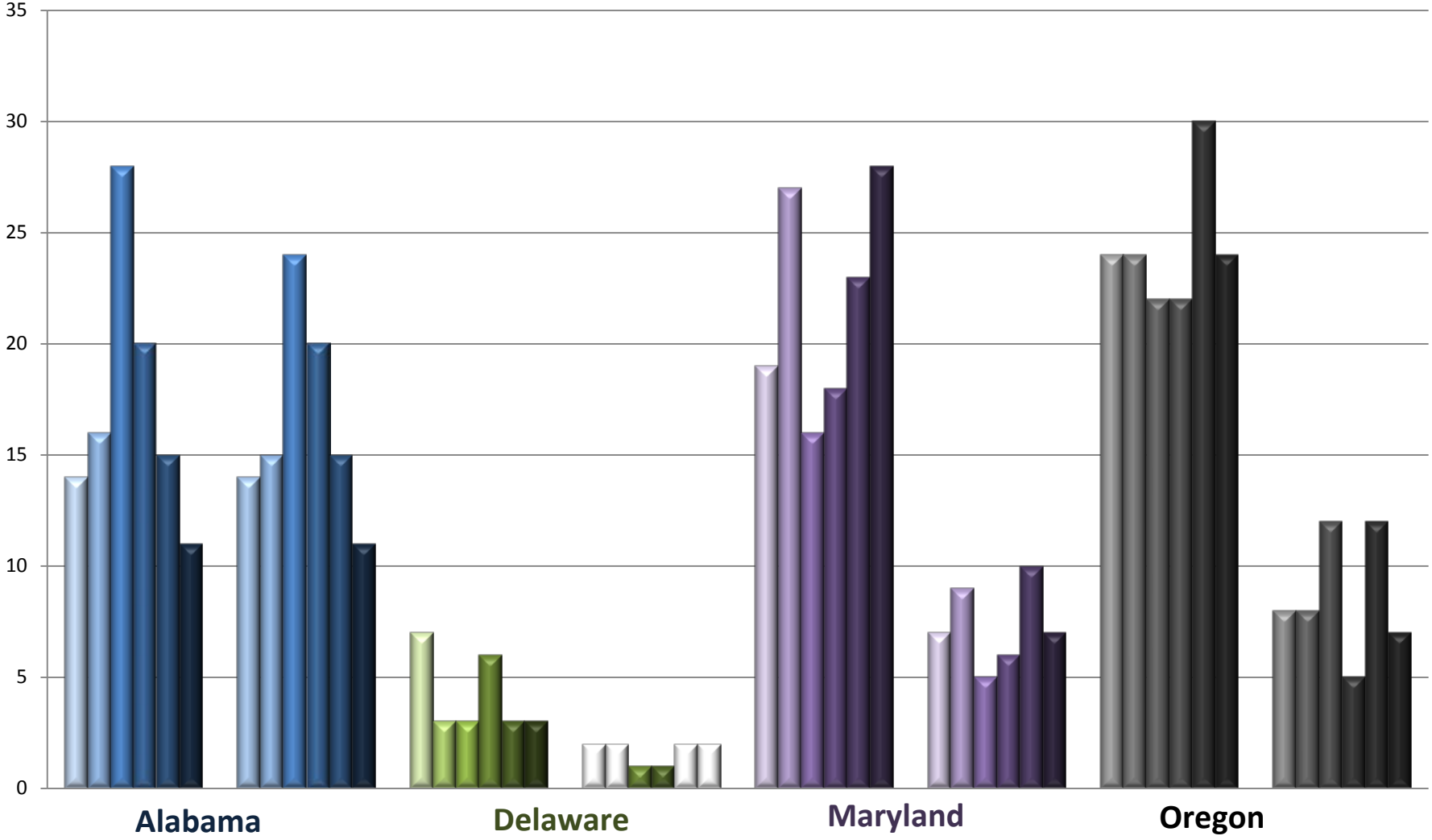


# Congenital Adrenal Hyperplasia
# Confirmed by Second Screen
# 2003 - 2008

**white bars = no data reported*



# Congenital Hypothyroidism
# Primary and Secondary Screen
# 2003 - 2008



# Next Steps

- Complete data collection for all states with IRB's approved
- Seek completion of pending IRBs and gather data into electronic files
- Analyze and interpret the laboratory and medical data – designated work group
- Report back to the participant states and newborn screening community
- Submit data and conclusions for publication – peer-reviewed journal

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# Questions