UPDATES ON IMPLEMENTATION OF SCREENING FOR SEVERE COMBINED IMMUNODEFICIENCY, CRITICAL CONGENITAL HEART DISEASE, AND POMPE DISEASE

JELILI OJODU, MPH, ASSOCIATION OF PUBLIC HEALTH LABORATORIES
MARCI SONTAG, PHD, COLORADO SCHOOL OF PUBLIC HEALTH

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Dynamic newborn screening systems have access to and utilize accurate, relevant information to achieve and maintain excellence through continuous quality improvement.

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BACKGROUND

The Foundation for SCID Newborn Screening

Immune deficiencies, infection, and systemic immune disorders

Development of a routine newborn screening protocol for severe combined immunodeficiency

Mei W. Baker, MD,[a,b] William J. Grossman, MD, PhD,[c] Ronald H. Laessig, PhD,[a] Gary L. Hoffman, BS,[a] Charles D. Brokopp, DrPH,[a] Daniel F. Kurtycz, MD,[a] Michael F. Cogley, BS,[a] Thomas J. Litsheim, BS,[a] Murray L. Katcher, MD, PhD,[b,d] and John M. Routes, MD[c] *Madison and Milwaukee, Wis*

Background: Severe combined immunodeficiency (SCID) is characterized by the absence of functional T cells and B cells. Without early diagnosis and treatment, infants with SCID die from severe infections within the first year of life.
Objective: To determined the feasibility of detecting SCID in newborns by quantitating T-cell receptor excision circles (TRECs) from dried blood spots (DBSs) on newborn screening (NBS) cards.
Methods: DNA was extracted from DBSs on deidentified NBS cards, and real-time quantitative PCR (RT-qPCR) was used to determine the number of TRECs. Positive controls consisted of DBS from a 1-week-old $T^-B^-NK^+$ patient with SCID and whole blood specimens selectively depleted of naive T cells.
Results: The mean and median numbers of TRECs from 5766 deidentified DBSs were 827 and 708, respectively, per 3.2-mm punch (~3 μL whole blood). Ten samples failed to amplify TRECs on initial analysis; all but 1 demonstrated normal TRECs and β-actin amplification on retesting. No TRECs were detected in either the SCID or naive T-cell–depleted samples, despite the presence of normal levels of β-actin.
Conclusions: The use of RT-qPCR to quantitate TRECs from DNA extracted from newborn DBSs is a highly sensitive and specific screening test for SCID. This assay is currently being used in Wisconsin for routine screening infants for SCID.
(J Allergy Clin Immunol 2009;124:522-7.)

Key words: *Dried blood spots, hematopoietic stem cell transplantation, newborn screening, real-time quantitative PCR, severe combined immunodeficiency, T-cell receptor excision circles*

The goal of newborn screening (NBS) is to identify presymptomatic newborns with potentially serious or fatal disorders that can be successfully treated, leading to significant reductions in morbidity and mortality. The 45-year history of NBS demonstrates that it is an extremely successful and cost-efficient public health undertaking and provides useful information in the field of preventive medicine.[1,2] Routine NBS began in the1960s with a single disorder, phenylketonuria, and grew to a core panel of 29 disorders as recommended by the American College of Medical Genetics.[3] As knowledge of the causes of genetic disorders increases, detection technologies advance, and better treatment regimens emerge, more diseases will be added to the NBS panel.

Severe combined immunodeficiency (SCID) was recognized as a disorder that meets the criteria for inclusion in NBS in a Centers for Disease Control and Prevention 2004 conference entitled "Applying Public Health Strategies to Primary Immunodeficiency Diseases."[4] Criteria include infants who are asymptomatic at birth, serious medical consequences without treatment, availability of confirmatory tests and effective treatment, and improved outcomes with early intervention. The National Advisory Committee of Heritable Disorders in Newborns and Children has selected SCID as the focus of an evidentiary review regarding recommendations for NBS.[5]

J Inherit Metab Dis (2010) 33 (Suppl 2):S273–S281
DOI 10.1007/s10545-010-9103-9

NEWBORN SCREENING

Guidelines for implementation of population-based newborn screening for severe combined immunodeficiency

Anne Marie Comeau · Jaime E. Hale · Sung-Yun Pai · Francisco A. Bonilla · Luigi D. Notarangelo · Mark S. Pasternack · H. Cody Meissner · Ellen Rae Cooper · Alfred DeMaria · Inderneel Sahai · Roger B. Eaton

Received: 22 January 2010 / Revised: 26 March 2010 / Accepted: 1 April 2010 / Published online: 20 May 2010

Abstract Severe combined immunodeficiency (SCID) is a Primary Immune Deficiency that is under consideration for population-based newborn screening (NBS) by many NBS programs, and has recently been recommended for inclusion in the US uniform panel of newborn screening conditions. A marker of SCID, the T cell receptor excision circle (TREC), is detectable in the newborn dried blood spot using a unique molecular assay as a primary screen. The New England Newborn Screening Program developed and validated a multiplex TREC assay in which both the TREC analyte and an internal control are acquired from a single punch and run in the same reaction. Massachusetts then implemented a statewide pilot SCID NBS program. The authors describe the rationale for a pilot SCID NBS program, a comprehensive strategy for successful implementation, the screening test algorithm, the screening follow-up algorithm and preliminary experience based on statewide screening in the first year. The Massachusetts experience demonstrates that SCID NBS is a program that can be implemented on a population basis with reasonable rates of false positives.

Communicated by: Rodney Pollitt

Competing interest: None declared.

A. M. Comeau (✉) · J. E. Hale · I. Sahai · R. B. Eaton
New England Newborn Screening Program,
UMass Medical School,
305 South Street,
Jamaica Plain, MA 02130, USA
e-mail: anne.comeau@umassmed.edu

S.-Y. Pai · F. A. Bonilla · L. D. Notarangelo
Children's Hospital,
Boston, MA, USA

S.-Y. Pai
Dana-Farber Cancer Institute,

Introduction

Severe combined immunodeficiency (SCID) denotes a group of diseases in the spectrum of primary immunodeficiency (PID). SCID is particularly worthy of consideration for inclusion in the list of conditions subject to population-

Rostrums

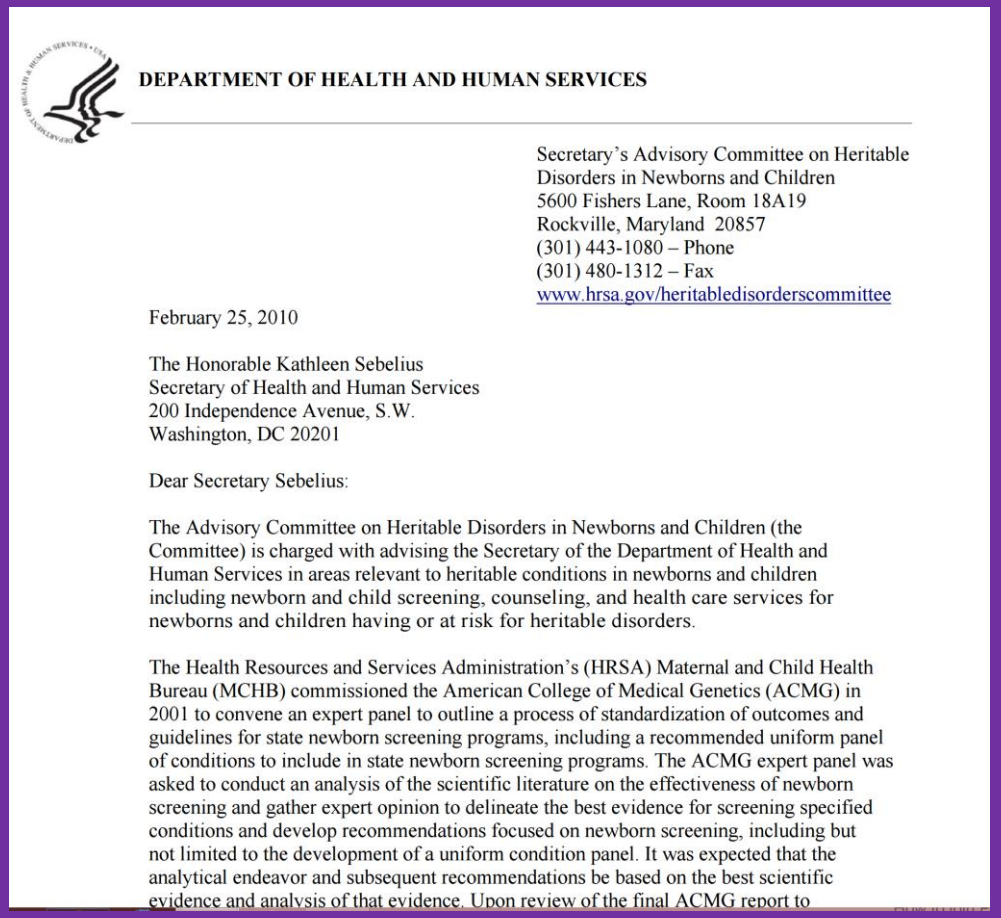
Population-based newborn screening for severe combined immunodeficiency: Steps toward implementation

Jennifer M. Puck, MD,[a] on behalf of The SCID Newborn Screening Working Group[b]
San Francisco, Calif

Severe combined immune deficiency (SCID) has been identified as a disorder of high priority for population-based newborn screening. Most affected infants are not brought to medical attention until they develop serious infectious complications, and SCID is fatal if untreated. Effective treatment with allogeneic hematopoietic stem cell transplantation is widely established. The best outcome for SCID, as with many other conditions for which newborn screening is now done, is achieved if hematopoietic stem cell transplantation is performed in the first months of life, ideally before clinical presentation with infections and failure to thrive. A meeting in San Francisco in May 2007 brought together experts from newborn screening programs; the pediatric immunology community; pediatric transplant centers; and federal, state, and nongovernmental agencies to consider obstacles to and implications of developing newborn screening for SCID. Development of an appropriate low-cost, high-throughput screening algorithm has been a challenge,

From [a]the Department of Pediatrics, University of California, San Francisco.
[b]The SCID Newborn Screening Working Group met in San Francisco, May 14-15, 2007. The group includes John C. Baker (Kaiser Permanente, Oakland Medical Center, Oakland, Calif); Mei W. Baker (University of Wisconsin, Madison); Marcia Boyle (Immune Deficiency Foundation, Towson, Md); Amy Brower (Third Wave Technologies, Madison, Wis); Rebecca H. Buckley (Duke University Medical Center, Durham, NC); Fabio Candotti (National Human Genome Research Institute, National Institutes of Health, Bethesda, Md); Anne Marie Comeau (University of Massachusetts Medical School, Jamaica Plain); Morton Cowan (University of California, San Francisco); Joie Davis (National Human Genome Research Institute, National Institutes of Health, Bethesda, Md); Elaine Eastman (Kaiser Permanente, Oakland Medical Center, Oakland, Calif); Gilian Engelson (National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Md); Diana Gonzalez-Espinosa (University of California, San Francisco); Nancy S. Green (Columbia University Medical Center, New York, NY); Howard Grodman (Tufts New England Medical Center, Boston, Mass); William Grossman (Medical College of Wisconsin, Milwaukee); R. Rodney Howell (National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Md); Naynesh R. Kamani (Children's National Medical Center, Washington, DC); Martin Kharrazi (California Department of Public Health, Richmond); Alan P. Knutsen (St Louis University School of Medicine, St Louis, Mo); Ronald H. Laessig (University of Wisconsin/State Lab of Hygiene, Madison); Tonya Lebet (University of California, San Francisco); Howard M. Lederman, Johns Hopkins School of Medicine, Baltimore, Md); David Lewis (Stanford University Medical Center, Palo Alto, Calif); Fred Lorey (California Department of Public Health, Richmond); Fizza Gulamali-Majid (Maryland State Department of Health and Mental Hygiene, Baltimore); Elaine Mansfield (Affymetrix, Santa Clara, Calif); Louis Matis (Immune Tolerance Institute, Michele A. Lloyd-Puryear (Maternal and Child Health Bureau, Health Resources Services Administration, Department of Health and Human Services, Rockville, Md); John M. Routes (Medical College of Wisconsin, Milwaukee); John E. Sherwin (California Department of Public Health, Richmond); Bradford L. Therrell, Jr (National Newborn Screening and Genetics Resource Center, University of Texas Health Science Center at San Antonio); Troy Torgerson (University of Washington and Seattle Childrens Hospital, Seattle); Robert F. Vogt, Jr (Centers for Disease Control and Prevention, Atlanta, Ga); Diane Wara (University of California, San Francisco); and Kenneth Weinberg (Stanford University Medical Center, Palo Alto, Calif).
The meeting from which this report originated was supported by the National Newborn Screening and Genetic Resource Center, Austin, Tex; the Genetic Services Branch, Maternal and Child Health Bureau, Department of Health and Human Services, Rockville, Md; and the Jeffrey Modell Foundation. Dr Puck is supported by a Clinical and Translational Sciences Award to the University of California, San Francisco, National Institutes of Health National Center for Research Resources (UL RR024131-01); the Jeffrey Modell Foundation; and a National Institute of Allergy and Infectious Diseases and National Institute for Child Health and Human Development–sponsored US Immunodeficiency Network research award.
Disclosure of potential conflict of interest: M. Boyle has received grants support from the Immune Deficiency Foundation. A. Brower is employed by and owns stock in Third Wave Technologies. R. R. Howell has consulting arrangements with Genzyme Corp, is on the speakers' bureau for ZLB-Behring, and is on the advisory board for Cryocell. A. P. Knutsen is on the speakers' bureau for Novartis, ZLB-Behring, and Talecris. E. Mansfield is employed by Affymetrix. L. Matis is employed by the Immune Tolerance Institute. S. R. Panny has received grant support from the Health Resources Services Administration. J. M. Puck is a consultant for the US Immunodeficiency Network and has received research support

Addition to the RUSP: February 2010



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Secretary's Advisory Committee on Heritable Disorders in Newborns and Children
5600 Fishers Lane, Room 18A19
Rockville, Maryland 20857
(301) 443-1080 – Phone
(301) 480-1312 – Fax
www.hrsa.gov/heritabledisorderscommittee

February 25, 2010

The Honorable Kathleen Sebelius
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

Dear Secretary Sebelius:

The Advisory Committee on Heritable Disorders in Newborns and Children (the Committee) is charged with advising the Secretary of the Department of Health and Human Services in areas relevant to heritable conditions in newborns and children including newborn and child screening, counseling, and health care services for newborns and children having or at risk for heritable disorders.

The Health Resources and Services Administration's (HRSA) Maternal and Child Health Bureau (MCHB) commissioned the American College of Medical Genetics (ACMG) in 2001 to convene an expert panel to outline a process of standardization of outcomes and guidelines for state newborn screening programs, including a recommended uniform panel of conditions to include in state newborn screening programs. The ACMG expert panel was asked to conduct an analysis of the scientific literature on the effectiveness of newborn screening and gather expert opinion to delineate the best evidence for screening specified conditions and develop recommendations focused on newborn screening, including but not limited to the development of a uniform condition panel. It was expected that the analytical endeavor and subsequent recommendations be based on the best scientific evidence and analysis of that evidence. Upon review of the final ACMG report to

When developing its recommendations to the Secretary, the Committee considers the nature of the science itself underlying the potential additions of the technology and the heritable conditions to the R
implications of implementat
recommends a tiered approa
T-cell lymphocyte deficienc
deficiencies are rare in the S
an iterative implemental dev
evaluation, surveillance, educ
lymphocyte deficiencies, the Committee therefore recommends to the Secretary:

It is with these issues in mind that the Committee recommends a tiered approach to the screening of SCID and related T-cell related lymphocyte deficiencies.

- The addition of SCID to the uniform panel, and related T-cell lymphocyte deficiencies to the list of secondary targets as a comprehensive entity, with the understanding that the following activities will also take place in a timely manner.
  - The National Institutes of Health shall fund surveillance activities to determine health outcomes of affected newborns with any T-cell lymphocyte deficiency receiving treatment as a result of prospective newborn screening;
  - The Health Resources and Services Administration shall fund the development of appropriate education and training materials for families and public health and health care professionals relevant to the screening and treatment of SCID and related T-cell lymphocyte deficiencies.
  - The Centers for Disease Control and Prevention shall develop and distribute to performing laboratories suitable dried blood spot specimens for quality control and quality assurance purposes.

This is the first condition determined to be ready for addition to the Committee's Recommended Uniform Screening Panel since 2005. It is a milestone for this Committee and represents the success of the Committee's evidence review system. Thank you for your consideration of this important topic.

Sincerely yours,

R. Rodney Howell, M.D.
Chairperson

Challenges in SCID NBS Implementation

Approval/Legislation

- Funding
- Priorities

Laboratory

- Equipment/Work flow
- Training
- Technical Challenges and Analysis

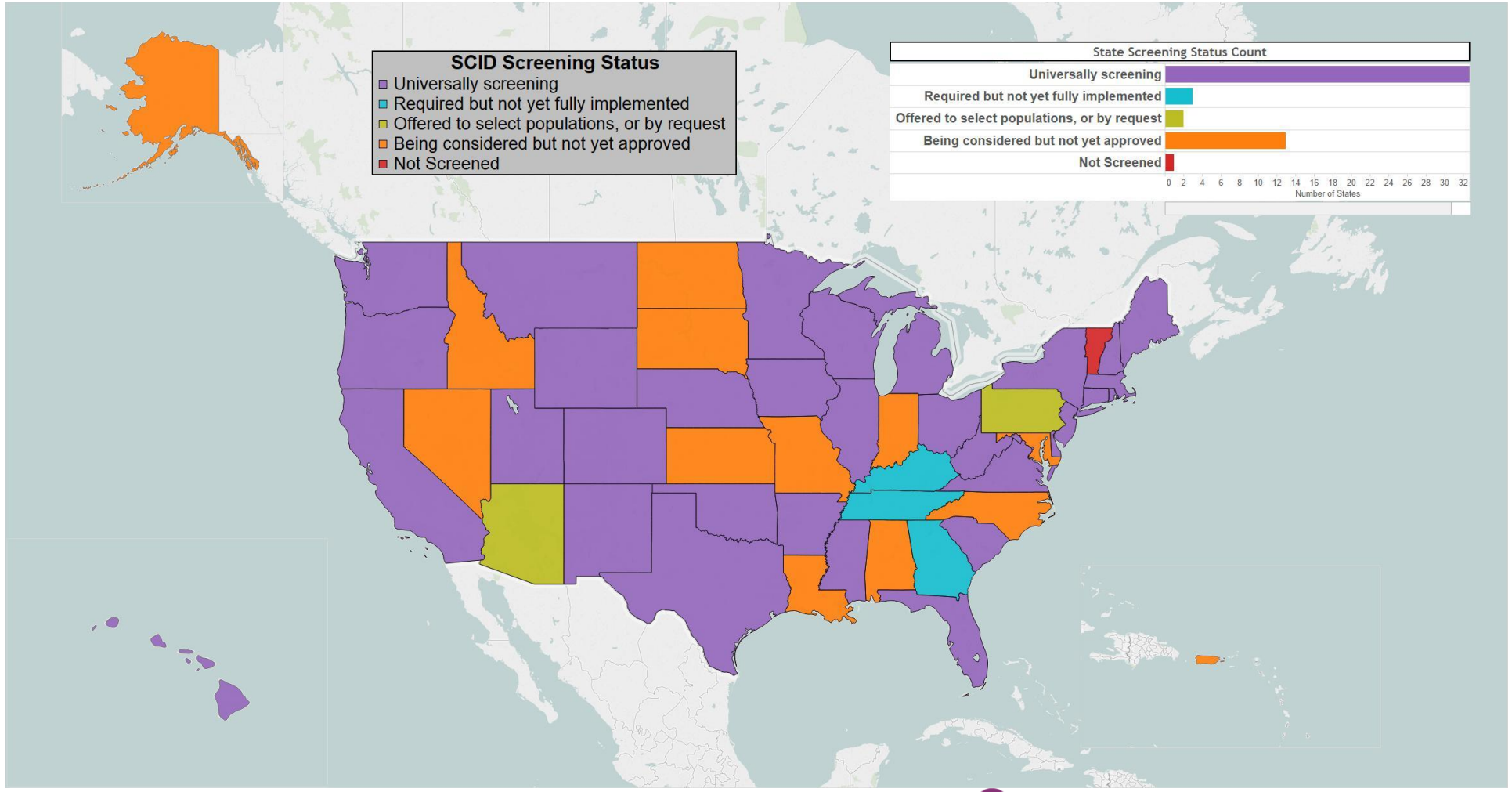
Follow-up and Clinical

- Availability of Immunologists
- Developing Relationships

Education

- Staff
- Leadership
- Clinicians
- Community/Advocacy

SCID Current Status | August 2015



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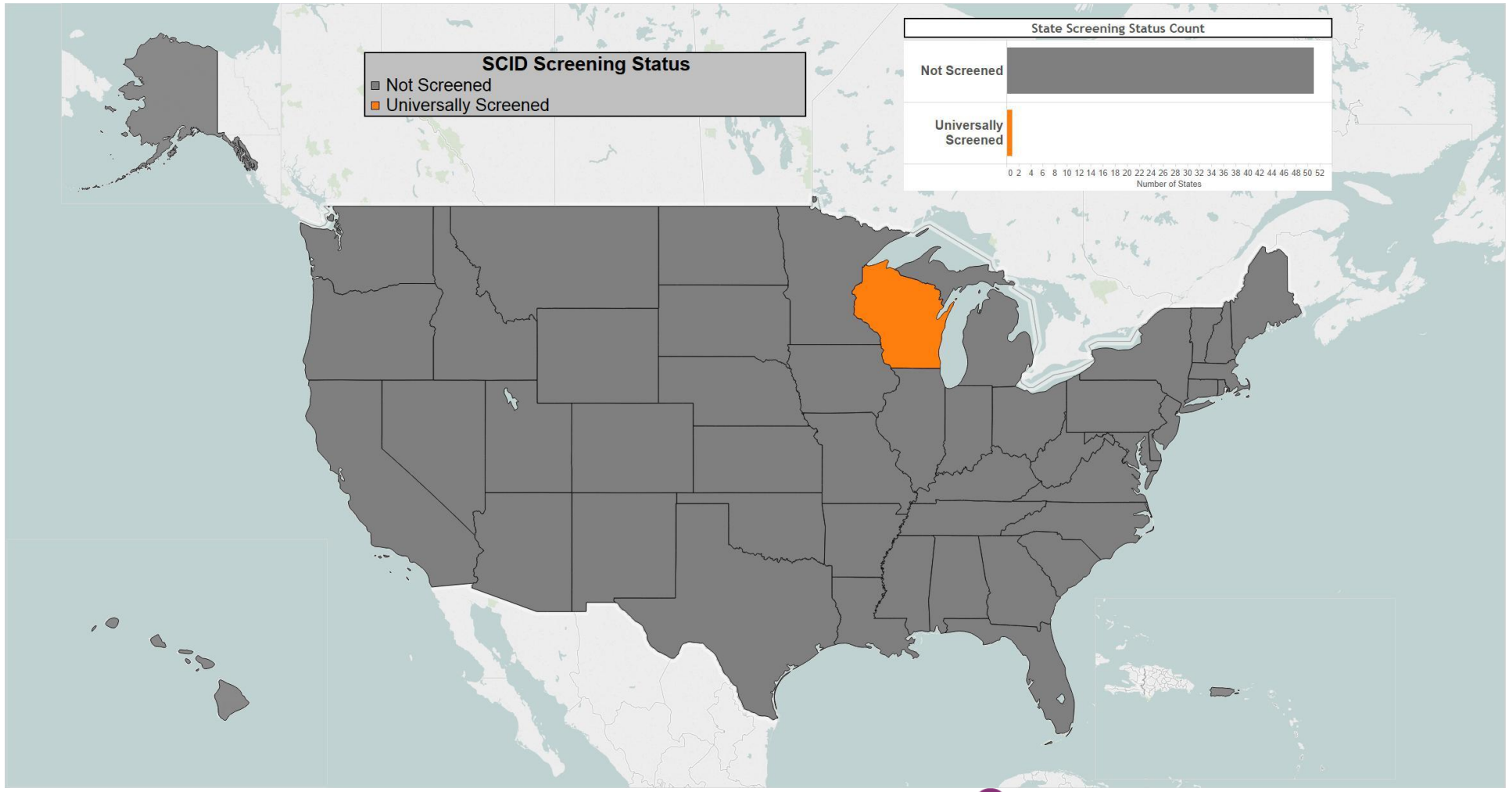
PROGRESS IN SCID IMPLEMENTATION

2008



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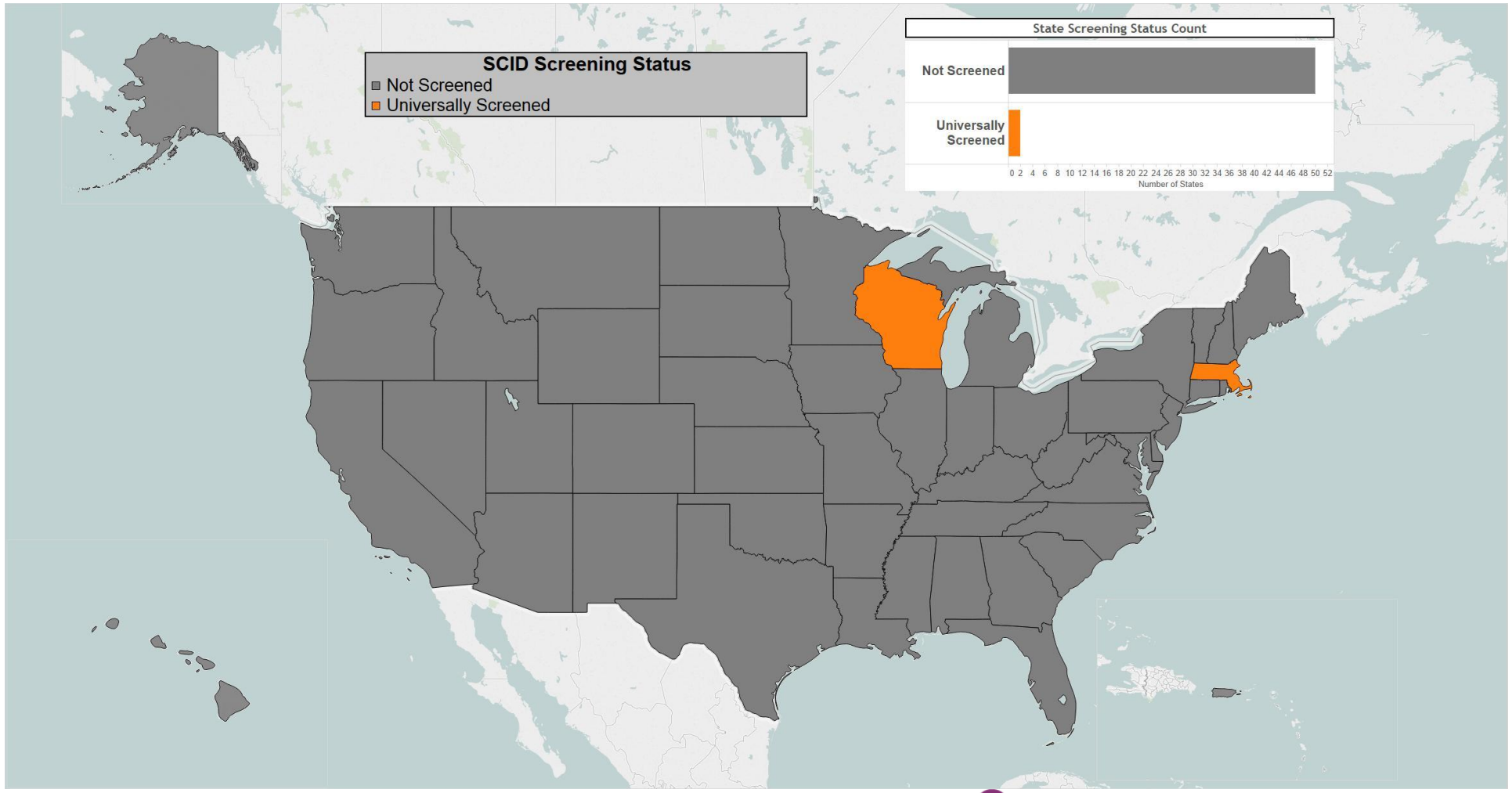
2009



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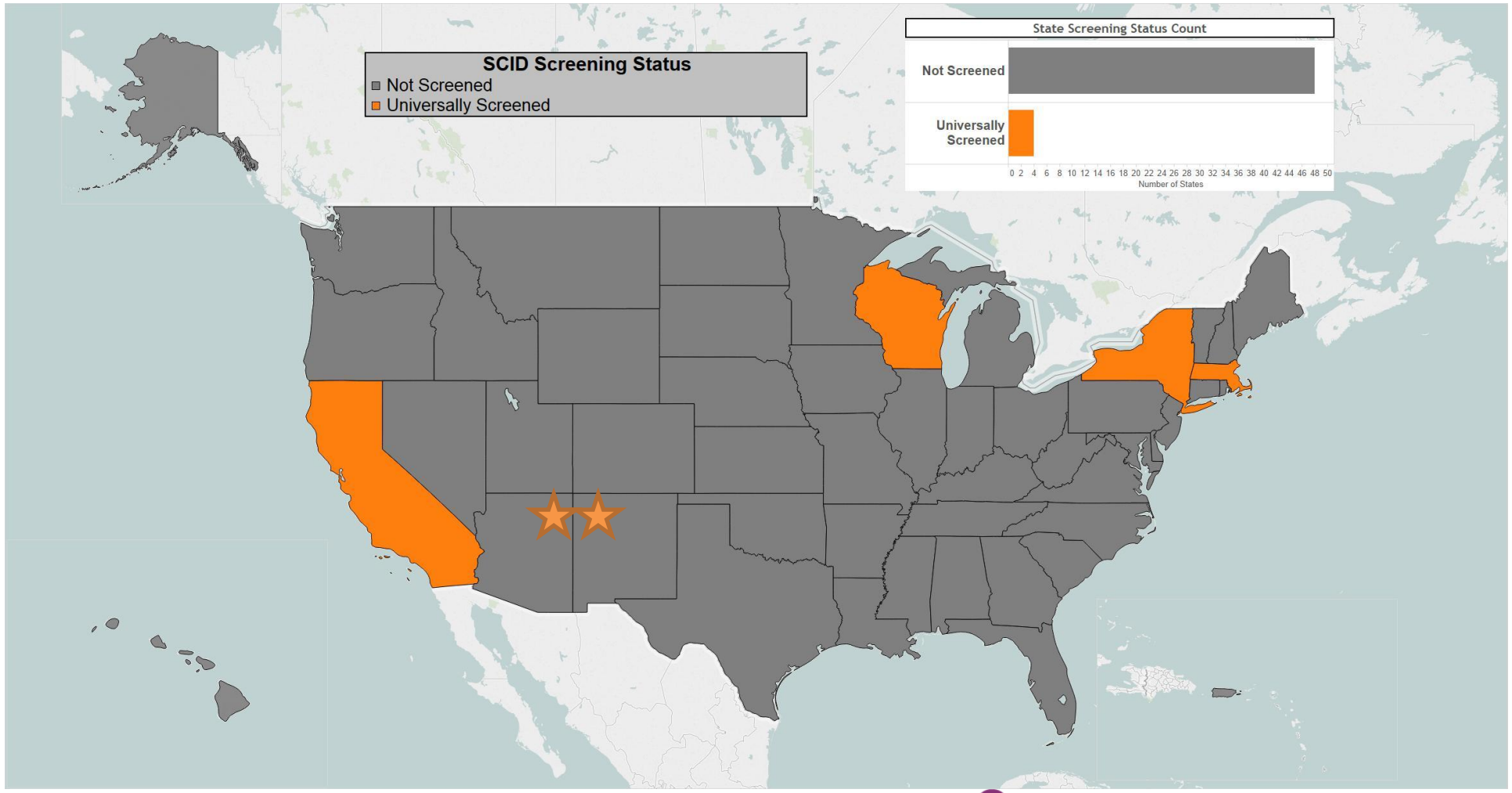
2010



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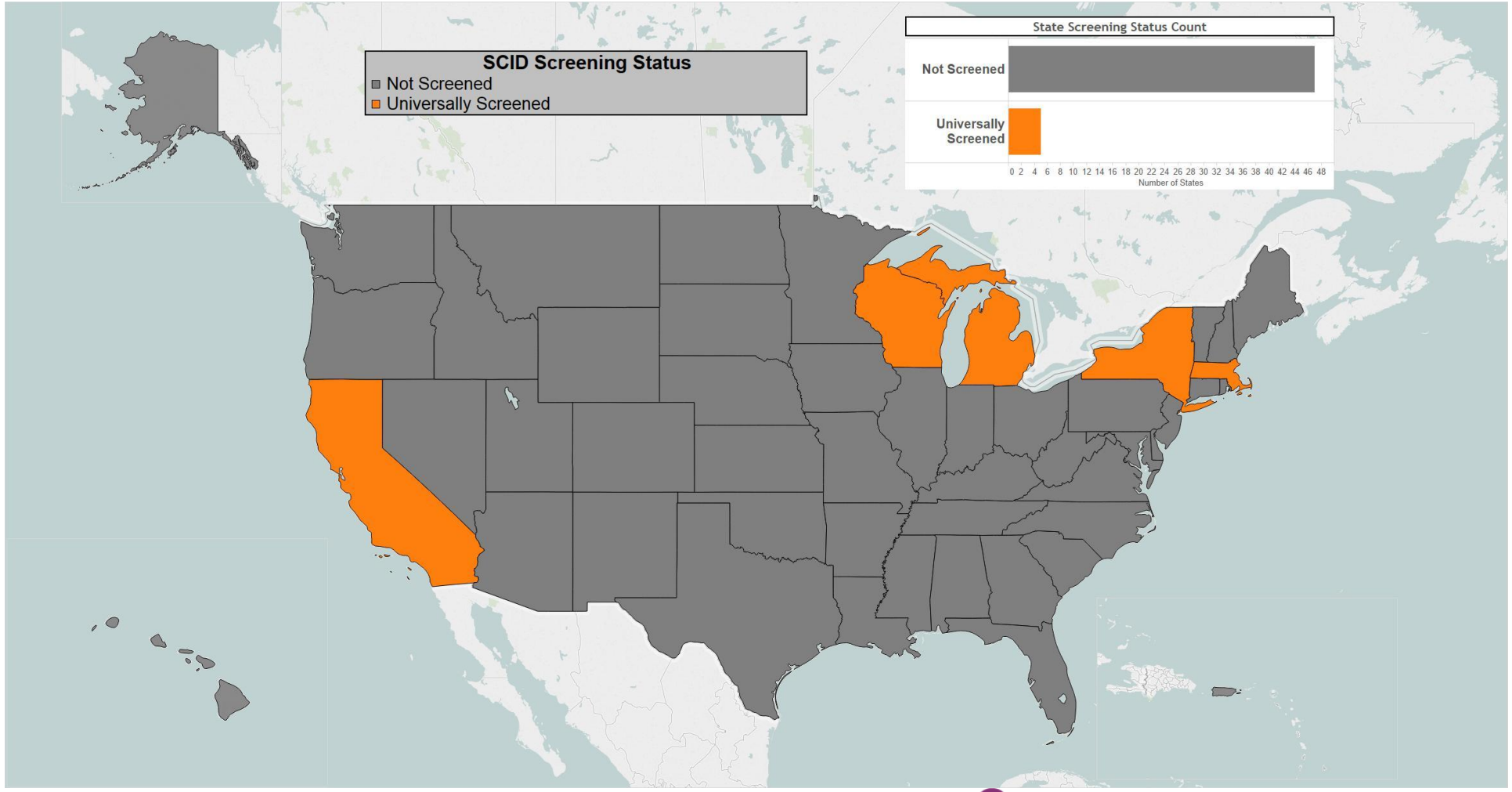
2011



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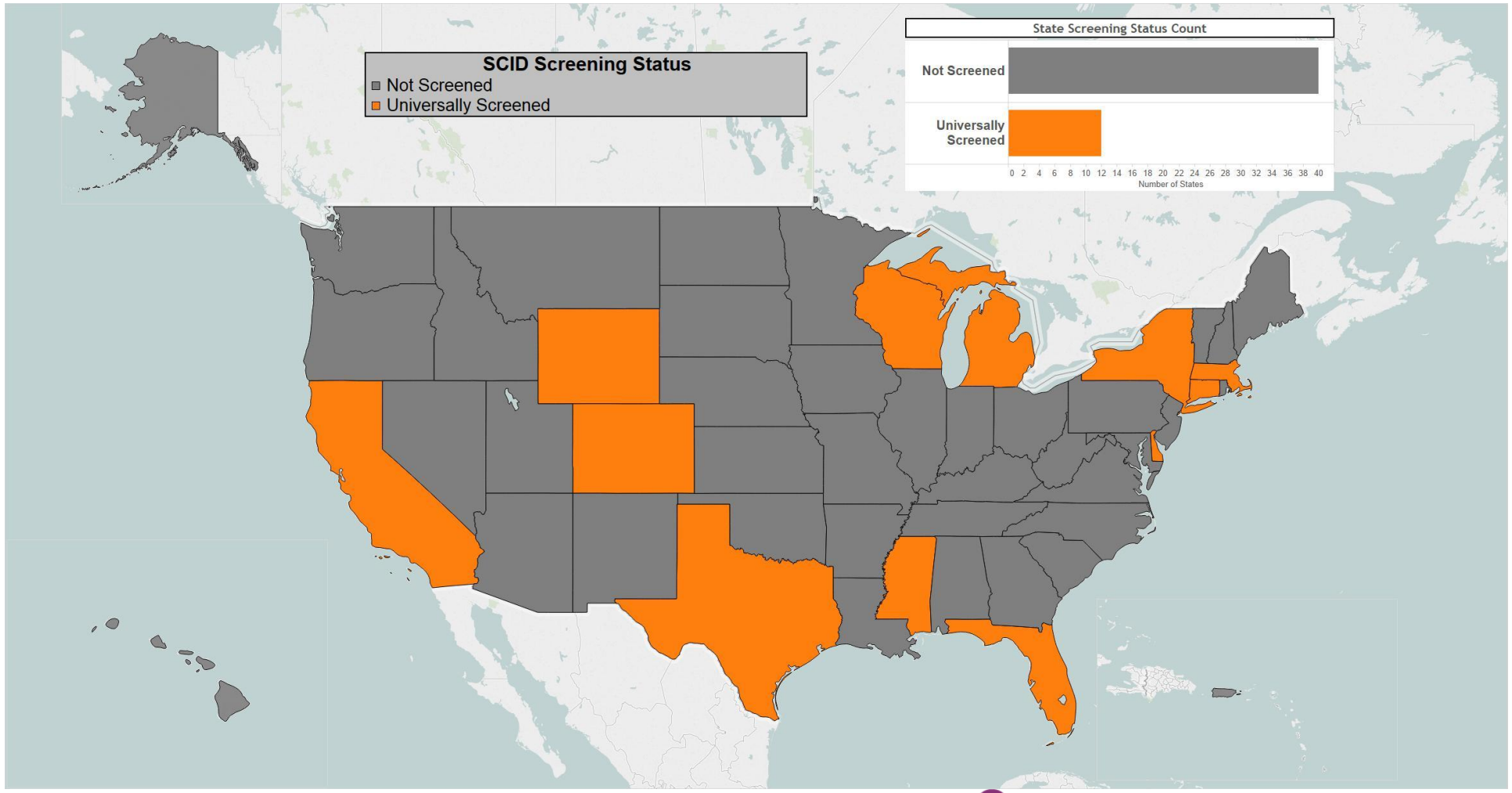
2012



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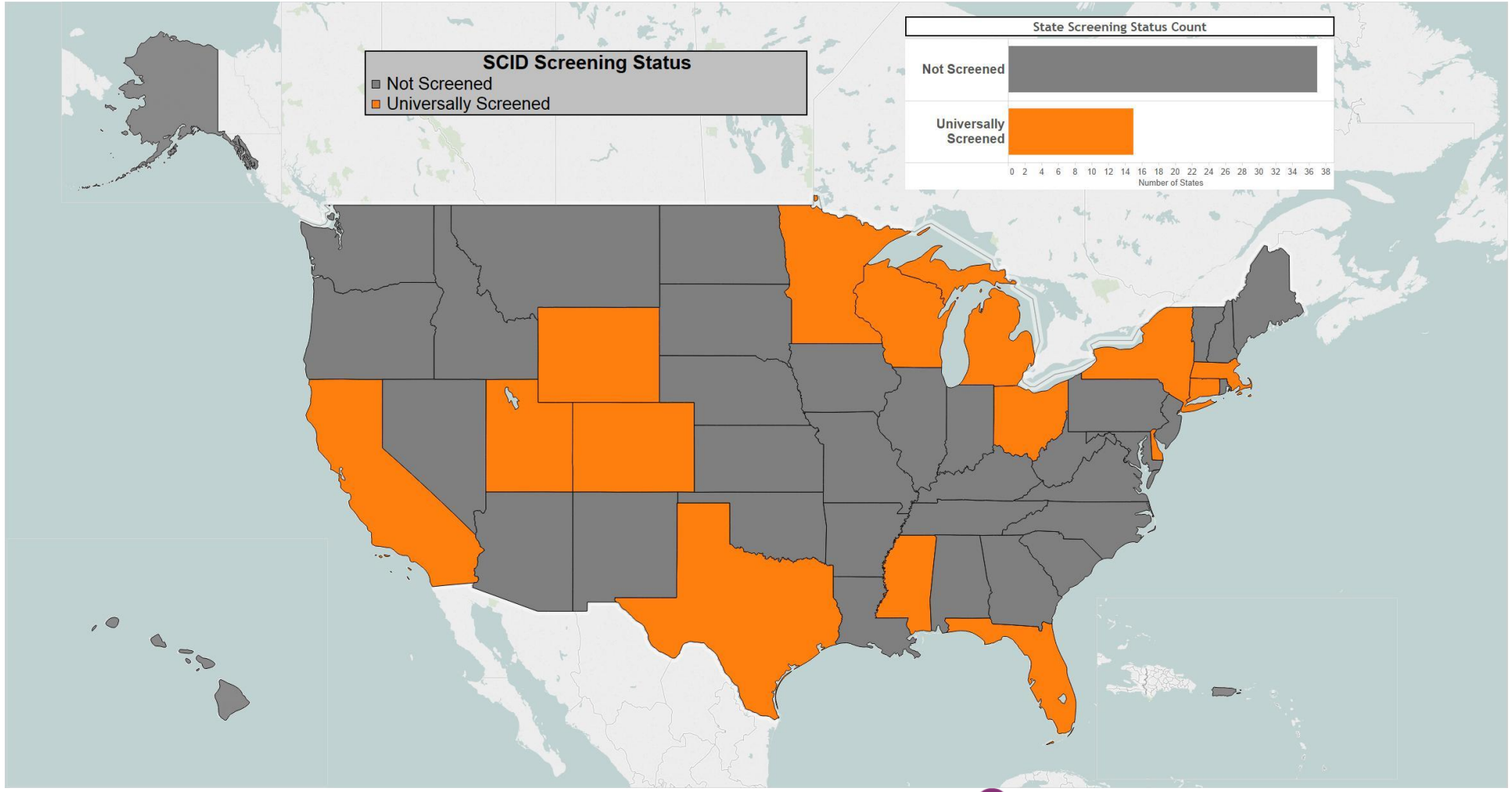
2013



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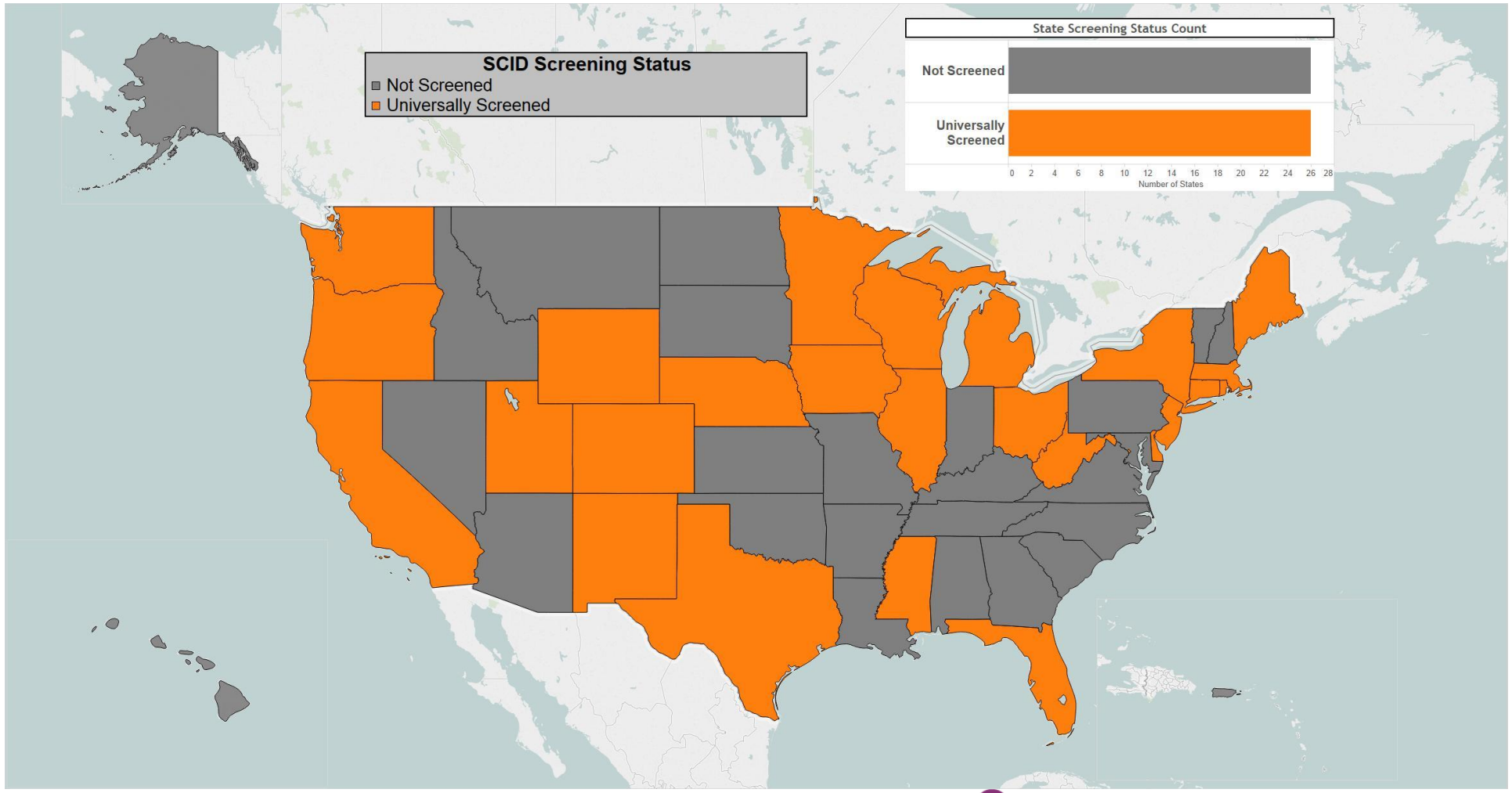
2014



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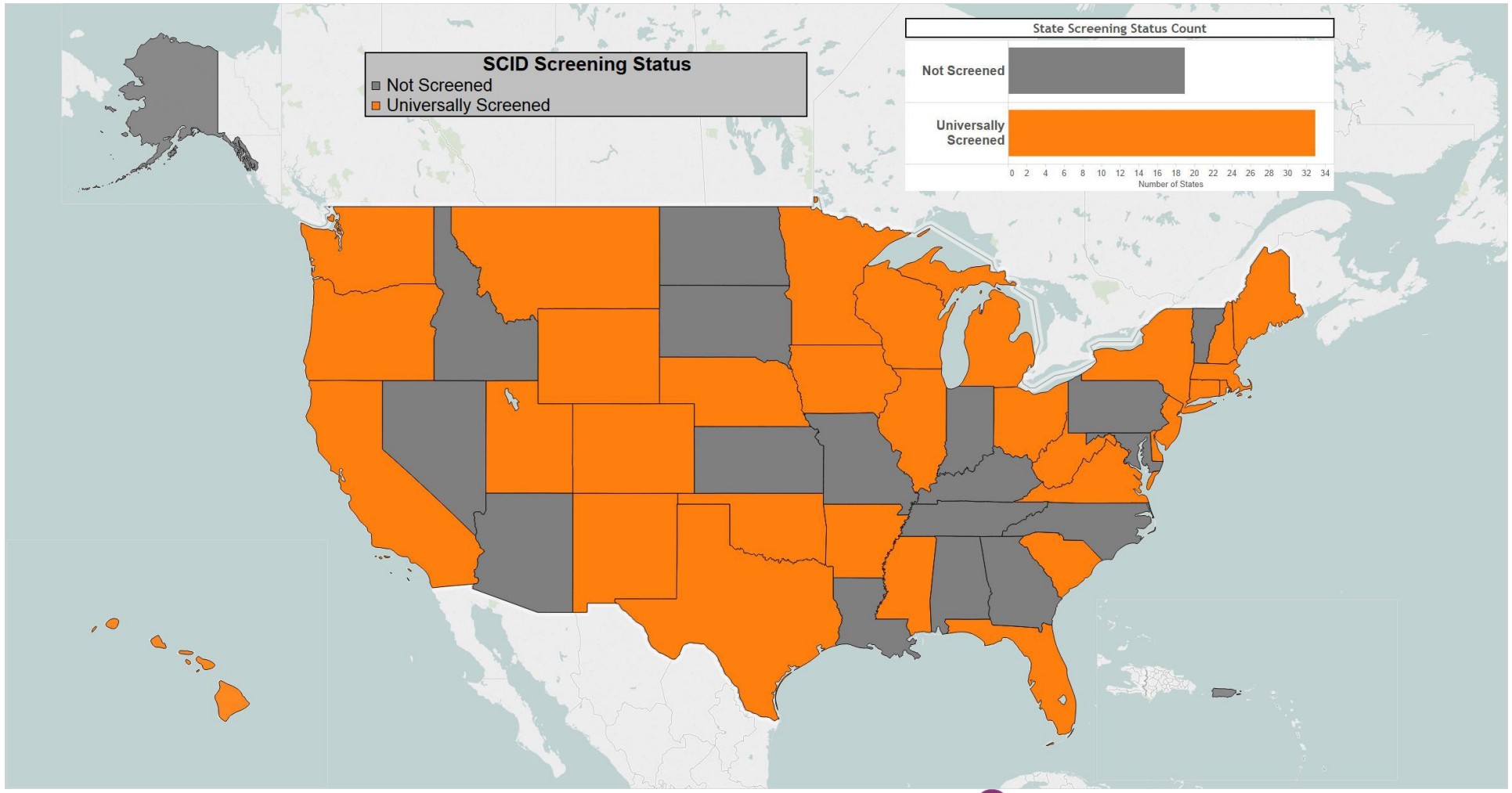
2015



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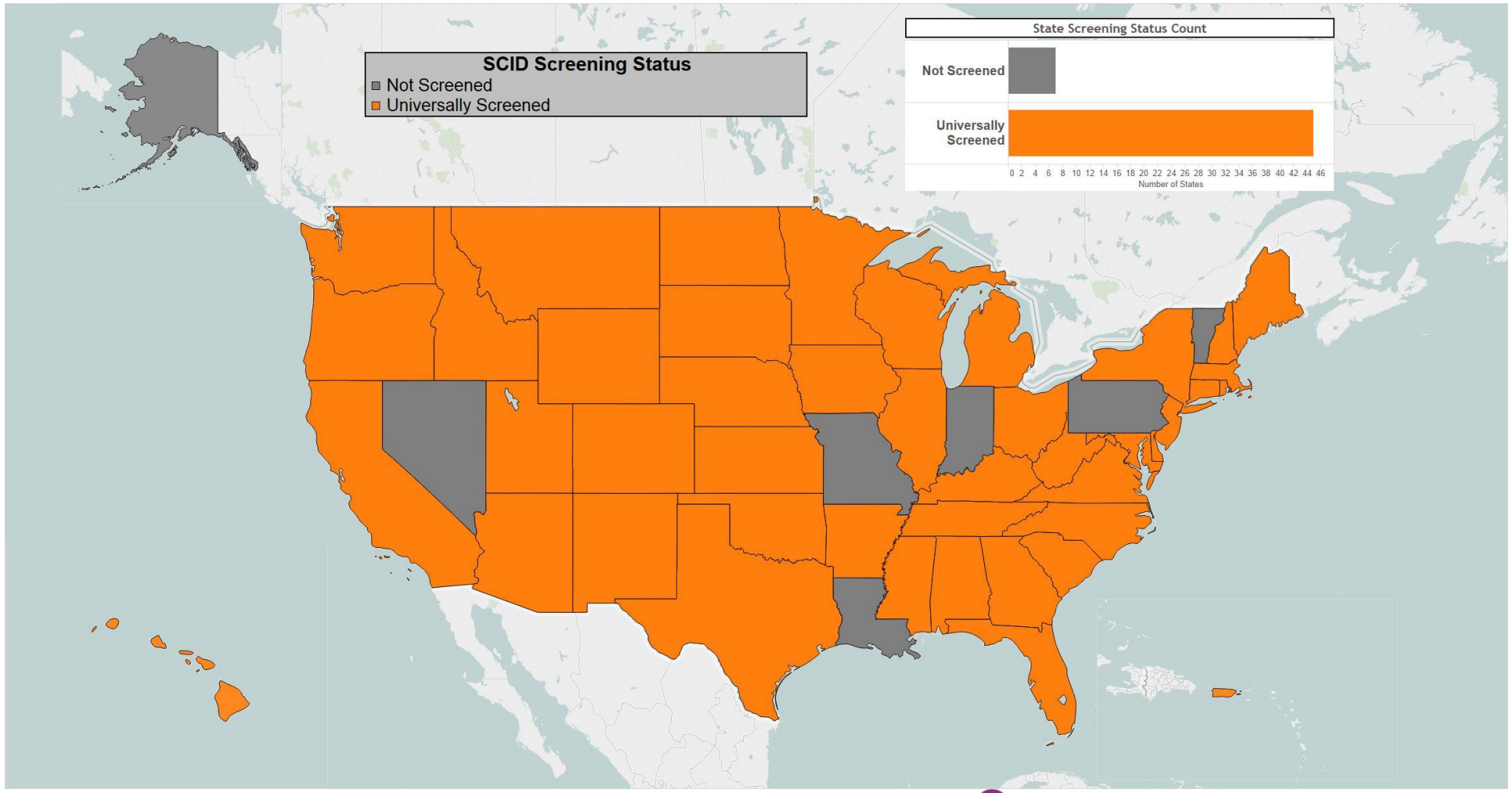
2016



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SCID Technical Assistance

- Funding Opportunities
- CDC Technical Assistance and Trainings
- Monthly Call: NBSTRN/NewSTEPs
- Technical Assistance In-Person Meeting (July 2015)
- 12 Grantees awarded up to $150,000/year for two years from APHL for SCID Implementation
- Resources shared on www.nbstrn.org and www.newsteps.org

SCID Grantees

- Educational Resources
- Technical Assistance
- Molecular Screening Capacity
- In-House Screening
- Expert Advisors
- Clinical Referral Networks
- Algorithm Development

SCID Updates

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FDA News Release

FDA allows marketing of the first newborn screening test to help detect Severe Combined Immunodeficiency

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For Immediate Release December 15, 2014

Release

Español

The U.S. Food and Drug Administration today allowed marketing of the EnLite Neonatal TREC Kit, the first screening test permitted to be marketed by FDA for Severe Combined Immunodeficiency (SCID) in newborns.

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The Newborn Screening Technical assistance and Evaluation Program (NewSTEPs), funded through a cooperative agreement to the Association of Public Health Laboratories (APHL) by the Genetic Services Branch of the Health Resources and Services Administration (HRSA), provides quality improvement initiatives, an innovative data repository and technical resources for newborn screening programs.

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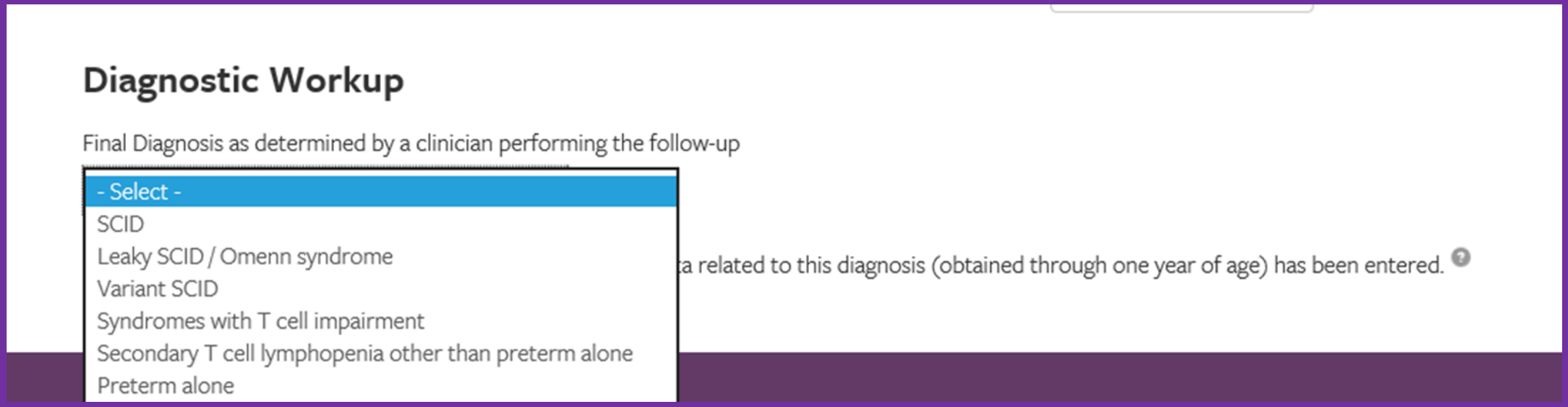
Measuring the Impact of SCID NBS

- NewSTEPs Repository
  - Count newborns identified by NBS with SCID



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SCID Summary

- 72% of newborns in the U.S. are born in states with universal screening for SCID.
- By the end of 2016, 86% of newborns in the U.S. will be born in states offering universal screening for SCID.
- Universal screening for SCID is influenced by a dynamic environment.

Critical Congenital Heart Disease (CCHD)

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The Foundation for CCHD Newborn Screening

BMJ

RESEARCH

Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39 821 newborns

Anne de-Wahl Granelli, cardiac sonographer,[1,11] Margareta Wennergren, consultant obstetrician,[2] Kenneth Sandberg, consultant neonatologist,[3] Mats Mellander, consultant paediatric cardiologist,[1] Carina Bejlum, consultant obstetrician,[4] Leif Inganäs, consultant paediatrician,[5] Monica Eriksson, consultant obstetrician,[6] Niklas Segerdahl, consultant paediatrician,[7] Annelie Ågren, research midwife,[8] Britt-Marie Ekman-Joelsson, consultant paediatrician,[9] Jan Sunnegårdh, consultant paediatric cardiologist,[1] Mario Verdicchio, consultant forensic pathologist,[10] Ingegerd Östman-Smith, professor of paediatric cardiology[1,11]

[1]Department of Paediatric Cardiology, Queen Silvia Children's Hospital, S-416 85 Göteborg, Sweden
[2]Department of Obstetrics, Sahlgrenska University Hospital, S-416 85 Göteborg
[3]Department of Neonatology, Queen Silvia Children's Hospital
[4]Department of Obstetrics, NÄL Hospital, S-461 85 Trollhättan, Sweden
[5]Children's Department, NÄL Hospital
[6]Obstetric Department, Södra Älvsborgs Hospital, S-501 85 Borås, Sweden
[7]Children's Department, Södra Älvsborgs Hospital
[8]Department of Neonatology, Hospital of Skövde, S-541 85 Skövde, Sweden
[9]Children's Department, Hospital of Skövde

ABSTRACT

Objective To evaluate the use of pulse oximetry to screen for early detection of life threatening congenital heart disease.

Design Prospective screening study with a new generation pulse oximeter before discharge from well baby nurseries in West Götaland. Cohort study comparing the detection rate of duct dependent circulation in West Götaland with that in other regions not using pulse oximetry screening. Deaths at home with undetected duct dependent circulation were included.

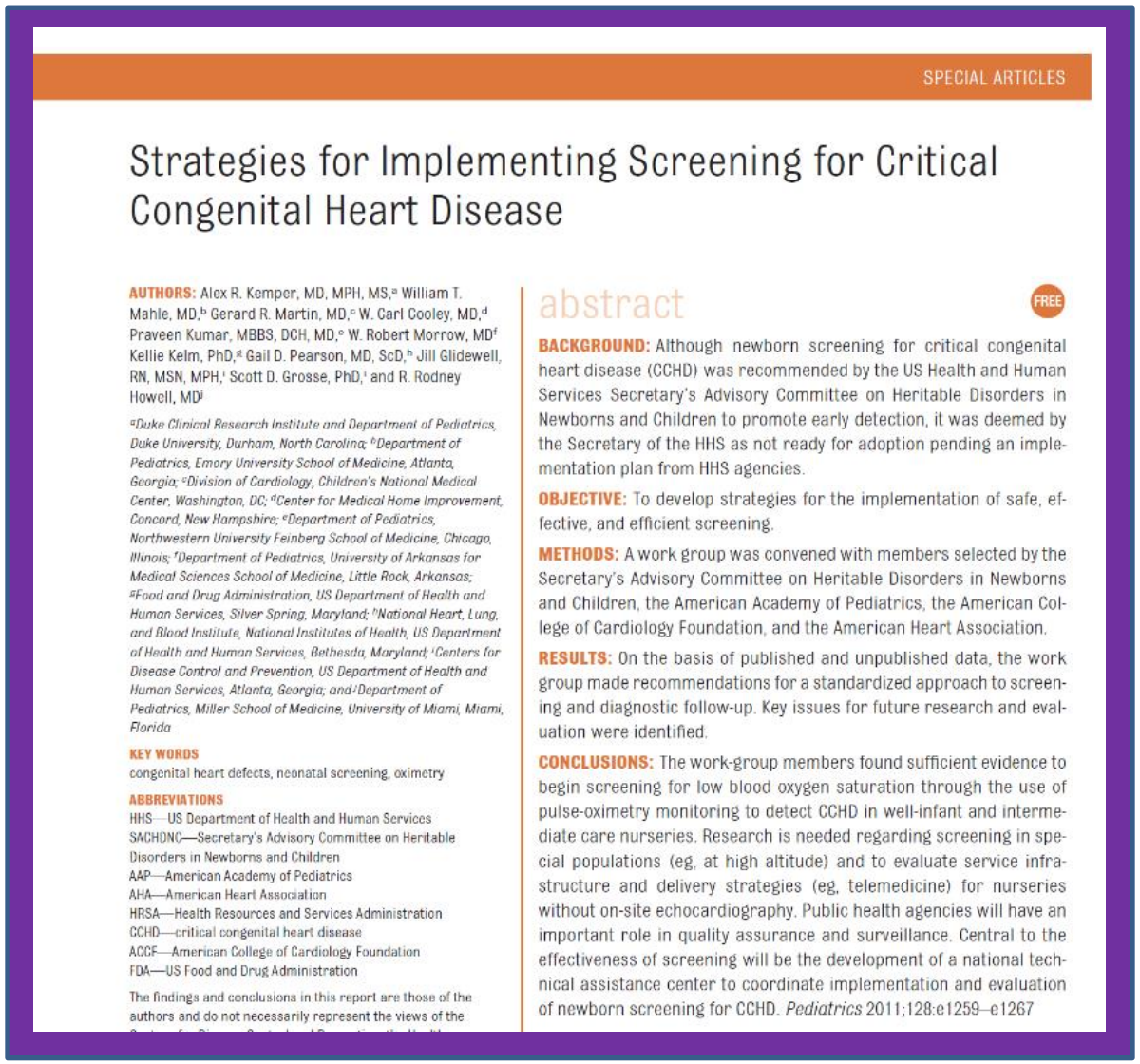
Setting All 5 maternity units in West Götaland and the supraregional referral centre for neonatal cardiac surgery.

Participants 39 821 screened babies born between 1 July 2004 and 31 March 2007. Total duct dependent circulation cohorts: West Götaland n=60, other referring regions n=100.

Main outcome measures Sensitivity, specificity, positive and negative predictive values, and likelihood ratio for

resulted in only 2.3 echocardiograms with normal cardiac findings for every true positive case of duct dependent circulation. In the cohort study, the risk of leaving hospital with undiagnosed duct dependent circulation was 28/100 (28%) in other referring regions versus 5/60 (8%) in West Götaland (P=0.0025, relative risk 3.36 (95% CI 1.37 to 8.24)). In the other referring regions 11/25 (44%) of babies with transposition of the great arteries left hospital undiagnosed versus 0/18 in West Götaland (P=0.0010), and severe acidosis at diagnosis was more common (33/100 (33%) v 7/60 (12%), P=0.0025, relative risk 2.8 (1.3 to 6.0)). Excluding premature babies and Norwood surgery, babies discharged without diagnosis had higher mortality than those diagnosed in hospital (4/27 (18%) v 1/110 (0.9%), P=0.0054). No baby died from undiagnosed duct dependent circulation in West Götaland versus five babies from the other referring regions.

Conclusion Introducing pulse oximetry screening before discharge improved total detection rate of duct dependent



Strategies for Implementing Screening for Critical Congenital Heart Disease

AUTHORS: Alex R. Kemper, MD, MPH, MS,[a] William T. Mahle, MD,[b] Gerard R. Martin, MD,[c] W. Carl Cooley, MD,[d] Praveen Kumar, MBBS, DCH, MD,[e] W. Robert Morrow, MD[f] Kellie Kelm, PhD,[g] Gail D. Pearson, MD, ScD,[h] Jill Glidewell, RN, MSN, MPH,[i] Scott D. Grosse, PhD,[i] and R. Rodney Howell, MD[j]

[a]*Duke Clinical Research Institute and Department of Pediatrics, Duke University, Durham, North Carolina;* [b]*Department of Pediatrics, Emory University School of Medicine, Atlanta, Georgia;* [c]*Division of Cardiology, Children's National Medical Center, Washington, DC;* [d]*Center for Medical Home Improvement, Concord, New Hampshire;* [e]*Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, Illinois;* [f]*Department of Pediatrics, University of Arkansas for Medical Sciences School of Medicine, Little Rock, Arkansas;* [g]*Food and Drug Administration, US Department of Health and Human Services, Silver Spring, Maryland;* [h]*National Heart, Lung, and Blood Institute, National Institutes of Health, US Department of Health and Human Services, Bethesda, Maryland;* [i]*Centers for Disease Control and Prevention, US Department of Health and Human Services, Atlanta, Georgia; and* [j]*Department of Pediatrics, Miller School of Medicine, University of Miami, Miami, Florida*

KEY WORDS
congenital heart defects, neonatal screening, oximetry

ABBREVIATIONS
HHS—US Department of Health and Human Services
SACHDNC—Secretary's Advisory Committee on Heritable Disorders in Newborns and Children
AAP—American Academy of Pediatrics
AHA—American Heart Association
HRSA—Health Resources and Services Administration
CCHD—critical congenital heart disease
ACCF—American College of Cardiology Foundation
FDA—US Food and Drug Administration

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the

abstract

FREE

BACKGROUND: Although newborn screening for critical congenital heart disease (CCHD) was recommended by the US Health and Human Services Secretary's Advisory Committee on Heritable Disorders in Newborns and Children to promote early detection, it was deemed by the Secretary of the HHS as not ready for adoption pending an implementation plan from HHS agencies.

OBJECTIVE: To develop strategies for the implementation of safe, effective, and efficient screening.

METHODS: A work group was convened with members selected by the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children, the American Academy of Pediatrics, the American College of Cardiology Foundation, and the American Heart Association.

RESULTS: On the basis of published and unpublished data, the work group made recommendations for a standardized approach to screening and diagnostic follow-up. Key issues for future research and evaluation were identified.

CONCLUSIONS: The work-group members found sufficient evidence to begin screening for low blood oxygen saturation through the use of pulse-oximetry monitoring to detect CCHD in well-infant and intermediate care nurseries. Research is needed regarding screening in special populations (eg, at high altitude) and to evaluate service infrastructure and delivery strategies (eg, telemedicine) for nurseries without on-site echocardiography. Public health agencies will have an important role in quality assurance and surveillance. Central to the effectiveness of screening will be the development of a national technical assistance center to coordinate implementation and evaluation of newborn screening for CCHD. *Pediatrics* 2011;128:e1259–e1267

Addition to the RUSP: September 2011

THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

September 21, 2011

R. Rodney Howell, M.D.
Committee Chairperson
Secretary's Advisory Committee on Heritable
Disorders in Newborns and Children
5600 Fishers Lane, Room 18A19
Rockville, MD 20857

Dear Dr. Howell:

As indicated in my letter to you on April 20, 2011, I determined that the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children's (SACHDNC) recommendations pertaining to the addition of Critical Congenital Heart Disease (CCHD) screening to the Recommended Uniform Screening Panel (RUSP) were not yet ready for adoption. Consequently, I referred the SACHDNC's recommendations to the Interagency Coordinating Committee on Screening in Newborns and Children (ICC) for additional review and input regarding implementation. I asked the ICC to review the evidence gaps described by the SACHDNC and propose a plan of action to address: identification of effective screening technologies, development of diagnostic proces
public, and strengthening service infrastructure
received and reviewed the requested ICC Plan

I have decided to adopt the SACHDNC's first recommendation to add CCHD to the RUSP

As you know, congenital heart disease causes u
life. Heart defects affect about 7 to 9 of every 1000 live bi
quarter of which could be detected and potentially treated by measuring blood oxygen saturation. Given this reality and the available information on the effectiveness of screening, I have decided to adopt the SACHDNC's first recommendation to add CCHD to the RUSP. In addition, I am requesting that the SACHDNC collaborate with the Health Resources and Services Administration (HRSA) to complete a thorough evaluation of the potential public health impact of universal screening for CCHD, as required by the authorizing statute, section 1111 of the Public Health Service Act (42 U.S.C. § 300b-10(b)(4)).

- What will be the impact on state health departments, including staffing needs, to implement this program? What are the roles of the state health departments?
- What capability is present to ensure that all babies are screened and their results are communicated to providers, including assuring that those not screened at birth receive a screen?

Regarding the four SACHDNC recommendations for action by the National Institutes of Health, Centers for Disease Control and Prevention, and HRSA to address recognized evidence gaps (Recommendations #2-#5), I have decided to adopt these recommendations. I will direct the named agencies, as well as other relevant HHS agencies, to proceed expeditiously with implementation, as described in the attachment, as feasible. I am taking this action because I believe that as we move forward, these activities will add important foundational information regarding the potential impact of implementing universal screening for CCHD, strengthen the platform on which to build the critical infrastructure for universal screening, and provide states with the data necessary to consider requiring that this condition be added to their existing newborn screening programs.

I would like to commend the SACHDNC on your success in creating and implementing an external scientific evidence review process for rare conditions that incorporates systematic evidence-based and peer-reviewed recommendations. I am encouraged by the emerging evidence base for the utility of early diagnosis and detection of CCHD via measurement of blood oxygen saturation, as well as the momentum and commitment that is evidenced at the state and federal levels to support implementation and investigation of successful screening programs. While we collectively engage in the remaining work that needs to be completed, HHS will continue to encourage states, health care facilities, and individual clinicians to provide this screening and contribute to the knowledge base in this important area.

I am committed to advancing screening for CCHD, and I appreciate the contributions of the SACHDNC in assisting HHS and states to explore ways to enhance newborn and child screening to improve the health of infants born in the United States.

Sincerely,

Kathleen Sebelius

Kathleen Sebelius

Challenges and Opportunities
CCHD NBS Implementation

- **Approval/Legislation**
  - Funding
  - Priorities
- **Point of Care Testing**
  - Equipment/Work flow in hospitals
  - Training/Education of nursery staff
  - Determining best algorithm
- **Special populations**
  - NICUs
  - Home births
  - High Altitude
  - Rural areas/lack of cardiology support

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Unique Challenges and Opportunities CCHD NBS Implementation

- **Data Collection**
  - State authority to collect data
  - Mechanisms to collect data
  - Hospital time and buy-in to report data
  - Defining minimum data set
  - Funding for surveillance
  - Quality assurance/Quality control
- **Birth Defects Registry**
  - Partner to collect long-term follow-up data
  - Identify false negatives
- **Education**
  - Staff
  - Leadership
  - Clinicians
  - Community/Advocacy

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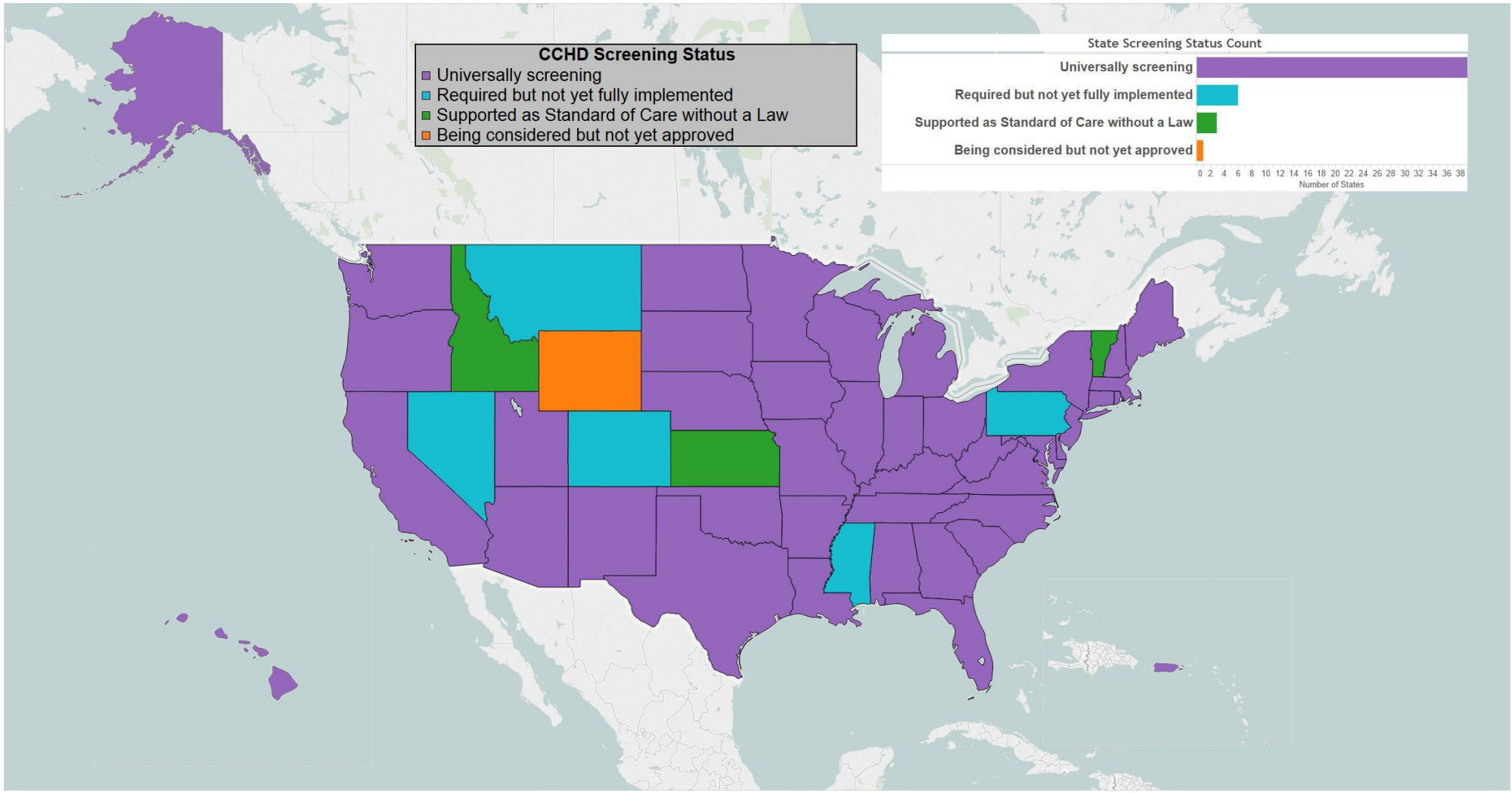
Current Status | August 2015



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CCHD Screening Progression

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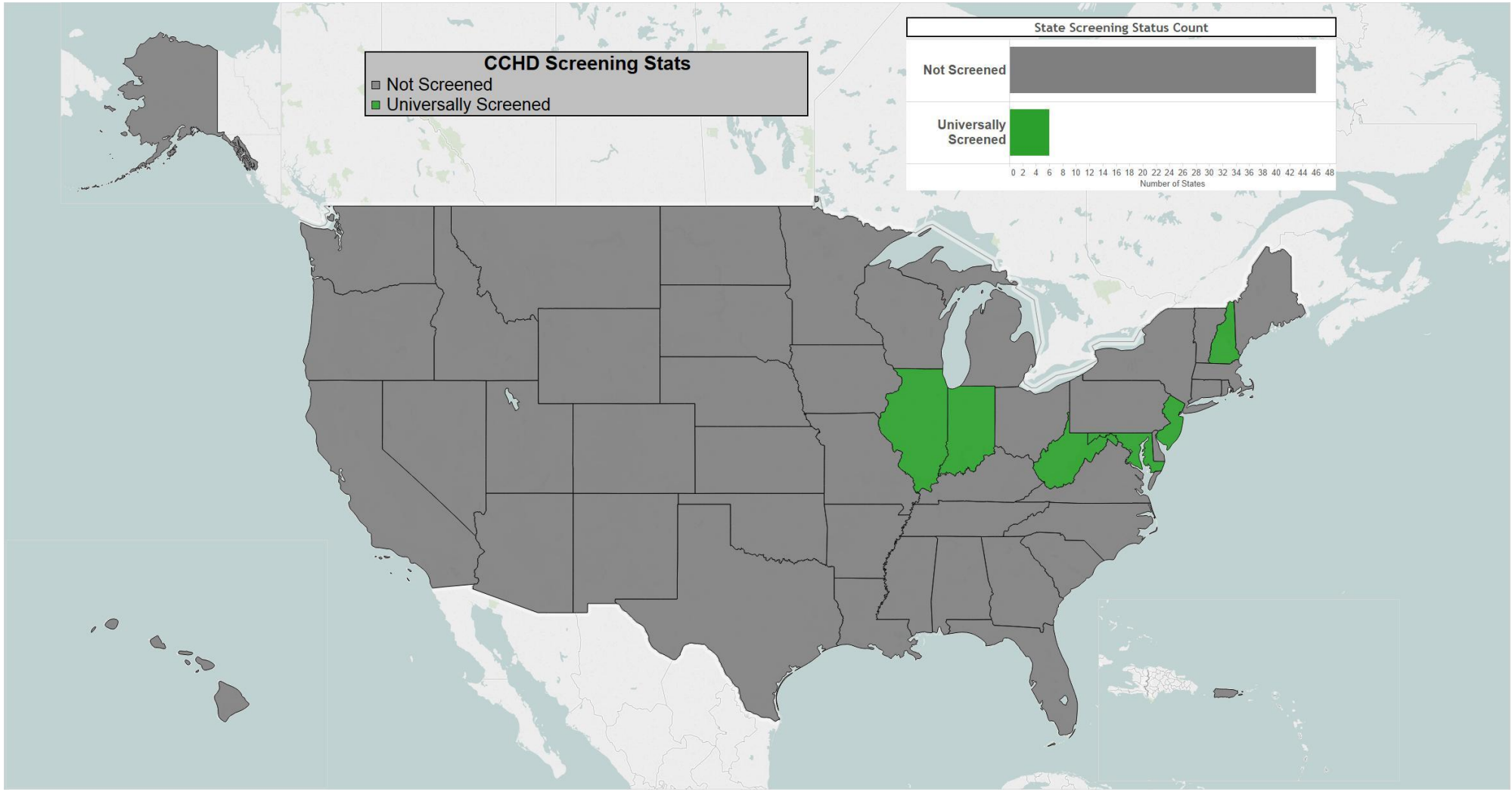
2012



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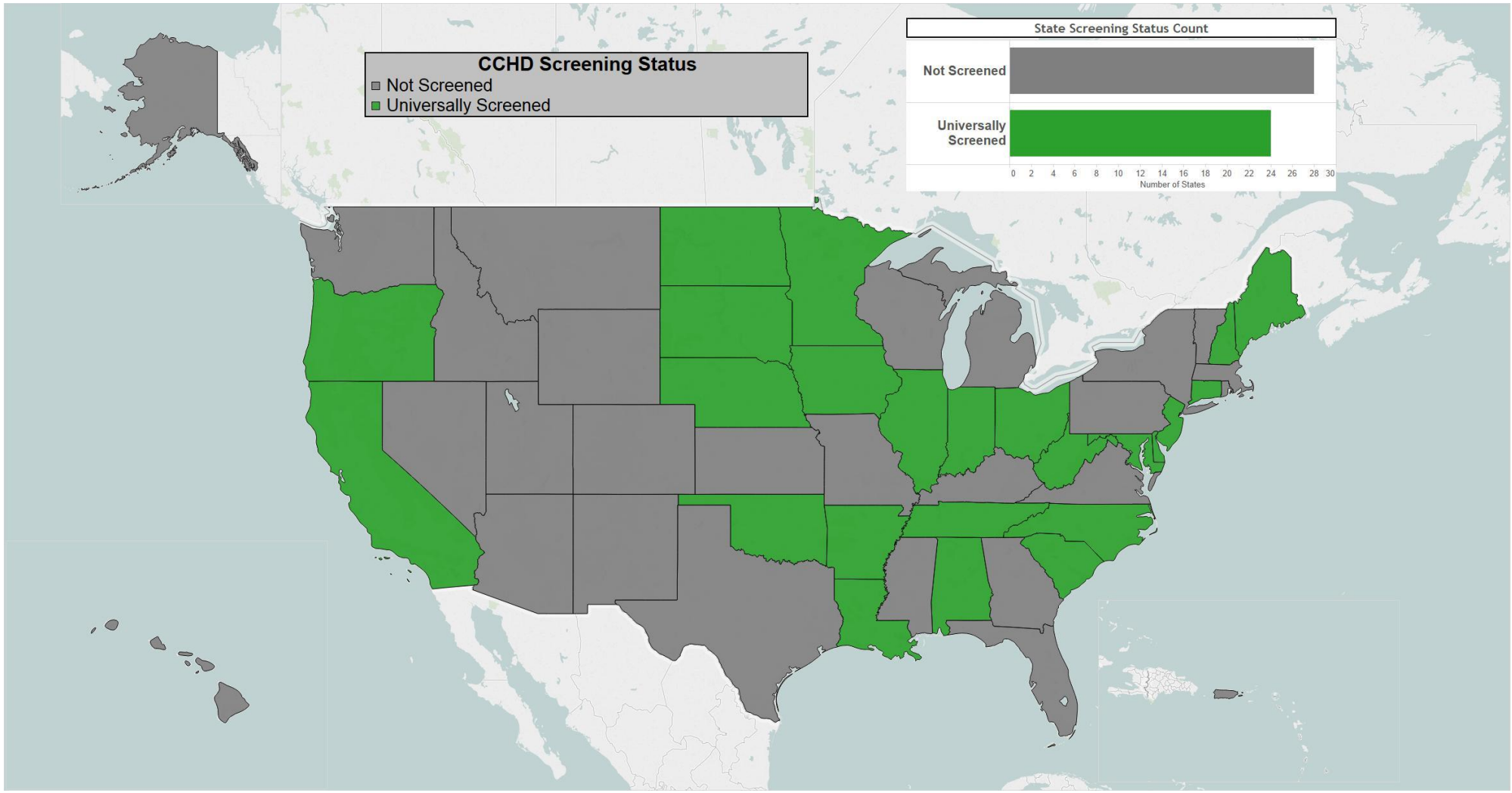
2013



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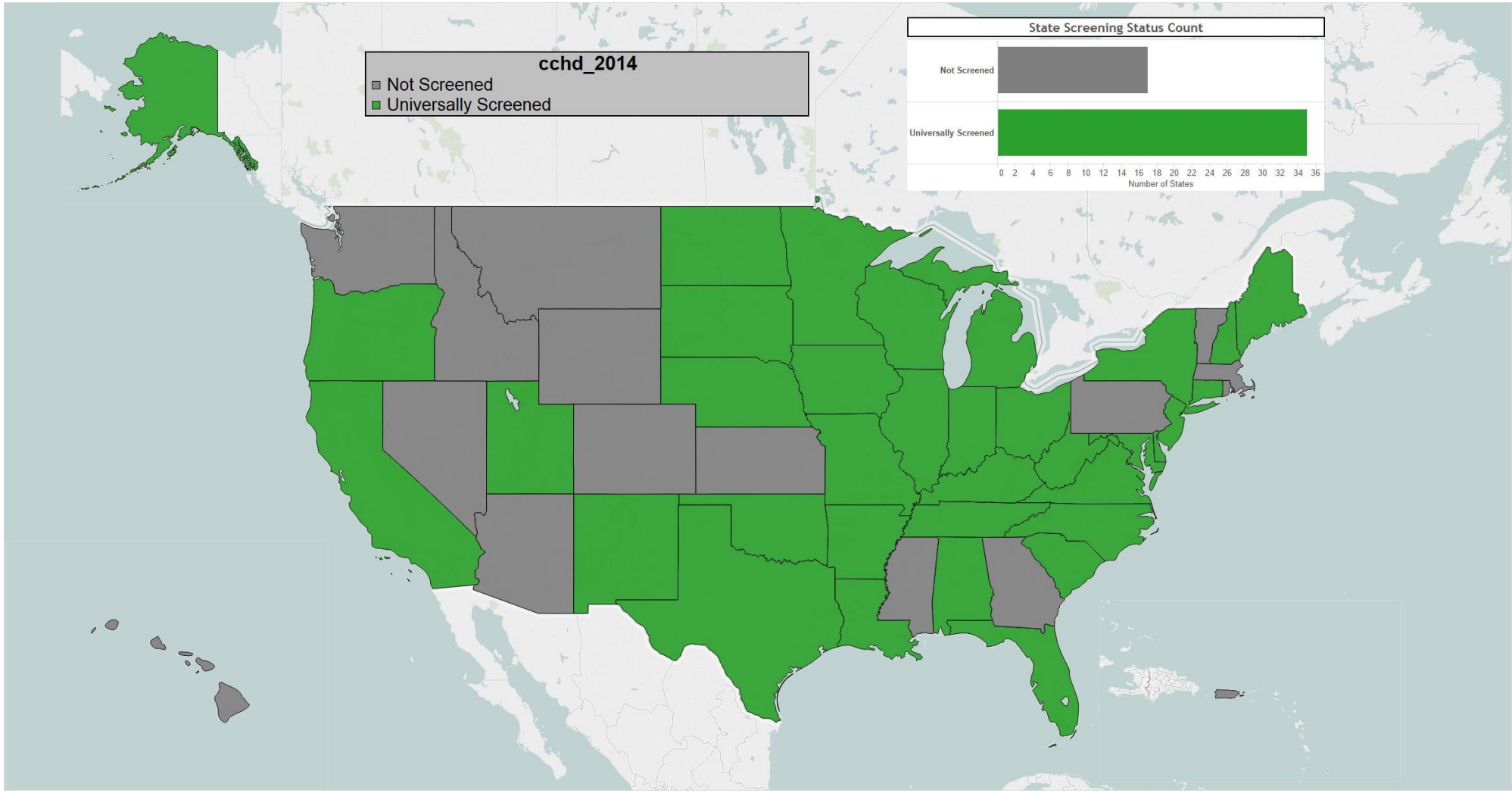
2014



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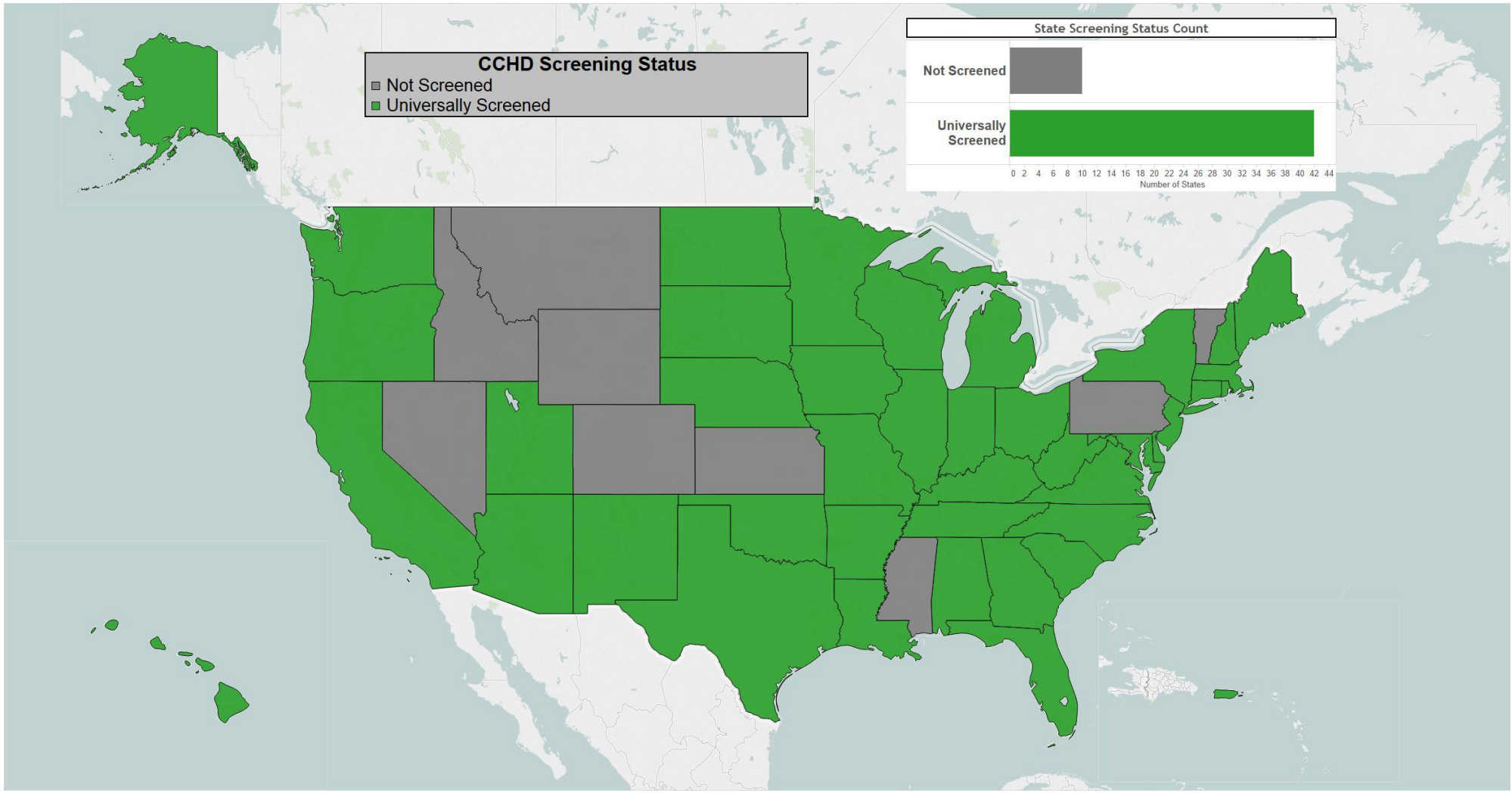
2015



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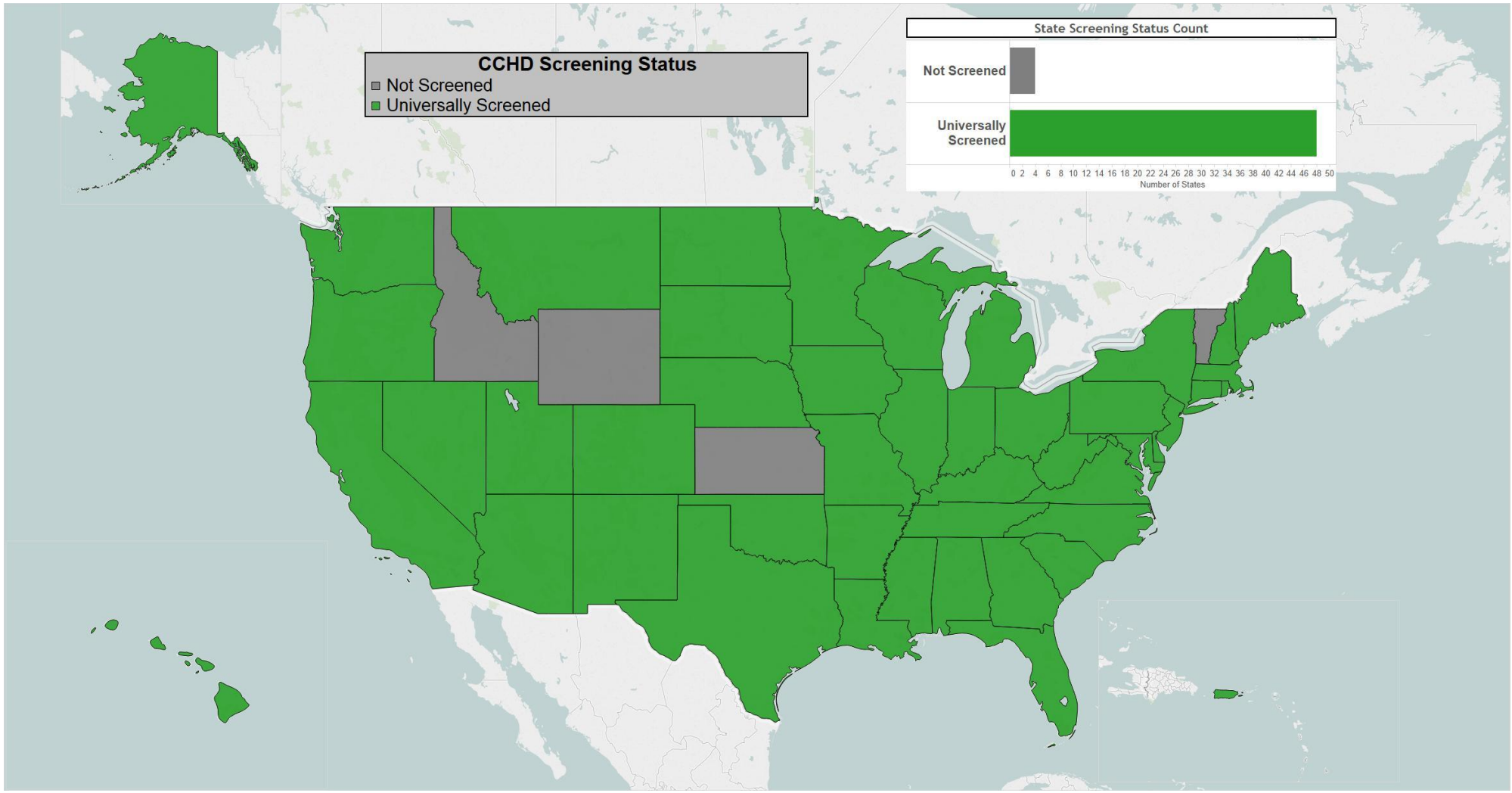
2016



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MMWR Summarizes CCHD Experience in U.S.

- Data Collection:
  - States that have implemented/ planning to implement CCHD screening
    - 24 current data collection,
    - 14 future data collection
    - 13 no plans for data collection
  - Types of data collection:
    - Aggregate data collection only
    - Pass/fail results on all newborns
    - O_2 saturation results on all newborns,
    - O_2 saturation results on failed newborns only

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 64 / No. 23
June 19, 2015

State Legislation, Regulations, and Hospital Guidelines for Newborn Screening for Critical Congenital Heart Defects — United States, 2011–2014

Jill Glidewell, MSN[1]; Richard S. Olney, MD[1]; Cynthia Hinton, PhD[2]; Jim Pawelski, MS[3]; Marci Sontag, PhD[4]; Thalia Wood, MPH[5]; James E. Kucik, PhD[6]; Rachel Daskalov, MHA[3]; Jeff Hudson, MA[3] (Author affiliations at end of text)

Critical congenital heart defects (CCHD) occur in approximately two of every 1,000 live births (*1*). Newborn screening provides an opportunity for reducing infant morbidity and mortality (*2,3*). In September 2011, the U.S. Department of Health and Human Services (HHS) Secretary endorsed the recommendation that critical congenital heart defects be added to the Recommended Uniform Screening Panel (RUSP) for all newborns (*4*). In 2014, CDC collaborated with the American Academy of Pediatrics (AAP) Division of State Government Affairs and the Newborn Screening Technical Assistance and Evaluation Program (NewSTEPs) to assess states' actions for adopting newborn screening for CCHD. Forty-three states have taken action toward newborn screening for CCHD through legislation, regulations, or hospital guidelines. Among those 43, 32 (74%) are collecting or planning to collect CCHD screening data; however, the type of data collected by CCHD newborn screening programs varies by state. State mandates for newborn screening for CCHD will likely increase the number of newborns screened, allowing for the possibility of early identification and prevention of morbidity and mortality. Data collection at the state level is important for surveillance, monitoring of outcomes, and evaluation of state CCHD newborn screening programs.

needed following an abnormal pulse oximetry screen (*1*) to determine whether CCHD are present (or to determine the cause of the abnormal result). Thus, unlike most newborn screening conditions, screening for CCHD is not based on performing a blood test. In addition, hypoxemia detected by screening could indicate a medical problem, and requires immediate follow-up before discharge from the hospital.

When accompanied by early identification and treatment, newborn screening provides an opportunity to reduce infant morbidity and mortality (*2,3*). The Secretary's Advisory Committee on Heritable Disorders in Newborns and Children has provided national guidelines and recommendations on

INSIDE

Mechanisms to collect CCHD NBS Data

- Electronic Birth Certificate
- Birth defects registry
- Hospital electronic medical record
- Dried blood spot card
- Paper forms
- Health level-7 messaging; automatic file transfer

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Quality Practice Resources Evaluation Program News and Education Maps and Reports

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About NewSTEPs

The Newborn Screening Technical assistance and Evaluation Program (NewSTEPs), funded through a cooperative agreement to the Association of Public Health Laboratories (APHL) by the Genetic Services Branch of the Health Resources and Services Administration (HRSA), provides quality improvement initiatives, an innovative data repository and technical resources for newborn screening programs.

STATE PROFILES

Check out map explorer for your state's data

Explore profiles

DATA REPOSITORY

Access data and more with NewSTEPs Data Repository

Visit Data Repository

TECHNICAL ASSISTANCE

Evaluation Site Visits, Model Practices, and more.

Learn more

Measuring the Impact of CCHD NBS

- NewSTEPs Repository
  - Count newborns identified by NBS with CCHD

Diagnostic Workup

Primary Screening Targets

- ☐ Hypoplastic left heart syndrome
- ☐ Pulmonary atresia with intact septum
- ☐ Tetralogy of fallot
- ☐ Total anomalous pulmonary venous return
- ☐ Transposition of the great arteries
- ☐ Tricuspid atresia
- ☐ Truncus arteriosus

Secondary Screening Targets

- ☐ Coarctation of the aorta
- ☐ Double outlet right ventricle
- ☐ Ebstein anomaly
- ☐ Interrupted aortic arch
- ☐ Single ventricle

- Birth Defects Registries

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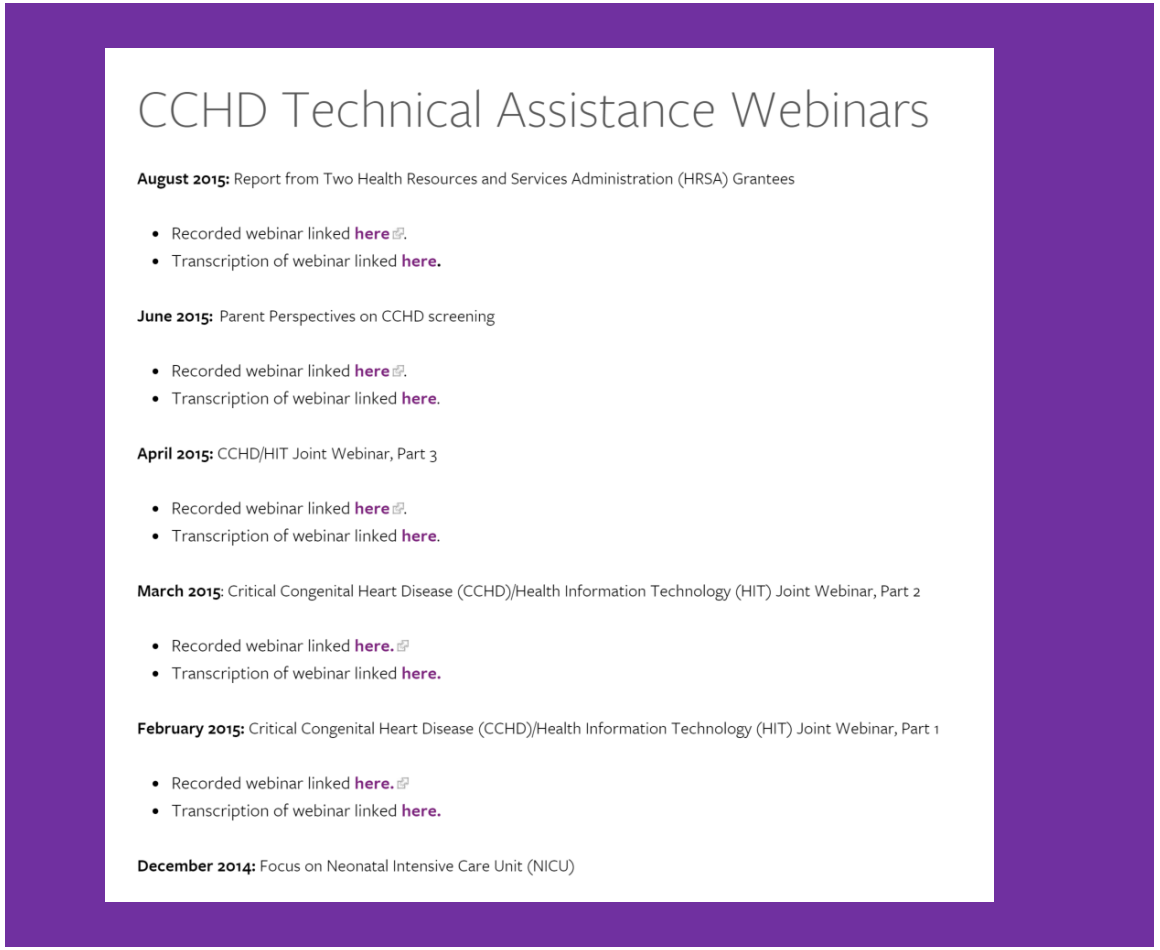
Technical Assistance Webinars

- Initiated by NYMAC Regional Genetics Collaborative (New York and Mid-Atlantic Region)
- Responsibility transferred to NewSTEPs in 2013
- Recorded and transcribed, (available at www.newsteps.org)



CCHD Technical Assistance Webinars

August 2015: Report from Two Health Resources and Services Administration (HRSA) Grantees

- Recorded webinar linked **here**.
- Transcription of webinar linked **here.**

June 2015: Parent Perspectives on CCHD screening

- Recorded webinar linked **here**.
- Transcription of webinar linked **here**.

April 2015: CCHD/HIT Joint Webinar, Part 3

- Recorded webinar linked **here**.
- Transcription of webinar linked **here**.

March 2015: Critical Congenital Heart Disease (CCHD)/Health Information Technology (HIT) Joint Webinar, Part 2

- Recorded webinar linked **here.**
- Transcription of webinar linked **here.**

February 2015: Critical Congenital Heart Disease (CCHD)/Health Information Technology (HIT) Joint Webinar, Part 1

- Recorded webinar linked **here.**
- Transcription of webinar linked **here.**

December 2014: Focus on Neonatal Intensive Care Unit (NICU)

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POMPE

Addition to the RUSP: March 2015

THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

MAR 0 2 2015

Joseph A. Bocchini, Jr., MD
Committee Chairperson
Discretionary Advisory Committee on Heritable Disorders
in Newborns and Children
Professor and Chairperson
Department of Pediatrics
Louisiana State University
1501 Kings Highway
Shreveport, LA 71130

Dear Dr. Bocchini:

As indicated in the January 27, 2014 letter from Secretary Sebelius, the Secretary's Discretionary Advisory Committee on Heritable Disorders in Newborns and Children (DACHDNC) recommendations regarding the addition of Pompe di... ...led Uniform Screening Panel (RUSP) were forwarded to the Inte... ...on Screening in Newborns and Children (ICC) for addi... ...ation.

I accept the DACHDNC recommendation to add Pompe disease to the RUSP.

The ICC reviewed the DACHDNC's recommendati... ...thod evaluation studies, information on test quality, natio... ...rrent state screening activities. In its report to me, the ICC noted challenges associated with the implementation of state newborn screening for Pompe disease including resource limitations for laboratory testing, management of late-onset cases, and increased burden on treatment and follow-up systems. However, the ICC emphasized that over time, adoption of this recommendation will help increase the number of newborns screened and decrease the morbidity

the complex issues surrounding newborn screening for Pompe disease and encourage Federal agencies to support states as they build capacity and implement state-wide screening.

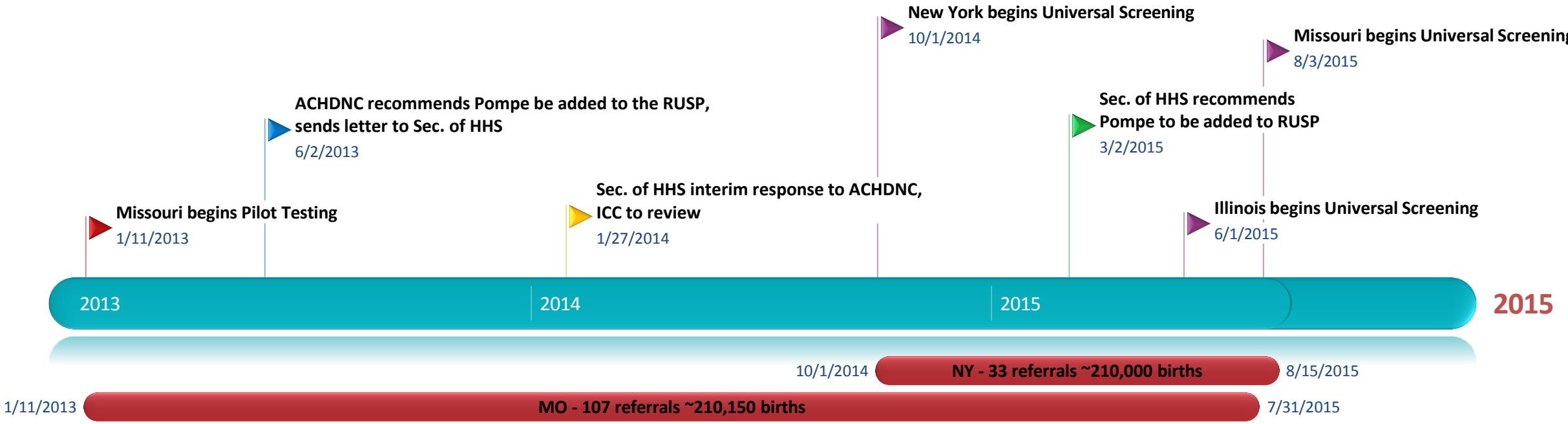
I appreciate the DACHDNC's dedication and continued hard work to improve the health of our nation's infants and children.

Sincerely,

[redacted]

Sylvia M. Burwell

Pompe Screening in the US



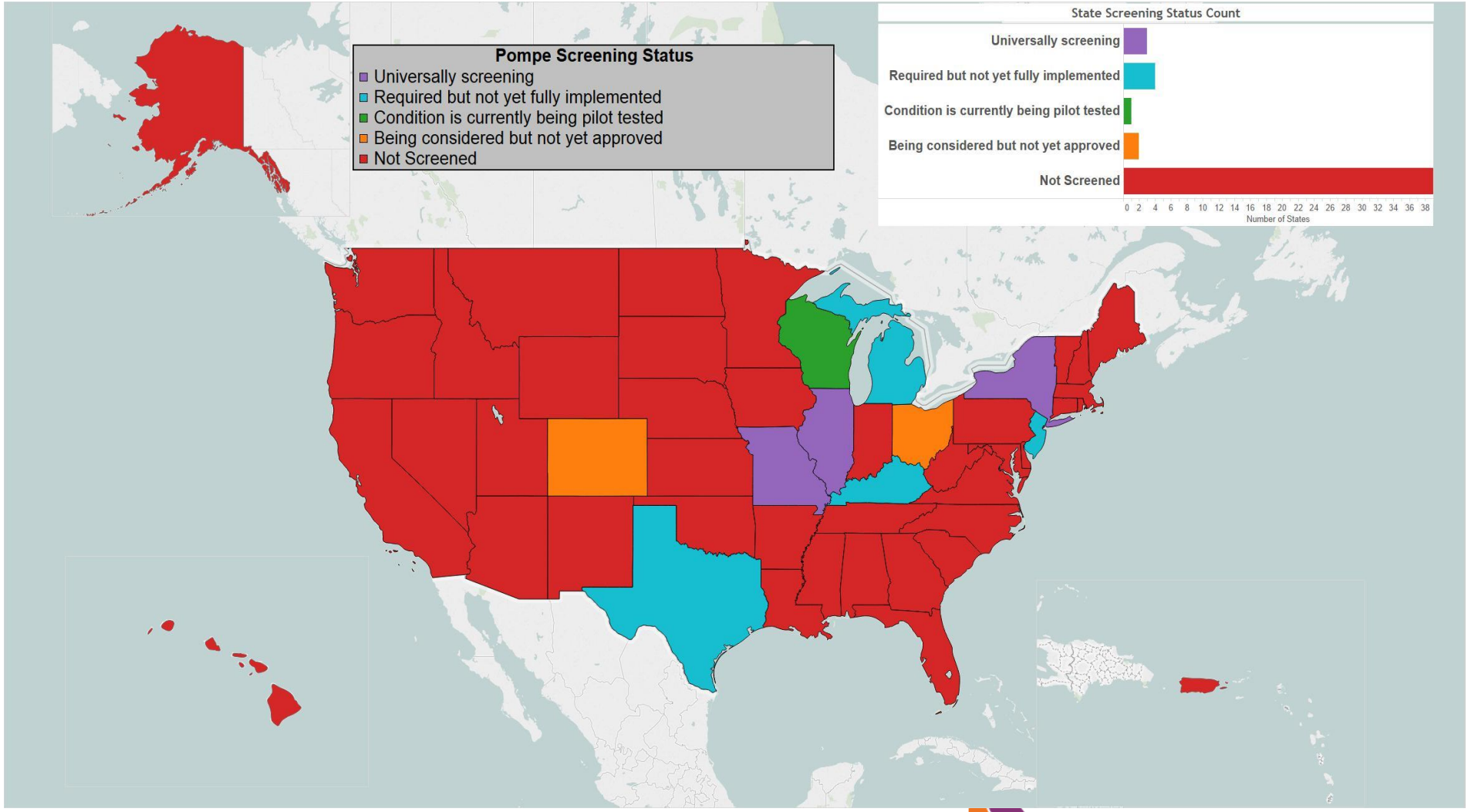
Screening Methodologies:

NY – FIA MS/MS + Molecular

IL – LC MS/MS moving towards FIA MS/MS

MO- Digital microfluidics fluorescent assay

Pompe Current Status | August 2015



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Pompe and Other LSD Activities in the US

Pilot/Research Study

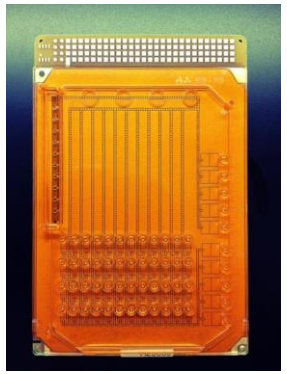
- Missouri
  - Pompe + 3 LSDs by digital microfludics
  - Krabbe, Niemann Pick A/B by stand-alone fluorometry (in validation)

- Wisconsin
  - NIH funded Pompe NBS pilot study
  - NBS for 6 LSDs bill introduced: Krabbe, Fabry, Pompe, Niemann−Pick, Gaucher, MPS-1

Pompe and Other LSD Activities in the US

- New York
  - NIH funded Pompe NBS pilot study
  - Pilot testing (Four NY City hospitals: Fabry, Gaucher, Niemann-Pick A/B, MPS-1)
  - Live screening: Krabbe, Pompe
- Washington
  - Pompe, Fabry and Gaucher
  - De-identified samples, FIA-MS/MS + molecular
  - Recently expanded to include 3 more LSDs

Digital microfluidics fluorescent assay



Tandem mass spectrometry assay

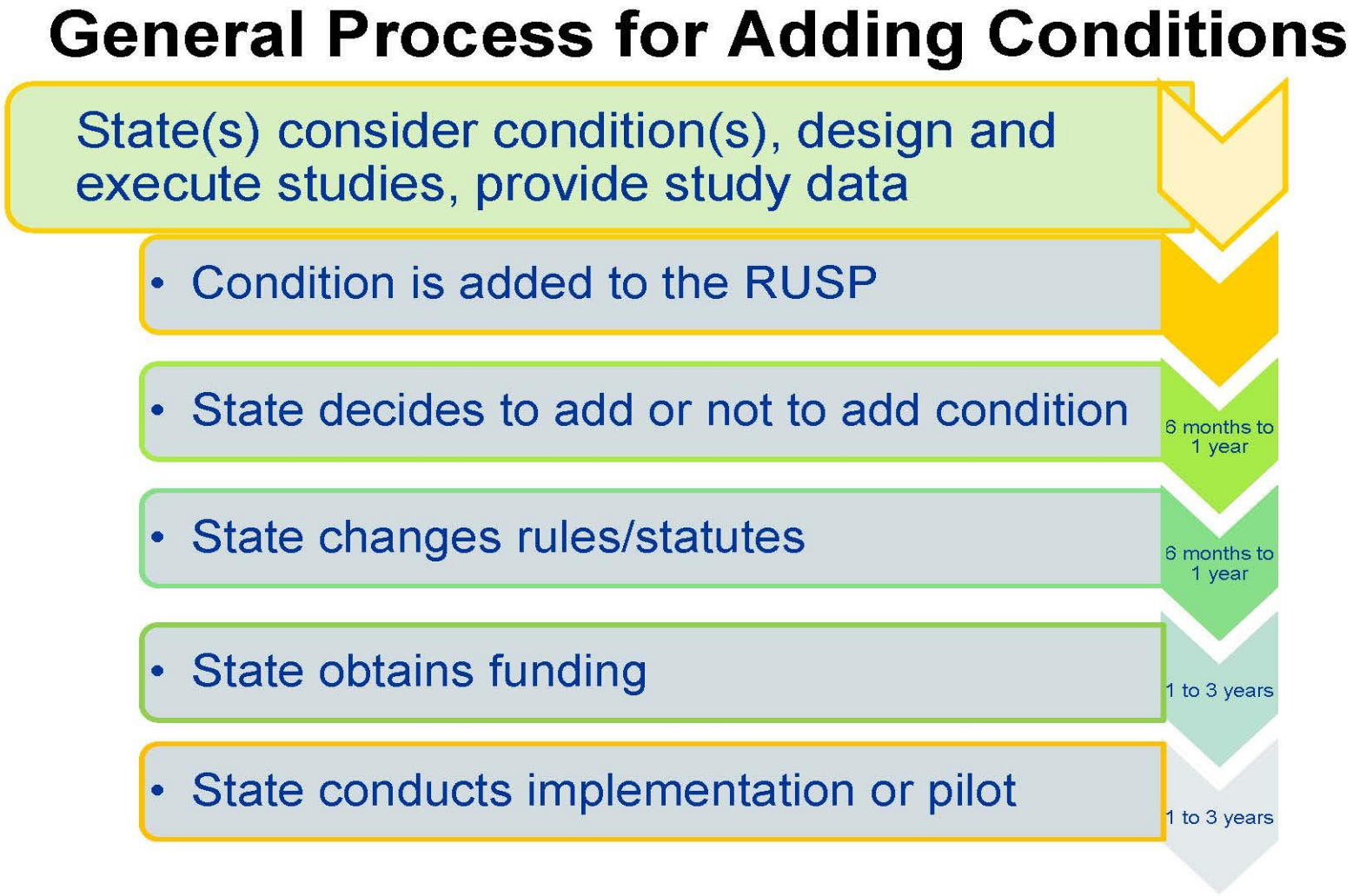
Future Pompe Screening

Status of Pompe Screening	NBS Program
Required but not fully implemented	New Jersey
	Kentucky
	Texas
	Michigan
Being considered, not yet approved	Colorado
	Ohio

Challenges in Pompe NBS Implementation

- Progression of disease – late onset
- Cost of treatment
- Recently added to RUSP
- Dedicated instrumentation
- LIMS software
- Staffing

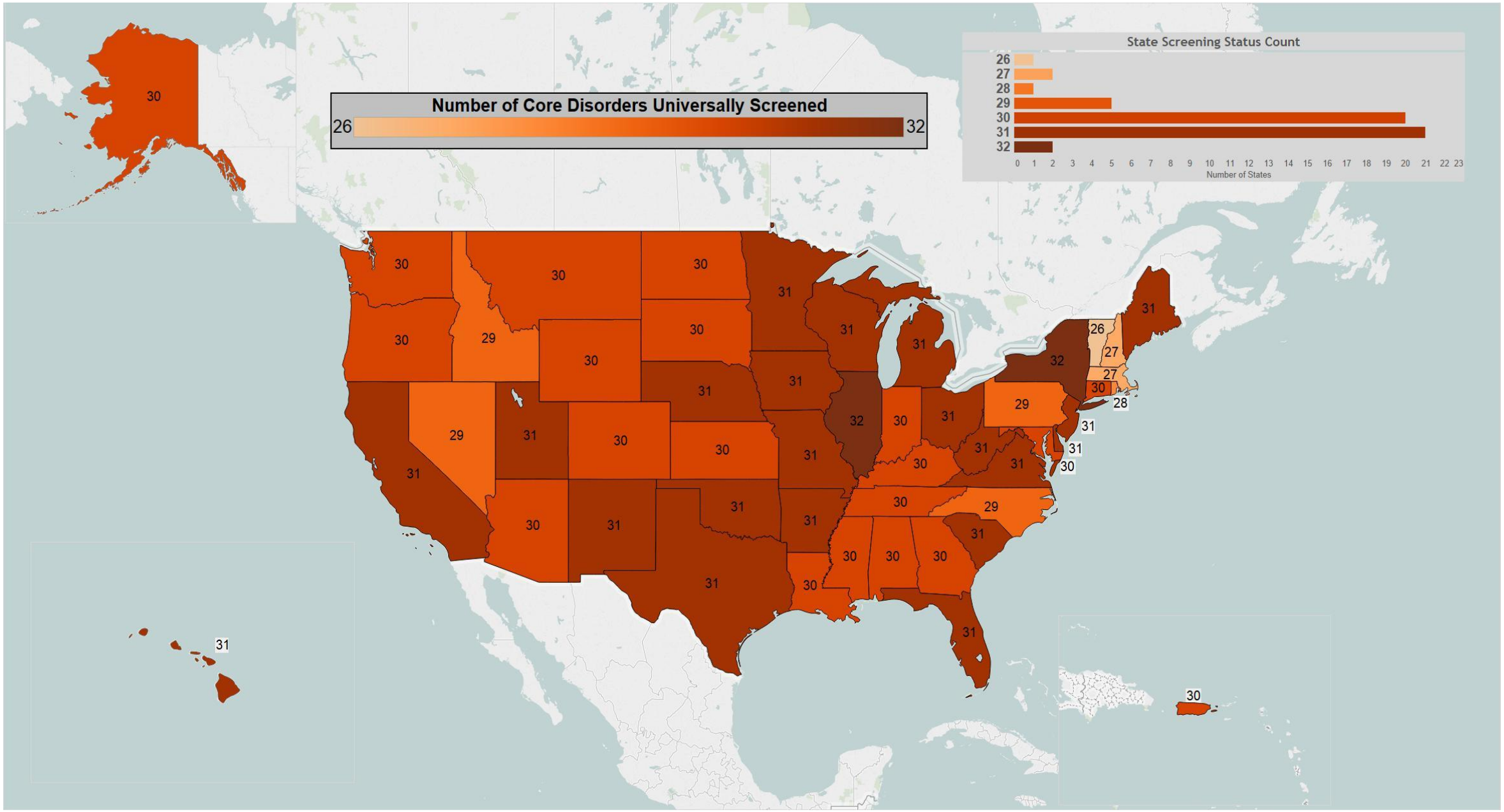
Timeline of adding to state panel



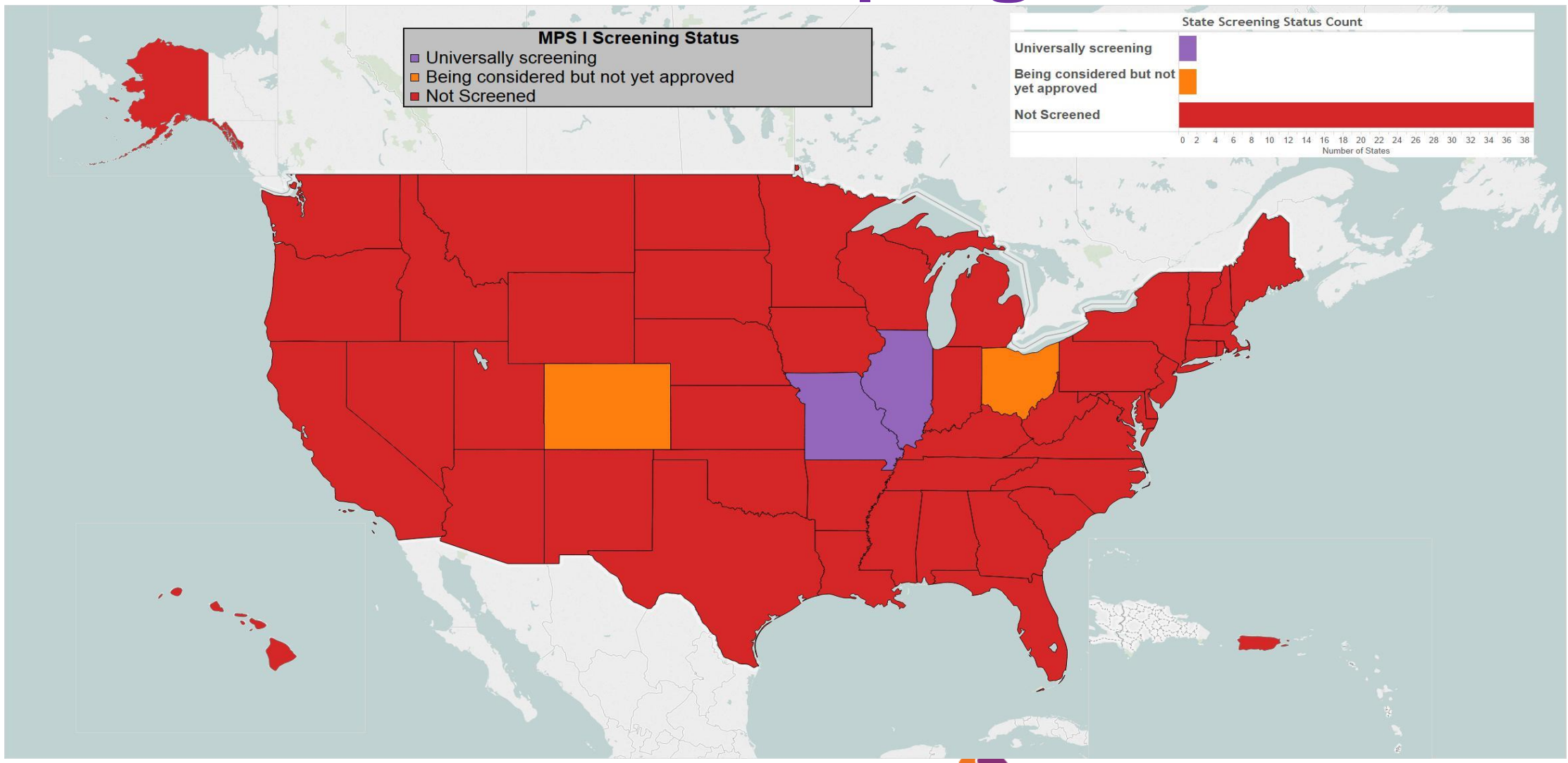
Public Health Impact Assessment

- **Past:** Limited and lack of formal public health impact assessments conducted prior to recommending the addition of CCHD, SCID and Pompe to the RUSP.
- **Present:**
  - MPS-1 Public Health Impact Assessment: Complete
  - X-ALD Public Health Impact Assessment: Complete
- **Future:** Public Health Impact remains a key component of assessment when evaluating additional conditions to be added to RUSP.

Number of Core Disorders Screened



MPS-1 Current Status | August 2015



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