DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

August 17, 2020

Allison Lucas
Siri & Glimstad
200 Park Ave
17th Floor
New York, NY 10166
Via email: foia@sirillp.com

Dear Ms. Lucas:

This letter is regarding to your Centers for Disease Control and Prevention and Agency for Toxic Substances and Disease Registry (CDC/ATSDR) Freedom of Information Act (FOIA) request of December 31, 2019, assigned #20-00395-FOIA, for:

1. Each and every email communication between January 1, 2012, to December 31, 2014 which includes Jon Baio or his email address on the "To", "From", "Cc" or "Bcc" line and also includes any one of the following names or email addresses on the "To", "From", "Cc" or "Bcc" line:
    - Christine Lasalle and/or christine.lasalle@hsc.utah.edu
    - Judith Zimmerman and/or judith.zimmerman@hsc.utah.edu and/or pinzim15@gmail.com
    - Dan Hogge and/or dan.hogge@hsc.utah.edu
    - Jocelyn Taylor and/or jocelyn.taylor@schools.utah.edu and/or jotaylor@dsdmail.net
    - Jeffrey Botkin and/or jeffrey.botkin@hsc.utah.edu
    - Jerry Smith and /or jerry.smith@utah.edu
    - Amanda Bakian and/or amanda.bakian@hsc.utah.edu
    - William McMahon and/or william.mcmahon@hsc.utah.edu
    - Amy Henderson and/or amy.henderson@hsc.utah.edu
    - Deborah Bilder and/or deborah.bilder@hsc.utah.edu

2. Each and every email communication between January 1, 2012, to December 31, 2014 which includes the name of a CDC employee from the National Center of Birth Defects and Developmental Disabilities division and/or email address on the "To", "From", "Cc" or "Bcc" line and also includes any of the following names or email addresses on the "To", "From", "Cc" or "Bcc" line:
    - Christine Lasalle and/or christine.lasalle@hsc.utah.edu
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    - Jeffrey Botkin and/or jeffrey.botkin@hsc.utah.edu
    - Jerry Smith and /or jerry.smith@utah.edu
    - Amanda Bakian and/or amanda.bakian@hsc.utah.edu

- William McMahon and/or william.mcmahon@hsc.utah.edu
- Amy Henderson and/or amy.henderson@hsc.utah.edu
- Deborah Bilder and/or deborah.bilder@hsc.utah.edu

3. Each and every written CDC communication (including electronic communication) between January 1, 2012, to December 31, 2014 which includes Jon Baio or his email address on the "To", "From", "Cc" or "Bcc" line and also includes any one of the following terms in the subject line or body of the communication: "Evaluating Prevalence Changes and Identifying Risk Factors of Autism Spectrum Disorders"; "Population Based Surveillance of Autism Spectrum Disorders"; "00011805"; "00049415"; "Utah Department of Health"; "Utah Registry of Autism and Developmental Disabilities"; "Prevalence and Characteristics of Autism Spectrum Disorder" and/or "URADD."

4. Each and every written CDC communication (including electronic communication) between January 1, 2012, to December 31, 2014 which includes the name of a CDC employee from the National Center of Birth Defects and Developmental Disabilities division and/or email address on the "To", "From", "Cc" or "Bcc" line and also includes any one of the following terms in the subject line or body of the communication: "Evaluating Prevalence Changes and Identifying Risk Factors of Autism Spectrum Disorders"; "Population Based Surveillance of Autism Spectrum Disorders"; "00011805"; "00049415"; "Utah Department of Health"; "Utah Registry of Autism and Developmental Disabilities"; "Prevalence and Characteristics of Autism Spectrum Disorder" and/or "URADD."

On January 10, 2020, you clarified the scope of your request. You withdrew item 2 of your request and modified items 3 and 4 of your request.

1. Each and every email communication between January 1, 2012, to December 31, 2014 which includes Jon Baio or his email address on the "To", "From", "Cc", or "Bcc" line and also includes any one of the following names or email addresses on the "To", "From", "Cc" or "Bcc" line:

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- William McMahon and/or william.mcmahon@hsc.utah.edu
- Amy Henderson and/or amy.henderson@hsc.utah.edu
- Deborah Bilder and/or deborah.bilder@hsc.utah.edu

2. Item 2 is withdrawn.

3. Each and every email communication between January 1, 2012, to December 31, 2014 which includes any of the following the names or his or her email address on the "To", "From", "Cc" or "Bcc" line:

Coleen Boyle, Stephanie Dulin, Georgina Peacock, Peggy Honein, Craig Hooper, Betsy Mitchell, Sascha Chaney, James Scales, Stuart Shapira, Gloria Krahn, Cynthia Moore, Salvatore Lucido, and/or Esther Sumartojo

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Jon Baio, Coleen Boyle, Stephanie Dulin, Georgina Peacock, Peggy Honein, Craig Hooper, Betsy Mitchell, Sascha Chaney, James Scales, Stuart Shapira, Gloria Krahn, Cynthia Moore, Salvatore Lucido, and/or Esther Sumartojo

and also includes any of one of the following terms in the subject line or body of the communication: "Autism Spectrum Disorders"; "ASD"; "Population Based Surveillance of Autism Spectrum Disorders"; "00011805"; "00049415"; "Utah Registry of Autism and Developmental Disabilities"; "Prevalence and Characteristics of Autism Spectrum Disorder" and/or "URADD."

We located 850 pages of responsive records (328 pages released in full; 13 pages disclosed in part; 50 pages withheld in full; 357 pages referred to the Department of Health and Human Services (HHS); 102 pages referred to the National Institutes of Health (NIH)). After a careful review of these pages, some information was withheld from release pursuant to 5 U.S.C. §552 Exemptions (b)(4), (b)(5) and (b)(6).

**EXEMPTION 4**

Exemption 4 protects trade secrets and commercial or financial information obtained from a person that is privileged or confidential. The information withheld is commercial or financial information, such as journal articles, and we have determined that the individuals to whom this information pertains have a substantial commercial or financial interest in withholding it.

**EXEMPTION 5**

Exemption 5 protects inter-agency or intra-agency memorandums or letters which would not be available by law to a party other than an agency in litigation with the agency. Exemption 5 therefore incorporates the privileges that protect materials from discovery in litigation, including the deliberative process, attorney work-product, and attorney-client privileges. Information withheld under this exemption was protected under the deliberative process privilege. The deliberative process privilege protects the decision-making process of

government agencies. The deliberative process privilege protects materials that are both predecisional and deliberative. The materials that have been withheld under the deliberative process privilege of Exemption 5 are both predecisional and deliberative, and do not contain or represent formal or informal agency policies or decisions. Examples of information withheld include draft documents.

**EXEMPTION 6**

Exemption 6 protects information in personnel and medical files and similar files when disclosure would constitute a clearly unwarranted invasion of personal privacy. The information that has been withheld under Exemption 6 consists of personal information, such as: personal e-mail addresses; phone numbers; bridge lines and pass codes. We have determined that the individuals to whom this information pertains has a substantial privacy interest in withholding it.

In accordance with the Department's implementing regulations, 45 CFR Part 5, a fee of $368.00 is assessed (see attached invoice). Please follow mailing instructions on the invoice or your payment may not be credited.

You may contact our FOIA Public Liaison at 770-488-6277 for any further assistance and to discuss any aspect of your request. Additionally, you may contact the Office of Government Information Services (OGIS) at the National Archives and Records Administration to inquire about the FOIA mediation services they offer. The contact information for OGIS is as follows: Office of Government Information Services, National Archives and Records Administration, 8601 Adelphi Road-OGIS, College Park, Maryland 20740-6001, e-mail at ogis@nara.gov; telephone at 202-741-5770; toll free at 1-877-684-6448; or facsimile at 202-741-5769.

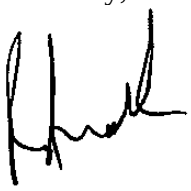
If you are not satisfied with the response to this request, you may administratively appeal by writing to the Deputy Agency Chief FOIA Officer, Office of the Assistant Secretary for Public Affairs, U.S. Department of Health and Human Services, Hubert H. Humphrey Building, 200 Independence Avenue, Suite 729H, Washington, D.C. 20201.You may also transmit your appeal via email to FOIARequest@psc.hhs.gov. Please mark both your appeal letter and envelope “FOIA Appeal.” Your appeal must be postmarked or electronically transmitted by October 18, 2020.

Documents belonging to other agencies were found in our search: Department of Health and Human Services (357 pages) and National Institutes of Health (102 pages). In accordance with the Department’s implementing regulations, CDC does not make decisions on the release or denial of other agencies’ documents. We have referred your request to the following agencies for their release determination and direct reply to you:

Department of Health and Human Services (HHS)
Freedom of Information Officer
Hubert H. Humphrey Building, Room 729H
200 Independence Avenue, SW
Washington, D.C. 20201
Email: FOIARequest@hhs.gov
Phone: 202-690-7453
Fax: 202-690-8320
FOIA Officer: Brandon Gaylord

NIH FOIA Office
Building 31 Room 5B35
31 Center Drive, MSC 2107
Bethesda, MD 20892
PH: 301-496-5633
Fax: 301-402-4541
E-mail: nihfoia@mail.nih.gov

Sincerely,



Roger Andoh
CDC/ATSDR FOIA Officer
Office of the Chief Operating Officer
(770) 488-6399
Fax: (404) 235-1852

Enclosures

20-00395-FOIA

**From:** Alex Kemper, M.D.
**Sent:** 9 Jun 2012 03:01:30 +0000
**To:** Chris Kus;Maribeth Ostrander;Anne Comeau;Boyle, Coleen (CDC/ONDIEH/NCBDDD);Dougherty, Denise (AHRQ);Marie Mann;Jeff Botkin
**Cc:** Green, Nancy;Sara Copeland
**Subject:** Good News - Point-of-Care manuscript
**Attachments:** A Framework for Considering Point-of-Care Newborn Screening-Revision 2.doc

Hi All,

I hope everyone is doing well.

As I think many of you know, Genetics in Medicine initially gave our point-of-care paper a "Revise and Resubmit" - the requested revisions were quite reasonable and did strengthen the work. Nancy and I made those revisions and we were just notified that the paper has been accepted pending minor revisions. Nancy and I have made those. Attached here is what we hope is the final draft of the manuscript. The manuscript has no "new" thoughts.

I will submit this on Tuesday unless I hear about any particular concern from any of you.

Thanks,
Alex

**A Framework for Considering Point-of-Care Newborn Screening**

2012-GIM-0073-R2

Short Title: Point-of-Care Newborn Screening

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Christopher A. Kus, MD, MPH[2]
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on behalf of the United States Secretary of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children

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[5]Centers for Disease Control and Prevention, Atlanta, GA
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[7]Health Resources and Services Administration, Rockville, MD
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[9]Department of Pediatrics, Columbia University Medical Center, New York, NY

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**Word Counts:** Abstract - 123 Main Text – 1,812
Figures: 0 Tables: 1

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**Conflict of Interest Notification Page**

**Conflict of Interest:** None of the authors has a commercial association that might pose or create a conflict of interest with the information presented in this manuscript.

**Disclaimer:** The views expressed herein are solely those of the authors and do not necessarily reflect the views of the Secretary of the United States Department of Health and Human Services or of the individual members of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children.

**Abstract**

Newborn screening is performed under public health authority, with analysis primarily performed by public health or other centralized laboratories. Increasingly, opportunities to improve infant health will arise from including screening tests that are completed within individual birth centers instead of in centralized laboratories, which is a paradigm shift for newborn screening. This report summarizes a framework developed by the United States Secretary of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children based on a series of meetings held during 2011 and 2012 for evaluating whether conditions identifiable through point-of-care screening should be added to the recommended universal screening panel and to identify key considerations for birth hospitals, public health agencies, and clinicians when point-of-care newborn screening is implemented.

**Abbreviations:** critical congenital heart disease (CCHD), dried-blood spots (DBS), Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC), United States Preventive Services Task Force (USPSTF)

## Introduction

In 2011, the United States Secretary of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) recommended that newborns be screened for critical congenital heart disease (CCHD) by pulse oximetry based on the evidence of the effectiveness of screening and the benefit of early intervention to child health.[1] Other than screening for CCHD and congenital hearing loss, public health newborn screening is based on the use of centralized laboratories to analyze infant samples (i.e., dried-blood spots [DBS]). At the time of the CCHD recommendation, the SACHDNC recognized that state public health departments face significant challenges in adopting screening recommendations that do not involve centralized laboratories.

The central issue is determining the degree to which newborn screening that occurs outside of centralized laboratories should be overseen by newborn screening programs as opposed to being conducted within the context of usual clinical care overseen by local health care providers. The SACHDNC recognized the need to develop a standard approach to evaluating nursery-based newborn screening. Over a one-year period of time, the SACHDNC developed a framework for considering nursery-based newborn screening that does not rely on centralized laboratories. This report describes the findings from this work, including key definitions, specific challenges, criteria for determining whether screening should be recommended, and the unique roles and responsibilities related to such screening activities.

## Point-of-Care Newborn Screening

Point-of-care testing refers to those tests administered and interpreted outside of a laboratory but close to the site of direct delivery of medical care for a patient.[2] Point-of-care newborn screening differs from the expected usual care provided by the healthcare system

because the former includes universal access to follow-up diagnosis and treatment, aided by some degree of public health oversight. Usual care does not include these attributes, although it reflects current standards for care delivery, is supported by clinical guidelines produced by professional societies, and includes screening for a wide array of conditions (e.g., the physical exam of otherwise well-appearing newborns for conditions such as congenital hip dysplasia or visual impairment). Evidence-based recommendations for such clinical preventive activities for newborns are available from sources such as Bright Futures and the United States Preventive Services Task Force (USPSTF).[3,4] However, these components of routine care are not provided under public health authority, nor do public agencies provide direct oversight for performing screening, ensuring uniform quality of procedures, follow-up care, and reporting. A key feature of newborn screening, regardless of how it is implemented, is that it assures universal access to diagnostic and follow-up treatment services, and thus plays an important role in eliminating disparities for conditions of public health importance.

**Challenges Related to Screening for Congenital Hearing Loss and CCHD**

In the 1990s, newborn hearing screening for the early identification of hearing loss began through hospital-based initiatives. By 2002, early hearing detection and intervention programs were established as part of the public health system in all 50 states and the District of Columbia.[5] Unlike newborn screening based on the analysis of DBS within centralized laboratories, the screening test for congenital hearing loss is conducted in the newborn nursery and is based on assessment of physiologic parameters (e.g., auditory evoked brainstem response, oto-acoustic emissions)[6] with diagnostic follow-up for those with an abnormal screen as an outpatient by three months of age. To implement the public health mandate for newborn hearing screening, birth hospitals acquired equipment; developed protocols to assure screening and communication

of results to families, healthcare providers and state public health agencies; and trained their personnel in these protocols.[7] Although nearly all newborns in the United States are screened for hearing loss before hospital discharge,[8] assuring follow-up for those infants with abnormal results remains challenging.[9,10] Hearing screening programs have not functioned under a standardized approach to structuring program operation or responsibilities. In some states, the newborn hearing screening program assumes responsibility for monitoring hospital screening programs, follow-up of newborns who did not pass screening, and tracking and reporting progress. In other states, tracking of infants with abnormal newborn hearing screening results is primarily the responsibility of the institutions where testing is performed. In most states, the public health responsibility for newborn hearing screening is primarily related to surveillance rather than individual case management, probably contributing to incomplete follow-up or reporting.[9]

As with congenital hearing loss, CCHD screening requires a physiologic test (i.e., pulse oximetry). However, unlike screening for congenital hearing loss, those with a positive screen for critical congenital heart disease require an urgent diagnostic testing prior to hospital discharge. Important challenges for implementation include the need for a validated screening algorithm that takes into account local effects such as altitude differences between nurseries, as yet undeveloped quality assurance methods for the screening test, difficulties in obtaining off-site diagnostic testing capabilities in some newborn nurseries, and the lack of established methods to report screening results and diagnostic follow-up to state newborn screening programs.

**Criteria for Point-of-Care Newborn Screening**

In developing recommendations for point-of-care newborn screening, the SACHDNC will first evaluate the degree to which the following four criteria are met: 1) urgent treatment of the condition is required earlier than the feasible turnaround time for a public health laboratory; 2) the screening is based on physiologic testing that requires the presence of the newborn at the time the results are generated; 3) the public health impact of screening for early diagnosis and treatment is of sufficiently health importance; and 4) universal screening and/or follow-up and treatment for the condition is not currently performed under standard clinical practice. The first two criteria establish the need for point-of-care screening. The first criterion, the need for urgent treatment based on the rapid turnaround of a test, is the strongest argument for point-of-care screening. The second criterion, the need for the presence of the newborn for a physiologic test (e.g. hearing screening), is a compelling but less crucial argument. The SACHDNC would not need to consider this criterion if the first was met. However, the SACHDNC would consider the need for the presence of the newborn for a physiologic test if there were compelling evidence that universal screening was not feasible outside of the newborn nursery. The third and fourth criteria establish the need for screening within a public health context. Both of these would need to be met before recommending the adoption of POC-NBS for the condition.

For conditions that meet these criteria, consideration for inclusion in the recommended universal screening panel should include an assessment of the feasibility of decentralized implementation, including not only the screening test but also the follow-up services. Before point-of-care newborn screening is recommended, it must be demonstrated that screening technology is readily available and can be standardized, the screening protocol can feasibly be administered in the often chaotic newborn nursery setting without significant loss of clinical validity, and that appropriate follow-up diagnosis and care can be begun promptly for those with

a positive screen. Ultimately, the decision about whether a condition meets the threshold for point-of-care newborn screening is predicated upon evidence that substantially better health outcomes are attainable if screening is performed under a public health mandate than feasibly could be obtained through usual clinical care.

**Roles and Responsibilities in Point-of-Care Newborn Screening**

The table summarizes roles and responsibilities for public health programs and health care providers across the components of point-of-care newborn screening. The degree to which public health agencies are directly involved in point-of-care newborn screening will depend on the legislation and regulations authorizing the particular screening test within each state. Factors that can help determine the degree of public health involvement include: the risk of a missed affected case; the complexity of the screening procedure; the degree to which the screening test is not already a component of standard clinical care; the challenge of providing confirmatory diagnostic follow-up after an abnormal screen; and variability between sites on quality measures related to screening and diagnosis, as well as health outcomes. Regardless of the level of involvement, at a minimum, public health departments have roles in: informing the public about a new screened condition; facilitating standardized implementation of screening; participating in quality assurance; developing systems for diagnostic confirmation and follow-up; data collection on screening and diagnosis; and evaluating the degree to which the newborn screening is effective in improving child health. For some screening procedures or conditions, public health may need to take a greater role in implementation and follow-up for point-of-care screening than for those conditions screened within the context of routine care. For example, if screening for a condition requires special equipment or staff training, public health expertise may be needed for establishing standardized procedures and evaluation of the quality of the implementation.

Another example is if availability of confirmatory diagnostic testing or treatment exists at only a limited number of sites, public health agencies could help facilitate transfer. For example, public health agencies might play a role in financing for these rare but potentially costly activities. For some conditions, public health roles may be limited to educating the public and providers and standardizing the implementation.

**Costs Related to Point-of-Care Newborn Screening**

Central to the success of point-of-care newborn screening will be the availability of sufficient funding to meet the needs of a comprehensive screening program. Undoubtedly, this will require commitments from both state legislatures and payers. As with any screening program, the costs associated with point-of-care newborn screening include the costs of both testing and follow-up. Important costs beyond administration of the screening test include those associated with purchase of screening equipment, start-up and continuous hospital staff training; the development of information systems to track short- and long-term follow-up; entering of results into these information systems; quality assurance monitoring; and program evaluation. The scientific evidence base for screening, diagnosis and treatment must provide a clear rationale for allocation of resources from clinical care and public health agencies to support point-of-care newborn screening programmatic activities.

**Summary and Next Steps**

We expect that the number of conditions to be considered for inclusion in point-of-care newborn screening by the SACHDNC will continue to increase. It is likely that continued rapid development of testing methodologies will transition more testing from state public health laboratories to the newborn nursery, transforming how newborn screening services are delivered. In contrast to usual clinical care, screening with public health oversight helps to assure universal

access and uptake of testing; high-quality standardized screening; coordinated follow-up with effective linkage to diagnosis, intervention, and family support; and, surveillance. Expanding use of electronic medical records and health information exchanges may help with documentation of screening and tracking of population health; such strategies will facilitate public health monitoring and evaluation of the delivery of point-of-care newborn screening services, from test administration through short- and long-term follow-up. The SACHDNC will continue to make recommendations for newborn screening based on the potential benefit of screening on health outcomes. At the same time, the SACHDNC will also consider feasibility in making recommendations regarding point-of-care newborn screening.

**References**


1. Kemper AR, Mahle WT, Martin GR, et al. Strategies for implementing screening for critical congenital heart disease. *Pediatrics*; 2011:128;e1259-e1267.
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9. Russ SA, Hanna D, DesGeorges J, Fosman I. Improving follow-up to newborn hearing screening: a learning-collaborative experience. *Pediatrics.* 2010;126:S59-S69.

10. Liu C, Farrell J, MacNeil JR, Stone S, Barfield W. Evaluating loss to follow-up in newborn hearing screening in Massachusetts. *Pediatrics.* 2008;121:e335-e343.

Table. Summary of roles and responsibilities related to point-of-care newborn screening.

| Component | Public Health Agencies | Health Care Providers |
|---|---|---|
| Screening Test | • Promote standard algorithm<br>• Provide quality assurance<br>• Train health care providers<br>• Provide educational material | • Adopt standard algorithm<br>• Assure all newborns are screened<br>• Participate in quality assurance<br>• Educate families<br>• Document results<br>• Share results with families |
| Diagnostic Evaluation | • Assure the availability of diagnostic evaluation | • Assure that those with an abnormal screening result receive timely diagnostic evaluation |
| Surveillance | • Track results of screening and diagnostic evaluation | • Report results of screening and diagnostic evaluation |
| Long-term Follow-up | • Monitor long-term follow-up | • Provide long-term follow-up |

**From:** Boyle, Coleen (CDC/ONDIEH/NCBDDD)
**Sent:** 9 Jun 2012 16:56:53 +0000
**To:** 'alex.kemper@duke.edu';'cak03@health.state.ny.us';(b)(6);'anne.comeau@umassmed.edu';Dougherty, Denise (AHRQ);'MMann@hrsa.gov';'Jeffrey.Botkin@hsc.utah.edu'
**Cc:** 'nsg11@mail.cumc.columbia.edu';'SCopeland@hrsa.gov'
**Subject:** Re: Good News - Point-of-Care manuscript

Thanks Alex and Nancy for your continued guidance on this project.

Coleen Boyle, Ph.D
cboyle@cdc.gov
Director

National Center on Birth Defects and Developmental Disabilities, CDC
Follow me on Twitter at https://twitter.com/#!/DrBoyleCDC

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---

Sent from my BlackBerry Wireless Device

---

**From**: Alex Kemper, M.D. [mailto:alex.kemper@duke.edu]
**Sent**: Friday, June 08, 2012 11:01 PM
**To**: Chris Kus <cak03@health.state.ny.us>; Maribeth Ostrander (b)(6); Anne Comeau <Anne.Comeau@umassmed.edu>; Boyle, Coleen (CDC/ONDIEH/NCBDDD); Dougherty, Denise (AHRQ); Marie Mann <MMann@hrsa.gov>; Jeff Botkin <Jeffrey.Botkin@hsc.utah.edu>
**Cc**: Green, Nancy <nsg11@mail.cumc.columbia.edu>; Sara Copeland <SCopeland@hrsa.gov>
**Subject**: Good News - Point-of-Care manuscript

Hi All,

I hope everyone is doing well.

As I think many of you know, Genetics in Medicine initially gave our point-of-care paper a "Revise and Resubmit" - the requested revisions were quite reasonable and did strengthen the work. Nancy and I made those revisions and we were just notified that the paper has been accepted pending minor revisions. Nancy and I have made those. Attached here is what we hope is the final draft of the manuscript. The manuscript has no "new" thoughts.

I will submit this on Tuesday unless I hear about any particular concern from any of you.

Thanks,
Alex

**From:** Judith Zimmerman
**Sent:** 3 Apr 2012 16:10:21 +0000
**To:** Boyle, Coleen (CDC/ONDIEH/NCBDDD)
**Cc:** Rice, Catherine (CDC/ONDIEH/NCBDDD)
**Subject:** RE: Congratulations on an excellent 2008 ADDM report

Thanks Coleen for your kind words. My sincere thanks to everyone at the CDC and in particular Cathy Rice. She has gone above and beyond in providing extraordinary support to the Utah team. Although the findings from Utah were not good news, we hope our cumulative research can be used to improve the lives of all those impacted by autism. Judy

Judith Pinborough Zimmerman, Ph.D.
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**Sent:** Tuesday, April 03, 2012 9:34 AM
**To:** Allison Hudson; AMANDA BAKIAN; AMY HENDERSON; Beverly Mulvihill; Carrie Arneson; Chris Cunniff; Corry Robinson; Eldon Schulz; Ellen Giarelli; Eric Lott; Gina Quintana; Jane Charles; John Constantino; Josephine Shenouda; Joyce Nicholas; Judith Zimmerman; Julie Daniels; Kathy Gotschall; Kelly Kast; Phillips, Keydra (CDC/ONDIEH/NCBDDD); Kristen Clancy Mancilla; Jolly, Kwinettaion (CDC/ONDIEH/NCBDDD) (CTR); Laura Arnstein Carpenter; Li-Ching Lee; Miller, Lisa (CDC state.co.us); Lydia King; Martha Slay Wingate; Marygrace Yale Kaiser; Matt Maenner; Maureen Durkin; Paula Bell; Rebecca Harrington; Robert Fitzgerald; kirby S. Russell (CDC health.usf.edu); Sydney Pettygrove; Thaer Baroud; Walter Jenner; Walter Zahorodny; William McMahon; lisa.miller@dphe.state.co.us; Ellen Giarelli; mgkaiser@eureka.edu
**Cc:** Franklin, C. Leah (CDC/ONDIEH/NCBDDD) (CTR); Stevens, Melody (CDC/ONDIEH/NCBDDD); Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD); Baio, Jon (CDC/ONDIEH/NCBDDD); Richardson, Julia (CDC/ONDIEH/NCBDDD); Galatas, Katherine (CDC/ONDIEH/NCBDDD); Lucido, Sal (CDC/ONDIEH/NCBDDD)
**Subject:** Congratulations on an excellent 2008 ADDM report

Dear Colleagues:

Thank you for your hard work and dedication to the Autism and Developmental Disabilities Monitoring (ADDM) Network. It took an incredible effort to produce our latest autism prevalence report, and no matter how large or small any one person's contribution, it all made a difference.

Because of the ADDM Network's efforts over the past decade, we know so much more about autism. We know more about which children are more likely to have autism, at what age they are likely to be diagnosed, and whether progress has been made in diagnosing children with autism early. The ADDM Network also paints a picture of autism in the local ADDM Network communities. Having such detailed information from a broad array of communities shows us how unique each site is and highlights the very real impact of autism upon children and families in communities across the country.

The latest autism prevalence report has garnered a great deal of positive attention on the work we do and the utility of our findings. Our work has contributed to increased awareness of autism, and the public seems more receptive than ever to the knowledge we share. Ultimately, the ADDM Network is helping to bring about a sense of hope and giving communities the information they need to plan for services and understand where improvements can be made to help children.

Yet between the milestones of releasing our latest prevalence reports, the ADDM Network maintains the highest quality in our day-to-day work and our investigators have no shortage of ideas for analyses to further explore the data we collect. We thank you for your commitment to scientific integrity and your relentless drive to know more about autism and other developmental disabilities.

I feel personally fortunate to have been working with CDC's National Center on Birth Defects and Developmental since its inception and have been watching our ADDM Network grow and develop--from a seed planted in metropolitan Atlanta community 30 years ago to a surveillance system that has global impact and bears scientific fruit that can be used to help us understand autism and other developmental disabilities locally, nationally, and globally. We hope that you and your sites share in our pride as we release these new data and continue our work.

I, along with my colleagues at CDC, look forward to continued collaboration with the talented and dedicated individuals working on behalf of the ADDM Network and hope we can continue to contribute to the field of autism in a meaningful way.

Thanks again to you and your teams for all you do!

Warm Regards,

Coleen

*Coleen A. Boyle, PhD, MS Hyg*
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**Sent:** 3 Apr 2012 15:34:10 +0000
**To:** Allison Hudson;Amanda Bakian;Amy Henderson;Beverly Mulvihill;Carrie Arneson;Chris Cunniff;Corry Robinson;Eldon Schulz;Ellen Giarelli;Eric Lott;Gina Quintana;Jane Charles;John Constantino;Josephine Shenouda;Joyce Nicholas;Judith Zimmerman;Julie Daniels;Kathy Gotschall;Kelly Kast;Phillips, Keydra (CDC/ONDIEH/NCBDDD);Kristen Clancy Mancilla;Jolly, Kwinettaion (CDC/ONDIEH/NCBDDD) (CTR);Laura Arnstein Carpenter;Li-Ching Lee;Miller, Lisa (CDC state.co.us);Lydia King;Martha Slay Wingate;Marygrace Yale Kaiser;Matt Maenner;Maureen Durkin;Paula Bell;Rebecca Harrington;Robert Fitzgerald;kirby S. Russell (CDC health.usf.edu);Sydney Pettygrove;Thaer Baroud;Walter Jenner;Walter Zahorodny;William McMahon;lisa.miller@dphe.state.co.us;Ellen Giarelli;mgkaiser@eureka.edu
**Cc:** Franklin, C. Leah (CDC/ONDIEH/NCBDDD) (CTR);Stevens, Melody (CDC/ONDIEH/NCBDDD);Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD);Baio, Jon (CDC/ONDIEH/NCBDDD);Richardson, Julia (CDC/ONDIEH/NCBDDD);Galatas, Katherine (CDC/ONDIEH/NCBDDD);Lucido, Sal (CDC/ONDIEH/NCBDDD)
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Warm Regards,

Coleen

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**Sent:** 7 Mar 2012 13:44:19 -0500
**To:** Correa, Adolfo (CDC/ONDIEH/NCBDDD);'amanda.bakian@hsc.utah.edu';'as16@columbia.edu';'ccunniff@peds.arizona.edu';Lawler, Cindy P. (NIH/NIEHS/DERT);'cjn32@drexel.edu';'clarneso@wisc.edu';'constantino@wustl.edu';Phillips, Keydra (CDC/ONDIEH/NCBDDD);Shapira, Stuart (CDC/ONDIEH/NCBDDD);(b)(6);Washington, Anita (CDC/ONDIEH/NCBDDD);Schendel, Diana (CDC/ONDIEH/NCBDDD);'fitzgerr@psychiatry.wustl.edu';'Gayle.Windham@cdph.ca.gov';'gdawson@autismspeaks.org';'Gerald.McGwin@ccc.uab.edu';'hgf2103@columbia.edu';'ihp@phs.ucdavis.edu';(b)(6);(b)(6);'julie_daniels@unc.edu';Van Naarden-Braun, Kim (CDC/ONDIEH/NCBDDD);Crider, Krista (CDC/ONDIEH/NCBDDD);'Lisa.A.Croen@kp.org';'lisam@smtpgate.dphe.state.co.us';Schieve, Laura (CDC/ONDIEH/NCBDDD);'llee2@jhsph.edu';'maenner@Waisman.Wisc.Edu';'mandelld@mail.med.upenn.edu';(b)(6);'mdurkin@wisc.edu';Kogan, Michael (HRSA/MCHB/ODPD);'mrosanoff@autismspeaks.org';'mwingate@ms.soph.uab.edu';Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD);Zack, Matthew M. (CDC/ONDIEH/NCCDPHP);(b)(6);'nicholjs@musc.edu';King, Michael (CDC/ONDIEH/NCEH);Devine, Owen (CDC/ONDIEH/NCBDDD);'pbell@autismspeaks.org';'perner@marshall.usc.edu';'Prisca@alum.mit.edu';(b)(6);'pshattuck@wustl.edu';'qyang@thepi.org';'rgrink@gwu.edu';Visser, Susanna (CDC/ONDIEH/NCBDDD);'sgalea@columbia.edu';'sydneyp@u.arizona.edu';Bartenfeld, Thomas (CDC/ONDIEH/NCBDDD);Baroud, Thaer (CDC healthyarkansas.com);'william.mcmahon@hsc.utah.edu';'young-shin.kim@yale.edu';'zahorodn@umdnj.edu';'cv111@columbia.edu';'Alison Singer';'lgrossman@autism-society.org';(b)(6);Yoon, Paula (CDC/OSELS/EAPO);'Charles, Jane M.';'Beverly Mulvihill, MEd, Ph.D.';'Judith Zimmerman';kirby S. Russell (CDC health.usf.edu);'King, Lydia A';'Rob Fitzgerald (fitzgerr@psychiatry.wustl.edu)';'brownst@psychiatry.wustl.edu';'Eldon Schulz - AR';'Andria Ratchford';'King, Lydia A';'Lopez, Maya L';Merikangas, Kathleen R. (NIH/NIMH/DIRP);(b)(6);'Dunaway, Wolf';'retzioni@fhcrc.org'
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**Subject:** 2011 Workshop on US Data to Evaluate Changes in ASD Prevalence Summary
**Attachments:** CS225567_ExecutiveSummary_Final Print.pdf, CS225567_WorkshopSummary_Final Print.pdf

Dear Panelists,

Thank you so much for your participation in last year's *Workshop on U.S. Data to Evaluate Changes in Prevalence of the Autism Spectrum Disorders (ASDs)*. The workshop was co-sponsored by CDC's National Centers on Birth Defects and Developmental Disabilities (NCBDDD) and Autism Speaks. The Executive and Full Workshop summaries are attached and are also available on the CDC's and Autism Speaks' websites.

The purpose of the workshop was to bring together scientists and stakeholders in the field of autism surveillance and research to:

- Summarize where we are in our current understanding of changes in ASD prevalence in the US;
- Learn from different perspectives, including experts who have studied prevalence changes among other complex conditions;
- Share ideas for the field to move forward in understanding trends in ASD prevalence.
- Stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

The key suggestions for framing the path forward centered around the following themes:

- Increase collaboration efforts
- Better utilize existing data
- Use data on prevalence and characteristics of individuals with an ASD to better inform service and support efforts
- Implement new types of data collection and studies

It is hoped that the information, research, and opinions shared during this workshop will add to the knowledge about ASD prevalence and encourage further work among public and private groups to understand the multiple factors influencing increasing ASD prevalence in the U.S. and beyond.

CDC is moving forward and is addressing several of the panelist suggestions. For example, CDC:

- Continues to monitor the prevalence of ASDs among 8-year-old children through the multi-site collaboration of the Autism and Developmental Disabilities Monitoring (ADDM) Network. An updated prevalence report is expected this Spring and ongoing data collection is underway for another cohort of children in areas of the United States.
- Has begun projects in 6 ADDM Network sites to determine the prevalence of ASDs among children at 4 years of age.
- Has supported 2 projects (CA and FL) currently underway to examine the prevalence of ASDs in young children with one study conducting community-based screening for ASDs in pediatric practices.
- Is working with NIH and Autism Speaks to support a project by the University of Minnesota through the Association of University Centers on Disabilities (AUCD) to study autism in a Minnesota Somali community to follow-up concerns about higher autism prevalence than in other communities.
- Has implemented analyses related to how specific identification and risk factors in the population have changed and whether they could have a significant impact on increasing ASD prevalence.
    - An analysis was completed and a paper published indicating that population changes in select perinatal factors such as low birth weight and gestational age have had a minimal effect on ASD prevalence changes reported in the ADDM Network (Schieve et al., 2011).
    - Several other analyses by ADDM Network investigators examining other identification and risk factors in relation to ASD prevalence change are underway.

- Has partnered with Autism Speaks to build on the ADDM Network infrastructure to evaluate the completeness of ASD prevalence estimates. Autism Speaks is funding a project in the SC ADDM site through the Medical University of South Carolina to add community screening and assessment to the existing ADDM record-review surveillance method.
- Continues to work as part of the Interagency Autism Coordinating Committee (IACC) to identify and implement a Strategic Plan for Autism Research coordinated among public and private organizations. This workshop summary will be shared with the IACC and can be used to inform the next iteration of the IACC Strategic Plan.
- Is conducting one of the largest studies in the United States to help identify factors that may put children at risk. This study, being conducted across a 6 site network known as the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE), is called SEED, the Study to Explore Early Development. SEED is looking at numerous risk factors of autism such as genetics, environmental exposures, pregnancy factors, and behavioral factors. The study enrollment is on schedule, and first reports are expected from SEED later this year.
- Continues to work with the community to increase awareness of early signs of ASDs and other developmental disabilities. Our "Learn the Signs. Act Early." program is working to address critical gaps in early identification of autism and other developmental disabilities in two ways:
    - First, we know that all parents play a critical role in monitoring their children's developmental milestones. Our program offers free online resources for parents to help them do that. We also have resources for health professionals and early childhood teachers. www.cdc.gov/actearly
    - Second, we are working with representatives from public health, medicine, education, and advocates in states to improve early identification, screening, and referral practices so children and their families can access the services and supports.
- For more information: www.cdc.gov

If you would like to have hard copies of the Workshop Report and/or Executive Summary mailed to you, please send your name, mailing address, and number of copies (up to 5) to Lekeisha Jones at lfj9@cdc.gov.

Thank you for your work and commitment for people with ASDs. Hopefully, this workshop summary will be a helpful resource for others as it has been for CDC.

*Cathy* and *Marshalyn*

Catherine E. Rice, PhD and Marshalyn Yeargin-Allsopp, MD
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Co-Sponsored by Autism Speaks

# Workshop on U.S. Data to Evaluate Changes in the Prevalence of Autism Spectrum Disorders (ASDs)

## Executive Summary

**Tuesday, February 1, 2011**

**Centers for Disease Control and Prevention**
**Tom Harkin Global Communications Center | 1600 Clifton Road, N.E. | Atlanta, Georgia**

National Center on Birth Defects and Developmental Disabilities
Division of Birth Defects and Developmental Disabilities

# Acknowlegement


## Co-Sponsored by the National Center on Birth Defects and Developmental Disabilities (NCBDDD), Centers for Disease Control and Prevention (CDC) and Autism Speaks


*Panel members* were representatives from:*

Autism Science Foundation
Autism Society of America (invited)
Colorado Department of Health
Columbia University
Drexel University
George Washington University
Health Resources and Services Administration (HRSA)
Johns Hopkins University
Kaiser Permanente®, California
Medical University of South Carolina
National Institutes of Health (NIEHS, NIMH)
Parkinson's Institute
SafeMinds
Parents of children with an Autism Spectrum Disorder
Persons with an Autism Spectrum Disorder
University of Alabama at Birmingham
University of Arizona, Tucson
University of Arkansas
University of California, Davis – MIND Institute
University of North Carolina, Chapel Hill
University of Pennsylvania
University of South Florida
University of Southern California, Marshall
University of Utah
Washington University in Saint Louis
University of Washington
University of Wisconsin, Madison
Yale University


### Workshop Planning Committee

| | |
|---|---|
| Carrie Arneson, MsC | University of Wisconsin, Madison |
| Amanda Bakian, PhD (Feb 2011) | University of Utah |
| Tom Bartenfeld, PhD | NCBDDD, CDC |
| Julie Daniels, PhD | University of North Carolina, Chapel Hill |
| Geraldine Dawson, PhD | Autism Speaks |
| Keydra Phillips, MsC | NCBDDD, CDC |
| Catherine Rice, PhD | NCBDDD, CDC |
| Michael Rosanoff, MPH | Autism Speaks |
| Anita Washington, MPH | Research Triangle Institute |
| Martha Wingate, DrPH | University of Alabama, Birmingham |
| Marshalyn Yeargin-Allsopp, MD | NCBDDD, CDC |


**Refer to Appendix B in full workshop summary for biographies of panel members*

*The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC). This summary report reflects statements made by individuals attending the workshop and does not constitute consensus recommendations made to the CDC.*

# Workshop Summary

## PURPOSE

Autism spectrum disorders (ASDs) are estimated to occur among about 1% of children in the U.S. This is in line with estimates from other industrialized countries. However, the identified prevalence of ASDs has increased significantly in a short time period based on data from multiple studies including the Centers for Disease Control and Prevention's (CDC) Autism and Developmental Disabilities Monitoring (ADDM) Network (http://www.cdc.gov/ncbddd/autism/addm.html). Whether increases in ASD prevalence are partly attributable to a true increase in the risk of developing ASD symptoms or solely to changes in community awareness and identification patterns is not known. It is clear that more children are identified with an ASD now than in the past and the impact on individuals, families, and communities is significant. However, disentangling the many potential reasons for ASD prevalence increases has been challenging. Understanding the relative contribution of multiple factors such as variation in study methods, changes in diagnostic and community identification, and potential changes in risk factors is an important priority for the ADDM Network and for CDC. This workshop was co-sponsored by CDC and Autism Speaks as a forum for sharing knowledge and opinions of a diverse range of stakeholders about changes in ASD prevalence. This summary report reflects statements made by individuals at the forum and discussions that were held among the attendees, and does not constitute formal consensus recommendations to CDC. The information, research, and opinions shared during this workshop add to the knowledge base about ASD prevalence in an effort to stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

## FRAMEWORK

The workshop brought together epidemiologic prevalence and surveillance experts in ASDs and other conditions as well as representatives from autism organizations, parents of children with ASDs, adults with an ASD, and other stakeholders. A total of 342 people registered to attend the workshop (143 in person and 199 via webinar).

Prior to the meeting, the panel members met via teleconference and were asked to submit at least two publications that they viewed as important background reading for understanding ASD prevalence trends. Panel members were provided with the compiled reference list (Appendix C) and articles and were asked to review, at a minimum, the priority readings prior to the workshop.

Presentations during the morning of the workshop summarized current knowledge and issues related to ASD prevalence and provided perspectives from subject matter experts in cancer, Parkinson disease, asthma, schizophrenia, and analytic modeling of prevalence changes.

Following the morning's presentations, the public was invited to provide statements, and there was an open invitation to provide written comments before and after the workshop. Workshop organizers, panelists, and stakeholders were asked to consider these comments when expressing their opinions on priorities for evaluating changes in ASD prevalence.

After hearing open comments from the community, the workshop was divided into four panels:

- Panel 1 – Utility of ASD Prevalence Data
- Panel 2 – U.S.-Based ASD Service Data
- Panel 3 – Autism and Developmental Disabilities Monitoring (ADDM) Network Data
- Panel 4 – What Else Is Needed To Understand ASD Trends?

For the workshop panel sessions, members of each panel were asked to reflect on questions along the following themes to better understand ASD prevalence trends:

- What can we do now with existing data?
- What should we do next to build on existing data systems?
- What else is needed in terms of new analyses, data collection, or other efforts?

## SUMMARY POINTS

Panel members and attendees commented that the effort to increase transparency and expand the dialogue related to ASD prevalence change was appreciated and necessary to move the community forward around the issue of understanding ASD prevalence changes. Additional key points made during the workshop included:

- The identified prevalence of ASD has increased significantly in a short time period across multiple studies, including data from the CDC's U.S.-based Autism and Developmental Disabilities Monitoring (ADDM) Network.
- CDC is the source for ASD prevalence estimates in the U.S., but other data systems exist or could be developed to better understand trends in ASDs.
- ASDs are conditions estimated to occur among about 1% of children in the U.S. There is an urgent demand to address the many needs associated with ASDs. Prevalence estimates have, for example, fueled action by advocacy groups and the Interagency Autism Coordinating Committee (IACC) and driven the creation of legislation and presidential priority. However, individuals, families, and communities continue to struggle to address unmet needs across the lifespan of people with ASDs. ASD prevalence estimates are important to stakeholders for program planning and making policy changes, in addition to highlighting the need for research into causes and interventions.
- In terms of reasons for increased ASD prevalence, the debate has been dichotomized by researchers, advocacy groups, and the media to indicate that increases must be explained either by identification factors or by increased risk among the population. In reality, a more complex understanding is needed. It is clear that some of the increase has been related to intrinsic and extrinsic identification factors. However, although a true increase in ASD symptoms cannot be ruled out, such an increase has been difficult to prove. Panels discussed needing to identify and use methods to better understand the role of potential identification and risk factors in the changing prevalence of ASD.
- Some people expressed hope that understanding why ASD prevalence has increased may help identify modifiable risk factors. There was debate about the roles of prevalence and surveillance in answering questions about risk and causes of ASDs. Prevalence studies provide descriptive data on the number of people with a condition in a defined population. These types of studies are not sufficient to identify what causes ASDs. However, prevalence studies can be used as tools to examine variation in occurrence of ASDs across place, groups, time, and exposures, which may provide clues about groups who are at increased risk for ASDs. Other study designs would then be necessary to fully investigate the reasons behind observed variation in prevalence.
- There are likely multiple forms of ASDs with multiple causes that are poorly understood. It was noted that sufficient evidence exists that biologic and environmental factors, alone and in interaction, need to be considered as causes. It is not necessary to have confirmation that a portion of the increase in ASD prevalence is due to increased risk in the population to motivate the active pursuit of causes of ASDs. By better understanding what causes ASDs, maybe we can understand the increases in measured prevalence.

- A risk factor might be strongly associated with ASD and might be modifiable, but it might not have increased sufficiently in the population during the time frame of interest. Therefore, this risk factor might be related to an individual's risk for ASD but not related to the increase in population prevalence of ASD. The model demonstrated that for any factor to have made a noteworthy contribution to population changes in ASD prevalence during a short time period, three conditions must be met: the factor has to be fairly prevalent in the population, it has to have increased substantially, and it has to be strongly associated with diagnosed ASD.
- There was a shared recognition of the importance of, and commitment to, obtaining and using prevalence and epidemiologic information to improve the lives of people with ASDs.

## PANEL DISCUSSION SUMMARIES

The four panel chairs compiled main discussion points brought forth by their members for building on existing infrastructure and for developing new initiatives to better understand ASD trends. These discussion points are summarized below.

### Collaboration

The panels indicated that collaboration among professionals and stakeholders is important, and the following points were made to assist collaborative efforts among those interested in understanding ASDs and supporting the ASD community through science:

- Continue efforts of this workshop to develop and enhance communication among families, individals affected, researchers, service providers, advocates, and government entities about ASD prevalence, research, and service needs.
- Seek public–private partnerships to support data collection, analyses, and usage.
- Seek input from and collaboration with those in other fields, such as cancer epidemiology, to identify and utilize methodologies for evaluating changes in the prevalence of complex conditions.
- Collaborate with other data systems, such as the Environmental Public Health Tracking Network, to improve access to population-level environmental data.

### Analytic Activities

Points were made on better utilizing existing data to understand ASD prevalence trends:

- Provide funding opportunities to encourage analyses and dissemination of findings from existing datasets.
- Link existing datasets identifying children with ASDs to other health, service, and research databases.
- Conduct analyses that will help explain variations in ASD prevalence across subgroups (e.g., race and ethnicity, sex, diagnostic subtype, and geographic groups) and if variation persists over time.
- Use complex modeling and multifactorial analyses to better understand variation in ASD prevalence such as by possible etiologic subgroups (e.g., specific genetic conditions and family history), geogrphy, and sex, and by potentially harmful exposures among cohorts.
- Conduct simulation studies to predict the anticipated course of ASD prevalence.

### Data Enhancements to Inform Practice

The panels discussed the importance of using data on the prevalence and characteristics of people with an ASD to better inform service and support efforts:

- In addition to prevalence estimates, provide more in-depth information on population characteristics of people with an ASD (such as functional level and impact of functional limitations, subtype, developmental characteristics, and associated conditions) to improve program planning and support needs.
- Examine data to better understand lags and disparities in ASD identification to, in turn, inform screening, identification, and program planning.
- Conduct analyses to provide better estimates of current and future needs of adults with an ASD.

## Additional Studies

Beyond enhancements to existing data systems and uses, the panels discussed new types of data collection and studies including:

- Expand ASD prevalence efforts to include very young children and adults.
- Examine prevalence over time among older children by following up with those identified in previous studies
- Conduct additional validation studies at various ADDM Network sites and use the results to enhance estimates of ASD
  prevalence.
- Conduct further studies to better understand who is identified and who is not identified in national parent report surveys and in service-based data such as special education child counts.
- Develop ways of better capturing the heterogeneity of ASD phenotypes including the complexity of core and associated features that may present in different combinations for people with an ASD.
- Improve tools for culturally sensitive screening and case confirmation among large populations.
- Identify ways to measure and monitor the traits associated with ASDs among the general population to reflect various degrees (dimensional) rather than categorical (having an ASD or not having an ASD) case vs. not case) levels. This includes characterizing how these traits overlap with other conditions and typical development.
- Conduct cross-sectional and longitudinal studies following cohorts over time. This could include examining trends in characteristics of the population, such as ASDs among specific subgroups (based on, for example, race and ethnicity, immigrant status, and socioeconomic status), age of identification, diagnoses, comorbidities, services use, and family characteristics.
- Monitor trends in ASD prevalence prospectively to rule out identification factors by consistently conducting developmental and ASD screening at a given age with diagnostic follow-up and documentation of each step and outcome.
- Conduct prospective studies that examine biology, phenotype, identification patterns, and service needs and use of people with an ASD.
- Examine trends in other behaviorally defined conditions (e.g., attention-deficit/hyperactivity disorder, depression, and anxiety).

## NEXT STEPS

The workshop summary will be made freely available to the community through posting on the CDC's and Autism Speaks' websites. It is hoped that the information, research, and opinions shared during this workshop will add to the knowledge base about ASD prevalence and stimulate further work among public and private groups to understand the multiple reasons behind changes in identified ASD prevalence in the U.S.

# Notes

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Autism Speaks
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CS225567

Co-Sponsored by Autism Speaks

# Workshop on U.S. Data to Evaluate Changes in the Prevalence of Autism Spectrum Disorders (ASDs)

**Tuesday, February 1, 2011**

**Centers for Disease Control and Prevention**
**Tom Harkin Global Communications Center | 1600 Clifton Road, N.E. | Atlanta, Georgia**

*Full agenda available in Appendix A*

National Center on Birth Defects and Developmental Disabilities
Division of Birth Defects and Developmental Disabilities

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*Panel members* were representatives from:*

Autism Science Foundation
Autism Society of America (invited)
Colorado Department of Health
Columbia University
Drexel University
George Washington University
Health Resources and Services Administration (HRSA)
Johns Hopkins University
Kaiser Permanente®, California
Medical University of South Carolina
National Institutes of Health (NIEHS, NIMH)
Parkinson's Institute
SafeMinds
Parents of children with an Autism Spectrum Disorder
Persons with an Autism Spectrum Disorder
University of Alabama at Birmingham
University of Arizona, Tucson
University of Arkansas
University of California, Davis – MIND Institute
University of North Carolina, Chapel Hill
University of Pennsylvania
University of South Florida
University of Southern California, Marshall
University of Utah
Washington University in Saint Louis
University of Washington
University of Wisconsin, Madison
Yale University

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**Refer to Appendix B for biographies of panel members*

*The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC). This summary report reflects statements made by individuals attending the workshop and does not constitute consensus recommendations made to the CDC.*

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# Workshop Summary

## PURPOSE

Autism spectrum disorders (ASDs) are estimated to occur among about 1% of children in the U.S. This is in line with estimates from other industrialized countries. However, the identified prevalence of ASDs has increased significantly in a short time period based on data from multiple studies including the Centers for Disease Control and Prevention's (CDC) Autism and Developmental Disabilities Monitoring (ADDM) Network (http://www.cdc.gov/ncbddd/autism/addm.html). Whether increases in ASD prevalence are partly attributable to a true increase in the risk of developing ASD symptoms or solely to changes in community awareness and identification patterns is not known. It is clear that more children are identified with an ASD now than in the past and the impact on individuals, families, and communities is significant. However, disentangling the many potential reasons for ASD prevalence increases has been challenging. Understanding the relative contribution of multiple factors such as variation in study methods, changes in diagnostic and community identification, and potential changes in risk factors is an important priority for the ADDM Network and for CDC. This workshop was co-sponsored by CDC and Autism Speaks as a forum for sharing knowledge and opinions of a diverse range of stakeholders about changes in ASD prevalence. This summary report reflects statements made by individuals at the forum and discussions that were held among the attendees, and does not constitute formal consensus recommendations to CDC. The information, research, and opinions shared during this workshop add to the knowledge base about ASD prevalence in an effort to stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

## FRAMEWORK

The workshop brought together epidemiologic prevalence and surveillance experts in ASDs and other conditions as well as representatives from autism organizations, parents of children with ASDs, adults with an ASD, and other stakeholders. A total of 342 people registered to attend the workshop (143 in person and 199 via webinar).

Prior to the meeting, the panel members met via teleconference and were asked to submit at least two publications that they viewed as important background reading for understanding ASD prevalence trends. Panel members were provided with the compiled reference list (Appendix C) and articles and were asked to review, at a minimum, the priority readings prior to the workshop.

Presentations during the morning of the workshop summarized current knowledge and issues related to ASD prevalence and provided perspectives from subject matter experts in cancer, Parkinson disease, asthma, schizophrenia, and analytic modeling of prevalence changes.

Following the morning's presentations, the public was invited to provide statements, and there was an open invitation to provide written comments before and after the workshop. Workshop organizers, panelists, and stakeholders were asked to consider these comments when expressing their opinions on priorities for evaluating changes in ASD prevalence.

After hearing open comments from the community, the workshop was divided into four panels:

- Panel 1 – Utility of ASD Prevalence Data
- Panel 2 – U.S.-Based ASD Service Data
- Panel 3 – Autism and Developmental Disabilities Monitoring (ADDM) Network Data
- Panel 4 – What Else Is Needed To Understand ASD Trends?

For the workshop panel sessions, members of each panel were asked to reflect on questions along the following themes to better understand ASD prevalence trends:

- What can we do now with existing data?
- What should we do next to build on existing data systems?
- What else is needed in terms of new analyses, data collection, or other efforts?

## SUMMARY POINTS

Panel members and attendees commented that the effort to increase transparency and expand the dialogue related to ASD prevalence change was appreciated and necessary to move the community forward around the issue of understanding ASD prevalence changes. Additional key points made during the workshop included:

- The identified prevalence of ASD has increased significantly in a short time period across multiple studies, including data from the CDC's U.S.-based Autism and Developmental Disabilities Monitoring (ADDM) Network.
- CDC is the source for ASD prevalence estimates in the U.S., but other data systems exist or could be developed to better understand trends in ASDs.
- ASDs are conditions estimated to occur among about 1% of children in the U.S. There is an urgent demand to address the many needs associated with ASDs. Prevalence estimates have, for example, fueled action by advocacy groups and the Interagency Autism Coordinating Committee (IACC) and driven the creation of legislation and presidential priority. However, individuals, families, and communities continue to struggle to address unmet needs across the lifespan of people with ASDs. ASD prevalence estimates are important to stakeholders for program planning and making policy changes, in addition to highlighting the need for research into causes and interventions.
- In terms of reasons for increased ASD prevalence, the debate has been dichotomized by researchers, advocacy groups, and the media to indicate that increases must be explained either by identification factors or by increased risk among the population. In reality, a more complex understanding is needed. It is clear that some of the increase has been related to intrinsic and extrinsic identification factors. However, although a true increase in ASD symptoms cannot be ruled out, such an increase has been difficult to prove. Panels discussed needing to identify and use methods to better understand the role of potential identification and risk factors in the changing prevalence of ASD.
- Some people expressed hope that understanding why ASD prevalence has increased may help identify modifiable risk factors. There was debate about the roles of prevalence and surveillance in answering questions about risk and causes of ASDs. Prevalence studies provide descriptive data on the number of people with a condition in a defined population. These types of studies are not sufficient to identify what causes ASDs. However, prevalence studies can be used as tools to examine variation in occurrence of ASDs across place, groups, time, and exposures, which may provide clues about groups who are at increased risk for ASDs. Other study designs would then be necessary to fully investigate the reasons behind observed variation in prevalence.
- There are likely multiple forms of ASDs with multiple causes that are poorly understood. It was noted that sufficient evidence exists that biologic and environmental factors, alone and in interaction, need to be considered as causes. It is not necessary to have confirmation that a portion of the increase in ASD prevalence is due to increased risk in the population to motivate the active pursuit of causes of ASDs. By better understanding what causes ASDs, maybe we can understand the increases in measured prevalence.

- A risk factor might be strongly associated with ASD and might be modifiable, but it might not have increased sufficiently in the population during the time frame of interest. Therefore, this risk factor might be related to an individual's risk for ASD but not related to the increase in population prevalence of ASD. The model demonstrated that for any factor to have made a noteworthy contribution to population changes in ASD prevalence during a short time period, three conditions must be met: the factor has to be fairly prevalent in the population, it has to have increased substantially, and it has to be strongly associated with diagnosed ASD.
- There was a shared recognition of the importance of, and commitment to, obtaining and using prevalence and epidemiologic information to improve the lives of people with ASDs.

## PANEL DISCUSSION SUMMARIES

The four panel chairs compiled main discussion points brought forth by their members for building on existing infrastructure and for developing new initiatives to better understand ASD trends. These discussion points are summarized below.

### Collaboration

The panels indicated that collaboration among professionals and stakeholders is important, and the following points were made to assist collaborative efforts among those interested in understanding ASDs and supporting the ASD community through science:

- Continue efforts of this workshop to develop and enhance communication among families, individals affected, researchers, service providers, advocates, and government entities about ASD prevalence, research, and service needs.
- Seek public–private partnerships to support data collection, analyses, and usage.
- Seek input from and collaboration with those in other fields, such as cancer epidemiology, to identify and utilize methodologies for evaluating changes in the prevalence of complex conditions.
- Collaborate with other data systems, such as the Environmental Public Health Tracking Network, to improve access to population-level environmental data.

### Analytic Activities

Points were made on better utilizing existing data to understand ASD prevalence trends:

- Provide funding opportunities to encourage analyses and dissemination of findings from existing datasets.
- Link existing datasets identifying children with ASDs to other health, service, and research databases.
- Conduct analyses that will help explain variations in ASD prevalence across subgroups (e.g., race and ethnicity, sex, diagnostic subtype, and geographic groups) and if variation persists over time.
- Use complex modeling and multifactorial analyses to better understand variation in ASD prevalence such as by possible etiologic subgroups (e.g., specific genetic conditions and family history), geogrphy, and sex, and by potentially harmful exposures among cohorts.
- Conduct simulation studies to predict the anticipated course of ASD prevalence.

### Data Enhancements to Inform Practice

The panels discussed the importance of using data on the prevalence and characteristics of people with an ASD to better inform service and support efforts:

- In addition to prevalence estimates, provide more in-depth information on population characteristics of people with an ASD (such as functional level and impact of functional limitations, subtype, developmental characteristics, and associated conditions) to improve program planning and support needs.
- Examine data to better understand lags and disparities in ASD identification to, in turn, inform screening, identification, and program planning.
- Conduct analyses to provide better estimates of current and future needs of adults with an ASD.

## Additional Studies

Beyond enhancements to existing data systems and uses, the panels discussed new types of data collection and studies including:

- Expand ASD prevalence efforts to include very young children and adults.
- Examine prevalence over time among older children by following up with those identified in previous studies
- Conduct additional validation studies at various ADDM Network sites and use the results to enhance estimates of ASD
  prevalence.
- Conduct further studies to better understand who is identified and who is not identified in national parent report surveys and in service-based data such as special education child counts.
- Develop ways of better capturing the heterogeneity of ASD phenotypes including the complexity of core and associated features that may present in different combinations for people with an ASD.
- Improve tools for culturally sensitive screening and case confirmation among large populations.
- Identify ways to measure and monitor the traits associated with ASDs among the general population to reflect various degrees (dimensional) rather than categorical (having an ASD or not having an ASD) case vs. not case) levels. This includes characterizing how these traits overlap with other conditions and typical development.
- Conduct cross-sectional and longitudinal studies following cohorts over time. This could include examining trends in characteristics of the population, such as ASDs among specific subgroups (based on, for example, race and ethnicity, immigrant status, and socioeconomic status), age of identification, diagnoses, comorbidities, services use, and family characteristics.
- Monitor trends in ASD prevalence prospectively to rule out identification factors by consistently conducting developmental and ASD screening at a given age with diagnostic follow-up and documentation of each step and outcome.
- Conduct prospective studies that examine biology, phenotype, identification patterns, and service needs and use of people with an ASD.
- Examine trends in other behaviorally defined conditions (e.g., attention-deficit/hyperactivity disorder, depression, and anxiety).

## NEXT STEPS

The workshop summary will be made freely available to the community through posting on the CDC's and Autism Speaks' websites. It is hoped that the information, research, and opinions shared during this workshop will add to the knowledge base about ASD prevalence and stimulate further work among public and private groups to understand the multiple reasons behind changes in identified ASD prevalence in the U.S.

# Background and Purpose

## WELCOME

## C. Boyle and G. Dawson

Dr. Boyle welcomed everyone, thanked the organizing committee and co-sponsor Autism Speaks, and indicated that she looked forward to the discussions and sharing of information and ideas on understanding autism spectrum disorder (ASD) prevalence trends. Dr. Dawson stated that we all have concerns about the increase in ASD prevalence. She expressed her hope that everyone would come away from the workshop with a path forward in understanding ASD prevalence changes and stated that we are much better prepared to address problems than ever before because of better data and analytic tools. These data and tools are from the Centers for Disease Control and Prevention's (CDC) Autism and Developmental Disabilities Monitoring (ADDM) Network, as well as other informative datasets from California and Europe. She remarked that many published papers cite several reasons for the possible increase in ASD prevalence including better analytic tools and broader awareness and diagnosis. However, these papers all have included the statement "a true increase in prevalence cannot be ruled out." She ventured that she looked forward to lively and productive discussion and concrete actions that can improve the understanding of why ASD prevalence has been increasing, with the ultimate goal of addressing the needs of people with autism.

## Background: What Do We Know About ASD Prevalence?

## M. Yeargin-Allsopp

Autism once was thought to be a rare condition, affecting about 1 in 2,000 individuals. It was thought of as mental illness, specifically schizophrenia of childhood, and was believed to be due to poor parenting. The "refrigerator mother" perception was prominent until the 1970s, continuing even into the 1980s. Today, autism is recognized as having a biologic basis and a range or spectrum of presentations. The autism spectrum disorders have been shown to occur among about 1% of children in several different countries. In addition to the core areas of impairment in social, communication, and behavioral domains, people with ASDs can have associated challenges in other areas such as sleeping, eating, attention, mood regulation, and gastrointestinal issues. It is recognized widely that ASDs have a strong genetic basis, but this is not a simple association and there is increasing recognition of the role of environmental factors. ASDs are now recognized as a complex disorder, most likely due to interactions between genes and the environment.

Beginning in the mid-1990s, concerns arose about increases in the numbers of individuals with autism identified in service systems. For example, starting in the early 1990s, the California Department of Developmental Services and the U.S. Department of Education's Office of Special Education documented increases in the need for autism services. Not all people with an ASD are identified by these service systems, so methods are needed to identify who else might have an ASD among the general population. CDC's ADDM Network conducts surveillance to estimate ASD prevalence in multiple areas of the U.S. and provides data to describe variations and changes over time. The ADDM Network reports ASD prevalence, or the total number of children with an ASD at a specified age in a specified year per 1,000 children in the population. The ADDM Network does not use incidence because incidence is based on new cases where a clear onset time can be documented. Typically, the onset of an ASD is not known, although it usually manifests by the time a child is 3 years of age. However, there is a great deal of variability in when a child actually manifests symptoms and then is diagnosed with an ASD.

There are several potential explanations that can account for an increase in the number of individuals diagnosed with ASDs, including better identification and screening methods, changes in diagnostic criteria, increased awareness among parents and clinicians, and changes in the availability of services. There also have been some studies that have examined how much of an increase is accounted for by other factors, such as increasing parental age. However, a full explanation must consider multiple factors that are not independent of each other. Prevalence estimates are important for planning policy and service needs and identifying promising clues about who is at risk for an ASD.

## Framework For This Workshop

### C. Rice

The identified prevalence of ASDs has increased significantly in a short time period across multiple studies, including the CDC's ADDM Network. ASDs are conditions estimated to occur among about 1% of all children. There is an urgent demand to address the many needs associated with ASDs, and concerns about ASD prevalence numbers have fueled local, state, and national action in terms of advocacy, policies, research, and creation of the Interagency Autism Coordinating Committee (IACC) among other activities. However, individuals and families continue to struggle to address and meet the needs associated with ASDs across their lifespan. Although prevalence estimates can help with service and policy efforts, increases in ASD prevalence beg the questions "Why?" and "Is the increase an actual increase in risk for ASDs?" The implication is that, if there is an increase in actual ASD risk, there might be modifiable risk factors to prevent ASDs from occurring. These questions get to the heart of what causes ASDs. Although multiple, complex genetic and environmental interactions are likely, we still have very limited information on what predisposes a fetus or child to have an ASD, what might increase risk, and which risks lead to the development of an ASD.

A prevalence study is an epidemiologic tool that describes the occurrence of a condition in a defined population in a defined time period. Surveillance is the ongoing monitoring of prevalence in a defined population over time. These studies provide descriptive data on the number of people with a condition in a defined population. These types of studies are not sufficient to identify what causes ASDs. However, prevalence studies can be used as tools to examine variation in occurrence of ASDs across place, groups, time, and exposures, and this may provide clues about groups who are at increased risk for ASDs. Prevalence studies can provide observations that might need further causal examination. For example, prevalence studies have shown that there are about 4 to 5 boys for every girl with an ASD. However, basic studies of the biology of individuals with an ASD are necessary to explain the mechanism that results in boys being at greater risk than girls.

Debates about reasons for ASD prevalence increases often have been dichotomized to point to explanations of better identification or evidence of increased risk implicating specific environmental factors. At this point, although we do know that some of the increase is related to identification factors, a true increase cannot be ruled out—but, it is hard to prove. We also know enough about potential causal mechanisms of ASDs to not pigeonhole the search for ASD causes to only genetic factors; complex biologic and environmental factors must be pursued as well. In order to evaluate ASD prevalence changes, scientists tend to use a systematic approach based on training in scientific methods where the first step is to rule out alternative explanations. This approach begins by examining factors that could explain a difference over time that are attributable to artifacts, rather than "true" increases. This approach tends to examine identification and methodological factors, as these variables are often more observable than the many potential and unknown risk factors that might contribute to ASD prevalence changes. As more data are collected and analyzed and different hypotheses evaluated over time and across studies, additional conclusions can be drawn. Understandably, this methodical approach is frustrating, especially when most people want to know *the* definitive reason for changes in ASD prevalence and whether it is something in the environment we can do something about. The fact that, despite many efforts, we have not found a single, simple explanation indicates that there are likely multiple, overlapping factors contributing to increases in ASD prevalence.

The purpose of the workshop was to bring together experts in epidemiologic prevalence and surveillance of ASDs and other conditions as well as stakeholders to: summarize where we are; learn from efforts to document prevalence changes among other conditions; and improve the specificity in quantifying and qualifying the multiple factors that might be influencing trends in ASD prevalence, including:

1. **Intrinsic Identification**—Internal methodology or measurement factors involved in documenting ASD prevalence trends (e.g., differences in study methods may lead to different individuals being counted or

not counted as having an ASD such as using a registry of children identified with an ASD or active screening).

2. **Extrinsic Identification**—External classification and awareness factors involved in identifying people with ASDs in the population (e.g., changes in diagnostic criteria or access to services based on an ASD label may influence who is identified for ASD prevalence studies).
3. **Risk**—Possible etiologic or true change in ASD symptoms among the population in relation to single or combined genetic, biologic, or environmental factors, or a combination thereof (e.g., specific biologic vulnerabilities or exposures in the environment that increase the risk of developing an ASD).

Four panels were formed for this workshop:

- Panel 1 – Utility of ASD Prevalence Data
- Panel 2 – U.S.-Based ASD Service Data
- Panel 3 – Autism and Developmental Disabilities Monitoring (ADDM) Network Data
- Panel 4 – What Else Is Needed To Understand ASD Trends?

After hearing the morning's presentations, members of the four panels were asked to discuss the following questions to provide a better understand of ASD prevalence trends:

1. What can we do now with existing data?
2. What should we do next to build on existing data systems?
3. What else is needed in terms of new analyses, data collection, or other efforts?

The goal of this workshop was to learn from different perspectives to inform the community and stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

## A Model for Assessing the Contribution of Various Risk Factors to Recent ASD Prevalence Increase in the U.S.

### L. Schieve

This presentation reviewed preliminary results of a study to formulate a mathematical model to assess the likely effects that given risk factors had on recent ASD prevalence increase and to apply the model to specific prenatal and perinatal risk factors previously found to be associated with ASDs. According to the ADDM Network report from 2009, there was a 57% increase in the prevalence of autism spectrum disorders (ASDs) from 2002 to 2006. The effect of a given risk factor on prevalence depends on the baseline prevalence of the risk factor (RFP), the change in RFP over time (cRFP), and the magnitude of the relative risk (RR). A number of previous studies consistently have indicated that preterm birth and low birthweight are risk factors for ASDs, and some other studies have implicated multiple birth, cesarean delivery, breech presentation, and assisted reproductive technology (ART) as possible risk factors. However, none have had sufficient values for RFP, cRFP, and RR to have contributed substantively to the recently observed ASD increase. While at an individual level, having one or more perinatal risk factors might convey a moderate or strong risk for having an ASD, these factors are unlikely to explain a large proportion of the population increase in ASD prevalence. Although examples were given using selected prenatal and perinatal risk factors, this model could be extended to assess various other risk factors.

A risk factor might be strongly associated with ASD and might be modifiable, but it might not have increased sufficiently in the population during the time frame of interest. Therefore, this risk factor might be related to an individual's risk for ASD but not related to the increase in population prevalence of ASD. The model demonstrated that for any factor to have made a noteworthy contribution to population changes in ASD prevalence during a short time period, three conditions must be met: the factor has to be fairly prevalent in the population, it has to have increased substantially, and it has to be strongly associated with diagnosed ASD.

### *Panel member discussion:*

A panel member asked if broad social changes, as opposed to individual risk factors, also were considered. The panel member was concerned that, by not fully examining population-level changes, the model might be underestimating the contribution of the change in that risk factor in the population on ASD prevalence. Dr. Schieve indicated that a large increase still would need to have an individual effect, and the model is accurate for shorter time intervals such as a few years. As the time period gets longer, then a different analytic model might be needed.

## ASD Genetic Variation and Gene–Environment Interaction

## K. Crider

This presentation summarized how genetic variations and gene-environment interactions could play a role in ASDs and provided background on how these factors may or may not change in a way that would affect ASD prevalence over a short period of time. Typically, to examine heritability of a condition, twin studies are used. More than 30 studies to date consistently have shown higher concordance between monozygotic than dizygotic twins, suggesting there is a strong genetic component associated with ASDs. ASDs have been associated with the following genetic variations: mutation of a gene, deletion of a large or small region of a gene, mutation of another gene, methylation of a gene, or creation of another copy of the gene or the region or chromosome. It is estimated that all genetic variants discovered to date are present in 10% to 15% of people with an ASD and many are implicated in other conditions (e.g., attention deficit hyperactivity disorder and schizophrenia). In general, there would not be an epidemic of a purely genetic condition because genes change over evolutionary time. However, shorter term changes can be seen if there are increases in mutations or breaks, or both, in chromosomes, changes occur in epigenetic patterning (e.g., DNA methylation) or in selective mating patterns.

Gene–environment interactions such as infection, stress, obesity, and trauma all can create the same type of cell damage. Specific causes may or may not have the statistical power to show the true association individually because multiple genetic and environmental factors can lead to the same disorder therefor, studies should be designed to take this into consideration. In some conditions, the magnitude of gene–environment interaction varies. Exposures associated with an increased risk for autism also are associated with other conditions, such as birth defects and cerebral palsy. Single exposures (genetic or environmental) are unlikely (but possible) to show a dramatic increased risk among the general population. Not every individual who carries these forms of genetic variation will have an ASD, which suggests the importance of interactions among multiple genes or gene–environment interaction, or both, in the occurrence of ASDs.

### *Panel member discussion:*

A panel member questioned the accuracy of the statistic that about 10% to 15% of children with an ASD have an identifiable genetic condition. Dr. Crider stated that the statistic is used by others in the field and is a best estimate, but noted the statistic needs better evaluation.

## Autism and Developmental Disabilities Monitoring (ADDM) Network

## C. Rice

### ADDM Network Overview

The ADDM Network is a collaboration of multiple sites in the U.S. to determine and monitor the prevalence of ASDs among 8-year-old children and to track peak prevalence over time. Children are identified through multiple education or health evaluation records if there is an ASD diagnosis, a special education classification, a suspicion of an ASD, or a social behavior associated with an ASD, even when an ASD has not been diagnosed. Clinician reviewers apply the current diagnostic standard criteria of the American Psychiatric Association's D*iagnostic and Statistical Manual, 4th edition, text revision (DSM-IVTR)*. The

strengths and limitations of the ADDM Network were discussed. The most recent ADDM Network estimates indicated that an average of 1 in 110 children (range from 1 in 80 to 1 in 240) had an ASD and that ASD prevalence had increased 57% over a 4-year period from 2002 to 2006. According to the ADDM Network data, the overall trend in ASD prevalence showed consistent increases, but variation existed among sites and among subgroups. While the increase in observed ASD prevalence at ADDM Network sites could be partly explained by identification factors—such as better information available in records, a more stable population at some sites, and improved identification of specific subgroups such as Hispanic children and children without cognitive impairment—these identification factors did not explain the total increase in prevalence. A neat explanation of all factors that could explain completely the observed increase is unlikely, and further work is needed to evaluate multiple identification and risk factors.

### Changes in ASD Diagnostic Criteria

This presentation reported on a preliminary analysis of how an identification factor could be evaluated using the ADDM Network data. Although it often has been stated that the changes in diagnostic criteria that occurred in the *DSM* in 1980 *(DSM III)*, 1987 *(DSM III-R)*, and 1994 (*DSM-IV* and minor changes for *DSM-IV-TR* in 2000) have affected reported ASD prevalence, no known studies have quantified this effect directly. Recoding the ADDM Network data based on the three diagnostic standards (*DSM III*, *III-R*, and *IV-TR*), it was found that autism and ASD prevalence were similar using *DSM III* and *III-R* standards, but increased significantly using *DSM-IV-TR* standards. A portion of the prevalence increase over time might have been attributed to differences in the definitions of ASD used for identification of ASDs by community professionals and service systems. This recoding analysis represents one example of an effort to provide more concrete estimates regarding the effects of a single factor on ASD prevalence.

### *Panel member discussion:*

Panel members raised several questions regarding reasons or theories to explain the wide range of ASD prevalence observed among ADDM Network sites, including the quality of data sources or records and the effect it might have had on prevalence and the inclusion or exclusion criteria used by the ADDM Network sites. Dr. Rice indicated there were some identifiable reasons explaining why the ASD prevalence estimates were lower at some ADDM Network sites (e.g., limited availability of education records) and higher at others (e.g., better quality of documentation in the records). Also, it is easier to identify reasons for lower prevalence estimates than for higher estimates. However, if a site had a low prevalence not due to a methodologic issue, it would be important to consider whether protective factors were at work at that particular site. A question was raised about the reason why the number of sites varied over the surveillance years. Dr. Rice explained that the number of ADDM Network sites depends on available funding and that sites go through a competitive application process in which the applicant must demonstrate a minimum population, partnerships with health departments, and other criteria based on independent peer review. A panel member also questioned when CDC was going to take the issue of rising ASD prevalence seriously. Dr. Rice indicated that CDC has been providing data actively to document these concerns and has been calling attention to the urgency of addressing the needs of the ASD community for years. She continued by stating that the workshop was an effort to broaden the conversation and share ideas on how CDC and others can all learn from other fields and improve collaboration to better understand ASD trends.

## Analyses of ADDM Network Data Related to: Parental Age, Age at Autism Identification, and Socioeconomic Inequalities in the Prevalence of ASD in the U.S.

## M. Durkin

This presentation summarized some analyses of data from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network related to parental age, age of autism identification, and socioeconomic

status. A major strength of ADDM Network data on ASD prevalence is that a sizeable proportion (27%) of children identified with ASDs for surveillance did not have a documented ASD classification. This allows us to investigate factors associated with having a previous ASD diagnosis and receiving services for ASD as distinct from having ASD, and to evaluate whether associations are due to differences in ASD risk or to disparities in identification. A consistent finding in recent epidemiologic studies is a positive association between both maternal and paternal age and risk of ASD in offspring. Despite this association and the increasing trend in mean parental age in recent decades, only a very small (less than .5%) proportion of the recent increase in ASD prevalence can be attributed to the increasing age of parents. ASD differs from developmental disabilities overall in its positive association with higher socioeconomic status (SES). Examining SES among Wisconsin ADDM Network data, it was found that the ASD prevalence increased with increasing SES. However, is this due to increased risk or identification disparities? For example, do educated parents have a disproportionate influence on autism awareness or does the risk of autism increase with a higher socioeconomic status? Is a knowledgeable and determined parent of a child with autism more likely to obtain an informed diagnosis? This is likely to be the case, and there is also the potential role of clinician bias and the possible evidence of disparity in access to care. ASD prevalence estimates likely underestimate prevalence in lower SES groups, which implies that we are still underestimating ASD prevalence and can expect some increases if disparity gaps are closed over time. But the fact that we saw a positive association between socioeconomic status and ASD risk in both those with and those without a previous ASD diagnosis suggests that the association might not be entirely due to under-ascertainment of ASD in economically disadvantaged groups.

## *Panel member discussion:*

Panel members raised the question of whether birth order and the effects of stoppage (a family deciding not to have another child after having a child with a disability) have been studied, and if plans are under way to study miscarriages and autism risk. Dr. Durkin indicated that the effect of birth order combined with parental age and sex appear to be additive. The role of stoppage and pregnancy loss cannot be directly or adequately investigated using ADDM data but require longitudinal, birth cohort studies. CDC's Study to Explore Early Development (SEED) will examine prenatal and perinatal risk factors, such as miscarriages. Studying these factors is important because past adverse pregnancy outcomes are understudied. The importance of examining characteristics (such as parental age, and SES) across cohorts to look at changes among subgroups will be important in understanding potential identification and risk factors contributing to ASD prevalence increases.

# ASD Trends: U.S. Service-Based Datasets

## U.S. Special Education Data

## P. Shattuck

This presentation provided an overview of U.S. Department of Education data related to documenting the presence of ASDs among special education students. U.S. Department of Education's Special Education Child Count data is an annual count of children enrolled in special education services. It is an accountability measure required by the Individuals with Disabilities Education Act (IDEA) to show nonexclusion of children with a disability based on select eligibility categories for each state. Autism was not initially a category within the child count dataset, but was added in 1990 with statesreporting to the U.S. Department of Education in 1991. The number of children classified as having autism and receiving special education services has increased since the early 1990s. However, the number is still fewer than would be expected given current prevalence estimates. A special education label is only mildly sensitive, but highly specific, and enrollment counts might not have provided a true prevalence of ASD. Child Count data vary by area and race or ethnicity. The special education system never was intended to serve a public health surveillance role. Thus, several important questions have been raised that focus on (1) understanding how state-level special education criteria for ASDs vary, (2) exploring referral pathways that lead to identification, (3) examining barriers to timely identification, and (4) developing more effective partnerships with the education sector to maximize data sharing. This will lead to a better understanding of the social, economic, and political factors that influence ASD identification in the community and that might contribute to the rise in identification ASDs in prevalence estimates.

### *Panel member discussion:*

Panel members asked how to integrate ASD screening in schools. Dr. Shattuck indicated that a school equivalent of CDC's Learn the Signs. Act Early. program is needed to increase awareness among educators of the signs of ASDs, and should be followed up with a systematic screening protocol to identify children with an ASD. This is important because, until everyone in the schools uses the same criteria, it will be difficult to rely on the validity of the Child Count data for monitoring changes in the actual prevalence of ASDs. Dr. Shattuck also indicated the need for legislative support to allow education and public health to form effective partnerships; often, school systems do not see the value in the Child Count data from a public health perspective. Especially now, schools are working to meet the service needs of the students rather than addressing broader public health issues such as identifying all children with an ASD in the population.

## California Department of Developmental Services Data I

## I. Hertz-Picciotto

This presentation provided an overview of some ways the California Department of Developmental Services (CA DDS) administrative data have been used to evaluate trends among children receiving services for ASD. Whether due to an artifact or a true increase, ASD prevalence has been high and there is a need to identify the causes. In addition, there already is enough evidence to suggest the importance of environmental causes. There are three main measures of occurrence of a condition: prevalence (the number of cases divided by the number of people in the population at a given time), incidence (the number of new cases among a given population in a defined time divided by the amount of person-time observed during the same period), and cumulative incidence (the number of new cases identified in an extended time period [e.g., from birth] divided by the size of the population without the disorder at the start of the time period). All measures are affected by changes in identification patterns and diagnostic practices. Prevalence data are most useful for service planning and incidence data are useful for etiology. However, a condition where the diagnosis tends to be stable (low mortality rate and it is rare for the diagnosis to change), can result in prevalence and cumulative incidence measures that will be virtually identical over a defined time or age period. For this reason, examining existing data may help us understand ASD trends.

The CA DDS has a statewide database with data from 21 regional centers in the state. The DDS database tracks 5 conditions (autism, epilepsy, cerebral palsy, intellectual disability, and intellectual disability-related conditions). Data collection is passive in that a child must be brought to a CA DDS center and a parent or guardian must request an evaluation to determine if they meet the service provision eligibility criteria. Comparing births in 1990 with those in 2001 (followed to age ten), the cumulative incidence in autism in the CA DDS rose 600%. About 200% of this increase in autism from 1990 through 2001 in the CA DDS database could be explained by trends toward younger age at diagnosis, inclusion of more mild cases, changes in diagnostic criteria, and older ages of mothers. Thus, artifacts related to criteria and methods for ascertainment might explain part but not all of the increase in ASD cumulative incidence in the CA DDS system. To date, there appears to be no leveling off of autism diagnoses, indicating there is considerable likelihood that there has been a true increase in incidence (or risk).

### *Panel member discussion:*

Panel members questioned how the identification artifacts played out across regions. Dr. Hertz-Picciotto indicated that there was substantial variability among the centers (Los Angeles traditionally has had higher ASD rates than other regions of the state). .Each DDS center is run by independent contractors and are managed slightly differently from each other. There also are clusters of ASDs near places where there are well-known treatment centers. A panel member pointed out that it is important to study these identification factors at multiple locations beyond California service data to areas of the U.S. and to also consider international patterns of occurrence.

## California Department of Developmental Services Data II

## P. Bearman

This presentation summarized additional analyses of data from the CA DDS related to trends in ASD prevalence conducted by Dr. Bearman and colleagues. During the past 30 years, the prevalence of autism has increased dramatically. Examining California birth data from the period 1992 through 2007, there were 8 million births (about 500,000 births per year). Using a sophisticated mapping program of all births and addresses and linking to CA DDS autism data, researchers were able to ascertain parental characteristics, prenatal conditions, and residence during the in utero period and link to data on neighborhoods, socioeconomic status, local toxicants, and other conditions. Examining these data was useful in examining the contribution of diagnostic change to increased prevalence, gaining insight into genetic mechanisms, understanding the spatial structuring or geographic patterns of autism at birth and age of diagnosis, considering diverse individual and community level risk factors, and measuring the potential role of sharing information on autism.

Analysis of the data showed that changes in ASD diagnoses in relation to those for intellectual disability (mental retardation) explained 24% of the increase in autism prevalence in the CA DDS data during the time period analyzed. An analysis was also done to see how administrative data might provide insight into genetic mechanisms. There was a high ASD concordance between identical twins and low concordance between fraternal twins. Over time, there was an increase in ASD among same sex twins and a decrease among opposite sex twins. Another analysis examined the spatial structure (geographic mapping) of the birth residence of children later identified with ASD by DDS. The researchers concluded that ASD birth clusters have been robust over time and do not appear to be due to factors such as education or socioeconomic status. Examining the DDS administrative data has provided insight into risk factors for autism. For example, findings indicated maternal age might be more critical than paternal age; community level characteristics such as geographic spacing are increasingly less salient as ascertainment increases, but still significant; and shorter interpregnancy intervals might confer excess risk. About 50% of ASD prevalence increases in the CA DDS data could be explained by several factors, such as diagnostic change, advancing parental age, social influence of people sharing information on ASDs, and spatial structure. Work is needed to understand what accounts for the other 50%. A project currently is under way to investigate

whether assistive reproductive technology (ART) is related to increased risk of having a child with ASD as identified in CA DDS data by linking with CDC data on births involving ART.

## *Panel member discussion:*

Questions were raised about the autism clusters that were identified using CA DDS data. There was a question as to whether these were true etiologic clusters or if there appeared to be shared identification patterns. Dr. Bearman discussed the idea that clusters might have been due to a shared exposure, such as toxicant, or to a social risk factor. For example, people with children the same age who shared a workplace or social activity might have been more likely to discuss their children and share information about autism, thus leading to increased identification. Or, there might have been reluctance among some groups to reach out to the health care or services system, resulting in decreased identification. A panel member expressed caution about the conclusion of being able to explain about 50% of the increase in DDS ASD prevalence as the approach used to arrive at this estimate was too simplistic and did not take the overlapping relationships between different factors into account. Dr. Bearman relayed his belief that some of the factors operate on different aspects of the spectrum and that the 50% figure was a way of summarizing what is known to date. For example, identification factors, such as shifts in the use of the intellectual disability diagnosis to add autism as another diagnosis or an alternative diagnosis, may operate on the lower end of the spectrum and social influence may operate on the higher end of the spectrum. Factors such as parental age and shorter pregnancy intervals are more likely to be risk factors contributing to ASD increases.

# Lessons Learned From Other Conditions and Analytic Methodologies

## Cancer

### R. Etzioni

Changes in cancer trends can be seen from changes in (1) exposures (e.g., smoking, diet, and obesity), (2) diagnosis or detection (e.g., screening and biopsy techniques), and (3) classification (e.g., staging and grading techniques). Dr. Etzioni presented three examples of changes in different types of cancer:

- Lung Cancer—The greatest modifiable risk factor for lung cancer is smoking. The trend line for lung cancer incidence plots has sloped similarly with the trend line for smoking prevalence, meaning the incidence rates of lung cancer have decreased over time (Surveillance, Epidemiology and End Results registry data) as smoking behavior has decreased over time (National Health and Nutrition Examination Survey).
- Colorectal Cancer—Screening rates for colorectal cancer have been increasing over time and the consumption of two or more servings of red meat per week has been decreasing over time. As screening has increased and red meat consumption has decreased, the incidence of colorectal cancer has decreased.
- Prostate Cancer—Prostate-specific antigen (PSA) screening was first introduced in the 1990s, which correlated with the first peak of prostate prevalence. The second prevalence peak occurred when follow-up biopsies became more routine. Researchers attributed the prevalence changes to differences in recording techniques and improvements in grading of cancer (from poorly to moderately to well-differentiated).

Examining patterns of change among a population might explain disease trends due to changes in factors such as the annual frequencies of exposures, availability of screenings, use of new diagnostic technologies, and changes in disease coding. It is important to have data on the occurrence of a condition before and after the change factor being evaluated. It is also helpful if there is a clear change factor that has occurred.

Modeling change is an integral part of cancer surveillance. There are several important lessons learned from this modeling that can be useful when examining changes in ASD prevalence. The basic steps of modeling change are:

- Characterizing changes in disease trends;
- Quantifying changes in the population that might explain trends;
- Identifying a mechanism for the effect of the population trend;
- Estimating the size of the effect on the risk of disease diagnosis; and
- Modeling or simulating experience among the population.

All of these steps are equally necessary and applicable in explaining changes in ASD prevalence. However, modeling techniques might be useful if the potential effects of a factor on prevalence are not known. There is a group called the Cancer Intervention and Surveillance Modeling Network (www.cisnet.cancer.gov) that is working to develop techniques for modeling changes in cancer based on multiple factors. Working with this group might be helpful in understanding ASD prevalence changes.

## Parkinson Disease

### C. Tanner

Parkinson's disease is a relatively rare disorder that does not have a diagnostic test or definitive marker. Symptoms occur later in life and share some features, such as cognitive decline, with other conditions such as Alzheimer's. The best diagnosis is a face-to-face exam. As with ASDs, population-based surveillance is challenging and there have been changes in diagnostic criteria over time. Also similar to autism, there are questions about the higher prevalence in males and differences by race. One example of examining diagnostic incidence trends of Parkinson's is a study conducted in the Kaiser Permanente Medical Care Program of Northern California (KPMCP). Researchers used active surveillance to examine electronic

medical records, physician referrals, and computerized databases to identify patients receiving services in community settings. Researchers have identified increased incidence of Parkinson's disease among men and with increasing age, a pattern that has been seen in most populations world-wide. Patterns that were suggested, but not supported by evidence, were higher incidence among Hispanics and the lowest incidence among Blacks. Environmental and genetic risk factors have been associated with Parkinson's disease. At this point, there are few sources of data to examine population trends in Parkinson's disease. The CA Parkinson's Disease Registry is a pilot effort to create a population-based database with active ascertainment and case validation, but is active in only a few counties and no state funds are designated to support the effort. Other efforts at population-based registries have been tried, but in these there is no active mechanism for reporting. Advocacy groups support a national surveillance system for Parkinson's disease, but this has yet to be realized. Researchers are also examining conditions with similar symptoms and/or risk factors to identify common biologic mechanisms. It may be useful to study prevalence changes in other disorders with symptoms that overlap with ASDs and among adults.

### *Panel member discussion:*

A panel member asked if there is a spectrum of conditions similar to ASDs. Dr. Tanner indicated that there are similar clinical syndromes including Parkinsonism. Different disorders have different clinical features and prognoses, but definitive diagnosis is post-mortem.

## Asthma

## M. King

Asthma is a highly prevalent chronic disease. Studies have shown persistent demographic differences in prevalence, as well as health care use. Asthma surveillance relies on several national datasets to determine prevalence and severity. One of these is the National Health Interview Survey (NHIS). Before 1997, the NHIS measured 12-month prevalence based on self-reports of "having asthma." After 1997, the NHIS measured prevalence by self-report of a "doctor's diagnosis" of asthma and included lifetime, past 12-months, and whether an attack occurred in past 12-months. The current measure of prevalence is similar to the projected 12-month rate, and the prevalence is higher among children than adults with racial differences observed as well. The Behavioral Risk Factor Surveillance System (BRFSS) allows state-specific estimates of asthma and enables CDC to conduct an asthma call-back survey. The BRFSS allows CDC to determine a population-based prevalence, as well as an at-risk–based rate. An at-risk–based rate is the number of affected people within the population having certain risk factors. While asthma prevalence has increased over time, actual asthma attack rates have been relatively stable. The reasons for overall prevalence increases are not known, but there are sociodemographic disparities in identification and service use. Changes in survey measurement have affected asthma estimates.

### *Panel member discussion:*

There was a question about the content of the call-back survey. Dr. King indicated this that this survey provides a chance to find out more about health care needs and use, effects on quality of life, and other information on the functional effect of asthma and service use related to asthma. Another question was about the availability of linking asthma data with environmental factors such as air pollution. Dr. King stated that data are not available to look at direct measures among individuals in the population over time, but different datasets could be linked to conduct ecologic analysis of asthma survey data based on residence and air quality, for example.

## Schizophrenia

## E. Susser

There are many parallels between schizophrenia and ASDs in the attempts to estimate incidence and historical changes in incidence. With respect to schizophrenia and related psychoses, two landmark

World Health Organization (WHO) studies can be used to mark shifts in thinking about schizophrenia, as well as about how studies of schizophrenia should be conducted. First, the International Pilot Study of Schizophrenia (IPSS), conducted in the 1960s, was designed to determine if schizophrenia was a culturally bound disorder and if it was a "real" disorder (some people hypothesized that schizophrenia was a social construction). The study used standardized criteria in a multinational study and many regions of the world were included. Researchers found schizophrenia in all settings; that finding is still questioned, but is supported by the findings of other types of studies. Second, the WHO "Ten Country Study" examined whether the incidence and course of schizophrenia varied across sociocultural settings. The study also had a novel design for determining incidence. It inaugurated the "first contact" design, now widely used and considered a "gold standard", in which researchers ascertain all people seeking help for a possible psychosis for the first time, within a defined population.

Based on misinterpretation of the results of these (and other) studies, the prevailing summary of schizophrenia from 1980 to about 2005 was that there was a lifetime risk of schizophrenia of 1%, and that this figure remained constant over time and place. The current view on schizophrenia is different; it is clear that the occurrence varies across populations and population subgroups, the clearest example being the very high rates among some immigrants who are ethnic minorities (mainly documented among immigrant groups in the United Kingdom and Netherlands). This variation is not inconsistent with the results of the WHO studies, but is inconsistent with the way these results were interpreted by most schizophrenia researchers and clinicians as showing constant rates overtime (not by the authors themselves, who were cautious in their conclusions). The WHO studies were not designed to examine change over time. Although other studies have attempted to examine change over time (e.g. registry studies), the results have been inconsistent, and the data weak (e.g. due to changes in diagnostic practices and systems). As a result, with the exception of one or two particular locations, we cannot at present draw conclusions as to whether schizophrenia incidence has changed over time. The discrepancy between studies of the course of schizophrenia, and interpretation of those results (again, not by the authors) is even more striking, but I do not have time to elaborate on this during this presentation.

There are several important lessons learned from studies of schizophrenia that could be useful when examining changes in ASD prevalence. For example, with regard to the notion of "constant" incidence over place and time, fixed thinking about schizophrenia was allowed to override the available data. The idea that schizophrenia occurred worldwide and that there was at most a very modest variation in incidence was accepted as true for a long time, and still taught in many psychiatry and other mental health professional training programs. This lesson is relevant to ASDs to help understand how to interpret ASD data. There have been different waves of ideology which have influenced the way in which the data on incidence of ASDs have been interpreted, and in particular, on whether they demonstrate a "true" increase or not ("true" means over and above an increase due to changes in ascertainment and help-seeking). The schizophrenia story helps one to recognize the power of ideology in the interpretation of such data, and the need to be cognizant of it. He noted his personal view is that the data on whether there has been a "true" increase in autism are simply inconclusive, but that the overall evidence favors the position that a part of the increase is "true".

## *Panel member discussion:*

Panel members asked if there was a specific way in which those in the ASD field could learn from the schizophrenia example? Dr. Susser responded that there have been different waves of ideology in how autism and related conditions have been interpreted and people tend to look at data as either, "yes, there has been an increase", or "no, there has not been an increase". It would be really helpful for those working with ASDs to not look through the data using those lenses, but to ask questions openly. Dr. Susser further stated that we do not need to be committed to either position to use data to advocate and to improve services. There was another question on subtypes of schizophrenia. Dr. Susser indicated that subtypes typically have not been reliable over time. Dr. Susser also commented that if a disorder persists

over generations, we also should be consider examining if there are selective mutations occurring or reframing to consider a selective advantage associated with the condition.

## Simulation Studies

### S. Galea

This presentation provided a brief overview of simulation studies as a method to understand prevalence changes. Changes in ASD prevalence have been and continue to be an observed phenomenon, yet the problem lies in identifying the causes for the changes. Causal models, including sufficient-component cause models, can shed some light on the joint effects of multiple exposures. However, these models are unable to consider timing in a dynamic way or connections between individuals. A possible solution is to use complex systems models. Complex systems approaches are computational approaches that use computer-based algorithms to model dynamic interactions between individuals within and across levels of influence (such as social networks and neighborhoods) using simulated populations. Complex systems models can incorporate multilevel determinants of population health, connections between individuals, and patterns of feedback between exposures and outcomes over time.

An example of trying to understand health problems seen after disasters was presented using a type of analytic strategy called "agent-based modeling" to predict changes among heterogeneous populations. The goal was to model outcomes observed by varying the variables that might have contributed to the observed pattern. There could have been several different sets of variables that produced the same outcome. A lesson that might be important when examining reasons for ASD trends is that complex systems models point to different possible explanations for observed phenomenon. However, they can be used in conjunction with empirical data to narrow down possible explanations and can play a central role in epidemiological analyses.

# Open Comments

The workshop included presentations and discussions among panel members. However, the meeting was open to anyone to register and attend in person or via webinar. Nonpanel members were able to provide written comments before and after the workshop, as well oral statements during an open period of the workshop. Comments included concern about increases in ASDs, the need to find out what has changed in our environment, the larger than expected number of children and young adults with an ASD, and the cost to society. Many of the public comments focused on concern about the role of vaccines in autism, with disappointment expressed about the lack of research on vaccine safety. In particular, studies of vaccinated and unvaccinated children and mitochondrial disease were requested. In addition, concerns were raised about the cumulative effect of the vaccine schedule and vaccine ingredients, as well as the need to consider a child's immune status prior to giving vaccinations. Suggestions were made for other studies such as of young children's development from birth to 2 years of age and to determine if there are specific subgroups of children with ASDs, such as those with gastrointestinal sensitivities. A man with an ASD expressed the belief that it is possible to be successful with an ASD and offered himself as an example of someone who once relied on public assistance, but is now successfully employed and lives independently. He also expressed gratitude for CDC's work in vaccine safety and satisfaction with receiving vaccines to protect from known diseases. Other comments included frustration with the delays parents face in getting a diagnosis of autism, despite bringing concerns to the attention of professionals. Other comments included concern about non-scientific expertise among panelists and interest in the latest research findings and plans for future research related to ASDs. Workshop organizers, panelists, and stakeholders were asked to consider these comments when discussing priorities for evaluating changes in ASD prevalence.

# Panel Session Summaries

The workshop featured four breakout panel discussions, with each panel asked to discuss questions related to ASD prevalence. The panelists' discussion, ideas, and suggestions were compiled by the panel chairs. Panel members consisted of epidemiologists and scientists with experience in epidemiology and surveillance of autism or other complex conditions and community stakeholders (representatives from autism organizations, parents of children with an ASD, and adults with an ASD). Following is a summary of the panel discussions and their ideas for addressing questions related to ASD prevalence trends.

## Panel 1: Utility of ASD Prevalence Data

Panel Chair: *A. Singer*

**Panelists:** *C. Cunniff, W. Zahorodny, R. Kirby, M. Lopez, R. Grinker, D. Mandell*, L. Grossman*, W. Dunaway, M. Rosanoff, J. Zimmerman, B. Mulvihill, J. Charles*

**Invited participant unable to attend remotely or in-person at last minute due to unforeseen circumstances.*

The discussion and questions addressed by Panel 1 focused on how ASD prevalence data are used in the community by different stakeholders and sought to identify ways in which data collection and reporting on the population prevalence and characteristics of people with an ASD could be further developed.

### *Q1. What does having ASD prevalence information do for stakeholders (parents, professionals, people with an ASD, researchers, scientists, policy makers, service providers)?*

The panelists indicated that ASD prevalence data are used to:

- Empower the community, confirming what parents and educators experience
- Drive public policy
- Support the need for service provisions and development
- Support the need for professional development and systems planning
- Support the need for additional research

At the community level, prevalence data have informed stakeholders about needed improvements in identifying people with an ASD and helped direct research which may ultimately lead to information about etiology. Similarly, the resulting increase in ASD awareness and knowledge among parents, caregivers, and communities has increased the quality of social and behavioral descriptions by clinicians and service providers when a child has been referred for an evaluation. This has resulted in parents being more equipped to discuss concerns with professionals. Clinicians have found that having ASD prevalence information increases awareness of the need to identify children and facilitates having a conversation with parents about concerns. It also has provided information to help clinicians advocate for needed resources for identification, referral, and intervention. Researchers have used prevalence data as justification for etiologic and intervention research, and the increased awareness of ASD has increased their own career choices to be engaged in meaningful work. Individuals with an ASD have also benefitted from ASD prevalence data. Increased ASD awareness has resulted in positive community connections and increased information has allowed them to help themselves and others understand their experience.

Prevalence data also have empowered communities by confirming what parents and educators have been experiencing and providing evidence for robust advocacy. ASD prevalence estimates have provided a starting point to assess service and support needs for individuals, families, and communities. On a policy level, awareness of the Autism and Developmental Disabilities Monitoring (ADDM) Network has allowed scientists and researchers, in some states, easier access to data sources and records for surveillance purposes, thus increasing the accuracy of ASD estimates. Prevalence estimates also have informed policy efforts to create an infrastructure to support children with an ASD (e.g., child care, intervention, education, transition services); understand and address lifespan issues (e.g, housing training, employment, health

and wellness); drive public policy and programs (e.g., insurance coverage and health care legislation); and support the need for service deployment, systems planning, and additional research funding.

### *Q2. How are stakeholders actually using ASD prevalence information?*

ASD prevalence data are included at the beginning of many, if not most, research publications and grant applications related to ASDs because they provide an estimate of the population-level effect of the conditions. In particular, recent estimates indicating that ASDs are more common than previously thought have motivated the need to better understand the course, causes, and supports related to ASDs. In addition to putting the scope of need into perspective, recent ASD prevalence estimates have prompted some states to pass mandatory reporting laws, establish autism task force groups or autism councils, pass legislation affecting service provision, or offer grants to school districts for supplemental funding related to autism. Examples of how states have used ASD prevalence data follow:

- South Carolina used prevalence data to show the need for improving access to services when drafting and passing insurance reform.
- New Jersey passed laws related to ASDs and mandatory reporting, compelling insurance companies to provide services and providing additional grants to schools.
- Alabama appointed an autism coordinator for the state based on the effects of the prevalence data.

### *Q3. What types of ASD prevalence information and descriptions of the population are useful to stakeholders?*

For individuals, families, and communities, having ASD prevalence data that are applicable to more specific local areas and states can better inform advocacy and service planning efforts. ASD prevalence data are population-based and are not easily applicable at the individual level. In addition to understanding the population effects of ASDs, families and communities continue to seek ways of making the information more relevant for their individual circumstances. Specific recommendations included:

- Improving communication with the community (e.g., families, individuals with an ASD, professionals, policy makers, and researchers) to help put the prevalence data into context.
- Providing more in-depth information on what an ASD diagnosis means for an individual across his or her lifespan, and what support systems such an individual needs or will need.
- Collecting and reporting data on functional level and effects of ASD, subtypes, developmental characteristics, and associated conditions (in addition to overall ASD prevalence estimates).

### *Q4. What questions do stakeholders expect epidemiology and prevalence studies, in particular, to answer?*

The panel noted that community stakeholders want the data to be useful at the community and individual levels. At the community level, ASD prevalence estimates can inform larger needs (identification, supports, policy, and research). For the individual person, as suggested in Q3's discussion, more detailed data on functioning and characteristics would be helpful. Prevalence numbers should inform preparation for the needs of a growing population. In addition to describing the population, prevalence studies could provide a baseline for evaluating interventions and gauging service needs. Some panel members called for more data on the link between prevalence and etiology. For example, would lower prevalence in some areas or subgroups indicate potential protective mechanisms? Prevalence studies should be accompanied by data collection on specific symptoms or biological measures, interventions, and trajectories over time.

## Panel 2: U.S.-Based ASD Service Data

### Panel Chair: *L. Croen*

**Panelists:** *P. Shattuck, P. Bearman, M. Kogan, S. Visser, I. Hertz-Picciotto, L. Miller, A. Bakian, K. Van Naarden Braun, L. Lee, T. Baroud, P. Bell, R. Etzioni, Y. Kim*

Panel 2 discussed databases that exist to serve the administrative functions of tracking service use, or were developed for specific studies. Although not designed to identify all children with an ASD among the population, these databases might serve as useful tools for looking at trends in identification, characteristics, and service use that will help explain population-based ASD prevalence trends. Some of the databases or datasets noted that could be explored for examining administrative or reported prevalence issues include:

All-Payer Claims Database (APCD; combines outpatient data from all claims databases)
California Department of Developmental Services (CA DDS) database
Department of Education/Individuals with Disabilities Education Act (IDEA) Child Count (also, Special Education Longitudinal Study)
Hospital Discharge Data
Interactive Autism Network (IAN) survey
Kaiser Permanente® membership databases
Centers for Medicaid and Medicare Services (CMS)
National Health Interview Survey (NHIS)
National Survey of Children's Health (NSCH)
National Survey of Children with Special Health Care Needs (NSCSHCN)
State registries (New Jersey, Utah, West Virginia)
Vaccine Adverse Event Reporting System (VAERS)

***Q1. What are the top three immediate (within 1 to 2 years) priority analyses needed to understand ASD trends using existing U.S.-based datasets?***

Panelists discussed several analyses that could be pursued, including:

- Conducting a life-course study of ASD identification, service use, and characteristics. Tracking life history can help determine if the ways people come into the system are changing. Researchers could examine first concerns and average age at first diagnosis, and what happens before and after an ASD diagnosis occurs among those in successive birth cohorts. Kaiser Permanente® membership data could be used to explore this.
- Examining trends in comorbidities among children with ASDs over time and trends in the use of treatments among parents over time. For example, a potential research question might include "Does survivorship of a mental or physical illness by parents (e.g., bipolar disorder) affect the trend in ASD prevalence among children? Kaiser Permanente® membership data or perhaps Medicaid data could be used to explore this type of question.
- Examining behavioral screening data to investigate trends in ASD diagnosis over time. Potential data sources could include the ADDM Network, as well as research programs, insurer databases, and primary care practices that have administered developmental screening tests over time.
- Examining trends in other behaviorally defined conditions (e.g., attention-deficit/hyperactivity disorder, depression, and anxiety) in U.S. population-based datasets (e.g., the National Survey of Children's Health). This could be addressed by ADDM Network data (among children with an ASD).

- Looking at ASD prevalence trends over time among different immigrant groups. This might inform trends and prevalence rates in terms of eliminating certain risk factors. However, it is difficult to disentangle if observed rates are lower among immigrants either because of immigrants' lack of familiarity with the U.S. health care system U.S. (including how it operates), or because of reluctance on the part of immigrants to seek medical attention for developmental disorders, or both.
- Further examining the respondents to national surveys who had at least one child ever diagnosed with an ASD and who reported the child no longer had an ASD diagnosis at the time of the survey There is a need to understand why some children may have been reported to have an ASD at one time, but not at the time of the survey.

***Q2. What are the top three next (within 3 to 5 year) priority analyses needed to understand ASD trends using existing U.S.-based datasets?***

Panelists discussed several potential analyses, including:

- Conducting multilevel modeling with Special Education Child Count or other datasets. Enhanced analysis might help answer questions regarding administrative prevalence trends in schools and communities.
- Using Special Education Child Count data from both IDEA Part C Early Intervention for 0-3 year-olds and IDEA Part B for 3-21 year-olds to track identification, services, and developmental trajectories at the individual level.
- Linking all-payer claims databases with state autism registries to track ASD diagnostic or billing codes, along with additional billing and pharmaceutical claims, to provide information concerning comorbid conditions.
- Taking simulation-based approaches to data analysis, and evaluating the models using real data from epidemiologic studies.
- Using Medicaid data to examine trends over time in ASD and related diagnoses among those receiving Medicaid services. Also, evaluate children longitudinally to examine changes in diagnoses and services.
- Collaborating with the National Institute of Mental Health (NIMH) to better understand the factors associated with the persistence of parent-reported ASD diagnosis. (NIMH has partnered with the Health Resources and Services Administration and the Centers for Disease Control and Prevention, and currently is conducting a follow-up study of the NSCSHCN for families of children who were reported ever to have had a diagnosis of an ASD.)

***Q3. Can the existing data systems be enhanced (e.g., adding analyses, data collection) to better answer questions about the changing ASD prevalence? If not, why not and what else is needed?***

Panelists discussed several enhancements, including:

- Enhancing use of Child Count Special Education Data by
  - » Documenting state differences in identifying children as eligible for autism special education services and documenting the methodology for obtaining and reporting these data to make better sense of special education data.
  - » Conducting studies to evaluate how children with autism are identified at schools.
  - » Enabling individual-level child data to be accessed for study purposes and pooled together.

- Enhancing use of surveys by
  - » Conducting needed validation studies of parent-reported data.
  - » Exploring whether national surveys (e.g., National Immunization Survey, NHIS, NSCH, VAERS) could be used to examine ASDs among vaccinated versus unvaccinated groups.
  - » Using national surveys to examine service use and needs.
  - » Adding questions to the IAN Survey to assess beliefs about causes of ASDs.
- Enhancing data access and coordination by
  - » Partnering with analytic powerhouses (e.g., Google) to develop new strategies to take advantage of the huge amounts of data that will become available in upcoming years (e.g., data enhancements from health care reform and electronic health records). This will require public and private partnerships.
  - » Making ASDs reportable conditions in more states. However, it was noted that making a condition reportable does not improve the ability to understand trends, but it is a useful method to establish public health authority to collect additional data to track trends.
  - » Collaborating with the National Environmental Public Health Tracking Network (EPHTN) to potentially access environmental risk factor and other environmental public health tracking data at the population-level.
- Creating new data collections for
  - » Using qualitative methods to understand pathways to screening and diagnosis.
  - » Monitoring trends in ASD prevalence prospectively to rule out "artificial" factors. Consistently conduct developmental and ASD screening at given ages with diagnostic follow-up and documentation of each step and outcomes.
  - » Developing methods to track the effects of information dissemination across parent networks via the Internet or other social media.

## Panel 3: Autism and Developmental Disabilities (ADDM) Network Data

### Panel Chair: *G. Dawson*

**Panelists:** *S. Galea, G. McGwin, O. Devine, A. Correa, M. Zack, P. Yoon, M. Maenner, J. Daniels, L. Schieve, S. Pettygrove, M. Wingate, J. E. Robison, P. C. Marvin*

The questions and discussion of Panel 3 focused on identifying immediate, next, and future priorities for enhancing the data collection, analysis, and reporting of ASD prevalence and descriptive data by the ADDM Network to betterunderstand trends.

***Q1. What are the top three immediate (next 1 to 2 years) priority analyses needed to understand ASD trends using existing ADDM Network data?***

Panelists discussed the following priorities:

- Conducting simulation studies to predict the anticipated course of ASD prevalence, informed by existing ADDM Network data, by
  - » Identifying and using more complex, nuanced modeling approaches to simultaneously examine multiple identification (intrinsic and extrinsic) and risk factors across cohorts (this will be challenging because several factors are confounded).
  - » Using ADDM Network data to inform assumptions in simulation models of ASD prevalence trends.

- Conducting analyses that will help explain variations in ASD prevalence across geography and subgroups by
  - » Providing information about risk factors related to parental age.
  - » Examining data on ASD prevalence for disparities in identification to inform diagnostic and access to service needs.
  - » Comparing changes in ASD prevalence among children with more a narrowly defined autistic disorder diagnosis to with those with a broader ASD diagnosis, as autistic disorder might be less influenced by increased public awareness.
- Using methods to maximize the number of children with an ASD in the population identified by the ADDM Network by
  - » Performing additional validation studies including direct screening and assessment at other ADDM Network sites and using the results to enhance estimates of ASD prevalence. [Note that a validation study in the Atlanta site (Avchen et al., 2010) found that the records-based approach had good specificity but low sensitivity indicating that ADDM Network ASD case classifications are consistent with clinical examination, but that some children with ASDs are not identified using current methods. Therefore, ADDM Network prevalence estimates likely underestimate ASD prevalence.]

***Q2. What are the top three (within 3 to 5 years) priority analyses needed to understand ASD trends using existing ADDM Network data?***

Panelists discussed the following potential next priorities:

- Conducting analyses to better understand ASD prevalence trends and current and future needs of adolescents and adults with an ASD by
  - » Examining an older cohort to better understand the changes in prevalence over time. This could be done by
    - * Surveying a previously-characterized cohort of 8-year-olds when they are older to determine if prevalence estimates are the same in this cohort at older ages.
  - » Identifying methods for estimating lifetime prevalence and characterizing developmental trajectories by
    - * Examining how ASD symptom presentation may change across cohorts and individuals across the lifespan.
    - * Identifying methods to examine the effects of early intervention and whether changing symptom profiles may have on ASD prevalence estimates.
  - » Conducting studies of ASD prevalence among adults by
    - * Identifying appropriate methods for characterizing ASD prevalence at different ages.
    - * Addressing the ethical concerns of identifying adults with an ASD who may not want that classification.
    - * Characterizing outcomes and service and support needs.
  - » Using ADDM Network data to better understand risk factors for ASDs by

* Recognizing that ADDM Network data might not be well-designed to examine risk factors at the individual level; however, use the data to characterize whether some risk factors have changed among the population and correlate to ASD prevalence changes.

***Q3. Can the ADDM Network be enhanced to better answer questions about changing ASD prevalence? If yes, how? If no, why not and what else is needed?***

Panelists discussed building on the existing ADDM Network infrastructure by

- Developing ways of better capturing the heterogeneity and complexity of ASD phenotypes.
- Expanding ADDM Network dataset linkages to other datasets (e.g., health, education, service, environmental data) to enrich data completeness and use for examining risk factors.
- Collecting follow-up data on cohorts studied previously at later ages to better understand trends over time and outcomes.
- Collecting more extensive data as part of ongoing surveillance using additional methods such as direct screening and diagnostic confirmation to obtain the most complete estimates of ASD prevalence in the U.S.

## Panel 4 –What Else Is Needed To Understand ASD Trends?

### Panel Chair: *M. Durkin*

**Panelists:** *K. Crider, E. Susser, C. Lawler, C. Tanner, M. King, S. Shapira, D. Schendel, J. Nicholas, W. McMahon, J. Constantino, C. Newschaffer, L. Perner, M. Blaxill, E. London, G. Windham, K. Merikangas*

Panel 4 engaged in an open discussion on some of the "big picture" issues related to understanding ASD trends, including whether it is possible to fully understand reasons for ASD prevalence increases, ways to move forward with collaborations and new methods, and what else could be done to improve the understanding of ASD trends.

***Q1. Can the question of the relative contribution of identification or risk factors, or both, on ASD prevalence during the last 20 years be answered? If not, why not? If yes, what are the three primary questions that need to be addressed by epidemiology?***

Panel members offered a range of perspectives on whether it will ever be possible to understand the relative contributions of identification and risk in increasing ASD prevalence. There was agreement that the ASD prevalence is a huge public health problem and that many individuals and families are affected globally. Panel members did not agree about whether it was possible ever to understand fully all the reasons behind increasing ASD prevalence. One panelist asserted that the question already has been answered: Of course there has been an increase because there has an increase in the number of cases and autism is an epidemic and needs to be treated as a public health emergency. Others noted that autism is a disorder of social behavior and that trends over time in its frequency are affected by corresponding changes in social context, perceptions, awareness, knowledge, diagnostic practices, and availability of services. However, there was a general sense that it is possible to move forward and to be more specific in documenting potential reasons for ASD prevalence trends. Several challenges were mentioned, such as insurmountable measurement error, overlap and confounding of multiple identification and risk factors, and poorly defined subtypes with limited information on biological underpinnings to explain phenotypes. It is unlikely that prevalence trend data will explain the etiology of a complex set of conditions, such as ASDs, but these data can identify clues for further mechanistic studies (e.g., increased risk by sex, geography, and birth characteristics). By better understanding what causes autism, maybe we can understand the

increases in measured prevalence. In addition, panelists noted that we need more clarity on phenotypes, expression across the lifespan, and trends in other conditions. Others thought that, although we might not be able to use prevalence data to make discoveries about how to prevent or cure ASDs, we can use prevalence data to assess needs and improve the lives of those affected by ASDs. This could lead to a focus on services and figuring out how to improve identification and access to such services.

***Q2. How can efforts to understand ASD trends be informed by other fields or conditions (e.g., comparison with other conditions, sharing methodology, analytic techniques, etc.)? How can that best be accomplished?***

Panelists discussed several potential collaborations, including:

- Comparing ASD prevalence trends to trends in other neurodevelopmental disorders.
- Collaborating with scientists investigating epigenetic effects in cancer and other fields to better understand gene–environment interactions in neurodevelopment.
- Examining subgroups of children with an ASD (e.g., children with fragile X syndrome and ASD) to determine if there are specific risk factors that can be identified among these children with increased risk for developing ASD.
- Analyzing new bioinformatics and computational tools and approaches to better understand complicated systems and interactions.
- Conducting translational research because existing ASD criteria are not mapped to biology and etiology. Translational investigators could help bridge the gap between diagnostic criteria and biology.

***Q3. What else is needed to understand reasons for trends?***

During the discussions for Questions 1 and 2, several propositions were made for better understanding ASD prevalence trends, including:

- Seeking public–private partnerships to support data collection, analyses, and usage of data.
- Providing funding opportunities to encourage use of existing datasets.
- Expanding use of analytic techniques for examining population trend data by
  - » Using modeling approaches to supplement observed data.
  - » Comparing multiple identification and risk factors that might contribute to prevalence changes.
- Expanding ASD prevalence efforts to include very young children and adults.
- Understanding patterns in ASD prevalence among subgroups (e.g., subtypes, males and females, geographic variation, comorbidities) to evaluate whether changes likely are due to identification or risk factors:
- Expanding the methodology for looking at ASD prevalence by
  - » Developing methods to conduct cross-sectional studies across successive birth cohorts that simultaneously ascertain parent-reported descriptions of developmental characteristics, intellectual functioning, ASD and comorbid symptoms, research diagnosis (categorical or observational), community diagnoses, and family characteristics (sibling recurrence).
- Understanding and improving ASD identification by
  - » Measuring ASDs dimensionally and quantifying the traits that make up the ASDs.

- » Measuring any overlap with other conditions and typical development, determining if is there a continuum of symptoms.
- » Improving tools for culturally sensitive screening and case confirmation among large populations.
- » Developing methods for measuring disability and monitoring functional limitations in individuals with ASD.
- » Using data on identification of ASDs to identify gaps and improve community practice.

- Improving community engagement and communication between individuals and families affected by autism, professionals providing services for people with autism, researchers, and policy makers by
  - » Fostering broader understanding of the strengths and challenges associated with ASDs so people with ASDs have access to the community.
  - » Utilizing ASD prevalence estimates to develop programs and practices that support the positive development of people with ASDs.
  - » Realizing that autism is not an academic issue for the many individuals and families affected by ASD, and listening to the concerns of parents of children and individuals with an ASD.
  - » Sharing information with leadership and policy makers to respond to this health crisis.
- Making sure public health is part of the Interagency Autism Coordinating Committee (IACC) Strategic Plan and input is sought from a range of stakeholders via annual research plan updates.
- Noting that, while trends are important, understanding them might require a better understanding of the etiology and heterogeneity of autism, as well as changes over time in diagnostic practices. These goals can be achieved by
  - » Advancing basic science on biologic and environmental mechanisms.
  - » Increasing the types of study methods used in research and service studies such as
    - * Conducting prospective studies that examine biology, phenotypes, identification patterns, and service needs and use.

# Appendix A: Workshop Agenda

## Workshop on U.S. Data to Evaluate Changes in the Prevalence of the Autism Spectrum Disorders (ASDs)

**Co-Sponsored by the National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC) and Autism Speaks**

## Tuesday, February 1, 2011

## Location: Centers for Disease Control and Prevention,

Tom Harkin Global Communications Center, 1600 Clifton Road, N.E., Atlanta, Georgia
Building 19, Auditorium B1/B2

**7:30–8:00** . ..... **Check-in**

**8:00–8:05** . ..... **Welcome** — *C. Boyle and G. Dawson*

**8:05–10:00** . ..... **Background and purpose**

- What do we know about ASD prevalence? — *M. Yeargin-Allsopp*
  - » General summary of ASD prevalence
- Framework for this meeting — *C. Rice*
  - » What might be influencing temporal patterns in prevalence?
    - * Intrinsic Identification – methodology/measurement
    - * Extrinsic Identification - (awareness and classification)
    - * Risk – (multiple biologic and environmental)
  - » Questions to address (For U.S. service data, ADDM, and the field, more generally)
    - * What we can do now? (analysis with existing data)
    - * What should we do next? (building on existing data systems)
    - * What else is needed? (analyses, data collection, others)
- 8:30–8:45 . ..... A mode for assessing the contribution of various risk factors to recent ASD prevalence increase in the U.S. — *L. Schieve*
  - » Examples using selected prenatal and perinatal risk factors.
- 8:45–9:00 . ..... ASD genetic variation and gene-environment interaction — K. Crider
- 9:00–9:45 . ..... Examples of analyses in progress from the Autism and Developmental Disabilities Monitoring (ADDM) Network
  - » ADDM Network Overview — C. Rice
  - » Changes in ASD diagnostic criteria
  - » Parental age, dx age, SES — M. Durkin
    - * Hypothesis
    - * Methods
    - * Findings
    - * What else could be done to understand ASD trends using this dataset?
    - * What else could be done to understand ASD trends?

**10:00–10:50** . . . . . **ASD Trends: U.S. single source datasets (ED and CA DDS data)**

- U.S. Special Education Data — P. Shattuck
- CA DDS Data — I. Hertz-Picciotto, P. Bearman
  - » Brief overview of evidence of prevalence changes.
  - » What factors contribute to the change in prevalence over time? (is it possible to distinguish the relative contribution of various intrinsic identification, extrinsic identification, and/or risk factors influencing prevalence change?)
  - » What are the strengths/limitations of these approaches?
  - » What else could be done to understand ASD trends using this dataset?
  - » What else is needed to understand ASD trends?

**10:50–11:05** . . . . . **Break**

**11:05–12:30** . . . . . **Lessons from other conditions and analytic methodologies**

- Cancer — R. Etzioni
- Parkinson's — C. Tanner
- Asthma — M. King
- Schizophrenia — E. Susser
- Simulation Studies — S. Galea

Given a change in prevalence/ incidence, what has been done to understand the reason(s)?

- Brief overview of evidence of prevalence changes.
- What factors contribute to the change in prevalence over time? (is it possible to distinguish the relative contribution of various intrinsic identification, extrinsic identification, and/or risk factors influencing prevalence change?)
- What are the strengths/ limitations of these approaches?
- What lessons may be important when looking at reasons for ASD trends?

**12:30–1:00** . . . . . **Open Comment**

**1:00–1:20** . . . . . **Pick up lunch and transition to Panel Breakouts**

**1:20–2:45** . . . . . **Panel Discussion Breakouts**

## Panel 1 – Utility of ASD Prevalence Information (Room 117)

Panel Chair: *A. Singer*

Recorder: *C. Arneson*

**Panelists:** *C. Cunniff, W. Zahorodny, R. Kirby, M. Lopez, R. Grinker, D. Mandell*, L. Grossman*, W. Dunaway, M. Rosanoff, J. Zimmerman, B. Mulvihill, J Charles*

- What does having ASD prevalence information do for stakeholders (parents, professionals, people with

ASD, policy makers, service providers)?

- How are stakeholders actually using ASD prevalence information?
- What types of ASD prevalence information and descriptions of the population are useful to stakeholders?
- What questions do stakeholders expect epidemiology and prevalence reports, in particular, to answer?

## Panel 2 – Other US-Based ASD Data (Room 255)

Panel Chair: *L. Croen*

Recorder: *L. King*

**Panelists:** *P. Shattuck, P. Bearman, M. Kogan, S. Visser, I. Hertz-Piciotto, L. Miller, A. Bakian, K. Van Naarden Braun, L. Lee, T. Baroud, P. Bell, R. Etzioni, Y. Kim*

- What are the top 3 immediate (1–2 year) priority analyses needed to understand ASD trends using existing US-based datasets?
- What are the top 3 next (3–5 year) priority analyses needed to understand ASD trends using existing US-based datasets?
- Can these data systems be enhanced (analyses, data collection, others) to better answer questions about changing prevalence of ASDs? If yes, how? If no, why not and what else is needed?

## Panel 3 – ADDM Network Data (Room 257)

Panel Chair: *G. Dawson*

Recorder: *K. Phillips*

**Panelists:** *S. Galea, G. McGwin, O. Devine, A. Correa, M. Zack, P. Yoon, M. Maenner, J. Daniels, L. Schieve, S. Pettygrove, M. Wingate, J. E. Robison, P. C. Marvin*

- What are the top 3 immediate (1 -2 year) priority analyses needed to understand ASD trends using existing ADDM data?
- What are the top 3 next (3-5 year) priority analyses needed to understand ASD trends using existing ADDM data?
- Can the ADDM Network be enhanced (analyses, data collection, others) to better answer questions about changing prevalence of ASDs? If yes, how? If no, why not and what else is needed?

## Panel 4 –What else could be done to understand ASD Trends? (Room B1/B2)

Panel Chair: *M. Durkin*

Recorder: *R. Fitzgerald*

**Panelists:** *K. Crider, E. Susser, C. Lawler, C. Tanner, M. King, S. Shapira, D. Schendel, J. Nicholas, W. McMahon, J. Constantino, C. Newschaffer, L. Perner, M. Blaxill, E. London, G. Windham, K. Merikangas*

- Can the question of the relative contribution of identification and/or risk factors on ASD prevalence in the last 20 years be answered?
  - » If not, why?
  - » If yes, what are the 3 primary questions which need to be addressed by epidemiology?
- How can the ASD field work with other fields / conditions to evaluate trends (comparison to other conditions, sharing methodology, analytic techniques, etc.)? How best can that be accomplished (give specific

conditions with possible analyses/activities)?

- What else is needed for the ASD larger field to understand reasons for trends?

**2:45–3:00** . ..... **Break**

**3:00–5:00** . ..... **Report from Each Panel (Aud A)**

Facilitator: P. Yoon

- 3:00–4:45 . ..... For Panel 1, 2, 3, and 4
  - » 10 minute summary report for each panel
  - » 15 minute Larger Panel Discussion
- 4:45–5:00 . ..... Meeting adjournment

# Appendix B: Panelist Biographies

Amanda V. Bakian, MS, PhD, is the epidemiologist and data manager for the Utah Registry of Autism and Developmental Disabilities (URADD) and the Utah ADDM Network site. She has collaborated on a variety of research studies investigating the prenatal, perinatal, neonatal, socio-demographic, and environmental risk factors associated with ASDs and intellectual disabilities.

Thaer Baroud, BSN, MA, MHSA, is a senior epidemiologist with the Arkansas comprehensive tobacco control program and he is the epidemiologist for the Arkansas ADDM Network site. He has worked as an epidemiologist at the Arkansas Center for Health Statistics.

Peter Bearman, PhD, is the Director of the Lazarsfeld Center for the Social Sciences, the Cole Professor of Social Science, and Co-Director of the Health & Society Scholars Program at Columbia University. He is currently investigating the social determinants of the autism epidemic. He has researched topics including adolescent sexual networks, networks of disease transmission, genetic influences on same-sex preference, and historical sociology.

Peter Bell, MBA, is Executive Vice President for Programs and Services at Autism Speaks and the father of a son with autism. He oversees the foundation's government relations and family services activities and also serves as an advisor to the science division. Mr. Bell was president and CEO of Cure Autism Now following a marketing career at McNeil Consumer & Specialty Pharmaceuticals, a member of the Johnson & Johnson family of companies.

Mark Blaxill, MBA, is the father of a daughter with autism, editor-at-large for Age of Autism, a director of SafeMinds, and a frequent speaker at autism conferences. He writes often on autism, science, and public policy. In his professional career, he is managing partner for 3LP Advisors, an advisory firm focused on intellectual property transactions.

Coleen A. Boyle, PhD, MSHyg, is the Director of the National Center on Birth Defects and Developmental Disabilities (NCBDDD) at CDC. She has worked on public health issues such as agent orange and cancer. Her interest and expertise is in the epidemiology and prevention of birth defects and developmental disabilities.

Jane Charles, MD, is a Developmental-Behavioral Pediatrician in the Department of Pediatrics at Medical University of South Carolina. Her areas of specialization are in the fields of ASDs and intellectual disabilities. For the past ten years, she has been Co-Principal Investigator for the South Carolina ADDM Network site.

Prisca Chen Marvin, JD, is the mother of a daughter with autism, a member of the Visiting Committee at Massachusetts Institute of Technology's Brain and Cognitive Science Department, a board member of REACH at the University of Iowa, and a Member of the Executive Council of the Associates of the Yale Child Study Center.

John N. Constantino, MD, is the Blanche F. Ittleson Professor of Psychiatry and Pediatrics at Washington University, Associate Director of a Eunice Kennedy Shriver Intellectual and Developmental Disabilities Research Center at the Washington University School of Medicine, and Director of the School's Division of Child Psychiatry. In addition to his role as Principal Investigator of the Missouri ADDM Network site, he leads a federally-funded program in autism research that is centered on a prospective longitudinal study of sibling pairs in families affected by autism.

Adolfo Correa, MD, MPH, PhD, is a Medical Officer and Birth Defects Surveillance Team Lead with the CDC's National Center on Birth Defects and Developmental Disabilities, Birth Defects Branch. He has worked extensively with the Metropolitan Atlanta Congenital Defects Program (MACDP). His current work focuses on surveillance of congenital heart defects and on the epidemiology of maternal diabetes and birth defects.

Krista S. Crider, MA, PhD, is a Geneticist with the CDC's National Center on Birth Defects and Developmental Disabilities, Pediatric Genetics Team. She has worked on epigenetics changes in DNA methylation and folic acid supplementation, antibiotic use and the risk of birth defects, trends in trisomies, and genetics of preterm birth among other projects with the National Birth Defects Prevention Study, Metropolitan Congenital Defects Program, and the China collaboration.

Lisa A. Croen, PhD, is a Senior Research Scientist and the Director of the Kaiser Permanente® Autism Research Program. Currently, she is leading or collaborating on several federally funded autism studies, including the Study to Explore Early Development (SEED), the Early Autism Risk Longitudinal Investigation Study (EARLI), the Early Markers for Autism Study (EMA), the California Autism Twins Study (CATS), and the Mental Health Research Network Autism Registry project.

Christopher Cunniff, MD, FACMG, FAAP, is a Professor of Pediatrics and Chief of the Section of Medical and Molecular Genetics at the University of Arizona, College of Medicine. His research focuses on public health genetics and the surveillance of developmental disabilities including ASDs, intellectual disability, muscular dystrophy, and fetal alcohol syndrome.

Julie Daniels, PhD, is a pediatric epidemiologist and Associate Professor in the Department of Epidemiology and Maternal and Child Health at University of North Carolina at Chapel Hill. She is the Principal Investigator of the North Carolina ADDM Network site and the CDC's Study to Explore Early Development (SEED) North Carolina site since 2002. Her research focuses on perinatal exposures, specifically nutrition and environmental exposures that may be associated with child health and development.

Geraldine Dawson, PhD, is Chief Science Officer for Autism Speaks, Research Professor of Psychiatry at the University of North Carolina at Chapel Hill, Adjunct Professor of Psychiatry at Columbia University, and Professor Emeritus of Psychology at University of Washington. She is a licensed clinical psychologist who has published extensively on autism, focusing on early detection and intervention and early patterns of brain dysfunction.

Owen Devine, PhD, is a Mathematical Statistician with the CDC's National Center on Birth Defects and Developmental Disabilities. He provides guidance on the analysis of epidemiologic data related to birth defects and developmental disabilities. His areas of interest included Bayesian methods, missing and miss measured data, and the interface of mathematical modeling and statistical techniques as applied to public health.

Wolf F. Dunaway works for the federal government as an Information Technology Specialist. He speaks at various colleges, universities, and symposiums on issues associated with autism and other disabilities and helps others better understand childhood autism through his own autism life experiences.

Maureen Durkin, PhD, DrPH, is a Professor of Population Health Sciences and Pediatrics and Waisman Center Investigator at the University of Wisconsin-Madison and the Principal Investigator of the Wisconsin ADDM Network site. She is an epidemiologist specializing in population-based studies of the frequency, prevention, antecedents, and consequences of developmental disabilities.

Ruth Etzioni, PhD, is a biostatistician and a full member at the Fred Hutchinson Cancer Research Center in Seattle. She studies population trends in prostate cancer incidence and mortality and is one of the principal investigators on the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network. She is currently adapting models for use in policy development for PSA screening.

Sandro Galea, MD, MPH, DrPH, is a physician, epidemiologist, and the Anna Cheskis Gelman and Murray Charles Gelman Professor and Chair of the Department of Epidemiology at Columbia University's Mailman School of Public Health. He has conducted large population-based studies in several countries,

and his primary research has been on the causes of mental disorders, substance abuse and on the role of traumatic events in shaping population health.

Roy Richard Grinker, PhD, is Professor of Anthropology at the George Washington University and editor-in-chief of The Anthropological Quarterly. He has published on topics such as the ethnic conflict in central Africa, intellectual history of African Studies, north-south Korean relations, and autism. He was a collaborator on a prevalence study of autism in South Korea and is a Co-Investigator on an NIMH-funded project entitled "Early Social Communication Characteristics of ASD in Diverse Cultures in the US and Africa".

Lee Grossman*, CAE, was the President and CEO of the Autism Society of America through early 2011 and the father of a son with autism. He has more than 20 years of experience with autism related issues, notably autism services and supports, adult issues, education, and research. He has served on numerous government and non-government advisory boards related to autism. Mr. Grossman has owned and operated a small business specializing in marketing, distribution, and consulting for medical manufacturers throughout the Pacific Basin.

Irva Hertz-Picciotto, PhD, is a Professor of Health Sciences at the University of California, Davis. She has published extensively on the effects of environmental exposures on pregnancy and child development. She is the Principal Investigator of CHARGE (Childhood Autism Risks from Genetics and Environment) Study, the first large, comprehensive population-based study of environmental factors in autism, and MARBLES (Markers of Autism Risk in Babies – Learning Early Signs), to search for early biologic markers that will predict autism.

Young Shin Kim, MD, MPH, PhD, is a researcher at Yale University. Her major research efforts focus on school bullying, the epidemiology of childhood onset neuropsychiatric disorders, and the genetic epidemiology of childhood onset neuropsychiatric disorders. She was the lead author on an epidemiological study of ASD prevalence in South Korea.

Michael King MSW, PhD, is a Commander in the US Public Health Service and an epidemiologist with the CDC's National Center for Environmental Health, Division of Environmental Hazards & Health Effects, Air Pollution and Respiratory Health Branch. His research has focused on using national surveys to monitor asthma-related morbidity, health-service use, and other respiratory health outcomes, including unintentional carbon monoxide poisoning.

Russell S. Kirby, PhD, MS, FACE, is Professor and Marrell-endowed Chair in the Department of Community and Family Health, College of Public Health, University of South Florida. He is a pediatric and perinatal epidemiologist with extensive experience in population health informatics and public health surveillance of birth defects and developmental disabilities and has been involved with the ADDM Network since 2002.

Michael D. Kogan, PhD, is Director of the Office of Epidemiology, Policy, and Evaluation for the US Health Resources and Services Administration's Maternal and Child Health Bureau. He also directs the US National Surveys of Children's Health and the National Surveys of Children with Special Health Care Needs. He has published over 100 articles and book chapters on numerous topics in pediatric and perinatal epidemiology, including the prevalence of ASDs, as well as the health care experiences of families with children who have an ASD.

Cindy Lawler, PhD, is a Program Director in the Division of Extramural Research and Training at the National Institute for Environmental Health Sciences (NIEHS), one of the National Institutes of Health. She is the NIEHS representative for extramural autism activities; this includes responsibilities as a program official for the NIH-funded Early Autism Risk Longitudinal Investigation (EARLI) study.

Li-Ching Lee, PhD, ScM, is a Research Scientist with the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health at the Johns Hopkins University. She has a background is in psychiatric epidemiology and a research interest in developmental disabilities in the US, China, and Taiwan. She has been involved with Maryland ADDM Network site since early in its inception and is currently the Principal Investigator.

Eric London, MD, is trained as a general psychiatrist and has a son with autism. He and his wife started the National Alliance for Autism Research (NAAR) in 1994, which later merged with Autism Speaks. He now serves on the Board of the Autism Science Foundation. Dr. London was the Director of the Autism Treatment Laboratory at the New York State Institute for Basic Research, and is now the Research Director at the the Center for Discovery in Harris, New York. His primary interests are in very early identification of autism and creating novel methods for autism treatment research.

Maya Lopez, MD, is a Developmental-Behavioral Pediatrician and Assistant Professor in the Developmental-Behavioral and Rehabilitative Pediatrics in the Department of Pediatrics College of Medicine at University of Arkansas Medical Sciences. She is the current Principal Investigator on the Autism Treatment Network (ATN) Grant for her institution and is Co-Principal Investigator for the Arkansas ADDM Network site.

David S. Mandell*, ScD, is Associate Professor of Psychiatry and Pediatrics at the University of Pennsylvania School of Medicine, an Associate Director of the Center for Mental Health Policy and Services Research, and Associate Director of the Center for Autism Research at The Children's Hospital of Philadelphia. The goal of his research is to improve the quality of care individuals with autism receive in their communities.

Matthew Maenner is a PhD candidate at the University of Wisconsin and works as an epidemiologist and data manager for the Wisconsin site of the ADDM network. He is currently funded by the Autism Science Foundation to explore the phenotypic heterogeneity of autism and its relationship to early identification.

Gerald McGwin, PhD, is a Professor and Vice Chairman in the Department of Epidemiology in the School of Public Health at the University of Alabama at Birmingham. He is an associate editor for the American Journal of Epidemiology, and has a lengthy and distinguished scientific reputation as a researcher, having authored or co-authored over 300 peer-reviewed manuscripts, with an emphasis on injury and ophthalmic epidemiology.

William M. McMahon, MD, is the Chairman of the Department of Psychiatry and a Professor of Psychiatry, Pediatrics, Psychology and Educational Psychology at the University of Utah. His research interests include the genetics and epidemiology of autism, Tourette's Disorder, nicotine addiction, and suicide. He is a Senior Investigator for the Autism Genome Project and is currently Principal Investigator of an Autism Speaks funded follow-up study of the Utah Autism Studies sample.

Kathleen Ries Merikangas, PhD, is a Senior Investigator and Chief of the Genetic Epidemiology Branch in the Intramural Research Program at the National Institute of Mental Health (NIMH). Her research interests have included clinical research on affective disorders and genetic epidemiology.

Lisa Miller, MD, MSPH, is the director of the Disease Control and Environmental Epidemiology Division at the Colorado Department of Public Health and Environment. She is the Co-Principal Investigator of the CDC-funded Colorado sites of the ADDM Network site and the Study to Explore Early Development (SEED). She currently directs epidemiologic programs concerning communicable diseases, environmental health, autism, and muscular dystrophy.

Beverly Mulvihill MEd, PhD, is currently an Associate Professor in the Department of Health Care Organization and Policy and a Research Scientist with the Civitan International Research Center at the University of Alabama at Birmingham. She has been Principal Investigator or Co-Principal Investigator of the Alabama ADDM Network site since 2008. Her research interests include child development; children with and at-risk for disabilities, especially autism spectrum disorders; and early identification, intervention, and inclusion for children in need of special services.

Craig Newschaffer, PhD, is Professor and Chairman of the Department of Epidemiology and Biostatistics at Drexel University School of Public Health. He leads an NIH-funded EARLI Study, which is designed specifically to study pre, peri- and neonatal autism risk factors and biomarkers. He is also a Principal Investigator on other major autism epidemiology initiatives. Prior to focusing his research on autism, he worked extensively in cancer epidemiology.

Joyce S. Nicholas PhD, is an Associate Professor in the Medical University of South Carolina's Department of Medicine, Division of Biostatistics and Epidemiology, with a dual appointment in the Department of Neurosciences. She specializes in neuro-epidemiology, in particular neurodevelopmental and other neurologic conditions. She is a Co-Principal Investigator for the South Carolina ADDM Network site.

Lars Perner, PhD, is an Assistant Professor of Clinical Marketing at the Marshall School of Business of the University of Southern California. His research interests focus on consumer behavior, "win-win" deals, non-profit marketing, and autism subtypes. He currently serves as Chair of the Panel of Persons on the Spectrum of Autism Advisors for the Autism Society.

Sydney Pettygrove, PhD, is an Assistant Professor of Epidemiology, College of Public Health, at the University of Arizona, Tucson. She primarily works on the effects of environmental and occupational exposures on reproductive outcomes including birth defects and developmental disabilities. She is the Co-Principal Investigator of the Arizona ADDM Network site.

Catherine E. Rice, PhD, is an Epidemiologist with CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch and has worked with people with an ASD through teaching, diagnostic assessment, intervention, training, and research. She has been a lead scientist with the ADDM Network since 2001. She works on public health programs related to autism with specific interests in early identification, diagnosis, prevalence, and risk factors for autism.

John Elder Robison is a self-identified "free range" Aspergian male. He is the founder of a specialty automobile company, pioneered specialty guitars for the band KISS, and worked on some of the first talking toys for Milton Bradley. He serves as adjunct faculty in the department of Communication Sciences and Disorders at Elms College in Massachusetts and has served on several national autism science boards as a community member. He is the author of Look Me in the Eye: My life with Asperger's.

Michael Rosanoff, MPH, is the Associate Director of Public Health Research and Scientific Review for Autism Speaks. He is a member of Autism Speaks etiology team and manages the organization's epidemiology and public health research grants. He is also the staff lead in overseeing the International Autism Epidemiology Network (IAEN) and is part of the development team for the Global Autism Public Health Initiative (GAPH).

Diana E. Schendel, PhD, is Lead Health Scientist and Epidemiology Team Lead with the CDC's National Center for Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. She serves as Principal Investigator for the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) which includes the Study to Explore Early Development (SEED). She is Project Lead for the International Collaboration for Autism Registry Epidemiology (iCARE). Her research interests include risk factors for cerebral palsy and autism.

Laura A. Schieve, PhD is an Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. Dr. Schieve is one of the Principal Investigators on the CDC's Study to Explore Early Development (SEED). Her current research includes prevalence of autism and other developmental disabilities, maternal and perinatal risk factors for developmental disability, health care needs and family functioning in families with a disabled child, and epidemiologic methods for assessing maternal and child risk factors in populations.

Stuart K. Shapira, MD, PhD, is a Medical Officer with CDC's National Center on Birth Defects and Developmental Disabilities, Pediatric Genetics Team. He is an investigator on the CDC Study to Explore Early Development (SEED). His current interests include birth defects epidemiologic research, dysmorphology of autism, gene and nutritional interactions for adverse reproductive outcomes, and newborn screening.

Paul T. Shattuck, PhD, is an Assistant Professor at the George Warren Brown School of Social Work at Washington University in St. Louis. Dr. Shattuck conducts research aimed at improving systems of care and services for people with autism and their families. He is especially interested in two key service transitions: getting a diagnosis in early childhood and exiting high school in adolescence.

Ezra Susser, MD, DrPH, is Professor of Epidemiology and Psychiatry at Columbia University. Dr. Susser heads the Imprints Center for Genetic and Environmental Lifecourse Studies, a collaborative birth cohort research program in which epidemiologists seek to uncover the causes of a broad range of disease and health outcomes, including psychiatric and neurodevelopmental disorders, obesity, cardiovascular disease, reproductive performance, and breast and ovarian cancers. His own studies focus on schizophrenia and autism.

Alison Singer, MBA, is Co-Founder and President of the Autism Science Foundation, a not-for-profit organization that funds autism research and serves to increase awareness of ASDs and the needs of individuals and families affected by autism. She has been very involved in advocacy for autism as the mother of a child with autism and legal guardian of her adult brother with autism. She spent 14 years at CNBC and NBC in a variety of positions, including vice president of programming in NBC's cable and business development division and as a producer. Ms. Singer has served on several research, advocacy, and government advisory boards for autism.

Caroline M. Tanner, MD, PhD, FAAN, is Director of Clinical Research at the Parkinson's Institute in Sunnyvale, California, a Visiting Professor at Xuan Wu Hospital and Capital University in Beijing, China, and an Adjunct Professor in the Department of Health Research and Policy at Stanford University. Her current research includes epidemiologic investigations of the genetic and environmental determinants of Parkinson's disease, multiple system atrophy, dystonia, Huntington's disease and essential tremor in a variety of populations in the US.

Kim Van Naarden Braun, PhD, is an Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch and with the New Jersey Department of Health and Senior Services. She is the Principal Investigator for the Metropolitan Atlanta Developmental Disabilities Surveillance Program (MADDSP) and also serves an epidemiologist for the ADDM Network and the ADDM Cerebral Palsy Network. Research interests include developmental disabilities, perinatal epidemiology, genetic epidemiology, environmental health, and child health and development.

Susanna Visser, MS, is the lead Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Child Development Studies Team. Her current research interests include population-based epidemiological studies of neurobehavioral and mental health conditions, including ADHD and Tourette Syndrome, medication treatment among youth with ADHD, and factors associated with ADHD medication treatment.

Gayle Windham, PhD, is a Research Scientist and Chief of the Epidemiological Surveillance Section at the California Department of Public Health in the Division of Environmental and Occupational Disease Control. She currently works with the Centers for Autism and Developmental Disabilities Research (CADDRE) team and is the lead investigator on a study of early ASD prevalence in California. Her areas of research and expertise include children's health in relation to environmental risk factors, pregnancy outcomes such as spontaneous abortion and fetal growth, and other aspects of reproductive health including puberty, infertility, and menstrual function.

Martha S. Wingate, DrPH, is an Assistant Professor at University of Alabama at Birmingham in the Department of Health Care Organization and Policy. She is the Co-Principal Investigator of the Alabama ADDM Network site. Much of her work focuses on preterm birth, fetal and infant mortality, racial and ethnic disparities in birth outcomes, and health policies related to pregnancy and infant health.

Marshalyn Yeargin-Allsopp, MD, is a Medical Epidemiologist and Branch Chief with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. She designed and implemented the first U.S. population-based study of developmental disabilities in school-age children in an urban area, which has served as the basis for the ADDM Network and the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE). She has presented internationally and published extensively on the epidemiology of developmental disabilities, including autism and cerebral palsy.

Paula Yoon, MPH, ScD, is currently the Team Lead for the Health Services Research and Registries Team in the Division for Heart Disease and Stroke Prevention, Epidemiology and Surveillance Branch. She is also leading an initiative to establish a National Cardiovascular Disease Surveillance System. She is the Chair of the Surveillance Science Advisory Group at CDC and is spearheading an effort to develop an agency-wide surveillance report to track the impact of health care reform on prevention in health care.

Matthew Zack, MD, is a Medical Epidemiologist with the CDC's National Center for Chronic Disease Prevention and Health Promotion, Division of Adult and Community Health, State Support, Arthritis, Epilepsy, & Quality of Life Branch. He has worked extensively on issues related to chronic diseases and environmental health.

Walter Zahorodny, PhD, is a clinical psychologist and Assistant Professor of Pediatrics at the New Jersey Medical School. He has over twenty years of experience in pediatric neurodevelopment and is the Principal Investigator of the New Jersey ADDM Network site for population-based ASD surveillance system. He is a founding member of the New Jersey Medical School Autism Center and was instrumental in development of the New Jersey Governor's Council on Medical Research and Treatment of Autism.

Judith Pinborough Zimmerman, PhD, CCC, is an Assistant Professor in the Department of Psychiatry at the University of Utah. She is the for the Utah Registry for Autism and Developmental Disabilities (URADD) and the Principal Investigator for the Utah ADDM Network site. She is particularly interested in the utility of ASD prevalence data for state Maternal and Child Health Programs.

## RECORDERS

Carrie Arneson, MSc, serves as Project Coordinator for the Wisconsin ADDM Network site located at the Waisman Center at University of Wisconsin-Madison.

Jon Baio, EdS, is an Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. He currently serves as Principal Investigator on the ADDM Network, studying the prevalence of autism and other developmental disabilities in several communities throughout the U.S.

Thomas A. Bartenfeld, PhD, specializes in program evaluation with the CDC's National Center on Birth Defects and Developmental Disabilities. His most recent work has focused on using evaluation to promote information to action and organizational integration with NCBDDD's surveillance, research, and prevention programs.

Robert Fitzgerald, MPH is currently a staff scientist in the Department of Psychiatry at the Washington University School of Medicine in St. Louis, and is a PhD candidate in Epidemiology at the St. Louis University School of Public Health. He has served as Project Coordinator for the Missouri ADDM Network site since its inception in 2003 and has served as Co-Principal Investigator since April of 2009.

Lydia King, PhD, is an Assistant Professor of Pediatrics at the Medical University of South Carolina and is an Epidemiologist specializing in ASDs. She has served as the Project Coordinator for the South Carolina ADDM site since 2003. She is also Faculty Director for the Global Education Masters in Clinical Research Program.

Keydra Phillips, MSc, is a Health Scientist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. She is a member of an interdisciplinary team of researchers of the ADDM Network, and her research interests include public health informatics and surveillance of chronic diseases.

Andria M. Ratchford, MSPH, has served as the Project Coordinator for the Colorado ADDM Network site at the Colorado Department of Public Health and Environment since 2002. She has considerable surveillance and project management experience through her experience with ADDM and the Colorado Center of Autism and Developmental Disabilities Research and Epidemiology (CADDRE) activities.

Anita Washington, MPH, is a Research Public Health Analyst with Research Triangle Institute (RTI) as part of the Atlanta Regional Office. For the past 6 years, she has been working as a contract employee in the role of the ADDM Network Project Coordinator for CDC's National Center on Birth Defects and Developmental Disabilities, Division of Birth Defects and Developmental Disabilities, Developmental Disabilities Branch.

**Invited participant unable to attend remotely or in-person at last minute due to unforeseen circumstances.*

# Appendix C: Reference List

References were compiled based on panel member nominations for suggested background reading on ASD prevalence.

Panel members were asked to read the articles indicated with an * prior to the workshop.

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# Notes

# Notes

Centers for Disease Control and Prevention
www.cdc.gov/autism
cdcinfo@cdc.gov
1-800-CDC-INFO

Autism Speaks
www.autismspeaks.org
research@autismspeaks.org
1-212-252-8584

CS225567

**From:** Boyle, Coleen (CDC/ONDIEH/NCBDDD)
**Sent:** 30 Jan 2012 15:33:11 +0000
**To:** Alex Kemper, M.D.;Chris Kus;Maribeth Ostrander;Anne Comeau;Dougherty, Denise (AHRQ);Marie Mann;Jeff Botkin;Green, Nancy
**Subject:** POC Manuscript -- CDC clearance
**Attachments:** Implementing Point-of-Care Newborn Screening.docx

Hi All: To put this manuscript through CDC publication clearance, I will need an email statement from each of you indicating your '*approval of the paper entitled "Implementing Point of Care Newborn Screening" for CDC Clearance'*. You can just cut and paste if you like.

Thanks,

Coleen

*Coleen A. Boyle, PhD, MS Hyg*
Director, National Center on Birth Defects and Developmental Disabilities
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**From:** Alex Kemper, M.D. [mailto:alex.kemper@duke.edu]
**Sent:** Sunday, December 18, 2011 2:32 PM
**To:** Jill Shuger; Sara Copeland; Chris Kus; Maribeth Ostrander; Anne Comeau; Boyle, Coleen (CDC/ONDIEH/NCBDDD); Dougherty, Denise (AHRQ); Marie Mann; Jeff Botkin
**Cc:** Green, Nancy
**Subject:** Next Draft

Nancy and I would like to thank everyone for their thoughtful and helpful comments. We've combined them all here into the attached draft. Please let us know if we have fully captured the important points.

Thanks so much,

Alex

**Implementing Point-of-Care Newborn Screening**

Short Title: Point-of-Care Newborn Screening

Alex R. Kemper, MD, MPH, MS[1]
Christopher A. Kus, MD, MPH[2]
Robert J. Ostrander, MD[3]
Anne Marie Comeau, PhD[4]
Coleen A. Boyle, PhD[5]
Denise Dougherty, PhD[6]
Marie Y Mann, MD, MPH[7]
Jeffrey R. Botkin, MD, MPH[8]
Nancy S. Green, MD[9]
on behalf of the United States Secretary of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children

[1]Department of Pediatrics, Duke University, Durham, NC
[2]New York State Department of Health, Albany, NY
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Figures: 0 Tables: 0

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**Conflict of Interest Notification Page**

**Conflict of Interest:** None of the authors has a commercial association that might pose or create a conflict of interest with the information presented in this manuscript.

**Disclaimer:** The views expressed in this article are those of the authors and do not necessarily reflect those of the authors' respective agencies within the U.S. Department of Health and Human Services or the U.S. Department of Health and Human Services.

**Abstract**

Newborn screening is performed under public health authority, with analysis primarily performed by public health or other centralized laboratories. Increasingly, opportunities to improve infant health will arise from including screening tests that are completed within individual birth centers instead of in centralized laboratories. This is a paradigm shift for which the roles of those involved in screening have not been resolved. This report summarizes a framework developed by the United States Secretary of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children for evaluating whether conditions identifiable through point-of-care screening should be added to the recommended universal screening panel and to identify key considerations for birth hospitals, public health agencies, and clinicians when point-of-care newborn screening is implemented.

**Abbreviations:** dried-blood spots (DBS), Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC), United States Preventive Services Task Force (USPSTF)

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(b)(5)

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**From:** Washington, Anita (CDC/ONDIEH/NCBDDD)
**Sent:** 13 May 2013 19:15:29 -0400
**To:** 'Eric Lott';mslay@uab.edu;Julie K Preskitt (preskitt@uab.edu);kirby S. Russell (CDC health.usf.edu);'Chris Cunniff';'Sydney Pettygrove';'kgotscha@email.arizona.edu';Mancilla, Kristen M C - (kclancy);Lopez, Maya L;Thaer Baroud;Hudson, Allison;Ghosh, Tista (CDC state.co.us);Kast - CDPHE, Kelly;Li-Ching Lee;'achang@jhsph.edu';Fitzgerald, Robert;'John Constantino';'Josephine P Shenouda';'zahorodn@umdnj.edu';Daniels, Julie L;'Jane Charles';'Joyce Nicholas';'Walter Jenner';'Lydia King';'Carpenter, Laura Arnstein';William McMahon;Deborah Bilder (Deborah.Bilder@hsc.utah.edu);'AMANDA BAKIAN';colin.kingsbury@hsc.utah.edu;'Maureen Durkin';'Carrie Arneson - WI (clarneso@wisc.edu)';kalkbren@uwm.edu;amy@ursid.com;'mmorrie@emory.edu';Talboy, Amy (Amy.Talboy@choa.org);Wright, Victoria (CDC/OCOO/OD);Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD);Baio, Jon (CDC/ONDIEH/NCBDDD);Rice, Catherine (CDC/ONDIEH/NCBDDD);Christensen, Deborah (Daisy) (CDC/ONDIEH/NCBDDD);Green, Santrell (CDC/ONDIEH/NCBDDD) (CTR);Jones, Lekeisha F. (CDC/OD/OADC);Goodman, Alyson B. (CDC/ONDIEH/NCCDPHP);Schieve, Laura (CDC/ONDIEH/NCBDDD);Wiggins, Lisa (CDC/ONDIEH/NCBDDD);Chan, C. Leah (CDC/ONDIEH/NCBDDD);Tian, Lin Hui (CDC/ONDIEH/NCBDDD);Van Naarden-Braun, Kim (CDC/ONDIEH/NCBDDD);Barritt, Lisa (CDC/ONDIEH/NCBDDD);Jolly, Kwinettaion (CDC/ONDIEH/NCBDDD);Frenkel, Gal (CDC/ONDIEH/NCBDDD);Augustus, Eric L. (CDC/ONDIEH/NCBDDD) (CTR);Williams, Susan (CDC/ONDIEH/NCBDDD);Cleveland, Michael (CDC/ONDIEH/NCBDDD) (CTR);Bell, Paula;Hobson, Nancy (CDC/ONDIEH/NCBDDD) (CTR);Dirienzo, Monica A. (CDC/ONDIEH/NCBDDD) (CTR);Clayton, Heather B. (CDC/OID/NCHHSTP);lynn.almli@emory.edu;Talboy, Amy (Amy.Talboy@choa.org);Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD);Boyle, Coleen (CDC/ONDIEH/NCBDDD);Shapira, Stuart (CDC/ONDIEH/NCBDDD);Devine, Owen (CDC/ONDIEH/NCBDDD) (CTR);Stevens, Melody (CDC/ONDIEH/NCBDDD);Sniezek, Joe (CDC/ONDIEH/NCBDDD);Honein, Margaret (Peggy) (CDC/ONDIEH/NCBDDD);Moore, Cynthia (CDC/ONDIEH/NCBDDD);Dowling, Nicole (CDC/ONDIEH/NCBDDD);Whitney, Julia (CDC/ONDIEH/NCBDDD) (CTR);Washington, Anita (CDC/ONDIEH/NCCDPHP)
**Subject:** Updated ADDM Meeting Agenda
**Attachments:** ADDM Network Meeting Agenda for May 14-16 2013.docx

Hi everyone,
I made a few updates to the agenda. I'll see everyone in the lobby of the hotel at 7:50am tomorrow.

Thank you,
Anita

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**From:** Washington, Anita (CDC/ONDIEH/NCBDDD)
**Sent:** Wednesday, May 08, 2013 7:29 PM
**To:** 'Eric Lott'; mslay@uab.edu; Julie K Preskitt (preskitt@uab.edu); kirby S. Russell (CDC health.usf.edu); 'Chris Cunniff'; 'Sydney Pettygrove'; 'kgotscha@email.arizona.edu'; Mancilla, Kristen M C - (kclancy); Lopez, Maya L; Thaer Baroud; Hudson, Allison; Ghosh, Tista (CDC state.co.us); Kast - CDPHE, Kelly; Li-Ching Lee; 'achang@jhsph.edu'; Fitzgerald, Robert; 'John Constantino'; 'Josephine P Shenouda'; 'zahorodn@umdnj.edu'; Daniels, Julie L; 'Jane Charles'; 'Joyce Nicholas'; 'Walter Jenner'; 'Lydia King'; 'Carpenter, Laura Arnstein'; William McMahon; Deborah Bilder (Deborah.Bilder@hsc.utah.edu); 'AMANDA BAKIAN'; colin.kingsbury@hsc.utah.edu; 'Maureen Durkin'; 'Carrie Arneson - WI (clarneso@wisc.edu)'; kalkbren@uwm.edu; amy@ursid.com; 'mmorrie@emory.edu'; Talboy, Amy (Amy.Talboy@choa.org); Wright, Victoria (CDC/ONDIEH/NCBDDD);

Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD); Baio, Jon (CDC/ONDIEH/NCBDDD); Rice, Catherine (CDC/ONDIEH/NCBDDD); Christensen, Deborah (Daisy) (CDC/ONDIEH/NCBDDD); Green, Santrell (CDC/ONDIEH/NCBDDD) (CTR); Jones, Lekeisha F. (CDC/ONDIEH/NCBDDD); Goodman, Alyson B. (CDC/ONDIEH/NCBDDD); Schieve, Laura (CDC/ONDIEH/NCBDDD); Wiggins, Lisa (CDC/ONDIEH/NCBDDD); Franklin, C. Leah (CDC/ONDIEH/NCBDDD) (CTR); Tian, Lin Hui (CDC/ONDIEH/NCBDDD); Van Naarden-Braun, Kim (CDC/ONDIEH/NCBDDD); Barritt, Lisa (CDC/ONDIEH/NCBDDD) (CTR); Jolly, Kwinettaion (CDC/ONDIEH/NCBDDD) (CTR); Frenkel, Gal (CDC/ONDIEH/NCBDDD); Augustus, Eric L. (CDC/ONDIEH/NCBDDD) (CTR); Williams, Susan (CDC/ONDIEH/NCBDDD); Cleveland, Michael (CDC/ONDIEH/NCBDDD) (CTR); Bell, Paula; Hobson, Nancy (CDC/ONDIEH/NCBDDD) (CTR); Dirienzo, Monica A. (CDC/ONDIEH/NCBDDD) (CTR); Clayton, Heather B. (CDC/ONDIEH/NCBDDD); lynn.almli@emory.edu
**Cc:** Washington, Anita (CDC/ONDIEH/NCBDDD)
**Subject:** ADDM Meeting Agenda

Hi Everyone,

Please see attached the final agenda for our meeting. If you have any questions please let me know.

Thanks,
Anita

Anita Washington, MPH
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**Telework: Thursday – 678-984-4698**

**Autism and Developmental Disabilities Monitoring (ADDM) Network**
**Agenda for May 2013 Investigator Meeting**
**Building 19, Tom Harkin Global Communications Center**
**Centers for Disease Control and Prevention**
**Atlanta, Georgia**
**May 14-16, 2013**

## Tuesday, May 14 (Distance Learning Auditorium)*

| Time | Topic | Presenter | Room |
|---|---|---|---|
| **8:00 - 8:30** | **Arrive at CDC and check-in / load presentations** | | |
| **8:30 - 8:45** | **Welcome and introductions** | Jon Baio | **DLA*** |
| **8:45 - 10:00** | **Preliminary SY2010 ASD prevalence data**<br>a. Preliminary findings<br>b. Topics to highlight in manuscript<br>c. SY2010 ASD prevalence reporting and trend comparisons | Jon Baio | **DLA** |
| **10:00 - 10:15** | **Break** | | |
| **10:15 - 11:30** | **Preliminary SY2010 Early ADDM ASD prevalence data**<br>a. Preliminary findings<br>b. Topics to highlight in manuscript<br>c. Options for reporting Early ADDM ASD prevalence results | Daisy Christensen | **DLA** |
| **11:30 - 1:00** | **Lunch** (CDC cafeteria or Emory Point across from CDC)<br>**CP SIG working lunch** (neuroimaging discussion) | | **116** |
| **1:00 - 1:45** | **Preliminary SY2010 ID surveillance data** | Sydney Pettygrove | **DLA** |
| **1:45 - 2:30** | **Preliminary SY2010 CP surveillance data** | Daisy Christensen | **DLA** |
| **2:30 - 2:45** | **Break** | | |
| **2:45 - 4:00** | **Denominator discussion**<br>a. Curtailing for SY2010<br>b. Planned discussions with concerned parties; Trend analyses<br>c. Manuscript on choice of denominator | <br>Jon / Daisy<br>Kim Van Naarden Braun<br>Amy Kalkbrenner | **DLA** |
| **4:00 - 4:45** | **Miscellaneous discussions**<br>a. Updated confidentiality policy for SY2012/ARCHEv4<br>b. Public use datasets<br>c. Informal discussion of community outreach activities in ADDM sites, new ideas for data dissemination | <br>Anita Washington<br>Jon Baio<br>(moderator TBD) | **DLA** |
| **5:00** | **A walk in the park** (meet at Emory Conference Center) | | |
| **6:30** | **Group dinner at Highland Tap** (meet at Emory Conference Center) | | |

**Autism and Developmental Disabilities Monitoring (ADDM) Network**
**Agenda for May 2013 Investigator Meeting**

**Wednesday, May 15**

| Time | Topic | Presenter | Room |
|---|---|---|---|
| **8:30 - 9:00** | **Arrive at CDC and check-in / load presentations** | | **CDC** |
| **9:00 - 10:30** | **Methodologic analyses and evaluations in-progress** | | **247/248** |
| | a. ICD and exceptionality DNR | Kim Van Naarden Braun | |
| | b. Sensitivity analysis | Julie Daniels | |
| | c. Trigger analysis | Carrie Arneson | |
| **10:30 - 10:45** | **Break** | | |
| **10:45 - 11:45** | **Scientific analyses and evaluations in-progress** | | **247/248** |
| | a. DSM-IV and discriminator analysis | Sydney Pettygrove | |
| | b. Manuscript on maternal prenatal weight gain | Deb Bilder | |
| | c. NC spatial time trend analysis | Julie Daniels | |
| **11:45 - 1:00** | **Lunch** (CDC cafeteria or Emory Point across from CDC)<br>**Available meeting rooms : 245 and 246** | | |
| **1:00 - 1:45** | **SY2012 timeline and updates** | | **247/248** |
| | a. Abstraction and clinician review | Anita Washington | |
| | b. Phase 4 ADDM FOA | Jon Baio | |
| **1:45 - 2:45** | **Workgroup formation** | | **247/248** |
| | a. Reconstituting the Spatial Analysis Workgroup | Amanda Bakian | |
| | b. Charge for a DSM-5 Workgroup | Jon Baio | |
| | c. Updates on DSM-5 transition | L. Carpenter & C. Rice | |
| **2:45 - 3:00** | **Break** | | |
| **3:00 - 3:30** | **SharePoint system for tracking proposals and analyses in-progress** | Leah Franklin | **247/248** |
| **3:30 - 5:00** | **Break-out session for Principal Investigators on datasharing policy** | Jon Baio | **247/248** |
| | a. Satisfaction with proposal submission/approval process | | |
| | b. Tracking site-specific analyses | | |
| | c. Ideas for new tracking system | | |
| **3:30 - 5:00** | **Break-out session for Project Coordinators** | Anita Washington | **245** |
| | a. QC Workgroup | Lisa Barritt | |
| | b. Training needs (Abstraction/Clinician Review) | Lisa Barritt | |
| | c. ARCHE v4 | E. Augustus & K. Jolly | |
| | d. ASD and CP Community Reports | Leah Franklin | |
| | e. Manuscript ideas? | Anita Washington | |
| **6:00** | **Small-group dinners at various Emory Point restaurants** | | |

## Autism and Developmental Disabilities Monitoring (ADDM) Network
## Agenda for May 2013 Investigator Meeting

**Thursday, May 16**

| Time | Topic | Presenter | Room |
|---|---|---|---|
| 8:30 - 9:00 | Arrive at CDC and check-in | | **CDC** |
| **9:00 - 12:00** | **ADDM Paper Group (9:00-9:30)**<br>Multi04: Follow-up on parental age and birth order on the prevalence of ASD using 2002, 2006, and 2008 | | **246** |
| | **ADDM Paper Group (9:30-10:00)**<br>Multi12: Follow manuscript on the association between the prevalence of ASD and SES, 2002-2008 | | **246** |
| | **ADDM Paper Group (10-10:30)**<br>Multi24: Trends over time (2002-2008) in the association between the prevalence of ASD and 2000 and 2010 census based measures of SES | | **246** |
| | **ADDM Paper Group (10:30-11)**<br>Multi22: Relationship between ASD prevalence and ADDM Network catchment area characteristics, 2002-2008 | | **246** |
| **12:00 - 1:00** | **Lunch** (CDC cafeteria or Emory Point across from CDC) | | |
| **1:00 - 5:00** | **ADDM Paper Groups / Atlanta Community Engagement Event** | | |

**From:** jjcannell@vitamindcouncil.org
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**Subject:** new paper

**Attachments:** 2014 Faroe Vtamin D JADD.pdf

Dear Expert:

I attach the first family study of ASD and vitamin D with Christopher Gillberg as senior author.

It suggests the genetics of ASD may be connected to the genetics of the vitamin D system.

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ORIGINAL PAPER

# Vitamin D in the General Population of Young Adults with Autism in the Faroe Islands

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**Abstract** Vitamin D deficiency has been proposed as a possible risk factor for developing autism spectrum disorder (ASD). 25-Hydroxyvitamin $D_3$ ($25(OH)D_3$) levels were examined in a cross-sectional population-based study in the Faroe Islands. The case group consisting of a total population cohort of 40 individuals with ASD (aged 15–24 years) had significantly lower $25(OH)D_3$ than their 62 typically-developing siblings and their 77 parents, and also significantly lower than 40 healthy age and gender matched comparisons. There was a trend for males having lower $25(OH)D_3$ than females. Effects of age, month/season of birth, IQ, various subcategories of ASD and Autism Diagnostic Observation Schedule score were also investigated, however, no association was found. The very low $25(OH)D_3$ in the ASD group suggests some underlying pathogenic mechanism.

**Keywords** Autism · ASD · Vitamin D · Calcitriol · Total population · Faroe Islands

## Introduction

Autism spectrum disorders (ASDs) are a heterogeneous group of complex, biologically based neurodevelopmental disorders. There are several known risk factors including a variety of mutated and variant genes, advanced paternal age, exposure to toxins and medications in early development, prematurity, and birth complications (Kolevzon et al. 2007; Gardener et al. 2009; Coleman and Gillberg 2012; Munger et al. 2012; Cannell and Grant 2013). Recently, maternal/neonatal vitamin D deficiency has been proposed

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as a possible environmental risk factor for ASD (Cannell and Grant 2013; Grant and Soles 2009; Kočovská et al. 2012a, b) due to its involvement in early neurodevelopment (Eyles et al. 2013), the immune system (Hayes et al. 2003), and gene regulation (Ramagopalan et al. 2010) processes.

Ergocalciferol (often called vitamin $D_2$), a direct analogue of cholecalciferol (vitamin $D_3$), is made from ergosterol (obtained from yeast) and has been used for food fortification and supplements. The LC–MS/MS assay in blood (used in this study, see below) can differentiate between and determine levels of both 25(OH)$D_2$ and vitamin 25(OH)$D_3$. The 25(OH)$D_2$ level reflects vitamin $D_2$ intake from supplements and the 25(OH)$D_3$ level reflects the vitamin $D_3$ intake from diet, supplements or sun exposure. The overall result is a sum of both circulating forms and it was this overall sum that this study has used (Feldman et al. 2011).

Indirect support for the involvement of vitamin D in ASD comes from ecological studies, according to which vitamin D levels vary with season and latitude and with the degree of skin pigmentation (Grant and Soles 2009; Dealberto 2011). The prevalence of ASD has been suggested to be raised at higher latitudes and in children of migrant mothers with darker skin (Grant and Soles 2009; Fernell et al. 2010; Dealberto 2011).

The end product of vitamin D metabolism is calcitriol (1,25-dihydroxyvitamin $D_3$ or 1,25$(OH)_2D_3$) that has now been recognized inter alia as a neuroactive hormone that signals via nuclear receptors (Eyles et al. 2005, 2013). It has been shown to be required for normal brain homeostasis and brain development (Garcion et al. 2002). The last 15 years have witnessed great advances in explaining the biochemical mechanisms of the diverse actions of calcitriol in the brain, especially its role in early neurodevelopment and in degenerative processes: (1) cell differentiation and axonal growth; (2) stimulation of neurotrophic factor expression (e.g., cytokines); (3) regulation of calcium signalling directly in the brain; (4) modulation of the production of the brain-derived reactive oxygen species; (5) stimulation of glutathione (a potent anti-oxidant, involved in DNA synthesis and repair) and thereby down-regulating excitotoxicity (Eyles et al. 2005, 2013; Garcion et al. 2002). Outcomes of many of these mechanisms during neurodevelopment might be relevant in a number of Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations (ESSENCE) (Gillberg 2010)—conditions that are now being linked with deficits of this vitamin/hormone, including ASD (Eyles et al. 2013).

To date, there have only been six clinical studies measuring vitamin D levels of individuals with ASD. These are: Humble et al. (2010) (without a comparison group); Molloy et al. (2010) (with a problematic comparison group); Meguid et al. (2010); Mostafa and AL-Ayadhi (2012); De Souza Tostes et al. (2012) and Gong et al. (2014), four of which showed significantly lower levels of vitamin D in individuals with this diagnosis as compared to healthy comparison group ("Appendix"). Fernell et al. (2010) demonstrated extremely low vitamin D levels in mothers of Somali origin living in Sweden with a child with ASD as compared to control group of Swedish mothers.

An apparent epidemic of vitamin D deficiency is now being recognised (Holick 2007; Adams and Hewison 2010), and this prompted us to explore the vitamin D levels in a general population cohort of young individuals with ASD (aged 15–24 years) and their siblings and parents, and in a typically-developing comparison group in the Faroe Islands. We chose the Faroe Islands for this study for various reasons. The islands' location in the North Atlantic Ocean at 62°00′N, and its maritime climate (high rainfall, strong winds, an average summer temperature of 9 °C), negatively affect the availability of the UVB radiation of sun rays necessary for vitamin D metabolism. Conversely, the Faroe Islanders have a diet rich in large oily fish containing vitamin D that could possibly, at least in part, compensate for the lack of UVB exposure, which in turn might mean that overall vitamin D status in the Faroe Islands could be adequate. In addition, many variables are unusually stable, including socioeconomic status, education, health care, familial/genetic history, and diet. This unique total population study in the Faroe Islands therefore offers an ideal environment for examining associations between vitamin D levels and ASD.

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## Methods

### Study Population

Participants with ASD were recruited during a two-phase screening process of the entire Faroe Islands population (n = 47,962) in the relevant school age group (7–16 years, n = 7,689) for the study of ASD prevalence in the Faroe Islands in 2002 (Ellefsen et al. 2007) (n = 43) and 2009 (n = 24) (Kočovská et al. 2012a, b). Thus the 67 individuals diagnosed with ASD represent an entire age-cohort of individuals with ASD in the Faroe Islands and therefore the present study represents the first ever entire population sample of vitamin D levels in ASD population. This current cross-sectional population-based study involved 219 individuals, all of white European origin: 40 participants with a diagnosis of ASD (31 males/9 females), their 62 typically developing siblings (29 brothers/33 sisters), their 77 parents (40 mothers/37 fathers), and 40 healthy comparisons (28 males/12 females).

In 2008–2009, 40 of the 67 individuals with ASD from the general population—24 participants (56 %) from the 2002 screening phase cohort and 16 (67 %) from the 2008–2009 cohort—and their close family members agreed to have blood drawn for analysis of various environmental factors (informed consent was obtained either from the individual or, if younger than 18, from the parent). The 40 participants with ASD were 15–24 years old [Mean 18.9 (SD 2.9)] at the time of blood sampling, and 31 were male. The comparison group was matched as closely as possible for age [Mean 18.5 (SD 2.5)], season of birth and gender. The reasons for non-participation in blood sampling among the ASD group (n = 27) were as follows: non-participation in the follow-up study in 2009 of those with ASD first diagnosed in 2002 (n = 10), participation but not willingness to give blood sample (n = 14), and participation but practical difficulties in blood drawing (n = 3). The group of 40 with blood samples had a similar gender profile and Autism Diagnostic Observation Schedule (ADOS) (Lord et al. 1989) scores to those from whom blood samples were not obtained (77/73 % and 12.5/9.4 respectively, $p = 0.1$.

Although some degree of genetic relatedness in the Faroe Islands can be assumed—due to the small population and its genetic isolate character, the prevalence of autism in the Faroe Islands has been found to be similar to other western nations, namely 0.56 % in 2002 (Ellefsen et al. 2007) and 0.94 % in the follow up study in 2009 (Kočovská et al. 2012a, b). The fact that in the follow up screening process an additional 24 individuals were diagnosed with autism, who were originally missed, and nearly half of these were females (n = 11), supports the findings of other studies, suggesting that girls are often missed at a young age and that screening and diagnostic processes need to address this phenomenon in the future (Giarelli 2010; Kočovská et al. 2013). There is good evidence (e.g. Kopp et al. 2010) that girls with ASD are missed or misdiagnosed at early ages and that, in fact, they had the symptoms from a very early age. There is little to indicate that girls develop ASD later than boys. There were only two families with an index child with ASD with another sibling also diagnosed with ASD but these siblings were not part of our study due to the age restriction (our participants had to be born between 1985 and 1994). During the diagnostic process in 2009, several families had siblings with some ASD traits but without an ASD diagnosis. Thus, in this vitamin D study there were no multi-ASD families.

### Ethics

The study was approved by the Scientific Ethics Committee of the Faroe Islands.

### Clinical Evaluation of Individuals with ASD

Participants with ASD were clinically examined in depth, their family history was reported by their primary caregiver, and they were assessed using a variety of standardized structured and semi-structured instruments and tests: the diagnostic interview for social and communication disorders (DISCO) (Wing et al. 2002), Wechsler Intelligence Scales (Wechsler 1981, 1992) and the ADOS (Lord et al. 1989) (see below). All were clinically diagnosed according to the International Classification of Diseases, Tenth Edition (ICD-10) (World Health Organization 1993), and the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (American Psychiatric Association 1994) criteria: childhood autism/autistic disorder; Asperger syndrome/disorder (without application of the age criterion); atypical autism/pervasive developmental disorder not otherwise specified (PDDNOS). The subcategories were collapsed into a broader ASD study group.

The DISCO-interview is an investigator-based structured and semi-structured instrument developed with a view to serving as a research and clinical interview with a collateral informant (usually one of the parents, as in the present context) for differential diagnosis within the spectrum of autism and other social communication disorders (Wing et al. 2002). The DISCO-10 was used in 2002, and the DISCO-11 in 2009.

The difference between the tenth (DISCO-10) and the eleventh (DISCO-11) versions of the DISCO is marginal. Stability of DISCO-algorithm subcategory diagnoses has been shown to be more variable than that of clinical diagnosis but still good for AD. In terms of "any ASD" diagnosis, DISCO-11 diagnoses showed excellent stability

over the 7-year period from school age through early adult life (Kočovská et al. 2013).

Wechsler intelligence scales were used age-appropriately for the cognitive assessment: Wechsler Intelligence Scale for Children (WISC-III) (Wechsler 1992) in a majority of the cases in 2002 and Wechsler Adult Intelligence Scale (WAIS-R) (Wechsler 1981) in 2009.

ADOS-assessment was performed only in 2009. The ADOS is an instrument used for diagnosing and assessing autism, allowing a standardised assessment of autistic symptoms (Lord et al. 1989).

## Blood Sampling and Assay of $25(OH)D_3$

Over a period of a year during 2008–2009, all participants had their blood drawn (EDTA monovette) at Torshavn Hospital, Faroe Islands, to determine the levels of $25(OH)D_3$. More than three quarters of the families with an index child with autism (78 %) had their blood drawn in summer (Jun–Aug) and autumn (Sep–Nov). The rest of the families were blood sampled in spring (Mar–May). No ASD participants had their blood sample drawn during the winter months. Thus it can be expected that the ASD group might demonstrate a certain seasonal elevation in their levels of vitamin D. In contrast, all healthy comparisons had their blood drawn in schools during a relatively short period between February and April 2009. In some participants with ASD, the blood samples were drawn at their homes due to needle phobia and/or other behavioural/care-taking problems.

Samples were then frozen at −80 °C and stored at the Department of Biochemistry of the Biobank of Faroes. The long-term stability of $25(OH)D_3$ serum concentrations for more than 10 years has been demonstrated under similar storage conditions (Agborsangaya et al. 2010). The stored, frozen whole blood samples were thawed in early 2013 and the required amount of 0.5 mL of haemolysed full blood separated, packed, and posted to the Department of Clinical Biochemistry, City Hospital, Birmingham, UK, where the laboratory analyses were performed by using the "gold-standard" method—liquid chromatography–tandem mass spectrometry (LC–MS/MS), details of which have been described by (Schottker et al. 2012). The laboratory staff were blind to the identity and diagnostic/comparison status of the individuals. The assay is accredited by the Vitamin D External Quality Assessment Scheme (DEQAS) and the laboratory is CPA accredited (available at: http://www.deqas.org/).

By using the haematocrit (hct) of the sample, the concentrations of $25(OH)D_3$ were calculated after measurement of the haemolysed sample (Shea and Berg 2013) which enabled the use of the haemolysed whole blood samples. All samples from all participants and the entire control group were haemolysed.

We resolved to use the same reference range as (Holick et al. 2011), since this range has been used in several recently published studies of vitamin D levels in patients with autism (e.g. Humble et al. 2010; Meguid et al. 2010; Dalgård et al. 2010; De Souza Tostes et al. 2012). The Swedish reference range for $25(OH)D_3$ levels awaits revision and the cut off for deficiency and insufficiency are expected to correspond to 50 and 75 nmol/L respectively. This scale, based on the latest research, seems plausible and practical to adopt (Priemel et al. 2010; Heaney and Holick 2011). The cut off for 'severe deficiency' (25 nmol/L–10 ng/mL) fulfils a practical function in clinical settings for the prescribed supplementation of vitamin D.

The reference range used in this study:

| | nmol/L | ng/mL |
|---|---|---|
| Severe deficiency | <25 | 10 |
| Deficiency | ≥25–<50 | 10–20 |
| Insufficiency | ≥50–<75 | 20–29 |
| Sufficiency | ≥75 | 30 |

## Statistical Analyses

Statistical analysis was performed in Minitab (version 16.0) and SPSS (version 19). Continuous data are presented as 'mean' and 'standard deviation' (SD) if normally distributed or as 'median' and 'inter-quartile range' (IQR) if not normally distributed. All data on vitamin D levels for all groups were not normally distributed, therefore we used non-parametric tests. We treated the groups of individuals with ASD and their siblings and parents as related.

The comparison group was selected to match as closely as possible in terms of gender, season of birth and age to give comparable groups for the statistical analysis.

Group comparisons of normally distributed data were made using Student's $t$ test. For continuous data that were not normally distributed (~all vitamin D levels in all groups), Mann–Whitney tests and Kruskal–Wallis tests were used when performing pairwise-comparisons and several-group-comparisons respectively. A significance level of 0.05 was considered significant for all analyses.

A linear model was used to correct for season of sampling. The vitamin D levels were not normally distributed (Anderson–Darling $p < 0.005$) however, a log transformation of the vitamin D levels was ($p = 0.525$).

Chi squared test or the Mantel–Haenszel linear-by-linear association Chi squared test for trend was used to assess categorical variables. Pearson correlation and logistic

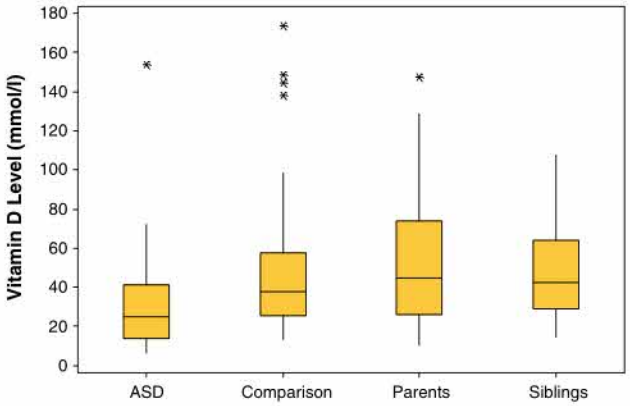


**Fig. 1** *Box plots* for 25(OH)$D_3$ levels for ASD, comparison ($p = 0.002$), parent ($p < 0.001$) and sibling ($p < 0.001$) groups, (95 % CI) (*asterisk* outliers)

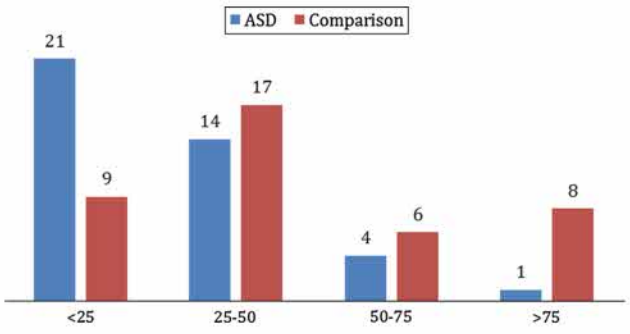


**Fig. 2** 25(OH)$D_3$ status among ASD and comparison groups (95 % CI, $p = 0.003$)

regression were used for analysis of the association between vitamin 25(OH)$D_3$ levels and certain background variables.

## Results

As there were several outliers with very high levels in all groups apart from siblings, all the statistical analyses were re-calculated with all outliers removed. However, we consider inclusion of the outliers important and as the results have remained unchanged and significant after exclusion of all the outliers, we present the original results including all the outliers unless specifically stated otherwise.

### 25(OH)$D_3$ Levels

The ASD group had significantly lower levels of 25(OH)$D_3$ [median (IQR) = 24.8 (27.5) nmol/L] compared to the healthy comparison group [median (IQR) = 37.6 (32.3) nmol/L], (95 % CI 5.0–22.5), $p = 0.002$ to their siblings [median (IQR) = 46.1 (28.3) nmol/L] (95 % CI 9.4–24.8), and parents [median (IQR) = 46.7 (36.2) nmol/L) (95 % CI 11.0–27.74], ($p < 0.001$ in both instances) (Fig. 1).

In the ASD group, 88 % were vitamin D deficient (Fig. 2). Among their siblings, parents, and the comparison group, the corresponding rates were 58, 58, and 65 % respectively ($p < 0.001$) (Table 1): for clarity and comparability of our results with several recently published studies of vitamin D levels in patients with autism we resolved to use the same reference ranges as (Holick et al. 2011) and we used values of nmol per litre (nmol/L).

### Analysis of Season of Blood Sampling

Medians of vitamin D levels of individuals with ASD varied according to season of the year in which they were sampled: spring (n = 9) = 13.80 nmol/L, summer (n = 18) = 39.90 nmol/L and autumn (n = 12) = 22.95 nmol/L ($p = 0.017$) reflecting a similar trend as that found in the study of Faroese elder population (Dalgård et al. 2010). Therefore, the vitamin D data was adjusted for month of sampling in our analysis.

### Comparison of 25(OH)$D_3$ Levels Across and Within Gender

The trend for males having lower vitamin D levels was observed in the ASD and sibling groups, although this gender difference was statistically significant only in the sibling group ($p = 0.03$). In the comparison and parent groups both males and females had comparable levels (Table 2).

Because of the variability in male:female ratio in all groups (ASD group ~3:1; sibling and parent groups ~1:1 and the comparison group ~2:1), a combined comparison of vitamin D levels was also carried out for 'males only' in all groups. There was a significant difference between the groups ($p = 0.001$). Males with ASD had significantly lower levels of 25(OH)$D_3$ [median (IQR) = 24.7 (20.6) nmol/L] compared to their brothers [median (IQR) = 34.6 (25.2) nmol/L] ($p = 0.004$) and fathers [median (IQR) = 44.9 (49.8) nmol/L] ($p < 0.001$) and also to the healthy comparison males [median (IQR) = 37.4 (31.0) nmol/L] ($p = 0.002$).

### Comparison of 25(OH)$D_3$ Levels in Individuals with ASD Recruited in 2002 and 2009

As there were only 2 females diagnosed in 2002 and one of them was 'an outlier' i.e. her 25(OH)$D_3$ level was much higher than all other participants' at 153 nmol/L, it was not meaningful to compare 25(OH)$D_3$ levels across gender in this 2002 group. In the 2009 group there was no difference

**Table 1** Vitamin D status: Chi squared test or table of percentages of participants with severe deficiency, deficiency, insufficiency and sufficiency of vitamin D (nmol/L) in the comparison group, ASD group and in siblings and parents of the individuals with ASD (Pearson Chi square = 26.730, $df = 9$, $p = 0.002$)

| Vitamin D status (nmol/L) | Count % within groups | Groups | | | | Total |
|---|---|---|---|---|---|---|
| | | Comparison | ASD | Sibling | Parent | |
| Severe deficiency <25 | Count | 9 | 21 | 10 | 18 | 58 |
| | % | 22.5 | 52.5 | 16.1 | 23.4 | 25.5 |
| Deficiency 25–50 | Count | 17 | 14 | 26 | 27 | 84 |
| | % | 42.5 | 35.0 | 41.9 | 35.1 | 38.4 |
| Insufficiency 50–75 | Count | 6 | 4 | 17 | 13 | 40 |
| | % | 15.0 | 10.0 | 27.4 | 16.9 | 18.3 |
| Sufficiency >75 | Count | 8 | 1 | 9 | 19 | 37 |
| | % | 20.0 | 2.5 | 14.5 | 24.7 | 16.9 |
| Total | Count | 40 | 40 | 62 | 77 | 219 |
| | % | 100 | 100 | 100 | 100 | 100 |

**Table 2** $25(OH)D_3$ gender differences in individual groups

| GROUP (n) | Vitamin D level median (nmol/L) | | $p$ (CI 95 %) |
|---|---|---|---|
| | Male | Female | |
| ASD (40) | 24.70 | 42.00 | 0.1 (5.6–31.1) |
| Comparison (40) | 37.40 | 43.95 | 0.6 (12.7–23.5) |
| Siblings (62) | 34.60 | 54.00 | 0.03 (1.2–27.3) |
| Parents (77) | 44.90 | 44.45 | 0.9 (11.7–11.29) |

between males [median 24.9 nmol/L (IQR = 20.3)] and females [median 22.2 (IQR = 27.1)] ($p = 0.37$).

For comparison between 2002 and 2009 groups this outlier was removed—there was no difference between the $25(OH)D_3$ levels of the 2002 group [median (IQR) = 24.7 (28.80) nmol/L] and the 2009 group [median(IQR) = 23.6 (24.38) nmol/L] (95 % CI 9.10–11.40) ($p = 0.965$).

Among the 24 participants (22 males/2 females) recruited in 2002, 12 (50 %) had severely deficient, eight (30 %) deficient, three (13 %) insufficient, and one (=female) (4 %) sufficient levels of $25(OH)D_3$.

Among the 16 participants (9 males/7females) recruited in 2009, nine (56 %) had severely deficient, six (38 %) deficient, one (=female) (6 %) insufficient, and zero (0 %) sufficient levels of $25(OH)D_3$.

Although the 2002 and 2009 cohorts were diagnosed at two different time points, it should be noted that both groups were blood sampled for vitamin D analysis during the same period in 2008–2009.

### $25(OH)D_3$ Levels and Other Variables

There was no association between $25(OH)D_3$ levels and age, IQ, subcategories of ASD or ADOS score. When investigating 'season of birth' in the ASD group, those born in the spring season (March–May) had the lowest levels of $25(OH)D_3$ (median 13.8 nmol/L; $p = 0.17$) in agreement with previous literature (Grant and Soles 2009). Among the ASD group there were 13 (32.5 %) spring births (the comparison group was matched for season of birth therefore included the same number of spring births). There was no correlation between $25(OH)D_3$ levels and ADOS scores ($p = 0.3$). There was also no correlation between $25(OH)D_3$ levels and the diagnosis—Asperger syndrome (n = 18): 23.55 nmol/L (20.2); atypical autism (n = 11): 24.7 nmol/L (29.6); autism (n = 11): 30.3 (51.8) ($p = 0.3$).

## Discussion

This first-ever population-based study of vitamin D in ASD showed significantly lower levels in young adolescents/adults with ASD than in their siblings and parents, and also than healthy comparisons.

Our findings are consistent with those of several studies published since 2010, although some of these had methodological problems e.g., no comparison group or a problematic comparison group (Nseir et al. 2012; Kočovská et al. 2012a, b) (see "Appendix").

The finding that 80 % of the comparison group (which can be considered representative of the general population in the Faroe Islands) were in the 'deficient/insufficient' range and 22.5 % in the 'severely deficient' range (<25 nmol/L–<10 ng/mL) that is indicative of the risk of osteomalacia/rickets (Holick 2007), adds to the mosaic of perceived global vitamin D deficiency in various regions of the world. It is of note that the levels of $25(OH)D_3$ found in ASD participants of the present study from the Faroe Islands are even lower than those in other regions (see "Appendix"). It might be that the severity of this region's climate and its high Northern latitude, both diminishing the

production of vitamin D by UVB rays, cannot be compensated for by a diet albeit rich in large oily fish.

The only other report on vitamin D levels in the Faroe Islands was the Faroese elder study (Dalgård et al. 2010) that found the median $25(OH)D_3$ concentration of 47.6 (29.8–64.8) nmol/L and a small seasonal variation in the $25(OH)D_3$ levels in Faroese elders, with a winter nadir of 42.6 nmol/L and a summer peak of 56.5 nmol/L (females 51.0 nmol/L; males 44.6 nmol/L). Our study found a similarly small, insignificant seasonal variation in our ASD group corresponding to the season of blood sampling.

Unlike in the Meguid (2010) and Gong (2014) studies our group with the most severe diagnosis of autism had the highest levels of vitamin D (30.30 nmol/L; $p = 0.3$). This could be partially explained by the fact that 9 out of 11 individuals with autism diagnoses were blood sampled during the summer holidays while for the two other diagnoses there was a greater variability in season of sampling.

The slight over-representation of spring births among the ASD group (32.5 %) and corresponding lowest level of vitamin D in this group (median 13.8 nmol/L; $p = 0.17$) is interesting and warrants follow up. A hypothetical explanation as to why ASD cases born in the spring had the lowest $25(OH)D_3$ status in adolescence could be that low maternal $25(OH)D_3$ levels led to epigenetic processes at the CYP24A1 gene. This gene encodes the 24-hydroxylase that degrades calcitriol and $25(OH)D_3$ is subject to epigenetic regulation (methylation) during neonatal life (Novakovic et al. 2009): epigenetic marking and silencing of the CYP24A1 gene could occur due to low maternal vitamin D levels preventing $25(OH)D_3$ from reaching a level that adequately supports CNS development. Further investigation of this potential mechanism may be of interest. To date the Faroese population generally has not been supplementing with vitamin D, even in pregnancy (apart from ordinary multivitamins with no more than 400 IU of cholecalciferol or ergoclaciferol per day), and the use of solaria in the Faroe Islands is also rare.

The trend towards lower levels of vitamin D in males in ASD and sibling groups presented another interesting finding. There are no acknowledged sun exposure differences between males and females among Faroese adolescents. Dalgård's Faroese elder study also reported that female gender was associated with higher $25(OH)D_3$ levels (Dalgård et al. 2010). Previous research has demonstrated various gender differences in vitamin D metabolism (Spach and Hayes 2005; Orton et al. 2006; Novakovic et al. 2009; Feldman et al. 2011). Thus, future research is warranted, as it would shed light on this phenomenon.

Here we only aimed at cross-sectional comparison of vitamin D levels and we did not investigate mechanisms involved in the differences found. It can be expected that both diet and availability of UVB rays can influence vitamin D levels. We did not measure calcium, parathyroid hormone (PTH), or phosphate, which might reveal more about the nature of the deficiency either from inadequate sun exposure and/or inadequate dietary intake (Holick 2007). An individual's underlying hormonal imbalance could also play a role (Cannell and Grant 2013; Holick 2007; Feldman et al. 2011). The apparatus regulating the hormone calcitriol (e.g. vitamin D receptors, vitamin D binding protein, associated enzymes) is all under genetic control and might exacerbate environmentally determined low vitamin D status or amplify its consequences to elevate ASD risk (Fu et al. 2009; Ahn et al. 2010; Hiraki et al. 2013). Thus future research is expected to shed light on a possible role of genetic factors. We intend to follow up and treat the diagnosed hypovitaminosis D among participants with ASD and try to obtain further information on the origin of low vitamin D status.

We have no evidence regarding the direction of causality as the blood samples of our ASD group were drawn when they were 15–24 years of age. The low vitamin D levels in the ASD group could be either a result of autism impacting on a family/child's lifestyle and/or diet (indoor activities, selective eater, etc.) or the underlying biology of autism altering the metabolism of vitamin D in some way or vitamin D deficiency itself contributing to the pathogenesis of ASD. As all groups were exposed to low levels of sunlight, the very low $25(OH)D_3$ in the ASD group suggests some other underlying pathogenic mechanism may be involved.

Children with Williams syndrome very often have high $25(OH)D_3$ levels in early infancy due to a single gene mutation, which also involves abnormal vitamin D metabolism (Feldman et al. 2011; Stamm et al. 2001). It would be interesting to explore whether altered vitamin D metabolism could also be involved in the development of autism. One of the supportive features for causality is biological mechanism (Hennekens et al. 1987).

High 'Body Mass Index' (BMI) has been associated with vitamin D deficiency (Holick 2007). We did not have exact BMI values available for either of our comparison groups. In our ASD group, eight participants (20 %) were noted by diagnosing clinicians as overweight/obese. Thus, this factor itself does not offer an exhaustive explanation for our overall result.

An increasing body of research indicates that ASD may be associated with a variety of complex immune dysregulations, including autoimmunity, and may have a neuroimmunecomponent (Cannell and Grant 2013; Mostafa and AL-Ayadhi 2012; Gentile et al. 2013). Thus, future investigation utilizing a combination of genetic, epigenetic, and mechanistic studies of this complex interplay between

autism, vitamin D deficiency, steroid metabolism, and autoimmunity will be desirable.

### Limitations

The main limitations of the present study were the modest size of our sample, a lack of data regarding BMI—only known in the some of the ASD group and lacking in all other control groups—and a lack of information about the participants habits with regards to indoor/outdoor activities or their vitamin D supplementation. Also there was an inconsistency of blood sampling across seasons among various groups. These research findings require replication with larger numbers. Because it would be challenging for any one centre to produce data on sufficient number of children with ASD, a multicentre international collaboration would be desirable in order to achieve more conclusive results.

## Conclusions

This first-ever population study of vitamin D levels in ASD showed significantly lower vitamin D levels in participants with ASD (aged 15–24 years) living in the Faroe Islands, as compared to their siblings, parents, and typically developing comparisons. A trend of lower levels in males compared to females in the ASD, comparison and sibling groups was also observed.

The findings could reflect the consequences of ASD per se impacting on a person's lifestyle and diet or the underlying biology of ASD impacting in some way directly on the metabolism of vitamin D. Alternatively, the low vitamin D levels could be an indication of life-long vitamin D deficiency in ASD, and this hormone deficiency could, at least theoretically, have been involved in early aberrant development of the brain in these individuals, leading to the development of ASD.

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**Conflict of interest** The authors declare that they have no competing interests.

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## Appendix

See Table 3.

**Table 3** Overview of studies of vitamin D levels in individuals with autism

| Author (year) | Country: study participants (n) | ASD group | | Comparison group | | *p* |
|---|---|---|---|---|---|---|
| | | nmol/L | ng/mL | nmol/L | ng/mL | |
| Humble et al. (2010)* | Sweden: adults (121) | 31.5 | 12.6 | – | | – |
| Molloy et al. (2010) | USA: boys 4–8 years (89) | 49.4 | 19.8 | 44.0 | 17.6 | 0.4 |
| Meguid et al. (2010) | Egypt: children 2–8 years (112) | 71.3 | 28.5 | 100.3 | 40.1 | <0.001 |
| Mostafa and AL-Ayadhi (2012) | Saudi Arabia: children 5–12 years (80) | 46.3 | 18.5 | 82.5 | 33.0 | <0.001 |
| De SouzaTostes et al. (2012) | Brazil: children ±7 years (48) | 66.2 | 26.5 | 101.3 | 40.5 | <0.001 |
| Gong et al. (2014) | China: children ±4 years (96) | 49.8 | 19.9 | 56.5 | 22.6 | 0.002 |
| Kočovská et al. (present study) | Faroe Islands: young adults 15–24 years (219) | 24.8 | 9.9 | 37.6 | 15.0 | 0.002 |

* The Humble et al. (2010) study did not have a control group. For more details see (Kočovská et al. 2012a)

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Original Investigation

# Late Detection of Critical Congenital Heart Disease Among US Infants

## Estimation of the Potential Impact of Proposed Universal Screening Using Pulse Oximetry

Cora Peterson, PhD; Elizabeth Ailes, PhD, MPH; Tiffany Riehle-Colarusso, MD, MSE, MPH; Matthew E. Oster, MD, MPH; Richard S. Olney, MD, MPH; Cynthia H. Cassell, PhD; David E. Fixler, MD, MSc; Suzan L. Carmichael, PhD; Gary M. Shaw, DrPH; Suzanne M. Gilboa, PhD, MHS

**IMPORTANCE** Critical congenital heart disease (CCHD) was added to the Recommended Uniform Screening Panel for Newborns in the United States in 2011. Many states have recently adopted or are considering requirements for universal CCHD screening through pulse oximetry in birth hospitals. Limited previous research is directly applicable to the question of how many US infants with CCHD might be identified through screening.

**OBJECTIVES** To estimate the proportion of US infants with late detection of CCHD (>3 days after birth) based on existing clinical practice and to investigate factors associated with late detection.

**DESIGN, SETTING, AND PARTICIPANTS** Descriptive and multivariable analysis. Data were obtained from a multisite population-based study of birth defects in the United States, the National Birth Defects Prevention Study (NBDPS). We included all live-born infants with estimated dates of delivery from January 1, 1998, through December 31, 2007, and nonsyndromic, clinically verified CCHD conditions potentially detectable through screening via pulse oximetry.

**MAIN OUTCOMES AND MEASURES** The main outcome measure was the proportion of infants with late detection of CCHD through echocardiography or at autopsy under the assumption that universal screening at birth hospitals might reduce the number of such late diagnoses. Secondary outcome measures included prevalence ratios for associations between selected demographic and clinical factors and late detection of CCHD.

**RESULTS** Of 3746 live-born infants with nonsyndromic CCHD, late detection occurred in 1106 (29.5% [95% CI, 28.1%-31.0%]), including 6 (0.2%) (0.1%-0.4%) first receiving a diagnosis at autopsy more than 3 days after birth. Late detection varied by CCHD type from 9 of 120 infants (7.5% [95% CI, 3.5%-13.8%]) with pulmonary atresia to 497 of 801 (62.0% [58.7%-65.4%]) with coarctation of the aorta. In multivariable analysis, late detection varied significantly by CCHD type and study site, and infants with extracardiac defects were significantly less likely to have late detection of CCHD (adjusted prevalence ratio, 0.58 [95% CI, 0.49-0.69]).

**CONCLUSIONS AND RELEVANCE** We estimate that 29.5% of live-born infants with nonsyndromic CCHD in the NBDPS received a diagnosis more than 3 days after birth and therefore might have benefited from routine CCHD screening at birth hospitals. The number of infants in whom CCHD was detected through screening likely varies by several factors, including CCHD type. Additional population-based studies of screening in practice are needed.

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Journal Club Slides and Supplemental content at jamapediatrics.com

CME Quiz at jamanetworkcme.com and CME Questions page 395

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**Subject:** Meeting date

Thanks to all of you for your quick response to our meeting poll. Obviously within this short time frame it was nearly impossible to find a time that everyone could meet, but the best dates are February 5-6. The meeting will be in the D.C. area, beginning first thing the morning of February 5 and concluding by noon on Friday the 6th. More details will follow about logistics, agenda, etc., but I wanted to get this out to you quickly so that you could hold the dates.

A couple of you are available on the 5th but not the 6th. If you can't change your commitments on the 6th, that's OK as I would still like for you to come on the 6th. However, for those of you who cannot come on the 5th but are available on the 6th, it would not be worth it for you to come for the half-day. I will be in touch directly with each of you with potential conflicts to discuss options.

Thanks again – the enthusiastic response to this project has been overwhelming, and I look forward to a very engaging meeting. More later…

Best regards,

Don

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**Subject:** Early ADDM report
**Attachments:** Early ADDM prevalence_Pediatrics_12_05_14.docx

Good evening everyone,

The Early ADDM prevalence report is ready to go to Pediatrics. Please check over the attached manuscript to make sure that your information (affiliation, etc) is correct. I plan to send it on Friday, December 19.

Happy holidays!

Daisy

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# Prevalence and Characteristics of Autism Spectrum Disorder among 4-year-old Children: a Pilot Study of the Early Autism and Developmental Disabilities Monitoring Network

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The findings and conclusions in this study are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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**Short Title**: Autism Spectrum Disorder among 4-Year-Old Children

**Abbreviations**: ASD – autism spectrum disorder; ID – intellectual disability; ADDM Network – Autism and Developmental Disabilities Monitoring Network

**Key words**: Prevalence, Autism Spectrum Disorder

**Funding Source**: All phases of this study were supported by

**Financial Disclosure**: The authors have no financial disclosures relevant to this article to disclose.

**Conflict of Interest**: The authors have no conflicts of interest to disclose.

**What's Known on This Subject**:

Population-based surveillance for ASD has focused primarily on school-aged children; less is known about the prevalence and characteristics of ASD among preschool-aged children. Surveillance among this population provides information on changes in ASD prevalence and characteristics in this age group as well as timely feedback on progress towards decreasing the age of ASD identification.

**What This Study Adds**:

ASD surveillance among 4-year-olds provides a baseline for assessing trends in ASD prevalence among children in this younger age group and informs health and education professionals of upcoming service needs. The Early ADDM Network offers valuable insight into the early identification of children with ASD and suggests some progression towards lowering the age of first ASD evaluation in participating communities.

**Contributors' Statement Page**

Deborah L. Christensen: Dr. Christensen implemented the study, carried out the analyses, drafted the initial manuscript, and approved the final manuscript as submitted.

Deborah A. Bilder: Dr. Bilder designed and implemented the study, critically reviewed the manuscript, and approved the final manuscript as submitted.

Walter Zahorodny: Dr. Zahorodny designed and implemented the study, critically reviewed the manuscript, and approved the final manuscript as submitted.

Sydney Pettygrove: Dr. Pettygrove designed and implemented the study, critically reviewed the manuscript, and approved the final manuscript as submitted.

Maureen S. Durkin: Dr. Durkin designed and implemented the study, critically reviewed the manuscript, and approved the final manuscript as submitted.

Robert Fitzgerald: Dr. Fitzgerald designed and implemented the study, critically reviewed the manuscript, and approved the final manuscript as submitted.

Catherine S. Rice: Dr. Rice designed and implemented the study, critically reviewed the manuscript, and approved the final manuscript as submitted.

Margaret Kurzius-Spencer: Dr. Kurzius-Spencer implemented the study, critically reviewed the manuscript, and approved the final manuscript as submitted.

Jon Baio: Dr. Baio implemented and study, critically reviewed the manuscript, and approved the final manuscript as submitted.

Marshalyn Yeargin-Allsopp: Dr. Yeargin-Allsopp designed and implemented the study, critically reviewed the manuscript, and approved the final manuscript as submitted.

**Word count**: 2996

**Abstract**

**Background**: Early identification of children with Autism Spectrum Disorder (ASD) facilitates timely access to intervention services.

**Methods**: We conducted a pilot study of ASD prevalence and characteristics among 4-year-old children in five of eleven sites participating in the Autism and Developmental Disabilities Monitoring Network in 2010. Children with ASD were identified through a multi-stage process of screening health and education records for ASD indicators, abstraction of relevant data, multisource data compilation for each child, and clinician review of composite records. ASD prevalence estimates, ages at first evaluation and ASD diagnosis, and demographics for 4-year-old children were compared with those for 8-year-old children living in the same areas.

**Results**: Among 58,467 children in these five sites, 4-year-old ASD prevalence was 13.4 per 1,000; 8-year-old ASD prevalence was 43% higher. Prevalence of ASD without intellectual disability was 80% higher among 8-year-olds compared with 4-year-olds, but prevalence of ASD with intellectual disability was similar between age groups. Among 4-year-olds with ASD, female and non-Hispanic white children were more likely to receive their first comprehensive evaluation by age 36 months compared with male and non-Hispanic black children, respectively. Among children diagnosed with ASD by age 48 months, median age at first comprehensive evaluation was 27 months for 4-year-olds compared with 32 months for 8-year-olds.

**Conclusions**: Although population-based ASD surveillance at 4 years of age may underestimate ASD prevalence, it provides insight into the early identification of children with ASD and indicates progression towards lowering the age of first ASD evaluation within participating ADDM communities.

Word count: 250

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**Cc:** Guttmacher, Alan (NIH/NICHD) [E];Boyle, Coleen (CDC/ONDIEH/NCBDDD)
**Subject:** Blame Mothers: Failure to Control for Iatrogenic Perinatal Trauma as Etiology of Increased Autism Risk Following (High Risk) Pregnancy
**Attachments:** autismhearing.pdf, Official CorrespondencesNIHCDCASHBJUIntEditorialBoardmember.pdf

Dear Autism Researchers/Public Health Advocates:

The recent publication of an extraordinary association between country-level rates of circumcision with their respective country-level rates of autism (r=0.98, p<0.000005) [http://www.ncbi.nlm.nih.gov/pubmed/23656698 ] explains the recent observation of a lower than expected rate of autism prevalence in Spain where an equal male to female autism prevalence (compared to the 5-6:1 male to female autism prevalence in the U.S.) was also observed (http://www.ncbi.nlm.nih.gov/pubmed/23746744 ) as Spain (http://www.ncbi.nlm.nih.gov/pubmed/16177149 ) (and Hispanics in the U.S.) have the lowest circumcision rates (2% in Spain) and Hispanics in the U.S. also have a lower than expected autism prevalence (http://www.ncbi.nlm.nih.gov/pubmed/20019320 ).

The exceptionally high rate of autism in Utah (http://www.cdc.gov/ncbddd/autism/states/addm-utah-fact-sheet.pdf ) where the overall circumcision rate is reported to be 39% (http://www.deseretnews.com/article/765598967/Study-Declining-circumcision-rates-could-lead-to-increase-in-health-care-costs-disease.html?pg=all ) may be attributable to Mormons who may have a much higher circumcision rate (http://www.examiner.com/article/circumcision-christianity-mormon-and-other-religions-traditon-vs-urantia-book ).

Similarly, South Korea which has reported an exceedingly high prevalence of autism in school age children with male:female autism prevalence of 2.5-5:1 (http://www.ncbi.nlm.nih.gov/pubmed/21558103 ) also has an extraordinarily high rate of circumcision (http://www.biomedcentral.com/1471-2458/12/1067 ).

Recent studies placing the onus for the increased autismrisk following high risk pregnancies on mothers with underlying pregnancy risk factors, all fail to control for confounding by iatrogenic perinatal trauma, i.e., circumcision rates which as cited above have been reported to be significantly associated with autism rates:

Examples of seriously deficient maternal-child autism research studies which have failed to control for iatrogenic perinatal trauma- circumcision - in this respect are as follows:

Increased rate of autism following preterm birth http://www.ncbi.nlm.nih.gov/pubmed/24068297

Increased rate of autism from mothers with lupus (http://www.medicaldaily.com/children-born-mothers-lupus-have-twice-risk-autism-261098 )

Increased rate of autism from mothers with metabolic conditions http://www.ncbi.nlm.nih.gov/pubmed/22492772

The recent study of placental abnormalities in association with autism (http://www.ncbi.nlm.nih.gov/pubmed/23623455 ) fails to address the gender disparity in autism spectrum disorders and confounding by disparate gender perinatal iatrogenic trauma as an autism risk factor. Mothers who have "at-risk pregnancies" are held responsible for risk of autism in their children based on placental abnormalities rather than the more likely gender disparate perinatal iatrogenic trauma of circumcision which is significantly associated with autism ($r=0.98$, $p < 0.000005$) (http://www.ncbi.nlm.nih.gov/pubmed/23656698 ).

In the ObGyn studies cited below and in the air pollution-autism studies (http://www.ncbi.nlm.nih.gov/pubmed/23816781 ; http://www.ncbi.nlm.nih.gov/pubmed/23404082 ) where pollution exposure was based on "time and place of birth" or "mother's address from birth certificate", no control for gender disparate confounding by perinatal iatrogenic trauma of circumcision for autism risk in boys was carried out.

This is seriously deficient research design/methodology for which ObGyn researchers should be well aware of, since ObGyns perform most hospital circumcisions in the U.S.

Similarly, the recent article on children with ADHD who express autism traits (http://www.ncbi.nlm.nih.gov/pubmed/23979086 ) fails to address the disparate gender prevalence of ASD and ADHD in males and the gender disparate risk of perinatal iatrogenic trauma associated with circumcision on the risk of ADHD/ASD. This is a serious inadequacy in research design. Adding insult to injury the authors after referring to perinatal trauma as a likely potential etiology for ADHD/ASD, while ignoring the perinatal trauma of circumcision, refer to the "…role of maternal infection during pregnancy…" as the potential etiology of ADHD/ASD.

Similarly a recent article on induced labor increasing risk of autism especially in males (http://archpedi.jamanetwork.com/article.aspx?articleid=1725449 ) also fails to address the gender disparate confounding perinatal iatrogenic trauma of circumcision (see autismhearing) on the risk of autism following induced labor.

Just as ObGyn surgeons induce labor, attend at high riskpregnancies/deliveries as cited above, they also commonly perform circumcisions post-delivery in the U.S., thus confounding any high risk pregnancy resulting in autism in males with the reported association of circumcision with autism. The induced labor – autism study casts suspicion on labor, a physiologic process, and thus on the mother as being responsible for autism risk rather than the likely iatrogenic traumatic procedure, circumcision, that accounts for the 5:1 male to femaleautism/ADHD prevalence.

The appropriately designed epidemiologic studies to determine whether circumcision as a risk for autism are straightforward and need to be carried out. However when NIH previously studied circumcision as a risk factor for chronic pelvic pain and serious comorbidities including neuropsychiatric diseases, erectile dysfunction among other sequelae, NIH suppressed the data (see official correspondences).

If there is interest in discussing this further, please contact me.

Sincerely,

Paul C. Turkeltaub, M.D.

Date: For 29 November 2012 Autism Hearing

To: The House Oversight and Government Reform Committee
Rayburn House Office Building
Washington, D.C. 20515-0001

From: Testimony of Paul C. Turkeltaub, M.D.
p.turkeltaub@att.net

Subject: **The Missing Risk Factor To Explain the 5 to 1 Male to Female Autism Prevalence is Circumcision. The Pain of the Vaccine Schedule is Also A Missing Risk Factor for Autism in At-Risk Girls and Boys**

I want to apprise the House Committee of the potential for serious unintended consequences for public health related to the risk of circumcised boys developing autism.

Porges reported significantly increased autonomic arousal (decreased vagal tone), severe pain behaviors, high pitched cry with circumcision (http://www.ncbi.nlm.nih.gov/pubmed?term=porges%20and%20circumcision) where "..individual differences in vagal tone measured prior to circumcision surgery were predictive of physiological and acoustic reactivity to subsequent stress". The severity of procedural pain is therefore dependent on vagal tone. Vagal tone therefore defines the at-risk child.

Taddio observed significantly increased pain responses in toddlers associated with routine immunizations 3-5 months post circumcision compared to uncircumcised immunized controls ((http://www.ncbi.nlm.nih.gov/pubmed/9057731). The increased pain responses of circumcised boys to the pain of the vaccine schedule indicates that circumcision causes traumatic brain injury which enhances their pain responses. This traumatic brain injury is called central sensitization (http://www.ncbi.nlm.nih.gov/pubmed/20961685) which is defined by enhanced central pain processing following trauma.

Although autistic children do not have apparent overt behavioral responses to suggest increased pain responses, their physiologic baseline indicates arousal as evidenced by increased heart rate (decreased vagal tone) which increases to a significantly greater extent than normal controls following a routine "minimal risk" painful medical procedure, such as venipuncture (http://www.ncbi.nlm.nih.gov/pubmed/19707566 ).

Girls with decreased vagal tone would also be likely to be at-risk for developing central sensitization following the traumatic painful dosage associated with the multiple needle sticks/vaccine reactogenicity of the vaccine schedule.

Despite the 5 to 1 male to female prevalence of autism by age 8 reported by CDC,

**CDC has not considered the increased burden of the vaccine schedule pain dose on circumcised boys/at-risk children with respect to the prevalence of Autism Spectrum Disorder. By age 2, children receive as many as 24 injections and may receive up to 5 injections in one visit. Children are receiving far more injections (needle pain dose/vaccine reactogenicity) now than they ever did.**

Old Order Amish who do not practice infant circumcision have a low prevalence of autism (http://imfar.confex.com/imfar/2010/webprogram/Paper7336.html). Somali immigrants in Sweden who practice male circumcision early in childhood have a high prevalence of autism in their children compared to Swedish children (http://www.ncbi.nlm.nih.gov/pubmed/20964674) who have a low rate of male circumcision ((http://en.wikipedia.org/wiki/Prevalence_of_circumcision ).

Autism prevalence is higher in whites than in blacks. Autism prevalence in blacks is higher than in Hispanics. Autism prevalence is higher in the children of parents with high socioeconomic status. (http://www.ncbi.nlm.nih.gov/pubmed?term=halperin%20and%20autism ). Circumcision rates are higher in whites than in blacks. Circumcision rates are higher in blacks than in Hispanics (http://www.ncbi.nlm.nih.gov/pubmed/17413536). Circumcision rates are higher in children whose parents have high socioeconomic status/educational attainment (see Wikipedia above).

**None of the epidemiologic studies of Autism Spectrum Disorder (ASD) prevalence have looked at circumcision status/ or heart rate variability (vagal tone) as risk factors for prevalence of Autism Spectrum Disorder / or with respect to the pain dosage of the vaccine schedule in at-risk children.**

Although chronic pelvic pain in males is likely to follow a surgical procedure on the male genitalia, such as infant circumcision, due to scarring and central sensitization as discussed above, NIH omitted circumcision risk data from an NIH published study of risk factors for chronic pelvic pain (http://www.ncbi.nlm.nih.gov/pubmed/16104910 ) which CDC classified as "publication bias" (see Official Correspondences attached). Chronic pelvic pain in the NIH funded/coauthored paper is associated with significant increased risk of neurologic disease and psychiatric conditions in addition to erectile dysfunction and other serious comorbidities. Thus NIH has been identified by CDC as suppressing important risk/safety data for a procedure, circumcision, which DHHS is promoting worldwide. The same NIH omission/suppression appears to be the case for not evaluating the safety of the pain dosage of the vaccine schedule in at-risk children/circumcised boys despite the observation that circumcised boys have significantly increased pain responses to childhood immunization (see Taddio above).

It is essential to protect the public health that there be adequate Congressional oversight of DHHS to ensure that the long term risk of both the pain/trauma of circumcision and the pain/trauma of the vaccine schedule on developmental disability be determined in at-risk children/circumcised boys.

In the absence of the complete analyses/publication of the circumcision/vaccine safety data, Informed Consents for these procedures should therefore include wording to the effect:

***"The US Government has collected data on whether circumcision is a risk factor for chronic pelvic pain in males. This NIH funded/coauthored study found that chronic pelvic pain is found in approximately 9% of adult males and is associated with serious long term adverse effects: increased lifetime risk of cardiovascular and neurologic disease, psychiatric conditions, nonspecific urethritis and erectile dysfunction. DHHS has declined to completely analyze and publish whether the circumcision data collected in this study is a risk factor for chronic pelvic pain and the associated serious comorbidities (see Official Correspondences). Despite circumcised boys being reported to have significantly increased pain responses to childhood immunization, DHHS has also failed to determine the long term safety of childhood immunization in circumcised boys with respect to the development of Autism Spectrum Disorder (ASD) and the ASD comorbidity ADHD."***

# CDC is Proposing Universal Circumcision for the United States while NIH is Suppressing Serious Long Term U.S. Adverse Event Data for Circumcision

## This PHS Policy Has Disparate Impact/Treatment in Persons of African Descent

### I. Chronic Pelvic Pain in Males (CPP) is Associated with Serious Comorbidities (BJU Int 2005; 96(4): 559-565; http://www.ncbi.nlm.nih.gov/pubmed/16104910/ Exhibit A)

NIDDK funded a study of chronic pelvic pain in males which found that CPP is associated with significant comorbidities: increased lifetime prevalence of cardiovascular disease, neurologic disease, psychiatric conditions, hematopoietic, lymphatic, or infectious disease, gastrointestinal disease, nonspecific urethritis, erectile dysfunction.

### II. NIDDK Collected Circumcision Data in the Study of CPP, but Omitted the Circumcision Data From the Above Published Study (NIDDK Letter dated 19 May 2009 & NIDDK email dated 19 October 2009/ Exhibits B & C)

NIDDK refuses to completely analyze the circumcision data, publish it, post the data on its website, or give public notice of the availability of the circumcision data for others to analyze and publish.

This study to determine the risk of CPP following circumcision is the only study ever carried out and is very important for making an accurate long term risk-benefit assessment, since it is based on U.S. subjects.

### III. Disparate Impact/Treatment in Persons of African Descent (Exhibits D/E/F)

NIDDK collected questionnaire data and performed a physical examination of the circumcision surgical site in the above study (email from Board Member of BJU Int 2005 dated 16 April 2009/Exhibit D), but has not reported the complete analysis (questionnaire plus physical examination data) of these data. In the NIDDK correspondence cited, NIDDK states that a "preliminary" analysis of the circumcision data indicates no associated risk of CPP.

"Preliminary" analysis based solely on questionnaire data is likely to be inaccurate, because self reported classification of circumcision status by subjects is inaccurate (up to 35% misclassification/ Exhibit E) in (minority) males

(http://www.cdc.gov/hiv/resources/factsheets/circumcision.htm; see "Status of Male Circumcision in the United States", para.1). Thus the physical examination data must be analyzed to accurately determine the risk of CPP due to circumcision and additionally whether subjects with a "pathological" scar (physical examination of the genitalia included whether foreskin was abnormal-see 16 April 2009 email) are at increased risk of CPP.

Because self reports of circumcision status by minority males are likely to be inaccurate and the incidence of pathological scars (e.g, hypertrophic/depressed scars) is higher in males of African descent (i.e., keloid specifically), it is essential that a complete analyses of the circumcision data collected be carried out for an accurate determination of the risk of CPP, not just a "preliminary" analysis as specified in the NIDDK correspondence.

The Medical Research Council, South Africa, has therefore stated "Since self-report of circumcision status may be a poor means of assessing exposure, it would seem reasonable to favor the results generated from those studies that used direct observation only." (The Lancet Infectious Diseases 2005; 5 (3):165-173; p.170 "Methodological Issues", para. 2&3/
http://www.ncbi.nlm.nih.gov/pubmed/15766651/
Exhibit F).

CDC and NIDDK, to make a scientifically sound judgment of the associated risk of CPP following circumcision, must analyze the complete physical examination data and include these analyses in the CDC assessment of risk-benefit of circumcision.

## IV. CDC Is Aware That NIDDK Is Suppressing Long Term Adverse Event Data for Circumcision, but is Proceeding with A Universal Circumcision Recommendation Nonetheless (Letter from CDC dated 19 November 2009 in response to email to CDC dated 26 October 2009/ Exhibit G).

In official correspondence, CDC in response to being provided the attached NIDDK correspondence indicates their awareness that there is "publication bias", but plans to proceed with its recommendation for universal circumcision based on the "available" risk data, rather than requesting the complete adverse event data from NIDDK.

It should be noted that the authors of the study omitting the circumcision data are practitioners of circumcision and are funded by NIDDK which has funded studies in Africa on the benefit of circumcision.

## V. Response From ASH (Letter dated 7 June 2010/ Exhibit H)

Dr. Koh indicates circumcision data will be posted on the NIDDK website. There is no indication whether the circumcision data to be posted will be the complete (questionnaire plus physical examination) data or not.

More problematic is that there is no indication that a notice of public availability of the circumcision data will published. Furthermore data availability/accessibility will be based on approval by NIDDK officials/ funded scientists who omitted/ suppressed the data.

Since PHS health policy formulation must be based on an accurate risk-benefit assessment, posting of these circumcision risk data by itself is inadequate.

## VI. Remedy

Analyze and publish the complete circumcision data collected to determine risk of CPP and incorporate this U.S. risk data in the CDC risk-benefit assessment of circumcision. Currently the CDC web site indicates there is no long term risk of circumcision based on published short term studies in Africa (http://www.cdc.gov/hiv/resources/factsheets/circumcision.htm; "Risks Associated with Male Circumcision", para.1, lines 10-11/ Exhibit I) which is misleading, since there is U.S. long term risk data that CDC is aware of which is not included in the current CDC risk assessment for "universal" circumcision in the U.S., nor in any of the Informed Consents for DHHS studies of circumcision in the U.S./Africa.

In this circumstance where national health policy is involved and there is "direct to consumer" labeling/health promotion by DHHS (CDC website/CDC publications), there needs to be appropriate regulatory oversight of the claims made, adequacy of the benefit-risk data used in the PHS assessment including ascertainment of the integrity of the data in view of the history of omission/suppression by NIDDK officials.

DHHS has a number of regulatory resources/oversight Agencies tasked with evaluating claims of risk/benefit, direct to consumer labeling, and ascertainment of data integrity to accomplish this task.

In addition, promulgation of compliance/enforcement mechanisms and a bioethics code of conduct/SOP pertaining to publication bias by federal funded science/scientists/officials to insure that research data used to formulate PHS policy has not been adversely impacted by publication bias is needed.

**"IF YOU WANT THE PRESENT TO BE DIFFERENT FROM THE PAST, STUDY THE PAST"**

**BDS**

Exhibit A

BJU Int. 2005 Sep;96(4):559-65.

# A case-control study of risk factors in men with chronic pelvic pain syndrome.

Pontari MA, McNaughton-Collins M, O'leary MP, Calhoun EA, Jang T, Kusek JW, Landis JR, Knauss J, Litwin MS; CPCRN Study Group.

Temple University School of Medicine, Philadelphia, PA 19140, USA. Pontarm@tuhs.temple.edu

## Abstract

**OBJECTIVE:** To compare the demographic, behavioural, clinical and medical history characteristics of men with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and asymptomatic controls, to identify characteristics that might be associated with this syndrome.

**PATIENTS AND METHODS:** Self-administered epidemiological questionnaires were completed by 463 men with CP/CPPS and 121 asymptomatic age-matched controls. We compared the prevalence of possible risk factors between men with CP/CPPS and controls, using generalized Mantel-Haenszel tests, and developed multivariate predictive models using logistic regression methods, adjusting for clustering by clinical centre within both methods.

**RESULTS:** Compared to controls, men with CP/CPPS reported a significantly greater lifetime prevalence of nonspecific urethritis (12% vs 4%, P = 0.008), cardiovascular disease (11% vs 2%, P = 0.004), neurological disease (41% vs 14%, P < 0.001), psychiatric conditions (29% vs 11%, P < 0.001), and haematopoietic, lymphatic or infectious disease (41% vs 20%, P < 0.001).

**CONCLUSION:** A wide range of self-reported medical conditions was associated with CP/CPPS. Further studies are necessary to determine whether they play a role in the pathogenesis of CP/CPPS.

PMID: 16104910 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Grant Support

LinkOut - more resources

Exhibit B

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

National Institute of Diabetes and
Digestive and Kidney Diseases
Bethesda, Maryland 20892

May 19, 2009

Dear [redacted]

Dr. Raynard Kington, Acting Director, NIH, has asked that I reply to your letter of May 2, 2009, in which you discuss a published paper on risk factors for chronic prostatitis. I believe that you are referring to the manuscript: "A case-control study of risk-factors in men with chronic pelvic pain syndrome," Pontari MA, et al, published in the *British Journal of Urology International,* vol 96, 559-565, 2005. This was a report of the Chronic Prostatitis Clinical Research Network (CPCRN) Cohort Study.

You have expressed interest in the data on circumcision that was collected from study participants by the CPCRN investigators, but which was not among the characteristics listed in the 2005 paper. This type of study typically collects numerous pieces of data, and investigators are faced with the sometimes difficult choice of what information to include in a particular manuscript--a choice that is driven by scientific considerations as well as the journal's peer review process and page limitations. Circumcision was one of a number of factors not encompassed by the referenced publication.

Dr. Leroy Nyberg, Senior Urology Advisor and Director, Urology Programs, NIDDK, has discussed the circumcision data with the biostatisticians for the CPCRN study. They noted that, based on a preliminary analysis, there is no evidence from the study that the absence of a foreskin is a risk factor for CP/CPPS.

Although the referenced manuscript was published in 2005, the overall CPCRN study did not end until 2008, and additional publications based upon study data are anticipated. Consistent with our policy on multi-site clinical trials, which allows study investigators time to complete manuscripts from study data while ensuring that the data will become publicly available to the investigative community, the CPCRN data are now being prepared for submission to the NIDDK Repository and should be in place by 2010. Information about access to data in the Repository is listed on the NIDDK website. The specific data from the CPCRN will not be listed on the website; you will need to follow application procedures to obtain the data from the Repository.

I hope this addresses your concerns.

Sincerely,

Robert Star

Robert A. Star, M.D.
Director, Division of Kidney Urologic
and Hematologic Diseases

[redacted]

**From:** Star, Robert (NIH/NIDDK) [E] [starr@niddk.nih.gov]

**Sent:** Monday, October 19, 2009 2:08 PM

**To:** [redacted]

**Subject:** circumcision

Dear [redacted]

Dr. Francis Collins, Director, National Institutes of Health (NIH), has asked that I reply to your emails of August 24 and September 29, 2009, concerning universal male circumcision.

The NIH does not have a policy on male circumcision. The Centers for Disease Control and Prevention (CDC) is currently developing public health recommendations regarding male circumcision for HIV prevention in the United States; these are not yet final. Please see http://www.cdc.gov/hiv/topics/research/male-circumcision.htm for information on the status of these recommendations (last modified: August 27, 2009; accessed, October 13, 2009). Key issues under consideration, including health risks and benefits, are outlined there and in a 2008 CDC fact sheet, "Male Circumcision and Risk for HIV Transmission and Other Health Conditions: Implications for the United States" (http://www.cdc.gov/hiv/resources/factsheets/circumcision.htm ). For example, randomized clinical trials conducted in Africa, supported by NIH and other organizations, have shown that circumcising HIV-negative men reduced their risk of acquiring HIV infection by at least 55 percent. In light of the global epidemic of HIV/AIDS, these research findings are potentially very significant both for individual men and their partners and for broader public health policy. However, the results of these studies are not the CDC's only consideration in developing a public health recommendation for male circumcision to prevent HIV transmission in the United States. Furthermore, according to the website above, the CDC intends to provide a period of public comment for its draft recommendations. Finally, the CDC website also notes that, "Whatever the content may include, CDC's final circumcision recommendations will be completely voluntary."

In my May 19, 2009, letter to you, I attempted to address your concerns regarding data on circumcision collected by the Chronic Prostatitis Clinical Research Network (CPCRN) Cohort Study, which ended in 2008. You had expressed interest in the data on circumcision that was collected from study participants by the CPCRN investigators, but which was not among the characteristics listed in the 2005 paper, "A case-control study of risk-factors in men with chronic pelvic pain syndrome," Pontari MA, et al, published in the *British Journal of Urology International* 2005; 96: 559-565. In May of this year, in response to your inquiry, Dr. Leroy Nyberg (retired), then Senior Urology Advisor and Director, Urology Programs, NIDDK, discussed the circumcision data with the biostatisticians for the CPCRN study. They noted that, based on a preliminary analysis, there is no evidence from the study that the absence of a foreskin is a risk factor for CP/CPPS. Research data collected as part of the CPCRN are now being prepared for submission to the NIDDK Repository and should be in place within the next six months. This will provide investigators from the research community with an opportunity to review the data and perform additional analyses. Information regarding access to data in the NIDDK Repository is listed on the NIDDK website. We welcome research grant applications that propose to use this data to uncover previously unidentified risk factors for CP/CPPS. Also, as you may be aware, we are currently supporting a new, multi-site research group, the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Network, which will also be examining risk factors and etiologies for CP/CPPS.

I hope this addresses your concerns.

Sincerely,

Robert Star

Robert A. Star, M.D.
Director, Division of Kidney Urologic and Hematologic Diseases
NIDDK/NIH

[redacted]

**From:** jcn [jcn@queensu.ca]
**Sent:** Thursday, April 16, 2009 9:26 AM
**To:** [redacted] downeyj@queensu.ca
**Cc:** pontarm@tuhs.temple.edu; cpcrn2-exec@mail.med.upenn.edu
**Subject:** RE: circumcision and CPP

Dear [redacted]:
Dr. Nyberg is correct. We did collect data as part of a comprehensive data collection plan which included a yes/no question as part of the clinical trials and for the cohort study we indicated during physical examination if the foreskin was absent, normal or abnormal.
I am not sure whether that data was made available to Dr. Pontari when he did the cohort analysis for the BJUInt paper on risk factors, but I have cc'd him with your query.
I am not sure how to initiate an analysis in respect to answering your question since the funding for the NIH CPCRN group which collected and analyzed the data has now run out. The data is certainly available in the Data Coordinating Center data base, but not sure who would pay for its extraction and analysis. I have cc'd the CPCRN executive committee with your query. Public access to the data will be available in the near future.
Appreciate your interest and agree that looking at this question, particularly with all the recent interest in the prophylactic employment of circumcision for infections such as HIV, make it important as well. Lets see what the people who control the data and money say.
J. Curtis Nickel MD

---

**From:** [redacted]
**Sent:** Wednesday, April 15, 2009 4:51 PM
**To:** jcn@post.queensu.ca
**Subject:** circumcision and CPP

Dear Dr. Nickel,

Dr. Nyberg has recently confirmed that "The data on circumcision was collected on participants in the CPCRN trials.'

Since these data were omitted from the published BJU Int paper on CPP risk factors and you were on the Editorial Board at the time of publication, can you analyze these data and publish them with a cite to the published paper or have Dr. Pontari do that or suggest another route for analyses and publication of these data?

Public access to these data according to NIDDK will be in 2010 in the NIDDK repository, but I think the delay in analyses and publication to date has already been inordinate.

Thanks,

[redacted]

Exhibit E

**Status of Male Circumcision in the United States**

In national probability samples of adults surveyed during 1999–2004, the National Health and Nutrition Examination Surveys (NHANES) found that 79% of men reported being circumcised, including 88% of non-Hispanic white men, 73% of non-Hispanic black men, 42% of Mexican American men, and 50% of men of other races/ ethnicities [30]. It is important to note that reported circumcision status may be subject to misclassification. In a study of adolescents, only 69% of circumcised and 65% of uncircumcised young men correctly identified their circumcision status as verified by physical exam [31].

**PubMed**

Exhibit F

U.S. National Library of Medicine
National Institutes of Health

THE LANCET Infectious Diseases
FULL-TEXT ARTICLE

Display Settings: Abstract

Lancet Infect Dis. 2005 Mar;5(3):165-73.

# HIV and male circumcision--a systematic review with assessment of the quality of studies.

Siegfried N, Muller M, Deeks J, Volmink J, Egger M, Low N, Walker S, Williamson P.

South African Cochrane Centre, Medical Research Council, South Africa. nsiegfried@cochrane.co.uk

## Abstract

This Cochrane systematic review assesses the evidence for an interventional effect of male circumcision in preventing acquisition of HIV-1 and HIV-2 by men through heterosexual intercourse. The review includes a comprehensive assessment of the quality of all 37 included observational studies. Studies in high-risk populations consisted of four cohort studies, 12 cross-sectional studies, and three case-control studies; general population studies consisted of one cohort study, 16 cross-sectional studies, and one case-control study. There is evidence of methodological heterogeneity between studies, and statistical heterogeneity was highly significant for both general population cross-sectional studies (chi(2)=132.34; degrees of freedom [df]=15; p<0.00001) and high-risk cross-sectional studies (chi(2)=29.70; df=10; p=0.001). Study quality was very variable and no studies measured the same set of potential confounding variables. Therefore, conducting a meta-analysis was inappropriate. Detailed quality assessment of observational studies can provide a useful visual aid to interpreting findings. Although most studies show an association between male circumcision and prevention of HIV, these results may be limited by confounding, which is unlikely to be adjusted for.

PMID: 15766651 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms

LinkOut - more resources

[redacted] Exhibit G

**From:** [redacted]

**Sent:** Monday, October 26, 2009 10:35 AM

**To:** 'ileana.arias@cdc.hhs.gov'

**Subject:** Omission of circumcision adverse event data from NIH publication on chronic pelvic pain while CDC considers recommending "universal" circumcision

**Attachments:** RE: circumcision and CPP; Star final response.pdf; Dear Dr.doc

Dear Dr. Frieden,

Noted CDC (Dr. Kilmarx) consideration of a universal circumcision recommendation for the U.S.population.

I have been aware for some time that potential adverse event data related to circumcision as a risk factor for chronic pelvic pain was omitted from an NIH funded/coauthored publication on risk factors for chronic pelvic pain (see attached Star final response; Dear Dr.). The unanalyzed data include physical examination of the genitalia of the subjects with respect to whether the foreskin was absent, normal, or abnormal (see attached email: RE:circumcision and CPP).

The authors of the paper are urologists, practitioners of the procedure, and the decision not to include the circumcision data among the extensive list of risk factors looked at in the published paper raises in my mind the appearance of conflict of self interest. The funding entity NIDDK is funding studies overseas of the benefits of circumcision as a public health intervention; thus there is the appearance of a conflict of Institutional interest/competing public health interests in suppressing/omitting these potential U.S. adverse event data from analyses/publication.

I am concerned that decisions regarding an accurate benefit-risk assessment / informed consent for circumcision will be made without all the relevant U.S. adverse event data being analyzed and made public/publicly available.

I am therefore requesting that all the relevant adverse event data related to circumcision be analyzed and published as part of the decision bearing on "universal" circumcision for the U.S. population.

A reply is requested.

Sincerely,

[redacted]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention

November 19, 2009

[redacted]

Dear [redacted]

Thank you for your recent correspondence to the Centers for Disease Control and Prevention (CDC) regarding male circumcision as it relates to HIV prevention in the United States. The potential role of male circumcision in addressing health outcomes in the United States, including HIV infections, is an important consideration for public health.

CDC believes it is critical that we promote evidence-based practices that are grounded in the best science currently available. CDC has been actively reviewing data and consulting with subject matter experts to determine the most appropriate response regarding the role of male circumcision in HIV prevention efforts in the United States. We have considered the results of numerous studies, and are aware of the risks and benefits of male circumcision, including ethical concerns regarding potential human rights violations and adverse health events occurring in relation to circumcision.

I understand your concern that any such review of the risks and benefits associated with male circumcision may be skewed by publication bias—specifically, a bias towards publicizing evidence of the benefits of circumcision while withholding or minimizing data on adverse effects. It is impossible for us to quantify the potential impact of such bias on the relative weighting of risks and benefits associated with male circumcision. However, as we develop recommendations regarding male circumcision and its impact on HIV prevention, CDC has striven to consistently apply a conservative, risk-averse lens to the available data, thereby minimizing any tendency towards underestimating the adverse consequences--or overstating the advantages—of male circumcision. We also intend to include a detailed discussion of the relative benefits and risks of male circumcision in the recommendations, so that both the evidence and logic underlying our recommendations are transparent to potential policy-makers and end-users.

Once draft recommendations are developed, a notice will be published in the Federal Register for a formal public comment period. The draft recommendations will be posted on our website to provide an opportunity for the public to comment through a formal public review period. CDC will carefully review and analyze the comments received through this process before issuing a final set of recommendations. We invite you to provide any additional comments or concerns you may have regarding the draft recommendations during the public review period.

CDC continues to support a combination of evidence-based strategies, particularly traditional approaches that encourage safer sexual behaviors, such as condom use. By promoting a comprehensive approach to HIV prevention, we will be better equipped to reduce the impact of HIV on America's communities.

Thank you for contacting CDC and we look forward to your continued commitment to HIV prevention.

Sincerely,

Kevin A. Fenton

Kevin A. Fenton, MD, PhD, FFPH
Director
National Center for HIV/AIDS, Viral Hepatitis,
STD and TB Prevention

Exhibit H

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Assistant Secretary for Health
Office of Public Health and Science
Washington D.C. 20201

JUN - 7 2010

[redacted]

Thank you for your email of April 9, 2010, regarding your concerns with the analysis of circumcision data by investigators participating in the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)-sponsored Chronic Prostatitis Collaborative Research Network (CPCRN).

I have contacted senior staff at the NIDDK regarding this matter. They have informed me that the NIDDK is currently working with the Data Coordinating Center for the CPCRN, which was terminated in 2008, to transfer data collected from the various studies conducted by the Network to the NIDDK Central Data Repository. NIDDK staff anticipate that the first database transfer will be from the CPCRN Cohort Study, including information on circumcision, on or about July 1, 2010. Transfer of data from two other clinical trials conducted by CPCRN investigators will take place later in the summer. Once archived at the NIDDK Central Data Repository, you and other researchers may request access to the data through the established policy of the Repository which can be found at the following Web site: https://www.niddkrepository.org/niddk/home.do.

I hope this information addresses your concerns. If you require additional information, please do not hesitate to contact me.

Sincerely yours,

Howard K. Koh, M.D., M.P.H.
Assistant Secretary for Health

Exhibit I

## Risks Associated with Male Circumcision

Reported complication rates depend on the type of study (e.g., chart review vs. prospective study), setting (medical vs. nonmedical facility), person operating (traditional vs. medical practitioner), patient age (infant vs. adult), and surgical technique or instrument used. In large studies of infant circumcision in the United States, reported inpatient complication rates range from 0.2% to 2.0% [1, 14, 15]. The most common complications in the United States are minor bleeding and local infection. In the recently completed African trials of adult circumcision, the rates of adverse events possibly, probably, or definitely attributable to circumcision ranged from 2% to 8%. The most commonly reported complications were pain or mild bleeding. There were no reported deaths or long-term sequelae documented [9, 10, 11, 16]. A recent case-control study of two outbreaks of methicillin-resistant Staphylococcus aureus (MRSA) in otherwise healthy male infants at one hospital identified circumcision as a potential risk factor. However, in no case did MRSA infections involve the circumcision site, anesthesia injection site, or the penis, and MRSA was not found on any of the circumcision equipment or anesthesia vials tested [17].

**From:** Bailey, Don
**Sent:** 14 Nov 2014 21:02:47 +0000
**To:** aaron.goldenberg@case.edu;alex.kemper@duke.edu;Wheeler, Anne;Annie Kennedy (annie@parentprojectmd.org);btarini@umich.edu;Boyle, Coleen (CDC/ONDIEH/NCBDDD);Riley, Catharine (CDC/ONDIEH/NCBDDD);c-wicklund@northwestern.edu;elizabeth_m_berry-kravis@rush.edu;Gehtland, Lisa;George Hatch;Cuthbert, Carla (CDC/ONDIEH/NCEH);McEwen, Jean (NIH/NHGRI) [E];jeffrey.botkin@hsc.utah.edu;Jerry Mendell (Jerry.Mendell@nationwidechildrens.org);Jill Jarecki;Bolen, Julie (CDC/ONDIEH/NCBDDD);kclapp@fraxa.org;Marsha R. Mailick;michele.lloyd-puryear@nih.gov;Raspa, Melissa;muenzer@med.unc.edu;Nancy Stockford (nstockford@jmfund.org);Street, Natalie (CDC/ONDIEH/NCBDDD);Paquin, Ryan;powellcm@med.unc.edu;rhowell@miami.edu;Samiah Al-Zaidy (Samiah.Al-Zaidy@nationwidechildrens.org);Scott Zimmerman (scott.j.zimmerman@dhhs.nc.gov);Susan.Tanksley@dshs.state.tx.us;swoboda@genetics.utah.edu;Tony Ferlenda;Trina Whitridge;tu36j@nih.gov;Valerie Cwik (vcwik@mdausa.org)
**Subject:** Tier 2 Newborn screening meeting
**Attachments:** Tier 2 concept.pdf

Dear Colleagues,

I have spoken with many of you about the effort now underway to envision and do the planning necessary to evaluate the acceptability and usefulness of a voluntary "Tier 2" newborn screening program for conditions that are not yet ready for the Recommended Uniform Screening Panel. Attached is a brief one-page summary of what we are up to. If I have not spoken directly with you about this yet, please accept my apologies. I wanted to go ahead and get this email poll out today, and will continue to follow up with phone calls with each of you and others not yet on the list.

We are planning a meeting in January or February, bringing together key stakeholders (researchers, patient advocacy groups, federal agencies) to help move the planning forward. I hope that you will be able to join us for this very important event. We need to set a date soon, so below is a link to a Doodle poll. Note that there are 19 possible day options, so please indicate each day that you could potentially be available. Please include days on which you have commitments that you might be able to change, as this is a lot of schedules to try to coordinate in a relatively short period of time. We anticipate a 1.5 day meeting either here in North Carolina or in D.C. More details will follow once we finalize a date.

http://doodle.com/ybmy6kbaauc68t22

Thanks so much for considering this, and please feel free to get in touch with me to discuss further.

Best,

Don

Don Bailey, Ph.D., Distinguished Fellow
RTI International
3040 Cornwallis Road
Research Triangle Park, NC 27709-2194 USA
(919) 541-6488 (tel)
(919) 485-2617 (fax)

dbailey@rti.org

(b)(4)

**From:** Bailey, Don
**Sent:** 19 Nov 2014 15:00:58 +0000
**To:** aaron.goldenberg@case.edu;alex.kemper@duke.edu;Wheeler, Anne;Annie Kennedy (annie@parentprojectmd.org);btarini@umich.edu;Boyle, Coleen (CDC/ONDIEH/NCBDDD);Riley, Catharine (CDC/ONDIEH/NCBDDD);c-wicklund@northwestern.edu;elizabeth_m_berry-kravis@rush.edu;Gehtland, Lisa;George Hatch;Cuthbert, Carla (CDC/ONDIEH/NCEH);McEwen, Jean (NIH/NHGRI) [E];jeffrey.botkin@hsc.utah.edu;Jerry Mendell (Jerry.Mendell@nationwidechildrens.org);Jill Jarecki;Bolen, Julie (CDC/ONDIEH/NCBDDD);kclapp@fraxa.org;Marsha R. Mailick;Raspa, Melissa;muenzer@med.unc.edu;Nancy Stockford (nstockford@jmfund.org);Street, Natalie (CDC/ONDIEH/NCBDDD);Paquin, Ryan;powellcm@med.unc.edu;rhowell@miami.edu;Samiah Al-Zaidy (Samiah.Al-Zaidy@nationwidechildrens.org);Scott Zimmerman (scott.j.zimmerman@dhhs.nc.gov);Susan.Tanksley@dshs.state.tx.us;swoboda@genetics.utah.edu;Tony Ferlenda;Trina Whitridge;tu36j@nih.gov;Valerie Cwik (vcwik@mdausa.org)
**Subject:** Correction

Well, I sent this out too quickly and Alex Kemper noted an error in my email below. The sentence should read:

A couple of you are available on the 5th but not the 6th. If you can't change your commitments on the 6th, that's OK as I would still like for you to come on the 5th.

Thanks Alex!

Don

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---

**From:** Bailey, Don
**Sent:** Wednesday, November 19, 2014 9:54 AM
**To:** aaron.goldenberg@case.edu; alex.kemper@duke.edu; Anne Wheeler (acwheeler@rti.org); Annie Kennedy (annie@parentprojectmd.org); btarini@umich.edu; cab3@cdc.gov; Catharine Riley (xan2@cdc.gov); c-wicklund@northwestern.edu; elizabeth_m_berry-kravis@rush.edu; Gehtland, Lisa (lgehtland@rti.org); George Hatch; ijz6@cdc.gov; Jean McEwen (mcewenj@mail.nih.gov); jeffrey.botkin@hsc.utah.edu; Jerry Mendell (Jerry.Mendell@nationwidechildrens.org); Jill Jarecki; Julie Bolen (jbolen@cdc.gov); kclapp@fraxa.org; Marsha R. Mailick; mraspa@rti.org; muenzer@med.unc.edu; Nancy Stockford (nstockford@jmfund.org); Natalie Street (ntl2@cdc.gov); Paquin, Ryan; powellcm@med.unc.edu; rhowell@miami.edu; Samiah Al-Zaidy (Samiah.Al-Zaidy@nationwidechildrens.org); Scott Zimmerman (scott.j.zimmerman@dhhs.nc.gov); Susan.Tanksley@dshs.state.tx.us; swoboda@genetics.utah.edu; Tony Ferlenda; Trina Whitridge; tu36j@nih.gov; Valerie Cwik (vcwik@mdausa.org)
**Subject:** Meeting date

Thanks to all of you for your quick response to our meeting poll. Obviously within this short time frame it was nearly impossible to find a time that everyone could meet, but the best dates are February 5-6. The meeting will be in the D.C. area, beginning first thing the morning of February 5 and concluding by noon on Friday the 6th. More details will follow about logistics, agenda, etc., but I wanted to get this out to you quickly so that you could hold the dates.

A couple of you are available on the 5th but not the 6th. If you can't change your commitments on the 6th, that's OK as I would still like for you to come on the 6th. However, for those of you who cannot come on the 5th but are available on the 6th, it would not be worth it for you to come for the half-day. I will be in touch directly with each of you with potential conflicts to discuss options.

Thanks again – the enthusiastic response to this project has been overwhelming, and I look forward to a very engaging meeting. More later…

Best regards,

Don

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**From:** Van Naarden-Braun, Kim (CDC/ONDIEH/NCBDDD)
**Sent:** 10 Dec 2014 12:53:51 -0500
**To:** Baio, Jon (CDC/ONDIEH/NCBDDD);Allison Hudson;Goodman, Alyson B. (CDC/ONDIEH/NCBDDD);Amanda Bakian;Andrea Boan;Ann Chang;Colin Kingsbury;Corry Robinson;Christensen, Deborah (Daisy) (CDC/ONDIEH/NCBDDD);Deborah Bilder;Eldon Schulz;Eric Lott;Jane Charles;John Constantino;Josephine Shenouda;Julie Daniels;Kathy Gotschall;Kelly Kast;Kristen Clancy Mancilla;Laura Arnstein Carpenter;Li-Ching Lee;Barritt, Lisa (CDC/ONDIEH/NCBDDD) (CTR);Margaret Kurzius-Spencer;Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD);Martha Slay Wingate;Maureen Durkin;Maya Lopez;Pamela Imm;Paula Bell;Rebecca Harrington;Robert Fitzgerald;Sydney Pettygrove;Ghosh, Tista (CDC state.co.us);Walter Jenner;Walter Zahorodny;William McMahon;Joyce Nicholas;Schieve, Laura (CDC/ONDIEH/NCBDDD);Franklin, C. Leah (CDC/ONDIEH/NCBDDD);Tian, Lin Hui (CDC/ONDIEH/NCBDDD);Wiggins, Lisa (CDC/ONDIEH/NCBDDD);Maenner, Matthew J. (CDC/ONDIEH/NCBDDD);kirby S. Russell (CDC health.usf.edu);Thaer Baroud;Peacock, Georgina (CDC/ONDIEH/NCBDDD);Rice, Catherine (CDC/ONDIEH/NCBDDD);Dowling, Nicole (CDC/ONDIEH/NCBDDD);Boyle, Coleen (CDC/ONDIEH/NCBDDD)
**Subject:** Exciting opportunity at George Washington University School of Public Health

Good afternoon,
I want to let you know of an exciting job opportunity. I gave a keynote talk last Friday at the Autism Transition Project's Conference, a project housed within the George Washington University School of Public Health. It was a wonderful day focusing on the myriad of challenges and opportunities surrounding transition from high school to adulthood for young adults on the autism spectrum.

They are recruiting for the Founding Director/Professor of the Autism & Neurodevelopmental Disorders (AND) Initiative which was endowed $2.5 M for the position and activities. I have included links below to both the AND Initiative and the position description.

https://www.gwu.jobs/postings/24907
http://andinitiative.gwu.edu/

Feel free to pass this on to anyone who might be interested.
Best,
Kim

Kim Van Naarden Braun, Ph.D.
Epidemiologist
Developmental Disabilities Branch
National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention
1600 Clifton Road MS E-86
Atlanta , GA 30333
phone: 404-498-3860 (Atlanta)
phone: 908-233-8303 (Westfield)
phone: 609-777-7715 (Trenton)
fax: 404-498-3550
email: kbn5@cdc.gov

**From:** Jenner, Walter H
**Sent:** 1 Aug 2012 12:14:04 -0400
**To:** ngarner@ms.soph.uab.edu;Lee Li-Ching (llee2@jhsph.edu);jemerson@email.arizona.edu;Rhodes, Cheryl (CDC/ONDIEH/NCBDDD) (CTR);melanie@autism-alabama.org;achang@jhsph.edu;desposfr@umdnj.edu;zahorodn@umdnj.edu;MEWilson@uams.edu;Richardson, Julia (CDC/ONDIEH/NCBDDD);Wise, Jasina B.;AEHudson@uams.edu;McConnell, Anna;Frenkel, Gal (CDC/ONDIEH/NCBDDD);Franklin, C. Leah (CDC/ONDIEH/NCBDDD) (CTR);Kelly.Kast@dphe.state.co.us;Bama Hager;Barritt, Lisa (CDC/ONDIEH/NCBDDD) (CTR);Charles, Jane M.;clarneso@wisc.edu;paula_bell@unc.edu;kgotscha@email.arizona.edu;fitzgeraldr@wustl.edu;Green, Katie (Kilker) (CDC/ONDIEH/NCBDDD);Van Naarden-Braun, Kim (CDC/ONDIEH/NCBDDD);Carolyn Skowyra;Peacock, Georgina (CDC/ONDIEH/NCBDDD);Rice, Catherine (CDC/ONDIEH/NCBDDD);judith.zimmerman@hsc.utah.edu;Stevens, Melody (CDC/ONDIEH/NCBDDD);Washington, Anita (CDC/ONDIEH/NCBDDD);Whitney, Julia (CDC/ONDIEH/NCBDDD) (CTR);Jenner, Walter H
**Subject:** FW: Education and Outreach Conference call
**Attachments:** 8-1-2012 The Arc and Autism NOW Presentation.pdf

We have a webinar scheduled but in case there are any IT problems
Attached are slides for the E+O call today

Walter Jenner M.S., C.A.S.
Autism and Developmental Disabilities Monitoring Network
ADDM Act Early Ambassador
Division of Developmental Pediatrics
Medical University of South Carolina
135 Rutledge Avenue
MSC 567
Charleston, SC 29425
843-532-4992
jennerw@musc.edu

---

From: Jennifer Sladen [jsladen@AutismNow.org]
Sent: Wednesday, August 01, 2012 10:21 AM
To: Jenner, Walter H
Subject: RE: Education and Outreach Conference call

Hello!

Sorry I have been slow to write back this morning. Attached are the slides in pdf form. Please let me know if I can provide you any further information.

Would you like me to be on a few minutes early?

Thanks,
Jennifer

Jennifer Sladen, Senior Program Associate
Autism NOW Center
1825 K Street NW, Suite 1200, Washington, D.C. 20006
Phone: 202.600.3490 | Toll free: 800.433.5255
Fax: 202.534.3731
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www.autismnow.org

Follow us online at:

A national initiative of The Arc. Funded by the Administration on Intellectual and Developmental Disabilities.

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-----Original Message-----
From: Jenner, Walter H [mailto:jennerw@musc.edu]
Sent: Tuesday, July 31, 2012 3:33 PM
To: Jennifer Sladen
Subject: Education and Outreach Conference call

Hello Jennifer
Tomorrow is our ADDM Education and Outreach conference call.

Wednesday August 1, 2012
1-2 PM EST
Telephone (b)(6)
Passcode (b)(6) then hit #

I have also set up a webinar to allow you to put your screen up and can control slide presentations

Copy this address and paste it into your web browser:
https://www.livemeeting.com/cc/cdc/join
Copy and paste the required information:
Meeting ID: (b)(6)
Entry Code: (b)(6)

Also if you want some insurance send me any Power Point slides and I can send them out to members if the webinar crashes

I take roll and do some housekeeping at the start

Please feel free to e-mail me with any questions.
My best
Walter

Walter Jenner M.S., C.A.S.
Autism and Developmental Disabilities Monitoring Network ADDM Act Early Ambassador Division of

Developmental Pediatrics Medical University of South Carolina
135 Rutledge Avenue
MSC 567
Charleston, SC 29425
843-532-4992
jennerw@musc.edu

# The Arc's Efforts in Engaging People with Autism Spectrum Disorders

The Arc Chapter Network and Autism NOW: The National Autism Resource and Information Center

The Arc

For people with intellectual and developmental disabilities

August 1, 2012

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# The Arc - Who We Are

- Largest national community-based organization advocating for and serving people with intellectual and developmental disabilities and their families.

- Network includes over 140,000 members and more than 700 chapters nationwide

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# The Arc - Mission

- We promote the human rights of people with ID and support full inclusion and participation in the community

- We believe in the principles of people first, equity, community, diversity, and self-determination for all.

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# Presentation Outline

- Overview of The Arc and its support of people with ASD, their families, and professionals via state and local Chapter Networks

- Overview of The Arc's national initiatives, particularly Autism NOW and its activities that assist people with ASD, families, and professionals

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# The Arc Chapter Network - What We Do

- Provide individual, community, and family services and support for people with ID

- Conduct systems-based and individual advocacy for people with ID and their families at local, state, and national levels

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# The Arc Chapter Network - Populations Supported

- The Arc network serves people with various different types of intellectual and developmental disabilities, including ASDs. Services and advocacy work provided supports people with ASDs, families, and professionals on issues affecting people across the lifespan.

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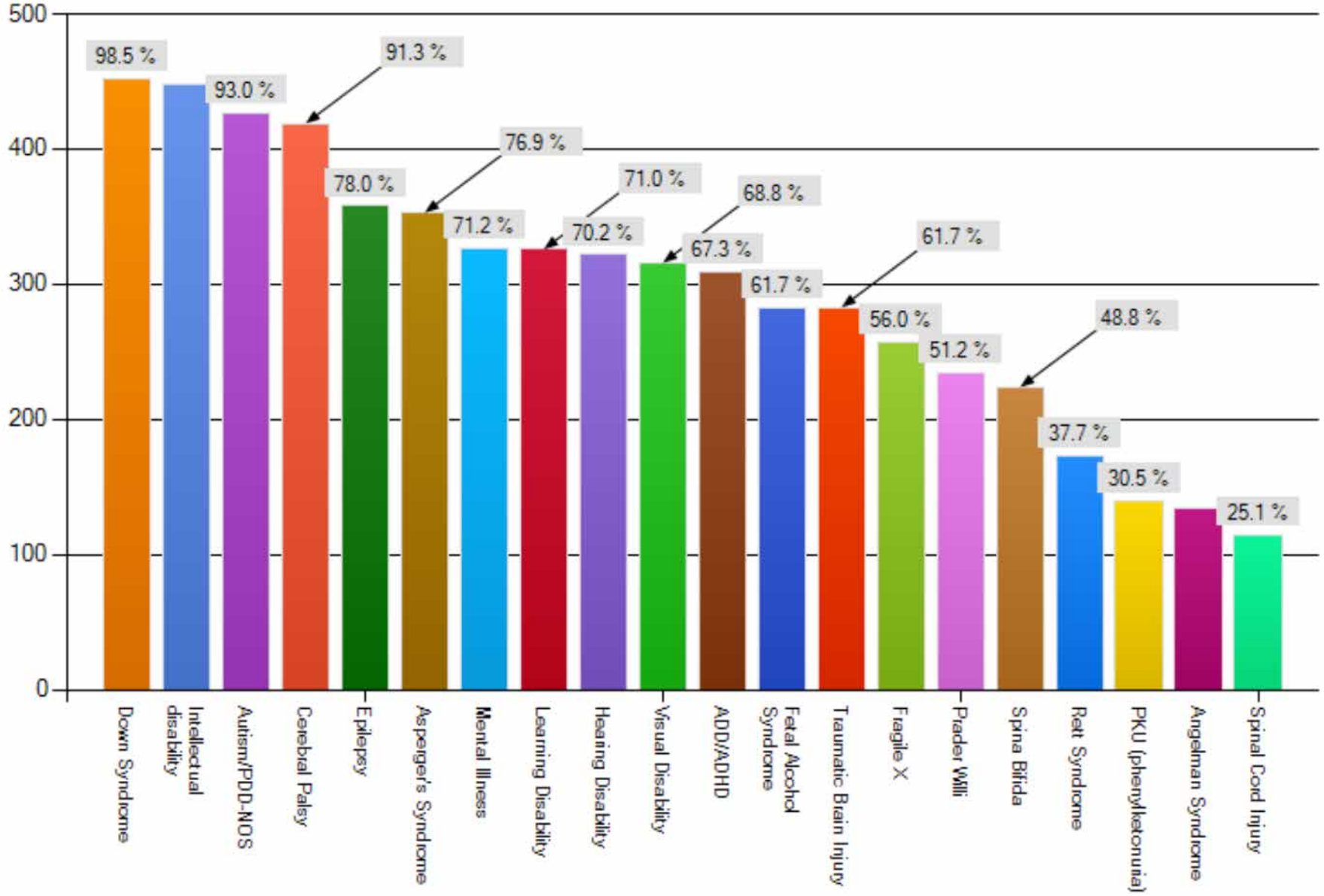
**Please indicate all of the different types of disabilities that are represented among the people who are served by your chapter. Check all that apply.**



# The Arc Chapter Network - Services Provided

Programs at Chapters of The Arc provide services to individuals with ID, their families, and the wider community. Services include:

- Public Awareness
- Parent Support
- Recreational Services
- Day Habilitation Services
- Early Childcare Services
- Respite
- Education/Transition Services
- Sibling Support
- Grandparent Support
- Future Planning
- Employment Services
- Transportation Training
- Professional Training
- Therapeutic Services

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# The Arc Chapter Network - Advocacy Work

Chapters of The Arc also advocate for system change as well as for individual rights. Common advocacy issues include:

- Health Care Policy and Access to Health Care/Treatment
- Home/Community Based Services
- Employment Policy and Discrimination
- Transportation
- Criminal Justice
- Civil Rights/ADA
- Housing Policy and Discrimination
- Funding, appropriations
- Public Benefits Policy/Access
- Education Policy/IEP
- Direct Service Workforce
- Individual Accommodations

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# The Arc - National Initiatives

In addition to national advocacy and Chapter support, The Arc national office implements initiatives to improve the qualifies of life of people with ID and best practices in service provision.

- School to Community Transition Program
- Self-Advocates with FASD in Action
- Down Syndrome Grant
- Medicaid Reference Desk
- eXplore eRecycling
- Autism NOW

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# How You Can Connect with The Arc Network!

- Check out www.thearc.org to follow our advocacy work and national initiatives
- Reach out to local Chapters of The Arc at http://www.thearc.org/page.aspx?pid=2437
- Connect with Chapters that offer autism and early intervention services (list found at conclusion of presentation)

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THE NATIONAL AUTISM RESOURCE & INFORMATION CENTER

# autism NOW

## you, empowered.

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# About Us

- Autism NOW: The National Autism Resource and Information Center is a central point of quality resources and information for individuals with Autism Spectrum Disorders (ASD) and other developmental disabilities, their families, and other targeted key stakeholders.

- We are funded by the Administration on Intellectual and Developmental Disabilities.

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# Our Partners

Autism Society of America

Autistic Self Advocacy Network

National Youth Leadership Network

Self Advocates Becoming Empowered

Sibling Leadership Network

University of Illinois at Chicago

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# Major Activities

- Develop Website with High-Quality Topical/Community Resources
- Implement Webinars to Share Key Autism-Related Information/Resources
- Publish Research Reviews, Toolkits, and Fact Sheets
- Discuss Lifespan Issues through Blog and Newsletter Articles
- Unite Autism Community via Regional Summits, Social Media, and Social Forum to Discuss Current Needs
- Provide Information and Referral Services to People with ASD, Families, and Professionals

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# Website

- Autism NOW's website houses over 700 resources relevant to issues across the lifespan, including news; articles; blogs; topical resource links to high-quality, vetted websites; books, guides, and other materials; and local and community resources.

- Additionally, it houses program activity archives, including blog posts, social forums and over 90 archived webinars.

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# Website

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# Webinars

- Free webinars offered every Tuesday 2:00-3:00 pm
- Designed for self-advocates, families, professionals, and the general public
- Popular topics include relationships and sexuality; iPad applications and assistive technology; safety; education and employment; and early intervention and screening and diagnosis issues.

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# Published Materials

- Autism NOW regularly works with partners to publish research reviews, toolkits for people with ASD and families, and fact sheets on key issue areas.
- Navigating College, Autistic Self Advocacy Network
- Upcoming materials will focus on self-advocacy, stigmatization and bullying, transition, IEPs and education, Social Security issues, and more!

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# Blog and Newsletter

- At least monthly, Autism NOW releases newsletters and blog posts around current disability-related topics.

## Recent Topics include:

- Vacation Planning for Parents of Children with Special Needs
- All About Bullying
- Typing to Communicate and Finding a Voice
- Things my Sibling Taught Me, and
- Autism, Being Autistic, and Acceptance

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# Regional Summits

- In 2011, implemented 5 regional summits across the country to bring together over 650 people with ASDs and ID, families, professionals and other stakeholders.

- Summits not only provided opportunities for people to discuss issues and policies that had impacted them, but also brought in local and regional experts to present on topics across the lifespan.

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# Regional Summits

## Critical Issues (for Parents of Children with ASD)

- Education - Training Teachers, Funding to Support Needs, Communicating Accommodations
- Finding Early Child Care
- Developing Relationships
- Funding Public Programs
- Access to Doctors
- Persistence in Finding Answers to Questions
- Managing Parent Expectations of "Normal"
- Accepting Child for Who They Are and Having Them Accept Themselves
- Parent Health and Stress

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# Regional Summits

"I am moved and encouraged by the energy, compassion, and dedication that the speakers presented with....

I need these types of conferences to remind myself that I am not alone as a parent of a child on the autism spectrum. I also loved meeting people on the autism spectrum and seeing how well they are doing."

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# Social Media and Forums

- Maintain an online presence on social media (Twitter, Facebook, and YouTube).

- We recently launched social forums so that people with ASD, families, professionals, the general public, experts, and Autism NOW partners could share information on resources, webinars, and current topics in the disability field. Check out the website to learn more!

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# Call Center

- Our Information and Referral Call Center is powered by the Autism Society of America. Information Specialists trained in providing referrals are available by phone or email to respond to individual needs.

- Anyone needing information can call our center toll free at 1.855.8AUTISM (1.855.828.8476) or email the center at info@autismnow.org.

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# How You Can Participate in Autism NOW!

- Visit our website at http://autismnow.org
- Help us reach out to families by letting others know about our initiative
- Connect with us on social media and in our forums
- Share feedback on our website or any topical or community resources that you know at http://autismnow.org/what-we-do/participate/

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# Any Questions?

Jennifer Sladen
(202) 600-3490
jsladen@autismnow.org

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# THANK YOU!

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# The Arc Chapters - Autism/Early Intervention Resources in Your State

## Alabama

- The Arc of Alabama, www.TheArcofAlabama.com
- The Arc of Jefferson County, http://www.arcofjeff.org/

## Arizona

- The Arc Arizona, http://www.arcarizona.org/
- Douglas ARC, http://www.douglasarc.org/

## Arkansas

- The Arc Arkansas, http://www.arcark.org/
- The Arc for the River Valley, http://www.arcrivervalley.org/

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# The Arc Chapters - Autism/Early Intervention Resources in Your State

## Colorado

- The Arc Colorado, http://www.thearcofco.org/

## Florida

- Arc Florida, www.arcflorida.org
- ARC Gateway, http://www.arc-gateway.org/
- The Arc of Palm Beach County, http://www.arcpbc.org/
- The Arc of the St. Johns, http://www.arcsj.org/
- The Arc of South Florida, http://www.thearcsofla.org/

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# The Arc Chapters - Autism/Early Intervention Resources in Your State

## Georgia

- The Arc of Georgia, http://www.thearcofgeorgia.org/
- Albany ARC, http://www.albanyarc.org/
- The Arc Macon, http://www.arcmacon.org/

## Maryland

- The Arc of Maryland, http://www.thearcmd.org/
- The Arc Baltimore, http://www.arcofbaltimore.org/
- The Arc of Frederick County, http://www.arcfc.org/
- The Arc of Prince George's County, http://www.thearcofpgc.org/

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# The Arc Chapters - Autism/Early Intervention Resources in Your State

## Missouri

- The Arc Missouri, http://www.arcofmissouri.org/
- The Arc of the Ozarks, http://www.thearcoftheozarks.org
- Saint Louis Arc, http://www.slarc.org/

## North Carolina

- The Arc of North Carolina, http://www.arcnc.org/
- Monarch, http://www.monarchnc.org/

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# The Arc Chapters - Autism/Early Intervention Resources in Your State

## New Jersey

- The Arc of New Jersey, www.arcnj.org
- The Arc of Bergen & Passaic, http://www.arcbergenpassaic.org/
- The Arc of Somerset County, http://www.thearcofsomerset.org/
- The Arc of Union County, http://www.arcunion.org/
- Arc of Warren County, http://www.arcwarren.org/

## Pennsylvania

- The Arc of Pennsylvania, http://www.thearcpa.org/
- The Arc-Crawford County, http://www.arcofcrawfordcounty.org/
- ACHIEVA, http://www.achieva.info/

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# The Arc Chapters - Autism/Early Intervention Resources in Your State

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- The Arc of South Carolina, www.arcsc.org
- The Arc of Pickens County, http://pcbdsn.org/Arc%20of%20Pickens%20County.html

## Wisconsin

- The Arc of Wisconsin, http://www.arc-wisconsin.org/
- Life Navigators, http://www.lifenavigators.org/

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**To:** Jenner, Walter H;ngarner@ms.soph.uab.edu;Lee Li-Ching (llee2@jhsph.edu);jemerson@email.arizona.edu;Rhodes, Cheryl (CDC/ONDIEH/NCBDDD) (CTR);melanie@autism-alabama.org;achang@jhsph.edu;desposfr@umdnj.edu;zahorodn@umdnj.edu;MEWilson@uams.edu;Richardson, Julia (CDC/ONDIEH/NCBDDD);Wise, Jasina B.;AEHudson@uams.edu;McConnell, Anna;Frenkel, Gal (CDC/ONDIEH/NCBDDD);Franklin, C. Leah (CDC/ONDIEH/NCBDDD) (CTR);Kelly.Kast@dphe.state.co.us;Bama Hager;Barritt, Lisa (CDC/ONDIEH/NCBDDD) (CTR);Charles, Jane M.;clarneso@wisc.edu;paula_bell@unc.edu;kgotscha@email.arizona.edu;fitzgeraldr@wustl.edu;Green, Katie (Kilker) (CDC/ONDIEH/NCBDDD);Van Naarden-Braun, Kim (CDC/ONDIEH/NCBDDD);sokec@wustl.edu;Peacock, Georgina (CDC/ONDIEH/NCBDDD);Rice, Catherine (CDC/ONDIEH/NCBDDD);judith.zimmerman@hsc.utah.edu;Stevens, Melody (CDC/ONDIEH/NCBDDD);Washington, Anita (CDC/ONDIEH/NCBDDD);Whitney, Julia (CDC/ONDIEH/NCBDDD) (CTR)
**Subject:** RE: Education and Outreach Conference call

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From: Jenner, Walter H
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To: ngarner@ms.soph.uab.edu; Lee Li-Ching (llee2@jhsph.edu); jemerson@email.arizona.edu; CRhodes1@cdc.gov; melanie@autism-alabama.org; achang@jhsph.edu; desposfr@umdnj.edu; zahorodn@umdnj.edu; MEWilson@uams.edu; gun2@cdc.gov; Wise, Jasina B.; AEHudson@uams.edu; McConnell, Anna; Frenkel, Gal (CDC/ONDIEH/NCBDDD); inu4@cdc.gov; Kelly.Kast@dphe.state.co.us; Bama Hager; Barritt, Lisa (CDC/ONDIEH/NCBDDD) (CTR); Charles, Jane M.; clarneso@wisc.edu; paula_bell@unc.edu; kgotscha@email.arizona.edu; fitzgeraldr@wustl.edu; kpk9@CDC.GOV; Kim Van Naarden; sokec@wustl.edu; ghn3@CDC.GOV; Cathy Rice; judith.zimmerman@hsc.utah.edu; sme1@cdc.gov; czo9@cdc.gov; asn0@cdc.gov; Jenner, Walter H
Subject: Education and Outreach Conference call

Hi Everyone
Our Education and Outreach conference call will be
Wednesday August 1, 2012
1-2 PM EST

It will be a webinar with Jennifer Sladen, Senior Program Associate, The ARC's Autism Now Center

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**Subject:** Simon's Foundation review
**Attachments:** Clinical research stable.docx

See attached review by the Simon's Foundation.

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SFARI SIMONS FOUNDATION AUTISM RESEARCH INITIATIVE

# Clinical research: Autism diagnosis stable over time

E-mail Print Share This

By Jessica Wright

24 July 2012

**Early promise**: Children diagnosed with autism when younger than 30 months are more likely to lose that diagnosis than those diagnosed when older.

Nearly all children diagnosed with autism retain their diagnosis when screened again at 8 years of age, according to a population-based study of more than 1,000 children, published in June in the *Journal of Developmental Behavioral Pediatrics*[1].

However, children first diagnosed when younger than 30 months are more likely to lose their diagnosis than those diagnosed after that age, the study found. These children may have benefited from early interventions. Alternatively, autism may be more difficult to diagnose accurately in children that young, the researchers say.

Other studies have reported that up to 90 percent of children diagnosed with autism at 2 years of age have an autism diagnosis when tested at 9 years[2]. But these children may be diagnosed with a different disorder on the spectrum — for example, Asperger syndrome or pervasive developmental disorder-not otherwise specified[3].

In the new study, researchers analyzed data collected by the Autism and

Developmental Disabilities Monitoring (ADDM) Network, a program funded by the Centers for Disease Control and Prevention.

The researchers used data from an ADDM study that screened 8-year-olds for autism in 2006 and 2008. That study screened health records to identify children who might have autism by looking for indications of a diagnosis, such as insurance billing codes or special education status. ADDM researchers then screened these children's health records for autism-like behaviors, which served as the basis for an autism diagnosis by trained clinicians.

The ADDM screened 4,958 children across the U.S. of whom 1,392 had a prior diagnosis of autism. They identified another 932 children with autism, and concluded that 61 of the 1,392 did not have autism at 8 years of age. Of the 61, they diagnosed 59 with an alternative disorder, such as attention deficit hyperactivity disorder or intellectual disability.

In the new study, the researchers looked for the potential reasons for this loss of diagnosis. They considered various factors, including the age at initial diagnosis, the presence of certain symptoms, such as language delay, and the credentials of the individual who made the original diagnosis.

They found that the age at initial diagnosis is the primary factor. Specifically, of 139 children diagnosed when younger than 30 months, 11 (eight percent) lost their diagnosis, compared with 50 of 1,192 children (four percent) diagnosed when older than 30 months.

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1: Wiggins L.D. *et al. J. Dev. Behav. Pediatr.* **33**, 387-395 (2012) PubMed

2: Lord C. *et al. Arch. Gen. Psychiatry* **63**, 694-701 (2006) PubMed

3: van Daalen E. *et al. Eur. Child Adolesc. Psychiatry* **18**, 663-674 (2009) PubMed


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**Sent:** 11 Jul 2012 10:57:43 -0400
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**Subject:** FW: Administrative prevalence numbers
**Attachments:** fulltext.pdf

FYI

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ORIGINAL PAPER

# Changes in the Administrative Prevalence of Autism Spectrum Disorders: Contribution of Special Education and Health from 2002–2008

**Judith Pinborough-Zimmerman · Amanda V. Bakian · Eric Fombonne · Deborah Bilder · Jocelyn Taylor · William M. McMahon**

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**Abstract** This study examined changes in the administrative prevalence of autism spectrum disorders (ASD) in Utah children from 2002 to 2008 by record source (school and health), age (four, six, and eight), and special education classification. Prevalence increased 100% with 1 in 77 children aged eight identified with ASD by 2008. Across study years and age groups rates were higher when health and school data were combined with a greater proportion of cases ascertained from health. The proportion of children with both a health ASD diagnosis and a special education autism classification did not significantly change. Most children with an ASD health diagnosis did not have an autism special education classification. Findings highlight the growing health and educational impact of ASD.

**Keywords** Autism · Prevalence · Epidemiology · Special education classification

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## Introduction

Once thought to be a rare condition, autism and related spectrum disorders have recently emerged as relatively common childhood neurodevelopmental disorders. In the United States (US), the current autism spectrum disorder (ASD) prevalence rate reported by the Centers for Disease Control and Prevention (CDC) in children aged eight was 1 in 110 children, reflecting a significant increase (57%) in the ten US sites that tracked prevalence changes from 2002 to 2006 (CDC 2009). ASD prevalence based on education administrative data from the US Department of Education, Office of Special Education and Programs is significantly lower than rates reported by the CDC, however, the proportion of children in special education with an autism classification nearly doubled from 2.3% in the 2002–2003 school year to 4.4% in 2007–2008 (Office of Special Education Programs 2008a, 2008b). The question remains whether similar prevalence increases are found in other US based ASD data sets such as individual state administrative registries with access to single and multiple administrative data sources.

Several reasons for increased ASD prevalence have been proposed. They include shifts in provider diagnostic patterns (Bishop et al. 2008; Grether et al. 2009; King and Bearman 2009; Nassar et al. 2009), increased awareness (Barbaresi et al. 2005; Fombonne et al. 2006; Kogan et al. 2009), and changes in administrative diagnostic criteria or program eligibility requirements (Fombonne 2009; Gurney et al. 2003; Kielinen et al. 2000; Newschaffer et al. 2005; Shattuck 2006). Two prominent changes are the broadening of the ASD diagnostic criteria in 1994 by the American Psychiatric Association (2000) and the addition of an autism special education classification with mandated implementation by the 1992–1993 school-year.

Variability across ASD epidemiology studies further complicates the interpretation of rising prevalence rates. Methods and data sources used for ASD case ascertainment and definition vary and impede clear comparisons across studies. Increased availability and access to more data sources has been correlated with higher ASD prevalence in previous studies (CDC 2007; CDC 2009). Conversely, prevalence has been consistently lower in studies in which case ascertainment has been based on health-only or special education-only administrative records (CDC 2007; CDC 2009; Fombonne 2001; Laidler 2005; Newschaffer et al. 2005; Pinborough-Zimmerman et al. 2010). Demographic factors such as population age also influence prevalence rates. Rates in children between 5 and 10 years of age are generally higher than in other age groups (Kogan et al. 2009; Yeargin-Allsopp et al. 2003).

Here, we report on the prevalence of ASD using multiple administrative datasets (health and education) spanning a 6 year time period in the same geographic region and age groups. The primary aims are to quantify changes in the measured ASD administrative prevalence (ASD health diagnosis and/or special education autism classification) and to examine how the completeness of surveillance and the magnitude of prevalence estimates vary when relying on administrative data from single versus multiple data sources and age groups. Our hypotheses are (1) that with minimal changes to the health and special education ASD diagnostic/classification criteria since the early 1990's, changes in the ASD administrative prevalence will begin to slow or plateau; (2) ASD administrative prevalence rates will be significantly lower when derived from one data source (health versus school), and lower in the youngest age group compared to older age groups; (3) with dramatic increases observed nationally in the proportion of children in special education with an autism classification, the proportion of total ASD cases identified from special education administrative data will significantly increase; and (4) with greater provider awareness and efforts to improve early diagnosis and access to services, the proportion of children with both an ASD health diagnosis and special education autism classification will significantly increase.

## Method

### Target Population

This study was conducted using ASD cases identified from the population of all children aged eight living in one of the three most densely populated counties in Utah (Davis, Salt Lake, and Utah) in study years (SY) 2002 ($n = 26{,}213$), 2006 ($n = 29{,}494$), and 2008 ($n = 33{,}757$). Additionally, ASD cases were identified from the same geographic region from the population of children aged four and six in SY 2006 ($n = 33{,}955$ and $n = 32{,}801$, respectively) and SY 2008 ($n = 35{,}803$ and $n = 34{,}368$, respectively). Growth in the target population was non-linear which likely was due to a number of factors. Utah was the fourth fastest growing state from 1990 through 2000 (Governor's Office of Planning and Budget 2001) and historically has had the highest fertility rate and largest family size in the US (Hamilton et al. 2009; U.S. Census Bureau 2009). Approval was obtained from the institutional review board at the University of Utah.

### Case Ascertainment

Ascertainment of records was facilitated by Utah law requiring providers to report ASD cases upon request to the Utah Department of Health or their agent. Cases were identified from administrative child records obtained from multiple electronic datasets including all major public education and health sources. Children receiving special education services were identified through a contractual agreement with the Utah State Office of Education. Special education data was comprised of lists of all students receiving special services by school and district as described by an Individualized Education Program (IEP) as mandated by Individuals with Disability Education Act (IDEA). We reduced the special education data to produce unduplicated lists of children receiving special education eligibility by year along with their primary classification. Children were counted as cases if they received Autism special education eligibility as their primary classification during a given study year.

Health sources included the Utah Department of Health's direct service programs, private and public clinics, child disability diagnostic centers, mental health centers and hospitals, and individual providers specializing in services for children with disabilities. Health sources were requested to provide birth date, gender, race/ethnicity, residential address, and date of service information from billing records containing at least one of approximately 200 International Classification of Diseases, Ninth Revision (ICD-9) diagnostic codes (ICD 1988) for ASD, and related developmental disabilities and medical conditions such as intellectual disability, language delay, Fragile X, etc.

Data linkages across all data sources were conducted utilizing a deterministic method using SAS software, version 9.2 (SAS Institute 2008) to obtain unduplicated counts from which overall ASD prevalence rates were determined. First, children were assigned unique identifiers based on a combination of parts of their first name, last name and date of birth. Next, we produced a master list containing all ASD cases from each source. This list was hand-checked

for accidental duplicates based on errors in the unique identifier. After hand-cleaning of the data, the master list was transposed to create a database containing one entry per child. Residential address and/or school address were verified for study year and records were then de-identified for further analysis. In children with both a school and residential address, we did not identify any cases in which children received educational services outside their county of residence.

### Administrative ASD case definitions

ASD cases were assigned to at least one of the following groups: (1) a special education autism classification (a special education disability classification of autism as defined by IDEA), (2) a health diagnosis of ASD (a previously documented ICD-9 ASD diagnosis–299.00, 299.80, 299.90–by a qualified provider), and (3) a special education autism classification plus a health ASD diagnosis.

### Analyses

Outcome variables of interest were ASD prevalence rates by administrative classification (a special education autism classification and/or an ASD health diagnostic code), study year (SY; 2002, 2006, and 2008), age group (children aged four, six, and eight), and gender. Period prevalence estimates were calculated using as the denominator the number of same-aged children residing in the three county surveillance area according to the Utah Department of Health's Center for Health Data (Utah Department of Health 2010). Prevalence results were reported per 1,000 children. Normal approximation to the binomial distribution was used to calculate 95% confidence intervals for prevalence rates. Chi-square tests were used to test for differences in prevalence rates across years and across age groups and to test for differences in special education classification within and across years and age groups. Prevalence rate ratios and percentage change were calculated to investigate trends in prevalence across years within age groups. Changes in the contribution of ascertainment source type to overall ASD prevalence was found by counting the number of ASD administrative cases derived from special education classification-only, health-only diagnosis, and both. Changes in ascertainment source contribution to ASD prevalence within age groups across years were tested using Welch's *t*-tests of proportions. Statistical analyses were conducted in SAS software, version 9.2 (SAS Institute 2008), and an alpha level of .05 was used for all statistical tests.

## Results

### Overall Prevalence Trends

ASD administrative prevalence per 1,000 children aged four, six, and eight in the three county surveillance region in Utah by year, sex, and record ascertainment source are shown in Fig. 1. In children aged eight prevalence increased from 6.5 (CI = 5.5-7.5) per 1000 in SY 2002, to 10.2 per 1000 (CI = 9.1–11.3) in SY 2006 ($\chi^2_{(1,\ N\ =\ 56{,}179)} = 21.4$,

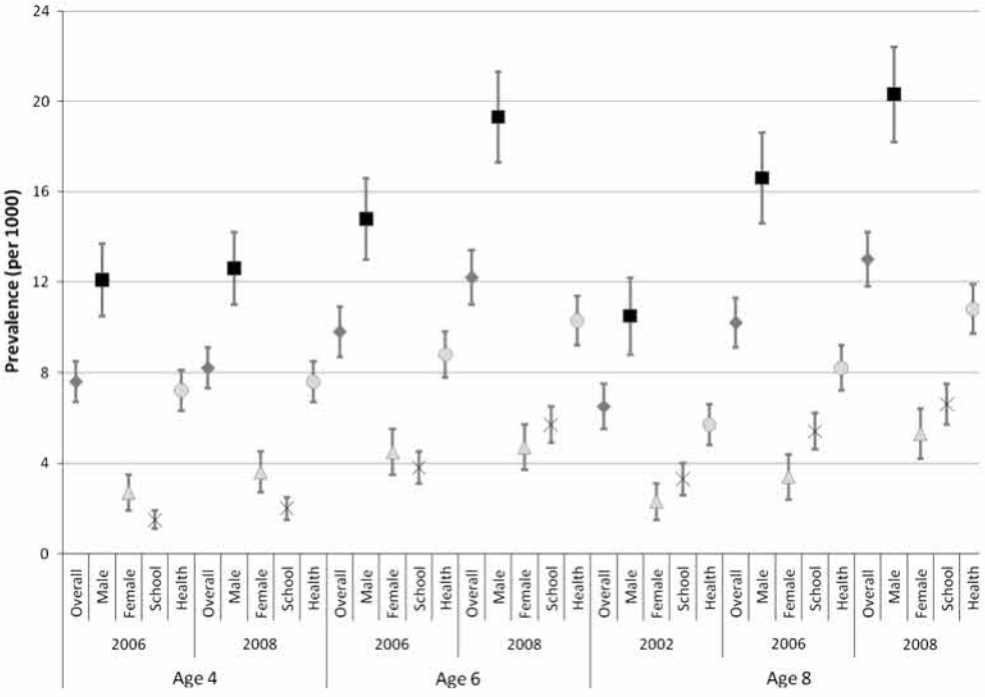


**Fig. 1** ASD administrative prevalence in children aged 4, 6, and 8 in the three county surveillance region in Utah by study year, gender, and record ascertainment source: school-only, health-only and overall (both school and health)

**Table 1** Number of ASD cases (*N*), rate ratio, percentage change in prevalence (%), and chi-square test *p*-values (*p*) by age and record ascertainment source

| | *N* | | | 2002–2006 | | | 2006–2008 | | | 2002–2008 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Group | 2002 | 2006 | 2008 | Rate ratio | % Change | *p* | Rate ratio | % Change | *p* | Rate ratio | % Change | *p* |
| *8 year-olds* | | | | | | | | | | | | |
| Overall | 171 | 301 | 432 | 1.6 | 57.0 | <.0001 | 1.3 | 27.5 | .001 | 2.0 | 100.0 | <.0001 |
| Male | 142 | 253 | 346 | 1.6 | 58.1 | <.0001 | 1.2 | 22.3 | .01 | 1.9 | 93.3 | <.0001 |
| Female | 29 | 48 | 86 | 1.5 | 47.8 | .08 | 1.6 | 55.9 | .01 | 2.3 | 130.4 | <.0001 |
| *Record ascertainment source* | | | | | | | | | | | | |
| School | 87 | 158 | 218 | 1.6 | 63.6 | .0003 | 1.2 | 22.2 | .05 | 2.0 | 100.0 | <.0001 |
| Health | 150 | 241 | 359 | 1.4 | 43.9 | .0005 | 1.3 | 31.7 | .0007 | 1.9 | 89.5 | <.0001 |
| *6 year-olds* | | | | | | | | | | | | |
| Overall | – | 322 | 418 | – | – | – | 1.2 | 24.5 | .004 | – | – | – |
| Male | – | 250 | 342 | – | – | – | 1.3 | 30.0 | .001 | – | – | – |
| Female | – | 72 | 76 | – | – | – | 1.0 | 4.4 | .96 | – | – | – |
| *Record ascertainment source* | | | | | | | | | | | | |
| School | – | 125 | 196 | – | – | – | 1.5 | 49.7 | .003 | – | – | – |
| Health | – | 287 | 353 | – | – | – | 1.2 | 17.0 | .05 | – | – | – |
| *4 year-olds* | | | | | | | | | | | | |
| Overall | – | 256 | 293 | – | – | – | 1.1 | 7.9 | .39 | – | – | – |
| Male | – | 211 | 229 | – | – | – | 1.0 | 4.1 | .71 | – | – | – |
| Female | – | 45 | 64 | – | – | – | 1.3 | 33.3 | .14 | – | – | – |
| *Record ascertainment source* | | | | | | | | | | | | |
| School | – | 50 | 54 | – | – | – | 1.3 | 33.3 | .90 | – | – | – |
| Health | – | 244 | 263 | – | – | – | 1.1 | 5.6 | .80 | – | – | – |

*Note*: Dashes indicate that data was not obtained

$p = < .0001$), and to 13.0 per 1000 (CI = 11.8–14.2) in SY 2008 ($\chi^2_{(1,\ N = 60,026)} = 61.3, p = < .0001$). In children aged 6 years prevalence significantly increased from 9.8 per 1000 (CI = 8.7–10.9) in SY 2006 to 12.2 (11.0–13.4) in study year 2008 ($\chi^2_{(1,\ N = 67,909)} = 8.5, p = .004$). The overall ASD administrative prevalence in children aged 4 years was 7.6 (CI = 6.7–8.5) in SY 2006. Prevalence increased to 8.2 (7.3–9.1) per 1000 in SY 2008 however this increase was not statistically significant ($\chi^2_{(1,\ N = 70,308)} = 0.9, p = .36$). Rate ratio and percentage of prevalence change by age group, source and gender are shown in Table 1. The greatest increase in prevalence (130.4%; $\chi^2_{(1,\ N\ =\ 28,976)} = 16.5$, $p = < .0001$) was found within the female group aged eight from SY 2002 to SY 2008.

The overall prevalence rates for children aged six and eight within the same SY were not significantly different in SY 2006 ($\chi^2_{(1,\ N = 62,918)} = 0.37, p = .54$) or SY 2008 ($\chi_{(1,\ N\ =\ 68,428)}{}^2 = 0.97, p = .32$). Prevalence in the same SY was significantly lower for children aged four compared with children aged eight in SY 2006 ($\chi^2_{(1,\ N = 64,007)} = 12.6$, $p = .0004$) and SY 2008 ($\chi^2_{(1,\ N = 69,738)} = 39.0, p < .0001$) and children aged four compared with children aged six in SY 2006 ($\chi^2_{(1,\ N\ =\ 67,335)} = 9.1, p = .0025$) and SY 2008 ($\chi^2_{(1,\ N\ =\ 70,882)} = 27.7, p < .0001$).

## Prevalence by Ascertainment Source

Prevalence rates for each age group varied as a function of ascertainment source with rates generally higher when both health and school ascertainment sources were used (Fig. 1). Prevalence rates based on health records alone were significantly higher than prevalence rates based on school records alone for children aged eight across all study years (SY 2002 versus SY 2006[$\chi^2_{(1,\ N\ =\ 55,952)} = 16.8$, $p < .0001$], SY 2006 vs. SY 2008 [$\chi^2_{(1,\ N\ =\ 63,080)} = 17.4$, $p < .0001$], and SY 2002 vs. SY 2008 [$\chi^2_{(1,\ N\ =\ 59,728)} = 24.8, p < .0001$])).

The proportion of ASD cases by age, year, and source type is displayed in Fig. 2. Of the total ASD administrative cases, on average, 49% of children aged eight, 59% of children aged six, and 81% of children aged four were only captured by a health diagnosis. The proportion of ASD cases aged four, six and eight captured by health-only sources did not significantly vary by year. Similarly, the proportion of ASD cases captured by both health and special education sources did not vary as a function of year. The proportion of total ASD administrative cases captured only by a special education autism classification, however, did significantly increase in children aged four and six from

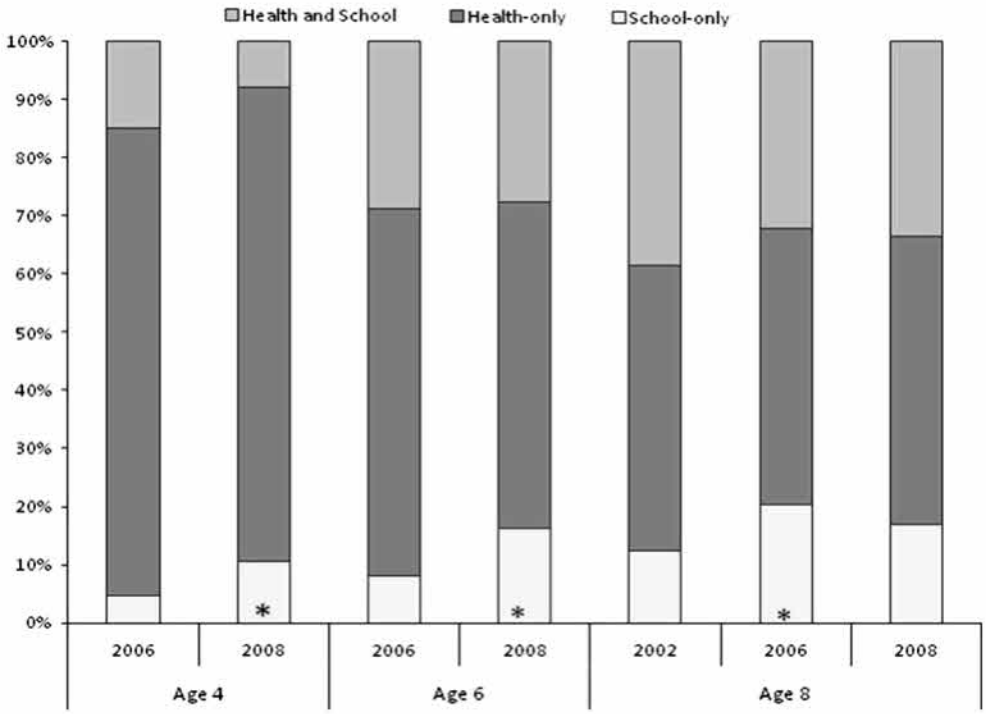


**Fig. 2** Proportion of ASD cases identified by source type (school-only, health-only, and both health and school) by year and age group. The * indicates a statistically significant change (at $\alpha = .05$) in the proportion of ASD cases captured by the school-only source between two study years. The significant change is between the year containing the * and the proceeding study year

SY 2006 to SY 2008 ($\chi^2_{(1,\ N\ =\ 593)} = 6.6$, $p = .01$, and $\chi^2_{(1,\ N\ =\ 834)} = 11.9$, $p = .0006$, respectively) and children aged eight from SY 2002 to SY 2006 ($\chi^2_{(1,\ N\ =\ 554)} = 4.8$, $p = .03$).

### School Special Education Services and an Autism Classification

A large proportion of children (20–50%) across age groups and study years with an ASD health diagnosis did not receive any special education services (Table 2). The proportion of children with an ASD diagnosis with an autism special education exceptionality ranged from 8% in children aged four in SY 2008 to 43% of children aged eight in SY 2002. As shown in Table 3, children aged eight with an ASD health diagnosis were not significantly more likely to receive an autism special education classification than an alternative special education classification in SY 2002 ($\chi^2_{(1,\ N\ =\ 152)} = 1.68$, $p = .20$) and SY 2006 ($\chi^2_{(1,\ N\ =\ 241)} = .04$, $p = .85$). In SY 2008, children aged six with an ASD health diagnosis were significantly more likely to receive non-ASD special education classification than ASD special education classification ($\chi^2_{(1,\ N\ =\ 353)} = 5.26$, $p = .02$), and children aged eight were about as likely to receive ASD than non-ASD special education classification ($\chi^2_{(1,\ N\ =\ 359)} = 3.58$, $p = .06$). Children aged four with an ASD health diagnosis, however, were significantly less likely to receive an autism special education classification in SY 2006 ($\chi^2_{(1,\ N\ =\ 244)} = 33.24$, $p < .0001$) and SY 2008 ($\chi^2_{(1,\ N\ =\ 263)} = 76.94$, $p < .0001$).

## Discussion

Several key findings emerge from this study. First, with the significant increases in ASD prevalence in young children aged six and eight, this study provides little or no evidence that the ASD administrative rates are slowing in our state. The measured administrative prevalence doubled from 2002 to 2008 in children aged eight with the best estimate of ASD risk to Utah children now 1 in 77. ASD rates in males rose to above 2% in children aged eight in 2008 with a 2.3 fold increase in females. Prevalence rates in children aged six significantly increased from SY 2006 to SY 2008 by 24.5% but no significant change in prevalence was found in children aged four during the same time period.

Two published studies conducted outside of the US investigated the positive predictive value of an ASD diagnosis contained in a record on receiving a secondary ASD diagnosis through an alternative surveillance approach. In Great Britain a diagnosis of pervasive developmental disorders was confirmed 92.5% of the time after independent expert record reviews (Fombonne et al. 2004). Similarly Danish researchers (Lauritsen et al. 2010) found a slightly higher rate at 94%. A preliminary multisite US analysis of the CDC's Autism and Developmental Disabilities Monitoring Network data for study years 2002 and 2006 obtained through personal correspondence with the CDC showed that of the total number of children abstracted with a previous ASD diagnosis and/or autism education classification, between 89.3% (2006) to 93.2% (2002) were classified as an ASD case using the network surveillance

**Table 2** Number (*N*) and percentage (%) of children with an ASD health diagnosis, special education classification, and autism special education classification by age and study year

| Study year | *N* ASD health diagnosis | *N* special education | *N* autism special education | % special education | % autism special education |
|---|---|---|---|---|---|
| *Statewide 8 year-old special education population* | | | | | |
| 2002 | – | 4470 | 109 | 12% | 2%* |
| 2006 | – | 5044 | 184 | 12%† | 4%† |
| 2008 | – | 5348 | 271 | 11%** | 5%** |
| *8 year-olds with ASD health diagnosis* | | | | | |
| 2002 | 150 | 121 | 66 | 80% | 43% |
| 2006 | 241 | 152 | 89 | 75% | 37% |
| 2008 | 359 | 210 | 134 | 68%** | 37% |
| *6 year-olds with an ASD health diagnosis* | | | | | |
| 2006 | 287 | 146 | 86 | 62%† | 30% |
| 2008 | 353 | 222 | 108 | 69% | 31% |
| *4 year-olds with an ASD health diagnosis* | | | | | |
| 2006 | 244 | 99 | 33 | 50% | 14% |
| 2008 | 263 | 118 | 22 | 50% | 8% |

*Note*: Dashes indicate that data was not obtained

* Significant change, 2002–2006, $p < .05$

† Significant change, 2006–2008, $p < .05$

** Significant change, 2002–2008, $p < .05$

**Table 3** Risk that a child with a health diagnosis of ASD receives an autism special education classification versus a non-autism special education classification by study year and age

| Age | *N* ASD | *N* non-ASD | Risk | 95% C.I. | *p* |
|---|---|---|---|---|---|
| *SY 2002* | | | | | |
| 8 | 66 | 55 | 1.20 | 0.93–1.46 | .20 |
| *SY 2006* | | | | | |
| 8 | 89 | 91 | 0.98 | 0.82–1.18 | .85 |
| 6 | 86 | 92 | 0.95 | 0.80–1.14 | .59 |
| 4 | 33 | 88 | 0.47 | 0.35–0.64 | <.0001 |
| *SY 2008* | | | | | |
| 8 | 134 | 110 | 1.16 | 1.00–1.34 | .06 |
| 6 | 108 | 137 | 0.83 | 0.70–0.98 | .02 |
| 4 | 22 | 109 | 0.28 | 0.19–0.41 | <.0001 |

methodology. The question yet to be answered is whether or not the positive predictive value of a recorded diagnosis of ASD will remain high should administrative prevalence rates continue to rise.

In light of the magnitude of increases in our administrative prevalence it is important to note that the true ASD prevalence in our state is still unknown. Use of administrative data in isolation as used in this study raises the potential for both false positives and negatives. Even though study findings are higher than current national rates, we are concerned that our 2008 prevalence findings may be actually an underestimate of prevalence in our state. The CDC's record review system has been found to be conservative in determining ASD case status (Avchen et al. 2010). A number of researchers have made the point that surveillance methods that rely on a previous clinical diagnosis only or on single administrative datasets potentially under estimates the number of children with ASD in the population (Barbaresi et al. 2005; CDC 2007; CDC 2009; Laidler 2005; Newschaffer et al. 2005; Pinborough-Zimmerman et al. 2010; Shattuck 2006). With this in mind efforts are underway to validate Utah's administrative prevalence in a subset of our surveillance population using the CDC's surveillance approach which includes an expert review of abstracted charts for the identification of previously undiagnosed children meeting study ASD case definitions (Van Naarden Braun et al. 2007) and verification of the ASD diagnosis in the record. Additionally the CDC's surveillance method gives us the ability to capture important phenotypic information missing in administrative datasets.

The consistency of our 2002 and 2006 administrative ASD prevalence rates in children aged eight (6.5 per 1,000 and 10.2 per 1,000 respectively) compared with those reported using CDC's MADDSP in study year 2002 (6.6 per 1,000; CDC 2007) and four of the six sites with access to school and health records in SY 2006 (CDC 2009) give us confidence that our 2008 rates are likely not an over

estimate of prevalence. Interestingly, the rise in administrative prevalence found in this study among children aged eight from SY 2002 to SY 2006 mirrored the 57% average increase reported by the CDC in ten US sites (Utah excluded) using the MADDSP surveillance approach during the same study years (CDC 2009).

With national and local efforts aimed at improving the identification of children with ASD at younger ages, an encouraging finding was that no significant difference was found within the same study year in the measured ASD administrative prevalence between children aged six and eight. Conversely, prevalence in children aged four was significantly lower than both prevalence in children aged six and eight in the same study year suggesting continued efforts are still needed to improve early diagnosis of ASD. Since the average age of diagnosis in the US exceeds 4 years of age (CDC 2009), the invariable prevalence in the 4 year old population in SY 2006 and SY 2008 along with the lower prevalence of this age group compared to 6 years old from the same study year may reflect slow improvements in the identification of ASD among young children in our study area.

Understanding the severity of ASD and co-morbid intellectual disability may provide additional insight into changes in ASD prevalence by age, study year, and gender. The relatively higher proportion of children in the older age groups being ascertained, in particular, females suggests that providers have made improvements in diagnosing females and children with milder forms of ASD either with or without intellectual impairment. Unfortunately very few measures of severity of ASD are captured by the administrative datasets used for this study with the exception of health data diagnostic codes and those specifically for autism (299.00) and other specified pervasive developmental disorder (299.80 and 299.90). However, an ad-hoc analysis of ASD diagnostic codes by year and age group showed no discernable pattern emerging. Across age groups and study years the proportion of ASD cases identified from health sources with only a 299.80 ICD code ranged from 27% to 36% while cases with only a 299.00 ICD code ranged from 31% to 42%. Similarly cases with greater than one ASD ICD-9 code ranged from 28% to 32%.

The American Psychiatric Association (APA) reported that distinctions among the ASD subcategories are inconsistent over time and may vary across regions (APA 2010). In the APA's proposed changes to the Diagnostic and Statistical Manual (DSM) V, 299.00 and 299.80 have been collapsed into a single category with the inclusion of clinical specifiers such as severity. The addition of a severity level scale may improve our ability in the future to capture and understand changes in prevalence related to severity.

A second major finding of this study was, as we hypothesized, that ASD administrative prevalence rates are significantly lower when derived from only a single data source, and rates are lowest in the youngest age group. The proportion of overall cases derived from health versus school administrative data varied significantly by age group, and although the proportion of children aged 4 and 6 ascertained by school-only sources increased between 2006 and 2008, a higher proportion of children were consistently captured at health than school sources across years and age groups. Not surprisingly, preschool-age children were predominately captured by health data.

Like other states, Utah is experiencing significant increases in the number of children receiving services under an autism special education classification (Office of Special Education Programs 2008a, 2008b). Statewide, the proportion of children aged eight in special education with an autism classification more than doubled from 2002 (2%) to 2008 (5%). The number of students with two other classification categories–communication disorders and developmental disabilities—has also risen; yet, enrollment has dropped for students qualifying under intellectual disabilities, specific learning disabilities, and behavior disorders exceptionalities. Shattuck (2006) suggested that changes in autism prevalence may reflect diagnostic substitution for those who previously may have qualified under intellectual and learning disability categories. Although not able to address Shattuck's hypothesis directly, the findings of this study may yield important information on special education's role on increases in overall ASD administrative prevalence.

We found that special education's contribution to overall prevalence was measurable, but small compared to the proportion of health administrative cases for a number of reasons. Health sources consistently diagnose ASD almost twice as frequently as special education sources assign an autism classification. Second, the growth in the number of children with autism special education classification parallels the growth in ASD health diagnoses but a large gap remains between the administrative prevalence based on health versus special education datasets. Third, without special education autism classification data, the overall ASD administrative prevalence in children aged eight in our region would have been reduced only by 12% in 2002 and 17% in 2008. Contrary to our third hypothesis, the majority of children with a health ASD diagnosis were not receiving school special education services under an autism classification. While one-third of children aged eight with a health ASD diagnosis were receiving services under an autism special education classification, another one-third of children aged six and eight with a health ASD diagnosis were not receiving any type of special education services. It is unknown if these children were in regular

public education programs, home-schooled, or private school which is a limitation of this study. In addition, we do not have any information concerning the cognitive functioning in this group of children. Lastly, contrary to our fourth hypothesis, the proportion of children with both an ASD health diagnosis and autism classification did not significantly change over time for children aged six and eight.

It is not totally clear why healthcare data would show greater prevalence and increase than special education administrative data. Nor do we know the reasons for ongoing discordance between children with ASD health diagnosis that do not receive a school autism classification. School practitioners are not required to use the health criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) (APA 2000) to identify children whom qualify for an autism special education classification. Rather, school teams assign a special education classification based on the US Code of Federal Regulations (CFR; National Archives and Records Administration 2010). Both DSM and CFR guidelines emphasize deficits in three general domains: social interaction, communication, and restrictive/stereotypical behaviors. Distinctions between DSM criteria and CFR classification vary across states (MacFarlane and Kanaya 2009), however, federal code requires that students eligible for special education services receive only one classification. Utah State Board of Education special education rules state that an autism classification is used if autism adversely affects the student's educational performance, necessitates special education and related services, and is recognized by the IEP team as the student's primary disability even in the presence of other disabling conditions such as emotional disturbance or intellectual disability (Utah State Board of Education, 2010). Furthermore, as part of the US Individuals with Disability Act, schools by law are required to educate pupils with disabilities and other special needs in the least restrictive environment that is appropriate to the individual pupil's needs. As children with disabilities, such as ASD, must have the opportunity to be educated with non-disabled peers to the greatest extent appropriate, pupils with ASD may not require special education services and may be receiving instruction and necessary accommodations in a general education classroom. These students would not be captured in a special education administrative dataset. So in other words, like elsewhere in the US, our school practitioner's operational definitions differ from DSM criteria, educators are able to only assign one primary special education classification, and special education data does not capture pupils with ASD for whom the regular classroom has been deemed the least restrictive environment.

Our study's findings have important policy implications. Given disparities between the proportion of children with an ASD health diagnosis and special education autism classifications shown by this study, the potential exists for families and providers to become disgruntled or confused by differences in special education classifications and health diagnoses. Baird (1999) reported that disputes between parents of pupils with autism and school district programs represent the fastest growing and most expensive area of litigation in special education. Eleven US states (excluding Utah) now require that a pediatrician, clinician, or ASD diagnosis be part of the education evaluation (MacFarlane and Kanaya 2009). With Utah's per public funding in education ranked last in the nation and high special education costs for children with an autism classification (Center for Special Education Finance 2003), it could be particularly helpful for health providers, upon appropriate parental consent, to provide diagnostic and prognostic information to the education team. This communication is particularly critical for general education personnel who may be educating students with ASD that are not eligible for an autism classification yet need accommodations in the general education setting. To improve communication between health and education, Utah education teams are currently developing autism specific guidelines for health care providers that outline the type of information that may be most beneficial for the schools to receive. Health provider awareness of laws for special education is key for physicians who are caring for families and children in a medical home. Cross health and education collaboration on providing specialized autism training could further understanding of the distinctions between an ASD diagnosis and special education autism classification and may improve overall communication.

Several additional limitations of this study should be noted. First, individual child records were not reviewed to substantiate an ASD diagnosis through an independent review process. Race/ethnicity could not be captured across all data sources and were thus not available for analysis. Next, US healthcare providers face numerous challenges getting reimbursed for ASD-related services. It is common for insurance companies to have exemptions specific to autism. Providers subsequently may choose not to use ASD diagnostic codes in health administrative datasets despite the presence of an ASD and these children would not have been captured in this study. Measuring trends in co-morbid diagnostic codes of cases and non-cases in future studies may provide insight into this potential trend. With lack of healthcare coverage or the potential for non-health insurance reimbursement, the only option for some US families may be to obtain autism related services through the public schools making special education data crucial to US administrative prevalence estimates. Regional variations in service availability through health and education sources

are likely to exist across the US so our findings may not apply to other regions in the US.

Limitations of this study are balanced with a number of strengths. Surveillance data was examined across multiple administrative datasets which allowed for the matching of individual children across sources. As we have shown, access to both health and education datasets results in a more accurate estimate of ASD administrative prevalence in our community. This surveillance method demonstrates a cost effective means of monitoring changes in ASD prevalence over time. Data from our surveillance activities assist in program planning and provide a potential mechanism to study long-term ASD trends. The identification of disparities in prevalence rates as a function of data source (health versus school) may support efforts to improve communication and understanding of ASD diagnosis and classification requirements across sources.

Reasons for such marked changes in ASD prevalence in Utah remain unclear. The magnitude of this measure necessitates an investigation as to whether or not it represents a true rise in risk for the development of an ASD in Utah. In the present study, there is no definitive way to measure the portions of the increase that can be attributed to improved ASD awareness, diagnostic changes, or service mandates. It remains possible that in addition to these factors there is a true increase in incidence due to a yet unknown environmental risk mechanism. Regardless, increases in ASD prevalence of the magnitude we document in this study place severe burdens on public health and education services in our state.

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New information on the burden of ASD

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# The Co-Morbidity Burden of Children and Young Adults with Autism Spectrum Disorders

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## Abstract

***Objectives:*** Use electronic health records Autism Spectrum Disorder (ASD) to assess the comorbidity burden of ASD in children and young adults.

***Study Design:*** A retrospective prevalence study was performed using a distributed query system across three general hospitals and one pediatric hospital. Over 14,000 individuals under age 35 with ASD were characterized by their co-morbidities and conversely, the prevalence of ASD within these comorbidities was measured. The comorbidity prevalence of the younger (Age<18 years) and older (Age 18–34 years) individuals with ASD was compared.

***Results:*** 19.44% of ASD patients had epilepsy as compared to 2.19% in the overall hospital population (95% confidence interval for difference in percentages 13.58–14.69%), 2.43% of ASD with schizophrenia vs. 0.24% in the hospital population (95% CI 1.89–2.39%), inflammatory bowel disease (IBD) 0.83% vs. 0.54% (95% CI 0.13–0.43%), bowel disorders (without IBD) 11.74% vs. 4.5% (95% CI 5.72–6.68%), CNS/cranial anomalies 12.45% vs. 1.19% (95% CI 9.41–10.38%), diabetes mellitus type I (DM1) 0.79% vs. 0.34% (95% CI 0.3–0.6%), muscular dystrophy 0.47% vs 0.05% (95% CI 0.26–0.49%), sleep disorders 1.12% vs. 0.14% (95% CI 0.79–1.14%). Autoimmune disorders (excluding DM1 and IBD) were not significantly different at 0.67% vs. 0.68% (95% CI −0.14-0.13%). Three of the studied comorbidities increased significantly when comparing ages 0–17 vs 18–34 with $p<0.001$: Schizophrenia (1.43% vs. 8.76%), diabetes mellitus type I (0.67% vs. 2.08%), IBD (0.68% vs. 1.99%) whereas sleeping disorders, bowel disorders (without IBD) and epilepsy did not change significantly.

***Conclusions:*** The comorbidities of ASD encompass disease states that are significantly overrepresented in ASD with respect to even the patient populations of tertiary health centers. This burden of comorbidities goes well beyond those routinely managed in developmental medicine centers and requires broad multidisciplinary management that payors and providers will have to plan for.

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**Subject:** 2011 Workshop on US Data to Evaluate Changes in ASD Prevalence Summary
**Attachments:** CS225567_ExecutiveSummary_Final Print.pdf, CS225567_WorkshopSummary_Final Print.pdf

Dear Panelists,

Thank you so much for your participation in last year's *Workshop on U.S. Data to Evaluate Changes in Prevalence of the Autism Spectrum Disorders (ASDs)*. The workshop was co-sponsored by CDC's National Centers on Birth Defects and Developmental Disabilities (NCBDDD) and Autism Speaks. The Executive and Full Workshop summaries are attached and are also available on the CDC's and Autism Speaks' websites.

The purpose of the workshop was to bring together scientists and stakeholders in the field of autism surveillance and research to:

- Summarize where we are in our current understanding of changes in ASD prevalence in the US;
- Learn from different perspectives, including experts who have studied prevalence changes among other complex conditions;
- Share ideas for the field to move forward in understanding trends in ASD prevalence.
- Stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

The key suggestions for framing the path forward centered around the following themes:

- Increase collaboration efforts
- Better utilize existing data
- Use data on prevalence and characteristics of individuals with an ASD to better inform service and support efforts
- Implement new types of data collection and studies

It is hoped that the information, research, and opinions shared during this workshop will add to the knowledge about ASD prevalence and encourage further work among public and private groups to understand the multiple factors influencing increasing ASD prevalence in the U.S. and beyond.

CDC is moving forward and is addressing several of the panelist suggestions. For example, CDC:

- Continues to monitor the prevalence of ASDs among 8-year-old children through the multi-site collaboration of the Autism and Developmental Disabilities Monitoring (ADDM) Network. An updated prevalence report is expected this Spring and ongoing data collection is underway for another cohort of children in areas of the United States.
- Has begun projects in 6 ADDM Network sites to determine the prevalence of ASDs among children at 4 years of age.
- Has supported 2 projects (CA and FL) currently underway to examine the prevalence of ASDs in young children with one study conducting community-based screening for ASDs in pediatric practices.
- Is working with NIH and Autism Speaks to support a project by the University of Minnesota through the Association of University Centers on Disabilities (AUCD) to study autism in a Minnesota Somali community to follow-up concerns about higher autism prevalence than in other communities.
- Has implemented analyses related to how specific identification and risk factors in the population have changed and whether they could have a significant impact on increasing ASD prevalence.
    - An analysis was completed and a paper published indicating that population changes in select perinatal factors such as low birth weight and gestational age have had a minimal effect on ASD prevalence changes reported in the ADDM Network (Schieve et al., 2011).
    - Several other analyses by ADDM Network investigators examining other identification and risk factors in relation to ASD prevalence change are underway.

- Has partnered with Autism Speaks to build on the ADDM Network infrastructure to evaluate the completeness of ASD prevalence estimates. Autism Speaks is funding a project in the SC ADDM site through the Medical University of South Carolina to add community screening and assessment to the existing ADDM record-review surveillance method.
- Continues to work as part of the Interagency Autism Coordinating Committee (IACC) to identify and implement a Strategic Plan for Autism Research coordinated among public and private organizations. This workshop summary will be shared with the IACC and can be used to inform the next iteration of the IACC Strategic Plan.
- Is conducting one of the largest studies in the United States to help identify factors that may put children at risk. This study, being conducted across a 6 site network known as the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE), is called SEED, the Study to Explore Early Development. SEED is looking at numerous risk factors of autism such as genetics, environmental exposures, pregnancy factors, and behavioral factors. The study enrollment is on schedule, and first reports are expected from SEED later this year.
- Continues to work with the community to increase awareness of early signs of ASDs and other developmental disabilities. Our "Learn the Signs. Act Early." program is working to address critical gaps in early identification of autism and other developmental disabilities in two ways:
    - First, we know that all parents play a critical role in monitoring their children's developmental milestones. Our program offers free online resources for parents to help them do that. We also have resources for health professionals and early childhood teachers. www.cdc.gov/actearly
    - Second, we are working with representatives from public health, medicine, education, and advocates in states to improve early identification, screening, and referral practices so children and their families can access the services and supports.
- For more information: www.cdc.gov

If you would like to have hard copies of the Workshop Report and/or Executive Summary mailed to you, please send your name, mailing address, and number of copies (up to 5) to Lekeisha Jones at lfj9@cdc.gov.

Thank you for your work and commitment for people with ASDs. Hopefully, this workshop summary will be a helpful resource for others as it has been for CDC.

*Cathy* and *Marshalyn*

Catherine E. Rice, PhD and Marshalyn Yeargin-Allsopp, MD
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Co-Sponsored by Autism Speaks

# Workshop on U.S. Data to Evaluate Changes in the Prevalence of Autism Spectrum Disorders (ASDs)

## Executive Summary

**Tuesday, February 1, 2011**

**Centers for Disease Control and Prevention**
**Tom Harkin Global Communications Center | 1600 Clifton Road, N.E. | Atlanta, Georgia**

National Center on Birth Defects and Developmental Disabilities
Division of Birth Defects and Developmental Disabilities

# Acknowlegement


## Co-Sponsored by the National Center on Birth Defects and Developmental Disabilities (NCBDDD), Centers for Disease Control and Prevention (CDC) and Autism Speaks


*Panel members* were representatives from:*

Autism Science Foundation
Autism Society of America (invited)
Colorado Department of Health
Columbia University
Drexel University
George Washington University
Health Resources and Services Administration (HRSA)
Johns Hopkins University
Kaiser Permanente®, California
Medical University of South Carolina
National Institutes of Health (NIEHS, NIMH)
Parkinson's Institute
SafeMinds
Parents of children with an Autism Spectrum Disorder
Persons with an Autism Spectrum Disorder
University of Alabama at Birmingham
University of Arizona, Tucson
University of Arkansas
University of California, Davis – MIND Institute
University of North Carolina, Chapel Hill
University of Pennsylvania
University of South Florida
University of Southern California, Marshall
University of Utah
Washington University in Saint Louis
University of Washington
University of Wisconsin, Madison
Yale University


### Workshop Planning Committee

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| Amanda Bakian, PhD (Feb 2011) | University of Utah |
| Tom Bartenfeld, PhD | NCBDDD, CDC |
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| Martha Wingate, DrPH | University of Alabama, Birmingham |
| Marshalyn Yeargin-Allsopp, MD | NCBDDD, CDC |


**Refer to Appendix B in full workshop summary for biographies of panel members*

*The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC). This summary report reflects statements made by individuals attending the workshop and does not constitute consensus recommendations made to the CDC.*

# Workshop Summary

## PURPOSE

Autism spectrum disorders (ASDs) are estimated to occur among about 1% of children in the U.S. This is in line with estimates from other industrialized countries. However, the identified prevalence of ASDs has increased significantly in a short time period based on data from multiple studies including the Centers for Disease Control and Prevention's (CDC) Autism and Developmental Disabilities Monitoring (ADDM) Network (http://www.cdc.gov/ncbddd/autism/addm.html). Whether increases in ASD prevalence are partly attributable to a true increase in the risk of developing ASD symptoms or solely to changes in community awareness and identification patterns is not known. It is clear that more children are identified with an ASD now than in the past and the impact on individuals, families, and communities is significant. However, disentangling the many potential reasons for ASD prevalence increases has been challenging. Understanding the relative contribution of multiple factors such as variation in study methods, changes in diagnostic and community identification, and potential changes in risk factors is an important priority for the ADDM Network and for CDC. This workshop was co-sponsored by CDC and Autism Speaks as a forum for sharing knowledge and opinions of a diverse range of stakeholders about changes in ASD prevalence. This summary report reflects statements made by individuals at the forum and discussions that were held among the attendees, and does not constitute formal consensus recommendations to CDC. The information, research, and opinions shared during this workshop add to the knowledge base about ASD prevalence in an effort to stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

## FRAMEWORK

The workshop brought together epidemiologic prevalence and surveillance experts in ASDs and other conditions as well as representatives from autism organizations, parents of children with ASDs, adults with an ASD, and other stakeholders. A total of 342 people registered to attend the workshop (143 in person and 199 via webinar).

Prior to the meeting, the panel members met via teleconference and were asked to submit at least two publications that they viewed as important background reading for understanding ASD prevalence trends. Panel members were provided with the compiled reference list (Appendix C) and articles and were asked to review, at a minimum, the priority readings prior to the workshop.

Presentations during the morning of the workshop summarized current knowledge and issues related to ASD prevalence and provided perspectives from subject matter experts in cancer, Parkinson disease, asthma, schizophrenia, and analytic modeling of prevalence changes.

Following the morning's presentations, the public was invited to provide statements, and there was an open invitation to provide written comments before and after the workshop. Workshop organizers, panelists, and stakeholders were asked to consider these comments when expressing their opinions on priorities for evaluating changes in ASD prevalence.

After hearing open comments from the community, the workshop was divided into four panels:

- Panel 1 – Utility of ASD Prevalence Data
- Panel 2 – U.S.-Based ASD Service Data
- Panel 3 – Autism and Developmental Disabilities Monitoring (ADDM) Network Data
- Panel 4 – What Else Is Needed To Understand ASD Trends?

For the workshop panel sessions, members of each panel were asked to reflect on questions along the following themes to better understand ASD prevalence trends:

- What can we do now with existing data?
- What should we do next to build on existing data systems?
- What else is needed in terms of new analyses, data collection, or other efforts?

## SUMMARY POINTS

Panel members and attendees commented that the effort to increase transparency and expand the dialogue related to ASD prevalence change was appreciated and necessary to move the community forward around the issue of understanding ASD prevalence changes. Additional key points made during the workshop included:

- The identified prevalence of ASD has increased significantly in a short time period across multiple studies, including data from the CDC's U.S.-based Autism and Developmental Disabilities Monitoring (ADDM) Network.
- CDC is the source for ASD prevalence estimates in the U.S., but other data systems exist or could be developed to better understand trends in ASDs.
- ASDs are conditions estimated to occur among about 1% of children in the U.S. There is an urgent demand to address the many needs associated with ASDs. Prevalence estimates have, for example, fueled action by advocacy groups and the Interagency Autism Coordinating Committee (IACC) and driven the creation of legislation and presidential priority. However, individuals, families, and communities continue to struggle to address unmet needs across the lifespan of people with ASDs. ASD prevalence estimates are important to stakeholders for program planning and making policy changes, in addition to highlighting the need for research into causes and interventions.
- In terms of reasons for increased ASD prevalence, the debate has been dichotomized by researchers, advocacy groups, and the media to indicate that increases must be explained either by identification factors or by increased risk among the population. In reality, a more complex understanding is needed. It is clear that some of the increase has been related to intrinsic and extrinsic identification factors. However, although a true increase in ASD symptoms cannot be ruled out, such an increase has been difficult to prove. Panels discussed needing to identify and use methods to better understand the role of potential identification and risk factors in the changing prevalence of ASD.
- Some people expressed hope that understanding why ASD prevalence has increased may help identify modifiable risk factors. There was debate about the roles of prevalence and surveillance in answering questions about risk and causes of ASDs. Prevalence studies provide descriptive data on the number of people with a condition in a defined population. These types of studies are not sufficient to identify what causes ASDs. However, prevalence studies can be used as tools to examine variation in occurrence of ASDs across place, groups, time, and exposures, which may provide clues about groups who are at increased risk for ASDs. Other study designs would then be necessary to fully investigate the reasons behind observed variation in prevalence.
- There are likely multiple forms of ASDs with multiple causes that are poorly understood. It was noted that sufficient evidence exists that biologic and environmental factors, alone and in interaction, need to be considered as causes. It is not necessary to have confirmation that a portion of the increase in ASD prevalence is due to increased risk in the population to motivate the active pursuit of causes of ASDs. By better understanding what causes ASDs, maybe we can understand the increases in measured prevalence.

- A risk factor might be strongly associated with ASD and might be modifiable, but it might not have increased sufficiently in the population during the time frame of interest. Therefore, this risk factor might be related to an individual's risk for ASD but not related to the increase in population prevalence of ASD. The model demonstrated that for any factor to have made a noteworthy contribution to population changes in ASD prevalence during a short time period, three conditions must be met: the factor has to be fairly prevalent in the population, it has to have increased substantially, and it has to be strongly associated with diagnosed ASD.
- There was a shared recognition of the importance of, and commitment to, obtaining and using prevalence and epidemiologic information to improve the lives of people with ASDs.

## PANEL DISCUSSION SUMMARIES

The four panel chairs compiled main discussion points brought forth by their members for building on existing infrastructure and for developing new initiatives to better understand ASD trends. These discussion points are summarized below.

### Collaboration

The panels indicated that collaboration among professionals and stakeholders is important, and the following points were made to assist collaborative efforts among those interested in understanding ASDs and supporting the ASD community through science:

- Continue efforts of this workshop to develop and enhance communication among families, individals affected, researchers, service providers, advocates, and government entities about ASD prevalence, research, and service needs.
- Seek public–private partnerships to support data collection, analyses, and usage.
- Seek input from and collaboration with those in other fields, such as cancer epidemiology, to identify and utilize methodologies for evaluating changes in the prevalence of complex conditions.
- Collaborate with other data systems, such as the Environmental Public Health Tracking Network, to improve access to population-level environmental data.

### Analytic Activities

Points were made on better utilizing existing data to understand ASD prevalence trends:

- Provide funding opportunities to encourage analyses and dissemination of findings from existing datasets.
- Link existing datasets identifying children with ASDs to other health, service, and research databases.
- Conduct analyses that will help explain variations in ASD prevalence across subgroups (e.g., race and ethnicity, sex, diagnostic subtype, and geographic groups) and if variation persists over time.
- Use complex modeling and multifactorial analyses to better understand variation in ASD prevalence such as by possible etiologic subgroups (e.g., specific genetic conditions and family history), geogrphy, and sex, and by potentially harmful exposures among cohorts.
- Conduct simulation studies to predict the anticipated course of ASD prevalence.

### Data Enhancements to Inform Practice

The panels discussed the importance of using data on the prevalence and characteristics of people with an ASD to better inform service and support efforts:

- In addition to prevalence estimates, provide more in-depth information on population characteristics of people with an ASD (such as functional level and impact of functional limitations, subtype, developmental characteristics, and associated conditions) to improve program planning and support needs.
- Examine data to better understand lags and disparities in ASD identification to, in turn, inform screening, identification, and program planning.
- Conduct analyses to provide better estimates of current and future needs of adults with an ASD.

## Additional Studies

Beyond enhancements to existing data systems and uses, the panels discussed new types of data collection and studies including:

- Expand ASD prevalence efforts to include very young children and adults.
- Examine prevalence over time among older children by following up with those identified in previous studies
- Conduct additional validation studies at various ADDM Network sites and use the results to enhance estimates of ASD
  prevalence.
- Conduct further studies to better understand who is identified and who is not identified in national parent report surveys and in service-based data such as special education child counts.
- Develop ways of better capturing the heterogeneity of ASD phenotypes including the complexity of core and associated features that may present in different combinations for people with an ASD.
- Improve tools for culturally sensitive screening and case confirmation among large populations.
- Identify ways to measure and monitor the traits associated with ASDs among the general population to reflect various degrees (dimensional) rather than categorical (having an ASD or not having an ASD) case vs. not case) levels. This includes characterizing how these traits overlap with other conditions and typical development.
- Conduct cross-sectional and longitudinal studies following cohorts over time. This could include examining trends in characteristics of the population, such as ASDs among specific subgroups (based on, for example, race and ethnicity, immigrant status, and socioeconomic status), age of identification, diagnoses, comorbidities, services use, and family characteristics.
- Monitor trends in ASD prevalence prospectively to rule out identification factors by consistently conducting developmental and ASD screening at a given age with diagnostic follow-up and documentation of each step and outcome.
- Conduct prospective studies that examine biology, phenotype, identification patterns, and service needs and use of people with an ASD.
- Examine trends in other behaviorally defined conditions (e.g., attention-deficit/hyperactivity disorder, depression, and anxiety).

## NEXT STEPS

The workshop summary will be made freely available to the community through posting on the CDC's and Autism Speaks' websites. It is hoped that the information, research, and opinions shared during this workshop will add to the knowledge base about ASD prevalence and stimulate further work among public and private groups to understand the multiple reasons behind changes in identified ASD prevalence in the U.S.

# Notes

Centers for Disease Control and Prevention
www.cdc.gov/autism
cdcinfo@cdc.gov
1-800-CDC-INFO

Autism Speaks
www.autismspeaks.org
research@autismspeaks.org
1-212-252-8584

CS225567

Co-Sponsored by Autism Speaks

# Workshop on U.S. Data to Evaluate Changes in the Prevalence of Autism Spectrum Disorders (ASDs)

**Tuesday, February 1, 2011**

**Centers for Disease Control and Prevention**
**Tom Harkin Global Communications Center | 1600 Clifton Road, N.E. | Atlanta, Georgia**

*Full agenda available in Appendix A*

National Center on Birth Defects and Developmental Disabilities
Division of Birth Defects and Developmental Disabilities

# Acknowlegement


## Co-Sponsored by the National Center on Birth Defects and Developmental Disabilities (NCBDDD), Centers for Disease Control and Prevention (CDC) and Autism Speaks


*Panel members* were representatives from:*

Autism Science Foundation
Autism Society of America (invited)
Colorado Department of Health
Columbia University
Drexel University
George Washington University
Health Resources and Services Administration (HRSA)
Johns Hopkins University
Kaiser Permanente®, California
Medical University of South Carolina
National Institutes of Health (NIEHS, NIMH)
Parkinson's Institute
SafeMinds
Parents of children with an Autism Spectrum Disorder
Persons with an Autism Spectrum Disorder
University of Alabama at Birmingham
University of Arizona, Tucson
University of Arkansas
University of California, Davis – MIND Institute
University of North Carolina, Chapel Hill
University of Pennsylvania
University of South Florida
University of Southern California, Marshall
University of Utah
Washington University in Saint Louis
University of Washington
University of Wisconsin, Madison
Yale University

### Workshop Planning Committee

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**Refer to Appendix B for biographies of panel members*

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- Some people expressed hope that understanding why ASD prevalence has increased may help identify modifiable risk factors. There was debate about the roles of prevalence and surveillance in answering questions about risk and causes of ASDs. Prevalence studies provide descriptive data on the number of people with a condition in a defined population. These types of studies are not sufficient to identify what causes ASDs. However, prevalence studies can be used as tools to examine variation in occurrence of ASDs across place, groups, time, and exposures, which may provide clues about groups who are at increased risk for ASDs. Other study designs would then be necessary to fully investigate the reasons behind observed variation in prevalence.
- There are likely multiple forms of ASDs with multiple causes that are poorly understood. It was noted that sufficient evidence exists that biologic and environmental factors, alone and in interaction, need to be considered as causes. It is not necessary to have confirmation that a portion of the increase in ASD prevalence is due to increased risk in the population to motivate the active pursuit of causes of ASDs. By better understanding what causes ASDs, maybe we can understand the increases in measured prevalence.

- A risk factor might be strongly associated with ASD and might be modifiable, but it might not have increased sufficiently in the population during the time frame of interest. Therefore, this risk factor might be related to an individual's risk for ASD but not related to the increase in population prevalence of ASD. The model demonstrated that for any factor to have made a noteworthy contribution to population changes in ASD prevalence during a short time period, three conditions must be met: the factor has to be fairly prevalent in the population, it has to have increased substantially, and it has to be strongly associated with diagnosed ASD.
- There was a shared recognition of the importance of, and commitment to, obtaining and using prevalence and epidemiologic information to improve the lives of people with ASDs.

## PANEL DISCUSSION SUMMARIES

The four panel chairs compiled main discussion points brought forth by their members for building on existing infrastructure and for developing new initiatives to better understand ASD trends. These discussion points are summarized below.

### Collaboration

The panels indicated that collaboration among professionals and stakeholders is important, and the following points were made to assist collaborative efforts among those interested in understanding ASDs and supporting the ASD community through science:

- Continue efforts of this workshop to develop and enhance communication among families, individals affected, researchers, service providers, advocates, and government entities about ASD prevalence, research, and service needs.
- Seek public–private partnerships to support data collection, analyses, and usage.
- Seek input from and collaboration with those in other fields, such as cancer epidemiology, to identify and utilize methodologies for evaluating changes in the prevalence of complex conditions.
- Collaborate with other data systems, such as the Environmental Public Health Tracking Network, to improve access to population-level environmental data.

### Analytic Activities

Points were made on better utilizing existing data to understand ASD prevalence trends:

- Provide funding opportunities to encourage analyses and dissemination of findings from existing datasets.
- Link existing datasets identifying children with ASDs to other health, service, and research databases.
- Conduct analyses that will help explain variations in ASD prevalence across subgroups (e.g., race and ethnicity, sex, diagnostic subtype, and geographic groups) and if variation persists over time.
- Use complex modeling and multifactorial analyses to better understand variation in ASD prevalence such as by possible etiologic subgroups (e.g., specific genetic conditions and family history), geogrphy, and sex, and by potentially harmful exposures among cohorts.
- Conduct simulation studies to predict the anticipated course of ASD prevalence.

### Data Enhancements to Inform Practice

The panels discussed the importance of using data on the prevalence and characteristics of people with an ASD to better inform service and support efforts:

- In addition to prevalence estimates, provide more in-depth information on population characteristics of people with an ASD (such as functional level and impact of functional limitations, subtype, developmental characteristics, and associated conditions) to improve program planning and support needs.
- Examine data to better understand lags and disparities in ASD identification to, in turn, inform screening, identification, and program planning.
- Conduct analyses to provide better estimates of current and future needs of adults with an ASD.

## Additional Studies

Beyond enhancements to existing data systems and uses, the panels discussed new types of data collection and studies including:

- Expand ASD prevalence efforts to include very young children and adults.
- Examine prevalence over time among older children by following up with those identified in previous studies
- Conduct additional validation studies at various ADDM Network sites and use the results to enhance estimates of ASD
  prevalence.
- Conduct further studies to better understand who is identified and who is not identified in national parent report surveys and in service-based data such as special education child counts.
- Develop ways of better capturing the heterogeneity of ASD phenotypes including the complexity of core and associated features that may present in different combinations for people with an ASD.
- Improve tools for culturally sensitive screening and case confirmation among large populations.
- Identify ways to measure and monitor the traits associated with ASDs among the general population to reflect various degrees (dimensional) rather than categorical (having an ASD or not having an ASD) case vs. not case) levels. This includes characterizing how these traits overlap with other conditions and typical development.
- Conduct cross-sectional and longitudinal studies following cohorts over time. This could include examining trends in characteristics of the population, such as ASDs among specific subgroups (based on, for example, race and ethnicity, immigrant status, and socioeconomic status), age of identification, diagnoses, comorbidities, services use, and family characteristics.
- Monitor trends in ASD prevalence prospectively to rule out identification factors by consistently conducting developmental and ASD screening at a given age with diagnostic follow-up and documentation of each step and outcome.
- Conduct prospective studies that examine biology, phenotype, identification patterns, and service needs and use of people with an ASD.
- Examine trends in other behaviorally defined conditions (e.g., attention-deficit/hyperactivity disorder, depression, and anxiety).

## NEXT STEPS

The workshop summary will be made freely available to the community through posting on the CDC's and Autism Speaks' websites. It is hoped that the information, research, and opinions shared during this workshop will add to the knowledge base about ASD prevalence and stimulate further work among public and private groups to understand the multiple reasons behind changes in identified ASD prevalence in the U.S.

# Background and Purpose

## WELCOME

## C. Boyle and G. Dawson

Dr. Boyle welcomed everyone, thanked the organizing committee and co-sponsor Autism Speaks, and indicated that she looked forward to the discussions and sharing of information and ideas on understanding autism spectrum disorder (ASD) prevalence trends. Dr. Dawson stated that we all have concerns about the increase in ASD prevalence. She expressed her hope that everyone would come away from the workshop with a path forward in understanding ASD prevalence changes and stated that we are much better prepared to address problems than ever before because of better data and analytic tools. These data and tools are from the Centers for Disease Control and Prevention's (CDC) Autism and Developmental Disabilities Monitoring (ADDM) Network, as well as other informative datasets from California and Europe. She remarked that many published papers cite several reasons for the possible increase in ASD prevalence including better analytic tools and broader awareness and diagnosis. However, these papers all have included the statement "a true increase in prevalence cannot be ruled out." She ventured that she looked forward to lively and productive discussion and concrete actions that can improve the understanding of why ASD prevalence has been increasing, with the ultimate goal of addressing the needs of people with autism.

## Background: What Do We Know About ASD Prevalence?

## M. Yeargin-Allsopp

Autism once was thought to be a rare condition, affecting about 1 in 2,000 individuals. It was thought of as mental illness, specifically schizophrenia of childhood, and was believed to be due to poor parenting. The "refrigerator mother" perception was prominent until the 1970s, continuing even into the 1980s. Today, autism is recognized as having a biologic basis and a range or spectrum of presentations. The autism spectrum disorders have been shown to occur among about 1% of children in several different countries. In addition to the core areas of impairment in social, communication, and behavioral domains, people with ASDs can have associated challenges in other areas such as sleeping, eating, attention, mood regulation, and gastrointestinal issues. It is recognized widely that ASDs have a strong genetic basis, but this is not a simple association and there is increasing recognition of the role of environmental factors. ASDs are now recognized as a complex disorder, most likely due to interactions between genes and the environment.

Beginning in the mid-1990s, concerns arose about increases in the numbers of individuals with autism identified in service systems. For example, starting in the early 1990s, the California Department of Developmental Services and the U.S. Department of Education's Office of Special Education documented increases in the need for autism services. Not all people with an ASD are identified by these service systems, so methods are needed to identify who else might have an ASD among the general population. CDC's ADDM Network conducts surveillance to estimate ASD prevalence in multiple areas of the U.S. and provides data to describe variations and changes over time. The ADDM Network reports ASD prevalence, or the total number of children with an ASD at a specified age in a specified year per 1,000 children in the population. The ADDM Network does not use incidence because incidence is based on new cases where a clear onset time can be documented. Typically, the onset of an ASD is not known, although it usually manifests by the time a child is 3 years of age. However, there is a great deal of variability in when a child actually manifests symptoms and then is diagnosed with an ASD.

There are several potential explanations that can account for an increase in the number of individuals diagnosed with ASDs, including better identification and screening methods, changes in diagnostic criteria, increased awareness among parents and clinicians, and changes in the availability of services. There also have been some studies that have examined how much of an increase is accounted for by other factors, such as increasing parental age. However, a full explanation must consider multiple factors that are not independent of each other. Prevalence estimates are important for planning policy and service needs and identifying promising clues about who is at risk for an ASD.

## Framework For This Workshop

### C. Rice

The identified prevalence of ASDs has increased significantly in a short time period across multiple studies, including the CDC's ADDM Network. ASDs are conditions estimated to occur among about 1% of all children. There is an urgent demand to address the many needs associated with ASDs, and concerns about ASD prevalence numbers have fueled local, state, and national action in terms of advocacy, policies, research, and creation of the Interagency Autism Coordinating Committee (IACC) among other activities. However, individuals and families continue to struggle to address and meet the needs associated with ASDs across their lifespan. Although prevalence estimates can help with service and policy efforts, increases in ASD prevalence beg the questions "Why?" and "Is the increase an actual increase in risk for ASDs?" The implication is that, if there is an increase in actual ASD risk, there might be modifiable risk factors to prevent ASDs from occurring. These questions get to the heart of what causes ASDs. Although multiple, complex genetic and environmental interactions are likely, we still have very limited information on what predisposes a fetus or child to have an ASD, what might increase risk, and which risks lead to the development of an ASD.

A prevalence study is an epidemiologic tool that describes the occurrence of a condition in a defined population in a defined time period. Surveillance is the ongoing monitoring of prevalence in a defined population over time. These studies provide descriptive data on the number of people with a condition in a defined population. These types of studies are not sufficient to identify what causes ASDs. However, prevalence studies can be used as tools to examine variation in occurrence of ASDs across place, groups, time, and exposures, and this may provide clues about groups who are at increased risk for ASDs. Prevalence studies can provide observations that might need further causal examination. For example, prevalence studies have shown that there are about 4 to 5 boys for every girl with an ASD. However, basic studies of the biology of individuals with an ASD are necessary to explain the mechanism that results in boys being at greater risk than girls.

Debates about reasons for ASD prevalence increases often have been dichotomized to point to explanations of better identification or evidence of increased risk implicating specific environmental factors. At this point, although we do know that some of the increase is related to identification factors, a true increase cannot be ruled out—but, it is hard to prove. We also know enough about potential causal mechanisms of ASDs to not pigeonhole the search for ASD causes to only genetic factors; complex biologic and environmental factors must be pursued as well. In order to evaluate ASD prevalence changes, scientists tend to use a systematic approach based on training in scientific methods where the first step is to rule out alternative explanations. This approach begins by examining factors that could explain a difference over time that are attributable to artifacts, rather than "true" increases. This approach tends to examine identification and methodological factors, as these variables are often more observable than the many potential and unknown risk factors that might contribute to ASD prevalence changes. As more data are collected and analyzed and different hypotheses evaluated over time and across studies, additional conclusions can be drawn. Understandably, this methodical approach is frustrating, especially when most people want to know *the* definitive reason for changes in ASD prevalence and whether it is something in the environment we can do something about. The fact that, despite many efforts, we have not found a single, simple explanation indicates that there are likely multiple, overlapping factors contributing to increases in ASD prevalence.

The purpose of the workshop was to bring together experts in epidemiologic prevalence and surveillance of ASDs and other conditions as well as stakeholders to: summarize where we are; learn from efforts to document prevalence changes among other conditions; and improve the specificity in quantifying and qualifying the multiple factors that might be influencing trends in ASD prevalence, including:

1. **Intrinsic Identification**—Internal methodology or measurement factors involved in documenting ASD prevalence trends (e.g., differences in study methods may lead to different individuals being counted or

not counted as having an ASD such as using a registry of children identified with an ASD or active screening).

2. **Extrinsic Identification**—External classification and awareness factors involved in identifying people with ASDs in the population (e.g., changes in diagnostic criteria or access to services based on an ASD label may influence who is identified for ASD prevalence studies).
3. **Risk**—Possible etiologic or true change in ASD symptoms among the population in relation to single or combined genetic, biologic, or environmental factors, or a combination thereof (e.g., specific biologic vulnerabilities or exposures in the environment that increase the risk of developing an ASD).

Four panels were formed for this workshop:

- Panel 1 – Utility of ASD Prevalence Data
- Panel 2 – U.S.-Based ASD Service Data
- Panel 3 – Autism and Developmental Disabilities Monitoring (ADDM) Network Data
- Panel 4 – What Else Is Needed To Understand ASD Trends?

After hearing the morning's presentations, members of the four panels were asked to discuss the following questions to provide a better understand of ASD prevalence trends:

1. What can we do now with existing data?
2. What should we do next to build on existing data systems?
3. What else is needed in terms of new analyses, data collection, or other efforts?

The goal of this workshop was to learn from different perspectives to inform the community and stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

## A Model for Assessing the Contribution of Various Risk Factors to Recent ASD Prevalence Increase in the U.S.

### L. Schieve

This presentation reviewed preliminary results of a study to formulate a mathematical model to assess the likely effects that given risk factors had on recent ASD prevalence increase and to apply the model to specific prenatal and perinatal risk factors previously found to be associated with ASDs. According to the ADDM Network report from 2009, there was a 57% increase in the prevalence of autism spectrum disorders (ASDs) from 2002 to 2006. The effect of a given risk factor on prevalence depends on the baseline prevalence of the risk factor (RFP), the change in RFP over time (cRFP), and the magnitude of the relative risk (RR). A number of previous studies consistently have indicated that preterm birth and low birthweight are risk factors for ASDs, and some other studies have implicated multiple birth, cesarean delivery, breech presentation, and assisted reproductive technology (ART) as possible risk factors. However, none have had sufficient values for RFP, cRFP, and RR to have contributed substantively to the recently observed ASD increase. While at an individual level, having one or more perinatal risk factors might convey a moderate or strong risk for having an ASD, these factors are unlikely to explain a large proportion of the population increase in ASD prevalence. Although examples were given using selected prenatal and perinatal risk factors, this model could be extended to assess various other risk factors.

A risk factor might be strongly associated with ASD and might be modifiable, but it might not have increased sufficiently in the population during the time frame of interest. Therefore, this risk factor might be related to an individual's risk for ASD but not related to the increase in population prevalence of ASD. The model demonstrated that for any factor to have made a noteworthy contribution to population changes in ASD prevalence during a short time period, three conditions must be met: the factor has to be fairly prevalent in the population, it has to have increased substantially, and it has to be strongly associated with diagnosed ASD.

### *Panel member discussion:*

A panel member asked if broad social changes, as opposed to individual risk factors, also were considered. The panel member was concerned that, by not fully examining population-level changes, the model might be underestimating the contribution of the change in that risk factor in the population on ASD prevalence. Dr. Schieve indicated that a large increase still would need to have an individual effect, and the model is accurate for shorter time intervals such as a few years. As the time period gets longer, then a different analytic model might be needed.

## ASD Genetic Variation and Gene–Environment Interaction

## K. Crider

This presentation summarized how genetic variations and gene-environment interactions could play a role in ASDs and provided background on how these factors may or may not change in a way that would affect ASD prevalence over a short period of time. Typically, to examine heritability of a condition, twin studies are used. More than 30 studies to date consistently have shown higher concordance between monozygotic than dizygotic twins, suggesting there is a strong genetic component associated with ASDs. ASDs have been associated with the following genetic variations: mutation of a gene, deletion of a large or small region of a gene, mutation of another gene, methylation of a gene, or creation of another copy of the gene or the region or chromosome. It is estimated that all genetic variants discovered to date are present in 10% to 15% of people with an ASD and many are implicated in other conditions (e.g., attention deficit hyperactivity disorder and schizophrenia). In general, there would not be an epidemic of a purely genetic condition because genes change over evolutionary time. However, shorter term changes can be seen if there are increases in mutations or breaks, or both, in chromosomes, changes occur in epigenetic patterning (e.g., DNA methylation) or in selective mating patterns.

Gene–environment interactions such as infection, stress, obesity, and trauma all can create the same type of cell damage. Specific causes may or may not have the statistical power to show the true association individually because multiple genetic and environmental factors can lead to the same disorder therefor, studies should be designed to take this into consideration. In some conditions, the magnitude of gene–environment interaction varies. Exposures associated with an increased risk for autism also are associated with other conditions, such as birth defects and cerebral palsy. Single exposures (genetic or environmental) are unlikely (but possible) to show a dramatic increased risk among the general population. Not every individual who carries these forms of genetic variation will have an ASD, which suggests the importance of interactions among multiple genes or gene–environment interaction, or both, in the occurrence of ASDs.

### *Panel member discussion:*

A panel member questioned the accuracy of the statistic that about 10% to 15% of children with an ASD have an identifiable genetic condition. Dr. Crider stated that the statistic is used by others in the field and is a best estimate, but noted the statistic needs better evaluation.

## Autism and Developmental Disabilities Monitoring (ADDM) Network

## C. Rice

### ADDM Network Overview

The ADDM Network is a collaboration of multiple sites in the U.S. to determine and monitor the prevalence of ASDs among 8-year-old children and to track peak prevalence over time. Children are identified through multiple education or health evaluation records if there is an ASD diagnosis, a special education classification, a suspicion of an ASD, or a social behavior associated with an ASD, even when an ASD has not been diagnosed. Clinician reviewers apply the current diagnostic standard criteria of the American Psychiatric Association's D*iagnostic and Statistical Manual, 4th edition, text revision (DSM-IVTR)*. The

strengths and limitations of the ADDM Network were discussed. The most recent ADDM Network estimates indicated that an average of 1 in 110 children (range from 1 in 80 to 1 in 240) had an ASD and that ASD prevalence had increased 57% over a 4-year period from 2002 to 2006. According to the ADDM Network data, the overall trend in ASD prevalence showed consistent increases, but variation existed among sites and among subgroups. While the increase in observed ASD prevalence at ADDM Network sites could be partly explained by identification factors—such as better information available in records, a more stable population at some sites, and improved identification of specific subgroups such as Hispanic children and children without cognitive impairment—these identification factors did not explain the total increase in prevalence. A neat explanation of all factors that could explain completely the observed increase is unlikely, and further work is needed to evaluate multiple identification and risk factors.

### Changes in ASD Diagnostic Criteria

This presentation reported on a preliminary analysis of how an identification factor could be evaluated using the ADDM Network data. Although it often has been stated that the changes in diagnostic criteria that occurred in the *DSM* in 1980 *(DSM III)*, 1987 *(DSM III-R)*, and 1994 (*DSM-IV* and minor changes for *DSM-IV-TR* in 2000) have affected reported ASD prevalence, no known studies have quantified this effect directly. Recoding the ADDM Network data based on the three diagnostic standards (*DSM III*, *III-R*, and *IV-TR*), it was found that autism and ASD prevalence were similar using *DSM III* and *III-R* standards, but increased significantly using *DSM-IV-TR* standards. A portion of the prevalence increase over time might have been attributed to differences in the definitions of ASD used for identification of ASDs by community professionals and service systems. This recoding analysis represents one example of an effort to provide more concrete estimates regarding the effects of a single factor on ASD prevalence.

### *Panel member discussion:*

Panel members raised several questions regarding reasons or theories to explain the wide range of ASD prevalence observed among ADDM Network sites, including the quality of data sources or records and the effect it might have had on prevalence and the inclusion or exclusion criteria used by the ADDM Network sites. Dr. Rice indicated there were some identifiable reasons explaining why the ASD prevalence estimates were lower at some ADDM Network sites (e.g., limited availability of education records) and higher at others (e.g., better quality of documentation in the records). Also, it is easier to identify reasons for lower prevalence estimates than for higher estimates. However, if a site had a low prevalence not due to a methodologic issue, it would be important to consider whether protective factors were at work at that particular site. A question was raised about the reason why the number of sites varied over the surveillance years. Dr. Rice explained that the number of ADDM Network sites depends on available funding and that sites go through a competitive application process in which the applicant must demonstrate a minimum population, partnerships with health departments, and other criteria based on independent peer review. A panel member also questioned when CDC was going to take the issue of rising ASD prevalence seriously. Dr. Rice indicated that CDC has been providing data actively to document these concerns and has been calling attention to the urgency of addressing the needs of the ASD community for years. She continued by stating that the workshop was an effort to broaden the conversation and share ideas on how CDC and others can all learn from other fields and improve collaboration to better understand ASD trends.

## Analyses of ADDM Network Data Related to: Parental Age, Age at Autism Identification, and Socioeconomic Inequalities in the Prevalence of ASD in the U.S.

## M. Durkin

This presentation summarized some analyses of data from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network related to parental age, age of autism identification, and socioeconomic

status. A major strength of ADDM Network data on ASD prevalence is that a sizeable proportion (27%) of children identified with ASDs for surveillance did not have a documented ASD classification. This allows us to investigate factors associated with having a previous ASD diagnosis and receiving services for ASD as distinct from having ASD, and to evaluate whether associations are due to differences in ASD risk or to disparities in identification. A consistent finding in recent epidemiologic studies is a positive association between both maternal and paternal age and risk of ASD in offspring. Despite this association and the increasing trend in mean parental age in recent decades, only a very small (less than .5%) proportion of the recent increase in ASD prevalence can be attributed to the increasing age of parents. ASD differs from developmental disabilities overall in its positive association with higher socioeconomic status (SES). Examining SES among Wisconsin ADDM Network data, it was found that the ASD prevalence increased with increasing SES. However, is this due to increased risk or identification disparities? For example, do educated parents have a disproportionate influence on autism awareness or does the risk of autism increase with a higher socioeconomic status? Is a knowledgeable and determined parent of a child with autism more likely to obtain an informed diagnosis? This is likely to be the case, and there is also the potential role of clinician bias and the possible evidence of disparity in access to care. ASD prevalence estimates likely underestimate prevalence in lower SES groups, which implies that we are still underestimating ASD prevalence and can expect some increases if disparity gaps are closed over time. But the fact that we saw a positive association between socioeconomic status and ASD risk in both those with and those without a previous ASD diagnosis suggests that the association might not be entirely due to under-ascertainment of ASD in economically disadvantaged groups.

## *Panel member discussion:*

Panel members raised the question of whether birth order and the effects of stoppage (a family deciding not to have another child after having a child with a disability) have been studied, and if plans are under way to study miscarriages and autism risk. Dr. Durkin indicated that the effect of birth order combined with parental age and sex appear to be additive. The role of stoppage and pregnancy loss cannot be directly or adequately investigated using ADDM data but require longitudinal, birth cohort studies. CDC's Study to Explore Early Development (SEED) will examine prenatal and perinatal risk factors, such as miscarriages. Studying these factors is important because past adverse pregnancy outcomes are understudied. The importance of examining characteristics (such as parental age, and SES) across cohorts to look at changes among subgroups will be important in understanding potential identification and risk factors contributing to ASD prevalence increases.

# ASD Trends: U.S. Service-Based Datasets

## U.S. Special Education Data

## P. Shattuck

This presentation provided an overview of U.S. Department of Education data related to documenting the presence of ASDs among special education students. U.S. Department of Education's Special Education Child Count data is an annual count of children enrolled in special education services. It is an accountability measure required by the Individuals with Disabilities Education Act (IDEA) to show nonexclusion of children with a disability based on select eligibility categories for each state. Autism was not initially a category within the child count dataset, but was added in 1990 with statesreporting to the U.S. Department of Education in 1991. The number of children classified as having autism and receiving special education services has increased since the early 1990s. However, the number is still fewer than would be expected given current prevalence estimates. A special education label is only mildly sensitive, but highly specific, and enrollment counts might not have provided a true prevalence of ASD. Child Count data vary by area and race or ethnicity. The special education system never was intended to serve a public health surveillance role. Thus, several important questions have been raised that focus on (1) understanding how state-level special education criteria for ASDs vary, (2) exploring referral pathways that lead to identification, (3) examining barriers to timely identification, and (4) developing more effective partnerships with the education sector to maximize data sharing. This will lead to a better understanding of the social, economic, and political factors that influence ASD identification in the community and that might contribute to the rise in identification ASDs in prevalence estimates.

### *Panel member discussion:*

Panel members asked how to integrate ASD screening in schools. Dr. Shattuck indicated that a school equivalent of CDC's Learn the Signs. Act Early. program is needed to increase awareness among educators of the signs of ASDs, and should be followed up with a systematic screening protocol to identify children with an ASD. This is important because, until everyone in the schools uses the same criteria, it will be difficult to rely on the validity of the Child Count data for monitoring changes in the actual prevalence of ASDs. Dr. Shattuck also indicated the need for legislative support to allow education and public health to form effective partnerships; often, school systems do not see the value in the Child Count data from a public health perspective. Especially now, schools are working to meet the service needs of the students rather than addressing broader public health issues such as identifying all children with an ASD in the population.

## California Department of Developmental Services Data I

## I. Hertz-Picciotto

This presentation provided an overview of some ways the California Department of Developmental Services (CA DDS) administrative data have been used to evaluate trends among children receiving services for ASD. Whether due to an artifact or a true increase, ASD prevalence has been high and there is a need to identify the causes. In addition, there already is enough evidence to suggest the importance of environmental causes. There are three main measures of occurrence of a condition: prevalence (the number of cases divided by the number of people in the population at a given time), incidence (the number of new cases among a given population in a defined time divided by the amount of person-time observed during the same period), and cumulative incidence (the number of new cases identified in an extended time period [e.g., from birth] divided by the size of the population without the disorder at the start of the time period). All measures are affected by changes in identification patterns and diagnostic practices. Prevalence data are most useful for service planning and incidence data are useful for etiology. However, a condition where the diagnosis tends to be stable (low mortality rate and it is rare for the diagnosis to change), can result in prevalence and cumulative incidence measures that will be virtually identical over a defined time or age period. For this reason, examining existing data may help us understand ASD trends.

The CA DDS has a statewide database with data from 21 regional centers in the state. The DDS database tracks 5 conditions (autism, epilepsy, cerebral palsy, intellectual disability, and intellectual disability-related conditions). Data collection is passive in that a child must be brought to a CA DDS center and a parent or guardian must request an evaluation to determine if they meet the service provision eligibility criteria. Comparing births in 1990 with those in 2001 (followed to age ten), the cumulative incidence in autism in the CA DDS rose 600%. About 200% of this increase in autism from 1990 through 2001 in the CA DDS database could be explained by trends toward younger age at diagnosis, inclusion of more mild cases, changes in diagnostic criteria, and older ages of mothers. Thus, artifacts related to criteria and methods for ascertainment might explain part but not all of the increase in ASD cumulative incidence in the CA DDS system. To date, there appears to be no leveling off of autism diagnoses, indicating there is considerable likelihood that there has been a true increase in incidence (or risk).

### *Panel member discussion:*

Panel members questioned how the identification artifacts played out across regions. Dr. Hertz-Picciotto indicated that there was substantial variability among the centers (Los Angeles traditionally has had higher ASD rates than other regions of the state). .Each DDS center is run by independent contractors and are managed slightly differently from each other. There also are clusters of ASDs near places where there are well-known treatment centers. A panel member pointed out that it is important to study these identification factors at multiple locations beyond California service data to areas of the U.S. and to also consider international patterns of occurrence.

## California Department of Developmental Services Data II

## P. Bearman

This presentation summarized additional analyses of data from the CA DDS related to trends in ASD prevalence conducted by Dr. Bearman and colleagues. During the past 30 years, the prevalence of autism has increased dramatically. Examining California birth data from the period 1992 through 2007, there were 8 million births (about 500,000 births per year). Using a sophisticated mapping program of all births and addresses and linking to CA DDS autism data, researchers were able to ascertain parental characteristics, prenatal conditions, and residence during the in utero period and link to data on neighborhoods, socioeconomic status, local toxicants, and other conditions. Examining these data was useful in examining the contribution of diagnostic change to increased prevalence, gaining insight into genetic mechanisms, understanding the spatial structuring or geographic patterns of autism at birth and age of diagnosis, considering diverse individual and community level risk factors, and measuring the potential role of sharing information on autism.

Analysis of the data showed that changes in ASD diagnoses in relation to those for intellectual disability (mental retardation) explained 24% of the increase in autism prevalence in the CA DDS data during the time period analyzed. An analysis was also done to see how administrative data might provide insight into genetic mechanisms. There was a high ASD concordance between identical twins and low concordance between fraternal twins. Over time, there was an increase in ASD among same sex twins and a decrease among opposite sex twins. Another analysis examined the spatial structure (geographic mapping) of the birth residence of children later identified with ASD by DDS. The researchers concluded that ASD birth clusters have been robust over time and do not appear to be due to factors such as education or socioeconomic status. Examining the DDS administrative data has provided insight into risk factors for autism. For example, findings indicated maternal age might be more critical than paternal age; community level characteristics such as geographic spacing are increasingly less salient as ascertainment increases, but still significant; and shorter interpregnancy intervals might confer excess risk. About 50% of ASD prevalence increases in the CA DDS data could be explained by several factors, such as diagnostic change, advancing parental age, social influence of people sharing information on ASDs, and spatial structure. Work is needed to understand what accounts for the other 50%. A project currently is under way to investigate

whether assistive reproductive technology (ART) is related to increased risk of having a child with ASD as identified in CA DDS data by linking with CDC data on births involving ART.

## *Panel member discussion:*

Questions were raised about the autism clusters that were identified using CA DDS data. There was a question as to whether these were true etiologic clusters or if there appeared to be shared identification patterns. Dr. Bearman discussed the idea that clusters might have been due to a shared exposure, such as toxicant, or to a social risk factor. For example, people with children the same age who shared a workplace or social activity might have been more likely to discuss their children and share information about autism, thus leading to increased identification. Or, there might have been reluctance among some groups to reach out to the health care or services system, resulting in decreased identification. A panel member expressed caution about the conclusion of being able to explain about 50% of the increase in DDS ASD prevalence as the approach used to arrive at this estimate was too simplistic and did not take the overlapping relationships between different factors into account. Dr. Bearman relayed his belief that some of the factors operate on different aspects of the spectrum and that the 50% figure was a way of summarizing what is known to date. For example, identification factors, such as shifts in the use of the intellectual disability diagnosis to add autism as another diagnosis or an alternative diagnosis, may operate on the lower end of the spectrum and social influence may operate on the higher end of the spectrum. Factors such as parental age and shorter pregnancy intervals are more likely to be risk factors contributing to ASD increases.

# Lessons Learned From Other Conditions and Analytic Methodologies

## Cancer

### R. Etzioni

Changes in cancer trends can be seen from changes in (1) exposures (e.g., smoking, diet, and obesity), (2) diagnosis or detection (e.g., screening and biopsy techniques), and (3) classification (e.g., staging and grading techniques). Dr. Etzioni presented three examples of changes in different types of cancer:

- Lung Cancer—The greatest modifiable risk factor for lung cancer is smoking. The trend line for lung cancer incidence plots has sloped similarly with the trend line for smoking prevalence, meaning the incidence rates of lung cancer have decreased over time (Surveillance, Epidemiology and End Results registry data) as smoking behavior has decreased over time (National Health and Nutrition Examination Survey).
- Colorectal Cancer—Screening rates for colorectal cancer have been increasing over time and the consumption of two or more servings of red meat per week has been decreasing over time. As screening has increased and red meat consumption has decreased, the incidence of colorectal cancer has decreased.
- Prostate Cancer—Prostate-specific antigen (PSA) screening was first introduced in the 1990s, which correlated with the first peak of prostate prevalence. The second prevalence peak occurred when follow-up biopsies became more routine. Researchers attributed the prevalence changes to differences in recording techniques and improvements in grading of cancer (from poorly to moderately to well-differentiated).

Examining patterns of change among a population might explain disease trends due to changes in factors such as the annual frequencies of exposures, availability of screenings, use of new diagnostic technologies, and changes in disease coding. It is important to have data on the occurrence of a condition before and after the change factor being evaluated. It is also helpful if there is a clear change factor that has occurred.

Modeling change is an integral part of cancer surveillance. There are several important lessons learned from this modeling that can be useful when examining changes in ASD prevalence. The basic steps of modeling change are:

- Characterizing changes in disease trends;
- Quantifying changes in the population that might explain trends;
- Identifying a mechanism for the effect of the population trend;
- Estimating the size of the effect on the risk of disease diagnosis; and
- Modeling or simulating experience among the population.

All of these steps are equally necessary and applicable in explaining changes in ASD prevalence. However, modeling techniques might be useful if the potential effects of a factor on prevalence are not known. There is a group called the Cancer Intervention and Surveillance Modeling Network (www.cisnet.cancer.gov) that is working to develop techniques for modeling changes in cancer based on multiple factors. Working with this group might be helpful in understanding ASD prevalence changes.

## Parkinson Disease

### C. Tanner

Parkinson's disease is a relatively rare disorder that does not have a diagnostic test or definitive marker. Symptoms occur later in life and share some features, such as cognitive decline, with other conditions such as Alzheimer's. The best diagnosis is a face-to-face exam. As with ASDs, population-based surveillance is challenging and there have been changes in diagnostic criteria over time. Also similar to autism, there are questions about the higher prevalence in males and differences by race. One example of examining diagnostic incidence trends of Parkinson's is a study conducted in the Kaiser Permanente Medical Care Program of Northern California (KPMCP). Researchers used active surveillance to examine electronic

medical records, physician referrals, and computerized databases to identify patients receiving services in community settings. Researchers have identified increased incidence of Parkinson's disease among men and with increasing age, a pattern that has been seen in most populations world-wide. Patterns that were suggested, but not supported by evidence, were higher incidence among Hispanics and the lowest incidence among Blacks. Environmental and genetic risk factors have been associated with Parkinson's disease. At this point, there are few sources of data to examine population trends in Parkinson's disease. The CA Parkinson's Disease Registry is a pilot effort to create a population-based database with active ascertainment and case validation, but is active in only a few counties and no state funds are designated to support the effort. Other efforts at population-based registries have been tried, but in these there is no active mechanism for reporting. Advocacy groups support a national surveillance system for Parkinson's disease, but this has yet to be realized. Researchers are also examining conditions with similar symptoms and/or risk factors to identify common biologic mechanisms. It may be useful to study prevalence changes in other disorders with symptoms that overlap with ASDs and among adults.

### *Panel member discussion:*

A panel member asked if there is a spectrum of conditions similar to ASDs. Dr. Tanner indicated that there are similar clinical syndromes including Parkinsonism. Different disorders have different clinical features and prognoses, but definitive diagnosis is post-mortem.

## Asthma

## M. King

Asthma is a highly prevalent chronic disease. Studies have shown persistent demographic differences in prevalence, as well as health care use. Asthma surveillance relies on several national datasets to determine prevalence and severity. One of these is the National Health Interview Survey (NHIS). Before 1997, the NHIS measured 12-month prevalence based on self-reports of "having asthma." After 1997, the NHIS measured prevalence by self-report of a "doctor's diagnosis" of asthma and included lifetime, past 12-months, and whether an attack occurred in past 12-months. The current measure of prevalence is similar to the projected 12-month rate, and the prevalence is higher among children than adults with racial differences observed as well. The Behavioral Risk Factor Surveillance System (BRFSS) allows state-specific estimates of asthma and enables CDC to conduct an asthma call-back survey. The BRFSS allows CDC to determine a population-based prevalence, as well as an at-risk–based rate. An at-risk–based rate is the number of affected people within the population having certain risk factors. While asthma prevalence has increased over time, actual asthma attack rates have been relatively stable. The reasons for overall prevalence increases are not known, but there are sociodemographic disparities in identification and service use. Changes in survey measurement have affected asthma estimates.

### *Panel member discussion:*

There was a question about the content of the call-back survey. Dr. King indicated this that this survey provides a chance to find out more about health care needs and use, effects on quality of life, and other information on the functional effect of asthma and service use related to asthma. Another question was about the availability of linking asthma data with environmental factors such as air pollution. Dr. King stated that data are not available to look at direct measures among individuals in the population over time, but different datasets could be linked to conduct ecologic analysis of asthma survey data based on residence and air quality, for example.

## Schizophrenia

## E. Susser

There are many parallels between schizophrenia and ASDs in the attempts to estimate incidence and historical changes in incidence. With respect to schizophrenia and related psychoses, two landmark

World Health Organization (WHO) studies can be used to mark shifts in thinking about schizophrenia, as well as about how studies of schizophrenia should be conducted. First, the International Pilot Study of Schizophrenia (IPSS), conducted in the 1960s, was designed to determine if schizophrenia was a culturally bound disorder and if it was a "real" disorder (some people hypothesized that schizophrenia was a social construction). The study used standardized criteria in a multinational study and many regions of the world were included. Researchers found schizophrenia in all settings; that finding is still questioned, but is supported by the findings of other types of studies. Second, the WHO "Ten Country Study" examined whether the incidence and course of schizophrenia varied across sociocultural settings. The study also had a novel design for determining incidence. It inaugurated the "first contact" design, now widely used and considered a "gold standard", in which researchers ascertain all people seeking help for a possible psychosis for the first time, within a defined population.

Based on misinterpretation of the results of these (and other) studies, the prevailing summary of schizophrenia from 1980 to about 2005 was that there was a lifetime risk of schizophrenia of 1%, and that this figure remained constant over time and place. The current view on schizophrenia is different; it is clear that the occurrence varies across populations and population subgroups, the clearest example being the very high rates among some immigrants who are ethnic minorities (mainly documented among immigrant groups in the United Kingdom and Netherlands). This variation is not inconsistent with the results of the WHO studies, but is inconsistent with the way these results were interpreted by most schizophrenia researchers and clinicians as showing constant rates overtime (not by the authors themselves, who were cautious in their conclusions). The WHO studies were not designed to examine change over time. Although other studies have attempted to examine change over time (e.g. registry studies), the results have been inconsistent, and the data weak (e.g. due to changes in diagnostic practices and systems). As a result, with the exception of one or two particular locations, we cannot at present draw conclusions as to whether schizophrenia incidence has changed over time. The discrepancy between studies of the course of schizophrenia, and interpretation of those results (again, not by the authors) is even more striking, but I do not have time to elaborate on this during this presentation.

There are several important lessons learned from studies of schizophrenia that could be useful when examining changes in ASD prevalence. For example, with regard to the notion of "constant" incidence over place and time, fixed thinking about schizophrenia was allowed to override the available data. The idea that schizophrenia occurred worldwide and that there was at most a very modest variation in incidence was accepted as true for a long time, and still taught in many psychiatry and other mental health professional training programs. This lesson is relevant to ASDs to help understand how to interpret ASD data. There have been different waves of ideology which have influenced the way in which the data on incidence of ASDs have been interpreted, and in particular, on whether they demonstrate a "true" increase or not ("true" means over and above an increase due to changes in ascertainment and help-seeking). The schizophrenia story helps one to recognize the power of ideology in the interpretation of such data, and the need to be cognizant of it. He noted his personal view is that the data on whether there has been a "true" increase in autism are simply inconclusive, but that the overall evidence favors the position that a part of the increase is "true".

## *Panel member discussion:*

Panel members asked if there was a specific way in which those in the ASD field could learn from the schizophrenia example? Dr. Susser responded that there have been different waves of ideology in how autism and related conditions have been interpreted and people tend to look at data as either, "yes, there has been an increase", or "no, there has not been an increase". It would be really helpful for those working with ASDs to not look through the data using those lenses, but to ask questions openly. Dr. Susser further stated that we do not need to be committed to either position to use data to advocate and to improve services. There was another question on subtypes of schizophrenia. Dr. Susser indicated that subtypes typically have not been reliable over time. Dr. Susser also commented that if a disorder persists

over generations, we also should be consider examining if there are selective mutations occurring or reframing to consider a selective advantage associated with the condition.

## Simulation Studies

### S. Galea

This presentation provided a brief overview of simulation studies as a method to understand prevalence changes. Changes in ASD prevalence have been and continue to be an observed phenomenon, yet the problem lies in identifying the causes for the changes. Causal models, including sufficient-component cause models, can shed some light on the joint effects of multiple exposures. However, these models are unable to consider timing in a dynamic way or connections between individuals. A possible solution is to use complex systems models. Complex systems approaches are computational approaches that use computer-based algorithms to model dynamic interactions between individuals within and across levels of influence (such as social networks and neighborhoods) using simulated populations. Complex systems models can incorporate multilevel determinants of population health, connections between individuals, and patterns of feedback between exposures and outcomes over time.

An example of trying to understand health problems seen after disasters was presented using a type of analytic strategy called "agent-based modeling" to predict changes among heterogeneous populations. The goal was to model outcomes observed by varying the variables that might have contributed to the observed pattern. There could have been several different sets of variables that produced the same outcome. A lesson that might be important when examining reasons for ASD trends is that complex systems models point to different possible explanations for observed phenomenon. However, they can be used in conjunction with empirical data to narrow down possible explanations and can play a central role in epidemiological analyses.

# Open Comments

The workshop included presentations and discussions among panel members. However, the meeting was open to anyone to register and attend in person or via webinar. Nonpanel members were able to provide written comments before and after the workshop, as well oral statements during an open period of the workshop. Comments included concern about increases in ASDs, the need to find out what has changed in our environment, the larger than expected number of children and young adults with an ASD, and the cost to society. Many of the public comments focused on concern about the role of vaccines in autism, with disappointment expressed about the lack of research on vaccine safety. In particular, studies of vaccinated and unvaccinated children and mitochondrial disease were requested. In addition, concerns were raised about the cumulative effect of the vaccine schedule and vaccine ingredients, as well as the need to consider a child's immune status prior to giving vaccinations. Suggestions were made for other studies such as of young children's development from birth to 2 years of age and to determine if there are specific subgroups of children with ASDs, such as those with gastrointestinal sensitivities. A man with an ASD expressed the belief that it is possible to be successful with an ASD and offered himself as an example of someone who once relied on public assistance, but is now successfully employed and lives independently. He also expressed gratitude for CDC's work in vaccine safety and satisfaction with receiving vaccines to protect from known diseases. Other comments included frustration with the delays parents face in getting a diagnosis of autism, despite bringing concerns to the attention of professionals. Other comments included concern about non-scientific expertise among panelists and interest in the latest research findings and plans for future research related to ASDs. Workshop organizers, panelists, and stakeholders were asked to consider these comments when discussing priorities for evaluating changes in ASD prevalence.

# Panel Session Summaries

The workshop featured four breakout panel discussions, with each panel asked to discuss questions related to ASD prevalence. The panelists' discussion, ideas, and suggestions were compiled by the panel chairs. Panel members consisted of epidemiologists and scientists with experience in epidemiology and surveillance of autism or other complex conditions and community stakeholders (representatives from autism organizations, parents of children with an ASD, and adults with an ASD). Following is a summary of the panel discussions and their ideas for addressing questions related to ASD prevalence trends.

## Panel 1: Utility of ASD Prevalence Data

Panel Chair: *A. Singer*

**Panelists:** *C. Cunniff, W. Zahorodny, R. Kirby, M. Lopez, R. Grinker, D. Mandell*, L. Grossman*, W. Dunaway, M. Rosanoff, J. Zimmerman, B. Mulvihill, J. Charles*

**Invited participant unable to attend remotely or in-person at last minute due to unforeseen circumstances.*

The discussion and questions addressed by Panel 1 focused on how ASD prevalence data are used in the community by different stakeholders and sought to identify ways in which data collection and reporting on the population prevalence and characteristics of people with an ASD could be further developed.

### *Q1. What does having ASD prevalence information do for stakeholders (parents, professionals, people with an ASD, researchers, scientists, policy makers, service providers)?*

The panelists indicated that ASD prevalence data are used to:

- Empower the community, confirming what parents and educators experience
- Drive public policy
- Support the need for service provisions and development
- Support the need for professional development and systems planning
- Support the need for additional research

At the community level, prevalence data have informed stakeholders about needed improvements in identifying people with an ASD and helped direct research which may ultimately lead to information about etiology. Similarly, the resulting increase in ASD awareness and knowledge among parents, caregivers, and communities has increased the quality of social and behavioral descriptions by clinicians and service providers when a child has been referred for an evaluation. This has resulted in parents being more equipped to discuss concerns with professionals. Clinicians have found that having ASD prevalence information increases awareness of the need to identify children and facilitates having a conversation with parents about concerns. It also has provided information to help clinicians advocate for needed resources for identification, referral, and intervention. Researchers have used prevalence data as justification for etiologic and intervention research, and the increased awareness of ASD has increased their own career choices to be engaged in meaningful work. Individuals with an ASD have also benefitted from ASD prevalence data. Increased ASD awareness has resulted in positive community connections and increased information has allowed them to help themselves and others understand their experience.

Prevalence data also have empowered communities by confirming what parents and educators have been experiencing and providing evidence for robust advocacy. ASD prevalence estimates have provided a starting point to assess service and support needs for individuals, families, and communities. On a policy level, awareness of the Autism and Developmental Disabilities Monitoring (ADDM) Network has allowed scientists and researchers, in some states, easier access to data sources and records for surveillance purposes, thus increasing the accuracy of ASD estimates. Prevalence estimates also have informed policy efforts to create an infrastructure to support children with an ASD (e.g., child care, intervention, education, transition services); understand and address lifespan issues (e.g, housing training, employment, health

and wellness); drive public policy and programs (e.g., insurance coverage and health care legislation); and support the need for service deployment, systems planning, and additional research funding.

### *Q2. How are stakeholders actually using ASD prevalence information?*

ASD prevalence data are included at the beginning of many, if not most, research publications and grant applications related to ASDs because they provide an estimate of the population-level effect of the conditions. In particular, recent estimates indicating that ASDs are more common than previously thought have motivated the need to better understand the course, causes, and supports related to ASDs. In addition to putting the scope of need into perspective, recent ASD prevalence estimates have prompted some states to pass mandatory reporting laws, establish autism task force groups or autism councils, pass legislation affecting service provision, or offer grants to school districts for supplemental funding related to autism. Examples of how states have used ASD prevalence data follow:

- South Carolina used prevalence data to show the need for improving access to services when drafting and passing insurance reform.
- New Jersey passed laws related to ASDs and mandatory reporting, compelling insurance companies to provide services and providing additional grants to schools.
- Alabama appointed an autism coordinator for the state based on the effects of the prevalence data.

### *Q3. What types of ASD prevalence information and descriptions of the population are useful to stakeholders?*

For individuals, families, and communities, having ASD prevalence data that are applicable to more specific local areas and states can better inform advocacy and service planning efforts. ASD prevalence data are population-based and are not easily applicable at the individual level. In addition to understanding the population effects of ASDs, families and communities continue to seek ways of making the information more relevant for their individual circumstances. Specific recommendations included:

- Improving communication with the community (e.g., families, individuals with an ASD, professionals, policy makers, and researchers) to help put the prevalence data into context.
- Providing more in-depth information on what an ASD diagnosis means for an individual across his or her lifespan, and what support systems such an individual needs or will need.
- Collecting and reporting data on functional level and effects of ASD, subtypes, developmental characteristics, and associated conditions (in addition to overall ASD prevalence estimates).

### *Q4. What questions do stakeholders expect epidemiology and prevalence studies, in particular, to answer?*

The panel noted that community stakeholders want the data to be useful at the community and individual levels. At the community level, ASD prevalence estimates can inform larger needs (identification, supports, policy, and research). For the individual person, as suggested in Q3's discussion, more detailed data on functioning and characteristics would be helpful. Prevalence numbers should inform preparation for the needs of a growing population. In addition to describing the population, prevalence studies could provide a baseline for evaluating interventions and gauging service needs. Some panel members called for more data on the link between prevalence and etiology. For example, would lower prevalence in some areas or subgroups indicate potential protective mechanisms? Prevalence studies should be accompanied by data collection on specific symptoms or biological measures, interventions, and trajectories over time.

## Panel 2: U.S.-Based ASD Service Data

### Panel Chair: *L. Croen*

**Panelists:** *P. Shattuck, P. Bearman, M. Kogan, S. Visser, I. Hertz-Picciotto, L. Miller, A. Bakian, K. Van Naarden Braun, L. Lee, T. Baroud, P. Bell, R. Etzioni, Y. Kim*

Panel 2 discussed databases that exist to serve the administrative functions of tracking service use, or were developed for specific studies. Although not designed to identify all children with an ASD among the population, these databases might serve as useful tools for looking at trends in identification, characteristics, and service use that will help explain population-based ASD prevalence trends. Some of the databases or datasets noted that could be explored for examining administrative or reported prevalence issues include:

All-Payer Claims Database (APCD; combines outpatient data from all claims databases)
California Department of Developmental Services (CA DDS) database
Department of Education/Individuals with Disabilities Education Act (IDEA) Child Count (also, Special Education Longitudinal Study)
Hospital Discharge Data
Interactive Autism Network (IAN) survey
Kaiser Permanente® membership databases
Centers for Medicaid and Medicare Services (CMS)
National Health Interview Survey (NHIS)
National Survey of Children's Health (NSCH)
National Survey of Children with Special Health Care Needs (NSCSHCN)
State registries (New Jersey, Utah, West Virginia)
Vaccine Adverse Event Reporting System (VAERS)

***Q1. What are the top three immediate (within 1 to 2 years) priority analyses needed to understand ASD trends using existing U.S.-based datasets?***

Panelists discussed several analyses that could be pursued, including:

- Conducting a life-course study of ASD identification, service use, and characteristics. Tracking life history can help determine if the ways people come into the system are changing. Researchers could examine first concerns and average age at first diagnosis, and what happens before and after an ASD diagnosis occurs among those in successive birth cohorts. Kaiser Permanente® membership data could be used to explore this.
- Examining trends in comorbidities among children with ASDs over time and trends in the use of treatments among parents over time. For example, a potential research question might include "Does survivorship of a mental or physical illness by parents (e.g., bipolar disorder) affect the trend in ASD prevalence among children? Kaiser Permanente® membership data or perhaps Medicaid data could be used to explore this type of question.
- Examining behavioral screening data to investigate trends in ASD diagnosis over time. Potential data sources could include the ADDM Network, as well as research programs, insurer databases, and primary care practices that have administered developmental screening tests over time.
- Examining trends in other behaviorally defined conditions (e.g., attention-deficit/hyperactivity disorder, depression, and anxiety) in U.S. population-based datasets (e.g., the National Survey of Children's Health). This could be addressed by ADDM Network data (among children with an ASD).

- Looking at ASD prevalence trends over time among different immigrant groups. This might inform trends and prevalence rates in terms of eliminating certain risk factors. However, it is difficult to disentangle if observed rates are lower among immigrants either because of immigrants' lack of familiarity with the U.S. health care system U.S. (including how it operates), or because of reluctance on the part of immigrants to seek medical attention for developmental disorders, or both.
- Further examining the respondents to national surveys who had at least one child ever diagnosed with an ASD and who reported the child no longer had an ASD diagnosis at the time of the survey There is a need to understand why some children may have been reported to have an ASD at one time, but not at the time of the survey.

***Q2. What are the top three next (within 3 to 5 year) priority analyses needed to understand ASD trends using existing U.S.-based datasets?***

Panelists discussed several potential analyses, including:

- Conducting multilevel modeling with Special Education Child Count or other datasets. Enhanced analysis might help answer questions regarding administrative prevalence trends in schools and communities.
- Using Special Education Child Count data from both IDEA Part C Early Intervention for 0-3 year-olds and IDEA Part B for 3-21 year-olds to track identification, services, and developmental trajectories at the individual level.
- Linking all-payer claims databases with state autism registries to track ASD diagnostic or billing codes, along with additional billing and pharmaceutical claims, to provide information concerning comorbid conditions.
- Taking simulation-based approaches to data analysis, and evaluating the models using real data from epidemiologic studies.
- Using Medicaid data to examine trends over time in ASD and related diagnoses among those receiving Medicaid services. Also, evaluate children longitudinally to examine changes in diagnoses and services.
- Collaborating with the National Institute of Mental Health (NIMH) to better understand the factors associated with the persistence of parent-reported ASD diagnosis. (NIMH has partnered with the Health Resources and Services Administration and the Centers for Disease Control and Prevention, and currently is conducting a follow-up study of the NSCSHCN for families of children who were reported ever to have had a diagnosis of an ASD.)

***Q3. Can the existing data systems be enhanced (e.g., adding analyses, data collection) to better answer questions about the changing ASD prevalence? If not, why not and what else is needed?***

Panelists discussed several enhancements, including:

- Enhancing use of Child Count Special Education Data by
  - » Documenting state differences in identifying children as eligible for autism special education services and documenting the methodology for obtaining and reporting these data to make better sense of special education data.
  - » Conducting studies to evaluate how children with autism are identified at schools.
  - » Enabling individual-level child data to be accessed for study purposes and pooled together.

- Enhancing use of surveys by
  - » Conducting needed validation studies of parent-reported data.
  - » Exploring whether national surveys (e.g., National Immunization Survey, NHIS, NSCH, VAERS) could be used to examine ASDs among vaccinated versus unvaccinated groups.
  - » Using national surveys to examine service use and needs.
  - » Adding questions to the IAN Survey to assess beliefs about causes of ASDs.
- Enhancing data access and coordination by
  - » Partnering with analytic powerhouses (e.g., Google) to develop new strategies to take advantage of the huge amounts of data that will become available in upcoming years (e.g., data enhancements from health care reform and electronic health records). This will require public and private partnerships.
  - » Making ASDs reportable conditions in more states. However, it was noted that making a condition reportable does not improve the ability to understand trends, but it is a useful method to establish public health authority to collect additional data to track trends.
  - » Collaborating with the National Environmental Public Health Tracking Network (EPHTN) to potentially access environmental risk factor and other environmental public health tracking data at the population-level.
- Creating new data collections for
  - » Using qualitative methods to understand pathways to screening and diagnosis.
  - » Monitoring trends in ASD prevalence prospectively to rule out "artificial" factors. Consistently conduct developmental and ASD screening at given ages with diagnostic follow-up and documentation of each step and outcomes.
  - » Developing methods to track the effects of information dissemination across parent networks via the Internet or other social media.

## Panel 3: Autism and Developmental Disabilities (ADDM) Network Data

### Panel Chair: *G. Dawson*

**Panelists:** *S. Galea, G. McGwin, O. Devine, A. Correa, M. Zack, P. Yoon, M. Maenner, J. Daniels, L. Schieve, S. Pettygrove, M. Wingate, J. E. Robison, P. C. Marvin*

The questions and discussion of Panel 3 focused on identifying immediate, next, and future priorities for enhancing the data collection, analysis, and reporting of ASD prevalence and descriptive data by the ADDM Network to betterunderstand trends.

***Q1. What are the top three immediate (next 1 to 2 years) priority analyses needed to understand ASD trends using existing ADDM Network data?***

Panelists discussed the following priorities:

- Conducting simulation studies to predict the anticipated course of ASD prevalence, informed by existing ADDM Network data, by
  - » Identifying and using more complex, nuanced modeling approaches to simultaneously examine multiple identification (intrinsic and extrinsic) and risk factors across cohorts (this will be challenging because several factors are confounded).
  - » Using ADDM Network data to inform assumptions in simulation models of ASD prevalence trends.

- Conducting analyses that will help explain variations in ASD prevalence across geography and subgroups by
  - » Providing information about risk factors related to parental age.
  - » Examining data on ASD prevalence for disparities in identification to inform diagnostic and access to service needs.
  - » Comparing changes in ASD prevalence among children with more a narrowly defined autistic disorder diagnosis to with those with a broader ASD diagnosis, as autistic disorder might be less influenced by increased public awareness.
- Using methods to maximize the number of children with an ASD in the population identified by the ADDM Network by
  - » Performing additional validation studies including direct screening and assessment at other ADDM Network sites and using the results to enhance estimates of ASD prevalence. [Note that a validation study in the Atlanta site (Avchen et al., 2010) found that the records-based approach had good specificity but low sensitivity indicating that ADDM Network ASD case classifications are consistent with clinical examination, but that some children with ASDs are not identified using current methods. Therefore, ADDM Network prevalence estimates likely underestimate ASD prevalence.]

***Q2. What are the top three (within 3 to 5 years) priority analyses needed to understand ASD trends using existing ADDM Network data?***

Panelists discussed the following potential next priorities:

- Conducting analyses to better understand ASD prevalence trends and current and future needs of adolescents and adults with an ASD by
  - » Examining an older cohort to better understand the changes in prevalence over time. This could be done by
    - * Surveying a previously-characterized cohort of 8-year-olds when they are older to determine if prevalence estimates are the same in this cohort at older ages.
  - » Identifying methods for estimating lifetime prevalence and characterizing developmental trajectories by
    - * Examining how ASD symptom presentation may change across cohorts and individuals across the lifespan.
    - * Identifying methods to examine the effects of early intervention and whether changing symptom profiles may have on ASD prevalence estimates.
  - » Conducting studies of ASD prevalence among adults by
    - * Identifying appropriate methods for characterizing ASD prevalence at different ages.
    - * Addressing the ethical concerns of identifying adults with an ASD who may not want that classification.
    - * Characterizing outcomes and service and support needs.
  - » Using ADDM Network data to better understand risk factors for ASDs by

* Recognizing that ADDM Network data might not be well-designed to examine risk factors at the individual level; however, use the data to characterize whether some risk factors have changed among the population and correlate to ASD prevalence changes.

***Q3. Can the ADDM Network be enhanced to better answer questions about changing ASD prevalence? If yes, how? If no, why not and what else is needed?***

Panelists discussed building on the existing ADDM Network infrastructure by

- Developing ways of better capturing the heterogeneity and complexity of ASD phenotypes.
- Expanding ADDM Network dataset linkages to other datasets (e.g., health, education, service, environmental data) to enrich data completeness and use for examining risk factors.
- Collecting follow-up data on cohorts studied previously at later ages to better understand trends over time and outcomes.
- Collecting more extensive data as part of ongoing surveillance using additional methods such as direct screening and diagnostic confirmation to obtain the most complete estimates of ASD prevalence in the U.S.

## Panel 4 –What Else Is Needed To Understand ASD Trends?

### Panel Chair: *M. Durkin*

**Panelists:** *K. Crider, E. Susser, C. Lawler, C. Tanner, M. King, S. Shapira, D. Schendel, J. Nicholas, W. McMahon, J. Constantino, C. Newschaffer, L. Perner, M. Blaxill, E. London, G. Windham, K. Merikangas*

Panel 4 engaged in an open discussion on some of the "big picture" issues related to understanding ASD trends, including whether it is possible to fully understand reasons for ASD prevalence increases, ways to move forward with collaborations and new methods, and what else could be done to improve the understanding of ASD trends.

***Q1. Can the question of the relative contribution of identification or risk factors, or both, on ASD prevalence during the last 20 years be answered? If not, why not? If yes, what are the three primary questions that need to be addressed by epidemiology?***

Panel members offered a range of perspectives on whether it will ever be possible to understand the relative contributions of identification and risk in increasing ASD prevalence. There was agreement that the ASD prevalence is a huge public health problem and that many individuals and families are affected globally. Panel members did not agree about whether it was possible ever to understand fully all the reasons behind increasing ASD prevalence. One panelist asserted that the question already has been answered: Of course there has been an increase because there has an increase in the number of cases and autism is an epidemic and needs to be treated as a public health emergency. Others noted that autism is a disorder of social behavior and that trends over time in its frequency are affected by corresponding changes in social context, perceptions, awareness, knowledge, diagnostic practices, and availability of services. However, there was a general sense that it is possible to move forward and to be more specific in documenting potential reasons for ASD prevalence trends. Several challenges were mentioned, such as insurmountable measurement error, overlap and confounding of multiple identification and risk factors, and poorly defined subtypes with limited information on biological underpinnings to explain phenotypes. It is unlikely that prevalence trend data will explain the etiology of a complex set of conditions, such as ASDs, but these data can identify clues for further mechanistic studies (e.g., increased risk by sex, geography, and birth characteristics). By better understanding what causes autism, maybe we can understand the

increases in measured prevalence. In addition, panelists noted that we need more clarity on phenotypes, expression across the lifespan, and trends in other conditions. Others thought that, although we might not be able to use prevalence data to make discoveries about how to prevent or cure ASDs, we can use prevalence data to assess needs and improve the lives of those affected by ASDs. This could lead to a focus on services and figuring out how to improve identification and access to such services.

***Q2. How can efforts to understand ASD trends be informed by other fields or conditions (e.g., comparison with other conditions, sharing methodology, analytic techniques, etc.)? How can that best be accomplished?***

Panelists discussed several potential collaborations, including:

- Comparing ASD prevalence trends to trends in other neurodevelopmental disorders.
- Collaborating with scientists investigating epigenetic effects in cancer and other fields to better understand gene–environment interactions in neurodevelopment.
- Examining subgroups of children with an ASD (e.g., children with fragile X syndrome and ASD) to determine if there are specific risk factors that can be identified among these children with increased risk for developing ASD.
- Analyzing new bioinformatics and computational tools and approaches to better understand complicated systems and interactions.
- Conducting translational research because existing ASD criteria are not mapped to biology and etiology. Translational investigators could help bridge the gap between diagnostic criteria and biology.

***Q3. What else is needed to understand reasons for trends?***

During the discussions for Questions 1 and 2, several propositions were made for better understanding ASD prevalence trends, including:

- Seeking public–private partnerships to support data collection, analyses, and usage of data.
- Providing funding opportunities to encourage use of existing datasets.
- Expanding use of analytic techniques for examining population trend data by
  - » Using modeling approaches to supplement observed data.
  - » Comparing multiple identification and risk factors that might contribute to prevalence changes.
- Expanding ASD prevalence efforts to include very young children and adults.
- Understanding patterns in ASD prevalence among subgroups (e.g., subtypes, males and females, geographic variation, comorbidities) to evaluate whether changes likely are due to identification or risk factors:
- Expanding the methodology for looking at ASD prevalence by
  - » Developing methods to conduct cross-sectional studies across successive birth cohorts that simultaneously ascertain parent-reported descriptions of developmental characteristics, intellectual functioning, ASD and comorbid symptoms, research diagnosis (categorical or observational), community diagnoses, and family characteristics (sibling recurrence).
- Understanding and improving ASD identification by
  - » Measuring ASDs dimensionally and quantifying the traits that make up the ASDs.

- » Measuring any overlap with other conditions and typical development, determining if is there a continuum of symptoms.
- » Improving tools for culturally sensitive screening and case confirmation among large populations.
- » Developing methods for measuring disability and monitoring functional limitations in individuals with ASD.
- » Using data on identification of ASDs to identify gaps and improve community practice.

- Improving community engagement and communication between individuals and families affected by autism, professionals providing services for people with autism, researchers, and policy makers by
  - » Fostering broader understanding of the strengths and challenges associated with ASDs so people with ASDs have access to the community.
  - » Utilizing ASD prevalence estimates to develop programs and practices that support the positive development of people with ASDs.
  - » Realizing that autism is not an academic issue for the many individuals and families affected by ASD, and listening to the concerns of parents of children and individuals with an ASD.
  - » Sharing information with leadership and policy makers to respond to this health crisis.
- Making sure public health is part of the Interagency Autism Coordinating Committee (IACC) Strategic Plan and input is sought from a range of stakeholders via annual research plan updates.
- Noting that, while trends are important, understanding them might require a better understanding of the etiology and heterogeneity of autism, as well as changes over time in diagnostic practices. These goals can be achieved by
  - » Advancing basic science on biologic and environmental mechanisms.
  - » Increasing the types of study methods used in research and service studies such as
    - * Conducting prospective studies that examine biology, phenotypes, identification patterns, and service needs and use.

# Appendix A: Workshop Agenda

## Workshop on U.S. Data to Evaluate Changes in the Prevalence of the Autism Spectrum Disorders (ASDs)

**Co-Sponsored by the National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC) and Autism Speaks**

## Tuesday, February 1, 2011

## Location: Centers for Disease Control and Prevention,

Tom Harkin Global Communications Center, 1600 Clifton Road, N.E., Atlanta, Georgia
Building 19, Auditorium B1/B2

**7:30–8:00** . ..... **Check-in**

**8:00–8:05** . ..... **Welcome** — *C. Boyle and G. Dawson*

**8:05–10:00** . ..... **Background and purpose**

- What do we know about ASD prevalence? — *M. Yeargin-Allsopp*
  - » General summary of ASD prevalence
- Framework for this meeting — *C. Rice*
  - » What might be influencing temporal patterns in prevalence?
    - * Intrinsic Identification – methodology/measurement
    - * Extrinsic Identification - (awareness and classification)
    - * Risk – (multiple biologic and environmental)
  - » Questions to address (For U.S. service data, ADDM, and the field, more generally)
    - * What we can do now? (analysis with existing data)
    - * What should we do next? (building on existing data systems)
    - * What else is needed? (analyses, data collection, others)
- 8:30–8:45 . ..... A mode for assessing the contribution of various risk factors to recent ASD prevalence increase in the U.S. — *L. Schieve*
  - » Examples using selected prenatal and perinatal risk factors.
- 8:45–9:00 . ..... ASD genetic variation and gene-environment interaction — K. Crider
- 9:00–9:45 . ..... Examples of analyses in progress from the Autism and Developmental Disabilities Monitoring (ADDM) Network
  - » ADDM Network Overview — C. Rice
  - » Changes in ASD diagnostic criteria
  - » Parental age, dx age, SES — M. Durkin
    - * Hypothesis
    - * Methods
    - * Findings
    - * What else could be done to understand ASD trends using this dataset?
    - * What else could be done to understand ASD trends?

**10:00–10:50** . . . . . **ASD Trends: U.S. single source datasets (ED and CA DDS data)**

- U.S. Special Education Data — P. Shattuck
- CA DDS Data — I. Hertz-Picciotto, P. Bearman
  - » Brief overview of evidence of prevalence changes.
  - » What factors contribute to the change in prevalence over time? (is it possible to distinguish the relative contribution of various intrinsic identification, extrinsic identification, and/or risk factors influencing prevalence change?)
  - » What are the strengths/limitations of these approaches?
  - » What else could be done to understand ASD trends using this dataset?
  - » What else is needed to understand ASD trends?

**10:50–11:05** . . . . . **Break**

**11:05–12:30** . . . . . **Lessons from other conditions and analytic methodologies**

- Cancer — R. Etzioni
- Parkinson's — C. Tanner
- Asthma — M. King
- Schizophrenia — E. Susser
- Simulation Studies — S. Galea

Given a change in prevalence/ incidence, what has been done to understand the reason(s)?

- Brief overview of evidence of prevalence changes.
- What factors contribute to the change in prevalence over time? (is it possible to distinguish the relative contribution of various intrinsic identification, extrinsic identification, and/or risk factors influencing prevalence change?)
- What are the strengths/ limitations of these approaches?
- What lessons may be important when looking at reasons for ASD trends?

**12:30–1:00** . . . . . **Open Comment**

**1:00–1:20** . . . . . **Pick up lunch and transition to Panel Breakouts**

**1:20–2:45** . . . . . **Panel Discussion Breakouts**

## Panel 1 – Utility of ASD Prevalence Information (Room 117)

Panel Chair: *A. Singer*

Recorder: *C. Arneson*

**Panelists:** *C. Cunniff, W. Zahorodny, R. Kirby, M. Lopez, R. Grinker, D. Mandell*, L. Grossman*, W. Dunaway, M. Rosanoff, J. Zimmerman, B. Mulvihill, J Charles*

- What does having ASD prevalence information do for stakeholders (parents, professionals, people with

ASD, policy makers, service providers)?

- How are stakeholders actually using ASD prevalence information?
- What types of ASD prevalence information and descriptions of the population are useful to stakeholders?
- What questions do stakeholders expect epidemiology and prevalence reports, in particular, to answer?

## Panel 2 – Other US-Based ASD Data (Room 255)

Panel Chair: *L. Croen*

Recorder: *L. King*

**Panelists:** *P. Shattuck, P. Bearman, M. Kogan, S. Visser, I. Hertz-Piciotto, L. Miller, A. Bakian, K. Van Naarden Braun, L. Lee, T. Baroud, P. Bell, R. Etzioni, Y. Kim*

- What are the top 3 immediate (1–2 year) priority analyses needed to understand ASD trends using existing US-based datasets?
- What are the top 3 next (3–5 year) priority analyses needed to understand ASD trends using existing US-based datasets?
- Can these data systems be enhanced (analyses, data collection, others) to better answer questions about changing prevalence of ASDs? If yes, how? If no, why not and what else is needed?

## Panel 3 – ADDM Network Data (Room 257)

Panel Chair: *G. Dawson*

Recorder: *K. Phillips*

**Panelists:** *S. Galea, G. McGwin, O. Devine, A. Correa, M. Zack, P. Yoon, M. Maenner, J. Daniels, L. Schieve, S. Pettygrove, M. Wingate, J. E. Robison, P. C. Marvin*

- What are the top 3 immediate (1 -2 year) priority analyses needed to understand ASD trends using existing ADDM data?
- What are the top 3 next (3-5 year) priority analyses needed to understand ASD trends using existing ADDM data?
- Can the ADDM Network be enhanced (analyses, data collection, others) to better answer questions about changing prevalence of ASDs? If yes, how? If no, why not and what else is needed?

## Panel 4 –What else could be done to understand ASD Trends? (Room B1/B2)

Panel Chair: *M. Durkin*

Recorder: *R. Fitzgerald*

**Panelists:** *K. Crider, E. Susser, C. Lawler, C. Tanner, M. King, S. Shapira, D. Schendel, J. Nicholas, W. McMahon, J. Constantino, C. Newschaffer, L. Perner, M. Blaxill, E. London, G. Windham, K. Merikangas*

- Can the question of the relative contribution of identification and/or risk factors on ASD prevalence in the last 20 years be answered?
  - » If not, why?
  - » If yes, what are the 3 primary questions which need to be addressed by epidemiology?
- How can the ASD field work with other fields / conditions to evaluate trends (comparison to other conditions, sharing methodology, analytic techniques, etc.)? How best can that be accomplished (give specific

conditions with possible analyses/activities)?

- What else is needed for the ASD larger field to understand reasons for trends?

**2:45–3:00** . ..... **Break**

**3:00–5:00** . ..... **Report from Each Panel (Aud A)**

Facilitator: P. Yoon

- 3:00–4:45 . ..... For Panel 1, 2, 3, and 4
  - » 10 minute summary report for each panel
  - » 15 minute Larger Panel Discussion
- 4:45–5:00 . ..... Meeting adjournment

# Appendix B: Panelist Biographies

Amanda V. Bakian, MS, PhD, is the epidemiologist and data manager for the Utah Registry of Autism and Developmental Disabilities (URADD) and the Utah ADDM Network site. She has collaborated on a variety of research studies investigating the prenatal, perinatal, neonatal, socio-demographic, and environmental risk factors associated with ASDs and intellectual disabilities.

Thaer Baroud, BSN, MA, MHSA, is a senior epidemiologist with the Arkansas comprehensive tobacco control program and he is the epidemiologist for the Arkansas ADDM Network site. He has worked as an epidemiologist at the Arkansas Center for Health Statistics.

Peter Bearman, PhD, is the Director of the Lazarsfeld Center for the Social Sciences, the Cole Professor of Social Science, and Co-Director of the Health & Society Scholars Program at Columbia University. He is currently investigating the social determinants of the autism epidemic. He has researched topics including adolescent sexual networks, networks of disease transmission, genetic influences on same-sex preference, and historical sociology.

Peter Bell, MBA, is Executive Vice President for Programs and Services at Autism Speaks and the father of a son with autism. He oversees the foundation's government relations and family services activities and also serves as an advisor to the science division. Mr. Bell was president and CEO of Cure Autism Now following a marketing career at McNeil Consumer & Specialty Pharmaceuticals, a member of the Johnson & Johnson family of companies.

Mark Blaxill, MBA, is the father of a daughter with autism, editor-at-large for Age of Autism, a director of SafeMinds, and a frequent speaker at autism conferences. He writes often on autism, science, and public policy. In his professional career, he is managing partner for 3LP Advisors, an advisory firm focused on intellectual property transactions.

Coleen A. Boyle, PhD, MSHyg, is the Director of the National Center on Birth Defects and Developmental Disabilities (NCBDDD) at CDC. She has worked on public health issues such as agent orange and cancer. Her interest and expertise is in the epidemiology and prevention of birth defects and developmental disabilities.

Jane Charles, MD, is a Developmental-Behavioral Pediatrician in the Department of Pediatrics at Medical University of South Carolina. Her areas of specialization are in the fields of ASDs and intellectual disabilities. For the past ten years, she has been Co-Principal Investigator for the South Carolina ADDM Network site.

Prisca Chen Marvin, JD, is the mother of a daughter with autism, a member of the Visiting Committee at Massachusetts Institute of Technology's Brain and Cognitive Science Department, a board member of REACH at the University of Iowa, and a Member of the Executive Council of the Associates of the Yale Child Study Center.

John N. Constantino, MD, is the Blanche F. Ittleson Professor of Psychiatry and Pediatrics at Washington University, Associate Director of a Eunice Kennedy Shriver Intellectual and Developmental Disabilities Research Center at the Washington University School of Medicine, and Director of the School's Division of Child Psychiatry. In addition to his role as Principal Investigator of the Missouri ADDM Network site, he leads a federally-funded program in autism research that is centered on a prospective longitudinal study of sibling pairs in families affected by autism.

Adolfo Correa, MD, MPH, PhD, is a Medical Officer and Birth Defects Surveillance Team Lead with the CDC's National Center on Birth Defects and Developmental Disabilities, Birth Defects Branch. He has worked extensively with the Metropolitan Atlanta Congenital Defects Program (MACDP). His current work focuses on surveillance of congenital heart defects and on the epidemiology of maternal diabetes and birth defects.

Krista S. Crider, MA, PhD, is a Geneticist with the CDC's National Center on Birth Defects and Developmental Disabilities, Pediatric Genetics Team. She has worked on epigenetics changes in DNA methylation and folic acid supplementation, antibiotic use and the risk of birth defects, trends in trisomies, and genetics of preterm birth among other projects with the National Birth Defects Prevention Study, Metropolitan Congenital Defects Program, and the China collaboration.

Lisa A. Croen, PhD, is a Senior Research Scientist and the Director of the Kaiser Permanente® Autism Research Program. Currently, she is leading or collaborating on several federally funded autism studies, including the Study to Explore Early Development (SEED), the Early Autism Risk Longitudinal Investigation Study (EARLI), the Early Markers for Autism Study (EMA), the California Autism Twins Study (CATS), and the Mental Health Research Network Autism Registry project.

Christopher Cunniff, MD, FACMG, FAAP, is a Professor of Pediatrics and Chief of the Section of Medical and Molecular Genetics at the University of Arizona, College of Medicine. His research focuses on public health genetics and the surveillance of developmental disabilities including ASDs, intellectual disability, muscular dystrophy, and fetal alcohol syndrome.

Julie Daniels, PhD, is a pediatric epidemiologist and Associate Professor in the Department of Epidemiology and Maternal and Child Health at University of North Carolina at Chapel Hill. She is the Principal Investigator of the North Carolina ADDM Network site and the CDC's Study to Explore Early Development (SEED) North Carolina site since 2002. Her research focuses on perinatal exposures, specifically nutrition and environmental exposures that may be associated with child health and development.

Geraldine Dawson, PhD, is Chief Science Officer for Autism Speaks, Research Professor of Psychiatry at the University of North Carolina at Chapel Hill, Adjunct Professor of Psychiatry at Columbia University, and Professor Emeritus of Psychology at University of Washington. She is a licensed clinical psychologist who has published extensively on autism, focusing on early detection and intervention and early patterns of brain dysfunction.

Owen Devine, PhD, is a Mathematical Statistician with the CDC's National Center on Birth Defects and Developmental Disabilities. He provides guidance on the analysis of epidemiologic data related to birth defects and developmental disabilities. His areas of interest included Bayesian methods, missing and miss measured data, and the interface of mathematical modeling and statistical techniques as applied to public health.

Wolf F. Dunaway works for the federal government as an Information Technology Specialist. He speaks at various colleges, universities, and symposiums on issues associated with autism and other disabilities and helps others better understand childhood autism through his own autism life experiences.

Maureen Durkin, PhD, DrPH, is a Professor of Population Health Sciences and Pediatrics and Waisman Center Investigator at the University of Wisconsin-Madison and the Principal Investigator of the Wisconsin ADDM Network site. She is an epidemiologist specializing in population-based studies of the frequency, prevention, antecedents, and consequences of developmental disabilities.

Ruth Etzioni, PhD, is a biostatistician and a full member at the Fred Hutchinson Cancer Research Center in Seattle. She studies population trends in prostate cancer incidence and mortality and is one of the principal investigators on the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network. She is currently adapting models for use in policy development for PSA screening.

Sandro Galea, MD, MPH, DrPH, is a physician, epidemiologist, and the Anna Cheskis Gelman and Murray Charles Gelman Professor and Chair of the Department of Epidemiology at Columbia University's Mailman School of Public Health. He has conducted large population-based studies in several countries,

and his primary research has been on the causes of mental disorders, substance abuse and on the role of traumatic events in shaping population health.

Roy Richard Grinker, PhD, is Professor of Anthropology at the George Washington University and editor-in-chief of The Anthropological Quarterly. He has published on topics such as the ethnic conflict in central Africa, intellectual history of African Studies, north-south Korean relations, and autism. He was a collaborator on a prevalence study of autism in South Korea and is a Co-Investigator on an NIMH-funded project entitled "Early Social Communication Characteristics of ASD in Diverse Cultures in the US and Africa".

Lee Grossman*, CAE, was the President and CEO of the Autism Society of America through early 2011 and the father of a son with autism. He has more than 20 years of experience with autism related issues, notably autism services and supports, adult issues, education, and research. He has served on numerous government and non-government advisory boards related to autism. Mr. Grossman has owned and operated a small business specializing in marketing, distribution, and consulting for medical manufacturers throughout the Pacific Basin.

Irva Hertz-Picciotto, PhD, is a Professor of Health Sciences at the University of California, Davis. She has published extensively on the effects of environmental exposures on pregnancy and child development. She is the Principal Investigator of CHARGE (Childhood Autism Risks from Genetics and Environment) Study, the first large, comprehensive population-based study of environmental factors in autism, and MARBLES (Markers of Autism Risk in Babies – Learning Early Signs), to search for early biologic markers that will predict autism.

Young Shin Kim, MD, MPH, PhD, is a researcher at Yale University. Her major research efforts focus on school bullying, the epidemiology of childhood onset neuropsychiatric disorders, and the genetic epidemiology of childhood onset neuropsychiatric disorders. She was the lead author on an epidemiological study of ASD prevalence in South Korea.

Michael King MSW, PhD, is a Commander in the US Public Health Service and an epidemiologist with the CDC's National Center for Environmental Health, Division of Environmental Hazards & Health Effects, Air Pollution and Respiratory Health Branch. His research has focused on using national surveys to monitor asthma-related morbidity, health-service use, and other respiratory health outcomes, including unintentional carbon monoxide poisoning.

Russell S. Kirby, PhD, MS, FACE, is Professor and Marrell-endowed Chair in the Department of Community and Family Health, College of Public Health, University of South Florida. He is a pediatric and perinatal epidemiologist with extensive experience in population health informatics and public health surveillance of birth defects and developmental disabilities and has been involved with the ADDM Network since 2002.

Michael D. Kogan, PhD, is Director of the Office of Epidemiology, Policy, and Evaluation for the US Health Resources and Services Administration's Maternal and Child Health Bureau. He also directs the US National Surveys of Children's Health and the National Surveys of Children with Special Health Care Needs. He has published over 100 articles and book chapters on numerous topics in pediatric and perinatal epidemiology, including the prevalence of ASDs, as well as the health care experiences of families with children who have an ASD.

Cindy Lawler, PhD, is a Program Director in the Division of Extramural Research and Training at the National Institute for Environmental Health Sciences (NIEHS), one of the National Institutes of Health. She is the NIEHS representative for extramural autism activities; this includes responsibilities as a program official for the NIH-funded Early Autism Risk Longitudinal Investigation (EARLI) study.

Li-Ching Lee, PhD, ScM, is a Research Scientist with the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health at the Johns Hopkins University. She has a background is in psychiatric epidemiology and a research interest in developmental disabilities in the US, China, and Taiwan. She has been involved with Maryland ADDM Network site since early in its inception and is currently the Principal Investigator.

Eric London, MD, is trained as a general psychiatrist and has a son with autism. He and his wife started the National Alliance for Autism Research (NAAR) in 1994, which later merged with Autism Speaks. He now serves on the Board of the Autism Science Foundation. Dr. London was the Director of the Autism Treatment Laboratory at the New York State Institute for Basic Research, and is now the Research Director at the the Center for Discovery in Harris, New York. His primary interests are in very early identification of autism and creating novel methods for autism treatment research.

Maya Lopez, MD, is a Developmental-Behavioral Pediatrician and Assistant Professor in the Developmental-Behavioral and Rehabilitative Pediatrics in the Department of Pediatrics College of Medicine at University of Arkansas Medical Sciences. She is the current Principal Investigator on the Autism Treatment Network (ATN) Grant for her institution and is Co-Principal Investigator for the Arkansas ADDM Network site.

David S. Mandell*, ScD, is Associate Professor of Psychiatry and Pediatrics at the University of Pennsylvania School of Medicine, an Associate Director of the Center for Mental Health Policy and Services Research, and Associate Director of the Center for Autism Research at The Children's Hospital of Philadelphia. The goal of his research is to improve the quality of care individuals with autism receive in their communities.

Matthew Maenner is a PhD candidate at the University of Wisconsin and works as an epidemiologist and data manager for the Wisconsin site of the ADDM network. He is currently funded by the Autism Science Foundation to explore the phenotypic heterogeneity of autism and its relationship to early identification.

Gerald McGwin, PhD, is a Professor and Vice Chairman in the Department of Epidemiology in the School of Public Health at the University of Alabama at Birmingham. He is an associate editor for the American Journal of Epidemiology, and has a lengthy and distinguished scientific reputation as a researcher, having authored or co-authored over 300 peer-reviewed manuscripts, with an emphasis on injury and ophthalmic epidemiology.

William M. McMahon, MD, is the Chairman of the Department of Psychiatry and a Professor of Psychiatry, Pediatrics, Psychology and Educational Psychology at the University of Utah. His research interests include the genetics and epidemiology of autism, Tourette's Disorder, nicotine addiction, and suicide. He is a Senior Investigator for the Autism Genome Project and is currently Principal Investigator of an Autism Speaks funded follow-up study of the Utah Autism Studies sample.

Kathleen Ries Merikangas, PhD, is a Senior Investigator and Chief of the Genetic Epidemiology Branch in the Intramural Research Program at the National Institute of Mental Health (NIMH). Her research interests have included clinical research on affective disorders and genetic epidemiology.

Lisa Miller, MD, MSPH, is the director of the Disease Control and Environmental Epidemiology Division at the Colorado Department of Public Health and Environment. She is the Co-Principal Investigator of the CDC-funded Colorado sites of the ADDM Network site and the Study to Explore Early Development (SEED). She currently directs epidemiologic programs concerning communicable diseases, environmental health, autism, and muscular dystrophy.

Beverly Mulvihill MEd, PhD, is currently an Associate Professor in the Department of Health Care Organization and Policy and a Research Scientist with the Civitan International Research Center at the University of Alabama at Birmingham. She has been Principal Investigator or Co-Principal Investigator of the Alabama ADDM Network site since 2008. Her research interests include child development; children with and at-risk for disabilities, especially autism spectrum disorders; and early identification, intervention, and inclusion for children in need of special services.

Craig Newschaffer, PhD, is Professor and Chairman of the Department of Epidemiology and Biostatistics at Drexel University School of Public Health. He leads an NIH-funded EARLI Study, which is designed specifically to study pre, peri- and neonatal autism risk factors and biomarkers. He is also a Principal Investigator on other major autism epidemiology initiatives. Prior to focusing his research on autism, he worked extensively in cancer epidemiology.

Joyce S. Nicholas PhD, is an Associate Professor in the Medical University of South Carolina's Department of Medicine, Division of Biostatistics and Epidemiology, with a dual appointment in the Department of Neurosciences. She specializes in neuro-epidemiology, in particular neurodevelopmental and other neurologic conditions. She is a Co-Principal Investigator for the South Carolina ADDM Network site.

Lars Perner, PhD, is an Assistant Professor of Clinical Marketing at the Marshall School of Business of the University of Southern California. His research interests focus on consumer behavior, "win-win" deals, non-profit marketing, and autism subtypes. He currently serves as Chair of the Panel of Persons on the Spectrum of Autism Advisors for the Autism Society.

Sydney Pettygrove, PhD, is an Assistant Professor of Epidemiology, College of Public Health, at the University of Arizona, Tucson. She primarily works on the effects of environmental and occupational exposures on reproductive outcomes including birth defects and developmental disabilities. She is the Co-Principal Investigator of the Arizona ADDM Network site.

Catherine E. Rice, PhD, is an Epidemiologist with CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch and has worked with people with an ASD through teaching, diagnostic assessment, intervention, training, and research. She has been a lead scientist with the ADDM Network since 2001. She works on public health programs related to autism with specific interests in early identification, diagnosis, prevalence, and risk factors for autism.

John Elder Robison is a self-identified "free range" Aspergian male. He is the founder of a specialty automobile company, pioneered specialty guitars for the band KISS, and worked on some of the first talking toys for Milton Bradley. He serves as adjunct faculty in the department of Communication Sciences and Disorders at Elms College in Massachusetts and has served on several national autism science boards as a community member. He is the author of Look Me in the Eye: My life with Asperger's.

Michael Rosanoff, MPH, is the Associate Director of Public Health Research and Scientific Review for Autism Speaks. He is a member of Autism Speaks etiology team and manages the organization's epidemiology and public health research grants. He is also the staff lead in overseeing the International Autism Epidemiology Network (IAEN) and is part of the development team for the Global Autism Public Health Initiative (GAPH).

Diana E. Schendel, PhD, is Lead Health Scientist and Epidemiology Team Lead with the CDC's National Center for Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. She serves as Principal Investigator for the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) which includes the Study to Explore Early Development (SEED). She is Project Lead for the International Collaboration for Autism Registry Epidemiology (iCARE). Her research interests include risk factors for cerebral palsy and autism.

Laura A. Schieve, PhD is an Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. Dr. Schieve is one of the Principal Investigators on the CDC's Study to Explore Early Development (SEED). Her current research includes prevalence of autism and other developmental disabilities, maternal and perinatal risk factors for developmental disability, health care needs and family functioning in families with a disabled child, and epidemiologic methods for assessing maternal and child risk factors in populations.

Stuart K. Shapira, MD, PhD, is a Medical Officer with CDC's National Center on Birth Defects and Developmental Disabilities, Pediatric Genetics Team. He is an investigator on the CDC Study to Explore Early Development (SEED). His current interests include birth defects epidemiologic research, dysmorphology of autism, gene and nutritional interactions for adverse reproductive outcomes, and newborn screening.

Paul T. Shattuck, PhD, is an Assistant Professor at the George Warren Brown School of Social Work at Washington University in St. Louis. Dr. Shattuck conducts research aimed at improving systems of care and services for people with autism and their families. He is especially interested in two key service transitions: getting a diagnosis in early childhood and exiting high school in adolescence.

Ezra Susser, MD, DrPH, is Professor of Epidemiology and Psychiatry at Columbia University. Dr. Susser heads the Imprints Center for Genetic and Environmental Lifecourse Studies, a collaborative birth cohort research program in which epidemiologists seek to uncover the causes of a broad range of disease and health outcomes, including psychiatric and neurodevelopmental disorders, obesity, cardiovascular disease, reproductive performance, and breast and ovarian cancers. His own studies focus on schizophrenia and autism.

Alison Singer, MBA, is Co-Founder and President of the Autism Science Foundation, a not-for-profit organization that funds autism research and serves to increase awareness of ASDs and the needs of individuals and families affected by autism. She has been very involved in advocacy for autism as the mother of a child with autism and legal guardian of her adult brother with autism. She spent 14 years at CNBC and NBC in a variety of positions, including vice president of programming in NBC's cable and business development division and as a producer. Ms. Singer has served on several research, advocacy, and government advisory boards for autism.

Caroline M. Tanner, MD, PhD, FAAN, is Director of Clinical Research at the Parkinson's Institute in Sunnyvale, California, a Visiting Professor at Xuan Wu Hospital and Capital University in Beijing, China, and an Adjunct Professor in the Department of Health Research and Policy at Stanford University. Her current research includes epidemiologic investigations of the genetic and environmental determinants of Parkinson's disease, multiple system atrophy, dystonia, Huntington's disease and essential tremor in a variety of populations in the US.

Kim Van Naarden Braun, PhD, is an Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch and with the New Jersey Department of Health and Senior Services. She is the Principal Investigator for the Metropolitan Atlanta Developmental Disabilities Surveillance Program (MADDSP) and also serves an epidemiologist for the ADDM Network and the ADDM Cerebral Palsy Network. Research interests include developmental disabilities, perinatal epidemiology, genetic epidemiology, environmental health, and child health and development.

Susanna Visser, MS, is the lead Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Child Development Studies Team. Her current research interests include population-based epidemiological studies of neurobehavioral and mental health conditions, including ADHD and Tourette Syndrome, medication treatment among youth with ADHD, and factors associated with ADHD medication treatment.

Gayle Windham, PhD, is a Research Scientist and Chief of the Epidemiological Surveillance Section at the California Department of Public Health in the Division of Environmental and Occupational Disease Control. She currently works with the Centers for Autism and Developmental Disabilities Research (CADDRE) team and is the lead investigator on a study of early ASD prevalence in California. Her areas of research and expertise include children's health in relation to environmental risk factors, pregnancy outcomes such as spontaneous abortion and fetal growth, and other aspects of reproductive health including puberty, infertility, and menstrual function.

Martha S. Wingate, DrPH, is an Assistant Professor at University of Alabama at Birmingham in the Department of Health Care Organization and Policy. She is the Co-Principal Investigator of the Alabama ADDM Network site. Much of her work focuses on preterm birth, fetal and infant mortality, racial and ethnic disparities in birth outcomes, and health policies related to pregnancy and infant health.

Marshalyn Yeargin-Allsopp, MD, is a Medical Epidemiologist and Branch Chief with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. She designed and implemented the first U.S. population-based study of developmental disabilities in school-age children in an urban area, which has served as the basis for the ADDM Network and the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE). She has presented internationally and published extensively on the epidemiology of developmental disabilities, including autism and cerebral palsy.

Paula Yoon, MPH, ScD, is currently the Team Lead for the Health Services Research and Registries Team in the Division for Heart Disease and Stroke Prevention, Epidemiology and Surveillance Branch. She is also leading an initiative to establish a National Cardiovascular Disease Surveillance System. She is the Chair of the Surveillance Science Advisory Group at CDC and is spearheading an effort to develop an agency-wide surveillance report to track the impact of health care reform on prevention in health care.

Matthew Zack, MD, is a Medical Epidemiologist with the CDC's National Center for Chronic Disease Prevention and Health Promotion, Division of Adult and Community Health, State Support, Arthritis, Epilepsy, & Quality of Life Branch. He has worked extensively on issues related to chronic diseases and environmental health.

Walter Zahorodny, PhD, is a clinical psychologist and Assistant Professor of Pediatrics at the New Jersey Medical School. He has over twenty years of experience in pediatric neurodevelopment and is the Principal Investigator of the New Jersey ADDM Network site for population-based ASD surveillance system. He is a founding member of the New Jersey Medical School Autism Center and was instrumental in development of the New Jersey Governor's Council on Medical Research and Treatment of Autism.

Judith Pinborough Zimmerman, PhD, CCC, is an Assistant Professor in the Department of Psychiatry at the University of Utah. She is the for the Utah Registry for Autism and Developmental Disabilities (URADD) and the Principal Investigator for the Utah ADDM Network site. She is particularly interested in the utility of ASD prevalence data for state Maternal and Child Health Programs.

## RECORDERS

Carrie Arneson, MSc, serves as Project Coordinator for the Wisconsin ADDM Network site located at the Waisman Center at University of Wisconsin-Madison.

Jon Baio, EdS, is an Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. He currently serves as Principal Investigator on the ADDM Network, studying the prevalence of autism and other developmental disabilities in several communities throughout the U.S.

Thomas A. Bartenfeld, PhD, specializes in program evaluation with the CDC's National Center on Birth Defects and Developmental Disabilities. His most recent work has focused on using evaluation to promote information to action and organizational integration with NCBDDD's surveillance, research, and prevention programs.

Robert Fitzgerald, MPH is currently a staff scientist in the Department of Psychiatry at the Washington University School of Medicine in St. Louis, and is a PhD candidate in Epidemiology at the St. Louis University School of Public Health. He has served as Project Coordinator for the Missouri ADDM Network site since its inception in 2003 and has served as Co-Principal Investigator since April of 2009.

Lydia King, PhD, is an Assistant Professor of Pediatrics at the Medical University of South Carolina and is an Epidemiologist specializing in ASDs. She has served as the Project Coordinator for the South Carolina ADDM site since 2003. She is also Faculty Director for the Global Education Masters in Clinical Research Program.

Keydra Phillips, MSc, is a Health Scientist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. She is a member of an interdisciplinary team of researchers of the ADDM Network, and her research interests include public health informatics and surveillance of chronic diseases.

Andria M. Ratchford, MSPH, has served as the Project Coordinator for the Colorado ADDM Network site at the Colorado Department of Public Health and Environment since 2002. She has considerable surveillance and project management experience through her experience with ADDM and the Colorado Center of Autism and Developmental Disabilities Research and Epidemiology (CADDRE) activities.

Anita Washington, MPH, is a Research Public Health Analyst with Research Triangle Institute (RTI) as part of the Atlanta Regional Office. For the past 6 years, she has been working as a contract employee in the role of the ADDM Network Project Coordinator for CDC's National Center on Birth Defects and Developmental Disabilities, Division of Birth Defects and Developmental Disabilities, Developmental Disabilities Branch.

**Invited participant unable to attend remotely or in-person at last minute due to unforeseen circumstances.*

# Appendix C: Reference List

References were compiled based on panel member nominations for suggested background reading on ASD prevalence.

Panel members were asked to read the articles indicated with an * prior to the workshop.

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# Notes

# Notes

Centers for Disease Control and Prevention
www.cdc.gov/autism
cdcinfo@cdc.gov
1-800-CDC-INFO

Autism Speaks
www.autismspeaks.org
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**Subject:** Education and Outreach

Hello to Education and Outreach members and guests

The Education and Outreach conference call will be
Wednesday March 6th
1-2 PM EST
Telephone (b)(6)
Passcode (b)(6) #

My best
Walter Jenner M.S., C.A.S.
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Reminder

The Education and Outreach conference call will be
Wednesday March 6th
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**To:** 'Eric Lott';mslay@uab.edu;Julie K Preskitt (preskitt@uab.edu);kirby S. Russell (CDC health.usf.edu);'Chris Cunniff';'Sydney Pettygrove';'kgotscha@email.arizona.edu';Mancilla, Kristen M C - (kclancy);Lopez, Maya L;Thaer Baroud;Hudson, Allison;Ghosh, Tista (CDC state.co.us);Kast - CDPHE, Kelly;Li-Ching Lee;'achang@jhsph.edu';Fitzgerald, Robert;'John Constantino';'Josephine P Shenouda';'zahorodn@umdnj.edu';Daniels, Julie L;'Jane Charles';'Joyce Nicholas';'Walter Jenner';'Lydia King';'Carpenter, Laura Arnstein';William McMahon;Deborah Bilder (Deborah.Bilder@hsc.utah.edu);'AMANDA BAKIAN';colin.kingsbury@hsc.utah.edu;'Maureen Durkin';'Carrie Arneson - WI (clarneso@wisc.edu)';kalkbren@uwm.edu;amy@ursid.com;'mmorrie@emory.edu';Talboy, Amy (Amy.Talboy@choa.org);Wright, Victoria (CDC/ONDIEH/NCBDDD);Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD);Baio, Jon (CDC/ONDIEH/NCBDDD);Rice, Catherine (CDC/ONDIEH/NCBDDD);Christensen, Deborah (Daisy) (CDC/ONDIEH/NCBDDD);Green, Santrell (CDC/ONDIEH/NCBDDD) (CTR);Jones, Lekeisha F. (CDC/ONDIEH/NCBDDD);Goodman, Alyson B. (CDC/ONDIEH/NCBDDD);Schieve, Laura (CDC/ONDIEH/NCBDDD);Wiggins, Lisa (CDC/ONDIEH/NCBDDD);Franklin, C. Leah (CDC/ONDIEH/NCBDDD) (CTR);Tian, Lin Hui (CDC/ONDIEH/NCBDDD);Van Naarden-Braun, Kim (CDC/ONDIEH/NCBDDD);Barritt, Lisa (CDC/ONDIEH/NCBDDD) (CTR);Jolly, Kwinettaion (CDC/ONDIEH/NCBDDD) (CTR);Frenkel, Gal (CDC/ONDIEH/NCBDDD);Augustus, Eric L. (CDC/ONDIEH/NCBDDD) (CTR);Williams, Susan (CDC/ONDIEH/NCBDDD);Cleveland, Michael (CDC/ONDIEH/NCBDDD) (CTR);Bell, Paula;Hobson, Nancy (CDC/ONDIEH/NCBDDD) (CTR);Dirienzo, Monica A. (CDC/ONDIEH/NCBDDD) (CTR);Clayton, Heather B. (CDC/ONDIEH/NCBDDD);lynn.almli@emory.edu;Talboy, Amy (Amy.Talboy@choa.org);Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD);Boyle, Coleen (CDC/ONDIEH/NCBDDD);Shapira, Stuart (CDC/ONDIEH/NCBDDD);Devine, Owen (CDC/ONDIEH/NCBDDD);Stevens, Melody (CDC/ONDIEH/NCBDDD);Sniezek, Joe (CDC/ONDIEH/NCBDDD);Honein, Margaret (Peggy) (CDC/ONDIEH/NCBDDD);Moore, Cynthia (CDC/ONDIEH/NCBDDD);Dowling, Nicole (CDC/ONDIEH/NCBDDD);Whitney, Julia (CDC/ONDIEH/NCBDDD) (CTR);Washington, Anita (CDC/ONDIEH/NCBDDD)
**Subject:** Updated ADDM Meeting Agenda
**Attachments:** ADDM Network Meeting Agenda for May 14-16 2013.docx

Hi everyone,
I made a few updates to the agenda. I'll see everyone in the lobby of the hotel at 7:50am tomorrow.

Thank you,
Anita

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**From:** Washington, Anita (CDC/ONDIEH/NCBDDD)
**Sent:** Wednesday, May 08, 2013 7:29 PM
**To:** 'Eric Lott'; mslay@uab.edu; Julie K Preskitt (preskitt@uab.edu); kirby S. Russell (CDC health.usf.edu); 'Chris Cunniff'; 'Sydney Pettygrove'; 'kgotscha@email.arizona.edu'; Mancilla, Kristen M C - (kclancy); Lopez, Maya L; Thaer Baroud; Hudson, Allison; Ghosh, Tista (CDC state.co.us); Kast - CDPHE, Kelly; Li-Ching Lee; 'achang@jhsph.edu'; Fitzgerald, Robert; 'John Constantino'; 'Josephine P Shenouda'; 'zahorodn@umdnj.edu'; Daniels, Julie L; 'Jane Charles'; 'Joyce Nicholas'; 'Walter Jenner'; 'Lydia King'; 'Carpenter, Laura Arnstein'; William McMahon; Deborah Bilder (Deborah.Bilder@hsc.utah.edu); 'AMANDA BAKIAN'; colin.kingsbury@hsc.utah.edu; 'Maureen Durkin'; 'Carrie Arneson - WI (clarneso@wisc.edu)'; kalkbren@uwm.edu; amy@ursid.com; 'mmorrie@emory.edu'; Talboy, Amy (Amy.Talboy@choa.org); Wright, Victoria (CDC/ONDIEH/NCBDDD);

Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD); Baio, Jon (CDC/ONDIEH/NCBDDD); Rice, Catherine (CDC/ONDIEH/NCBDDD); Christensen, Deborah (Daisy) (CDC/ONDIEH/NCBDDD); Green, Santrell (CDC/ONDIEH/NCBDDD) (CTR); Jones, Lekeisha F. (CDC/ONDIEH/NCBDDD); Goodman, Alyson B. (CDC/ONDIEH/NCBDDD); Schieve, Laura (CDC/ONDIEH/NCBDDD); Wiggins, Lisa (CDC/ONDIEH/NCBDDD); Franklin, C. Leah (CDC/ONDIEH/NCBDDD) (CTR); Tian, Lin Hui (CDC/ONDIEH/NCBDDD); Van Naarden-Braun, Kim (CDC/ONDIEH/NCBDDD); Barritt, Lisa (CDC/ONDIEH/NCBDDD) (CTR); Jolly, Kwinettaion (CDC/ONDIEH/NCBDDD) (CTR); Frenkel, Gal (CDC/ONDIEH/NCBDDD); Augustus, Eric L. (CDC/ONDIEH/NCBDDD) (CTR); Williams, Susan (CDC/ONDIEH/NCBDDD); Cleveland, Michael (CDC/ONDIEH/NCBDDD) (CTR); Bell, Paula; Hobson, Nancy (CDC/ONDIEH/NCBDDD) (CTR); Dirienzo, Monica A. (CDC/ONDIEH/NCBDDD) (CTR); Clayton, Heather B. (CDC/ONDIEH/NCBDDD); lynn.almli@emory.edu
**Cc:** Washington, Anita (CDC/ONDIEH/NCBDDD)
**Subject:** ADDM Meeting Agenda

Hi Everyone,

Please see attached the final agenda for our meeting. If you have any questions please let me know.

Thanks,
Anita

Anita Washington, MPH
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National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention
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**Telework: Thursday – 678-984-4698**

**Autism and Developmental Disabilities Monitoring (ADDM) Network**
**Agenda for May 2013 Investigator Meeting**
**Building 19, Tom Harkin Global Communications Center**
**Centers for Disease Control and Prevention**
**Atlanta, Georgia**
**May 14-16, 2013**

## Tuesday, May 14 (Distance Learning Auditorium)*

| Time | Topic | Presenter | Room |
|---|---|---|---|
| **8:00 - 8:30** | **Arrive at CDC and check-in / load presentations** | | |
| **8:30 - 8:45** | **Welcome and introductions** | Jon Baio | **DLA*** |
| **8:45 - 10:00** | **Preliminary SY2010 ASD prevalence data**<br>a. Preliminary findings<br>b. Topics to highlight in manuscript<br>c. SY2010 ASD prevalence reporting and trend comparisons | Jon Baio | **DLA** |
| **10:00 - 10:15** | **Break** | | |
| **10:15 - 11:30** | **Preliminary SY2010 Early ADDM ASD prevalence data**<br>a. Preliminary findings<br>b. Topics to highlight in manuscript<br>c. Options for reporting Early ADDM ASD prevalence results | Daisy Christensen | **DLA** |
| **11:30 - 1:00** | **Lunch** (CDC cafeteria or Emory Point across from CDC)<br>**CP SIG working lunch** (neuroimaging discussion) | | **116** |
| **1:00 - 1:45** | **Preliminary SY2010 ID surveillance data** | Sydney Pettygrove | **DLA** |
| **1:45 - 2:30** | **Preliminary SY2010 CP surveillance data** | Daisy Christensen | **DLA** |
| **2:30 - 2:45** | **Break** | | |
| **2:45 - 4:00** | **Denominator discussion**<br>a. Curtailing for SY2010<br>b. Planned discussions with concerned parties; Trend analyses<br>c. Manuscript on choice of denominator | <br>Jon / Daisy<br>Kim Van Naarden Braun<br>Amy Kalkbrenner | **DLA** |
| **4:00 - 4:45** | **Miscellaneous discussions**<br>a. Updated confidentiality policy for SY2012/ARCHEv4<br>b. Public use datasets<br>c. Informal discussion of community outreach activities in ADDM sites, new ideas for data dissemination | <br>Anita Washington<br>Jon Baio<br>(moderator TBD) | **DLA** |
| **5:00** | **A walk in the park** (meet at Emory Conference Center) | | |
| **6:30** | **Group dinner at Highland Tap** (meet at Emory Conference Center) | | |

**Autism and Developmental Disabilities Monitoring (ADDM) Network**
**Agenda for May 2013 Investigator Meeting**

**Wednesday, May 15**

| Time | Topic | Presenter | Room |
|---|---|---|---|
| **8:30 - 9:00** | **Arrive at CDC and check-in / load presentations** | | **CDC** |
| **9:00 - 10:30** | **Methodologic analyses and evaluations in-progress** | | **247/248** |
| | a. ICD and exceptionality DNR | Kim Van Naarden Braun | |
| | b. Sensitivity analysis | Julie Daniels | |
| | c. Trigger analysis | Carrie Arneson | |
| **10:30 - 10:45** | **Break** | | |
| **10:45 - 11:45** | **Scientific analyses and evaluations in-progress** | | **247/248** |
| | a. DSM-IV and discriminator analysis | Sydney Pettygrove | |
| | b. Manuscript on maternal prenatal weight gain | Deb Bilder | |
| | c. NC spatial time trend analysis | Julie Daniels | |
| **11:45 - 1:00** | **Lunch** (CDC cafeteria or Emory Point across from CDC)<br>**Available meeting rooms : 245 and 246** | | |
| **1:00 - 1:45** | **SY2012 timeline and updates** | | **247/248** |
| | a. Abstraction and clinician review | Anita Washington | |
| | b. Phase 4 ADDM FOA | Jon Baio | |
| **1:45 - 2:45** | **Workgroup formation** | | **247/248** |
| | a. Reconstituting the Spatial Analysis Workgroup | Amanda Bakian | |
| | b. Charge for a DSM-5 Workgroup | Jon Baio | |
| | c. Updates on DSM-5 transition | L. Carpenter & C. Rice | |
| **2:45 - 3:00** | **Break** | | |
| **3:00 - 3:30** | **SharePoint system for tracking proposals and analyses in-progress** | Leah Franklin | **247/248** |
| **3:30 - 5:00** | **Break-out session for Principal Investigators on datasharing policy** | Jon Baio | **247/248** |
| | a. Satisfaction with proposal submission/approval process | | |
| | b. Tracking site-specific analyses | | |
| | c. Ideas for new tracking system | | |
| **3:30 - 5:00** | **Break-out session for Project Coordinators** | Anita Washington | **245** |
| | a. QC Workgroup | Lisa Barritt | |
| | b. Training needs (Abstraction/Clinician Review) | Lisa Barritt | |
| | c. ARCHE v4 | E. Augustus & K. Jolly | |
| | d. ASD and CP Community Reports | Leah Franklin | |
| | e. Manuscript ideas? | Anita Washington | |
| **6:00** | **Small-group dinners at various Emory Point restaurants** | | |

## Autism and Developmental Disabilities Monitoring (ADDM) Network
## Agenda for May 2013 Investigator Meeting

**Thursday, May 16**

| Time | Topic | Presenter | Room |
|---|---|---|---|
| 8:30 - 9:00 | Arrive at CDC and check-in | | **CDC** |
| **9:00 - 12:00** | **ADDM Paper Group (9:00-9:30)**<br>Multi04: Follow-up on parental age and birth order on the prevalence of ASD using 2002, 2006, and 2008 | | **246** |
| | **ADDM Paper Group (9:30-10:00)**<br>Multi12: Follow manuscript on the association between the prevalence of ASD and SES, 2002-2008 | | **246** |
| | **ADDM Paper Group (10-10:30)**<br>Multi24: Trends over time (2002-2008) in the association between the prevalence of ASD and 2000 and 2010 census based measures of SES | | **246** |
| | **ADDM Paper Group (10:30-11)**<br>Multi22: Relationship between ASD prevalence and ADDM Network catchment area characteristics, 2002-2008 | | **246** |
| **12:00 - 1:00** | **Lunch** (CDC cafeteria or Emory Point across from CDC) | | |
| **1:00 - 5:00** | **ADDM Paper Groups / Atlanta Community Engagement Event** | | |

**From:** Rice, Catherine (CDC/ONDIEH/NCBDDD)
**Sent:** 7 Mar 2012 13:44:19 -0500
**To:** Correa, Adolfo (CDC/ONDIEH/NCBDDD);'amanda.bakian@hsc.utah.edu';'as16@columbia.edu';'ccunniff@peds.arizona.edu';Lawler, Cindy P. (NIH/NIEHS/DERT);'cjn32@drexel.edu';'clarneso@wisc.edu';'constantino@wustl.edu';Phillips, Keydra (CDC/ONDIEH/NCBDDD);Shapira, Stuart (CDC/ONDIEH/NCBDDD);(b)(6);Washington, Anita (CDC/ONDIEH/NCBDDD);Schendel, Diana (CDC/ONDIEH/NCBDDD);'fitzgerr@psychiatry.wustl.edu';'Gayle.Windham@cdph.ca.gov';'gdawson@autismspeaks.org';'Gerald.McGwin@ccc.uab.edu';'hgf2103@columbia.edu';'ihp@phs.ucdavis.edu';(b)(6) (b)(6);'julie_daniels@unc.edu';Van Naarden-Braun, Kim (CDC/ONDIEH/NCBDDD);Crider, Krista (CDC/ONDIEH/NCBDDD);'Lisa.A.Croen@kp.org';'lisam@smtpgate.dphe.state.co.us';Schieve, Laura (CDC/ONDIEH/NCBDDD);'llee2@jhsph.edu';'maenner@Waisman.Wisc.Edu';'mandelld@mail.med.upenn.edu';(b)(6);'mdurkin@wisc.edu';Kogan, Michael (HRSA/MCHB/ODPD);'mrosanoff@autismspeaks.org';'mwingate@ms.soph.uab.edu';Yeargin-Allsopp, Marshalyn (CDC/ONDIEH/NCBDDD);Zack, Matthew M. (CDC/ONDIEH/NCCDPHP);(b)(6);'nicholjs@musc.edu';King, Michael (CDC/ONDIEH/NCEH);Devine, Owen (CDC/ONDIEH/NCBDDD);'pbell@autismspeaks.org';'perner@marshall.usc.edu';'Prisca@alum.mit.edu';(b)(6) (b)(6);'pshattuck@wustl.edu';'qyang@thepi.org';'rgrink@gwu.edu';Visser, Susanna (CDC/ONDIEH/NCBDDD);'sgalea@columbia.edu';'sydneyp@u.arizona.edu';Bartenfeld, Thomas (CDC/ONDIEH/NCBDDD);Baroud, Thaer (CDC healthyarkansas.com);'william.mcmahon@hsc.utah.edu';'young-shin.kim@yale.edu';'zahorodn@umdnj.edu';'cv111@columbia.edu';'Alison Singer';'lgrossman@autism-society.org';(b)(6);Yoon, Paula (CDC/OSELS/EAPO);'Charles, Jane M.';'Beverly Mulvihill, MEd, Ph.D.';'Judith Zimmerman';kirby S. Russell (CDC health.usf.edu);'King, Lydia A';'Rob Fitzgerald (fitzgerr@psychiatry.wustl.edu)';'brownst@psychiatry.wustl.edu';'Eldon Schulz - AR';'Andria Ratchford';'King, Lydia A';'Lopez, Maya L';Merikangas, Kathleen R. (NIH/NIMH/DIRP);(b)(6);'Dunaway, Wolf';'retzioni@fhcrc.org'
**Cc:** Baio, Jon (CDC/ONDIEH/NCBDDD);Wright, Victoria (CDC/ONDIEH/NCBDDD);Jones, Lekeisha F. (CDC/ONDIEH/NCBDDD);Jackson, Bisi (CDC/OID/NCEZID) (CTR);Ayers, Kimberly P. (CDC/ONDIEH/NCEH);'Alycia Halladay';Boyle, Coleen (CDC/ONDIEH/NCBDDD);Colson, Angela S. (CDC/ONDIEH/NCBDDD);Ward-Cameron, Conne (CDC/OPHPR/DEO);Sumartojo, Esther (CDC/ONDIEH/NCBDDD);Stevens, Melody (CDC/ONDIEH/NCBDDD);Richardson, Julia (CDC/ONDIEH/NCBDDD);Moore, Cynthia (CDC/ONDIEH/NCBDDD)
**Subject:** 2011 Workshop on US Data to Evaluate Changes in ASD Prevalence Summary
**Attachments:** CS225567_ExecutiveSummary_Final Print.pdf, CS225567_WorkshopSummary_Final Print.pdf

Dear Panelists,

Thank you so much for your participation in last year's *Workshop on U.S. Data to Evaluate Changes in Prevalence of the Autism Spectrum Disorders (ASDs)*. The workshop was co-sponsored by CDC's National Centers on Birth Defects and Developmental Disabilities (NCBDDD) and Autism Speaks. The Executive and Full Workshop summaries are attached and are also available on the CDC's and Autism Speaks' websites.

The purpose of the workshop was to bring together scientists and stakeholders in the field of autism surveillance and research to:

- Summarize where we are in our current understanding of changes in ASD prevalence in the US;
- Learn from different perspectives, including experts who have studied prevalence changes among other complex conditions;
- Share ideas for the field to move forward in understanding trends in ASD prevalence.
- Stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

The key suggestions for framing the path forward centered around the following themes:

- Increase collaboration efforts
- Better utilize existing data
- Use data on prevalence and characteristics of individuals with an ASD to better inform service and support efforts
- Implement new types of data collection and studies

It is hoped that the information, research, and opinions shared during this workshop will add to the knowledge about ASD prevalence and encourage further work among public and private groups to understand the multiple factors influencing increasing ASD prevalence in the U.S. and beyond.

CDC is moving forward and is addressing several of the panelist suggestions. For example, CDC:

- Continues to monitor the prevalence of ASDs among 8-year-old children through the multi-site collaboration of the Autism and Developmental Disabilities Monitoring (ADDM) Network. An updated prevalence report is expected this Spring and ongoing data collection is underway for another cohort of children in areas of the United States.
- Has begun projects in 6 ADDM Network sites to determine the prevalence of ASDs among children at 4 years of age.
- Has supported 2 projects (CA and FL) currently underway to examine the prevalence of ASDs in young children with one study conducting community-based screening for ASDs in pediatric practices.
- Is working with NIH and Autism Speaks to support a project by the University of Minnesota through the Association of University Centers on Disabilities (AUCD) to study autism in a Minnesota Somali community to follow-up concerns about higher autism prevalence than in other communities.
- Has implemented analyses related to how specific identification and risk factors in the population have changed and whether they could have a significant impact on increasing ASD prevalence.
    - An analysis was completed and a paper published indicating that population changes in select perinatal factors such as low birth weight and gestational age have had a minimal effect on ASD prevalence changes reported in the ADDM Network (Schieve et al., 2011).
    - Several other analyses by ADDM Network investigators examining other identification and risk factors in relation to ASD prevalence change are underway.

- Has partnered with Autism Speaks to build on the ADDM Network infrastructure to evaluate the completeness of ASD prevalence estimates. Autism Speaks is funding a project in the SC ADDM site through the Medical University of South Carolina to add community screening and assessment to the existing ADDM record-review surveillance method.
- Continues to work as part of the Interagency Autism Coordinating Committee (IACC) to identify and implement a Strategic Plan for Autism Research coordinated among public and private organizations. This workshop summary will be shared with the IACC and can be used to inform the next iteration of the IACC Strategic Plan.
- Is conducting one of the largest studies in the United States to help identify factors that may put children at risk. This study, being conducted across a 6 site network known as the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE), is called SEED, the Study to Explore Early Development. SEED is looking at numerous risk factors of autism such as genetics, environmental exposures, pregnancy factors, and behavioral factors. The study enrollment is on schedule, and first reports are expected from SEED later this year.
- Continues to work with the community to increase awareness of early signs of ASDs and other developmental disabilities. Our "Learn the Signs. Act Early." program is working to address critical gaps in early identification of autism and other developmental disabilities in two ways:
    - First, we know that all parents play a critical role in monitoring their children's developmental milestones. Our program offers free online resources for parents to help them do that. We also have resources for health professionals and early childhood teachers. www.cdc.gov/actearly
    - Second, we are working with representatives from public health, medicine, education, and advocates in states to improve early identification, screening, and referral practices so children and their families can access the services and supports.
- For more information: www.cdc.gov

If you would like to have hard copies of the Workshop Report and/or Executive Summary mailed to you, please send your name, mailing address, and number of copies (up to 5) to Lekeisha Jones at lfj9@cdc.gov.

Thank you for your work and commitment for people with ASDs. Hopefully, this workshop summary will be a helpful resource for others as it has been for CDC.

*Cathy* and *Marshalyn*

Catherine E. Rice, PhD and Marshalyn Yeargin-Allsopp, MD
Developmental Disabilities Branch
National Center on Birth Defects and Developmental Disabilities
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Co-Sponsored by Autism Speaks

# Workshop on U.S. Data to Evaluate Changes in the Prevalence of Autism Spectrum Disorders (ASDs)

## Executive Summary

**Tuesday, February 1, 2011**

**Centers for Disease Control and Prevention**
**Tom Harkin Global Communications Center | 1600 Clifton Road, N.E. | Atlanta, Georgia**

National Center on Birth Defects and Developmental Disabilities
Division of Birth Defects and Developmental Disabilities

# Acknowlegement


## Co-Sponsored by the National Center on Birth Defects and Developmental Disabilities (NCBDDD), Centers for Disease Control and Prevention (CDC) and Autism Speaks


*Panel members* were representatives from:*

Autism Science Foundation
Autism Society of America (invited)
Colorado Department of Health
Columbia University
Drexel University
George Washington University
Health Resources and Services Administration (HRSA)
Johns Hopkins University
Kaiser Permanente®, California
Medical University of South Carolina
National Institutes of Health (NIEHS, NIMH)
Parkinson's Institute
SafeMinds
Parents of children with an Autism Spectrum Disorder
Persons with an Autism Spectrum Disorder
University of Alabama at Birmingham
University of Arizona, Tucson
University of Arkansas
University of California, Davis – MIND Institute
University of North Carolina, Chapel Hill
University of Pennsylvania
University of South Florida
University of Southern California, Marshall
University of Utah
Washington University in Saint Louis
University of Washington
University of Wisconsin, Madison
Yale University


### Workshop Planning Committee

| | |
|---|---|
| Carrie Arneson, MsC | University of Wisconsin, Madison |
| Amanda Bakian, PhD (Feb 2011) | University of Utah |
| Tom Bartenfeld, PhD | NCBDDD, CDC |
| Julie Daniels, PhD | University of North Carolina, Chapel Hill |
| Geraldine Dawson, PhD | Autism Speaks |
| Keydra Phillips, MsC | NCBDDD, CDC |
| Catherine Rice, PhD | NCBDDD, CDC |
| Michael Rosanoff, MPH | Autism Speaks |
| Anita Washington, MPH | Research Triangle Institute |
| Martha Wingate, DrPH | University of Alabama, Birmingham |
| Marshalyn Yeargin-Allsopp, MD | NCBDDD, CDC |


**Refer to Appendix B in full workshop summary for biographies of panel members*

*The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC). This summary report reflects statements made by individuals attending the workshop and does not constitute consensus recommendations made to the CDC.*

# Workshop Summary

## PURPOSE

Autism spectrum disorders (ASDs) are estimated to occur among about 1% of children in the U.S. This is in line with estimates from other industrialized countries. However, the identified prevalence of ASDs has increased significantly in a short time period based on data from multiple studies including the Centers for Disease Control and Prevention's (CDC) Autism and Developmental Disabilities Monitoring (ADDM) Network (http://www.cdc.gov/ncbddd/autism/addm.html). Whether increases in ASD prevalence are partly attributable to a true increase in the risk of developing ASD symptoms or solely to changes in community awareness and identification patterns is not known. It is clear that more children are identified with an ASD now than in the past and the impact on individuals, families, and communities is significant. However, disentangling the many potential reasons for ASD prevalence increases has been challenging. Understanding the relative contribution of multiple factors such as variation in study methods, changes in diagnostic and community identification, and potential changes in risk factors is an important priority for the ADDM Network and for CDC. This workshop was co-sponsored by CDC and Autism Speaks as a forum for sharing knowledge and opinions of a diverse range of stakeholders about changes in ASD prevalence. This summary report reflects statements made by individuals at the forum and discussions that were held among the attendees, and does not constitute formal consensus recommendations to CDC. The information, research, and opinions shared during this workshop add to the knowledge base about ASD prevalence in an effort to stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

## FRAMEWORK

The workshop brought together epidemiologic prevalence and surveillance experts in ASDs and other conditions as well as representatives from autism organizations, parents of children with ASDs, adults with an ASD, and other stakeholders. A total of 342 people registered to attend the workshop (143 in person and 199 via webinar).

Prior to the meeting, the panel members met via teleconference and were asked to submit at least two publications that they viewed as important background reading for understanding ASD prevalence trends. Panel members were provided with the compiled reference list (Appendix C) and articles and were asked to review, at a minimum, the priority readings prior to the workshop.

Presentations during the morning of the workshop summarized current knowledge and issues related to ASD prevalence and provided perspectives from subject matter experts in cancer, Parkinson disease, asthma, schizophrenia, and analytic modeling of prevalence changes.

Following the morning's presentations, the public was invited to provide statements, and there was an open invitation to provide written comments before and after the workshop. Workshop organizers, panelists, and stakeholders were asked to consider these comments when expressing their opinions on priorities for evaluating changes in ASD prevalence.

After hearing open comments from the community, the workshop was divided into four panels:

- Panel 1 – Utility of ASD Prevalence Data
- Panel 2 – U.S.-Based ASD Service Data
- Panel 3 – Autism and Developmental Disabilities Monitoring (ADDM) Network Data
- Panel 4 – What Else Is Needed To Understand ASD Trends?

For the workshop panel sessions, members of each panel were asked to reflect on questions along the following themes to better understand ASD prevalence trends:

- What can we do now with existing data?
- What should we do next to build on existing data systems?
- What else is needed in terms of new analyses, data collection, or other efforts?

## SUMMARY POINTS

Panel members and attendees commented that the effort to increase transparency and expand the dialogue related to ASD prevalence change was appreciated and necessary to move the community forward around the issue of understanding ASD prevalence changes. Additional key points made during the workshop included:

- The identified prevalence of ASD has increased significantly in a short time period across multiple studies, including data from the CDC's U.S.-based Autism and Developmental Disabilities Monitoring (ADDM) Network.
- CDC is the source for ASD prevalence estimates in the U.S., but other data systems exist or could be developed to better understand trends in ASDs.
- ASDs are conditions estimated to occur among about 1% of children in the U.S. There is an urgent demand to address the many needs associated with ASDs. Prevalence estimates have, for example, fueled action by advocacy groups and the Interagency Autism Coordinating Committee (IACC) and driven the creation of legislation and presidential priority. However, individuals, families, and communities continue to struggle to address unmet needs across the lifespan of people with ASDs. ASD prevalence estimates are important to stakeholders for program planning and making policy changes, in addition to highlighting the need for research into causes and interventions.
- In terms of reasons for increased ASD prevalence, the debate has been dichotomized by researchers, advocacy groups, and the media to indicate that increases must be explained either by identification factors or by increased risk among the population. In reality, a more complex understanding is needed. It is clear that some of the increase has been related to intrinsic and extrinsic identification factors. However, although a true increase in ASD symptoms cannot be ruled out, such an increase has been difficult to prove. Panels discussed needing to identify and use methods to better understand the role of potential identification and risk factors in the changing prevalence of ASD.
- Some people expressed hope that understanding why ASD prevalence has increased may help identify modifiable risk factors. There was debate about the roles of prevalence and surveillance in answering questions about risk and causes of ASDs. Prevalence studies provide descriptive data on the number of people with a condition in a defined population. These types of studies are not sufficient to identify what causes ASDs. However, prevalence studies can be used as tools to examine variation in occurrence of ASDs across place, groups, time, and exposures, which may provide clues about groups who are at increased risk for ASDs. Other study designs would then be necessary to fully investigate the reasons behind observed variation in prevalence.
- There are likely multiple forms of ASDs with multiple causes that are poorly understood. It was noted that sufficient evidence exists that biologic and environmental factors, alone and in interaction, need to be considered as causes. It is not necessary to have confirmation that a portion of the increase in ASD prevalence is due to increased risk in the population to motivate the active pursuit of causes of ASDs. By better understanding what causes ASDs, maybe we can understand the increases in measured prevalence.

- A risk factor might be strongly associated with ASD and might be modifiable, but it might not have increased sufficiently in the population during the time frame of interest. Therefore, this risk factor might be related to an individual's risk for ASD but not related to the increase in population prevalence of ASD. The model demonstrated that for any factor to have made a noteworthy contribution to population changes in ASD prevalence during a short time period, three conditions must be met: the factor has to be fairly prevalent in the population, it has to have increased substantially, and it has to be strongly associated with diagnosed ASD.
- There was a shared recognition of the importance of, and commitment to, obtaining and using prevalence and epidemiologic information to improve the lives of people with ASDs.

## PANEL DISCUSSION SUMMARIES

The four panel chairs compiled main discussion points brought forth by their members for building on existing infrastructure and for developing new initiatives to better understand ASD trends. These discussion points are summarized below.

### Collaboration

The panels indicated that collaboration among professionals and stakeholders is important, and the following points were made to assist collaborative efforts among those interested in understanding ASDs and supporting the ASD community through science:

- Continue efforts of this workshop to develop and enhance communication among families, individals affected, researchers, service providers, advocates, and government entities about ASD prevalence, research, and service needs.
- Seek public–private partnerships to support data collection, analyses, and usage.
- Seek input from and collaboration with those in other fields, such as cancer epidemiology, to identify and utilize methodologies for evaluating changes in the prevalence of complex conditions.
- Collaborate with other data systems, such as the Environmental Public Health Tracking Network, to improve access to population-level environmental data.

### Analytic Activities

Points were made on better utilizing existing data to understand ASD prevalence trends:

- Provide funding opportunities to encourage analyses and dissemination of findings from existing datasets.
- Link existing datasets identifying children with ASDs to other health, service, and research databases.
- Conduct analyses that will help explain variations in ASD prevalence across subgroups (e.g., race and ethnicity, sex, diagnostic subtype, and geographic groups) and if variation persists over time.
- Use complex modeling and multifactorial analyses to better understand variation in ASD prevalence such as by possible etiologic subgroups (e.g., specific genetic conditions and family history), geogrphy, and sex, and by potentially harmful exposures among cohorts.
- Conduct simulation studies to predict the anticipated course of ASD prevalence.

### Data Enhancements to Inform Practice

The panels discussed the importance of using data on the prevalence and characteristics of people with an ASD to better inform service and support efforts:

- In addition to prevalence estimates, provide more in-depth information on population characteristics of people with an ASD (such as functional level and impact of functional limitations, subtype, developmental characteristics, and associated conditions) to improve program planning and support needs.
- Examine data to better understand lags and disparities in ASD identification to, in turn, inform screening, identification, and program planning.
- Conduct analyses to provide better estimates of current and future needs of adults with an ASD.

## Additional Studies

Beyond enhancements to existing data systems and uses, the panels discussed new types of data collection and studies including:

- Expand ASD prevalence efforts to include very young children and adults.
- Examine prevalence over time among older children by following up with those identified in previous studies
- Conduct additional validation studies at various ADDM Network sites and use the results to enhance estimates of ASD
  prevalence.
- Conduct further studies to better understand who is identified and who is not identified in national parent report surveys and in service-based data such as special education child counts.
- Develop ways of better capturing the heterogeneity of ASD phenotypes including the complexity of core and associated features that may present in different combinations for people with an ASD.
- Improve tools for culturally sensitive screening and case confirmation among large populations.
- Identify ways to measure and monitor the traits associated with ASDs among the general population to reflect various degrees (dimensional) rather than categorical (having an ASD or not having an ASD) case vs. not case) levels. This includes characterizing how these traits overlap with other conditions and typical development.
- Conduct cross-sectional and longitudinal studies following cohorts over time. This could include examining trends in characteristics of the population, such as ASDs among specific subgroups (based on, for example, race and ethnicity, immigrant status, and socioeconomic status), age of identification, diagnoses, comorbidities, services use, and family characteristics.
- Monitor trends in ASD prevalence prospectively to rule out identification factors by consistently conducting developmental and ASD screening at a given age with diagnostic follow-up and documentation of each step and outcome.
- Conduct prospective studies that examine biology, phenotype, identification patterns, and service needs and use of people with an ASD.
- Examine trends in other behaviorally defined conditions (e.g., attention-deficit/hyperactivity disorder, depression, and anxiety).

## NEXT STEPS

The workshop summary will be made freely available to the community through posting on the CDC's and Autism Speaks' websites. It is hoped that the information, research, and opinions shared during this workshop will add to the knowledge base about ASD prevalence and stimulate further work among public and private groups to understand the multiple reasons behind changes in identified ASD prevalence in the U.S.

# Notes

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www.cdc.gov/autism
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Autism Speaks
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CS225567

Co-Sponsored by Autism Speaks

# Workshop on U.S. Data to Evaluate Changes in the Prevalence of Autism Spectrum Disorders (ASDs)

**Tuesday, February 1, 2011**

**Centers for Disease Control and Prevention**
**Tom Harkin Global Communications Center | 1600 Clifton Road, N.E. | Atlanta, Georgia**

*Full agenda available in Appendix A*

National Center on Birth Defects and Developmental Disabilities
Division of Birth Defects and Developmental Disabilities

# Acknowlegement


## Co-Sponsored by the National Center on Birth Defects and Developmental Disabilities (NCBDDD), Centers for Disease Control and Prevention (CDC) and Autism Speaks


*Panel members* were representatives from:*

Autism Science Foundation
Autism Society of America (invited)
Colorado Department of Health
Columbia University
Drexel University
George Washington University
Health Resources and Services Administration (HRSA)
Johns Hopkins University
Kaiser Permanente®, California
Medical University of South Carolina
National Institutes of Health (NIEHS, NIMH)
Parkinson's Institute
SafeMinds
Parents of children with an Autism Spectrum Disorder
Persons with an Autism Spectrum Disorder
University of Alabama at Birmingham
University of Arizona, Tucson
University of Arkansas
University of California, Davis – MIND Institute
University of North Carolina, Chapel Hill
University of Pennsylvania
University of South Florida
University of Southern California, Marshall
University of Utah
Washington University in Saint Louis
University of Washington
University of Wisconsin, Madison
Yale University

### Workshop Planning Committee

| | |
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| Amanda Bakian, PhD (Feb 2011) | University of Utah |
| Tom Bartenfeld, PhD | NCBDDD, CDC |
| Julie Daniels, PhD | University of North Carolina, Chapel Hill |
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| Keydra Phillips, MsC | NCBDDD, CDC |
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| Michael Rosanoff, MPH | Autism Speaks |
| Anita Washington, MPH | Research Triangle Institute |
| Martha Wingate, DrPH | University of Alabama, Birmingham |
| Marshalyn Yeargin-Allsopp, MD | NCBDDD, CDC |

**Refer to Appendix B for biographies of panel members*

*The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC). This summary report reflects statements made by individuals attending the workshop and does not constitute consensus recommendations made to the CDC.*

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# Workshop Summary

## PURPOSE

Autism spectrum disorders (ASDs) are estimated to occur among about 1% of children in the U.S. This is in line with estimates from other industrialized countries. However, the identified prevalence of ASDs has increased significantly in a short time period based on data from multiple studies including the Centers for Disease Control and Prevention's (CDC) Autism and Developmental Disabilities Monitoring (ADDM) Network (http://www.cdc.gov/ncbddd/autism/addm.html). Whether increases in ASD prevalence are partly attributable to a true increase in the risk of developing ASD symptoms or solely to changes in community awareness and identification patterns is not known. It is clear that more children are identified with an ASD now than in the past and the impact on individuals, families, and communities is significant. However, disentangling the many potential reasons for ASD prevalence increases has been challenging. Understanding the relative contribution of multiple factors such as variation in study methods, changes in diagnostic and community identification, and potential changes in risk factors is an important priority for the ADDM Network and for CDC. This workshop was co-sponsored by CDC and Autism Speaks as a forum for sharing knowledge and opinions of a diverse range of stakeholders about changes in ASD prevalence. This summary report reflects statements made by individuals at the forum and discussions that were held among the attendees, and does not constitute formal consensus recommendations to CDC. The information, research, and opinions shared during this workshop add to the knowledge base about ASD prevalence in an effort to stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

## FRAMEWORK

The workshop brought together epidemiologic prevalence and surveillance experts in ASDs and other conditions as well as representatives from autism organizations, parents of children with ASDs, adults with an ASD, and other stakeholders. A total of 342 people registered to attend the workshop (143 in person and 199 via webinar).

Prior to the meeting, the panel members met via teleconference and were asked to submit at least two publications that they viewed as important background reading for understanding ASD prevalence trends. Panel members were provided with the compiled reference list (Appendix C) and articles and were asked to review, at a minimum, the priority readings prior to the workshop.

Presentations during the morning of the workshop summarized current knowledge and issues related to ASD prevalence and provided perspectives from subject matter experts in cancer, Parkinson disease, asthma, schizophrenia, and analytic modeling of prevalence changes.

Following the morning's presentations, the public was invited to provide statements, and there was an open invitation to provide written comments before and after the workshop. Workshop organizers, panelists, and stakeholders were asked to consider these comments when expressing their opinions on priorities for evaluating changes in ASD prevalence.

After hearing open comments from the community, the workshop was divided into four panels:

- Panel 1 – Utility of ASD Prevalence Data
- Panel 2 – U.S.-Based ASD Service Data
- Panel 3 – Autism and Developmental Disabilities Monitoring (ADDM) Network Data
- Panel 4 – What Else Is Needed To Understand ASD Trends?

For the workshop panel sessions, members of each panel were asked to reflect on questions along the following themes to better understand ASD prevalence trends:

- What can we do now with existing data?
- What should we do next to build on existing data systems?
- What else is needed in terms of new analyses, data collection, or other efforts?

## SUMMARY POINTS

Panel members and attendees commented that the effort to increase transparency and expand the dialogue related to ASD prevalence change was appreciated and necessary to move the community forward around the issue of understanding ASD prevalence changes. Additional key points made during the workshop included:

- The identified prevalence of ASD has increased significantly in a short time period across multiple studies, including data from the CDC's U.S.-based Autism and Developmental Disabilities Monitoring (ADDM) Network.
- CDC is the source for ASD prevalence estimates in the U.S., but other data systems exist or could be developed to better understand trends in ASDs.
- ASDs are conditions estimated to occur among about 1% of children in the U.S. There is an urgent demand to address the many needs associated with ASDs. Prevalence estimates have, for example, fueled action by advocacy groups and the Interagency Autism Coordinating Committee (IACC) and driven the creation of legislation and presidential priority. However, individuals, families, and communities continue to struggle to address unmet needs across the lifespan of people with ASDs. ASD prevalence estimates are important to stakeholders for program planning and making policy changes, in addition to highlighting the need for research into causes and interventions.
- In terms of reasons for increased ASD prevalence, the debate has been dichotomized by researchers, advocacy groups, and the media to indicate that increases must be explained either by identification factors or by increased risk among the population. In reality, a more complex understanding is needed. It is clear that some of the increase has been related to intrinsic and extrinsic identification factors. However, although a true increase in ASD symptoms cannot be ruled out, such an increase has been difficult to prove. Panels discussed needing to identify and use methods to better understand the role of potential identification and risk factors in the changing prevalence of ASD.
- Some people expressed hope that understanding why ASD prevalence has increased may help identify modifiable risk factors. There was debate about the roles of prevalence and surveillance in answering questions about risk and causes of ASDs. Prevalence studies provide descriptive data on the number of people with a condition in a defined population. These types of studies are not sufficient to identify what causes ASDs. However, prevalence studies can be used as tools to examine variation in occurrence of ASDs across place, groups, time, and exposures, which may provide clues about groups who are at increased risk for ASDs. Other study designs would then be necessary to fully investigate the reasons behind observed variation in prevalence.
- There are likely multiple forms of ASDs with multiple causes that are poorly understood. It was noted that sufficient evidence exists that biologic and environmental factors, alone and in interaction, need to be considered as causes. It is not necessary to have confirmation that a portion of the increase in ASD prevalence is due to increased risk in the population to motivate the active pursuit of causes of ASDs. By better understanding what causes ASDs, maybe we can understand the increases in measured prevalence.

- A risk factor might be strongly associated with ASD and might be modifiable, but it might not have increased sufficiently in the population during the time frame of interest. Therefore, this risk factor might be related to an individual's risk for ASD but not related to the increase in population prevalence of ASD. The model demonstrated that for any factor to have made a noteworthy contribution to population changes in ASD prevalence during a short time period, three conditions must be met: the factor has to be fairly prevalent in the population, it has to have increased substantially, and it has to be strongly associated with diagnosed ASD.
- There was a shared recognition of the importance of, and commitment to, obtaining and using prevalence and epidemiologic information to improve the lives of people with ASDs.

## PANEL DISCUSSION SUMMARIES

The four panel chairs compiled main discussion points brought forth by their members for building on existing infrastructure and for developing new initiatives to better understand ASD trends. These discussion points are summarized below.

### Collaboration

The panels indicated that collaboration among professionals and stakeholders is important, and the following points were made to assist collaborative efforts among those interested in understanding ASDs and supporting the ASD community through science:

- Continue efforts of this workshop to develop and enhance communication among families, individals affected, researchers, service providers, advocates, and government entities about ASD prevalence, research, and service needs.
- Seek public–private partnerships to support data collection, analyses, and usage.
- Seek input from and collaboration with those in other fields, such as cancer epidemiology, to identify and utilize methodologies for evaluating changes in the prevalence of complex conditions.
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### Analytic Activities

Points were made on better utilizing existing data to understand ASD prevalence trends:

- Provide funding opportunities to encourage analyses and dissemination of findings from existing datasets.
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- Conduct analyses that will help explain variations in ASD prevalence across subgroups (e.g., race and ethnicity, sex, diagnostic subtype, and geographic groups) and if variation persists over time.
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- Conduct simulation studies to predict the anticipated course of ASD prevalence.

### Data Enhancements to Inform Practice

The panels discussed the importance of using data on the prevalence and characteristics of people with an ASD to better inform service and support efforts:

- In addition to prevalence estimates, provide more in-depth information on population characteristics of people with an ASD (such as functional level and impact of functional limitations, subtype, developmental characteristics, and associated conditions) to improve program planning and support needs.
- Examine data to better understand lags and disparities in ASD identification to, in turn, inform screening, identification, and program planning.
- Conduct analyses to provide better estimates of current and future needs of adults with an ASD.

## Additional Studies

Beyond enhancements to existing data systems and uses, the panels discussed new types of data collection and studies including:

- Expand ASD prevalence efforts to include very young children and adults.
- Examine prevalence over time among older children by following up with those identified in previous studies
- Conduct additional validation studies at various ADDM Network sites and use the results to enhance estimates of ASD
  prevalence.
- Conduct further studies to better understand who is identified and who is not identified in national parent report surveys and in service-based data such as special education child counts.
- Develop ways of better capturing the heterogeneity of ASD phenotypes including the complexity of core and associated features that may present in different combinations for people with an ASD.
- Improve tools for culturally sensitive screening and case confirmation among large populations.
- Identify ways to measure and monitor the traits associated with ASDs among the general population to reflect various degrees (dimensional) rather than categorical (having an ASD or not having an ASD) case vs. not case) levels. This includes characterizing how these traits overlap with other conditions and typical development.
- Conduct cross-sectional and longitudinal studies following cohorts over time. This could include examining trends in characteristics of the population, such as ASDs among specific subgroups (based on, for example, race and ethnicity, immigrant status, and socioeconomic status), age of identification, diagnoses, comorbidities, services use, and family characteristics.
- Monitor trends in ASD prevalence prospectively to rule out identification factors by consistently conducting developmental and ASD screening at a given age with diagnostic follow-up and documentation of each step and outcome.
- Conduct prospective studies that examine biology, phenotype, identification patterns, and service needs and use of people with an ASD.
- Examine trends in other behaviorally defined conditions (e.g., attention-deficit/hyperactivity disorder, depression, and anxiety).

## NEXT STEPS

The workshop summary will be made freely available to the community through posting on the CDC's and Autism Speaks' websites. It is hoped that the information, research, and opinions shared during this workshop will add to the knowledge base about ASD prevalence and stimulate further work among public and private groups to understand the multiple reasons behind changes in identified ASD prevalence in the U.S.

# Background and Purpose

## WELCOME

## C. Boyle and G. Dawson

Dr. Boyle welcomed everyone, thanked the organizing committee and co-sponsor Autism Speaks, and indicated that she looked forward to the discussions and sharing of information and ideas on understanding autism spectrum disorder (ASD) prevalence trends. Dr. Dawson stated that we all have concerns about the increase in ASD prevalence. She expressed her hope that everyone would come away from the workshop with a path forward in understanding ASD prevalence changes and stated that we are much better prepared to address problems than ever before because of better data and analytic tools. These data and tools are from the Centers for Disease Control and Prevention's (CDC) Autism and Developmental Disabilities Monitoring (ADDM) Network, as well as other informative datasets from California and Europe. She remarked that many published papers cite several reasons for the possible increase in ASD prevalence including better analytic tools and broader awareness and diagnosis. However, these papers all have included the statement "a true increase in prevalence cannot be ruled out." She ventured that she looked forward to lively and productive discussion and concrete actions that can improve the understanding of why ASD prevalence has been increasing, with the ultimate goal of addressing the needs of people with autism.

## Background: What Do We Know About ASD Prevalence?

## M. Yeargin-Allsopp

Autism once was thought to be a rare condition, affecting about 1 in 2,000 individuals. It was thought of as mental illness, specifically schizophrenia of childhood, and was believed to be due to poor parenting. The "refrigerator mother" perception was prominent until the 1970s, continuing even into the 1980s. Today, autism is recognized as having a biologic basis and a range or spectrum of presentations. The autism spectrum disorders have been shown to occur among about 1% of children in several different countries. In addition to the core areas of impairment in social, communication, and behavioral domains, people with ASDs can have associated challenges in other areas such as sleeping, eating, attention, mood regulation, and gastrointestinal issues. It is recognized widely that ASDs have a strong genetic basis, but this is not a simple association and there is increasing recognition of the role of environmental factors. ASDs are now recognized as a complex disorder, most likely due to interactions between genes and the environment.

Beginning in the mid-1990s, concerns arose about increases in the numbers of individuals with autism identified in service systems. For example, starting in the early 1990s, the California Department of Developmental Services and the U.S. Department of Education's Office of Special Education documented increases in the need for autism services. Not all people with an ASD are identified by these service systems, so methods are needed to identify who else might have an ASD among the general population. CDC's ADDM Network conducts surveillance to estimate ASD prevalence in multiple areas of the U.S. and provides data to describe variations and changes over time. The ADDM Network reports ASD prevalence, or the total number of children with an ASD at a specified age in a specified year per 1,000 children in the population. The ADDM Network does not use incidence because incidence is based on new cases where a clear onset time can be documented. Typically, the onset of an ASD is not known, although it usually manifests by the time a child is 3 years of age. However, there is a great deal of variability in when a child actually manifests symptoms and then is diagnosed with an ASD.

There are several potential explanations that can account for an increase in the number of individuals diagnosed with ASDs, including better identification and screening methods, changes in diagnostic criteria, increased awareness among parents and clinicians, and changes in the availability of services. There also have been some studies that have examined how much of an increase is accounted for by other factors, such as increasing parental age. However, a full explanation must consider multiple factors that are not independent of each other. Prevalence estimates are important for planning policy and service needs and identifying promising clues about who is at risk for an ASD.

## Framework For This Workshop

### C. Rice

The identified prevalence of ASDs has increased significantly in a short time period across multiple studies, including the CDC's ADDM Network. ASDs are conditions estimated to occur among about 1% of all children. There is an urgent demand to address the many needs associated with ASDs, and concerns about ASD prevalence numbers have fueled local, state, and national action in terms of advocacy, policies, research, and creation of the Interagency Autism Coordinating Committee (IACC) among other activities. However, individuals and families continue to struggle to address and meet the needs associated with ASDs across their lifespan. Although prevalence estimates can help with service and policy efforts, increases in ASD prevalence beg the questions "Why?" and "Is the increase an actual increase in risk for ASDs?" The implication is that, if there is an increase in actual ASD risk, there might be modifiable risk factors to prevent ASDs from occurring. These questions get to the heart of what causes ASDs. Although multiple, complex genetic and environmental interactions are likely, we still have very limited information on what predisposes a fetus or child to have an ASD, what might increase risk, and which risks lead to the development of an ASD.

A prevalence study is an epidemiologic tool that describes the occurrence of a condition in a defined population in a defined time period. Surveillance is the ongoing monitoring of prevalence in a defined population over time. These studies provide descriptive data on the number of people with a condition in a defined population. These types of studies are not sufficient to identify what causes ASDs. However, prevalence studies can be used as tools to examine variation in occurrence of ASDs across place, groups, time, and exposures, and this may provide clues about groups who are at increased risk for ASDs. Prevalence studies can provide observations that might need further causal examination. For example, prevalence studies have shown that there are about 4 to 5 boys for every girl with an ASD. However, basic studies of the biology of individuals with an ASD are necessary to explain the mechanism that results in boys being at greater risk than girls.

Debates about reasons for ASD prevalence increases often have been dichotomized to point to explanations of better identification or evidence of increased risk implicating specific environmental factors. At this point, although we do know that some of the increase is related to identification factors, a true increase cannot be ruled out—but, it is hard to prove. We also know enough about potential causal mechanisms of ASDs to not pigeonhole the search for ASD causes to only genetic factors; complex biologic and environmental factors must be pursued as well. In order to evaluate ASD prevalence changes, scientists tend to use a systematic approach based on training in scientific methods where the first step is to rule out alternative explanations. This approach begins by examining factors that could explain a difference over time that are attributable to artifacts, rather than "true" increases. This approach tends to examine identification and methodological factors, as these variables are often more observable than the many potential and unknown risk factors that might contribute to ASD prevalence changes. As more data are collected and analyzed and different hypotheses evaluated over time and across studies, additional conclusions can be drawn. Understandably, this methodical approach is frustrating, especially when most people want to know *the* definitive reason for changes in ASD prevalence and whether it is something in the environment we can do something about. The fact that, despite many efforts, we have not found a single, simple explanation indicates that there are likely multiple, overlapping factors contributing to increases in ASD prevalence.

The purpose of the workshop was to bring together experts in epidemiologic prevalence and surveillance of ASDs and other conditions as well as stakeholders to: summarize where we are; learn from efforts to document prevalence changes among other conditions; and improve the specificity in quantifying and qualifying the multiple factors that might be influencing trends in ASD prevalence, including:

1. **Intrinsic Identification**—Internal methodology or measurement factors involved in documenting ASD prevalence trends (e.g., differences in study methods may lead to different individuals being counted or

not counted as having an ASD such as using a registry of children identified with an ASD or active screening).

2. **Extrinsic Identification**—External classification and awareness factors involved in identifying people with ASDs in the population (e.g., changes in diagnostic criteria or access to services based on an ASD label may influence who is identified for ASD prevalence studies).
3. **Risk**—Possible etiologic or true change in ASD symptoms among the population in relation to single or combined genetic, biologic, or environmental factors, or a combination thereof (e.g., specific biologic vulnerabilities or exposures in the environment that increase the risk of developing an ASD).

Four panels were formed for this workshop:

- Panel 1 – Utility of ASD Prevalence Data
- Panel 2 – U.S.-Based ASD Service Data
- Panel 3 – Autism and Developmental Disabilities Monitoring (ADDM) Network Data
- Panel 4 – What Else Is Needed To Understand ASD Trends?

After hearing the morning's presentations, members of the four panels were asked to discuss the following questions to provide a better understand of ASD prevalence trends:

1. What can we do now with existing data?
2. What should we do next to build on existing data systems?
3. What else is needed in terms of new analyses, data collection, or other efforts?

The goal of this workshop was to learn from different perspectives to inform the community and stimulate further work to understand the multiple reasons behind increasing ASD prevalence in the U.S.

## A Model for Assessing the Contribution of Various Risk Factors to Recent ASD Prevalence Increase in the U.S.

### L. Schieve

This presentation reviewed preliminary results of a study to formulate a mathematical model to assess the likely effects that given risk factors had on recent ASD prevalence increase and to apply the model to specific prenatal and perinatal risk factors previously found to be associated with ASDs. According to the ADDM Network report from 2009, there was a 57% increase in the prevalence of autism spectrum disorders (ASDs) from 2002 to 2006. The effect of a given risk factor on prevalence depends on the baseline prevalence of the risk factor (RFP), the change in RFP over time (cRFP), and the magnitude of the relative risk (RR). A number of previous studies consistently have indicated that preterm birth and low birthweight are risk factors for ASDs, and some other studies have implicated multiple birth, cesarean delivery, breech presentation, and assisted reproductive technology (ART) as possible risk factors. However, none have had sufficient values for RFP, cRFP, and RR to have contributed substantively to the recently observed ASD increase. While at an individual level, having one or more perinatal risk factors might convey a moderate or strong risk for having an ASD, these factors are unlikely to explain a large proportion of the population increase in ASD prevalence. Although examples were given using selected prenatal and perinatal risk factors, this model could be extended to assess various other risk factors.

A risk factor might be strongly associated with ASD and might be modifiable, but it might not have increased sufficiently in the population during the time frame of interest. Therefore, this risk factor might be related to an individual's risk for ASD but not related to the increase in population prevalence of ASD. The model demonstrated that for any factor to have made a noteworthy contribution to population changes in ASD prevalence during a short time period, three conditions must be met: the factor has to be fairly prevalent in the population, it has to have increased substantially, and it has to be strongly associated with diagnosed ASD.

### *Panel member discussion:*

A panel member asked if broad social changes, as opposed to individual risk factors, also were considered. The panel member was concerned that, by not fully examining population-level changes, the model might be underestimating the contribution of the change in that risk factor in the population on ASD prevalence. Dr. Schieve indicated that a large increase still would need to have an individual effect, and the model is accurate for shorter time intervals such as a few years. As the time period gets longer, then a different analytic model might be needed.

## ASD Genetic Variation and Gene–Environment Interaction

## K. Crider

This presentation summarized how genetic variations and gene-environment interactions could play a role in ASDs and provided background on how these factors may or may not change in a way that would affect ASD prevalence over a short period of time. Typically, to examine heritability of a condition, twin studies are used. More than 30 studies to date consistently have shown higher concordance between monozygotic than dizygotic twins, suggesting there is a strong genetic component associated with ASDs. ASDs have been associated with the following genetic variations: mutation of a gene, deletion of a large or small region of a gene, mutation of another gene, methylation of a gene, or creation of another copy of the gene or the region or chromosome. It is estimated that all genetic variants discovered to date are present in 10% to 15% of people with an ASD and many are implicated in other conditions (e.g., attention deficit hyperactivity disorder and schizophrenia). In general, there would not be an epidemic of a purely genetic condition because genes change over evolutionary time. However, shorter term changes can be seen if there are increases in mutations or breaks, or both, in chromosomes, changes occur in epigenetic patterning (e.g., DNA methylation) or in selective mating patterns.

Gene–environment interactions such as infection, stress, obesity, and trauma all can create the same type of cell damage. Specific causes may or may not have the statistical power to show the true association individually because multiple genetic and environmental factors can lead to the same disorder therefor, studies should be designed to take this into consideration. In some conditions, the magnitude of gene–environment interaction varies. Exposures associated with an increased risk for autism also are associated with other conditions, such as birth defects and cerebral palsy. Single exposures (genetic or environmental) are unlikely (but possible) to show a dramatic increased risk among the general population. Not every individual who carries these forms of genetic variation will have an ASD, which suggests the importance of interactions among multiple genes or gene–environment interaction, or both, in the occurrence of ASDs.

### *Panel member discussion:*

A panel member questioned the accuracy of the statistic that about 10% to 15% of children with an ASD have an identifiable genetic condition. Dr. Crider stated that the statistic is used by others in the field and is a best estimate, but noted the statistic needs better evaluation.

## Autism and Developmental Disabilities Monitoring (ADDM) Network

## C. Rice

### ADDM Network Overview

The ADDM Network is a collaboration of multiple sites in the U.S. to determine and monitor the prevalence of ASDs among 8-year-old children and to track peak prevalence over time. Children are identified through multiple education or health evaluation records if there is an ASD diagnosis, a special education classification, a suspicion of an ASD, or a social behavior associated with an ASD, even when an ASD has not been diagnosed. Clinician reviewers apply the current diagnostic standard criteria of the American Psychiatric Association's D*iagnostic and Statistical Manual, 4th edition, text revision (DSM-IVTR)*. The

strengths and limitations of the ADDM Network were discussed. The most recent ADDM Network estimates indicated that an average of 1 in 110 children (range from 1 in 80 to 1 in 240) had an ASD and that ASD prevalence had increased 57% over a 4-year period from 2002 to 2006. According to the ADDM Network data, the overall trend in ASD prevalence showed consistent increases, but variation existed among sites and among subgroups. While the increase in observed ASD prevalence at ADDM Network sites could be partly explained by identification factors—such as better information available in records, a more stable population at some sites, and improved identification of specific subgroups such as Hispanic children and children without cognitive impairment—these identification factors did not explain the total increase in prevalence. A neat explanation of all factors that could explain completely the observed increase is unlikely, and further work is needed to evaluate multiple identification and risk factors.

### Changes in ASD Diagnostic Criteria

This presentation reported on a preliminary analysis of how an identification factor could be evaluated using the ADDM Network data. Although it often has been stated that the changes in diagnostic criteria that occurred in the *DSM* in 1980 *(DSM III)*, 1987 *(DSM III-R)*, and 1994 (*DSM-IV* and minor changes for *DSM-IV-TR* in 2000) have affected reported ASD prevalence, no known studies have quantified this effect directly. Recoding the ADDM Network data based on the three diagnostic standards (*DSM III*, *III-R*, and *IV-TR*), it was found that autism and ASD prevalence were similar using *DSM III* and *III-R* standards, but increased significantly using *DSM-IV-TR* standards. A portion of the prevalence increase over time might have been attributed to differences in the definitions of ASD used for identification of ASDs by community professionals and service systems. This recoding analysis represents one example of an effort to provide more concrete estimates regarding the effects of a single factor on ASD prevalence.

### *Panel member discussion:*

Panel members raised several questions regarding reasons or theories to explain the wide range of ASD prevalence observed among ADDM Network sites, including the quality of data sources or records and the effect it might have had on prevalence and the inclusion or exclusion criteria used by the ADDM Network sites. Dr. Rice indicated there were some identifiable reasons explaining why the ASD prevalence estimates were lower at some ADDM Network sites (e.g., limited availability of education records) and higher at others (e.g., better quality of documentation in the records). Also, it is easier to identify reasons for lower prevalence estimates than for higher estimates. However, if a site had a low prevalence not due to a methodologic issue, it would be important to consider whether protective factors were at work at that particular site. A question was raised about the reason why the number of sites varied over the surveillance years. Dr. Rice explained that the number of ADDM Network sites depends on available funding and that sites go through a competitive application process in which the applicant must demonstrate a minimum population, partnerships with health departments, and other criteria based on independent peer review. A panel member also questioned when CDC was going to take the issue of rising ASD prevalence seriously. Dr. Rice indicated that CDC has been providing data actively to document these concerns and has been calling attention to the urgency of addressing the needs of the ASD community for years. She continued by stating that the workshop was an effort to broaden the conversation and share ideas on how CDC and others can all learn from other fields and improve collaboration to better understand ASD trends.

## Analyses of ADDM Network Data Related to: Parental Age, Age at Autism Identification, and Socioeconomic Inequalities in the Prevalence of ASD in the U.S.

## M. Durkin

This presentation summarized some analyses of data from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network related to parental age, age of autism identification, and socioeconomic

status. A major strength of ADDM Network data on ASD prevalence is that a sizeable proportion (27%) of children identified with ASDs for surveillance did not have a documented ASD classification. This allows us to investigate factors associated with having a previous ASD diagnosis and receiving services for ASD as distinct from having ASD, and to evaluate whether associations are due to differences in ASD risk or to disparities in identification. A consistent finding in recent epidemiologic studies is a positive association between both maternal and paternal age and risk of ASD in offspring. Despite this association and the increasing trend in mean parental age in recent decades, only a very small (less than .5%) proportion of the recent increase in ASD prevalence can be attributed to the increasing age of parents. ASD differs from developmental disabilities overall in its positive association with higher socioeconomic status (SES). Examining SES among Wisconsin ADDM Network data, it was found that the ASD prevalence increased with increasing SES. However, is this due to increased risk or identification disparities? For example, do educated parents have a disproportionate influence on autism awareness or does the risk of autism increase with a higher socioeconomic status? Is a knowledgeable and determined parent of a child with autism more likely to obtain an informed diagnosis? This is likely to be the case, and there is also the potential role of clinician bias and the possible evidence of disparity in access to care. ASD prevalence estimates likely underestimate prevalence in lower SES groups, which implies that we are still underestimating ASD prevalence and can expect some increases if disparity gaps are closed over time. But the fact that we saw a positive association between socioeconomic status and ASD risk in both those with and those without a previous ASD diagnosis suggests that the association might not be entirely due to under-ascertainment of ASD in economically disadvantaged groups.

## *Panel member discussion:*

Panel members raised the question of whether birth order and the effects of stoppage (a family deciding not to have another child after having a child with a disability) have been studied, and if plans are under way to study miscarriages and autism risk. Dr. Durkin indicated that the effect of birth order combined with parental age and sex appear to be additive. The role of stoppage and pregnancy loss cannot be directly or adequately investigated using ADDM data but require longitudinal, birth cohort studies. CDC's Study to Explore Early Development (SEED) will examine prenatal and perinatal risk factors, such as miscarriages. Studying these factors is important because past adverse pregnancy outcomes are understudied. The importance of examining characteristics (such as parental age, and SES) across cohorts to look at changes among subgroups will be important in understanding potential identification and risk factors contributing to ASD prevalence increases.

# ASD Trends: U.S. Service-Based Datasets

## U.S. Special Education Data

## P. Shattuck

This presentation provided an overview of U.S. Department of Education data related to documenting the presence of ASDs among special education students. U.S. Department of Education's Special Education Child Count data is an annual count of children enrolled in special education services. It is an accountability measure required by the Individuals with Disabilities Education Act (IDEA) to show nonexclusion of children with a disability based on select eligibility categories for each state. Autism was not initially a category within the child count dataset, but was added in 1990 with statesreporting to the U.S. Department of Education in 1991. The number of children classified as having autism and receiving special education services has increased since the early 1990s. However, the number is still fewer than would be expected given current prevalence estimates. A special education label is only mildly sensitive, but highly specific, and enrollment counts might not have provided a true prevalence of ASD. Child Count data vary by area and race or ethnicity. The special education system never was intended to serve a public health surveillance role. Thus, several important questions have been raised that focus on (1) understanding how state-level special education criteria for ASDs vary, (2) exploring referral pathways that lead to identification, (3) examining barriers to timely identification, and (4) developing more effective partnerships with the education sector to maximize data sharing. This will lead to a better understanding of the social, economic, and political factors that influence ASD identification in the community and that might contribute to the rise in identification ASDs in prevalence estimates.

### *Panel member discussion:*

Panel members asked how to integrate ASD screening in schools. Dr. Shattuck indicated that a school equivalent of CDC's Learn the Signs. Act Early. program is needed to increase awareness among educators of the signs of ASDs, and should be followed up with a systematic screening protocol to identify children with an ASD. This is important because, until everyone in the schools uses the same criteria, it will be difficult to rely on the validity of the Child Count data for monitoring changes in the actual prevalence of ASDs. Dr. Shattuck also indicated the need for legislative support to allow education and public health to form effective partnerships; often, school systems do not see the value in the Child Count data from a public health perspective. Especially now, schools are working to meet the service needs of the students rather than addressing broader public health issues such as identifying all children with an ASD in the population.

## California Department of Developmental Services Data I

## I. Hertz-Picciotto

This presentation provided an overview of some ways the California Department of Developmental Services (CA DDS) administrative data have been used to evaluate trends among children receiving services for ASD. Whether due to an artifact or a true increase, ASD prevalence has been high and there is a need to identify the causes. In addition, there already is enough evidence to suggest the importance of environmental causes. There are three main measures of occurrence of a condition: prevalence (the number of cases divided by the number of people in the population at a given time), incidence (the number of new cases among a given population in a defined time divided by the amount of person-time observed during the same period), and cumulative incidence (the number of new cases identified in an extended time period [e.g., from birth] divided by the size of the population without the disorder at the start of the time period). All measures are affected by changes in identification patterns and diagnostic practices. Prevalence data are most useful for service planning and incidence data are useful for etiology. However, a condition where the diagnosis tends to be stable (low mortality rate and it is rare for the diagnosis to change), can result in prevalence and cumulative incidence measures that will be virtually identical over a defined time or age period. For this reason, examining existing data may help us understand ASD trends.

The CA DDS has a statewide database with data from 21 regional centers in the state. The DDS database tracks 5 conditions (autism, epilepsy, cerebral palsy, intellectual disability, and intellectual disability-related conditions). Data collection is passive in that a child must be brought to a CA DDS center and a parent or guardian must request an evaluation to determine if they meet the service provision eligibility criteria. Comparing births in 1990 with those in 2001 (followed to age ten), the cumulative incidence in autism in the CA DDS rose 600%. About 200% of this increase in autism from 1990 through 2001 in the CA DDS database could be explained by trends toward younger age at diagnosis, inclusion of more mild cases, changes in diagnostic criteria, and older ages of mothers. Thus, artifacts related to criteria and methods for ascertainment might explain part but not all of the increase in ASD cumulative incidence in the CA DDS system. To date, there appears to be no leveling off of autism diagnoses, indicating there is considerable likelihood that there has been a true increase in incidence (or risk).

### *Panel member discussion:*

Panel members questioned how the identification artifacts played out across regions. Dr. Hertz-Picciotto indicated that there was substantial variability among the centers (Los Angeles traditionally has had higher ASD rates than other regions of the state). .Each DDS center is run by independent contractors and are managed slightly differently from each other. There also are clusters of ASDs near places where there are well-known treatment centers. A panel member pointed out that it is important to study these identification factors at multiple locations beyond California service data to areas of the U.S. and to also consider international patterns of occurrence.

## California Department of Developmental Services Data II

## P. Bearman

This presentation summarized additional analyses of data from the CA DDS related to trends in ASD prevalence conducted by Dr. Bearman and colleagues. During the past 30 years, the prevalence of autism has increased dramatically. Examining California birth data from the period 1992 through 2007, there were 8 million births (about 500,000 births per year). Using a sophisticated mapping program of all births and addresses and linking to CA DDS autism data, researchers were able to ascertain parental characteristics, prenatal conditions, and residence during the in utero period and link to data on neighborhoods, socioeconomic status, local toxicants, and other conditions. Examining these data was useful in examining the contribution of diagnostic change to increased prevalence, gaining insight into genetic mechanisms, understanding the spatial structuring or geographic patterns of autism at birth and age of diagnosis, considering diverse individual and community level risk factors, and measuring the potential role of sharing information on autism.

Analysis of the data showed that changes in ASD diagnoses in relation to those for intellectual disability (mental retardation) explained 24% of the increase in autism prevalence in the CA DDS data during the time period analyzed. An analysis was also done to see how administrative data might provide insight into genetic mechanisms. There was a high ASD concordance between identical twins and low concordance between fraternal twins. Over time, there was an increase in ASD among same sex twins and a decrease among opposite sex twins. Another analysis examined the spatial structure (geographic mapping) of the birth residence of children later identified with ASD by DDS. The researchers concluded that ASD birth clusters have been robust over time and do not appear to be due to factors such as education or socioeconomic status. Examining the DDS administrative data has provided insight into risk factors for autism. For example, findings indicated maternal age might be more critical than paternal age; community level characteristics such as geographic spacing are increasingly less salient as ascertainment increases, but still significant; and shorter interpregnancy intervals might confer excess risk. About 50% of ASD prevalence increases in the CA DDS data could be explained by several factors, such as diagnostic change, advancing parental age, social influence of people sharing information on ASDs, and spatial structure. Work is needed to understand what accounts for the other 50%. A project currently is under way to investigate

whether assistive reproductive technology (ART) is related to increased risk of having a child with ASD as identified in CA DDS data by linking with CDC data on births involving ART.

## *Panel member discussion:*

Questions were raised about the autism clusters that were identified using CA DDS data. There was a question as to whether these were true etiologic clusters or if there appeared to be shared identification patterns. Dr. Bearman discussed the idea that clusters might have been due to a shared exposure, such as toxicant, or to a social risk factor. For example, people with children the same age who shared a workplace or social activity might have been more likely to discuss their children and share information about autism, thus leading to increased identification. Or, there might have been reluctance among some groups to reach out to the health care or services system, resulting in decreased identification. A panel member expressed caution about the conclusion of being able to explain about 50% of the increase in DDS ASD prevalence as the approach used to arrive at this estimate was too simplistic and did not take the overlapping relationships between different factors into account. Dr. Bearman relayed his belief that some of the factors operate on different aspects of the spectrum and that the 50% figure was a way of summarizing what is known to date. For example, identification factors, such as shifts in the use of the intellectual disability diagnosis to add autism as another diagnosis or an alternative diagnosis, may operate on the lower end of the spectrum and social influence may operate on the higher end of the spectrum. Factors such as parental age and shorter pregnancy intervals are more likely to be risk factors contributing to ASD increases.

# Lessons Learned From Other Conditions and Analytic Methodologies

## Cancer

### R. Etzioni

Changes in cancer trends can be seen from changes in (1) exposures (e.g., smoking, diet, and obesity), (2) diagnosis or detection (e.g., screening and biopsy techniques), and (3) classification (e.g., staging and grading techniques). Dr. Etzioni presented three examples of changes in different types of cancer:

- Lung Cancer—The greatest modifiable risk factor for lung cancer is smoking. The trend line for lung cancer incidence plots has sloped similarly with the trend line for smoking prevalence, meaning the incidence rates of lung cancer have decreased over time (Surveillance, Epidemiology and End Results registry data) as smoking behavior has decreased over time (National Health and Nutrition Examination Survey).
- Colorectal Cancer—Screening rates for colorectal cancer have been increasing over time and the consumption of two or more servings of red meat per week has been decreasing over time. As screening has increased and red meat consumption has decreased, the incidence of colorectal cancer has decreased.
- Prostate Cancer—Prostate-specific antigen (PSA) screening was first introduced in the 1990s, which correlated with the first peak of prostate prevalence. The second prevalence peak occurred when follow-up biopsies became more routine. Researchers attributed the prevalence changes to differences in recording techniques and improvements in grading of cancer (from poorly to moderately to well-differentiated).

Examining patterns of change among a population might explain disease trends due to changes in factors such as the annual frequencies of exposures, availability of screenings, use of new diagnostic technologies, and changes in disease coding. It is important to have data on the occurrence of a condition before and after the change factor being evaluated. It is also helpful if there is a clear change factor that has occurred.

Modeling change is an integral part of cancer surveillance. There are several important lessons learned from this modeling that can be useful when examining changes in ASD prevalence. The basic steps of modeling change are:

- Characterizing changes in disease trends;
- Quantifying changes in the population that might explain trends;
- Identifying a mechanism for the effect of the population trend;
- Estimating the size of the effect on the risk of disease diagnosis; and
- Modeling or simulating experience among the population.

All of these steps are equally necessary and applicable in explaining changes in ASD prevalence. However, modeling techniques might be useful if the potential effects of a factor on prevalence are not known. There is a group called the Cancer Intervention and Surveillance Modeling Network (www.cisnet.cancer.gov) that is working to develop techniques for modeling changes in cancer based on multiple factors. Working with this group might be helpful in understanding ASD prevalence changes.

## Parkinson Disease

### C. Tanner

Parkinson's disease is a relatively rare disorder that does not have a diagnostic test or definitive marker. Symptoms occur later in life and share some features, such as cognitive decline, with other conditions such as Alzheimer's. The best diagnosis is a face-to-face exam. As with ASDs, population-based surveillance is challenging and there have been changes in diagnostic criteria over time. Also similar to autism, there are questions about the higher prevalence in males and differences by race. One example of examining diagnostic incidence trends of Parkinson's is a study conducted in the Kaiser Permanente Medical Care Program of Northern California (KPMCP). Researchers used active surveillance to examine electronic

medical records, physician referrals, and computerized databases to identify patients receiving services in community settings. Researchers have identified increased incidence of Parkinson's disease among men and with increasing age, a pattern that has been seen in most populations world-wide. Patterns that were suggested, but not supported by evidence, were higher incidence among Hispanics and the lowest incidence among Blacks. Environmental and genetic risk factors have been associated with Parkinson's disease. At this point, there are few sources of data to examine population trends in Parkinson's disease. The CA Parkinson's Disease Registry is a pilot effort to create a population-based database with active ascertainment and case validation, but is active in only a few counties and no state funds are designated to support the effort. Other efforts at population-based registries have been tried, but in these there is no active mechanism for reporting. Advocacy groups support a national surveillance system for Parkinson's disease, but this has yet to be realized. Researchers are also examining conditions with similar symptoms and/or risk factors to identify common biologic mechanisms. It may be useful to study prevalence changes in other disorders with symptoms that overlap with ASDs and among adults.

### *Panel member discussion:*

A panel member asked if there is a spectrum of conditions similar to ASDs. Dr. Tanner indicated that there are similar clinical syndromes including Parkinsonism. Different disorders have different clinical features and prognoses, but definitive diagnosis is post-mortem.

## Asthma

## M. King

Asthma is a highly prevalent chronic disease. Studies have shown persistent demographic differences in prevalence, as well as health care use. Asthma surveillance relies on several national datasets to determine prevalence and severity. One of these is the National Health Interview Survey (NHIS). Before 1997, the NHIS measured 12-month prevalence based on self-reports of "having asthma." After 1997, the NHIS measured prevalence by self-report of a "doctor's diagnosis" of asthma and included lifetime, past 12-months, and whether an attack occurred in past 12-months. The current measure of prevalence is similar to the projected 12-month rate, and the prevalence is higher among children than adults with racial differences observed as well. The Behavioral Risk Factor Surveillance System (BRFSS) allows state-specific estimates of asthma and enables CDC to conduct an asthma call-back survey. The BRFSS allows CDC to determine a population-based prevalence, as well as an at-risk–based rate. An at-risk–based rate is the number of affected people within the population having certain risk factors. While asthma prevalence has increased over time, actual asthma attack rates have been relatively stable. The reasons for overall prevalence increases are not known, but there are sociodemographic disparities in identification and service use. Changes in survey measurement have affected asthma estimates.

### *Panel member discussion:*

There was a question about the content of the call-back survey. Dr. King indicated this that this survey provides a chance to find out more about health care needs and use, effects on quality of life, and other information on the functional effect of asthma and service use related to asthma. Another question was about the availability of linking asthma data with environmental factors such as air pollution. Dr. King stated that data are not available to look at direct measures among individuals in the population over time, but different datasets could be linked to conduct ecologic analysis of asthma survey data based on residence and air quality, for example.

## Schizophrenia

## E. Susser

There are many parallels between schizophrenia and ASDs in the attempts to estimate incidence and historical changes in incidence. With respect to schizophrenia and related psychoses, two landmark

World Health Organization (WHO) studies can be used to mark shifts in thinking about schizophrenia, as well as about how studies of schizophrenia should be conducted. First, the International Pilot Study of Schizophrenia (IPSS), conducted in the 1960s, was designed to determine if schizophrenia was a culturally bound disorder and if it was a "real" disorder (some people hypothesized that schizophrenia was a social construction). The study used standardized criteria in a multinational study and many regions of the world were included. Researchers found schizophrenia in all settings; that finding is still questioned, but is supported by the findings of other types of studies. Second, the WHO "Ten Country Study" examined whether the incidence and course of schizophrenia varied across sociocultural settings. The study also had a novel design for determining incidence. It inaugurated the "first contact" design, now widely used and considered a "gold standard", in which researchers ascertain all people seeking help for a possible psychosis for the first time, within a defined population.

Based on misinterpretation of the results of these (and other) studies, the prevailing summary of schizophrenia from 1980 to about 2005 was that there was a lifetime risk of schizophrenia of 1%, and that this figure remained constant over time and place. The current view on schizophrenia is different; it is clear that the occurrence varies across populations and population subgroups, the clearest example being the very high rates among some immigrants who are ethnic minorities (mainly documented among immigrant groups in the United Kingdom and Netherlands). This variation is not inconsistent with the results of the WHO studies, but is inconsistent with the way these results were interpreted by most schizophrenia researchers and clinicians as showing constant rates overtime (not by the authors themselves, who were cautious in their conclusions). The WHO studies were not designed to examine change over time. Although other studies have attempted to examine change over time (e.g. registry studies), the results have been inconsistent, and the data weak (e.g. due to changes in diagnostic practices and systems). As a result, with the exception of one or two particular locations, we cannot at present draw conclusions as to whether schizophrenia incidence has changed over time. The discrepancy between studies of the course of schizophrenia, and interpretation of those results (again, not by the authors) is even more striking, but I do not have time to elaborate on this during this presentation.

There are several important lessons learned from studies of schizophrenia that could be useful when examining changes in ASD prevalence. For example, with regard to the notion of "constant" incidence over place and time, fixed thinking about schizophrenia was allowed to override the available data. The idea that schizophrenia occurred worldwide and that there was at most a very modest variation in incidence was accepted as true for a long time, and still taught in many psychiatry and other mental health professional training programs. This lesson is relevant to ASDs to help understand how to interpret ASD data. There have been different waves of ideology which have influenced the way in which the data on incidence of ASDs have been interpreted, and in particular, on whether they demonstrate a "true" increase or not ("true" means over and above an increase due to changes in ascertainment and help-seeking). The schizophrenia story helps one to recognize the power of ideology in the interpretation of such data, and the need to be cognizant of it. He noted his personal view is that the data on whether there has been a "true" increase in autism are simply inconclusive, but that the overall evidence favors the position that a part of the increase is "true".

## *Panel member discussion:*

Panel members asked if there was a specific way in which those in the ASD field could learn from the schizophrenia example? Dr. Susser responded that there have been different waves of ideology in how autism and related conditions have been interpreted and people tend to look at data as either, "yes, there has been an increase", or "no, there has not been an increase". It would be really helpful for those working with ASDs to not look through the data using those lenses, but to ask questions openly. Dr. Susser further stated that we do not need to be committed to either position to use data to advocate and to improve services. There was another question on subtypes of schizophrenia. Dr. Susser indicated that subtypes typically have not been reliable over time. Dr. Susser also commented that if a disorder persists

over generations, we also should be consider examining if there are selective mutations occurring or reframing to consider a selective advantage associated with the condition.

## Simulation Studies

### S. Galea

This presentation provided a brief overview of simulation studies as a method to understand prevalence changes. Changes in ASD prevalence have been and continue to be an observed phenomenon, yet the problem lies in identifying the causes for the changes. Causal models, including sufficient-component cause models, can shed some light on the joint effects of multiple exposures. However, these models are unable to consider timing in a dynamic way or connections between individuals. A possible solution is to use complex systems models. Complex systems approaches are computational approaches that use computer-based algorithms to model dynamic interactions between individuals within and across levels of influence (such as social networks and neighborhoods) using simulated populations. Complex systems models can incorporate multilevel determinants of population health, connections between individuals, and patterns of feedback between exposures and outcomes over time.

An example of trying to understand health problems seen after disasters was presented using a type of analytic strategy called "agent-based modeling" to predict changes among heterogeneous populations. The goal was to model outcomes observed by varying the variables that might have contributed to the observed pattern. There could have been several different sets of variables that produced the same outcome. A lesson that might be important when examining reasons for ASD trends is that complex systems models point to different possible explanations for observed phenomenon. However, they can be used in conjunction with empirical data to narrow down possible explanations and can play a central role in epidemiological analyses.

# Open Comments

The workshop included presentations and discussions among panel members. However, the meeting was open to anyone to register and attend in person or via webinar. Nonpanel members were able to provide written comments before and after the workshop, as well oral statements during an open period of the workshop. Comments included concern about increases in ASDs, the need to find out what has changed in our environment, the larger than expected number of children and young adults with an ASD, and the cost to society. Many of the public comments focused on concern about the role of vaccines in autism, with disappointment expressed about the lack of research on vaccine safety. In particular, studies of vaccinated and unvaccinated children and mitochondrial disease were requested. In addition, concerns were raised about the cumulative effect of the vaccine schedule and vaccine ingredients, as well as the need to consider a child's immune status prior to giving vaccinations. Suggestions were made for other studies such as of young children's development from birth to 2 years of age and to determine if there are specific subgroups of children with ASDs, such as those with gastrointestinal sensitivities. A man with an ASD expressed the belief that it is possible to be successful with an ASD and offered himself as an example of someone who once relied on public assistance, but is now successfully employed and lives independently. He also expressed gratitude for CDC's work in vaccine safety and satisfaction with receiving vaccines to protect from known diseases. Other comments included frustration with the delays parents face in getting a diagnosis of autism, despite bringing concerns to the attention of professionals. Other comments included concern about non-scientific expertise among panelists and interest in the latest research findings and plans for future research related to ASDs. Workshop organizers, panelists, and stakeholders were asked to consider these comments when discussing priorities for evaluating changes in ASD prevalence.

# Panel Session Summaries

The workshop featured four breakout panel discussions, with each panel asked to discuss questions related to ASD prevalence. The panelists' discussion, ideas, and suggestions were compiled by the panel chairs. Panel members consisted of epidemiologists and scientists with experience in epidemiology and surveillance of autism or other complex conditions and community stakeholders (representatives from autism organizations, parents of children with an ASD, and adults with an ASD). Following is a summary of the panel discussions and their ideas for addressing questions related to ASD prevalence trends.

## Panel 1: Utility of ASD Prevalence Data

Panel Chair: *A. Singer*

**Panelists:** *C. Cunniff, W. Zahorodny, R. Kirby, M. Lopez, R. Grinker, D. Mandell*, L. Grossman*, W. Dunaway, M. Rosanoff, J. Zimmerman, B. Mulvihill, J. Charles*

**Invited participant unable to attend remotely or in-person at last minute due to unforeseen circumstances.*

The discussion and questions addressed by Panel 1 focused on how ASD prevalence data are used in the community by different stakeholders and sought to identify ways in which data collection and reporting on the population prevalence and characteristics of people with an ASD could be further developed.

### *Q1. What does having ASD prevalence information do for stakeholders (parents, professionals, people with an ASD, researchers, scientists, policy makers, service providers)?*

The panelists indicated that ASD prevalence data are used to:

- Empower the community, confirming what parents and educators experience
- Drive public policy
- Support the need for service provisions and development
- Support the need for professional development and systems planning
- Support the need for additional research

At the community level, prevalence data have informed stakeholders about needed improvements in identifying people with an ASD and helped direct research which may ultimately lead to information about etiology. Similarly, the resulting increase in ASD awareness and knowledge among parents, caregivers, and communities has increased the quality of social and behavioral descriptions by clinicians and service providers when a child has been referred for an evaluation. This has resulted in parents being more equipped to discuss concerns with professionals. Clinicians have found that having ASD prevalence information increases awareness of the need to identify children and facilitates having a conversation with parents about concerns. It also has provided information to help clinicians advocate for needed resources for identification, referral, and intervention. Researchers have used prevalence data as justification for etiologic and intervention research, and the increased awareness of ASD has increased their own career choices to be engaged in meaningful work. Individuals with an ASD have also benefitted from ASD prevalence data. Increased ASD awareness has resulted in positive community connections and increased information has allowed them to help themselves and others understand their experience.

Prevalence data also have empowered communities by confirming what parents and educators have been experiencing and providing evidence for robust advocacy. ASD prevalence estimates have provided a starting point to assess service and support needs for individuals, families, and communities. On a policy level, awareness of the Autism and Developmental Disabilities Monitoring (ADDM) Network has allowed scientists and researchers, in some states, easier access to data sources and records for surveillance purposes, thus increasing the accuracy of ASD estimates. Prevalence estimates also have informed policy efforts to create an infrastructure to support children with an ASD (e.g., child care, intervention, education, transition services); understand and address lifespan issues (e.g, housing training, employment, health

and wellness); drive public policy and programs (e.g., insurance coverage and health care legislation); and support the need for service deployment, systems planning, and additional research funding.

### *Q2. How are stakeholders actually using ASD prevalence information?*

ASD prevalence data are included at the beginning of many, if not most, research publications and grant applications related to ASDs because they provide an estimate of the population-level effect of the conditions. In particular, recent estimates indicating that ASDs are more common than previously thought have motivated the need to better understand the course, causes, and supports related to ASDs. In addition to putting the scope of need into perspective, recent ASD prevalence estimates have prompted some states to pass mandatory reporting laws, establish autism task force groups or autism councils, pass legislation affecting service provision, or offer grants to school districts for supplemental funding related to autism. Examples of how states have used ASD prevalence data follow:

- South Carolina used prevalence data to show the need for improving access to services when drafting and passing insurance reform.
- New Jersey passed laws related to ASDs and mandatory reporting, compelling insurance companies to provide services and providing additional grants to schools.
- Alabama appointed an autism coordinator for the state based on the effects of the prevalence data.

### *Q3. What types of ASD prevalence information and descriptions of the population are useful to stakeholders?*

For individuals, families, and communities, having ASD prevalence data that are applicable to more specific local areas and states can better inform advocacy and service planning efforts. ASD prevalence data are population-based and are not easily applicable at the individual level. In addition to understanding the population effects of ASDs, families and communities continue to seek ways of making the information more relevant for their individual circumstances. Specific recommendations included:

- Improving communication with the community (e.g., families, individuals with an ASD, professionals, policy makers, and researchers) to help put the prevalence data into context.
- Providing more in-depth information on what an ASD diagnosis means for an individual across his or her lifespan, and what support systems such an individual needs or will need.
- Collecting and reporting data on functional level and effects of ASD, subtypes, developmental characteristics, and associated conditions (in addition to overall ASD prevalence estimates).

### *Q4. What questions do stakeholders expect epidemiology and prevalence studies, in particular, to answer?*

The panel noted that community stakeholders want the data to be useful at the community and individual levels. At the community level, ASD prevalence estimates can inform larger needs (identification, supports, policy, and research). For the individual person, as suggested in Q3's discussion, more detailed data on functioning and characteristics would be helpful. Prevalence numbers should inform preparation for the needs of a growing population. In addition to describing the population, prevalence studies could provide a baseline for evaluating interventions and gauging service needs. Some panel members called for more data on the link between prevalence and etiology. For example, would lower prevalence in some areas or subgroups indicate potential protective mechanisms? Prevalence studies should be accompanied by data collection on specific symptoms or biological measures, interventions, and trajectories over time.

## Panel 2: U.S.-Based ASD Service Data

### Panel Chair: *L. Croen*

**Panelists:** *P. Shattuck, P. Bearman, M. Kogan, S. Visser, I. Hertz-Picciotto, L. Miller, A. Bakian, K. Van Naarden Braun, L. Lee, T. Baroud, P. Bell, R. Etzioni, Y. Kim*

Panel 2 discussed databases that exist to serve the administrative functions of tracking service use, or were developed for specific studies. Although not designed to identify all children with an ASD among the population, these databases might serve as useful tools for looking at trends in identification, characteristics, and service use that will help explain population-based ASD prevalence trends. Some of the databases or datasets noted that could be explored for examining administrative or reported prevalence issues include:

All-Payer Claims Database (APCD; combines outpatient data from all claims databases)
California Department of Developmental Services (CA DDS) database
Department of Education/Individuals with Disabilities Education Act (IDEA) Child Count (also, Special Education Longitudinal Study)
Hospital Discharge Data
Interactive Autism Network (IAN) survey
Kaiser Permanente® membership databases
Centers for Medicaid and Medicare Services (CMS)
National Health Interview Survey (NHIS)
National Survey of Children's Health (NSCH)
National Survey of Children with Special Health Care Needs (NSCSHCN)
State registries (New Jersey, Utah, West Virginia)
Vaccine Adverse Event Reporting System (VAERS)

***Q1. What are the top three immediate (within 1 to 2 years) priority analyses needed to understand ASD trends using existing U.S.-based datasets?***

Panelists discussed several analyses that could be pursued, including:

- Conducting a life-course study of ASD identification, service use, and characteristics. Tracking life history can help determine if the ways people come into the system are changing. Researchers could examine first concerns and average age at first diagnosis, and what happens before and after an ASD diagnosis occurs among those in successive birth cohorts. Kaiser Permanente® membership data could be used to explore this.
- Examining trends in comorbidities among children with ASDs over time and trends in the use of treatments among parents over time. For example, a potential research question might include "Does survivorship of a mental or physical illness by parents (e.g., bipolar disorder) affect the trend in ASD prevalence among children? Kaiser Permanente® membership data or perhaps Medicaid data could be used to explore this type of question.
- Examining behavioral screening data to investigate trends in ASD diagnosis over time. Potential data sources could include the ADDM Network, as well as research programs, insurer databases, and primary care practices that have administered developmental screening tests over time.
- Examining trends in other behaviorally defined conditions (e.g., attention-deficit/hyperactivity disorder, depression, and anxiety) in U.S. population-based datasets (e.g., the National Survey of Children's Health). This could be addressed by ADDM Network data (among children with an ASD).

- Looking at ASD prevalence trends over time among different immigrant groups. This might inform trends and prevalence rates in terms of eliminating certain risk factors. However, it is difficult to disentangle if observed rates are lower among immigrants either because of immigrants' lack of familiarity with the U.S. health care system U.S. (including how it operates), or because of reluctance on the part of immigrants to seek medical attention for developmental disorders, or both.
- Further examining the respondents to national surveys who had at least one child ever diagnosed with an ASD and who reported the child no longer had an ASD diagnosis at the time of the survey There is a need to understand why some children may have been reported to have an ASD at one time, but not at the time of the survey.

***Q2. What are the top three next (within 3 to 5 year) priority analyses needed to understand ASD trends using existing U.S.-based datasets?***

Panelists discussed several potential analyses, including:

- Conducting multilevel modeling with Special Education Child Count or other datasets. Enhanced analysis might help answer questions regarding administrative prevalence trends in schools and communities.
- Using Special Education Child Count data from both IDEA Part C Early Intervention for 0-3 year-olds and IDEA Part B for 3-21 year-olds to track identification, services, and developmental trajectories at the individual level.
- Linking all-payer claims databases with state autism registries to track ASD diagnostic or billing codes, along with additional billing and pharmaceutical claims, to provide information concerning comorbid conditions.
- Taking simulation-based approaches to data analysis, and evaluating the models using real data from epidemiologic studies.
- Using Medicaid data to examine trends over time in ASD and related diagnoses among those receiving Medicaid services. Also, evaluate children longitudinally to examine changes in diagnoses and services.
- Collaborating with the National Institute of Mental Health (NIMH) to better understand the factors associated with the persistence of parent-reported ASD diagnosis. (NIMH has partnered with the Health Resources and Services Administration and the Centers for Disease Control and Prevention, and currently is conducting a follow-up study of the NSCSHCN for families of children who were reported ever to have had a diagnosis of an ASD.)

***Q3. Can the existing data systems be enhanced (e.g., adding analyses, data collection) to better answer questions about the changing ASD prevalence? If not, why not and what else is needed?***

Panelists discussed several enhancements, including:

- Enhancing use of Child Count Special Education Data by
  - » Documenting state differences in identifying children as eligible for autism special education services and documenting the methodology for obtaining and reporting these data to make better sense of special education data.
  - » Conducting studies to evaluate how children with autism are identified at schools.
  - » Enabling individual-level child data to be accessed for study purposes and pooled together.

- Enhancing use of surveys by
  - » Conducting needed validation studies of parent-reported data.
  - » Exploring whether national surveys (e.g., National Immunization Survey, NHIS, NSCH, VAERS) could be used to examine ASDs among vaccinated versus unvaccinated groups.
  - » Using national surveys to examine service use and needs.
  - » Adding questions to the IAN Survey to assess beliefs about causes of ASDs.
- Enhancing data access and coordination by
  - » Partnering with analytic powerhouses (e.g., Google) to develop new strategies to take advantage of the huge amounts of data that will become available in upcoming years (e.g., data enhancements from health care reform and electronic health records). This will require public and private partnerships.
  - » Making ASDs reportable conditions in more states. However, it was noted that making a condition reportable does not improve the ability to understand trends, but it is a useful method to establish public health authority to collect additional data to track trends.
  - » Collaborating with the National Environmental Public Health Tracking Network (EPHTN) to potentially access environmental risk factor and other environmental public health tracking data at the population-level.
- Creating new data collections for
  - » Using qualitative methods to understand pathways to screening and diagnosis.
  - » Monitoring trends in ASD prevalence prospectively to rule out "artificial" factors. Consistently conduct developmental and ASD screening at given ages with diagnostic follow-up and documentation of each step and outcomes.
  - » Developing methods to track the effects of information dissemination across parent networks via the Internet or other social media.

## Panel 3: Autism and Developmental Disabilities (ADDM) Network Data

### Panel Chair: *G. Dawson*

**Panelists:** *S. Galea, G. McGwin, O. Devine, A. Correa, M. Zack, P. Yoon, M. Maenner, J. Daniels, L. Schieve, S. Pettygrove, M. Wingate, J. E. Robison, P. C. Marvin*

The questions and discussion of Panel 3 focused on identifying immediate, next, and future priorities for enhancing the data collection, analysis, and reporting of ASD prevalence and descriptive data by the ADDM Network to betterunderstand trends.

***Q1. What are the top three immediate (next 1 to 2 years) priority analyses needed to understand ASD trends using existing ADDM Network data?***

Panelists discussed the following priorities:

- Conducting simulation studies to predict the anticipated course of ASD prevalence, informed by existing ADDM Network data, by
  - » Identifying and using more complex, nuanced modeling approaches to simultaneously examine multiple identification (intrinsic and extrinsic) and risk factors across cohorts (this will be challenging because several factors are confounded).
  - » Using ADDM Network data to inform assumptions in simulation models of ASD prevalence trends.

- Conducting analyses that will help explain variations in ASD prevalence across geography and subgroups by
  - » Providing information about risk factors related to parental age.
  - » Examining data on ASD prevalence for disparities in identification to inform diagnostic and access to service needs.
  - » Comparing changes in ASD prevalence among children with more a narrowly defined autistic disorder diagnosis to with those with a broader ASD diagnosis, as autistic disorder might be less influenced by increased public awareness.
- Using methods to maximize the number of children with an ASD in the population identified by the ADDM Network by
  - » Performing additional validation studies including direct screening and assessment at other ADDM Network sites and using the results to enhance estimates of ASD prevalence. [Note that a validation study in the Atlanta site (Avchen et al., 2010) found that the records-based approach had good specificity but low sensitivity indicating that ADDM Network ASD case classifications are consistent with clinical examination, but that some children with ASDs are not identified using current methods. Therefore, ADDM Network prevalence estimates likely underestimate ASD prevalence.]

***Q2. What are the top three (within 3 to 5 years) priority analyses needed to understand ASD trends using existing ADDM Network data?***

Panelists discussed the following potential next priorities:

- Conducting analyses to better understand ASD prevalence trends and current and future needs of adolescents and adults with an ASD by
  - » Examining an older cohort to better understand the changes in prevalence over time. This could be done by
    - * Surveying a previously-characterized cohort of 8-year-olds when they are older to determine if prevalence estimates are the same in this cohort at older ages.
  - » Identifying methods for estimating lifetime prevalence and characterizing developmental trajectories by
    - * Examining how ASD symptom presentation may change across cohorts and individuals across the lifespan.
    - * Identifying methods to examine the effects of early intervention and whether changing symptom profiles may have on ASD prevalence estimates.
  - » Conducting studies of ASD prevalence among adults by
    - * Identifying appropriate methods for characterizing ASD prevalence at different ages.
    - * Addressing the ethical concerns of identifying adults with an ASD who may not want that classification.
    - * Characterizing outcomes and service and support needs.
  - » Using ADDM Network data to better understand risk factors for ASDs by

* Recognizing that ADDM Network data might not be well-designed to examine risk factors at the individual level; however, use the data to characterize whether some risk factors have changed among the population and correlate to ASD prevalence changes.

***Q3. Can the ADDM Network be enhanced to better answer questions about changing ASD prevalence? If yes, how? If no, why not and what else is needed?***

Panelists discussed building on the existing ADDM Network infrastructure by

- Developing ways of better capturing the heterogeneity and complexity of ASD phenotypes.
- Expanding ADDM Network dataset linkages to other datasets (e.g., health, education, service, environmental data) to enrich data completeness and use for examining risk factors.
- Collecting follow-up data on cohorts studied previously at later ages to better understand trends over time and outcomes.
- Collecting more extensive data as part of ongoing surveillance using additional methods such as direct screening and diagnostic confirmation to obtain the most complete estimates of ASD prevalence in the U.S.

## Panel 4 –What Else Is Needed To Understand ASD Trends?

### Panel Chair: *M. Durkin*

**Panelists:** *K. Crider, E. Susser, C. Lawler, C. Tanner, M. King, S. Shapira, D. Schendel, J. Nicholas, W. McMahon, J. Constantino, C. Newschaffer, L. Perner, M. Blaxill, E. London, G. Windham, K. Merikangas*

Panel 4 engaged in an open discussion on some of the "big picture" issues related to understanding ASD trends, including whether it is possible to fully understand reasons for ASD prevalence increases, ways to move forward with collaborations and new methods, and what else could be done to improve the understanding of ASD trends.

***Q1. Can the question of the relative contribution of identification or risk factors, or both, on ASD prevalence during the last 20 years be answered? If not, why not? If yes, what are the three primary questions that need to be addressed by epidemiology?***

Panel members offered a range of perspectives on whether it will ever be possible to understand the relative contributions of identification and risk in increasing ASD prevalence. There was agreement that the ASD prevalence is a huge public health problem and that many individuals and families are affected globally. Panel members did not agree about whether it was possible ever to understand fully all the reasons behind increasing ASD prevalence. One panelist asserted that the question already has been answered: Of course there has been an increase because there has an increase in the number of cases and autism is an epidemic and needs to be treated as a public health emergency. Others noted that autism is a disorder of social behavior and that trends over time in its frequency are affected by corresponding changes in social context, perceptions, awareness, knowledge, diagnostic practices, and availability of services. However, there was a general sense that it is possible to move forward and to be more specific in documenting potential reasons for ASD prevalence trends. Several challenges were mentioned, such as insurmountable measurement error, overlap and confounding of multiple identification and risk factors, and poorly defined subtypes with limited information on biological underpinnings to explain phenotypes. It is unlikely that prevalence trend data will explain the etiology of a complex set of conditions, such as ASDs, but these data can identify clues for further mechanistic studies (e.g., increased risk by sex, geography, and birth characteristics). By better understanding what causes autism, maybe we can understand the

increases in measured prevalence. In addition, panelists noted that we need more clarity on phenotypes, expression across the lifespan, and trends in other conditions. Others thought that, although we might not be able to use prevalence data to make discoveries about how to prevent or cure ASDs, we can use prevalence data to assess needs and improve the lives of those affected by ASDs. This could lead to a focus on services and figuring out how to improve identification and access to such services.

***Q2. How can efforts to understand ASD trends be informed by other fields or conditions (e.g., comparison with other conditions, sharing methodology, analytic techniques, etc.)? How can that best be accomplished?***

Panelists discussed several potential collaborations, including:

- Comparing ASD prevalence trends to trends in other neurodevelopmental disorders.
- Collaborating with scientists investigating epigenetic effects in cancer and other fields to better understand gene–environment interactions in neurodevelopment.
- Examining subgroups of children with an ASD (e.g., children with fragile X syndrome and ASD) to determine if there are specific risk factors that can be identified among these children with increased risk for developing ASD.
- Analyzing new bioinformatics and computational tools and approaches to better understand complicated systems and interactions.
- Conducting translational research because existing ASD criteria are not mapped to biology and etiology. Translational investigators could help bridge the gap between diagnostic criteria and biology.

***Q3. What else is needed to understand reasons for trends?***

During the discussions for Questions 1 and 2, several propositions were made for better understanding ASD prevalence trends, including:

- Seeking public–private partnerships to support data collection, analyses, and usage of data.
- Providing funding opportunities to encourage use of existing datasets.
- Expanding use of analytic techniques for examining population trend data by
  - » Using modeling approaches to supplement observed data.
  - » Comparing multiple identification and risk factors that might contribute to prevalence changes.
- Expanding ASD prevalence efforts to include very young children and adults.
- Understanding patterns in ASD prevalence among subgroups (e.g., subtypes, males and females, geographic variation, comorbidities) to evaluate whether changes likely are due to identification or risk factors:
- Expanding the methodology for looking at ASD prevalence by
  - » Developing methods to conduct cross-sectional studies across successive birth cohorts that simultaneously ascertain parent-reported descriptions of developmental characteristics, intellectual functioning, ASD and comorbid symptoms, research diagnosis (categorical or observational), community diagnoses, and family characteristics (sibling recurrence).
- Understanding and improving ASD identification by
  - » Measuring ASDs dimensionally and quantifying the traits that make up the ASDs.

- » Measuring any overlap with other conditions and typical development, determining if is there a continuum of symptoms.
- » Improving tools for culturally sensitive screening and case confirmation among large populations.
- » Developing methods for measuring disability and monitoring functional limitations in individuals with ASD.
- » Using data on identification of ASDs to identify gaps and improve community practice.

- Improving community engagement and communication between individuals and families affected by autism, professionals providing services for people with autism, researchers, and policy makers by
  - » Fostering broader understanding of the strengths and challenges associated with ASDs so people with ASDs have access to the community.
  - » Utilizing ASD prevalence estimates to develop programs and practices that support the positive development of people with ASDs.
  - » Realizing that autism is not an academic issue for the many individuals and families affected by ASD, and listening to the concerns of parents of children and individuals with an ASD.
  - » Sharing information with leadership and policy makers to respond to this health crisis.
- Making sure public health is part of the Interagency Autism Coordinating Committee (IACC) Strategic Plan and input is sought from a range of stakeholders via annual research plan updates.
- Noting that, while trends are important, understanding them might require a better understanding of the etiology and heterogeneity of autism, as well as changes over time in diagnostic practices. These goals can be achieved by
  - » Advancing basic science on biologic and environmental mechanisms.
  - » Increasing the types of study methods used in research and service studies such as
    - * Conducting prospective studies that examine biology, phenotypes, identification patterns, and service needs and use.

# Appendix A: Workshop Agenda

## Workshop on U.S. Data to Evaluate Changes in the Prevalence of the Autism Spectrum Disorders (ASDs)

**Co-Sponsored by the National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC) and Autism Speaks**

## Tuesday, February 1, 2011

## Location: Centers for Disease Control and Prevention,

Tom Harkin Global Communications Center, 1600 Clifton Road, N.E., Atlanta, Georgia
Building 19, Auditorium B1/B2

**7:30–8:00** . ..... **Check-in**

**8:00–8:05** . ..... **Welcome** — *C. Boyle and G. Dawson*

**8:05–10:00** . ..... **Background and purpose**

- What do we know about ASD prevalence? — *M. Yeargin-Allsopp*
  - » General summary of ASD prevalence
- Framework for this meeting — *C. Rice*
  - » What might be influencing temporal patterns in prevalence?
    - * Intrinsic Identification – methodology/measurement
    - * Extrinsic Identification - (awareness and classification)
    - * Risk – (multiple biologic and environmental)
  - » Questions to address (For U.S. service data, ADDM, and the field, more generally)
    - * What we can do now? (analysis with existing data)
    - * What should we do next? (building on existing data systems)
    - * What else is needed? (analyses, data collection, others)
- 8:30–8:45 . ..... A mode for assessing the contribution of various risk factors to recent ASD prevalence increase in the U.S. — *L. Schieve*
  - » Examples using selected prenatal and perinatal risk factors.
- 8:45–9:00 . ..... ASD genetic variation and gene-environment interaction — K. Crider
- 9:00–9:45 . ..... Examples of analyses in progress from the Autism and Developmental Disabilities Monitoring (ADDM) Network
  - » ADDM Network Overview — C. Rice
  - » Changes in ASD diagnostic criteria
  - » Parental age, dx age, SES — M. Durkin
    - * Hypothesis
    - * Methods
    - * Findings
    - * What else could be done to understand ASD trends using this dataset?
    - * What else could be done to understand ASD trends?

**10:00–10:50** . . . . . **ASD Trends: U.S. single source datasets (ED and CA DDS data)**

- U.S. Special Education Data — P. Shattuck
- CA DDS Data — I. Hertz-Picciotto, P. Bearman
  - » Brief overview of evidence of prevalence changes.
  - » What factors contribute to the change in prevalence over time? (is it possible to distinguish the relative contribution of various intrinsic identification, extrinsic identification, and/or risk factors influencing prevalence change?)
  - » What are the strengths/limitations of these approaches?
  - » What else could be done to understand ASD trends using this dataset?
  - » What else is needed to understand ASD trends?

**10:50–11:05** . . . . . **Break**

**11:05–12:30** . . . . . **Lessons from other conditions and analytic methodologies**

- Cancer — R. Etzioni
- Parkinson's — C. Tanner
- Asthma — M. King
- Schizophrenia — E. Susser
- Simulation Studies — S. Galea

Given a change in prevalence/ incidence, what has been done to understand the reason(s)?

- Brief overview of evidence of prevalence changes.
- What factors contribute to the change in prevalence over time? (is it possible to distinguish the relative contribution of various intrinsic identification, extrinsic identification, and/or risk factors influencing prevalence change?)
- What are the strengths/ limitations of these approaches?
- What lessons may be important when looking at reasons for ASD trends?

**12:30–1:00** . . . . . **Open Comment**

**1:00–1:20** . . . . . **Pick up lunch and transition to Panel Breakouts**

**1:20–2:45** . . . . . **Panel Discussion Breakouts**

## Panel 1 – Utility of ASD Prevalence Information (Room 117)

Panel Chair: *A. Singer*

Recorder: *C. Arneson*

**Panelists:** *C. Cunniff, W. Zahorodny, R. Kirby, M. Lopez, R. Grinker, D. Mandell*, L. Grossman*, W. Dunaway, M. Rosanoff, J. Zimmerman, B. Mulvihill, J Charles*

- What does having ASD prevalence information do for stakeholders (parents, professionals, people with

ASD, policy makers, service providers)?

- How are stakeholders actually using ASD prevalence information?
- What types of ASD prevalence information and descriptions of the population are useful to stakeholders?
- What questions do stakeholders expect epidemiology and prevalence reports, in particular, to answer?

## Panel 2 – Other US-Based ASD Data (Room 255)

Panel Chair: *L. Croen*

Recorder: *L. King*

**Panelists:** *P. Shattuck, P. Bearman, M. Kogan, S. Visser, I. Hertz-Piciotto, L. Miller, A. Bakian, K. Van Naarden Braun, L. Lee, T. Baroud, P. Bell, R. Etzioni, Y. Kim*

- What are the top 3 immediate (1–2 year) priority analyses needed to understand ASD trends using existing US-based datasets?
- What are the top 3 next (3–5 year) priority analyses needed to understand ASD trends using existing US-based datasets?
- Can these data systems be enhanced (analyses, data collection, others) to better answer questions about changing prevalence of ASDs? If yes, how? If no, why not and what else is needed?

## Panel 3 – ADDM Network Data (Room 257)

Panel Chair: *G. Dawson*

Recorder: *K. Phillips*

**Panelists:** *S. Galea, G. McGwin, O. Devine, A. Correa, M. Zack, P. Yoon, M. Maenner, J. Daniels, L. Schieve, S. Pettygrove, M. Wingate, J. E. Robison, P. C. Marvin*

- What are the top 3 immediate (1 -2 year) priority analyses needed to understand ASD trends using existing ADDM data?
- What are the top 3 next (3-5 year) priority analyses needed to understand ASD trends using existing ADDM data?
- Can the ADDM Network be enhanced (analyses, data collection, others) to better answer questions about changing prevalence of ASDs? If yes, how? If no, why not and what else is needed?

## Panel 4 –What else could be done to understand ASD Trends? (Room B1/B2)

Panel Chair: *M. Durkin*

Recorder: *R. Fitzgerald*

**Panelists:** *K. Crider, E. Susser, C. Lawler, C. Tanner, M. King, S. Shapira, D. Schendel, J. Nicholas, W. McMahon, J. Constantino, C. Newschaffer, L. Perner, M. Blaxill, E. London, G. Windham, K. Merikangas*

- Can the question of the relative contribution of identification and/or risk factors on ASD prevalence in the last 20 years be answered?
  - » If not, why?
  - » If yes, what are the 3 primary questions which need to be addressed by epidemiology?
- How can the ASD field work with other fields / conditions to evaluate trends (comparison to other conditions, sharing methodology, analytic techniques, etc.)? How best can that be accomplished (give specific

conditions with possible analyses/activities)?

- What else is needed for the ASD larger field to understand reasons for trends?

**2:45–3:00** . ..... **Break**

**3:00–5:00** . ..... **Report from Each Panel (Aud A)**

Facilitator: P. Yoon

- 3:00–4:45 . ..... For Panel 1, 2, 3, and 4
  - » 10 minute summary report for each panel
  - » 15 minute Larger Panel Discussion
- 4:45–5:00 . ..... Meeting adjournment

# Appendix B: Panelist Biographies

Amanda V. Bakian, MS, PhD, is the epidemiologist and data manager for the Utah Registry of Autism and Developmental Disabilities (URADD) and the Utah ADDM Network site. She has collaborated on a variety of research studies investigating the prenatal, perinatal, neonatal, socio-demographic, and environmental risk factors associated with ASDs and intellectual disabilities.

Thaer Baroud, BSN, MA, MHSA, is a senior epidemiologist with the Arkansas comprehensive tobacco control program and he is the epidemiologist for the Arkansas ADDM Network site. He has worked as an epidemiologist at the Arkansas Center for Health Statistics.

Peter Bearman, PhD, is the Director of the Lazarsfeld Center for the Social Sciences, the Cole Professor of Social Science, and Co-Director of the Health & Society Scholars Program at Columbia University. He is currently investigating the social determinants of the autism epidemic. He has researched topics including adolescent sexual networks, networks of disease transmission, genetic influences on same-sex preference, and historical sociology.

Peter Bell, MBA, is Executive Vice President for Programs and Services at Autism Speaks and the father of a son with autism. He oversees the foundation's government relations and family services activities and also serves as an advisor to the science division. Mr. Bell was president and CEO of Cure Autism Now following a marketing career at McNeil Consumer & Specialty Pharmaceuticals, a member of the Johnson & Johnson family of companies.

Mark Blaxill, MBA, is the father of a daughter with autism, editor-at-large for Age of Autism, a director of SafeMinds, and a frequent speaker at autism conferences. He writes often on autism, science, and public policy. In his professional career, he is managing partner for 3LP Advisors, an advisory firm focused on intellectual property transactions.

Coleen A. Boyle, PhD, MSHyg, is the Director of the National Center on Birth Defects and Developmental Disabilities (NCBDDD) at CDC. She has worked on public health issues such as agent orange and cancer. Her interest and expertise is in the epidemiology and prevention of birth defects and developmental disabilities.

Jane Charles, MD, is a Developmental-Behavioral Pediatrician in the Department of Pediatrics at Medical University of South Carolina. Her areas of specialization are in the fields of ASDs and intellectual disabilities. For the past ten years, she has been Co-Principal Investigator for the South Carolina ADDM Network site.

Prisca Chen Marvin, JD, is the mother of a daughter with autism, a member of the Visiting Committee at Massachusetts Institute of Technology's Brain and Cognitive Science Department, a board member of REACH at the University of Iowa, and a Member of the Executive Council of the Associates of the Yale Child Study Center.

John N. Constantino, MD, is the Blanche F. Ittleson Professor of Psychiatry and Pediatrics at Washington University, Associate Director of a Eunice Kennedy Shriver Intellectual and Developmental Disabilities Research Center at the Washington University School of Medicine, and Director of the School's Division of Child Psychiatry. In addition to his role as Principal Investigator of the Missouri ADDM Network site, he leads a federally-funded program in autism research that is centered on a prospective longitudinal study of sibling pairs in families affected by autism.

Adolfo Correa, MD, MPH, PhD, is a Medical Officer and Birth Defects Surveillance Team Lead with the CDC's National Center on Birth Defects and Developmental Disabilities, Birth Defects Branch. He has worked extensively with the Metropolitan Atlanta Congenital Defects Program (MACDP). His current work focuses on surveillance of congenital heart defects and on the epidemiology of maternal diabetes and birth defects.

Krista S. Crider, MA, PhD, is a Geneticist with the CDC's National Center on Birth Defects and Developmental Disabilities, Pediatric Genetics Team. She has worked on epigenetics changes in DNA methylation and folic acid supplementation, antibiotic use and the risk of birth defects, trends in trisomies, and genetics of preterm birth among other projects with the National Birth Defects Prevention Study, Metropolitan Congenital Defects Program, and the China collaboration.

Lisa A. Croen, PhD, is a Senior Research Scientist and the Director of the Kaiser Permanente® Autism Research Program. Currently, she is leading or collaborating on several federally funded autism studies, including the Study to Explore Early Development (SEED), the Early Autism Risk Longitudinal Investigation Study (EARLI), the Early Markers for Autism Study (EMA), the California Autism Twins Study (CATS), and the Mental Health Research Network Autism Registry project.

Christopher Cunniff, MD, FACMG, FAAP, is a Professor of Pediatrics and Chief of the Section of Medical and Molecular Genetics at the University of Arizona, College of Medicine. His research focuses on public health genetics and the surveillance of developmental disabilities including ASDs, intellectual disability, muscular dystrophy, and fetal alcohol syndrome.

Julie Daniels, PhD, is a pediatric epidemiologist and Associate Professor in the Department of Epidemiology and Maternal and Child Health at University of North Carolina at Chapel Hill. She is the Principal Investigator of the North Carolina ADDM Network site and the CDC's Study to Explore Early Development (SEED) North Carolina site since 2002. Her research focuses on perinatal exposures, specifically nutrition and environmental exposures that may be associated with child health and development.

Geraldine Dawson, PhD, is Chief Science Officer for Autism Speaks, Research Professor of Psychiatry at the University of North Carolina at Chapel Hill, Adjunct Professor of Psychiatry at Columbia University, and Professor Emeritus of Psychology at University of Washington. She is a licensed clinical psychologist who has published extensively on autism, focusing on early detection and intervention and early patterns of brain dysfunction.

Owen Devine, PhD, is a Mathematical Statistician with the CDC's National Center on Birth Defects and Developmental Disabilities. He provides guidance on the analysis of epidemiologic data related to birth defects and developmental disabilities. His areas of interest included Bayesian methods, missing and miss measured data, and the interface of mathematical modeling and statistical techniques as applied to public health.

Wolf F. Dunaway works for the federal government as an Information Technology Specialist. He speaks at various colleges, universities, and symposiums on issues associated with autism and other disabilities and helps others better understand childhood autism through his own autism life experiences.

Maureen Durkin, PhD, DrPH, is a Professor of Population Health Sciences and Pediatrics and Waisman Center Investigator at the University of Wisconsin-Madison and the Principal Investigator of the Wisconsin ADDM Network site. She is an epidemiologist specializing in population-based studies of the frequency, prevention, antecedents, and consequences of developmental disabilities.

Ruth Etzioni, PhD, is a biostatistician and a full member at the Fred Hutchinson Cancer Research Center in Seattle. She studies population trends in prostate cancer incidence and mortality and is one of the principal investigators on the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network. She is currently adapting models for use in policy development for PSA screening.

Sandro Galea, MD, MPH, DrPH, is a physician, epidemiologist, and the Anna Cheskis Gelman and Murray Charles Gelman Professor and Chair of the Department of Epidemiology at Columbia University's Mailman School of Public Health. He has conducted large population-based studies in several countries,

and his primary research has been on the causes of mental disorders, substance abuse and on the role of traumatic events in shaping population health.

Roy Richard Grinker, PhD, is Professor of Anthropology at the George Washington University and editor-in-chief of The Anthropological Quarterly. He has published on topics such as the ethnic conflict in central Africa, intellectual history of African Studies, north-south Korean relations, and autism. He was a collaborator on a prevalence study of autism in South Korea and is a Co-Investigator on an NIMH-funded project entitled "Early Social Communication Characteristics of ASD in Diverse Cultures in the US and Africa".

Lee Grossman*, CAE, was the President and CEO of the Autism Society of America through early 2011 and the father of a son with autism. He has more than 20 years of experience with autism related issues, notably autism services and supports, adult issues, education, and research. He has served on numerous government and non-government advisory boards related to autism. Mr. Grossman has owned and operated a small business specializing in marketing, distribution, and consulting for medical manufacturers throughout the Pacific Basin.

Irva Hertz-Picciotto, PhD, is a Professor of Health Sciences at the University of California, Davis. She has published extensively on the effects of environmental exposures on pregnancy and child development. She is the Principal Investigator of CHARGE (Childhood Autism Risks from Genetics and Environment) Study, the first large, comprehensive population-based study of environmental factors in autism, and MARBLES (Markers of Autism Risk in Babies – Learning Early Signs), to search for early biologic markers that will predict autism.

Young Shin Kim, MD, MPH, PhD, is a researcher at Yale University. Her major research efforts focus on school bullying, the epidemiology of childhood onset neuropsychiatric disorders, and the genetic epidemiology of childhood onset neuropsychiatric disorders. She was the lead author on an epidemiological study of ASD prevalence in South Korea.

Michael King MSW, PhD, is a Commander in the US Public Health Service and an epidemiologist with the CDC's National Center for Environmental Health, Division of Environmental Hazards & Health Effects, Air Pollution and Respiratory Health Branch. His research has focused on using national surveys to monitor asthma-related morbidity, health-service use, and other respiratory health outcomes, including unintentional carbon monoxide poisoning.

Russell S. Kirby, PhD, MS, FACE, is Professor and Marrell-endowed Chair in the Department of Community and Family Health, College of Public Health, University of South Florida. He is a pediatric and perinatal epidemiologist with extensive experience in population health informatics and public health surveillance of birth defects and developmental disabilities and has been involved with the ADDM Network since 2002.

Michael D. Kogan, PhD, is Director of the Office of Epidemiology, Policy, and Evaluation for the US Health Resources and Services Administration's Maternal and Child Health Bureau. He also directs the US National Surveys of Children's Health and the National Surveys of Children with Special Health Care Needs. He has published over 100 articles and book chapters on numerous topics in pediatric and perinatal epidemiology, including the prevalence of ASDs, as well as the health care experiences of families with children who have an ASD.

Cindy Lawler, PhD, is a Program Director in the Division of Extramural Research and Training at the National Institute for Environmental Health Sciences (NIEHS), one of the National Institutes of Health. She is the NIEHS representative for extramural autism activities; this includes responsibilities as a program official for the NIH-funded Early Autism Risk Longitudinal Investigation (EARLI) study.

Li-Ching Lee, PhD, ScM, is a Research Scientist with the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health at the Johns Hopkins University. She has a background is in psychiatric epidemiology and a research interest in developmental disabilities in the US, China, and Taiwan. She has been involved with Maryland ADDM Network site since early in its inception and is currently the Principal Investigator.

Eric London, MD, is trained as a general psychiatrist and has a son with autism. He and his wife started the National Alliance for Autism Research (NAAR) in 1994, which later merged with Autism Speaks. He now serves on the Board of the Autism Science Foundation. Dr. London was the Director of the Autism Treatment Laboratory at the New York State Institute for Basic Research, and is now the Research Director at the the Center for Discovery in Harris, New York. His primary interests are in very early identification of autism and creating novel methods for autism treatment research.

Maya Lopez, MD, is a Developmental-Behavioral Pediatrician and Assistant Professor in the Developmental-Behavioral and Rehabilitative Pediatrics in the Department of Pediatrics College of Medicine at University of Arkansas Medical Sciences. She is the current Principal Investigator on the Autism Treatment Network (ATN) Grant for her institution and is Co-Principal Investigator for the Arkansas ADDM Network site.

David S. Mandell*, ScD, is Associate Professor of Psychiatry and Pediatrics at the University of Pennsylvania School of Medicine, an Associate Director of the Center for Mental Health Policy and Services Research, and Associate Director of the Center for Autism Research at The Children's Hospital of Philadelphia. The goal of his research is to improve the quality of care individuals with autism receive in their communities.

Matthew Maenner is a PhD candidate at the University of Wisconsin and works as an epidemiologist and data manager for the Wisconsin site of the ADDM network. He is currently funded by the Autism Science Foundation to explore the phenotypic heterogeneity of autism and its relationship to early identification.

Gerald McGwin, PhD, is a Professor and Vice Chairman in the Department of Epidemiology in the School of Public Health at the University of Alabama at Birmingham. He is an associate editor for the American Journal of Epidemiology, and has a lengthy and distinguished scientific reputation as a researcher, having authored or co-authored over 300 peer-reviewed manuscripts, with an emphasis on injury and ophthalmic epidemiology.

William M. McMahon, MD, is the Chairman of the Department of Psychiatry and a Professor of Psychiatry, Pediatrics, Psychology and Educational Psychology at the University of Utah. His research interests include the genetics and epidemiology of autism, Tourette's Disorder, nicotine addiction, and suicide. He is a Senior Investigator for the Autism Genome Project and is currently Principal Investigator of an Autism Speaks funded follow-up study of the Utah Autism Studies sample.

Kathleen Ries Merikangas, PhD, is a Senior Investigator and Chief of the Genetic Epidemiology Branch in the Intramural Research Program at the National Institute of Mental Health (NIMH). Her research interests have included clinical research on affective disorders and genetic epidemiology.

Lisa Miller, MD, MSPH, is the director of the Disease Control and Environmental Epidemiology Division at the Colorado Department of Public Health and Environment. She is the Co-Principal Investigator of the CDC-funded Colorado sites of the ADDM Network site and the Study to Explore Early Development (SEED). She currently directs epidemiologic programs concerning communicable diseases, environmental health, autism, and muscular dystrophy.

Beverly Mulvihill MEd, PhD, is currently an Associate Professor in the Department of Health Care Organization and Policy and a Research Scientist with the Civitan International Research Center at the University of Alabama at Birmingham. She has been Principal Investigator or Co-Principal Investigator of the Alabama ADDM Network site since 2008. Her research interests include child development; children with and at-risk for disabilities, especially autism spectrum disorders; and early identification, intervention, and inclusion for children in need of special services.

Craig Newschaffer, PhD, is Professor and Chairman of the Department of Epidemiology and Biostatistics at Drexel University School of Public Health. He leads an NIH-funded EARLI Study, which is designed specifically to study pre, peri- and neonatal autism risk factors and biomarkers. He is also a Principal Investigator on other major autism epidemiology initiatives. Prior to focusing his research on autism, he worked extensively in cancer epidemiology.

Joyce S. Nicholas PhD, is an Associate Professor in the Medical University of South Carolina's Department of Medicine, Division of Biostatistics and Epidemiology, with a dual appointment in the Department of Neurosciences. She specializes in neuro-epidemiology, in particular neurodevelopmental and other neurologic conditions. She is a Co-Principal Investigator for the South Carolina ADDM Network site.

Lars Perner, PhD, is an Assistant Professor of Clinical Marketing at the Marshall School of Business of the University of Southern California. His research interests focus on consumer behavior, "win-win" deals, non-profit marketing, and autism subtypes. He currently serves as Chair of the Panel of Persons on the Spectrum of Autism Advisors for the Autism Society.

Sydney Pettygrove, PhD, is an Assistant Professor of Epidemiology, College of Public Health, at the University of Arizona, Tucson. She primarily works on the effects of environmental and occupational exposures on reproductive outcomes including birth defects and developmental disabilities. She is the Co-Principal Investigator of the Arizona ADDM Network site.

Catherine E. Rice, PhD, is an Epidemiologist with CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch and has worked with people with an ASD through teaching, diagnostic assessment, intervention, training, and research. She has been a lead scientist with the ADDM Network since 2001. She works on public health programs related to autism with specific interests in early identification, diagnosis, prevalence, and risk factors for autism.

John Elder Robison is a self-identified "free range" Aspergian male. He is the founder of a specialty automobile company, pioneered specialty guitars for the band KISS, and worked on some of the first talking toys for Milton Bradley. He serves as adjunct faculty in the department of Communication Sciences and Disorders at Elms College in Massachusetts and has served on several national autism science boards as a community member. He is the author of Look Me in the Eye: My life with Asperger's.

Michael Rosanoff, MPH, is the Associate Director of Public Health Research and Scientific Review for Autism Speaks. He is a member of Autism Speaks etiology team and manages the organization's epidemiology and public health research grants. He is also the staff lead in overseeing the International Autism Epidemiology Network (IAEN) and is part of the development team for the Global Autism Public Health Initiative (GAPH).

Diana E. Schendel, PhD, is Lead Health Scientist and Epidemiology Team Lead with the CDC's National Center for Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. She serves as Principal Investigator for the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) which includes the Study to Explore Early Development (SEED). She is Project Lead for the International Collaboration for Autism Registry Epidemiology (iCARE). Her research interests include risk factors for cerebral palsy and autism.

Laura A. Schieve, PhD is an Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. Dr. Schieve is one of the Principal Investigators on the CDC's Study to Explore Early Development (SEED). Her current research includes prevalence of autism and other developmental disabilities, maternal and perinatal risk factors for developmental disability, health care needs and family functioning in families with a disabled child, and epidemiologic methods for assessing maternal and child risk factors in populations.

Stuart K. Shapira, MD, PhD, is a Medical Officer with CDC's National Center on Birth Defects and Developmental Disabilities, Pediatric Genetics Team. He is an investigator on the CDC Study to Explore Early Development (SEED). His current interests include birth defects epidemiologic research, dysmorphology of autism, gene and nutritional interactions for adverse reproductive outcomes, and newborn screening.

Paul T. Shattuck, PhD, is an Assistant Professor at the George Warren Brown School of Social Work at Washington University in St. Louis. Dr. Shattuck conducts research aimed at improving systems of care and services for people with autism and their families. He is especially interested in two key service transitions: getting a diagnosis in early childhood and exiting high school in adolescence.

Ezra Susser, MD, DrPH, is Professor of Epidemiology and Psychiatry at Columbia University. Dr. Susser heads the Imprints Center for Genetic and Environmental Lifecourse Studies, a collaborative birth cohort research program in which epidemiologists seek to uncover the causes of a broad range of disease and health outcomes, including psychiatric and neurodevelopmental disorders, obesity, cardiovascular disease, reproductive performance, and breast and ovarian cancers. His own studies focus on schizophrenia and autism.

Alison Singer, MBA, is Co-Founder and President of the Autism Science Foundation, a not-for-profit organization that funds autism research and serves to increase awareness of ASDs and the needs of individuals and families affected by autism. She has been very involved in advocacy for autism as the mother of a child with autism and legal guardian of her adult brother with autism. She spent 14 years at CNBC and NBC in a variety of positions, including vice president of programming in NBC's cable and business development division and as a producer. Ms. Singer has served on several research, advocacy, and government advisory boards for autism.

Caroline M. Tanner, MD, PhD, FAAN, is Director of Clinical Research at the Parkinson's Institute in Sunnyvale, California, a Visiting Professor at Xuan Wu Hospital and Capital University in Beijing, China, and an Adjunct Professor in the Department of Health Research and Policy at Stanford University. Her current research includes epidemiologic investigations of the genetic and environmental determinants of Parkinson's disease, multiple system atrophy, dystonia, Huntington's disease and essential tremor in a variety of populations in the US.

Kim Van Naarden Braun, PhD, is an Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch and with the New Jersey Department of Health and Senior Services. She is the Principal Investigator for the Metropolitan Atlanta Developmental Disabilities Surveillance Program (MADDSP) and also serves an epidemiologist for the ADDM Network and the ADDM Cerebral Palsy Network. Research interests include developmental disabilities, perinatal epidemiology, genetic epidemiology, environmental health, and child health and development.

Susanna Visser, MS, is the lead Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Child Development Studies Team. Her current research interests include population-based epidemiological studies of neurobehavioral and mental health conditions, including ADHD and Tourette Syndrome, medication treatment among youth with ADHD, and factors associated with ADHD medication treatment.

Gayle Windham, PhD, is a Research Scientist and Chief of the Epidemiological Surveillance Section at the California Department of Public Health in the Division of Environmental and Occupational Disease Control. She currently works with the Centers for Autism and Developmental Disabilities Research (CADDRE) team and is the lead investigator on a study of early ASD prevalence in California. Her areas of research and expertise include children's health in relation to environmental risk factors, pregnancy outcomes such as spontaneous abortion and fetal growth, and other aspects of reproductive health including puberty, infertility, and menstrual function.

Martha S. Wingate, DrPH, is an Assistant Professor at University of Alabama at Birmingham in the Department of Health Care Organization and Policy. She is the Co-Principal Investigator of the Alabama ADDM Network site. Much of her work focuses on preterm birth, fetal and infant mortality, racial and ethnic disparities in birth outcomes, and health policies related to pregnancy and infant health.

Marshalyn Yeargin-Allsopp, MD, is a Medical Epidemiologist and Branch Chief with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. She designed and implemented the first U.S. population-based study of developmental disabilities in school-age children in an urban area, which has served as the basis for the ADDM Network and the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE). She has presented internationally and published extensively on the epidemiology of developmental disabilities, including autism and cerebral palsy.

Paula Yoon, MPH, ScD, is currently the Team Lead for the Health Services Research and Registries Team in the Division for Heart Disease and Stroke Prevention, Epidemiology and Surveillance Branch. She is also leading an initiative to establish a National Cardiovascular Disease Surveillance System. She is the Chair of the Surveillance Science Advisory Group at CDC and is spearheading an effort to develop an agency-wide surveillance report to track the impact of health care reform on prevention in health care.

Matthew Zack, MD, is a Medical Epidemiologist with the CDC's National Center for Chronic Disease Prevention and Health Promotion, Division of Adult and Community Health, State Support, Arthritis, Epilepsy, & Quality of Life Branch. He has worked extensively on issues related to chronic diseases and environmental health.

Walter Zahorodny, PhD, is a clinical psychologist and Assistant Professor of Pediatrics at the New Jersey Medical School. He has over twenty years of experience in pediatric neurodevelopment and is the Principal Investigator of the New Jersey ADDM Network site for population-based ASD surveillance system. He is a founding member of the New Jersey Medical School Autism Center and was instrumental in development of the New Jersey Governor's Council on Medical Research and Treatment of Autism.

Judith Pinborough Zimmerman, PhD, CCC, is an Assistant Professor in the Department of Psychiatry at the University of Utah. She is the for the Utah Registry for Autism and Developmental Disabilities (URADD) and the Principal Investigator for the Utah ADDM Network site. She is particularly interested in the utility of ASD prevalence data for state Maternal and Child Health Programs.

## RECORDERS

Carrie Arneson, MSc, serves as Project Coordinator for the Wisconsin ADDM Network site located at the Waisman Center at University of Wisconsin-Madison.

Jon Baio, EdS, is an Epidemiologist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. He currently serves as Principal Investigator on the ADDM Network, studying the prevalence of autism and other developmental disabilities in several communities throughout the U.S.

Thomas A. Bartenfeld, PhD, specializes in program evaluation with the CDC's National Center on Birth Defects and Developmental Disabilities. His most recent work has focused on using evaluation to promote information to action and organizational integration with NCBDDD's surveillance, research, and prevention programs.

Robert Fitzgerald, MPH is currently a staff scientist in the Department of Psychiatry at the Washington University School of Medicine in St. Louis, and is a PhD candidate in Epidemiology at the St. Louis University School of Public Health. He has served as Project Coordinator for the Missouri ADDM Network site since its inception in 2003 and has served as Co-Principal Investigator since April of 2009.

Lydia King, PhD, is an Assistant Professor of Pediatrics at the Medical University of South Carolina and is an Epidemiologist specializing in ASDs. She has served as the Project Coordinator for the South Carolina ADDM site since 2003. She is also Faculty Director for the Global Education Masters in Clinical Research Program.

Keydra Phillips, MSc, is a Health Scientist with the CDC's National Center on Birth Defects and Developmental Disabilities, Developmental Disabilities Branch. She is a member of an interdisciplinary team of researchers of the ADDM Network, and her research interests include public health informatics and surveillance of chronic diseases.

Andria M. Ratchford, MSPH, has served as the Project Coordinator for the Colorado ADDM Network site at the Colorado Department of Public Health and Environment since 2002. She has considerable surveillance and project management experience through her experience with ADDM and the Colorado Center of Autism and Developmental Disabilities Research and Epidemiology (CADDRE) activities.

Anita Washington, MPH, is a Research Public Health Analyst with Research Triangle Institute (RTI) as part of the Atlanta Regional Office. For the past 6 years, she has been working as a contract employee in the role of the ADDM Network Project Coordinator for CDC's National Center on Birth Defects and Developmental Disabilities, Division of Birth Defects and Developmental Disabilities, Developmental Disabilities Branch.

**Invited participant unable to attend remotely or in-person at last minute due to unforeseen circumstances.*

# Appendix C: Reference List

References were compiled based on panel member nominations for suggested background reading on ASD prevalence.

Panel members were asked to read the articles indicated with an * prior to the workshop.

## ASD Prevalence Reviews


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# Notes

# Notes

Centers for Disease Control and Prevention
www.cdc.gov/autism
cdcinfo@cdc.gov
1-800-CDC-INFO

Autism Speaks
www.autismspeaks.org
research@autismspeaks.org
1-212-252-8584

CS225567

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**Sent:** 13 May 2013 19:15:29 -0400
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**Subject:** Updated ADDM Meeting Agenda
**Attachments:** ADDM Network Meeting Agenda for May 14-16 2013.docx

Hi everyone,
I made a few updates to the agenda. I'll see everyone in the lobby of the hotel at 7:50am tomorrow.

Thank you,
Anita

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**From:** Washington, Anita (CDC/ONDIEH/NCBDDD)
**Sent:** Wednesday, May 08, 2013 7:29 PM
**To:** 'Eric Lott'; mslay@uab.edu; Julie K Preskitt (preskitt@uab.edu); kirby S. Russell (CDC health.usf.edu); 'Chris Cunniff'; 'Sydney Pettygrove'; 'kgotscha@email.arizona.edu'; Mancilla, Kristen M C - (kclancy); Lopez, Maya L; Thaer Baroud; Hudson, Allison; Ghosh, Tista (CDC state.co.us); Kast - CDPHE, Kelly; Li-Ching Lee; 'achang@jhsph.edu'; Fitzgerald, Robert; 'John Constantino'; 'Josephine P Shenouda'; 'zahorodn@umdnj.edu'; Daniels, Julie L; 'Jane Charles'; 'Joyce Nicholas'; 'Walter Jenner'; 'Lydia King'; 'Carpenter, Laura Arnstein'; William McMahon; Deborah Bilder (Deborah.Bilder@hsc.utah.edu); 'AMANDA BAKIAN'; colin.kingsbury@hsc.utah.edu; 'Maureen Durkin'; 'Carrie Arneson - WI (clarneso@wisc.edu)'; kalkbren@uwm.edu; amy@ursid.com; 'mmorrie@emory.edu'; Talboy, Amy (Amy.Talboy@choa.org); Wright, Victoria (CDC/ONDIEH/NCBDDD);

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**Cc:** Washington, Anita (CDC/ONDIEH/NCBDDD)
**Subject:** ADDM Meeting Agenda

Hi Everyone,

Please see attached the final agenda for our meeting. If you have any questions please let me know.

Thanks,
Anita

Anita Washington, MPH
Health Scientist
National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention
1600 Clifton Road, MS E-86
Atlanta, Georgia 30333
(Overnight delivery: 1825 Century Blvd. NE, Room 3093, Atlanta, GA 30345)

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**Telework: Thursday – 678-984-4698**

**Autism and Developmental Disabilities Monitoring (ADDM) Network**
**Agenda for May 2013 Investigator Meeting**
**Building 19, Tom Harkin Global Communications Center**
**Centers for Disease Control and Prevention**
**Atlanta, Georgia**
**May 14-16, 2013**

## Tuesday, May 14 (Distance Learning Auditorium)*

| Time | Topic | Presenter | Room |
|---|---|---|---|
| **8:00 - 8:30** | **Arrive at CDC and check-in / load presentations** | | |
| **8:30 - 8:45** | **Welcome and introductions** | Jon Baio | **DLA*** |
| **8:45 - 10:00** | **Preliminary SY2010 ASD prevalence data**<br>a. Preliminary findings<br>b. Topics to highlight in manuscript<br>c. SY2010 ASD prevalence reporting and trend comparisons | Jon Baio | **DLA** |
| **10:00 - 10:15** | **Break** | | |
| **10:15 - 11:30** | **Preliminary SY2010 Early ADDM ASD prevalence data**<br>a. Preliminary findings<br>b. Topics to highlight in manuscript<br>c. Options for reporting Early ADDM ASD prevalence results | Daisy Christensen | **DLA** |
| **11:30 - 1:00** | **Lunch** (CDC cafeteria or Emory Point across from CDC)<br>**CP SIG working lunch** (neuroimaging discussion) | | **116** |
| **1:00 - 1:45** | **Preliminary SY2010 ID surveillance data** | Sydney Pettygrove | **DLA** |
| **1:45 - 2:30** | **Preliminary SY2010 CP surveillance data** | Daisy Christensen | **DLA** |
| **2:30 - 2:45** | **Break** | | |
| **2:45 - 4:00** | **Denominator discussion**<br>a. Curtailing for SY2010<br>b. Planned discussions with concerned parties; Trend analyses<br>c. Manuscript on choice of denominator | <br>Jon / Daisy<br>Kim Van Naarden Braun<br>Amy Kalkbrenner | **DLA** |
| **4:00 - 4:45** | **Miscellaneous discussions**<br>a. Updated confidentiality policy for SY2012/ARCHEv4<br>b. Public use datasets<br>c. Informal discussion of community outreach activities in ADDM sites, new ideas for data dissemination | <br>Anita Washington<br>Jon Baio<br>(moderator TBD) | **DLA** |
| **5:00** | **A walk in the park** (meet at Emory Conference Center) | | |
| **6:30** | **Group dinner at Highland Tap** (meet at Emory Conference Center) | | |

**Autism and Developmental Disabilities Monitoring (ADDM) Network**
**Agenda for May 2013 Investigator Meeting**

**Wednesday, May 15**

| Time | Topic | Presenter | Room |
|---|---|---|---|
| **8:30 - 9:00** | **Arrive at CDC and check-in / load presentations** | | **CDC** |
| **9:00 - 10:30** | **Methodologic analyses and evaluations in-progress** | | **247/248** |
| | a. ICD and exceptionality DNR | Kim Van Naarden Braun | |
| | b. Sensitivity analysis | Julie Daniels | |
| | c. Trigger analysis | Carrie Arneson | |
| **10:30 - 10:45** | **Break** | | |
| **10:45 - 11:45** | **Scientific analyses and evaluations in-progress** | | **247/248** |
| | a. DSM-IV and discriminator analysis | Sydney Pettygrove | |
| | b. Manuscript on maternal prenatal weight gain | Deb Bilder | |
| | c. NC spatial time trend analysis | Julie Daniels | |
| **11:45 - 1:00** | **Lunch** (CDC cafeteria or Emory Point across from CDC)<br>**Available meeting rooms : 245 and 246** | | |
| **1:00 - 1:45** | **SY2012 timeline and updates** | | **247/248** |
| | a. Abstraction and clinician review | Anita Washington | |
| | b. Phase 4 ADDM FOA | Jon Baio | |
| **1:45 - 2:45** | **Workgroup formation** | | **247/248** |
| | a. Reconstituting the Spatial Analysis Workgroup | Amanda Bakian | |
| | b. Charge for a DSM-5 Workgroup | Jon Baio | |
| | c. Updates on DSM-5 transition | L. Carpenter & C. Rice | |
| **2:45 - 3:00** | **Break** | | |
| **3:00 - 3:30** | **SharePoint system for tracking proposals and analyses in-progress** | Leah Franklin | **247/248** |
| **3:30 - 5:00** | **Break-out session for Principal Investigators on datasharing policy** | Jon Baio | **247/248** |
| | a. Satisfaction with proposal submission/approval process | | |
| | b. Tracking site-specific analyses | | |
| | c. Ideas for new tracking system | | |
| **3:30 - 5:00** | **Break-out session for Project Coordinators** | Anita Washington | **245** |
| | a. QC Workgroup | Lisa Barritt | |
| | b. Training needs (Abstraction/Clinician Review) | Lisa Barritt | |
| | c. ARCHE v4 | E. Augustus & K. Jolly | |
| | d. ASD and CP Community Reports | Leah Franklin | |
| | e. Manuscript ideas? | Anita Washington | |
| **6:00** | **Small-group dinners at various Emory Point restaurants** | | |

## Autism and Developmental Disabilities Monitoring (ADDM) Network
## Agenda for May 2013 Investigator Meeting

**Thursday, May 16**

| Time | Topic | Presenter | Room |
|---|---|---|---|
| 8:30 - 9:00 | Arrive at CDC and check-in | | **CDC** |
| **9:00 - 12:00** | **ADDM Paper Group (9:00-9:30)**<br>Multi04: Follow-up on parental age and birth order on the prevalence of ASD using 2002, 2006, and 2008 | | **246** |
| | **ADDM Paper Group (9:30-10:00)**<br>Multi12: Follow manuscript on the association between the prevalence of ASD and SES, 2002-2008 | | **246** |
| | **ADDM Paper Group (10-10:30)**<br>Multi24: Trends over time (2002-2008) in the association between the prevalence of ASD and 2000 and 2010 census based measures of SES | | **246** |
| | **ADDM Paper Group (10:30-11)**<br>Multi22: Relationship between ASD prevalence and ADDM Network catchment area characteristics, 2002-2008 | | **246** |
| **12:00 - 1:00** | **Lunch** (CDC cafeteria or Emory Point across from CDC) | | |
| **1:00 - 5:00** | **ADDM Paper Groups / Atlanta Community Engagement Event** | | |

**From:** Grosse, Scott (CDC/ONDIEH/NCBDDD)
**Sent:** 1 Feb 2014 15:25:20 -0500
**To:** 'K.K. Lam, Ph.D.';Comeau, Anne;Alex Kemper, M.D.;Aaron Goldenberg PhD;'Nancy Green MD (nsg11@columbia.edu)';Ojodu, Jelili (CDC aphl.org);Lisa Prosser PhD;Susan Tanksley PhD
**Cc:** Sarkar, Debi (HRSA);Vasquez, Lisa (HRSA);Stephanie Mascaro;Scott, Joan (HRSA);Jeff Botkin (Jeffrey.Botkin@hsc.utah.edu);Boyle, Coleen (CDC/ONDIEH/NCBDDD)
**Subject:** New article from the EU
**Attachments:** Cornel EJHG 2014.pdf

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3865414/

I just came across this open-access article in the European Journal of Human Genetics authored by Martina Cornel and colleagues, including Stephanie Weinreich. It is the product of several years of work supported by the EU. It presents a proposal that the EU establish a committee not dissimilar to the SACHDNC and follow a comparable process of evidence review and synthesis, working in collaboration with the SACHDNC and other groups. I was pleased to see that they mention economic considerations.

Scott

European Journal of Human Genetics (2014) 22, 12–17
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EJHG Open

POLICY

# A framework to start the debate on neonatal screening policies in the EU: an Expert Opinion Document

Martina C Cornel*[,1], Tessel Rigter[1], Stephanie S Weinreich[1], Peter Burgard[2], Georg F Hoffmann[2], Martin Lindner[2], J Gerard Loeber[3], Kathrin Rupp[2], Domenica Taruscio[4] and Luciano Vittozzi[4]

**The European Union (EU) Council Recommendation on rare diseases urged the member states to implement national and EU collaborative actions to improve the health care of rare disease patients. Following this recommendation, the European Commission launched a tender on newborn screening (NBS) to report on current practices of laboratory testing, form a network of experts and provide guidance on how to further implement NBS screening in a responsible way, the latter of which was provided in an Expert Opinion document. After consultation of experts from EU member states, (potential) candidate member states and European Free Trade Association countries, in a consensus meeting in June 2011, 70 expert opinions were finalized. They included the need to develop case definitions for all disorders screened for to facilitate assessment and international outcome studies. Decision whether a screening program should be performed can be based on screening criteria updated from the traditional Wilson and Jungner (1968) criteria, relating to disease, treatment, test and cost. The interest of the child should be central in the assessment of pros and cons. A European NBS body should assess evidence on (new) screening candidate disorders. For rare conditions, best level evidence should be used. The health system should ensure treatment to cases diagnosed by screening, controlled and revised by follow-up outcome studies. Screening methodology should aim to avoid unintended findings, such as mild forms and carrier status information, as much as possible. Activities to improve NBS in Europe, such as training and scientific evaluation, could benefit from collaboration at EU level and beyond.**
*European Journal of Human Genetics* (2014) **22,** 12–17; doi:10.1038/ejhg.2013.90; published online 8 May 2013

The European Union (EU) Council Recommendation[1] on Rare Diseases (9 June 2009)[2] identified rare diseases (ie, a life-threatening or chronically debilitating condition affecting not more than five in 10 000 persons in the community) as a public health concern and highlighted the need for public health actions, promoting the development of research on rare disorders and the improvement of the health care of rare disease patients. Following this recommendation, the European Commission launched a tender on neonatal screening ( = newborn screening, NBS) in July 2009 (http://ec.europa.eu/eahc/health/tenders_H09C2.html) in order to (1) report on the practices of neonatal screening for rare disorders implemented in all the member states, including number of centers, estimate the number of infants screened and the number of disorders included in the NBS, as well as reasons for the selection of these disorders, (2) to identify types of medical management and follow-up implemented in the member states, (3) to establish a network of experts analyzing the information and formulating a final opinion containing recommendations on best practices, and recommending a core panel of NBS conditions that could be included in all MS practices, and (4) to develop a decision-making matrix that could be used by member states' programs to systematically expand (or contract) screening mandates.

The focus of the tender activities was on NBS by using laboratory testing techniques (blood spot screening). All reports are available on the internet (http://www.iss.it/cnmr/prog/cont.php?id=1621&lang=1&tipo=64).

To get some insight into the current practices (points 1 and 2 above), an online survey was compiled and filled out by EU member states, (potential) member states and European Free Trade Association countries – in total 40 countries. Apart from the final report, available on the internet, the current practices are summarized in two journal articles: the first publication addresses the steps in screening programmes from blood spot to screening result[3] and the second publication addresses the steps from screening laboratory results to treatment, follow-up and quality assurance.[4]

As a third part of the activity and work methodology requested by the tender specifications, a European Union Network of Experts on Newborn Screening (EUNENBS) had to be constituted. Criteria for the inclusion of experts in EUNENBS (http://www.iss.it/cnmr/prog/cont.php?id=1621&lang=1&tipo=64) include that all member states' authorities should be represented in the network. Each countries' competent authorities were invited to identify their experts to represent the country at the workshops in 2010 and 2011. Further experts represent European professional and scientific organizations involved in NBS, the representative of the US Secretary's Advisory Committee on Heritable Disorders in Newborns and Children, additional fields of expertise (eg, ethics) and patient organizations. The list of EUNENBS members is available as Appendix 1 of the Expert Opinion document (http://www.iss.it/cnmr/prog/cont.php?id=1621&lang=1&tipo=64). Most EUNENBS members have a background in health policy making, health technology assessment

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(HTA) and/or coordinating screening programs, many are involved in the service delivery of NBS in pediatrics, laboratory medicine and genetics. The task of EUNENBS was to supervise the work of the tender and participate in the revision of the tender deliverables, including the Expert Opinion document. The EUNENBS members have provided informally their input and advice without implying any obligation or commitment of their national authorities or organizations. Working documents were prepared reviewing most relevant scientific literature on the development of NBS policy and submitted to EUNENBS to stimulate the discussion during its meeting held on 6–7 December 2010, where the future of NBS was discussed in a workshop. Conclusions were integrated in a draft of the Expert Opinion document that was circulated by e-mail on 9 March 2011 to the membership of EUNENBS and to European Union Committee of Experts on Rare Diseases members from the Candidate and European Economic Area/European Free Trade Association countries inviting comments. This consultation ended on 6 April 2011. The preparation of the second draft, integrating the suggestions received, took place until 6 May 2011. Before the consensus meeting on 20 and 21 June 2011 in Luxembourg, the document was circulated for a second consultation, which took place from 11 to 27 May 2011, and amended considering the comments received. The Expert Opinion document was endorsed by the Boards of the International Society for Neonatal Screening and the European Society of Human Genetics in August and October 2011.

Experiences from other countries have served as useful sources, although their applicability may need to be checked against information from EU countries and agreement needs to be sought with EUNENBS. This article presents the 70 Expert Opinions, resulting from the debate among the EUNENBS members with respect to the elements that are part of a system to evaluate the quality and ethical aspects of neonatal screening in the light of available literature, as well as the proposal for a decision matrix. We furthermore provide a brief discussion.

## RESULTS 1: EXPERT OPINIONS

### Governance of neonatal screening

1. Screening is different from diagnostics. Screening is offered to people who either do not have or have not recognized the symptoms of the disease(s) that the screening relates to. A screening test is not intended to be diagnostic. Screening aims to identify people at sufficient risk to benefit from referral for diagnostics.
2. Haven taken notice of the fact that a European body for the HTA will be developed (European Network for Health Technology Assessment),[5,6] the EUNENBS recommends a committee for neonatal screening.
3. This EU NBS committee should summarize the scientific developments (evidence, economics and ethics)[7] and advice transparently. It should update relevant information at national and European level. In addition, because it will gather the widest expertise on NBS at the EU level, it should act as a central point for any stakeholder (eg, learned societies, industry and patient groups) to propose and discuss new NBS procedures.
4. The EU NBS body should promote synergies and best practice guidelines on policies concerning consent, storage of samples, pretest information for parents, etc. (benchmarking, reviewing, updating and so on).
5. The body should have a clear governance structure and accountability. It should have a role in offering advice to (national) policy makers.
6. In each country, national bodies should assess the country-specific factors, including epidemiological, economical, ethical and legal issues, and perform the monitoring and evaluation of the program.
7. A formalised decision process is needed to start the HTA of a screening and to re-evaluate the evidence for screening either periodically or on demand.
8. Actors to be involved in NBS decision making include patients' and parents' organizations, laboratory scientists, health-care workers and professional organizations, ethical, legal and economic experts, governmental and non-governmental agencies and health-care providers.
9. The role of industry, commercial parties or industrial researchers should be limited to consultation.
10. Existing examples of written policies should be translated and published, so that they could serve as examples for the countries that do not have such policies yet, but which are considering their development. The criteria used by national committees when considering new screening programs should be published. The examples of policies should cover both national and European practices in a way that could allow the assessment of trans-border issues (eg, equipment-related issues, access to relevant new technologies and appropriate screening for people moving from one country to another).
11. Systems should be in place within the EU to learn from potential generic adverse incidents that may cross national boundaries, for example, equipment-related issues.
12. Once the EU NBS body is in place and examples of good practices are available, it should be discussed to what extent harmonization of NBS in Europe is possible.

### Criteria to evaluate whether a screening program should be performed

1. There is a clear need to develop and publish agreed case definitions for all disorders screened. There should be an attempt made to achieve agreement on these case definitions within the EU to facilitate assessment and international outcome studies.
2. The decision whether a screening program should be performed can be based on a framework of screening criteria updated from the traditional Wilson and Jungner criteria (W&J), relating to disease, treatment, test and cost.
3. The interest of the child should be central in the assessment of pros and cons.
4. The European NBS body (or the national NBS bodies) should further elaborate the specifications and the operative application of the screening criteria through discussion and agreement with the EU national authorities.
5. HTA to evaluate the evidence on the effectiveness of early detection through neonatal screening and treatment should be achievable in practice. For rare conditions, best level evidence should be used. Methods need to be developed to both optimize health benefit and careful evaluation.
6. Universal screening is generally preferable to ethnical targeted screening. If there are sound reasons (eg, health gain) for targeted screening, it is important to avoid stigmatization.
7. The health system should ensure treatment to all confirmed cases diagnosed by screening. In case of suboptimal availability of treatment, it should plan to make treatment available for all confirmed cases (based on common values and principles in EU Health Systems (universality and access to good quality care)).

8. Systems should be developed in order to support universal screening in countries where it would be beneficial, but not affordable, for economic and/or social reasons.
9. Systems should be put in place by the EU for helping the countries, where treatment is not available yet for all confirmed cases. The target of treatment for all confirmed cases should be achieved without reducing the quality of treatment.
10. The European NBS body (or the national NBS bodies) should consider other potential advantages, especially (a) avoiding a diagnostic odyssey and (b) informed reproductive choice for the next pregnancy(ies) of the parents, and later for the child, and the provision of genetic counseling to the family.
11. Screening methodology should aim to avoid unintended findings, such as cases with mild forms of the disorder screened for and information on carrier status, as much as possible.
12. If unintended results are found (such as carrier status), member states need to consider carefully how results are communicated. Parents need to be informed adequately in a way that is consistent with the individual data protection rights and the right to privacy, as well as patient rights. (Pretest information is discussed in Chapter 5 of the Expert Opinion document)(http://www.iss.it/cnmr/prog/cont.php?id=1621&lang=1&tipo=64.)
13. Economic evaluations of NBS programs are needed. Balancing the right to care of all patients' needs to take rare disorders into account.
14. Even if a program may be cost effective in the long run, the initial costs may represent a barrier to start. Raising specific initial funding should be considered.
15. Systems should be in place at EU level in order to support the countries, which for reasons of economic development might have difficulties in covering those initial costs.

**Criteria on how a screening program should be performed**

1. Before the start of an NBS program, all health-care professionals involved must be offered adequate training and sufficient participation must be achieved.
2. The provision of information needs to be organized at program management level by public health authorities and is the responsibility of the NBS program management. This should be developed in collaboration with the relevant users.
3. The information contents and communication guidelines should be defined at program management level; it may take advantage from sharing existing examples and experiences.
4. Sufficient general information on NBS should be given to prospective parents, starting during pregnancy. This could also come up in preconceptional care. Detailed information should be available upon request. On a program level, the responsibility for this pretest information needs to be clarified: public health authorities could mandate obstetric-care providers.
5. Evidence-based patient information on NBS in appropriate language should be made available on websites of the institutions responsible for the screening.

**Informed consent**

1. NBS must be offered to all infants in the EU.
2. It should be offered as a service governed by appropriate legal provisions, which also ensures compliance with quality requirements of other legislation (such as patient's rights, personal data protection, biobanks, research approval by ethics committee, genetic testing and genetic counseling). The health-care system should cover the costs.
3. The importance of NBS in the best interest of their child should be clarified to parents. Participation should be voluntary.
4. A specific consent should be sought for activities not strictly related to the benefit of the newborn, such as the use for research purposes.
5. The informed consent protocols should be defined at jurisdictional level, in consultation with the appropriate stakeholders; it may take advantage from sharing existing examples and experiences.

**Blood spot sampling**

1. Blood spot sampling between 48 and 72 h is preferable for most disorders in NBS programs.
2. Uptake needs to be monitored, an uptake of 100% is pursued. If informed consent is taken seriously, this value may not be reached.
3. Systems should be in place to maximize uptake and ensure that babies are not missed
4. Systems should be in place to deal with the families moving into the area and crossing national boundaries to ensure that appropriate screening has been carried out or is offered.

**Laboratory procedures**

1. The target values and benchmarks ensuring the quality and efficacy of laboratory procedures should be defined at program management level;
2. The development of laboratory procedures should take advantage from sharing existing examples and experiences.
3. Defined screening protocols should be published by each member state and reviewed every 1–5 years or on demand in case of recognized developments.
4. Test turnaround time within the laboratory should be kept short: for example, a maximum of 48 h is recommended.

**Blood spot storage**

1. Blood spots need to be stored for quality control in the NBS screening laboratory for at least 5 years.
2. Blood spot storage should ensure appropriate protection of sensitive personal information and of biological samples (eg, compliance with the relevant regulations).
3. Informed consent should be asked, at least for activities not strictly related to the benefit of the newborn, such as storage for quality control and research. For use of the blood spot after 18 years, the child should have the possibility to consent or dissent.
4. Use of blood spots for research purposes is subject to national specific ethical regulations (eg, definition of research objectives and timing, informed consent and approval by the ethical committee). The potential interest for research and the possible misuse of residual NBS specimens have increased the need for regulation of specimen storage and access policies at the European level for both ethical and legal reasons. At the European level, major differences in regulations should be avoided in view of trans-border health care and international research.

**Communication of positive result**

1. Communication of the need for additional clinical investigations should be preferably carried out by specialists. In case good information has been provided to parents before the sampling/birth, this communication may be carried out also by non-experts, if clearly instructed what to communicate.
2. The information contents and communication guidelines, for the communication of the need for additional clinical investigations to parents, should be defined at program management level and published; there may be advantages to sharing existing examples and experiences.
3. For every positive NBS result a diagnostic confirmation test, performed by established laboratory methods according to predefined standards, must take place, for most disorders within 24 h or the next working day after communicating a positive screening result.
4. Communication means should ensure timely delivery to parents, with check on receipt and understanding. Communication of any result, including negative results, may contribute to quality control and parental well-being.

**Confirmation of diagnosis and treatment**

1. Defined 'diagnostic protocols' should be developed, which relate directly to the case definition. Protocols on whom to treat as patient, including referral to clinical services, should be available at program level.
2. Protocols for confirmation of diagnosis and guidelines for treatment should be defined at program management level; there may be advantages to sharing existing examples and experiences.
3. Communication after a confirmed diagnosis is extremely important. Personal communication by physicians can be supported by information from accredited webportals.

**Communication of unintended findings**

1. Parents should be given the possibility to be informed of any unintended finding that could be relevant, to the extent this is consistent with laws, individual data protection rights and the right to privacy.
2. Different positions have been taken in the debate on unintended findings. Discussion is needed in countries to develop policy and legislation, if appropriate. This should be published.
3. As far as unintended but relevant information for the health of the child or mother is concerned, parents should be given the possibility to be informed. For the return of information on carrier status, a separate decision, consistent with other relevant national health regulations, is needed in each country. This is because carrier information is mainly important for reproductive choice of the parents and not directly for the health of the screened newborn. The content of the information and guidelines for its communication to parents should be defined at program management level; it may take advantage from sharing existing examples and experiences.

**Quality assurance of laboratory results**

1. NBS laboratories should be certified and participate in external quality assurance/control programs. The EU NBS committee should advise on EQA and poor performance, and offer educational support to poorly performing laboratories.
2. Within a jurisdiction the number of laboratories should be limited. Optimal quality performance and cost effectiveness requires a minimum number of samples handled, such as 30 000–50 000 samples per year.

**Screening program evaluation**

1. The quality of the process of the program needs to be monitored regularly (possibly annually) to allow the identification of steps requiring improvement and the adoption of appropriate corrective measures. Results should be made available by open access.
2. Evaluation of specific aspects of NBS programs must be considered for aspects other than those regularly monitored, such as recently changed information policies.
3. Databases are needed to monitor and evaluate the program. As all NBS conditions are rare, international collaboration may help to facilitate evaluation.
4. Systems should be in place to ensure that feedback of confirmed diagnosis and long-term outcomes are available for program evaluation, also in case of screened children moving abroad.

**Epidemiological evaluation**

1. Collaborative international projects are needed to assess the long-term follow-up of the patients with rare conditions identified in NBS programs. Both evaluation of programs (expert opinion no. 65), and the success of screening and treatment for patients and families are needed. The EU should take a pro-active approach to organize long-term follow-up.

**Features of disorders, which might be considered in the gradual expansion of NBS in EU**

1. Training on all aspects of improving NBS programs should be facilitated at EU level.
2. EU countries should consider the assessment of the first group of disorders (Chapter 5 of the Expert Opinion document) (http://www.iss.it/cnmr/prog/cont.php?id=1621&lang=1&tipo=64) on the basis of local/national conditions in case that they intend to expand their NBS. This process and conclusions should be published.
3. The EU NBS body, charged with the assessment of the evidence and possibilities for neonatal screening,[8] might consider initiating its activity with reviewing the evidence for disorders to be screened. For the first group of disorders, several countries have assessed the evidence already. Especially the conditions in the second group (Chapter 5 of the Expert Opinion document) (http://www.iss.it/cnmr/prog/cont.php?id=1621&lang=1&tipo=64), where limited evidence is available or different conclusions were reached need to be prioritized.
4. There is an opportunity to use the moment of blood spot screening for other screening programs concerning, for example, hearing loss, hips, eyes and heart.

## RESULT 2: PROPOSED MODEL OF DECISION-MAKING MATRIX

(1) Does your country or health-care jurisdiction have a neonatal screening program?

  (a) If no: start neonatal screening for congenital hypothyroidism (the reason for the choice of congenital hypothyroidism is twofold: (1) congenital hypothyroidism is (one of) the most prevalent congenital disorders, the prevalence being largely independent of ethnicity; (2) the screening and confirmatory methodology is relatively simple. All European countries that contributed to the current Practices Document (http://www.iss.it/cnmr/prog/cont.php?id=1621&lang=1&tipo=64; refs 3,4) screen for congenital hypothyroidism.).

(2) If YES, consider disorders for which a neonatal screening program exists elsewhere, or for which research shows promising results. For each disorder:

  (a) Can, according to international experience, considerable, irreparable damage be prevented by neonatal screening or other benefits for the patient and the family be achieved? Assessment includes:
    (i) The condition sought should be an important health problem (W&J1).[1]
    (ii) There should be an accepted benefit for patients with recognized disease (W&J2).
    (iii) There should be a recognizable latent or early symptomatic stage (W&J4).
    (iv) The natural history of the condition, including development from latent to declared disease, should be adequately understood (W&J7).

  (b) Is, according to international experience, a good test available? (Sensitivity, specificity, positive predictive value and acceptability) Assessment includes:
    (i) There should be a suitable test or examination (W&J5).
    (ii) The test should be acceptable to the population (W&J6).
    (iii) There should be an agreed policy on whom to treat as patients (W&J8).

(3) If both questions YES, consider desirability in your country/region:

  (a) Is the disorder an important health problem *in your country*?
  (b) Is the test acceptable for the population from cultural/ethical perspective (unintentional findings; carrier status; mild and late-onset forms).

(4) If the previous questions are answered YES, consider the feasibility:

  (a) Compare the burden of the disorders for the health system with the cost of screening, with a view to ensuring equity of access to health care and considering other feasible options.
    (i) The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole (W&J9).
    (ii) What is the birth prevalence of the disorder(s)?
  (b) Can facilities be made available for adequate surveillance, prevention, treatment, education, counseling and social support? Assessment includes:
    (i) Facilities for diagnosis and treatment should be available (W&J3).
    (ii) Case finding should be a continuing process and not a 'once and for all' project (W&J10).
    (iii) Is a good test available in your country?
    (iv) Are sufficient diagnostic specialists available?
    (v) Is treatment available in your country?
    (vi) Are sufficient treatment specialists available?
    (vii) Are there patients' associations which may provide support to the patient and/or the family?

(5) If NBS is considered desirable and feasible, take care of adequate quality of the program, including:

  (a) Training of relevant health-care providers.
  (b) Information to prospective parents.
  (c) Informed consent, both general and specific, on communication of carrier status information and sample storage for research use.
  (d) Procedures for blood spot sampling, laboratory handling and storage of cards.
  (e) Protocols for communication of health-care providers in case of positive results.

## DISCUSSION

Experts from a diversity of backgrounds in health policy making, coordinating screening programs, laboratory and clinic engaged in a series of meetings in 2010 and 2011 to analyze the diversity of NBS practices in EU and other countries and to develop Expert Opinions on NBS policy. NBS programmes are very diverse in these countries. Given the fast technological changes and the increasing possibilities to treat or even cure rare diseases diagnosed after NBS, the importance of developing a reference framework for NBS practices and policy making became clear.

Not only in Europe, also in the USA and other continents NBS is under revision. Horizon scanning, quality control, epidemiological follow-up and other activities may profit from international collaboration, for instance with the USA Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (http://www.thefederalregister.com/d.p/2010-04-26-2010-9625). For the follow-up, it is of great importance that case definitions are the same world-wide (expert opinion no. 13). The International Society for Neonatal Screening could have an important role here.

The analyses and opinions agreed by the EUNENBS experts within this tender have been presented to the European Union Committee of Experts on Rare Diseases. This advisory committee for EU policy on rare diseases is now debating on collaborative solutions to further improve their NBS programs and fill the gaps highlighted in the tender documents without impacting on their national prerogatives in the delivery of care.

Beside the initiatives that will be taken at EU level, the analyses and opinions produced by the tender activities may guide further national policy developments, bilateral and international initiatives.

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