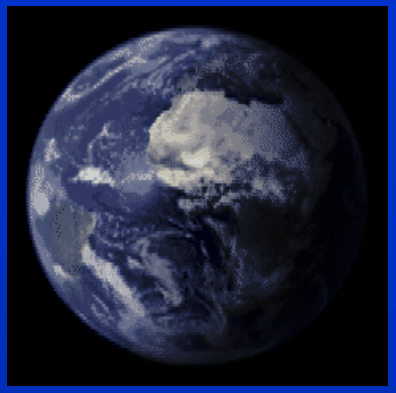

Epidemiology and Autism Speaks: Global Opportunities

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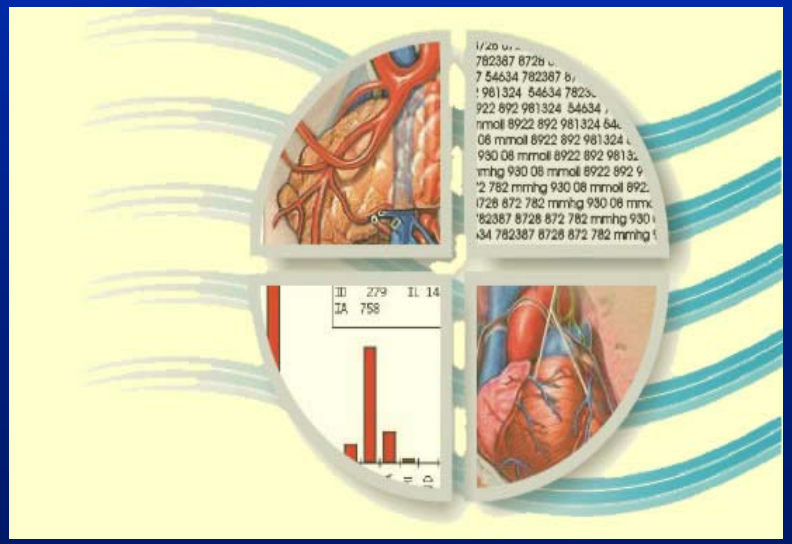
AUTISM SPEAKS™ & cure Autism now FOUNDATION Working Together

Overview

- What is epidemiology?
- Why is it important?
- What kinds of questions can epidemiology answer?
- History of NAAR/AS epidemiology efforts
- International Autism Epidemiology Network
  - Purpose
  - History
    - Summary of 3 meetings
  - Future Direction

What is Epidemiology?

The branch of medicine that deals with the study of the causes, distribution, and control of diseases or disorders in populations.



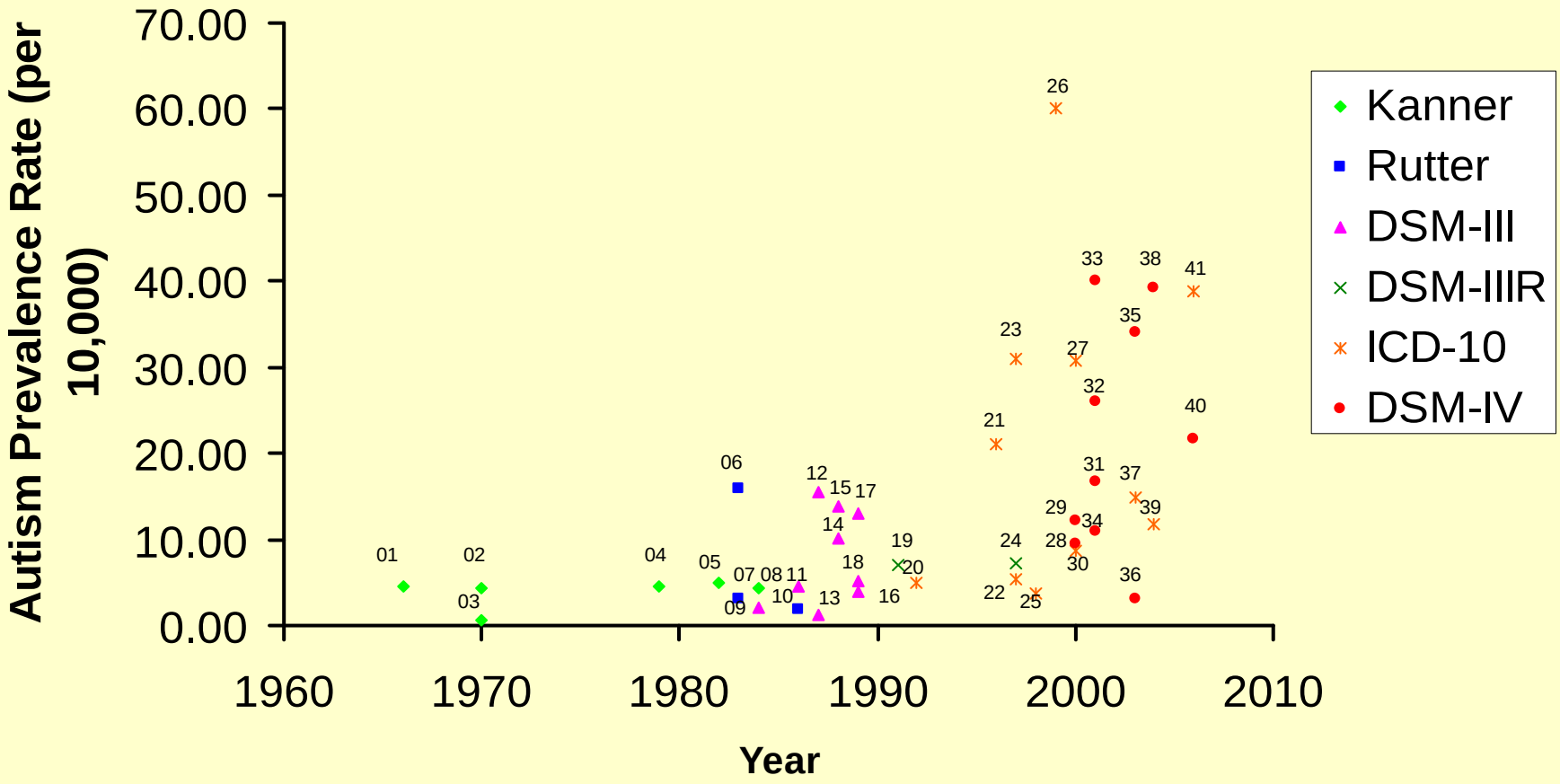
Strengths of Epidemiologic Studies

- Based on entire population, not select groups
- Fewer biases: who is in and who is out
- Often representative of all affected individuals, not just select few
- Allows for international comparisons
- Large sample size increases power to study multiple factors

Examples of questions epidemiology can help to answer

- How common is autism? Is the prevalence similar all around the world? Are some subgroups more affected than others?
- Has the prevalence increased over time and if so, why?
- What are the risk factors/causes of autism?
- How do genes and the environment interact in terms of causation? What are specific environmental “triggers”?
- How common are GI disorders in children with ASD?
- What is the role of immune factors (parental and child) in ASD?
- How to define the broader phenotype?
- How to create homogenous subtypes for basic and clinical studies?
- Which, if any therapies are “effective”?
- Are there public health programs that have unintended consequences , e.g., vaccines?, vitamins (folic acid), etc.

Comparison of Autism Prevalence Rates



Why International Epidemiology?

Is the prevalence the same everywhere?

- Within one country-urban/rural, hot spots
- Across the developed world
- Across the world
- Across latitudes
- Across different ethnic groups
- Across different socioeconomic groups
- Across time

Why International Epidemiology?

Given finite resources, what are the benefits?

- **"Natural experiments"**
  - Novel contrasts in genetic and environmental features applicable to fundamental questions of prevalence and etiology
- **Increased "public will", locally and abroad**
  - Among international partners, attention on results raises awareness of public health burden and may leverage increased local commitment of resources

Why an International Epidemiology Network?

- Epidemiology is the best methodology to study MANY key issues in autism:
  - Environmental factors
  - GI issues

- Resource to help researchers get started with epidemiological studies
- Provide access to information on a variety of systems that can be used around the world to ask various questions about autism

Purpose of the International Autism Epidemiology Network

- Develop network for exchange and collaboration of epidemiology activities across countries
- Examine successful international collaborative models applied to other health conditions and identify common features to facilitate autism surveillance and research
- Identify epidemiology's unique role in understanding causes of autism, particularly in comparisons across diverse genetic and cultural settings

NAAR planning meeting: building an international autism epidemiology network

November 3-4, 2005
Washington DC
22 participants

- Review of ongoing epi studies
  - China
  - Korea and Canada
  - India
  - UK
  - Denmark
  - Sweden
  - Aruba/Curaco
  - Norway
  - US
- Discussion of forming a network
  - Facilitate collaboration
  - Institute standards for epi studies

IMFAR 2006 AS International Epidemiology Planning Workshop II

May 31, 2006
Montreal, Canada
40 participants

- Overview of November meeting and discussion
- Feasibility and approaches to expand epi research, especially in developing countries
- Feasibility and approaches to data sharing
- Vision for the future and next steps
  - **3 working group concept**

Goals of the May 2007 International Autism Epidemiology Network Meeting

May 2, 2007
Seattle, WA

- Network
- Share experiences and epidemiologic methods
- Generate ideas for collaborative or single country international epidemiologic projects

The Autism Epidemiologic Olympics
79 individuals
22 countries

- Australia (2)
- Brazil (1)
- Canada (1)
- China (2)
- Denmark (1)
- Finland (1)
- Iceland (3)
- India (7)
- Kenya (1)
- Korea (1)
- Mexico (1)
- Portugal (1)
- Saudi Arabia (3)
- Scotland (1)
- Spain (1)
- Sweden (1)
- Taiwan (3)
- Thailand (1)
- Uganda (2)
- United Kingdom (4)
- United States (40)
- Venezuela (1)

Challenge: International Field is Uneven

Global diversity in local capacity to support autism epidemiology research

Principles of Global Collaborative Research

- Benefit to target population, especially in low resource settings
- Capacity-building, especially in low resource settings
- Original data maintained by host, data sharing by all
- Locally appropriate measures, comparable data across locales

Format: Three Workgroups

- Records – Based Workgroup
  - Countries with structured services/school records – USA, Korea
- Registry Workgroup
  - Countries with registries – Norway, Denmark, Iceland, Australia
- Screening Workgroup
  - Countries with no structured service – door to door surveillance – Developing World

Records-Based Workgroup

Purpose:

Improve understanding of descriptive epidemiology of the Autism Spectrum Disorders (ASDs)

Question:

- Can a multiple source record review methodology work outside the US?
- How do we determine the feasibility for investigators that are interested in considering this method?

Records-Based Environment

- **Advantages:**
  - Minimal burden on children and families
  - Minimize response bias
  - Population-based, reference rates provide better understanding of occurrence patterns/clues regarding potential risk factors
  - Pool of potential participants for research studies

- **Feasibility considerations:**
  - Local service infrastructure in place
  - Record keeping (completeness, location)
  - Who owns the data in records?
  - Validation possible?

- **Sustainability**
  - Ongoing relationship building

Registry Workgroup

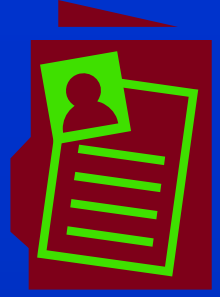
Purpose:

Promote access to, use, and value of population-based registry systems for collaborative activities among members of the international autism research community.

Goals:

- **Enhance knowledge of, accessibility, and use of registry-based research resources related to autism to the autism scientific community through development programs for autism researchers.**
- **Enhance value and quality of registry-based research resources, with a special emphasis on biobanks.**

"Registry"



- Data file of compiled individual information (in a defined population)
  - Disease
  - Other health-relevant condition or characteristic
  - Exposure
  - Biologic specimens (biobanks)
- Established for administrative, service, or research purposes
  - May be product of centralized service delivery or record keeping

Research Value of Registries

- Pre-existing data
  - Independent data collection
    - Avoid reporting bias by participant
  - Economical (time and resource needs)
  - Enriched analytic opportunities through other data linkages
- Often, population-based coverage
  - Representative
- Large size
  - Rare events with enhanced precision
- Ongoing, prospective collection
  - Longitudinal effects
  - Historical cohorts
- Pool of potential participants for further data collection

Research Challenges of Registries

- Questions regarding data quality
  - Completeness
  - Validity
- Availability of data on confounders
- In naïve hands, easily misused
- Biobanks
  - Availability of appropriate technology
  - Specimen quality
- Vulnerable to wax/wane of support (funds, personnel, public/political)

Challenges in Low Income Settings

- Identification of affected children in absence of local child-find infrastructure
- Absence of
  - culturally valid measures
  - locally appropriate identification techniques
- Identification measures adapted to:
  - Low literacy
  - Poor caregiver recognition of relevant behaviors or developmental milestones

Two-Phase Design for Child Identification in Low Income Settings

Screening → Assessment → Weighted analysis

- Good News:
  - Ten Question (TQ) Screen addresses basic methodologic challenges of low income settings
  - Risk factor studies of disability based on TQ identified environmental factors with implications for primary prevention and health care policy

TQ Gaps

- Not designed to identify ASD
- Adaptation of TQ for screening behavioral disorders, e.g. ADHD and ASD, in process
  - Requires more questions

Next Big Challenge → Cross-culturally valid and feasible clinical assessment tools to confirm ASD diagnosis

Screening Workgroup: Developing Countries

Recommendation:

- **Develop a clinical tool for epidemiologic research**
  - a series of workshops to include a core group of clinical experts, epidemiologists, and representatives from several key countries to draft such a tool.
  - pilot studies in at least two different developing country settings to test and improve upon the attributes of the draft tool