Making Sense of Autistic Spectrum Disorders

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January 17, 2014

Etiology, Epidemiology, and Quackery [10:30 -12:00]

- The autism “explosion”
  - Where did it come from? What does it mean?
  - Impact of DSM5
- Causes of ASD: Proven, unproven, and disproven
  - Genetics, and why you should care about it
  - The signs and symptoms of quackery

LUNCH [12:00 – 1:00]

The ASD “Explosion”

- Are we in an epidemic?
- If so:
  - Is there a smoking gun?
  - Are there preventive or therapeutic measures?
- If not:
  - Where did all these kids come from?
  - Where are the “missing” adults?

DEFINITIONS

- Incidence
- Prevalence
- Epidemic
- “Explosion”

Incidence = Rate

- The number of new cases of a disorder, over a specified period of time, in a defined population
  - New cases of Influenza / 100,000 persons / wk
  - Incidence of ASD =
    - Birth rate of newborns who will have ASD +
    - Attack rate of autistic regression among children
  - The Incidence of ASD is Unknown

Prevalence = Proportion

- The percent of the population that is affected, at one point in time
  - The % of people with the Flu at a given time
  - The % of people with ASD
- We do not know the prevalence of ASD. What we know is the number of children being served with a diagnosis of ASD (the “administrative prevalence”).
Administrative Prevalence ("Explosion")

INCIDENCE (Epidemic)

You cannot get a speeding ticket for having a full tank of gas

Scientific Illiteracy

What difference does it make?

- If we are really in an epidemic:
  - Is there a smoking gun?
    - Immunizations
    - Mercury
    - Other?
  - Is there a cure or preventive measure?

Known Causes of Administrative Prevalence of ASD

- Broadening diagnostic criteria
- Broadening Federal service & reporting requirements
- Diagnostic substitution
- Broadening ascertainment methods
Relationship between diagnostic criteria and apparent prevalence

What is the prevalence of “Tall Stature”
- If the cutoff for “Tall” = 7 feet?
- If the cutoff for “Tall” = 6 ft 10”
- If the cutoff for “Tall” = 6 ft 6”
- If the cutoff for “Tall” = 6 ft
- Etc…..

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**DSM III**

<table>
<thead>
<tr>
<th>Yr</th>
<th>Event</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>DSM-III: First appearance of:</td>
<td>6 mandatory, severe criteria for Dx of autism, including:</td>
</tr>
<tr>
<td></td>
<td>- Infantile autism</td>
<td>- Pervasive lack of responsiveness to other people</td>
</tr>
<tr>
<td></td>
<td>- Autism-residual state:</td>
<td>- Gross deficits in language development</td>
</tr>
<tr>
<td></td>
<td>Children who once met criteria for infantile autism but no longer do.</td>
<td>- Bizarre responses to various aspects of the environment</td>
</tr>
</tbody>
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**DSM III-R**

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Comment</th>
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</table>
| 1987 | DSM-III-R:  
+"Infantile autism" replaced by “Autistic Disorder”  
+"Autism-Residual State" replaced by PDD-NOS | PDD-NOS encompasses children who never met full criteria for Autism, as well as children who once met such criteria but improved over time. |

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**DSM IV**

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Comment</th>
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<tbody>
<tr>
<td>1994</td>
<td>DSM-IV:</td>
<td>6 of 12 milder criteria, such as:</td>
</tr>
<tr>
<td></td>
<td>- Three Domains</td>
<td>- Lack of spontaneous seeking to share achievements with other people</td>
</tr>
<tr>
<td></td>
<td>- Social</td>
<td>- Difficulty sustaining a conversation</td>
</tr>
<tr>
<td></td>
<td>- Language</td>
<td>- Lack of varied social imitative play</td>
</tr>
<tr>
<td></td>
<td>- Repetitive Behavior</td>
<td>- Persistent preoccupation with parts of objects</td>
</tr>
<tr>
<td></td>
<td>- Menu of qualifying symptoms</td>
<td>- &quot;No gross delay in language&quot;</td>
</tr>
<tr>
<td></td>
<td>- Asperger’s Disorder first appears</td>
<td>* &quot;Polythetic&quot; approach</td>
</tr>
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### DSM Criteria and the ASD Explosion

![Diagram showing IQ and Atypicality]

1994: DSM-IV
- Menu Dx of Autism
- Asperger Syndrome

#### Shifting epidemiology of ASD

- IQ < 70
- IQ ≥ 70

<table>
<thead>
<tr>
<th>Period</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1950's</td>
<td>2-4/10,000</td>
</tr>
<tr>
<td>2000's</td>
<td>100/10,000</td>
</tr>
</tbody>
</table>

### Autism Spectrum Disorder

**Two Clinical Domains (vs. 3 in DSMIV, and 4 in Kanner)**

A. Deficits in Social Communication and Interaction
   - Combines Social & Language domains
B. Restricted, Repetitive, Behaviors, Interests, and Activities

### DSM5 - ASD

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following,* currently or by history (examples are illustrative, not exhaustive):…

* Doesn’t say “all” of the following: intent unclear

### Social Communication & Interaction

- Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.

Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

DSM5 - ASD

B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive)…

Restricted, repetitive patterns of behavior, interests, or activities

- Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases)

- Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day)

- Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests)
Restricted, repetitive patterns of behavior, interests, or activities

• Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement)

• “Because symptoms change with development and may be masked by compensatory mechanisms, the diagnostic criteria may be met based on historical information, although the current presentation must cause significant impairment.

C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).

D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.

E. These disturbances are not better explained by intellectual disability or global developmental delay.

Note: Individuals with a well-established DSM-IV diagnosis of autistic disorder, Asperger’s disorder, or PDD-NOS should be given the diagnosis of ASD. Individuals who have marked deficits in social communication, but whose symptoms do not otherwise meet criteria for ASD, should be evaluated for social (pragmatic) communication disorder.

ASD vs. Social (Pragmatic) Communication D/O

<table>
<thead>
<tr>
<th>Symptom Domain*</th>
<th>Autism Spectrum D/O</th>
<th>Social (Pragmatic) Communication D/O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social and Language</td>
<td>√Deficits in social-emotional reciprocity and maintaining/understanding relationships</td>
<td>‘Deficits in social communication resulting in functional limitations in effective communication, social participation, development of social relationships, academic achievement, or occupational performance’</td>
</tr>
<tr>
<td>Restricted, repetitive patterns of behavior, interests, or activities</td>
<td>√Stereotyped or repetitive motor movements, use of objects, or speech ‘Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior’</td>
<td>NO</td>
</tr>
<tr>
<td></td>
<td>√Highly restricted, fixated interests that are abnormal in intensity or focus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>√Hyper- or hyporeactivity to sensory input (at least 2 out of 4)</td>
<td></td>
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</tbody>
</table>

DSM5: ASD vs. Social Communication D/O

“Current absence of symptoms would not preclude a diagnosis of autism spectrum disorder, if the restricted interests and repetitive behaviors were present in the past. A diagnosis of social (pragmatic) communication disorder should be considered only if the developmental history fails to reveal any evidence of restricted/repetitive patterns of behavior, interests, or activities.”
Molecular Autism
http://www.molecularautism.com/series/dsm5
http://www.molecularautism.com/content/4/1/12

Review Autism in DSM-5: progress and challenges
Fred R Volkmar and Brian Fischhoff
* Corresponding author: Fred R Volkmar fred.volkmar@yale.edu
Author affiliations
Child Study Center, Yale University School of Medicine, PO Box 207900, New Haven, CT 06520-7900, USA

The electronic version of this article is the complete one and can be found online at:
http://www.molecularautism.com/content/4/1/12

Autism in DSM-5: progress and challenges
Fred R Volkmar and Brian Fischhoff

- “The impact is probably greatest among the most cognitively able cases and those with less classic autism presentations;” up to 10% may lose Dx of ASD
- Impact will be greatest in settings where reliance is placed exclusively on testing, w/o diligent review of early developmental history

Announcing DSM Criteria and the ASD Explosion

Up to 10% of children with ASD may lose their Dx: Risk is greatest for children with “High Functioning Autism”

Implications for School Psychology
Stephen E. Brock & Shelly R. Hart

“Ultimately, we ask the question as school psychologists: What does this mean for us?...The short answer is: Nothing...

The work of school psychologists is, and always has been, informed by DSM. DSM has never been a controlling authority....

Autism in DSM-5: progress and challenges
Fred R Volkmar and Brian Fischhoff

- DSM-IV: 3 categories (Language, Social, Repetitive Behavior) and a menu of qualifying criteria within each category gave >2,000 combinations of criteria that would yield an autism diagnosis
- Combining Social and Language into one category, and requiring 3 out of 3 criteria to be met for Repetitive Behavior results in many fewer potential combinations
- “Despite the name change to Autism Spectrum Disorder, the concept actually proposed is apparently more restricted than the DSM-IV approach”

The simple presence of a DSM diagnosis for a student we serve can and should direct our attention, but it never should direct our action.

The education codes and regulations that do direct our action (i.e. IDEA) require clear evidence of an adverse effect on educational functioning, and, as a result, some might argue are more restrictive in this setting than DSM...”

(* Some of us would beg to differ: Anxiety w/o academic failure, e.g.)
Known causes of prevalence of children with a Dx of ASD

- Broadening diagnostic criteria
- Broadening Federal service & reporting requirements
- Diagnostic substitution
- Broadening ascertainment methods

Changes in Federal Law - 1

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Comment</th>
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<tbody>
<tr>
<td>1975</td>
<td>Congress enacts Public Law 94-142: Education for All Handicapped Children (EAHC)</td>
<td>First Federal law requiring the States to provide free and appropriate public education (FAPE) to “all children &gt;5 yrs old, regardless of disability”</td>
</tr>
</tbody>
</table>

But…....

“Handicapping Conditions” (PL 94-142; 1975)

- Mentally Retarded
- Learning Disabled
- Speech impaired
- Hearing / Vision Impaired
- Seriously emotionally disturbed
- Orthopedically impaired
- Multi-handicapped
- Other health impaired

Where is autism?

Changes in Federal Law - 2

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Comment</th>
</tr>
</thead>
</table>
| 1986 | PL 99-457: Early Intervention Amendments to PL 94-142 | Extends FAPE to children age 3-5, mandated to take effect by 1991 (Section 619, Part B)
| | | Creates Early Intervention for children 0-3 (Section 619, Part H). |

Where is autism?

Changes in Federal Law - 3

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Comment</th>
</tr>
</thead>
</table>
| 1990 | Congress Amends PL 94-142 again (PL101-476) | Renamed Individuals with Disabilities Education Act (IDEA)
| | | Includes Autism & Traumatic Brain Injury (TBI) as “eligible disabilities” under the scope of the law |

Prior to 1990, according to Federal regulations, Autism did not exist.

Changes in Federal Law - 4

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Comment</th>
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</thead>
</table>
Impact of Federal Law & Regulations

• EI & 3 to 5 Services begin: 1986
• Autism recognized as a fundable D/O: 1990
  – Re-classification of children already in the system (diagnostic substitution)
  – Correct classification of new children with autism entering the system
• Reporting autism to US DOE required: 1992


Known causes of ↑ prevalence of children with a Dx of ASD

• Broadening diagnostic criteria
• Broadening Federal service & reporting requirements
  ➢ Diagnostic substitution
• Broadening ascertainment methods

Ascertainment Methods for ASD

• Old: Count already-identified cases
  – School data
  – Medical clinics
• New: Search for unrecognized cases
  – Population Screening (EI, ACA, etc.)
• Ascertainment Bias?
Population Screening

- **Subjects**
  - Missouri Twin Study
  - 788 twin pairs, age 7-15
  - No identified developmental disorder

- **Methods**
  - Social Responsiveness Scale (SRS); mother = informant (97%)

Constantino JN and Todd, RD. Arch Gen Psych 2003; 60(5):524-30

Prevalence of Autistic Traits in “Normal” Children

- SRS scores of 1,576 unselected twins
- Constantino JN and Todd, RD. Arch Gen Psych 2003; 60(5):524-30

Cutoff for ASD

- Boys: 1.4% 1 in 71
- Girls: 0.3% 1 in 333

The Affordable Care Act and Autism-Related Conditions

- New health insurance plans or insurance policies must cover preventive services without cost-sharing, including autism screening for children at 18 and 24 months

Ascertainment Bias

- **Differential ascertainment**
  - By race
  - By geographic region
  - By socioeconomic status

CDC Prevalence Estimates for ASD, 2008

- Autism and Developmental Disabilities Monitoring Network (ADDM)
  - 14 Sites (Universities, State Depts of health; not demographically representative of the US as a whole)

- Data sources:
  - Healthcare organizations (general & specialty)
  - Schools (some sites)

- N = 337,093 children, age 8

- 3,820 met surveillance case criteria for ASD
  - 79% had a pre-existing Dx of ASD in their records
  - 21% had no ASD Dxs in their records


http://www.cdc.gov/mmwr/preview/mmwrhtml/ss6103a1.htm?s_cid=ss6103a1_w
TABLE 2. Estimated prevalence of autism spectrum disorders (ASDs) per 1,000 children aged 8 years, by sex and race/ethnicity — Autism and Developmental Disabilities Monitoring Network, 14 sites, United States, 2008. MMWR 3/30/2012

<table>
<thead>
<tr>
<th></th>
<th>White</th>
<th>Black</th>
<th>Hispanic</th>
<th>W.B</th>
<th>W.H</th>
<th>B.H</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td>12.0</td>
<td>10.2</td>
<td>7.9</td>
<td>1.2 : 1</td>
<td>1.5 : 1</td>
<td>1.3 : 1</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td>5.0 – 40.0</td>
<td>4.0 – 25.9</td>
<td>1.4 – 20.0</td>
<td>1.0 – 1.9 : 1</td>
<td>0.6 – 3.5 : 1</td>
<td>0.4 – 5.8 : 1</td>
</tr>
</tbody>
</table>

Socioeconomic Inequality in the Prevalence of Autism Spectrum Disorder: Evidence from a U.S. Cross-Sectional Study
Durkin MS, Maenner MJ, Maeney FJ, et al.

Prevalence increased with increasing SES* in a dose-response manner, with prevalence ratios relative to medium SES of 0.70 for low SES, and of 1.25 for high SES, (P<0.001).

*SES: Socioeconomic status (income, education)

"Hot Spots"
- Increased risk of having a child with Autism, compared to state-wide average

The spatial structure of autism in California, 1993–2001
Durkin MS, Maenner MJ, Meaney FJ, et al.

Prevalence increased with increasing SES* in a dose-response manner, with prevalence ratios relative to medium SES of 0.70 for low SES, and of 1.25 for high SES, (P<0.001).

*SES: Socioeconomic status (income, education)
Following the money
• $ earmarked for children with ASD
• Pressure to classify children with borderline symptoms as ASD in order to access to services
  – Improved recognition of children with mild ASD, or
  – Artificial increase in number of children with autism diagnosis?

Lawmakers Want More Autism Training For Teachers
http://www.disabilityscoop.com/2012/04/30/lawmakers-autism-training/
April 30, 2012
A bill introduced in Congress … would establish a five-year federal grant program to allow school districts to team with universities and nonprofits to train general education teachers and other school staff to best support students with autism … Under the bill, the program would be available in school districts where at least 10 percent of special education students have an autism diagnosis …

Where have all the adults gone?
“Since 1% of adults don’t have ASD, doesn’t that prove we’re in an epidemic?”

“Missing” adults: NHS Survey
http://www.ic.nhs.uk/pubs/asdpsychiatricmorbidity07
NHS Survey 2007
Phase 1
• Autism Quotient (20-Item Screen)
  • N=2,854

Phase 2
• ADOS (Autism Diagnostic Observation Schedule)
  • N=618

Prevalence of ASD: 1%
• Male: 1.8% (1 in 56)
• Female: 0.2% (1 in 500)

NHS Survey 2007
• National sample of survey of adults living in the community
  • Excludes persons in residential care
  • Therefore, under-counts adults with severe disability
NHS Survey 2007

Prevalence of ASD (ADOS 10+), by age

<table>
<thead>
<tr>
<th>Age group</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-44</td>
<td>%</td>
</tr>
<tr>
<td>45-74</td>
<td>%</td>
</tr>
<tr>
<td>75+</td>
<td>%</td>
</tr>
<tr>
<td>ASD (ADOS score of 10+)</td>
<td>1.1 0.9 0.8</td>
</tr>
</tbody>
</table>

Prevalence x Age: Not statistically significant

http://www.ic.nhs.uk/pubs/asdpsychiatricmorbidity07

“Missing adults”

• Reality:
  – The prevalence of ASD among today's senior citizens is roughly the same as among today's children.

Outline

Etiology, Epidemiology, and Quackery [10:45-12:00]
• The autism “explosion”
  • Where did it come from? What does it mean?
  • Impact of DSM5
  ✓ Causes of ASD: Proven, unproven, and disproven
    • Genetics, and why you should care about it
    • The signs and symptoms of quackery

LUNCH

“Losing the diagnosis”

• Just because someone outgrows childhood criteria for ASD does not mean that they are cured

ASD (Autism, PDD-NOS, AS)

Extended Family

- Social Impairment
- Communication Impairment
- Restricted, repetitive behaviors & interests
- Anxiety Disorders
- Obsessive-Compulsive Disorder
- Depression, Bipolar Disorder
- Alcoholism

NLD: Non-Verbal LD, SPLD: Semantic-Pragmatic Lang. Disorder

Non-ASD Psych D/V

Presentation in Childhood

NLD, SPLD

Broad Autism Phenotype

Copyright, 2010, in press
• Social Impairment
• Communication Impairment
• Restricted, repetitive behaviors & interests
• Anxiety Disorders
• Obsessive-Compulsive Disorder
• Depression, Bipolar Disorder
• Alcoholism

Outcome for children with High Functioning ASD

Anxiety, OCD, ASD

Anxiety, Depression, ASD, Agitation

BPD, OCD, Anxiety, AS

Causes of ASD

- Prenatal
  - Genetic: Nearly all cases of ASD with a known etiology
  - Teratogenic (rare: rubella, valproate)
  - Associations: Parental Age; Infertility, ?ART

- Perinatal:
  - Associations: (extreme prematurity), but no proven causes

- Postnatal:
  - Some associations, but no proven causes
  - No proof: Diet, immunizations
Gluten / Casein

Elimination Diets in Autism Spectrum Disorders: Any Wheat Amidst the Chaff?

GEORGE W. CHRISTISON, M.D.
Department of Psychiatry, Loma Linda University School of Medicine, Loma Linda, California
KRISTIN IVANY, M.D.
Department of Psychiatry, Emory School of Medicine, Atlanta, Georgia


Testing: No proven benefit

• Stool for yeast, parasites, metals
• Urine porphyrins
• Red Blood Cell elements
• Hair analysis
• Allergy or Food Sensitivity (Gluten)

Network Topologies and Convergent Aetiologies Arising from Deletions and Duplications Observed in Individuals with Autism

PLOS Genetics, June 6 2013
http://www.plosgenetics.org/article/info%3Adoi%2F10.1371%2Fjournal.pgen.1003523
doi:10.1371/journal.pgen.1003523

• 192 genes form an interconnected cluster
• Patients with copy number variations within this cluster possess on average, 3 CNV’s
• Many of these genes are implicated in psychiatric disorders in humans (anxiety, e.g.), and/or behavioral abnormalities in animal models (abnormal nurturing behavior, e.g.)
Morena De Luca et al, 2013

Mental Illness & ASD: The Elephant in the Room

Child w. ASD + Parent with MH D/O =

Quackery - 1

“The promotion, for profit, of a medical remedy known to be false or unproven”
(FDA)

Quack Therapies: The Pitch

- Simple yet mysterious
- All-powerful, yet safe
- Able to cure multiple conditions
-Supported by Testimonials
-Thrive as the underdog: persecuted by, or challenger to, standard medical practice

Promotional Techniques

- Create a demand
- Deliver the pitch
- Close the sale

- Modern advertising originated with 19th Century “patent medicines”
- Safe & Effective!
- Satisfaction guaranteed!

Creating Demand for Prescription Drugs: A Content Analysis of Television Direct-to-Consumer Advertising
http://www.annfammed.org/content/5/1/6.full
Show me the data

- Epidemiologic evidence & animal models to confirm causation
- Randomized Controlled Trials to demonstrate safety & efficacy
  - Parents need to demand, and then be willing to enroll their children, in RCTs

Expectation Bias - 1

- *We see what we expect to see*

Expectation Bias – 2

*(If you wish it hard enough, it is no dream)*

- Pygmalion Effect
  - aka Rosenthal Effect; Teacher Expectation effect
- Randomly selected students were labeled “exceptionally bright”
- “Bright” students’ scores rose on objective measures, compared to controls
- Moral: If you believe in a therapy strongly enough, *your belief alone is enough to create objective change*

Follow the money

- Who else is advocating a particular therapy, *other than*
  - parents who have already spent money it, and
  - vendors who make their livelihood providing it?
Implications

• Beware of any arguments that rest on the claim that we are in an epidemic
  – Allegations as to cause
  – Promises of cure

Summary

• Epidemiology:
  – Administrative Prevalence of ASD has risen
  – No proof that actual prevalence has changed
  – No info on Incidence
• Genetics
  – Accounts for most cases of known cause
  – Co-morbid mental health disorders
    • In the affected child
    • In parents
• Quackery
  – Show me the data
  – Follow the money

LUNCH!!!