ELSI Issues Related to ASD Screening and Diagnosis Research

- Ethical issues in the conduct and uptake of ASD screening research-**Lonnie Zwaigenbaum, M.D.**
- Identifying and communicating meaningful genetic results used in ASD screening and diagnosis-**Fiona Miller, Ph.D.**
- Lessons from newborn screening for Fragile X syndrome-**Don Bailey, Ph.D.**
- Ethical issues in adult diagnosis – **Catherine Lord, Ph.D.**

Ethical issues in the conduct and uptake of ASD screening research

Lonnie Zwaigenbaum MD FRCPC
Department of Pediatrics, University of Alberta

Ethical, Legal and Societal Implications of Autism Research

NIH Workshop, Bethesda, MD

September 26th, 2011

Context

- **Post-natal** (generally 18-30 months)
- **Symptomatic**- ASD-related behaviors as measured by parental questionnaires and/or clinical observation
- **Universal vs. targeted** ('first-level' versus 'second-level' screening)
- **Current practice parameters: e.g., AAP**

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

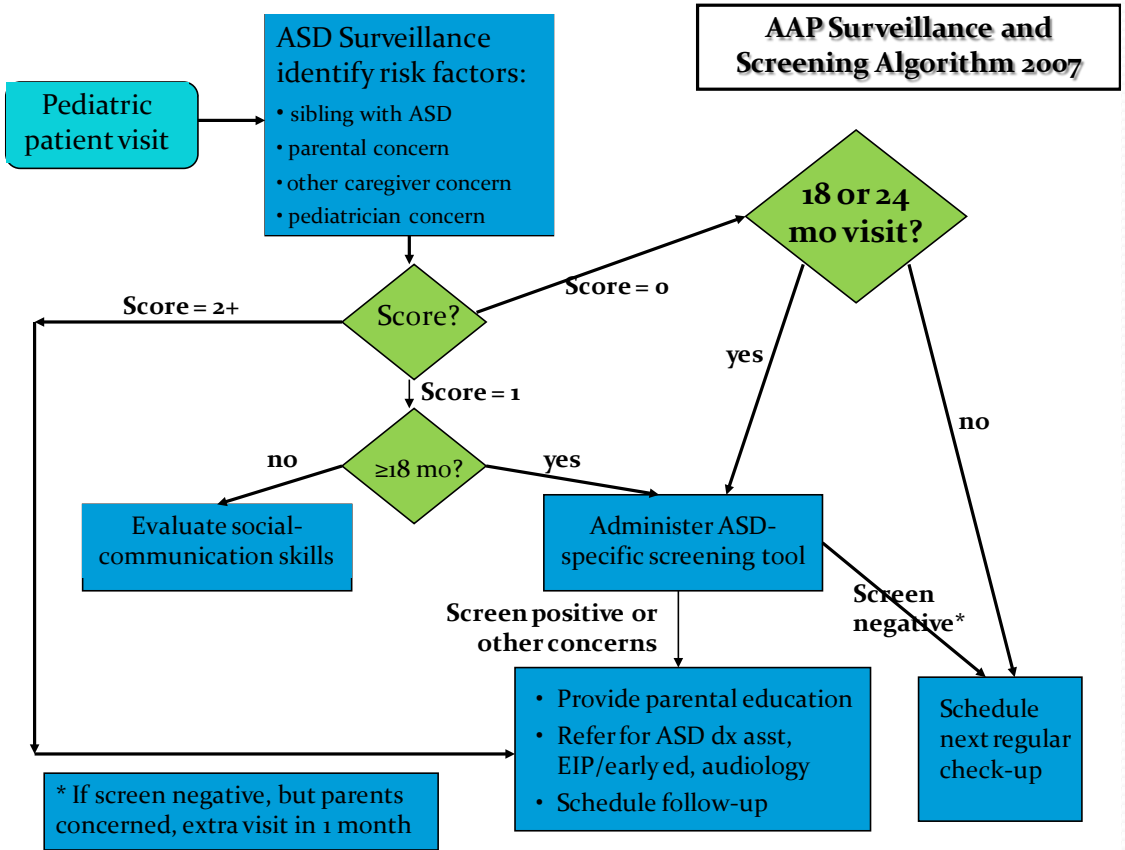
CLINICAL REPORT

Identification and Evaluation of Children With Autism Spectrum Disorders

Guidance for the Clinician in Rendering Pediatric Care

Chris Plauché Johnson, MD, MEd, Scott M. Myers, MD, and the Council on Children With Disabilities

Oct, 2007



- **Monitor for early signs of ASD at each visit**
- **Universal screening for ASD at 18 and 24 months**
- **E.g., M-CHAT, ITC**

Important ethical and societal issues

- **Beneficence vs. Nonmaleficence**
  - Benefits and risks
  - Individuals, autism community, society
  - Criteria for uptake into 'best practice', public policy
- **Evaluation of ASD screening**
  - What determines optimal balance of sensitivity and specificity?
  - Focus on individual classification vs. clinically meaningful endpoints
- **Broader health care perspective**
  - Importance of system capacity – but what drives what?

Criteria for 'screening effectiveness' in health care (proposed by Cadman et al, 1984; cited by Al Quabandi, Gorter & Rosenbaum, 2011)

- **Is a valid screening test available?**
- **Has the effectiveness of the screening program been established in a randomized controlled trial**
  - Implicit is the identification of meaningful end-points
- **Are there efficacious treatments and/or preventative strategies?**
- **Will the screening program reach a high proportion of the persons for whom it was intended?**
- **Will those with positive screens follow-up with further assessment and intervention?**
- **Can the health care system adequately respond?**

Letter to the editor, Pediatrics: Dawson, Fein, Rogers, Zwaigenbaum

(http://pediatrics.aappublications.org/content/early/2011/06/08/peds.2010-1881/reply#pediatrics_el_51471)

- "In conclusion, while Al-Qabandi et al. pose important questions that should be considered prior to the implementation of a community screening program for any health condition, we disagree with the conclusions drawn regarding the availability of accurate autism screening tools, the evidence base for effective early intervention, and the feasibility of care provision for children with ASD identified through early screening…"

Are there valid ASD screening tests?

- **CHAT** – important contributions, but insufficient sensitivity to have utility as 1st or 2nd level screen
- **M-CHAT and ITC** – recent community level data support use as 1st level screen as part of overall early detection strategy (also M-CHAT as 2nd level screen)
- **STAT** – utility as 2nd level screen
- **SCQ** – some utility as 2nd level screen in clinical samples, poorer sensitivity/specificity for < 4-year-olds
- The **ESAT** experience: education and engagement may be as important as screening...

Are there effective interventions for children with early ASD diagnoses?

- **ESDM Clinical Trial (Dawson et al., 2010)**
- 18-30-month-old toddlers with ASD (n=48)
- Randomized to 24 months of:
  - ESDM (20 hr/wk, plus parent sessions and other community interventions)
  - 'Assess and monitor' (include community interventions – about 10 hr/wk)
- ESDM group showed marked improvements:
  - Advances in language and cognitive skills
  - Tendency to shift to milder diagnostic subtype

Are there controlled clinical trials of ASD screening?

- **Oosterling et al. (2010)**
  - Evaluated ASD screen (ESAT) as part of an overall early detection *strategy*
  - Compared changes in age of diagnosis in two regions with similar demographics and service structure, one of which had the novel strategy implemented
  - Strategy consisted of training for (and interaction between) professionals and front-line workers, 2nd level screening with the ESAT (<36 months), establishment of an enhanced multi-disciplinary diagnostic team
  - Mean age of diagnosis dropped from age 7 to about age 5 in 'experimental region'; stable at age 7 in 'control region'
  - Previous research suggests ESAT has limited sensitivity and classification accuracy; yet the overall strategy was effective!

Will the screening program reach a high proportion of children for whom it was intended? Will those with positive screens follow-up with further assessment and intervention?

- **Data are somewhat mixed**
- e.g., Pierce et al., 2011; 'One-year Well Baby Check-up'
  - Efficiacy study (i.e., ideal circumstances) – well-engaged pediatricians, streamlined access to expert diagnostic assessment and intervention in research context
  - 1319 of 10479 (13%) of 1-year-olds failed ITC screen
    - Only 346 (26%) were referred
    - Only 184 were seen in follow-up (53% of those who were referred, or 28% of those with positive screens)
- Loss to follow-up also noted in M-CHAT research

How do we study the potential benefits and risks of ASD screening?

- **From whose perspective?**
  - **Individual child:** What is the impact of being correctly identified as having ASD? Or incorrectly identified as having ASD (or as not having ASD)?
  - **Research and advocacy community:** Can we identify, diagnose and treat ASD earlier? Can we improve long-term outcomes for children (and families)?
  - **Societal:** What are the resource and opportunity costs and benefits, both short- and long-term? Does ASD screening strain or build system capacity?

Challenges in ASD diagnosis in children under age 2 years (Zwaigenbaum et al., *Pediatrics* 2009)

- **Limited clinical experience and research evidence base for reliability/stability**
  - Minimal data outside of highly specialized tertiary care setting
- **Minimum cognitive level needed to assess critical developmental domains;** e.g., joint attention behaviors
- **'Fuzzy boundaries' between ASD and other developmental impairments**
- **However, experience to date in 'baby sib' samples suggests stability of early diagnosis is high, but sensitivity is fairly low**

Priorities in ASD Screening Research: Through an ELSI Lens

- **Family experience related to ASD screening**
  - Communication of findings
  - Navigating the system after a positive screen
  - Impacts of misclassification
    - Importance of longer term follow-up
  - Impacts of earlier detection
- **ASD Screening *Effectiveness***
  - ASD screening as part of overall early detection *strategy*
  - Focus on short- and long-term meaningful outcomes
- **Setting ethical standards for early detection and screening research**
  - e.g., 'infant sibling' research

Acknowledgements

- **University of Toronto**
  - **Wendy Roberts MD**
  - **Jessica Brian PhD**
  - Becky Baatjes BA
  - Bonnie MacKinnon MEd
  - Jonathan Leef MA
- **University of Alberta**
  - Heather Wagg BSc
  - Jana Roberto BSc
  - Carol Wilson MHS
- **Dalhousie University**
  - **Susan Bryson PhD**
  - **Isabel Smith PhD**
  - Theresa McCormick BSc
- **McMaster University**
  - **Peter Szatmari MD**
  - **Caroline Roncadin PhD**
  - Ann Thompson MSc
- **University of Ottawa**
  - **Tracy Vaillancourt PhD**

Our Research is supported by

Autism Speaks

Canadian Institutes of Health Research

NIMH

Alberta Innovates

Stollery Children Hospital Foundaation

Many wonderful children and families!