Pediatric Antipsychotic Use: Indications, Guidelines, and Options

February 3, 2012

Improving People's Lives
through innovations in personalized health care

THE OHIO STATE UNIVERSITY Medical Center

Objectives

- **To provide an overview of existing clinical practices with atypical antipsychotic agents (AAAs) in youth**
- **To review FDA approved indications and the evidence for common off-label pediatric uses for AAAs**
- **To highlight prescription practices for AAAs that are without support, known to be ineffective, or contraindicated.**

Atypical Antipsychotic Agents (AAA)

2nd Generation Antipsychotic Agents

- **"Atypical" due to reduced EPS compared to "typical" AAs**
- **Not necessarily more effective than typical AAs**
- **Prescription increasing in youth, including very young**
- **Most pediatric use is "off-label" (i.e, no FDA indication)**
  - ***Most often for non-psychotic disorders***
  - ***Aggression the most common target symptom in youth***
- **Disproportionate use in several populations**
  - ***Males, foster care, Medicaid***
- **Little is known about long term safety of AAAs**
- **Although in same class, AAAs are not interchangeable**
  - ***All block dopamine D2 receptor, but each has unique effects***

Atypical Antipsychotic Agents (AAA)

2nd Generation Antipsychotic Agents

Generic	Proprietary
• Asenapine	*Saphris*
• Aripiprazole*	*Abilify*
• Clozapine	*Clozaril*
• Iloperidone	*Fanapt*
• Lurasidone	*Latuda*
• Olanzapine*	*Zyprexa*
• Olanzapine/Fluoxetine	*Symbax*
• Paliperidone	*Invega*
• Quetiapine*	*Seroquel*
• Risperidone*	*Risperdal*
• Ziprasidone	*Geodon*

**** FDA approved for at least one pediatric indication***

AAAs Approved by FDA For Pediatric Use

- **Risperidone (*Risperdal)***
  - ***Irritability in Autism, Bipolar I (mixed/manic), Schizophrenia***
  - ***Best studied AAA in youth***
- **Aripiprazole (*Abilify)***
  - ***Irritability in Autism, Bipolar I (mixed/manic), Schizophrenia***
- **Olanzapine (*Zyprexa)***
  - ***Bipolar I (mixed/manic), Schizophrenia***
- **Quetiapine (*Seroquel)***
  - ***Bipolar I (mixed/manic), Schizophrenia***

FDA Approved Indications
For AAAs in youth

- **Irritability associated with Autistic Disorder**
  - ***Risperidone (5 to 16 years), Aripiprazole (6 to 17 years)***
- **Bipolar I Disorder, mixed or manic (ages 10 to 17)**
  - ***Risperidone, Aripiprazole, Olanzapine, Quetiapine***
- **Schizophrenia (ages 13 to 17)**
  - ***Risperidone, Aripiprazole, Olanzapine, Quetiapine***

Common Off-Label Pediatric AAA Use

- **Aggression/Disruptive behavior disorders**
  - ***Most common target symptom for youth treated with AAAs***
- **Anorexia Nervosa/Eating Disorders**
- **Mood disorders**
  - ***Bipolar NOS, Mood NOS, MDD adjunct***
- **Poor impulse control (e.g., in Personality Disorders)**
- **Post-traumatic stress disorder (PTSD)**
- **Refractory OCD**
- **Tics/Tourette's Disorder**

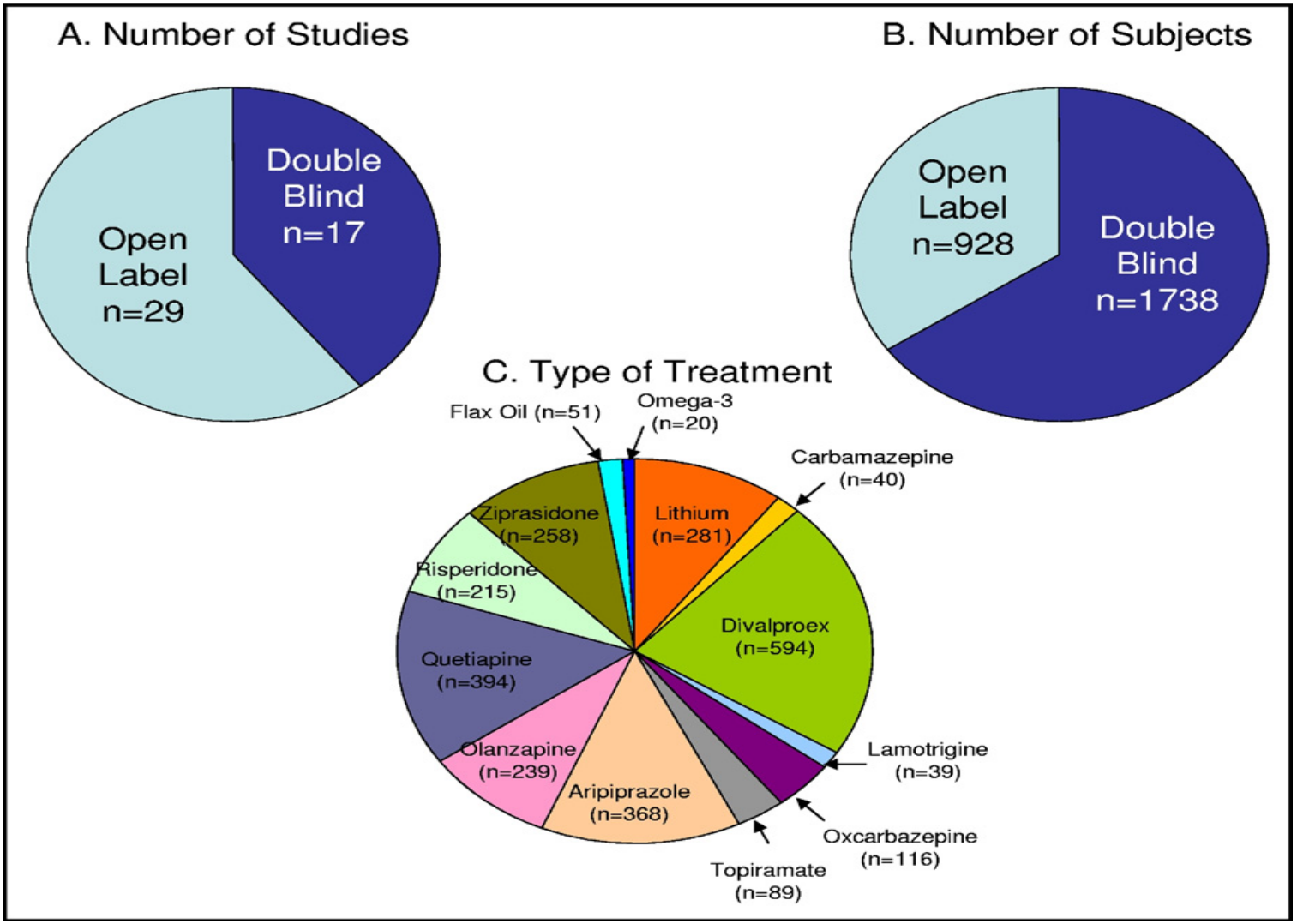
Evidence for Pediatric AAA Use

RCT = Randomized Control Trial, UCT = Uncontrolled Trial, CS = Case Study

	CLOZ	RISP	OLAN	QUET	ZIP	ARI
Schizophrenia/Psychosis	1 RCT	1 RCT	>1 RCT	>1 RCT	CS	>1 RCT
Bipolar d/o	UCT	1 RCT	1 RCT	>1 RCT	1 RCT	>1 RCT
Aggression/ DBD	UCT	1 RCT	1 RCT	UCT	CS	CS
Autism/PDD Irritability	CS	>1 RCT	1 RCT	CS	CS	>1 RCT
Tics/ Tourette's		>1 RCT	CS		1 RCT	
Anorexia/ED			CS			
PTSD		CS		CS		

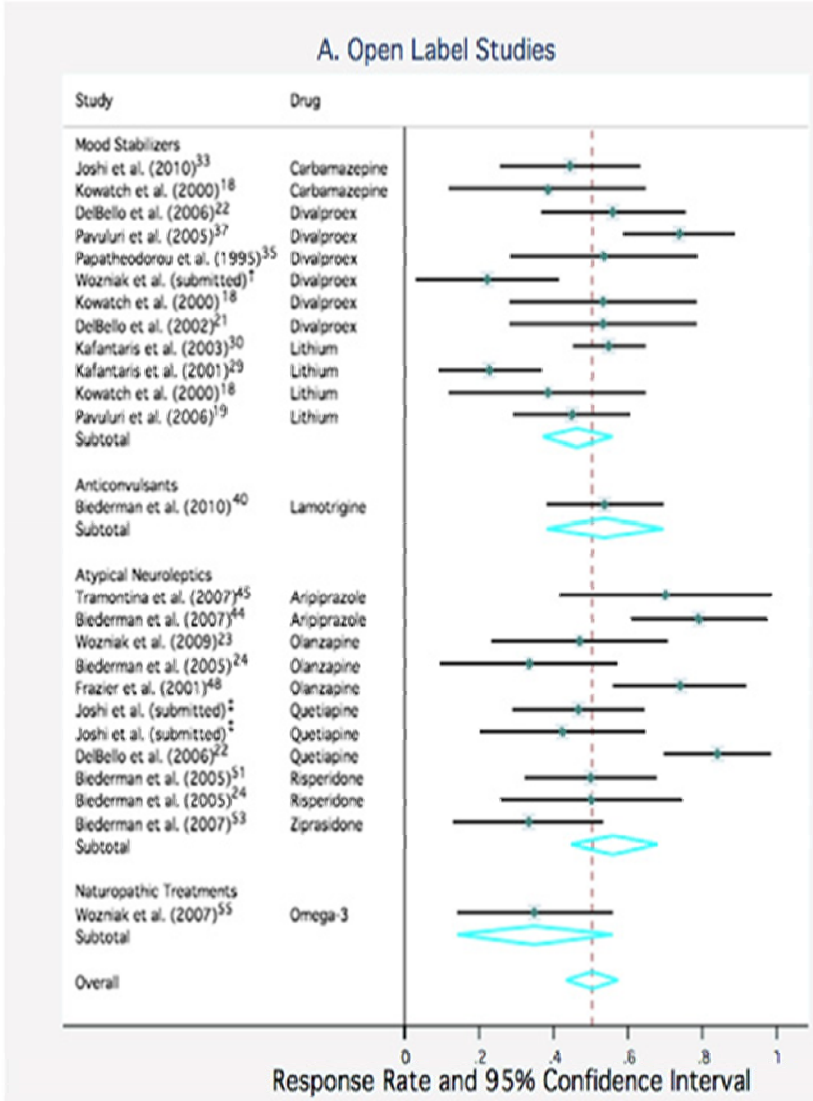
Treatment of Pediatric Bipolar Disorder

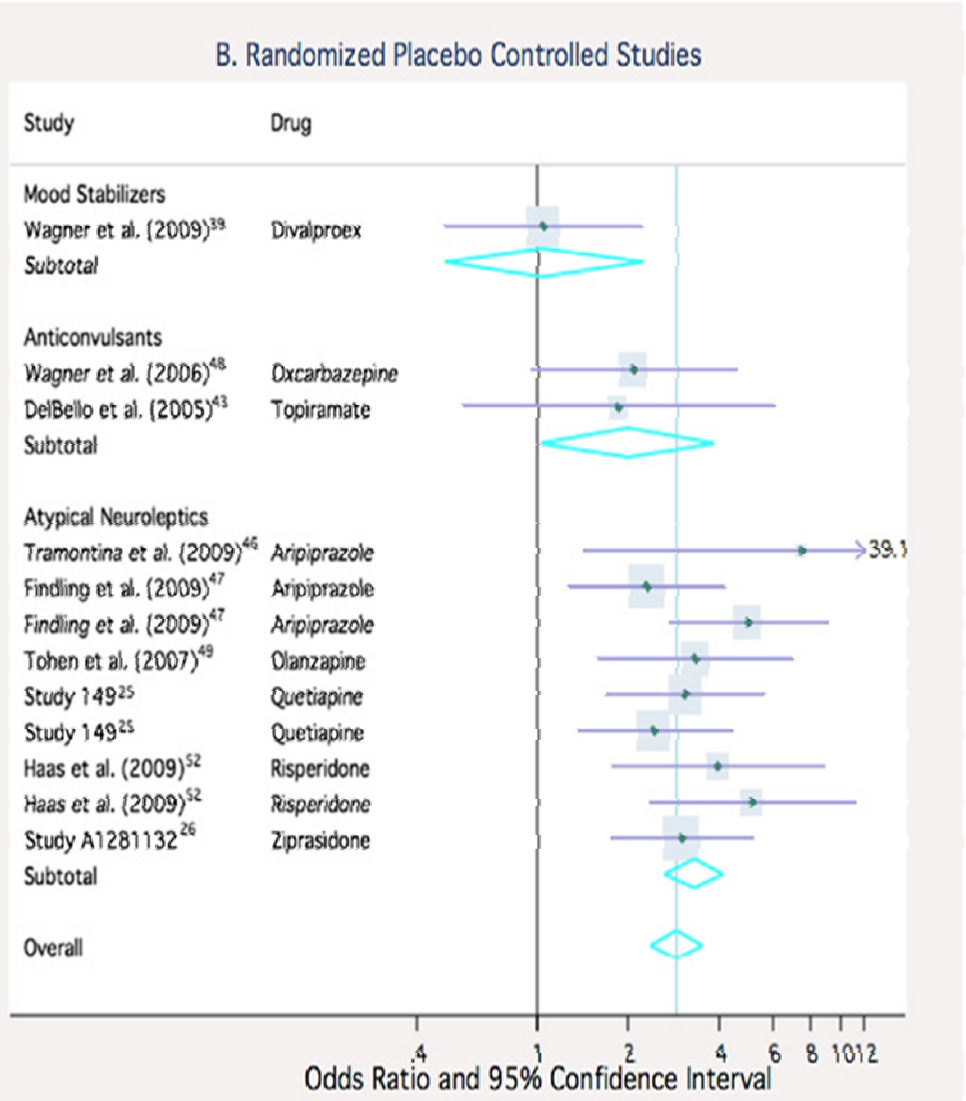
Liu et al., JAACAP 2011



Treatment of Pediatric Bipolar Disorder

Liu et al., JAACAP 2011





Adverse Effects of AAAs

- **Weight gain**
  - ***Vulnerability to weight gain varies by agent***
- **Metabolic effects**
  - ***Hyperglycemia, Diabetes (BLACK BOX WARNING)***
    - **Risk may be weight independent and varies by agent**
  - ***Hyperlipidemia, Hypercholesterolemia***
  - ***Hyperprolactinemia***
  - ***Hepatic dysfunction***

Adverse Effects of AAAs (cont.)

- **Extrapyramidal effects (dystonia, Parkinsonism)**
  - ***Risk likely greater risk for youth than adults***
- **Akathisia**
- **Tardive dyskinesia**
- **Withdrawal dyskinesia**
- **Neuroleptic Malignant Syndrome**
- **Agranulocytosis and neutropenia**
- **Cardiovascular effects**
  - ***Prolonged QTc, tachycardia, orthostatic hypotension***
- **Seizures**

Atypical Antipsychotics

Safety and Tolerability (cont.)

	Aripiprazole ABIL	Olanzapine OLZ	Quetiapine QTP	Risperidone RISP	Ziprasidone ZIP
EPS	+	+	0	++	+
Akathisia	++	+	+	+	+
↑Glucose	0/+	+++	++	+	0/+
↑Lipids	0/+	++	+	+	0/+
↑Prolactin	0	++	0	+++	+
Sedation	0/+	0/+	+	+	++
↑Weight	+	+++	++	++	+
↑ QTc	0/+	0/+	+	+	++

Adapted from Correll CU, JAACAP 2008

Suggested Principles for Use of AAAs

- **Apply best available evidence**
- **Prescribe in context of overall health status of patient**
- **Use lowest effective dose for target symptom(s)**
- **Caution with polypharmacy**
  - ***Limited data on long term combination treatments***
- **Avoid simultaneous use of multiple AAAs**
- **Careful monitoring for potential adverse effects**
  - ***Baseline weight/BMI, fasting glucose, lipids, AIMS***
- **Determine planned duration of treatment**
- **Avoid abrupt discontinuation when possible**