FORWARD FOCUS: TRANSITIONING FROM CHILDHOOD TO ADOLESCENCE WITH ADHD
Learning Objectives

• Identify the different challenges in the management of ADHD in child and adolescent patients

• Differentiate the spectrum of medication options available for use in pediatric ADHD based on formulation and pharmacokinetic profile

• Optimize treatment of pediatric ADHD to fit the specific needs of the patient and their caregivers
Overview

• DSM-5 criteria
• Epidemiology brain development and persistence of symptoms
• Academic challenges
• Social challenges
• Long term data on comorbidity in boys and girls
• Management of the whole patient given the social, academic, and comorbidity demands
DSM-5
What is ADHD?

• Core symptoms include inattention and/or hyperactivity and impulsivity
• Symptoms begin before the age of *12*
• Impairment present in two or more settings
• Clear evidence of impairment in social, academic, or occupational functioning
• Range from mild to severe
Diagnostic Criteria

Either A or B

A. Six (or more) of the following symptoms of inattention have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:
   - often fails to pay close attention to details or makes careless mistakes in schoolwork, work, or other activities
   - often has difficulty sustaining attention in tasks or play activities
   - often does not seem to listen when spoken to directly
   - often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace
   - often has difficulty organizing tasks and activities
   - often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort
   - often loses things necessary for tasks or activities
   - is often distracted by extraneous stimuli
   - is often forgetful in daily activities
B. Six (or more) of the following symptoms of hyperactivity-impulsivity have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:
   - often fidgets with hands or feet, or squirms in seat
   - often leaves seat in classroom or in other situations wherein remaining seated is expected
   - often runs about or climbs excessively in situations wherein it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)
   - often has difficulty playing or engaging in leisure activities quietly
   - is often “on the go” or acts as if “driven by a motor”
   - often talks excessively
   - often blurts out answers before questions have been completed
   - often has difficulty awaiting turn
   - often interrupts or intrudes on others
Epidemiology
Prevalence and Persistence

- Estimated that 3-10% of children have ADHD
- 50-80% of children diagnosed with ADHD will continue to meet full criteria during adolescence
- 18-65% of children diagnosed with ADHD will continue to meet full criteria into adulthood
- Estimated that 4% of adults have ADHD
Brain Development
Brain Development

Brain development is finalized in early 20s.
- Longitudinal structural MRI study
- Measuring cortical thickness
- Cortical thickness decreases from age 5 to 20 due to neuronal pruning
- Thinning proceeds posterior \(\rightarrow\) anterior
Brain Development

1. Male brains develop later than female brains

2. Different areas develop at different rates

For example: striatum develops earlier than cortex

Striatum – modulates reward seeking

Cortex – executive functioning, cognitive control, response inhibition
ADHD is characterized by a delay in cortical maturation.


C. Tang 2018
Dev. Neurosci
Showed a delay in functional connectivity in default mode network

Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation.

ADHD: Delay in Prefrontal Cortex Maturation

![Graph showing maturation curves for All Cortical Points and Prefrontal Cortex comparing ADHD and Typically developing groups.](image)
Academic Challenges
Academic Challenges by School Grades

• Kindergarten: sitting-in-circle time and staying in line on school trips
• Grades 1 and 2: increasing demands to listen to teacher, remain in your seat, and complete math and reading/writing worksheets
• Grade 3: first time synthesis of material is needed for work projects; must have organizational skills to do this; posters and essays are done
• Middle school/junior high: now required to be fully independent in work product (i.e., complete long-term projects with no scaffolding or academic training, hand in all assignments on time and without being asked), remember to maintain work due dates and calendar; ability to complete new assignments; ability to study for exams, including statewide exams
Which presentation of ADHD comes to attention?

• Kindergarten-grade 2 combined and hyperactive/impulsive presentation moderate to severe
• Grades 3-middle school children with inattentive ADHD who now are struggling to do projects, hand in homework and are too social in the classroom
• Middle school-high school students with milder presentations of all three ADHD varieties who do well on classwork and quizzes but fail the statewide end-of-year exams or class finals. Parents and students often feel that grades do not reflect raw ability
Social Challenges
Social Challenges

• Being silly, goofy, and hyperactive is fun early in school and then starts to interfere insofar as making and maintaining friends
• Classmates may continue to encourage off-task and goofy behavior, and the child becomes the “class clown”
• Dropping grades in elementary and middle school may prompt parental interventions and reinforce the idea that school is not fun/not for them/they are stupid
• Impulsivity in speaking with friends may further isolate and alienate losing the good kids
• Pre-teen and adolescent may then move to peer groups that embrace early sex, substance use, and conduct issues
• Teens with ADHD will have more driving issues such as moving and non-moving violations
Long-Term Data on Co-Morbidity
Comorbidity in the MTA vs. Girls


GIRLS

- ADHD only: 55%
- Anxiety: 34%, 7%
- Mood: 20%, 7%
- Conduct: 8%

BOYS

ODD: Oppositional defiant disorder

- ADHD only: 67 (12%)
- Anxiety + ODD: 67 (12%)
- Anxiety: 58 (10%)
- Mood: 5
- Conduct: 43 (7%)
- Tics: 14

- GIRLS: Anxiety: 7%
- BOYS: Anxiety: 34%
- GIRLS: Mood: 20%
- BOYS: Mood: 8%
- GIRLS: Conduct: 8%
- BOYS: Conduct: 7%

Conditions Coexistent With ADHD

Long-Term Prospective Studies by Biederman

• Took boys and girls with ADHD along with normal controls and followed out at regular intervals for other comorbid disorders
• Looked at time of onset of different disorders
• Showed (see management section) that treatment can reduce incidence of other comorbid disorders
A Prospective 4-Year Follow-Up Study of Attention-Deficit Hyperactivity and Related Disorders

Table 1. Demographic Information*

<table>
<thead>
<tr>
<th></th>
<th>Baseline (N=128)</th>
<th>Control Group (N=109)</th>
<th>Year 1 (N=126)</th>
<th>Control Group (N=106)</th>
<th>Year 4 (N=128)</th>
<th>Control Group (N=109)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age</td>
<td>10.6 (3.0)</td>
<td>11.6 (3.7)</td>
<td>11.7 (3.1)</td>
<td>12.7 (3.7)</td>
<td>14.4 (3.1)</td>
<td>15.2 (3.7)</td>
</tr>
<tr>
<td>Socioeconomic status, mean (SD)</td>
<td>1.9 (0.97)</td>
<td>1.5 (0.73)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Intactness No. (%)‡</td>
<td>96 (75)</td>
<td>90 (82)</td>
<td>89 (70)</td>
<td>87 (80)</td>
<td>84 (66)</td>
<td>84 (77)</td>
</tr>
<tr>
<td>Diagnosis of ADHD No. (%)</td>
<td>126 (100)</td>
<td>0 (0)</td>
<td>121 (96)</td>
<td>1 (1)</td>
<td>83 (65)</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>

*ADHD indicates attention-deficit hyperactivity disorder; ellipses, not reassessed.

ƗP<.01, t test.

ǂIntactness Indicates no divorce or separation of the child's parents.

Table 2. Cumulative Rates of Lifetime Diagnoses at Each Assessment*

<table>
<thead>
<tr>
<th></th>
<th>Baseline (N=128)</th>
<th>Control Group (N=109)</th>
<th>Year 1 (N=126)</th>
<th>Control Group (N=106)</th>
<th>Year 4 (N=128)</th>
<th>Control Group (N=109)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conduct disorder</td>
<td>28 (22)†</td>
<td>3 (3)</td>
<td>30 (24)†</td>
<td>4 (4)</td>
<td>36 (29)†</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Oppositional disorder</td>
<td>83 (65)†</td>
<td>10 (9)</td>
<td>89 (71)†</td>
<td>12 (11)</td>
<td>93 (73)†</td>
<td>17 (16)†</td>
</tr>
<tr>
<td>Any alcohol/drug abuse or dependence</td>
<td>3 (2)</td>
<td>7 (6)</td>
<td>6 (5)</td>
<td>9 (8)</td>
<td>19 (16)§</td>
<td>18 (17)§</td>
</tr>
<tr>
<td>Major depression (severe)</td>
<td>37 (29)†</td>
<td>2 (2)</td>
<td>53 (42)†</td>
<td>4 (4)</td>
<td>58 (45)†</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>14 (11)†</td>
<td>0 (0)</td>
<td>22 (18)†</td>
<td>0 (0)</td>
<td>29 (23)†</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Multiple (≥2) anxieties</td>
<td>35 (27)†</td>
<td>5 (6)</td>
<td>42 (34)†</td>
<td>8 (7)</td>
<td>45 (35)†</td>
<td>10 (9)</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>3 (2)</td>
<td>1 (1)</td>
<td>6 (5)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>11 (9)†</td>
<td>1 (1)</td>
<td>18 (15)†</td>
<td>3 (3)</td>
<td>26 (20)†</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Overanxious disorder</td>
<td>39 (30)†</td>
<td>7 (6)</td>
<td>48 (38)†</td>
<td>8 (7)</td>
<td>56 (44)†</td>
<td>10 (9)</td>
</tr>
<tr>
<td>Simple phobia</td>
<td>24 (19)†</td>
<td>5 (5)</td>
<td>31 (25)†</td>
<td>10 (9)</td>
<td>33 (26)†</td>
<td>10 (9)</td>
</tr>
<tr>
<td>Social phobia</td>
<td>16 (13)†</td>
<td>4 (4)</td>
<td>23 (19)†</td>
<td>7 (6)</td>
<td>31 (24)†</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Separation anxiety</td>
<td>37 (29)†</td>
<td>6 (6)</td>
<td>38 (30)†</td>
<td>7 (7)</td>
<td>39 (30)†</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Obsessive-compulsive disorder</td>
<td>4 (3)</td>
<td>1 (1)</td>
<td>5 (4)</td>
<td>1 (1)</td>
<td>14 (11)†</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Tic disorder</td>
<td>22 (17)†</td>
<td>4 (4)</td>
<td>38 (30)†</td>
<td>5 (5)</td>
<td>42 (33)†</td>
<td>7 (6)</td>
</tr>
<tr>
<td>Enuresis</td>
<td>38 (30)†</td>
<td>15 (14)</td>
<td>42 (34)†</td>
<td>18 (17)</td>
<td>42 (33)†</td>
<td>18 (17)</td>
</tr>
</tbody>
</table>

*ADHD indicates attention-deficit hyperactivity disorder. At each follow-up the lifetime diagnosis was considered positive if it had been endorsed at the follow-up or any prior assessment.

ƗP≤.01 vs controls by Pearson's χ² test.

ǂP≤.01 vs baseline by McNemar's χ² test.

§P≤.01 vs year 1 by McNemar's χ² test.

Biederman J Arch Gen Psychiatry. 1996 May;53(5):437-46
A Prospective 4-Year Follow-Up Study of Attention-Deficit Hyperactivity and Related Disorders (cont’d)
Biederman 1996 (boys data)

<table>
<thead>
<tr>
<th>Baseline Comorbid Diagnosis</th>
<th>Conduct Disorder, No. (%) (n=28)</th>
<th>Major Depression, No. (%) (n=37)</th>
<th>Multiple (≥2) Anxieties, No. (%) (n=35)</th>
<th>Noncomorbid ADHD, No. (%) (n=61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conduct disorder</td>
<td>10 (36)† ‡ ‡</td>
<td>6 (15)</td>
<td>6 (17)</td>
<td>6 (10)</td>
</tr>
<tr>
<td>Oppositional disorder</td>
<td>20 (71)† ‡ ‡</td>
<td>25 (69)† ‡ ‡</td>
<td>19 (54)†</td>
<td>21 (34)† ‡</td>
</tr>
<tr>
<td>Major depression (severe)</td>
<td>7 (27)†</td>
<td>11 (32)† ‡ ‡</td>
<td>5 (16)†</td>
<td>4 (7)</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>8 (27)† ‡ ‡</td>
<td>9 (23)† ‡ ‡</td>
<td>4 (10)†</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Multiple (≥2) anxieties</td>
<td>21 (9)†</td>
<td>11 (30)† ‡ ‡</td>
<td>12 (34)† ‡</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>3 (11)†</td>
<td>2 (5)</td>
<td>4 (11)† ‡</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>4 (14)†</td>
<td>9 (24)† ‡ ‡</td>
<td>10 (29)† ‡</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Overanxious disorder</td>
<td>5 (18)†</td>
<td>10 (27)†</td>
<td>11 (31)† ‡</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Social phobia</td>
<td>4 (14)†</td>
<td>9 (24)† ‡ ‡</td>
<td>11 (31)† ‡</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Separation anxiety</td>
<td>3 (11)†</td>
<td>6 (15)† ‡ ‡</td>
<td>8 (23)† ‡ ‡</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Obsessive-compulsive disorder</td>
<td>2 (7)†</td>
<td>3 (8)†</td>
<td>5 (14)†</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>5 (18)†</td>
<td>3 (8)</td>
<td>1 (3)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Drug dependence</td>
<td>4 (15)†</td>
<td>2 (5)</td>
<td>1 (3)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Tic disorder</td>
<td>6 (21)†</td>
<td>7 (19)†</td>
<td>8 (23)†</td>
<td>9 (15)†</td>
</tr>
</tbody>
</table>

*ADHD indicates attention-deficit hyperactivity disorder. Boldface entries represent significant findings after correcting for socioeconomic status and other comorbidities using logistic regression. N=128 for all ADHD subjects; N=109 for all controls.
†P≤.01 vs controls by Pearson's χ² test.
‡P≤.01 vs ADHD without the respective comorbid diagnosis (conduct disorder, major depression, or anxiety) by Pearson's χ² test.
Change in Prevalence in Boys

**Lifetime Prevalence of Multiple Anxieties**
From Baseline to 4-year Follow-Up

**Lifetime Prevalence of Conduct Disorder**
From Baseline to 4-year Follow-Up

**Lifetime Prevalence of Major Depressive Disorder**
From Baseline to 4-year Follow-Up
Clinical Correlates of ADHD in Females: Findings From a Large Group of Girls Ascertained From Pediatric and Psychiatric Referral Sources

Biederman 1999 (original girls data)

TABLE 2
Lifetime Prevalence of Psychiatric Disorders

<table>
<thead>
<tr>
<th>Behavior disorders</th>
<th>ADHD (n = 140)</th>
<th>Control (n = 122)</th>
<th>Statistic</th>
<th>OR (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conduct disorder*</td>
<td>11 (8)</td>
<td>0</td>
<td>$\chi^2 = 48.0; p &lt; .001$</td>
<td></td>
</tr>
<tr>
<td>ODD</td>
<td>49 (35)</td>
<td>5 (4)</td>
<td>$\chi^2 = 27.7; p &lt; .001$</td>
<td>13.6 (3.8, 48.5)</td>
</tr>
<tr>
<td>Mood disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major depression (severe)</td>
<td>24 (17)</td>
<td>1 (1)</td>
<td>$\chi^2 = 10.4; p &lt; .001$</td>
<td>30.1 (2.1, 435.0)</td>
</tr>
<tr>
<td>Mania*</td>
<td>15 (11)</td>
<td>0</td>
<td>$\chi^2 = 13.5; p &lt; .001$</td>
<td></td>
</tr>
<tr>
<td>Dysthymia</td>
<td>13 (9)</td>
<td>1 (1)</td>
<td>$\chi^2 = 6.2; p &lt; .013$</td>
<td>13.6 (0.9, 202.3)</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple (≥2) anxiety disorders</td>
<td>47 (34)</td>
<td>6 (5)</td>
<td>$\chi^2 = 26.7; p &lt; .001$</td>
<td>10.9 (3.3, 35.9)</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>10 (7)</td>
<td>1 (1)</td>
<td>$\chi^2 = 4.9; p &lt; .03$</td>
<td>10.5 (0.7, 101.5)</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>22 (16)</td>
<td>3 (3)</td>
<td>$\chi^2 = 11.6; p &lt; .001$</td>
<td>8.8 (1.7, 45.2)</td>
</tr>
<tr>
<td>Overanxious disorder</td>
<td>40 (29)</td>
<td>2 (2)</td>
<td>$\chi^2 = 18.5; p &lt; .001$</td>
<td>25.0 (3.7, 168.2)</td>
</tr>
<tr>
<td>Simple phobia</td>
<td>40 (29)</td>
<td>13 (11)</td>
<td>$\chi^2 = 12.9; p &lt; .001$</td>
<td>3.6 (1.4, 8.8)</td>
</tr>
<tr>
<td>Social phobia</td>
<td>20 (14)</td>
<td>4 (3)</td>
<td>$\chi^2 = 9.7; p &lt; .002$</td>
<td>6.0 (1.4, 26.1)</td>
</tr>
<tr>
<td>Separation anxiety disorder</td>
<td>36 (26)</td>
<td>12 (10)</td>
<td>$\chi^2 = 10.6; p &lt; .002$</td>
<td>3.2 (1.2, 8.2)</td>
</tr>
<tr>
<td>OCD</td>
<td>7 (5)</td>
<td>1 (1)</td>
<td>$\chi^2 = 2.6; p = .1$</td>
<td>5.8 (0.4, 94.2)</td>
</tr>
<tr>
<td>PTSD</td>
<td>3 (2)</td>
<td>1 (1)</td>
<td>$\chi^2 = 0.7; p = .4$</td>
<td>2.7 (1.1, 54.3)</td>
</tr>
<tr>
<td>Avoidant disorder</td>
<td>3 (3)</td>
<td>3 (3)</td>
<td>$\chi^2 = 0.02; p = .9$</td>
<td>0.9 (0.1, 7.7)</td>
</tr>
<tr>
<td>SUD</td>
<td>9 (6)</td>
<td>0</td>
<td>$\chi^2 = 4.5; p &lt; .03$</td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse*</td>
<td>5 (4)</td>
<td>0</td>
<td>$\chi^2 = 0.9; p = .4$</td>
<td></td>
</tr>
<tr>
<td>Alcohol dependence*</td>
<td>1 (1)</td>
<td>0</td>
<td>$\chi^2 = 2.6; p = .1$</td>
<td></td>
</tr>
<tr>
<td>Drug abuse*</td>
<td>3 (2)</td>
<td>0</td>
<td>$\chi^2 = 5.4; p &lt; .02$</td>
<td></td>
</tr>
<tr>
<td>Drug dependence*</td>
<td>6 (4)</td>
<td>0</td>
<td>$\chi^2 = 5.9; p = .016$</td>
<td>4.6 (0.9, 23.4)</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>13 (10)</td>
<td>4 (3)</td>
<td>$\chi^2 = 7.9; p &lt; .005$</td>
<td>5.0 (1.1, 22.1)</td>
</tr>
<tr>
<td>Tic disorders</td>
<td>18 (13)</td>
<td>4 (3)</td>
<td>$\chi^2 = 9.2; p &lt; .002$</td>
<td>2.5 (1.1, 5.5)</td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>45 (34)</td>
<td>21 (18)</td>
<td>$\chi^2 = 23.2; p &lt; .001$</td>
<td></td>
</tr>
<tr>
<td>Elimination disorders</td>
<td></td>
<td></td>
<td>$\chi^2 = 13.8; p &lt; .001$</td>
<td>5.1 (1.6, 15.8)</td>
</tr>
<tr>
<td>Enuresis</td>
<td>35 (25)</td>
<td>7 (6)</td>
<td>$\chi^2 = 5.4; p = .02$</td>
<td></td>
</tr>
<tr>
<td>Encopresis*</td>
<td>6 (4)</td>
<td>0</td>
<td>$\chi^2 = 10.4; p = .006$</td>
<td></td>
</tr>
<tr>
<td>Language disorders</td>
<td></td>
<td></td>
<td>$\chi^2 = 6.5; p &lt; .011$</td>
<td>5.2 (1.0, 27.1)</td>
</tr>
<tr>
<td>Language disorder</td>
<td>18 (13)</td>
<td>3 (3)</td>
<td>$\chi^2 = 0.2; p = .7$</td>
<td>1.7 (0.1, 37.8)</td>
</tr>
<tr>
<td>Stuttering</td>
<td>3 (2)</td>
<td>1 (1)</td>
<td>$\chi^2 = 3.6; p = .2$</td>
<td></td>
</tr>
<tr>
<td>Eating disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anorexia*</td>
<td>2 (1)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bulimia*</td>
<td>2 (1)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Mean ± SD are reported for continuous variables; n and percent (in parentheses) are reported for categorical data. ADHD = attention-deficit hyperactivity disorder. t tests are reported for continuous variables and Pearson X2 is reported for categorical variables. Subscript numbers are degrees of freedom.

Psychopathology in Females With Attention-Deficit/Hyperactivity Disorder: a Controlled, 5-Year Prospective Study

<table>
<thead>
<tr>
<th>Major Psychopathology</th>
<th>Control N = 122</th>
<th>ADHD N = 140</th>
<th>Hazard Ratio</th>
<th>Test Statistic (df), P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Depressive Disorder</td>
<td>.03 (01, 10)</td>
<td>.40 (31, 50)</td>
<td>19.2</td>
<td>$X^2_{(m)} = 24.5, p &lt; .001$</td>
</tr>
<tr>
<td>Multiple Anxiety Disorder</td>
<td>.17 (11, 25)</td>
<td>.52 (44, 61)</td>
<td>3.8</td>
<td>not estimated*</td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td>.02 (00, 07)</td>
<td>.22 (16, 31)</td>
<td>15.3</td>
<td>$X^2_{(m)} = 13.9, p &lt; .001$</td>
</tr>
<tr>
<td>Psychosis</td>
<td>.00</td>
<td>.07 (04, 13)</td>
<td>—</td>
<td>not estimated*</td>
</tr>
<tr>
<td>Antisocial Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oppositional-Defiant Disorder</td>
<td>.07 (03, 13)</td>
<td>.56 (48, 66)</td>
<td>11.0</td>
<td>$X^2_{(m)} = 40.6, p &lt; .001$</td>
</tr>
<tr>
<td>Conduct Disorder</td>
<td>.03 (01, 09)</td>
<td>.23 (16, 33)</td>
<td>10.2</td>
<td>$X^2_{(m)} = 14.4, p &lt; .001$</td>
</tr>
<tr>
<td>ASPD</td>
<td>.00</td>
<td>.05 (01, 19)</td>
<td>—</td>
<td>not estimated*</td>
</tr>
<tr>
<td>Developmental Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enuresis</td>
<td>.09 (05, 16)</td>
<td>.28 (21, 37)</td>
<td>3.3</td>
<td>$X^2_{(m)} = 11.2, p = .001$</td>
</tr>
<tr>
<td>Tics/Tourette’s Disorder</td>
<td>.05 (02, 11)</td>
<td>.19 (13, 27)</td>
<td>4.1</td>
<td>$X^2_{(m)} = 9.5, p = .002$</td>
</tr>
<tr>
<td>Language Disorder</td>
<td>.03 (01, 09)</td>
<td>.17 (12, 25)</td>
<td>4.6</td>
<td>$X^2_{(m)} = 7.7, p = .006$</td>
</tr>
<tr>
<td>Encopresis</td>
<td>.00</td>
<td>.05 (02, 10)</td>
<td>—</td>
<td>not estimated*</td>
</tr>
<tr>
<td>Substance Dependence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotine Dependence</td>
<td>.12 (07, 20)</td>
<td>.38 (29, 49)</td>
<td>3.1</td>
<td>$X^2_{(m)} = 12.9, p &lt; .001$</td>
</tr>
<tr>
<td>Drug Dependence</td>
<td>.03 (01, 10)</td>
<td>.13 (08, 23)</td>
<td>4.6</td>
<td>$X^2_{(m)} = 7.3, p = .007$</td>
</tr>
<tr>
<td>Alcohol Dependence</td>
<td>.00</td>
<td>.04 (02, 11)</td>
<td>2.7</td>
<td>$X^2_{(m)} = 1.4, p = .231$</td>
</tr>
</tbody>
</table>

MR = Cumulative lifetime prevalence of disorder by age 16 as estimated by Kaplan-Meier failure function. All analyses adjusted for baseline SES and baseline age.

*Effect could not be estimated by the Cox regression model due to zero cases in the control group.

**Major depression with severe impairment.

*Greater than or equal to two anxiety disorders.

†Antisocial personality disorder; estimates based on the subset of subjects who were administered the SCID (42 controls and 40 ADHD subjects).
Psychopathology in Females With Attention-Deficit/Hyperactivity Disorder: a Controlled, 5-Year Prospective Study (mean age 16.7)

Figure 1. Cox proportional hazards models of lifetime psychiatric comorbidity in females with and without ADHD. Statistical comparison of ADHD (n = 140) and Control (n = 122) females: Psychotic, Mood and Anxiety Disorders: z=7.6, p<.001; Antisocial Disorders: z=6.5, p<.001; Developmental Disorders: z=4.5, p<.001; Substance Dependence Disorders: z=3.7, p<.001; Eating Disorders: z=1.9, p<.061.

Patterns of Comorbidity Among Girls With ADHD: A Meta-analysis

- Meta-analytically summarize rates of comorbid internalizing (anxiety, depression) and externalizing (oppositional defiant disorder [ODD], conduct disorder [CD]) psychopathology among girls with and without ADHD
- Literature searches (PubMed, Google Scholar) identified published studies examining comorbid psychopathology in girls with and without ADHD
- Eighteen studies (1997 participants) met inclusion criteria and had sufficient data for the meta-analysis
- Compared with girls without ADHD, girls with ADHD were significantly more likely to meet Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria for each comorbid disorder assessed. Relative odds were higher for externalizing (ODD: 5.6×; CD: 9.4×) relative to internalizing disorders (anxiety: 3.2×; depression: 4.2×)
- Meta-regression revealed larger effect sizes of ADHD on anxiety for studies using multiple diagnostic methods, featuring younger children, and including clinic-referred (versus community referred) girls; the effect of ADHD on ODD varied based on diagnostic informant

*FIGURE 5*

Forest plot graphing ORs for depression among girls with ADHD versus without. Each study is represented by one horizontal line and box, with location of the box on the x-axis corresponding to the point estimate for each study, and the size of the box indicating the weight (inverse of variance) of the study. The diamond and dotted vertical line depict the overall effect estimate for all 12 studies, with the width of the diamond representing the CI.
An Examination of the Association Between Anxiety and Social Functioning in Youth With ADHD: a Systematic Review

- Up to 50% of children with Attention-Deficit/Hyperactivity Disorder (ADHD) meet criteria for an anxiety disorder.
- Understanding the factors associated with social functioning in ADHD is important given the limited efficacy of existing social skills interventions for this population.
- This systematic review aimed to determine the association between anxiety and social functioning (social problems, peer status, and social skills/competence) in children and adolescents with ADHD.
- 4807 articles for screening with 31 included in the final review.
- Anxiety symptom severity was associated with lower levels of social skills and higher levels of social problems in young people with ADHD.
- Few differences emerged when defining anxiety based on diagnostic measures.
- Key variables emerged that influenced the associations between anxiety and social functioning, including the type of reporter and sample characteristics such as age, sex, ADHD subtype, and other comorbidites.
- Implications for social functioning interventions in ADHD given the role of anxiety symptoms in predicting poorer social functioning.

An Examination of the Association Between Anxiety and Social Functioning in Youth With ADHD: a Systematic Review

<table>
<thead>
<tr>
<th>(From Table 1)</th>
<th>Social Problems Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antshel 2014</td>
<td>No difference in peer problems</td>
</tr>
<tr>
<td>Bagwell 2006</td>
<td>Social problems associated with anxiety and ADHD</td>
</tr>
<tr>
<td>Biederman 1996</td>
<td>ADHD + Anxiety did not have more peer problems than ADHD alone</td>
</tr>
<tr>
<td>Biederman 2013</td>
<td>ADHD + PTSD had more peer problems than ADHD alone</td>
</tr>
<tr>
<td>Bowen 2008</td>
<td>Differences in capacity to make friends across comorbidity groups. No difference between children with ADHD + anxiety and ADHD alone</td>
</tr>
<tr>
<td>Farmer 2015</td>
<td>Small positive correlations between peer conflict levels and anxiety scores</td>
</tr>
<tr>
<td>Greene 1997</td>
<td>Children with ADHD plus social disability had higher rates of anxiety 4 years later</td>
</tr>
<tr>
<td>Lee 2012</td>
<td>Anxiety + ADHD had more social problems than ADHD alone but no difference in social impairment</td>
</tr>
<tr>
<td>Mulrany 2016</td>
<td>Peer problems significantly associated with anxiety in children with ADHD in unadjusted analyses; not significant in adjusted analyses</td>
</tr>
<tr>
<td>Newcorn 2004</td>
<td>ADHD + anxiety significantly associated with adolescent-rated social problems</td>
</tr>
<tr>
<td>Pollack 2016</td>
<td>Significant differences in social problems between ADHD + ODD + Anxiety &amp; ADHD + ODD &amp; ADHD alone</td>
</tr>
<tr>
<td>Sciberras 2014</td>
<td>Children with ADHD + more than 2 anxiety comorbidities had more peer problems than ADHD only in unadjusted analyses; no significant differences in adjusted analyses.</td>
</tr>
</tbody>
</table>
An Examination of the Association Between Anxiety and Social Functioning in Youth With ADHD: a Systematic Review. Bishop et al. (2019)

<table>
<thead>
<tr>
<th>(From Table 1)</th>
<th>Bullying/Aggression Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abikoff 2002</td>
<td>No differences in aggression between ADHD + Anxiety + DBD &amp; ADHD + Anxiety &amp; ADHD alone</td>
</tr>
<tr>
<td>Danforth 2017</td>
<td>No differences in aggression between ADHD + Anxiety &amp; ADHD alone</td>
</tr>
<tr>
<td>Gadow 2011</td>
<td>No difference in peer aggression between ADHD + Anxiety &amp; ADHD alone</td>
</tr>
<tr>
<td>Hu 2016</td>
<td>No association between bullying perpetration and anxiety in adolescents with ADHD</td>
</tr>
<tr>
<td>Mikami 2011</td>
<td>Significant negative interaction between anxiety and ADHD status in comparison children; no interaction for children with ADHD</td>
</tr>
<tr>
<td>Yen 2014</td>
<td>Cyberbullying perpetration not significantly associated with anxiety in children with ADHD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Victimisation Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becker 2016</td>
</tr>
<tr>
<td>Hu 2016</td>
</tr>
<tr>
<td>Yen 2014</td>
</tr>
</tbody>
</table>
An Examination of the Association Between Anxiety and Social Functioning in Youth With ADHD: a Systematic Review

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becker 2015</td>
<td>Youth with ADHD + anxiety had poorer social skills on some measures than youth without anxiety</td>
</tr>
<tr>
<td>Biederman 2013</td>
<td>No differences in ADHD alone &amp; ADHD + PTSD in how children engaged in activities with peers</td>
</tr>
<tr>
<td>Bowen 2008</td>
<td>Children with ADHD + anxiety had lower social competence compared to ADHD alone</td>
</tr>
<tr>
<td>Jensen 2001</td>
<td>Differences on some measures of social skills between children with ADHD + anxiety &amp; ADHD alone</td>
</tr>
<tr>
<td>Lee 2012</td>
<td>No differences in social skills of ADHD + anxiety &amp; ADHD alone</td>
</tr>
<tr>
<td>March 2000</td>
<td>Children with ADHD + anxiety + CD had poorer social skills than ADHD + anxiety &amp; ADHD alone</td>
</tr>
<tr>
<td>Mikami 2011</td>
<td>The influence of anxiety symptoms on social skills was stronger for comparison children than for children with ADHD</td>
</tr>
<tr>
<td>Pollack 2016</td>
<td>Significant difference in social problems of children with ADHD + ODD + anxiety &amp; ADHD + ODD &amp; ADHD alone</td>
</tr>
<tr>
<td>Ray 2017</td>
<td>No differences in anxiety symptoms when comparing socially healthy to socially impaired adolescents</td>
</tr>
<tr>
<td>Schneider 2009</td>
<td>In ADHD alone group, social competence was associated with global anxiety and social phobia</td>
</tr>
<tr>
<td>Sukhodolsky 2005</td>
<td>No difference in social competence of children with OCD + ADHD compared to ADHD alone</td>
</tr>
</tbody>
</table>
Management of the Whole Patient
Management of the Whole Patient

- Treat the ADHD with longer acting medications to cover the whole day
  - Longest amphetamines lisdexamfetamine (Vyvanse), mixed salts of a single-entity amphetamine product (Mydayis)
  - Longest methylphenidate transdermal methylphenidate (Daytrana), nighttime dosing of methylphenidate with morning onset (Jornay pm), oros methylphenidate (Concerta)
  - Nonstimulants are the long-acting clonidine, guanfacine, and atomoxetine
- May need combination treatment for better coverage
  - Use of stimulant plus long acting alpha agonist
  - Use of stimulant plus atomoxetine
  - Use of long- and short-acting stimulants
- Treat the comorbidity either with selection of ADHD agent or by adding in an agent for the comorbid condition
  - Anxiety: either use atomoxetine, which has approval and data for anxiety in ADHD, or add in SSRI/SNRI or CBT
Management of the Whole Patient (cont’d)

• Treat the comorbidity either with selection of ADHD agent or by adding an agent for the comorbid condition
  • Depression: may wish to select dopaminergic agent bupropion or add SSRI/SNRI or CBT
  • Bipolar: many treatment studies have allowed continued treatment of ADHD with stimulants; can use all FDA-approved bipolar meds
  • Autism: treat ADHD and may be more emotional on stimulants; atomoxetine study positive in this population
  • Tics: try non-stimulants first, may then do combination treatment of 2 ADHD agents or adding an antipsychotic, or use habit-reversal CBT to manage the tics
Management of the Whole Patient (cont’d)

• Remember school accommodations are important
  • 504 plan can help with preferential seating, extra time on tests, and later for standardized testing (ACT, SAT)
  • IEP goes into more support and spelling out everything teachers must do to help student succeed
  • Copies of notes in class, power points, textbooks at home, portal lists of all homework and due dates, reminders to hand in assignments

• Tutoring and coaching can help
  • Effective learning in class, critical reading, time management, and breaking down assignments into smaller chunks can be taught and mastered
  • Some students have an extra period to do work before going home
Protective Effects of Stimulants on Comorbidity

N=140 boys with ADHD at entry; 10 year follow-up data

N=82 subjects receiving stimulants [mean duration of 6 years] and 30 not on stimulants