

## The Adolescent with ADHD: Managing Transition

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Service



## Disclosure Statement: Philip Hazell

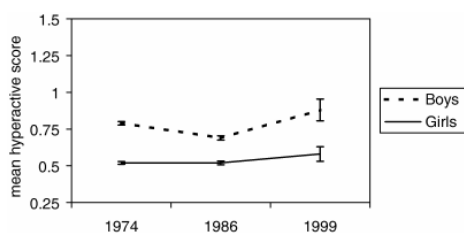
Source	Consultant	Advisory Board	Stock Equity >\$10,000	Speaker's Bureau	Research Contract
Eli Lilly	Submissions to Australian drug regulatory and funding bodies	International Australia	-	Oral and poster presentations	Atomoxetine relapse prevention study, ADHD + ODD study
Pfizer	-	-	-	Oral presentations	-
Janssen	-	Australia	-	Oral presentations	-
Celltech	-	-	-	-	Trial of Metadate CD for ADHD
Novartis	-	Australia	-	-	-
Shire	-	International	-	-	-

- Prevalence of attention-deficit/hyperactivity disorder (ADHD) declines from childhood to adolescence
- 50% reduction in prevalence per five years

## Gender and age influences on cross-sectional ADHD prevalence (NSMHW)

- Males (15.4%) > Females (6.8%)
- Prepubertal > Pubertal
  - Male: 6-12 = 19.3% > 13-17 = 10%
  - Female: 6-12 = 8.8% > 13-17 = 3.8%

## Historical trends in hyperactive problem scale scores (UK survey data)



Collishaw et al. J Child Psychol and Psychiatry 2004;45: 1350-1362

## Trend in US rates of stimulant prescribing by age band

Age	1987	1996	Increase
<6	0.22	0.31	41%
6-14	1.18	4.14	250%
15-18	0.15	1.56	940%

Adapted from Olsson et al. J Am Acad Child Adolesc Psychiatry 2002;41: 514-521

### Factors contributing to increase in prescribing to adolescent patients

- greater recognition of the disorder
- flow on effects from treatment in childhood
- cognitive demands of modern education
- availability of more 'user friendly' forms of medication

### New treatment initiations in adolescence

- predominantly inattentive type ADHD, usually because increasing academic demand has exposed the attentional impairment
- ADHD previously overlooked in the context of prominent conduct or emotional problems

### Service models

- Continuity of care from childhood through adolescence
- Adolescent specific services

### Lifestyle challenges

- Greater demand on executive function skills-greater impairment
- Greater concentration demands- up to 3 hrs for some assessment tasks
- More complex social interactions
- Evening activities
- Driving
- Workplace safety
- Exposure to disinhibiting substances

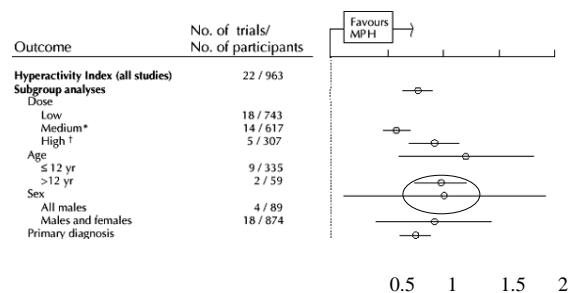
### Efficacy: Methylphenidate IR

Smith et al. Clin Child Family Psychol Rev 2000;3:243-67.

- As effective for adolescents as it is for younger children?
- Meta-analysis of 8 RCTS (199 participants, age range 12-18 years) found an effect size (ES) of 0.94 for ADHD symptoms
- Response rate around 50% in 3 RCTs

### Subgroup analyses, effect size for methylphenidate

Schachter et al. CMAJ 2001;165:1475-88

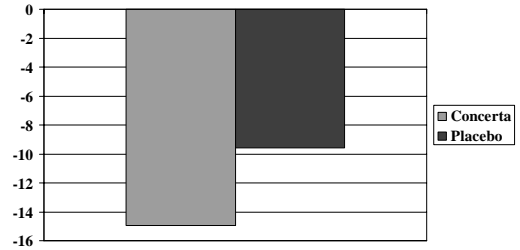


## Efficacy: OROS Methylphenidate (Concerta)

Wilens et al. Arch Pediatr Adolesc Med 2006;160:82-90.

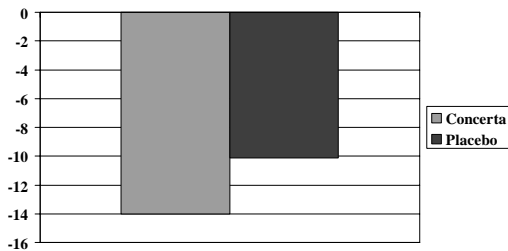
- 1 RCT randomized control trial involving 177 outpatients (age range 13 to 18 years)
- Greater proportion much or very much improved on Clinical Global Impressions (52% v 31%) after 2 weeks

## Mean change in clinician-rated ADHD symptoms after 2 weeks



$F_{1,158} = 11.21, p < .01$

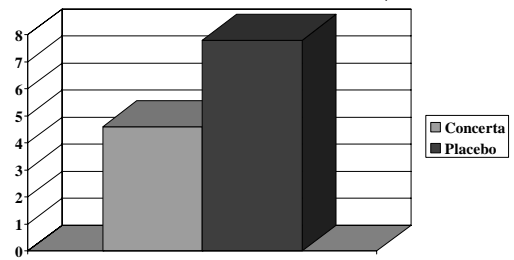
## Mean change in parent-rated ADHD symptoms after 2 weeks



$F_{1,158} = 7.29, p < .01$

## Mean number driving errors (patients 16-18 yrs)

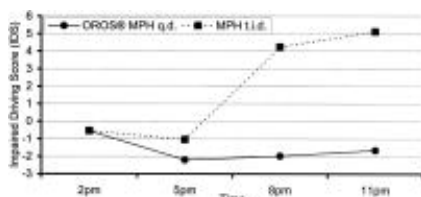
Cox et al. J Am Board Fam Pract 2004;17:235-9.



$t = 3.06, p < .05$

## Driving errors in simulator: OROS vs IR MPH (cross over, n = 6 males 16-19 yrs)

Cox et al. J Am Acad Child Adolesc Psychiatry 2004;43:269-275

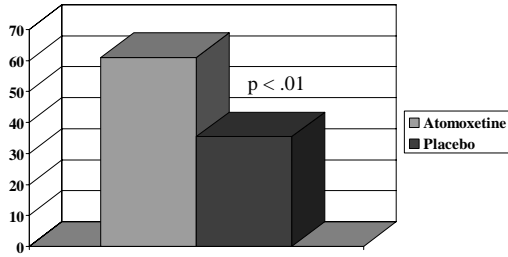


## Atomoxetine

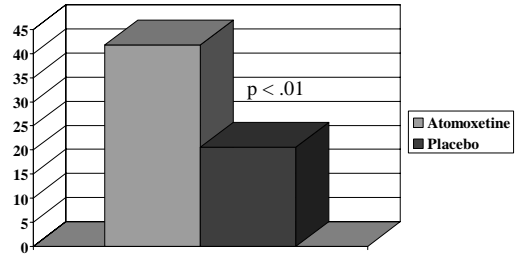
Wilens et al. J Am Acad Child Adolesc Psychiatry 2006;45:149-57.

- No trials specifically directed to adolescent patients
- But most trials have included adolescent patients
- Subgroup analyses of data pooled from 6 similarly conducted RCTs (atomoxetine n = 107, placebo n = 69)

Percentage responders to atomoxetine (25% reduction ADHD rating scale)



Percentage responders to atomoxetine (2 point reduction in CGI score)



### Atomoxetine

- Packaging carries a safety alert for suicidality, although the small number of patients who have developed suicidal ideation or behaviour during treatment trials have been pre adolescent.

### Bupropion

- Mostly studied in adolescents with comorbid substance abuse-open label studies found reductions in ADHD symptoms from 13-43%
- 'Equivalence' reported in crossover trial with methylphenidate in sample aged 7-17 but sample had insufficient power to support this conclusion
- Bupropion and methylphenidate no more effective than placebo in reducing symptoms of ADHD in adults with comorbid cocaine abuse

### Moclobemide

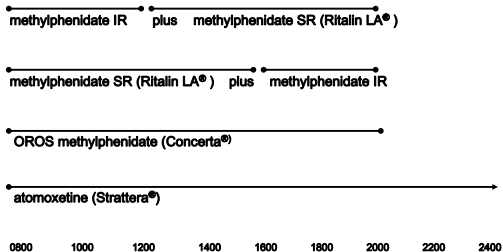
- No data specific to adolescents

### Clonidine

- No data specific to adolescents

School activities

Extracurricular, homework,  
driving, part time work



Hazell. CNS Drugs 2007;21:37-46

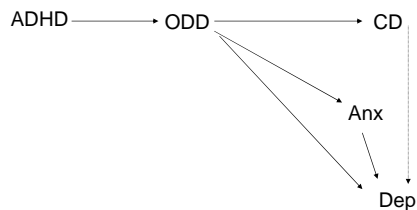
## Management issues

- Supervision by school staff of medication administration is no longer guaranteed
- Patients are likely to have activities in the afternoon and evening that continue to place attentional demands on them
- *Clear advantage for long acting medications*
- Some patients still require top up with immediate release
- Weight-based calculation of drug dosage is a less useful guide in adolescents than in younger children, as there is wide variability in dose requirement
- Greater reliance on self-report

## Emergent problems

- treatment induced dysphoria
- depression
- adolescent onset conduct problems
- substance abuse
- bipolar disorder
- psychosis
- drug diversion

## Developmental sequence to disruptive and mood disorder



Burke et al. JCPP 2005;46:1200-1210

## Factors that mediate association between ADHD, CD and Depression



Drabick et al. JCPP 2006;47:766-774

## Goh Study

- Most ADHD patients thought to have treatment emergent depression already had elevated Anx/Dep and Withdrawn subscale scores on the CBCL at intake

## Emergent MDD

Stage 1	If mild MDD, persist with stim, stim SR or consider switch to SNRI, TCA, RIMA
Stage 2 ±ADHD, -MDD	Withdraw stim (as can cause dysphoria)
Stage 3 ± ADHD, -MDD - ADHD, +MDD	SSRI Cautiously reintroduce stim after interval

+ treatment response  
- no treatment response

## Concurrent treatment

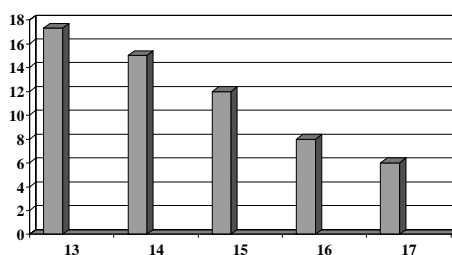
- Oral contraceptive
- Roaccutane
- *no known interactions between these agents and either the psychostimulants or atomoxetine*

## Pregnancy and breastfeeding

- Risk unknown for psychostimulants and atomoxetine

## Discontinuation

Rate per 1000 population of stimulant prescribing by age, NSW 2000



## Duration of maintenance treatment

- No guidelines exist
- While individual still impaired by ADHD or where a relapse in ADHD symptoms would cause significant impairment
- Typically at least until mid high school, often beyond
- If patient uncertain about whether to continue, structured trial off treatment for 3 months then review

## Clinical Global Impressions- ADHD Severity

- 1 Normal not ill
- 2 Minimally ill
- 3 Mildly ill
- 4 Moderately ill
- 5 Markedly ill
- 6 Severely ill
- 7 Very severely ill

## CGI-ADHD-Severity

- Increase in scores by two points from entry to maintenance treatment suggests lack of effectiveness. Consider increase in total daily dose and/or dose frequency.
- Scores of 1 continuously for 12 months suggest that a trial off treatment is indicated

## Possible reasons for unplanned discontinuation

- Remission
- Lower task demand eg apprenticeship rather than school
- Perceived lack of efficacy
- Adverse effects
- Non-adherence once parents do not supervise
- Lack of available services
- Lack of expertise

## Discontinuation syndrome

- Discontinuation syndrome reported for neither psychostimulant nor atomoxetine

## Transition to adult treatment

- access to treatment is a problem
  - ADHD is not considered 'core business' by publicly funded adult mental health services
  - few psychiatrists in private practice routinely treat such patients
- options
  - refer to child and adolescent trained psychiatrist who also treats adults
  - switch the patient to a non-stimulant medication that can be prescribed by a general practitioner