CO-OCCURRING ADHD AND DEPRESSION IN YOUTH

ASSESSMENT and TREATMENT CONSIDERATIONS

Dr. Nicole Martin, BSc, MD, FRCPC
Child and Adolescent Psychiatry, Ledger Program
Clinical Instructor, University of British Columbia
nicole.martin@islandhealth.ca

DISCLOSURES

- None

LEARNING OBJECTIVES

1. Discuss the relationship between ADHD and symptoms of depression
2. Determine an approach to assessment and treatment of these co-occurring conditions
3. Discuss of the rational for early detection and treatment of ADHD

ASSUMPTIONS/DISCLAIMERS

- Baseline knowledge of DSM V criteria for MDD and ADHD
- Baseline knowledge of biopsychosocial assessment process and tools for MDD and ADHD – eg. PHQ9 and SNAP forms, and first line pharmacologic treatment options for both
- Focus will be primarily on pharmacological treatment decisions. Specific behavioural, psychological and family interventions are important but will not be reviewed in detail

CASE EXAMPLE

- 14 yr (Grade 9) female comes to your office in October with presenting complaint of low mood and passive suicidal ideation with some superficial NSSI.
  - No previous psych history, medically well, no medication
  - Has tried MJ and ETOH 1-2x but not a regular user
  - Struggling with school attendance, can't concentrate on the work, grades are starting to slip, low energy, losing small amount of weight
  - Spending lots of time in bedroom, irritable and withdrawn from family and activities (e.g, soccer and dance.)
  - Sleep is highly disruptive with difficulty initiating and sustaining sleep

CASE EXAMPLE con't

- Early history:
  - Outgoing, "intense" personality. Lots of meltdowns
  - Social butterfly, no significant anxiety
  - Got reasonable grades in elementary school, often done early, careless mistakes - "would do better if applied self"
  - Middle school started having trouble with friend groups

CASE EXAMPLE con't

- Physical Exam
  - Thin, well appearing adolescent
  - Vitals normal
  - Fresh NSSI wounds – occurred after argument with parents about grades
  - MSE – downcast, withdrawn. Seems spaced out – loses focus on the questions asked. Endorsing intermittent passive SI, no plan.

- B/W – slightly low ferritin, otherwise unremarkable.

WHAT IS GOING ON?

- DIFFERENTIAL DIAGNOSIS:
  - **MDD**
  - **ADHD**
  - PTSD
  - Adjustment reaction (Family, social, school stressors – bullying)
  - Medical issues – eg. Eating disorder, thyroid issues

LEARNING OBJECTIVES

1. Discuss the relationship between ADHD and symptoms of depression
2. Determine an approach to assessment and treatment of these co-occurring conditions
3. Discuss of the rational for early detection and treatment of ADHD

THE PROBLEMS

- Diagnostic challenges
  - ADHD and MDD have symptom overlap
  - Some symptoms of ADHD do not become clinically relevant until middle school age, high school or college – eg. Inattentive subtype, which can coincide with MDD onset

- MDD and ADHD are highly comorbid
  - 6x more likely to have MDD 1 yr after ADHD dx (Gundel *et al.* 2018)
  - MDD on average 5x higher in ADHD youth (Beiderman, 2008)
  - 10-30% of youth with ADHD may also have MDD, up to 70% may eventually develop MDD (CHADD, 2023)

- Comorbid ADHD can worsen MDD trajectory. (Beiderman, 2008)
  - Earlier onset, greater symptom severity, longer duration, more hospitalizations, and increased risk of suicidality and NSSI

- Can be difficult to know what to prioritize with treatment when both ADHD and MDD occur together

WHY DO ADHD AND MDD CO-OCCUR?

- Can have similar risk factors/etiologic factors
  - Common genetic predisposing factors (Farone and Larsson, 2019; Demontis et al, 2019)
  - Early childhood trauma and adversity; high ACE scores (Walker et al. 2021; Brown et al, 2017.)
  - Prenatal exposures and in-utero experiences
- ADHD symptoms as a risk factor for developing MDD

HOW CAN ADHD LEAD TO MDD?

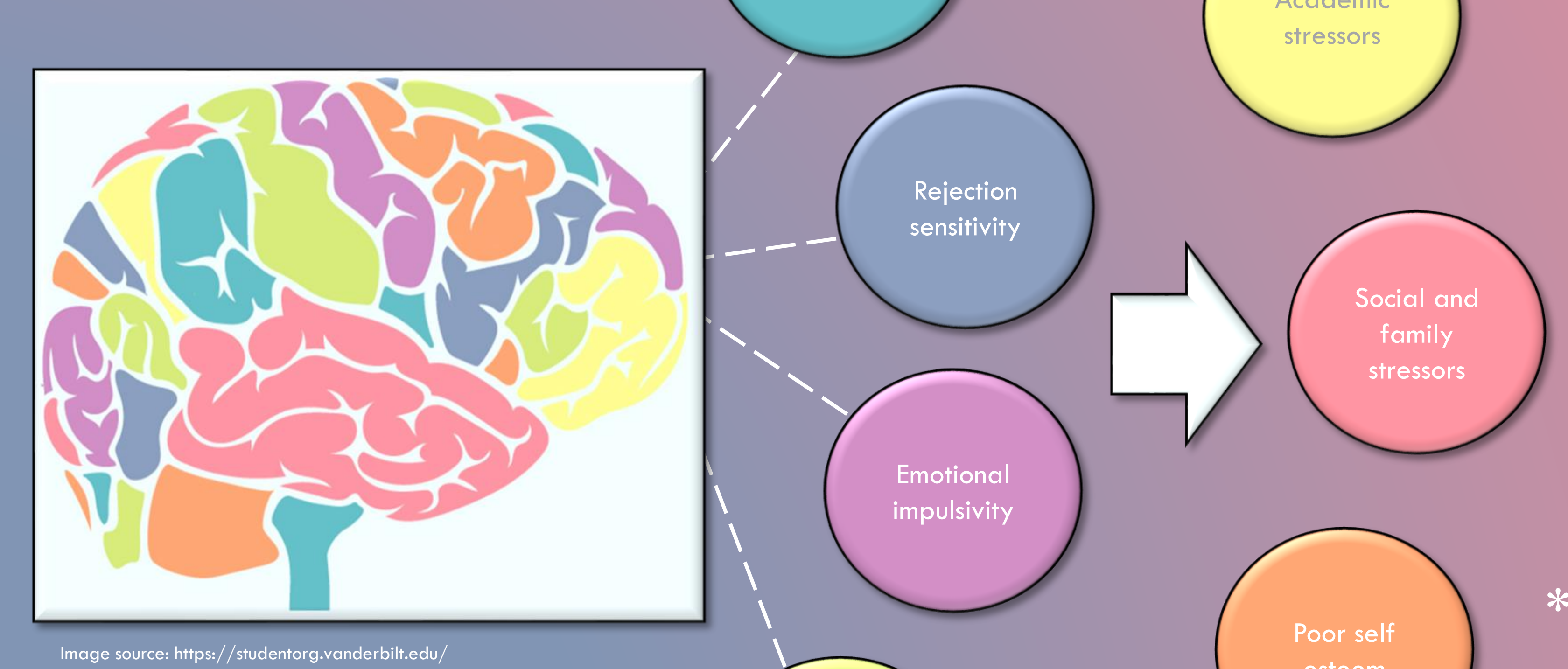
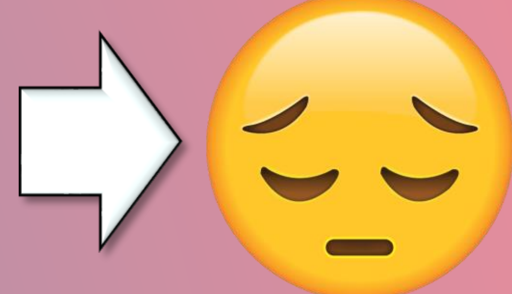


Image source: https://studentorg.vanderbilt.edu/



Poor self esteem

* High risk periods: transitions associated with large increase in cognitive demands

LEARNING OBJECTIVES

1. Discuss the relationship between ADHD and symptoms of depression

2. Determine an approach to assessment and treatment of these co-occurring conditions

3. Discuss of the rational for early detection and treatment of ADHD

ASSESSMENTS

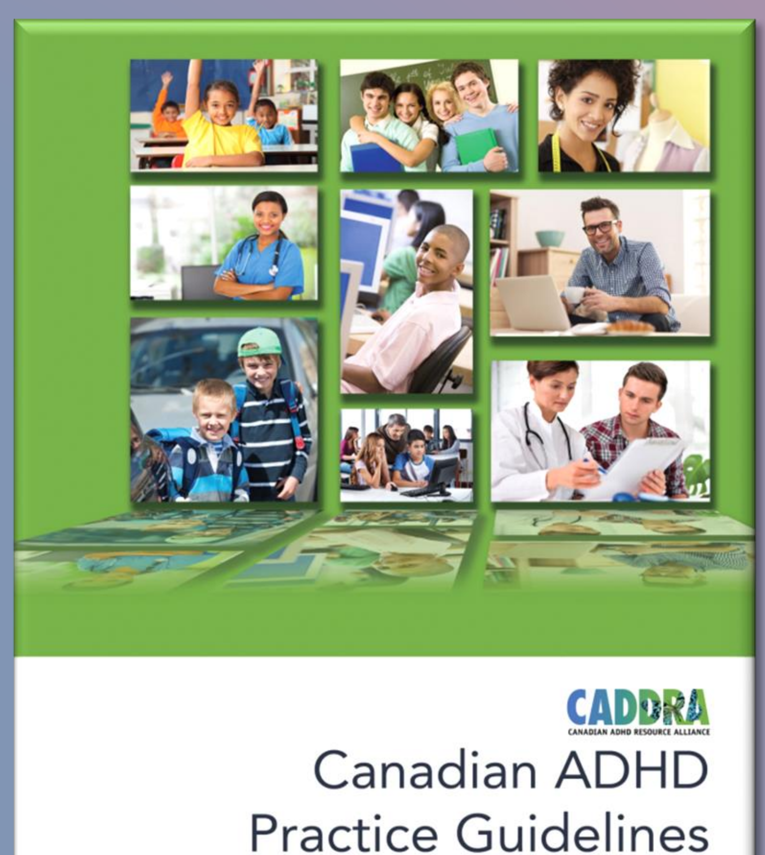
- Based on psycho-social history and collateral gathering – youth AND parent reports
  - Takes time!
  - Similar instruments – e.g SNAP – IV parents and teachers, PHQ9 – although may not be as accurate
  - **PHQ9 – question 3 (insomnia) and 7 (concentration) consider scoring only if deviation from baseline**
  - ***Focus on timelines*** – alter SNAP instructions to assess prior to depressive symptom onset. Consider different sources from current teacher (e.g previous coach, previous teacher)
  - Consider other diagnoses – eg. Substance use, PTSD, bipolar disorder, anxiety
  - Family history (ADHD?), medical history
  - Safety – suicidality, abuse, substances

ASSESSMENTS con't

- RS Diler *et al*. Differentiating major depressive disorder in youths with attention deficit hyperactivity disorder. 2007.
  - Symptoms unique to MDD:
    - social withdrawal
    - anhedonia
    - depressive cognitions
    - suicidal thoughts
    - psychomotor retardation

TREATMENT APPROACH: co-occurring ADHD AND MDD

- CADDRA (2022) and TEXAS (2007) Approach



The Texas Children's Medication Algorithm Project: Revision of the Algorithm for Pharmacotherapy of Attention-Deficit/Hyperactivity Disorder

STEVEN R. PLISZKA, M.D., M. LYNN CRISMON, PHARM.D., CARROLL W. HUGHES, PH.D., C. KEITH CONNERS, PH.D., GRAHAM J. EMSLIE, M.D., PETER S. JENSEN, M.D., JAMES T. McCRACKEN, M.D., JAMES M. SWANSON, PH.D., MOLLY LOPEZ, PH.D., AND THE TEXAS CONSENSUS CONFERENCE PANEL ON PHARMACOTHERAPY OF CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

ABSTRACT

Objective: In 1998, the Texas Department of Mental Health and Mental Retardation developed algorithms for medication treatment of attention-deficit/hyperactivity disorder (ADHD). Advances in the psychopharmacology of ADHD and results of a feasibility study of algorithm use in community mental health centers caused the algorithm to be modified and updated. **Method:** We convened a consensus conference of academic clinicians and researchers, practicing clinicians, administrators, consumers, and families to revise the algorithms for the pharmacotherapy of ADHD itself as well as ADHD with specific comorbid disorders. New research was reviewed by national experts, and rationales were provided for proposed changes and additions to the algorithms. The changes to the algorithms were discussed and approved both by the national experts and experienced clinicians from the Texas public mental health system. **Results:** The panel developed consensually agreed-upon algorithms for ADHD with and without comorbid disorders. The major changes included elimination of pemoline as a treatment option, adding atomoxetine to the algorithm, and refining guidelines for treating ADHD with comorbid depression, aggressive behaviors, and tic disorders. **Conclusions:** Medication algorithms for ADHD can be modified to keep abreast of developments in the field. Although these evidence- and consensus-based treatment recommendations may be a useful approach to guide the treatment of ADHD in children, additional research is needed to determine how these algorithms can be used to maximally benefit child outcomes. *J. Am. Acad. Child Adolesc. Psychiatry*, 2006;45(6):642–657. **Key Words:** attention-deficit/hyperactivity disorder, algorithm, psychopharmacology, practice parameters.

In 1998, the Texas Department of Mental Health and Mental Retardation (now the Texas Department of State Health Services [DSHS]) convened a consensus conference to develop algorithms for the medication treatment of attention-deficit/hyperactivity disorder (ADHD) with or without comorbid disorders (Pliszka et al., 2000a). Briefly, this algorithm recommended a stimulant (methylphenidate [MPH] or amphetamine [AMP]) as the first stage of treatment. If this stimulant did not produce a satisfactory result, then stage 2 would be the stimulant not used in stage 1. Stage 3 was a trial of pemoline, and stage 4 was a trial of either bupropion or a tricyclic antidepressant. Stage 5 was the agent not

Accepted December 14, 2005.

Dr. Pliszka is with the Department of Psychiatry, University of Texas Health Science Center at San Antonio; Dr. Crismon is with the College of Pharmacy, University of Texas at Austin; Dr. Hughes is with the Department of Psychology and Dr. Emslie is with the Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas; Dr. Conners is with the Department of Psychiatric & Behavioral Science, Duke University, Durham, NC; Dr. Jensen is with Columbia University, New York State Psychiatric Institute, New York; Dr. McCracken is with the UCLA Neuropsychiatric Institute, Los Angeles; Dr. Swanson is with the Department of Psychiatry, University of California at Irvine; and Dr. Lopez is with the Texas Department of State Health Services, Austin.

Correspondence to Steven R. Pliszka, M.D., Department of Psychiatry, MC 7792, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900; e-mail: pliszka@uthscsa.edu.

0890-8567/06/4506-0642©2006 by the American Academy of Child and Adolescent Psychiatry.

DOI: 10.1097/01.chi.0000215326.51175.eb

TREATMENT APPROACH: co-occurring ADHD AND MDD

- CADDRA (2022) and TEXAS (2007) Approach:
  - Determine the most impairing diagnosis and prioritize treatment of that. If unclear – ask the patient!
  - Acute suicidality in context of MDD – prioritize MDD treatment
    - CBT psychotherapy +/- SSRI's (**fluoxetine** vs sertraline or escitalopram) (CANMAT, 2016)
    - If ADHD symptoms persist – treat with second agent for ADHD
  - If mild to moderate depressive symptoms - esp if clearly related to functional impairments of ADHD, prioritizing ADHD
    - First line – long-acting psychostimulant (see CADDRA). - or short-line first for Pharmacare coverage
    - Two trials of psychostimulants (can switch class - MPH or AMP)
    - If depressive symptoms persist – treat with second agent (e.g. SSRI)

TREATMENT APPROACH: co-occurring ADHD AND MDD

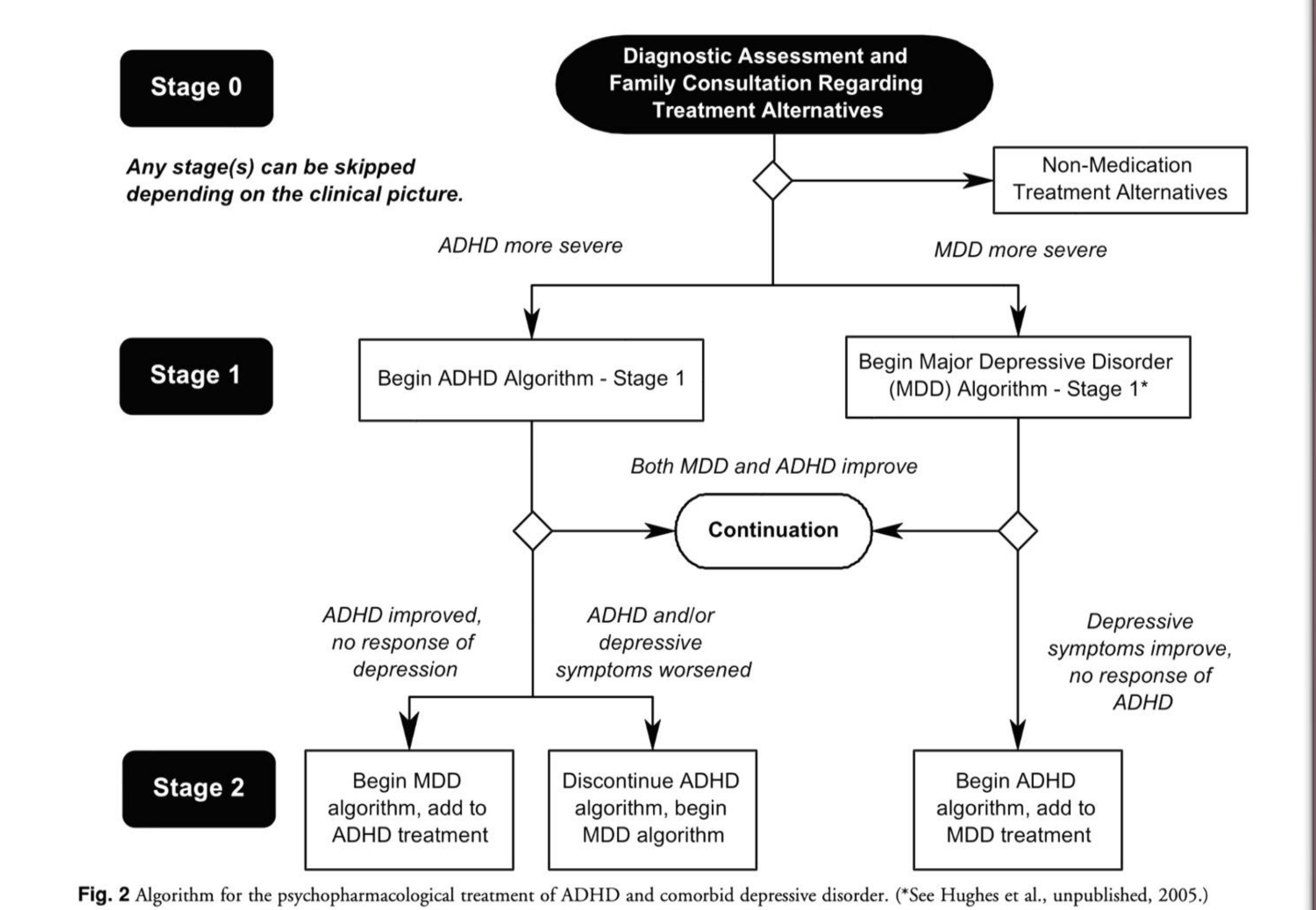


Fig. 2 Algorithm for the psychopharmacological treatment of ADHD and comorbid depressive disorder. (*See Hughes et al., unpublished, 2005.)

Source: Pliska *et al.* J. Am Acad Child Adolesc Psychiatry, 45:6, JUNE 2006

TREATMENT APPROACH:

CADDRA GUIDE TO ADHD PHARMACOLOGICAL TREATMENTS IN CANADA - NOVEMBER 2022

Medications & Illustrations			Delivery	Duration of action[1]	Starting dose[2]	Release mode Immediate/ Delayed (%)	Dose titration per product monograph[3]
AMPHETAMINE-BASED PSYCHOSTIMULANTS							
First Line	Adderall XR®	Capsules 5, 10, 15, 20, 25, 30 mg	Granules can be sprinkled	~12 h	5-10 mg q.d. a.m.	50/50	▲5-10 mg at weekly intervals Max. dose/day: Children = 30 mg Adolescents & Adults = 20-30 mg
First Line	Vyvanse®	Capsules 10, 20, 30, 40, 50, 60, 70[4] mg Chewable Tablets 10, 20, 30, 40, 50, 60 mg	Capsule content can be diluted in liquid or sprinkled Chewable tablets should be chewed thoroughly	~13-14 h	20-30 mg q.d. a.m.	Not Applicable (Prodrug)	▲10-20 mg by clinical discretion at weekly intervals Max. dose/day: All ages = 60 mg
Second Line	Dexedrine®	Tablets 5 mg Spansules 10, 15 mg	Scored Tablet Beaded Formulation	~4 h ~6-8 h	Tablets = 2.5 to 5 mg b.i.d. Spansules = 10 mg q.d. a.m.	100/0 50/50	▲5 mg at weekly intervals Max. dose/day: (q.d. or b.i.d.) Children & Adolescents = 20-30 mg Adults = 50 mg
METHYLPHENIDATE-BASED PSYCHOSTIMULANTS							
First Line	Biphentin®	Capsules 10, 15, 20, 30, 40, 50, 60, 80 mg	Granules can be sprinkled	~10-12 h	10-20 mg q.d. a.m.	40/60	▲10 mg at weekly intervals Max. dose/day: Children & Adolescents = 60 mg Adults = 80 mg
First Line	Concerta®	Extended Release Tablets 18, 27, 36, 54 mg	Osmotic-Controlled Release Oral Delivery System (OROS®)	~12 h	18 mg q.d. a.m.	22/78	▲18 mg at weekly intervals. Max. dose/day: Children & Adolescents = 54 mg Adults = 72 mg
First Line	Foquest®	Capsules 25, 35, 45, 55, 70, 85, 100 mg	Granules can be sprinkled	~13-16 h	25 mg q.d. a.m.	20/80	▲10-15 mg in intervals of no less than 5 days Max. dose/day: Children & Adolescents = 70 mg Adults = 100 mg
Second Line	Methylphenidate short-acting Ritalin®SR	Tablets 5 mg (generic) 10, 20 mg (Ritalin®) Tablets 20 mg	Scored Tablet Wax Matrix Preparation	~3-4 h ~8 h	5 mg b.i.d. to t.i.d. Adult: 20 mg q.d.	100/0 100/0	▲5-10 mg at weekly intervals Max. dose/day: All ages = 60 mg
NON-PSYCHOSTIMULANT - SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITOR							
Second Line	Strattera® (Atomoxetine)	Capsules 10, 18, 25, 40, 60, 80, 100 mg	Capsule needs to be swallowed whole to reduce GI side effects	Up to 24 h	Children & Adolescents: 0.5 mg/kg/day Adults = 40 mg q.d. for 7-14 days	Not Applicable	Maintain dose for a minimum of 7-14 days before adjusting: Children = 0.8 then 1.2 mg/kg/day 70 kg or Adults = 60 then 80 mg/day Max. dose/day: 1.4 mg/kg/day or 100 mg
NON-PSYCHOSTIMULANT - SELECTIVE ALPHA-2A ADRENERGIC RECEPTOR AGONIST							
Second Line	Intuniv XR® (Guanfacine XR)	Extended Release Tablets 1, 2, 3, 4 mg	Pills need to be swallowed whole to keep delivery mechanism intact	Up to 24 h	1 mg q.d. (morning or evening)	Not Applicable	Maintain dose for a minimum of 7 days before adjusting by no more than 1 mg increment weekly. Max. dose/day: Monotherapy: 6-12 years = 4 mg, 13-17 years = 7 mg As adjunctive therapy to psychostimulants: 6-17 years = 4 mg

Illustrations do not reflect actual size of pills/capsules. Longer-acting stimulants tend to have lower abuse potential than shorter-acting formulations. Non-stimulant formulations have no abuse potential. [1]Pharmacokinetic and pharmacodynamic responses vary from individual to individual. The clinician must use clinical judgment as to the duration of efficacy and not solely rely on reported values for PK-PD and duration of effect. [2]Starting doses in table are taken from product monographs. CADDRA recommends usually starting with the lowest dose available. [3]For specific details on how to start, adjust and switch ADHD medications, clinicians should refer to the Canadian ADHD Practice Guidelines (www.caddra.ca). [4]Vyvanse 70 mg is an off-label dosage for ADHD treatment in Canada. Original version of this sheet developed by Dr. Annick Vincent in collaboration with Direction des communications et de la philanthropie, Laval University. Access provincial and federal formulary information at tinyurl.com/uf3mxr1

CADDRA

LEARNING OBJECTIVES

1. Discuss the relationship between ADHD and symptoms of depression
2. Determine an approach to assessment and treatment of these co-occurring conditions
3. Discuss of the rational for early detection and treatment of ADHD

OUTCOMES - TREATMENT MATTERS!!

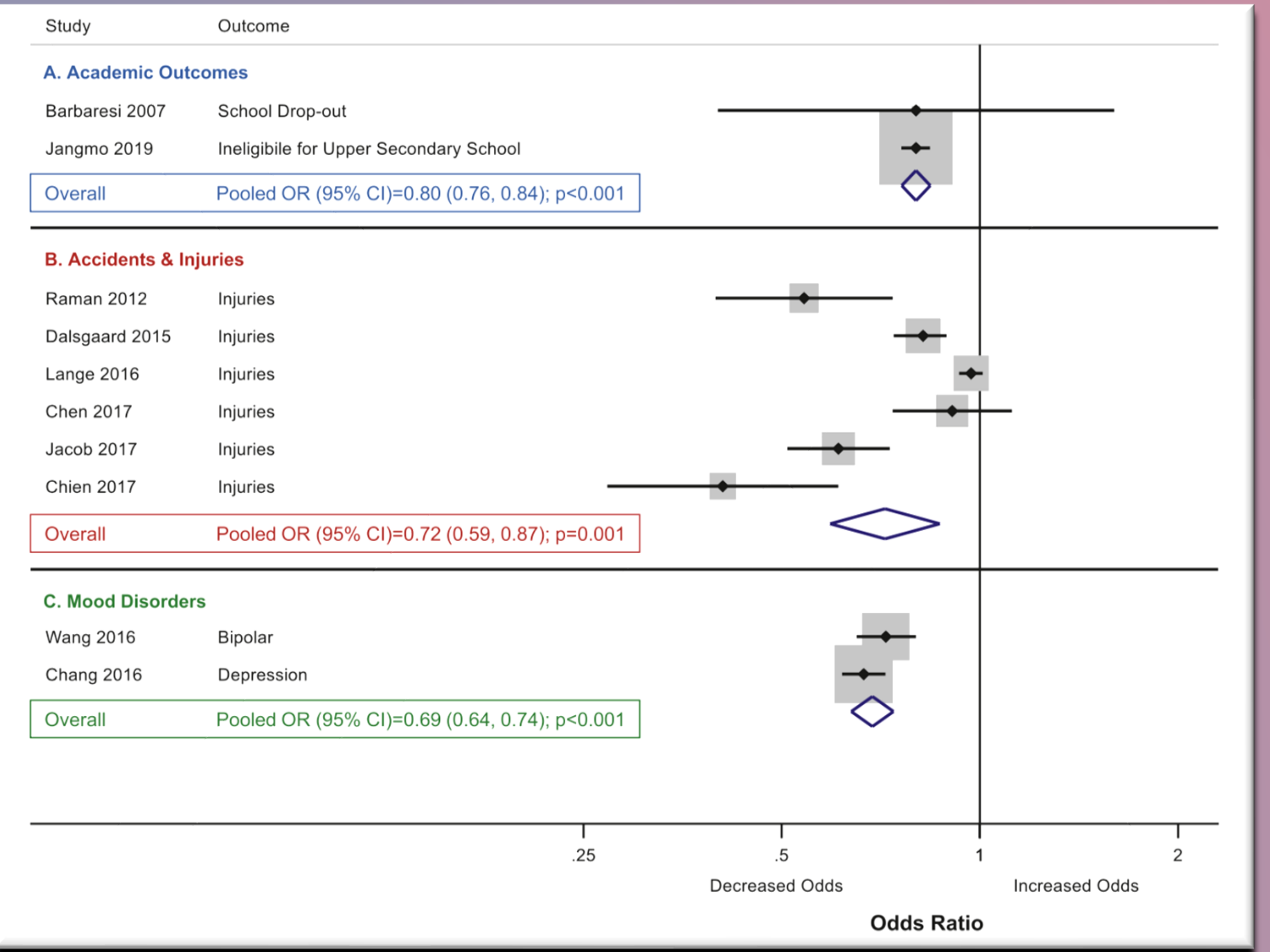
1. Beiderman *et al.* (2009):
   - Case control white male children with ADHD (n= 112) with 73% treated with stimulants
   - 10 year follow up:
     - "Participants with ADHD who were treated with stimulants were significantly less likely to subsequently develop depressive and anxiety disorders and disruptive behavior and less likely to repeat a grade compared with participants with ADHD who were not treated."

OUTCOMES - TREATMENT MATTERS!!

2. Chang *et al.* (2016) :
   - Retrospective study (n=38,752)
   - Treatment of ADHD associated with decreased risk of MDD development (approx. 20% ↓)
   - Moderated by duration of ADHD treatment

3. Park *et al.* (2022):
   - Nationwide cohort study (South Korea)
   - Long-term (n=1309) and short-term MPH (n=2199) users <18yr
   - Long-term MPH use significantly correlated to decreased MDD risk (and Conduct Disorder) HR:0.7

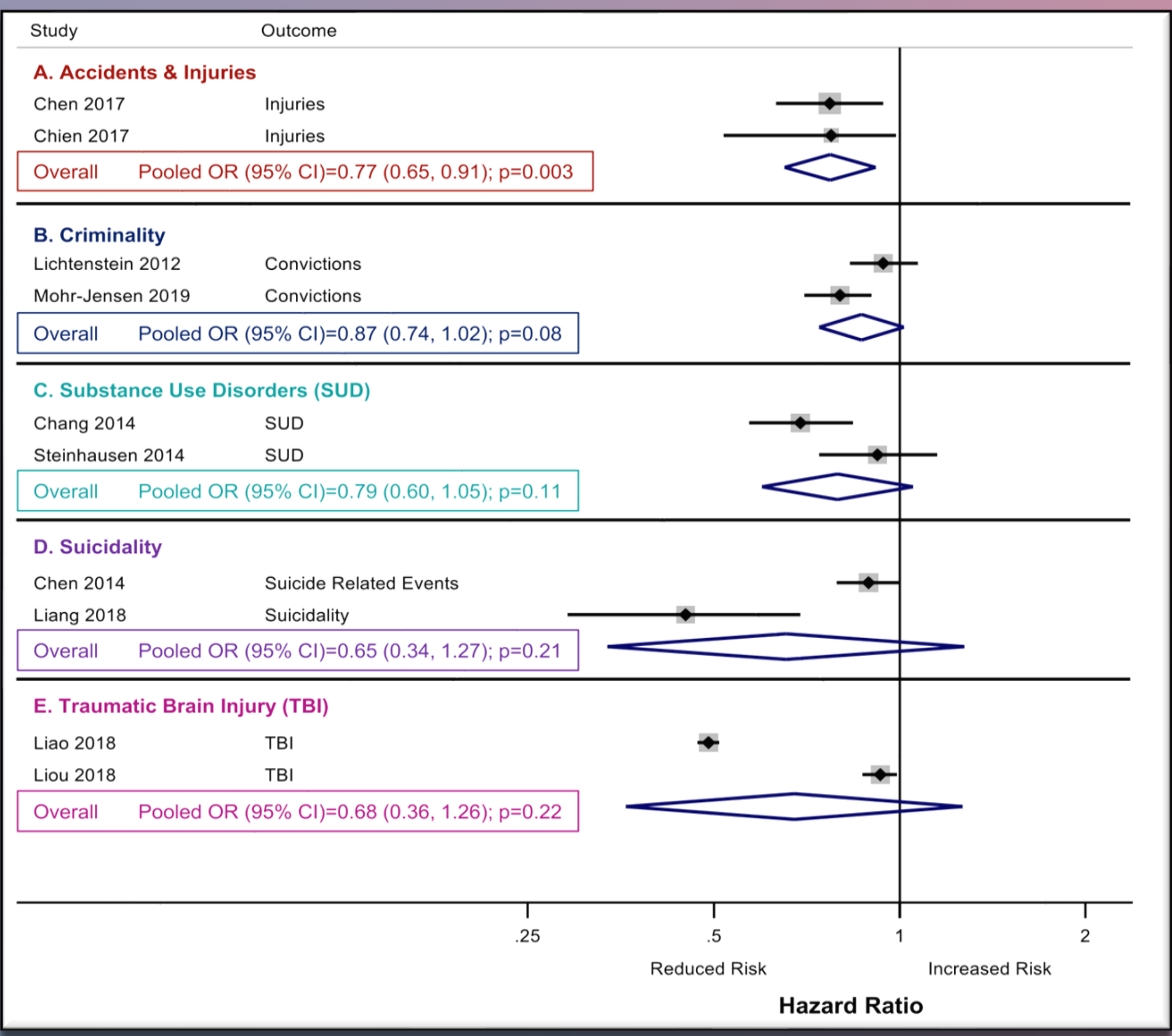
OUTCOMES - TREATMENT MATTERS!!



Boland et al. (2020): A literature review and meta-analysis on the effects of ADHD medications on functional outcomes. Journal of Psychiatric Research

- 40 studies included
- International studies
- N ranging from 5718 to 146,000,000
- "Overwhelming majority of medication treatment consisted of stimulants"

OUTCOMES - TREATMENT MATTERS!!



Boland et al. (2020): A literature review and meta-analysis on the effects of ADHD medications on functional outcomes.

- 40 studies included
- International studies
- N ranging from 5718 to 146,000,000
- ”Overwhelming majority of medication treatment consisted of stimulants”

CASE EXAMPLE con’t

- 14 yr (Grade 9) female comes to your office in October with presenting complaint of low mood and passive suicidal ideation with some superficial NSSI.
  - PHQ 9 – score 10, mild – moderate depression, no intent to SI
  - SNAP scores – 20/27 inattention, 14/27 hyperactive
  - MDD symptoms started with high school and feeling overwhelmed in school
  - Family conflict increasing around school avoidance
  - Social impulsivity has created more conflict

CASE EXAMPLE con't

- Reviewed options of treatment with youth and family
- Clarified cardiac history prior to initiation of stimulant
- RX lisdexamphetamine 20mg po daily
  - Given history of some substance use – this was prescribed over other long-acting and short-acting stimulants
  - Special Authority obtained
- Follow up in 2 weeks – ADHD symptoms improved. PHQ9 – decreased to 7

TAKE AWAYS

1. MDD and ADHD can be difficult to differentiate – assessments take time. Focus on timelines
2. MDD and ADHD often co-occur together with worse outcomes for MDD
3. When ADHD and MDD co-occur – treat the more impairing disorder first.
4. Treatment of ADHD early can decrease the risk of later onset of mood disorders and other negative outcomes

TAKE AWAYS

5. Consider school transition points high risk times for ADHD symptoms to present

6. Consider screening parents for ADHD when youth diagnosed

7. Consider review with COMPASS or referral to CYMH/Child and Adolescent Psychiatry services if not responding to first two medication trials.

8. Consider Ledger referral if struggling despite secondary services (eg. CYMH)

CLINICAL PEARLS

1. Use lisdexamphetamine preferentially if youth using substances

2. Younger children, especially neuro-diverse children may require lower starting doses of short-acting stimulants to start (e.g. 2.5 mg MPH BID).

3. Fluoxetine can be more activating than sertraline. Consider starting with sertraline in hyperactive youth.

RESOURCES

- For Clinicians
  - CADDRA (Canadian ADHD Resource Alliance)
  - BCCH Tool Kits – ADHD and MDD
  - **COMPASS - https://www.compassbc.ca/**
- For Families
  - BCCH “Rolling with ADHD” Series: https://healthymindslearning.ca/rollingwith-adhd/
  - BCCH: ADHD Info for families
  - CHADD: https://chadd.org/about/

RESOURCES

Practical Strategies for Parenting ADHD

Wish you could just roll with the ADHD in your family?

Need practical strategies to deal with the day to day parenting of a child with ADHD? Sign up today for this FREE learning series from BC Children's Hospital.

Click here

COMPASS

Child & Youth Mental Health Case Consultation & Education for Healthcare Providers

Are you a healthcare provider seeking guidance on **clinical care** for child & youth mental health and substance use disorders?

- Call **1-855-702-7272** or visit **compassbc.ca** for support with **medications, counselling, diagnosis or treatment planning** for children and youth in your practice.

Are you a healthcare provider seeking more **education** on common child & youth mental health and substance use disorders?

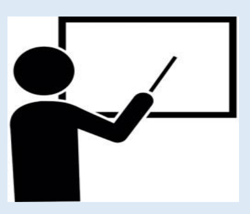
- Visit **compassbc.ca/education** to find clinical toolkits, webinar recordings, and curated resources.

Call: 1-855-702-7272 **Visit: CompassBC.ca**

Services

Telephone case consultation

Service navigation


Education for healthcare providers

Bibliography

1. Gundel LK, Pedersen CB, Munk-Olsen T, Dalsgaard S. Longitudinal association between mental disorders in childhood and subsequent depression - A nationwide prospective cohort study. *J Affect Disord*. 2018;227:56-64.
2. Biederman J, Ball SW, Monuteaux MC, et al. New insights into the comorbidity between ADHD and major depression in adolescent and young adult females. *J Am Acad Child Adolesc Psychiatry*. 2008;47(4):426-434.
3. CHADD. Children and Adults with Attention Deficit Disorder. Coexiting Condtions. https://chadd.org/about-adhd/depression/. Accessed May 26, 2023.
4. Faraone SV, Larsson H. Genetics of attention deficit hyperactivity disorder. *Mol Psychiatry*. 2019;24(4):562-575.
5. Demontis D, Walters RK, Martin J, et al. Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder. *Nat Genet*. 2019;51(1):63-75.
6. Walker CS, Walker BH, Brown DC, Buttross S, Sarver DE. Defining the role of exposure to ACEs in ADHD: Examination in a national sample of US children. *Child Abuse Negl*. 2021;112:104884.
7. Brown NM, Brown SN, Briggs RD, Germán M, Belamarich PF, Oyeku SO. Associations Between Adverse Childhood Experiences and ADHD Diagnosis and Severity. Acad Pediatr. 2017 May-Jun;17(4):349-355.
8. Diler RS, Daviss WB, Lopez A, Axelson D, Iyengar S, Birmaher B. Differentiating major depressive disorder in youths with attention deficit hyperactivity disorder. *J Affect Disord*. 2007;102(1-3):125-130.
9. CADDRA - Canadian ADHD Resource Alliance: Canadian ADHD Practice Guidelines, 4.1 Edition, Toronto ON; CADDRA, 2020.
10. Pliszka SR, Crismon ML, Hughes CW, et al. The Texas Children's Medication Algorithm Project: revision of the algorithm for pharmacotherapy of attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2006;45(6):642-657.
11. MacQueen GM, Frey BN, Ismail Z, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 6. Special Populations: Youth, Women, and the Elderly [published correction appears in Can J Psychiatry. 2017 May;62(5):356]. *Can J Psychiatry*. 2016;61(9):588-603. doi:10.1177/0706743716659276
12. Biederman J, Monuteaux MC, Spencer T, Wilens TE, Faraone SV. Do stimulants protect against psychiatric disorders in youth with ADHD? A 10-year follow-up study. *Pediatrics*. 2009;124(1):71-78.
13. Chang Z, D'Onofrio BM, Quinn PD, Lichtenstein P, Larsson H. Medication for Attention-Deficit/Hyperactivity Disorder and Risk for Depression: A Nationwide Longitudinal Cohort Study. *Biol Psychiatry*. 2016;80(12):916-922.
14. Park J, Lee DY, Kim C, et al. Long-term methylphenidate use for children and adolescents with attention deficit hyperactivity disorder and risk for depression, conduct disorder, and psychotic disorder: a nationwide longitudinal cohort study in South Korea. *Child Adolesc Psychiatry Ment Health*. 2022;16(1):80. Published 2022 Oct 11.
15. Boland H, DiSalvo M, Fried R, et al. A literature review and meta-analysis on the effects of ADHD medications on functional outcomes. *J Psychiatr Res*. 2020;123:21-30. doi:10.1016/j.jpsychires.2020.01.006