






Generic/ TRADE <small>g=generic avail</small> (Strength & forms) Pregnancy ⁹	Side effects / Contraindications C	√ = therapeutic use / Comments / Drug Interactions D / Monitor M	Initial ⁴ / Typical Dose ⁸ (Max mg/d) * Titration ⁴ {Child(up to 40 kg); Adolescent; Adult}	\$ Canada / 30 days
PSYCHOSTIMULANTS Response rate ~ 75%; SHORT-ACTING: (Ritalin, Dexedrine) are less expensive & flexible during initial Tx, esp. in small children. But, social stigmatization & drug diversion concerns related to in-school dosing. INTERMEDIATE-ACTING: (Ritalin SR, Dexedrine Spansules) may last up to 8 hours. CADDRA guidelines generally recommend long-acting agents as 1 st line; however expert opinion notes role for individualization of therapy.) LONG-ACTING: (Concerta, Biphentin, Adderall XR) are dosed once-daily & have less fluctuation in serum concentrations (may ↑ compliance). May affect evening appetite & sleep, & are more expensive (varying drug plan coverage). Less abuse potential.				
Amphetamine Mixed Salts dextroamphetamine and levoamphetamine salts (3:1) ADDERALL XR $\chi \otimes$ 5, 10, 15, 20, 25, 30mg cap 50% immediate release & 50% gradual release [MOA:↑ DA,NE] C	Common: appetite suppression, ↓ weight, insomnia, headache, dry mouth, rebound irritability, nausea/vomiting, constipation/diarrhea, GI upset, dizziness, anxiety, tremor, ↑ BP & ↑ HR, emotional lability; slow growth Infrequent: uncovering tics, sexual dysfunction, tactile & visual hallucinations, psychosis, ↓ seizure threshold Serious: sudden death (see Cardiac Risk note below) CI: advanced arteriosclerosis, symptomatic CV dx, hyperthyroidism ↑BP, hypersensitivity/idiosyncrasy to sympathomimetic amines, glaucoma, agitated states, drug abuse hx, or MAOI use within 14day	√ ADHD age ≥ 6yr ^(narcolepsy in the USA) May be opened & sprinkled on soft foods Duration: 8-12hr (long-acting) D: ↑amphetamine effect; acetazolamide, antacid; MAOI & linezolid [↑] effect & ↑BP; sympathomimetics [↑] HR & BP, & TCAs [↑] CV effects M: ADHD symptoms, behaviour & academic performance; rating scales e.g. SNAP-IV, Conners', CGI; physical exam, patient & family cardiac hx, ECG (at baseline & consider repeat if pt age <12yr at initial ECG or if change in patient symptoms eg. ^{palpitations/syncope}) BP, HR: At Day 0, 1 & 3months then q6-12months Pediatric patients: development, weight & growth	Peds: 10mg qam / 30mg qam (30 mg/d) Titrate 5-10mg q7d Adolescents: 10mg qam / 30mg qam (50mg/d) Titrate 5mg q7d Adults: 10mg qam / 60mg qam (60mg/d) Titrate 5-10mg q7d	86 / 123 (123) 86 / 123 (220) 86 / 240 (240)
Precautions: amphetamine misuse or if cardiac dx → ↑BP/↑HR, serious CV events or even sudden death; hx of drug dependence → ↑ abuse; hx seizures/EEG changes → may ↓ seizure threshold; pre-existing psychosis, bipolar or hx of tics or Tourette's ⁺ → may worsen disorder				
Dextroamphetamine DEXEDRINE 5 ^c mg tab C DEXEDRINE Spansule 10, 15mg cap [MOA: blocks re-uptake of DA; increases release of DA and NE] {SK Formulary: max \$15/Rx for age ≤14yrs as of Jul/08}	Common: as in Adderall XR Infrequent: as in Adderall XR Serious: as in Adderall XR CI: as in Adderall XR + patients with motor tics or with a family hx of diagnosis of Tourette's Syndrome ⁺ Precautions: as in Adderall XR + tartrazine (FD&C Yellow No. 5) sensitivity, esp. with aspirin sensitivity; may cause allergic-type reaction (tablets)	√ ADHD age ≥ 6 yr; adjunctive therapy for narcolepsy Duration: Tab: ~4-6hr (short); Spansule both IR & ER pellets; 6-8hr (intermediate) More potent than MPH (10mg MPH ≈ 5mg Dextroamp.) Short-acting often used as initial Tx in small kids, but bid-tid dosing; longer acting greater convenience, confidentiality but may ↓ evening appetite & ↓ sleep Spansules may be opened & sprinkled on soft foods D: as in Adderall XR M: as in Adderall XR	Peds: Tab: 2.5mg qam & qnoon / 10mg bid (30mg/d) Titrate 5mg q7d by adding 4pm dose Spansule: 10mg qam / 15mg qam (30mg/d) Titrate 10mg q7d by adding 4pm dose Adolescents: Tab: 2.5mg qam & qnoon / 10mg bid (30 mg/d) Titrate 5mg q7d by adding 4pm dose Spansule: 10mg qam / 15mg qam (30 mg/d) Titrate 10mg q7d by adding 4pm dose Adult: Tab: 5mg qam & qnoon / 15mg bid (50 mg/d) Titrate 5mg q7d by adding 4pm dose Spansule: 10mg qam / 30mg qam (45 mg/d) Titrate 10mg q7d by adding 4pm dose	26 / 82 (121) 34 / 40 (74) 26 / 82 (121) 34 / 40 (74) 44 / 121 (197) 34 / 74 (107)
Methylphenidate (MPH) RITALIN, g 5, 10 ^c , 20 ^c mg tab RITALIN SR, g 20mg tab -do not chew or crush tablet [MOA: blocks DA reuptake] wax matrix C {SK Formulary: max \$15/Rx for age ≤14yrs as of Jul/08}	Common: Insomnia 13%, ↓appetite 26%, nausea 12%, vomiting 10%, weight loss 9%, tic 7%, emotional instability 6%, anorexia 5%, nasal congestion 6%, nasopharyngitis 5%, headaches Serious: blood dyscrasia (very rare), angioedema, hallucinations, sudden death (see Cardiac Risk note below) CI: Anxiety, tension, agitation, thyrotoxicosis, advanced arteriosclerosis, symptomatic CV disease, ↑BP, glaucoma & pheochromocytoma, patients with motor tics or with a family hx or diagnosis of Tourette's syndrome ⁺ , MAOI use within 14 days.	√ ADHD age ≥ 6yr ^(narcolepsy in the USA) Duration: Tabs: ~3-5hr (short-acting); SR: ~3-8hr (intermediate-acting) Short-acting often used as initial Tx in small kids, but bid-tid dosing; Intermediate acting ↑ convenience & confidentiality but may ↓ evening appetite & ↓ sleep D: clonidine ECG changes & sudden death; linezolid & MAOI [↑] BP; phenobarbital & phenytoin [↑] level; sympathomimetic [↑] HR & BP, TCAs [↑] TCA levels, warfarin [↑] INR ↓ MPH level: carbamazepine M: as in Adderall XR. Also CBC, differential & platelets: periodically long-term Tx Consider abuse & diversion risk especially with any short acting stimulant (e.g. children may be targeted for the drug). Take reasonable precautions to ↓ risk (e.g. use of treatment agreement; refrain from informing others, etc.; consider long-acting stimulant or non-stimulant).	Peds: IR tab: 5mg qam & qnoon ^{0.3 mg/kg/day} / 10mg tid (60mg/d) Titrate 5-10mg ^{0.2 mg/kg/day} q7d by adding 4pm dose SR tab: 20mg qam / 40mg qam (60mg/d) Titrate 20mg q7d by adding 2pm dose Adolescents: IR tab: 5mg qam & qnoon / 20mg tid (60 mg/d) Titrate 5mg q7d by adding 4pm dose SR tab: 20mg qam / 60mg qam (80 mg/d) Titrate 20mg q7d by adding 2pm dose Adult: IR tab: 10mg qam & qnoon / 20mg tid (60 mg/d) Titrate 10mg q7d by adding 4pm dose SR tab: 20mg qam / 60mg qam (100 mg/d) Titrate 20mg q7d by adding 2pm dose (Combo strategies: e.g. kick start & avoid noon dosing → Ritalin SR qam + small Ritalin IR dose qam; "rebound" → Ritalin SR qam + small Ritalin IR dose late afternoon) (Ritalin no sub is typically \$15-30 more than generics/month; may crumble less when tabs split, but has ↑ street abuse value)	15 / 25 (41) 22 / 35 (49) 15 / 41 (41) 22 / 49 (63) 19 / 41 (41) 22 / 49 (77) (27-39)
Methylphenidate BIPHENTIN $\chi \otimes$ C 10, 15, 20, 30, 40, 50, 60, 80mg cap Multilayer-release delivery system: 40% immediate, 60% gradual	See Methylphenidate above	√ ADHD age ≥ 6yr (somewhat lower cost for once daily) Duration: 10-12hr (long-acting) Capsules should be swallowed whole & must never be crushed or chewed. Contents may be sprinkled on these soft foods: apple sauce, ice cream or yogurt.	Peds: 10mg qam / 30mg qam (60mg/d) Titrate 10mg q7d Adolescents: 10mg qam / 40mg qam (80 mg/d) Titrate 10mg q7d Adults: 10mg qam / 60mg qam (80 mg/d) Titrate 10mg q7d	31 / 66 (114) 31 / 82 (146) 31 / 114 (146)
Methylphenidate CONCERTA \otimes C 18, 27, 36, 54mg tab Osmotic release oral system OROS: 22% immediate, 78% gradual {SK Formulary: max \$15/Rx for age ≤14yrs as of Jul/08}	See Methylphenidate above; tablet does not change in shape in GI tract → should <u>not</u> be administered to pts with pre-existing GI narrowing Dx (e.g. small bowel inflammatory dx, "short gut" syndrome, hx of peritonitis, cystic fibrosis, intestinal pseudo-obstruction, or Meckel's diverticulum). ⁷ Dose conversion: Methylphenidate 5mg bid/tid or 20mg SR od → 18mg qam Methylphenidate 10mg bid/tid or 40mg SR od → 36mg qam Methylphenidate 15mg bid/tid or 60mg SR od → 54mg qam (A 27 mg is avail for Drs to prescribe between 18 mg & 36 mg dosages)	√ ADHD age ≥ 6yr Duration: 8-12hr (long-acting) Swallow whole with liquids; tablet shell may be in stool . Non-deformable shell makes it very difficult to break, cut or crush, which may dramatically ↓ its abuse risk (If inadequate immediate effects and/or effects too prolonged esp. at high doses → consider Biphentin)	Peds: 18mg qam / 36mg qam (54mg/d) Titrate 18mg q7d Adolescents: 18mg qam / 54mg qam (54 mg/d) Titrate 18mg q7d Adults: 18mg qam / 54mg qam (108 mg/d) Titrate 18mg q7d **Full formulary SK July/08 in effort to ↓ stimulant abuse & diversion** To get one responder after 6weeks: Concerta NNT=3 vs Strattera NNT=5 ^{Newcom'08 n=516}	80/ 103 (125) 80 / 125 (125) 80 / 125 (243)

Consider if...

Atomoxetine  Approved 2005
STRATTERA   
10, 18, 25, 40, 60mg cap
(in USA: also 80, 100 mg) 
♦cap can not be opened/sprinkled
[MOA: NE reuptake inhibitor]

Common: Headache ~20%, insomnia 16%, xerostomia ~10%, abdominal pain 20%, vomiting ~10%, ↓appetite ~10%, nausea 12%, cough 11%; mild ↑BP ~5% & HR 3%; fatigue 8%, ↓weight 2%, urinary hesitancy 1%
 {↑risk of vomiting & somnolence 7% vs MPH-IR; but ↓appetite concern.
 Poor ZD6 metabolizers have higher rates of ↓appetite}
Serious: liver toxicity rare, suicidal thinking 0.4%, blackbox warning, sudden death (see below), dyskinesia, seizures peds 0.2%, adults 0.1%, priapism rare
Cx: MAOI within 14days; narrow angle glaucoma; symptomatic CV D; ↑BP; advanced arteriosclerosis; uncontrolled hyperthyroidism

Peds: 10mg ^{0.5mg/kg/d} / 25mg qam ^{1.2mg/kg/d} (Lower of 1.4 mg/kg/d or 60mg/d) Titrate 0.8mg/kg/d at week 2 & 1.2mg/kg/d at week 4 -slower titration to ↓SE	150 / 150 (150)
Adolescents: 18mg ^{0.5mg/kg/d} / 40mg qam ^{1.2mg/kg/d} (Lower of 1.4mg/kg/d or 100mg/d) Titrate 0.8mg/kg/d at week 2 & 1.2mg/kg/d at week 4 -slower titration to ↓SE	150/ 150 (290)
Adults: 25mg ^{0.5mg/kg/d} / 60-80mg qam ^{1.2mg/kg/d} (Lower of 100mg/d or 1.4 mg/kg/d) Titrate 40mg, 60mg, 80mg & max 100mg q14days (slower titration will ↓SE or divide dose bid)	150/ 150-290 (290) same price/ can

Agents **WITHOUT** Official Indication for ADHD:

=↓ dose for renal dysfx **ζ**=scored tab **χ**=Non-formulary Sask **≡**=Exception Drug Status Sask **⊗**=not covered by NIHB **▼**=covered by NIHB **ac**=before meals **BMI**=body mass index **BP**=blood pressure **cc**=with meal **CGI**=Clinical Global Impression scale **CV**=cardiovascular disease
⊠=contraindication **DA**=dopamine **DI**=drug interaction **Dx**=diagnosis **fx**=function **HF**=heart failure **HR**=heart rate **ht**=height **IR**=immediate release **M**=monitor **MAOI**=monoamine oxidase inhibitor **MI**=myocardial infarction **MOA**=mechanism of action **MPH**=methylphenidate
NE=norepinephrine **Pt**=patient **Rx**=reactions **SNAP-IV**=revised version of Swanson, Nolan & Pelham Questionnaire **SR**=sustained release **Sx**=symptoms **SE**=side effect **Tx**=treatment **wt**=weight * MAX dose listed in 2007-08 Canadian ADHD Guidelines, which may differ from product monograph
 †Psychostimulants are used with precaution in tic spectrum disorders but the Canadian guidelines committee agrees that use can be indicated if ADHD symptoms warrant treatment. Medications for ADHD may be combined with other drugs for tics.⁴

COMORBID/ RESEMBLING CONDITIONS: age-appropriate behaviour, mental retardation, understimulating environments, learning disabilities; disorders (conduct, oppositional defiant, stereotypic movement, mood (e.g. bipolar), anxiety, personality (e.g. narcissistic, antisocial, borderline, passive-aggressive personality), substance-related, pervasive developmental, psychotic, depression, of impulse control); chronic fatigue, fetal alcohol syndrome, hyper- or hypothyroidism, drug/substance-induced (see below), OCD, pathological gambling, pheochromocytoma, PTSD, seizure, situational disturbances, Tourette's¹⁷⁻¹⁸

DRUG/SUBSTANCE-INDUCED: bronchodilators caffeine, isoniazid lead poisoning neuroleptics (from akathisia) phenobarbital phenytoin¹⁹⁻²⁰

DIAGNOSIS:⁴¹ a) **Inattentive subtype (10-20%):** ≥ 6 (of 9) inattentive Sx: inattention to details/makes careless mistakes, difficulty sustaining attention, seem not to listen, fail to finish tasks, difficulty organizing, avoid tasks requiring sustained attention, lose things, easily distracted, forgetful; b) **hyperactive-impulsive subtype (5-10%):** ≥ 6 (of 9) hyperactive-impulsive Sx: fidgety, unable to stay seated, inappropriate running/climbing, difficult engaging in leisure activities quietly, "on the go", talks excessively, blurt out answers before question finished, difficulty waiting turn, interrupt/intrude others; c) **combined subtype (70-80%):** if criteria met for both inattentive & hyperactive-impulsive subtypes. ADHD Sx must: persist for ≥ 6months, present prior to age 7, & present in ≥ 1 setting. Evidence of significant impairment in social, academic or occupational fx. Sx not explained by another mental dx.

SCREENING Tools: SNAP-IV, T-CAPS, Weiss Symptom Screen, Weiss Functional Impairment Rating Scale; psychoeducational testing. **Tools:** <http://www.caddra.ca/> **Tx GOALS:** core Sx; improve behaviour, academic, social & self-esteem; minimize med SE

NON-DRUG Interventions: behavioural therapy may be considered: for milder ADHD; when psychosocial Tx preferred; in preschool-age children; & adult ADHD²²⁻²³ In kids with ADHD & comorbid dxs, behavioural therapy alone was less effective than meds alone in ↓ ADHD core Sx.²⁴ Combined medication & behavioural Tx do not offer substantial improvement over meds alone in ↓ ADHD Sx, but may add benefit for some non-ADHD Sx areas^{25-26,27,28}; (eg. parent training, contingency management, daily school report cards) environmental interventions, e.g adherence to regular daily schedules, structured home & school settings, sitting at the front of the classroom, using white noise during homework time; role for academic remediation, social skills training, etc.; diet modifications has limited anecdotal evidence supporting benefits but ↑ food additives, preservatives (eg. sodium benzoate) & food colourings may be useful if true sensitivities; complementary & alternative medicine lack evidence;²⁹ natural health products (St. John's Wort, chamomile, melatonin, valerian for calming/sedating; others: blue-green algae, B vitamins, pycnogenol, omega-3), homeopathic, neurofeedback, hypnosis.

CARDIAC Risk: 45 deaths (31 kids, 14 adults), Jan 1992 to Feb 2005, related to stimulants or atomoxetine.³⁰ But the rate of sudden death in those taking psychostimulants or atomoxetine did not exceed the background rate.³¹ Pts with known CV diseases should not be prescribed these drugs.³² AHA cardiovascular guidelines suggest: prior to initiation of Tx to ↑ chance of identifying CV conditions: i) pt & family history, ii) physical examination, & iii) ECG read by a Dr with expertise in pediatric ECGs. Consult pediatric cardiology if significant findings.³³ Routine ECG not necessary AAP'08

PSYCHIATRIC Risk: Suicidal thinking at atomoxetine 0.4%; 55 Canadian cases reported. Although risk is small, it should be discussed with pts & family, & kids should be monitored for this esp. in the first few months of Tx.⁵ **Aggression/emotional lability:** Stimulants & atomoxetine trials show not ↑ aggression.^{5,34} Clinicians should distinguish between aggression/emotional lability that is present when the stimulant is active & ↑ hyperactivity/impulsivity in the evening when the stimulant is no longer effective.⁵ Note: oppositional-defiant Sx usually decrease with therapy.

GROWTH Suppression Risk: Stimulant Tx may be assoc. with a ↓ in height, at least in the first 1-3 yrs of Tx.³⁵ One study had ↓ growth rates after 3yrs of stimulant Tx compared to those with no meds (average growth of 2 cm & 2.7 kg less than non-med subgroup).^{36,37} Most kids achieve a satisfactory adult height but some growth may be permanently attenuated. Monitor: ht, wt & BMI at baseline & 1-2 times/yr during Tx. If pt has a change in height, weight or BMI that crosses two percentile lines, a drug holiday during weekends, summers or consider switching to an alternative med.⁵

ABUSE/DIVERSION: Lifetime diversion rates: 16-29% of students with stimulant scripts asked to give, sell, or trade their meds.³⁸ Strategies to ↓ risk → see ADHD Newsletter/Treatment Agreement. Stimulant Tx does not appear to ↑ risk for substance use Dx. It is unclear whether Tx ↓ risk.^{39,40,41}

Other Strategies: 1) Educate patient/family: *handle medication like you would your wallet!* 2) Refrain from informing others about being on the drug; 3) Remove labels when discarding; 4) Use random pill counts; 5) Weekly dispensing; 6) School program & collaboration; 7) Non-Ritalin options; 8)

MANAGEMENT: ^{4.6, 42} **headaches** → acetaminophen; usually ↓ after meds used for 1-3 weeks; divide dose ↓ **appetite** → give med with meals; give high-calorie meals when stimulant effects are low (breakfast, bedtime); supplemental Boost, Ensure; engage child in meal prep & shopping for favourite foods; manage drug-induced **dry mouth** → ↑ fluids intake; **rebound appetite** in the evening → spread out supper into 2 or 3 session to prevent GI distress; ↓ dose &/or titrate dose slowly; **insomnia** → optimal sleep hygiene; give doses earlier in the day; avoid stimulant dose after 2 pm if possible, change to shorter-acting meds; ↓ noon or afternoon stimulant dose; consider clonidine, trazodone, an antihistamine, or melatonin 3-6 mg ½ hr before bedtime; others: benzos, TCAs, atypical antipsychotics; **tics** → switch stimulant or switch to a non-stimulant; add clonidine or an atypical antipsychotic; **irritability** → ↓ dose; adjust longer-acting meds; assess for Sx of comorbid conditions; **rebound hyperactivity** → Overlap stimulant dosing pattern, switch to longer-acting stimulant, combine IR with SR forms, or add other meds; switch to a non-stimulant.

USA: Dexmethylphenidate: **Focalin** (2.5,5,10mg cap; **XR** 5,10,15,20mg cap); Methylphenidate: **Methylin** 5,10,20mg tab; **Methylin ER** 10,20mg tab; **Metadate ER** 10,20mg tab; **Metadate CD** 10,20,30,40,50,60mg cap can open & sprinkle; **Ritalin LA** 10,20,30,40mg cap; **Daytrana Patch** 10,15,20,30mg; Lisdexamfetamine **Vyvanse** 20,30,50,60,70mg cap; Mixed amphetamine salts: **Adderall** 5,7.5,10,12.5,20,30mg tab; Dextroamphetamine: **Dexostat** 5,10mg tab; **Medikinet**, Modafinil: **Sparlon** (Skin rx) **SJS** → Cephalon not to pursue ADHD indication; Guanfacine: **Tenex** 1,2mg tabs (FDA ADHD decision pending); Methamphetamine: **Desoxyn** 5mg tab (Biovail: Canadian approval **Altenade** - not yet marketed)

References: ADHD Treatment Chart

- ¹ Virani A. Attention-Deficity Hyperactivity Disorder. Therapeutic Choices 5th Edition 2007.
- ² Micromedex 2008
- ³ Lexi-comp 2008
- ⁴ Canadian Attention Deficit Hyperactivity Disorder Resource Alliance (**CADDRA**). *Canadian ADHD Practice Guidelines 2007-2008*. Toronto (ON): CADDRA; 2007. Available at: http://www.caddra.ca/english/2007-08_guidelines_pdfs/2007-08_Caddra_Guidelines.pdf (accessed April 22, 2008).
- ⁵ Pliszka SR *et al*. AACAP Official Action. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder. *J Am Acad Child Adolesc Psychiatry* 2007;46:894-921.
- ⁶ Virani A. Advances in ADHD Treatment: an overview for pharmacists. Canadian Pharmacists Association Advancement 2005 Learning Series.
- ⁷ Compendium of Pharmaceuticals and Specialties 2008. Available at: <http://www.e-cps.ca>
- ⁸ The Medical Letter. Drugs for the Treatment of ADHD. Treatment Guidelines from the Medical Letter. Nov 2006. Vol. 4 (Issue 51).
- ⁹ Briggs GG, Freeman RK, Sumner JY. Drugs in Pregnancy and Lactation 8th Edition. Williams & Wilkins, Baltimore, 2008.
- ¹⁰ Rappley M. Attention deficit-hyperactivity disorder. *NEJM* 2005; 352:165-173.
- ¹¹ Daviss W B et al. Clonidine for Attention-Deficit/Hyperactivity Disorder II. ECG Changes and Adverse Events Analysis. *J Am Acad Child Adolesc Psychiatry* 2008;47:189-198.
- ¹² Banaschewski T, Roessler V, Dittman RW, Santosh PJ, Rothenberger A. Non-stimulant medication in the treatment of ADHD. *Eur Child Adolesc Psychiatry* 2004;13(Suppl 1):102-116.
- ¹³ Einarson TR, Iskedian M. Novel antipsychotics for patients with attention-deficit hyperactivity disorder: A systematic review. 17. 2001. Ottawa, Canadian Coordinating Office for Health Technology Assessment (CCOHTA). Available at: http://cadth.ca/media/pdf/114_antipsychotic_adhd_tr_e.pdf. (accessed on May 7, 2008).
- ¹⁴ Food and Drug Administration. Modafinil Serious Skin Reactions http://www.fda.gov/cder/dsn/2007_fall/postmarketing.htm#modafinil. (accessed on May 9, 2008).
- ¹⁵ Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and meta-regression analysis. *Am J Psychiatry* 2007;164:942-8.
- ¹⁶ American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Text Revision. Arlington, VA: American Psychiatric Press, Inc.; 2000.
- ¹⁷ American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Text Revision. Arlington, VA: American Psychiatric Press, Inc.; 2000.
- ¹⁸ Hallowell EM, Ratey JJ. *Driven to Distraction*
- ¹⁹ American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Text Revision. Arlington, VA: American Psychiatric Press, Inc.; 2000.
- ²⁰ Hallowell EM, Ratey JJ. *Driven to Distraction*
- ²¹ American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Text Revision. Arlington, VA: American Psychiatric Press, Inc.; 2000.
- ²² Conners CK, March JS, Frances A, Wells KC, Ross R. The Expert Consensus Guideline Series: Treatment of Attention-Deficit/Hyperactivity Disorder. *J Attention Disord*. 2001;4(suppl 1):7-128.
- ²³ Safren SA. Cognitive-behavioural approaches to ADHD Treatment in adulthood. *J Clin Psychiatry* 2006;67(suppl 8):46-50.
- ²⁴ MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 1999;56:1073-1086. (n=579; 14months)
- ²⁵ MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 1999;56:1073-1086.
- ²⁶ Abikoff H, Hechtman L, Klein RG, et al. Symptomatic improvement in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *J Am Acad Child Adolesc Psychiatry* 2004;43:802-811.
- ²⁷ Jadad AR, Boyle M, Cunningham C, Kim M, Schachar R. Treatment of attention-deficit/hyperactivity disorder. Evid Rep Technol Assess (Summ). 1999 Nov; 1-341. Available at: <http://www.ahcpr.gov> (accessed May 1, 2008).
- ²⁸ Swanson JM, Kraemer HC, Hinshaw SP, Arnold LE et al. Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment. *J Am Acad Child Adolesc Psychiatry*. 2001;40:168-79.
- ²⁹ Chan E. The role of complementary and alternative medicine in attention-deficit hyperactivity disorder. *J Dev Behav Pediatr* 2002;23(1 Suppl):S37-45.
- Weber W, Vander Stoep A, McCarty RL, et al. Hypericum perforatum (St John's wort) for attention-deficit/hyperactivity disorder in children and adolescents: a randomized controlled trial. *JAMA*. 2008 Jun 11;299(22):2633-41. In this study, use of H. perforatum for treatment of ADHD over the course of 8 weeks did not improve symptoms.
- Cala S, Crismon ML, Baumgartner J. A survey of herbal use in children with attention-deficit-hyperactivity disorder or depression. *Pharmacotherapy*. 2003 Feb;23(2):222-30. Herbal medicines were given most frequently for a behavioral condition, with ginkgo biloba, echinacea, and St. John's wort most prevalent.
- ³⁰ Villalaba L. Follow up review of AERS search identifying cases of sudden death occurring with drugs used for the treatment of attention deficit hyperactivity disorder ADHD. Available at: http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4210b_07_01_safetyreview.pdf (accessed May 2, 2008).
- Gould, Madelyn S., Walsh, B. Timothy, et al. Sudden Death and Use of Stimulant Medications in Youths. *Am J Psychiatry* 2009 0: appi.ajp.2009.09040472.
- ³¹ Villalaba L. Follow up review of AERS search identifying cases of sudden death occurring with drugs used for the treatment of attention deficit hyperactivity disorder ADHD. Available at: http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4210b_07_01_safetyreview.pdf (accessed May 2, 2008).
- ³² a) Health Canada. Attention Deficit Hyperactivity Disorder (ADHD) Drugs: Updated and Standardized Labelling Regarding Very Rare Cardiac-Related Adverse Events. May 2006. Available at: http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/adhd-tdah_medic_hpc-cps_e.html (accessed May 2, 2008).
- b) Hechtman L, Greenfield B. Long-term use of stimulants in children with attention deficit hyperactivity disorder. *Pediatr Drugs* 2003; 5:787-794.
- c) Gould, Madelyn S., Walsh, B. Timothy, et al. **Sudden Death** and Use of Stimulant Medications in Youths. *Am J Psychiatry* 2009 0: appi.ajp.2009.09040472.
- ³³ Vetter VL *et al*. Cardiovascular Monitoring of Children and Adolescents with heart Disease Receiving Stimulant Drugs. A Scientific Statement from the American Heart Association Council on Cardiovascular disease in the Young Congenital Cardiac Defects Committee and the Council on Cardiovascular Nursing. *Circulation*. Published online April 21, 2008. DOI: 10.1161/CIRCULATIONAHA.107.189473.
- (Perrin JM, Friedman RA, Kniliens TK; Black Box Working Group; Section on Cardiology and Cardiac Surgery. Cardiovascular monitoring and stimulant drugs for attention-deficit/hyperactivity disorder. *Pediatrics*. 2008 Aug;122(2):451-3.)
- ³⁴ Polzer J, Bangs ME, Zhang S, Dellva MA, Tauscher-Visniewski S, Acharya N, et al. Meta-Analysis of Aggression or Hostility Events in Randomized, Controlled Clinical Trials of Atomoxetine for ADHD. *Biol Psychiatry* 2007;61:713-719.
- ³⁵ Poulton A. Growth on stimulant medication; clarifying the confusion: a review. *Arch Dis Child*. 2005;90:801-806.
- Swanson J, Greenhill L, Wigal T, et al. Stimulant-related reductions of growth rates in the **PATS**. *J Am Acad Child Adolesc Psychiatry*. 2006 Nov;45(11):1304-13. For 95 children who remained on medication, annual growth rates were 20.3% less than expected for height (5.41 cm/yr-6.79 cm/yr=-1.38 cm/yr) and 55.2% for weight (1.07 kg/yr-2.39 kg/yr=-1.32 kg/yr).
- Faraoane SV, Biederman J, Morley CP, Spencer TJ. Effect of Stimulants on Height and Weight: A Review of the Literature. *J Am Acad Child Adolesc Psychiatry*. 2008 Jun 20. [Epub ahead of print] Treatment with stimulants in childhood modestly reduced expected height and weight. Although these effects attenuate over time and some data suggest that ultimate adult growth parameters are not affected, more work is needed to clarify the effects of continuous treatment from childhood to adulthood. Although physicians should monitor height, deficits in height and weight do not appear to be a clinical concern for most children treated with stimulants.
- ³⁶ MTA Cooperative Group. National Institute of Mental Health multimodal treatment study of ADHD follow-up: changes in effectiveness and growth after the end of treatment. *Pediatrics* 2004;113:762-769.
- ³⁷ MTA Cooperative Group. Effects of stimulant medication on **growth rates across 3 years** in the MTA follow-up. *J Am Acad Child Adolesc Psychiatry* 2007;46:1015-1027.

- 38 Wilens TE, Lenard MD, Adler A, Adams J, Sgambati S, Rotrosen J, Sawtelle R, Utzinger L, Fusillo S. Misuse and diversion of stimulants prescribed for ADHD: a systematic review of the literature. *J Am Acad Child Adolesc Psychiatry* 2008;47:21-31.
- 39 Wilens TE, Faraone SV, Biederman J, Gunawardene S. Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. *Pediatrics* 2003;111:179-185.
- 40 Biederman J, Monuteaux MC, Spencer T, Wilens TE, MacPherson HA, Faraone SV. Stimulant therapy and risk for subsequent substance use disorders in male adults with ADHD: a naturalistic controlled 10-year follow-up study. *Am J Psychiatry* 2008;165: 597–603.
- 41 Mannuzza S, Klein RG, Truong NL, Moulton JL III, Roizen ER, Howell KH, Castellanos FX. Age of methylphenidate treatment initiation in children with ADHD and later substance abuse: prospective follow-up into adulthood. *Am J Psychiatry* 2008;165: 604–609.
- Wilens TE, Adamson J, Monuteaux MC, et al. Effect of prior stimulant treatment for attention-deficit/hyperactivity disorder on subsequent risk for cigarette smoking and alcohol and drug use disorders in adolescents. *Arch Pediatr Adolesc Med.* 2008 Oct;162(10):916-21. Stimulant therapy does not increase but rather reduces the risk for cigarette smoking and SUDs in adolescents with ADHD.
- 42 Dopheide JA, Theesen KA, Malkin M. Chapter 61: Childhood Disorders. In: DiPirio JT, Talbert RL, Hayes PE et al, eds. *Pathophysiologic Approach*. 6th Edition, McGraw-Hill Co., Inc., NY, 2005.

Acknowledgements: Contributors & Reviewers: Dr. D. Quinn (SHR-Psyc), Dr. G. Ferguson (SHR-Psych), Dr. H. McKee (SHR), Dr. P. Butt (SHR), Dr. M. Jutras (SHR), Dr. T. Laubscher (SHR), Dr. F.

Remillard (PharmD, College of Pharmacy, U of S.), C. Evans (BSP,PHD ^{Cand}) & the RxFiles Advisory Committee.

Prepared by: Monica Lee PharmD Cand L. Regier BSP, BA, B. Jensen BSP

DISCLAIMER: The content of this newsletter represents the research, experience and opinions of the authors and not those of the Board or Administration of Saskatoon Health Region (SHR). Neither the authors nor Saskatoon Health Region nor any other party who has been involved in the preparation or publication of this work warrants or represents that the information contained herein is accurate or complete, and they are not responsible for any errors or omissions or for the result obtained from the use of such information. Any use of the newsletter will imply acknowledgment of this disclaimer and release any responsibility of SHR, its employees, servants or agents. Readers are encouraged to confirm the information contained herein with other sources. Additional information and references online at: www.RxFiles.ca

Copyright 2008 – RxFiles, Saskatoon Health Region (SHR) www.RxFiles.ca

Additional ADHD Treatment References:

Candy B Jones L Williams R Tookman A King M. Psychostimulants for depression. *Cochrane Database Syst Rev.* 2008 Apr 16;(2):CD006722. There is some evidence that in the short-term, PS reduce symptoms of depression.

Whilst this reduction is statistically significant, the clinical significance is less clear.

Davidson MA. ADHD in adults: a review of the literature. *J Atten Disord.* 2008 May;11(6):628-41. Epub 2007 Dec 19.

Greenhill LL, Posner K, Vaughan BS, Kratochvil CJ. Attention deficit hyperactivity disorder in preschool children. *Child Adolesc Psychiatr Clin N Am.* 2008 Apr;17(2):347-66, ix.

Keenan HT, Hall GC, Marshall SW. Early head injury and attention deficit hyperactivity disorder: retrospective cohort study. *BMJ.* 2008 Nov 6;337:a1984. doi: 10.1136/bmj.a1984. Medically attended head injury before 2 years of age does not seem to be causal in the development of attention deficit hyperactivity disorder. Medically attended injury before 2 years of age may be a marker for subsequent diagnosis of attention deficit hyperactivity disorder.

King S, Griffin S, Hodges Z, Weatherly H, et al. A systematic review and economic model of the effectiveness and cost-effectiveness of methylphenidate, dexamfetamine and atomoxetine for the treatment of attention deficit hyperactivity disorder in children and adolescents. *Health Technol Assess.* 2006 Jul;10(23):iii-iv, xiii-146.

McCann D, Barrett A, Cooper A, et al. Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded, placebo-controlled trial. *Lancet.* 2007 Nov 3;370(9598):1560-7. Erratum in: *Lancet.* 2007 Nov 3;370(9598):1542.

Molina BS, Flory K, Hinshaw SP, et al. Delinquent behavior and emerging substance use in the MTA at 36 months: prevalence, course, and treatment effects. *J Am Acad Child Adolesc Psychiatry.* 2007 Aug;46(8):1028-40.

Mosholder AD, Gelperin K, Hammad TA, et al. Hallucinations and other psychotic symptoms associated with the use of attention-deficit/hyperactivity disorder drugs in children. *Pediatrics.* 2009 Feb;123(2):611-6.

Newcorn JH, et al. Atomoxetine and osmotically released methylphenidate for the treatment of attention deficit hyperactivity disorder: acute comparison and differential response. *Am J Psychiatry.* 2008 Jun;165(6):721-30. Epub 2008

Feb 15. Response was significantly greater with osmotically released methylphenidate than with atomoxetine. One-third of patients who received methylphenidate followed by atomoxetine responded better to one or the other, suggesting that there may be preferential responders.

NICE Sept/08 Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults <http://www.nice.org.uk/guidance/index.jsp?action=byID&o=12061> Kendall T, Taylor E, Perez A, Taylor C; Guideline Development Group. Diagnosis and management of attention-deficit/hyperactivity disorder in children, young people, and adults: summary of NICE guidance. *BMJ.* 2008 Sep 24;337:a1239. doi: 10.1136/bmj.a1239.

Pappadopoulos E et al. Medication adherence in the MTA: Saliva methylphenidate samples versus parent report and mediating effect of concomitant behavioral treatment. *J Am Acad Child Adolesc Psychiatry* 2009 May; 48:501.

Schachter HM, Pham B, King J, Langford S, Moher D. How efficacious and safe is short-acting methylphenidate for the treatment of attention-deficit disorder in children and adolescents? A meta-analysis. *CMAJ.* 2001 Nov 27;165(11):1475-88.

Shaw P, Sharp WS, Morrison M, et al. Psychostimulant treatment and the developing cortex in attention deficit hyperactivity disorder. *Am J Psychiatry.* 2009 Jan;166(1):58-63. Epub 2008 Sep 15. These findings show no evidence that psychostimulants were associated with slowing of overall growth of the cortical mantle.

Szobot CM, Bukstein O. Attention deficit hyperactivity disorder and substance use disorders. *Child Adolesc Psychiatr Clin N Am.* 2008 Apr;17(2):309-23, viii.

Thomson A, Maltezos S, Paliokosta E, et al. Risperidone for attention-deficit hyperactivity disorder in people with intellectual disabilities. *Cochrane Database Syst Rev.* 2009 Apr 15;(2):CD007011. There is no evidence from RCTs that risperidone is effective for the treatment of ADHD in people with ID. Prescribing in this population can only be based on open-label studies or extrapolation from research in people with autism and disruptive behaviour disorders; however these studies have not investigated people with ID separately so there are reservations regarding the applicability of these findings.