Psychiatric Pharmacology & the Role of Supplements in Pediatric Patients

Jane Bischoff, PharmD, BCPP

May 2022

Introduction

- No conflicts of interest to disclose
- Generic names will be used whenever possible, but the brand name drug may be referenced if appropriate. Inclusion of a brand name drug in this presentation does not represent endorsement

Preface

- Treatments, not diagnosis
  - Based on proper diagnostic assessment & ongoing evaluation and adjustments
- Therapy or Psychotherapy
- Focus on evidence & safety ≥ practicality
  - Practicality: ease of use, adherence, cost and insurance barriers

Outline

- Depression/Anxiety
  - Latest guidelines and landmark clinical trials
  - Considerations for pediatric vs adult patients
  - Prescribing trends among child psychiatrists and PCPs
  - (Clinically relevant) drug-drug interactions
  - How to safely titrate and cross-taper between agents
- ADD/ADHD
  - Review of guidelines and general recommendations
  - Newest formulations
  - Avoiding and overcoming common insurance barriers

Outline (continued)

- Role of supplements in pediatric psychiatry
  - Importance of diet
  - Risks of “natural” remedies
  - Integrative medicine and evidence-based recommendations
    - Vitamin D
    - Fish Oil
    - St. John’s Wort
    - Medical Marijuana
    - Iron
    - SAM-e
    - NAC
    - Melatonin
- Conclusion
- Q&A
- Case Presentation

Depression/Anxiety – Pediatric Considerations

- Medication is only recommended as adjunct to psychotherapy
- STAR*D trials
- Black Box Warning
- Bipolar Disorder
- Adherence is likely the biggest barrier to treatment
- Start low…go slowly

Antidepressants & Anxiolytics

Fluoxetine

Sertraline

Escitalopram

Venlafaxine

Duloxetine*

Bupropion

Citalopram

Paroxetine

Fluvoxamine

*Honorable mentions: Hydroxyzine, Trazodone, Mirtazapine

Antidepressants & Anxiolytics

Fluoxetine

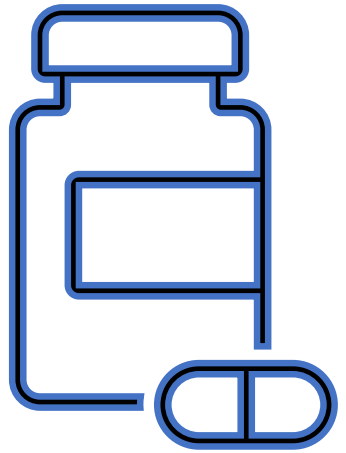
Sertraline

Escitalopram

- Most evidence in pediatric patients (except citalopram)
- Easy to titrate, taper, and cross taper
- Liquid formulations available, can also cut/crush
- Flexibility with dosing and schedule
  - Give any time of day
- 1st line for Pediatric GAD
- Weight neutral

Antidepressants & Anxiolytics

Fluoxetine



- CAPSULES not TABLETS
- 10-20mg starting dose – up to 60mg
- Long half-life
- Drug interactions
- FDA approved for pediatric Depression
- Most evidence for treatment, preferred initial choice in guidelines

Antidepressants & Anxiolytics

Sertraline

- 25-50mg starting dose – up to 200mg daily
- Take with food
- Liquid formulation needs to be further diluted
- Small tablets, scored

Antidepressants & Anxiolytics

Escitalopram

- S stereoisomer of citalopram
  - Half the dose of citalopram
- 5-10mg starting dose – up to 20mg
- Much less toxic in OD
- Less titrating to get to final dose
- FDA approved for pediatric depression

Mirtazapine

Antidepressants & Anxiolytics

- Also recommended first-line for pediatric GAD
- 20-30mg starting dose – up to 120mg
- Much less toxic in OD
- Only FDA approved agent for pediatric GAD

Duloxetine*

Venlafaxine

- Little evidence in peds
- Serotonergic until 150mg, then becomes an SNRI
- Weight neutral or weight loss
- Starting dose 37.5-75mg up to 300mg
- Poor choice for nonadherent patients
  - Given in the morning
- Withdrawal symptoms
  - ALWAYS use extended-release capsules

- Little evidence in peds
- Often used as adjunct
- Bupropion XL (24 hour formulation) 150mg-300mg daily
- Give in the morning
- Toxic in OD

Bupropion

- Least preferred options

Citalopram

Paroxetine

Fluvoxamine

- Toxic in OD
  - Seizures
  - QTC prolongation
- Tested in pediatrics
- Rarely prescribed over escitalopram

Citalopram

- No pediatric indications
- Hazardous to Handle
  - Cannot crush, split tablets
- Weight gain
- Drug interactions
- Withdrawals
- Poorly tolerated

Paroxetine

- Indicated for OCD
- Drug interactions – CYP1A2 inhibitor
- Short half-life, may need BID dosing
- Recently recommended for COVID19 – may see a shortage

Fluvoxamine

Hydroxyzine

- Often 10, 25, or 50mg PRN at the beginning of treatment for anxiety or sleep
- May receive alert for QTc prolongation

Trazodone

- Adjunct for sleep
- 25-50mg QHS PRN, may increase to 150mg

Mirtazapine

- 7.5mg more potent than 15mg for sleep
- May help with weight gain
- 7.5mg or 15mg used as adjunct for sleep, higher doses for depression

How to titrate and cross-taper

- To avoid insurance issues, prescribe the target dose and have patient **split tablet** for first 7-10 days
  - E.g. escitalopram 10mg: take ½ tablet by mouth once daily, then increase to a full tablet after one week
  - Exception: fluoxetine may take 2 prescriptions if insurance doesn't allow for more than one capsule/strength/day

How to titrate and cross-taper

- Do NOT put refills on a titration
  - Causes insurance issues and delays
- Cross taper between agents within a week or less
  - Fluoxetine self-tapers
- Plan for drug destruction in the event of discontinuation
- Determine an “adequate drug trial” appropriate for your patient

ADD/ADHD Medications

- Overall, medications haven’t changed
  - Formulations have multiplied
  - Generic availability has eased ability to access
  - Increased flexibility in dose timing
- One new medication in 2021, not widely used yet

Methylphenidate & Derivatives

Amphetamine & Derivatives

OR

Atomoxetine

Viloxazone

+/-

Guanfacine ER

Clonidine ER

Methylphenidate

- Immediate release – tablets, can all be cut/crushed, added to food
  - Ritalin ®, Methylin ®
- Extended release – all capsules can be poured out onto food, ER tablets cannot
- Liquid and chewable formulations

Methylphenidate Extended Release

- Monophasic: Methylphenidate ER tablets
  - Onset at 90 minutes, duration 3-8 hours
  - Generic
- Biphasic (IR:ER): Metadate CD ® (30:70), Ritalin LA ® (50:50) & Aptensio XR ® (40:60) capsules
  - Generic – Metadate CD ® & Ritalin LA ® (some forms)
- Triphasic: Concerta ® tablets & Adhansia XR ® capsules
  - Mimics BID-TID dosing (i.e. Concerta ® 18mg dose is the same as 5mg BID-TID; Adhansia XR ® 100mg similar to 20mg BID-TID)
  - Generic - Concerta ®
- Dexmethylphenidate: Focalin ® tablets & Focalin XR ® capsules

Methylphenidate Extended Release

- Quilivant XR ® liquid
  - Brand only – need to reconstitute an entire bottle
- Quilichew ® chewable tablet
  - Generic available
- Daytrana ® Patch
  - Brand only
  - Not well tolerated, not widely available or covered – 2 hours until onset, wear up to 9 hours total
- Jornay PM ® capsule
  - Brand only
  - 5% of drug released in first 10 hours

Amphetamine-based drugs

- Mixed Amphetamine Salts
  - Adderall ® IR tablets, Adderall XR ® capsules
- Mixed salts of a single-entity amphetamine
  - Mydayis ® ER capsules
- Amphetamine sulfate
  - Evekeo ® tablets, Evekeo ODT ®, Dynavel XR ® suspension, Adzenys ER ® suspension, Adzenys XR-ODT ®
- Lisdexamfetamine
  - Vyvanse ® capsules
- Dextroamphetamine
  - Dexedrine ® tablets and ER capsules, Dexedrine Spansule ®, Zenzedi ® tablets, ProCentra ® liquid

Mixed Amphetamine Salts (Adderall ® IR and XR)

- Most prescribed agents from this group
- All generic
- Predictable kinetics
- Easy to dose, titrate
- Can pour capsules into food, crush tablets
- Abuse and diversion potential

Lisdexamfetamine (Vyvanse ®)

- Brand name only – manufacturer coupon on website
- Unique mechanism of action means it has LOW abuse potential
  - Absorbed through GI tract into blood
  - Blood enzyme cleaves Lysine and releases dextroamphetamine throughout the day
  - May pour capsule into food

Dextroamphetamine

- Many generic forms available
- Dextro isomer only
- May be better tolerated in some patients
- Same abuse and diversion potential as Adderall formulations

Atomoxetine (Strattera ®)

- Generic, cost is coming down
- Alternative to stimulants, especially if concerns for abuse
- Delayed onset of action
- CANNOT open capsule – ocular irritation
  - Small capsules anyway
- Sometimes better tolerated than stimulants
- Dosing – 0.5mg/kg/day to 1.2mg/kg/day if <70kg, otherwise start at 40mg
  - 10mg, 18mg, 25mg, 40mg, 60mg, 80mg, 100mg

Viloxazine (Qelbree ®)

- Brand name only – manufacturer coupon on website
- Newest ADHD agent
- Similar place in therapy as atomoxetine
- May sprinkle capsule into applesauce

Clonidine (Kapvay ®)

- Generic available
- Duration of action ~12 hours
- Dosed twice daily
- 0.1mg-0.4mg daily dose

Guanfacine – Intuniv ®

- Generic available
- Duration of action ~18-24 hours
- Dosed once daily
- 1mg-4mg daily dose

Methylphenidate & Derivatives

Amphetamine & Derivatives

OR

Atomoxetine

Viloxazone

+/-

Guanfacine ER

Clonidine ER

Supplements

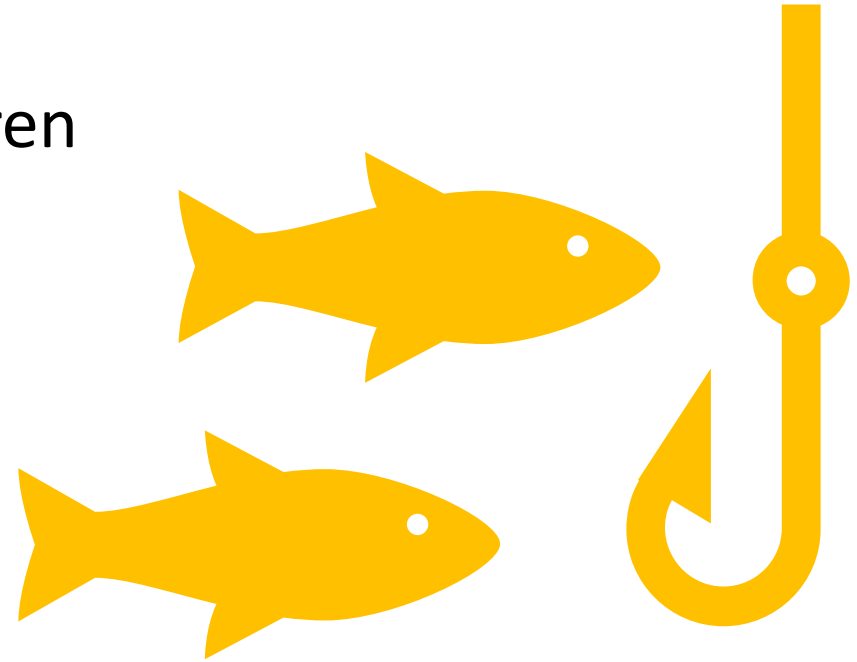
- Diet
- Safety/Risks
- Potency

Vitamin D

- Often difficult to treat in overweight and obese patients – stores in fat
- Low levels correlated with depression, little evidence to suggest that it is a causative agent
- Typically treated to above 30ng/ml
- Daily vs weekly supplementation

Fish Oil

- May have CV benefits, but no known efficacy in psychiatric illness in adults or children
- Potential adjunct for ADHD in children
- 1000-2000mg daily



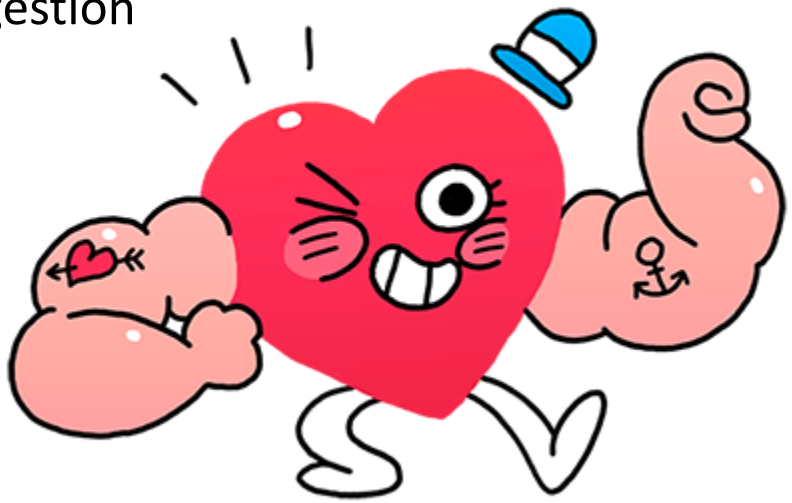
St John's Wort

- Evidence is modest for depression
- In the guidelines for mild depression for adults
  - Mild depression isn't treated with medication in pediatrics
- Major drug-drug interactions, including oral contraceptives
- Dosing is 300mg TID

Medical Marijuana

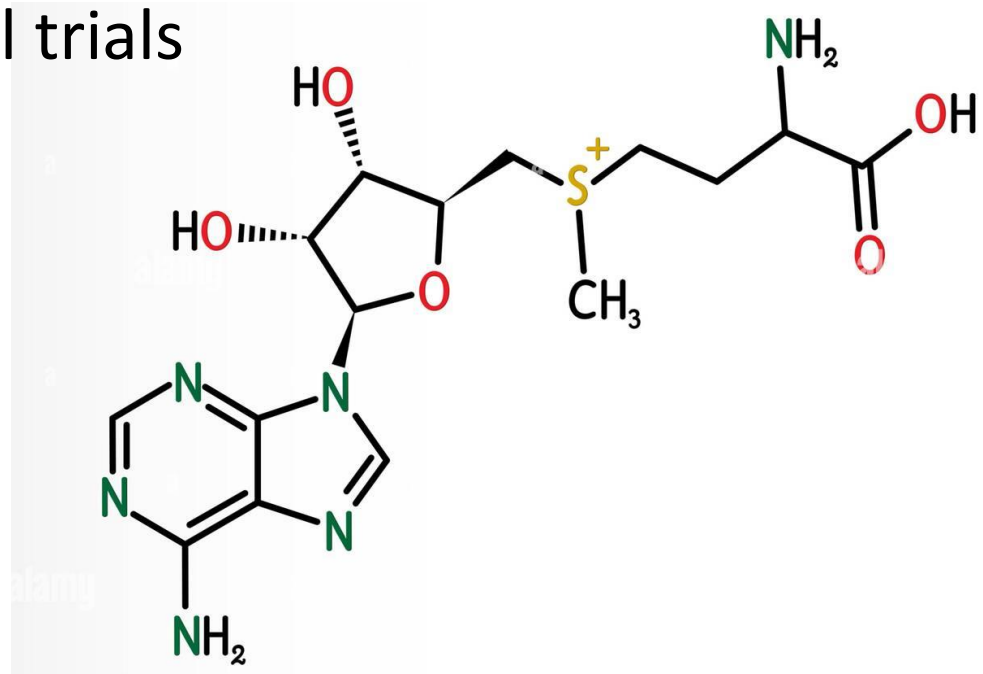
Iron

- May prefer to treat to a higher serum ferritin level due to low iron stores in children with ADHD
- Formulations that may improve adherence
  - Multivitamins with iron – 9-27mg elemental Fe per daily serving
    - Gummies do NOT contain iron
  - Vitron – C ®
    - Carbonyl iron with vitamin C to increase absorption and ease digestion
  - Slow Fe ®
  - Ferrous Gluconate
    - Only 45mg elemental iron
  - Adjunct Miralax ® to combat constipation



SAM-e

- Methyl donor in DA and 5HT synthesis
- Lower concentrations in CSF of those with severe depression
- PO 800-1600mg/day or IM 400mg/day
- No evidence of efficacy in several clinical trials

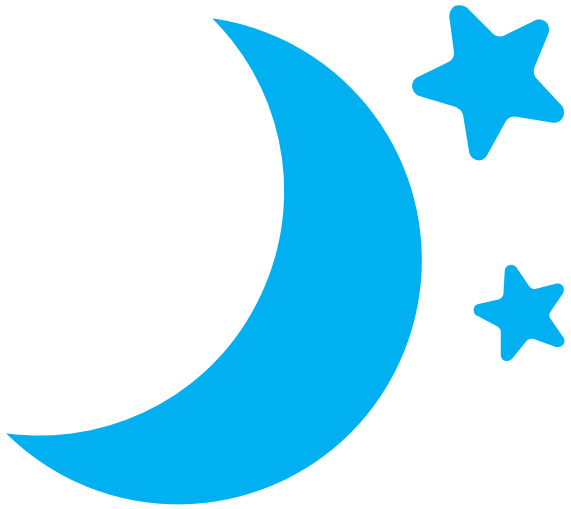


NAC (N-Acetylcysteine)

- Dosed 600-1200mg BID
  - Sulfur smell
- Some evidence in SUD
- Prescribing trend to use for self-harm, but no strong evidence available

Melatonin

- Some evidence
  - 1-3mg is recommended, more won’t hurt
- Very safe, even in OD
- Several formulations available, including ER (Natrol ® brand)



Conclusion

- Guidelines and recommendations have largely stayed the same
- Formulations and practice trends have changed

Questions?

Varigonda AL, Jakubovski E, Taylor MJ, Freemantle N, Coughlin C, Bloch MH. Systematic review and meta-analysis: early treatment responses of selective serotonin reuptake inhibitors in pediatric major depressive disorder. J Am Acad Child Adolesc Psychiatry. 2015;54(7):557-64.

Dobson ET, Strawn JR. Pharmacotherapy for pediatric generalized anxiety disorder: a systematic evaluation of efficacy, safety, and tolerability. Paediatr Drugs. 2016;18(1):45-53.

Strawn JR, Geracioti L, Rajdev N, Clemenza K, Levine A. Pharmacotherapy for generalized anxiety disorder in adult and pediatric patients: an evidence-based treatment review. Expert Opin Pharmacother. 2018;19(10):1057-70.

Strawn JR, Prakash A, Zhang Q, Pangallo BA, Stroud CE, Cai N, et al. A randomized, placebo-controlled study of duloxetine for the treatment of children and adolescents with generalized anxiety disorder. J Am Acad Child Adolesc Psychiatry. 2015;54(4):283-93.

Cheung AH, Zuckerbrot RA, Jensen PS, Laraque D, Stein REK. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): Part II. Treatment and Ongoing Management. Pediatrics. 2018;141(3).

Hammad TA, Laughren T, Racoosin J. Suicidality in pediatric patients treated with antidepressant drugs. Arch Gen Psychiatry. 2006;63(3):332-9.

Hopkins, Kathryn, et al. Diagnosis and management of depression in children and young people: summary of updated NICE guidance. *Bmj* 350 (2015).

Bolea-Alamañac B, Nutt DJ, Adamou M, Asherson P, Bazire S, Coghill D, et al.. Evidence-based guidelines for the pharmacological management of attention deficit hyperactivity disorder: update on recommendations from the British Association for Psychopharmacology. J Psychopharmacol. 2014;28(3):179-203.

Childress AC, Berry SA. Pharmacotherapy of attention-deficit hyperactivity disorder in adolescents. Drugs. 2012;72(3):309-25.

Kollins SH, Jain R, Brams M, Segal S, Findling RL, Wigal SB, et al. Clonidine extended-release tablets as add-on therapy to psychostimulants in children and adolescents with ADHD. Pediatrics. 2011;127(6):e1406-13.

Pliszka S. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2007;46(7):894-921.

Vaughan B, Kratochvil CJ. Pharmacotherapy of pediatric attention-deficit/hyperactivity disorder. Child Adolesc Psychiatr Clin N Am. 2012;21(4):941-55.

National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder: diagnosis and management.

Canadian ADHD Resource Alliance (CADDRA): Canadian ADHD Practice Guidelines, Fourth Edition, Toronto ON; CADDRA, 2018.

Gan J, Galer P, Ma D, Chen C, Xiong T. The effect of vitamin D supplementation on attention-deficit/hyperactivity disorder: a systematic review and meta-analysis of randomized controlled trials. J Child Adolesc Psychopharmacol. 2019;29(9):670-87.

Gillies D, Sinn JK, Lad SS, Leach MJ, Ross MJ. Polyunsaturated fatty acids (PUFA) for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. Cochrane Database Syst Rev. 2012;(7):CD007986.

Product Information: fluoxetine oral tablets, fluoxetine oral tablets. Edgemont Pharmaceuticals, LLC (per FDA), Austin, TX, 2011

Product Information: Lexapro(R) oral tablets, oral solution, escitalopram oxalate oral tablets, oral solution. Forest Pharmaceuticals, Inc. (per FDA), St. Louis, MO, 2014

Product Information: ZOLOFT oral tablets, oral solution, sertraline HCl oral tablets, oral solution. Roerig (per manufacturer), New York, NY, 2019.

Product Information: CYMBALTA(R) oral delayed-release capsules, duloxetine oral delayed-release capsules. Lilly USA LLC (per FDA), Indianapolis, IN, 2020

Product Information: PAXIL CR(R) oral extended-release tablets, paroxetine oral extended-release tablets. Apotex Corp (per FDA), Weston, FL, 2019.

Product Information: Citalopram oral capsules, citalopram oral capsules. Almatica Pharma LLC (per FDA), Morristown, NJ, 2022.

Product Information: EFFEXOR XR(R) extended-release oral capsules, venlafaxine hydrochloride extended-release oral capsules. Wyeth Pharmaceuticals Inc, Philadelphia, PA, 2008.

Product Information: WELLBUTRIN(R) XL oral extended-release tablets, bupropion hydrochloride oral extended-release tablets. Valeant Canada LP (per Health Canada), Laval, QC, Canada, 2016.

Product Information: Daytrana(TM) transdermal patches, methylphenidate transdermal system transdermal patches. Shire US Inc, Wayne, PA, 2009.

Product Information: JORNAY PM(TM) oral extended-release capsules, methylphenidate HCl oral extended-release capsules. Ironshore Pharmaceuticals & Development Inc (per manufacturer), Chesterbrook, PA, 2018.

Product Information: QUILLICHEW ER(TM) extended-release chewable tablets, methylphenidate HCl extended-release chewable tablets. Tris Pharma, Inc. (per manufacturer), Monmouth Junction, NJ, 2015.

Product Information: APTENSIO XR(TM) oral extended-release capsules, methylphenidate HCl oral extended-release capsules. Rhodes Pharmaceuticals L.P. (per FDA), Coventry, RI, 2015.

14. Product Information: QUILLIVANT XR(R) oral extended-release suspension, methylphenidate HCl oral extended-release suspension. NextWave Pharmaceuticals Inc (per FDA), Mommouth Junction, NJ, 2021.

Product Information: Metadate CD(R) oral extended release capsules, methylphenidate HCl oral extended release capsules. UCB, Inc. (per FDA), Smyrna, GA, 2013.

Product Information: CONCERTA(R) oral extended release tablets, methylphenidate HCl oral extended release tablets. Janssen Pharmaceuticals, Inc. (per FDA), Titusville, NJ, 2017.

Product Information: Ritalin LA(R) oral extended-release capsules, methylphenidate HCl oral extended-release capsules. Novartis Pharmaceuticals Corporation (per FDA), East Hanover, NJ, 2013.

Product Information: RITALIN(R) oral tablets, RITALIN-SR(R) sustained-release oral tablets, methylphenidate hcl oral tablets, sustained-release oral tablets. Novartis Pharmaceuticals Corporation, East Hanover, NJ, 2006.

Product Information: QUILLIVANT(TM) XR oral extended release suspension, methylphenidate HCl oral extended release suspension. NextWave Pharmaceuticals, Inc. (per FDA), New York, NY, 2013.

Product Information: VYVANSE(R) oral capsules, oral chewable tablets, lisdexamfetamine dimesylate oral capsules, oral chewable tablets. Shire US Inc. (per FDA), Lexington, MA, 2017.

Product Information: ADDERALL XR(R) oral capsules, dextroamphetamine sulfate dextroamphetamine saccharate amphetamine aspartate monohydrate amphetamine sulfate oral capsules. Shire US Inc. (per FDA), Lexington, MA, 2017.

Product Information: ADDERALL(R) oral tablets, dextroamphetamine saccharate amphetamine aspartate monohydrate dextroamphetamine sulfate amphetamine sulfate oral tablets. Barr Laboratories, Inc. (per FDA), Pomona, NY, 2015.

Product Information: MYDAYIS(R) oral extended-release capsules, dextroamphetamine sulfate, amphetamine sulfate, dextroamphetamine saccharate, amphetamine aspartate monohydrate oral extended-release capsules. Shire US Inc (per manufacturer), Lexington, MA, 2017.

Product Information: METADATE(R) ER extended-release tablets, methylphenidate hydrochloride . Celltech Pharmaceuticals, Inc, 2002.

Product Information: Focalin(R) oral tablets, dexmethylphenidate HCl oral tablets. Novartis Pharmaceuticals Corporation (per FDA), East Hanover, NJ, 2019.

Product Information: FOCALIN XR(R) oral extended-release capsules, dexmethylphenidate HCl oral extended-release capsules. Novartis Pharmaceuticals Corporation (per FDA), East Hanover, NJ, 2019.

Product Information: EVEKEO ODT(TM) orally disintegrating tablets, amphetamine sulfate orally disintegrating tablets. Arbor Pharmaceuticals LLC (per FDA), Atlanta, GA, 2019.

Product Information: EVEKEO(R) oral tablets, amphetamine sulfate oral tablets. Arbor Pharmaceuticals, LLC (per DailyMed), Atlanta, GA, 2016.

Product Information: DEXEDRINE(R) SPANSULE(R) oral sustained release capsules, dextroamphetamine sulfate oral sustained release capsules. Amedra Pharmaceuticals LLC (per FDA), Horsham, PA, 2017.

Product Information: INTUNIV(R) oral extended-release tablets, guanfacine oral extended-release tablets. Shire US Inc. (per FDA), Wayne, PA, 2015.

Product Information: KAPVAY(R) oral extended-release tablets, clonidine HCl oral extended-release tablets. Concordia Pharmaceuticals Inc (per FDA), Bannockburn, Il, 2014

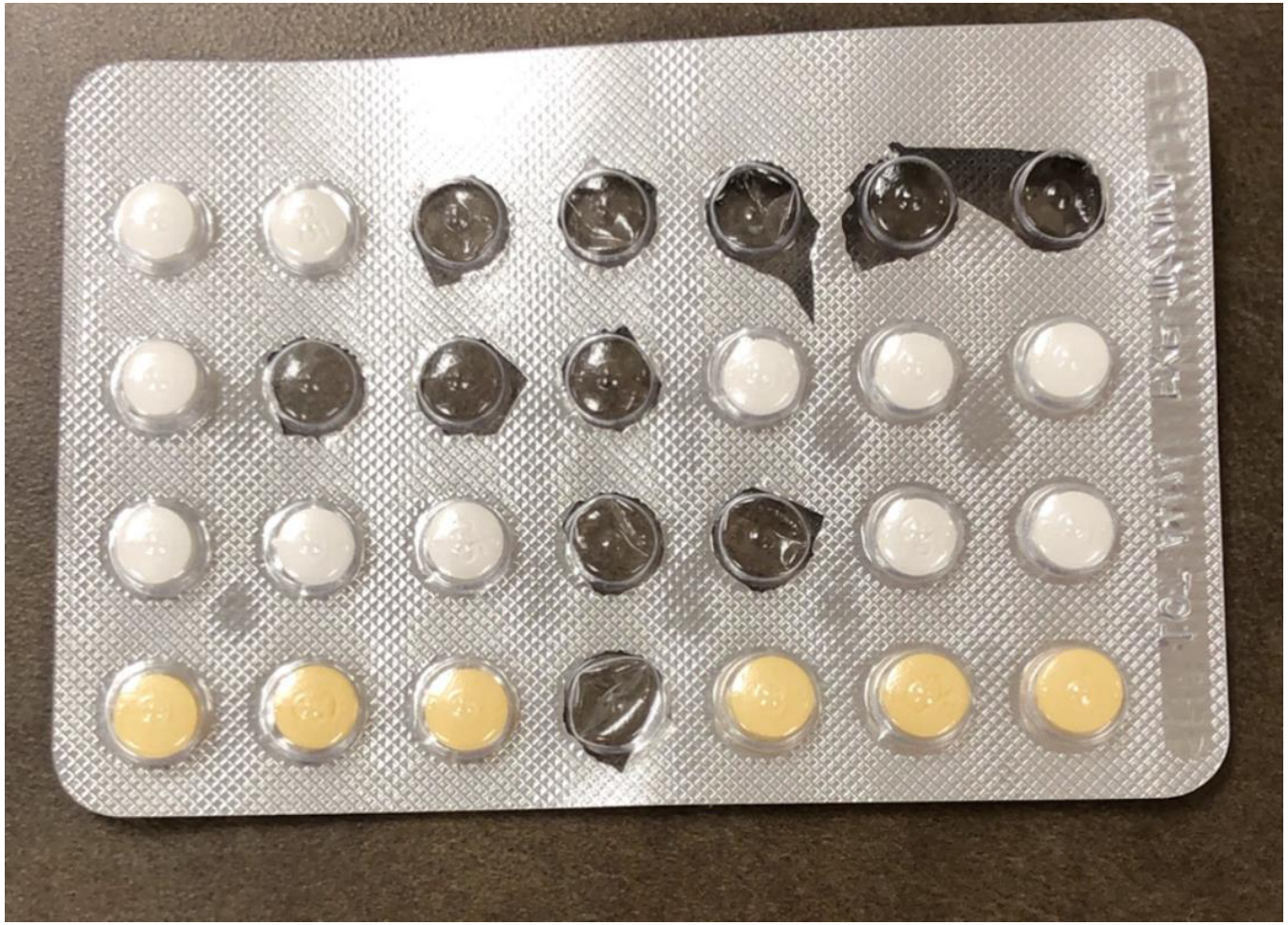
Case Presentation

- AM is a 12yo female diagnosed 2 months ago with depression, moderate, without psychotic features
- Diagnosed with ADHD at 7yo, takes Adderall XR ® 30mg once daily
- Started with therapy twice weekly, still has bothersome symptoms such as decreased appetite, difficulty sleeping
- Vitamin D levels WNL, thyroid levels normal
- Taking omeprazole for chronic GERD, oral contraceptive to regulate heavy menses
- Mother also has depression, controlled with weekly therapy and venlafaxine ER 150mg daily

Case Presentation

- What medication do you start, and how do you titrate it?
- How soon do you increase the dose?
- What if parents wanted a more “natural” approach?

Birth Control Package



One month later…

- Started on sertraline 50mg tablets, took 25mg for 6 days, then increased to 50mg
- Has about #10 50mg tablets left
- Increased GI upset
- Sleep is somewhat improved but still laying in bed for a couple hours 3-4 nights per week
- Next steps….?

Thank you!

- jmaxelrod30@gmail.com