ADHD Treatment in Perinatal Patients

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I have no relevant financial relationship with a commercial interest to disclose.

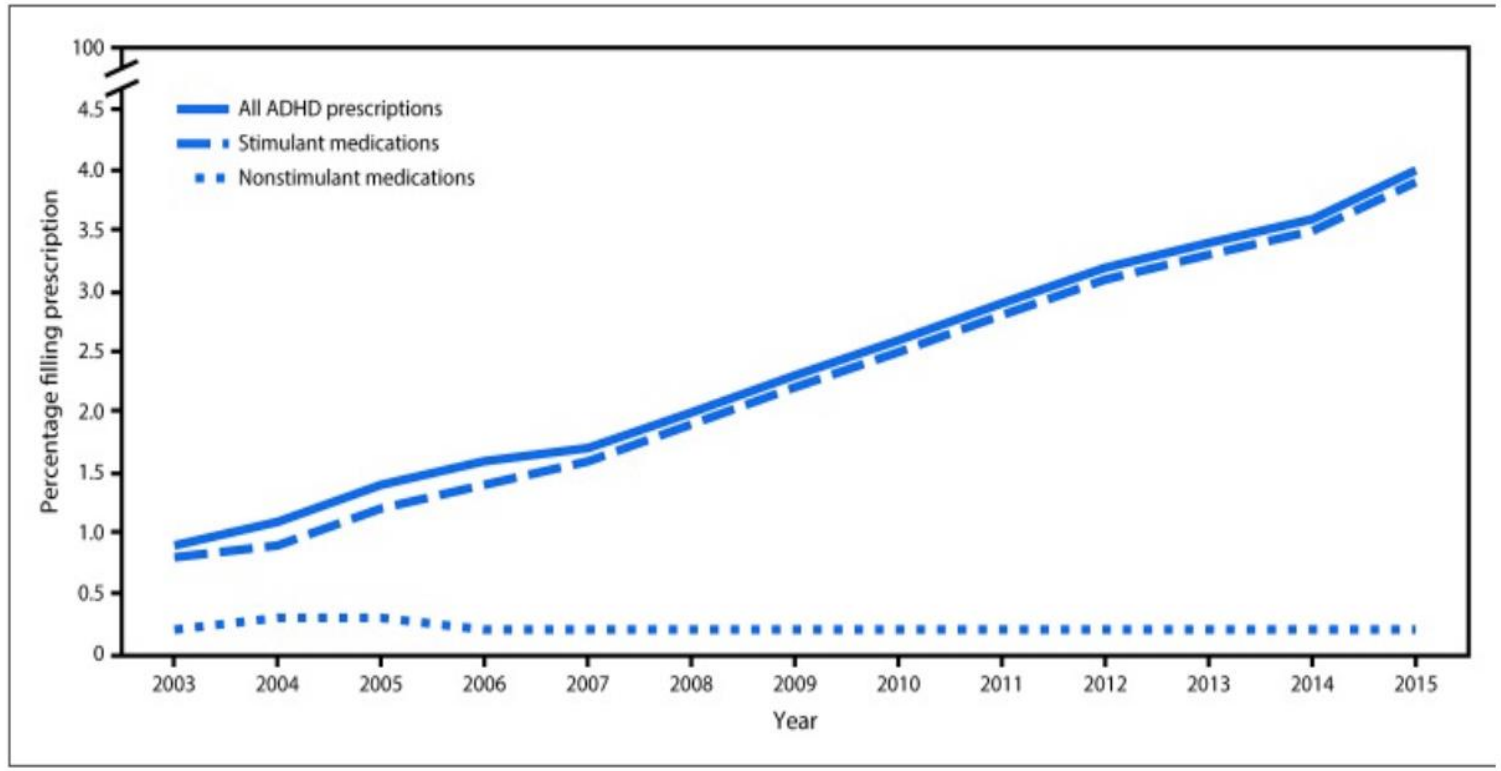
Objectives

- Review major known risks associated with untreated ADHD in perinatal patients
- Review Diagnosis/Differential Diagnosis of Peripartum ADHD
- Overview non-pharmacological options for perinatal patients with ADHD
- Discuss major known risks associated with pharmacological treatments for ADHD during the perinatal period

Scope:

- ADHD estimated to affect 4.4% of American adults[1]
- Estimated ratio in adults is 1.6:1 male to female[2]
- No longer viewed as “just a childhood illness”
  - An estimated 60% of children with ADHD will continue to have clinically relevant symptoms as adults[3]
  - Inattentive symptoms in particular frequently persist, although hyperactive symptoms may also persist in some cases

- Treatment for ADHD in adults is increasing
- The increase in prescriptions is largely being driven by stimulants



FIGURE

Percentage of women aged 15–44 years with private employer-sponsored insurance who filled one or more prescriptions for an attention-deficit/hyperactivity disorder (ADHD) medication, by medication class — United States, 2003–2015

Attention-Deficit/Hyperactivity Disorder Medication Prescription Claims Among Privately Insured Women Aged 15–44 Years — United States, 2003–2015

MMWR Morb Mortal Wkly Rep. 2018 Jan 19;67(2):66-70.

Impact of ADHD on pregnancy outcomes

- Limited studies have shown some specific perinatal risks
- Murray et al reported higher risk for maternal stress, comorbid depressive symptoms, and significant negative impact on social supports
  - They also found significantly higher rates of tobacco use and preterm birth, but this lost significance when adjusted for confounding factors[5]
- Poulton et al found an increased risk of multiple negative outcomes including pre-eclampsia, pre-term labor/birth, higher incidence of surgical delivery, and higher need for neonatal resuscitation and higher likelihood of neonatal admission, although they were unable to confidently ascribe these outcomes to parental ADHD, use of psychostimulants, or other correlated factors[6]

More broadly, untreated ADHD in adults is associated with numerous negative outcomes[1, 4, 5, 7, 8, 9, 20, 21, 22, 23]

- Elevated risk of multiple medical comorbidities, especially neurological, metabolic, musculoskeletal and respiratory illnesses
- Elevated risk of all cause mortality, especially non-natural mortality (e.g. accidental death, suicide)
- Higher rates of serious motor vehicle crashes
- Elevated rates of substance misuse
- Elevated risk of mood disorders and anxiety disorders
- Heightened impulsivity/increased risk-taking behaviors
- Elevated rates of criminal behavior/legal system involvement
- Decreased academic and vocational success, higher rates of financial stress
- Decreased social supports, higher rates of relational conflict/divorce

Why treat during pregnancy?

- Treatment of ADHD has been shown to reduce rates of morbidity/mortality[7] (including decreasing risk of motor vehicle crashes[21]), reduce substance abuse[22], and reduce symptoms of emotional dysregulation and impulsivity[4]
- Treatment of ADHD also has positive impact on[23]:
  - Successful employment and improved financial resources
  - Social connection and support
  - Engagement in health-promoting behaviors
  - Parenting

Diagnosis

- ADHD confounders:
  - Cognitive changes related to pregnancy and postpartum
  - Depressive disorders
  - Anxiety disorders
  - PTSD

Assessment

- Use a structured assessment tool
  - ASRS can be a helpful jumping off point
- Important elements:
  - Assess for childhood symptoms
  - Family history
  - Current level of functioning
  - Severity
    - Work
    - Relationships
    - Driving

Non-pharmacological interventions

- Psychoeducation
- CBT
- Neurofeedback
- Peer support
- Coaching
- Environmental modifications (e.g. prioritizing public transport over driving, accommodations in school/work, etc.)

Risks associated with pharmacological treatment of ADHD in pregnancy: Stimulants

- The most convincing data of adverse effects from stimulant exposure exists from studies of pregnant individuals abusing psychostimulants (in particular methamphetamine)
  - See higher rates of fetal demise, hypertensive disorders, in utero growth restriction, preterm birth, postpartum hemorrhage in this group
- Cannot automatically extrapolate these risks to therapeutic use

Risks associated with pharmacological treatment of ADHD in pregnancy: Stimulants

- Increased risk of birth defects
  - Possible small increase in cardiac malformations with methylphenidate
  - No known risk with amphetamine exposure[10]
  - Other studies have found no association between stimulant exposure and birth defects[11]
- *In utero* growth effects
  - Some evidence of growth acceleration and being large for gestational age[11]
  - However, other studies have shown growth restriction[13]

Risks associated with pharmacological treatment of ADHD in pregnancy: Stimulants

- Hypertensive disorders[6, 12, 14]
  - Data are conflicted on risk of pre-eclampsia with therapeutic stimulant exposure
- Increased risk of preterm birth[11, 14]
- Increased rates of neonatal morbidity
  - More likely to require NICU care, and more likely to experience CNS disorders (e.g. seizures)[11]
  - More likely to require caesarian delivery, have low APGAR scores, require NICU care[6]
  - No study has found stimulant associated increase in neonatal death

Risks associated with pharmacological treatment of ADHD in pregnancy: Bupropion

- Increased risk of birth defects?
  - Early studies said maybe, but more recent data are reassuring[15, 16]
- Few other reported negative pregnancy outcomes
- Low risk for postnatal adaptation
- Less effective than stimulants, but may be a reasonable option for patients with comorbid depression and/or nicotine use disorder

Risks associated with pharmacological treatment of ADHD in pregnancy: Atomoxetine

- Limited data available
- No evidence of increased risk of birth defects[17, 18]
- No evidence of increased risk of pre-eclampsia or preterm birth[14]
- No evidence of increased risk of long-term developmental problems including growth problems or autism[18]

Risks associated with pharmacological treatment of ADHD in pregnancy: α2 agonists

- Very little published data and what is known is confounded – most studies are from patients being treated for severe hypertension, which can have significant effects on pregnancy outcomes
- Clonidine was not associated with impairments in development or growth[18]
- Guanfacine was similarly not associated with development or growth impairments after exposure during pregnancy[19]

References

1. Kessler, R. C., Adler, L., Barkley, R., Biederman, J., Conners, C. K., Demler, O., Faraone, S. V., Greenhill, L. L., Howes, M. J., Secnik, K., Spencer, T., Ustun, T. B., Walters, E. E., & Zaslavsky, A. M. (2006). The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. *The American journal of psychiatry*, *163*(4), 716–723.
2. Quinn PO, Madhoo M. A review of attention-deficit/hyperactivity disorder in women and girls: uncovering this hidden diagnosis. Prim Care Companion CNS Disord. 2014;16(3):PCC.13r01596
3. Young, J. L., & Goodman, D. W. (2016). Adult attention-deficit/hyperactivity disorder diagnosis, management, and treatment in the *dsm-5* era. *The Primary Care Companion For CNS Disorders*.
4. Reimherr, F. W., Marchant, B. K., Gift, T. E., Steans, T. A., & Wender, P. H. (2015). Types of adult attention-deficit hyperactivity disorder (ADHD): baseline characteristics, initial response, and long-term response to treatment with methylphenidate. *Attention deficit and hyperactivity disorders*, *7*(2), 115–128.
5. Murray, A. L., Taut, D., Baban, A., Hemady, C. L., Walker, S., Osafo, J., Sikander, S., Tomlinson, M., Toit, S. D., Marlow, M., Ward, C. L., Fernando, A., Madrid, B., Van Thang, V., Tuyen, H. D., Dunne, M., Hughes, C., Fearon, P., Valdebenito, S., & Eisner, M. (2022). Associations Between ADHD Symptoms and Maternal and Birth Outcomes: An Exploratory Analysis in a Multi-Country Cohort of Expectant Mothers. *Journal of attention disorders*, *26*(14), 1882–1894.
6. Poulton, A. S., Armstrong, B., & Nanan, R. K. (2018). Perinatal Outcomes of Women Diagnosed with Attention-Deficit/Hyperactivity Disorder: An Australian Population-Based Cohort Study. *CNS drugs*, *32*(4), 377–386.

References

7. Du Rietz, E., Brikell, I., Butwicka, A., Leone, M., Chang, Z., Cortese, S., D'Onofrio, B. M., Hartman, C. A., Lichtenstein, P., Faraone, S. V., Kuja-Halkola, R., & Larsson, H. (2021). Mapping phenotypic and aetiological associations between ADHD and physical conditions in adulthood in Sweden: a genetically informed register study. *The lancet. Psychiatry*, *8*(9), 774–783.

8. Li, L., Zhu, N., Zhang, L., Kuja-Halkola, R., D'Onofrio, B. M., Brikell, I., Lichtenstein, P., Cortese, S., Larsson, H., & Chang, Z. (2024). ADHD Pharmacotherapy and Mortality in Individuals With ADHD. *JAMA*, *331*(10), 850–860.

9. Chang, Z., D'Onofrio, B. M., Quinn, P. D., Lichtenstein, P., & Larsson, H. (2016). Medication for Attention-Deficit/Hyperactivity Disorder and Risk for Depression: A Nationwide Longitudinal Cohort Study. *Biological psychiatry*, *80*(12), 916–922.

10. Huybrechts, K. F., Bröms, G., Christensen, L. B., Einarsdóttir, K., Engeland, A., Furu, K., Gissler, M., Hernandez-Diaz, S., Karlsson, P., Karlstad, Ø., Kieler, H., Lahesmaa-Korpinen, A. M., Mogun, H., Nørgaard, M., Reutfors, J., Sørensen, H. T., Zoega, H., & Bateman, B. T. (2018). Association Between Methylphenidate and Amphetamine Use in Pregnancy and Risk of Congenital Malformations: A Cohort Study From the International Pregnancy Safety Study Consortium. *JAMA psychiatry*, *75*(2), 167–175.

11. Nörby, U., Winbladh, B., & Källén, K. (2017). Perinatal Outcomes After Treatment With ADHD Medication During Pregnancy. *Pediatrics*, *140*(6), e20170747.

12. Newport, D. J., Hostetter, A. L., Juul, S. H., Porterfield, S. M., Knight, B. T., & Stowe, Z. N. (2016). Prenatal Psychostimulant and Antidepressant Exposure and Risk of Hypertensive Disorders of Pregnancy. *The Journal of clinical psychiatry*, *77*(11), 1538–1545. https://doi.org/10.4088/JCP.15m10506*chiatry*, *75*(2), 167–175.

References

13. Wright, T. E., Schuetter, R., Tellei, J., & Sauvage, L. (2015). Methamphetamines and pregnancy outcomes. *Journal of addiction medicine*, *9*(2), 111–117.

14. Cohen, J. M., Hernández-Díaz, S., Bateman, B. T., Park, Y., Desai, R. J., Gray, K. J., Patorno, E., Mogun, H., & Huybrechts, K. F. (2017). Placental Complications Associated With Psychostimulant Use in Pregnancy. *Obstetrics and gynecology*, *130*(6), 1192–1201.

15. Turner, E., Jones, M., Vaz, L. R., & Coleman, T. (2019). Systematic Review and Meta-Analysis to Assess the Safety of Bupropion and Varenicline in Pregnancy. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco*, *21*(8), 1001–1010.

16. Cole, J. A., Modell, J. G., Haight, B. R., Cosmatos, I. S., Stoler, J. M., & Walker, A. M. (2007). Bupropion in pregnancy and the prevalence of congenital malformations. *Pharmacoepidemiology and drug safety*, *16*(5), 474–484.

17. Bröms, G., Hernandez-Diaz, S., Huybrechts, K. F., Bateman, B. T., Kristiansen, E. B., Einarsdóttir, K., Engeland, A., Furu, K., Gissler, M., Karlsson, P., Klungsøyr, K., Lahesmaa-Korpinen, A. M., Mogun, H., Nørgaard, M., Reutfors, J., Sørensen, H. T., Zoega, H., & Kieler, H. (2023). Atomoxetine in Early Pregnancy and the Prevalence of Major Congenital Malformations: A Multinational Study. *The Journal of clinical psychiatry*, *84*(1), 22m14430.

18. Bang Madsen, K., Robakis, T. K., Liu, X., Momen, N., Larsson, H., Dreier, J. W., Kildegaard, H., Groth, J. B., Newcorn, J. H., Hove Thomsen, P., Munk-Olsen, T., & Bergink, V. (2023). In utero exposure to ADHD medication and long-term offspring outcomes. *Molecular psychiatry*, *28*(4), 1739–1746.

19. Philipp E. (1980). Guanfacine in the treatment of hypertension due to pre-eclamptic toxaemia in thirty women. *British journal of clinical pharmacology*, *10 Suppl 1*(Suppl 1), 137S–140S.

20. Klein, R. G., Mannuzza, S., Olazagasti, M. A., Roizen, E., Hutchison, J. A., Lashua, E. C., & Castellanos, F. X. (2012). Clinical and functional outcome of childhood attention-deficit/hyperactivity disorder 33 years later. *Archives of general psychiatry*, *69*(12), 1295–1303. https://doi.org/10.1001/archgenpsychiatry.2012.271

References

21. Chang, Z., Lichtenstein, P., D'Onofrio, B. M., Sjölander, A., & Larsson, H. (2014). Serious transport accidents in adults with attention-deficit/hyperactivity disorder and the effect of medication: a population-based study. *JAMA psychiatry*, *71*(3), 319–325. https://doi.org/10.1001/jamapsychiatry.2013.4174

22. Faraone, S. V., & Wilens, T. E. (2007). Effect of stimulant medications for attention-deficit/hyperactivity disorder on later substance use and the potential for stimulant misuse, abuse, and diversion. *The Journal of clinical psychiatry*, *68 Suppl 11*, 15–22.

23. Kosheleff, A. R., Mason, O., Jain, R., Koch, J., & Rubin, J. (2023). Functional Impairments Associated With ADHD in Adulthood and the Impact of Pharmacological Treatment. *Journal of attention disorders*, *27*(7), 669–697. https://doi.org/10.1177/10870547231158572