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Focusing on the Bu

Are Stimulants "Safe" to Use When Treating ADHD in Pregnancy?

August 14, 2025

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Presentation Outline

- Review ADHD diagnostic criteria & whether there are sex-based differences in symptoms
- Discuss relationship between ADHD & reproductive hormonal fluctuations
- Describe current reproductive safety data about using stimulant medications during pregnancy
- Identify key factors to consider when weighing the risks vs benefits of using stimulant medications during pregnancy
- Q&A

ADHD

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ADHD

- Neurodevelopmental disorder characterized by significant deficits in two domains: inattention and hyperactivity/impulsivity (American Psychiatric Association 2013)
- Often, but not always, diagnosed in childhood
- Leads to functional impairment in school, work & interpersonally

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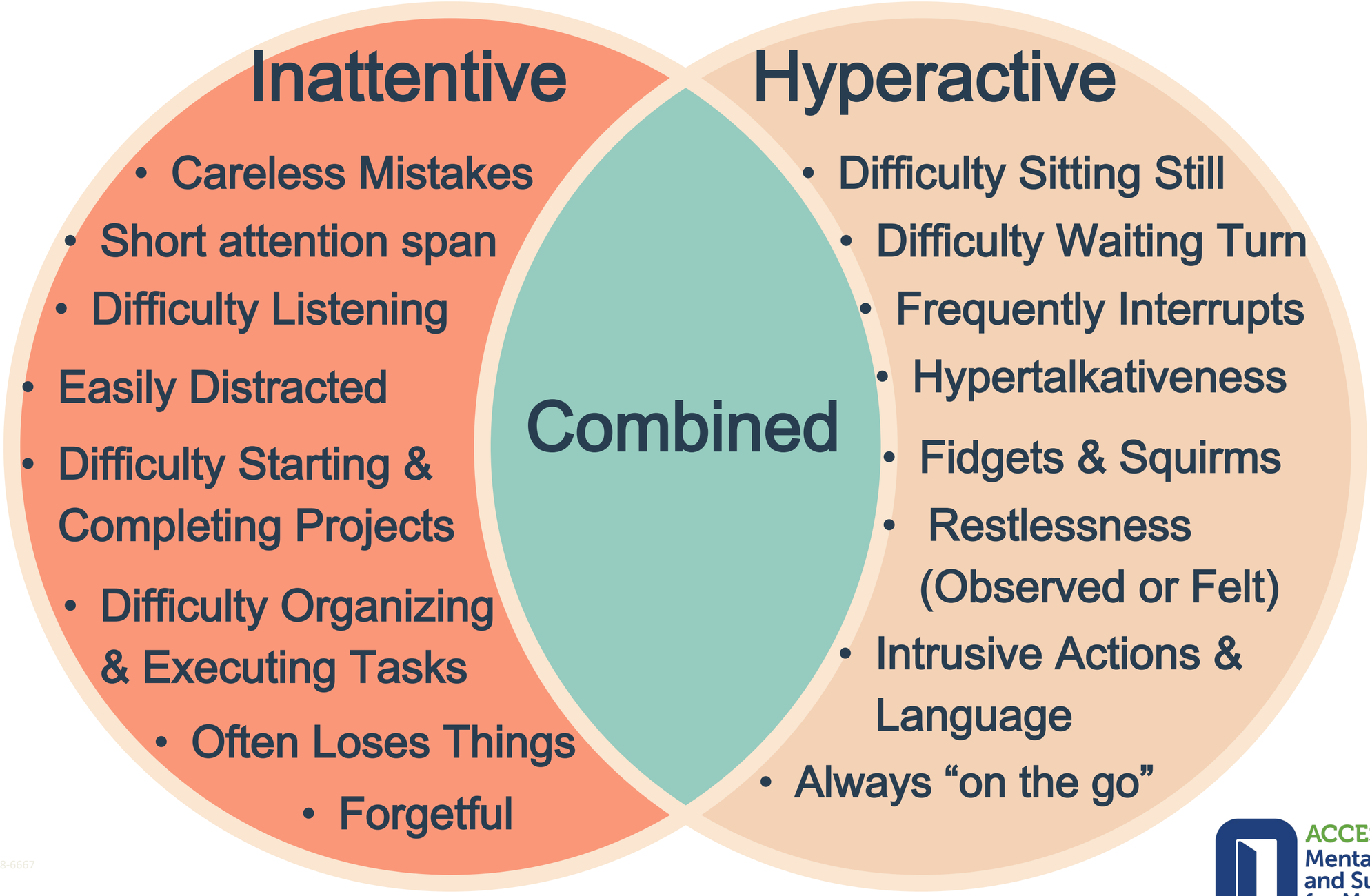

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Common Psychiatric Comorbidities

- Sleep issues
- Emotional dysregulation
  - Aggressive behavior, poor frustration tolerance, emotional lability, excessive excitability
- Cognitive dysfunction
  - Working memory impairment
  - Specific learning disabilities (dysgraphia, dyscalculia, dyslexia, dyspraxia)
- Alterations in motivation & processing of reinforcement

Common Psychiatric Comorbidities

- Autism spectrum disorder
- Anxiety disorders
- Mood disorders
- OCD
- Eating disorders
- PTSD
- Substance use disorders
- Impulse-control disorders
- Personality disorders
- Self-harming & suicidality risk

Presence of ADHD has been associated with ***less favorable prognosis*** *of other mental health conditions like depression, bipolar disorder & substance use disorders as well as* ***increased risk*** *of self -harm, suicide, harassment & abusive relationships*

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Prevalence

3-7% in children & adolescents

2-5% in adults

Symptoms often **decline** with age (particularly hyperactivity & impulsivity)

Prevalence **does not** seem to differ among race or ethnicity, yet **Black and Hispanic** children are diagnosed at **lower rates** than white children

- ODD, conduct disorder, bipolar disorder, PTSD, psychosis

Risks Factors for Persistence into Adulthood

- Family history of ADHD or other mental health conditions
- Combined subtype in childhood
- Greater symptom severity
- Co-morbid mental health conditions like depression
- Social stressors

Risks Associated with Un/Under - treated ADHD

- Substance misuse
- Binge eating
- Reckless behaviors
- Accidents and accidental death
- Unplanned pregnancies
- Poorer physical health
- Lower quality of life
- Impaired relationships
- Increased rates of divorce

Risks Associated with Un/Under - treated ADHD

- Difficulties with education and employment
- Financial distress
- Impaired driving safety
- Higher rates of imprisonment
- Increase mortality due to accidents
  - Rates higher in women with ADHD compared to men & persists even after controlling for comorbidities like substance use disorders
- Increased rate of suicide in all age groups & both sexes
- Increased vulnerability to sexual harassment, exploitation & abusive relationships

Sex Differences

Male to Female Ratios:

(Cortese et al. 2016; Rösler et al. 2006)

3 : 1 childhood

1: 1 adulthood

WHY?!?

Do boys get better moving into adulthood?

OR are we **missing it** in girls?

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Girls often present with more inattentive symptoms

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Girls often present with more inattentive symptoms

Quietly daydreaming in class, being easily distracted, forgetful, disorganized, overwhelmed, or lacking internal motivation

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Hyperactive/impulsive symptoms may look different in girls

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Hyperactive/impulsive symptoms may look different in girls

Hypertalkativeness & emotional reactivity rather than excessive motor activity

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Anxious, depressed & withdrawn

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Girls are socialized to be “good” & “quiet”

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Less disruptive?

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ADHD in Women

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Hormones & ADHD

ADHD & mood symptoms can worsen during **luteal phase** (Camara et al. 2022; de Jong et al. 2023)

ADHD is very hard to manage in context of **perinatal & postpartum** brain changes, increased executive function demands & sleep deprivation

ADHD is also hard to manage in context of **perimenopausal** “brain fog”

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Perinatal Implications

Pregnancy, new motherhood & perimenopause represent **transitions** associated with **more** psychosocial stress & executive function demands

Inattention symptoms are **more likely** to persist into adulthood & to become **problematic** at times of reproductive transition

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Perinatal Implications

Neurobiological brain changes during pregnancy & postpartum period:

- **Neuroplasticity** in areas important to social cognition & maternal attachment
- **Reduction in total brain volume** that reverses by 6mo postpartum (Oatridge et al 2002)
- Some evidence for **impaired verbal recall & working memory** related to hormonal changes

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Perinatal Implications

- Inattention
- Disorganization
- Time management difficulties
- Inner restlessness
- Procrastination
- Feeling easily overwhelmed or distracted
- Difficulty starting tasks
- Difficulty completing tasks once started

Perinatal Implications

Many women have coped & masked for **years** until executive function demands exceed their natural abilities

Many women present for **anxiety or depression** when underlying driving factor is undiagnosed or untreated ADHD

Household & parenting duties **disproportionately** borne by women (Treas and Tai 2016)

IMPULSIVITY

Ending relationships

Quitting jobs

More driving violations

Overspending, eating, drinking

HYPERACTIVITY

Restlessness

Verbosity

Constant activity

Active jobs

INATTENTION

Procrastination

Difficulty making decisions

Poor time management

Difficulty in organizing activities

Missing financial payments

EMOTIONAL REACTIVITY

Poor frustration tolerance

Parenting struggles

Arguing

Irritability

Anger

Perinatal Evaluation

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Perinatal ADHD Evaluation

(1) Screening

(2) History & Mental Status Exam

(3) Objective collateral information

- Partner, work performance reviews, academic records

(4) Medical Workup

- Baseline lab work including urine toxicology screening
- Further work-up like imaging or neuropsychiatric testing only when clinically indicated

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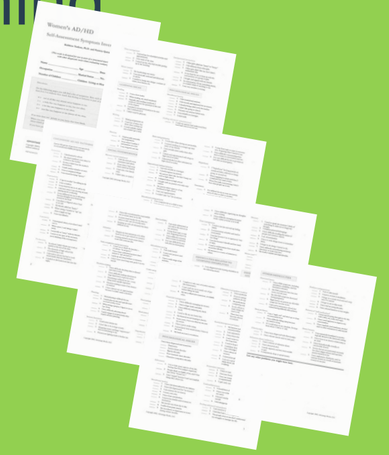
Perinatal ADHD Evaluation

ADHD is a **clinical** diagnosis!

Formal neuropsychiatric testing is **not** required, but can be helpful when trying to discern between ADHD and other disorders (like learning disabilities, GAD, PTSD, etc)



No rating scales specific to perinatal population

- Most rating scale norms are from male or mixed samples
- Nadeau & Quinn's Women's AD/HD Self-Assessment Symptom Inventory (SASI)

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Perinatal Treatment

MEDICATION?

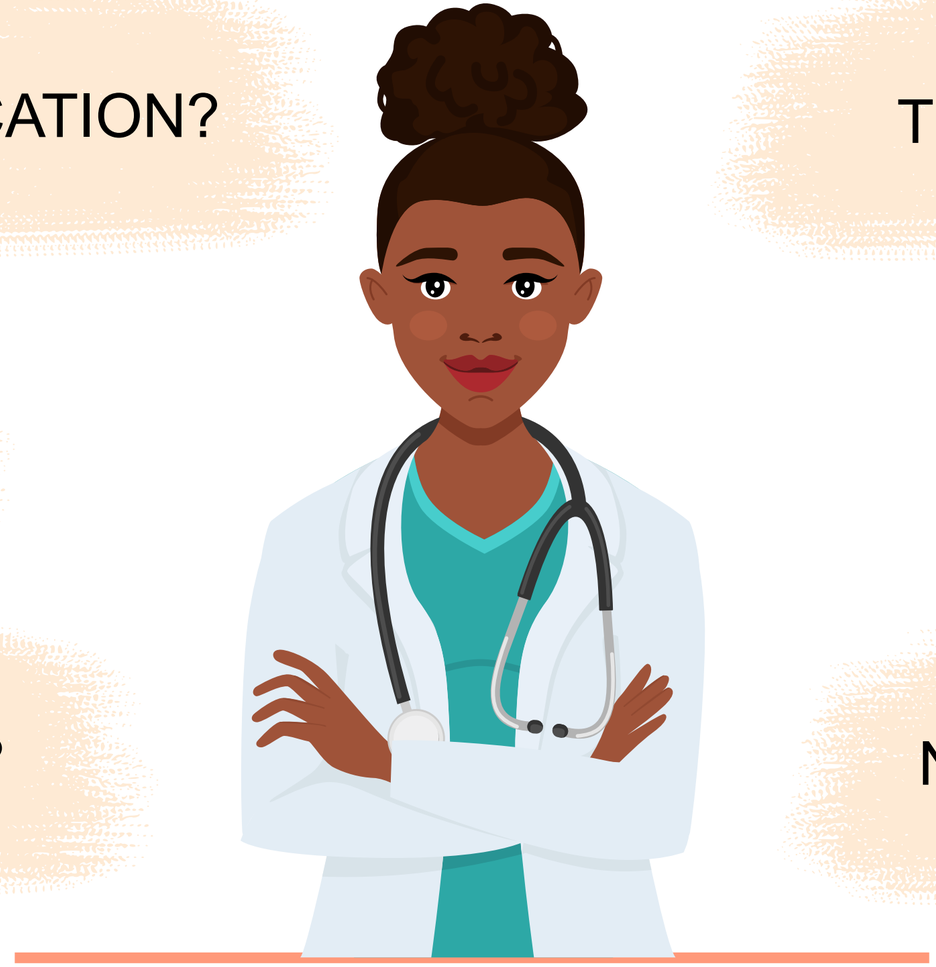
THERAPY?

SUPPLEMENTS?

SLEEP?

EXERCISE?

NUTRITION?



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Non - Pharmacologic Options

- Combined psychotherapy & medication management result in better therapeutic outcomes than either treatment alone (Cherkasova et al. 2020; Philipsen et al. 2015; Young et al. 2017)
- CBT with focus on executive dysfunction (Mongia and Hechtman 2012)
- Executive Function Coaching (Prevatt and Yelland 2015)
- Mindfulness-based interventions (Poissant et al. 2019; Scoten et al. 2024)
- Dialectical behavioral therapy (Scoten et al. 2024)
- Exercise
  - AM cardiovascular activity
- Nutrition, sleep, social support

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Perinatal Stimulant Use

Increasing numbers of women of reproductive age are taking stimulant medications

- From 2003 to 2015, number of reproductive-aged women annually filling prescriptions for ADHD Rx increased by **344%** to an overall prevalence of **4%** (Anderson et al. 2018)
- Approximately **1%** of US pregnant women use medications to treat ADHD
  - **One of the most commonly prescribed medications in pregnancy**

(Anderson et al. 2018; Lupattelli et al.

Amphetamines (APM)

alpha-methylphenethylamine

2 enantiomers

- Dextroamphetamine (D)
  - More potent
- Levoamphetamine (L)

IR formulations last ~4-6hrs
XR formulations last ~10-12hrs
Prodrug lasts up to 12-14hrs

Three options:

(1) Mixed amphetamine salts (MAS): 3:1 or 1:1

(2) Dextroamphetamine alone

(3) Lisdexamfetamine (prodrug)

Methylphenidate (MPH)

2 enantiomers

- Dexmethylphenidate (D)
  - More potent
- Levomethylphenidate (L)

IR formulations last ~3-5hrs
SR formulations last ~4-8h
XR formulations last ~8-12
Prodrug lasts up to 13hrs

Redistributes VMAT-2 but does not directly increase DA release so lower abuse potential compared to AMP

Three options:

(1) 50:50 racemic mixture

(2) Dexmethylphenidate alone

(3) Serdexmethylphenidate (prodrug) + dexmethylphenidate

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Stimulant Side Effects

- Increased HR & BP
- Orthostatic hypotension
- Insomnia
- Appetite suppression
- Anxiety
- Headaches
- Dry Mouth
- Tics
- Mood swings
- Potential for dependency, misuse & diversion

<u>Monitor</u>:

- Weight
- Hydration status
- Cardiac health
  - Baseline & annual EKG
  - BP, HR at each visit
- Mood & anxiety level

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Stimulants & Addiction

- **Tolerance:** decreased response to same dose after repeated use
- **Dependency:** physical or psychological reliance on a substance or behavior that can lead to cravings or withdrawal symptoms.
- **Addiction:** compulsive behavior where someone feels a strong, uncontrollable urge to engage in a particular activity or use a substance, despite negative consequences.

Risk - Risk Analysis

Undertreated or untreated mental illness has been shown to increase risk of pregnancy complications & perinatal death independent of medication use!!

- Medical complications like high blood pressure, preeclampsia or preterm birth
- Emergence or worsening of depression or anxiety
- Emergence or worsening of suicidal and/or infanticidal thoughts
- Drug or alcohol misuse or abuse
- Development of a postpartum psychiatric disorder
- Disrupted attachment

Risk - Risk Analysis

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THIS MAKES IT DIFFICULT TO DETERMINE HOW MUCH OF THESE OUTCOMES IN MEDICATION-EXPOSED INFANTS ARE ATTRIBUTABLE TO MEDICATION USE VS UNDERLYING MENTAL ILLNESS

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National Pregnancy
Registry for ADHD
Medications

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Perinatal Stimulant Use

Understanding of reproductive safety profile of stimulants is **limited & complicated** by **confounding variables**

- ADHD itself
- Alcohol, nicotine & other illicit exposures
- Poor nutrition or prenatal care
- Indication (using for anorectic properties)
- Medical & psychiatric comorbidities
- Other psychosocial variables

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MGH
National Pregnancy Registry for ADHD Medications

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Perinatal Stimulant Use

Also limited & complicated by **study design:**

- Small sample sizes & low power
- Heterogeneous definitions of ADHD and drug exposure timeline
- Many studies based on pharmacy registries
- Data from illicit stimulants like methamphetamine or cocaine
- Misuse and/or supra-therapeutic dosages
- Studies combine stimulant classes
- Significant differences in patient characteristics

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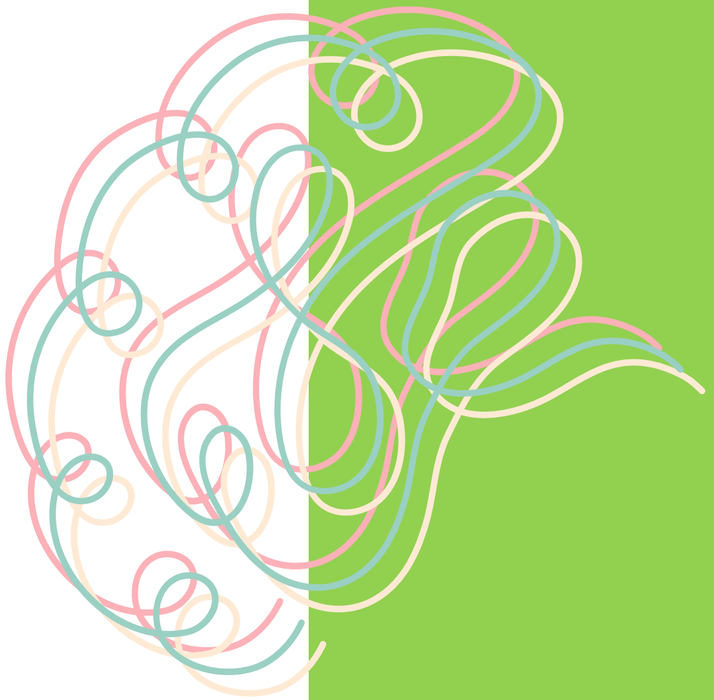
Risks Associated with Perinatal Stimulant Use

- Congenital Malformations
- Spontaneous Abortions
- Obstetrical Complications
- Neonatal Complications
- Long-Term Neurodevelopment

Congenital Malformations

Most studies **do not** suggest risk of overall congenital malformations

- Aktepe et al. 2009; Debooy et al.1993; Diav-Citrin et al. 2016; Dideriksen et al. 2013; Källén et al. 2013; Kolding et al. 2021; Milkovich and van der Berg 1977; Nörby et al. 2017; Pottegård et al. 2014



Congenital Malformations

A few studies have noted associations with the following malformations:

- **Cardiac** (Huybrechts et al. 2018; Jiang et al. 2019; Kolding et al. 2021)
- **Gastrointestinal** (Anderson et al. 2020; Elliott et al. 2009)
- **Limb** (Anderson et al. 2020)

ADHD medication use & individual birth defects were **rare**, thus absolute risk presumed to be **low**

Spontaneous Abortion

Some studies show association with **increased risk** but presence of **confounding variables** like:

- Polypharmacy (Haervig et al. 2014)
- Prior miscarriage (Diav-Citrin et al. 2016)
- Confounding by indication (Bro et al. 2015)

Obstetric Complications

Some studies show **association** with **increased risk** of:

- **Preterm delivery** (Cohen et al. 2017; Ladhani et al. 2011; Norby et al. 2017)
- **Hypertensive disorders** of pregnancy including preeclampsia (Newport et al. 2016; Cohen et al. 2017)

Obstetric Complications

However – presence of **confounding variables** (like age, smoking status, differences in group patient characteristics) & **small** absolute risk

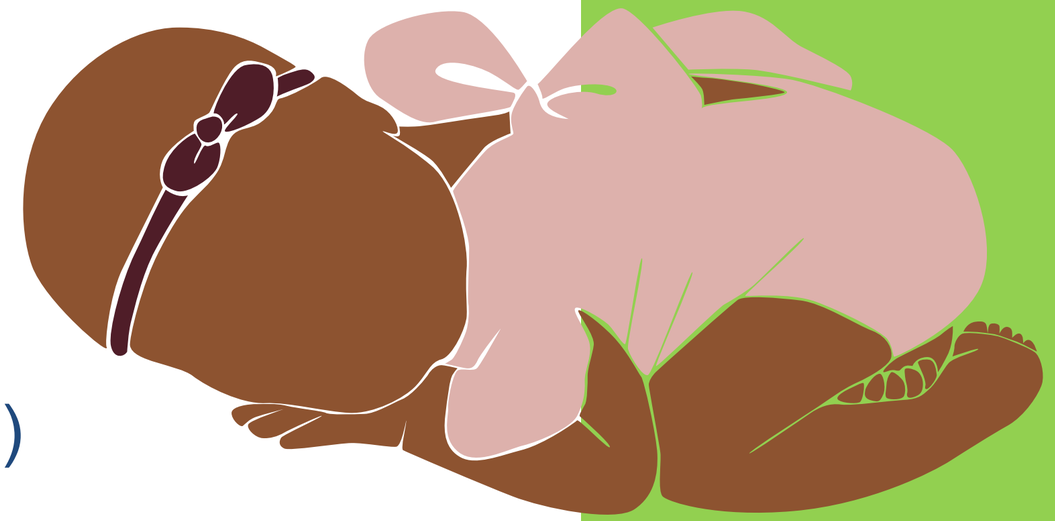
Cohen et al. 2017:

“women with significant ADHD should not be counseled to suspend their ADHD treatment based on these findings”

Neonatal Complications

Increased risk:

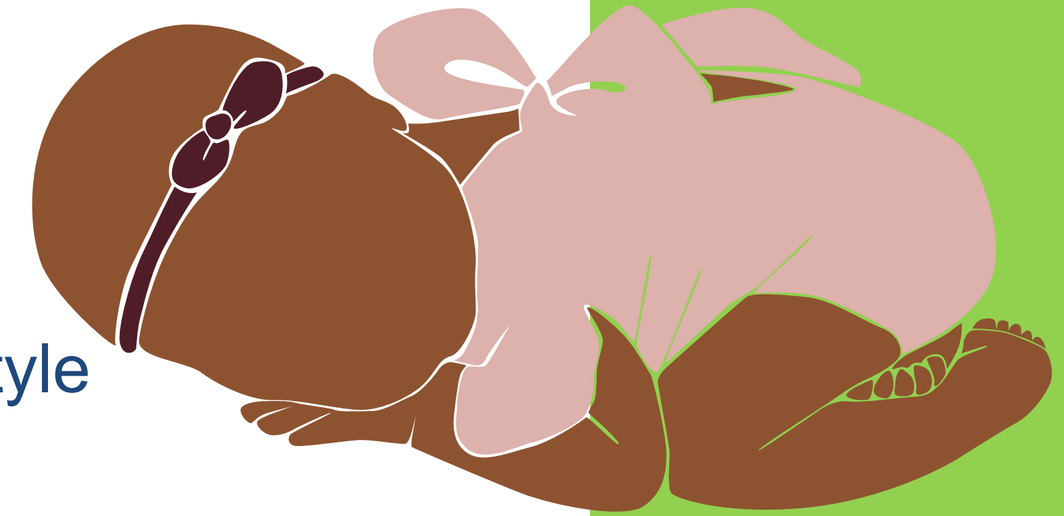
- LGA (Norby et al. 2017)
- SGA (Ladhani et al. 2011)
- NICU admission (Norby et al. 2017; Jiang et al. 2019)
- CNS-related disorders (Norby et al. 2017)
- Low APGAR scores (Bro et al. 2015)



Neonatal Complications

However:

- Small sample sizes
- Heterogenous populations
- Heterogenous medications evaluated
- Medications grouped for analyses
- Many confounding variables (like lifestyle factors & differences in group patient characteristics)
- Polypharmacy



Long - Term Development

Very limited evidence thus far is reassuring that in utero exposure to stimulants **does not increase risk** for adverse neurodevelopmental outcomes in children (Bang Madsen et al. 2023; Suarez et al. 2024)

Risks Associated with Perinatal ADHD

- 5-fold increased risk PPD & PPA (Andersson et al. 2023; Baker et al. 2022)
- Poor adherence to prenatal care
- Substance use (tobacco, alcohol, cannabis, etc)
- Poor nutrition & weight disruptions
- Increased maternal stress (occupational, $$)
- Increased risk of accidents
- Other mental health conditions requiring medication
- Hypothesized to struggle more with parenting, balancing work with household management, and maintaining partnerships & interpersonal relationships (Nadeau and Quinn 2002; Young et al. 2020)

Risk - Risk Analysis

Historically, women with **mild to moderate** symptoms have been advised to **discontinue** stimulant medication for pregnancy & focus on non-pharmacologic management

HOWEVER, more studies are showing **relative safety** of stimulant medications during pregnancy & **significant risks** associated with stopping medication for pregnancy (even in mild cases)

Risk - Risk Analysis

Undertreated or untreated ADHD symptoms increase risk of pregnancy complications (including PPD & PPA) independent of medication use

Risks of untreated perinatal ADHD may outweigh risk of medication exposure to fetus, depending on symptom severity

Must weigh potential risks associated with discontinuing stimulants (occupational, social, safety like driving) with risks to fetus (Freeman 2014)

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Perinatal Prescribing

Always counsel on reproductive safety profile regardless of desire for children

- **50%** of pregnancies are unintentional

Use what works – changing medication to “minimize” risk to fetus once a woman is already pregnant actually **increases risk**

- **Fetus exposed to:**
  - Original medication
  - New medication
- **Fetus potentially exposed to:**
  - Sequelae of mother’s psychiatric illness if new medication doesn’t work

Risk Mitigation Strategies

- Psychoeducation
- Use lowest effective dose
- Avoid polypharmacy
- “Drug holidays” as clinically indicated
- Check baseline urine toxicology prior to prescribing
- Regular appointments for refills with close monitoring of prescription drug monitoring programs (PDMP)
- Standardized policies for early refills & “lost” prescriptions

Risk Mitigation Strategies

- **Coordinate** with OB/midwife and pediatric providers
- **Reconsider** dosing based on maternal vitals and fetal growth
- **Document** risks discussed, alternatives considered, and patient's informed choice
- **Emphasize** ongoing collaboration and flexibility

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Lactation & Stimulants

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Lactation & Stimulants

Very limited data – 15 total case reports

AMP & MPH have been shown to **decrease PRL** (related to increased DA)

- Most studies did not report corresponding effects on milk production

Lactation & Stimulants

Amount of medication found in the breast milk **parallels** maternal blood levels

- **IR**
  - Maternal blood levels peak in **1-2 hrs**
- **ER**
  - Maternal blood levels rise more slowly & remain elevated for **6-8 hrs**

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Lactation & Stimulants

AMP estimated **RID 3.9-13.8%** (Illet et al. 2006)

MPH estimated RID ranged from **undetectable to 0.7%**

Do not appear to adversely affect infants when used at therapeutic dosages

Monitor infant growth, stimulation, insomnia, fussiness & feeding difficulties

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Lactation & Stimulants

Decisions about breastfeeding must weigh risks of infant medication exposure and maternal symptom severity, safety & potential sleep disruptions

As during pregnancy, recommend **avoiding** stimulants in **mild to moderate** cases if possible

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Lactation & Stimulants

Based on extremely limited data, thus far AMP & MPH **appear safe** to use at therapeutic dosages when breastfeeding full-term, healthy infants

Lactation & Stimulants

May consider using judiciously in **severe cases** of ADHD where lack of medication could lead to functional impairment that may negatively affect a woman's safety, economic security, or increase risk for depression/anxiety

Lactation & Stimulants

To **minimize** breastmilk transmission, mothers might consider:

- PRN use
- Switching to IR formulation
- Formula or combo feeding

Thank you

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