# ADHD in girls and women across the life span

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# Today

- Background on ADHD
- Gender and ADHD
- ADHD in times of hormonal change


- Throughout I will highlight ongoing research being conducted by my lab

# Background

Inattention:

- Easily distracted
- Not listening when spoken to
- Forgetful in daily activities

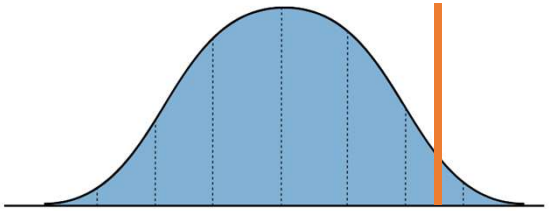
Hyperactivity/impulsivity:

- Talks excessively
- Fidgets with or taps hands or squirms in seat
- Unable to play or take part in activities quietly

- Results in impairment
- Pervasive (occurs in multiple settings)

# ADHD and neurodiversity

- An extreme of a continuum in the population



ADHD symptoms

- ADHD from a neurodiversity perspective:
- "…variations in brain structure and function, which lead to ways of thinking and behaving that are different from most people in society… Any impairment experienced by neurodiverse people occurs, not as an intrinsic part of a disorder, but because there is a mismatch between their ways of thinking and behaving and their environments"

Sonuga-Barke & Thapar 2021

# Gender and ADHD in childhood

- ADHD diagnosis has a strong male preponderance
  - 16:1-3:1 male:female gender ratio

- At least 2 broad (not mutually exclusive!) explanations:
  - True **higher risk** in males (female protective effect)
  - **Underdiagnosis** among girls

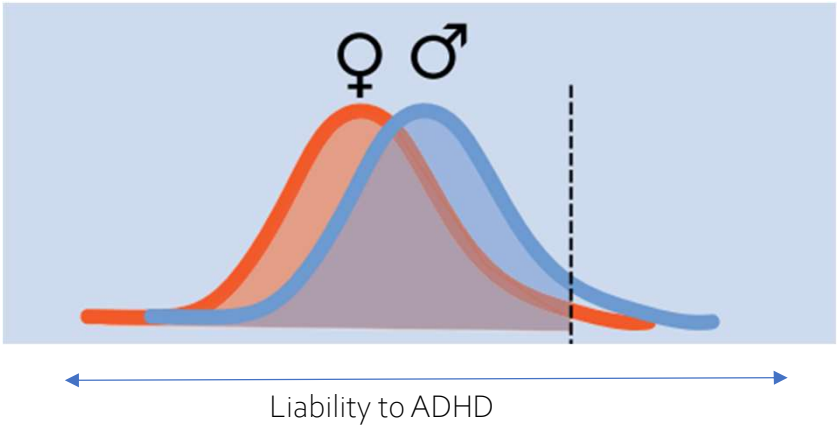
Young 2020, Novik 2006

# Note on language about sex/gender

- The vast majority of research on this topic is not-specific about sex vs gender
  - *Some* what I will talk about will have to do with sex (i.e. biological) factors, e.g. related to menstrual cycles
  - *Some* will be more to do with gender (i.e. social) factors, e.g. cultural expectations about how girls 'should' act
- My aim is to be as inclusive as possible– when talking about biological processes like the menstrual cycle, I mean all people with menstrual cycles (or menopause, etc).
- When talking about gender, I mean people who present as female

# Is ADHD more prevalent in boys?

- Female protective effect:
  - Hypothesizes that female individuals are resilient to developing ADHD
  - If this were the case:
    - Girls with ADHD undergo greater exposure to etiological factors than males in order to develop ADHD
    - Require a higher burden of risk factors to develop ADHD




Wigdor 2022

# Female protective effect?

Supportive evidence

- ↑ risk of ADHD in 1st degree relatives of girls/women with ADHD compared with males
  - i.e. families of affected girls have a genetic burden

Contradictory evidence

- Not all studies find ↑ risk of ADHD in 1st degree relatives of affected female individuals compared with affected males
- Study in large (n>50k) cohort in Sweden found no higher ADHD polygenic risk score amongst girls vs boys with ADHD

Rutter 2003, Martin 2018

# Underdiagnosis in girls

- Gender ratio varies from 16:1 in some clinical cohorts to 3:1-2:1 in population-based cohorts
- This difference in clinical sex ratio and population-based cohorts suggests *referral bias*

  → Girls are being missed

Young 2020, Novik 2006

# Underdiagnosis in girls

Historical bias of ADHD as a disorder affecting boys among clinicians, teachers and parents

## Clinicians

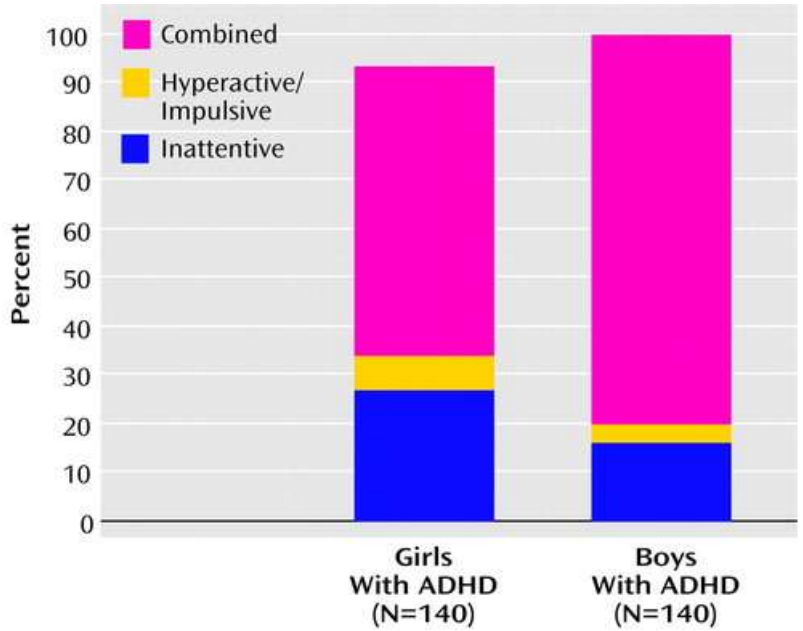
- Study presenting clinical vignettes with identical behaviours but the gender of the patient varying
- Clinicians 2x more likely to diagnose boys than girls based on identical clinical information (Bruchmuller 2012)

## Parents & teachers

- Evidence parents and teachers rate boys as more hyperactive even when objective indicators rated them similarly
- Study used the Classroom Observation Code used to rate ADHD behaviours by blinded classroom assessors
- Parent & teacher ratings significantly higher for males than females even when ratings by assessor did not differ by sex (Meyer 2020)

# Underdiagnosis among girls

- Many (not all) studies find girls are more likely to have predominantly inattentive versus hyperactive symptoms
  - Teachers less likely to raise as a potential problem inattention symptoms vs combined type ADHD
  - Teachers particularly important as they may initiate referral for diagnosis raising concerns about a child's behaviour




Biederman 2002, Moldavsky 2012, Sayal 2006

# Underdiagnosis among girls

ADHD symptom description reflects more "male" behaviours

- Many early studies of ADHD that helped establish the ADHD criteria included all boys or had extremely small female subsamples
  - DSM-IV criteria for ADHD are based primarily on observations of males and the DSM-5 field studies included a greater percentage of males
- Thus, the ADHD symptom description may itself be biases towards a more "male" presentation
  - E.g. physical overactivity vs excessive talkativeness

Lahey 1994, Barkley 2002, Clarke 2013, Mowlem 2019

# Underdiagnosis among girls

- Some studies find girls with ADHD are less likely to exhibit co-morbid disruptive behaviours (Gaub 1997)
  - Boys more likely to have comorbid conduct disorder
  - Boys exhibiting higher levels of externalizing behaviour

- More recent findings on this are inconsistent:
  - Several studies (Graetz 2005, Levy 2005, Bauermeister 2007) find no difference in the rates of disruptive disorders between girls and boys

# Underdiagnosis among girls

Girls more likely to exhibit 'prosocial' behaviour

- Study comparing boys and girls who met diagnostic criteria for ADHD to those with high levels of ADHD symptoms, but no ADHD diagnosis
- What other elements (impairment, other behavioural problems) associated with diagnosis?
  - In the presence of positive social behaviour, girls' symptoms may be 'masked' making them appear less impaired, which could reduce the likelihood of girls with ADHD symptoms being referred

Mowlem 2019

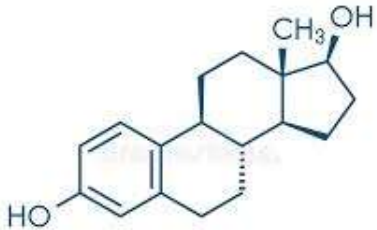
# Implications of underdiagnosis among girls

- Women diagnosed at later ages
  - Incidence peaked earlier in boys than girls in ADHD (8 vs 17 years of age)
- Already have more comorbidities:
  - Study from Stockholm finds women presenting with ADHD have significantly more comorbid anxiety, mood and substance use disorders compared to men
- Anecdotally, this is something women talked about a lot
  - Receiving diagnosis of anxiety, depression, etc prior to ADHD diagnosis in adulthood
  - Feeling derailed in their lives, especially around schooling, due to missed diagnosis in childhood
    - "I think of how much I could have done if it had been caught earlier"

Dalsgaard 2019, Skoglund 2023

# Sex hormones and ADHD

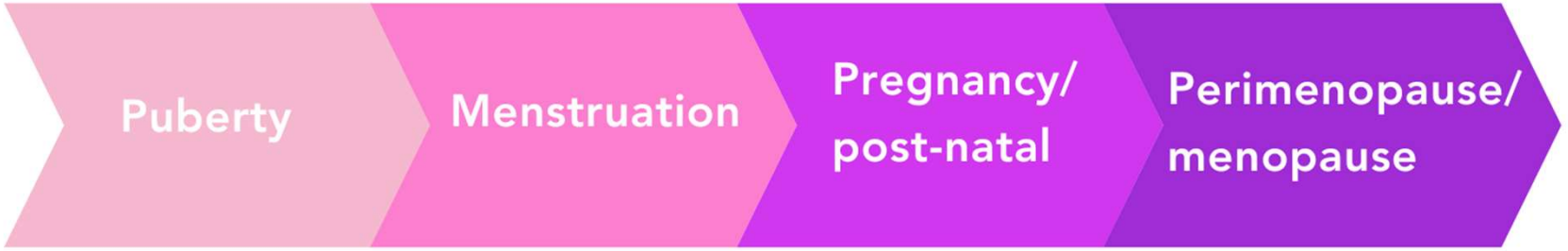
- Because of this historical under-recognition of ADHD in girls and women, female-specific factors have been under-researched
- Strong biological rationale linking estrogen and ADHD:
  - Dopamine a key neurotransmitter associated with ADHD
    - Stimulant medication acts by reducing dopamine reuptake
  - Estrogen can affect dopamine availability
    - Overall estrogen appears to have a facilitating effect on dopaminergic neurotransmission
    - Drops in estrogen (e.g. premenstrually) could result in lower dopamine availability
    - Much of this research comes from animal models (rats)



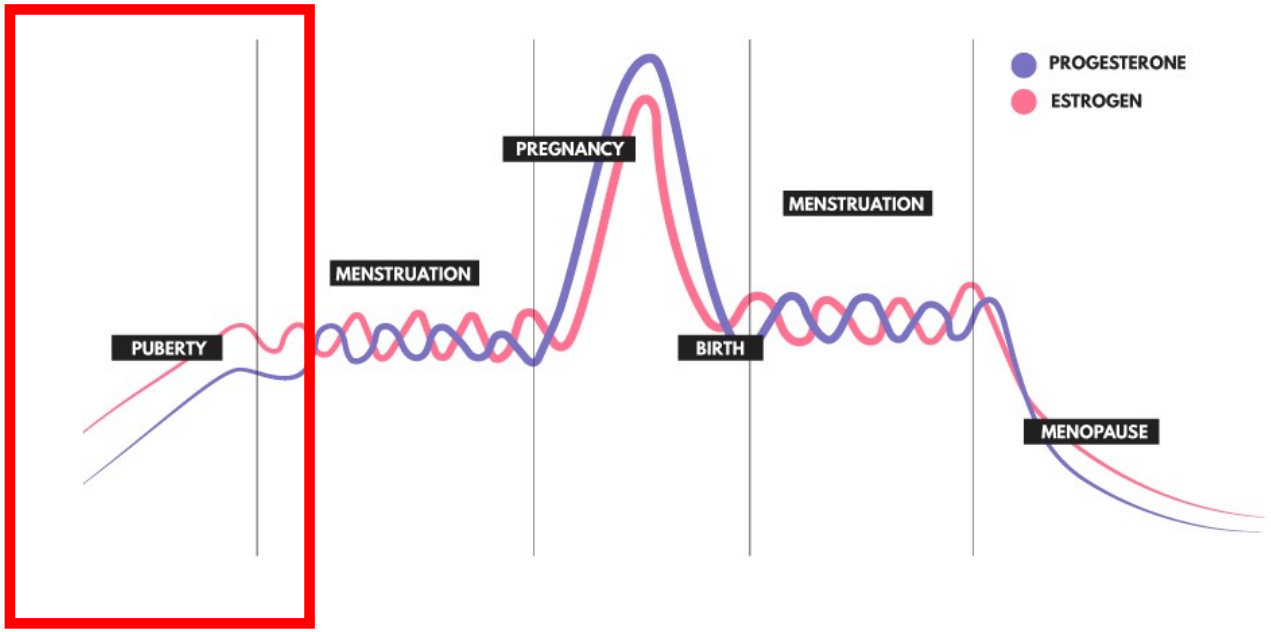
estradiol

Barth et al 2015

# Hormonal change and ADHD



# Puberty




*"As I hit puberty, it all came melting down"*

# Puberty

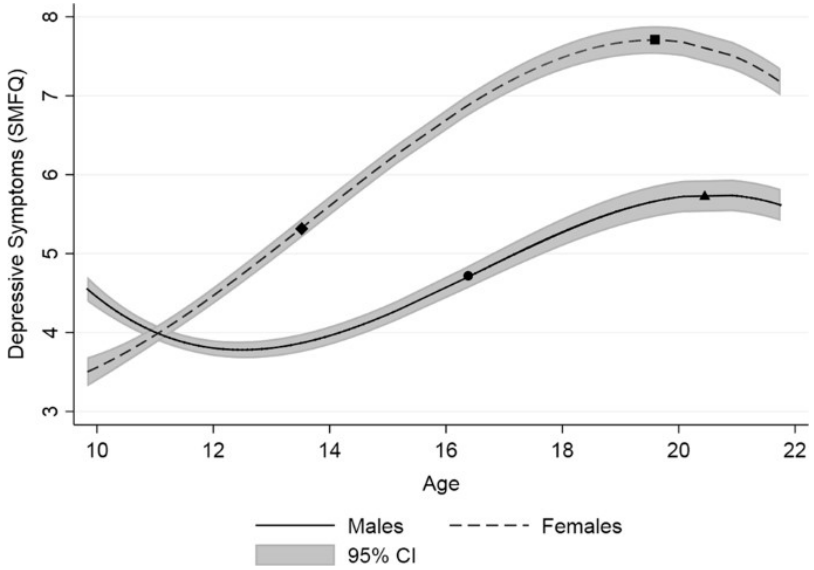


- Time of significant **hormonal** change
  - Increase in estradiol, which is responsible for developing secondary sexual characteristics
- Time of significant **neurological** change
  - The structure of the prefrontal cortex undergoes significant development
- Time of significant **educational, social** and **emotional** change

# Adolescence and mental health

PUBERTY

- Puberty is associated with onset of mental health problems in girls, especially depression:
  - In childhood, the prevalence of depression is similar in boys and girls but around the age of 12-13, incidence increases sharply in females
  - Millennium cohort study find by age 14, **1 in 4** girls have high levels of depressive symptoms
    - Compared to 1 in 9 boys, despite similar levels at age 11




Hankin 1998, Patalay 2017, Kwong 2019

# Adolescence and ADHD

PUBERTY

- Why do we think adolescence might be particularly important for girls and ADHD?
- In childhood, ADHD diagnosis has a strong male preponderance
  - 16:1-3:1 male:female gender ratio
  - By adulthood, the gender ratio equalizes, and ADHD diagnoses are 50% male, 50% female
  - Puberty/adolescence may represent a key transition point in ADHD among girls

Hinshaw et al 2022

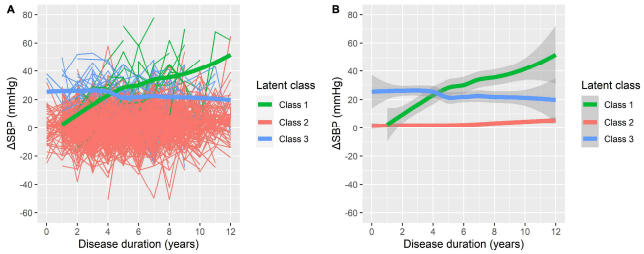
# ADHD and puberty

PUBERTY

Adolescent Brain Cognitive Development®
Teen Brains. Today's Science. Brighter Future.

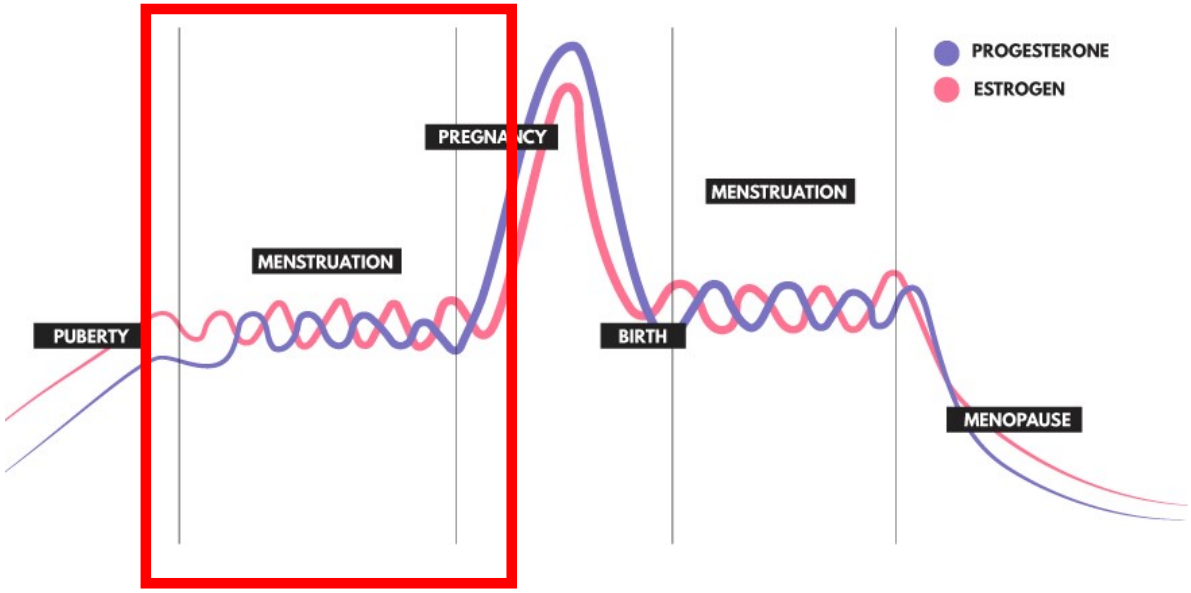
UKRI Medical Research Council

- New research study using a cohort from the US that follows children from age 9/10 to most recently 12/13 with:
  - Yearly ADHD symptom assessment
  - Questions on pubertal stage by parents and adolescents
  - Biological assessments of hormonal levels




- Research questions:
  - (1) Is there a subgroup of girls with increasing ADHD symptoms in adolescence?
  - (2) Is pubertal onset associated with ADHD symptom change in girls?

# Menstruation

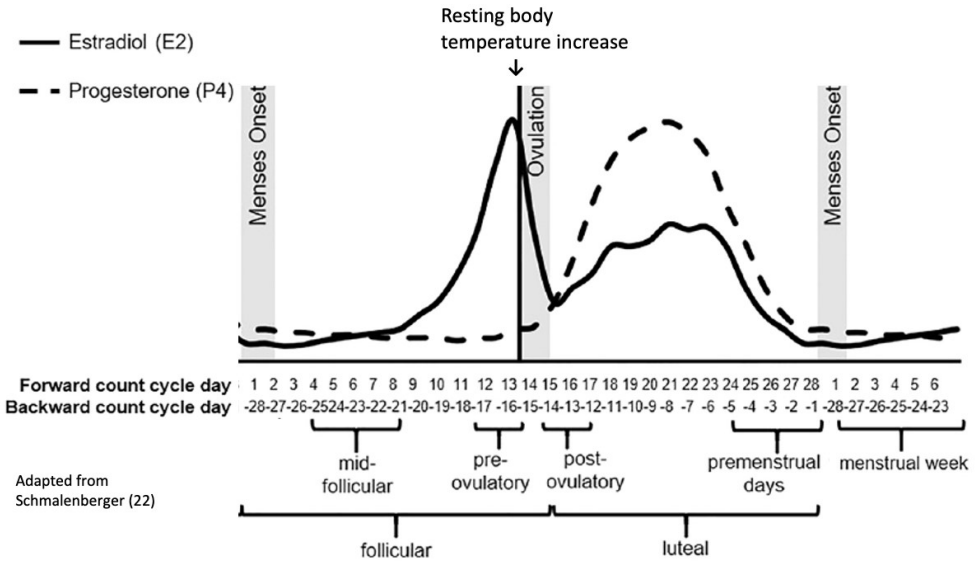



*"I've taken my meds, why can I not focus on things when last week I could…"*

# Menstrual cycle

MENSTRUATION

- Beginning of cycle characterised by low estrogen and progesterone
- Followed by a steep preovulatory increase in estrogen and sharp drop post ovulation
- Then both estrogen and progesterone rise in the luteal phase then drop sharply premenstrually
- Drops in estrogen may affect dopamine availability
  - Could exacerbate ADHD symptoms and compromise medication effectiveness



# Menstrual cycle hormonal fluctuations

MENSTRUATION

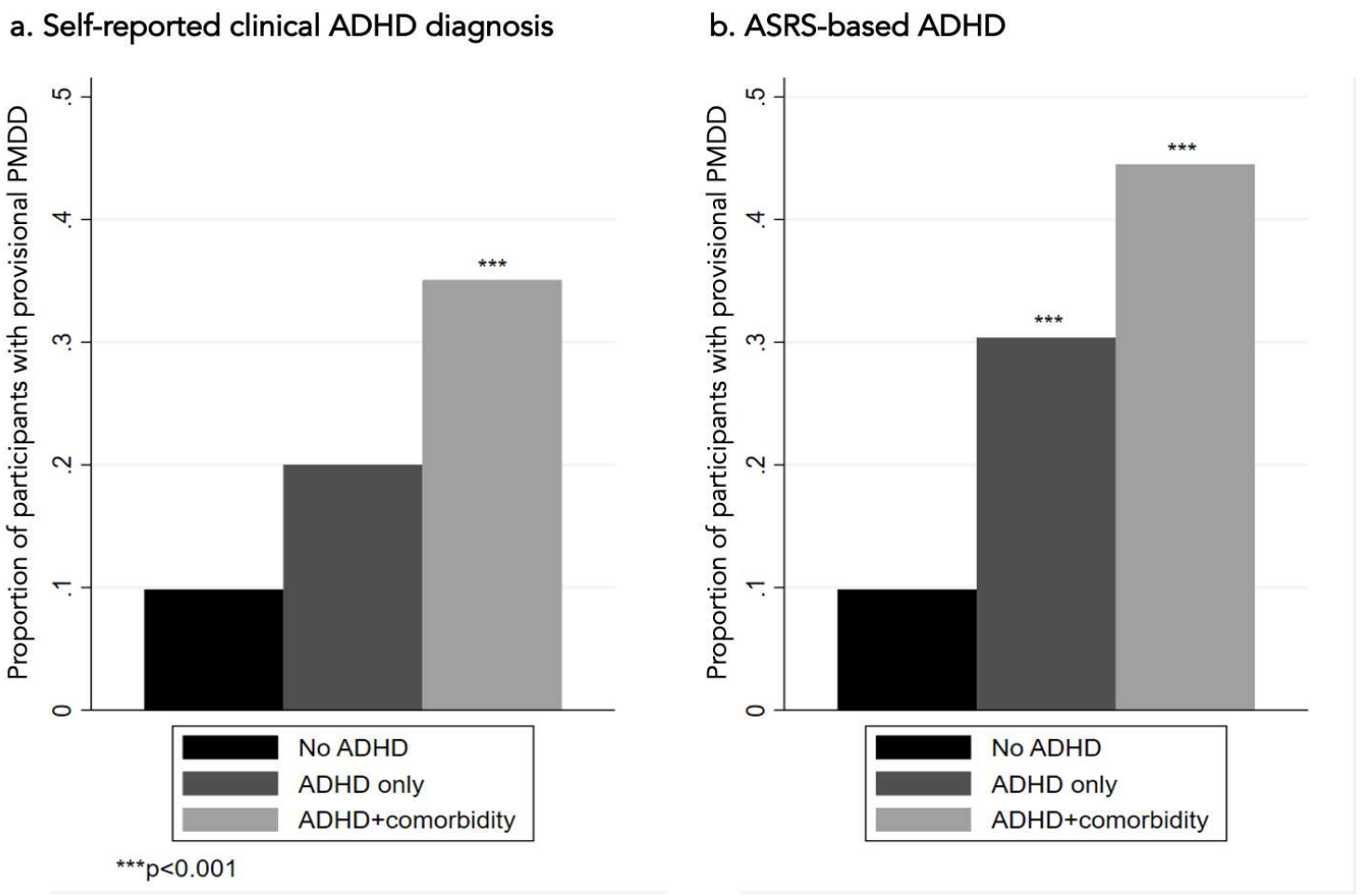
- Premenstrual Dysphoric Disorder (PMDD)
  - Mood and behavioural changes that occur in the few days prior to menstruation that are so severe they interfere with personal and professional relationships
  - Affects between 3-9% of menstruating women
  - Not caused by different levels of hormones, per se, but by differential sensitivity to these hormones
  - Studies of the post-natal period and post-initiation of hormonal contraception suggest women with ADHD might have higher rates of hormonal sensitivity

DSM-5, Backstrom 2003, Schmidt 1998, Lundin 2023, Andersson 2023

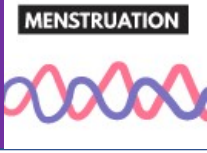
# ADHD and PMDD

- Online study of 715 women with and without ADHD
  - ADHD:
    - Self-reported clinical diagnosis (n=102)
    - ADHD scale-based ADHD (n=229)
  - Non-ADHD reference group (n=305)
- PMDD measured via the Premenstrual Symptoms Screening Tool (PSST)
  - 31.4% among participants self-reporting a clinical ADHD diagnosis
  - 41.1% among ADHD scale-based ADHD participants
  - 9.8% among non-ADHD reference group

# ADHD and PMDD



# Hormonal fluctuations on women's ADHD symptoms




- Clinical and anecdotal evidence for some role of hormonal fluctuation in ADHD symptom expression for women with ADHD
- Women discuss their symptoms getting worse premenstrually, medication being less effective during this time

Question for #ADHD people who get periods, esp #inattentive pals: Do you find your symptoms, energy and brain fog get way worse just before and during yo period? My meds become almost ineffective and all I want to do is wallow in bed!

Every month I'm like "I've been so distracted for the past couple days, what's going on?" And then my period arrives and I'm like 🤦‍♀️ THAT was the reason.

3 weeks later... "I'm so distracted, I wonder why".

Keep going on an eternal cycle #ADHD

# Measuring Adult ADHD and Menstruation (MAAM) Study

- To address this gap in the research we have funding for the MAAM study
- Research questions:

1. Are different cycle phases associated with changes in ADHD symptoms and functioning among women with ADHD?
2. Are changes in hormone levels across the menstrual cycle among women with ADHD are associated with the effectiveness of ADHD medication?
3. Do sleep and physical activity mediate the association between hormonal changes and ADHD symptoms/functioning among women with ADHD?

MAAM STUDY
MEASURING ADULT ADHD AND MENSTRUATION

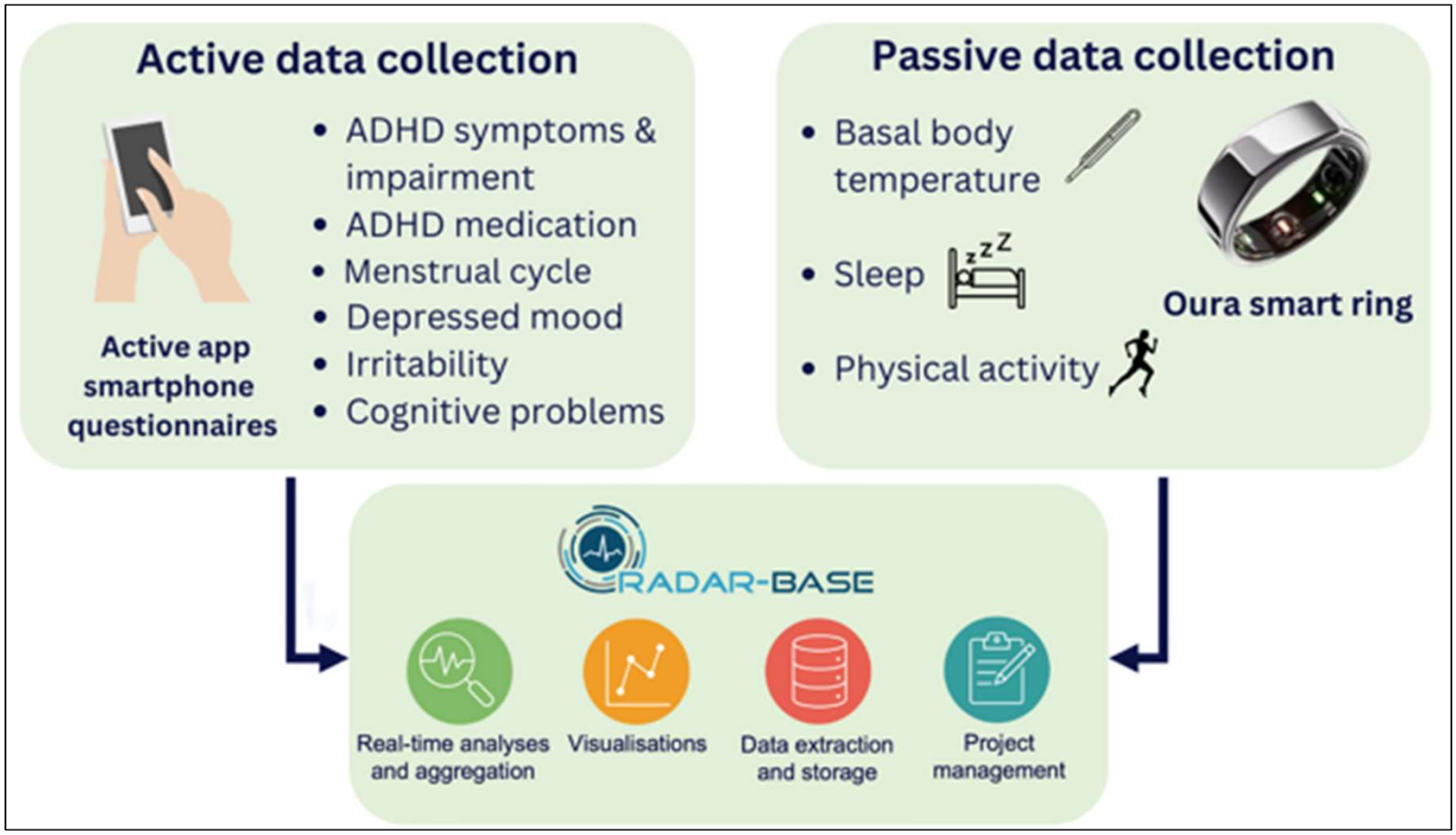
ADHD REMOTE TECHNOLOGY CARMA ART

https://www.adhdlifelab.com/maam-study

# Measuring Adult ADHD and Menstruation (MAAM) Study

MAAM STUDY
MEASURING ADULT ADHD AND MENSTRUATION

MENSTRUATION

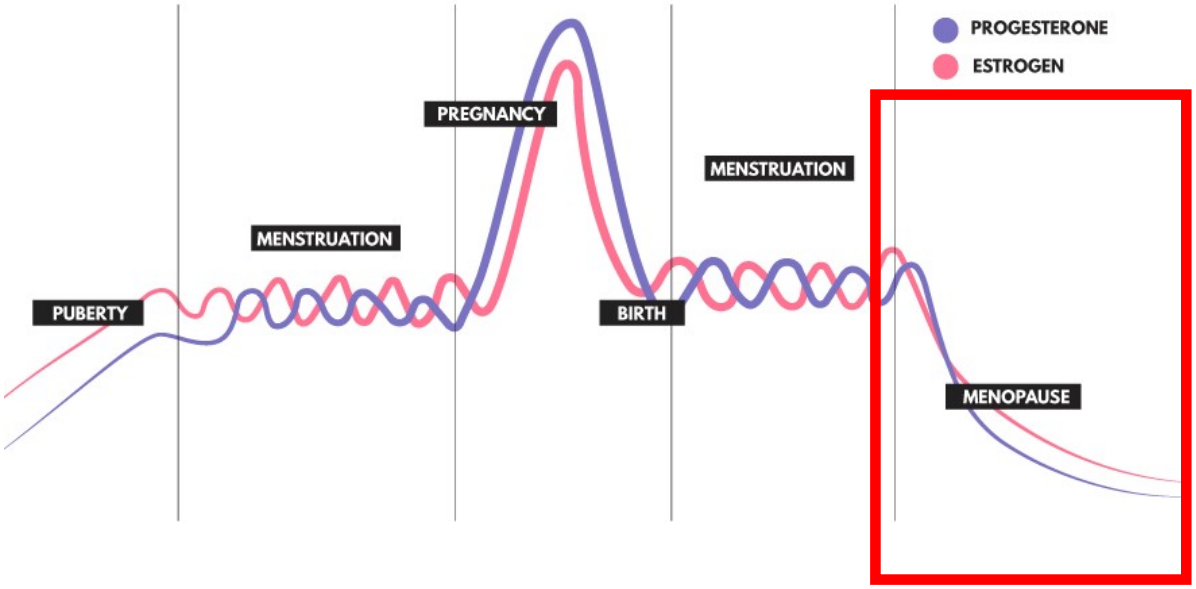



https://www.adhdlifelab.com/maam-study

# Menstrual cycle hormonal fluctuations and ADHD

Impact:

- Provide quantitative evidence regarding symptom change across the menstrual cycle
- A better understanding of the effect of menstrual cycle for women with ADHD may help them better anticipate/plan for symptom exacerbation
- If ADHD medication is less effective in certain cycle phases, this may suggest a benefit to increasing dose during these phases
- If sleep and physical activity are key mediators, interventions could focus on improving these areas to mitigate hormonal effects

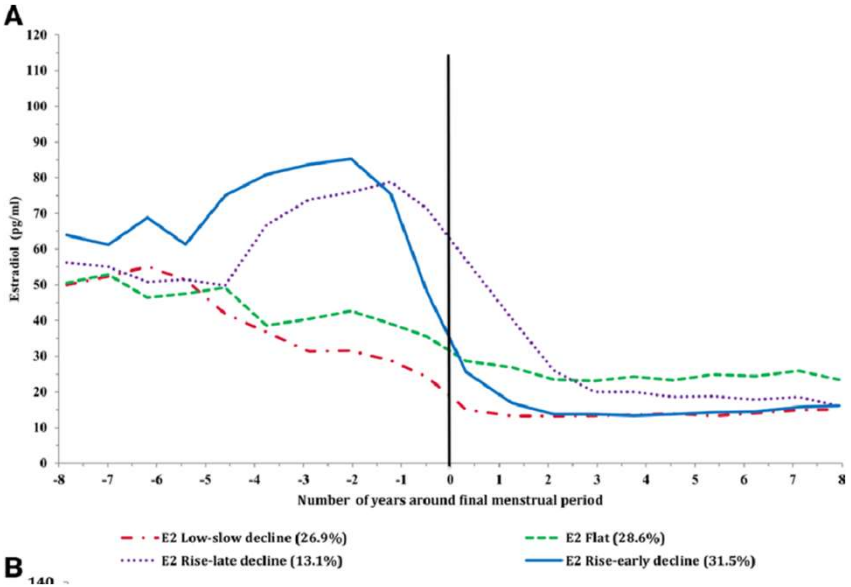



*"My friends and I are going through perimenopause, and my friends with ADHD… we just struggle more"*

*"The scatter of my memory is just on a different level… I thought I had early onset Alzheimer's"*

# Perimenopause/menopause

- The transition to menopause can occur over a 10–15 year period (around age 40-44)
- Early in perimenopause, menstrual cycles are typically more frequent and characterized by more hormonal extreme fluctuations
- Later in the menopausal transition, cycles become unpredictable and decrease in number exposing women to progressively longer periods of estrogen withdrawal




Morrison 2006, Santoro 1996, Deecher 2008, Khoudary 2020

# Perimenopause/menopause

- This is an area of huge concern for women with ADHD
- Currently forming a PPI group of women with ADHD in the menopausal transition who will inform on several PhD projects, including:
  - **Qualitative interviews** with women with ADHD about their experiences of the menopausal transition
  - **Analysis of data** from the US-based SWAN cohort examining how women with high genetic risk for ADHD experience menopause
  - **Survey study** comparing women with ADHD to those without a diagnosis on symptoms and experience of menopause

# In conclusion


- Times of hormonal transition may particularly affect women with ADHD
- We have many more questions than answers about how hormones affect women with ADHD (and women in general!)
- Women are asking us to answer these questions and we need to listen

Medical Research Council

# Thank you for listening!
# Questions?

**Ways to keep in touch:**

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