GODDESS-
hur möta ett kvinnligt liv med ADHD- ett liv med stora utmaningar

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Declaration of interest Helena Kopp Kallner

I receive honorariums for lectures on from: Abbvie, Actavis, Bayer, Gedeon Richter Exeltis, Nordic Pharma, Natural Cycles, Mithra, Teva, Merck, Organon, Ferring, Consilient Health Takeda and Medice.

I provide expert opinion for: Bayer, Evolan, Gedeon Richter, Exeltis, Merck, Teva, TV4 och Natural Cycles, Pharmiva, Dynamic Code (ended from my side), Ellen, Estercare, Pharmiva, Gedea, Gesynta, Essity and Preglife

I am an investigator in trials sponsored by Bayer, MSD, Mithra, Ethicon, Azanta/Norgine, Gedeon Richter, Gedea, planned study for Organon, Pharmiva and Takeda

I teach in courses sponsored by: Organon, Bayer and Gedeon Richter

I teach courses organized by: SFOG, Karolinska Institutet, Sophiahemmet (medical and nurse midwifery program) and participate in educational activities organised by county councils

I have written book chapters in: Guide for contraception (sponsored by Bayer) and in the Swedish medical Products agency recommendation for contraception and book chapters for 1,6 million club (Swedens largest social club for women)

I am president of the European Society of Contraception and Reproductive Health.


”De flesta förstår inte att vissa människor använder enorma mängder energi för att bara vara normala”
Albert Camus

GODDESS-projektet

- Ett samarbetsprojekt initierat av Helena Kopp Kallner och Charlotte Borg Skoglund

- Idag ett multidisciplinärt forskningsprojekt med gynekologer, psykiatriker, psykologer, barnpsykiatriker, barnmorskor
- Finansierat av privata donationer från familjen Tham och Susanne Hobohms stiftelse

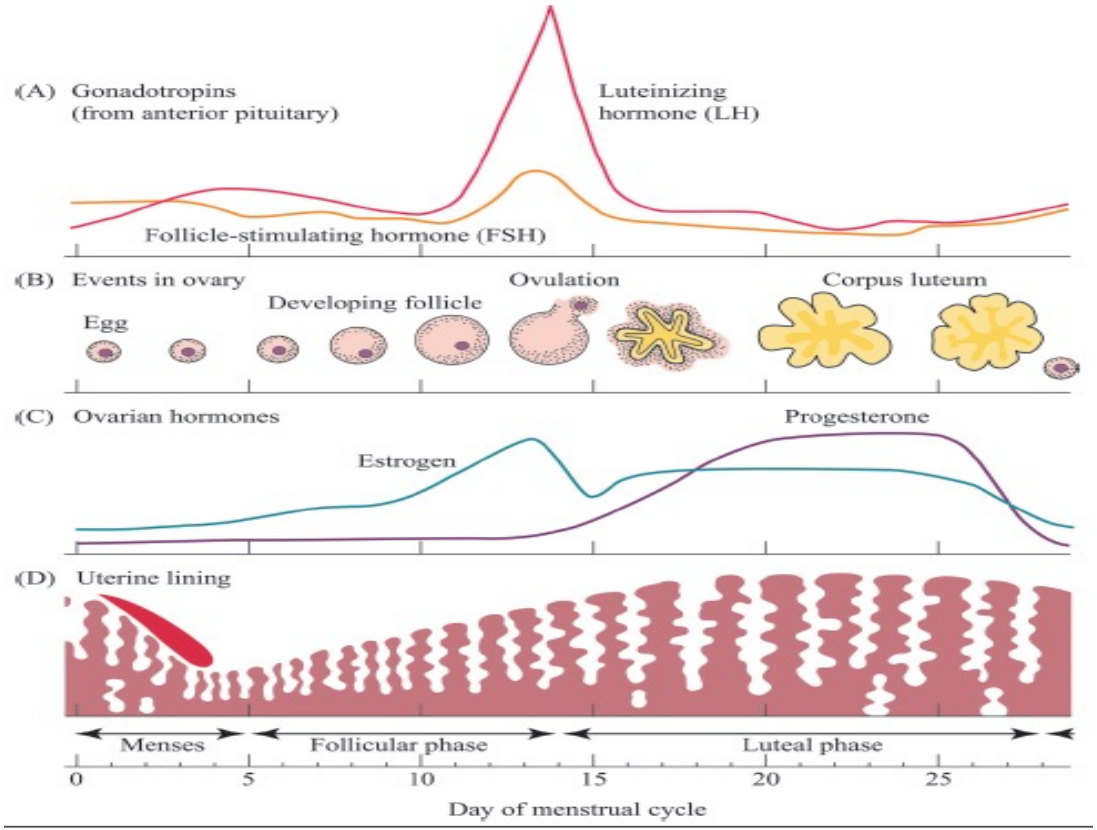
HORMONERNA

Genom livet och menscyklerna

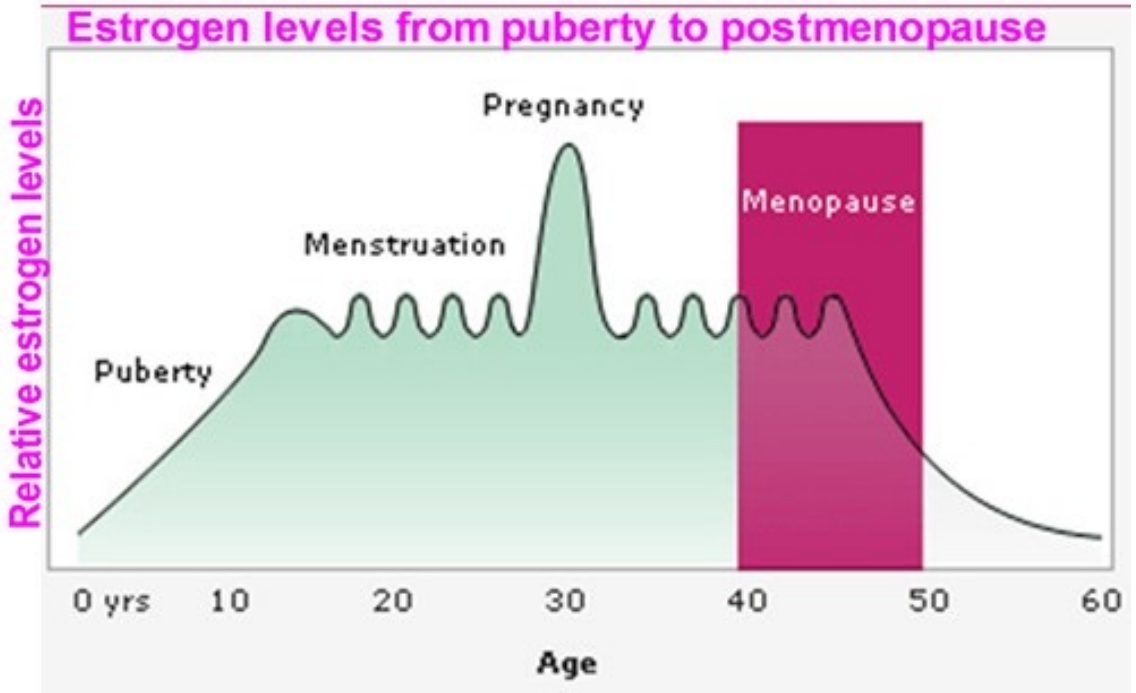
- Prepubertet
- Pubertet
- PMS/PMDS
- Graviditet
- Övergångsålder
- Klimakterium

→ Symtom
→ Sexuell hälsa
→ Läkemedelsbehandling

MENSCYKELN


(A) Gonadotropins
(from anterior pituitary)
Luteinizing
hormone (LH)
Follicle-stimulating hormone (FSH)
(B) Events in ovary
Egg
Developing follicle
Ovulation
Corpus luteum
(C) Ovarian hormones
Estrogen
Progesterone
(D) Uterine lining
Menses
Follicular phase
Luteal phase
0
5
10
15
20
25
Day of menstrual cycle

ÖSTROGENER GENOM LIVET



PROBLEMET

Flickor och kvinnor med adhd är ofta **o- eller feldiagnostiserade** och när de väl får sin diagnos sämre behandlade.

De har högre risk för:

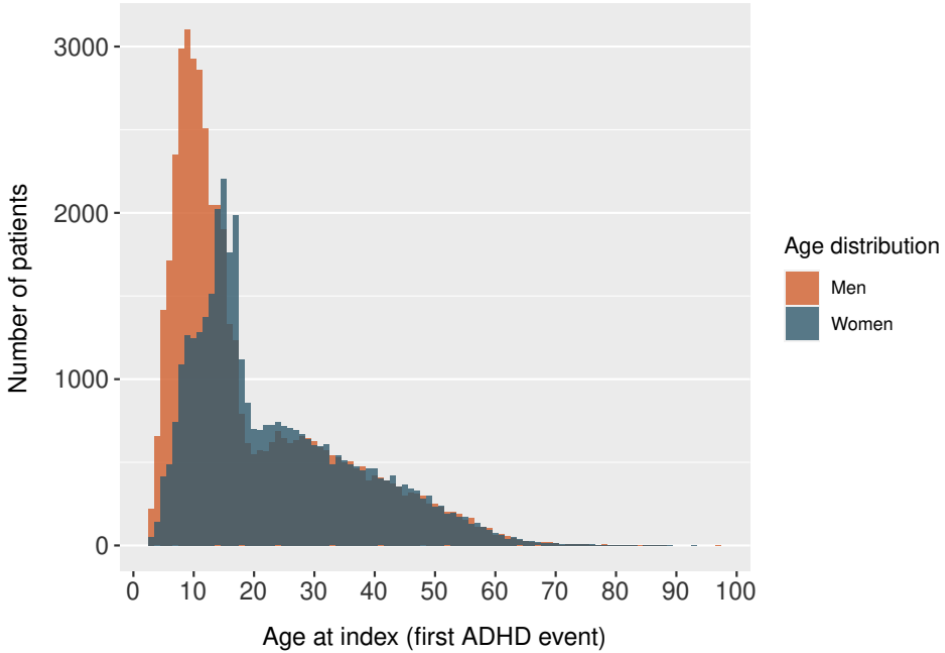
- Tidig sexual debut
- Sexuellt risktagande i ung ålder
- Sexuellt överförbara sjukdomar
- Sexuell exploatering och övergrepp
- Oönskade graviditeter och aborter
- Tonårsföräldraskap

Kvinnor med psykiatriska diagnoser utesluts ofta ur forskningsstudier

Kunskapen om behandling och stöd är låg

Dawson AE, Wymbs BT, Evans SW, DuPaul GJ. Exploring how adolescents with ADHD use and interact with technology. Journal of adolescence. 2019;71:119-137.Young S, Heptinstall E, Sonuga-Barke EJ, Chadwick O, Taylor E. The adolescent outcome of hyperactive girls: self-report of psychosocial status. Journal of child psychology and psychiatry, and allied disciplines. 2005;46(3):255-262. Skoglund C, Kopp Kallner H, Skalkidou A, et al. Association of Attention-Deficit/Hyperactivity Disorder With Teenage Birth Among Women and Girls in Sweden. JAMA network open. 2019;2(10):e1912463.

Kvinnor med adhd får sin diagnos senare



- Flickor och kvinnor får dubbelt så ofta diagnosen adhd ouppmärksam form (ADD) och
- har mer internaliserande symtom som inte ”stör andra” och kommer därför inte tilll utredning och behandling (Young 2021).
- Visades av Gershon i en meta-analys 2002.
- Visat av oss i Stockholm

A meta-analytic review of gender differences in ADHD. Gershon J. J Atten Disord. 2002 Jan;5(3):143-54

Time after time: failure to identify and support females with ADHD - a Swedish population register study. Skoglund C, Sundström Poromaa I, Leksell D, Ekholm Selling K, Cars T, Giacobini M, Young S, Kopp Kallner H. J Child Psychol Psychiatry. 2023 Nov 28.

UNGA KVINNOR MED ADHD

Samsjuklighet och risktagande

- Påtagligt försämrad funktionsnedsättning pga emotionell instabilitet
- Depression, ångest, ätstörningar, självskada
- Skadligt bruk och beroende
- Sexuellt risktagande & tonårsgraviditeter
- Utsatthet, trauma och övergrepp
- Olyckor, suicid och ökad dödlighet

Biederman 2002, Elkins 2007; ; Molina 2002, O Brien 2010, Lee 2010; Lehti 2012, Owens 2017, Skoglund 2019; Konstenius 2015; Lee &Hinshaw 2005 ,Lee 2010; Rucklidge Tannok 2001 Hinshaw 2012 Owens 2017; Dalsgaard 2015

SAMSJUKLIGHET ÄR REGEL

ASPD, antisocial personality disorder Image sourced by presenter

1. Franke B, et al. Eur Neuropsychopharmacol 20182;28:1059–88; **2.** Nigg JT. Clin Psychol Rev 2013;33:215–28; **3.** Biederman J, et al. Pediatrics 1999;104:e20; **4.** Hinshaw SP. J Consult Clin Psychol 2002;70:1086–98; **5.** Biederman J, et al. J Clin Psychiatry 2012;73:941–50; **6.** Kuja-Halkola R, et al. Mol Psychiatry 2018;Oct 15:doi: 10.1038/s41380-018-0248-5; **7.** Cortese S, et al. J Clin Psychiatry 2016;77:e421–8; **8.** Cortese S, Tessari L. Curr Psychiatry Rep . 2017;19:4

Women suffer a higher psychiatric co-morbidity

Table 1: Psychiatric comorbidities in females and males with ADHD

Psychiatric comorbidities*, n (%)	Females (n=37,591)	Males (n=47,739)	*P*-value† Females vs males
Anxiety disorders including stress	18,932 (50.4)	12,359 (25.9)	<0.001
Mood (affective) disorders	14,103 (37.5)	9,296 (19.5)	<0.001
Substance use disorders	4,834 (12.9)	5,703 (12.0)	<0.001
Autism	3,732 (9.9)	5,955 (12.5)	<0.001
Sleep disorders	2,812 (7.5)	2,300 (4.8)	<0.001
Eating disorders	2,094 (5.6)	273 (0.6)	<0.001
Personality disorders	2,357 (6.3)	1,001 (2.1)	<0.001
Conduct disorder	944 (2.6)	2,001 (4.2)	<0.001
Tics/Tourette syndrome	266 (0.7)	836 (1.8)	<0.001
Psychotic disorders	443 (1.2)	603 (1.3)	0.278
Mental retardation	403 (1.1)	596 (1.3)	0.019

*Expressed as ≥1 record of the condition pre- (or at time of) ADHD-index. †*P*-value for the two-sample proportion test.

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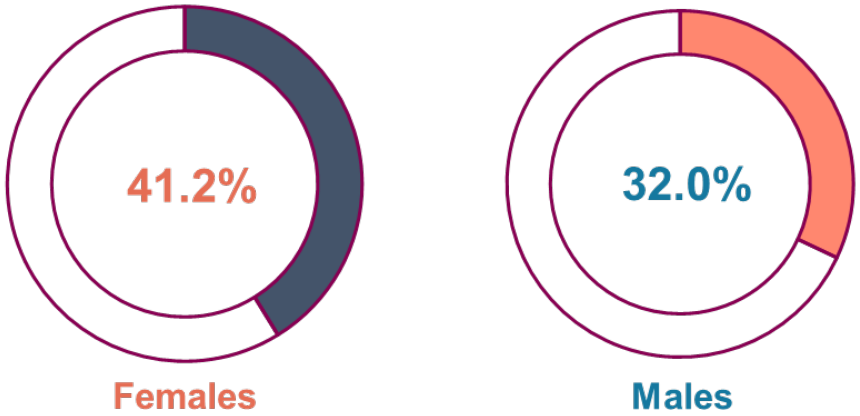
Samsjuklighet leder till att man söker lösningar– man mår inte bra!

Proportion of outpatients with ≥1 psychiatric healthcare visit 2 years prior to ADHD index



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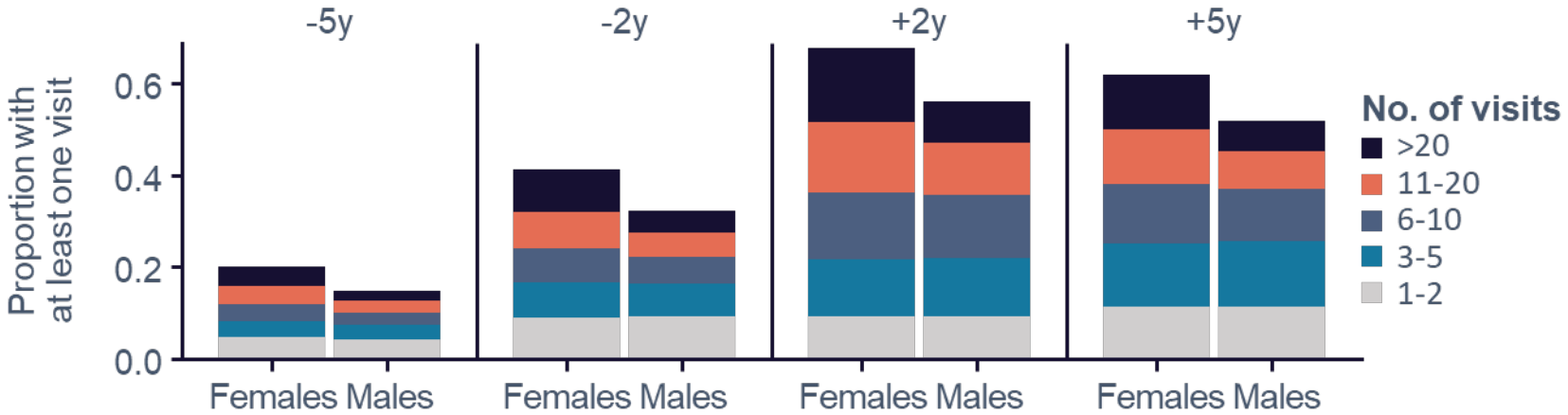
Enorm belastning på sjukvården

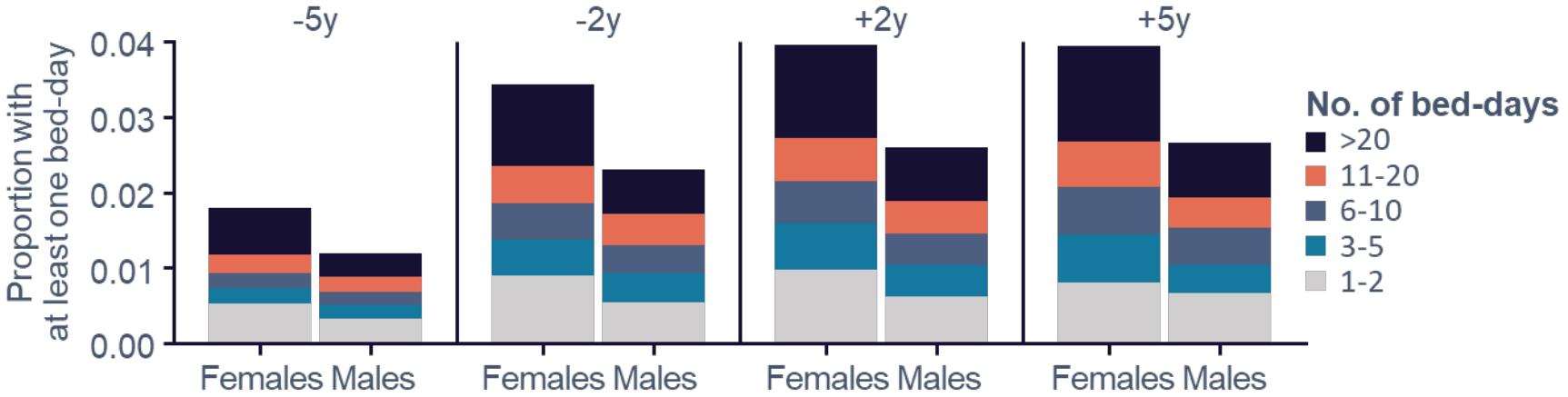
Figure 3: Outpatient psychiatric healthcare utilisation in patients with ADHD expressed as ≥1 visit over the period 5 years before ADHD-index and 5 years following ADHD-index*,†



Time after time: failure to identify and support females with ADHD – a Swedish population register study. Skoglund C, Sundström Poromaa I, Leksell D, Ekholm Selling K, Cars T, Giacobini M, Young S, Kopp Kallner H. J Child Psychol Psychiatry. 2023 Nov 28.

… och sjukhusen!

Figure 2: Inpatient psychiatric healthcare utilisation in patients with ADHD expressed as ≥1 inpatient bed-day over the period 5 years before ADHD-index and 5 years following ADHD-index*,†



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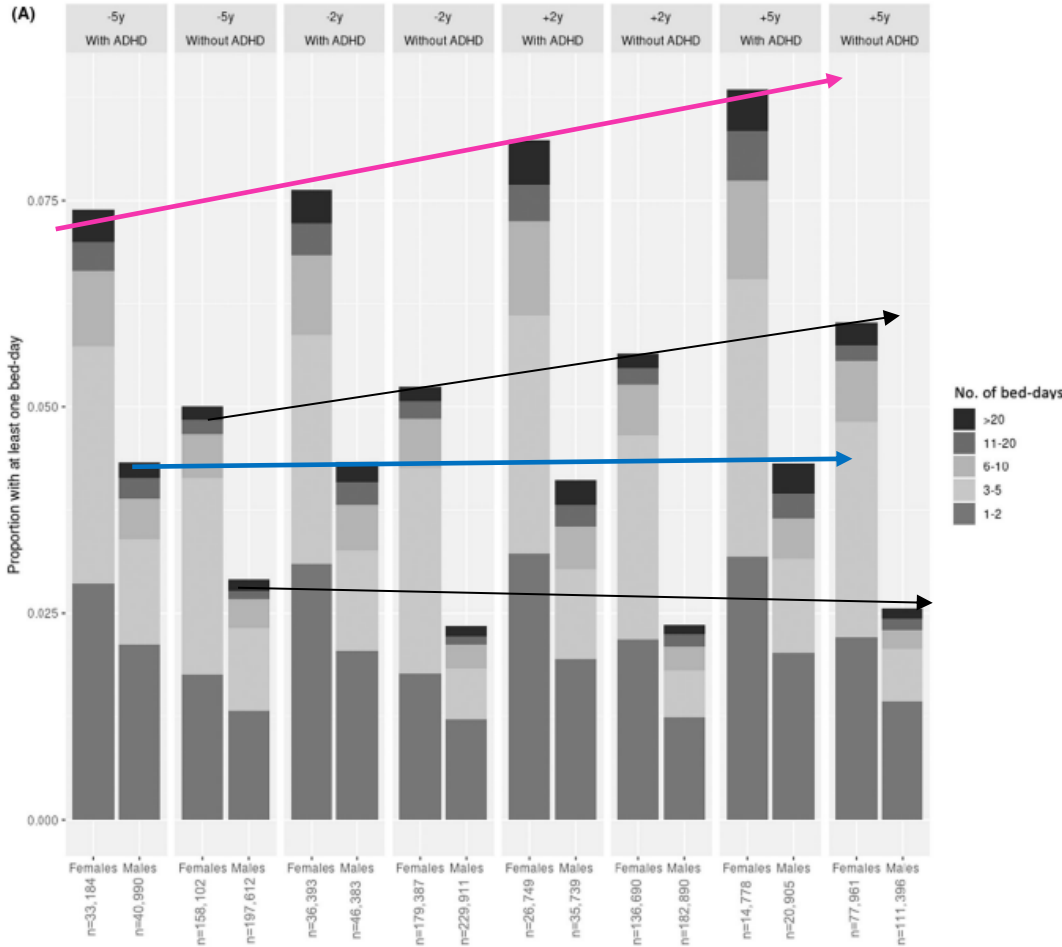
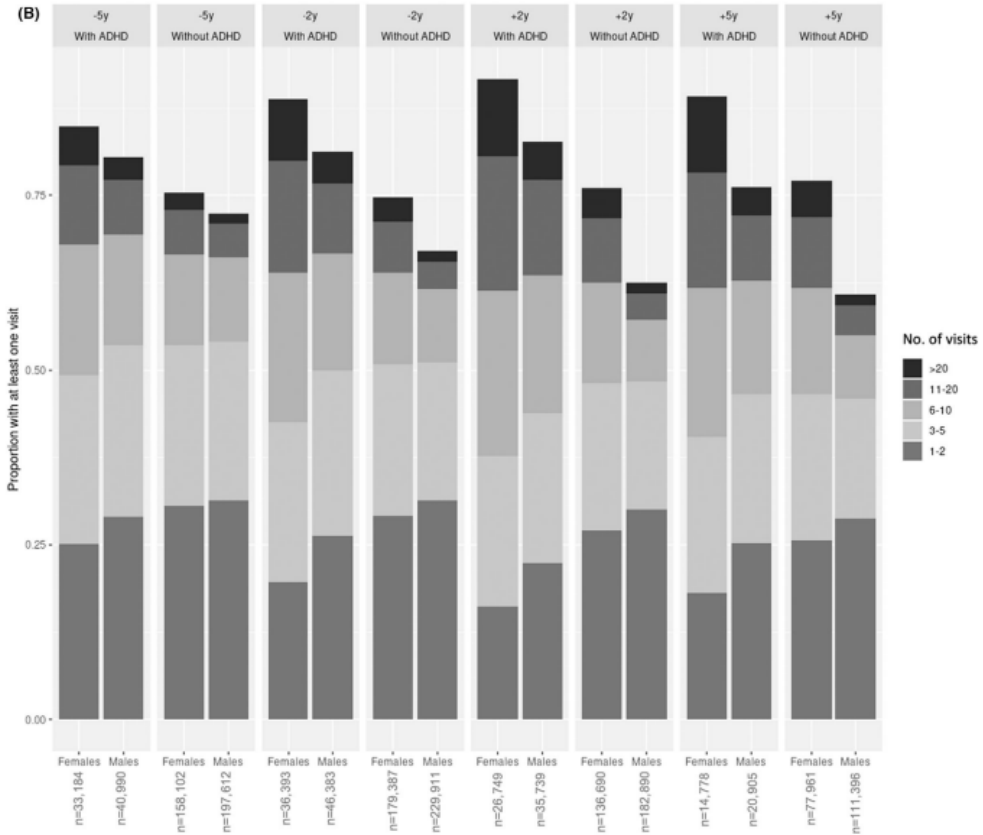
Somatisk inneliggande vård

kvinnor konsumerar mer vård med åldern både med och utan ADHD



Även poliklinisk somatisk vård

- > 30% av kvinnor med ADHD har 6 eller fler besök till läkare av somatisk orsak varje år.



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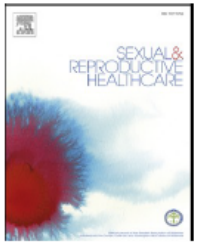

Knowledge, challenges, and standard of care of young women with ADHD at Swedish youth clinics

Anna-Karin Klint Carlander [a], Malin Thorsell [a,*], Youstina Demetry [b], Sky Nikodell [c], Helena Kopp Kallner [a,d], Charlotte Skoglund [e]

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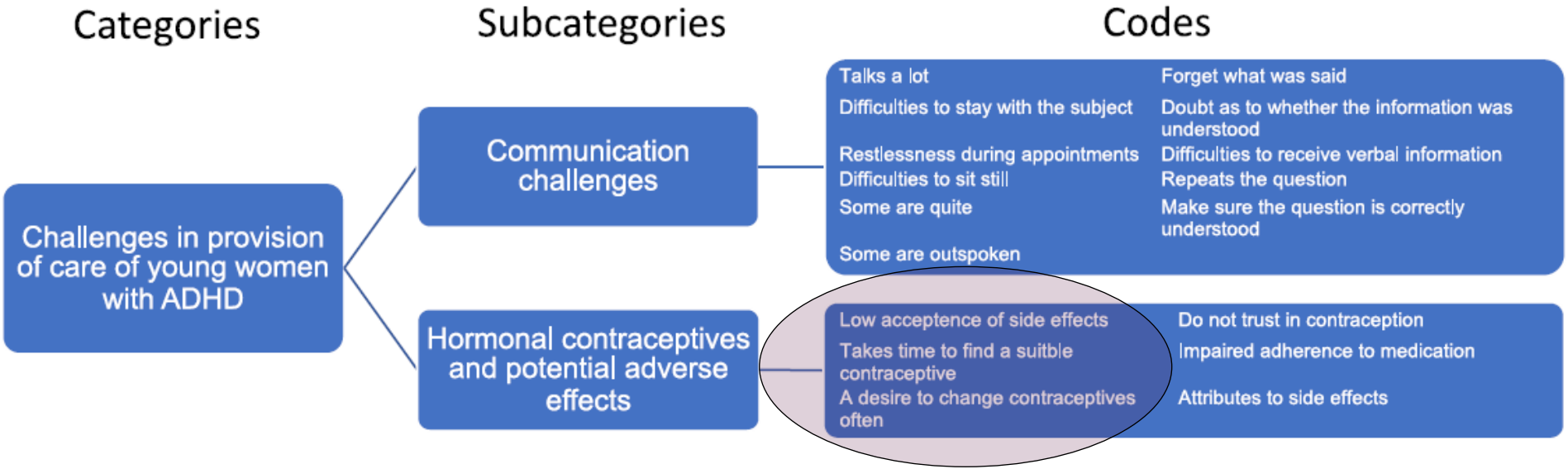
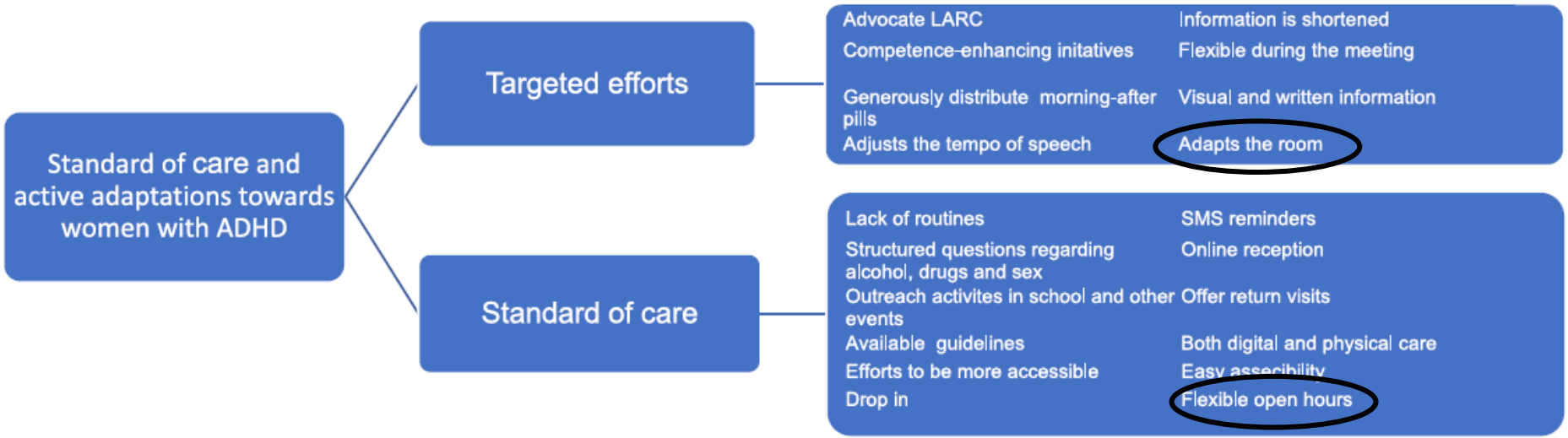
[b] Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden
[c] Medical Program, Linköping University, Linköping, Sweden
[d] Department of Obstetrics and Gynecology, Danderyd Hospital, Stockholm, Sweden
[e] Department of Neuroscience, Uppsala University, Uppsala, Sweden

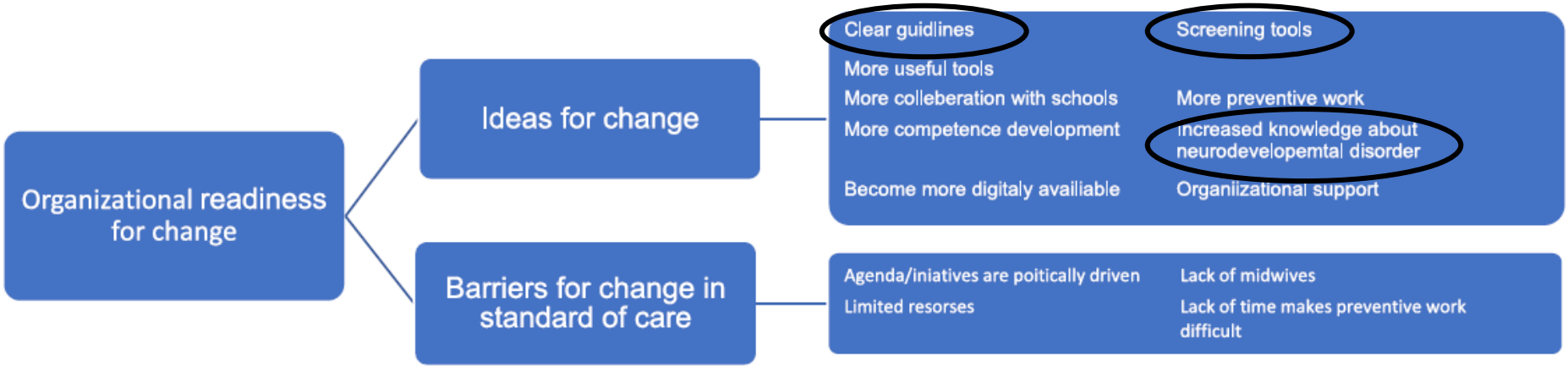
What are the challenges?



Hur gör man idag?



Vad skulle man vilja ha????



“Jag har aldrig tålt p-piller, jag får lösa det på nåt annat sätt”

Anja 21

Hormonal Contraceptive Use and Risk of Depression Among Young Women With Attention-Deficit/Hyperactivity Disorder

Cecilia Lundin, MD, PhD, Anna Wikman, PhD, Per Wikman, PhD, Helena Kopp Kallner, MD, PhD, Inger Sundström-Poromaa, MD, PhD, Charlotte Skoglund, MD, PhD

Objective: Women with attention-deficit/hyperactivity disorder (ADHD) have an increased risk of becoming teenage mothers. Adverse effects of hormonal contraception (HC), including depression, may affect adherence to user-dependent contraception and increase the risk for unplanned pregnancies and teenage births in women with ADHD. The current study analyzed whether girls and young women with ADHD are at increased risk for depression during HC use compared with women without ADHD.

Method: A linkage of Swedish national registers covering 29,767 girls and young women with ADHD aged 15 to 24 years and 763,146 without ADHD provided measures of ADHD and depression diagnoses (*International Classification of Diseases* [*ICD*] code) and prescription of stimulant medication, HC, and antidepressant medication (Anatomical Therapeutic Chemical [ATC] code). Cox regression models applying an interaction term (ADHD diagnosis × HC use) evaluated the excess risk of HC-induced depression in women with ADHD.

Results: Women with ADHD had a 3-fold higher risk of developing depression, irrespective of HC use (adjusted hazard ratio [aHR] = 3.69, 95% CI = 3.60-3.78). Oral combined HC users with ADHD had a 5 times higher risk of depression compared with women without ADHD who were not using oral combined HC (aHR = 5.19, 95% CI = 4.94-5.47), and a 6 times higher risk in comparison with women without ADHD who were on oral combined HC (aHR = 6.10 (95% CI = 5.79-6.43). The corresponding risk of depression in women with ADHD who used a progestogen-only pill (aHR = 5.00, 95% CI = 4.56-5.49). The risk of developing depression when using non-oral HC was similarly moderately increased in both groups.

Conclusion: Girls and young women with ADHD have an increased risk of developing depression when using oral HC compared with their unaffected peers. Information on risks with HCs as well as potential benefits with long-acting reversible contraceptives needs to be an integrated part of the shared decision making and contraception counseling for young women with ADHD.

Key words: ADHD; women; hormonal contraceptive; depression

J Am Acad Child Adolesc Psychiatry 2023;62(6):665-674.

Results

TABLE 2 Risk of Developing Depression in the Study Population, in Relation to Attention-Deficit/Hyperactivity Disorder (ADHD) Diagnosis (n = 29,767), Any Hormonal Contraceptive Use, and Other Covariates

Covariate	Events/person-years	aHR (95% CI)
None	56,491/2,425,833	1 (ref)
Psychiatric diagnosis	33,641/837,107	1.51 (1.49-1.53)
Parental suicide	721/15,026	1.76 (1.64-1.89)
Medical indication for HC		
Acne	5,567/161,792	1.29 (1.25-1.32)
Dysfunctional bleeding	7,048/146,026	1.40 (1.37-1.44)
Dysmenorrhea	6,937/118,250	1.80 (1.75-1.84)
Endometriosis	1,304/18,192	1.66 (1.57-1.76)
Polycystic ovary syndrome	2,162/52,828	1.36 (1.30-1.42)

Lundin C et al., J Am Acad Child Adolesc Psychiatry. 2023 Jun;62(6):665-674

Results

TABLE 3 Risk of Depression in Relation to Type of Hormonal Contraceptive and in Relation to Attention-Deficit/Hyperactivity Disorder (ADHD) Diagnosis (n = 29,767)

	Women with ADHD	Non-ADHD women	Main effect of HC exposure		HC × ADHD interaction	
Contraceptive	Events/person-years	Events/person-years	aHR (95% CI)	*p*	aHR (95% CI)	*p*
Combined oral contraceptive	1,524/9,832	16,899/773,693	0.85 (0.84-0.87)	<.001	1.60 (1.51-1.69)	<.001
Progestogen-only pill	453/2,929	4,595/173,518	1.01 (0.98-1.04)	.32	1.22 (1.10-1.34)	<.001
Patch and vaginal ring	168/981	1,811/57,745	1.24 (1.18-1.30)	<.001	1.12 (0.95-1.31)	.14
Implant	697/8,027	4,091/125,623	1.23 (1.19-1.27)	<.001	0.99 (0.91-1.07)	.91
Injection	16/135	156/9,179	1.21 (1.03-1.42)	.51	0.65 (0.39-1.09)	.12
Hormonal IUD	267/2,704	3,001/73,329	1.41 (1.36-1.47)	<.001	0.88 (0.78-1.00)	.06

Note: Values are adjusted for age, calendar year, level of education, parental country of origin, parental diagnoses of mental disorder, acne, dysmenorrhea, dysfunctional uterine bleeding, endometriosis, polycystic ovary syndrome, age, and calendar year. aHR = adjusted hazard ratio; COC = combined oral contraceptive; HC = hormonal contraceptive; POP = progestin-only pill.

Lundin C et al., J Am Acad Child Adolesc Psychiatry. 2023 Jun;62(6):665-674

Interpretation

- Our results show that women with ADHD are at increased risk for developing depression
- Further analyses showed that although use of oral HC had no influence on women without ADHD, they did in women with ADHD.
- Medical reasons for treatment with HC increases risk for depression. Medical reasons for HC were more common in women with ADHD, further placing them at risk for depression.

JAMA Network Open

Original Investigation | Obstetrics and Gynecology

Association of Attention-Deficit/Hyperactivity Disorder With Teenage Birth Among Women and Girls in Sweden

Charlotte Skoglund, PhD; Helena Kopp Kallner, PhD; Alkistis Skalkidou, PhD; Anna-Karin Wikström, PhD; Cecilia Lundin, MD; Susanne Hesselman, PhD; Anna Wikman, PhD; Inger Sundström Poromaa, PhD

Abstract

IMPORTANCE Attention-deficit/hyperactivity disorder (ADHD) is associated with a plethora of adverse health outcomes throughout life. While Swedish specialized youth clinics have carefully and successfully targeted risk of unplanned pregnancies in adolescents, important risk groups, such as women and girls with ADHD, might not be identified or appropriately assisted by these interventions.

OBJECTIVES To determine whether women and girls with ADHD are associated with increased risk of teenage birth compared with their unaffected peers and to examine the association of ADHD with risk factors for adverse obstetric and perinatal outcomes, such as smoking, underweight or overweight, and substance use disorder.

DESIGN, SETTING, AND PARTICIPANTS This nationwide cohort study included data from 6 national longitudinal population-based registries in Sweden. All nulliparous women and girls who gave birth in Sweden between January 1, 2007, and December 31, 2014, were included. Data analyses were conducted from October 7, 2018, to February 8, 2019.

EXPOSURES Women and girls treated with stimulant or nonstimulant medication for ADHD (Anatomic Therapeutic Chemical classification code N06BA) in the Swedish Prescribed Drug Register between July 1, 2005, and December 31, 2014.

Key Points

Question Is attention-deficit/hyperactivity disorder (ADHD) associated with increased risk of teenage birth?

Findings This nationwide cohort study of 384 103 women and girls in Sweden who gave birth for the first time between 2007 and 2014, including 6410 women and girls with ADHD, found that teenage deliveries occurred at a significantly higher rate among women and girls with ADHD than among those without ADHD (15.2% vs 2.8%).

Meaning This study suggests that women and girls with ADHD may have an increased risk of giving birth as teenagers compared with their unaffected peers.

Risks with teenage birth

- Teenage pregnancies are associated with several long- and short term adverse outcomes for
  - → both parents and
  - → children.
- Young parents are at risk of
  - → low educational attainment,
  - → single habitation,
  - → and use of public assistance.
- Risks for the children include perinatal morbidity and mortality, low socioeconomic status, and low quality of life.
- In Sweden, teenage birth rates have decreased from 15.3% of all births in 1973 to 2.4% in 2014, one of the lowest rates internationally.

Skoglund et al. JAMA Netw Open. 2019 Oct; 2(10): e1912463

Results

- The overall rate of teenage births in the study was 3.0% (11 615 births).

Teenage deliveries were significantly more common among women and girls with ADHD (15.3%) than in women and girls without ADHD (2.8%).

Women and girls with ADHD contributed to 8.4% of all teenage deliveries during the period.

- Compared with women and girls without ADHD, those with ADHD were associated with a **6-fold increased risk** of giving birth when they were younger than 20 years (OR, 6.23 [95%CI, 5.80-6.68]).

Hur ser graviditeten ut för unga kvinnor med ADHD

Table 3. Obstetric Risk Factors in Nulliparous Women and Girls With ADHD by Age at Birth

Variable	Women and Girls, No (%)		Odds Ratio (95% CI)
	Aged ≥20 y (n = 5430)	Aged <20 y (n = 980)	
Smoking during the first trimester	1284 (24.8)	375 (40.1)	2.02 (1.75-2.34)
Smoking during the third trimester	1001 (20.3)	293 (34.0)	2.02 (1.73-2.37)
Body mass index[a]			
<18.50	147 (3.0)	54 (6.1)	1.97 (1.42-2.73)
18.50-24.99	2749 (55.2)	512 (58.2)	1 [Reference]
25.00-29.99	1290 (25.9)	212) (24.1)	0.88 (0.74-1.05)
30.00-34.99	523 (10.5)	71 (8.1)	0.73 (0.56-0.95)
35.00-39.99	200 (4.0)	21 (2.4)	0.56 (0.36-0.89)
>40.00	68 (1.4)	10 (1.1)	0.79 (0.40-1.54)
Alcohol or substance use disorder	415 (14.1)	110 (11.2)	1.05 (0.88-1.25)
Alcohol or substance use disorder during 12 mo preceding the pregnancy	157 (5.3)	50 (5.1)	0.72 (0.53-0.98)
ADHD treatment during 12 mo preceding the pregnancy	685 (23.3)	341 (34.8)	1.80 (1.55-2.08)
ADHD treatment during pregnancy	213 (7.2)	112 (11.4)	1.73 (1.38-2.16)

Premenstruellt dysforiskt syndrom hos kvinnor med ADHD

- In a small study of 209 women, 95 (45.5%) fulfilled diagnostic criteria of PMDD
- Heavy overrepresentation compared to general population

Prevalence of hormone-related mood disorder symptoms in women with ADHD. Dorani F, Bijlenga D, Beekman ATF, van Someren EJW, Kooij JJS. J Psychiatr Res. 2021 Jan;133:10-15.

Vad är premenstrualt dysforiskt syndrom?

Each evening note the degree to which you experienced each of the problems listed below. Put an "x" in the box which corresponds to the severity:

1 - not at all **2 - minimal** 3 - mild **4 - moderate** 5 - severe **6 - extreme**

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Enter day of the week (e.g. Monday = 'M')																																
Note any spotting by entering 'S'																																
Note menstrual bleeding by entering 'M'																																
Date (i.e. 1 = 1st of the month)																																
1. Felt depressed, sad, "down,", or "blue" or felt hopeless; or felt worthless or guilty	6																															
	5																															
	4																															
	3																															
	2																															
	1																															
2. Felt anxious, tense, "keyed up" or "on edge"	6																															
	5																															
	4																															
	3																															
	2																															
	1																															
3. Had mood swings (i.e., suddenly feeling sad or tearful) or was sensitive to rejection or feelings were easily hurt	6																															
	5																															
	4																															
	3																															
	2																															
	1																															
4. Felt angry, or irritable	6																															
	5																															
	4																															
	3																															
	2																															
	1																															
5. Had less interest in usual activities (work, school, friends, hobbies)	6																															
	5																															
	4																															
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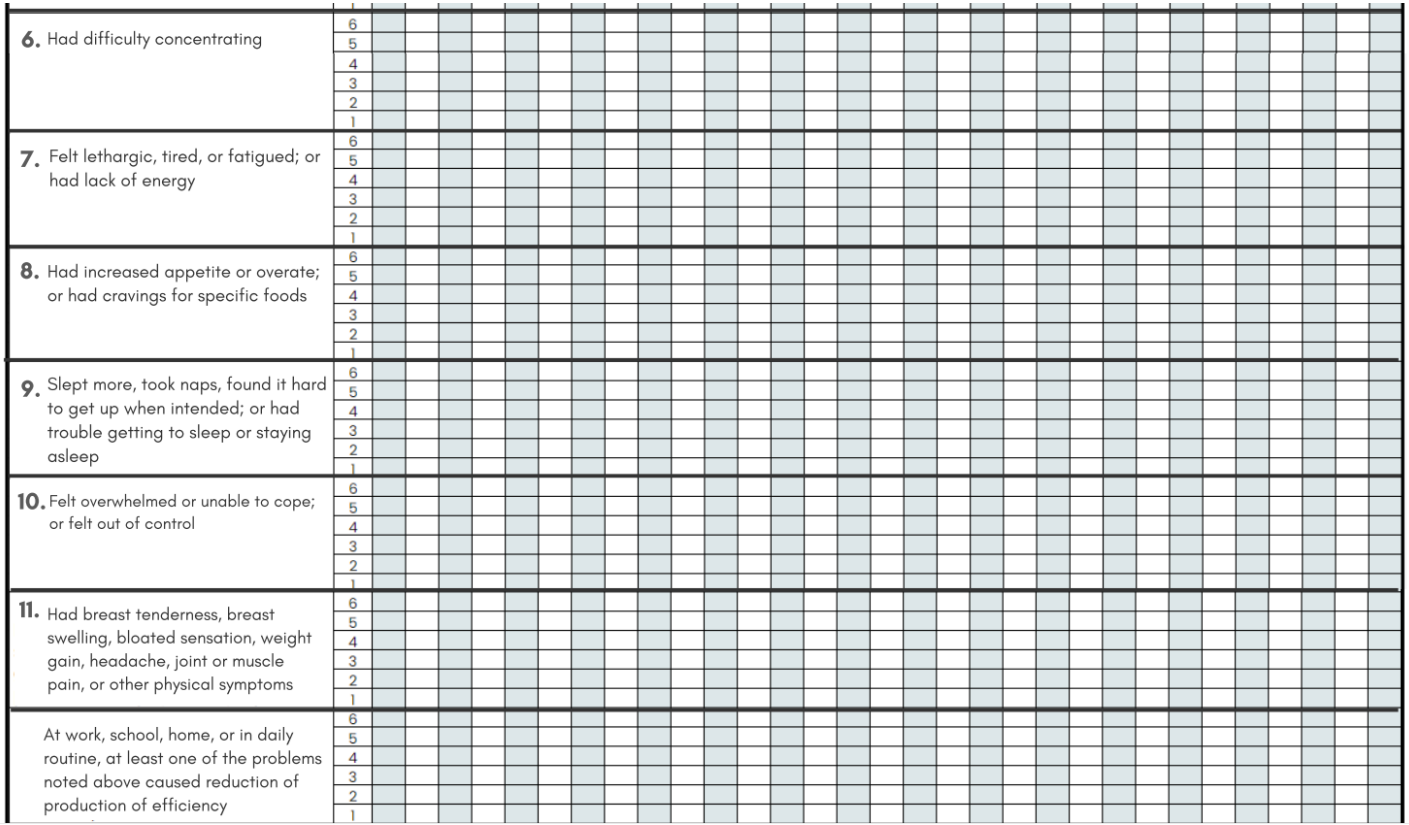
Fortsatt...


6. Had difficulty concentrating
7. Felt lethargic, tired, or fatigued; or had lack of energy
8. Had increased appetite or overate; or had cravings for specific foods
9. Slept more, took naps, found it hard to get up when intended; or had trouble getting to sleep or staying asleep
10. Felt overwhelmed or unable to cope; or felt out of control
11. Had breast tenderness, breast swelling, bloated sensation, weight gain, headache, joint or muscle pain, or other physical symptoms
At work, school, home, or in daily routine, at least one of the problems noted above caused reduction of production of efficiency
6
5
4
3
2
1

LÖSNINGEN?

Titrera adhd-läkemedel utifrån menscykel för optimal symptomkontroll?

- Större effekt av CS i follikulär fas?
- Premenstruell försämring av adhd-symtom?

- **Skräddarsydd sexual- och preventivmedelsrådgivning?**
  - Förbättrad sexuell och reproduktiv hälsa?
  - Förbättrad emotionell reglering?

Transdiciplinär forskning och klinisk verksamhet efterlyses!

Justice J and de Wit H. Psychopharmacology (Berl). 1999;145:67–75; Quin P. J Clin Psychol. 2005;61(5);579–87; Roberts B. Psychoendocrinology. 2018;88:105–14.