LECTURE · 27 MARCH 2025

Evidence-based ADHD treatment in 2025



Speaker: Dr. Aileen Doyle, psychiatrist

Originally presented in Dutch on 27 March 2025 (Praktijk Bunderbos). English translation by the author.

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Overview

Impact of ADHD

- How many of our patients have ADHD?
- Young vs old
- Women with ADHD
- Missed diagnoses
- Over vs underdiagnosis
- Genetics
- Comorbidities

Medication

- Why treat ADHD?
- How well does ADHD medication work?
- Is it addictive?
- Do’s and don’ts
- Build in breaks or keep going?

Take home message

Who am I?

- OLO-Rotonde:
  - Around 30 young people and young adults in residential care, more than half with ADHD (proportions vary)
- Own practice:
  - 20/49 pts ADHD
  - 14/49 pts autism (ASD)
  - 11/49 pts AuDHD
  - 4 without ADHD or autism (as far as known so far)
- Meclinas: medical trials on ADHD/autism in the future
- Projects: improving diagnostics, developing secondary prevention in ADHD, collaboration with companies, brainspark.be etc.



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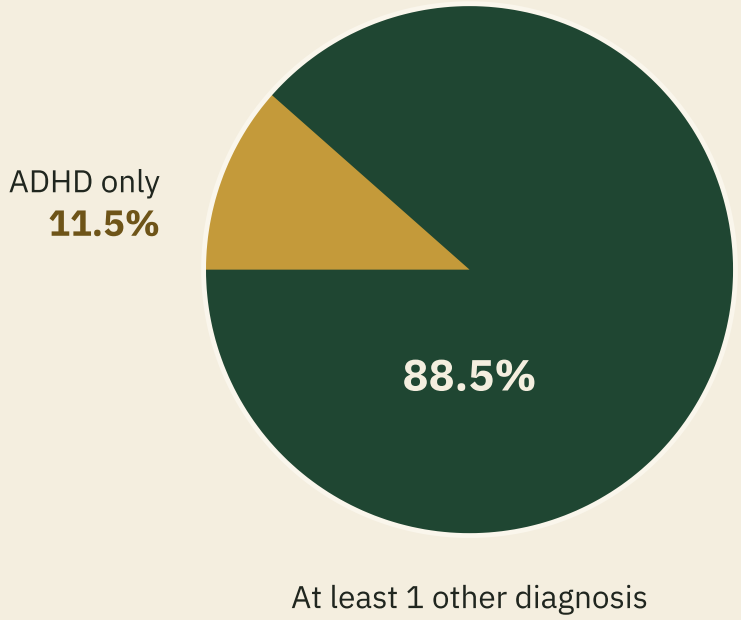
Disclosures

Companies and organisations	Speaker	Non-monetary reimbursement of expenses	Clinical trials
Takeda	X	X	
Janssen			X

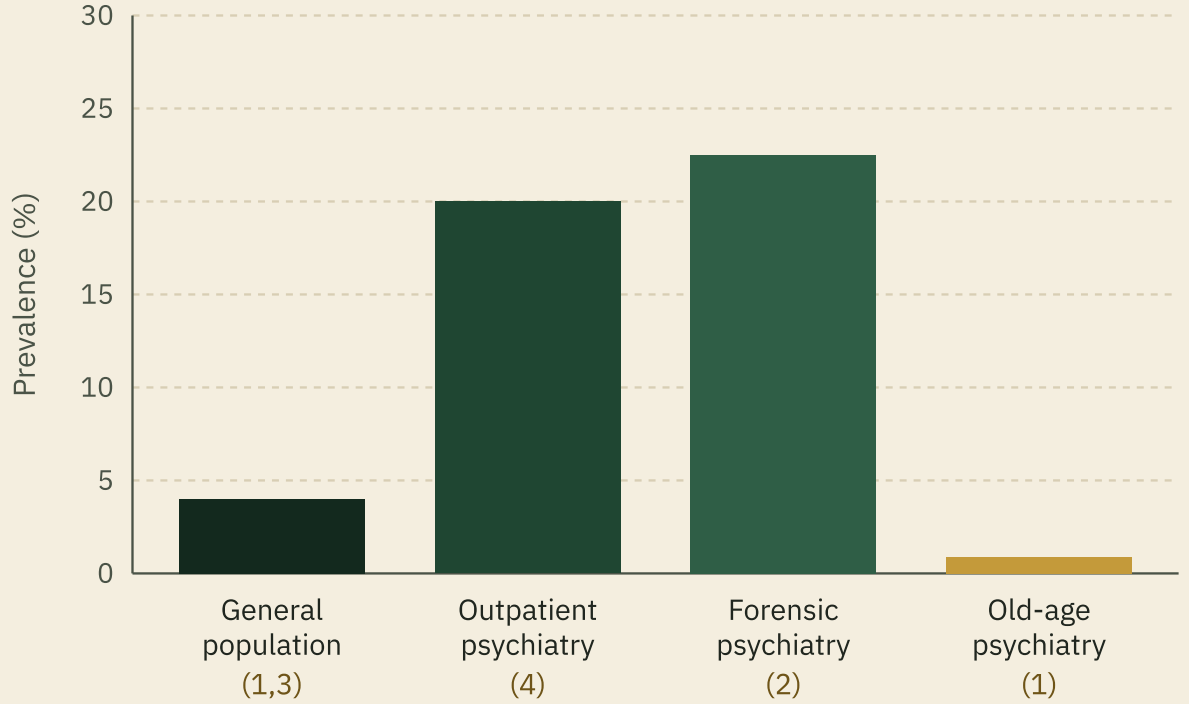
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How many of our patients have ADHD?

Outpatients with a diagnosis of ADHD (4)



Prevalence of ADHD in different populations



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Young versus old?



Why is it hard to diagnose? [6,7]

- Clinical blindness and bias among professionals:
  - “They don’t need it, they’ve had it their whole life”
  - “That’s cognitive decline, normal for their age”
- Influence of comorbidities and polypharmacy on the clinical picture
- Often no developmental history can be taken any more
- Symptoms persist into later life, but are given a different name

ADHD language	Old-age language
Hyperactivity	Restlessness, difficulty relaxing
Inattention	Forgetfulness
Executive dysfunction	Disorganisation, memory problems
Impulsivity	“Can’t wait”, making rash decisions

Women with ADHD?

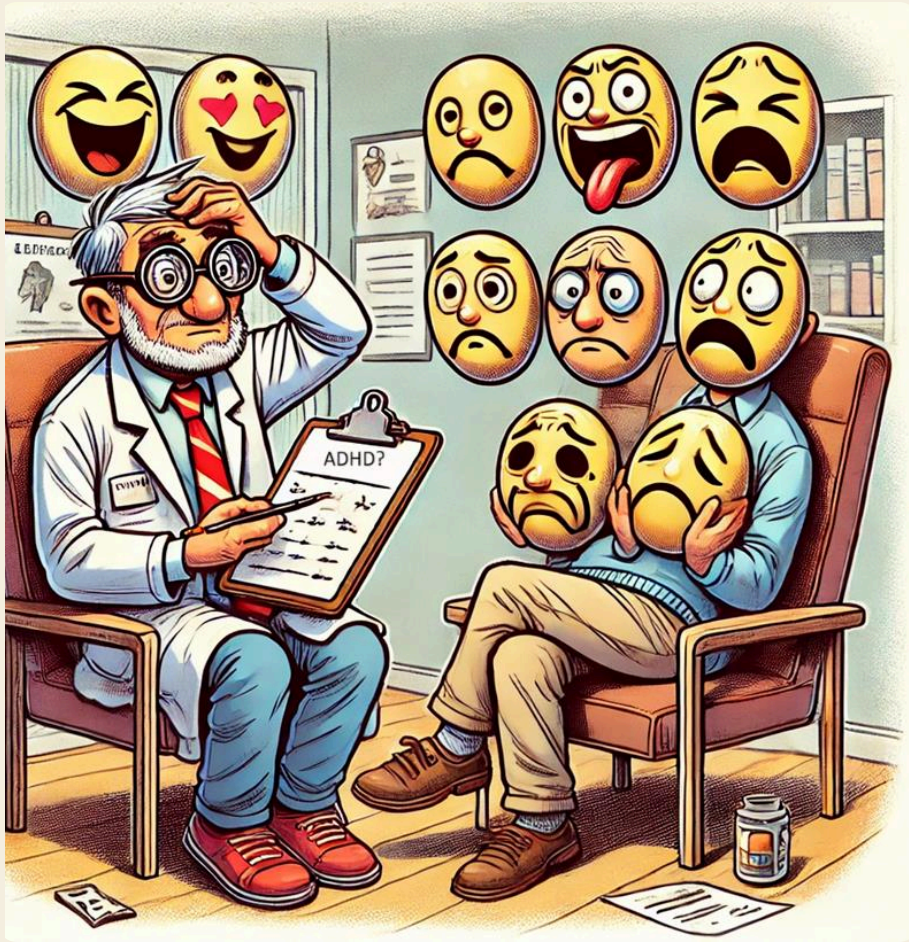
- Higher prevalence of premenstrual tension and PMDD in women with ADHD[28]
- After ovulation, ADHD symptoms increase until after menstruation. It can be worthwhile to address this with medication.[29]
- ADHD medication during pregnancy does not appear to be associated with immediate adverse maternal or neonatal outcomes[30]
- Think of ADHD if[28, 31]
  - First-degree relative with ADHD
  - Symptoms coincide with a transition period
  - Specific learning or educational problems
  - Increased sexualised behaviour in young women
- Postmenopausal: clinically more troubled by ADHD symptoms (DD biological DD life period changes)[31]



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Missed diagnoses in psychiatry

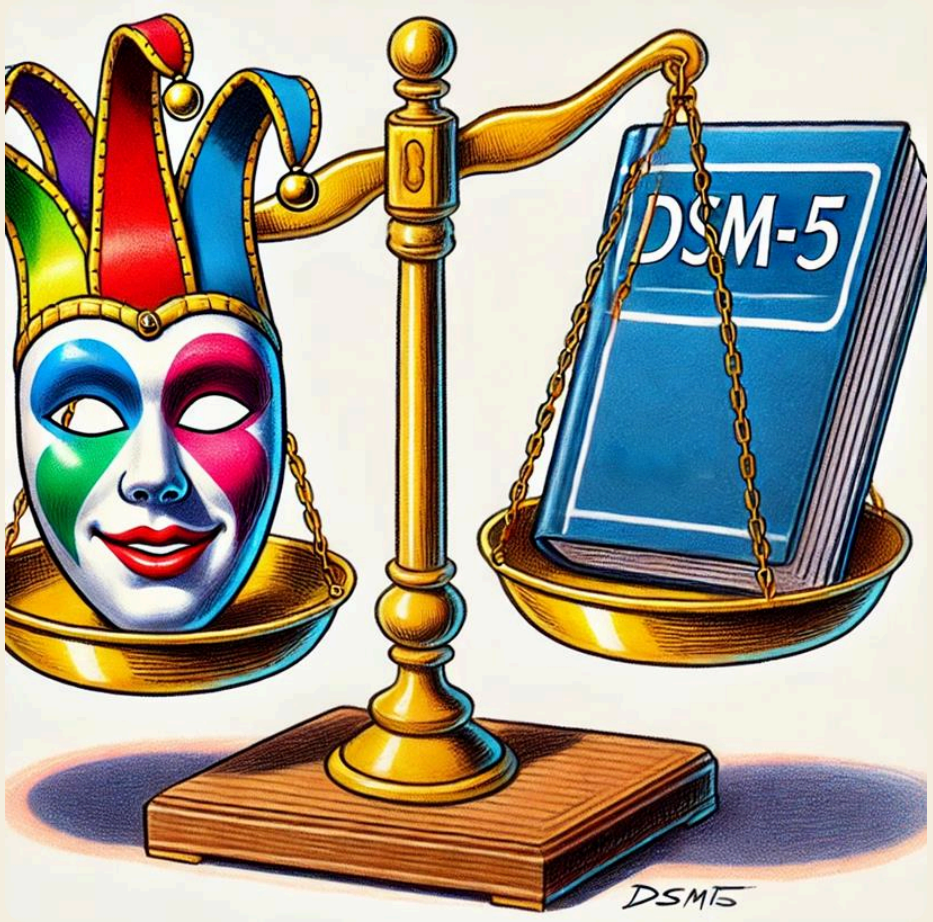
- ADHD camouflaging [32]
- 40% of people with ASD have ADHD [33]
- Adults with both ASD and ADHD are at higher risk[2]:
  - Anxiety and depression
  - Substance abuse disorder
- Executive dysfunction: large overlap between ADHD and ASD [34]
  - ADHD: also impaired inhibition
  - ASD: also impaired flexibility
- In people with a migration background or from minority groups[2]:
  - ADHD is missed more often
  - Less often correctly medicated according to the guidelines



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Overdiagnosis? Underdiagnosis?

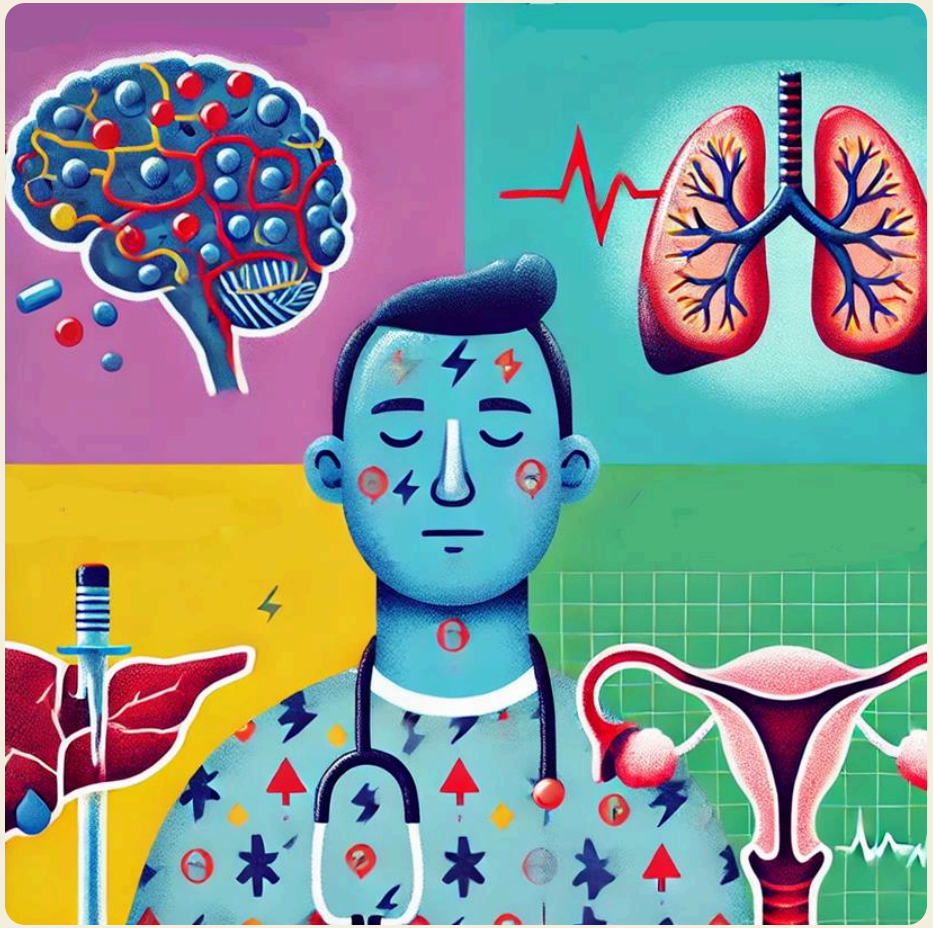
- There is no evidence that more children have ADHD when the diagnosis is made in a standardised way[9]. There is, however, research showing that ADHD is sometimes diagnosed and treated too often in young people[10,11]
- In adults, things only go wrong when the diagnosis is not made carefully according to the guideline[11]
- ADHD is recognised more often in boys and men than in girls and women[12]
- In adults who receive the diagnosis, 4/5 ADHD symptoms were missed in childhood[13]
- People are now encouraged to seek help more than in the past[13]
- Girls and women hide or compensate for ADHD more often. Because of this compensation, the problems often shift to internal complaints[14,15]



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Comorbidities: somatic[17]

- Metabolic: type 1 & 2 diabetes, obesity, raised cholesterol
- Cardiovascular
- Neurological conditions (migraine, epilepsy, Parkinson's)
- Neurodegenerative diseases
- Sleep disorders, dental caries
- Atopic eczema, asthma, psoriasis
- Chronic inflammatory bowel disease
- SLE, Bechterew's disease (ankylosing spondylitis), fibromyalgia
- UTIs, STIs, use less contraception
- Enuresis (up to 60+ years age group)
- Take part less in cancer screening
- Have more accidents and emergency visits for accidental injuries



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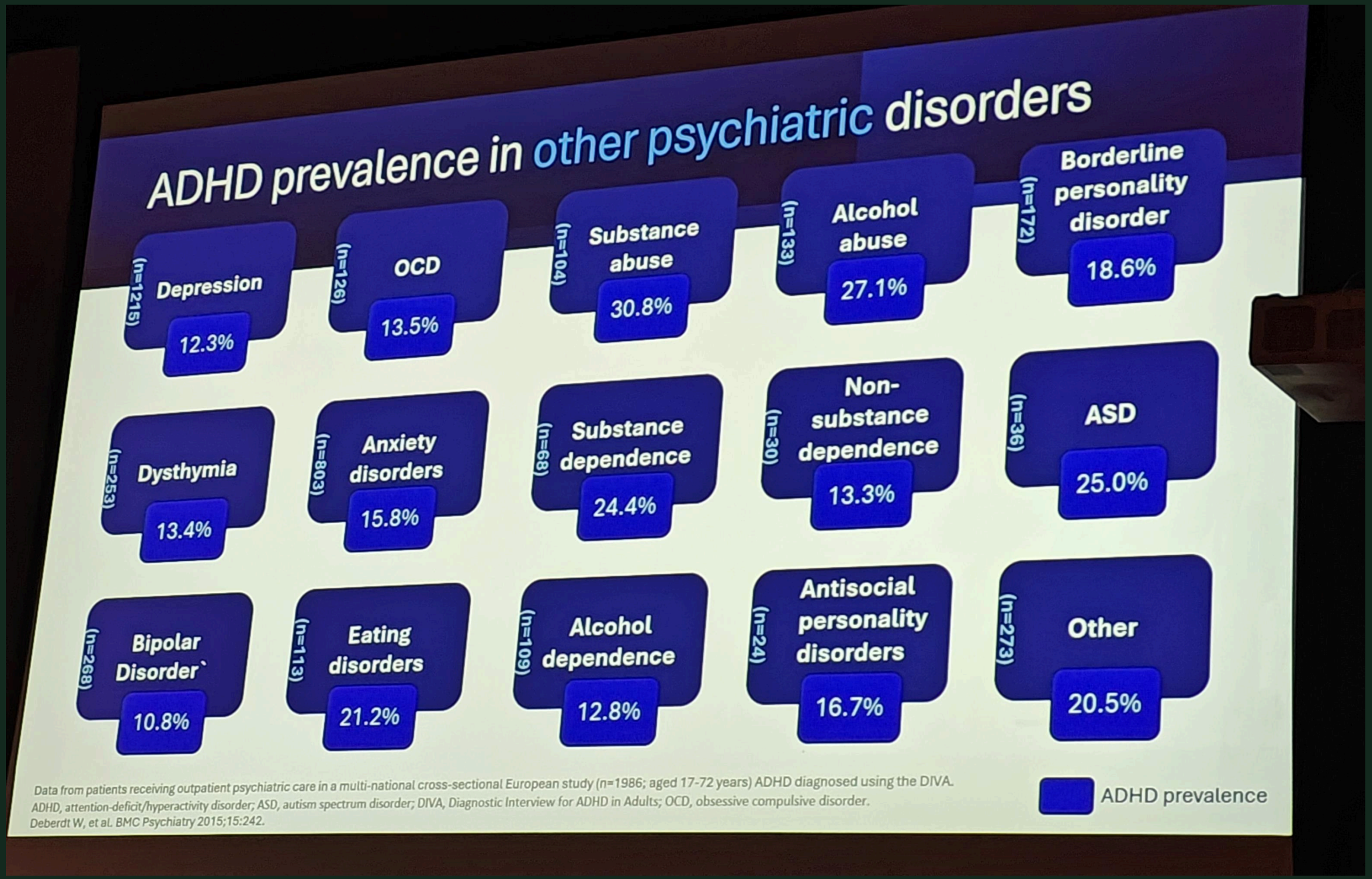
Comorbidities: psychiatric

Psychiatric [18]

- Depression and anxiety
- OCD
- Trauma and (c)PTSD
- Substance misuse or dependence
- Behavioural addictions (58.9%) [19]
- Bipolar disorder
- Borderline and antisocial PD



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ADHD prevalence in other psychiatric disorders
(n=1215) Depression 12.3%
(n=126) OCD 13.5%
(n=104) Substance abuse 30.8%
(n=133) Alcohol abuse 27.1%
(n=172) Borderline personality disorder 18.6%
(n=253) Dysthymia 13.4%
(n=803) Anxiety disorders 15.8%
(n=68) Substance dependence 24.4%
(n=30) Non-substance dependence 13.3%
(n=36) ASD 25.0%
(n=268) Bipolar Disorder` 10.8%
(n=113) Eating disorders 21.2%
(n=109) Alcohol dependence 12.8%
(n=24) Antisocial personality disorders 16.7%
(n=273) Other 20.5%
Data from patients receiving outpatient psychiatric care in a multi-national cross-sectional European study (n=1986; aged 17-72 years) ADHD diagnosed using the DIVA.
ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; DIVA, Diagnostic Interview for ADHD in Adults; OCD, obsessive compulsive disorder.
Deberdt W, et al. BMC Psychiatry 2015;15:242.
ADHD prevalence

Genome-wide analyses of attention deficit hyperactivity disorder identify 27 risk loci, refine the genetic architecture, and implicate several cognitive domains

Ditte Demontis[1,2,3,*], G. Bragi Walters[4,5,*], Georgios Athanasiadis[2,6,7,*], Raymond Walters[8,9,*], Karen Therrien[10,11,12,13,14,15], Trine Tollerup Nielsen[1,2,3], Leila Faraizadeh[1,2,3]

Genetics: what is relevant for us? [20]

- ADHD is polygenic, with 76 gene variants that are mainly active during early brain development and affect dopaminergic neurons
- There is no single ‘ADHD gene’; people with ADHD have different genetic risk profiles
- A polygenic risk score can estimate your risk
- A higher genetic predisposition to ADHD is associated with lower scores on cognitive tests, such as attention and reasoning ability.
- ADHD shares genetic factors with depression and autism, which points to overlap between these conditions



ADHD medication

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Why treat ADHD

- Lower life expectancy without treatment:
  - Men/Women: -6.78/-8.64 [5]
  - Strongest correlation with behavioural disinhibition[4]
- Prevention of comorbidities
- Treating ADHD costs society (much) less than not treating it[21]
  - Car crashes
  - Forensic population
  - Psychiatric/somatic comorbidities/injuries
  - Incapacity for work/unemployment

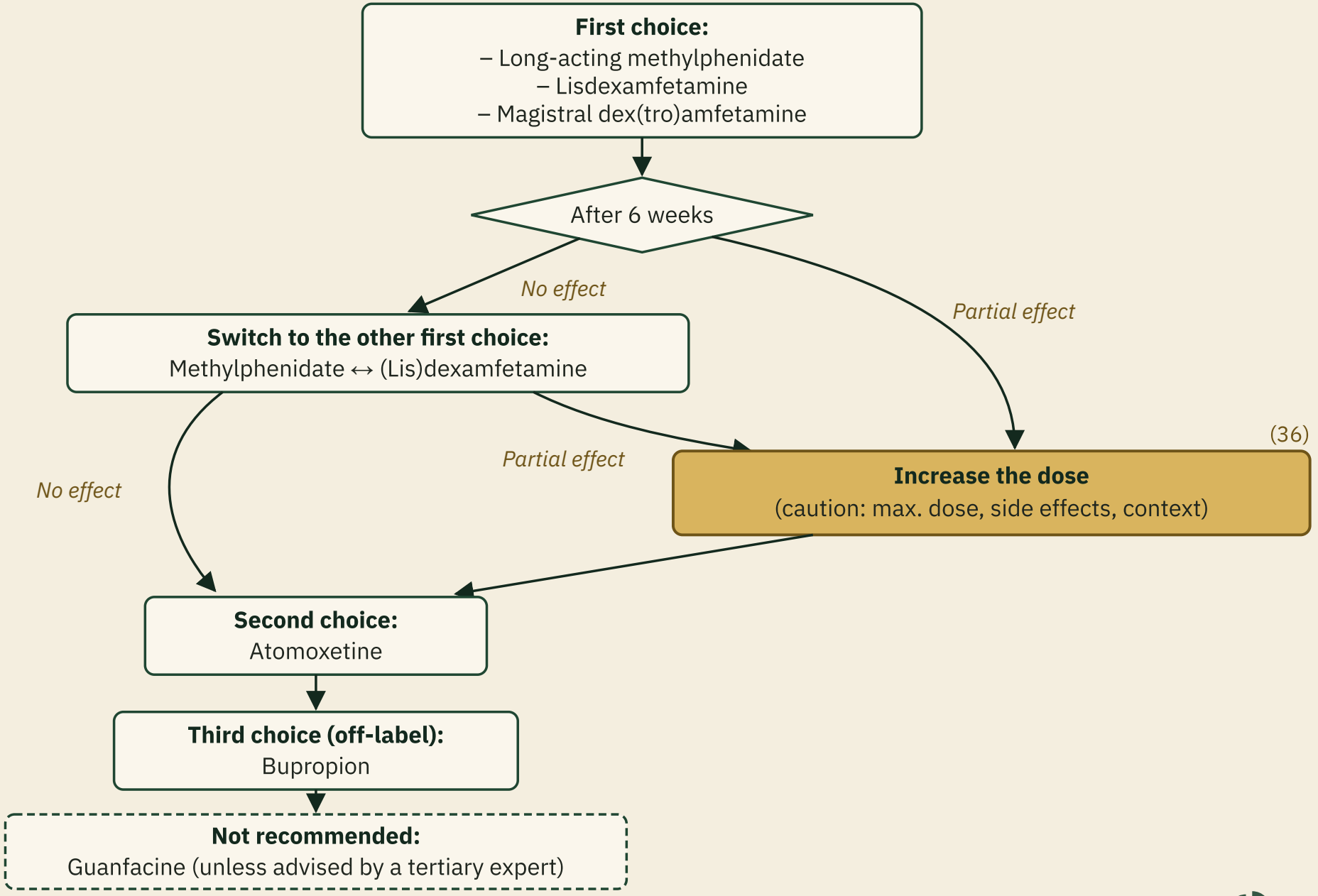
Guideline on ADHD in adults in Belgium [35]

- *“(Lis)dexamfetamine or methylphenidate are recommended as equivalent alternatives for first-choice pharmacological treatment in adults with ADHD”*
- *“Long-acting preparations are preferred because they improve adherence and therefore effectiveness, and because they carry less risk of misuse”*
- *(March 2021): “However, long-acting lisdexamfetamine is not yet on the market in Belgium. In practice, the HGR therefore considers long-acting methylphenidate the first choice, ahead of magistral dex(tro)amfetamine.”*
- *From Sept 2021: long-acting lisdexamfetamine available on the Belgian market*

Hoge Gezondheidsraad

HGR · Belgian Superior Health Council

Quotations translated from the Dutch advisory report no. 9547 (2021).
Magistral = compounded by the pharmacist.


First choice:
– Long-acting methylphenidate
– Lisdexamfetamine
– Magistral dex(tro)amfetamine
After 6 weeks
No effect
Partial effect
Switch to the other first choice:
Methylphenidate ↔ (Lis)dexamfetamine
No effect
Partial effect
(36)
Increase the dose
(caution: max. dose, side effects, context)
Second choice:
Atomoxetine
Third choice (off-label):
Bupropion
Not recommended:
Guanfacine (unless advised by a tertiary expert)

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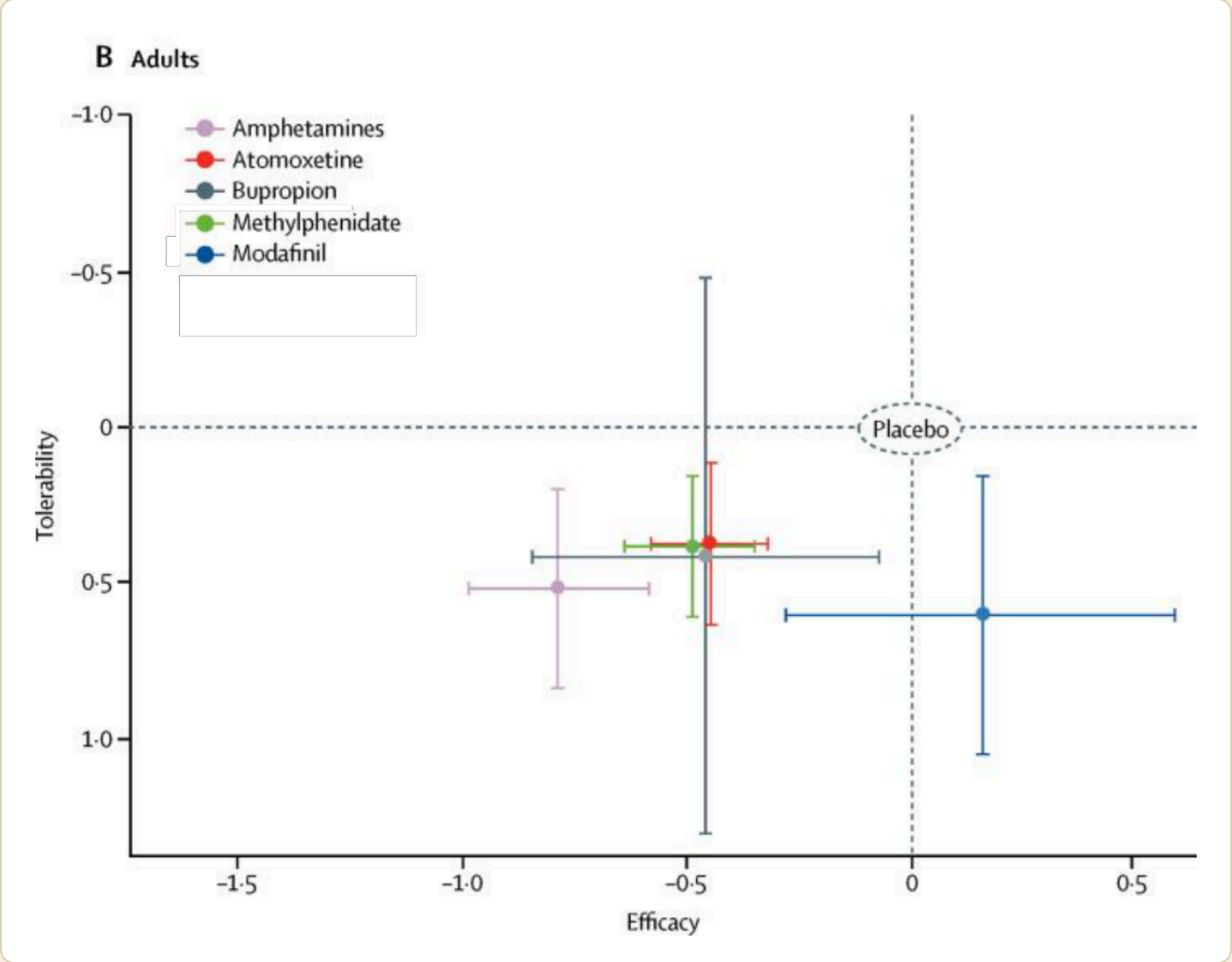
How well do ADHD medications work? [22]

Effect sizes for ADHD Medications *vs.* Other Psychiatric Medications

Standard Mean Difference	ADHD Medications	Other Psychiatric Medications
0.9+	Amphetamine: ~1.0 (0.91–1.10)	
0.8–0.89		Clozapine for positive symptoms of schizophrenia (0.8–0.9)
0.7–0.79	Methylphenidate: ~0.78 (0.64–0.91)	Benzodiazepines for anxiety (0.5–0.8)
0.6–0.69	Atomoxetine: 0.65 (0.52–0.82)	Clozapine (0.5–0.7)
0.5–0.59	Clonidine: 0.58	Second-gen. antipsychotics (SGA)/Haloperidol, Schizophrenia: 0.51–0.53 · Lithium (0.4–0.6)
0.4–0.49	Guanfacine (extended release): ~0.5 (0.43–0.52)	SGA/Mood Stabilizers, Bipolar: 0.40–0.53
0.3–0.39		Selective serotonin reuptake inhibitors, OCD: 0.31–0.41; Antidepressants, MDD: 0.31–0.32

Answer: very well[23]

(Study from The Lancet 2018)



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Is it addictive?

- If the substance does not peak in the brain within <30 min, it has little addictive potential
- Dopamine, if anything, has a protective function against addiction
- Never combine:
  - Cocaine and methylphenidate
  - Spice (synthetic cannabinoid) and MPH or lisdex
  - THC and ADHD medication in case of psychotic vulnerability

Prof. Dr. David Nutt, UK
Professor of Neuropsychopharmacology
Director of the Neuropsychopharmacology Unit in the Division of Brain Sciences.

Do’s and don’ts of medication

- Psychoeducation:
  - ADHD medication has a strong treatment effect
  - It helps prevent comorbidities and early death
- Link ADHD medication to advice to start therapy (emotion regulation and strategies/CBT for executive dysfunction)
- Do not give it during pregnancy or breastfeeding, unless stopping the medication would do more harm[24]
- In addiction and ADHD, the literature advises treating the ADHD with medication. Stimulants are prescribed with positive outcomes. Lisdexamfetamine is the safest option with regard to possible misuse



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Continue medication daily, or as little as possible?



- ADHD treated with medication shows lower ‘all cause mortality’, in particular a preventive effect on unnatural causes of death[25]
- Psychiatrists used to be trained to build in “medication holidays” as standard. This is no longer considered so evidence-based today. Always weigh up the pros and cons of interrupting medication together with the patient

ADHD medication and long-term risk of cardiovascular disease[26]

Study of 278 000 people with ADHD (6 yrs – 64 yrs):

- Followed up on medication for up to 14 years
- Nationwide health registers in Sweden
- Impact factor: 22.5

Conclusion:

- Increased risk of developing hypertension
- Increased risk of developing arterial disease
- Stimulants slightly more risk than non-stimulants
- No difference between men and women

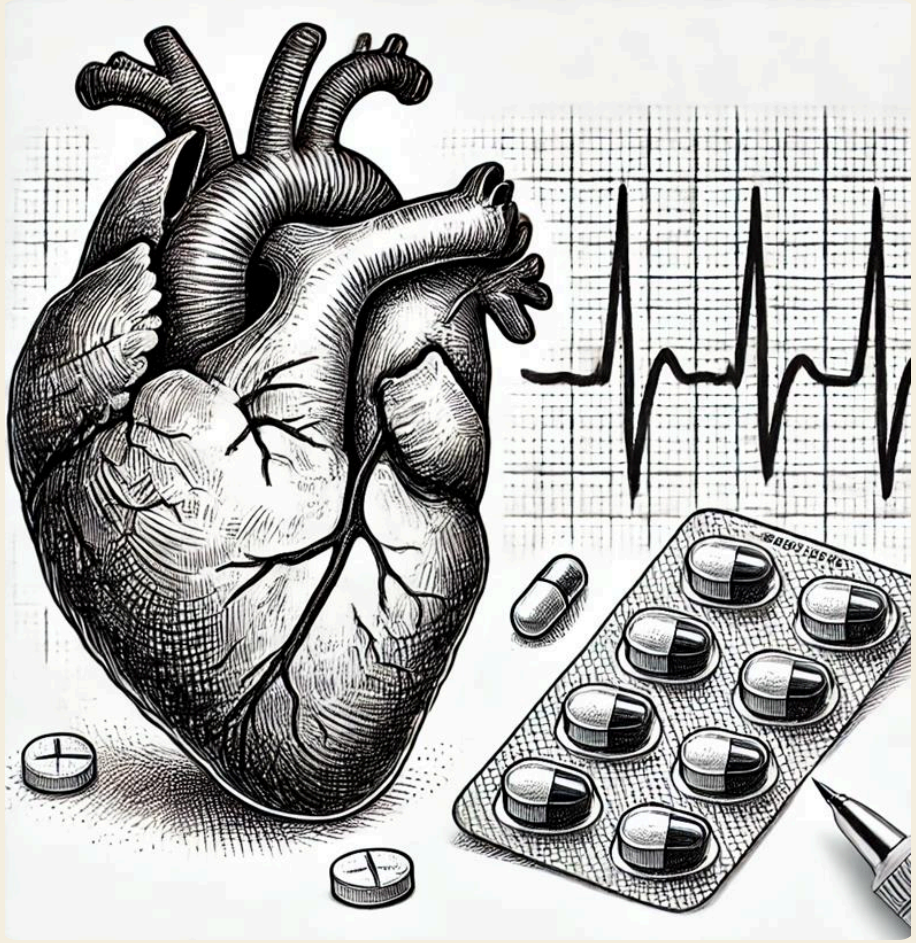
Limitations:

- Not corrected for other concurrent medication or lifestyle factors
- Severe ADHD, even with medication, has more comorbidities and a less healthy lifestyle
- ADHD without treatment also carries a risk of CVD



The use of ADHD meds in cardiac disease[27]

- Association with increased blood pressure and pulse
- *No* association with:
  - Sudden cardiac death
  - Myocardial infarction and death
- In cardiomyopathy and long QT syndrome/Brugada:
  - Consider alpha2-agonists (guanfacine) in consultation with a cardiologist
- Patients possibly more troubled by tachycardia/hypertension in case of CYP2D6 slow metabolising
- Genetic variability in drug metabolism influences the cardiac response





1. Correct diagnosis and treatment of ADHD makes a world of difference for the patient, for us and for society
2. ADHD is 10x more common in our populations than in the general population.
3. In treatment-resistant patients, rule out comorbid ADHD
4. Please treat people with ADHD and addiction with ADHD medication
5. Lisdexamfetamine is virtually impossible to misuse for a “high”
6. In terms of effectiveness, ADHD stimulants are comparable to clozapine
7. Balance the risk of hypertension and atherosclerosis against the downsides of untreated ADHD
8. Always advise combining it with non-pharmacological therapy

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