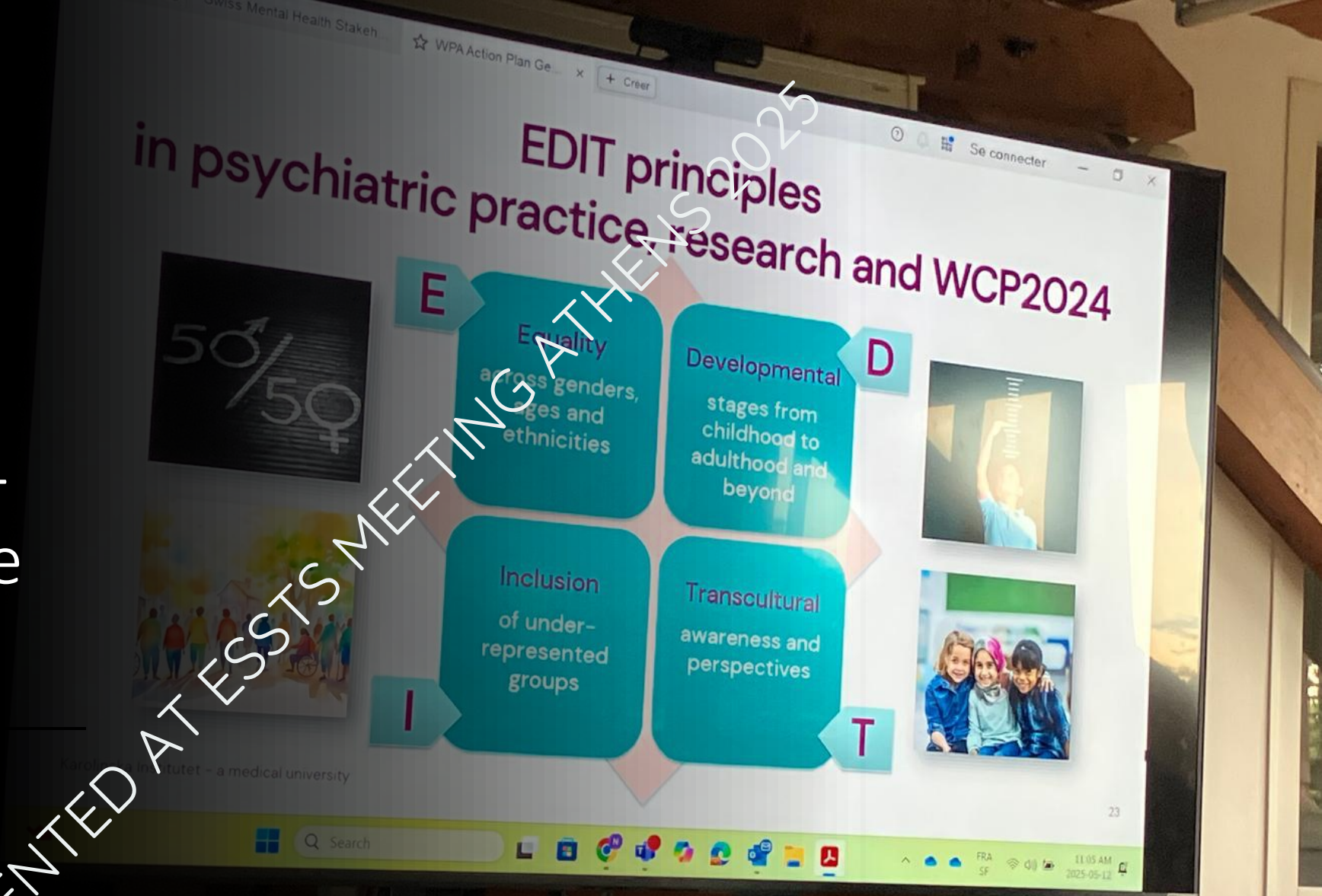
What is new in the treatment of ADHD?

PROF. KERSTIN JESSICA VON PLESSEN

Talking about the treatment is also talking about the news in research– ideally the two are linked..



PRESENTED AT ESSTS MEETING ATHENS 2025

Scientometric analysis of the scientific literature on ADHD (28,381 publications)

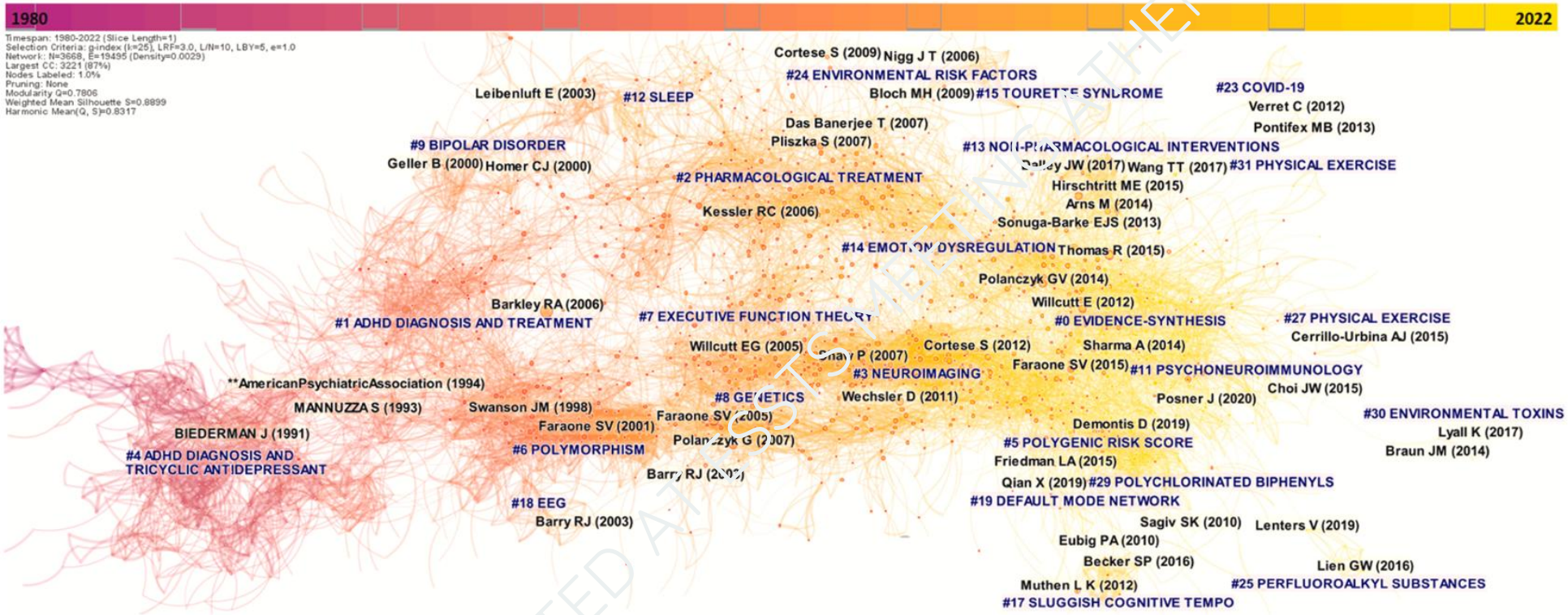
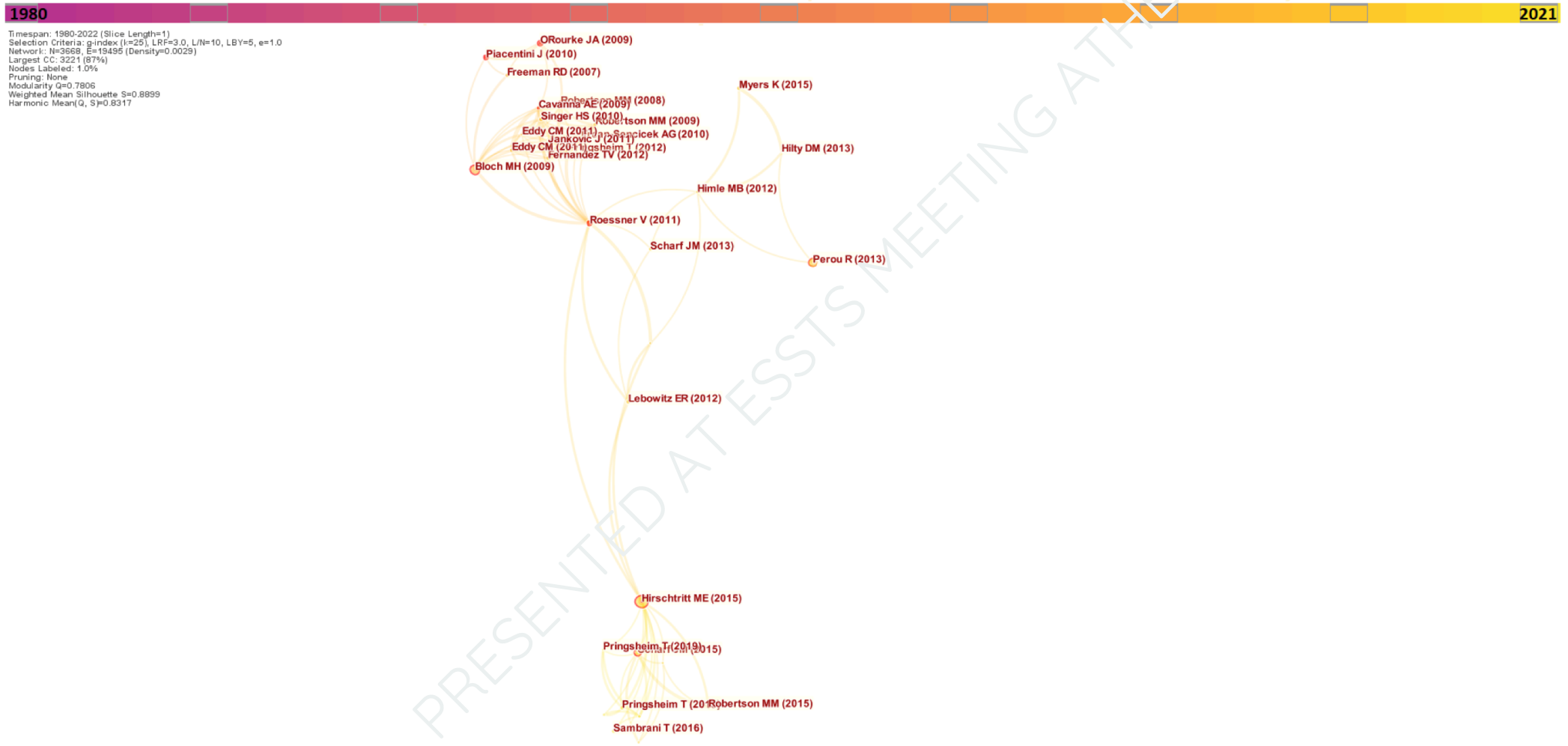


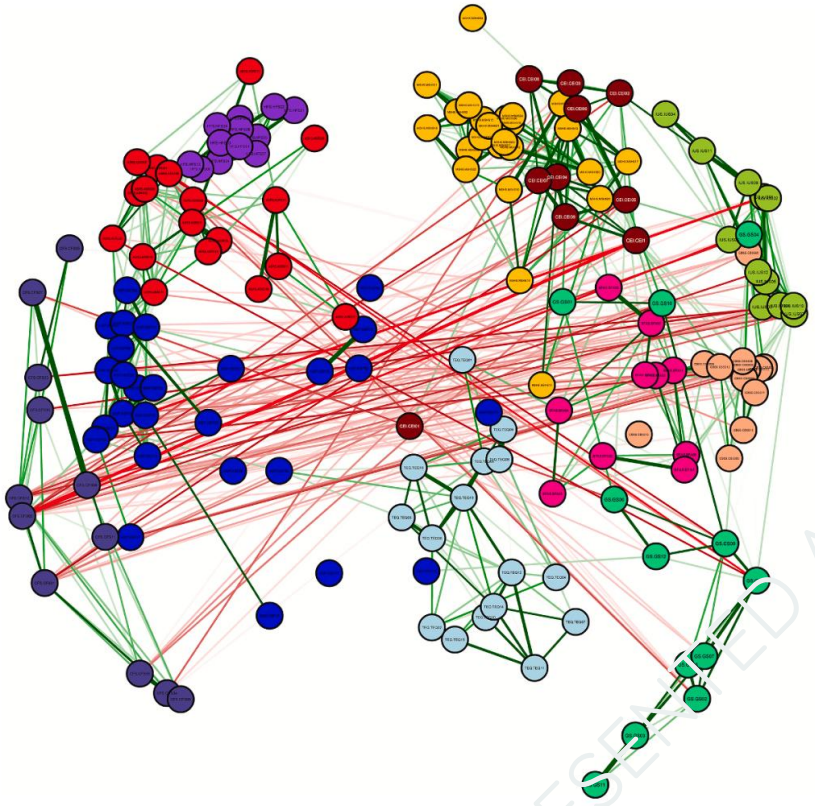
Fig. 1. Co-citation references network (1980–2022) with cluster visualization and burstness of hotspots obtained with CiteSpace. Note: Co-citation reference network with cluster visualization and burstness of hotspots. The position of the node correspond to the year of publication. The size of a node (article) is proportional to the number of times the node has been co-cited. Colored shades indicate the passage of the time, from past (purplish) to the present time (reddish). Colored tree rings refer to the nodes with high betweenness centrality (external purple tree rings) and burstness (central red tree rings). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

History of Research in ADHD

Cluster 15 ≠ Tourette syndrome: tourette syndrome (155.15, 1.0E-4); tics (135.74, 1.0E-4); tic disorders (88.41, 1.0E-4); deep brain stimulation (26.44, 1.0E-4); tourette (26.44, 1.0E-4)



ADHD and strengths in the general population



Contents lists available at ScienceDirect

Comprehensive Psychiatry

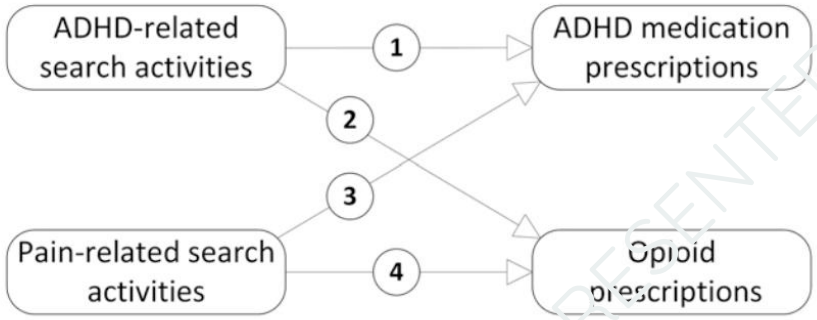
journal homepage: www.elsevier.com/locate/comppsych

Associations between ADHD traits and self-reported strengths in the general population

L.M. Schippers [a,b], C.U. Greven [c,d], M. Hoogman [a,b,*]

TikTok trends or the pandemic? What's behind the rise in ADHD diagnoses

By 2016, the reported incidence of adult ADHD rose by 123% in the US – increases in stimulant medication prescriptions suggest its rise continues



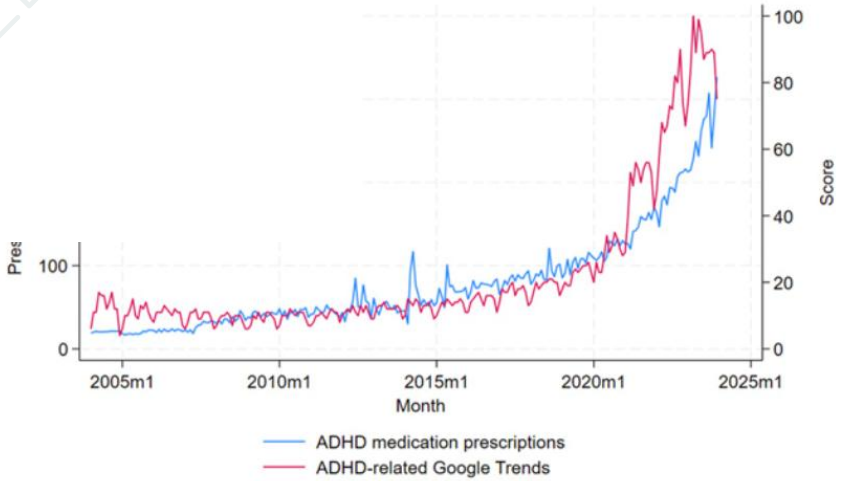
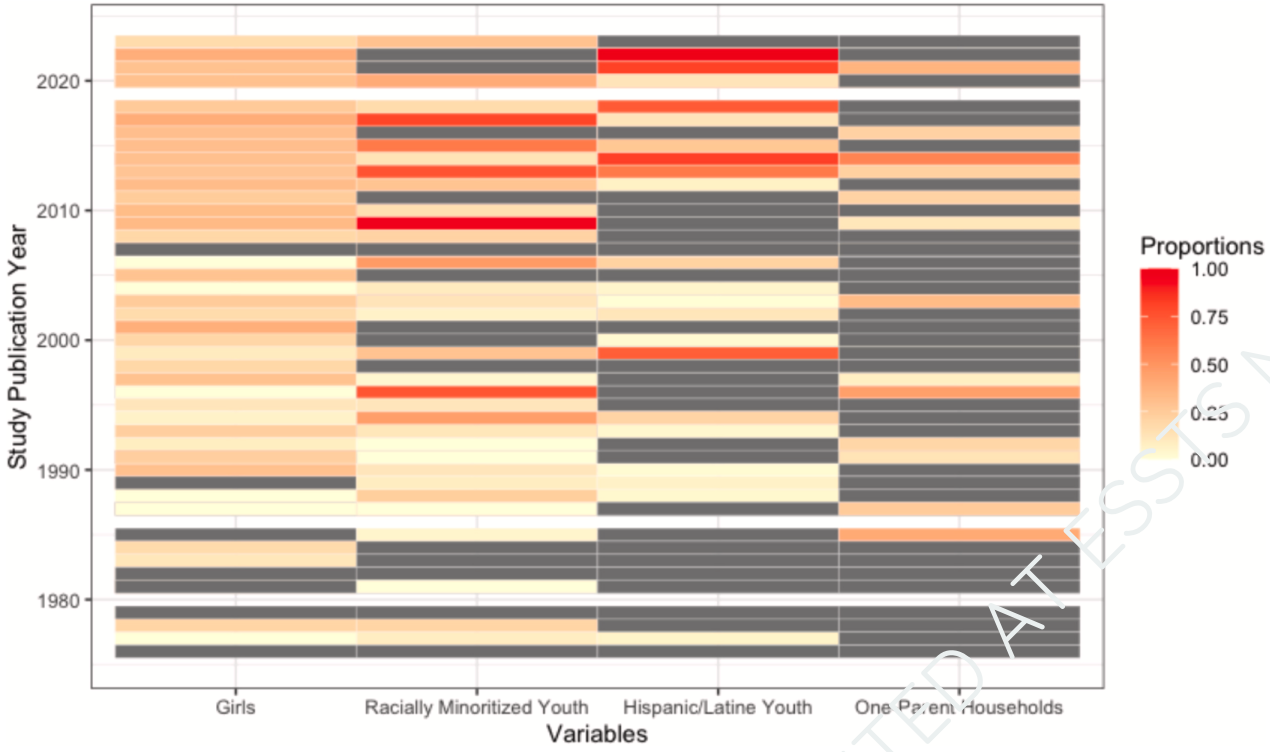


Figure 2. Time series plots of ADHD medication prescriptions and GT data for ADHD (right-side y-axis) from January 2004 to December 2023.

ADHD and Diversity ?



Clinical Psychology Review 112 (2024) 102461

Contents lists available at ScienceDirect

Clinical Psychology Review

journal homepage: www.elsevier.com/locate/clinpsychrev

Review

Diversity and representation in ADHD psychosocial treatment research: A comprehensive synthesis with data from over 10,000 participants

Demographic information of 10,604 youth in ADHD treatment studies.

	Number of participants	Percent of participants in studies that report	Percent of all participants (n = 10,604)
Gender, reported in k = 111 studies (88.10%), n = 9855			
Boys	7331	74.39%	69.13%
Girls	2411	24.47%	22.74%
Non-binary, transgender, or not listed gender identity[a]	0	0%	0%
Race, reported in k = 92 studies (73.02%), n = 8602			
American Indian/ Alaskan Native	8	0.09%	0.08%
Asian	151	1.76%	1.43%
Black/African American	1299	15.10%	12.25%
Middle Eastern/ North African	0	0%	0%
Native Hawaiian/ Pacific Islander	1	0.01%	0.01%
White/Caucasian	5380	62.54%	50.73%
Multiracial	270	3.14%	2.55%
Unspecified Race	823	9.56%	7.76%
Minoritized Race, combined	2440	28.37%	23.02%
Ethnicity, reported in k = 61 studies (48.41%), n = 6712			
Hispanic/Latine	1695	25.26%	15.99%
Family Status/Structure, reported in k = 37 studies (29.37%), n = 4119			
One-parent[b] household	1291	31.34%	12.24%

Same, same, but different!

- The classic idea of ADHD mainly affecting active little boys with obvious symptoms from a young age does not respond to reality anymore.
- It also includes a woman in her 20s who managed to cope with the the situation due to her parents supporting her during childhood and adolescence, she kept things together as a child but is now overwhelmed by adult life;
- …or, an autistic person who finds it really hard to focus due to his hyperactivity
- …or a creative african-american artist who didn't fit into regular school but is now thriving in her own artistic space.

The Journal of Child Psychology and Psychiatry

Journal of Child Psychology and Psychiatry 65:6 (2024), pp 832–844 doi:10.1111/jcpp.13920

Time after time: failure to identify and support females with ADHD – a Swedish population register study

Charlotte Skoglund,[1] Inger Sundström Poromaa,[2] Daniel Leksell,[3] Katarina Ekholm Selling,[2,4] Thomas Cars,[4] Maibritt Giacobini,[5,6] Susan Young,[7,8] and Helena Kopp Kallner[9,10]

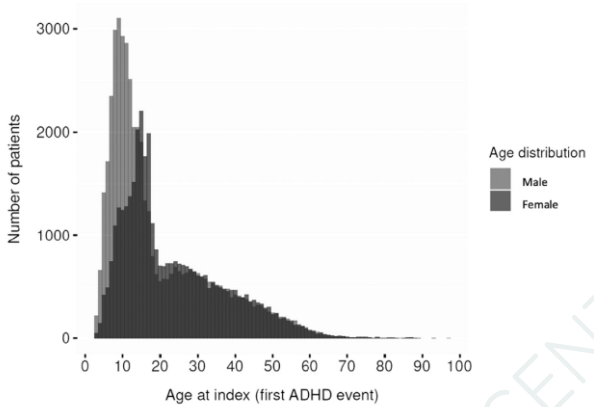
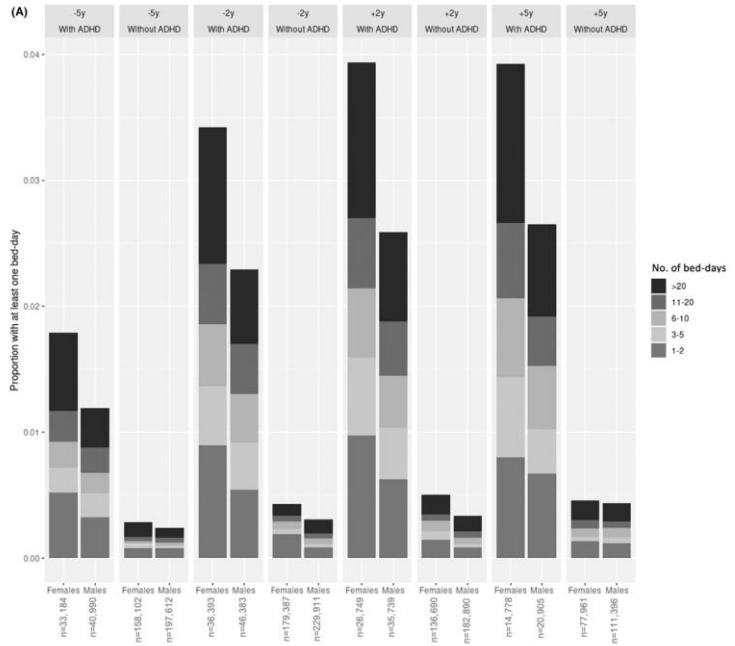


Figure 2 Age distribution at ADHD-index by sex

Table 1 Age and socioeconomic status at first record of ICD10: F90 and/or ADHD-medication in the study population

	Females N = 37,591		Males N = 47,739		p-Value
	With ADHD[1] N = 37,591	Matched controls Without ADHD[2] N = 187,946	With ADHD[1] N = 47,739	Matched controls Without ADHD[2] N = 238,680	Females versus males (ADHD-group)
Age at index					
Mean (*SD*)	23.5 (13.8)	23.5 (13.8)	19.6 (13.9)	19.6 (13.9)	<.001[3]
Median (IQR)	19.0 (13.0–32.0)	19.0 (13.0–32.0)	14.0 (9.0–28.0)	14.0 (9.0–28.0)	<.001[4]
Socioeconomic status, n (%)					
High	9,196 (24.4)	45,978 (24.4)	11,863 (24.9)	59,310 (24.9)	.069[5]
Middle	12,505 (33.3)	62,522 (33.3)	16,377 (34.3)	81,882 (34.3)	
Low	13,271 (35.3)	66,354 (35.3)	16,730 (35.0)	83,647 (35.0)	
Missing	2,619 (7.0)	13,092 (7.0)	2,769 (5.8)	13,841 (5.8)	

Consequences of a late diagnosis



ADHD and hormonal contraceptives– be aware!

- All Swedish-born women aged 15 to 24 years, and residing in Sweden were identied through the population registers and included in the study
- Exposures: ADHD and use of hormonal contraceptives HC
- Women with ADHD had a 3-fold higher risk of developing depression, irrespective of HC use.
- Overall, women with ADHD who used combined HC or progestogen-only pills had more than 5 times increased risk of depression compared to women without ADHD who did not use HCs.
- Information on risks with HCs as well as potential bene ts with long-acting reversible contraceptives needs to be an integrated part of the shared decision making and contraception counseling for young women with ADHD.

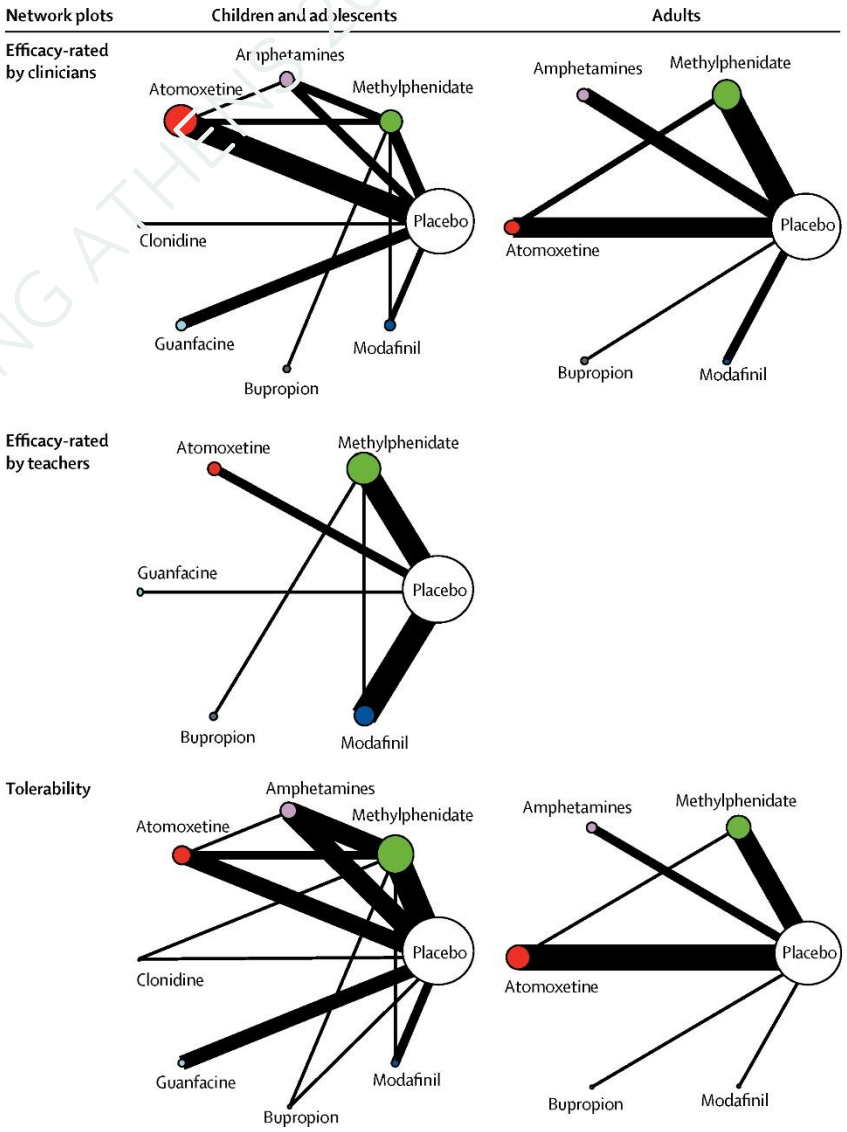
The best treatments…

Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: a systematic review and network meta-analysis

Samuele Cortese, Nicoletta Adamo, Cinzia Del Giovane, Christina Mohr-Jensen, Adrian J Hayes, Sara Carucci, Lauren Z Atkinson, Luca Tessari, Tobias Banaschewski, David Coghill, Chris Hollis, Emily Simonoff, Alessandro Zuddas, Corrado Barbui, Marianna Purgato, Hans-Christoph Steinhausen, Farhad Shokraneh, Jun Xia, Andrea Cipriani

133 studies
- 81 in children/adolescents,
- 51 in adults
- 1 including children, adolescents and adults

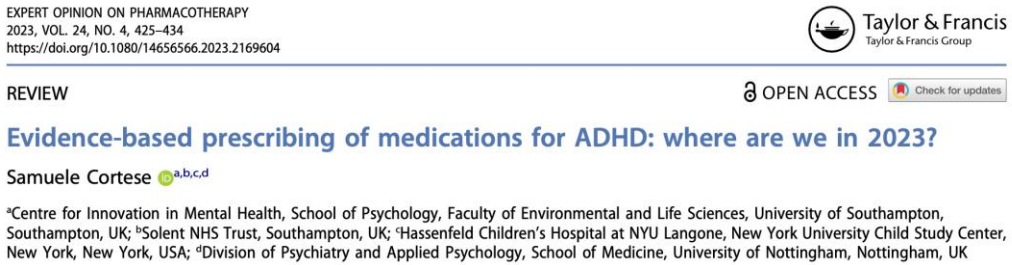
In total, 14,346 children/adolescents and 10,296 adults were included.



Cortese et al. Lancet Psychiatry 2018; 5(9):727-738.

Pharmacotherapy–the big picture

- Results of RCTs are not able to inform decision-making at the individual patient level.
- The «maximum» safe and effective doses, possibly beyond those currently recommended, are not well explored.
- Evidence from RCTs on augmenting strategies is still limited.
- No novel agents with the same or higher effect size of stimulants, in terms of efficacy have been found (taking into account tolerability and lower abuse potential) .
- Implementation of precision psychiatry approaches and stratification of patients in future RCTs will be key to, respectively, individualize the treatment strategies and test etiopathophysiology-based agents.



EXPERT OPINION ON PHARMACOTHERAPY
2023, VOL. 24, NO. 4, 425–434
https://doi.org/10.1080/14656566.2023.2169604

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REVIEW

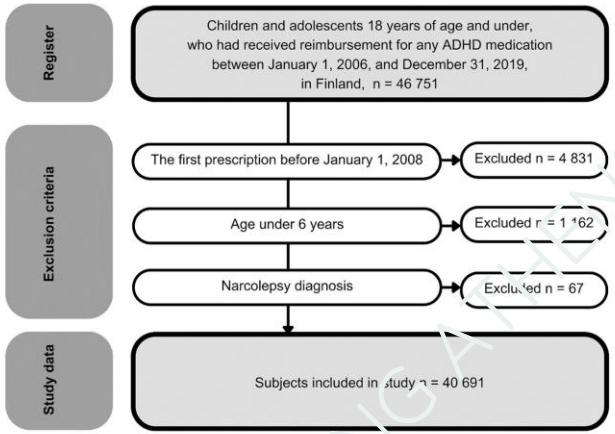
OPEN ACCESS Check for updates

Evidence-based prescribing of medications for ADHD: where are we in 2023?

Samuele Cortese [a,b,c,d]

[a]Centre for Innovation in Mental Health, School of Psychology, Faculty of Environmental and Life Sciences, University of Southampton, Southampton, UK; [b]Solent NHS Trust, Southampton, UK; [c]Hassenfeld Children's Hospital at NYU Langone, New York University Child Study Center, New York, New York, USA; [d]Division of Psychiatry and Applied Psychology, School of Medicine, University of Nottingham, Nottingham, UK

The mean duration of pharmacological treatment…



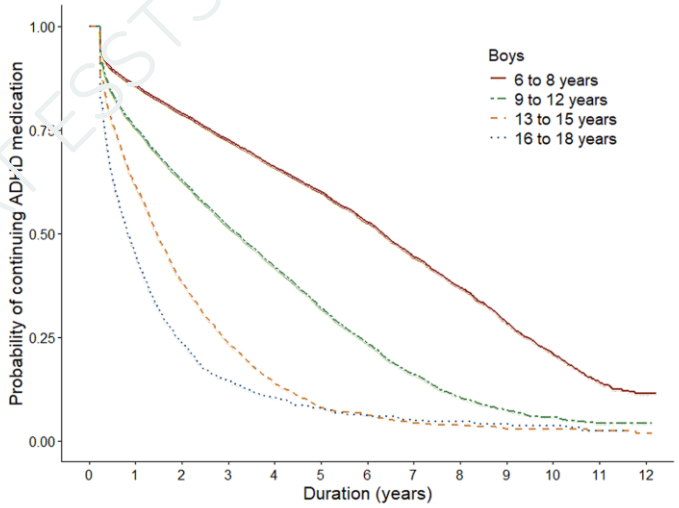
European Child & Adolescent Psychiatry
https://doi.org/10.1007/s00787-025-02735-4

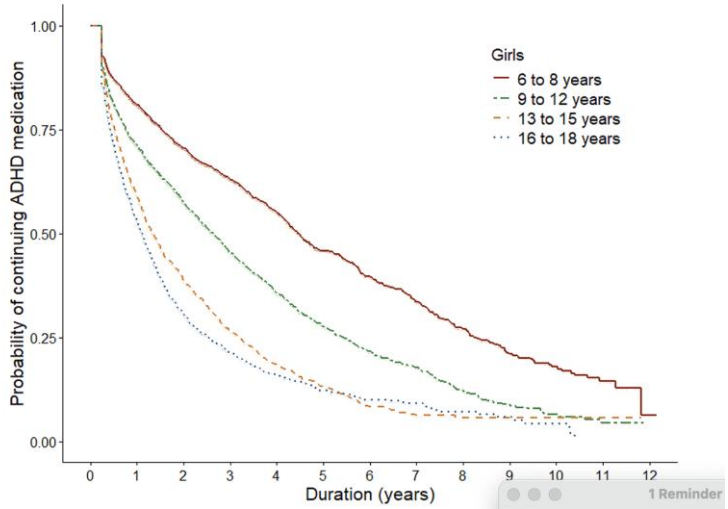
RESEARCH

Duration of ADHD medication treatment among Finnish children and adolescents – a nationwide register study

Terhi A. Kolari[1,12] · Miika Vuori[2,3] · Hanna Rättö[2,4] · Eveliina A. Varimo[5,6] · Eeva T. Aronen[5,6] · Kari Auranen[7,8] · Leena K. Saastamoinen[9] · Päivi T. Ruokoniemi[10,11]

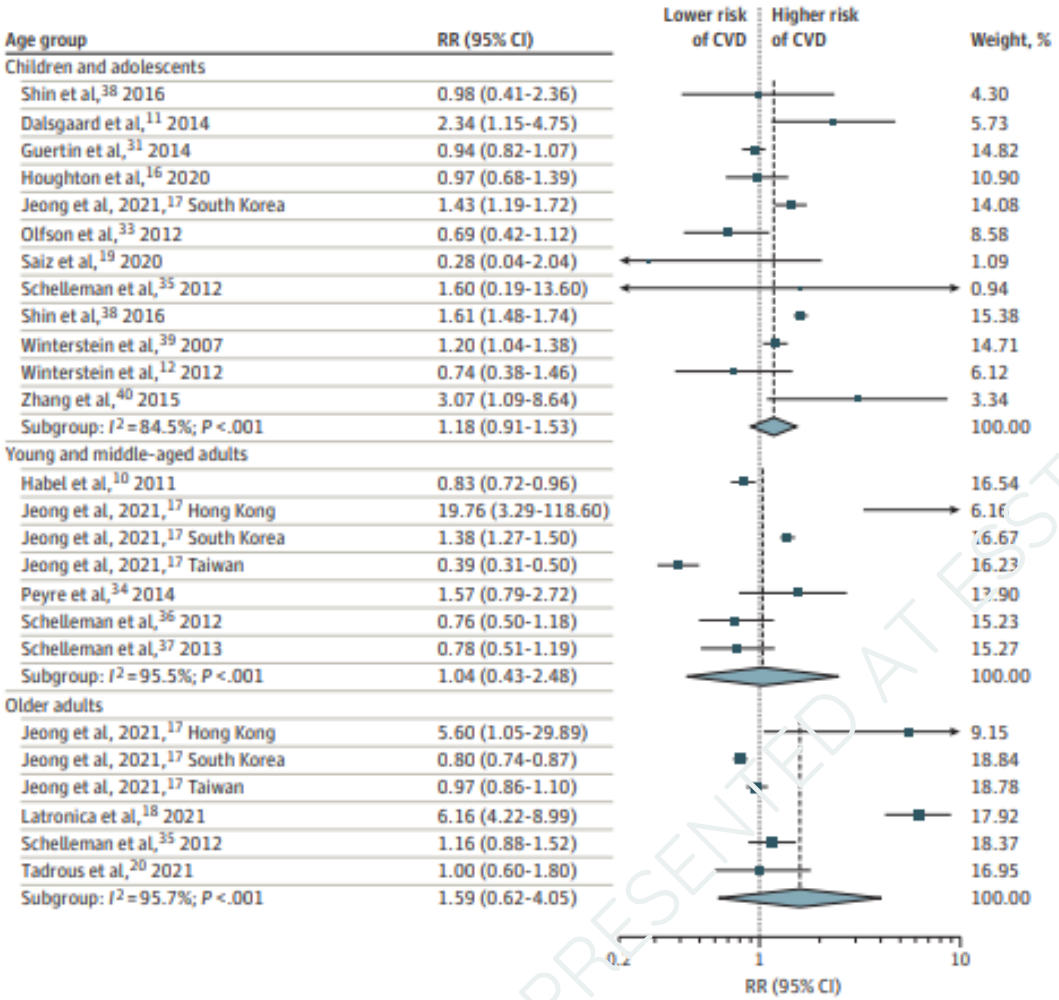
Received: 13 August 2024 / Accepted: 25 April 2025





Cardio-Vascular risk

Figure 2. Risk of Any Cardiovascular Event by Age Group Among Individuals Receiving Attention-Deficit/Hyperactivity Disorder Medication



CVD indicates cardiovascular disease; RR, risk ratio.

CONCLUSIONS AND RELEVANCE

This meta-analysis suggests **no statistically significant association between ADHD medications and the risk of CVD across age groups**, although a modest risk increase could not be ruled out, especially for the risk of cardiac arrest or tachyarrhythmias.

Further investigation is warranted for the cardiovascular risk in **female patients** and patients with **preexisting CVD** as well as **long-term risks** associated with ADHD medication use.

Zhang et al. JAMA Network Open. 2022;5(11):e2243597.

AE and Safety in an metaanalysis including all ages and broader diagnoses

- It is important to better understand the safety of stimulants, particularly in relation to drug diversion, misuse, and adult ADHD diagnoses.
- Prolonged exposure to stimulants lasting 5 to 14 years may increase the risk of cardiovascular disease.
- Safety of stimulant medications prescribed for various diagnoses, including ADHD, depression, binge-eating disorder, schizophrenia, Alzheimer's disease, and stimulant use disorders, as reported in RCTs investigating methylphenidate, lisdexamfetamine, and other amphetamines.
- This meta-analysis (studies published since 2000), including 93 RCTs with duration up to 52 weeks found an increased risk of AEs with stimulant use compared with placebo, without clinically significant cardiovascular outcomes.
- As adult ADHD diagnoses increase, studies with longer follow up periods assessing stimulant-related AEs are needed.

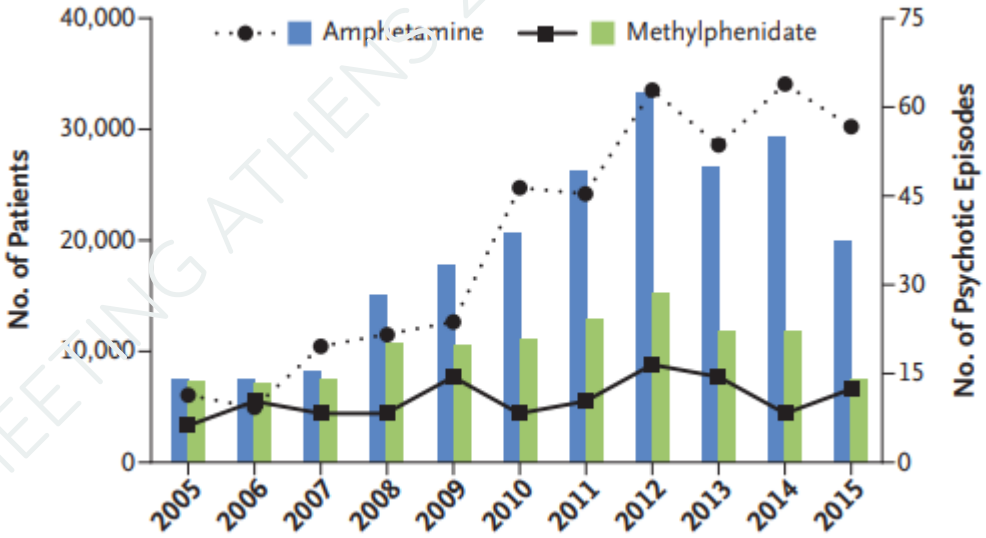
Nunes Pereira Oliva, JAMA Network, 2025

Treatment-Emergent Psychosis

ORIGINAL ARTICLE

Psychosis with Methylphenidate or Amphetamine in Patients with ADHD

Lauren V. Moran, M.D., Dost Ongur, M.D., Ph.D., John Hsu, M.D., M.S.C.E., Victor M. Castro, M.S., Roy H. Perlis, M.D., and Sebastian Schneeweiss, M.D., Sc.D.



Insurance claims databases to assess patients **13 to 25** years of age who had received a diagnosis of ADHD and who started taking methylphenidate or amphetamine between January 1, 2004, and September 30, 2015.

221,846 patients; 110,923 patients taking methylphenidate were matched with 110,923 patients taking amphetamines

343 episodes of psychosis (with an episode defined as a new diagnosis code for psychosis and a prescription for an antipsychotic medication)

106 episodes (0.10%) in the methylphenidate group
237 episodes (0.21%) in the amphetamine group

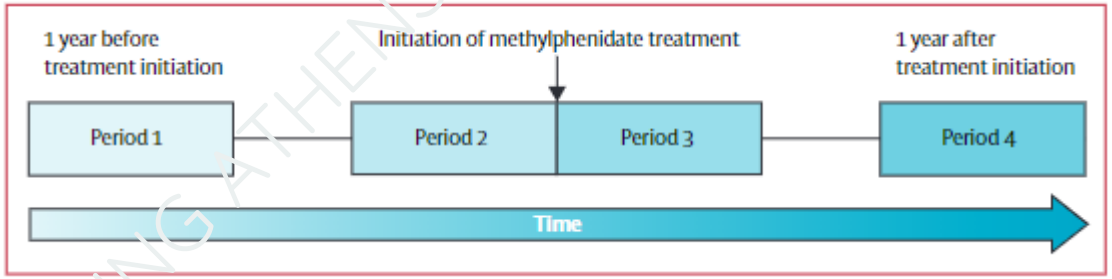
Moran, 2019

Methylphenidate-Emergent Psychosis

Articles

Methylphenidate and the risk of psychosis in adolescents and young adults: a population-based cohort study

Chris Hollis, Qi Chen, Zheng Chang, Patrick D Quinn, Alexander Viktorin, Paul Lichtenstein, Brian D'Onofrio, Mikael Landén, Henrik Larsson



Screened individuals on these registers to identify those receiving methylphenida tetreatment, and who were aged 12–30 years at the start of treatment

Characteristics (n=23 898)	
Sex, n (%)	
Female	9729 (40·7%)
Male	14 169 (59·3%)
Median age at treatment initiation (IQR), years	17 (14–22)
Individuals with at least one psychotic event, n (%)	
Period 1	89 (0·4%)
Period 2	114 (0·5%)
Period 3	110 (0·5%)
Period 4	94 (0·4%)

Period 1: the 12-week period one calendar year before treatment. Period 2: 12 weeks before treatment initiation. Period 3: 12 weeks after treatment initiation. Period 4: the 12-week period one calendar year after treatment.

Table 1: **Study population characteristics**

Hollis, 2019

Patients with a history of psychotic symptoms and current ADHD require careful, slow titration of stimulant medication.

Preferably with methylphenidate rather than amphetamines and, if necessary, simultaneous treatment with antipsychotic medication.

The high dosages of stimulants observed in substance abuse situations present greater risks for psychosis than smaller therapeutic dosages.

Risk of hospitalisation for first-onset psychosis or mania within a year of ADHD medication initiation

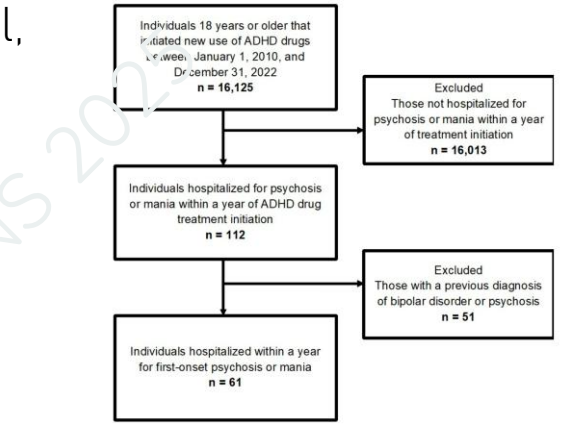


Figure 1 Flow chart of the study population. ADHD, attention deficit hyperactivity disorder.

In conclusion, the risk of hospitalisation for first-onset psychosis or mania was approximately 1 in 264 among adults of any age prescribed methylphenidate, amphetamines or atomoxetine to treat ADHD during the study period. Adjusting for the general population risk of hospitalisation for first-onset psychosis or mania, the NNH was 302. The risk of such first-onset admissions taking place within a year of ADHD treatment commencing was eight times higher than that of all other first-onset admissions for psychosis or mania combined in 2018–2020. The majority of patients hospitalised were represcribed ADHD drugs within a year following discharge, and one in four was readmitted within a year. This raises concerns about whether the prescribing clinicians as well as the admitted individuals are sufficiently aware of the potential causal role of ADHD drugs in the development of first-onset psychosis or mania.

To cite: Gudbrandsdottir RK, Sigurdsson E, Albertsson Þl, *et al*. *BMJ Ment Health* 2025;**28**:1–7.

JAMA Psychiatry | Original Investigation

Safety and Efficacy of Repeated Low-Dose LSD for ADHD Treat in Adults
A Randomized Clinical Trial

JAMA Psychiatry.doi:10.1001/jamapsychiatry.2025.0044
PublishedonlineMarch19,2025.

Lorenz Mueller, MD; Joyce Santos de Jesus; Yasmin Schmid, MD; Felix Müller, MD; Anna Becker, MSc; Aaron Klaiber, MSc; Isabelle Straumann, MSc; Dino Luethi, PhD; Eline C. H. M. Haijen, MSc; Petra P. M. Hurks, PhD; Kim P. C. Kuypers, PhD; Matthias E. Liechti, MD

Safety and Efficacy of Repeated Low-Dose LSD for ADHD Treatment in Adults

- A 6-week,multicenter, double-blind, placebo-controlled, parallel-group phase 2A randomized clinical trial
- Adults aged 18 to 65 years with a prior ADHD diagnosis who presented with moderate to severe symptoms
- Participants received either LSD (20µg) or placebo twice weekly for 6 weeks (total of 12 doses)
- 53 participants were randomized to LSD (n = 27) or placebo (n = 26)
- Mean(SD)participant age was 37 (12) years, and 22 participants (42%) were female
- In this randomized clinical trial, repeated low-dose LSD administration was safe in an outpatient setting but did not prove more effective than a placebo in reducing ADHD symptoms

Clinical Prediction models?

- Despite a wealth of literature, no established evidence-based prediction models inform individualized treatment strategies based on the patient's clinical, environmental, cognitive, genetic, or biological characteristics.
- The study comprehensively and specifically reviewed the status of validated prediction models in ADHD
- To test potential moderating factors that could affect the performance of available models
- Among the 100 prediction modelling studies included, 88% reported on diagnostic, 5% on prognostic, and 7% on treatment-response models
- 35% of studies used clinical, 31.0% neuroimaging, and 27.0% cognitive predictors. Notably, only 7.0% of models were externally validated.

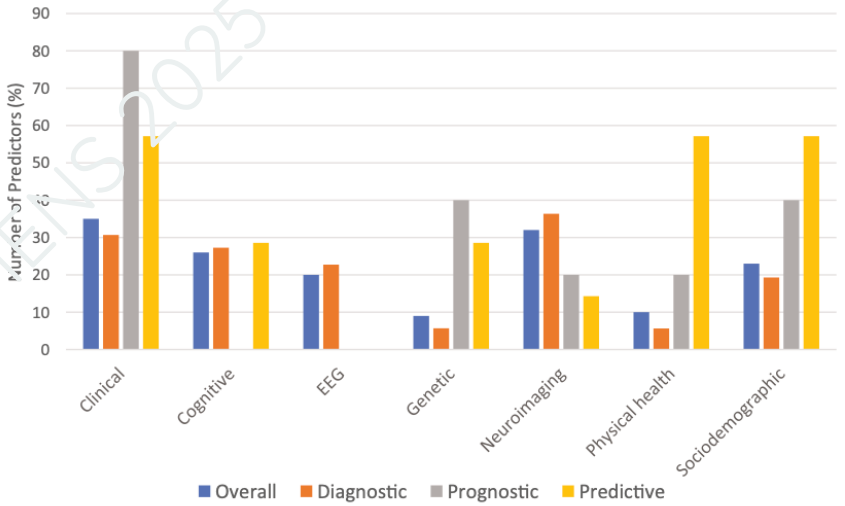


Fig. 2 Reported predictors. Most frequently reported predictors across prediction model types.

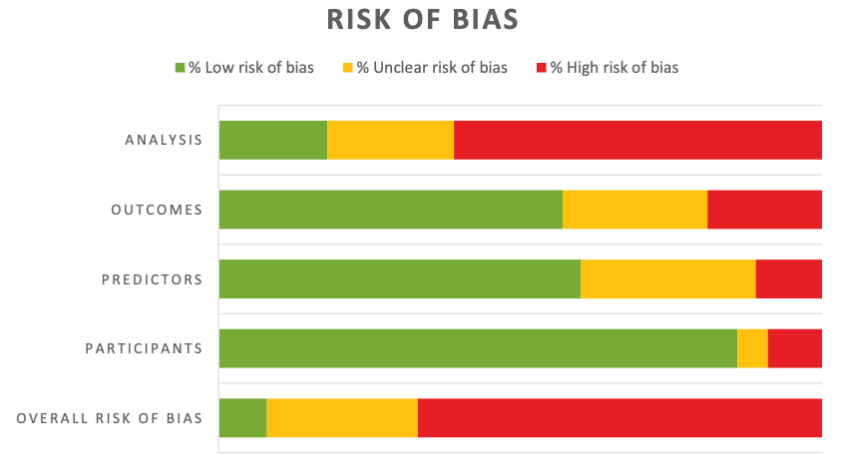


Fig. 3 Quality assessment. Risk of bias of the retrieved studies, as assessed by the PROBAST tool.

Salazar de Pablo, Molecular Psychiatry, 2024

Old Compounds, new formulas ?

- Methylphenidate (MPH) as Jornay PM, a very delayed-release formulation taken in the evening to be active the next morning.
- Serdexmethylphenidate-dexmethylphenidate as Azstarys, where serdexmethylphenidate acts as a prodrug, slowly converting to dexmethylphenidate over several hours.
- Amphetamines (AMP) in a transdermal (patch) form.
- Clonidine as a liquid in an extended-release formulation.
- Shows a trend towards modifying drug delivery systems to improve convenience, adherence, or pharmacokinetic profiles for patients.

Old Compounds, new formulas ?

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- Clonidine as a liquid in an extended-release formulation.
- Shows a trend towards modifying drug delivery systems to improve convenience, adherence, or pharmacokinetic profiles for patients.
- Viloxazine extended-release capsules (brand name Qelbree) were approved by the U.S. Food and Drug Administration (FDA) for the treatment of ADHD in pediatric patients aged 6 to 17 years in April 2021, later approved for adults in May 2022 (a non-stimulant medication for ADHD).

Where do we stand?

- Recent scientific evidence indicates that ADHD represents an extreme manifestation of complex, dimensional traits that are largely persistent and follow varied developmental paths.
- As with many neurodevelopmental and psychiatric disorders, the origins of ADHD are multifaceted and varied, involving a combination of interacting genetic and environmental factors that contribute to subtle differences in brain structure and function.
- Future research priorities include addressing clinical and causal heterogeneity and comorbidity, enhancing risk prediction, understanding gene–environment interactions, exploring how ADHD presents in females and other "minority" groups, examining the impact of social environments on impairment and stigma, and promoting resilience and personal development.
- Looking ahead, involving individuals with ADHD in participatory research will be essential.