Is ADHD Fake News?

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Conflict Disclosure Information

Diane McIntosh has received research support, spoken for, or sits on advisory boards for the following companies:

Lundbeck, Pfizer, Shire, Otsuka, Eli Lilly, Bristol Myers Squibb, Janssen-Ortho, Sunovion, Allergan, Valeant, Purdue

Mitigating Bias

- I will endeavor to use **generic names**
- I will inform you when I am referring to a drug use that is **off-label** or provide its **on-label indications**
- I urge everyone to recommend the treatment that is **the best option for your individual patient**, whether that treatment is **psychotherapy, exercise, or a medication that have been available for 2 years or 50 years.**

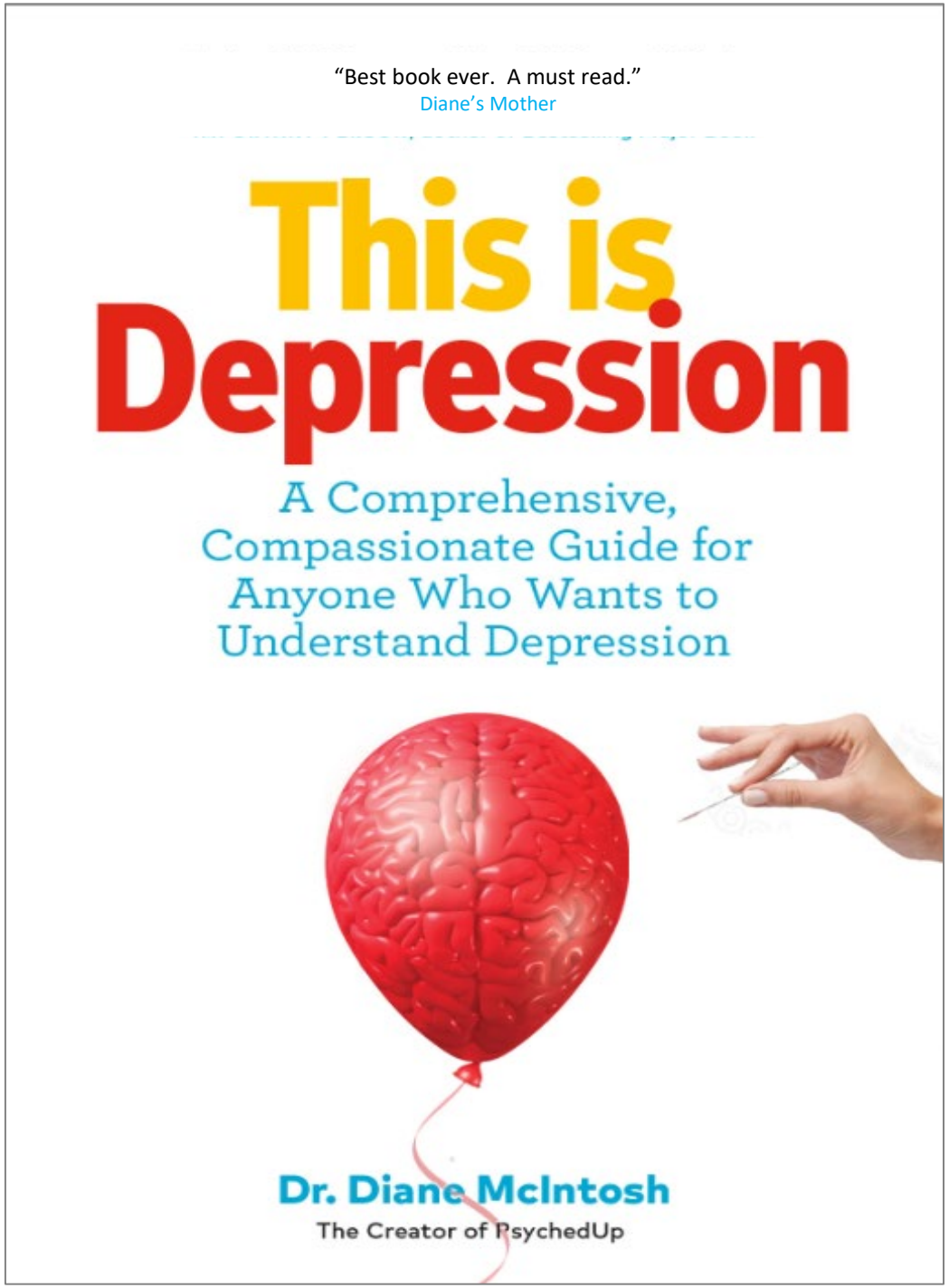
PSYCHEDUP

PsychedUpCME.com

Vancouver
May 31, 2019 and November 15, 2019
Okanagan
June 21, 2019

It's ACCREDITED!

4.5 Hrs/day: Group Learning Activity (Section 1) and Mainpro+


"Best book ever. A must read."
Diane's Mother
This is Depression
A Comprehensive, Compassionate Guide for Anyone Who Wants to Understand Depression
Dr. Diane McIntosh
The Creator of PsychedUp

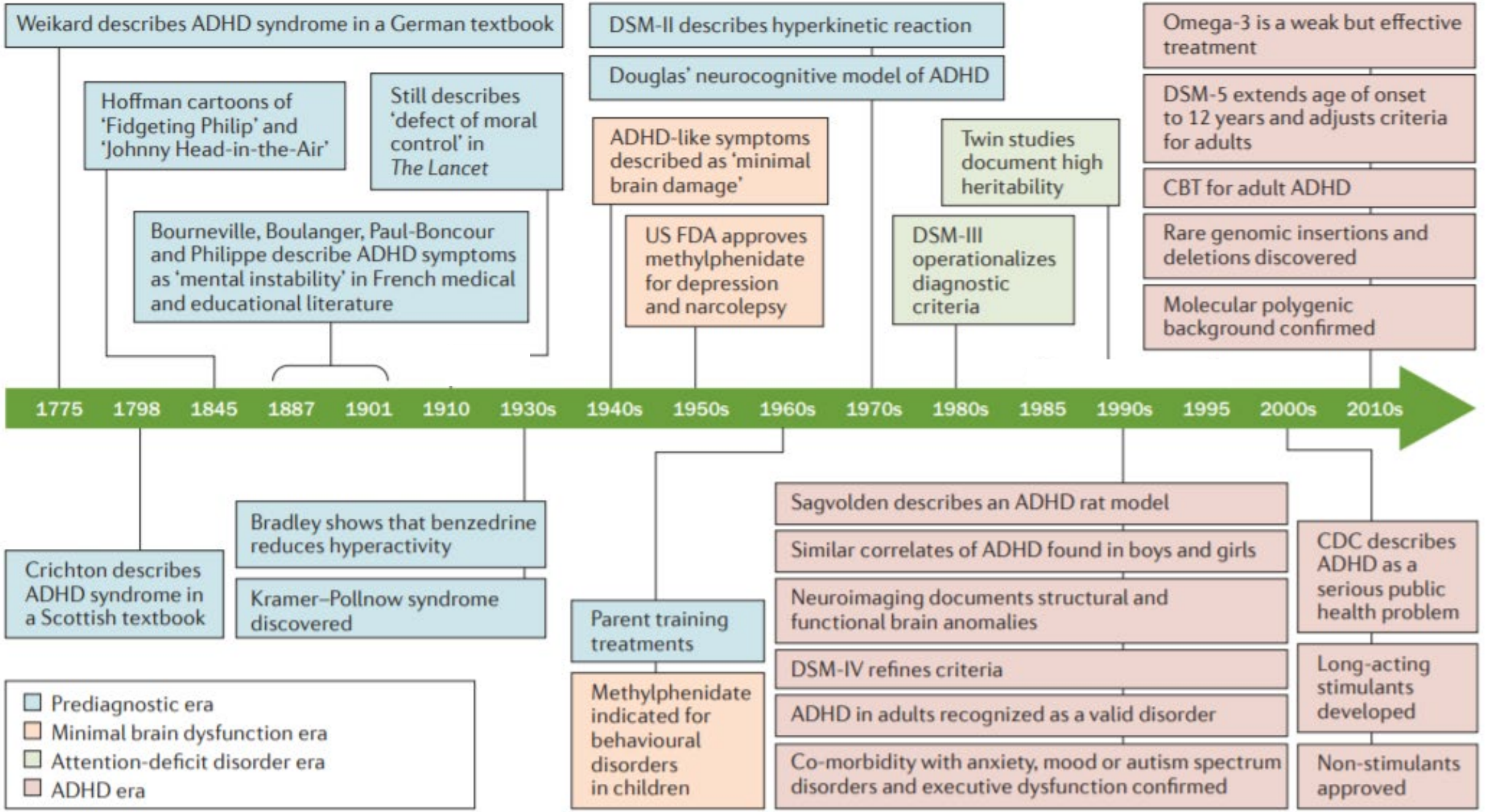
COMING SOON!

Learning Objectives

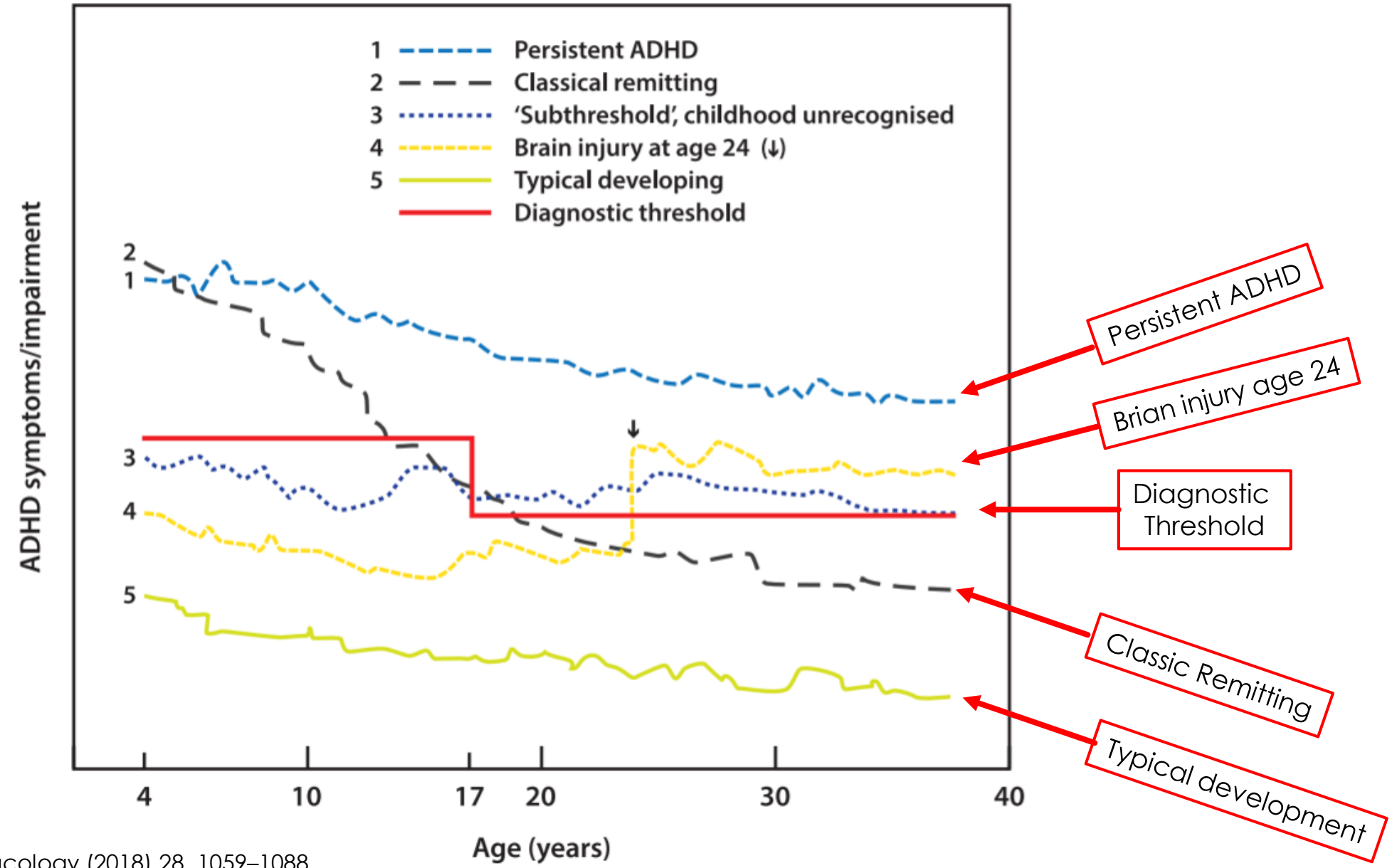
- **Is ADHD real?**
  - Review the **structural and functional brain dysfunction** that underlies a diagnosis of ADHD
- **Should ADHD be treated?**
  - Highlight research **evidence that supports or refutes** the benefits of **treating ADHD across the lifespan**.
- **Does the TI offer valuable insights to BC physicians?**
  - Debate the **Therapeutics Initiative's** approach to the treatment of mental illnesses, including the most recent newsletter regarding ADHD diagnosis and treatment

Is ADHD Real?

OR IS IT THE ORIGINAL LIFESTYLE DISORDER?

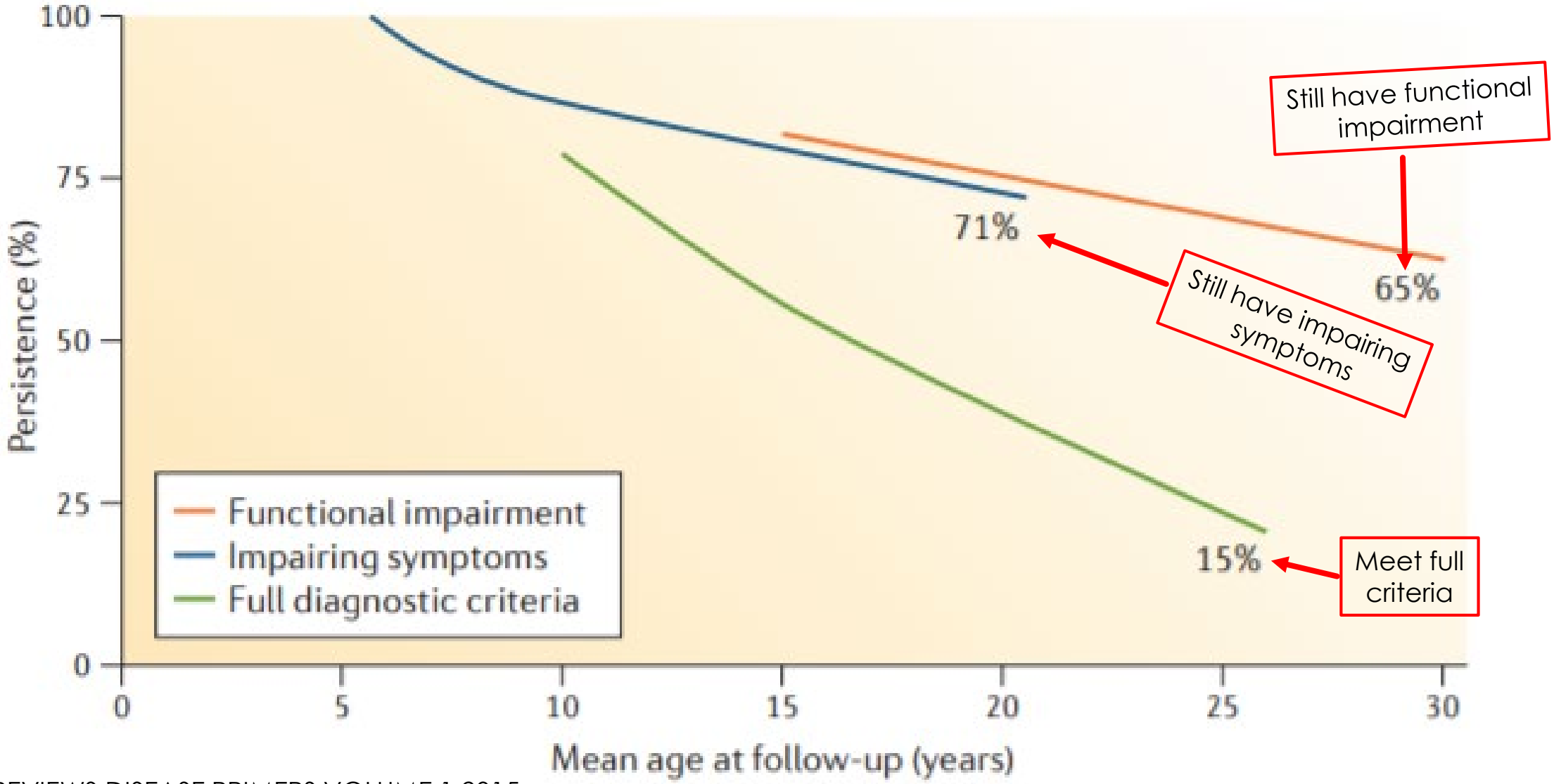

Weikard describes ADHD syndrome in a German textbook
Hoffman cartoons of 'Fidgeting Philip' and 'Johnny Head-in-the-Air'
Still describes 'defect of moral control' in The Lancet
Bourneville, Boulanger, Paul-Boncour and Philippe describe ADHD symptoms as 'mental instability' in French medical and educational literature
DSM-II describes hyperkinetic reaction
Douglas' neurocognitive model of ADHD
ADHD-like symptoms described as 'minimal brain damage'
US FDA approves methylphenidate for depression and narcolepsy
Twin studies document high heritability
DSM-III operationalizes diagnostic criteria
Omega-3 is a weak but effective treatment
DSM-5 extends age of onset to 12 years and adjusts criteria for adults
CBT for adult ADHD
Rare genomic insertions and deletions discovered
Molecular polygenic background confirmed
1775
1798
1845
1887
1901
1910
1930s
1940s
1950s
1960s
1970s
1980s
1985
1990s
1995
2000s
2010s
Crichton describes ADHD syndrome in a Scottish textbook
Bradley shows that benzedrine reduces hyperactivity
Kramer–Pollnow syndrome discovered
Parent training treatments
Methylphenidate indicated for behavioural disorders in children
Sagvolden describes an ADHD rat model
Similar correlates of ADHD found in boys and girls
Neuroimaging documents structural and functional brain anomalies
DSM-IV refines criteria
ADHD in adults recognized as a valid disorder
Co-morbidity with anxiety, mood or autism spectrum disorders and executive dysfunction confirmed
CDC describes ADHD as a serious public health problem
Long-acting stimulants developed
Non-stimulants approved
Prediagnostic era
Minimal brain dysfunction era
Attention-deficit disorder era
ADHD era

Developmental Trajectories of ADHD



European Neuropsychopharmacology (2018) 28, 1059–1088

The age-dependent decline and persistence of ADHD throughout the lifetime



NATURE REVIEWS DISEASE PRIMERS VOLUME 1 2015

Heterogeneity = ADHD

- Inter-individual differences are a **hallmark of neurodevelopmental disorders** such as ADHD[1]
- In ADHD, heterogeneity between diagnosed individuals originates from distinct **cognitive deficits** and **neural mechanisms**[1,2]

1. Faraone SV, Asherson P, Banaschewski T, et al. (2015) Nat Rev Dis Primers 1:15020. 2. Coghill DR, Seth S, Matthews K (2014) Psychol Med 44:1989–2001.

ADHD changes through development

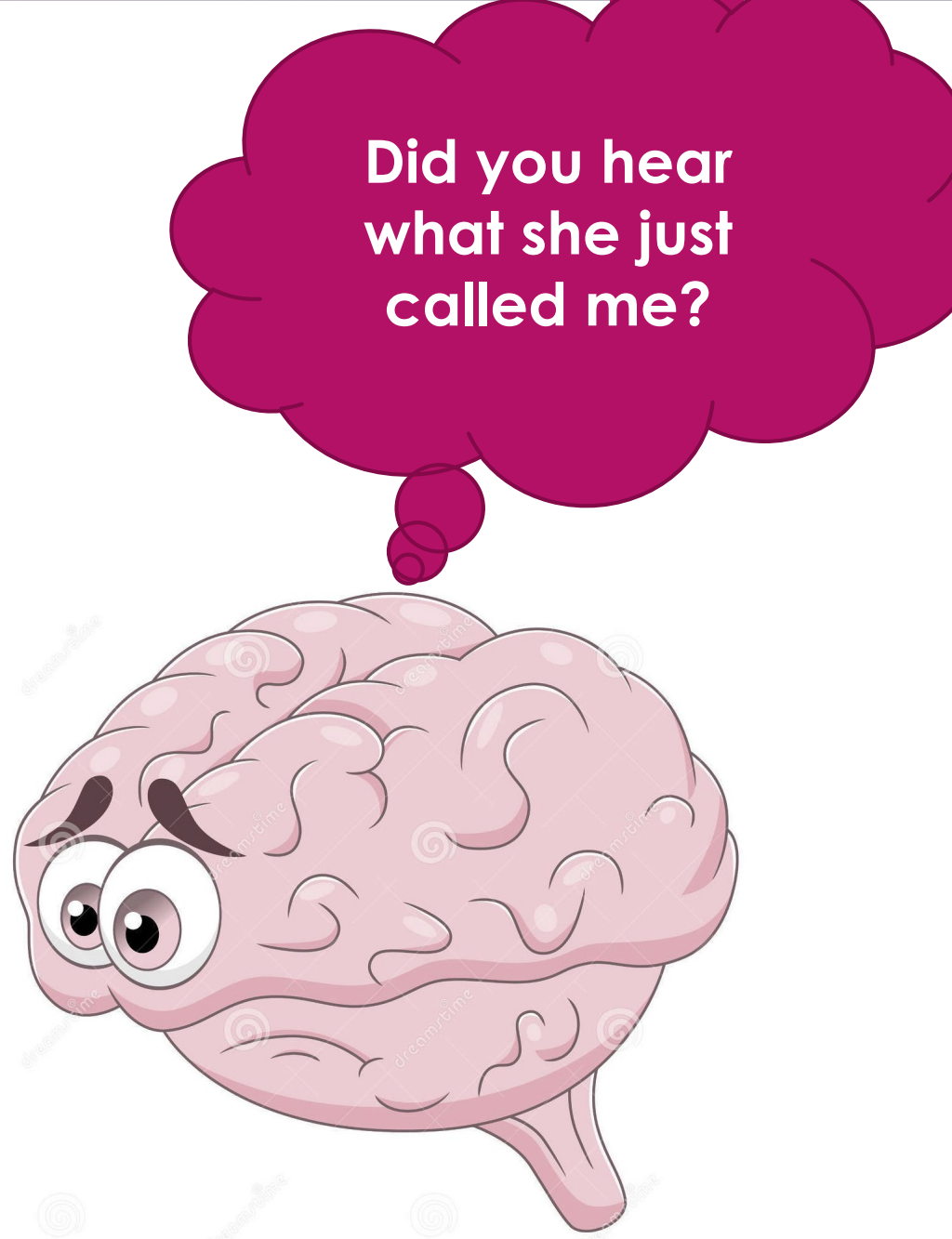
- Characteristic ADHD symptoms throughout development[1].
  - **Very young children**: more hyperactive-impulsive behaviour
  - **Middle childhood**: inattentive symptoms become more apparent
  - **Late adolescence and adulthood**: inattention persists and objective hyperactivity declines
    - **Emotional lability becomes a growing burden**, which may **dominate the clinical picture**.
- The changing clinical picture led the **DMS-5 committee** to move away from subtypes: predominantly inattentive, predominantly hyperactive-impulsive, and combined[2]
  - Now referred to as **clinical presentations in DSM-5.**

1. Cortex. 2015 Dec;73:62-72; 2. Neurotherapeutics. 2012 Jul;9(3):490-9.

The brain doesn't care about categories!

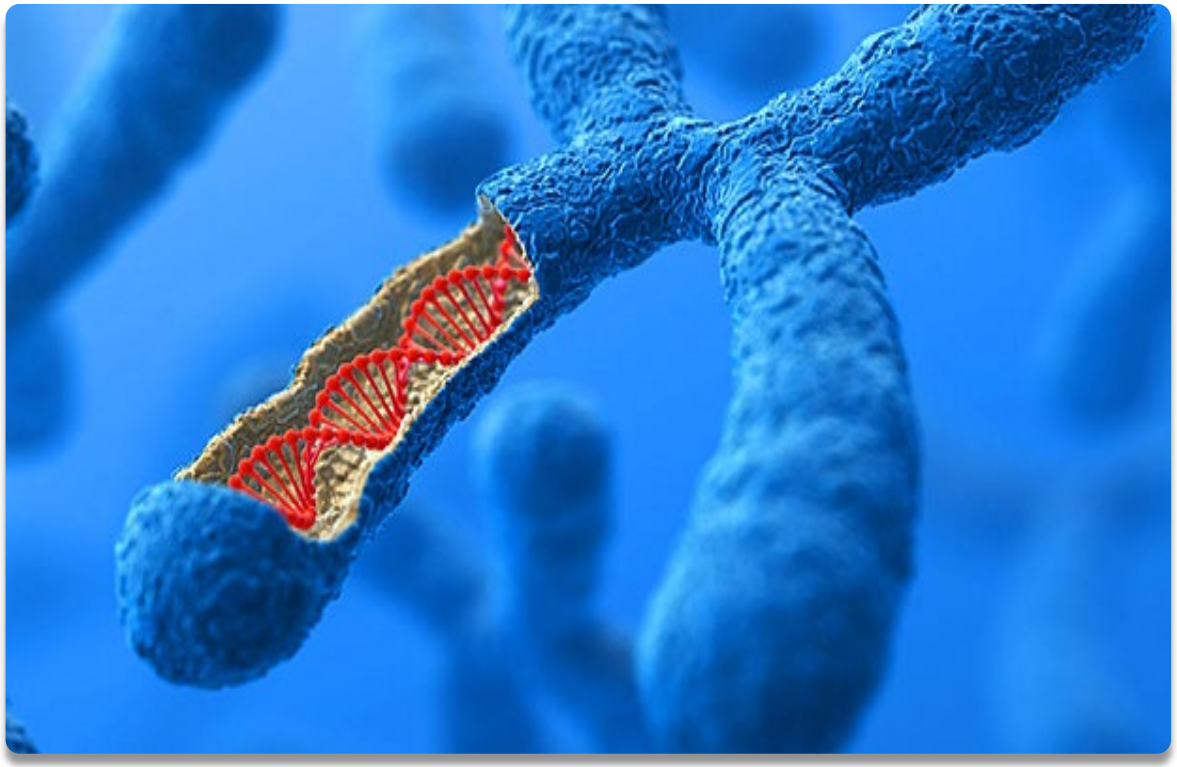
- "The current state-of-the-art in the understanding of the biology of brain disease underscores the notion that **neurobiology could not care less** about how to categorize neurodevelopmental and psychiatric disorders."

Zhao & Castellanos, 2016

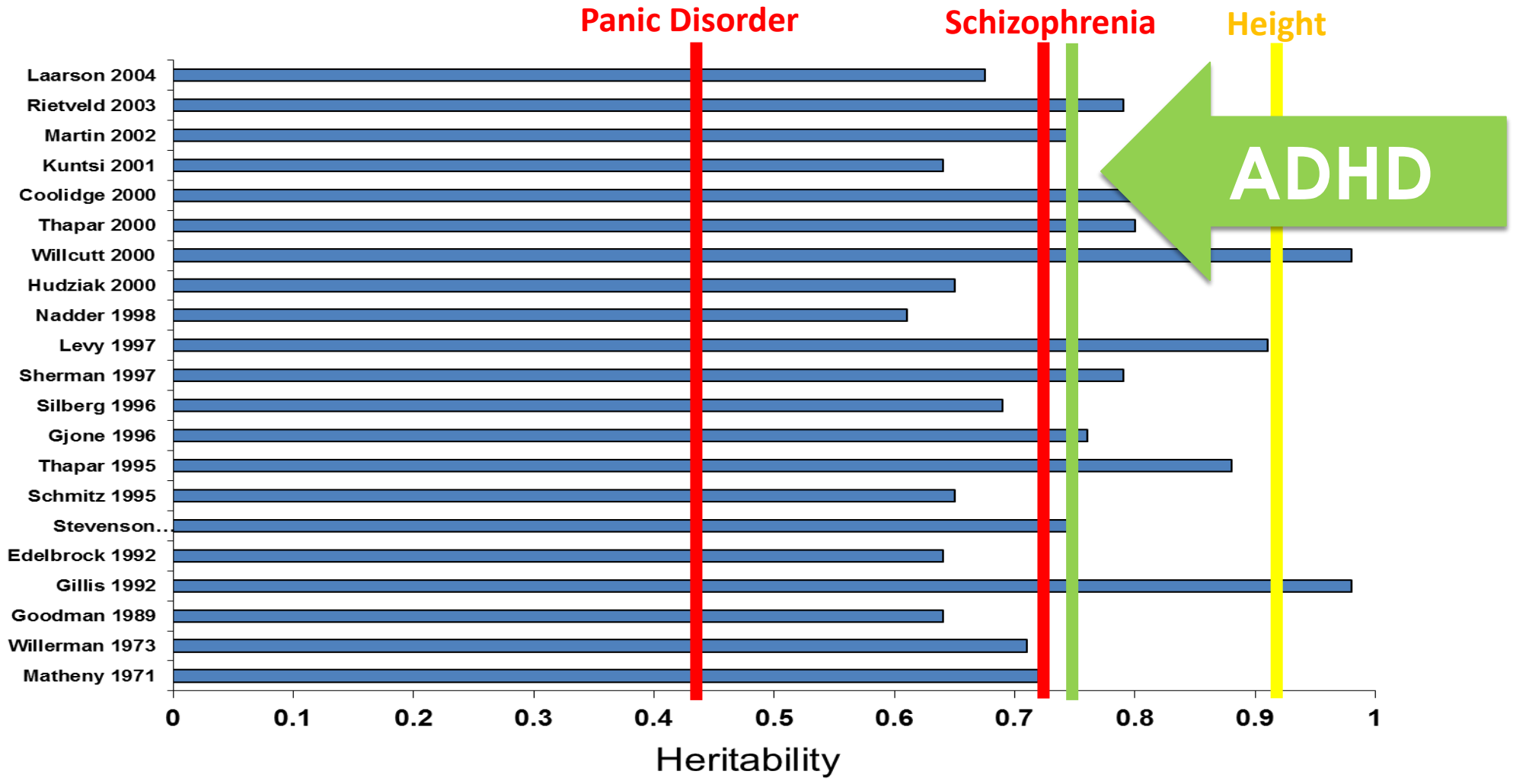


ADHD: genetic and environmental risk factors

- Epidemiologic and clinical studies implicate **genetic and environmental** risk factors
  - Affect the **structure and functional** capacity of **brain networks** involved in **behavior and cognition**
- **Polygenic inheritance**: the expression of a phenotype that is determined by **many genes at different loci**.
  - Each gene exerts an **cumulative effect**: none are dominant or recessive



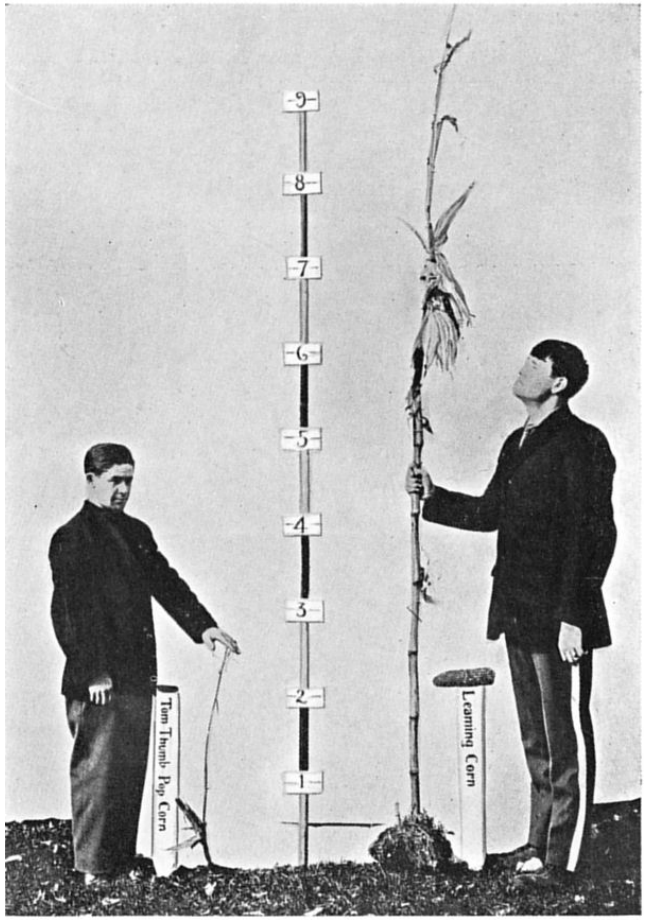
Mean Heritability of ADHD



Faraone SV, et al. *Biol Psychiatry*. 2005;57(11)1313-1323.

Heritability Facts

- Consensus estimates (>30 twin studies): **heritability of ADHD is 70–80%** throughout the lifespan[1,2]
- Environmental risks do not increase likelihood of ADHD between siblings (it is largely genetic) [3]
- Family and twin studies: genetic overlap between **ADHD and other conditions**[4]
  - ASPD[5], cognitive impairment[6], ASD[7,8], schizophrenia[9], bipolar[10], and MDD[11]



1. Franke, B. et al. Mol. Psychiatry 17, 960–987 (2012). 2. Faraone, S. V. et al. Biol. Psychiatry 57, 1313–1323 (2005). 3. Burt, S. A. Psychol. Bull. 135, 608–637 (2009). 5. Christiansen, H. et al. J. Neural Transm. (Vienna) 115, 163–175 (2008).6. Kuntsi, J. et al. J. Abnorm. Child Psychol. 42, 127–136 (2014). 7. Rommelse, N. N., Franke, B., Geurts, H. M., et al. Eur. Child Adolesc. Psychiatry 19, 281–295 (2010). 8. Ghirardi, L. et al. Mol. Psychiatry. 23, 257–262 (2018). 9. Larsson, H. et al. British J. Psychiatry 203, 103–106 (2013). 10. Faraone, S. V., Biederman, J. & Wozniak, J. Am. J. Psychiatry 169, 1256–1266 (2012). 11. Faraone, S. V. & Biederman, J. J. Nerv. Ment. Dis. 185, 533–541 (1997).

Big Data analysis or Mega-analytics

- The statistical handling of **enormous and complex data sets** furthers our understanding of the **heritability of common brain disorders** (The Brainstorm Consortium 2019).
- Taylor et al used the large population based cohort of the Child and Adolescent Twin Study in Sweden (CATSS)
  - Further validated the view that ADHD is **principally a neurodevelopmental disorder**
  - Characterized by a **potential persistence of profound cognitive, behavioral, and psychosocial impairments across the entire lifecycle.**

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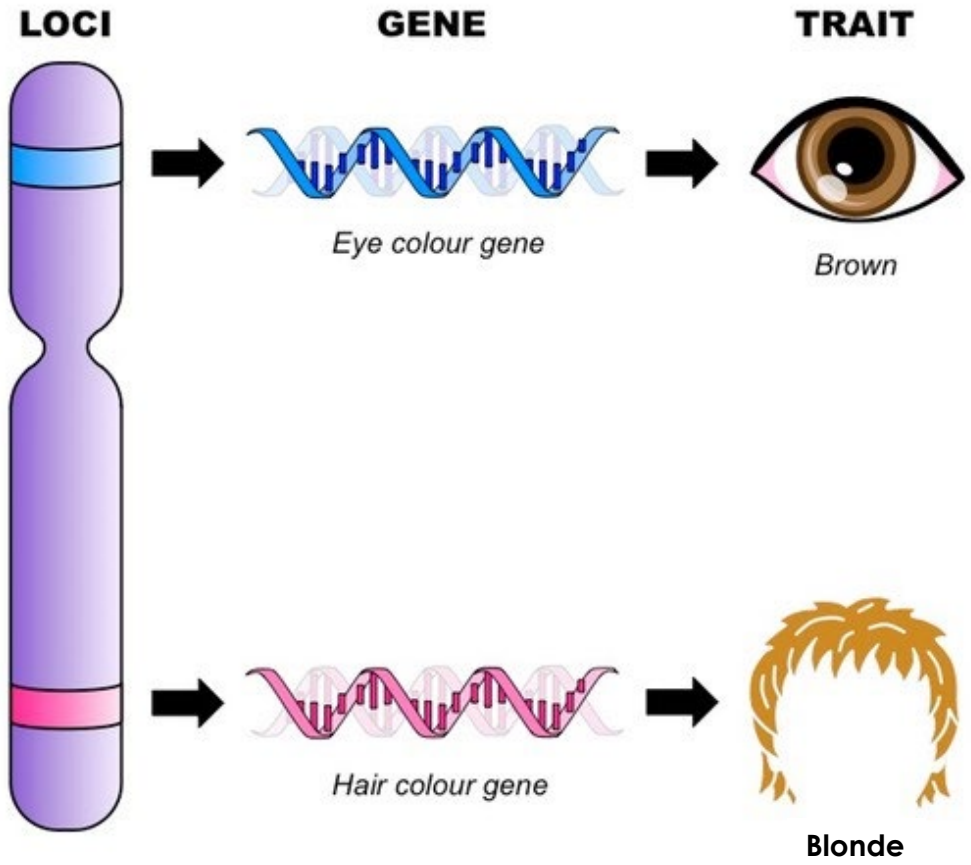
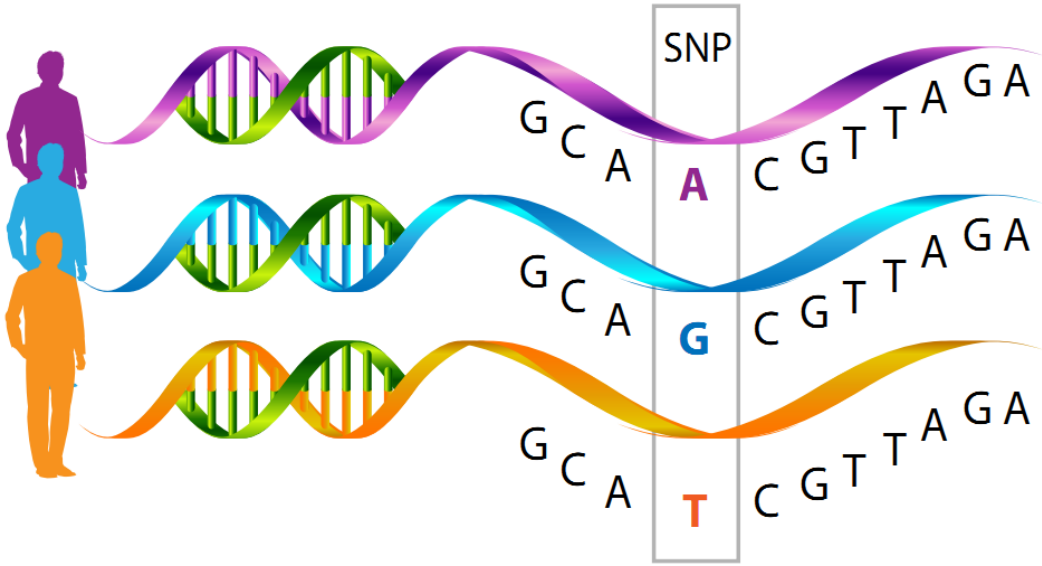
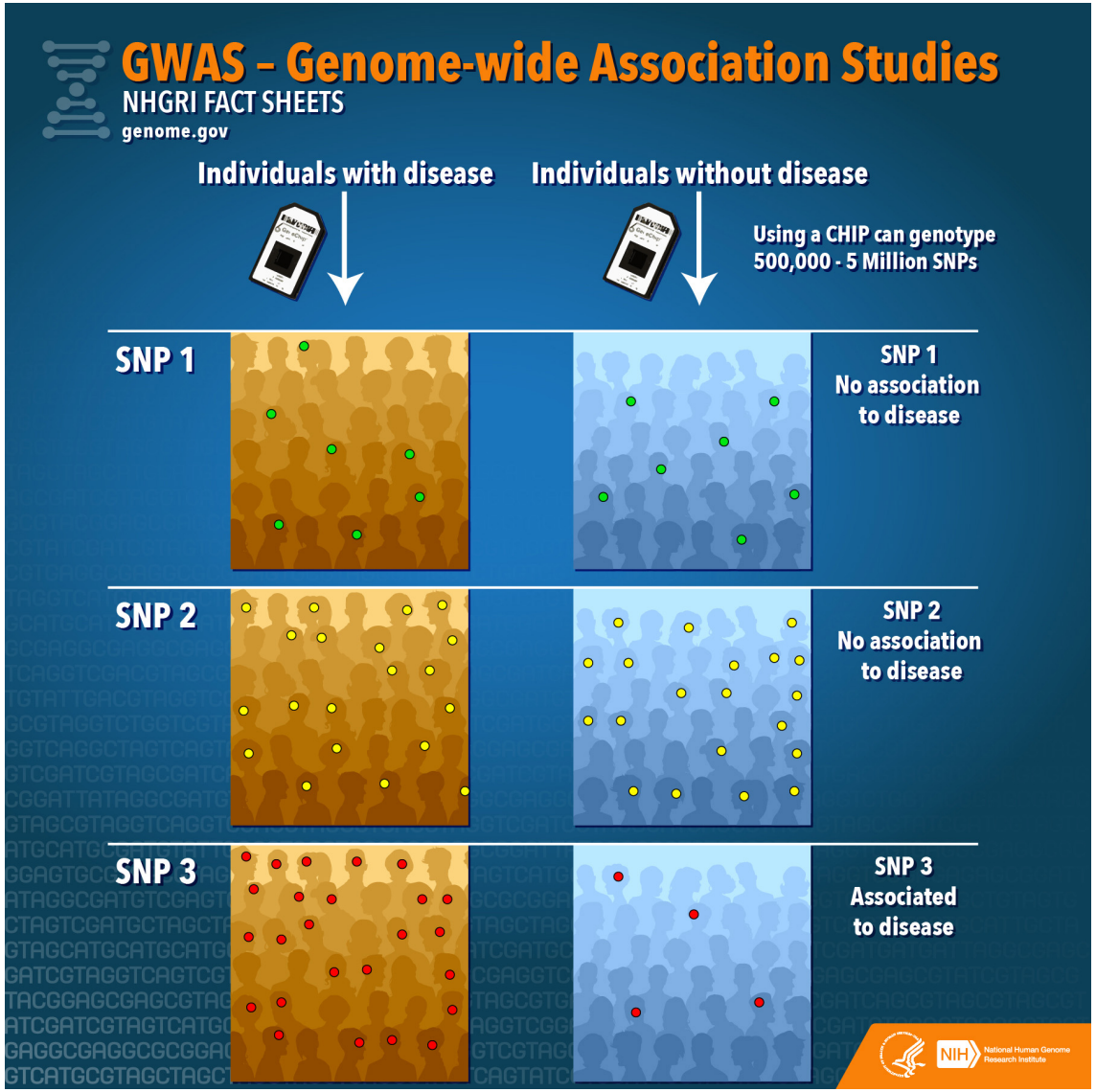
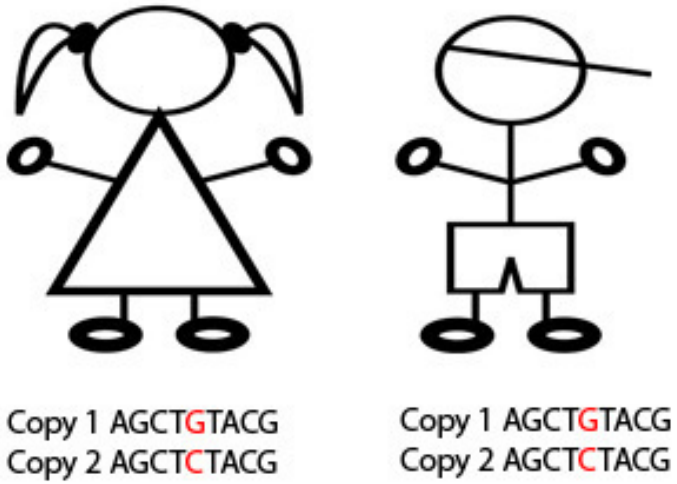


Single nucleotide polymorphisms




GWAS – Genome-wide Association Studies
NHGRI FACT SHEETS
genome.gov
Individuals with disease
Individuals without disease
Using a CHIP can genotype
500,000 - 5 Million SNPs
SNP 1
SNP 1
No association
to disease
SNP 2
SNP 2
No association
to disease
SNP 3
SNP 3
Associated
to disease
NIH
National Human Genome
Research Institute

ADHD Genome-wide Association Study



- **Genome-wide meta-analysis** published in January, 2019
- An international collaboration that **analyzed ~10 million positions (loci)** of the genome of **55,374 individuals** (20,183 with ADHD and 35,191 controls) from different countries in Europe, the US, Canada and China

Nature Genetics VOL 51 JANUARY 2019 63–75

Genome-wide Association Studies (GWASs): identified common DNA variants that increase the risk of ADHD

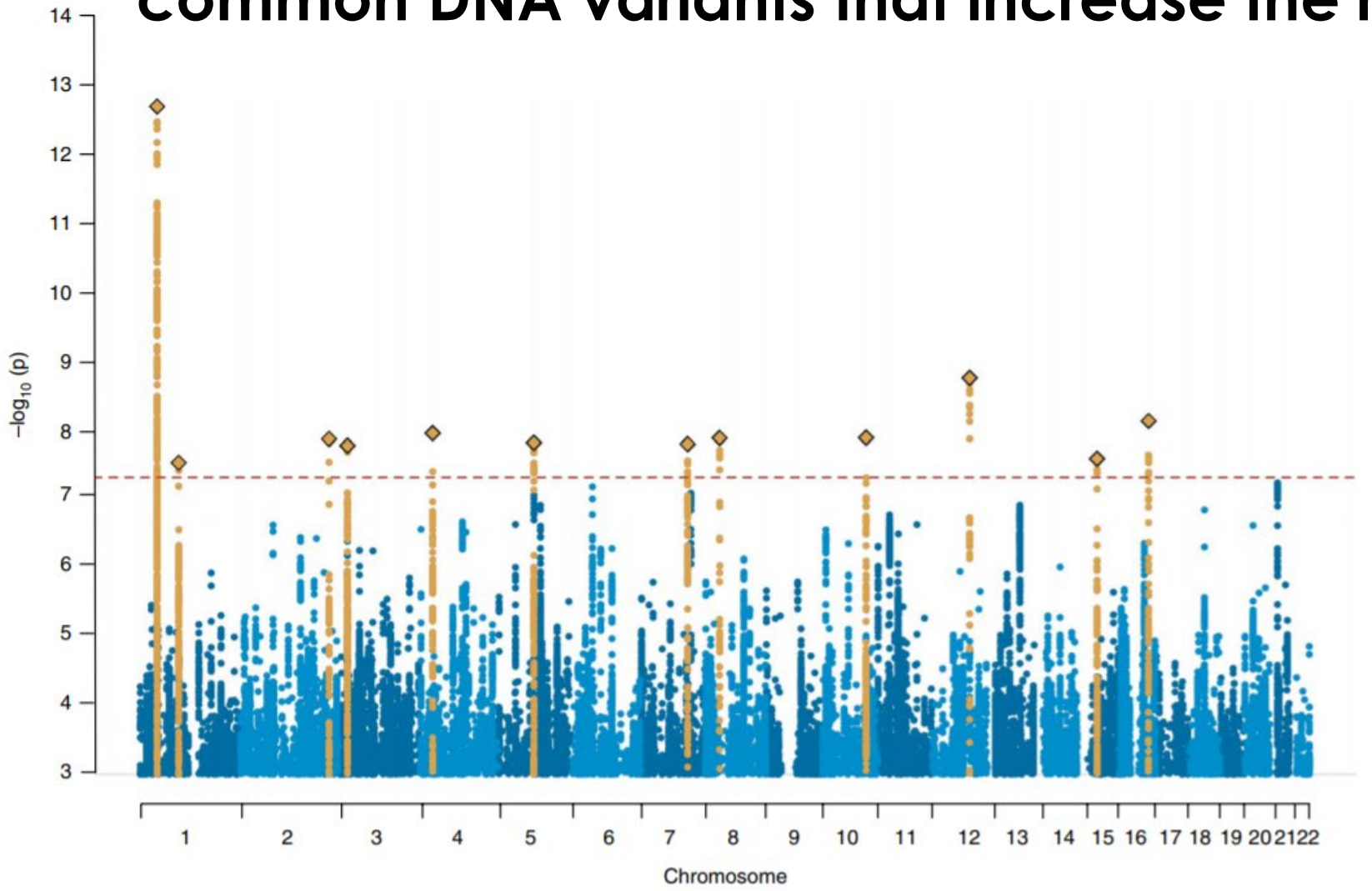


Fig. 1 | Manhattan plot of the results from the GWAS meta-analysis of ADHD. The index variants in the 12 genome-wide significant loci are highlighted as an orange diamond. Index variants located with a distance <400 kb are considered as one locus. The *y* axis represents −log(two-sided *P* values) for association of variants with ADHD, from meta-analysis using an inverse-variance weighted fixed effects model and a total sample size of 20,183 individuals with ADHD and 35,191 controls. The horizontal red line represents the threshold for genome-wide significance.

Identified **twelve specific fragments** of DNA related to the **vulnerability** of ADHD

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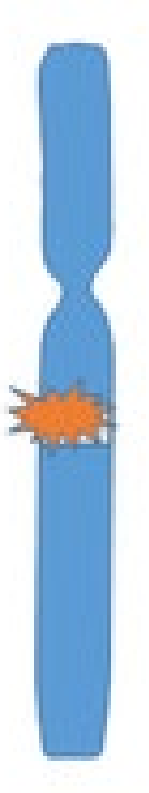
Key ADHD "Fragments" (loci)



- **FOXP2**- one of the most studied genes regarding **language development**
  - Encodes a protein required for synaptogenesis and learning.
- **DUSP6**- gene involved in the control of **dopaminergic neurotransmission**, the target of the most common ADHD pharmacological treatments.
- **SEMA6D**- this gene is expressed in the brain during the embryonic development: likely role in the creation of **neural branches.**

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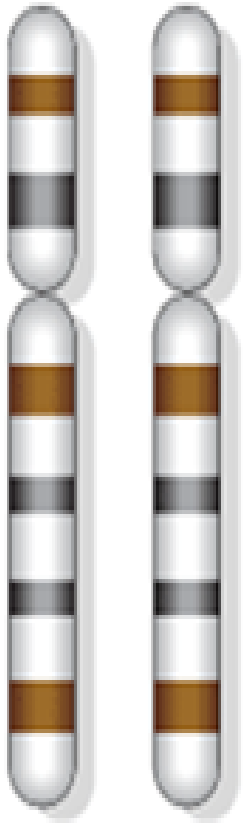
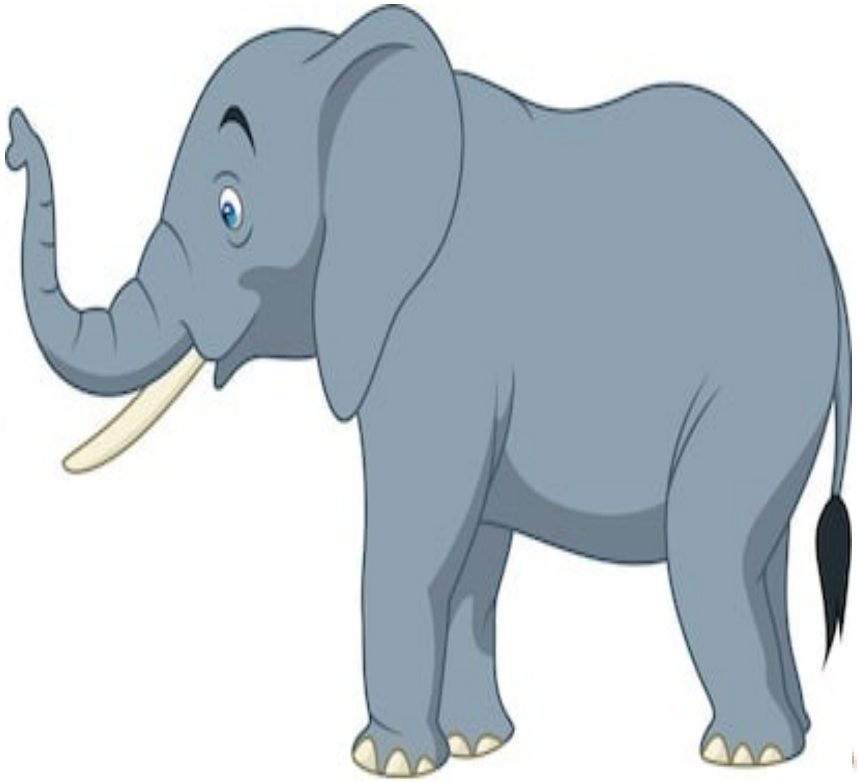
Genotype Vs. Phenotype

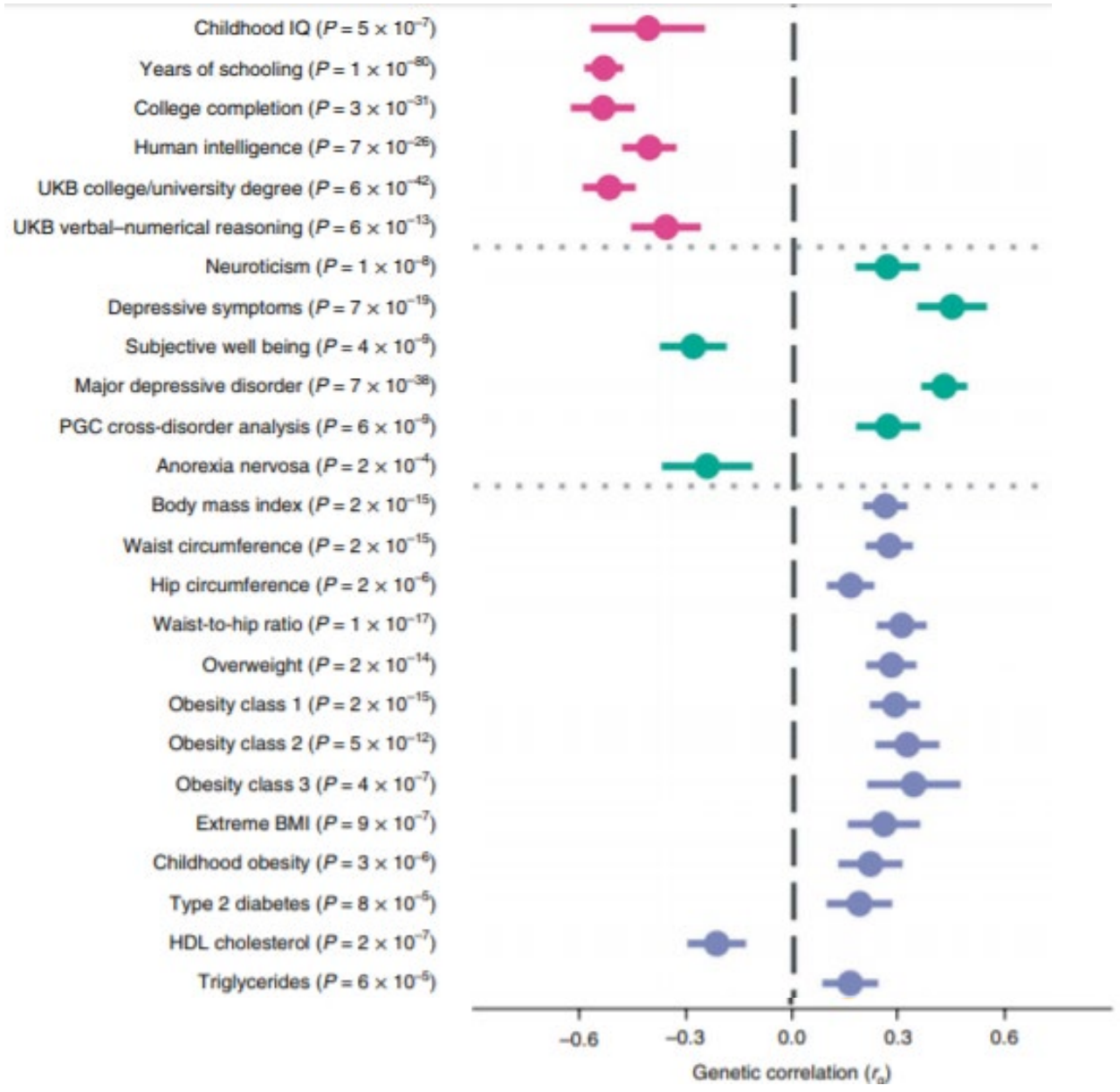


GENOTYPE



PHENOTYPE

Genetic correlations of ADHD with other phenotypes



ADHD positively correlated with:

- Major depression
- Obesity/ BMI
- Childhood obesity
- Type II diabetes
- Triglycerides

And negatively correlated with:

- Subjective wellbeing
- Childhood IQ
- Years of schooling
- University completion

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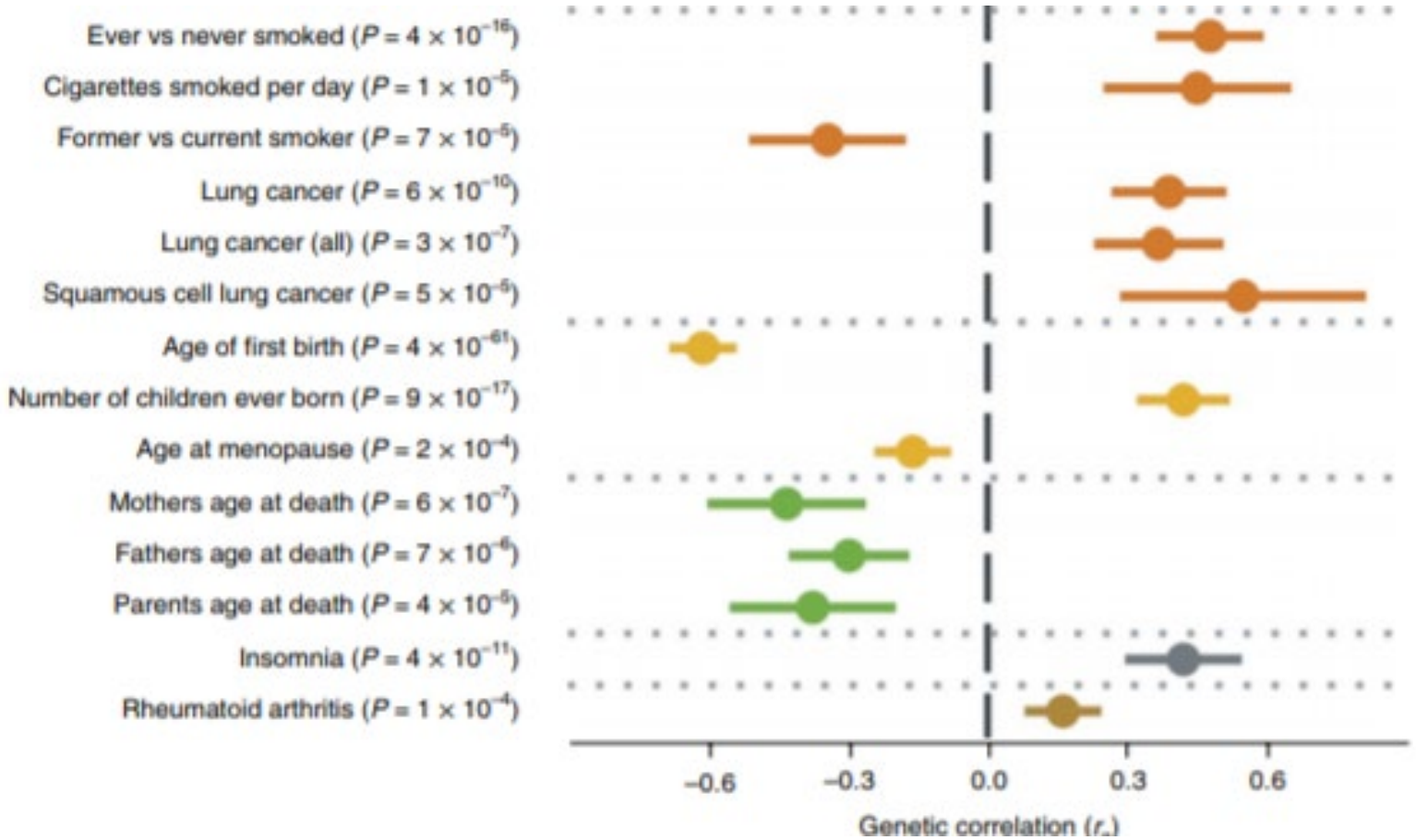
Genetic correlations of ADHD with other phenotypes



ADHD positively correlated with:

- Ever having smoked
- Number of cigarettes/day
- Lung cancer
- Number of children ever born

And negatively correlated with:

- Age of first birth

Nature Genetics VOL 51 JANUARY 2019 63–75 |

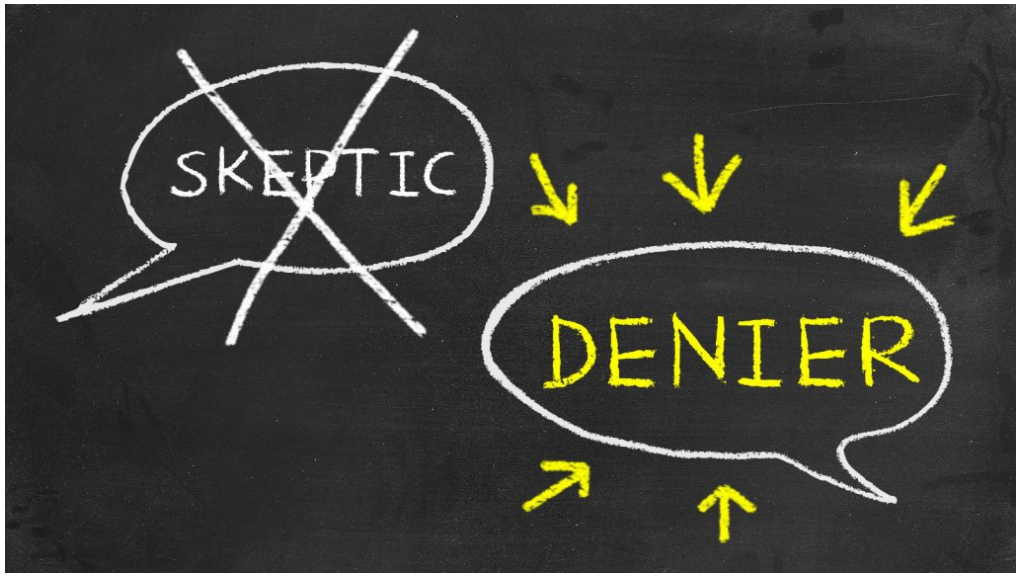
Clinical Correlates of Genetic Research

Phenotype (what we see)	Genotype
Poor educational outcomes	✓
MDD/ other psychiatric comorbidities	✓
Smoking/ obesity/ DMII	✓

The genetic landscape of ADHD

- "This study reinforces, against deniers, the idea that **ADHD is a disorder with a solid biological basis**, where genetics mean a lot."

Dr. Bru Cormand



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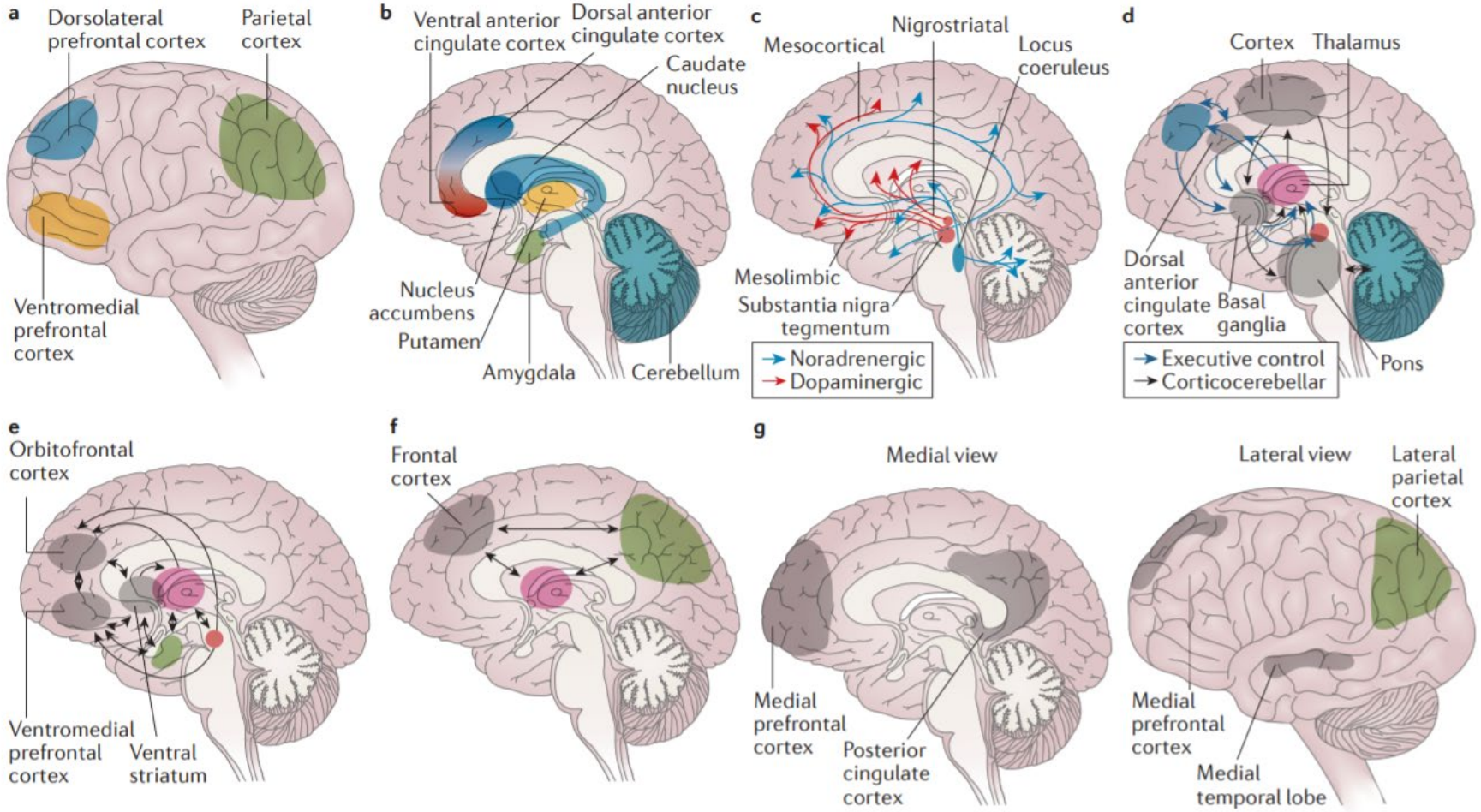
Brain dysfunction in ADHD

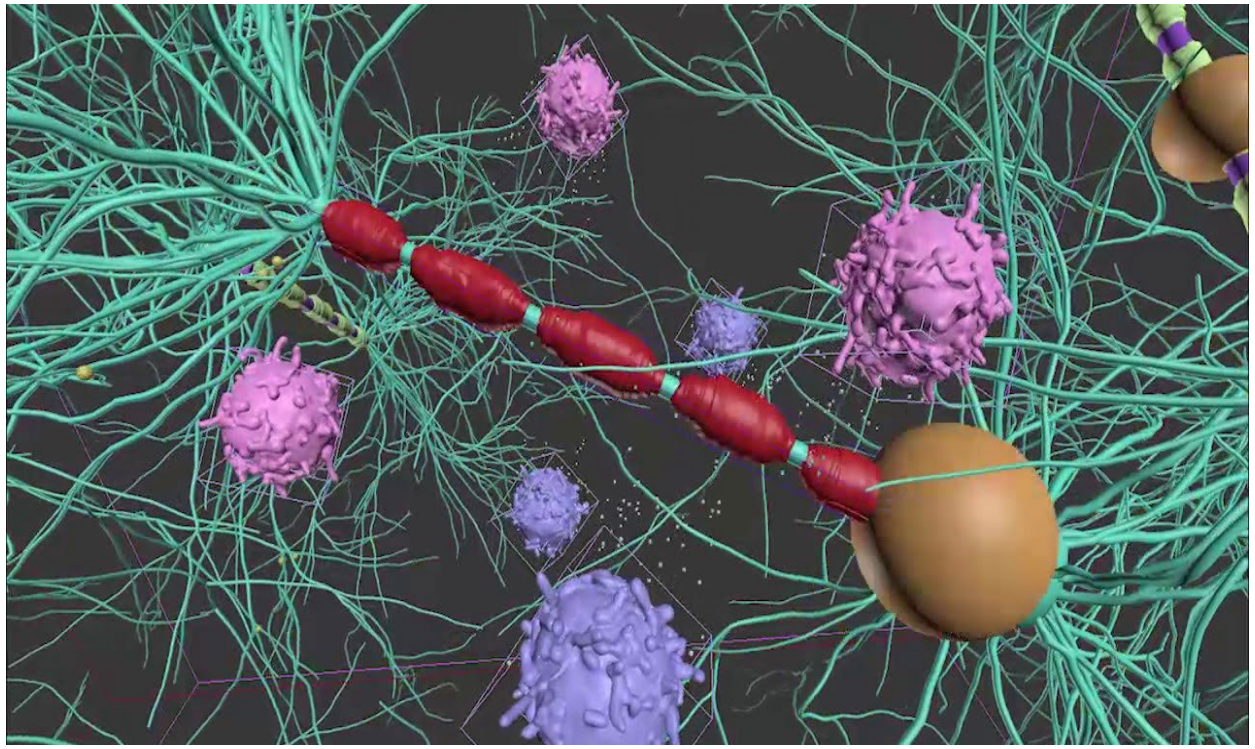


a. PFC- working memory, executive functioning, attention
b. Cingulate- executive control
c. Abnormal NTs
d. Executive dysfunction
e. Abnormal reward system
f. Impaired alert system
g. Default mode network

NATURE REVIEWS DISEASE PRIMERS VOLUME 1 2015

Myelin Dysfunction

- **Delayed and/or dysregulated myelination** may underpin developmental delay and explain persistence of ADHD into adulthood
- It represents pathophysiologic mechanisms **amenable to therapeutic intervention**.



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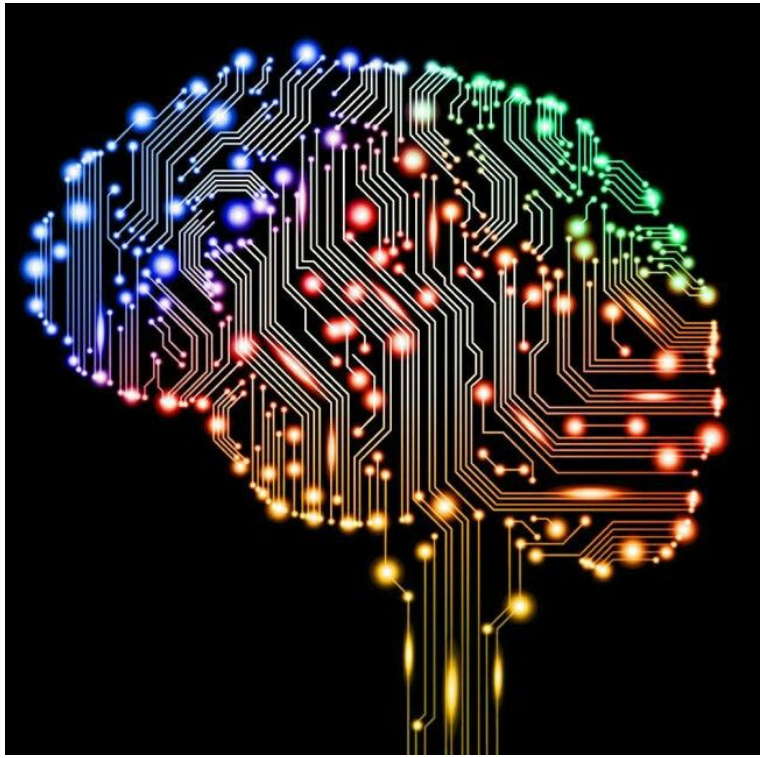
Why does ADHD persist into adulthood?

- ADHD is a **circuitopathy** (delayed development of fronto-striatal and limbic circuits)
  - Myelination begins early in 3rd trimester, progresses in infancy and continues through adolescence
  - Oligodendrocytes produce the myelin sheath: facilitates the growth of **neuron projections**
  - Alterations in **neuroplasticity** is another cause of **disrupted brain maturation** and the **persistence of destructive cognitive and emotional impairments**



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fMRI demonstrates ADHD changes over time

- **Symptom recovery** in ADHD was related to **stronger integration of prefrontal regions in the executive control network**.
- **Higher connectivity** within frontal executive control network was related to **decreases in ADHD symptoms.**
- The pattern and strength of resting state functional connectivity (RSFC) across remittent ADHD, persistent ADHD, and healthy controls potentially reflects the presence of **compensatory neural mechanisms that aid symptomatic remission.**

Cortex. 2015 Dec;73:62-72

Do we really need to treat ADHD?

Treatment helps Robert to hit the pause button

- Medication allows patients to pause and engage their executive brain
  - Forward thinking
  - Critical thinking
- Parenting, social reinforcement, and continued brain development help cultivate compensatory mechanisms

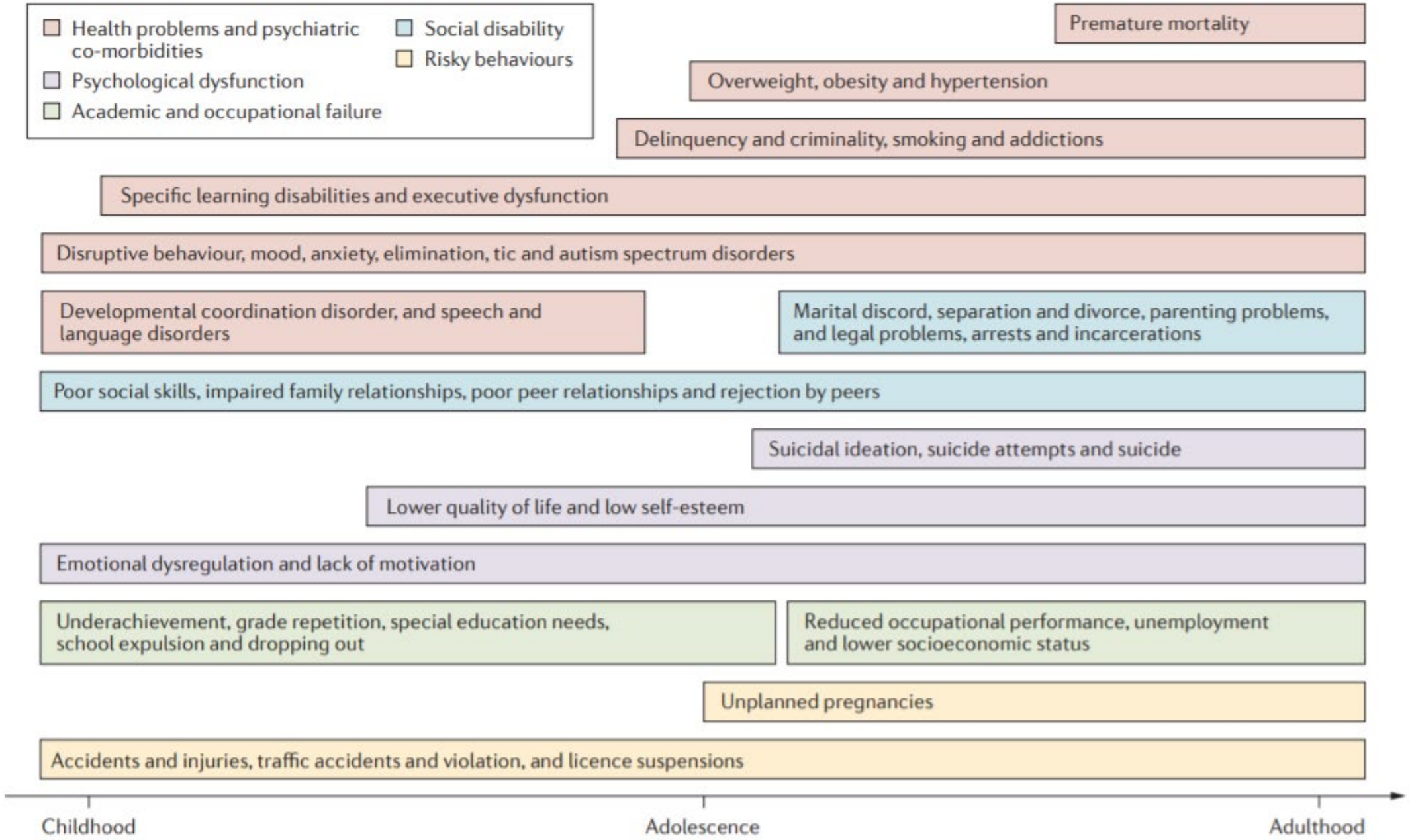
Long-term stimulant use: is it safe? Helpful?

- Stimulant treatment **enhanced orbitofrontal-striatal white matter connectivity**, and reinforced the importance of the orbitofrontal cortex and its connections in ADHD[1].
- Therapeutic oral doses of stimulants **decrease alterations in brain structure and function** in subjects with ADHD relative to unmedicated subjects and controls. These medication-associated brain effects parallel, and may underlie, the well-established clinical benefits[2].
- Preliminary evidence suggests that long-term stimulant medication use may be associated with **more normal activation** in the **right caudate** during the attention domain[3]
- Large, well matched long-term study found no evidence that stimulant treatment has a beneficial or detrimental effect on the long-term course of ADHD symptoms, social–emotional functioning, motor control, timing or verbal working memory[4].
  - Prospective longitudinal study design showed that clinical improvement of ADHD symptoms over the course of adolescence occurs in those who are or are not treated with stimulants during that time.

1. Eur Neuropsychopharmacol. 2016 Apr;26(4):674-83; 2. *J Clin Psychiatry 2013;74(9):902–917;* 3. JAMA Psychiatry. 2013 Feb;70(2):185-98. 4. Psychol Med. 2019 Jan;49(2):217-223.

What are the potential negative outcomes of untreated ADHD?

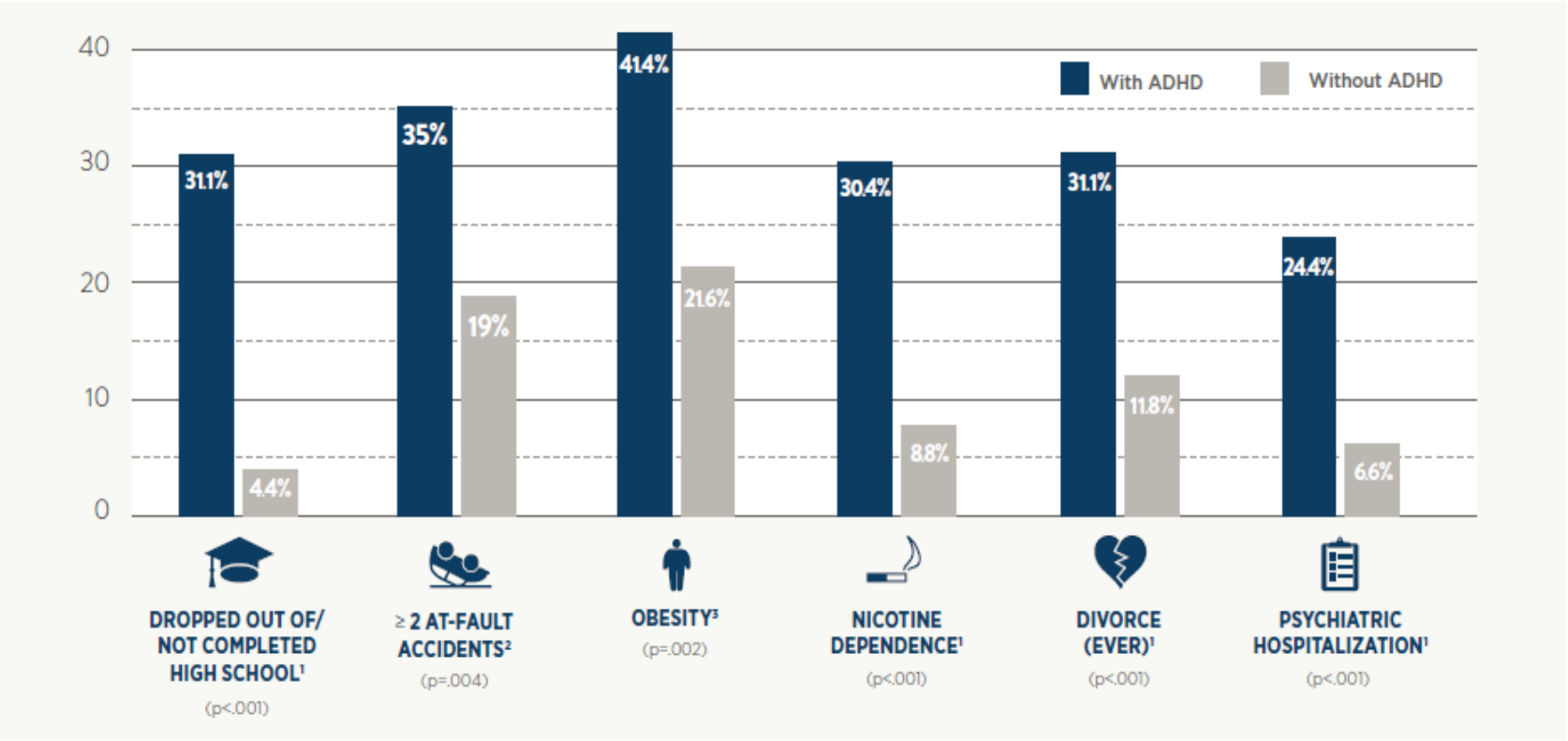
Quality of life and ADHD



NATURE REVIEWS DISEASE PRIMERS VOLUME 1 2015

Greater risk observed in almost every aspect of life:

In a **33-year follow-up**, children with ADHD were found to have a greater risk of poor long-term outcomes as adults in almost every aspect of life compared to their non-ADHD counterparts.*[1,2]



- 6- to 12-year-old boys referred between 1970-78.
- 135 probands in follow-up (mean age 41 years)

1. Klein RG, et al. *Arch Gen Psychiatry* 2012;69:1295; 2. Cortese S, et al. *Pediatrics* 2013:131:e1731

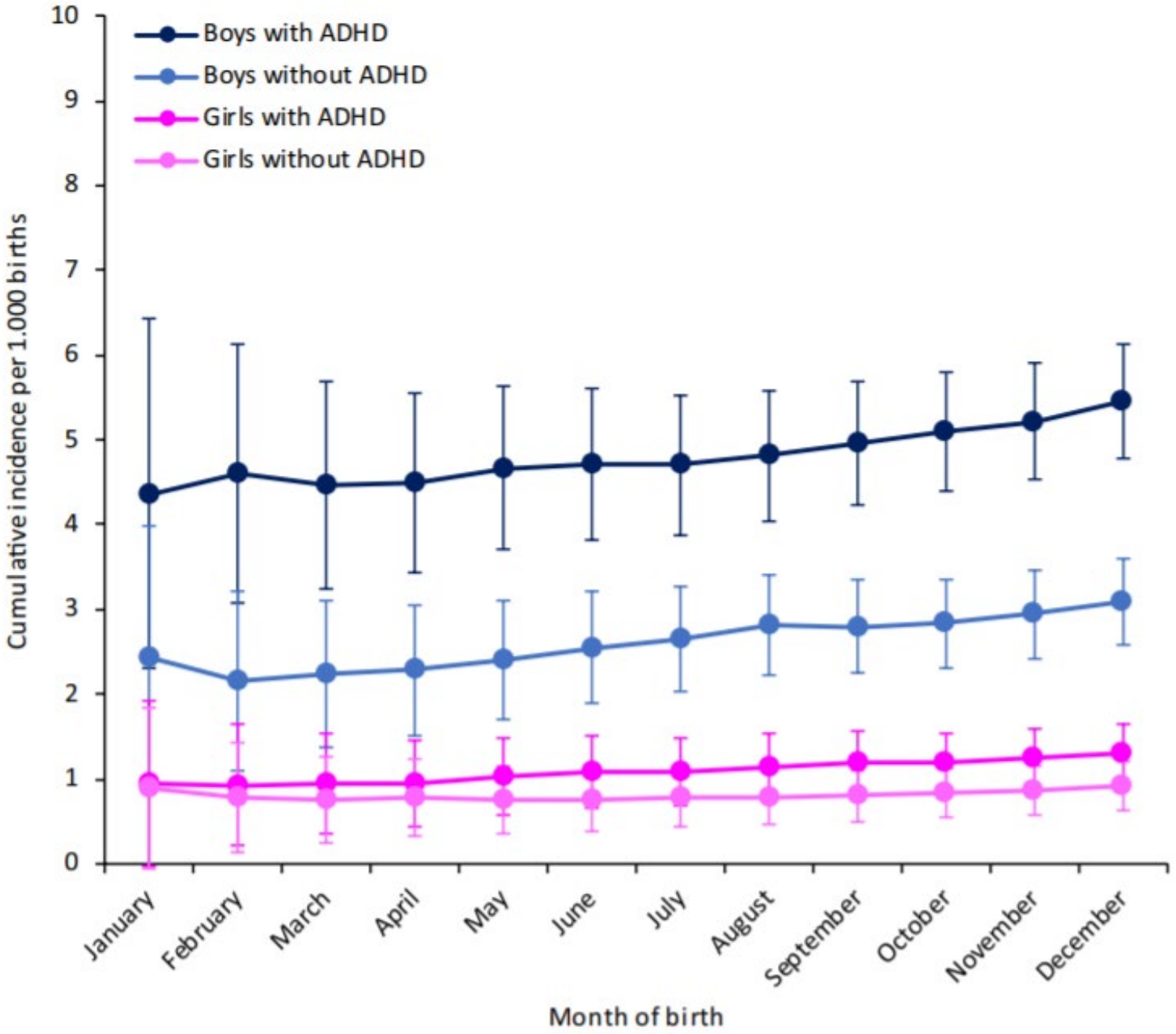
This leaves us with the question: Is the risk of not treating greater than the risk of treating?

Is ADHD caused by starting school too soon?

DSM-5 ADHD Diagnosis

- Requires evidence of a persistent pattern of **cross-situational impairment**
  - Functional difficulties attributable to ADHD at home and school.
- Those who diagnose and treat ADHD **depend on reports from teachers** re child's behaviour, developmental capabilities, and performance.
- Standardized questionnaires evaluate the child's **compared with their peers.**
  - Vanderbilt teacher rating scale: **"Each rating should be considered in the context of what is appropriate for the age of the child you are rating"**.
  - Despite this, teachers often rate a child compared to others at the same grade level, rather than age-level

Lancet Psychiatry. 2017 Nov;4(11):825-826.



European Child & Adolescent Psychiatry (2018) 27:1171–1180

Cumulative incidence of ADHD and other psychiatric disorders:

- 4070 children
- 85% male
- 70% met ADHD diagnostic criteria

The association between younger relative school age and ADHD diagnosis

- The cumulative incidence of **clinically diagnosed ADHD or other developmental disorders** is greater among children **within the school year**
  - The strength of the association is greater for **children born during September–December**[1].
  - This association is **independent of type and severity of ADHD**, presence of comorbidities, and medication at the end of the diagnostic assessment.
  - The association is **not exclusive to ADHD**: observed for other developmental disorders in children without ADHD.
- Consistent with other large studies[2]

1. European Child & Adolescent Psychiatry (2018) 27:1171–1180; 2. Sayal K, Chudal R, et al (2017) Lancet Psychiatry 4:868–875

Why does school age matter?

- Younger children are less mature in terms of **self-regulation**.
  - Relatively young children struggle to meet the **classroom behavioral expectations** compared to peers[1]
  - Teachers are **more likely to raise concerns** about these children to their parents, which could lead parents to seek an assessment[1]
- Early access to school may make a **latent disorder apparent**, even though it would have appeared anyway a year later[2]
  - In this context, the need to **refer and diagnose** mental disorders early and **treat appropriately** is well known, regardless of patient age[1]

1. Efron D (2017) Lancet Psychiatry 4:825–826; 2. Price A, Allen K, Ukoumunne OC, Hayes R, Ford T (2017) Child Care Healthh Dev 43:891–898.

Immature Brain Hypothesis

- The **relative age effect** was affected by **a child's actual age**
  - Relative age had a greater effect on clinical diagnosis in **younger children (age 6-9) attending school**.[1]
  - The effect tends to decline with age supporting the "immaturity hypothesis" of ADHD[2]
- Hypothesis supported by many neuroanatomical[3] and functional studies[4]
  - Children with ADHD show **relative cortical thinning in regions important for attentional control.**[3]
  - **Worse ADHD outcomes** associated with **"fixed" thinning of the left medial PFC**, compromising anterior attentional network and hampering clinical improvement.
  - **Right parietal cortex thickness normalized** in children with a **better outcome** may represent compensatory cortical change.

1. European Child & Adolescent Psychiatry (2018) 27:1171–1180; 2. Halldner L, Tillander A, Lundholm C et al (2014) J Child Psychol Psychiatry 55:897–904; 3. Shaw P, Lerch J, Greenstein D et al (2006) Arch Gen Psychiatry 63:540–549, 4. Marcos-Vidal L, Martínez-García M, Pretus C et al (2018) Hum Brain Mapp. https://doi.org/10.1002/hbm.24013].

Implications of over-diagnosis

- Many kids diagnosed with ADHD receive medication- often for years
- If ADHD dx is to a great extent related to immaturity, many children would be treated unnecessarily
  - **Response to treatment is non-specific** (most kids will attend better), thus medication might appear effective and be continued
  - Exposure to **side-effects**
  - **Missing another explanation**: a learning disorder, abuse, psychiatric comorbidity
  - **Stigmatization** by teachers, other parents, classmates
- **In practice, clinicians need to ensure they assess attentional capacity and impulse control relative to the child's chronological age and overall developmental status, rather than age for year level.**

Lancet Psychiatry. 2017 Nov;4(11):825-826.

What the heck do we do then?

- Your clinical experience is essential!
- Consider the child's age, not their grade
- Consider all functional domains
- Assess parents (ASRS) and siblings

Are ADHD Treatments Safe?

Are ADHD Treatments Safe?

- Hundreds of clinical studies have reported that ADHD drugs are generally well tolerated and that most of their adverse effects are mild and/or temporary [1-4].
- Several meta-analyses have addressed the safety of amphetamine, methylphenidate, atomoxetine, and alpha2-agonists in children and adults with ADHD [5-10].

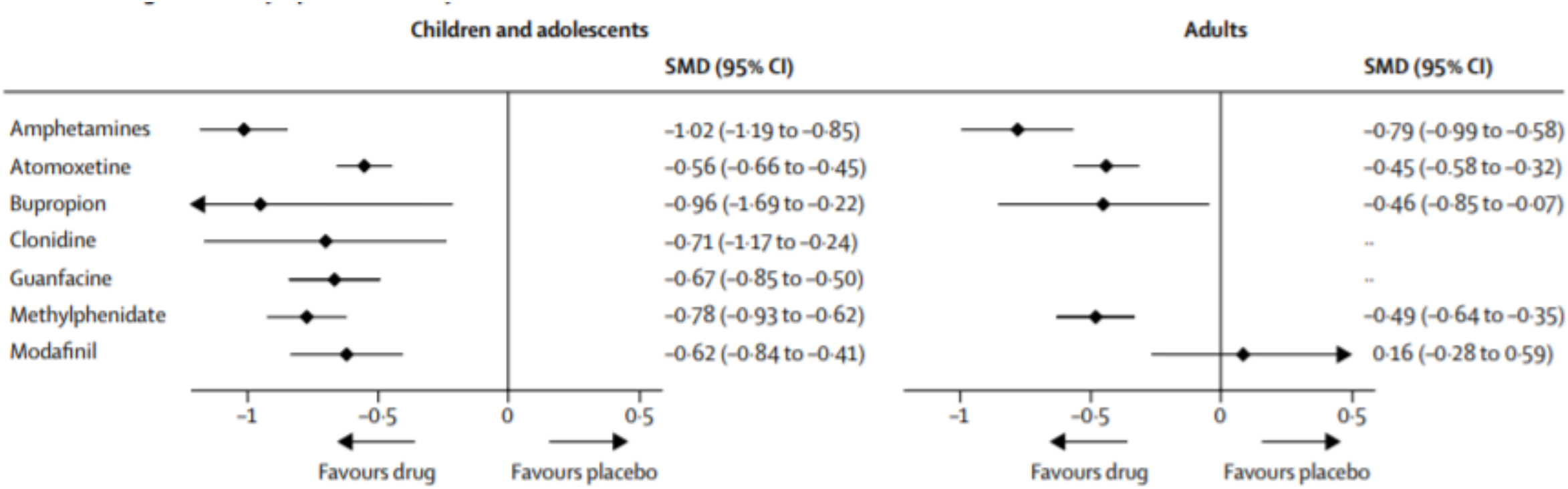
1 Aagaard L, Hansen EH. Neuropsychiatr Dis Treat. 2011;7:729–744. 2. Cortese S, Holtmann M, Banaschewski T, et al. J Child Psychol Psychiatry. 2013;54:227–246. 3. Graham J, Coghill D. CNS Drugs. 2008;22:213–237. 4. Graham J, Banaschewski T, Buitelaar J, et al. Eur Child Adolesc Psychiatry. 2011;20:17–37 5. Aagaard L, Hansen EH. BMC Res Notes. 2010;3:176. 6. Cheng JY, Chen RY, Ko JS, et al. Psychopharmacology (Berl). 2007;194:197–209. 7. Hirota T, Schwartz S, Correll CU. J Am Acad Child Adolesc Psychiatry. 2014;53:153–173. 8. Ruggiero S, Clavenna A, Reale L, et al. Eur Neuropsychopharmacol. 2014;24:1578– 1590. 9. Schachter HM, Pham B, King J, et al. Cmaj. 2001;165:1475–1488. 10. Schwartz S, Correll CU. J Am Acad Child Adolesc Psychiatry. 2014;53:174–187. Ann Pharmacother. 2019 Feb;53(2):121-133

2018 Lancet Meta-analysis

- "To the best of our knowledge, our network meta-analysis represents **the most comprehensive comparative synthesis to date on the efficacy and tolerability of medications** for children, adolescents, and adults with ADHD."
- Addressed limitations of previous network meta-analyses: all age groups and **included published and unpublished** material.
- 133 studies:14346 children and adolescents and 10296 adults were included.

Lancet Psychiatry, The, 2018-09-01, Volume 5, Issue 9, Pages 727-738

Clinician rates ADHD symptom scores



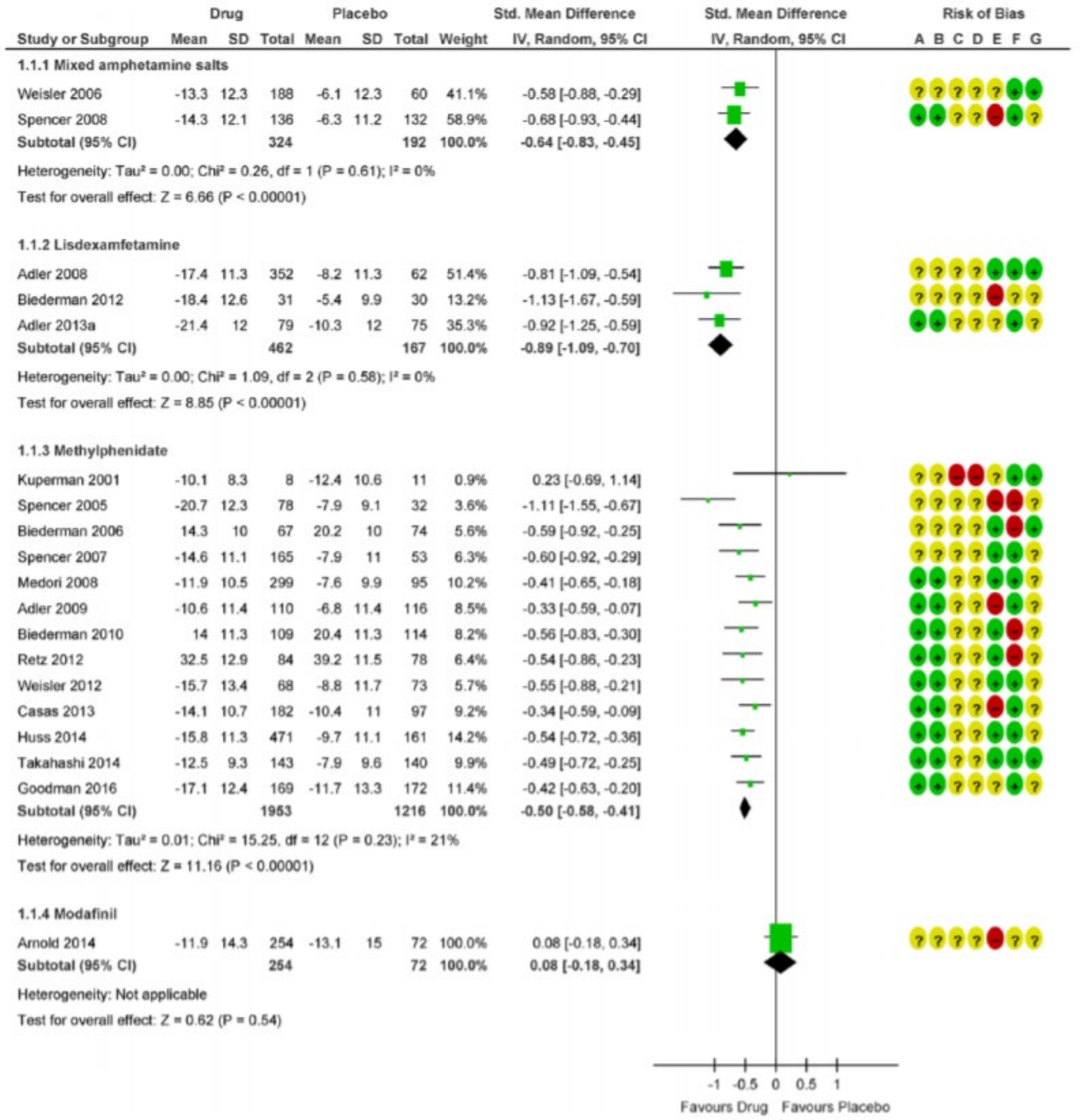
Parents' ratings of their child's ADHD core symptoms and adults' self-ratings of their own ADHD core symptoms, with respect to efficacy of active drugs versus placebo, were similar to clinicians' ratings

Lancet Psychiatry, The, 2018-09-01, Volume 5, Issue 9, 727-738

“All drugs were superior to placebo”

- **With respect to ADHD core symptoms** rated by clinicians in children and adolescents, all drugs were superior to placebo
  - In adults, **amphetamines, methylphenidate, bupropion, and atomoxetine** were superior to placebo.
  - In children, adolescents, and adults, **amphetamines were significantly superior to modafinil, atomoxetine, and methylphenidate.**
- With respect to tolerability:
  - in children and adolescents, **only guanfacine and amphetamines were less well tolerated than placebo**
  - In adults, **modafinil, amphetamines, methylphenidate, and atomoxetine were inferior to placebo.**

Lancet Psychiatry, The, 2018-09-01, Volume 5, Issue 9, 727-738



The authors received no financial support for the research, authorship, and/or publication of this article.

Ann Pharmacother.2019 Feb;53(2):121-133

Table 1 Reported effect sizes (standardised mean difference) from meta-analysis for studies of treatment efficacy for ADHD core symptoms in childhood and adulthood.

Treatment and age-group	Treatment type	Effect size	Reference
Childhood: pharmacological treatment	Methylphenidate	0.72	Faraone and Buitelaar (2010)
	Amphetamines	0.99	Faraone and Buitelaar (2010)
	Atomoxetine	0.64	Schwartz and Correll (2014)
	Guanfacine	0.63	Hirota et al. (2014)
	Clonidine	0.44	Hirota et al. (2014)
Childhood: non-pharmacological treatment	Omega-3	0.16	Sonuga-Barke et al. (2013)
	Diets	0.42	Sonuga-Barke et al. (2013)
	Neurofeedback	0.21	Hodgson et al. (2014)
	Multimodal psychosocial	0.09	Hodgson et al. (2014)
	Working memory training	−0.02−0.20	Cortese et al. (2015); Hodgson et al. (2014)
	Behaviour modification	−0.03	Hodgson et al. (2014)
	Parent training	−0.51	Hodgson et al. (2014)
	Self-monitoring	−5.91	Hodgson et al. (2014)
	School-based	−0.26−0.16	Hodgson et al. (2014); Richardson et al. (2015)
Adulthood: pharmacological treatment	Methylphenidate	0.42−0.72	Castells et al. (2011b; Epstein et al. (2014
	Amphetamines	0.72−1.07	Castells et al. (2011a); Fridman et al. (2015)
	Atomoxetine	0.38−0.60	Asherson et al. (2014); Fridman et al. (2015)
Adulthood: non-pharmacological treatment	Cognitive-behavioural therapy	0.43−1.0	Jensen et al. (2016); Knouse et al. (2017); Young et al. (2016)
	Mindfulness-based therapies	0.53−0.66	Cairncross and Miller (2016)

What does $15 million buy BC physicians?

Challenges Facing Psychiatry in BC

- Loss of public confidence because:
  - Abuse of mentally ill patients
  - Backlash against psychiatrists who speak out
  - Lack of access to psychiatric care and gold standard treatments
- Lack of public recognition of the essential nature of rational psychopharmacology
  - Failure to teach adequate psychopharmacology skills
- Lack of access to Health Canada approved psychiatric treatments through BC Pharmacare
  - Therapeutics Initiative

What is the Therapeutics Initiative?

- Claims to provide **unbiased "advice"** about **"evidence-based drug therapy"**
- Submitted for review **"to 60 experts and primary care physicians** in order to correct inaccuracies and to ensure that the information is concise and relevant to clinicians"
- Funded by the BC Ministry of Health through a grant to the University of British Columbia
  - **There are no psychiatrists on the TI**

therapeutics letter

January - February 2018

THERAPEUTICS INITIATIVE Evidence Based Drug Therapy

Stimulants for ADHD in children: Revisited

This Letter reviews our previous publications and research on this topic and explores whether our publications have led to a change in prescribing of stimulants to children in BC. Despite concerns, stimulant drug treatment of childhood attention-deficit/hyperactivity disorder (ADHD) has increased worldwide over the last two decades.[1] The optimal management of this behavioral condition remains unknown and this is reflected in the wide variation of stimulant treatment by country, jurisdiction, income, race and ethnicity.[1,2]

Children are particularly vulnerable to harms of long-term drug therapies and there should be a higher level

British Columbia birth month study

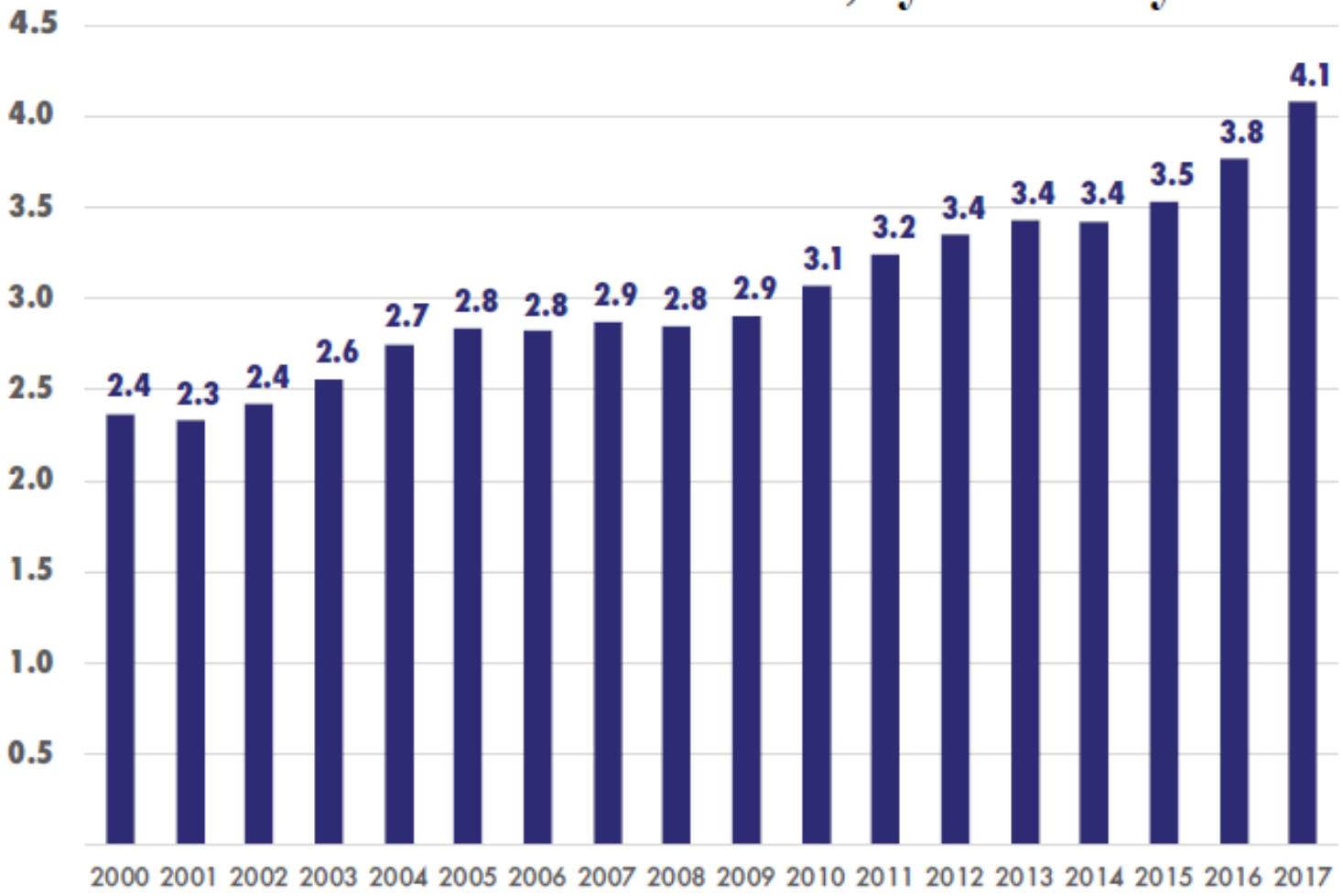
We undertook a study of the utilization of stimulant drugs by BC children 6 to 12 years of age between December 1st 1997 and November 30th 2008. This study found that boys were 41% more likely and girls 77% more likely to be prescribed

Jan-Feb 2018:
Stimulants for ADHD in children: Revisited

This TI conclusions:

- **Whether the benefits** of long-term CNS stimulants for ADHD in children **outweigh the harms** remains unknown.
- There is **convincing evidence** that a proportion of boys and girls treated with stimulants in BC and around the world are **simply the youngest in their class**.
- There is insufficient evidence to know whether our publications or research findings had an impact on the overall rate of stimulant drug prescribing in BC children.
- The **recent increase in CNS stimulant prescribing in BC is unexplained and concerning.**

Figure: Percent of 6-12 year old children receiving ADHD medications in BC, by calendar year



The Figure shows that the use of ADHD drugs in BC children between the ages of 6 to 12 grew between 2002 and 2005, remained steady for several years, then began to climb again in 2010. Over that 17 year period, the percent of BC children 6 to 12 years old receiving ADHD drugs increased from 2.4 to 4.1.

As an example of the TI's content…

- In the 2018 newsletter, they quoted their March 2009 Letter #73 entitled "Atomoxetine for ADHD in Children and Adolescents"

  We recommended: Without long-term RCTs showing that atomoxetine improves educational achievement, school completion, employment and future health and in view of the risk of serious harm, use of atomoxetine should be limited to exceptional cases intolerant to other ADHD drugs.

Let's break that paragraph down

- Use stimulants instead of atomoxetine- but don't use stimulants because there isn't enough data.
  - In 2008, they concluded that ***"better benefit and harm evidence is necessary before long-term stimulant treatment in children can be recommended."*** (also reprinted in 2018 newsletter)
- After a drug is developed, no one should use it (despite short and long-term safety data, post-marketing data and years of clinical use) until it is proven that treated children will:
  - Graduate with good marks
  - Get a good job
  - Be a healthy adult
- If that's the bar that needs to be cleared to use a drug, NO DRUG WOULD EVER BE PRESCRIBED.

Was the BC Birth Month Study Fake News?

- "We suggested that poor and disruptive behavior among the youngest children in a classroom might be driving rates of ADHD diagnosis and treatment."
- **"This strongly suggests that teachers, parents and physicians are medicalizing a social rather than a medical problem."**
- Impressively, their study was published in the high impact *Canadian Medical Association Journal*
  - "The study received global media attention and was reported in many media outlets both in Canada and abroad including **Time Magazine, The Globe and Mail, and ABC News."**

TI is not evidence-based

- Clear neurobiological underpinnings of ADHD
- ADHD is under-diagnosed and often untreated.
- **Misdiagnosis of some should not mean others should not be diagnosed and treated**
- This is especially true for **difficult to diagnose populations**- do we not diagnose kids who are the youngest in their grade because we might get is wrong?
  - We need to use more care, assess families, and assess kids based on their chronological AGE!
- Stimulant medications, and all psychiatric medications, already terrify our colleagues
  - **The TI inappropriately and unnecessarily deepens that fear**

- "The TI's **biased approach-cherry-picking data** without careful consideration or the involvement of actual doctors who treat these illnesses-**harms all British Columbians**."

Diane McIntosh (actual doctor who treats real patients who suffer from mental illnesses)


Thank you