



ADHD Across the Life Cycle: An Overview

Joseph Biederman, MD

Professor of Psychiatry

Harvard Medical School

Chief, Clinical and Research Programs in

Pediatric Psychopharmacology and Adult ADHD

Director, Bressler Program for Autism Spectrum Disorders

Trustees Endowed Chair in Pediatric Psychopharmacology

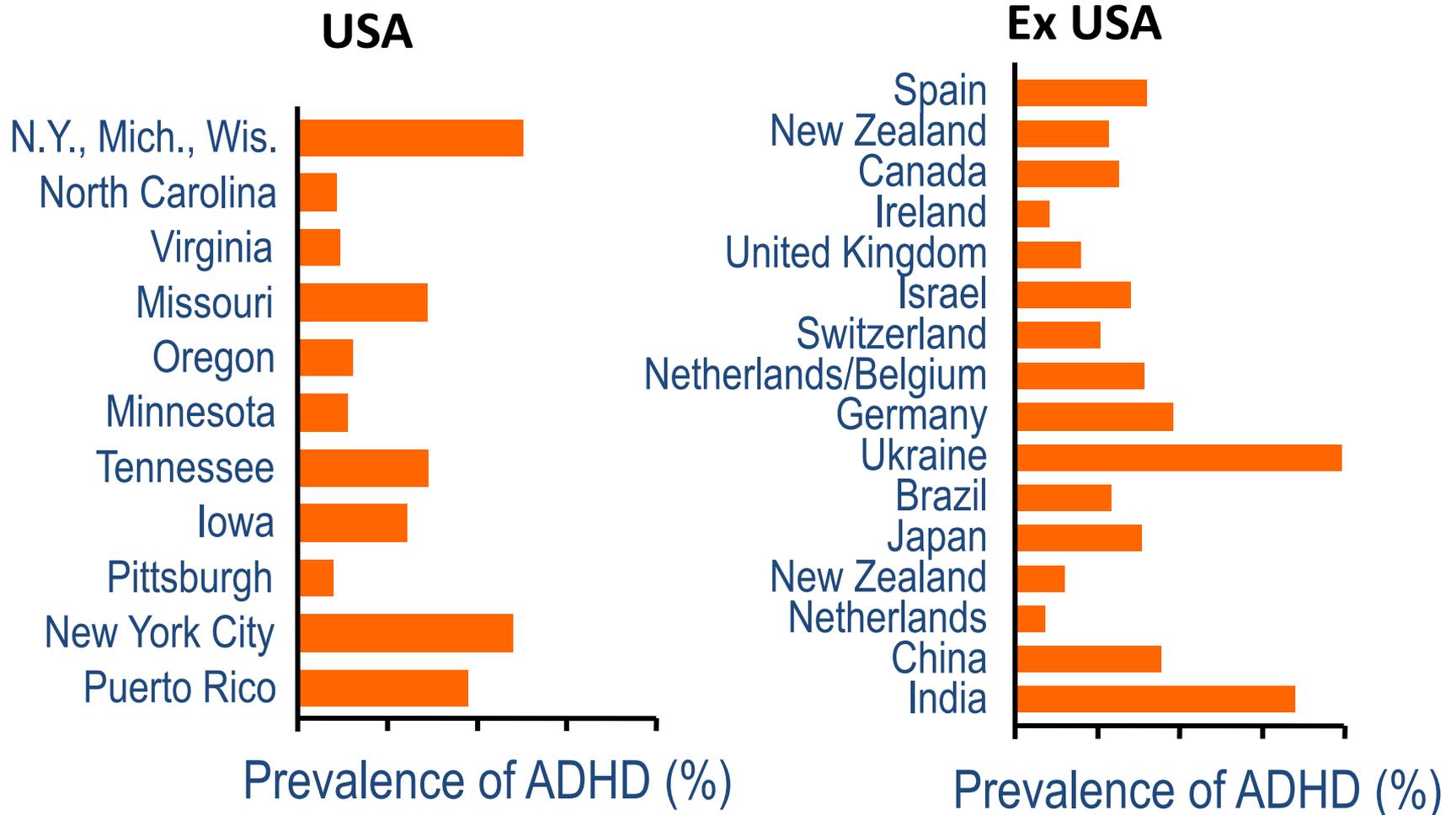
Massachusetts General Hospital

Disclosures 2019-2020

My spouse/partner and I have the following relevant financial relationships with commercial interests to disclose:

- *Research support:* Genentech, Headspace Inc., Lundbeck, Neurocentria Inc., Pfizer, Roche TCRC Inc., Shire Pharmaceuticals Inc., Sunovion, and Tris.
- *Consulting fees:* Akili, Avekshan LLC, Jazz Pharma, and Shire/Takeda
- *Scientific Advisory Board through MGH CTNI:* Supernus
- *Royalties paid to the Department of Psychiatry at MGH, for a copyrighted ADHD rating scale used for ADHD diagnoses:* Bracket Global, Ingenix, Prophase, Shire, Sunovion, and Theravance

Worldwide Prevalence of ADHD in Children



Key findings

Data from the National Health Interview Survey, 1998–2009

- The percentage of children ever diagnosed with attention deficit hyperactivity disorder (ADHD) increased from 7% to 9% from 1998–2000 through 2007–2009.

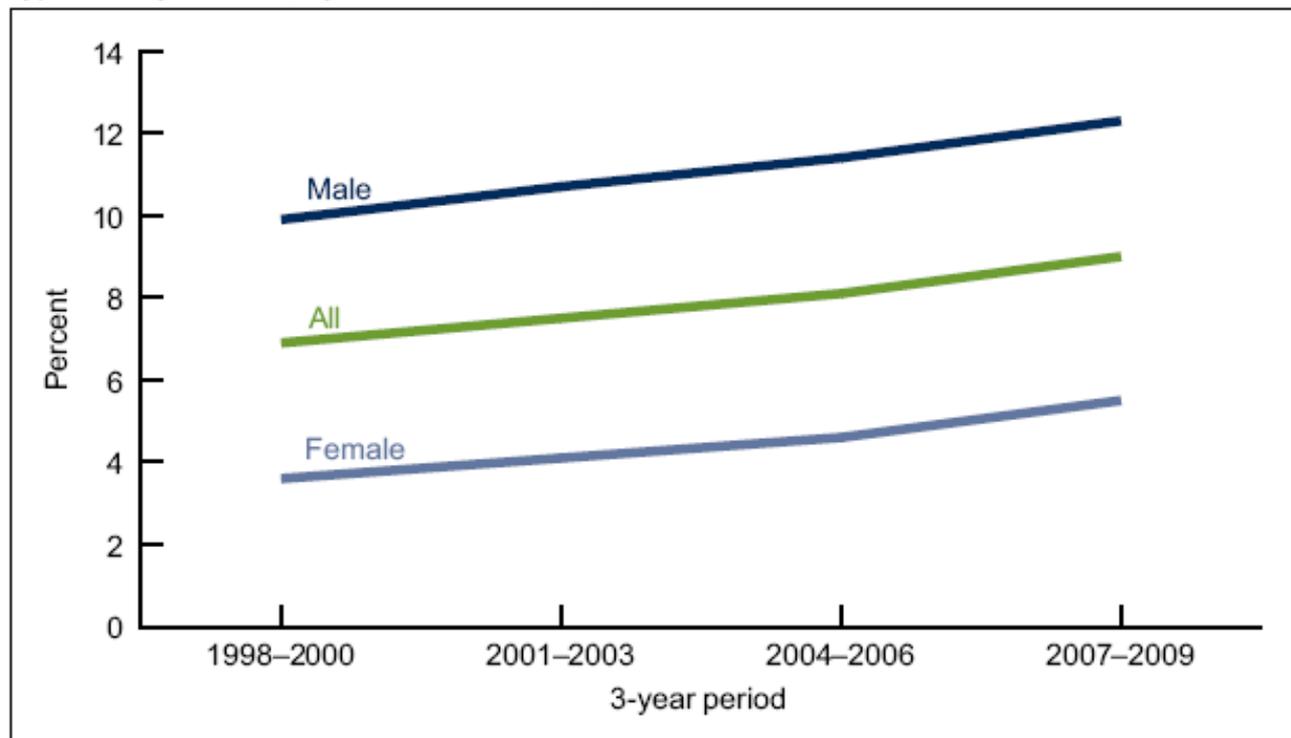
- ADHD prevalence trends varied by race and ethnicity. Differences between groups narrowed from 1998 through 2009; however, Mexican children had consistently lower ADHD prevalence than other racial or ethnic groups.

- From 1998 through 2009, ADHD prevalence increased to 10% for children with family income less than 100% of the poverty level and to 11% for those with family income between 100% and 199% of the poverty level.

- From 1998 through 2009, ADHD prevalence rose to 10% in the Midwest and South regions of the United States.

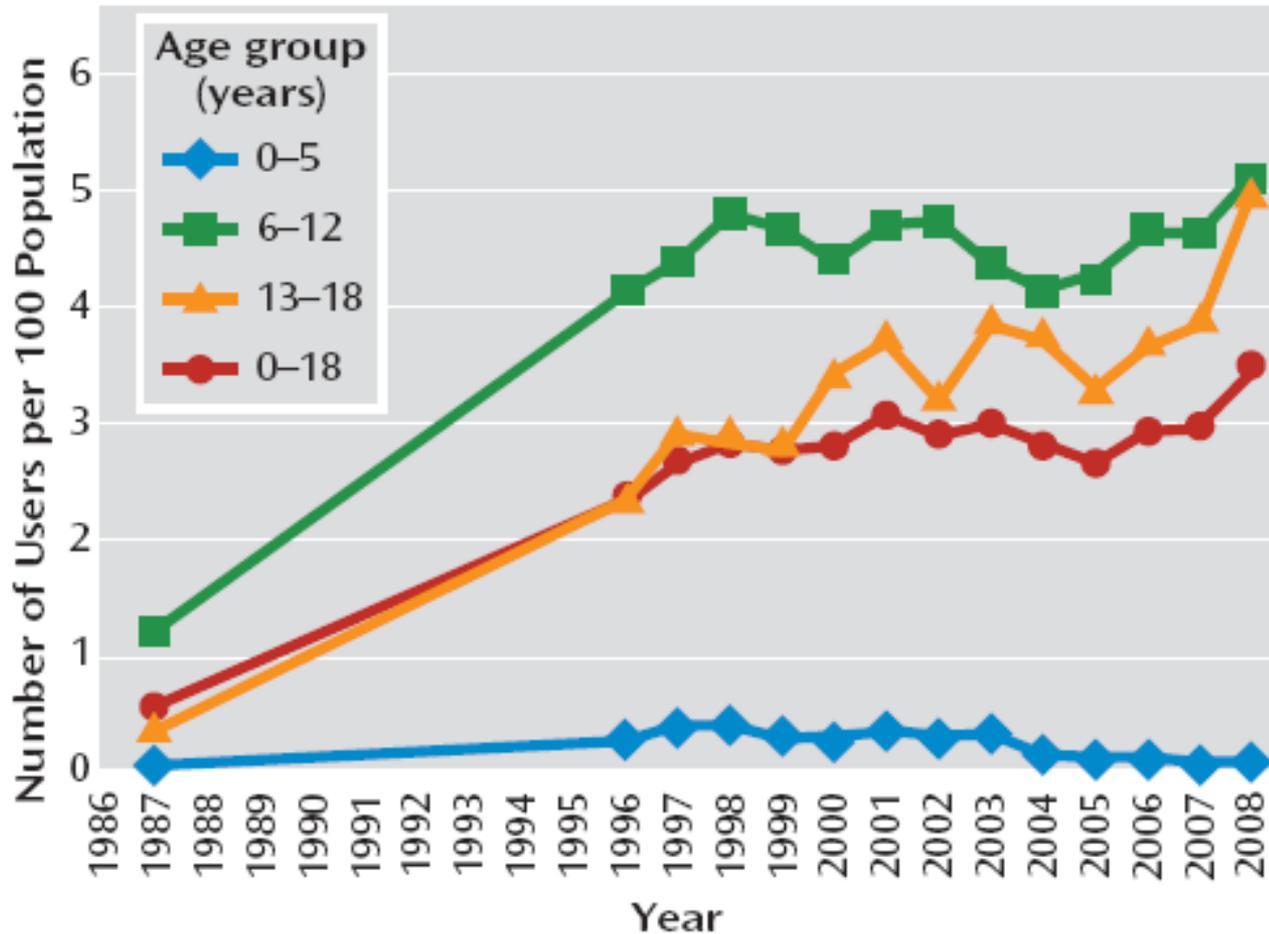
The percentage of children ever diagnosed with ADHD increased from 1998 through 2009 among both boys and girls.

Figure 1. Percentage of children aged 5–17 years ever diagnosed with attention deficit hyperactivity disorder, by sex: United States, 1998–2009



NOTE: Access data table for Figure 1 at: http://www.cdc.gov/nchs/data/databriefs/db70_tables.pdf#1.
SOURCES: CDC/NCHS, Health Data Interactive and National Health Interview Survey.

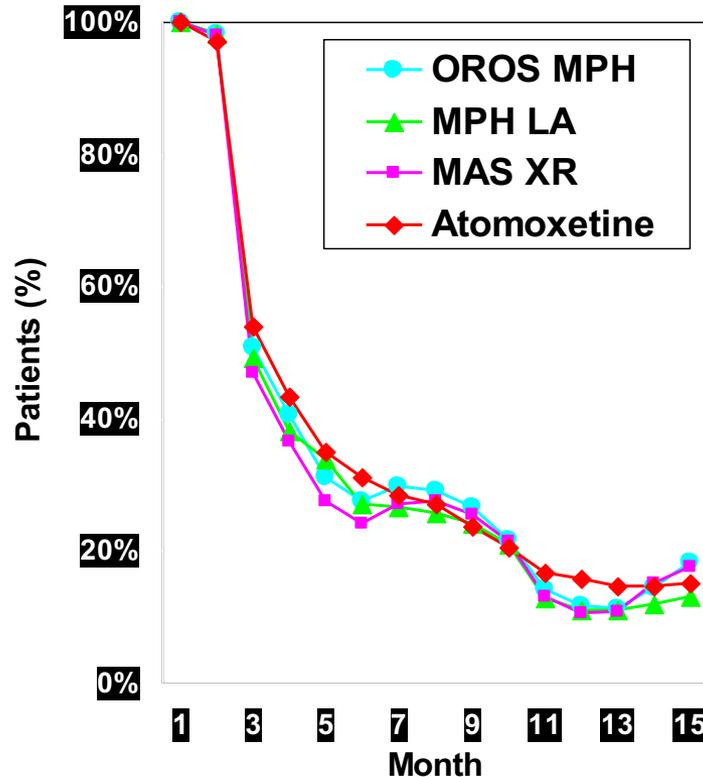
FIGURE 1. Trends in Prevalence of Stimulant Use in the U.S. Population Age 18 and Younger, 1987–2008^a



^a Based on the Medical Expenditure Panel Survey (1996–2008) and the National Medical Expenditure Survey (1987).

Adherence in ADHD is Dismal

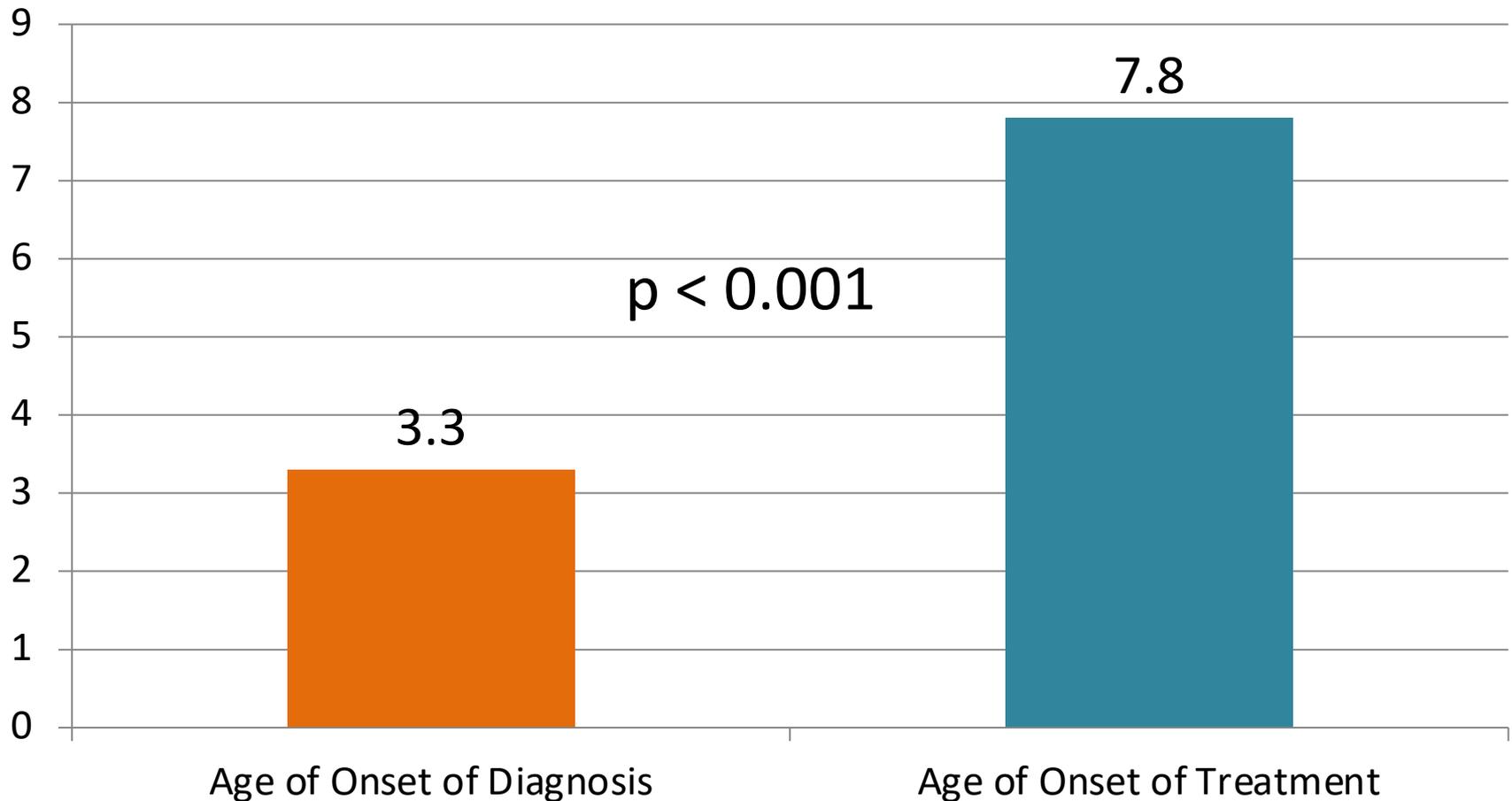
- **Only 13% of patients consistently take their medication one year out**



- **Within 2 to 3 months, a majority of patients with ADHD have stopped taking medication consistently**
- **Patients renewed their monthly prescriptions about 2 to 3 times per year¹**

1. Capone. Presented at CHADD Annual International Conference, Dallas, Texas; October 27, 2005.
2. Perwien et al. *J Manag Care Pharm.* 2004;10(2):122-129.
3. Sanchez et al. *Pharmacotherapy.* 2005;25(7):909-917.

Long Delays in the Initiation of Treatment (n=1498)



MGH Pediatric Psychopharmacology Clinic



School Readiness in Preschoolers With Symptoms of Attention-Deficit/Hyperactivity Disorder

Hannah T. Perrin, MD, Nicole A. Heller, BA, Irene M. Loe, MD

abstract

OBJECTIVE: To compare school readiness in preschoolers with and without attention-deficit/hyperactivity disorder (ADHD) symptoms using a comprehensive framework. We hypothesized that preschoolers with ADHD symptoms have higher odds of school readiness impairment.

METHODS: Children ages 4 to 5 years ($n = 93$) were divided into 2 groups on the basis of presence of ADHD symptoms (ADHD group, $n = 45$; comparison group, $n = 48$). School readiness was assessed through 10 component measures, including direct assessments and standardized questionnaires, regarding 5 school readiness domains: physical well-being and motor development, social and emotional development, approaches to learning, language, and

CONCLUSIONS: Preschoolers with ADHD symptoms are likely to have impaired school readiness. We recommend early identification of school readiness impairment by using a comprehensive 5-domain framework in children with ADHD symptoms paired with targeted intervention to improve outcomes.

measures and greater odds of impairment in all domains except for cognition and general knowledge. Overall, 79% of the ADHD group and 13% of the comparison group had school readiness impairment (odds ratio 21, 95% confidence interval 5.67–77.77, $P < .001$).

CONCLUSIONS: Preschoolers with ADHD symptoms are likely to have impaired school readiness. We recommend early identification of school readiness impairment by using a comprehensive 5-domain framework in children with ADHD symptoms paired with targeted intervention to improve outcomes.



Original Investigation | Psychiatry

Trends in the Prevalence and Incidence of Attention-Deficit/Hyperactivity Disorder Among Adults and Children of Different Racial and Ethnic Groups

CONCLUSIONS AND RELEVANCE This study confirmed the reported increases in rates of ADHD diagnosis among adults, showing substantially lower rates of detection among minority racial/ethnic subgroups in the United States. Higher odds of negative outcomes reflect the economic and personal consequences that substantiate the need to improve assessment and treatment of ADHD in adults.

States. However, there are limited data on recent trends of adult ADHD diagnosis among racial/ethnic subgroups.

OBJECTIVE To examine trends, including associated demographic characteristics, psychiatric diagnoses, and negative outcomes, in the prevalence and incidence of adult ADHD diagnosis among 7 racial/ethnic groups during a 10-year period.

incidence among racial and ethnic groups in the United States?

Findings In this cohort study of 5 282 877 patients who identified as African American or black, Native

Chung et al. *JAMA Network Open*. 2019;2(11):e1914344.

Diagnosis of ADHD

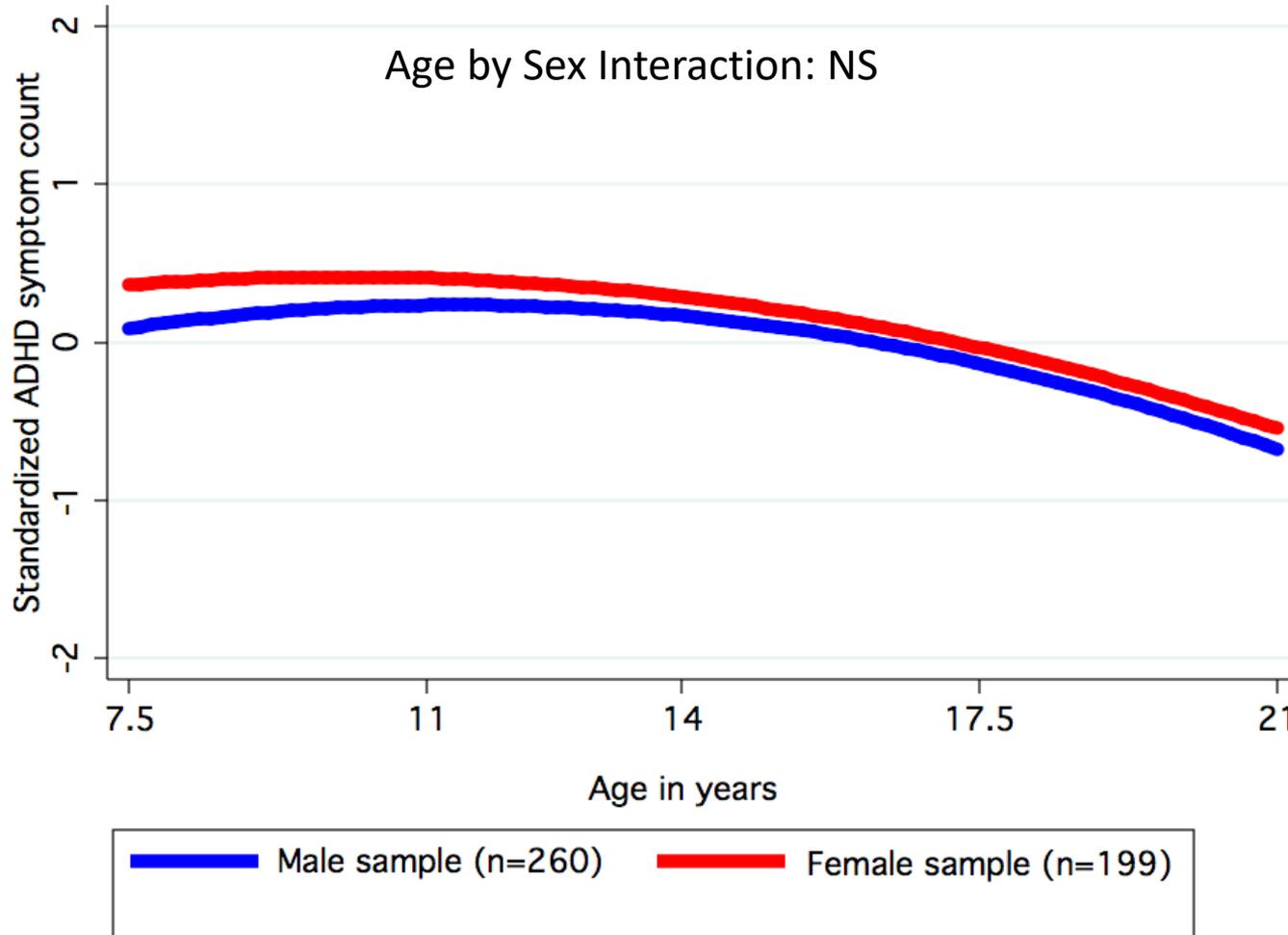
- Diagnosis is based on clinical assessment of symptoms, associated impairment and age of onset
- No test is available
- Symptoms are subjective, as well as developmentally and context sensitive

ADHD: Core Symptom Areas

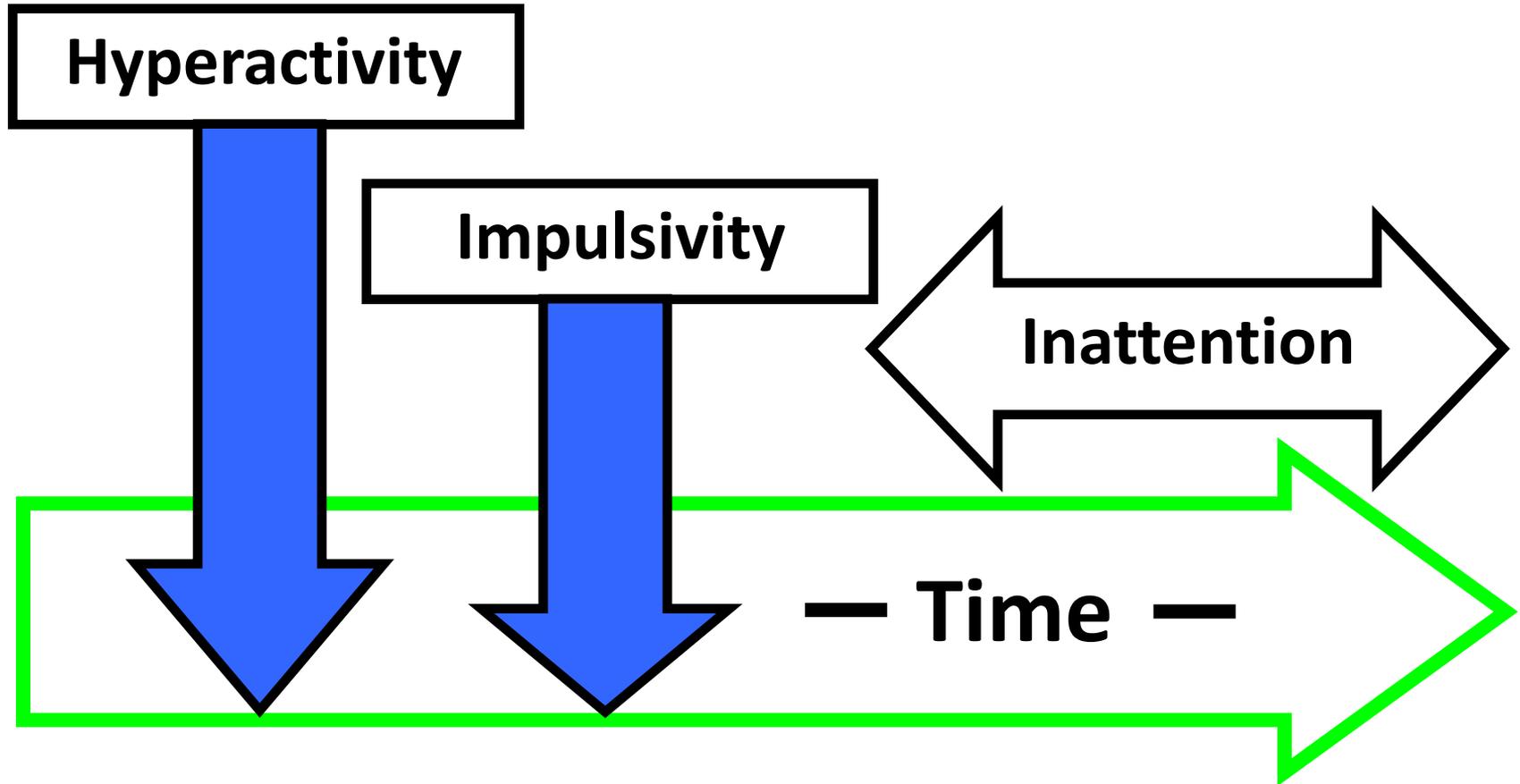
Inattention

Impulsivity/Hyperactivity

Course of ADHD Symptoms Over Time by Sex: A Growth Curve Model



ADHD: Course of the Disorder



Age-Dependent Decline and Persistence of ADHD Throughout the Lifetime

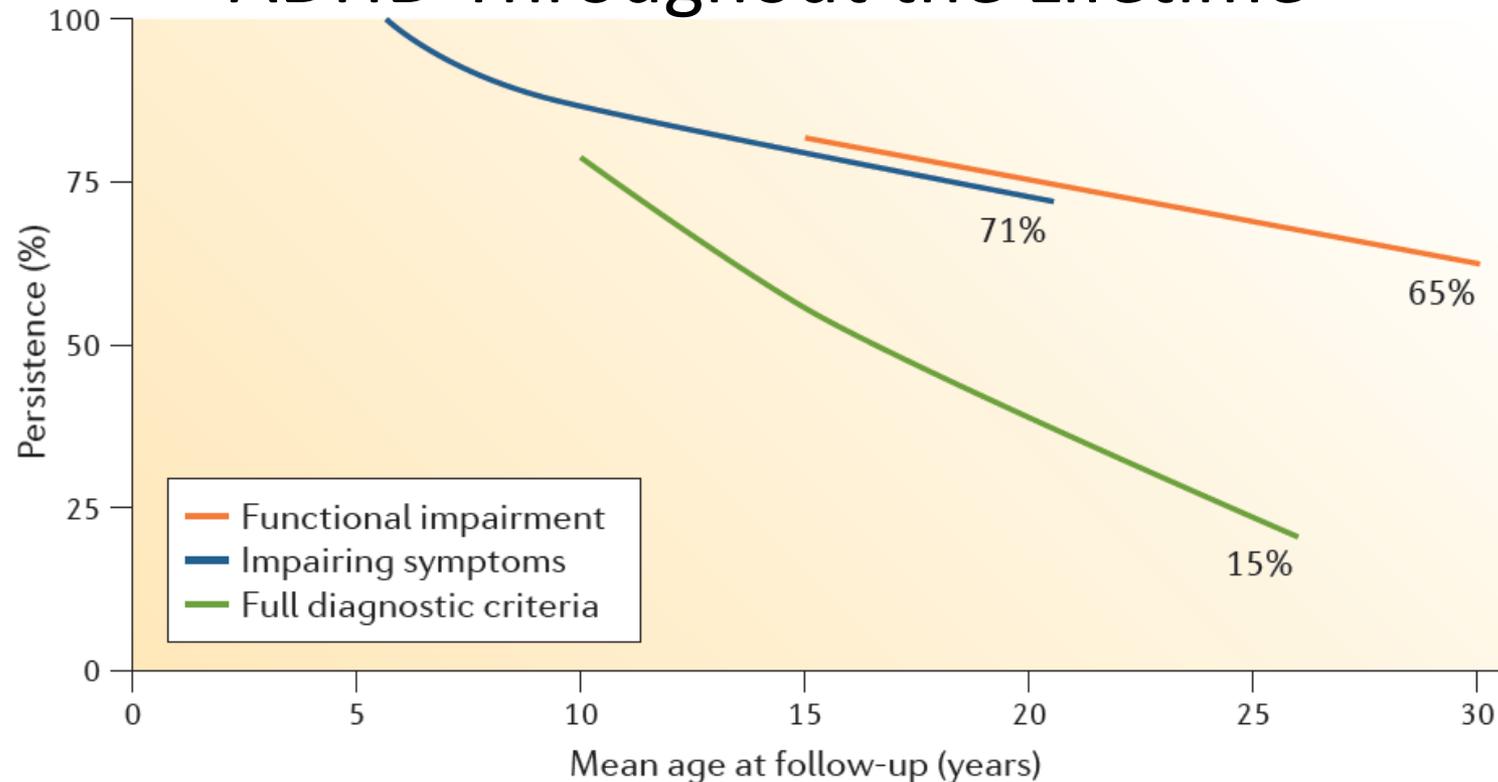


Figure 2 | **The age-dependent decline and persistence of attention-deficit/hyperactivity disorder throughout the lifetime.** Follow-up studies have assessed children with attention-deficit/hyperactivity disorder (ADHD) at multiple time points after their initial diagnosis. Although they document an age-dependent decline in ADHD symptoms, ADHD is also a highly persistent disorder when defined by the persistence of functional impairment⁷ or the persistence of subthreshold (three or fewer) impairing symptoms⁸. By contrast, many patients remit full diagnostic criteria⁷.

The Prevalence and Correlates of Adult ADHD in the United States: Results From the National Comorbidity Survey Replication

Ronald C. Kessler, M.D.,
Lenard Adler, M.D.,
Russell Barkley, Ph.D.,
Joseph Biederman, M.D.,
C. Keith Conroy, M.D.,
Olga Demler, M.D.,
Stephen V. Faraone, M.D.,
Laurence L. Greenberg, M.D.,
Mary J. Howes, M.D.,

Results: The estimated prevalence of current adult ADHD was 4.4%. Significant correlates included being male, previously married, unemployed, and non-Hispanic white. Adult ADHD was highly comorbid with many other DSM-IV disorders assessed in the survey and was associated with substantial role impairment. The majority of cases were untreated, although many individuals had obtained treatment for other comorbid mental and substance-related disorders.

154 respondents, with positive screen- ing was used to identify and correlates of clinical ADHD.

The prevalence of current adult ADHD was 4.4%. Significant correlates included being male, previously married, and non-Hispanic white. Adult ADHD was highly comorbid with many other DSM-IV disorders assessed in the survey and was associated with substantial role impairment. The majority of cases were untreated, although many individuals had obtained treatment for other comorbid mental and substance-related disorders.

Further research is needed to improve the diagnosis and treatment of adult ADHD. It is needed to determine whether effective treatment would reduce the onset, persistence, and severity of disorders that co-occur with adult ADHD.

diagnostic interview to assess a wide range of DSM-IV disorders. Blinded clinical follow-up interviews of adult ADHD

are needed to improve the diagnosis and treatment of adult ADHD. It is needed to determine whether effective treatment would reduce the onset, persistence, and severity of disorders that co-occur with adult ADHD.

The Long-Term Financial Outcome of Children Diagnosed With ADHD

William E. Pelham III
Arizona State University

Timothy F. Page, Amy R. Altszuler,
and Elizabeth M. Gnagy

Conclusion: The financial deficit of adults with history of childhood ADHD grows across early adulthood. Projections based on early financial trajectories suggest very large cumulative differences in earnings and savings. With or without persistence of the DSM symptoms, the adult sequela of childhood ADHD can be conceptualized as a chronic condition often requiring considerable support from others during adulthood.

during childhood ($N = 364$) and demographically matched controls ($N = 240$) for nearly 20 years.

HEAD TO HEAD

Is ADHD a valid diagnosis in adults?

Philip Asherson and colleagues argue that the concept of ADHD in adults is valid but **Joanna Moncrieff and Sami Timimi** believe that it is supported by little more than aggressive marketing



Philip Asherson, professor of molecular psychiatry and honorary consultant psychiatrist, MRC Social Genetic and Developmental Psychiatry, Institute of Psychiatry, King's College London
philip.asherson@kd.ac.uk

Marios Adamou, consultant psychiatrist, Service for adults with ADHD, Marygates Clinic, South West Yorkshire Partnership NHS Foundation Trust, Yorkshire; Blanca Bolea, consultant psychiatrist and honorary lecturer, University of Bristol, Bristol Adult ADHD Clinic, Avon and Wiltshire Partnership Mental Health Trust, Bristol; Ulrich Muller, university lecturer and honorary consultant psychiatrist, Adult ADHD Research Clinic, Department of Psychiatry, University of Cambridge and Peterborough NHS Foundation Trust, Addenbrooke's Hospital, Cambridge; Susan Dunn, Morua founder and chairwoman adult attention deficit disorder UK (AADD-UK), Adult Attention Deficit Disorder UK (AADD-UK), London, and Bristol; Mark Pitts, clinical nurse specialist, Adult ADHD Service, Maudsley Hospital, South London and Maudsley NHS Foundation Trust, London; Johannes Thome, professor of psychiatry, Swansea Medical School, University of Wales, Swansea; Susan Young, senior lecturer in clinical forensic psychology and consultant clinical and forensic psychologist, Department of Forensic Mental Health Science, Institute of Psychiatry, King's College London

YES Attention deficit hyperactivity disorder (ADHD) is well established in childhood, with 3.6% of children in the United Kingdom being affected.¹ Most regions have child and adolescent mental health or paediatric services for ADHD. Follow-up studies of children with ADHD find that 15% still have the full diagnosis at 25 years, and a further 50% are in partial remission, with some symptoms associated with clinical and psychosocial impairments persisting.²

ADHD is a clinical syndrome defined in the *Diagnostic and Statistical Manual of Mental Dis-*

orders, fourth edition, by high levels of hyperactive, impulsive, and inattentive behaviours in early childhood that persist over time, pervade across situations, and lead to notable impairments. ADHD is thought to result from complex interactions between genetic and environmental factors.³

Proof of validity

Using the Washington University diagnostic criteria, the National Institute for Health and Clinical Excellence (NICE) reviewed the validity of the system used to diagnose ADHD in children and adults.^{4,5}

Symptoms of ADHD are reliably identifiable. The symptoms used to define ADHD are found to cluster together in both clinical and population samples. Studies in such samples also separate ADHD symptoms from conduct problems and neurodevelopmental traits. Twin studies show a distinct pattern of genetic and environmental influences on ADHD compared with conduct problems,⁶ and overlapping genetic influences between ADHD and neurodevelopmental disorders such as autism and specific reading difficulties.^{7,8} Disorders that commonly, but not invariably, occur in adults with ADHD include antisocial personality, substance misuse, and depression.⁴

Symptoms of ADHD are continuously distributed throughout the population.⁹ As with anxiety and depression, most people have symptoms of ADHD at some time. The disorder is diagnosed by

perceptions and variation of diagnosis across sex and class,³ and serious adverse outcomes being more strongly related to co-occurring problems such as conduct disorder and familial conflict.⁴

Joanna Moncrieff senior lecturer and honorary consultant psychiatrist, University College London and North East London Mental Health Trust, UCL Department of Mental Health Sciences, London W1W 7EJ j.moncrieff@ucl.ac.uk
Sami Timimi consultant child and adolescent psychiatrist and

Changes in DSM-5 ADHD

- “Neurodevelopmental” - not “disruptive”
- $\geq 6/9$ inattentive or $\geq 6/9$ impulsive/hyperactive symptoms over last six months (>5 for adults)
- Symptoms caused impairment by age 12 (no longer 7)
- ASDs no longer exclusionary
- No more “subtypes”; Inattentive / Hyperactive-impulsive / Combined are now “Presentations”
- Restricted inattentive subtype: In Appendix, worthy of further study



ADHD as a Brain Disorder: Neuroimaging Findings

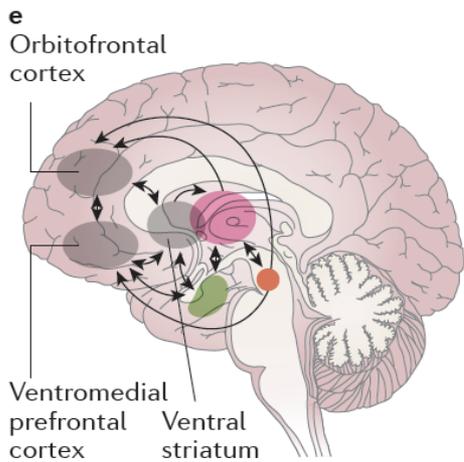
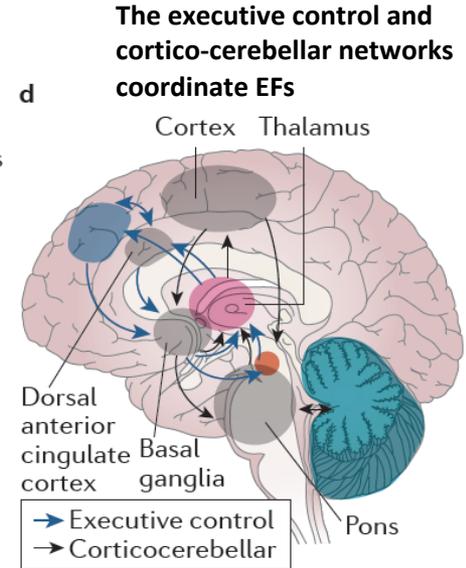
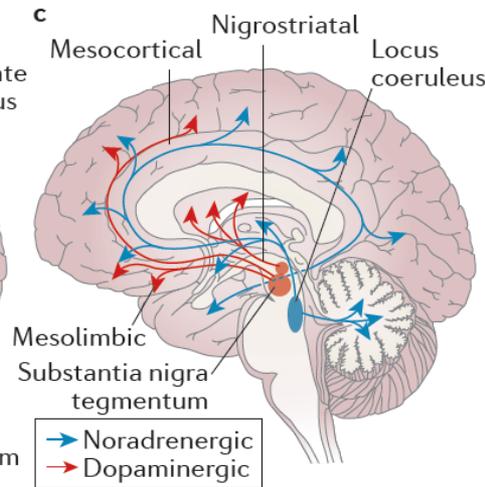
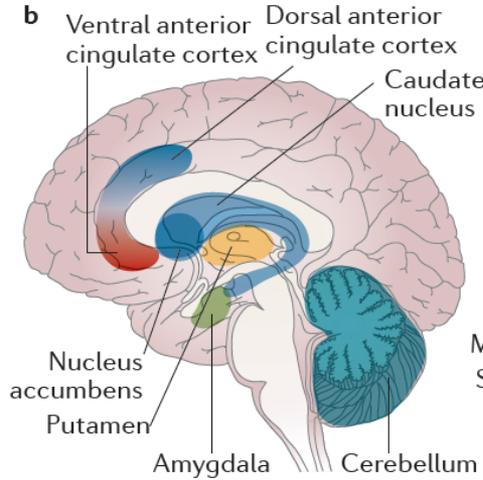
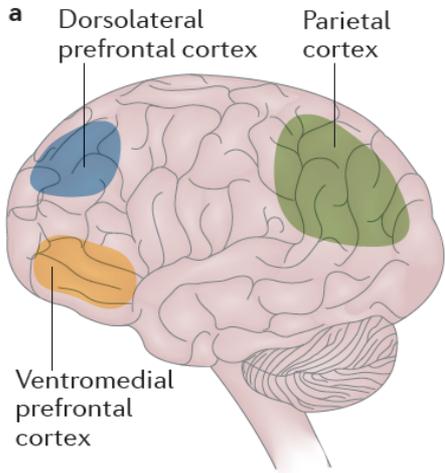
Attention-deficit/hyperactivity disorder

Stephen V. Faraone^{1,2}, Philip Asherson³, Tobias Banaschewski⁴, Joseph Biederman⁵, Jan K. Buitelaar⁶, Josep Antoni Ramos-Quiroga⁷⁻⁹, Luis Augusto Rohde^{10,11}, Edmund J. S. Sonuga-Barke^{12,13}, Rosemary Tannock^{14,15} and Barbara Franke¹⁶

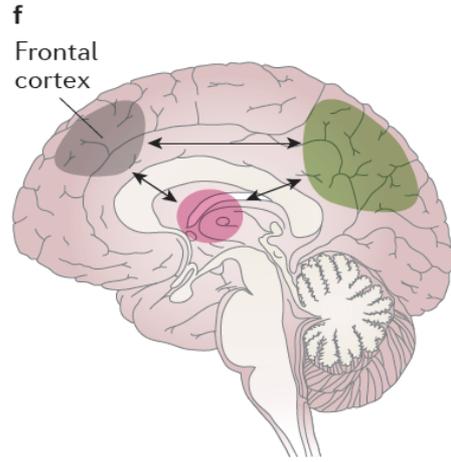
Abstract | Attention-deficit/hyperactivity disorder (ADHD) is a persistent neurodevelopmental disorder that affects 5% of children and adolescents and 2.5% of adults worldwide. Throughout an individual's lifetime, ADHD can increase the risk of other psychiatric disorders, educational and occupational failure, accidents, criminality, social disability and addictions. No single risk factor is necessary or sufficient to cause ADHD. In most cases ADHD arises from several genetic and environmental risk factors that each have a small individual effect and act together to increase susceptibility. The multifactorial causation of ADHD is consistent with the heterogeneity of the disorder, which is shown by its extensive psychiatric co-morbidity, its multiple domains of neurocognitive impairment and the wide range of structural and functional brain anomalies associated with it. The diagnosis of ADHD is reliable and valid when evaluated with standard criteria for psychiatric disorders. Rating scales and clinical interviews facilitate diagnosis and aid screening. The expression of symptoms varies as a function of patient developmental stage and social and academic contexts. Although there are no curative treatments for ADHD, evidenced-based treatments can markedly reduce its symptoms and associated impairments. For example, medications are efficacious and normally well tolerated, and various non-pharmacological approaches are also valuable. Ongoing clinical and neurobiological research holds the promise of advancing diagnostic and therapeutic approaches to ADHD. For an illustrated summary of this Primer, visit: <http://go.nature.com/l6jiwl>

The DLPC is linked to WM, the VMPFC to complex decision making and strategic planning, and the parietal cortex to attention

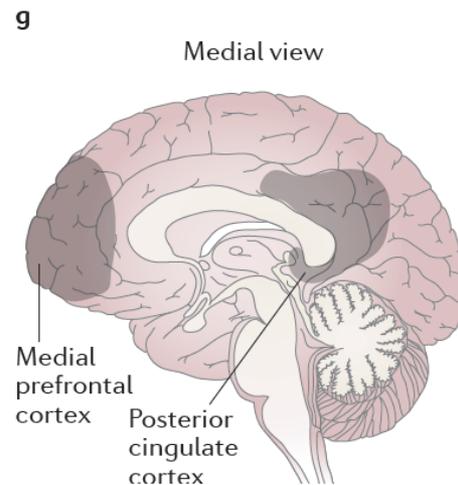
Brain Mechanisms in ADHD



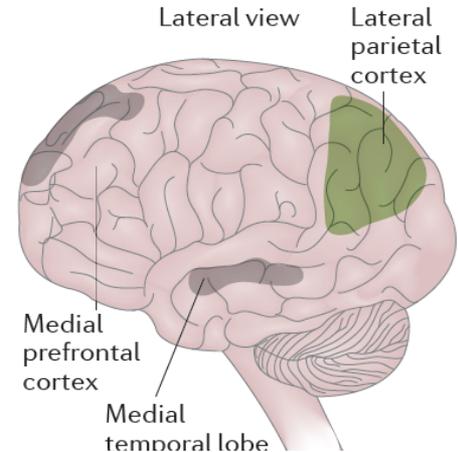
The VMPFC, OFC & ventral striatum are the brain network associated with anticipation and reward



The frontal and parietal cortices and the thalamus support attentional functioning



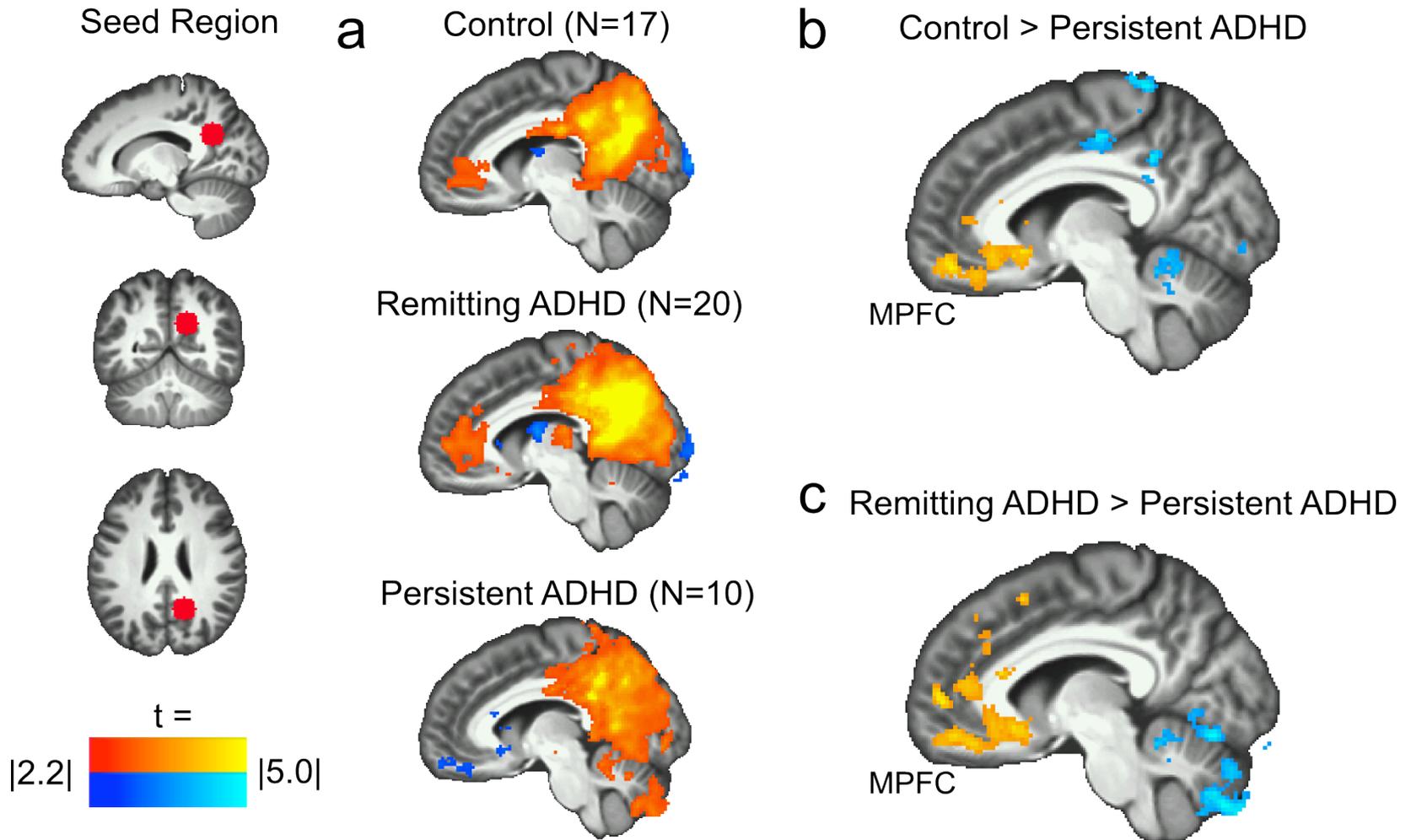
Negative correlations between the DMN and the frontoparietal control network are weaker in patients with ADHD





Resting-State Functional Connectivity in a Longitudinal Sample of ADHD Children Grown Up

Reduced MPFC-PCC Coupling Reflects Current Diagnostic State of ADHD



Neural Basis of Persistent ADHD

- Persistent ADHD alters intrinsic functional organization of the brain
- Findings supports the idea that adult ADHD diagnosis reflects a true brain difference

Mattfeld et al. *Brain: A Journal of Neurology* 2014, epub: June 10, 2014

REPORT**Brain differences between persistent and remitted attention deficit hyperactivity disorder**

Previous resting state studies examining the brain basis of attention deficit hyperactivity disorder have not distinguished between patients who persist versus those who remit from the diagnosis as adults. To characterize the neurobiological differences and similarities of persistence and remittance, we performed resting state functional magnetic resonance imaging in individuals who had been longitudinally and uniformly characterized as having or not having attention deficit hyperactivity disorder in childhood and again in adulthood (16 years after baseline assessment). Intrinsic functional brain organization was measured in patients who had a persistent diagnosis in childhood and adulthood ($n = 13$), in patients who met diagnosis in childhood but not in adulthood ($n = 22$), and in control participants who never had attention deficit hyperactivity disorder ($n = 17$). A positive functional correlation between posterior cingulate and medial prefrontal cortices, major components of the default-mode network, was reduced only in patients whose diagnosis persisted into adulthood. A negative functional correlation between medial and dorsolateral prefrontal cortices was reduced in both persistent and remitted patients. The neurobiological dissociation between the persistence and remittance of attention deficit hyperactivity disorder may provide a framework for the relation between the clinical diagnosis, which indicates the need for treatment, and additional deficits that are common, such as executive dysfunctions.

who had been longitudinally and uniformly characterized as having or not having attention deficit hyperactivity disorder in childhood and again in adulthood (16 years after baseline assessment). Intrinsic functional brain organization was measured in patients who had a persistent diagnosis in childhood and adulthood ($n = 13$), in patients who met diagnosis in childhood but not in adulthood ($n = 22$), and in control participants who never had attention deficit hyperactivity disorder ($n = 17$). A positive functional correlation between posterior cingulate and medial prefrontal cortices, major components of the default-mode network, was reduced only in patients whose diagnosis persisted into adulthood. A negative functional correlation between medial and dorsolateral prefrontal cortices was reduced in both persistent and remitted patients. The neurobiological dissociation between the persistence and remittance of attention deficit hyperactivity disorder may provide a framework for the relation between the clinical diagnosis, which indicates the need for treatment, and additional deficits that are common, such as executive dysfunctions.

Subcortical brain volume differences in participants with attention deficit hyperactivity disorder in children and adults: a cross-sectional mega-analysis



Martine Hoogman, Janita Bralten, Derrek P Hibar, Maarten Mennes, Marcel P Zwiers, Lizanne S J Schveren, Kimm J E van Hulzen, Sarah E Medland, Elena Shumskaya, Neda Jahanshad, Patrick de Zeeuw, Eszter Szekely, Gustavo Sudre, Thomas Wolfers, Alberdingk M H Onnink, Janneke T Dammers, Jeanette C Mostert, Yolanda Vives-Gilabert, Gregor Kohls, Eileen Oberwelland, Jochen Seitz, Martin Schulte-Rüther, Sara Ambrosino, Alysa E Doyle, Marie F Høvik, Margaretha Dramsdahl, Leanne Tamm, Theo G M van Erp, Anders Dale, Andrew Schork, Annette Conzelmann, Kathrin Zierhut, Ramona Baur, Hazel McCarthy, Yuliya N Yoncheva, Ana Cubillo, Kaylita Chantiluke, Mitul A Mehta, Yannis Paloyelis, Sarah Hohmann, Sarah Baumeister, Ivanei Bramati, Paulo Mattos, Fernanda Tovar-Moll, Pamela Douglas, Tobias Banaschewski, Daniel Brandeis, Jonna Kuntsi, Philip Asherson, Katya Rubia, Clare Kelly, Adriana Di Martino, Michael P Milham, Francisco X Castellanos, Thomas Frodl, Mariam Zentis, Klaus-Peter Lesch, Andreas Reif, Paul Pauli, Terry L Jernigan, Jan Haavik, Kerstin J Plessen, Astri J Lundervold, Kenneth Hugdahl, Larry J Seidman, Joseph Biederman, Nanda Rommelse, Dirk J Heslenfeld, Catharina A Hartman, Pieter J Hoekstra, Jaap Oosterlaan, Georg von Polier, Kerstin Konrad, Oscar Vilarroya, Josep Antoni Ramos-Quiroga, Joan Carles Soliva, Sarah Durston, Jan K Buitelaar, Stephen V Faraone, Philip Shaw, Paul M Thompson, Barbara Franke

Interpretation With the largest dataset to date, we add new knowledge about bilateral amygdala, accumbens, and hippocampus reductions in ADHD. We extend the brain maturation delay theory for ADHD to include subcortical structures and refute medication effects on brain volume suggested by earlier meta-analyses. Lifespan analyses suggest that, in the absence of well powered longitudinal studies, the ENIGMA cross-sectional sample across six decades of ages provides a means to generate hypotheses about lifespan trajectories in brain phenotypes.

collaboration, which in the present analysis was frozen at Feb 8, 2015. Individual sites analysed structural T1-weighted MRI brain scans with harmonised protocols of individuals with ADHD compared with those who do not have this diagnosis. Our primary outcome was to assess case-control differences in subcortical structures and intracranial volume through pooling of all individual data from all cohorts in this collaboration. For this analysis, p values were significant at the false discovery rate corrected threshold of $p=0.0156$.

Department of Human Genetics (M Hoogman PhD, J Bralten PhD, K J E van Hulzen PhD, E Shumskaya PhD, T Wolfers MSc, A M H Onnink PhD, J C Mostert PhD, Prof B Franke PhD), Department

■ REVIEW ARTICLE

Effect of Psychostimulants on Brain Structure and Function in ADHD: A Qualitative Literature Review of Magnetic Resonance Imaging–Based Neuroimaging Studies

*Thomas J. Spencer, MD; Ariel Brown, PhD; Larry J. Seidman, PhD;
Eve M. Valera, PhD; Nikos Makris, MD; Alexandra Lomedico, BA;
Stephen V. Faraone, PhD; and Joseph Biederman, MD*

ADHD Imaging Studies Summary

- Neuroimaging studies confirm that brain abnormalities in fronto-subcortical networks are associated with ADHD
- Neuroimaging techniques are not valid tools for ADHD diagnosis; imaging measures are not sensitive or specific enough to be used for diagnostic purposes
- Treatment attenuate neural deficits

Spencer et al. *J Clin Psychiatry* 2013 Sep;74(9):902-17.



ADHD as a Neurobiological Disorder: Catecholamine Dysregulation

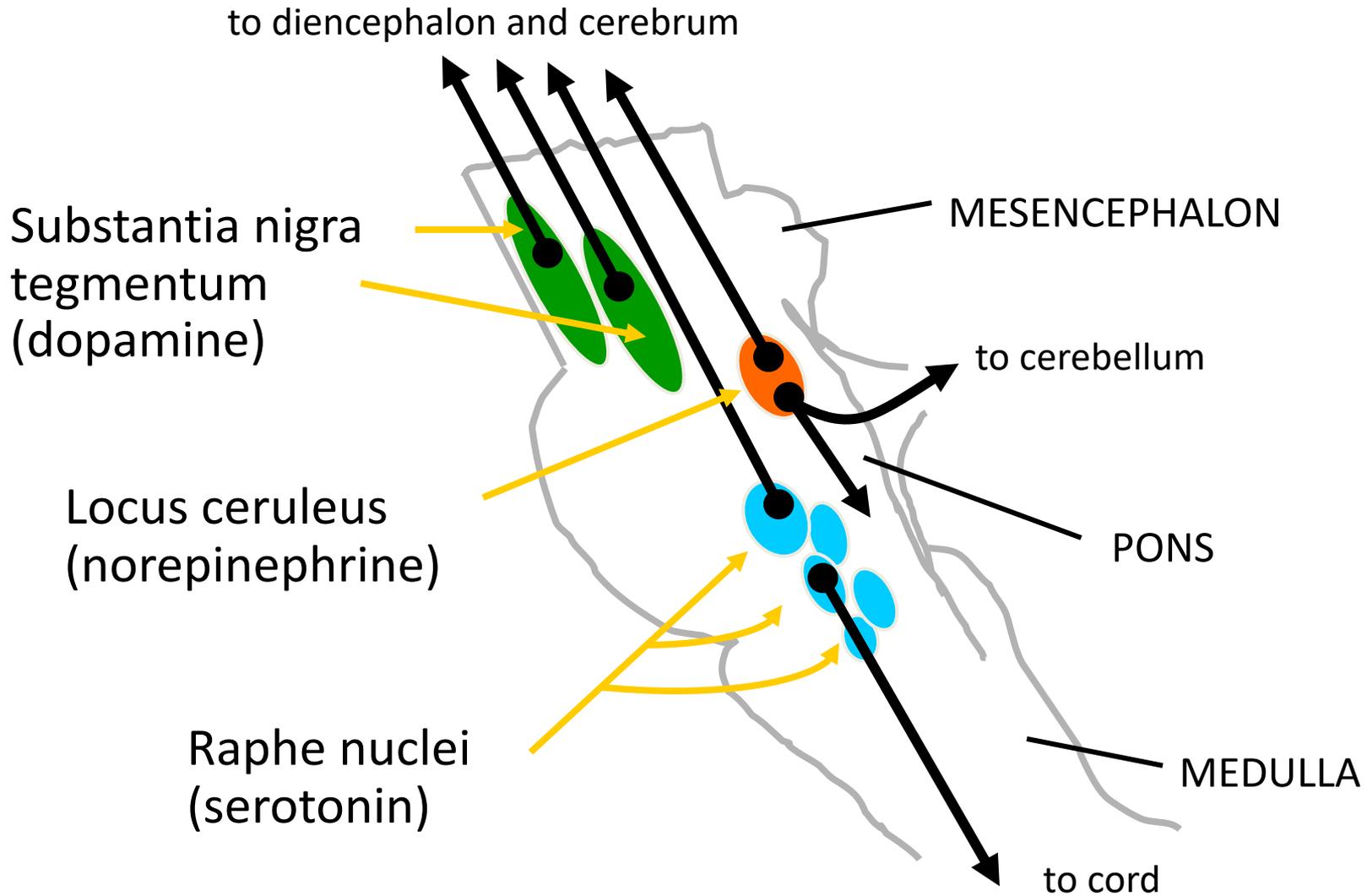
Frontosubcortical Networks and Catecholamines

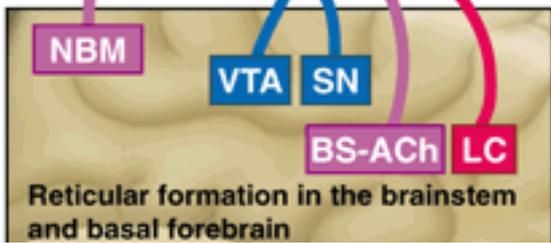
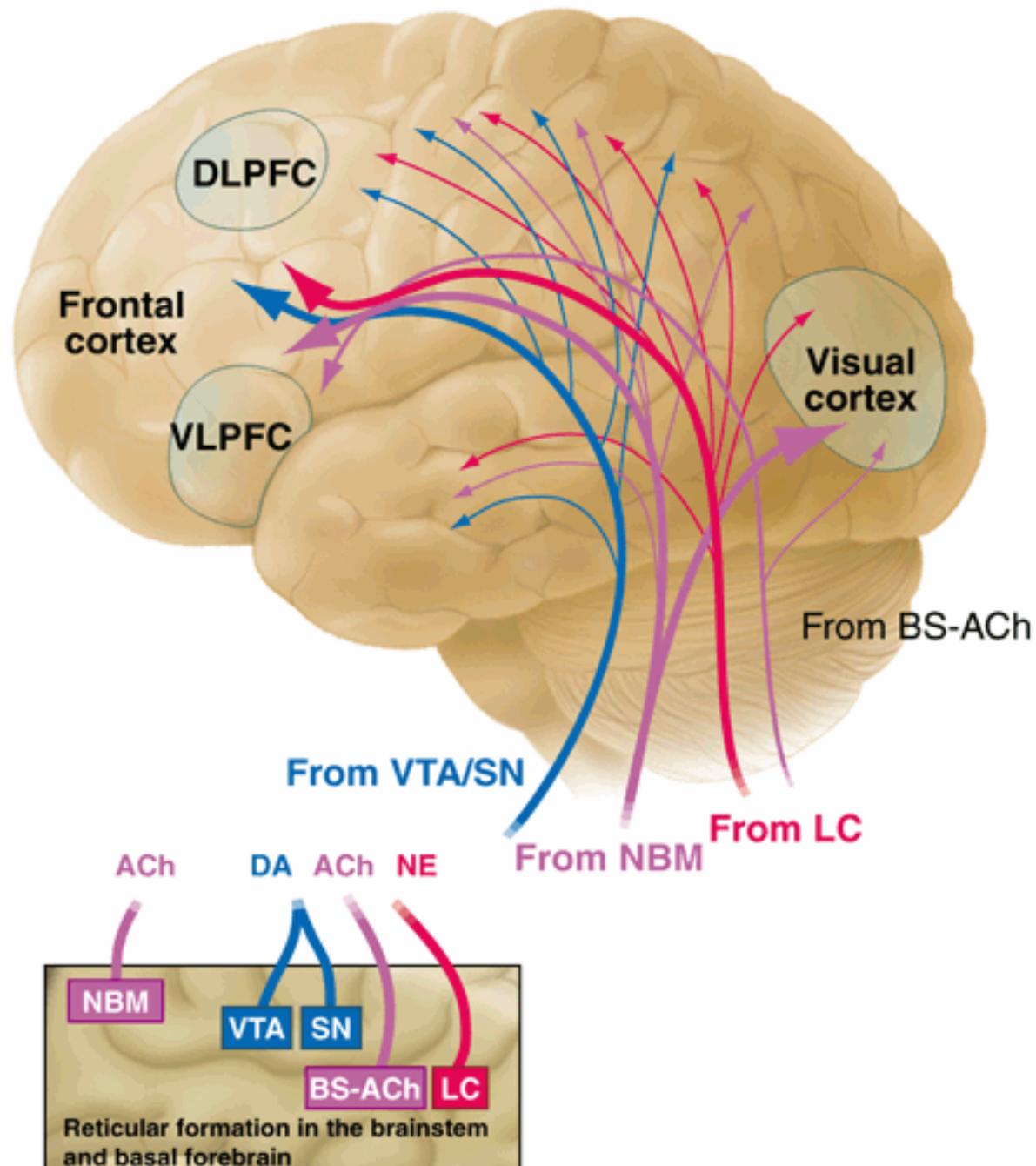
- Dopaminergic and noradrenergic dysregulation abnormalities in fronto subcortical pathways
- Medications that are effective in ADHD are either dopaminergic or noradrenergic

Zametkin. *J Am Acad Child Adolesc Psychiatry*. 1987;26(5):676-686

Zametkin. *J Am Acad Child Adolesc Psychiatry*. 1987;26(5):676-686.

Brain Stem





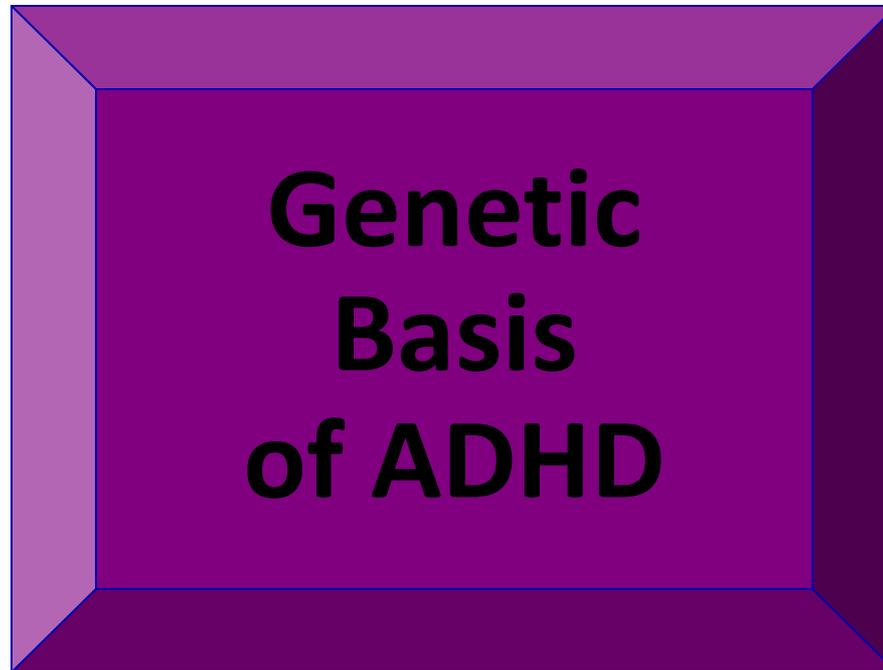


ADHD as a Neurobiological Disorder: Genetic Findings

ADHD: Genetics

Twin Studies

Family Studies

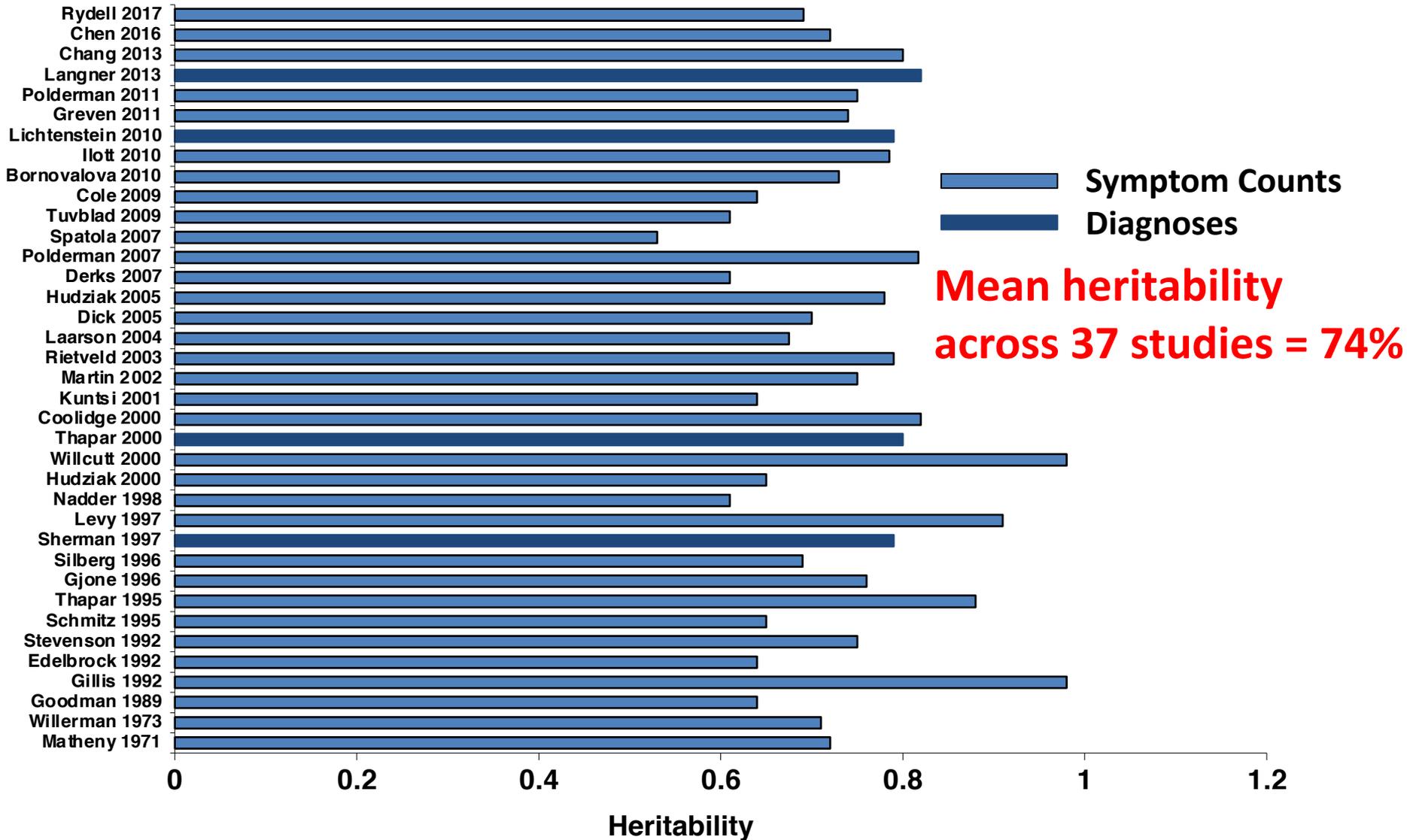


Adoption Studies

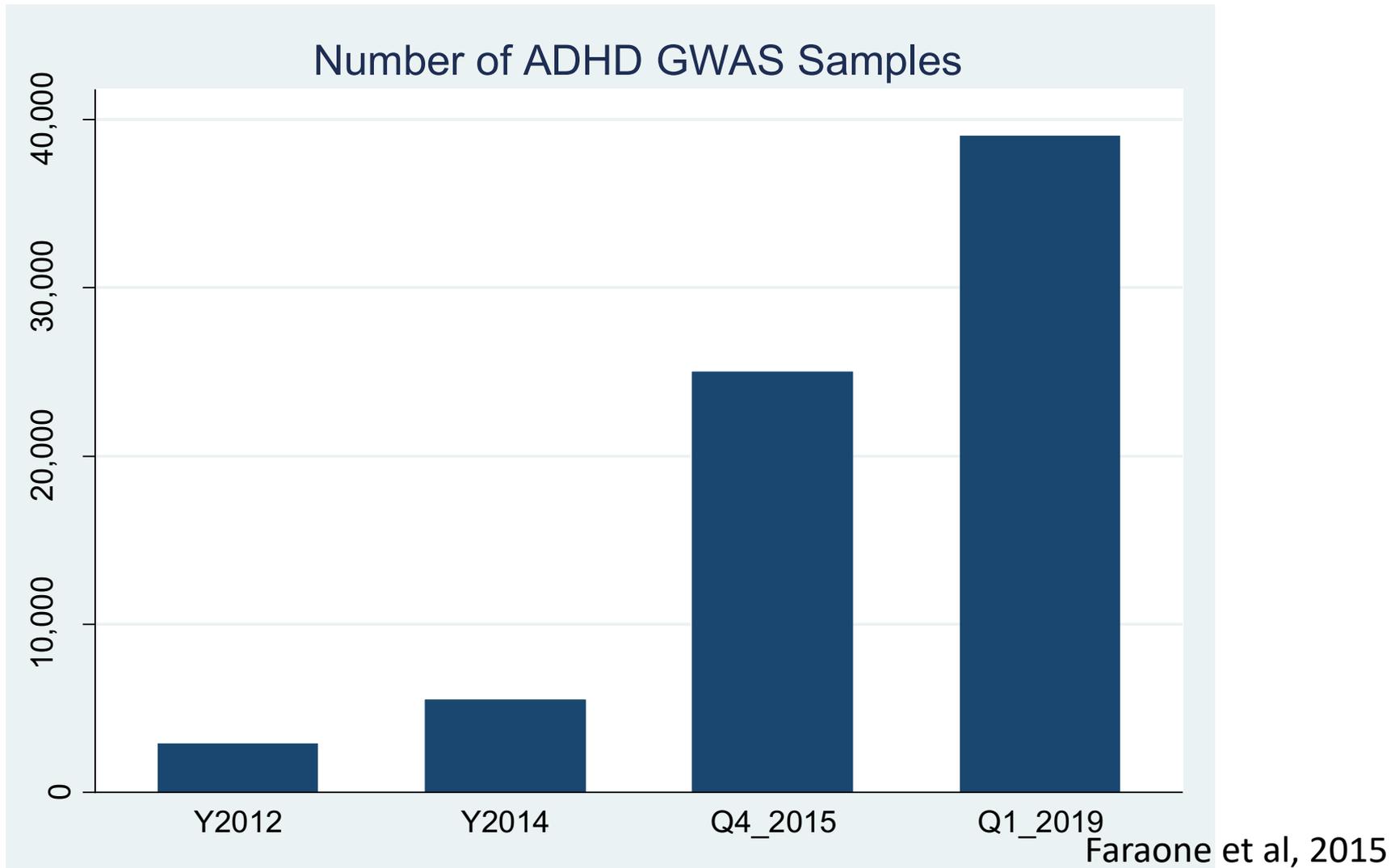
Molecular Genetics

Twin Studies of ADHD

(Faraone & Larsson, Molecular Psychiatry, 2018)

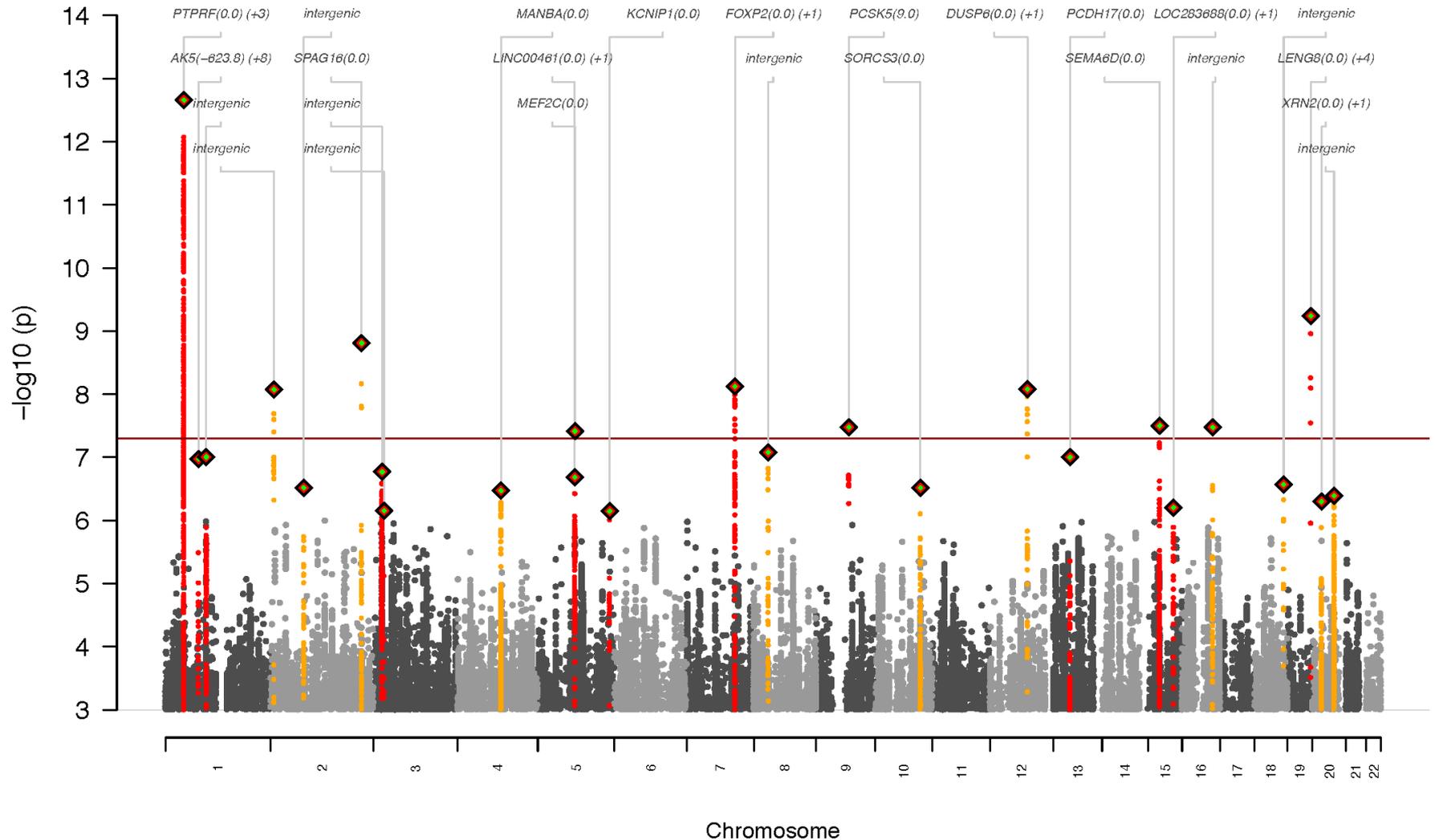


New Results from Genomewide Association Studies (GWAS)



Preliminary ADHD meta-analysis

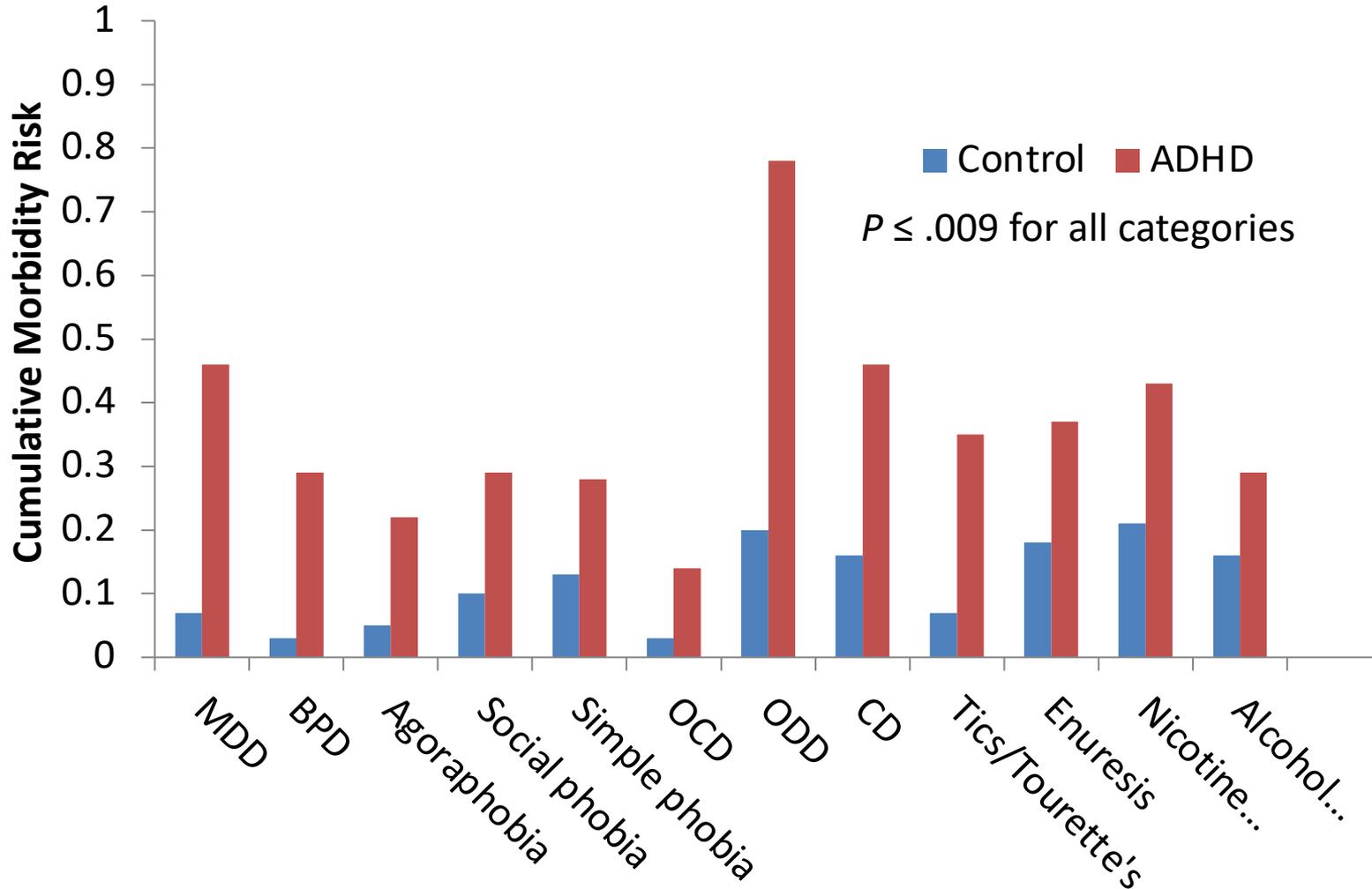
18,284 cases 33,836 controls



ADHD Diagnostic Considerations



Cumulative Morbidity Risks for Psychiatric Disorders in ADHD and Control Probands



THE AMERICAN JOURNAL OF PSYCHIATRY



Teaching Trainees to Negotiate
Research Collaborations With
Industry: A Mentorship Model
David B. Merrill, M.D., et al. 381

Morphological Abnormalities of
the Thalamus in Youths With
Attention Deficit Hyperactivity
Disorder
Iliyan Ivanov, M.D., et al. 397

◀ Adult Psychiatric Outcomes of Girls
With Attention Deficit Hyperactivity
Disorder: 11-Year Follow-Up in a
Longitudinal Case-Control Study
Joseph Biederman, M.D., et al. 409

Project Among African-Americans
to Explore Risks for Schizophrenia
(PAARTNERS): Evidence for
Impairment and Heritability of
Neurocognitive Functioning in
Families of Schizophrenia Patients
Monica E. Calkins, Ph.D., et al. 459

Continuing Medical Education 483

April 2010

Volume 167 • Number 4

Official Journal of the
AMERICAN PSYCHIATRIC ASSOCIATION

ajp.psychiatryonline.org

Biederman et al.
AJP. April 2010

Pharmacotherapy of ADHD

- ADHD remains the most treatable disorder in Psychiatry
- **Stimulants (amphetamines and methylphenidate compounds) remain the mainstay of treatment for ADHD due to their robust (High Effect Size) efficacy and safety**
- FDA-approved Non Stimulants (Atomoxetine and Alpha-2 Agonist (guanfacine and clonidine extended release) are generally less effective than the stimulants (moderate effect sizes of 0.4-0.6)

Do Stimulants Protect Against Psychiatric Disorders in Youth With ADHD? A 10-Year Follow-up Study

abstract

OBJECTIVE: Little is known about the effect of stimulant treatment in youth with attention-deficit/hyperactivity disorder (ADHD) on the subsequent development of comorbid psychiatric disorders. We tested the association between stimulant treatment and the subsequent development of psychiatric comorbidity in a longitudinal sample of patients

CONCLUSIONS: We found evidence that stimulant treatment decreases the risk for subsequent comorbid psychiatric disorders and academic failure in youth with ADHD. *Pediatrics* 2009;124:71–78

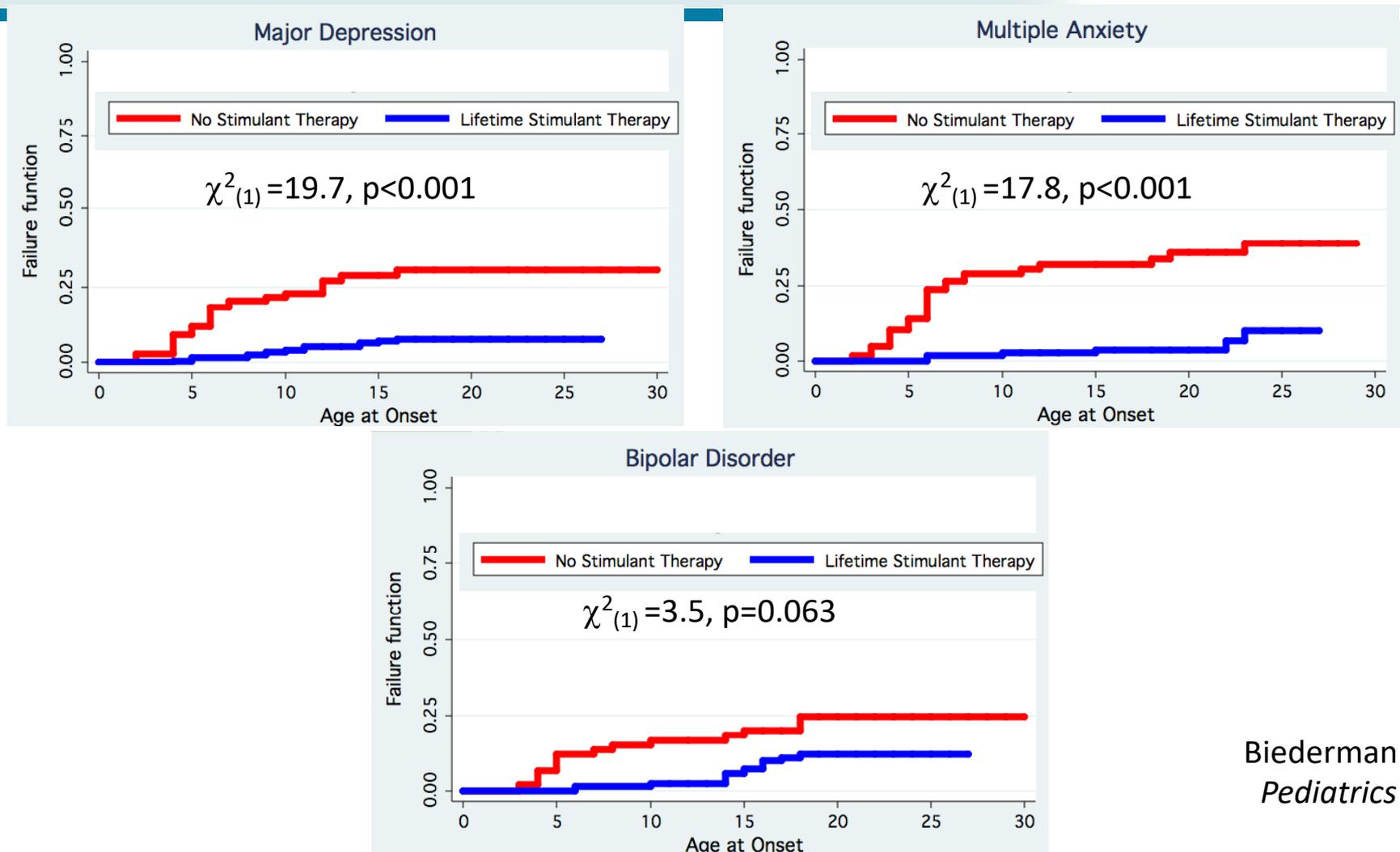
112 (80%) and 105 (88%) of the children in the ADHD and control groups, respectively, were reassessed (mean age: 22 years). We examined the association between stimulant treatment in childhood and adolescence and subsequent comorbid disorders and grade retention by using proportional hazards survival models.

RESULTS: Of the 112 participants with ADHD, 82 (73%) were previously treated with stimulants. Participants with ADHD who were treated with stimulants were significantly less likely to subsequently develop depressive and anxiety disorders and disruptive behavior and less likely to repeat a grade compared with participants with ADHD who were not treated.

CONCLUSIONS: We found evidence that stimulant treatment decreases the risk for subsequent comorbid psychiatric disorders and academic failure in youth with ADHD. *Pediatrics* 2009;124:71–78

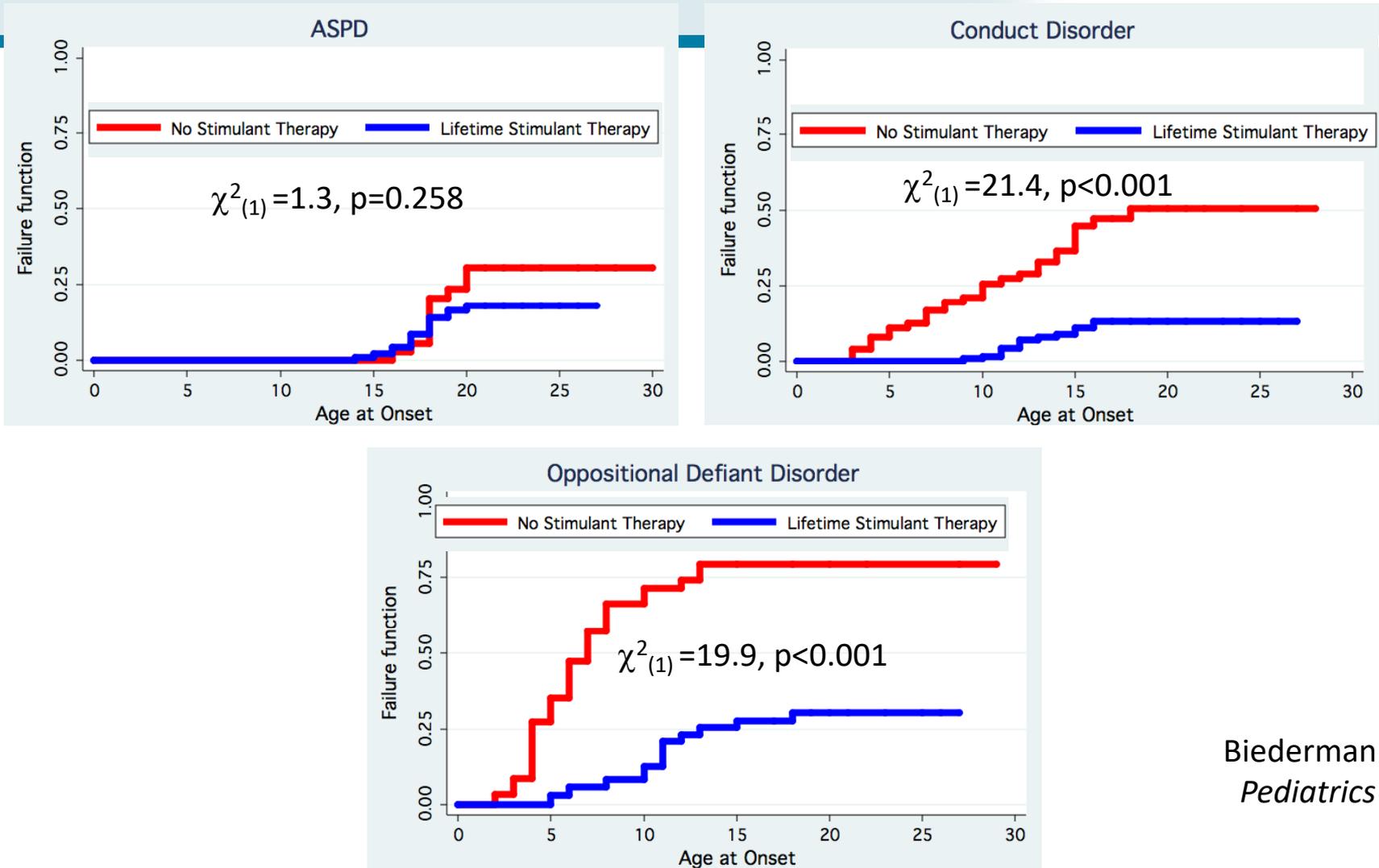
Biederman et al.
Pediatrics 2009
Jul;124(1):71-8.

Protective Effect of Stimulants on Comorbidity



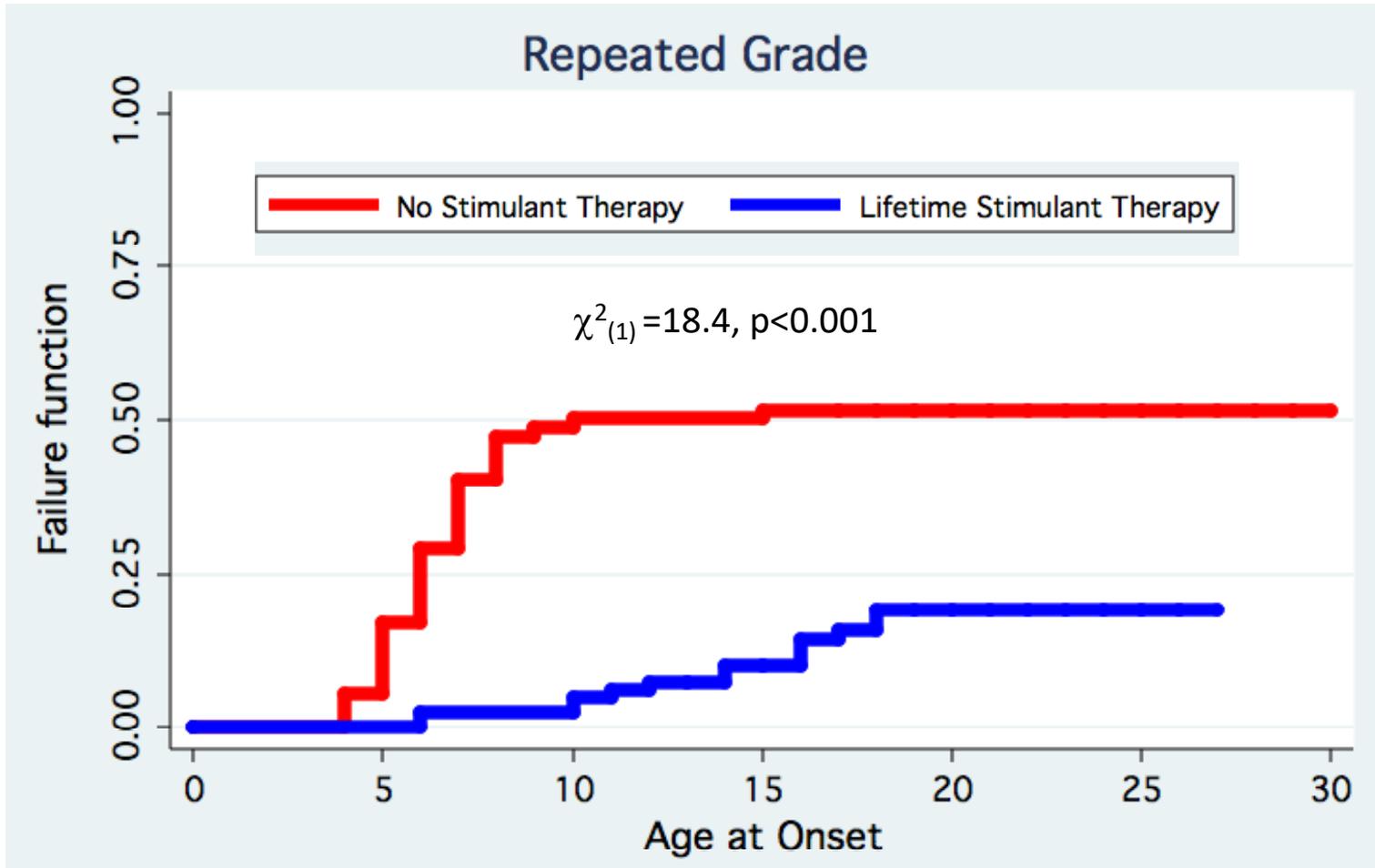
Biederman et al.
Pediatrics 2009

Protective Effect of Stimulants on Comorbidity



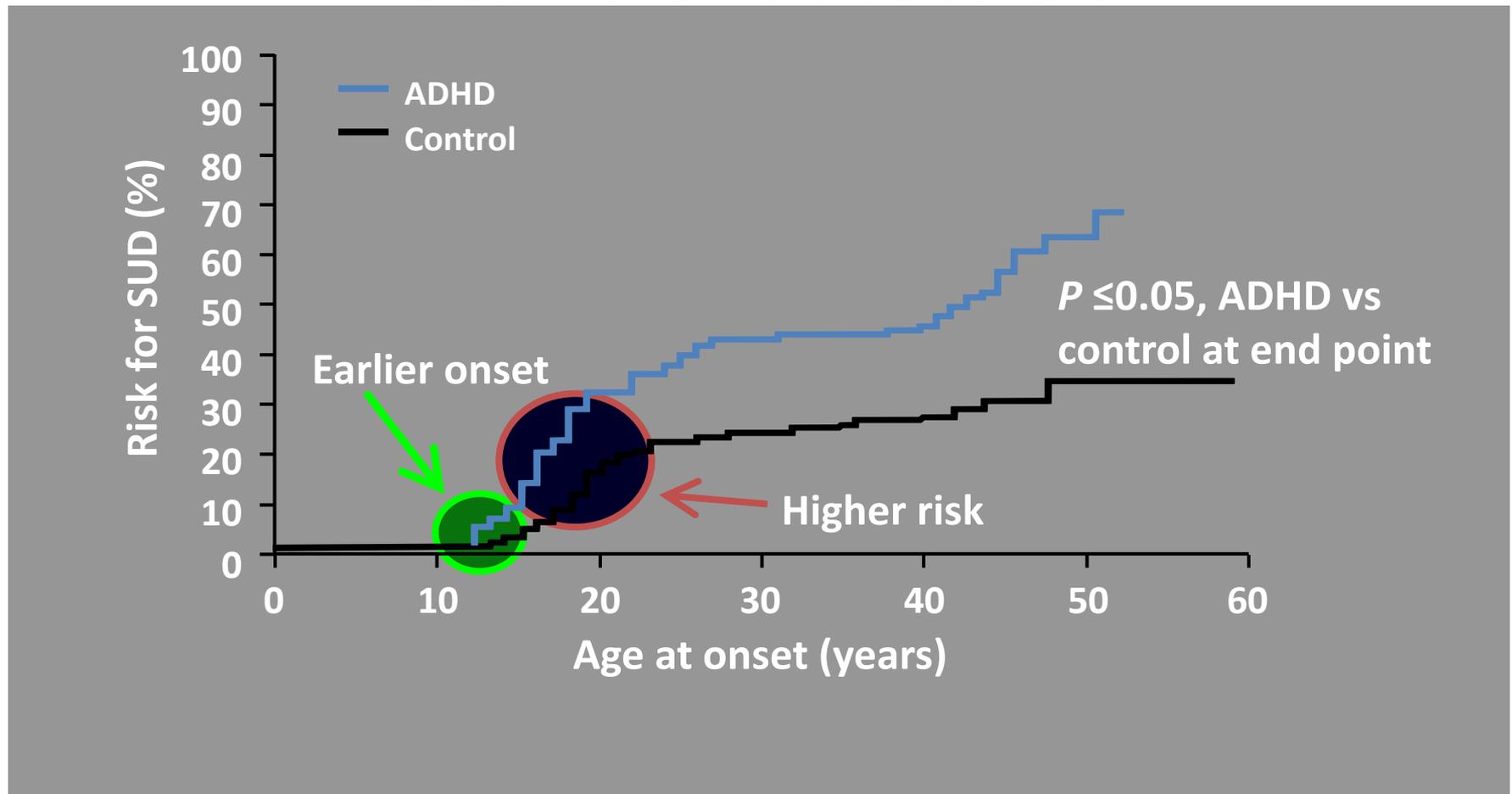
Biederman et al.
Pediatrics 2009

Protective Effect of Stimulants

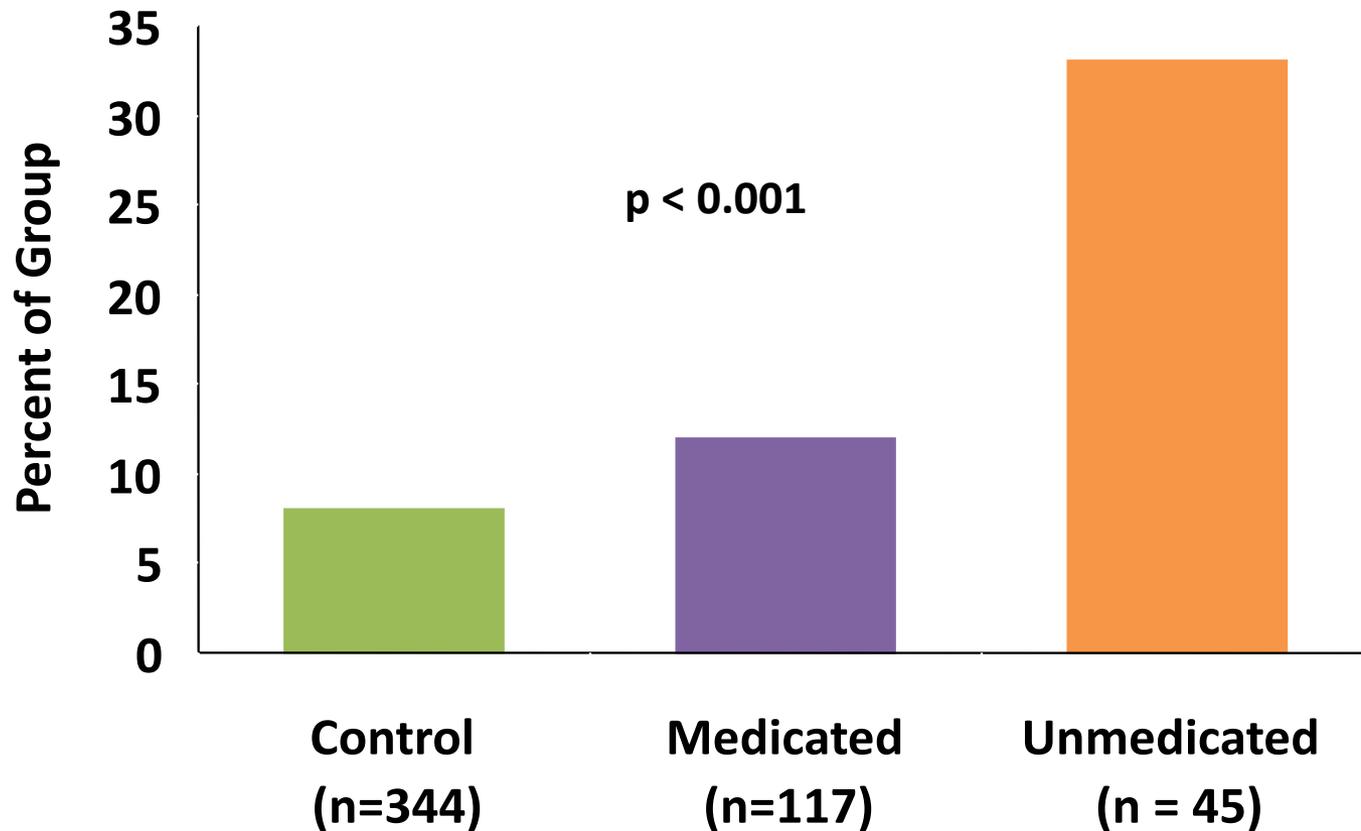


ADHD and Substance Abuse

Risk for Substance Use Disorder (SUD)
Onset in Adults With Untreated ADHD

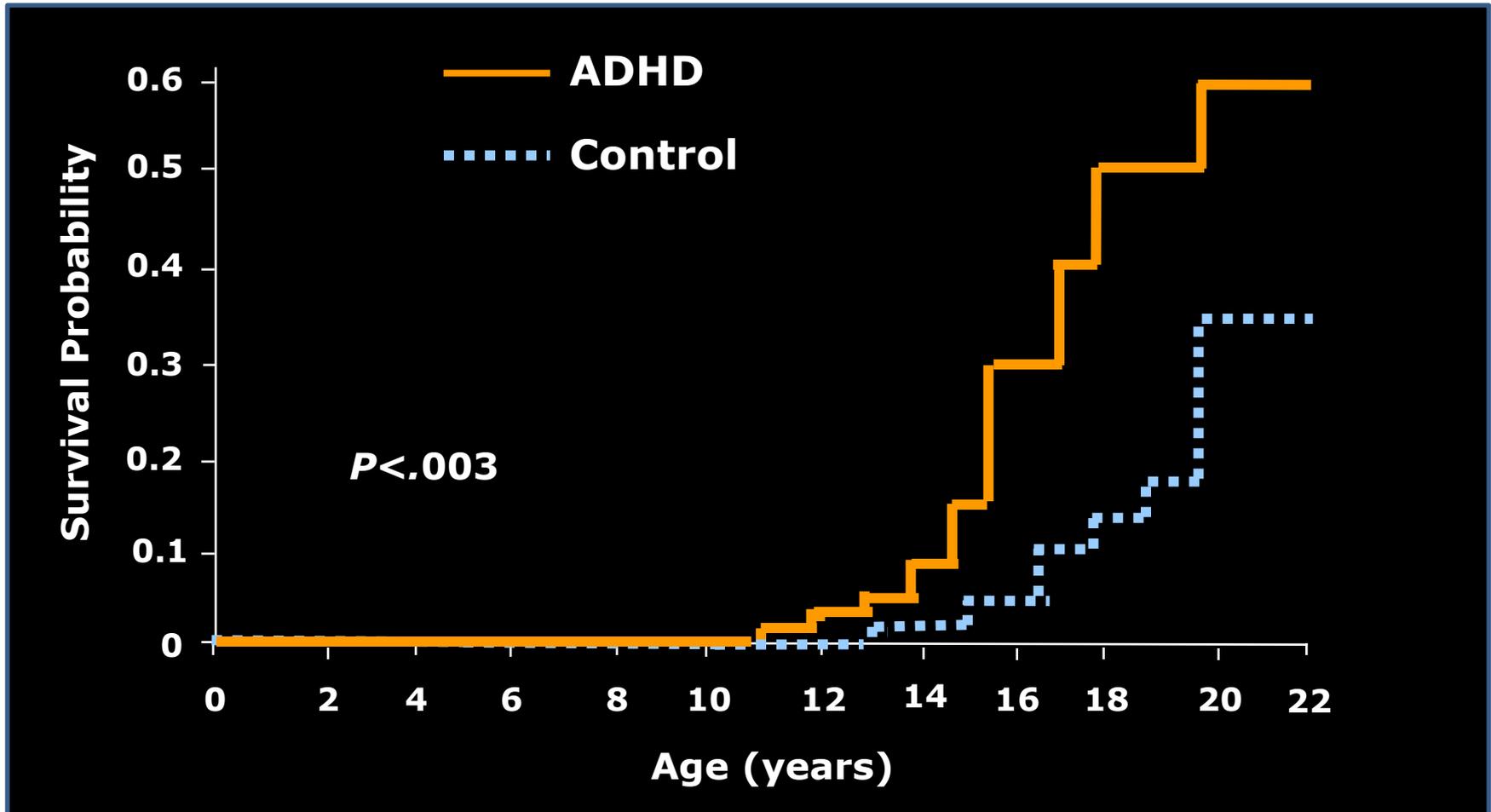


SUD in ADHD Youth Growing Up: Overall Rate of Substance Use Disorder



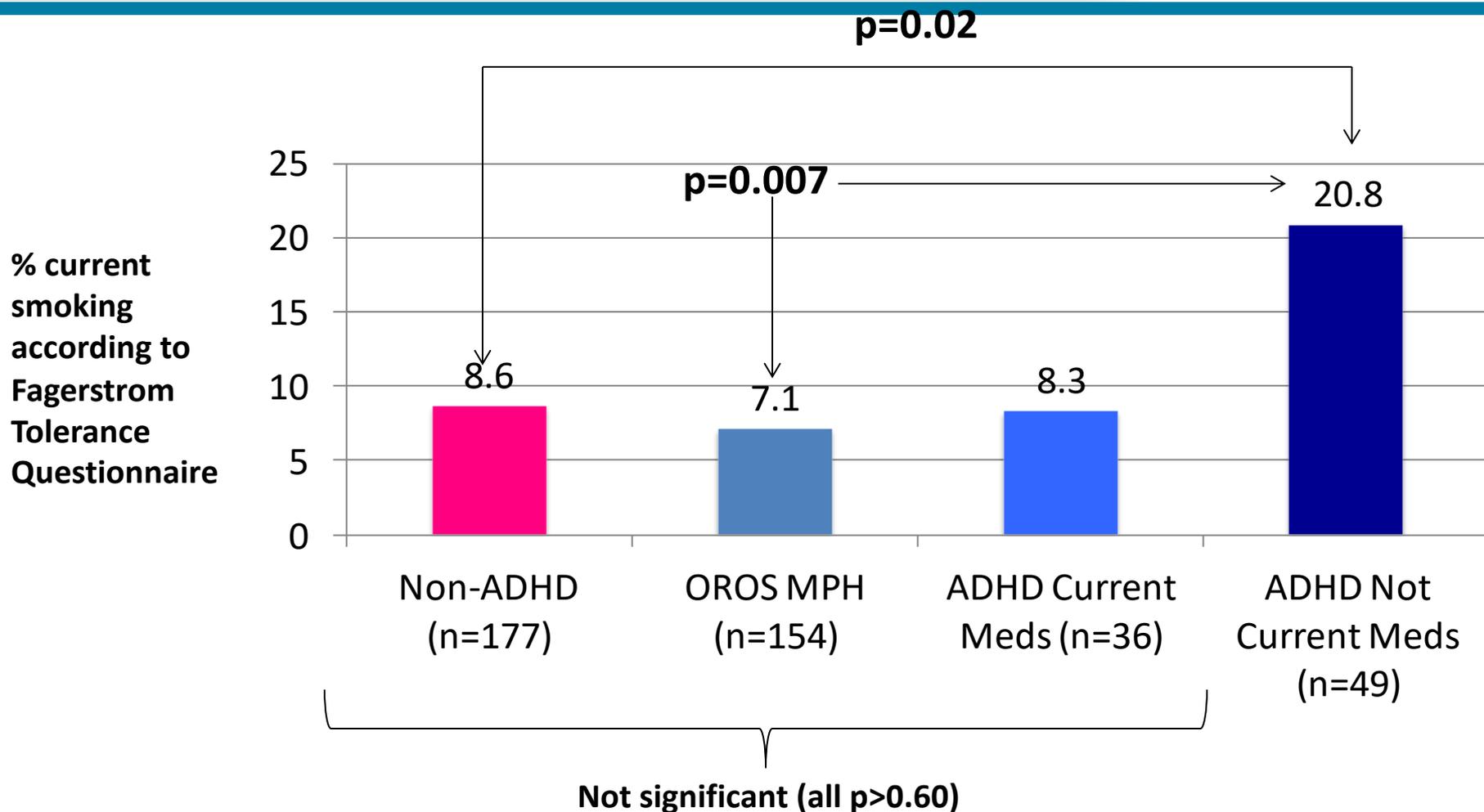
Biederman, Wilens, Mick et al., Pediatric 1999

Onset of **Nicotine Use** in Children and Adolescents with ADHD



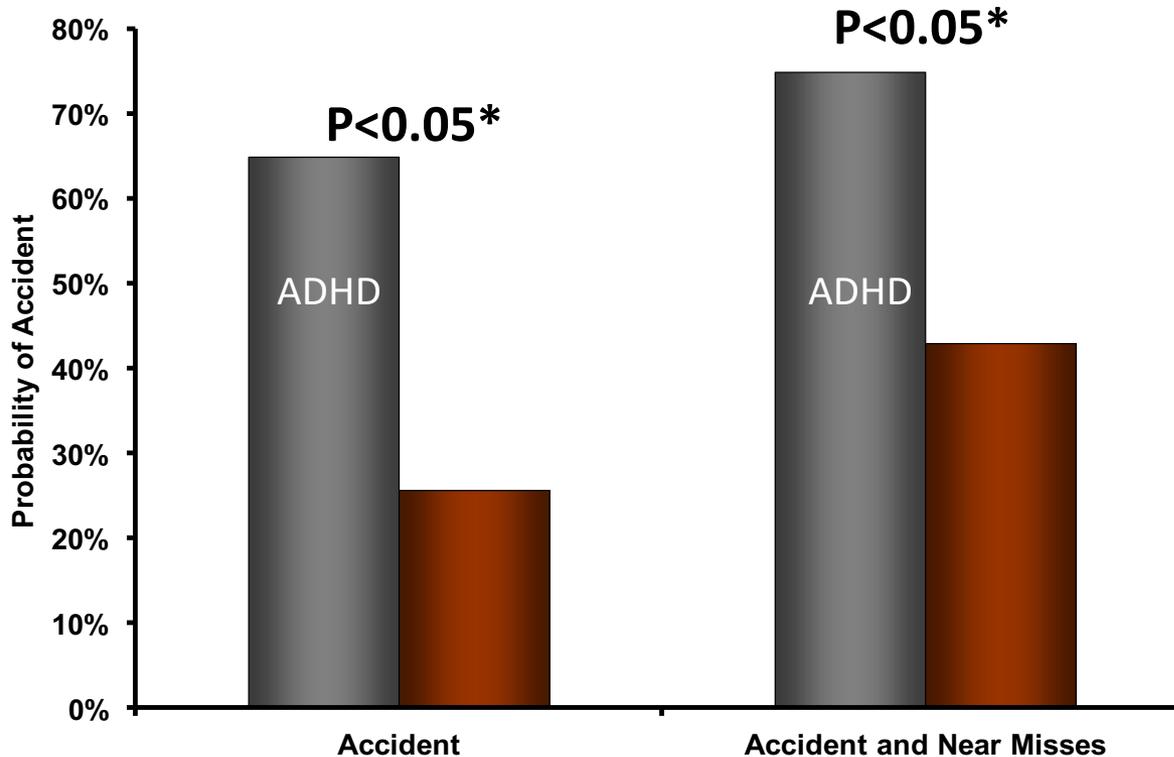
Prospective Study of OROS MPH vs. non-ADHD and ADHD

Omnibus test, chi-squared(1)=8.44, p=0.04



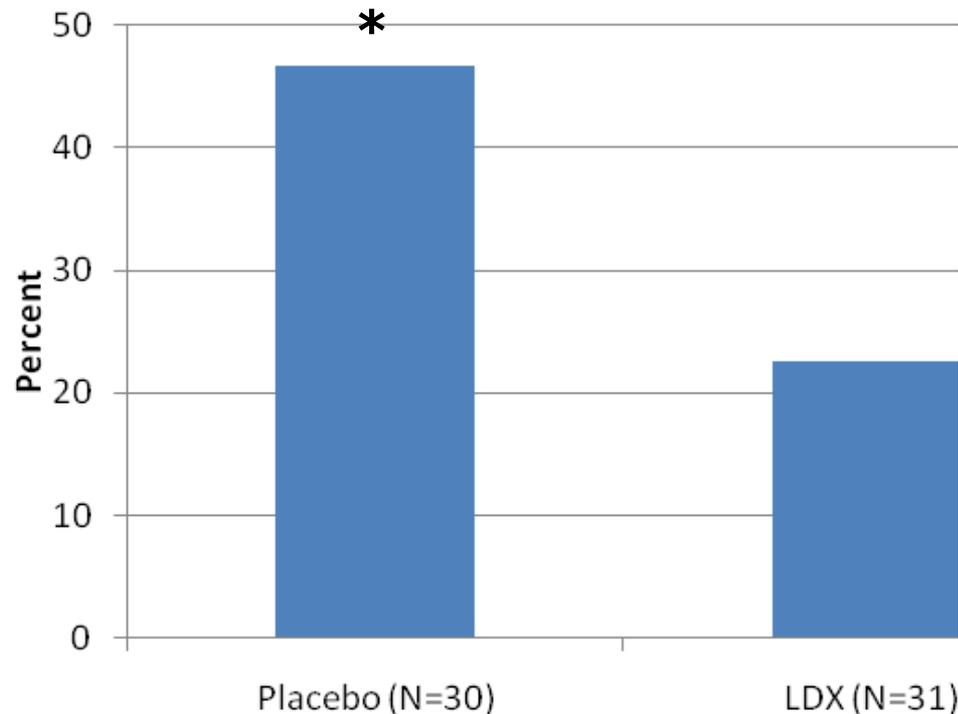
Hammerness and Biederman, Journal of Pediatrics 2012

Accidents and Near Misses



*Indicates P<0.05 after controlling for gender, age, time of day and the age*ADHD interaction

Percent of Subjects Involved in Collisions During Surprise Events



LDX = lisdexamfetamine dimesylate

- During the five surprise events, drivers in the medication group were 67% less likely to have a collision than drivers in the placebo group

Disease burden and direct medical costs of incident adult ADHD: A retrospective longitudinal analysis based on German statutory health insurance claims data

Conclusions. We conclude that earlier recognition of aADHD could prevent the development and aggravation of comorbid mental illnesses. At the same time, comorbid conditions may have masked (“over-shadowed”) aADHD and delayed diagnosis. The burden of disease in aADHD is high, which was noticeable especially among individuals who received initial ADHD-medication, suggesting that psychopharmacological treatment was mainly considered for the most severely ill. We conclude that measures to facilitate access of aADHD patients to clinical experts are required to improve reality of care in the outpatient setting.

Background. Adult attention-deficit/hyperactivity disorder (aADHD) is still a largely unrecognized psychiatric condition despite its strong impact on individuals’ well-being. Here, we describe the healthcare situation of individuals with incident aADHD over 4 years before and 4 years after initial administrative diagnosis.

Libutzki et al. *Eur Psychiatry*. 2020 Oct 1;63(1):e86.



Literature Review of Registries and Large Databases Examining the Effects of Stimulants on Functional Outcome

Summary of Results

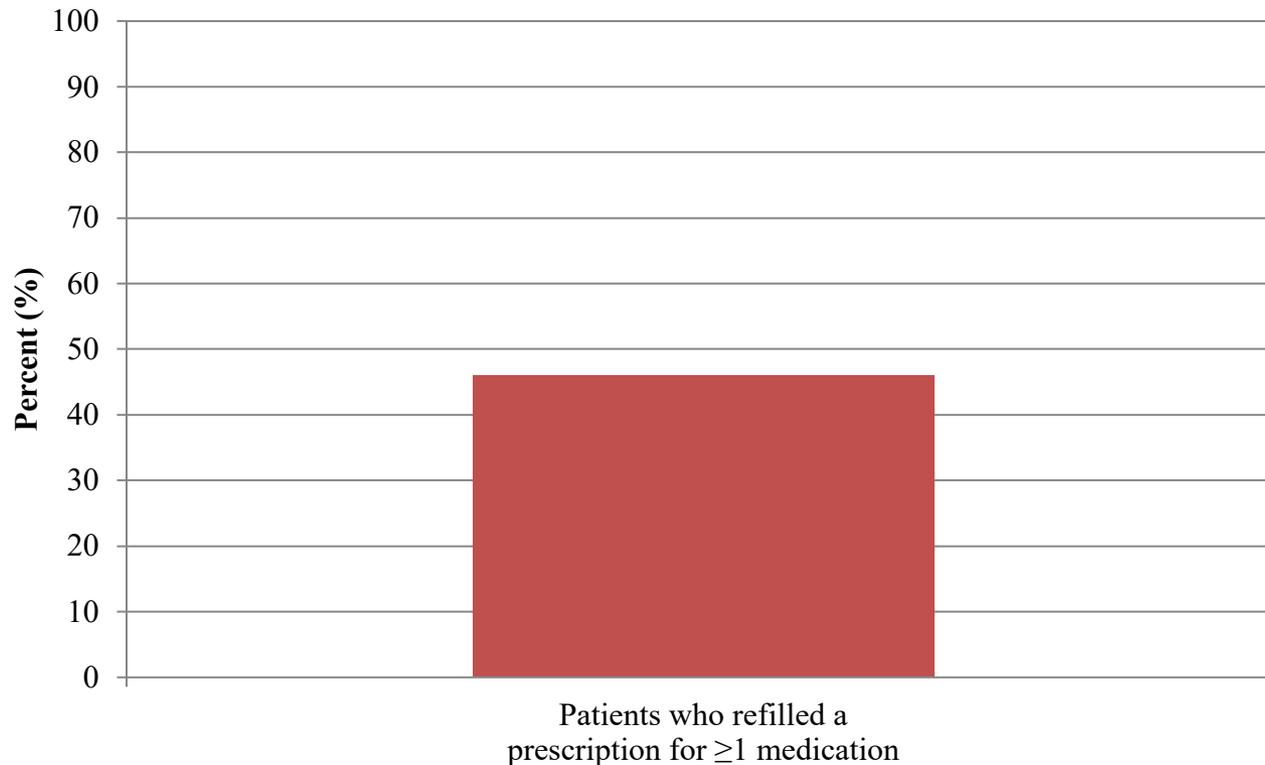
- The majority of the N=40 articles identified document a robust protective effect of ADHD medications on **mood disorders, suicidality, criminality, substance use disorders, accidents and injuries, traumatic brain injuries, motor vehicle crashes, and educational outcomes**
- Similarly, the meta-analyses demonstrated an overall protective effect of medication treatment on these functional outcomes



The Serious Problem of Non-Adherence

Percent of Patients with ADHD who Renewed their First Stimulant Rx: A Partners Healthcare EMR Review

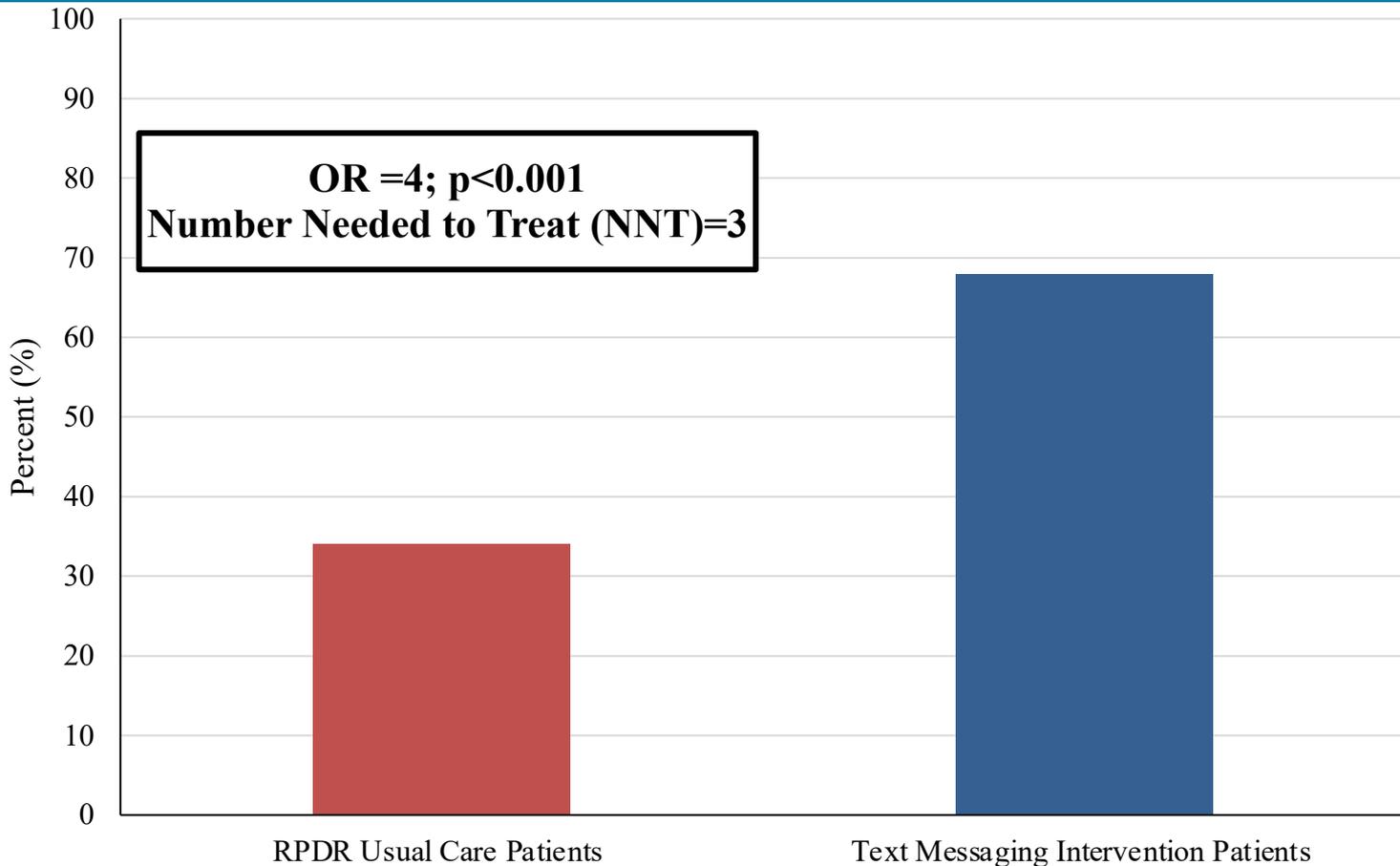
# of patients	# of patients who refilled a prescription for ≥ 1 medication	% of patients who refilled
2,206	1,023	46%





AN SMS-BASED DISEASE MANAGEMENT INTERVENTION FOR ADHD

Rate of Engagement to stimulant treatment in ADHD who received SMS Intervention (N=92) vs. age- and sex-matched Controls (N=460) who received treatment as usual in Partners Healthcare



Biederman et al. *J Clin Psychopharmacol* 2019;39: 351–356

Summary

- ADHD is a neurobehavioral disorder with a:
 - Complex etiology
 - Neurobiologic basis
 - Strong genetic component
- ADHD
 - Affects millions of people of both genders
 - Persists through adolescence and adulthood in a high percentage of cases
 - Can have negative impact on multiple areas of functioning
 - ADHD is a highly treatable disorder