



The Serious Problem of Non-Adherence to Treatment in ADHD

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Disclosures 2020-2021

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

- *Research support:* Genentech, Headspace Inc., Pfizer Pharmaceuticals, Roche TCRC Inc., Sunovion Pharmaceuticals Inc., Takeda/Shire Pharmaceuticals Inc., and Tris.
- *Consulting fees:* Akili, Avekshan LLC, Jazz Pharma, and Shire/Takeda
- *Honorarium for scientific presentation:* Tris
- *Royalties paid to the Department of Psychiatry at MGH, for a copyrighted ADHD rating scale used for ADHD diagnoses:* Biomarin, Bracket Global, Cogstate, Ingenix, Medavent Prophase, Shire, Sunovion, and Theravance
- Through Partners Healthcare Innovation, I have a partnership with MEMOTEXT to commercialize a digital health intervention to improve adherence in ADHD.

ADHD is a Prevalent and Chronic Disorder

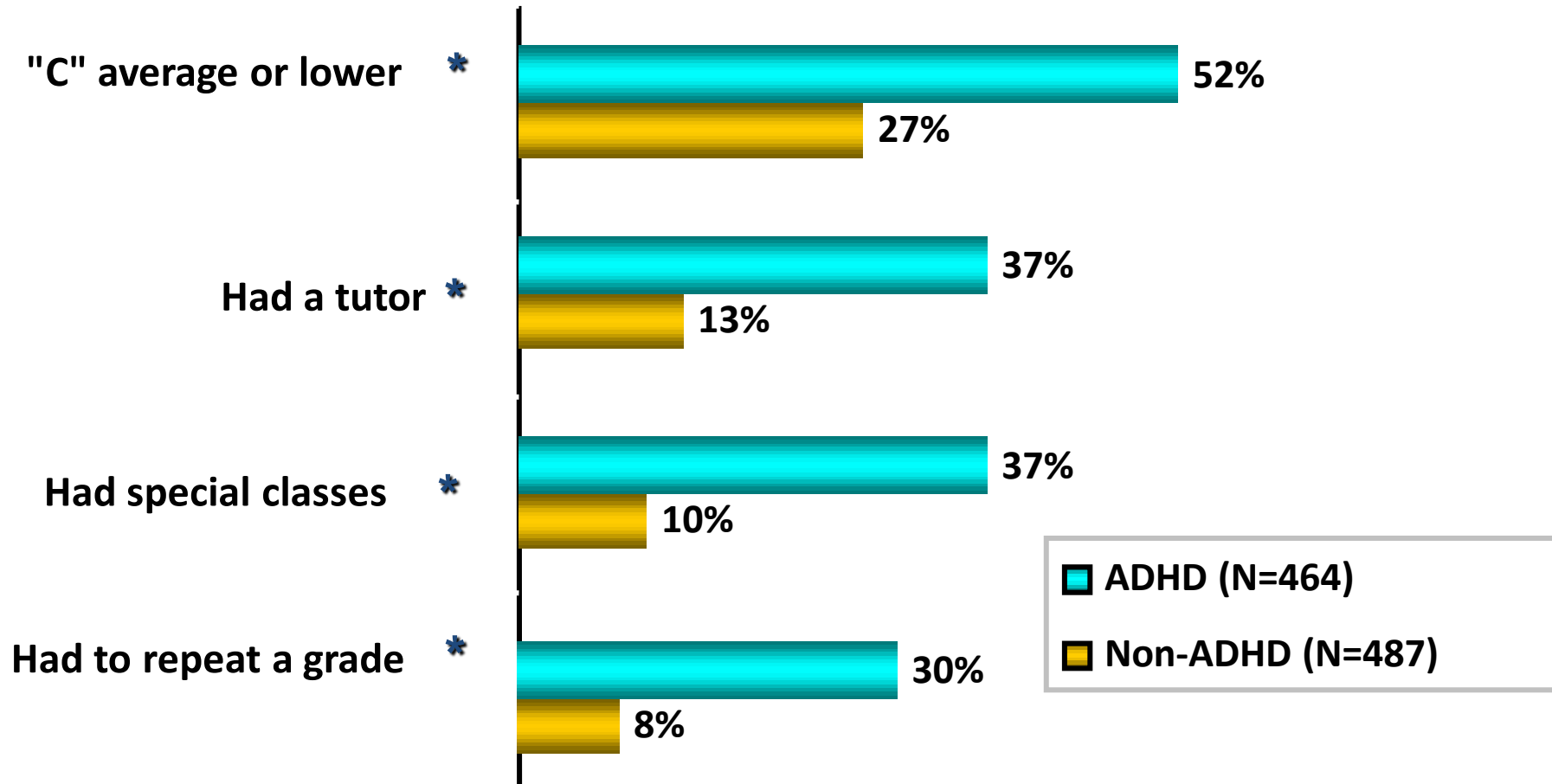
- Prevalence

ADHD in Children (10%)

ADHD in Adults (5%)

Educational Impairment in High School

Percentage of Those Who Attended High School



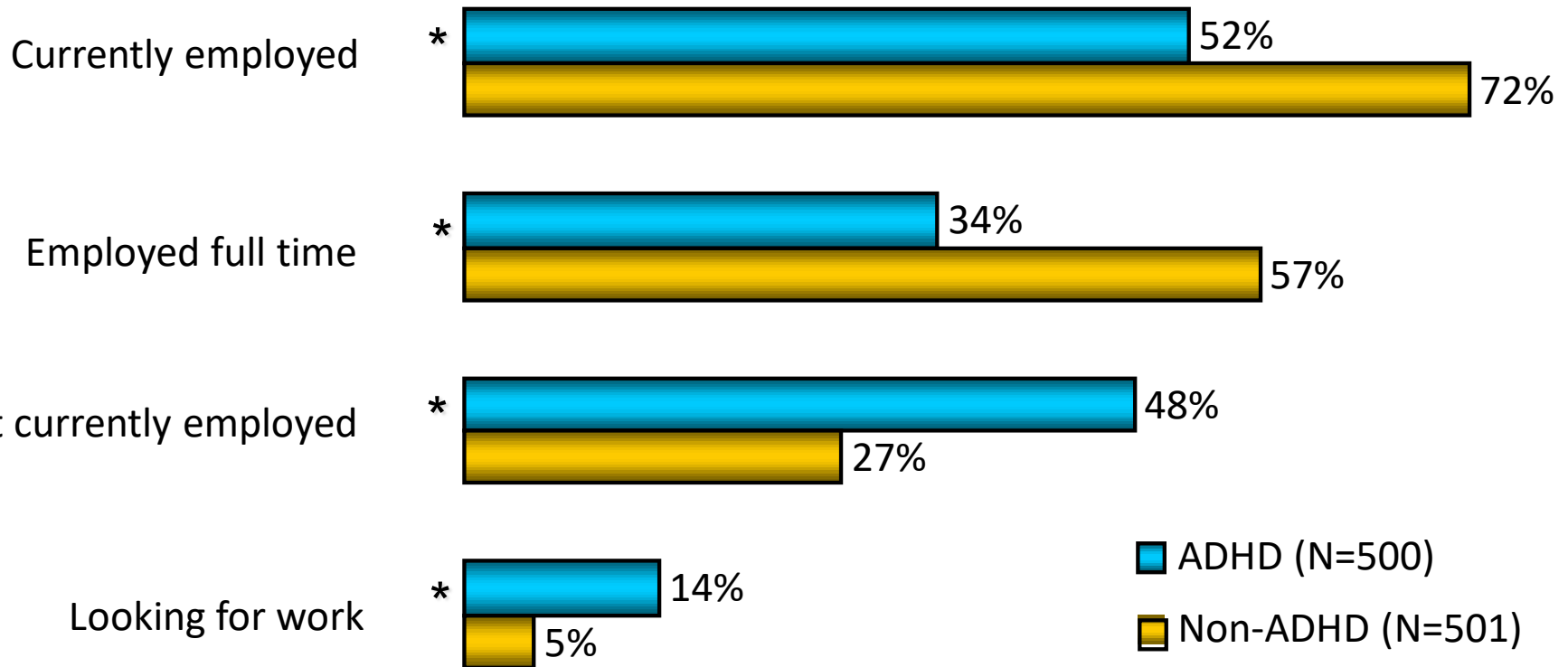
* $p \leq .001$

Biederman et al. *J Clin Psychiatry*. 2006 Apr; 67(4):524-40

www.mghcme.org

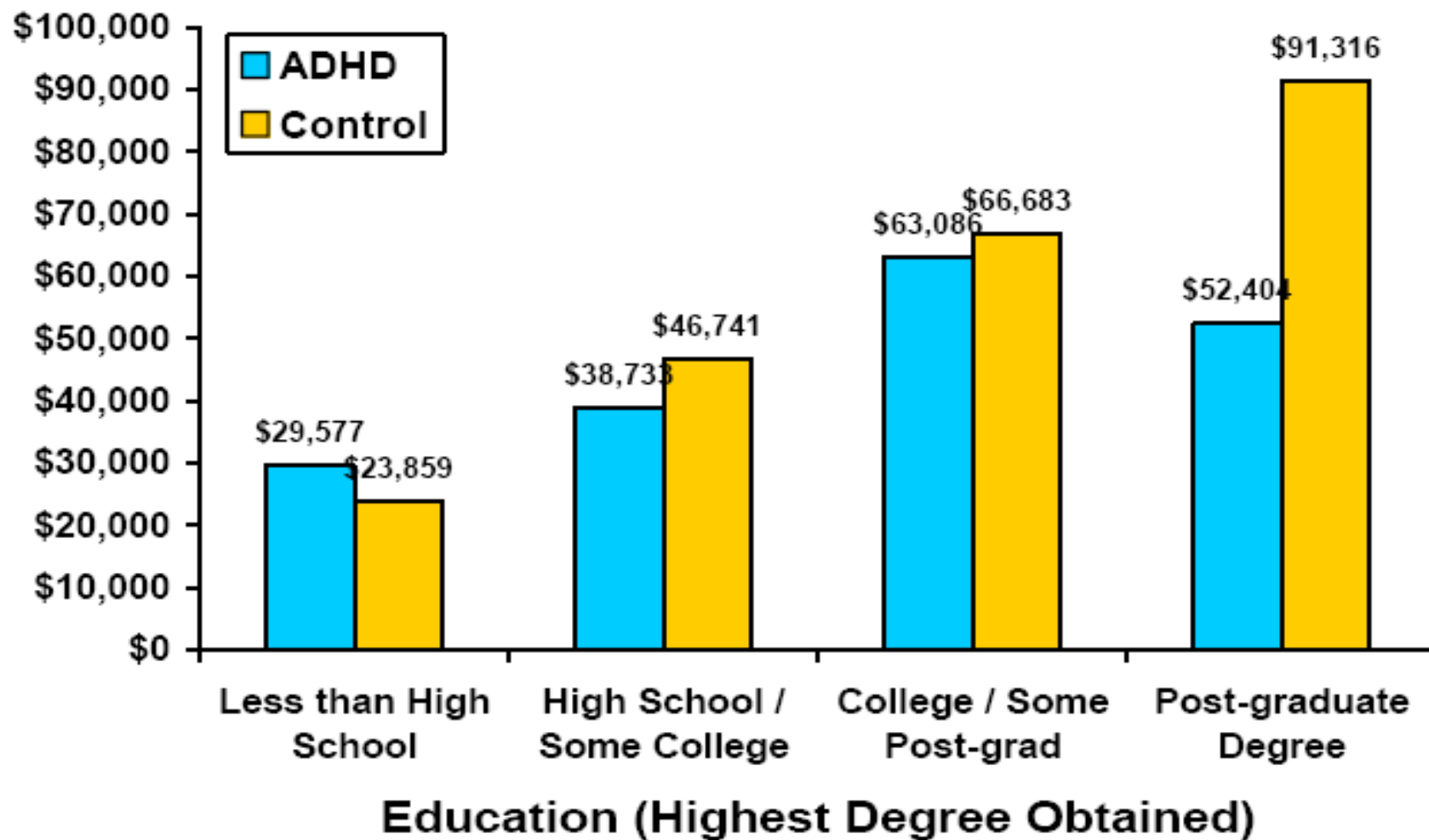
Current Employment Status

Percentage of Each Group



* $P \leq .001$

Average Household Income by Education Level Attained



Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study

Søren Dalsgaard, Søren Dinesen Østergaard, James F Leckman, Preben Bo Mortensen, Marianne Giørtz Pedersen

Summary

Background Attention deficit hyperactivity disorder (ADHD) is a common mental disorder associated with factors that are likely to increase mortality, such as oppositional defiant disorder or conduct disorder, criminality, accidents, and substance misuse. However, whether ADHD itself is associated with increased mortality remains unknown. We aimed to assess ADHD-related mortality in a large cohort of Danish individuals.

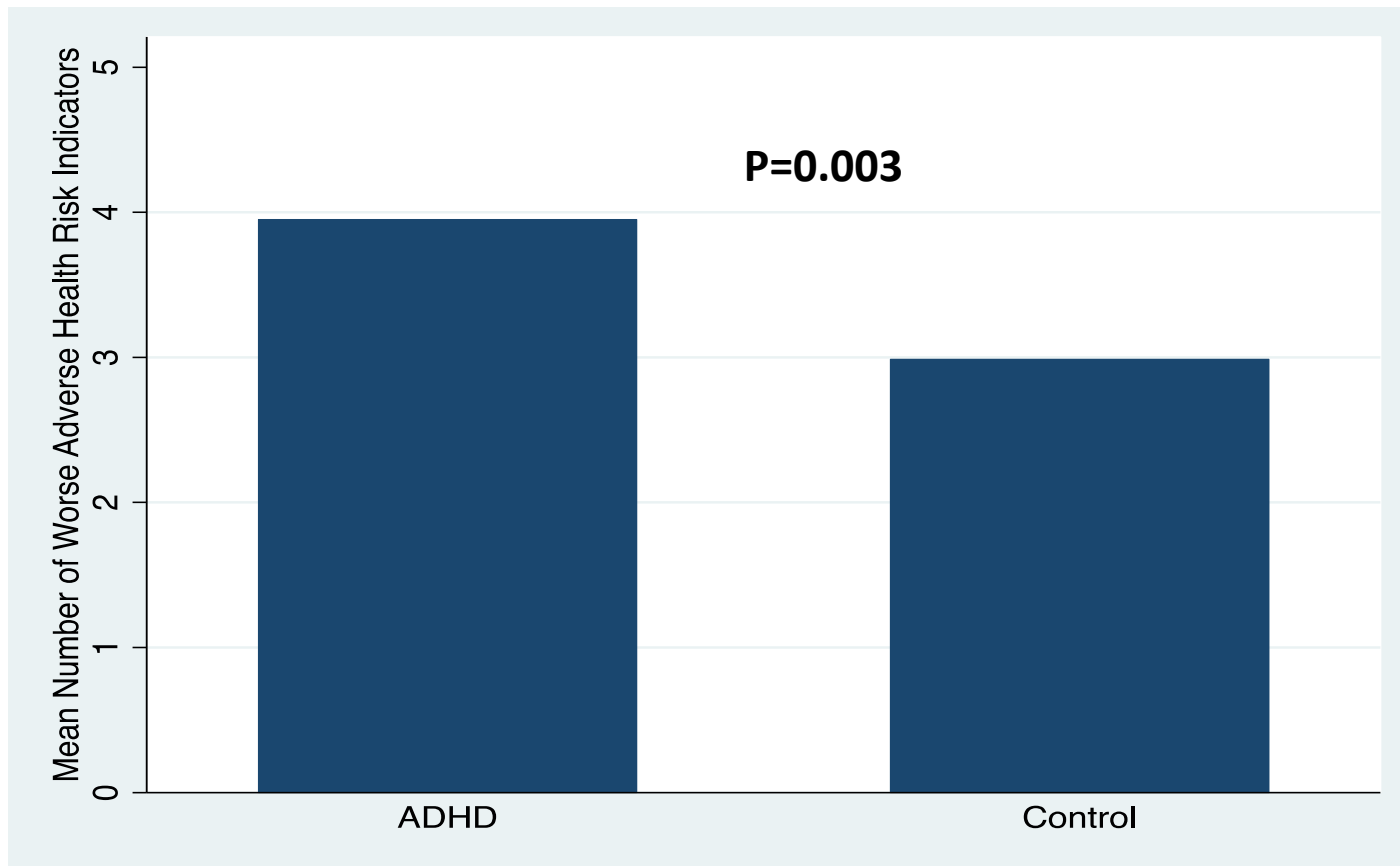
Methods By use of the Danish national registers, we followed up 1·92 million individuals, including 32 061 with ADHD, from their first birthday through to 2013. We estimated mortality rate ratios (MRRs), adjusted for calendar year, age, sex, family history of psychiatric disorders, maternal and paternal age, and parental educational and employment status, by Poisson regression, to compare individuals with and without ADHD.

Findings During follow-up (24·9 million person-years), 5580 cohort members died. The mortality rate per 10 000 person-years was 5·85 among individuals with ADHD compared with 2·21 in those without (corresponding to a fully adjusted MRR of 2·07, 95% CI 1·70–2·50; $p < 0·0001$). Accidents were the most common cause of death. Compared with individuals without ADHD, the fully adjusted MRR for individuals diagnosed with ADHD at ages younger than 6 years was 1·86 (95% CI 0·93–3·27), and it was 1·58 (1·21–2·03) for those aged 6–17 years, and 4·25 (3·05–5·78) for those aged 18 years or older. After exclusion of individuals with oppositional defiant disorder, conduct disorder, and substance use disorder, ADHD remained associated with increased mortality (fully adjusted MRR 1·50, 1·11–1·98), and was higher in girls and women (2·85, 1·56–4·71) than in boys and men (1·27, 0·89–1·76).

Interpretation ADHD was associated with significantly increased mortality rates. People diagnosed with ADHD in adulthood had a higher MRR than did those diagnosed in childhood and adolescence. Comorbid oppositional defiant disorder, conduct disorder, and substance use disorder increased the MRR even further. However, when adjusted for these comorbidities, ADHD remained associated with excess mortality, with higher MRRs in girls and women with ADHD than in boys and men with ADHD. The excess mortality in ADHD was mainly driven by deaths from unnatural causes, especially accidents.

Funding This study was supported by a grant from the Lundbeck Foundation.

Mean Number of Impaired Health Risk Indicators



Impaired Health Risk indicators: cutoffs defined by values outside the normal range

ADHD is a Highly Treatable Disorder

- ADHD is among the most treatable of all psychiatric disorders
- Stimulants are among the most effective treatments in medicine with effect sizes of 1
- **Studies show that many of ADHD-associated poor outcomes can be mitigated by treatment with stimulants**

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

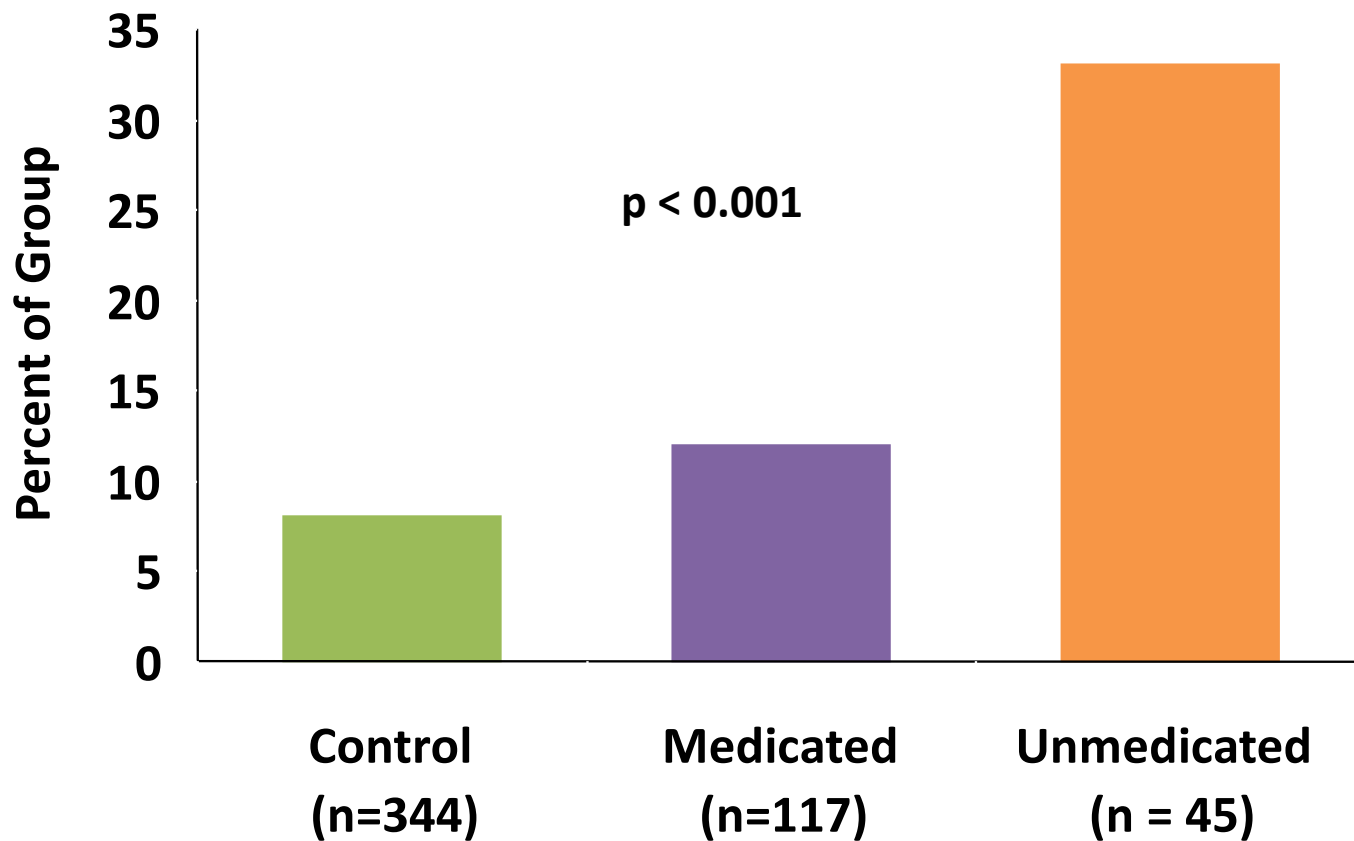
112 (80%) and 105 (88%) of the children in the ADHD and control groups, respectively, were reassessed (mean age: 22 years). We examined the association between stimulant treatment in childhood and adolescence and subsequent comorbid disorders and grade retention by using proportional hazards survival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

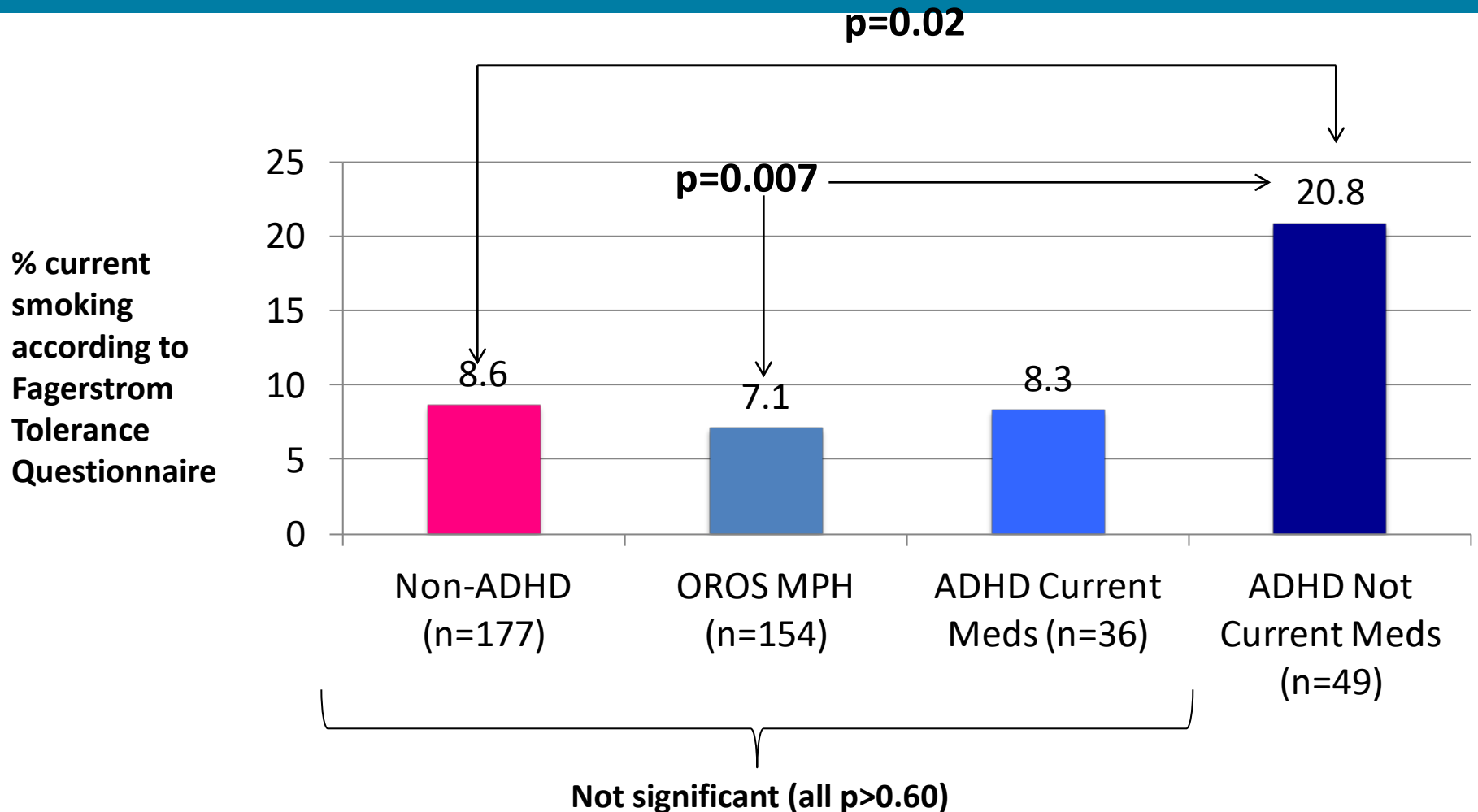
SUD in ADHD Youth Growing Up: Overall Rate of Substance Use Disorder



Biederman, Wilens, Mick et al., Pediatric 1999

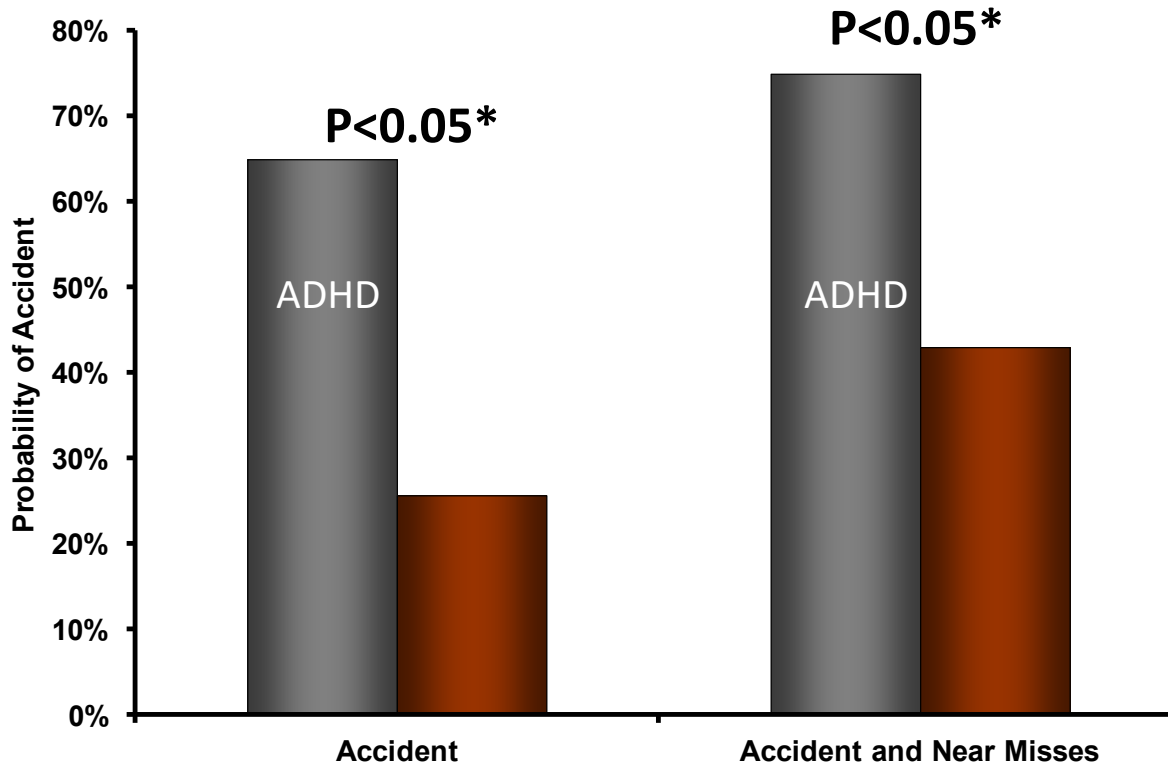
Prospective Study of OROS MPH vs. non-ADHD and ADHD

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



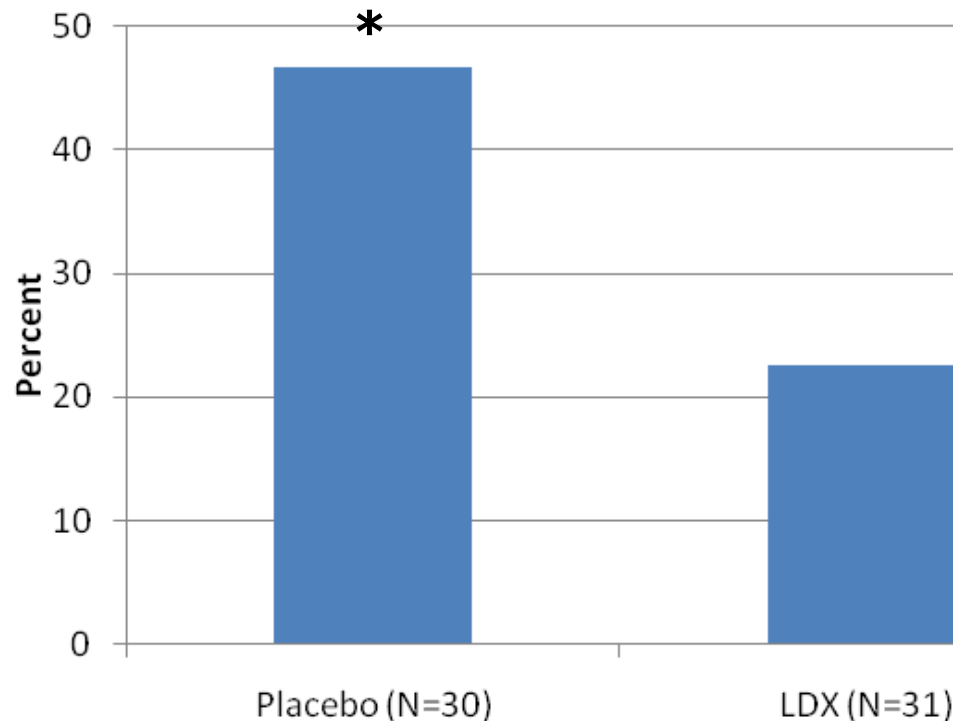
Hammerness and Biederman, Journal of Pediatrics 2012

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

***LITERTURE REVIEW OF LARGE DATASETS
EXAMINING THE IMPACT OF
TREATMENT OF FUNCTIONAL
OUTCOMES***

Literature Review: Main Aim

- The main aim of this study was to conduct a systematic review and meta-analysis of the extant literature from large databases to assess the effects of stimulant treatment on ADHD-associated functional outcomes
- We hypothesized that this literature would show that ADHD medications improve important ADHD-associated serious and morbid functional outcomes.

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

Conclusions

These findings indicate that ADHD medication treatments are associated with decreases in the risks for a wide range of ADHD-associated functional outcomes supporting efforts aimed at early diagnosis and treatment of individuals with ADHD.

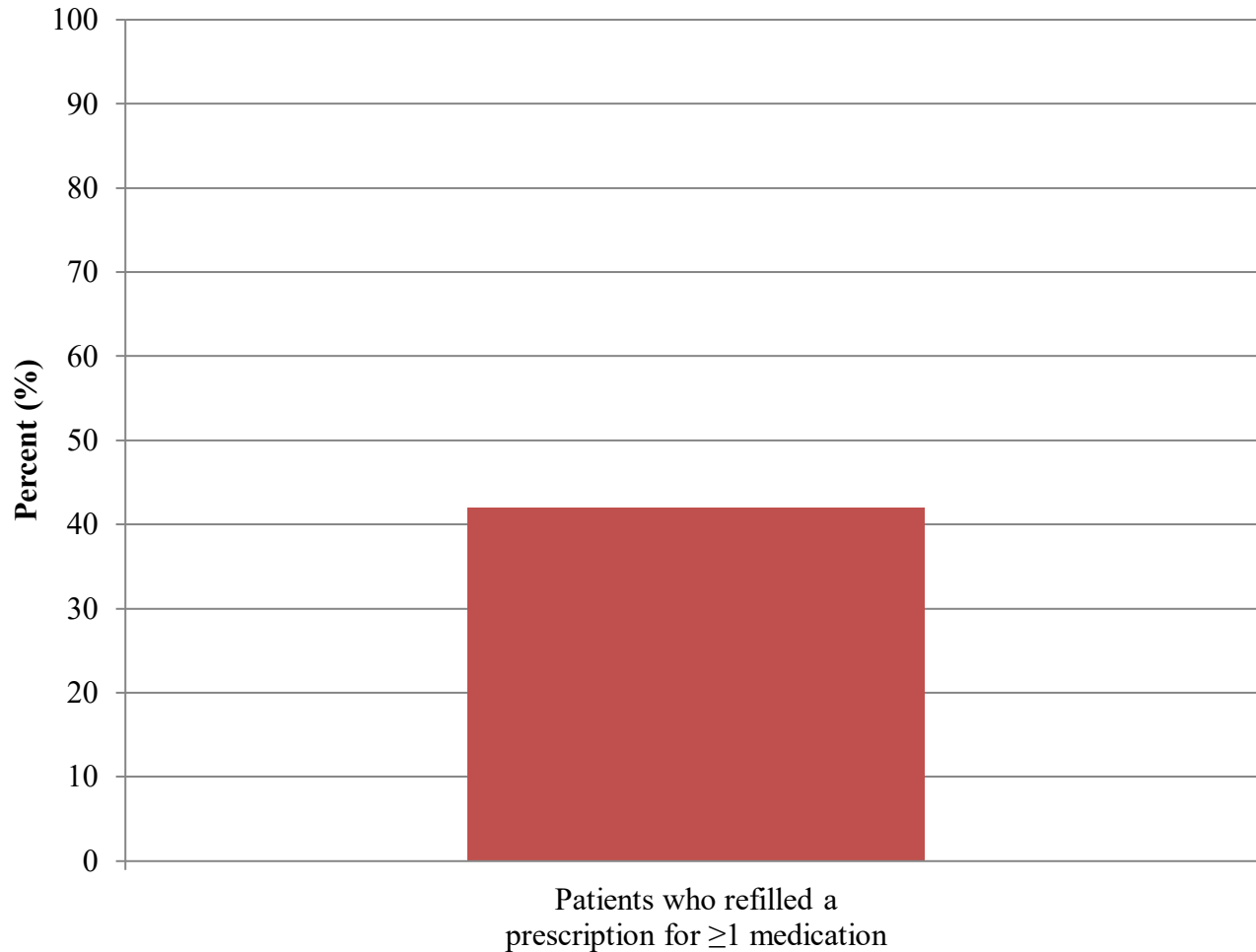
**MAJOR UNMET NEED: EXTREMELY
POOR ADHERENCE TO STIMULANT
MEDICATIONS IN ADHD**



ADULT ENGAGEMENT DATA AT PARTNERS


Percent of Adults with ADHD who Renewed their First Stimulant Rx at Partners Healthcare: An EMR Review

| Total # of Patients | # of Patients Who Renewed | % of Patients Who Renewed |
|---------------------|---------------------------|---------------------------|
| 2,689 | 1120 | 42% |





Further evidence of low adherence to stimulant treatment in adult ADHD: an electronic medical record study examining timely renewal of a stimulant prescription

Joseph Biederman^{1,2}  · Ronna Fried^{1,2} · Maura DiSalvo¹ · K. Yvonne Woodworth¹ · Itai Biederman¹ · Haley Driscoll¹ · Elizabeth Noyes¹ · Stephen V. Faraone^{3,4} · Roy H. Perlis^{1,2,5}

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Abstract

Rationale ADHD is a prevalent and morbid neurobiological disorder affecting up to 5% of adults. While stimulants have been documented to be safe and effective in adults with ADHD, uncertainties remain about adherence to these treatments.

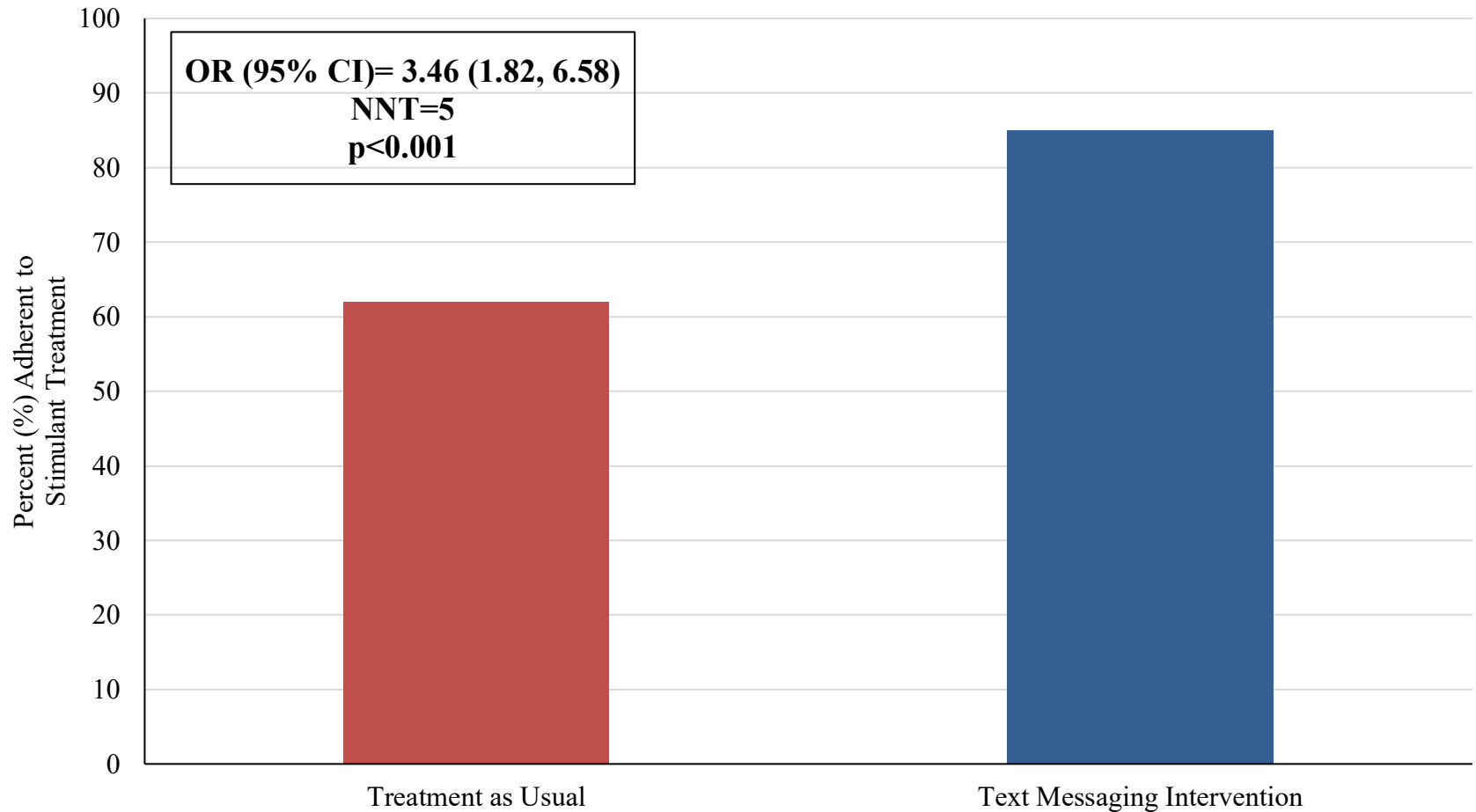
Objectives The main aim of this article was to evaluate contemporaneous rates and correlates of adherence to stimulants in adults with ADHD using data from electronic medical records from a large healthcare organization focusing on timely renewal of an initial prescription.

Biederman et al. *Psychopharmacology (Berl)*. 2020 Sep;237(9):2835-2843.



AN SMS-BASED DISEASE MANAGEMENT INTERVENTION FOR ADHD


Rate of patient adherence to stimulant treatment in pediatric patients who received the SMS intervention (N=87) and age- and sex-matched patients who did not participate in the intervention and received treatment as usual (N=246)



Biederman et al. *J Psychopharmacol* 2020 in press



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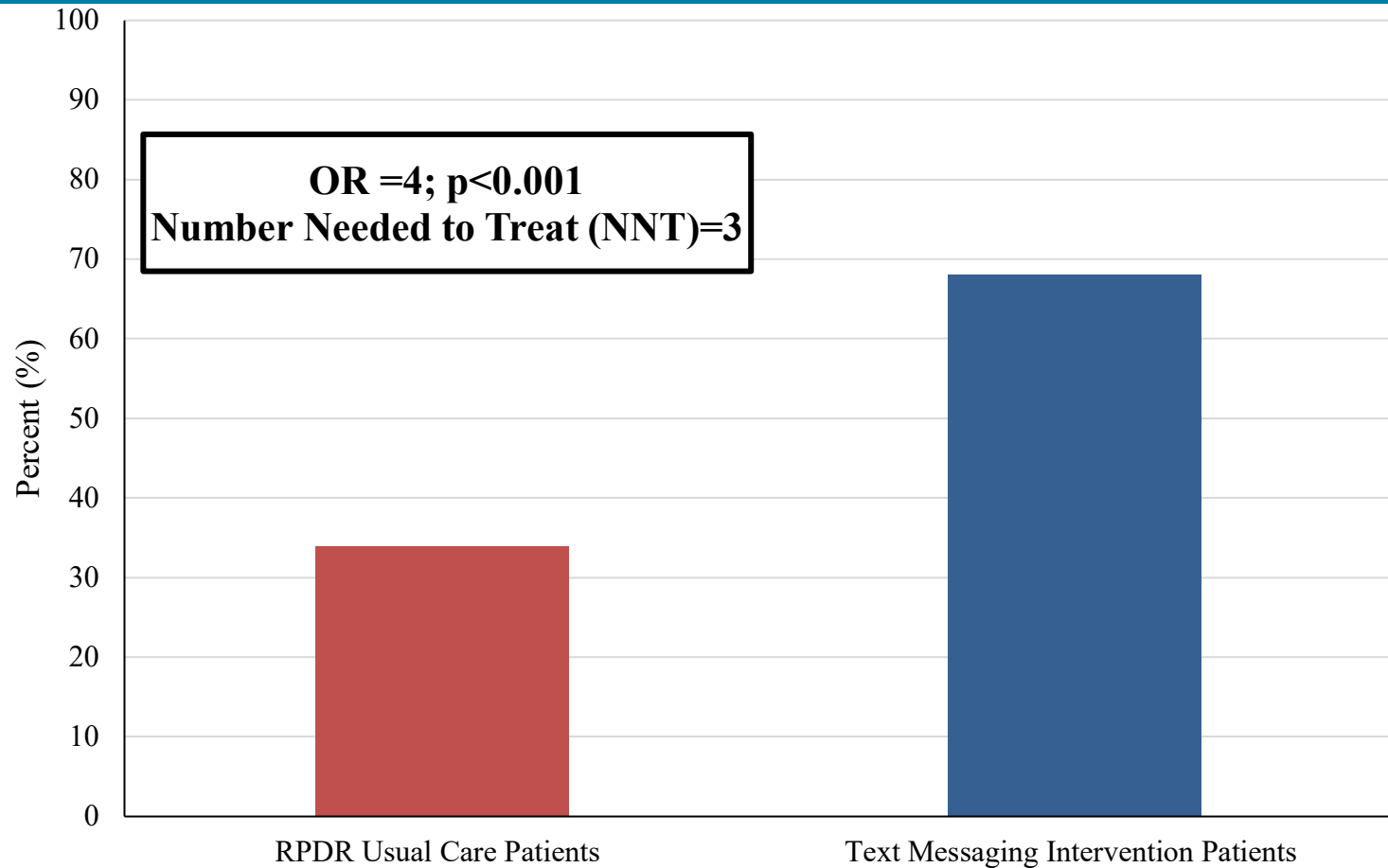
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Rate of Engagement to stimulant treatment in adult patients who received SMS Intervention (N=92) vs. age- and sex-matched patients (N=460) who received treatment as usual in Partners Healthcare



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

A Novel Text Message Intervention to Improve Adherence to Stimulants in Adults With Attention Deficit/Hyperactivity Disorder

Joseph Biederman, MD,† Ronna Fried, EdD,*† Maura DiSalvo, MPH,* K. Yvonne Woodworth, BA,* Itai Biederman, MBA,* Elizabeth Noyes, BA,* Stephen V. Faraone, PhD,‡§ and Roy H. Perlis, MD, MSc*†||*

Abstract:

Background: Attention deficit/hyperactivity disorder (ADHD) is a prevalent neurobiological disorder associated with a wide range of adverse outcomes. Although large data sets document that stimulants decrease the risks for many ADHD-associated adverse outcomes, compliance with stimulants remains very poor. The main aim of this study was to assess the effectiveness of a novel text messaging–based intervention aimed at improving the poor rate of adherence to stimulant medications in adults with ADHD.

Methods: Subjects were adults with ages 18 to 55, prescribed a stimulant medication for ADHD treatment. For comparators, we identified at a 5-to-1 ratio (age and sex matched) adult patients from the Partners HealthCare electronic medical record who had been prescribed stimulant medications over a 1-year period. We determined whether patients had timely prescription refills, defined as refilled within 37 days, using prescriptions documented in their electronic medical record.

Results: Our results showed that 68% of the SMS intervention group refilled their prescriptions in a timely manner. In contrast, only 34% of patients receiving treatment as usual refilled their prescriptions in a timely fashion (odds ratio, 4.04; 95% confidence interval, 2.49–6.56; $P < 0.001$).

Conclusions: These data indicate that an innovative ADHD-centric text messaging intervention significantly improved patient engagement to treat-

Attention deficit/hyperactivity disorder (ADHD) is a neurobehavioral disorder¹ estimated to afflict up to 5% of adults in this country.² The literature documents many negative outcomes of ADHD including high risk for academic/occupational underattainment and high school dropout,^{3–5} unemployment and underemployment,^{3–7} divorce and separation,⁴ traffic accidents,^{3,8–10} medical and psychiatric comorbidities,^{4,6} posttraumatic stress disorder,^{6,11} traumatic brain injury,^{12,13} and smoking and substance abuse,^{6,7,11,14,15} among many others. Although stimulants are safe and effective in treating ADHD^{16–24} and could help mitigate many of these complications,^{25,26} nonadherence to stimulant treatment in ADHD is very high (up to 87%).^{27–30}

Although the reasons for poor adherence to medications for ADHD remain unclear, it is possible that the core features of ADHD such as forgetfulness, inattention, and deficits in follow through contribute to this problem.^{31,32} Another important factor contributing to nonadherence in ADHD is the complexity associated with prescribing stimulants that are schedule II medicines requiring monthly written prescriptions and monthly contact with the prescriber. Finally, ongoing biases, prejudices, and misperceptions about ADHD and its treatment are also likely contributors to nonadherence.

Although high rates of poor adherence to stimulants for

Benefits of the Text Messaging Program

- Helps patients remain adherent
- Helps families support patient treatment
- Helps prescribers educate and support patient treatment, in a cost effective manner allowing the patient to be seen less frequently and diminishing the concern of the clinician about the uncertainty of patient's renewal of their treatment

Significance

- Text messaging is widely used, available in most geographic areas and is inexpensive
- Text messaging content can be adapted to any age group , geographic location, clinical need and clinical setting

The MGH SMS Program

- We developed a text messaging program aimed at improving adherence in ADHD patient populations thereby reducing costs of ADHD-associated complications while adding beneficial support and value to patients, families and prescribers

Questions?

- Email: jbiederman@partners.org
- THANK YOU