EDITORIAL

Protective Effects of ADHD Medication on Real-World Outcomes

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While attention-deficit/hyperactivity disorder (ADHD) has long been defined by its core symptoms, inattention, hyperactivity, and impulsivity, the true impact of ADHD extends beyond its symptomatology. For example, an ADHD diagnosis is linked to adverse educational outcomes, suicidal behavior, aggression, substance use, and dementia, risks that persist even after accounting for co-occurring mental health disorders.[1,2]

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In this issue of *JAMA Psychiatry*, Li and colleagues[3] report a large study using a self-controlled case series of 247 420 individuals with ADHD in Sweden from 2006 to 2020. The rigor of the study is strengthened by its self-control design. Ideal for pharmacoepidemiological research, in this method, individuals act as their own controls, allowing researchers to account for both measured and unmeasured confounders. Through this robust analysis, they found that periods receiving ADHD medication were consistently associated with lower rates of multiple serious outcomes, including self-harm, unintentional injuries, traffic crashes, and criminal arrests.[3] These findings reinforce a growing body of literature indicating that ADHD pharmacotherapy yields benefits beyond symptom control, cutting the risk of costly and dangerous events in patients' lives.

These new findings from Sweden are not isolated. Over the past decade, several large studies across countries have documented similar protective associations. A landmark within-patient study in Sweden found that ADHD medication was associated with a 41% reduction in criminal convictions in women and a 32% reduction in men.[4] In the US, MarketScan insurance data demonstrated that adolescents and adults had a 31% lower risk of substance-related emergency events in women and a 35% lower risk in men during months on ADHD medication.[5] Similarly, Chang and colleagues[6] reported a 42% lower rate of motor vehicle crashes in women and a 38% lower rate in men in medicated months.[6] This real-world benefit extends even further. A meta-analysis by Boland et al[7] demonstrated protective effects similar to those found by Li and colleagues,[3] showing 25% to 35% within-group improvement during the active treatment period and nearly 50% improvement between treated and never-treated groups across mood disorders, substance use disorders, accidents, crime, injuries, and educational outcomes.[7]

The accumulation of evidence makes one thing clear: when used appropriately, ADHD medications can help affected people not just feel better, but live safer, more productive lives. This message is important as many individuals with ADHD still do not receive medication as their first-line treatment, despite medications having the most robust evidence for ADHD.[8]

As the rate of ADHD medication treatment increases worldwide, extending to a population that would not previously have been treated and, therefore, is likely to have less severe symptoms, an emerging question is whether there remains a meaningful reduction in real-world harm. Li and colleagues[3] examine this. Between 2006 and 2020, the prevalence of ADHD medication use in Sweden increased 3-fold in children and more than 5-fold in adults. During this time, the protective association between ADHD medication and outcomes, such as unintentional injury, traffic crashes, and crime, attenuated, though it remained significant. Notably, this decline in effect size was not fully explained by changing demographics (eg, age or sex), suggesting that broader prescribing may be reaching individuals with milder impairments, and therefore, those less likely to experience these severe events associated with ADHD. Overall, these findings are significant because rising stimulant use in the US and elsewhere has come under increased scrutiny, particularly via telehealth.[9]

Historically, ADHD, once referred to as minimal brain dysfunction in the mid-20th century, was conceptualized primarily as a childhood condition marked by severe hyperactivity and impulsivity. Only the most overt cases, typically young boys with disruptive behavior, were diagnosed and treated. However, over the past 20 years, clinical understanding of ADHD has evolved into a broader, more inclusive construct across the life span. This shift is reflected in diagnostic criteria that now include examples of adult symptoms. ADHD awareness has also increased among clinicians and the public. As a result, many individuals who would have been overlooked in previous eras are now being diagnosed with ADHD and receiving medication, including greater numbers of adults and females.[9] New recipients of ADHD medication may have a lower likelihood of arrest or serious unintentional injuries in the first place, even without medication. Thus, giving them medication will not show as large an absolute reduction in those extreme outcomes.

While the results are still significant when controlling for sex, the inclusion of more females with ADHD likely contributes to a changing outcome profile. Females with ADHD, on average, display fewer externalizing behaviors (like recklessness or aggression) and more internalizing features (such as inattention or anxiety) compared with males with ADHD.[3] Consequently, untreated females with ADHD are less likely to incur outcomes like arrest, traffic crashes, or serious injuries than untreated males with ADHD. In Li and colleagues' data, the strongest medication-associated risk reductions in early years were seen in females, presumably because only the most impaired girls were treated then; however, as more girls entered the treated population, the relative benefit of medication on out-

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comes, like injuries and crime, in females declined toward the levels seen in males.[3]

Li and colleagues saw a parallel dynamic with age. Overall, ADHD symptoms diminish with age as the brain continues to mature, and many affected people stop taking medication as a result, though many more adults now take medication than in the past. Accordingly, they found that the protective effect of medication on unintentional injuries attenuated significantly in adults but not in children over time.[3] In other words, medicated youth today still show robust reductions in injury risk, but medicated adults today do not show as large a drop in injuries. This is likely because today's adult patients (a far larger group than before) include those with less severe impairment.

Critically, the purpose of ADHD treatment is not primarily to prevent arrests, car crashes, or self-harm crises. Reducing those serious externalizing outcomes is an important public health benefit of effective treatment, one that prior observational studies highlighted, but is only part of the story. ADHD medications are prescribed primarily to alleviate core symptoms (inattention, impulsivity, hyperactivity) and to improve patients' daily functioning and quality of life. Many of these positive outcomes are less visible in epidemiologic registries focused on hospital or legal records. As Li and colleagues acknowledge, their analysis captured only a subset of outcomes associated with ADHD,[3] and more evidence is crucial to draw conclusions about other domains such as academic or social functioning.

Had Li and colleagues examined such functional outcomes,[3] it is plausible that medication effects would remain just as strong over time because treatment decisions are made primarily based upon daily difficulties in function, rather than the long-term risk of severe events. Typically, medication treatment of ADHD is targeted to short-term and long-term improvements in life outcomes that matter deeply to individual patients and families, even if those outcomes are not as readily captured by population-level crime or injury statistics. Importantly, careful assessment of ADHD and its impact on daily function is crucial before starting pharmacological treatment, typically including input from multiple sources, such as family members or teachers. Sometimes, neuropsychological testing is helpful to differentiate from other reasons for learning difficulties. Key elements of the initial ADHD assessment are then repeated to evaluate response to treatment. Not studied here but also important, adjuvant psychosocial interventions, as well as educational or vocational accommodations, are usually indicated to create a plan tailored to the individual.[10]

ARTICLE INFORMATION

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