# Challenges and Limitations to Treating ADHD in Incarcerated Populations

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An often underappreciated and hard-to-treat condition in correctional institutions is attention-deficit/hyperactivity disorder (ADHD). Although there are many effective psychopharmacologic treatments for ADHD, such as various formulations of amphetamines, many physicians are hesitant to prescribe controlled stimulants in correctional settings because of concerns about abuse and safety. Although nonstimulant alternatives are available, they are generally seen as less effective than stimulants. However, there are many unique factors regarding corrections populations and their responses to treatment, which makes it difficult to know what the ideal treatment regimen would be for this population. We review the standard treatments for ADHD, for prescribing in correctional institutions, barriers to using medications for off-label treatment of ADHD, and suggest future research that could better guide correctional treatment staff on how to approach patients with ADHD.

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In this issue of the *Journal*, we are fortunate to have two papers that review U.S. Food and Drug Administration (FDA)–approved nonstimulant treatments for attention-deficit/hyperactivity disorder (ADHD): one by Jillani *et al.*,[1] on a juvenile incarcerated population, and one by Mattes,[2] who focused on an adult prison population. These papers complement each other by highlighting the multiple agents that can be used for ADHD treatment (Table 1), unique aspects of ADHD, such as differing symptom presentation (e.g., impulsivity, aggression), comorbid disorders (e.g., conduct disorder, substance abuse), and references to predecessors such as mentioned by Appelbaum[3] in his article on ADHD treatment protocols for the Massachusetts correctional system that have included stimulant and nonstimulant medications.

Although both of these papers add to the literature regarding treatment of ADHD in incarcerated populations, there are still many unanswered questions when it comes to how best to manage inmates with ADHD in corrections. Much of the work on inmates with attention-deficit spectrum disorders focuses on the hyperactivity symptom cluster, because it is those symptoms (e.g., impulsivity, restlessness, and intruding into others' space) that frequently pose the greatest disruption to institutional operation. However, we should remember that there is also the inattentive symptom cluster, which affects the inmate's quality of life and functioning, such as diminished participation in educational programs (e.g., GED test preparation, college level courses), rehabilitation activities, and therapeutic activities such as group therapy.[3] These diverse symptom clusters raise the question of which medications control which symptoms the best in this population.

An additional question asks whether incarcerated individuals with ADHD are similar to sufferers in the general population or whether they are unique subpopulations. If incarcerated individuals with ADHD represent a unique population in their mechanism of illness, symptom presentation, and comorbidity, it may be justified in most cases to treat them with medications other than those used by the general population. Even though stimulant medications such as amphetamines are the traditional gold stan-

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**Table 1.** Treatments for ADHD or ADD[1–3,8–11,37,38]

| Drug Categories/Drugs |
|---|
| FDA approved nonstimulant |
| Atomoxetine |
| Clonidine extended release |
| Guanfacine extended release |
| FDA approved stimulant |
| Dexmethylphenidate |
| Lisdexamfetamine |
| Methylphenidate |
| Mixed amphetamine salts (dextroamphetamine/amphetamine) |
| Psychotherapy |
| Behavioral: social skills training |
| CBT |
| Occupational therapy |
| Study skills |
| Off-label nonstimulants |
| Bupropion |
| Modafinil |
| SNRIs (e.g., venlafaxine, duloxetine) |
| Tricyclic antidepressants (e.g. desipramine) |
| Experimental/early studies/theoretical |
| Nicotinic/cholinergic analogs |
| Propranolol |
| SSRI (certain pathway responses) |
| Monoamine oxidase inhibitor (MAO-I) |
| Lithium (with certain comorbid conditions) |

dard for ADHD treatment in general, given the unique makeup of incarcerated populations, initial use of nonstimulants may make the most clinical sense.

To try to build on the papers by Jillani *et al.*[1] and Mattes[2] and address some of the questions raised above, we will review some general principles of attention spectrum disorders, discuss both stimulant and nonstimulant medication classes, and focus on some areas for additional research in this population.

## A General Review of ADHD and ADD

Although there are many potential causes of ADHD (genetics, brain injury, environmental exposure), the current psychobiologic explanations for the condition often involve abnormalities in the inferior frontal and dorsolateral prefrontal cortices, as well as in striatal, anterior cingulate, temporoparietal, basal ganglia, and cerebellar regions.[4–10] The primary neurotransmitters believed to be involved or affected in these regions, as related to ADHD presentations, are dopamine and norepinephrine.[8,10] Dopamine is thought to be responsible for regulating cognition and communication skills in the mesocortical pathway, whereas norepinephrine primarily helps with attention, motivation, and energy.[10] For this reason, most medications investigated or used for ADHD treatment often directly or indirectly affect these neurotransmitters. Some of these pathways (e.g., orbitofrontal–striatal tracts) are also receptive to serotonin modulations.[6,9–11] In addition some genetic studies suggest serotonin gene abnormalities (e.g., the serotonergic transporter 5-HTT and the serotonergic receptor HTR1B) also contribute to ADHD symptom presentation.[9]

Neuroimaging studies for adult ADHD show more neuroanatomy differences and variations from childhood ADHD (more inconsistent abnormalities in the frontostriatal, temporoparietal, and cerebellar regions), which are theorized to be related to natural disease progression (e.g., incomplete or spotty brain maturation), effects of medication and illicit drugs taken over the course of one's life, or an increased frequency of comorbid conditions that develop as one ages.[4,5] Changes in neuroimaging between childhood and adult ADHD may also show gender-related differences, with the male-to-female ratio being closer to 1:1 in adults than in children in whom there is a male predominance.[4,12]

Although it has been estimated that 30 to 70 percent of adult prison inmates have some degree of ADHD or ADD, the conditions have historically been thought of as "diseases of childhood" (children, 5–10%, and adults, 1–6%), with the thought being that, as children grow and their brains fully mature, the condition will largely resolve, resulting in their no longer needing medication such as stimulants.[4,6–9,12–14] Although there is a recognition that the presentation and symptoms of ADHD often change as the child ages (e.g., improvement in some hyperactive symptoms, with inattention, disorganization, and impulsivity more likely to remain), the condition does not necessarily fully abate (roughly 50–70% of children are still symptomatic to some degree as adults).[4,6–9,12–14] Some claim that ADHD can develop *de novo* in adults, which again raises a question about underlying pathologic mechanisms and which medications would best treat late-onset cases.[12,13] Although the Diagnostic and Statistical Manual of Mental Disorders (DSM), Fifth Edition[15] does not specifically recognize adult-onset ADHD, it relaxes the age limit diagnostic criteria from the Fourth Edition, Text Revision[16] (e.g., symptoms occur before age 12 rather than age 7; only five instead of six of nine symptoms are needed if 17 or older, as stated in the Attention and Hyperactivity Category; Ref. 15, pp 59–66).

These changes were made, because it may be difficult for people to remember how they behaved as young children and because many bright individuals with aspects of ADHD may have been able to compensate earlier in life, only to become more symptomatic with increasing demands as they age (e.g., transition from elementary to middle school and high school to college).[7,12–15]

Some studies have suggested that 50 to 90 percent of children and approximately 80 percent of adults with attention deficit disorder have at least one comorbid diagnosis, with as many as 50 percent having two or more.[7–9] For example, 50 percent of adults with ADHD have a comorbid substance abuse problem, 30 to 50 percent have had one or more depressive episodes, and 40 to 60 percent have had an anxiety disorder during their lifetime.[8] For children, the most frequent comorbid disorders are obsessive-compulsive disorder (OCD) and anxiety disorders (30%).[7] As referenced in Jillani *et al.*[1] and Mattes,[2] there is also a strong correlation with conduct disorder and antisocial personality disorder in the general population with ADHD, let alone in an incarcerated population.[7,9] Although there is a strong association with conduct spectrum disorders, it must be remembered that DSM-5 cautions "[ADHD] symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand instructions" (Ref. 15, p 59).

Stimulant medications are the most effective treatment for ADHD or ADD, although the exact mechanisms of actions are not fully appreciated.[7–9,14,17] Stimulants are thought to increase cytoplasmic vesical release of neurotransmitters, such as the catecholamines (dopamine, norepinephrine), inhibit degenerative enzymes, and block reuptake in the synaptic cleft.[8,18] These mechanisms can also affect other neurotransmitters, such as serotonin, providing theoretical support for varying antidepressants also having some effect on ADHD symptoms.[8,10,16] Many of the nonstimulant treatment mechanisms focus more on enhancing existing neurotransmitter levels (e.g., synaptic reuptake blockade), not necessarily on encouraging additional cytoplasmic vesical release.[1,2,8,10,14] This lack of additional cytoplasmic release, which can lead to depletion of vesicular monoamine storage, is thought to explain the decreased abuse and dependency potential for most nonstimulant medication when taken as prescribed.[17,18] That there may be various neurologic underpinnings may explain why different medications and differing mechanisms of action are effective for different patients. Although stimulants in general are the most well studied and efficacious ADHD and ADD medications, they are not 100 percent effective (e.g., 70–90% response rate).[7–10,14] Stimulants are believed to be most helpful for poor attention span, distraction, impulsive behavior, hyperactivity, restlessness, vigilance, cognition, reaction time, and short-term memory.[8] Although infrequent, serious side effects, such as seizures, hypertension, psychosis, hepatotoxicity, and sudden death can occur with stimulants.[7–9,14]

The risk of abuse for stimulants in the general population is not unheard of, with roughly 10 percent of patients reporting that they have sold their stimulant medications at some time and roughly 20 to 35 percent reporting that they have abused their stimulant medication at some point.[7,19] Although general advice is to avoid prescribing stimulants in an individual with substance use problems, some literature supports that stimulants may actually decrease the risk of children, adolescents, or adults with ADHD developing substance use problems (assuming stimulant treatment predates recreational substance use), as well as potentially reducing substance relapse (e.g., to cocaine use) if stimulant treatment is well supervised.[7,20–24] It is hypothesized that stimulant medications help protect against substance abuse by decreasing core ADHD symptoms, such as impulsivity; reduce tendency to self-treat; address underlying mechanisms of existing addiction pathways, such as dopamine abnormalities; and improve secondary factors, such as poor self-esteem, social skills deficits, and academic difficulties.[20–24]

## Concerns in Correctional Settings

As noted by Jillani *et al.*[1] and Mattes,[2] the use of stimulants is a very thorny problem for correctional psychiatry. In a commentary in the *Journal*, Burns[25] identified many reasons to limit controlled substances in a correction environment, such as the prevalence of substance use disorder (estimated to be 70–90% for incarcerated populations), the potential barter economy in correction facilities, security threats associated with controlled substances (e.g., risk of increased aggression and psychosis if abused), potential intimidation or victimization of inmates known to be receiving a controlled substance, and the possibility that access to controlled substances will foster malingering to obtain drugs. However, patients in a correctional facility are entitled both

legally and ethically to a standard of care equivalent to that applied within the community.[3,26–28] With this said, it must be acknowledged that incarcerated populations are not identical to community samples, and their differences can influence treatment planning. For instance, incarcerated populations have greater rates of traumatic life events, comorbidity, and substance use disorders that can worsen or even mimic ADHD symptoms, making careful diagnostic assessment crucial.[9,29–33] Because of this, a primary reliance on nonstimulant medications may actually be in line with general community treatment standards and recommendations (e.g., use of nonstimulants in individuals with substance use disorders), even though on the surface, it may appear that the incarcerated populations are being undertreated due to limited use of stimulant medication.[7–9,19]

Use of nonstimulant medications will not always reduce all potential risks for abuse in a correction population. The list of psychotropic drugs reported as having been diverted for abuse covers virtually every medication in psychiatry (e.g., antidepressant, antipsychotic, and antianxiety agents).[34] For example bupropion is a common drug of abuse in corrections, as it has amphetamine-like effects abused (e.g., excess oral dosing, nasal insufflation, intravenous injection).[34–37] Even FDA-approved nonstimulant medications such as $\alpha 2$ agonists have potential for misuse or barter value in a correctional environment since they are also used for symptomatic relief of opioid withdrawal.[38] Although many jails prescribe clonidine for opiate withdrawal, in a 2005 study, Fiscella *et al.*[38] found that roughly 50 percent of jails did not. This result indicates that there may be a diversion risk in jails and lockups for $\alpha$ agonists, just as is true of stimulants.

An additional challenge for those practicing in incarcerated settings is making sure the diagnosis of ADHD or ADD is accurate. Many of the symptoms can be nonspecific (e.g., concentration, impulsivity), which can result in a potentially wide differential diagnosis (e.g., intermittent explosive disorder, specific learning disorder, disruptive mood dysregulation disorder, or autism spectrum disorder).[7,9,14,15] Individuals dealing with high levels of stress may also exhibit symptoms of ADHD, such as decreased concentration, feeling overwhelmed, or forgetfulness.[7,8] These symptoms can especially affect an inmate who has just been incarcerated, is adjusting to a new environment (e.g., prison transfer), or is coming to terms with the stress of long-term incarceration. The diagnosis, particularly in adult correctional facilities, may be hard to confirm because many of the symptoms needed for a DSM-5 diagnosis are based on subjective reporting designed for youths rather than adults (e.g., difficulty in remaining seated in class or failure to finish schoolwork), are difficult to confirm through collateral sources (e.g., challenges in gaining access to teachers' reports or school records), and are easy to malinger (e.g., "yes I was a bad student but it was because I could not sit still").[7,8,15] Even with outpatient records or family reports, there is the potential concern for overdiagnosis of ADHD in the community or other institutions, resulting in the continuation of an inappropriate diagnosis in the correctional setting.[32–34]

A strict denial of an effective medication treatment, based solely on the status of being a prisoner, raises potential ethics concerns (e.g., limiting access to health care as part of the punitive action of imprisonment). For this reason, the approach advocated by Applebaum[3] of accessing many factors, such as diagnostic accuracy, current functioning, treatment history (e.g., participation with nonpharmacologic interventions and responses to nonstimulants), comorbid diagnoses, and correctional history (e.g., evidence for or against history of drug diversion) may be best for determining the use of stimulant or nonstimulant medications in a correction setting.

## Nonpharmacologic Treatment Approach

Unresolved or untreated ADHD may become more problematic in controlled environments because many individuals may not be able to use the coping mechanism, either good or bad, that they had relied on while not incarcerated (e.g., self-medication, flexible routines, or exercise). For example, many adults with ADHD may naturally choose more flexible environments where they can engage behavioral coping mechanisms to adapt to the condition (e.g., individuals with ADHD often choose work that focuses more on immediate problem solving, flexible deadlines, or scheduling or variation in tasks).[7–9,14] Although medications are helpful for ADHD, the most effective treatment regimens include a behavioral component.[7–9,14] Unfortunately, especially in short-term adult correctional settings, it may be difficult to incorporate aspects of behavioral

or environmental modification (i.e., inmates transferred in and out of an environment, schedule disrupted by events such as court, large open-space dormitory-style housing).[29] However, in long-term periods of incarceration, there may be greater benefits to approaches such as cognitive behavioral therapy, group therapy, or individual therapy to address attention deficit disorder, as well as comorbid conditions.[3,29]

## Off-Label Nonstimulant Medications

As Mattes[2] noted, many of the studies supporting use of nonstimulants for treatment of ADHD in adults were extrapolated from earlier research on FDA-approved medications for children and adolescents,[2,39] raising the question of whether other medications such as antidepressants, especially ones that affect norepinephrine, are not being studied or supported for FDA approval in part because of the 2004 black-box warning regarding antidepressant use in children.[7–11,39–43] The black-box warning had a profound impact on how antidepressants were perceived and prescribed, resulting in a reduction in use for both children and adults.[41–46] Even the already approved ADHD medication atomoxetine, (originally designed to be an antidepressant even though it did not obtain that indication), was required to add a black box warning regarding suicidality in 2005.[47] There may be little reason for pharmaceutical companies to risk market share of successful adult antidepressant medications on childhood or general ADHD trials (e.g., legal risk, perpetuation of further stigma regarding suicide, or risk of decrease in adult prescriptions if new side effects are discovered). Although there is research that supports serotonin–noradrenaline reuptake inhibitors (SNRIs) and other antidepressants for treatment of ADHD (50–70% efficacy), it is unlikely that these medications will ever receive FDA approval.[7–10,40,41,48,49] Many antidepressant medications that may be appropriate for study are off patent (e.g., venlafaxine, duloxetine), which makes it less likely that drug companies will spend the money to obtain FDA approval, even in an adult population. Although many community physicians prescribe medications off label, the lack of FDA approval may make it harder to justify unconventional use of medications. Well-regulated formularies, treatment protocols to limit legal exposure, costs, and potential abuse in correctional environments hinder issuing of off-label prescriptions.[3,29,50–52]

Bupropion is an antidepressant that can be used off label to treat ADHD and ADD because of its effects on norepinephrine and dopamine.[8–10,14,39] Some initial studies have found it to be roughly 50 percent effective in treating ADHD.[38] It may also have the benefit of being used in patients with bipolar disorder, because it is thought to be less likely to induce a manic switch than other antidepressants or stimulants.[8] In addition, a theoretical treatment approach combining bupropion with a selective serotonin reuptake inhibitor (SSRI) is thought to result in a combination that has properties similar to many stimulants (e.g., effects on dopamine, norepinephrine, and serotonin without the elevated dependency concerns). Although bupropion is frequently added as an adjunct medication to an SSRI or SNRI for treatment of depression, we are not aware of any direct investigations of this combination for treatment of ADHD.[53,54] Given that several manufacturers produce bupropion and the various forms of SSRIs, all of which are off patent, it is again very unlikely that this combination will receive funding from pharmaceutical companies for in-depth study for treatment of ADHD. Unfortunately, bupropion may not be an ideal medication for the correctional setting, given that it has the potential for abuse, as noted earlier.

Another nonstimulant off-label treatment is tricyclic antidepressants (TCAs).[8,10,14,39,41] Historically, they have been thought to help improve mood and decrease hyperactivity in open-label and controlled studies in children, but they are not necessarily as effective on concentration, nor do they have cognitive effects as stimulants.[8,14,39,41] TCAs are thought to be beneficial because of effects on norepinephrine.[8,10,39] The classic ADHD tricyclic is desipramine, but other members of this family, such as nortriptyline, amitriptyline, and imipramine, have also been discussed in the literature.[8,14,39] Although they have less potential for abuse in correctional settings, given their potential lethality in overdose, TCAs should be used with caution in incarcerated populations.

Modafinil, which is FDA approved for narcolepsy, has also been investigated as an off-label nonstimulant treatment for ADHD.[8,39] The study results for this drug have been somewhat inconsistent, though,

making further study advisable before it becomes a common alternative treatment.[8,39] In addition, the cost of modafinil and other nonstimulant wakefulness promoters is often prohibitive, making them difficult to justify for off-label use or to add to many correctional formularies.

## Future Research

Both Jillani *et al.*[1] and Mattes[2] address the use of nonstimulant ADHD medications from a daily functioning perspective in postconviction correctional systems. However, it must be remembered that ADHD and ADD disorders can have significant preadjudication implications. In general, the prominent symptom seen in adults with ADHD is trouble organizing and completing necessary tasks, which can affect preconviction functioning, such as being able to participate in court or prepare a defense with one's attorney. Although it is extremely rare for ADHD or ADD to be so severe on its own that a defendant lacks competency, it is easy to see how it could affect traditional *McGarry* criteria such as planning legal strategy, testifying relevantly, and controlling behavior, especially if a comorbid disorder is present.[55] Therefore, it may be beneficial to look for a medicine that helps treat both ADHD and comorbid conditions (e.g., select an SNRI over an SSRI for an individual with depression/anxiety and ADHD). Having future research that clearly identifies how stimulant and nonstimulant medicines control specific symptoms in incarcerated populations at all stages before and after conviction, may result in better due process protection for inmates, as well as improvement in general functioning.

More studies examining treatment of ADHD and improved rehabilitation, both in prison and in the community after release, are needed. Many studies looking at ADHD symptoms in prisoners may use a reduction in disciplinary actions or improved scores on screening instruments as markers of effectiveness, but it may also be as beneficial to measure academic achievements, such as obtaining a GED, completing college courses, or becoming certified in a trade.

Future studies may also have access to female inmates with ADD. Research has indicated that there may be a gender difference, with males more often having the hyperactivity form and females the inattention/concentration form.[4,8,12,15] It would be important to see whether benefits noted in male prisoners with stimulant or nonstimulant treatments carry over to female inmates as well.

Finally, additional study should focus on determining how an individual fares once released. Compliance with nonstimulant medication started in a correctional setting should be monitored to see whether it continues after discharge to the community. Would community treaters switch former inmates back to stimulants or maintain them on nonstimulants? If switched, would there be further improvement in symptoms or no significant change? Would individuals on stimulant or nonstimulant medication be more compliant with long-term treatment, and which group would have a lower risk of recidivism? It may be the answers to these questions that best determine whether incarcerated inmates are a unique population and whether a stimulant or nonstimulant should be prescribed as the first-line medication.

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