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Attention Deficit Hyperactivity Disorder:
Comparison of Medication Efficacy and Cost

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Abstract

Although a common psychological disorder, pharmacological treatment of Attention Deficit Hyperactivity Disorder can be a costly endeavor. Among 4-5 year olds, methylphenidate is a safe, efficacious, and cost-effective option for short-, intermediate-, and long-acting medication options. Short-acting methylphenidate, intermediate-acting methylphenidate ER and SR, and long-acting methylphenidate LA are the most efficacious and cost-effective medications.

Selection of non-stimulant medications should be based upon recommended guidelines rather than primarily on cost. For children incapable of swallowing pills, the most efficacious and cost-effective treatments are short-acting dextroamphetamine liquid and long-acting methylphenidate LA capsules that can be opened and sprinkled over food.

Attention Deficit Hyperactivity Disorder:
A Comparison of Medication Efficacy and Cost

According to the United States Surgeon General,¹ approximately 20% of children and adolescents in the United States (U.S.) exhibit signs or symptoms of a psychological or behavioral disorder.² Attention Deficit Hyperactivity Disorder (ADHD) is one of the more common childhood psychological disorders affecting three to seven percent of school-age children.³ ADHD often presents in early childhood with symptoms of hyperactivity, impulsivity, and/or inattention.^{4,5} Associated with a variety of complications, untreated ADHD has the potential to impair a child's cognitive, academic, behavioral, emotional, and social functioning.^{4,6}

With full implementation of the Patient Protection and Affordable Care Act (PPACA) on January 1, 2014,⁷ health insurance coverage is anticipated to assist an additional 32 million previously uninsured citizens, thereby reducing the total number of uninsured in the U.S.⁸ and achieving near-universal coverage.⁷ A portion of the PPACA is designed to expand the eligibility for Medicaid by 15 million Americans, limit insurance exclusions, and mandate employers or individuals to purchase health insurance.^{9,7} While the PPACA alters health care coverage for many, it does not achieve universal coverage.⁹ In fact, it has been estimated that 24 million people will remain without health insurance coverage, even after January 1, 2014.⁷ This number could be higher, though, depending on how many states implement the Medicaid expansion program.¹⁰ In addition, "adults with incomes of 250-400 percent of poverty could remain at risk for...premiums that are high relative to their incomes."¹¹

Unfortunately, obtaining ADHD medication can be a costly endeavor for the family with an ADHD child, especially if the family is either uninsured or underinsured. Between 1994 and 2003, the price of ADHD medications in the U.S. rose by 285%.¹² Considering the ever

increasing costs of ADHD medications, "...providers and consumers should consider the cost-effectiveness of a medication when making decisions about drug acceptance and coverage."¹²

Moreover, because untreated children with ADHD may suffer social, behavioral, and emotional consequences; healthcare providers (HCPs) must carefully assess ADHD medication costs and efficacy to meet the needs of the child and family. The purpose of this review, therefore, is to evaluate ADHD medications to promote effective management of pediatric patients in relation to efficacy and expense.

METHOD

Several electronic database searches were conducted to review studies related to medications and treatments for ADHD. The databases search included *MEDLINE*, *CINAHL*, *PsycINFO*, *UpToDate*, and the *Cochrane Library*. Various websites were also reviewed, including the Affordable Care Act, American Academy of Child & Adolescent Psychiatry, Centers for Disease Control and Prevention, Psych Central, CBS News, Healthline, National Institute of Mental Health, American Academy of Pediatrics, and United States Department of Health and Human Services.

Articles published in the past 10 years in English were included for review. Other inclusion criteria encompassed age groups related to children and adolescents, ages 0-18, and research articles using human studies. Systematic and integrative reviews of randomized controlled studies and drug trials related to ADHD were also obtained. While effective management of ADHD may incorporate behavioral, pharmacological, and multimodal approaches, only pharmacological treatment options were included for review. Articles which focused on adult treatment of ADHD or articles of ADHD diagnoses attached to other comorbidities such as psychiatric or cardiac issues were also excluded. Search terms included:

ADHD, Attention Deficit Hyperactivity Disorder, medication, efficacy, cost, pediatric, treatment, effectiveness, safety, side effects, expense, children, adolescent, drug therapy, and risk.

RESULTS

Stimulants

Stimulants are the first-line treatment option for 75-90% of children suffering with the hyperactivity, impulsivity, and inattention of ADHD.¹³⁻¹⁶ Despite a variety of preparations for the treatment of ADHD—short-acting, intermediate-acting, and long-acting—there is no evidence showing a clear benefit to using one stimulant over another in any of the preparations.¹⁷⁻²¹ It is possible, however, that individual children will respond more favorably to one stimulant or preparation.²² Therefore, clinical decisions guiding the use of a particular stimulant remains a point of caregiver preference with consideration of the patient's ability to swallow pills, needs regarding duration of action, age, co-morbidities, potential contraindications, and medication cost.¹³

Short-acting stimulants. Short-acting stimulants last approximately 3-6 hours and often require dosing more frequently than once per day. While the disadvantages from frequent dosing of short-acting stimulants include the possible disruption of the child's school day and confidentiality,²³ the frequent dosing also allows for greater precision when dosing. A list of short-acting stimulants, available doses, and associated costs is presented in Table 1.

Dextroamphetamine. Dextroamphetamine is available in tablet or liquid form and as the brand names Dexedrine (tablet), Dextrostat (tablet), Procentra (liquid), and Zenzedi (tablet). The medication is commonly prescribed more than once per day. All forms of dextroamphetamine are available as generic except the 2.5 mg and 7.5 mg doses which are only available as the brand name Zenzedi. Other available dosing options of dextroamphetamine include 5 mg, 10 mg,

15 mg, 20 mg, and 30 mg. The cost of Dexedrine and Dextrostat are the same – \$133.05 for 60 of the 5 mg tablets.²⁴ In comparison, 300 ml of 5 mg/5 ml Procentra is \$414.00.²⁴ For 60 tablets of the 5 mg Zenzedi, the cost is \$224.25.²⁴ All of the short-acting dextroamphetamine preparations are approved by the United States Food and Drug Administration (FDA) for use in children over the age of 3 years.²⁵

Methamphetamine. Desoxyn is the brand name preparation for methamphetamine and is available only in a 5 mg tablet that is commonly dosed twice per day. Methamphetamine is FDA approved for use in children 6 years old and older.²⁵ For 60 tablets of 5 mg methamphetamine, the cost is \$334.78,²⁶ almost triple the cost of the dextroamphetamines.

Methylphenidate. Methylphenidate is available in several forms: tablet (brand name Ritalin), chewable tablet (brand name Methylin), and liquid (Methylin),²⁴ all of which may need dosing twice a day.^{13,23} All formulations of methylphenidate are FDA approved for use in children 6 years old and older and all brand names are available as generics.²⁵ Ritalin (tablet) is available in 5 mg, 10 mg, and 20 mg doses. Methylin (chewable tablet) is available in 2.5 mg, 5 mg, and 10 mg doses. Finally, as a liquid Methylin is available in 5 mg/5 ml and 10 mg/5 ml forms. Methylphenidate tablets (Ritalin) costs \$33.55 for 60 of the 5 mg tablets,²⁴ a fraction of the cost of dextroamphetamines and methamphetamines. The chewable methylphenidate tablets (Methylin) are more costly with a price of \$268.80 for 60 5 mg tablets.²⁴ The liquid form of methylphenidate (Methylin) costs \$291.00 for 300 ml of the 10 mg/5 ml dose.²⁴

Dexmethylphenidate. Focalin is the common brand name for dexmethylphenidate, a tablet that is also available as a generic. Like Zenzedi (dextroamphetamine), dexmethylphenidate is available in smaller doses starting at 2.5 mg tablets and increasing in dosing to 5 mg and 10 mg tablets.^{13,27} Dexmethylphenidate is also approved for use in children 6 years of age or older.²⁵

Currently, dexamethylphenidate is available for \$46.20 for 60 tablets of the 5 mg dose,²⁴ which is similar to the cost of Ritalin.

Dextroamphetamine/amphetamine. The generic form of Adderall, dextroamphetamine/amphetamine is FDA approved for use in children aged 3 years old and older.²⁸ Dextroamphetamine/amphetamine generic is available in tablet form and in dosing increments of 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 20 mg, and 30 mg.²⁷ The current cost for 60 5 mg tablets is \$72.47.²⁴

Intermediate-acting stimulants. Intermediate-acting ADHD stimulants bridge the gap between short-acting and long-acting medications with an average duration of 6-10 hours. As extended release tablets, intermediate-acting stimulants are not to be chewed, crushed, or divided.^{24,27} A list of intermediate-acting stimulants, available doses, and associated costs is presented in Table 2.

Methylphenidate. None of the methylphenidate intermediate-acting stimulants are recommended for use in children under 6 years old.²⁵ Available formulations of immediate-acting methylphenidate include methylphenidate ER (Metadate ER), methylphenidate SR (Ritalin SR), and methylphenidate CD (Metadate CD).²³ Methylphenidate ER and SR formulations are available in tablet form and are only offered in a 20 mg dose. Methylphenidate CD is available as capsules and offered in 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, and 60 mg doses. The cost of methylphenidate ER and SR are identical—\$41.31 for 30 of the 20 mg tablets.²⁴ The cost of methylphenidate CD is \$112.50 for 30 20 mg capsules.²⁴

Long-acting stimulants. Long-acting stimulants are typically taken only once a day and have a duration ranging from 6-12 hours.²³ As with all extended release medications, the pills or capsules should not be divided, crushed or chewed.²⁴ The long-acting stimulants have the most

variety regarding route of administration, including tablets, capsules, liquid, and a transdermal patch. All of the long-acting stimulants are FDA approved for use in children who are 6 years and older.²⁵ A list of long-acting stimulants, available doses, and associated costs can be found in Table 3.

Dextroamphetamine. The brand name preparation of dextroamphetamine ER is Dexedrine Spansules and is available as capsules in 5 mg, 10 mg, and 15 mg doses. For children who find it difficult to swallow a capsule, dextroamphetamine ER can be opened and sprinkled over a small amount of applesauce as long as the beads are not chewed or crushed.¹³ The cost for 30 15 mg capsules is \$118.55.²⁴

Methylphenidate. Methylphenidate LA (Ritalin LA), methylphenidate ER (Concerta), methylphenidate transdermal (Daytrana), and methylphenidate XR (Quillivant XR) are all long-acting with a 10-12 hour duration.^{13,15} The available doses of methylphenidate LA include 10 mg, 20 mg, 30 mg, and 40 mg capsules. Methylphenidate ER is available in 18 mg, 27 mg, 36 mg, 54 mg, and 72 mg tablets. The methylphenidate transdermal patch can only be purchased as the brand name—Daytrana—in 10 mg, 15 mg, 20 mg, and 30 mg dosing increments. The only long-acting stimulant in liquid form is methylphenidate XR which is only sold as the brand name Quillivant XR with one available dose—25 mg/5 ml. Methylphenidate LA can be purchased for \$112.50 for 30 20 mg capsules.²⁴ The cost for 30 tablets of 18 mg methylphenidate ER is \$141.30.²⁴ Not surprisingly, Daytrana, which is only available as a brand name medication, is more expensive than the other long-acting methylphenidate preparations at \$246.88 for 30 patches of the 20 mg dose.²⁴ Quillivant XR is \$238.40 for 120 ml of the 25 mg/5 ml dose.²⁶

Dextroamphetamine/amphetamine. Adderall XR, the brand name for generic dextroamphetamine/amphetamine XR, is indicated for treatment of ADHD in children over the

age of 6 years old.¹⁵ Available as a capsule, dextroamphetamine/amphetamine XR is offered at dosing increments of 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, and 30 mg. The cost for 30 capsules of 20 mg dextroamphetamine/amphetamine XR is \$248.52.²⁴

Lisdexamfetamine. As with all other long-acting stimulants, lisdexamfetamine (Vyvanse) is only FDA approved for use in children over the age of 6 years old. Lisdexamfetamine is a capsule available in 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, and 70 mg doses. Preferably the medication is swallowed whole, although if the child has difficulty swallowing the capsule, it may be opened and poured into a glass of water prior to consumption.^{24,27} A generic form is currently unavailable for Vyvanse; the cost of 30 20 mg capsules is \$212.70.²⁴

Dexmethylphenidate ER. Dexmethylphenidate ER, also available as the brand name Focalin XR, is approved for use in children who are at least 6 years of age.²⁵ The generic preparation of dexmethylphenidate ER is only available in 15 mg, 30 mg, and 40 mg doses. While dexmethylphenidate ER is also available in dosing increments of 5 mg, 10 mg, 20 mg, 25 mg, and 35 mg, these doses are only available for purchase as the brand name, Focalin XR. While intended to be swallowed whole, the capsule may also be opened and sprinkled on applesauce. The cost for 30 capsules of the 20 mg dose is \$241.50.²⁴

Non-stimulants

Generally, non-stimulants are not considered first-line ADHD interventions^{13,22,16}; however, for patients who fail to respond to stimulants, for whom stimulants are contraindicated, or for patients in whom other comorbidities exist (e.g. tic disorder), a non-stimulant may be a viable treatment option.^{13,22,16} Non-stimulant treatment options for ADHD include atomoxetine (Strattera) which is a norepinephrine reuptake inhibitor and guanfacine (Intuniv) and clonidine ER (Kapvay) which are both alpha-2 adrenergic agonists. While each of the non-stimulant

medications are FDA approved for use in children aged 6 years and older, the AAP recommends a stepwise treatment of atomoxetine, guanfacine and then clonidine ER, in that specific order.²⁹ One disadvantage of non-stimulant ADHD medications is that achieving a therapeutic response takes time, sometimes several weeks before improvement is seen, whereas stimulants act quickly and results may be perceived to be immediate.³⁰ A list of non-stimulants, available doses, and associated costs can be found in Table 4.

Norepinephrine reuptake inhibitors. Atomoxetine is the generic form of Strattera, which is available in 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg, and 100 mg doses. The capsules may be administered as a one-time morning dose or as divided doses in the morning and late afternoon or early evening.^{24,27} The duration of atomoxetine is approximately 10-12 hours.¹³ The lowest dose, 10 mg, can be purchased for \$240.44 for 30 capsules.²⁴

Alpha-2 adrenergic agonists. Additionally, there are two options for ADHD treatment with alpha-2 adrenergic agonists: guanfacine (Intuniv) and clonidine ER (Kapvay). Guanfacine (Intuniv) is indicated as an alternative to stimulant use in the treatment of ADHD, although it should only be prescribed after failing on a trial of atomoxetine.²⁹ The duration of guanfacine is at least a 10-12 hour duration and is recommended as a once daily medication taken in either the morning or evening.²⁵ The price of guanfacine is \$16.50 for 30 tablets of the lowest dose, 1 mg.²⁴

Clonidine ER can be prescribed as 0.1 mg or 0.2 mg tablets and has a duration of at least 10-12 hours. While clonidine ER is FDA approved as a non-stimulant treatment option, a trial should be attempted only after the patient has first failed on atomoxetine and guanfacine.²⁹ The lowest dose of clonidine ER, 0.1 mg, can be purchased for \$141.60 for 30 tablets.²⁴

IMPLICATIONS FOR PRACTICE

While there are no intermediate- or long-acting ADHD medications approved for use in preschool-aged children aged 3-5 years, there are two main classes of short-acting ADHD medications that have received approval from the FDA for use in this age group, namely dextroamphetamine and dextroamphetamine/amphetamine.²⁷ However, despite the FDA's approval, the American Academy of Pediatrics (AAP) does not recommend the use of dextroamphetamine or dextroamphetamine/amphetamine in preschool-aged children²⁹ with the rationale that the FDA approval of these ADHD medications in children younger than 6 years old took place during a time when less stringent criteria was required. Thus, even though dextroamphetamine and dextroamphetamine/amphetamine have FDA approval for use in children as young as 3 years old, the empirical evidence regarding the safety and efficacy of these short-acting stimulants in preschoolers is lacking.²⁹

Most of the stimulant medication studies in preschoolers with ADHD have been conducted with methylphenidate, a medication proven to be safe and efficacious in preschool children. Notwithstanding the recommendation to use methylphenidate off-label in preschool children with ADHD, its use is recommended in children 4-5 years old and after trying behavior interventions first.^{13,29} According to Krull¹³, children suffering from ADHD who are younger than 6 years old should also be managed by or in consultation with a specialist.

Recommendations for Preschoolers with ADHD

Three-year old children are difficult to diagnose and have limited options for stimulant medications.²⁹ Thus, we recommend the diagnosis and management of 3 year old children with ADHD in coordination with a specialist. Because methylphenidate has been well studied and is recommended in guidelines set forth by the AAP for ADHD treatment in preschoolers ages 4-5

years old, we cautiously recommend its use as a first-line stimulant medication in this age group. Besides being recommended as the first-line stimulant medication for children ages 4-5, it is also the most cost-effective option of all the short-acting stimulants. The lowest available dose, however, is a 5 mg tablet that is unscored, meaning that it may not accurately split with a pill splitter. Thus, methylphenidate should be prescribed in 4-5 year old preschoolers only when the 5 mg dose can be swallowed whole.

Recommendations for Children Unable to Swallow Pills

Children over the age of 6 years who are unable to swallow pills whole should be provided other options. Among the short-acting stimulants, the most cost-effective option is methylphenidate (Methylin) chewable tablets at \$268.80 for 60 5 mg tablets. Non-tablet options, however, are unavailable in the intermediate-acting stimulant category. If a long-acting stimulant is clinically indicated, the most cost-effective option is dextroamphetamine ER, which is a capsule that can be opened and sprinkled over applesauce.

Recommendations for Short-, Intermediate-, and Long-acting Stimulants

Since there is no clear difference in efficacy of short-, intermediate-, and long-acting stimulants, cost should be an important factor when selecting a stimulant medication for children age 6 years and older. The most cost-effective short-acting stimulant is methylphenidate (Ritalin) at \$33.55 for 60 of the 5 mg tablets. The most cost-effective intermediate-acting stimulant is either methylphenidate ER or methylphenidate SR at a cost of \$41.31 for 30 of the 20 mg tablets. For long-acting stimulants, methylphenidate LA is the most cost-effective at \$112.50 for 30 of the 20 mg capsules, although for patients who cannot tolerate methylphenidate, dextroamphetamine ER is also cost-effective at \$118.55 for 30 of the 15 mg capsules.

Recommendations for Non-stimulants

While guanfacine is the most cost-effective option for non-stimulant treatment of ADHD, it is not the first-line non-stimulant medication as recommended by the AAP. While cost is an important consideration, our recommendation for non-stimulant medications is primarily based on AAP guidelines.²⁹ Thus, selection of a non-stimulant medication for the treatment of ADHD should be independent of cost, with atomoxetine first (\$240.44 for 30 of 10 mg capsules), guanfacine second (\$16.50 for 30 of the 1 mg tablets), and finally, clonidine ER (\$141.60 for 30 of the 0.1 mg).

CONCLUSION

ADHD is a commonly occurring condition in childhood; however, treatment of ADHD symptoms with medications can be a costly endeavor for the family of the pediatric ADHD patient. Consequently, HCPs should stay informed regarding the efficacy and cost of ADHD medications appropriate for use in pediatric patients. With careful consideration of medication cost and efficacy, HCPs can positively influence pharmacological treatment compliance for children with ADHD, which then influences the child's ability to function cognitively, academically, behaviorally, emotionally and socially.

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Table 1. Cost Comparison of Short-acting Stimulants

Availability as Generic	Generic Name	Brand Name	Available Doses	Type	Age	Cost
Yes*	Dextroamphetamine	Dexedrine	5, 10	Tablet	≥3	60 tab of 5 mg \$133.05 ²⁴
		Dextrostat	5, 10	Tablet	≥3	60 tab of 5 mg \$133.05 ²⁴
		Procentra	5 mg/5 ml	Liquid	≥3	300 ml of 5/5ml \$414.00 ²⁴
		Zenzedi	2.5, 5, 7.5, 10, 15, 20, 30	Tablet	≥3	60 tab of 5 mg \$224.25 ²⁴
Yes	Methamphetamine	Desoxyn	5	Tablet	≥6	60 tab of 5 mg \$334.78 ²⁶
Yes	Methylphenidate	Ritalin	5, 10, 20	Tablet	≥6	60 tab of 5 mg \$ 33.55 ²⁴
		Methylin	2.5, 5, 10	Chewable		60 tab of 5 mg \$268.80 ²⁴
		Methylin	5/5ml 10/5ml	Liquid		300 ml of 10/5 \$291.00 ²⁴
Yes	Dexmethylphenidate	Focalin	2.5, 5, 10	Tablet	>6	60 tab of 5 mg \$ 46.20 ²⁴
Yes	Dextroamphetamine/ amphetamine	Adderall	5, 7.5, 10, 12.5, 15, 20, 30	Tablet	≥3	60 tab of 5 mg \$ 72.47 ²⁴

Categorization of medications according to WebMD²³

* 2.5 mg and 7.5 mg only available as brand name Zenzedi

Table 2. Cost Comparison of Intermediate-acting Stimulants

Availability as Generic	Generic Name	Brand Name	Available Doses	Type	Age	Cost
Yes	Methylphenidate ER	Metadate ER	20	Tablet	≥6	30 tab of 20 mg \$ 41.31 ²⁴
Yes	Methylphenidate SR	Ritalin SR	20	Tablet	≥6	30 tab of 20 mg \$ 41.31 ²⁴
Yes	Methylphenidate CD	Metadate CD	10, 20, 30, 40, 50, 60	Capsule	≥6	30 cap of 20 mg \$112.50 ²⁴

Categorization of medications according to WebMD²³

Table 3. Cost Comparison of Long-acting Stimulants

Availability as Generic	Generic Name	Brand Name	Available Doses	Type	Age	Cost
Yes	Dextroamphetamine ER	Dexedrine Spansule	5, 10, 15	Capsule	≥6	30 cap of 15 mg \$118.55 ²⁴
Yes	Methylphenidate LA	Ritalin LA	10, 20, 30, 40	Capsule	≥6	30 cap of 20 mg \$112.50 ²⁴
Yes	Methylphenidate ER	Concerta	18, 27, 36, 54, 72	Tablet	≥6	30 tab of 18 mg \$141.30 ²⁴
No	Methylphenidate transdermal	Daytrana	10, 15, 20, 30	Patch	≥6	30 patches of 20 mg \$246.88 ²⁴
No	Methylphenidate XR	Quillivant XR	25 mg/5 ml	Liquid	≥6	120 ml of 25 mg/5ml \$238.40 ²⁶
Yes	Dextroamphetamine/amphetamine XR	Adderall XR	5, 10, 15, 20, 25, 30	Capsule	≥6	30 cap of 20 mg \$248.52 ²⁴
No	Lisdexamfetamine	Vyvanse	20, 30, 40, 50, 60, 70	Capsule	≥6	30 cap of 20 mg \$212.70 ²⁴
Yes*	Dexmethylphenidate XR	Focalin XR	5, 10, 15, 20, 25, 30, 35, 40	Capsule	≥6	30 cap of 20 mg \$241.50 ²⁴

Categorization of medications according to WebMD²³

* 5 mg, 10 mg, 20 mg, 25 mg, 35 mg only available as brand Focalin XR

Table 4. Cost Comparison of Non-stimulants

Availability as Generic	Classification	Generic Name	Brand Name	Available Doses	Type	Age	Cost
Yes	Norepinephrine Reuptake Inhibitors	Atomoxetine	Strattera	10, 18, 25, 40, 60, 80, 100	Capsule	≥6	30 cap of 10 mg \$240.44 ²⁴
Yes	Alpha 2 Adrenergic Agonists	Guanfacine	Intuniv	1, 2, 3, 4	Tablet	≥6	30 tab of 1 mg \$16.50 ²⁴
		Clonidine ER	Kapvay	0.1, 0.2	Tablet	≥6	30 tab of 0.1 mg \$141.60 ²⁴

Categorization of medications according to WebMD²³