A SUPPLEMENT TO Pediatric News

OCTOBER 2020

PEDIATRIC BEHAVIORAL AND MENTAL HEALTH

With commentary by Dr. Susan D. Swick

ONCE-DAILY
Vyvanse®
(lisdexamfetamine dimesylate)
10 • 20 • 30 • 40 • 50 • 60 • 70 mg capsules
10 • 20 • 30 • 40 • 50 • 60 mg chewable tablets

INDICATION AND LIMITATION OF USE

Vyvanse is indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in patients ages 6 and above. Vyvanse is not indicated or recommended for weight loss. Use of other sympathomimetic drugs for weight loss has been associated with serious cardiovascular adverse events. The safety and effectiveness of Vyvanse for the treatment of obesity have not been established.

VYVANSE IS PROVEN TO HELP TREAT PEDIATRIC PATIENTS (AGES 6-17) WITH ADHD[1-3]

For appropriate patients with ADHD

Start with Vyvanse[1]

See more at VyvansePro.com/pediatric

Hypothetical patient portrayal.
Individual results may vary.

IMPORTANT SAFETY INFORMATION

WARNING: ABUSE AND DEPENDENCE

- **CNS stimulants (amphetamines and methylphenidate-containing products), including Vyvanse, have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy.**

- **Contraindications**
  - Known hypersensitivity to amphetamines or other ingredients of Vyvanse. Anaphylactic reactions, Stevens-Johnson Syndrome, angioedema, and urticaria have occurred.
  - Use with monoamine oxidase inhibitors (MAOIs) or within 14 days of stopping MAOIs (including MAOIs such as linezolid or intravenous methylene blue), because of an increased risk of hypertensive crisis.

- **Warnings and Precautions**
  - Prior to and during treatment assess for the presence of cardiac disease. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, coronary artery disease, and other serious heart problems. Sudden death, stroke and myocardial infarction have been reported in adults with CNS stimulants at recommended doses, as well as sudden death in children and adolescents with structural cardiac abnormalities and other serious heart problems while taking CNS stimulants at recommended doses. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias while taking Vyvanse.
  - CNS stimulants cause increases in blood pressure (mean increase about 2-4 mm Hg) and heart rate (mean increase about 3-6 bpm). Monitor all patients for tachycardia and hypertension.
  - *Exacerbation of Pre-existing Psychosis:* May exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder. *Induction of a Manic Episode in Patients with Bipolar Disorder:* May induce a mixed/manic episode in patients with bipolar disorder. Prior to initiating treatment, screen for risk factors for developing a manic episode (e.g., comorbid or history of depressive symptoms, or a family history of suicide, bipolar disorder, and depression). *New Psychotic or Manic Symptoms:* At recommended doses, may cause psychotic or manic symptoms (e.g., hallucinations, delusional thinking, or mania) in patients with no prior history of psychotic illness or mania. Discontinue if symptoms occur.

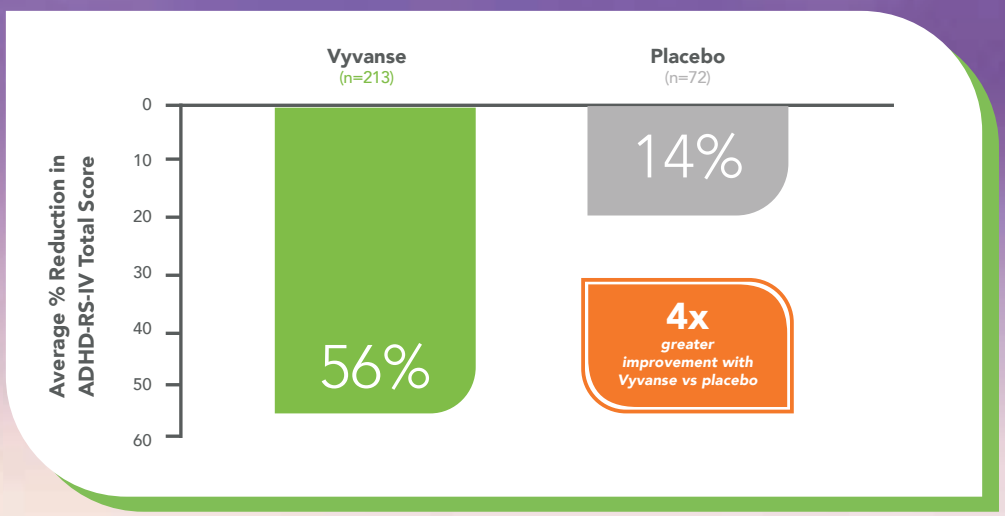
Study 301 Review Clinical Study

In a clinical study of children aged 6-12 years with ADHD, Vyvanse (lisdexamfetamine dimesylate) demonstrated a

Significant reduction in ADHD-RS-IV* total score[1-3]

PRIMARY ENDPOINT: Change from baseline to endpoint in ADHD-RS-IV total score†[1,2]

Vyvanse provided a 56% average reduction in ADHD-RS-IV total score (from 43.9 to 19.5) for all doses combined vs a 14% average reduction for placebo (from 42.4 to 36.6); P<.0001 for Vyvanse versus placebo.[1,3]



Study Design

Randomized, double-blind, parallel-group, placebo-controlled, 4-week study with forced-dose escalation to assess the efficacy and safety of Vyvanse 30, 50, and 70 mg/day compared with placebo in 290 children aged 6-12 years with ADHD (as defined by *DSM-IV-TR®*).‡[1,2]

*ADHD-RS-IV=Attention-Deficit/Hyperactivity Disorder Rating Scale, Version IV, a validated investigator-rated measure that consists of 18 items designed to reflect symptomatology of ADHD based on *DSM-IV-TR®* criteria.

†Last post-randomization treatment week for which a valid ADHD-RS-IV total score was obtained.

‡*DSM-IV-TR®=Diagnostic and Statistical Manual of Mental Disorders*, 4th ed, text revision.

- **Warnings and Precautions (continued)**
  - CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients (monitor weight and height). Treatment may need to be interrupted in children not growing or gaining weight as expected.
  - CNS stimulants, including Vyvanse, are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; very rare sequelae include digital ulceration and/or soft tissue breakdown. Observe patients during treatment for new numbness, pain, skin color change, or sensitivity to temperature in fingers and toes. Further evaluation may be required, including referral.
  - Increased risk of serotonin syndrome when co-administered with serotonergic agents (e.g., SSRIs, SNRIs, triptans) and CYP2D6 inhibitors, but also during overdosage situations. Discontinue Vyvanse if it occurs and initiate supportive treatment.
- **Adverse Reactions**
  The most common adverse reactions (≥5% and at least twice the rate of placebo) reported in clinical trials were:
  - *Children aged 6 to 12:* decreased appetite, insomnia, upper abdominal pain, irritability, vomiting, decreased weight, nausea, dry mouth, and dizziness;
  - *Adolescents aged 13 to 17:* decreased appetite, insomnia, and decreased weight;
  - *Adults:* decreased appetite, insomnia, dry mouth, diarrhea, nausea, anxiety, and anorexia.
- **Pregnancy and Lactation**
  - Vyvanse may cause fetal harm. Breastfeeding is not recommended during Vyvanse treatment.

Please see Brief Summary of Full Prescribing Information, including Boxed WARNING regarding Potential for Abuse and Dependence, on following pages.

References: 1. Vyvanse [package insert]. Lexington, MA: Shire US Inc. **2.** Biederman J, Krishnan S, Zhang Y, McGough JJ, Findling RL. Efficacy and tolerability of lisdexamfetamine dimesylate (NRP-104) in children with attention deficit/hyperactivity disorder: a phase III, multicenter, randomized, double-blind, forced-dose, parallel-group study. *Clin Ther.* 2007;29(3):450-463. **3.** Data on file; LDX006; Shire.

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VYVANSE® (lisdexamfetamine dimesylate)

Capsules 10, 20, 30, 40, 50, 60, 70 mg
Chewable tablets 10, 20, 30, 40, 50, 60 mg CII Rx Only

BRIEF SUMMARY: Consult the Full Prescribing Information for complete product information.

WARNING: ABUSE AND DEPENDENCE

CNS stimulants (amphetamines and methylphenidate-containing products), including VYVANSE, have a high potential for abuse and dependence.

Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy.

CONTRAINDICATIONS

VYVANSE is contraindicated in patients with:

- Known hypersensitivity to amphetamine products or other ingredients of VYVANSE. Anaphylactic reactions, Stevens-Johnson Syndrome, angioedema, and urticaria have been observed in postmarketing reports.
- Patients taking monoamine oxidase inhibitors (MAOIs), or within 14 days of stopping MAOIs (including MAOIs such as linezolid or intravenous methylene blue), because of an increased risk of hypertensive crisis.

WARNINGS AND PRECAUTIONS

Potential for Abuse and Dependence *(See Above)*

Serious Cardiovascular Reactions

Sudden death, stroke and myocardial infarction have been reported in adults with CNS stimulant treatment at recommended doses. Sudden death has been reported in children and adolescents with structural cardiac abnormalities and other serious heart problems taking CNS stimulants at recommended doses for ADHD. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, coronary artery disease, and other serious heart problems. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during VYVANSE treatment.

Blood Pressure and Heart Rate Increases

CNS stimulants cause an increase in blood pressure (mean increase about 2-4 mm Hg) and heart rate (mean increase about 3-6 bpm). Monitor all patients for potential tachycardia and hypertension.

Psychiatric Adverse Reactions

Exacerbation of Pre-existing Psychosis

CNS stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder.

Induction of a Manic Episode in Patients with Bipolar Disorder

CNS stimulants may induce a mixed/manic episode in patients with bipolar disorder. Prior to initiating treatment, screen patients for risk factors for developing a manic episode (e.g., comorbid or history of depressive symptoms or a family history of suicide, bipolar disorder, and depression).

New Psychotic or Manic Symptoms

CNS stimulants, at recommended doses, may cause psychotic or manic symptoms, e.g. hallucinations, delusional thinking, or mania in children and adolescents without a prior history of psychotic illness or mania. If such symptoms occur, consider discontinuing VYVANSE. In a pooled analysis of multiple short-term, placebo-controlled studies of CNS stimulants, psychotic or manic symptoms occurred in 0.1% of CNS stimulant-treated patients compared to 0% in placebo-treated patients.

Suppression of Growth

CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. Closely monitor growth (weight and height) in pediatric patients treated with CNS stimulants, including VYVANSE. In a 4-week, placebo-controlled trial of VYVANSE in patients ages 6 to 12 years old with ADHD, there was a dose-related decrease in weight in the VYVANSE groups compared to weight gain in the placebo group. Additionally, in studies of another stimulant, there was slowing of the increase in height.

Peripheral Vasculopathy, including Raynaud's Phenomenon

Stimulants, including VYVANSE, used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; however, very rare sequelae include digital ulceration and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud's phenomenon, were observed in postmarketing reports at different times and at therapeutic doses in all age groups throughout the course of treatment. Signs and symptoms generally improve after reduction in dose or discontinuation of drug. Careful observation for digital changes is necessary during treatment with ADHD stimulants. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients.

Serotonin Syndrome

Serotonin syndrome, a potentially life-threatening reaction, may occur when amphetamines are used in combination with other drugs that affect the serotonergic neurotransmitter systems such as monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort. Amphetamines and amphetamine derivatives are known to be metabolized, to some degree, by cytochrome P450 2D6 (CYP2D6) and display minor inhibition of CYP2D6 metabolism. The potential for a pharmacokinetic interaction exists with the co-administration of CYP2D6 inhibitors which may increase the risk with increased exposure to the active metabolite of VYVANSE (dextroamphetamine). In these situations, consider an alternative non-serotonergic drug or an alternative drug that does not inhibit CYP2D6. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

Discontinue treatment with VYVANSE and any concomitant serotonergic agents immediately if symptoms of serotonin syndrome occur, and initiate supportive symptomatic treatment. Concomitant use of VYVANSE with other serotonergic drugs or CYP2D6 inhibitors should only be used if the potential benefit justifies the potential risk. If clinically warranted, consider initiating VYVANSE with lower doses, monitoring patients for the emergence of serotonin syndrome during drug initiation or titration, and informing patients of the increased risk for serotonin syndrome.

ADVERSE REACTIONS

Clinical Trial Experience

Based on data from 4-week parallel-group controlled clinical studies of VYVANSE in pediatric and adult patients with ADHD.

Adverse Reactions Associated with Discontinuation of Treatment

In the controlled trial in patients ages 6 to 12 years, 8% (18/218) of VYVANSE-treated patients discontinued due to adverse reactions compared to 1% (1/72) of placebo-treated patients. The most frequently reported adverse reactions leading to discontinuation (1% or more and twice rate of placebo) were ECG voltage criteria for ventricular hypertrophy, tic, vomiting, psychomotor hyperactivity, insomnia, decreased appetite and rash [2 instances for each adverse reaction, i.e., 2/218 (1%)].

In the controlled trial in patients ages 13 to 17 years, 3% (7/233) of VYVANSE-treated patients discontinued due to adverse reactions compared to 1% (1/77) of placebo-treated patients. Most frequent adverse reactions leading to discontinuation were irritability (3/233; 1%), decreased appetite (2/233; 1%), and insomnia (2/233; 1%).

In the controlled adult trial, 6% (21/358) of VYVANSE-treated patients discontinued due to adverse reactions compared to 2% (1/62) of placebo-treated patients. The most frequently reported adverse reactions leading to discontinuation (1% or more and twice rate of placebo) were insomnia (8/358; 2%), tachycardia (3/358; 1%), irritability (2/358; 1%), hypertension (4/358; 1%), headache (2/358; 1%), anxiety (2/358; 1%), and dyspnea (3/358; 1%).

Adverse Reactions Occurring at an Incidence of ≥5% or More Among VYVANSE Treated Patients with ADHD in Clinical Trials

Most common adverse reactions (incidence ≥5% and at a rate at least twice placebo) reported in children, adolescents, and/or adults were anorexia, anxiety, decreased appetite, decreased weight, diarrhea, dizziness, dry mouth, irritability, insomnia, nausea, upper abdominal pain, and vomiting.

Adverse Reactions Occurring at an Incidence of 2% or More

Adverse reactions reported in the controlled trials in pediatric patients ages 6 to 12 years, adolescent patients ages 13 to 17 years, and adult patients treated with VYVANSE or placebo:

Adverse Reactions Reported by ≥2% of Children (Ages 6 to 12 Years) with ADHD Taking VYVANSE and at least Twice the Incidence in Patients Taking Placebo - VYVANSE (n=218), Placebo (n=72):

Decreased Appetite (39%, 4%), Insomnia (22%, 3%), Abdominal Pain Upper (12%, 6%), Irritability (10%, 0%), Vomiting (9%, 4%), Weight Decreased (9%, 1%), Nausea (6%, 3%), Dry Mouth (5%, 0%), Dizziness (5%, 0%), Affect lability (3%, 0%), Rash (3%, 0%), Pyrexia (2%, 1%), Somnolence (2%, 1%), Tic (2%, 0%), Anorexia (2%, 0%).

Adverse Reactions Reported by ≥2% of Adolescent (Ages 13 to 17 Years) Patients with ADHD Taking VYVANSE and at least Twice the Incidence in Patients Taking Placebo - VYVANSE (n=233), Placebo (n=77):

Decreased Appetite (34%, 3%), Insomnia (13%, 4%), Weight Decreased (9%, 0%), Dry Mouth (4%, 1%), Palpitations (2%,1%), Anorexia (2%, 0%), Tremor (2%,0%).

Adverse Reactions Reported by ≥2% of Adult Patients with ADHD Taking VYVANSE and at least Twice the Incidence in Patients Taking Placebo - VYVANSE (n=358), Placebo (n=62):

Decreased Appetite (27%, 2%), Insomnia (27%, 8%), Dry Mouth (26%, 3%), Diarrhea (7%, 0%), Nausea (7%, 0%), Anxiety (6%, 0%), Anorexia (5%, 0%),

Feeling Jittery (4%, 0%), Agitation (3%, 0%), Increased Blood Pressure (3%, 0%), Hyperhidrosis (3%, 0%), Restlessness (3%, 0%), Decreased Weight (3%, 0%), Dyspnea (2%, 0%), Increased Heart Rate (2%, 0%), Tremor (2%, 0%), Palpitations (2%, 0%).

In addition, in the adult population erectile dysfunction was observed in 2.6% of males on VYVANSE and 0% on placebo; decreased libido was observed in 1.4% of subjects on VYVANSE and 0% on placebo.

Postmarketing Experience

The following adverse reactions have been identified during post approval use of VYVANSE. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These events are as follows: cardiomyopathy, mydriasis, diplopia, difficulties with visual accommodation, blurred vision, eosinophilic hepatitis, anaphylactic reaction, hypersensitivity, dyskinesia, dysgeusia, tics, bruxism, depression, dermatillomania, alopecia, aggression, Stevens-Johnson Syndrome, chest pain, angioedema, urticaria, seizures, libido changes, frequent or prolonged erections, constipation, and rhabdomyolysis.

DRUG INTERACTIONS

Clinically Important Interactions with Amphetamines

MAO Inhibitors (MAOI)

Clinical Impact: MAOI antidepressants slow amphetamine metabolism, increasing amphetamines effect on the release of norepinephrine and other monoamines from adrenergic nerve endings causing headaches and other signs of hypertensive crisis. Toxic neurological effects and malignant hyperpyrexia can occur, sometimes with fatal results.

Intervention: Do not administer VYVANSE during or within 14 days following the administration of MAOI *[*see *Contraindications].*

Examples: selegiline, isocarboxazid, phenelzine, tranylcypromine

Serotonergic Drugs

Clinical Impact: The concomitant use of VYVANSE and serotonergic drugs increases the risk of serotonin syndrome.

Intervention: Initiate with lower doses and monitor patients for signs and symptoms of serotonin syndrome, particularly during VYVANSE initiation or dosage increase. If serotonin syndrome occurs, discontinue VYVANSE and the concomitant serotonergic drug(s) [see *Warnings and Precautions*].

Examples: selective serotonin reuptake inhibitors (SSRI), serotonin norepinephrine reuptake inhibitors (SNRI), triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John's Wort

CYP2D6 Inhibitors

Clinical Impact: The concomitant use of VYVANSE and CYP2D6 inhibitors may increase the exposure of dextroamphetamine, the active metabolite of VYVANSE compared to the use of the drug alone and increase the risk of serotonin syndrome.

Intervention: Initiate with lower doses and monitor patients for signs and symptoms of serotonin syndrome particularly during VYVANSE initiation and after a dosage increase. If serotonin syndrome occurs, discontinue VYVANSE and the CYP2D6 inhibitor [see *Warnings and Precautions* and *Overdosage*].

Examples: paroxetine and fluoxetine (also seratonergic drugs), quinidine, ritonavir.

Alkalinizing Agents

Clinical Impact: Urinary alkalinizing agents can increase blood levels and potentiate the action of amphetamine.

Intervention: Co-administration of VYVANSE and urinary alkalinizing agents should be avoided.

Examples: Urinary alkalinizing agents (e.g. acetazolamide, some thiazides).

Acidifying Agents

Clinical Impact: Urinary acidifying agents can lower blood levels and efficacy of amphetamines.

Intervention: Increase dose based on clinical response.

Examples: Urinary acidifying agents (e.g., ammonium chloride, sodium acid phosphate, methenamine salts).

Tricyclic Antidepressants

Clinical Impact: May enhance the activity of tricyclic or sympathomimetic agents causing striking and sustained increases in the concentration of d-amphetamine in the brain; cardiovascular effects can be potentiated.

Intervention: Monitor frequently and adjust or use alternative therapy based on clinical response.

Examples: desipramine, protriptyline

Drugs Having No Clinically Important Interactions with VYVANSE

From a pharmacokinetic perspective, no dose adjustment of VYVANSE is necessary when VYVANSE is co-administered with guanfacine, venlafaxine, or omeprazole. In addition, no dose adjustment of guanfacine or venlafaxine is needed when VYVANSE is co-administered.

From a pharmacokinetic perspective, no dose adjustment for drugs that are substrates of CYP1A2 (e.g. theophylline, duloxetine, melatonin), CYP2D6 (e.g. atomoxetine, desipramine, venlafaxine), CYP2C19 (e.g. omeprazole, lansoprazole, clobazam), and CYP3A4 (e.g. midazolam, pimozide, simvastatin) is necessary when VYVANSE is co-administered.

USE IN SPECIFIC POPULATIONS

Pregnancy

The limited available data from published literature and postmarketing reports on use of VYVANSE in pregnant women are not sufficient to inform a drug-associated risk for major birth defects and miscarriage. Adverse pregnancy outcomes, including premature delivery and low birth weight, have been seen in infants born to mothers dependent on amphetamines. Monitor infants born to mothers taking amphetamines for symptoms of withdrawal such as feeding difficulties, irritability, agitation, and excessive drowsiness.

Lactation

Lisdexamfetamine is a pro-drug of dextroamphetamine. Based on limited case reports in published literature, amphetamine (d-or d, l-) is present in human milk, at relative infant doses of 2% to 13.8% of the maternal weight-adjusted dosage and a milk/plasma ratio ranging between 1.9 and 7.5. There are no reports of adverse effects on the breastfed infant. Long-term neurodevelopmental effects on infants from amphetamine exposure are unknown. It is possible that large dosages of dextroamphetamine might interfere with milk production, especially in women whose lactation is not well established. Because of the potential for serious adverse reactions in nursing infants, including serious cardiovascular reactions, blood pressure and heart rate increase, suppression of growth, and peripheral vasculopathy, advise patients that breastfeeding is not recommended during treatment with VYVANSE.

Pediatric Use

Safety and efficacy in pediatric patients below the age of 6 years have not been established.

Geriatric Use

Clinical studies of VYVANSE did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

Renal Impairment

Due to reduced clearance in patients with severe renal impairment (GFR 15 to <30 mL/min/1.73 m^2), the maximum dose should not exceed 50 mg/day. The maximum recommended dose in ESRD (GFR <15 mL/min/1.73 m^2) patients is 30 mg/day.

Lisdexamfetamine and d-amphetamine are not dialyzable.

Gender

No dosage adjustment of VYVANSE is necessary on the basis of gender.

DRUG ABUSE AND DEPENDENCE

VYVANSE contains lisdexamfetamine, a prodrug of amphetamine, a Schedule II controlled substance.

OVERDOSAGE

Consult with a Certified Poison Control Center (1-800-222-1222) for up-to-date guidance and advice for treatment of overdosage. Individual patient response to amphetamines varies widely. Toxic symptoms may occur idiosyncratically at low doses.

Manifestations of amphetamine overdose include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states, hyperpyrexia, and rhabdomyolysis. Serotonin syndrome has been reported with amphetamine use, including VYVANSE. Fatigue and depression usually follow the central nervous system stimulation. Other reactions include arrhythmias, hypertension or hypotension, circulatory collapse, nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning is usually preceded by convulsions and coma.

Lisdexamfetamine and d-amphetamine are not dialyzable.

Manufactured for: Shire US Inc., Lexington, MA 02421 Made in USA
For more information call 1-800-828-2088

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Cultivating resilience in children at risk

BY SUSAN D. SWICK, MD

If I had to describe the themes of this mental health supplement, I would say that they are risk and resilience. There is no physical health and well-being without mental health and well-being, and pediatricians are in a powerful position to assess their patients for different types of risk and to promote resilience so that our patients don't only avoid illness or poor outcomes, but actually cultivate health and well-being – for themselves and beyond.

Knowledge of health risks can inform care and treatment in very specific ways in the pediatric office. Understanding the risks for treatment failure in ADHD helps to ensure more efficient and effective treatment of symptoms of inattention, impulsivity, and hyperactivity – psychiatric problems routinely managed by pediatricians. Routine screening for suicide risk in the primary care pediatric setting may be uniquely effective in identifying those adolescents who are suffering silently before it is too late.

Dr. Swick

When we understand the risk factors for youth running away from home, and the risks that being homeless can confer, we can devote appropriate time to our lesbian, gay, bisexual, transgender, and queer (LGBTQ) patients to learn about their home life. When we appreciate the nature of how adolescents assess risk and make decisions, we can help them (and their parents) ensure that they have accurate information and meaningful models regarding drug and alcohol use, stress management, and communication so that they can develop independence safely. When we broaden our understanding of developmental health in preschool children, we may be better equipped to properly assess and treat their behavioral problems and protect them against adverse educational outcomes. We appreciate that in youth adverse educational outcomes predict adverse outcomes outside of school as well.

Many of the interventions we review here involve rather straightforward education, but what sounds simple is rarely easy. Perhaps the most exciting and hopeful piece in the supplement describes how information, effectively shared, can confer resilience by diminishing stigma. This is the study of a curriculum for educating children just at the start of adolescence about common mental illnesses and how treatable they are. This simple educational intervention diminished stigma, which was measured in improved treatment-seeking in those with symptoms. We can imagine how this effect could multiply over time and support protective connections to peers with psychiatric symptoms, which help their friends to seek care when needed. When the silence and stigma that have for too long surrounded psychiatric illness are replaced by knowledge, compassion, and connectedness, we have good reason to be hopeful about the development of resilience for all of the children in our care.

portishead1/Getty Images

THERE IS NO **PHYSICAL HEALTH AND WELL-BEING** WITHOUT MENTAL HEALTH AND WELL-BEING.

Dr. Swick is physician in chief at Ohana, Center for Child and Adolescent Behavioral Health, Community Hospital of the Monterey (Calif.) Peninsula. Dr. Swick said she had no relevant financial disclosures.

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Intervention reduces mental illness stigma

School curriculum–based program increased treatment-seeking behavior

BY BIANCA NOGRADY
FROM PEDIATRICS

A school curriculum–based intervention aimed at reducing the stigma of mental illness was associated with a nearly fourfold increase in the likelihood of youth with significant symptoms seeking treatment.

Writing in Pediatrics, researchers reported the outcome of a 2-year, longitudinal, cluster-randomized trial involving 416 students in 6th-grade classes in 14 schools across Texas.

The intervention was a school-based curriculum program called Eliminating the Stigma of Differences (ESD); a 3-hour, three-module curriculum program delivered over 1 week, which contained a mix of teaching, group discussion, and homework exercises.

One module explored the idea of difference; the definition, causes, and consequences of stigma; ways to end stigma; and the description, causes, and treatments of mental illness, as well as the barriers to seeking help. The other two modules explored specific mental illnesses in more detail but with content designed to stimulate empathy.

The study compared this with two other interventions – in-class presentations and discussions led by two young adults with a history of mental illness; or exposure to anti-stigma printed materials – and a no-intervention control.

The study found that involvement with the curriculum program was associated with a significant and sustained increase in knowledge of and attitudes to mental illness compared with the control and other interventions, and with significant decreases in social distance, which measures the extent to which children are unwilling to interact with someone who is identified as having a mental illness. This association was seen even after the researchers controlled for other factors such as a participants' knowledge of or attitudes toward mental illness before the intervention, their age, sex, race or ethnicity, or their parents' educational level.

> "YOUTH CAN BE POSITIVELY INFLUENCED AT A RELATIVELY YOUNG AGE, **FOSTERING CHANGES IN MENTAL HEALTH ATTITUDES** AND BEHAVIORS."

"Our study, in combination with other studies, suggests strongly that youth can be positively influenced at a relatively young age, fostering changes in mental health attitudes and behaviors that last, as our study has shown, for at least 2 years," wrote Bruce G. Link, PhD, of the School of Public Policy at the University of California, Riverside, and coauthors.

The study also found that, among youth who were experiencing a high level of symptoms of mental illness, the curriculum-based intervention was associated with nearly fourfold higher odds of seeking treatment (odd ratio, 3.9; $P < .05$), after adjustment for similar covariates.

The authors looked separately at whether this self-reported treatment-seeking was the first time that students had sought treat-

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Ridofranz/Getty Images

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ment, a continuation of treatment-seeking, or a return to it. All three showed similar odds ratios but small sample sizes meant they did not reach statistical significance.

"We do know that negative attitudes toward mental illnesses and the exceptionally large percentage of people who experience but do not receive treatment for such illnesses are problems that have been with us for a long time," Dr. Link and associates said. "Interventions such as ESD represent a partial but positive response to this public mental health challenge."

The intervention didn't lead to a significant increase in treatment-seeking behavior among students with low levels of mental illness symptoms.

There were no significant differences in the effectiveness of the intervention across race or ethnicity, sex, education level of caregivers, or the baseline attitudes toward mental illness. The only exception was seen with Latino youth, where the intervention was not associated with a decrease in social distancing.

Contact intervention, in which two young people with a history of mental illness came to talk to classes and participate in discussions, was not associated with any significant changes in attitudes.

"A potential explanation is that contact is not as effective in youth, a possibility that is supported by a meta-analysis showing diminished effects of contact compared with educational interventions in adolescents," Dr. Link and associates said.

In an accompanying editorial, Nathaniel Beers, MD, of Children's National Hospital in Washington, and Shashank V. Joshi, MD, of Stanford (Calif.) University, wrote that more than one-fifth of children and youth in the United States are diagnosed with behavioral health needs before they reach the age of 18, but the perception of stigma can make families reluctant to access treatment.

> "THIS CURRICULUM COULD ADD A CRITICAL COMPONENT TO ADDRESSING THE **MENTAL HEALTH NEEDS OF CHILDREN AND YOUTH** IN THE UNITED STATES."

"Previous research has highlighted the importance of stigma reduction in school-based settings as a crucial component in changing the social norms about seeking help among diverse youth populations," they said. Reducing stigma also can reduce detrimental outcomes from social isolation and bullying.

Dr. Beers and Dr. Joshi noted that school-based interventions can have a substantial and lasting effect, with the benefit of influencing parents and staff in addition to students.

"Combined with screening and improved access to school-based mental health services, this curriculum could add a critical component to addressing the mental health needs of children and youth in the United States," they concluded.

The study was supported by the National Institute of Mental Health and National Institutes of Health. The authors said they had no relevant financial disclosures. Dr. Beers and Dr. Joshi received no external funding, and they said they had no relevant financial disclosures.

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Commentary by Dr. Swick / It is well established that most psychiatric illnesses emerge during youth: 50% by the age of 15 years and 75% by the age of 24. It also is well established that the great majority of youth experiencing a psychiatric illness do not access (professional) mental health care. Much of this is accounted for by the difficulty in accessing mental health care for youth in the United States, but it also is a function of the stigma that still surrounds mental illness and enforces silence and isolation around emerging symptoms. And internalizing symptoms (such as those for anxiety and depressive disorders), which are the most common psychiatric symptoms in youth, is less likely to be observed by connected adults, so they depend on the youth themselves to speak up and seek help. This is made even less likely because the symptoms themselves often include a sense of guilt, shame, or worthlessness: In effect depression and anxiety "lie" to the youth experiencing them, making them believe they are inadequate and burdensome, which discourages them from seeking help for their treatable illnesses.[1]

Prior research has demonstrated that a strong predictor of treatment-seeking for youth with psychiatric symptoms hinged on a parental history of psychiatric care. A 2014 study of adolescent use of mental health services found that "parental factors including recognition of the adolescent's internalizing symptoms and parental experience with depression/anxiety are strongly associated with mental health service use for depressed adolescents." Similar work done in Europe, where it is easier to access mental health treatment, concluded that low rates of accessing effective care for depression and anxiety in youth was caused primarily by youth not reporting symptoms and by parental failure to observe or suspect a problem: "The findings stress the importance of early interventions focusing on raising parental and child awareness of mental health problems."[2]

This exciting study reinforces the value of educational interventions directed at youth and the power of broad educational campaigns in school settings. It would be interesting to follow this cohort of youth and see if the rate of treatment-seeking behavior remains higher as de novo symptoms emerge in the months or years that follow this brief education. The protective power of destigmatizing, both in enhancing treatment-seeking for symptomatic youth and in decreasing social distance from others experiencing illness is real. It also is informative that the efficacy was greatest with a traditional curriculum and homework format, rather than a contact intervention, which has historically been used in school-based mental health destigmatization campaigns. What may be needed next are data exploring the cost-effectiveness of a universal 5th- or 6th-grade educational intervention that promotes early treatment of these common illnesses, compared with the cost of illnesses going untreated for longer and being more severe when they come to treatment. Such economic analysis might help establish policies – and funding – for a potent public health intervention.

REFERENCES

1. Gen Hosp Psychiatry. 2014 May-Jun;36(3):296-301.
2. Front Psychol. 2019 Aug 29. doi: 10.3389/fpsyg.2019.01915.

Ready for school? Not preschoolers with ADHD

Early identification and intervention necessary

BY RANDY DOTINGA
FROM PEDIATRICS

Are preschoolers with signs of ADHD ready for school? A new study suggests they're far from prepared.

A small sample of children with symptoms of moderate to severe ADHD scored markedly lower than comparable children on 8 of 10 measures of readiness for primary education.

"Preschool-aged children with parent- or clinician-reported ADHD symptoms are likely to have impaired school readiness. These children require early identification and intervention," Hannah T. Perrin, MD, of Stanford (Calif.) University and associates wrote.

Dr. Perrin and colleagues recruited 93 children aged 4-6 years from the community. Their parents, who were compensated, took the Early Childhood Inventory-4 (ECI-4) questionnaire. It revealed that 80% (n = 45) of those diagnosed with ADHD had scores considered signs of moderate or severe ADHD symptom severity based on the parent ratings. Those with lower scores made up the comparison group (n = 48).

The groups were similar, about 60% male and more than 50% white; neither difference between groups was statistically significant. However, those in the comparison group were much more likely to have non-Latino/non-Hispanic ethnicity; 61% in ADHD group vs. 91% in comparison group, $P = .001$. The children were tested for school readiness through several measures in two 1- to 1.5-hour sessions.

The researchers reported that 79% of children in the ADHD group were not ready for school (impaired) vs. 13% of the comparison group. (odds ratio, 21; $P = .001$).

"We found that preschool-aged children with ADHD symptoms demonstrated significantly worse performance on 8 of 10 school readiness measures," the authors added, "and significantly greater odds of impairment in four of five domains and overall school readiness."

Going forward, they wrote, "family dynamics and social-emotional functioning should be assessed for each preschool-aged child with ADHD symptoms, and appropriate therapeutic interventions and community supports should be prescribed to enhance school readiness."

The study authors had no disclosures. Study funders include the Maternal and Child Health Bureau, the Katharine McCormick Faculty Scholar Award, Stanford Children's Health and Child Health Research Institute Pilot Early Career Award, and the National Institutes of Health.

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Commentary by Dr. Swick / This thought-provoking report raises important issues about the diagnosis and treatment of ADHD in the youngest children. ADHD is a well-established neurodevelopmental disorder; the average age of diagnosis is 8 years, while primarily inattentive subtype is usually diagnosed at age 10.[1] Symptoms must be present from before the age of 7 years to be considered diagnostically valid. It cannot be diagnosed in children under the age of 4 years, given the degree of inattention, impulsivity, and hyperactivity that are developmentally normal in this age cohort.

The authors' focus on the matter of school readiness sets a broader frame for considering behavioral concerns in the youngest children. Their assessment of school readiness incorporates five domains: cognition and general knowledge, physical well-being and motor development, social-emotional development, approach to learning, and language development.

The finding that nearly 80% of clinically referred preschoolers with ADHD were markedly impaired in every domain except for cognition and general knowledge, compared with only 13% of their non-ADHD peers (who were referred by their parents but had more mild symptoms) suggests global impairment in preschoolers being treated for ADHD. It also suggests that their treatment had been of limited efficacy. First-line treatment in 4- to 5-year-olds is behavioral treatment for the child or parent,[2] and the authors noted that it was being utilized at very low rates: 36% of the ADHD group was receiving combined medication and behavioral therapy, and 23% was receiving only one or the other.

Are the youngest patients referred for behavioral problems not receiving the proper diagnoses and treatments? Or are they simply more likely to have severe disease that is more likely to be refractory to our treatments?

Both of these possibilities illustrate the importance of meticulous diagnostic practices in the youngest patients referred for hyperactivity, impulsivity, and inattention. Use of clinical observation across several visits, parent reports, and teacher reports are essential. Careful assessment of other causes of these behavioral disturbances in the youngest patients is critical, including assessment for adequate restful sleep and for the presence of significant adversity in the home. A failure to improve with first-line treatments should prompt a thoughtful reassessment and consideration of other etiologies of behavioral dysregulation in this age group, including primary anxiety disorders or exposure to neglect or abuse.

Finally, this study raises the critically important idea that universal assessment of school readiness has public health value: If our health care and school systems were united in tracking children across the domains of healthy development, we might better detect, diagnose, and manage the problems that can disrupt healthy development in our youngest children.

REFERENCES

1. Am J Psychiatry. 2010 Jan. doi: 10.1176/appi.ajp.2009.09060796.
2. Centers for Disease Control and Prevention. "Parent Training in Behavior Management for ADHD." www.cdc.gov/ncbddd/adhd/behavior-therapy.html.

Suicide continues to have high impact on youth

At-risk young populations are vulnerable to many threats to well-being

BY TARA HAELLE

Screening youth to identify those at risk for suicide is particularly important in medical settings, given the increasing rates of adolescent suicide, and screening can take as little as 20 seconds, according to Lisa Horowitz, PhD, MPH, a staff scientist and clinical psychologist at the National Institute of Mental Health, Bethesda, Md.

But clinicians need to use validated screening instruments that are both population specific and site specific, and they need practice guidelines to treat patients screening positive.

Currently, many practitioners use depression screens – such as question #9 on suicide ideation and self-harm on the Patient Health Questionnaire for Adolescents (PHQ-A) – to identify suicide risk, but preliminary data suggest these screens often are inadequate, Dr. Horowitz said. Just one question, especially one without precise language, does not appear to identify as many at-risk youths as more direct questions about suicidal thoughts and behaviors.

A Pathways to Clinical Care suicide risk screening work group therefore designed a three-tiered clinical pathway for suicide risk screenings in emergency departments, inpatient care, and outpatient primary care. It begins with the Ask Suicide-Screening Questions (ASQ), which takes about 20 seconds and was specifically developed for pediatric patients in the emergency department and validated in both inpatient and outpatient settings.

Dr. Horowitz, also the lead principal investigator for development of the ASQ, currently is leading six National Institute of Mental Health studies to validate and implement the screening tool in medical settings. She explained the three-tiered system during a session on youth suicide screening at the Pediatric Academic Societies annual meeting in Baltimore.

If a patient screens positive on the ASQ, a trained clinician should conduct a brief suicide safety assessment (BSSA), which takes approximately 10 minutes, Dr. Horowitz said. Those who screen positive on the BSSA should receive the Patient Resource List and then be referred for a full mental health and safety evaluation, which takes about 30 minutes. Resources, such as nurse scripts and parent/guardian flyers, are available at the NIMH website, as well as translations of the ASQ in Arabic, Chinese, Dutch, French, Hebrew, Italian, Japanese, Korean, Portuguese, Russian, Somali, Spanish, and Vietnamese.

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ACKNOWLEDGING THE IMPORTANCE OF SUICIDE SCREENING

During the same session, John V. Campo, MD, an assistant dean for behavioral health and professor of behavioral medicine and psychiatry at West Virginia University in Morgantown, discussed why suicide risk screening is so crucial in general medical settings. As someone who trained as a pediatrician before crossing over to behavioral health, he acknowledged that primary care physicians already have many priorities to cover in short visits, and that the national answer to most public health problems is to deal with it in primary care.

"Anyone who has done primary care pediatrics understands the challenges involved with screening for anything – particularly when you identify someone who is extensively at risk," he said.

But suicide has a disproportionately high impact on young populations, and "identifying youth at risk for suicide identifies a group of young people who are at risk for a variety of threats to their health and well-being," he said.

For youth aged 10-19 years in 2016, suicide was the second leading cause of death behind accidents, according to the Centers for Disease Control and Prevention (Natl Vital Stat Rep. 2018 Jun;67[4]:1-16). In fact, accidents, suicide, and homicide account for three-quarters of deaths among youth aged 10-24 years (Natl Vital Stat Rep. 2019 Jun;68[6]:1-77), yet it's typically the other 25% that most physicians trained for in residency.

"Suicide kills more kids than cancer, heart disease, infections – all kinds, sepsis, meningitis, pneumonia, influenza, HIV, respiratory conditions. Suicide kills more young people every year than all of that [combined]," Dr. Campo said. "And yet, when you walk through a modern emergency department, we see all these specialized programs for those who present with physical trauma or chest pain or all these other things, but zero specialized mental health services. There's a disconnect."

There is some good news in the data, he said. Observational data have shown that suicide rates negatively correlate with indicators of better access to health and medical health services, and researchers increasingly are identifying proven strategies that help prevent suicide in young people – once they have been identified.

But that's the problem, "and we all know it," Dr. Campo continued. "Most youth who are at risk for suicide aren't recognized, and those who are recognized most often are untreated or inadequately treated," he said. Further, "the best predictor of future behavior is past behavior," but most adolescents die by suicide on their first attempt.

Again, however, Dr. Campo pivoted to the good news. Data also have shown that most youth who die by suicide had at least one health contact in the previous year, which means there are opportunities for screening and intervention.

The most common risk factor for suicide is having a mental health or substance use condition, present in about 90% of completed suicides and affecting approximately one in five youth. Prevalence is even higher in those with physical health conditions and among those with Medicaid or no insurance (J Child Psychol Psychiatry. 2006 Mar-Apr;47[3-4]372-94).

Yet, "the majority of them have not been treated at all for mental disorder, which seems to be the most important remediable risk factor for suicide, and even fewer are in current treatment at the time of the death," Dr. Campo said. Suicide also is correlated with a number of other high-risk behaviors or circumstances, such as having "vulnerabilities to substance abuse, riding in a car with someone who is intoxicated, carrying a weapon to school, fighting, and meeting criteria for depression" (Pediatrics. 2010 May;125[5]:945-52). Screening for suicide risk therefore allows physicians to identify youth vulnerable to a wide range of risks, conditions, or death.

OVERCOMING BARRIERS TO SUICIDE SCREENING IN PRIMARY CARE

Given the high prevalence of suicide and its link to so many other risks for youth, screening in primary care can send the message that suicide screening "really is a part of health care," Dr. Campo said. Incorporating screening into primary care also can help overcome distrust of behavioral health specialists in the general public and stigma associated with behavioral health disorders.

Primary care screening emphasizes the importance and credibility of mental health and challenges attitudinal barriers to care, he said.

At the same time, however, he acknowledged that providers themselves often are uneasy about addressing behavioral health. Therefore, "having the guideline and the expectation [of suicide risk screening] really drives home the point that this needs to be integrated into the rest of primary care," he said. "It's also consistent with the idea of the medical home." With suicide the second leading cause of death among youth, "if there's anything that we're going to be thinking about screening for, one would think suicide would be high on the list."

In fact, observational evidence has shown that educating and training primary care providers to recognize people with depression or a high risk for suicide can reduce suicide attempts and the suicide rate, Dr. Campo said (JAMA Psychiatry. 2017 Jun 1;74[6]:563-70). It also can help with the mismatch between where at-risk patients are and where behavioral health specialists are. About 90% of behavioral health specialists work only in specialty settings, and only 5% typically work in general medical settings, he said. Yet "most people who are in mental distress or in crisis don't present in specialty behavioral health settings. They present in general medical settings."

More data are needed to demonstrate more definitively whether and how much suicide risk screening changes outcomes, but we know a few things, Dr. Campo said, summing up his key points: "We know suicide's a major source of mortality in youth that's been relatively neglected in pediatric health care. Second, we know that suicide risk is associated with risk for other important causes of death, for mental disorders, and for alcohol and substance use.

"We know that most suicide decedents are unrecognized prior to the time of death, and those who are recognized often are not treated. We know that the majority of suicide deaths occur on the very first attempt. We also know that we increasingly have treatments, mental disorders that can be identified, and remediable risk factors, and [that at-risk youth] typically present at general medical settings. Beyond that, focusing on the general medical setting has both conceptual and practical advantages as a site for really helping us to detect patients at risk and then managing them."

No funding was used for the presentations. Dr. Horowitz and Dr. Campo had no relevant financial disclosures.

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Commentary by Dr. Swick / Suicide has remained the second or third leading cause of death for 10- to 24-year-olds in the United States (after accidents) since 1975.[1] However, over the past decade, the rate of suicide has been steadily climbing in youth, increasing 56%.[2] While most outpatient pediatric offices screen for risk factors for accidents (such as presence of smoke detectors or firearms in the home, use of car seats or bike helmets, and so on), rates of screening for suicide risk remain stubbornly low. One survey found that, while 67% of primary care providers screened youth for mental health concerns, only 35% screened for suicide risk and only 14% used a validated screening instrument.[3] In another study, only 36% of primary care physicians screened for suicide risk when their patients presented with a request for antidepressants.[4]

Dr. Campo detailed the potential preventative power of screening all children from ages 10 to 24 years for suicide risk. While mental illness is estimated to be present in 90% of those who attempt suicide, screening for common mental illnesses (such as anxiety in prepubertal children or depression in adolescents) may not reveal all of those at risk. The availability of a free, fast, and valid screening instrument can help increase the screening rate. Other obstacles to adopting the suicide screening include time pressures, difficulty accessing further evaluation, and treatment resources and physician discomfort. Studies have demonstrated that adoption of a standardized suicide screen greatly increase the detection of risk with minimal increase in burden to the pediatric practice. In one study, the rate of inquiry doubled and detection increased by a factor of four, but this translated to a referral of approximately one patient per week to outpatient behavioral health.[5] When a pediatric practice has limited treatment resources, it may be useful to consider hiring a midlevel clinician, such as a psychiatric social worker, who could provide expanded assessments for those youth who screen in for suicide risk or may provide psychotherapy (both billable services), or who could coordinate referrals to outside resources. There are actually many practical and cost-effective models for integrated or collaborative systems of care for behavioral health within primary care practices.[6] Coupling this valuable information about suicide screening with these practical strategies would probably lead to more robust adoption of this straightforward intervention.

REFERENCES

1. JAMA Netw Open. 2019. doi: 10.1001/jamanetworkopen.2019.3886.
2. National Center for Health Statistics. "Death Rates Due to Suicide and Homicide Among Persons Aged 10–24: United States, 2000–2017," Data Brief No. 352, October 2019.
3. J Prim Care Community Health. 2012 Jan. doi: 10.1177/2150131911417878.
4. Ann Fam Med. 2007 Sep-Oct;5(5):412-8.
5. Pediatrics. 2010 May. doi: 10.1542/peds.2009-2458.
6. Mayo Clin Proc. 2011 Aug. doi: 10.4065/mcp.2011.0076.

Alcohol, opioid misuse tied to risky behaviors

Open communication and support from adults may be protective

BY JEFF CRAVEN
FROM PEDIATRICS

Binge drinking and misuse of opioids led to risky behavior during adolescence, two studies from the journal Pediatrics highlighted. And the binge drinking in high school may predict risky driving behaviors up to 4 years after high school.

Federico E. Vaca, MD, of the developmental neurocognitive driving simulation research center at Yale University, New Haven, Conn., and colleagues examined the associations between risky driving behaviors and binge drinking of 2,785 adolescents in the nationally representative, longitudinal NEXT Generation Health Study. The researchers studied the effects of binge drinking on driving while impaired (DWI), riding with an impaired driver (RWI), blackouts, extreme binge drinking, and risky driving.

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BINGE DRINKING IN HIGH SCHOOL MAY **PREDICT RISKY DRIVING BEHAVIORS** UP TO 4 YEARS AFTER HIGH SCHOOL.

The adolescents were studied across seven waves, with Wave 1 beginning in the 2009-2010 school year (10th grade; mean age, 16 years), and data extended up to 4 years after high school. Of all adolescents enrolled, 91% completed Wave 1, 88% completed Wave 2, 86% completed Wave 3 (12th grade), 78% completed Wave 4, 79% completed Wave 5, 84% completed Wave 6, and 83% completed Wave 7 (4 years after leaving high school) of the study.

HIGH SCHOOL BINGE DRINKING PREDICTS LATER RISKY BEHAVIOR

About one-quarter of adolescents reported binge drinking in Waves 1-3, with an incidence of 27% in Wave 1, 24% in Wave 2, and 27% in Wave 3. Adolescents who reported binge drinking in Wave 3 had a higher likelihood of DWI in subsequent waves, with nearly six times higher odds in Wave 5 and more than twice as likely in Wave 7, researchers said. Binge drinking in Wave 3 also was associated with greater than four times higher odds of RWI in Wave 4, and more than two and a half times higher odds of RWI in Wave 7. Among adolescents who reported binge drinking across 3 years in high school, there was a higher likelihood of extreme binge drinking in Wave 7, and higher likelihood of risky driving after graduating.

PARENTAL KNOWLEDGE OF DRINKING HAS IMPACT

Parental knowledge of drinking and support for not drinking alcohol was associated with lower likelihood of DWI and RWI in some waves. Father monitoring knowledge of drinking in Waves 1-3 lowered the odds of DWI by 30% in Wave 5 and 20% in Wave 6, while also lowering the odds of RWI in Wave 4 and Wave 7 by 20%. Mother knowledge of drinking in Waves 1-3 was associated with 60% lower odds of DWI in Wave 4, but did not lower odds in any wave for RWI.

Overall, parental support for not drinking lowered odds for DWI by 40% in Waves 4 and 5, and by 30% in Wave 7 while also lowering odds of RWI in Wave 4 by 20%.

The results are consistent with other studies examining risky driving behavior and binge drinking in adolescent populations, but researchers noted that "to an important but limited extent, parental practices while the teenager is in high school may protect against DWI, RWI, and blackouts as adolescents move into early adulthood."

"Our findings are relevant to prevention programs that seek to incorporate alcohol screening with intentional inquiry about binge drinking. Moreover, our results may be instructive to programs that seek to leverage facets of parental practices to reduce health-risk contexts for youth," Dr. Vaca and colleagues concluded. "Such prevention activities coupled with strengthening of policies and practices reducing adolescents' access to alcohol could reduce later major alcohol-related health-risk behaviors and their consequences."

OPIOID MISUSE INCREASED ODDS OF RISKY BEHAVIOR

In a second study, Devika Bhatia, MD, of the University of Colorado at Denver, Aurora, and colleagues examined opioid misuse in a nationally representative sample of 14,765 adolescents from the Centers for Disease Control and Prevention's 2017 Youth Risk Behavior Surveillance Survey. The researchers measured opioid misuse by categorizing adolescents into groups based on whether they had ever misused prescription opioids and whether they had engaged in risky driving behavior, violent behavior, or risky sexual behavior; had a history of substance abuse; or attempted suicide.

Dr. Bhatia and colleagues found 14% of adolescents in the study reported misusing opioids, with an overrepresentation of 17-year-old and 18-year-old participants

reporting opioid misuse (*P* less than .0001). There were no statistically significant difference between those who misused opioids and those who did not in terms of race, ethnicity, or sex.

Those adolescents who reported misusing opioids were 2.8 times more likely to not use a seatbelt; were 2.8 times more likely to have RWI; were 5.8 times more likely to have DWI; or 2.3 times more likely to have texted or emailed while driving. In each of these cases, *P* was less than .0001.

Adolescents who misused opioids also had significantly increased odds of engaging in risky sexual behaviors such as having sex before 13 years (3.9 times); having sex with four or more partners (4.8 times); using substances before sex (3.6 times); and not using a condom before sex (2.0 times). In each of these cases, *P* was less than .0001.

Additionally, adolescents in this category were between 5.4 times and 22.3 times more likely to use other substances (*P* less than .0001 for 10 variables); 4.9 times more likely to have attempted suicide (*P* less than .0001); or more likely to have engaged in violent behavior such as getting into physical fights (4.0 times), carrying a weapon (3.4 times), or carrying a gun (5.1 times) within the last 30 days. In the four latter cases, *P* was less than .0001.

"With the ongoing opioid epidemic, pediatricians and child psychiatrists are likely to be more attuned to opioid misuse in their patients," Dr. Bhatia and colleagues concluded. "If youth are screening positive for opioid misuse, pediatricians, nurses, social workers, child psychiatrists, and other providers assessing adolescents may have a new, broad range of other risky behaviors for which to screen regardless of the direction of the association."

Substance use screening for treating substance use disorder traditionally has been provided by a specialist, Jessica A. Kulak, PhD, MPH, said in an interview. "However, integration of care services may help to change societal norms around problematic substance use – both by decreasing stigma associated with substance use, as well as increasing clinicians' preparedness, knowledge, and confidence in preventing and intervening on adolescents' substance experimentation and use." She recommended that clinicians in primary care improve their training by using the Substance Abuse and Mental Health Services Administration's Screening, Brief Intervention, and Referral to Treatment program, which is available as a free online course.

Confidentiality is important in adolescent health, said Dr. Kulak, who is an assistant professor in the department of health, nutrition, and dietetics at State University of New York at Buffalo.

"When discussing sensitive topics, such as binge drinking and opioid misuse, adolescents may fear that these or other risky activities may be disclosed to parents or law enforcement officials. Therefore, adolescent health providers should be aware of local, state, and federal laws pertaining to the confidentiality of minors," she remarked

She added, "adolescents are often susceptible to others' influences, so having open communication and support from a trusted adult – be it a parent or clinician – may also be protective against risky behaviors."

The study by Vaca et al. was funded by the National Institutes of Health with support from the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development; the National Heart, Lung, and Blood Institute; the National Institute on Alcohol Abuse and Alcoholism; the National Institute on Drug Abuse; and the Maternal and Child Health Bureau of the Health Resources and Services Administration. The study by Bhatia et al. had no external funding. The authors from both studies reported no relevant financial disclosures. Dr. Kulak said she had no financial disclosures or other conflicts of interest.

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SOURCES: Vaca FE et al. Pediatrics. 2020. doi: 10.1542/peds.2018-4095; Bhatia D et al. Pediatrics. 2020. doi: 10.1542/peds.2019-2470.

Commentary by Dr. Swick / Both of the studies described here highlight a central challenge in adolescent health: risky behavior. It has long been considered a danger, even a flaw, of adolescent brain development that the brain's limbic system, the part of the brain that is wired for reward, matures long before the prefrontal cortex, the part of the brain that is responsible for executive function and control. Research in just the past 10 years has been expanding our understanding of adolescent brain development. There is strong evidence that, rather than being ignorant about risk, adolescents are actually excellent at assessing risk and are simply willing to tolerate higher levels of it in the pursuit of novelty. And this pursuit potentiates learning and mastery.[1] It seems to make some evolutionary sense that adolescent brain development promotes risk tolerance and learning, both necessary for moving into independence.

But when adolescents experiment with drugs and alcohol, their judgment and impulse control both become impaired, making novelty seeking much more dangerous. And we know that earlier first use of drugs or alcohol significantly raises their lifetime risk for addiction, which is the downside of their brain's reward sensitivity. We also know that adolescent decision-making is especially sensitive to social influences.[2] While this means that adolescents may underestimate risk in the presence of their friends, it also is cause for hope. Parents, and other caring adults, have more influence than they think on adolescent decision-making. When parents provide regular, clear, consistent information about risks, their children meaningfully absorb that information to use in their own risk assessment. This makes it critical that parents talk early and often about the known quantifiable risks of using specific substances: binge drinking, opioid pills that may seem safe because they came from someone's medicine cabinet, or the effects of "medical" marijuana on the developing brain. They also are very influential by modeling behaviors, such as tolerance of frustration or distress, curiosity with preserved critical thinking, patience, and honesty. Remind your patient's parents that they should talk early and often about the facts (and their house rules) around those areas that teenagers will be managing independently: sex, drugs, and mental health. And when they do that alongside modeling qualities such as honesty, restraint, self-awareness, and compassion, they inoculate their children against the most dangerous novelty-seeking in adolescence and well into adulthood.

REFERENCES

1. Neuron. 2016 Oct 5. doi: 10.1016/j.neuron.2016.08.031.
2. Front Psychol. 2019 Aug 29. doi: 10.3389/fpsyg.2019.01915.

Identify youth at high risk of running away

Knowing the risk factors and care needs can make a difference

BY CHRISTINE KILGORE
FROM PEDIATRICS

As many as 1 in 20 youth run away from home each year, and you can play a critical role in identifying adolescents at high risk through confidential social histories and discussions, according to a clinical report from the American Academy of Pediatrics.

The academy's data-rich report, "Runaway Youth: Caring for the Nation's Largest Segment of Missing Children," details how unaccompanied youth who run away – either on their own or who are asked to leave home – have high rates of trauma and neglect, mental illness, substance abuse, family dysfunction, and disengagement from school.

Children who identify as lesbian, gay, bisexual, transgender, and questioning or queer (LGBTQ) and youth in protective custody also are at high risk of running away and of becoming homeless – and once away from home, they and other runaways are at high risk for additional trauma, victimization, and violence, including sexual exploitation, according to the report published in Pediatrics.

"There clearly are certain populations at higher risk, and we really need to be aware of and in tune with these risks, and ask about the home and the household in order to try to decrease the risk of these kids getting into dangerous situations," Thresia B. Gambon, MD, said in an interview. She is coauthor of the report and a pediatrician with the Citrus Health Network in Miami.

Among the AAP's recommendations for practice is the guidance to conduct a thorough and confidential psychosocial assessment such as the HEEADSSS assessment (home environment, education and employment, eating, peer-related activities, drugs, sexuality, suicide/depression, and safety) and to use a validated depression screening tool for adolescents, such as the Patient Health Questionnaire for Adolescents (PHQ-A) and the primary care version of the Beck Depression Inventory (BDI).

In broad terms, pediatric practices should "consider assessing for previous runaway episodes and risk factors for running away using a trauma-informed approach, which involves being aware of trauma and adverse childhood experiences that can affect health," according to the report. The AAP Trauma Toolbox for Primary Care is mentioned as a resource.

Most surprising to Dr. Gambon in the research and report-writing process were data showing that disengagement from school is a significant risk factor. "This stood out to me," she said. "If there are school problems, kids might run away to avoid attending school."

Tasked with updating the AAP's 2004 clinical report, "The Pediatrician's Role in the Prevention of Missing Children," Dr. Gambon and coauthor, Janna R. Gewirtz O'Brien, MD, decided to look more closely at runaway youth after studying the numbers – some studies estimate that between 5% and 8% of adolescents run away every year. They saw that, "in general, the number of kids who just go missing has actually decreased [with the help of] cell phones," Dr. Gambon said in an interview.

"The numbers of kids who are actually running away are high," she said, "and probably we're underidentifying these in our primary care clinics."

"IF THERE ARE SCHOOL PROBLEMS, KIDS MIGHT RUN AWAY TO AVOID ATTENDING SCHOOL."

Commentary by Dr. Swick / This very important work from the American Academy of Pediatrics highlights the power of pediatricians to screen for risk in their patients and address the sources of risk. It is particularly important that the authors highlight the high level of risk among lesbian, gay, bisexual, transgender, and queer (LGBTQ) youth. Over a quarter of youth who identify as LGBTQ are kicked out of their homes after coming out to their parents.[1] Substance abuse is an independent risk factor for becoming a runaway, and again LGBTQ youth are at higher risk. In one meta-analysis, the odds of substance use for LGBTQ youth were, on average, 190% higher than for heterosexual youth.[2] Once homeless, LGBTQ youth are at higher risk than their heterosexual peers to use risky survival strategies and to experience sexual and other forms of victimization.[3] In their National Survey on LGBTQ Youth Mental Health in 2019, The Trevor Project found LGBTQ youth who experienced housing instability reported considering suicide at twice the rate and attempted suicide at more than three times the rate of LGBTQ youth who had not.[4] This finding remained even after controlling for the impact of related variables.

While it is important to screen for all of the risk factors described here, it is critical to have a low index of concern when you know your patient is an LGBTQ youth, especially if they have not come out to their family. If your patient also is abusing substances, their level of risk becomes very high, for homelessness and for suicide. It is always valuable to ask about sexual orientation and safety and connection at home, and to be prepared to offer targeted supports for LGBTQ youth and for their families, so that they may stay strongly connected through coming out and avoid the extraordinary risks of becoming homeless and the hazards that homelessness would bring them.

REFERENCES

1. SAMSHA "Homelessness Programs Resources to Help LGBT Youth." www.samhsa.gov/homelessness-programs-resources/hpr-resources/resources-help-lgbt-youth.
2. Addiction. 2008 Apr. doi: 10.1111/j.1360-0443.2008.02149.x.
3. "Mental Disorder, Subsistence Strategies, and Victimization Among Gay, Lesbian, and Bisexual Homeless and Runaway Adolescents" (Lincoln, Neb; Sociology Department, Faculty Publications. 53, 2004).
4. The Trevor Project. "Research Brief: Unstable Housing and LGBTQ Youth Suicidality." www.thetrevorproject.org/2019/08/28/research-brief-unstable-housing-and-lgbtq-youth-suicidality/.

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Because a significant number of runaway youth become homeless, data on the homeless offer a valuable window not only into the health risks of homelessness for teens (substance abuse, pregnancy, STDs,) but also into risk factors for leaving home in the first place, she noted. Research shows, for instance, that about 20%-40% of teenagers who are homeless identify as LGBTQ, compared with 4%-10% of their nonhomeless peers.

When an adolescent at high risk for running away is identified, you should use practice- and community-based resources to address key issues, support psychological and behavioral health needs of the child and family, and ensure safety.

For youth who have run away, you can share information on local resources, as well as the national Runaway Safeline (1-800-RUNAWAY), which provides 24-hour referrals to community resources, including shelter, food banks, social services, and counseling.

You also can ask adolescents whether they have sources of support and shelter (safe, supportive adults who might help in a crisis), and discuss safety plans for leaving home that include health care to mitigate risk, such as reliable contraception and access to mental health care.

"The goal with talking about a safety plan isn't, of course, to encourage a child to run away, but if they feel as if they need to find somewhere else to live or stay, to discuss what resources are available to them to try to keep them as safe as possible when they're out of their home," Dr. Gambon said.

Dr. Gambon speaks partly from experience. She works routinely with youth who have run away from foster care homes, youth who have been trafficked, and other runaways.

"I always try to talk with them about safety. I try not to put them down for their decisions but to work with them to make better decisions," she said. "I work closely with a psychologist because a big part of this is getting them to have self-worth. They often feel as if no one cares, and some just want to be heard and to be able to talk about their situations."

The AAP report notes that, of more than 70,000 contacts made to Runaway Safeline in 2017, 31% were about youth who were contemplating running away, 16% were about youth who had run away, 5% were about youth asked to leave home or prevented from returning, and 9% concerned youth experiencing homelessness. About three-quarters of the calls came from the youth themselves.

SOME STUDIES ESIMATE THAT BETWEEN **5% AND 8% OF ADOLESCENTS RUN AWAY EVERY YEAR**.

Dr. Gambon and Dr. Gewirtz O'Brien, of the department of pediatrics at the University of Minnesota in Minneapolis, worked with the AAP Committee on Psychosocial Aspects of Child and Family Health and the AAP Council on Community Pediatrics in producing the report. There was no external funding for this report and the authors said they had no conflicts of interest.

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FACTS AND MYTHS DECODED

To learn more, visit www.TEAM-ADHD.com/awareness, or scan here.

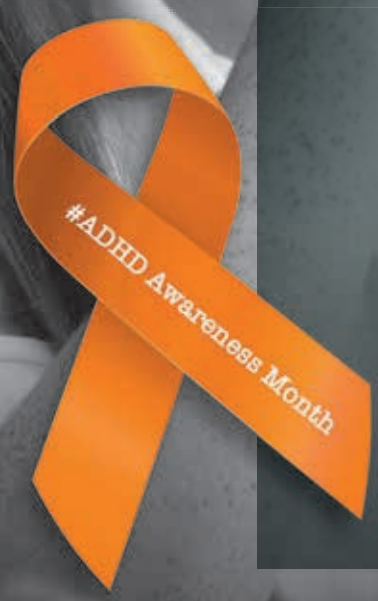
MYTH: ADHD IS A SIMPLE SCHOOL-DAY DISORDER

FACT: UP TO 75% OF CHILDREN AND ADOLESCENTS HAVE AT LEAST 1 OVERLAPPING COMORBIDITY[1]

In pediatric patients with ADHD, the following conditions are commonly reported[2,3]:

CO-OCCURRING IN UP TO 50% OF CASES[2,3]

- **Depression**
- **Anxiety disorders**
- **Oppositional defiant disorder**
- **Pervasive developmental disorders/ autism spectrum disorder**



You can help. Dive deeper into complex ADHD.

As a trusted resource for your patients and their caregivers, please encourage them to visit **MoreToADHD.com.** Here, they can learn more about the treatment complexities often associated with ADHD.

Actor Portrayal.

REFERENCES: 1. Banaschewski T, Becker K, Dopfner M, Holtmann M, Rosler M, Romanos M. Attention deficit/hyperactivity disorder. *Dtsch Arztebl Int*. 2017;114(9):149-159. **2.** Clemow DB, Bushe C, Mancini M, Ossipov MH, Upadhyaya H. A review of the efficacy of atomoxetine in the treatment of attention-deficit hyperactivity disorder in children and adult patients with common comorbidities. *Neuropsychiatr Dis Treat*. 2017;13:357-371. **3.** Turgay A, Ansari R. Major depression with ADHD in children and adults. *Psychiatry (Edgmont)*. 2006;3(4):2-32.

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