Mood, anxiety, and substance use disorders

Learning objectives

- Describe common mood, anxiety, and substance use disorders that occur during childhood and adolescence and their basic treatment options.

Depression in young people: prevalence[1]

- 2% in children
- 4-8% in adolescents[2]
  - 12-month period 11.0%
  - Severe impairment 3.0% (life); 2.3% (12 months)
- Male-female ratio of 1:1 during childhood and 1:2 during adolescence
- 20% of females by the age 18
- 1 in 4 adolescents have experienced a depressive episode by age 18
- 5-10% have subsyndromal symptoms of MDD
  - Significant psychosocial impairment
  - Increased risk of suicide and developing MDD

Co-morbidity is the norm

- 40-90% of youth with depressive disorders have a co-morbid disorder
  - Up to 50% have 2 or more

- Most common co-occurring mental health diagnoses:
  - Anxiety
  - Disruptive behavior disorders
  - Attention-Deficit/Hyperactivity Disorder
  - Substance Use Disorder
  - Autism Spectrum Disorder

Long-term consequences of depression

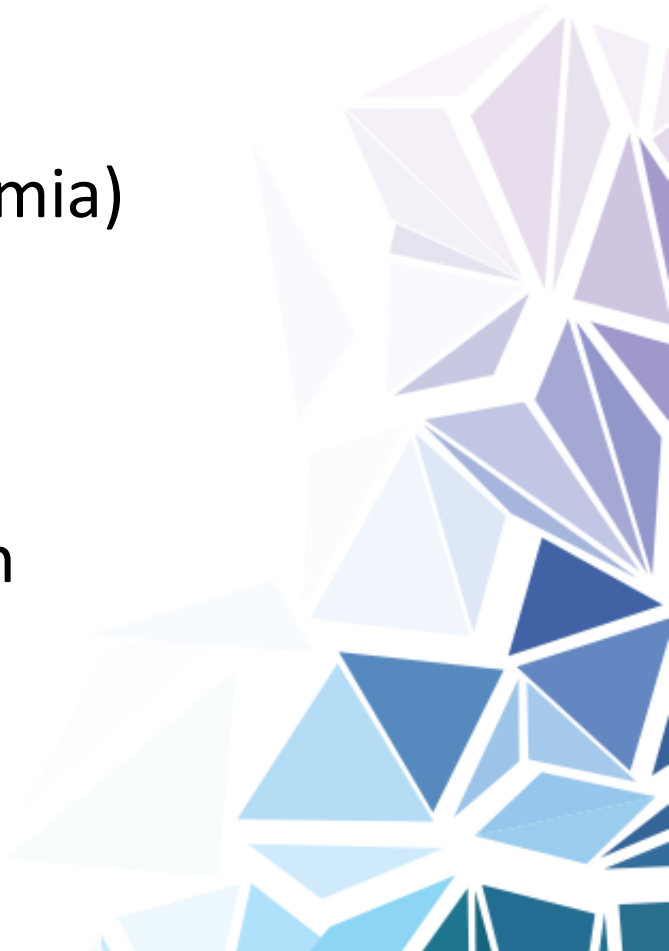
- School performance
- Work performance
- Substance use
- Suicide attempts
- Legal difficulties

Risk factors for depressive disorders[1]

- Parent or sibling with depression
- Negative outlook or poor coping strategies
- Chronic medical issues
- Previous depressive symptoms or depressive episodes
- Family stressors or dysfunction including conflict with caregiver
- Exposure to early adverse events (abuse, neglect, loss of loved one)

Depressive disorders

- Disruptive Mood Dysregulation Disorder (DMDD)
- **Major Depressive Disorder (MDD)**
- Persistent Depressive Disorder (formerly called Dysthymia)
- Premenstrual Dysphoric Disorder (PMDD)
- Substance or Medication-Induced Depressive Disorder
- Depressive Disorder Due to Another Medical Condition
- Other Specified Depressive Disorder



Major Depressive Disorder (MDD)

- Depressed mood or anhedonia and 5 or more SIGECAPS symptoms for at least 2 weeks
- Must cause marked distress or dysfunction

- **S**: sleep-too little or too much
- **I**: loss of interest in things previously found pleasurable
- **G**: excessive feelings of guilt
- **E**: low energy
- **C**: poor concentration
- **A**: appetite-increase or decrease
- **P**: psychomotor retardation; moving or responding very slowly
- **S**: suicidal thoughts

Bipolar Disorder

- Always monitor for bipolar symptoms when there is a concern for depression
- Evidence suggests that Bipolar is often diagnosed when not present, yet many cases also go undiagnosed
- Marked progress has been made in validating and honing assessment strategies and experts agree there is validity of DSM based diagnoses
- Ask about manic and hypomanic symptoms
- If there is a concern for bipolar disorder, refer for further evaluation by a psychiatric provider as this is beyond the scope of Collaborative Care

Manic/Hypomanic symptoms (DSM-5)

- A distinct period of abnormal and persistent elevated, expansive, or irritable mood with goal-directed behavior or energy, lasting at least 1 week and present most of the day, nearly every day (or any duration if hospitalization is necessary)

- During mood state and increased energy/activity need 3+ symptoms (4+ if only irritable mood):
  - Inflated self-esteem or grandiosity
  - Decreased need for sleep
  - More talkative than usual or pressure to keep talking
  - Flight of ideas or subjective experience that thoughts are racing
  - Distractibility, reported or observed
  - Increase in goal-directed activity or psychomotor agitation
  - Excessive involvement in activities that have a high potential for painful consequences

More descriptions of Bipolar Disorder

- Distinct change or acute onset
  - Significant change from baseline
- More episodic
- Persists
- Pathological elation or euphoria
  - Too silly, inappropriately silly or giddy

Decreased need for sleep

Hyper sexuality

Activity, speech, flow of ideas - "overdrive"

Extravagant plans

Delusional thinking and sometimes hallucinations

Screening for Bipolar

- Talk with caregivers
- Family history
- Screening instruments
  - Parent-completed General Behavior Inventory (P-GBI)
  - Parent-completed Child Mania Rating Scale (P-CMRS)
  - Parent-completed Young Mania Rating Scale (P-YMRS)
- Patient interview
  - Language? Psychosis? Suicidal behavior? Abuse? Illicit substance use? Racing thoughts? Flight of ideas?

Anxiety

- **Worry**: anxious apprehension and thoughts focused on the possibility of negative future events

- **Fear**: response to threat or danger that is perceived as actual or impending

- **Anxiety can be normal and adaptative**
  - Important to distinguish normal, transient, developmentally appropriate worries and fears from anxiety disorders

Characteristics of anxiety disorders

- Interferes with daily functioning and interpersonal relationships
- Persistent
- Excessive
- Intense
- Frequent
- Distressing
- Not helping
- Disruptive
- Overwhelming
- Difficult to control

Anxiety disorders: prevalence[3,4]

- Most common psychiatric illness of childhood
- Prevalence estimates ranging from 10% to 30%
- 12-month prevalence in adolescence aged 13- 18 years: 25% to 32%

Anxiety disorders: common comorbid conditions

- Obsessive Compulsive Disorder (OCD)
- Separation Anxiety Disorder (SAD), Social Anxiety, and Generalized Anxiety Disorder (GAD)
  - Less common to have pure anxiety
- Mood problems
- Externalizing disorders
- Greater risk of developing substance abuse and conduct problems

Anxiety disorders

- **Obsessive Compulsive Disorder (OCD)**

- Non-OCD Anxiety
  - **Generalized Anxiety**
  - Separation Anxiety
  - **Specific Phobia**
  - **Panic Disorder**
  - Selective Mutism

Obsessive Compulsive Disorder (OCD)

- Presence of obsessions, compulsions, or both, that are **time-consuming** (e.g., take more than 1 hour per day) or cause clinically **significant distress or impairment** in social, occupational, or other important areas of functioning

- **Obsessions**
  - Recurrent or persistent **thoughts**, urges, or images
  - Intrusive
  - Unwanted

- **Compulsions**
  - Repetitive **behaviors** or mental acts
  - Aimed at preventing or reducing anxiety or distress

Generalized Anxiety Disorder (GAD)

- Excessive anxiety and worry
- Occurring more days than not for at least 6 months, about a number of events or activities
- The anxiety and worry are associated with three or more of the following six symptoms:
  - Restlessness or feeling keyed up or on edge
  - Being easily fatigued
  - Difficulty concentrating or mind going blank
  - Irritability
  - Muscle tension
  - Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep)

Specific phobia

- Marked fear or anxiety about a specific object or situation which:
  - Almost always provokes fear or anxiety disproportionate to the actual danger posed or sociocultural context
  - Is actively avoided or endured with intense fear or anxiety
  - Persists 6 months or longer

Panic attack

- An abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur:
  - Palpitations, pounding heart, or accelerated heart rate
  - Sweating
  - Trembling or shaking
  - Sensations of shortness of breath or smothering
  - Feelings of choking
  - Chest pain or discomfort
  - Nausea or abdominal distress
  - Feeling dizzy, unsteady, light-headed, or faint
  - Chills or heat sensations
  - Paresthesia (numbness or tingling sensations)
  - Derealization (feelings of unreality) or depersonalization (being detached from oneself)
  - Fear of losing control or “going crazy”
  - Fear of dying

Panic Disorder

- Recurrent unexpected panic attacks

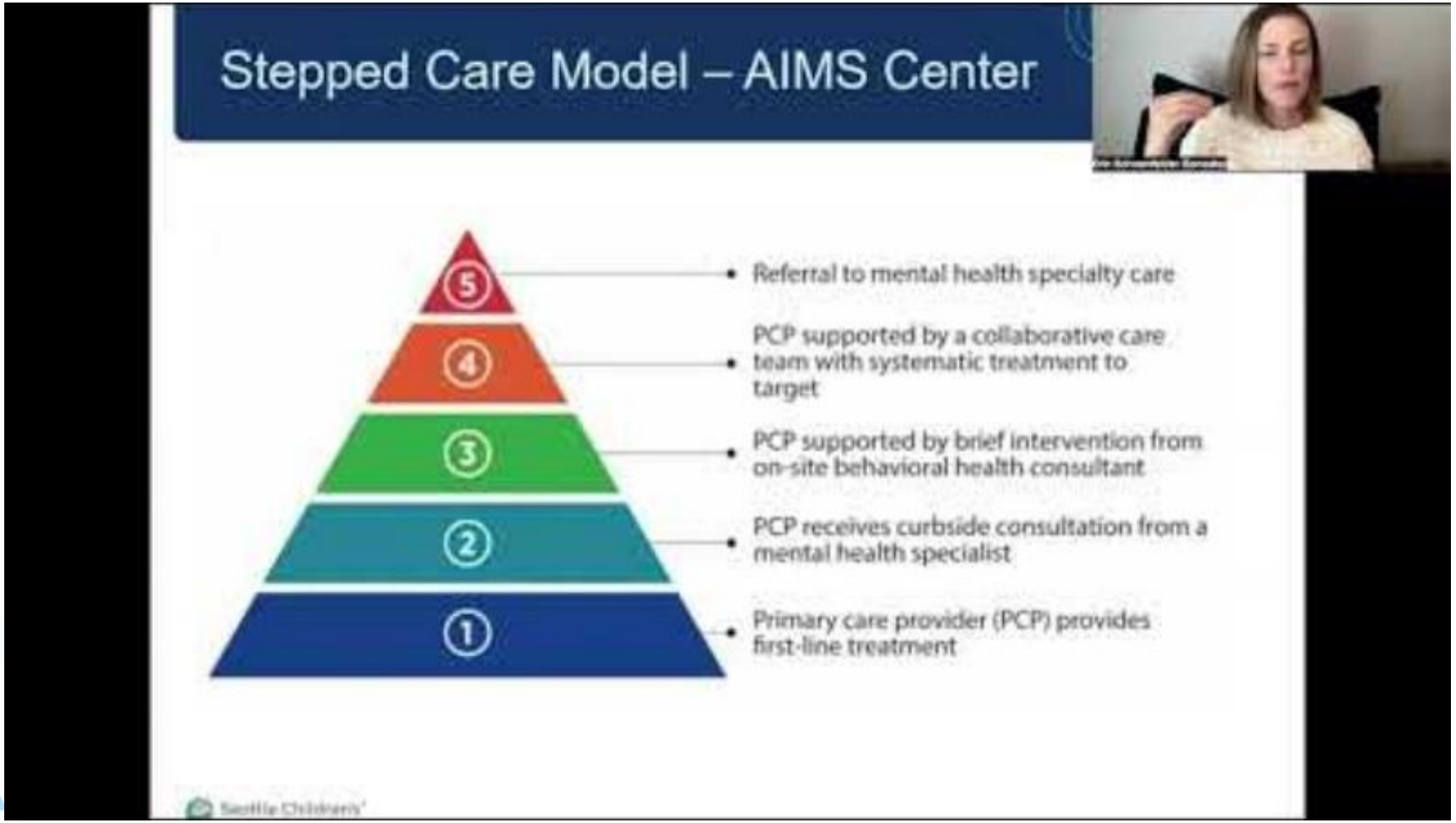
- At least one of the attacks has been followed by 1 month (or more) of one or both of the following:
  - Persistent concern or worry about additional panic attacks or their consequences (e.g., losing control, having a heart attack, “going crazy”)

  - A significant maladaptive change in behavior related to the attacks (e.g., behaviors designed to avoid having panic attacks, such as avoidance of exercise or unfamiliar situations)

Non-pharmacological treatment of depression and anxiety

- Usual Collaborative Care interventions
  - Psychoeducation
    - Impact of sleep, nutrition
  - Motivational Interviewing
  - Behavioral Activation
  - Problem Solving Treatment
- Involve parents in interventions
- Seattle Children's First Approach Skills Training (FAST) program
  - Anxiety (FAST-A)
  - Depression (FAST-D)

First Approach Skills Training (FAST) program



https://www.youtube.com/watch?v=JHcumBlcWJs

General psychopharmacology recommendations

- **Start low, go slow, and keep going**
- Continue to make slow, steady increases until arriving at the effective dose
- Help youth and family have **realistic expectations**
- Ensure the patient is taking them regularly

Landmark study: Treatment for Adolescents with Depression Study (TADS)

- Funded by the National Institute of Mental Health
- Conducted in 13 academic and community centers in the U.S.
- Randomized controlled trial that evaluated the effectiveness of four treatments for adolescents with moderate to severe major depression
- Highlights the value of combination treatment
- *"*Findings revealed that 6 to 9 months of combined fluoxetine + CBT should be the modal treatment from the public health perspective as well as to maximize benefits and minimize harm for individual patients.*"*[5]

Landmark study: Treatment of SSRI-Resistant Depression in Adolescents (TORDIA)

- "Switching to a combination of CBT and another antidepressant resulted in a higher rate of clinical response than switching to another medication without CBT."[6]
- Best results with 9 or more sessions
- CBT with problem-solving and social skills treatments, more likely had a reduction in depression
- No suicides in the study
- SNRI: a bit more activating than the SSRIs

Medication classes

- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin and norepinephrine reuptake inhibitors (SNRIs)
- Other antidepressants
  - Bupropion (Wellbutrin)
  - Mirtazapine (Remeron)
  - Tricyclic antidepressants (TCAs)

Selective serotonin reuptake inhibitors (SSRIs)

- Increase serotonin concentrations
- Generally reserved for moderate to severe symptoms
- Most common pharmacotherapy for youth with depression
- Caution in youth with bipolar disorder; SSRIs may induce a manic episode

FDA approved medications

- **Depression**: Fluoxetine (Prozac) and Escitalopram (Lexapro)
  - Fluoxetine 8 years old and older
  - Escitalopram 12 years old and older

- **OCD**: Fluoxetine (Prozac), Fluvoxamine (Luvox), Sertraline (Zoloft), Clomipramine

- **Anxiety**: Duloxetine
  - However, the evidence is stronger for SSRI's

- **For adolescents, it is common to use many psychotropic medications off-label both for depression and other mental health disorders**

FDA-approved indications and dose ranges

Medication	FDA-approved indication	Indication age range	Starting Dose	Dose range
Citalopram (Celexa)	Depression	Adults	10-20mg	10-40mg
Escitalopram (Lexapro)	Depression	12 years to adult	2.5-5mg	2.5-20mg
	GAD	Adults		
Fluoxetine (Prozac)	Depression	8 years to adult	5-10mg	10-60mg
	OCD	7 years to adult		
Fluvoxamine (Luvox)	OCD	8 years to adult	12.5-25mg	12.5-300mg
Sertraline (Zoloft)	Depression	Adults	12.5-25mg	12.5-200mg
	OCD	6 years to adult		

SSRI contraindications

- Youth with extreme irritability, agitation, or explosiveness on prior trials of SSRIs
- Children with evidence of bipolar disorder
  - Elevated, expansive, decreased need for sleep, pressured speech, explosiveness that is episodic in nature
- Many children with “bipolar” have relational issues, trauma, or more chronic characterological issues
- People taking triptans are at risk for serotonin syndrome when SSRIs are added

Go slow

- Dose Increase:
  - Typically, 2-6 weeks
  - May not reach maximum efficacy until 8 weeks

  - Allow several weeks at target dose before assessing full response to medication

Serotonin and norepinephrine reuptake inhibitors (SNRIs)

- Duloxetine (Cymbalta) and Venlafaxine (Effexor)
- Limited data
- Works in a similar way to SSRIs
- In adults, helpful for pain (e.g., diabetic peripheral neuropathic pain, fibromyalgia, chronic musculoskeletal pain)
- Remember to monitor blood pressure
- Given effects on norepinephrine, may be more energizing or activating and should be given in the morning
- Venlafaxine (Effexor): Can have more pronounced withdrawal if a teen stops this or is not taking regularly

Atypical antidepressants

Bupropion (Wellbutrin)

- **Advantage vs. SSRIs**: Suppresses appetite, less sexual dysfunction
- **Disadvantage vs. SSRIs**: Not effective for anxiety disorders
- **Mechanism**: Stimulates release of dopamine and norepinephrine
  - Also effective for smoking cessation
  - Caution in patients with seizure history, tics, and eating disorders

Mirtazapine (Remeron)

- **Advantage vs. SSRIs**: Sedating and stimulates appetite, useful for insomnia and weight loss
- **Disadvantage vs. SSRIs**: Sedation and weight gain
- **Mechanism**: Blocks serotonin receptors, increases serotonin and norepinephrine release

Tricyclic antidepressants (TCAs)

- Precursor to the safer SSRIs
- Examples: amitriptyline, desipramine, doxepin, nortriptyline
- In adults used for major depression, anxiety disorders, and pain syndromes
- Often used medically for children with headaches, pain syndrome, functional GI conditions, enuresis
- More side effects than SSRIs:
  - Drowsiness, dizziness, dry mouth, and constipation, GI distress
  - Irritability or angry outbursts
  - Sudden unexplained death in some case studies[7,8,9]
  - Possibility of cardiac toxicity, follow EKGs: use extreme caution in individuals with high suicide risk
- Little evidence to support frequent use of TCAs as a monotherapy for adolescents with depression or anxiety
- Given concerns for cardiac side effects, consider EKG monitoring especially when used with > 1 treatment that can elevate QTc interval

Common drug interactions

- Triptans: watch for serotonin syndrome when used together with SSRIs
- Fluoxetine (Prozac): more interactions with P450
- Consider EKG if there are multiple medications that may increase QT interval and risk for Torsades de Pointes

Antidepressant black box warning (2004)

- No suicides occurred in any of these studies
- FDA measured suicidal thinking and behavior by using "Adverse Event Reports“ (AER)
- 3% of all children/adolescents taking medication had an “adverse event", compared to 2% of those taking placebo
- Most of these events were an increase in suicidal thoughts; None were suicide deaths
- Since the FDA issued the black box warning, there has been a decline in antidepressant use, but an increase in suicide deaths
- Further analyses of clinical trials data revealed that there is overall improvement in suicidality in subjects treated with antidepressants, with only a few subjects reporting worsening or new onset suicidality

Increased suicide risk can be managed

- Careful monitoring
- Development of a safety plan
- Combination of medication + therapy
- For moderate to severe levels of depression, there is benefit in the use of medication
  - Higher rate of relief
  - More complete relief

Conclusion about black box warning

"Spontaneously reported SAEs appear to be more common with antidepressant treatment than placebo. Nevertheless, given the greater number of patients who benefit from antidepressant treatment, particularly the SSRIs, than who experience these SAEs, as well as the decline in overall suicidal ideation on rating scales, the **risk-benefit ratio for SSRI use in pediatric depression appears to be favorable**, with careful monitoring."

—Boris Birmaher, *Clinical Manual of Child and Adolescent Psychopharmacology, Second Edition*

Antidepressant discontinuation

- Maintain patient on medication for 9-12 months once remission in symptoms is reached
  - Helps to prevent relapse
- Typically discontinue over a 4–6-week period
- Tend to do it spring/summer or periods of low stress
- If multiple episodes of depression, may be best to stay on the medication

Substance use

- Adolescence is a crucial period of both susceptibility to the rewards of drugs and the vulnerability to the long-term effects of drug exploration
- 50% of all lifetime SUD's onset occurred prior to age 18 and 80% prior to age 24[10]
- Substance use initiation almost always occurs in adolescence[11]

"Addiction is a disease of adolescence."

—Nora Volkow, MD

Substance use screening: CRAFFT

- **C**: Have you ever ridden in a **CAR** driven by someone (including yourself) who was high or had been using alcohol or drugs?
- **R**: Do you ever use alcohol or drugs to **RELAX**, feel better about yourself or fit in?
- **A**: Do you ever use alcohol or drugs while you are by yourself? Or **ALONE**?
- **F**: Do you ever **FORGET** things you did while using alcohol or drugs?
- **F**: Do your **FAMILY** or **FRIENDS** ever tell you that you should cut down on your drinking or drug use?
- **T**: Have you ever gotten in **TROUBLE** while you were using alcohol or drugs?

Scoring: **Two** or more **YES** answers suggest a serious problem and need for further assessment

Youth Screening, Brief Intervention, and Referral to Treatment (YSBIRT)

- Evidence-based practice to prevent and reduce risky substance use among adolescents ages 12-18
- **Screening** to identify an adolescent's place on a spectrum from non-use to substance use
- **Brief intervention** to raise patient awareness of risks, elicit internal motivation for change, and help set behavior-change goals
- **Referral to treatment** to facilitate access to and engagement in specialized services and coordinated care for patients at highest risk

Screening to brief intervention (SB2I)[12]

In the past year, how many times have you used:	
• **Tobacco**? (Cigarettes, e-cigarettes, vapes) • **Alcohol**? • **Marijuana**? (Smoked, vaped, edibles)	❑ Never
STOP if all "Never." Otherwise CONTINUE	❑ Once or twice
• **Prescription drugs that were not prescribed for you**? (Adderall, pain medication) • **Illegal drugs**? (Cocaine, Ecstasy) • **Inhalants**? (Nitrous oxide) • **Herbs/synthetic drugs**? (Salvia, K2, bath salts)	❑ Monthly ❑ Weekly or more

Screening results inform brief intervention[12]

In the past year, how many times have you used: Tobacco? Alcohol? Marijuana?

Prevention Opportunity	Risk Level for Substance Use Disorder		
	Low Risk	Moderate Risk	High Risk
No use	Once or twice use	Monthly use	Weekly use or more
Anticipatory guidance: • Affirm health choices	Ask follow-up SB21 Questions: Prescription drugs? Illegal drugs? Inhalants? Herbs or synthetic drugs?		
	Brief intervention: • Provide cessation advice	Brief intervention: • Provide cessation advice • Reduce use and risky behavior	Brief intervention: • Provide cessation advice • Reduce use and risky behavior • Facilitate linkage to specialty treatment

Resources

- Parent-completed General Behavior Inventory (P-GBI)
- Parent-completed Child Mania Rating Scale (P-CMRS)
- Parent-completed Young Mania Rating Scale (P-YMRS)
- CRAFFT Questionnaire
- Youth Screening, Brief Intervention, and Referral to Treatment (YSBIRT)
- Seattle Children's First Approach Skills Training (FAST) program

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