Speaker Disclosures

I do not have any financial interest, arrangement or affiliation with medical/pharmaceutical or equipment companies.

I intend to reference off-label or investigational use of drugs or products in my presentation:

- Mirtazapine
- Citalopram
- Bupropion
- Duloxetine
Objectives

• *To be able to:* Identify the role of screening tools as part of a comprehensive assessment process for youth depression,

• *To be able to:* Discuss non-medication approaches to treatment for youth with depression

• *To be able to:* Describe first- and second-line medication treatment strategies for youth with depression
Statistics
• Adolescent depression affects 12-25% of adolescents
• Onset prior to age 12 linked to poor functioning, suicide attempts, more lifetime depression, psychiatric comorbidity.
• Generally associated with poor academic, social, and health outcomes; substance abuse, early pregnancy and parenthood, and increased healthcare costs
• Suicide is the 2nd-leading cause of death for our youth ages 10-24
• More teenagers and young adults die from suicide than from cancer, heart disease, AIDS, birth defects, stroke, pneumonia, influenza, and chronic lung disease, **COMBINED**
• Despite these statistics, 80% of adolescents do not receive appropriate treatment

Past Year Prevalence of Major Depressive Episode Among U.S. Adolescents (2016)

Data Courtesy of SAMHSA

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Race/Ethnicity</th>
</tr>
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<tbody>
<tr>
<td>Overall</td>
<td>12.8</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>19.4</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6.4</td>
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</tr>
<tr>
<td>13</td>
<td>9.4</td>
<td></td>
</tr>
<tr>
<td>14</td>
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<td>15</td>
<td>13.9</td>
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<td>Hispa...</td>
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<tr>
<td>White</td>
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<td>Black</td>
<td>9.1</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>11.9</td>
<td></td>
</tr>
<tr>
<td>Al/AN**</td>
<td>11.5</td>
<td></td>
</tr>
<tr>
<td>2 or ...</td>
<td>13.8</td>
<td></td>
</tr>
</tbody>
</table>
Past Year Prevalence of Major Depressive Episode Among U.S. Adolescents (2020)

Data Courtesy of SAMHSA

*Persons of Hispanic origin may be of any race; all other racial/ethnic groups are non-Hispanic. Note: Estimates for Native Hawaiian / Other Pacific Islander and American Indian / Alaskan Native groups are not reported in the above figure due to low precision of data collection in 2020.

https://www.nimh.nih.gov/health/statistics/major-depression#part_155721
WA Youth Survey 2021: Depression

Percent of students who report feeling so sad or hopeless almost every day for two weeks or more in a row that they stopped doing some usual activities in the past year.

- Source: 2021 Healthy Youth Survey
Depression
The problem of depression

- Only about 50% of adolescents with depression will be diagnosed prior to adulthood.
- Without screening, most depressed adolescents are not being identified in primary care.
- When depression is identified, only about 50% end up receiving appropriate care.
The natural history of depression

• **Prepubertal:**
  • depression more common in boys (1.6X more likely)

• **Puberty and beyond:**
  • 2:1 more likely in girls than boys

Systematic Review and Meta-Analysis: Adolescent Depression and Long-Term Psychosocial Outcomes.
Clayborne ZM, Varin M, Colman I
Why does depression present in adolescence?

• Hormonal changes of puberty
• Sleep disturbances
• Cognitive developmental changes
• Psychosocial pressures
  • identity, sexuality, school achievement issues
• Emotional and/or physical trauma
• Substance use/abuse
• Genetics
Manifestations of Depression in Adolescents (typical)

- Sadness and tearfulness
- Hopelessness
- Inability to concentrate
- Loss of energy
- Sleep and/or appetite changes
- Self-criticism and low self-esteem
- Suicidal thoughts

(These are also some of the diagnostic criteria)
Manifestations of Depression in Adolescents (more subtle)

- Withdrawal from family/social activities
- Irritability (fights, moodiness, etc.)
- School underachievement, failure, truancy
- Substance use and abuse (self-medication)
- Aches and pains, somatic symptoms
  - Increased # physician/ER visits
  - Increase in medical testing
Risk factors for depression

- Low birth weight
- Family history of depression and anxiety in first-degree relatives
- Family dysfunction or caregiver-child conflict
- Exposure to early adversity (e.g., abuse, neglect, or early loss)
- Psychosocial stressors (e.g., peer problems and victimization [bullying], and academic difficulties)
- LBGTQ youth, especially if youth is bullied, not supported
- Negative style of interpreting events and coping with stress
- History of anxiety disorders, SUD, LDs, ADHD
- Traumatic brain injury
- Chronic illness
Screening
Rating scales

• General Behavioral Health Screening
  • PSC-17 has an “Internalizing” subscale which can suggest a depressive disorder
  • SDQ “emotional problems” scale has 4 out of 5 items on anxiety, so less useful for depression
  • Much longer general screening scales like CBCL and BASC are not free, much more time consuming
Key principles of screening (in general)

- Communication with families regarding the “why” of screening is essential
- Screening has an important role in promotion and prevention, as well as for intervention
- Engage families with screening as conversation, and as partners in care.
- Engage the parent/caregiver as an expert on their child
- Utilize validated screening tools/questions
- Always have a conversation about results and incorporate primary care intervention
- Make effective referrals/linkages, prioritizing a warm handoff. (Note the need to implement outreach to build collaborative relationships with community partners before beginning screening)
- “Close the loop”
Rating scales

• Targeted Screen/Depression diagnostic aide
  • PHQ-9 or PHQ-9A for adolescents
  • SMFQ for kids over age 6
  • Others like CDI, Beck, CDRS-R available for a fee
    • These all can also track response to treatments
Recommendations for Screening

• AAP Bright Futures recommends annual depression screens for age 12 and up
  • Also, recommends maternal depression screens at 1, 2, 4 and 6 month well child visits

• US Preventive Services Task Force endorses depression screening in pediatric primary care for ages 12-18
  • Screening only if systems in place to ensure accurate diagnosis, therapy and follow-up

https://www.uspreventiveservicestaskforce.org/uspstf/draft-recommendation/screening-depression-suicide-risk-children-adolescents#:~:text=The%20USPSTF%20recommends%20screening%20for,ages%2012%20to%2018%20years.&text=The%20USPSTF%20concludes%20that%20the%20age%2011%20years%20or%20younger.

brightfutures.aap.org/Bright%20Futures%20Documents/MSRTable_AdolVisits_BF4.pdf
Screening for Depression and Suicide Risk in Children and Adolescents

The U.S. Preventive Services Task Force (USPSTF) concludes with moderate certainty that screening for MDD in asymptomatic adolescents ages 12 to 18 years has a moderate net benefit.

The USPSTF concludes that the evidence is insufficient on screening for MDD in asymptomatic children ages 11 years or younger. Evidence is lacking, and the balance of benefits and harms cannot be determined.

The USPSTF concludes that the evidence is insufficient on the benefit and harms of screening for suicide risk in asymptomatic children and adolescents due to a lack of evidence. As a result, the balance of benefits and harms cannot be determined.
Importance of Screening for Depression

• Depression may be unrecognized due to:
  • Stigma
  • Parent or patient denial of illness
  • Signs dismissed as “typical teenager” behavior
  • Focus on somatic symptoms may distract

• 2016 US adolescent MDD survey data (NSDUH)
  • 60% received no mental health treatment
  • 19% saw a health professional, used no medication
  • 21% saw a health professional, tried a medication

MDD= Major Depressive Disorder
https://www.nimh.nih.gov/health/statistics/major-depression#part_155721
Screening Questionnaires

• Pros:
  • Increased identification possible
  • Universal screening possible
  • Time efficient (can complete in waiting room)
  • Providers do not have to remember initiate the conversation
  • Can increase adolescent disclosure of symptoms
Screening Questionnaires

• **Cons:**
  • Can be time consuming to screen all teens
  • Negative impacts on practice flow
  • Research is less clear on when, where, and with what frequency to screen
  • Many instruments available – how to choose?
  • False-positives and false-negatives
  • Improved outcomes depends on proper follow-up of positive screens
Pediatric Symptom Checklist-17 (PSC-17)

<table>
<thead>
<tr>
<th>Internalizing</th>
<th>Depression</th>
<th>Anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>ODD</td>
<td>Conduct</td>
</tr>
</tbody>
</table>

35 item version also available

Age 8 and up

No fee for use


Formatting by seattlechildrens.org/PAL
SMFQ

- Age 6 and up
- No fee for use

By Angold and Costello, 1987

Free download at https://devepi.duhs.duke.edu/measures/the-mood-and-feelings-questionnaire-mfq/
Patient Health Questionnaire (PHQ-9)

NAME: _______________________________ DATE: _______________________________

Over the last 2 weeks, how often have you been bothered by any of the following problems? (use ‘✓’ to indicate your answer).

<table>
<thead>
<tr>
<th>Problem</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead, or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Add columns: [ ] [ ] [ ] [ ]

(Total: [ ] [ ] [ ] [ ] [ ])

PHQ-9

- Age 13 and up
- No fee for use
- PHQ-A is nearly identical, slight wording modifications, both supported for adolescents

Spitzer R et al 1999, Johnson JG et al 2002
Using Rating Scales

• Only as good as their information input
  • Patients may have a “positive ROS” vs. or may falsely deny having any symptoms

• Imperfect sensitivity/specificity numbers
  • PSC-17 (Internalizing) and major depression
    • 73% sensitivity, 74% specificity
  • SMFQ score and major depression
    • 60% sensitivity, 85% specificity
  • PHQ-9 and major depression (adolescent)
    • 73% sensitive, 94% specificity
Tips for Overcoming Screening Barriers

• Address where this fits in the office flow
  • Adolescent well child packet for waiting room…
• Develop an office procedure for responding to a child in crisis
  • Know mental health resources in community
  • Know your County crisis line number
• Practice asking questions in a manner which projects your wanting to know…
  • “Have you been feeling down or low recently?”
  • Not “You don’t feel depressed, do you?”
After Screening, Assess

• Review confidentiality and its limits
• Talk to teen alone and follow up on positive screening answers
  • Project interest in them, how they are doing
• Offer support and validation
  • “sounds like things are very hard for you right now”
• May diagnose Major Depression after a “SIGECAPS” neuro-vegetative symptom review (next slide)
Depression Symptom Mnemonic

- Major Depression per the DSM-5
- 2 weeks of depressed mood plus 4 of the following changes (5 if mood is just irritable):
  - Sleep
  - Interest
  - Guilt
  - Energy
  - Concentration
  - Appetite
  - Psychomotor
  - Suicidality
Medical and Other Potential Mimics or Contributors to Depression

• Consider possible medical causes:
  • Conditions
    • Thyroid and parathyroid disease
    • Anemia and iron deficiency
    • Malnutrition
    • Chronic pain
    • Any chronic/relapsing condition
  • Medication side effects
    • Steroids
    • Interferon
Medical and Other Potential Mimics or Contributors to Depression

• Housing or food insecurity (income, housing, legal status, personal safety/family stability)
• Consider alternative psychosocial issues
  • Trauma/abuse
  • Undiagnosed or under-treated cognitive problems
    • Especially learning or language disabilities that limit school or occupational achievement
Clinical judgement trumps all

- You may judge child has “Unspecified Depression” per DSM-5, even if not all specific criteria are met
  - Depressive symptoms with decreased functioning
  - Enough basis to initiate referrals for therapy
Asking About Suicidality

• Part of every depression evaluation
• Start broad
  • “Ever wish that you weren’t around?”
  • “Ever thought about killing yourself?”
• If positive, get specific
  • “In the past month, have you thought about killing yourself?”
  • “Have you made any plans for how you would kill yourself? What would you do?”
**Suicide Risk Screening Tool**

**Ask the patient:**

1. In the past few weeks, have you wished you were dead?
   - Yes
   - No

2. In the past few weeks, have you felt that you or your family would be better off if you were dead?
   - Yes
   - No

3. In the past week, have you been having thoughts about killing yourself?
   - Yes
   - No

4. Have you ever tried to kill yourself?
   - Yes
   - No
   If yes, how?
   
   
   When?

   
   If the patient answers Yes to any of the above, ask the following acuity question:

5. Are you having thoughts of killing yourself right now?
   - Yes
   - No

**Next steps:**

- If patient answers “No” to all questions 1 through 4, screening is complete (not necessary to ask question #5). No intervention is necessary (*Note: Clinical judgment can always override a negative screen*).
- If patient answers “Yes” to any of questions 1 through 4, or refuses to answer, they are considered a positive screen. Ask question #5 to assess acuity:
  - **“Yes”** to question #5 = acute positive screen (imminent risk identified)
    - Patient requires a STAT safety/full mental health evaluation.
    - Patient cannot leave until evaluated for safety.
    - Keep patient in sight. Remove all dangerous objects from room. Alert physician or clinician responsible for patient’s care.
  - **“No”** to question #5 = non-acute positive screen (potential risk identified)
    - Patient requires a brief suicide safety assessment to determine if a full mental health evaluation is needed. Patient cannot leave until evaluated for safety.
    - Alert physician or clinician responsible for patient’s care.

**Provide resources to all patients**

- 24/7 National Suicide Prevention Lifeline: 1-800-273-TALK (8255) En Español: 1-888-626-9454
- 24/7 Crisis Text Line: Text “HOME” to 741-741

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**Seattle Children’s**

**asQ Suicide Risk Screening Toolkit**

**NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)**

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**NIMH TOOLKIT**
Why Ask? Because Suicidality in Young People is Common

US High school students’ self report (2019), regarding the past 12 months:

18.8% seriously considered suicide
15.7% made a suicide plan
8.9% attempted suicide
2.5% needed treatment following attempt

CDC. Youth Risk Behavior Surveillance — 2019
For Washington State, teen suicide increased 38% from 11.4 to 15.7 deaths per 100,000 adolescents ages 15-19 between 2012-2014 and 2017-2019.

Among the total U.S. student population, the percentage of students who had attempted suicide ≥1 time during the 12 months before the survey experienced a significant linear increase from 6.3% during 2009 to 8.9% during 2019.
Suicide Risk Factors

- Past suicide attempts (greatest risk factor)
- Mental health or substance use disorder
- Recurrent self harm
- Family history of suicidal behavior
- Exposure to real or fictional accounts of suicide
- Parental mental health problems or substance abuse
- Gay or bisexual orientation
- History of child abuse
- Chronic medical illnesses (e.g., diabetes, epilepsy)
- Victim of bullying (e.g., cyberbullying)
Suicide Assessment Acronym: “Is Path Warm”

- Ideation
- Substance abuse
- Purposelessness
- Anxiety
- Trapped
- Hopelessness
- Withdrawal
- Anger
- Recklessness
- Mood changes
WA Youth Survey 2021: Contemplation of Suicide

Percent of students who report having seriously considered suicide in the past year

<table>
<thead>
<tr>
<th>Grade 6</th>
<th>Grade 8</th>
<th>Grade 10</th>
<th>Grade 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question not asked of this grade</td>
<td>19%</td>
<td>20%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Statewide
- Source: 2021 Healthy Youth Survey
FIGURE 2. Percentage of high school students who attempted suicide during the 12 months before the survey, by race/ethnicity — Youth Risk Behavior Survey, United States, 2009–2019
Caregiver acceptance and support of gender identity is essential to promote wellness and safety.
Why would kids self injure?

- Affect Regulation
  - Temp. distract from an intolerable mood state
- Self Punishment
- Interpersonal Influences
  - Friend does this, wanted to try too
- Anti-dissociation
  - An attempt to ground back in reality
- Anti-suicide
  - Self reports of it replacing a suicide attempt
Treatment
What you can do for depression

(before considering medications)
PAL Care Guide
summary approach to depression care
(seattlechildrens.org/PAL)
Patient and Family Engagement and psychoeducation

- Seek to align and engage patient and family members
- Help reduce stigma, possibly by comparing to other common and recurrent pediatric illnesses, such as asthma
- GLAD-PC recommends providing care in the pediatric clinic enlisting the help of mental health consultants and on-site behavioral therapy, which may serve to reduce stigma
- Educate about the typical symptoms, clinical course, and prognosis, especially the importance of adherence and avoiding premature termination, which can lead to recurrence
- Promote basics of good mood hygiene—keeping regular daily schedules, including sleep; moderate levels of exercise/activity; continuing to engage in pleasurable activities even if not motivated (opposite action)
Things You Can Do for Depression

• Schedule frequent follow up visits
  • Healthcare provider engagement alone has been shown to reduce suicidality
  • Says in essence “I care” and want to see you again

• Recommend and coach on:
  • behavioral activation, exercise
  • increased peer interactions
  • good sleep hygiene
  • reducing stressors, if possible
  • support groups, if they are available
More of What You Can Do

• New 988 nationwide mental health crisis/suicide prevention number rolling out July 2022
• Give them a crisis plan or phone number
  • County Crisis Line Phone Numbers: www.hca.wa.gov/health-care-services-and-supports/behavioral-health-recovery/mental-health-crisis-lines
  • Text HOME to 741741 or visit: https://www.crisistextline.org
  • Teen Link Hotline: 1-866-833-6546 or https://www.teenlink.org/
  • The National Suicide Hotline: 1-800-273-8255
• Provide psychoeducation about depression, and say that it does get better
• Talk about restricting access to lethal means
  • Guns and suffocation account for the vast majority of completed suicides
Review Basic Home Safety Recommendations

- Follow regular routines
- Parents pick your battles, stay low-key
- Provide appropriate supervision
  - (not left home alone for hours)
- For active suicidality restrict access to:
  - Knives and razors
  - Firearms
  - Materials that can be used for strangulation
  - Medications, including OTC, of all family members
Provide an Information Handout

Family Support Action Plan

What a Parent Can Do to Help Their Child/Adolescent

Family Support is a vital component in your child/adolescent’s recovery from depression. It makes you a more engaged participant in your child’s healthcare and helps rebuild your child/adolescent’s confidence and sense of accomplishment. However, it can also be extremely difficult after all, when your child/adolescent is depressed, she probably doesn’t feel like accomplishing anything at all.

To help with Family Support, set goals to help you focus on your child/adolescent’s recovery and recognize your child/adolescent’s progress. Find things that have helped your child/adolescent in the past—identify goals that are simple and realistic and match your child/adolescent’s natural “style” and personality. Work on only one goal at a time.

Adherence to Treatment Plan. Following through on health advice can be difficult when your child/adolescent is down. Your child/adolescent’s success will depend on the severity of his/her symptoms, the presence of other health conditions, and your child/adolescent’s comfort level in accepting your support. However, your child/adolescent’s choices for recovery are excellent if you understand how you and your family naturally prefer to deal with your child/adolescent’s health problems. Knowing what barriers are present will help you develop realistic health goals for your child/adolescent. Example goals reminder to give your child/adolescent his/her medications, participate in counseling, help your child/adolescent keep appointments.

MY GOAL: _____________________________

Relationships. It may be tempting for your child/adolescent to avoid contact with people when s/he is depressed, or to “shut out” concerned family and friends. Yet, fulfilling relationships will be a significant part of your child/adolescent’s recovery and long-term mental health. Understanding your child/adolescent’s natural relational style for asking for and accepting help should guide the design of your Family Support plan. Example goals: Encourage your child/adolescent to talk with a friend every day. Attend scheduled social functions. Schedule time to talk and “just be” with your child/adolescent.

MY GOAL: _____________________________

Nutrition and Exercise. Often, people who are depressed don’t eat a balanced diet or get enough physical exercise—which can make them feel worse. Help your child/adolescent set goals to ensure good nutrition and regular exercise. Example goals: Encourage your child/adolescent to drink plenty of water, eat fruits and vegetables. Avoid alcohol. Take a walk once a day. Do for a bike ride.

MY GOAL: _____________________________

Spirituality and Pleasurable activities. If spirituality has been an important part of your child/adolescent’s life in the past, you should help to include it in your child/adolescent’s current routine as well. Also, even though s/he may not feel as motivated, or get the same amount of pleasure as s/he used to, help her/him connect to a fun activity each day. Example goals: Recall a happy event. Go to a hobby. Listen to music. Attend community or cultural events. Meditate. Worship. Do fun family activities. Take your child/adolescent to a fun place s/he wants to go.

MY GOAL: _____________________________

(Adapted with permission from Entermission Healthcare)

Depression Resources

Information for Families

Books families may find helpful:

The Childhood Depression Sourcebook (1998), by Jeffrey Hiler
The Depressed Child: Overcoming Teen Depression (2005), by Marian Kaufman
The Explosive Child (2008), by Ross W. Greene

Books children may find helpful:

Taking Depression to School (2005), by Kathy Mahlab (for young children)
When Your Child’s Moods Are Out of Control (2007), by Carol Mahlab (for young children)
Feeling Good: The Mood Therapy Manual, by Barbara King (for adolescents)
My Feeling Better Workbook: Help for Kids Who Are Sad and Depressed (2004), by Tara Nana (for elementary school students)


Crisis Hotlines:

National Suicide Prevention Lifeline
1-800-273-TALK (1-800-273-8255)
www.suicidepreventionlifeline.org

Seniors’ Depression Hotline
1-800-273-TALK (1-800-273-8255)
www.suicidepreventionlifeline.org

Website links may find helpful:

Guides to depression medications from AIA and AACAP professional societies
www.aamhp.org

National Institute of Mental Health
www.nimh.nih.gov/health/topics/depression/index.shtml

National Alliance for Mental Illness
www.namh.org/

American Foundation for Suicide Prevention
www.aftsp.org

American Academy of Child and Adolescent Psychiatry
www.aacap.org/CE/Clinical_and_Support/Resources/Depression_Resource_Center/data.aspx

This resource page is now available in Spanish at www.seattlechildrens.org/PAL

Seattle Children’s®

Glad-PC

seattlechildrens.org/PAL
Initial treatment of depression

Mild/uncomplicated/brief
- Psychoeducation
- Supportive management - active listening and reflection, restoration of hope, problem solving, coping skills, and strategies for maintaining participation in treatment
- Case management – environmental stressors in family and school

Moderate
- CBT or Interpersonal Psychotherapy (IPT)
- Consider SSRI – not responding, not ready for therapy

Severe/suicidal ideation
- CBT (or IPT) and SSRI
Engaging Patients with Therapy

• WA State Mental Health Referral Service for Children & Teens: 833-303-5437
  • Age ≤17
• As few as 50% will attend a single appointment after your referral
• Find what motivates patient/family
  • Link pursuit of therapy as the best means to achieve that end
  • Not because you say so, but because they want help for what motivates them
• Address family member ambivalence
• Seek care by insurer-covered providers
Behavioral Activation

- Easily described, less easily enacted
- Patient identifies their own positively rewarding activities
  - Not a “should” do activity, but a “want to” do activity
- Select specific things, rather than vague activities like “get organized” or “get in shape”
- Come up with a variety of activities, list them out, rank in order of easier to harder
- Get support of others (parents) in pursuing
  - Motivation and avoidance are major hurdles
  - Rewards for progress
Other therapies

• Supportive counseling
  • Addressing current stressors
    • often done, less evidence supported than CBT/IPT

• Psychodynamic therapy
  • Freudian style, for longer-term treatment

• Any therapy can be effective when there is a good treatment alliance with the therapist
Need help finding therapy or resources for your patient?

• **Call the PAL Social Worker**
  • Can consult on patients up to age 19
  • **866-599-7257**
Medication
Medicating Major Depression—general tips

- Start low, go slow
- Change one medicine at a time
- Use the full dose range, wait 3-4 weeks before each increase
- Ask about previous antidepressant trials in family members
- Get baseline inventory of potential pre-medications somatic issues (e.g., frequency of headaches, sleep issues, etc.)
- Discuss potential SE with caregivers and (when appropriate) with the patient
- Discuss importance of compliance
### Evidence-Supported SSRIs for Adolescent Depression

<table>
<thead>
<tr>
<th>Medication</th>
<th>Usual Adolescent Starting Dose</th>
<th>Increase Increment (after 4-6 weeks)</th>
<th>Max Dosage</th>
<th>Youth RCT benefits</th>
<th>Youth FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>10mg/day</td>
<td>10-20mg</td>
<td>60mg</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Citalopram* (Celexa)</td>
<td>10mg/day</td>
<td>10-20mg</td>
<td>40mg</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>5mg/day</td>
<td>5-10mg</td>
<td>20mg</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sertraline* (Zoloft)</td>
<td>25mg/day</td>
<td>25-50mg</td>
<td>200mg</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

*Not FDA approved for depression

RCT=randomized controlled trial

Which SSRI to start with?

• Fluoxetine – multiple positive RCTs, FDA approved ages 8 and up
  • Very little SI signal in controlled studies
  • Long half-life means no withdrawal symptoms from missed doses
  • Covered by all plans, and available generic
  • Available in once-a-week dosing:
    • Start patient on short acting fluoxetine and stabilize at 20 mg dose
    • Then stop fluoxetine 20 mg/day and start fluoxetine 90 mg/week capsule 7 days after last 20 mg dose
  • Caution: Medication interactions
August 2016 Lancet article by Cipriani et al. “Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: a network meta-analysis”.

- Meta-analysis of 34 RCT’s for the acute treatment of MDD, included 5260 patients
- For SSRI monotherapy for depression in adolescents, fluoxetine is the only antidepressant with statistically significant change from placebo
- Take home: Fluoxetine should be first-line treatment if choosing an SSRI for a depressed youth with moderate-to-severe depression without access to psychotherapy or who is not responding to therapy alone
The Treatment of Adolescents with Depression Study (TADS)

• Design

• 439 12-17 y.o. with moderate to severe depression
  • ~30% with suicidality; more than half had comorbid psychiatric illness

• Fluoxetine, CBT, combo, or placebo

• 12 weeks blinded; 24 weeks un-blinded conducted in community and academic centers

1. TADs Study Team. JAMA 2004;292(7), 807
2. March et al. Arch Gen Psych 2007; 64(10):1132
• Starting dose fluoxetine 10mg
• Week two, increased to 20mg (if no side effects)
• Dose could be increased at weeks 4, 6, 9 and 12 if still significant symptoms
• Mean final dose was ~30mg/day

TADS Medication Protocol

TADS, J Am Acad Child Psychiatry, 2005
TADS Results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Response Rate (CGI ≤2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine plus CBT</td>
<td>73%</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>62%</td>
</tr>
<tr>
<td>CBT</td>
<td>48%</td>
</tr>
<tr>
<td>Placebo</td>
<td>35%</td>
</tr>
</tbody>
</table>

- Suicidal “events” decreased with all active treatments
- At 36-week follow up more common with fluoxetine alone (14%) than Combination (8%), or CBT (6%)
At one year follow-up benefits persisted

TADS TEAM

**FIGURE 1. Depression Scores From Baseline to End of Naturalistic Follow-Up for 327 Adolescents With Major Depressive Disorder Treated With Fluoxetine, Cognitive-Behavioral Therapy (CBT), or a Combination**

*Derived from the random coefficients regression model with adjustments for fixed and random effects.*
• Treatment of depression with fluoxetine alone or in combo with CBT accelerates response
• Adding CBT to meds enhances the safety of meds
• Therefore, combined treatment superior to monotherapy
Predictors of poor response to SSRIs with/without CBT

- Hopelessness
- Family conflict
- History of abuse
- Depression severity and chronicity
- Non-suicidal self injury (NSSI)

- Suicidal ideation
- Functional impairment
- Comorbidity (TADS)
- Older age and lower family income (TADS)
Treatment of Resistant Depression in Adolescents (TORDIA)

• Design

• 334 12-18 y.o. with MDD that had not responded to 2 mo on SSRI

• Switch to: (1) 2nd SSRI, (2) 2nd SSRI and CBT, (3) venlafaxine, (4) venlafaxine and CBT

• 12 weeks blind, 12 more open

1. Brent et al. JAMA 2008;299(8):901
Treatment of Resistant Depression in Adolescents (TORDIA)

• Results

• Rates of response (12 weeks):
  • CBT plus either med 54.8%>med alone 40.5%
  • No difference in response between 2nd SSRI and venlafaxine

1. Brent et al. JAMA 2008;299(8):901
Treatment of Resistant Depression in Adolescents (TORDIA)

• Adverse Effects
  • No differential treatment effects on SI
  • More AEs with venlafaxine
    • increase diastolic BP and pulse
    • skin problems
    • associated with a higher rate of self-harm adverse events in those with higher SI

1. Brent et al. JAMA 2008;299(8):901
TORDIA - Conclusions

• For adolescents with depression not responding to first SSRI:
  • Continued treatment results in remission in approximately 1/3 of patients
  • Eventual remission is evident within the first 6 weeks in many
    • Earlier intervention may be important
  • Switch to 2nd SSRI just as efficacious as a switch to venlafaxine
    • SSRI had fewer adverse effects
  • Combo of CBT + new med > new med alone
What Other Meds Can Be Tried?

• If first SSRI fails, a second SSRI will work approximately 1/3 of the time
  • Choose 2nd agent from the prior list (fluoxetine, sertraline, citalopram/escitalopram)

• How to switch?
  • If a major side effect—stop, wait till resolves, then start new med
    • The “side effect” may not be medication related
  • Consider a ~1-month cross taper (low dose of new med, at same time as starting lowered dose of old med)
  • If was on fluoxetine, long half life means it auto-tapers after stopping over 2 weeks.
Switching discussion (continued)

• Cross taper vs. switch over
• Potential concerns:
  • Discontinuation syndrome
  • Relapse of partially treated symptoms
  • Side effects to new medication
  • Medication interactions
    • Serotonin syndrome
    • P450 2D6
      • fluoxetine and paroxetine strongly inhibit it, most commonly used antidepressants are substrates
• Time to get to therapeutic dose of new med
• Complexity of instructions
After two SSRIs don’t work - depression

• Venlafaxine*
  • Combo of 2 RCTs (2ndary analysis) showed positive effect for adolescents
• Cymbalta*
  • 1 open label safety study
• Bupropion*
  • Open label positive studies in adolescents

*Not FDA approved for depression treatment <18

SNRIs

- Venlafaxine (Effexor®)*
  - SNRI side effects, withdrawal symptoms worse than SSRIs
  - Does have some research support for adolescent depression
  - I’d only recommend if an older adolescent with SSRI failure

- Duloxetine (Cymbalta®)*
  - SNRI like venlafaxine, but tends to be better tolerated
  - FDA indicated for GAD, but no data on youth depression
After two SSRIs don’t work (continued)

- **Tricyclic antidepressants***
  - Serious side effects, fatal in overdose
  - Meta-analysis – not superior over placebo in kids, therefore, **NOT** recommended

- **Trazodone (Desyrel®)***
  - Occasionally useful as sleep aide, usually up to 100 mg (interacts with fluoxetine through hepatic metabolism pathways, so caution advised)
  - Full adult antidepressant doses are typically not tolerated

*Not FDA approved for depression treatment <18

Other meds for depression (continued)

- After two SSRI failures, there are other options:
  - **Bupropion (Wellbutrin®)**
    - More agitation side effects
    - A reasonable third choice if two SSRIs failed, or an older adolescent or young adult
    - Reasonable if adolescent has ADHD too
  - **Mirtazapine (Remeron®)**
    - Sedating, increases appetite
    - Open label positive study in adolescents; older adolescents may respond like adults do for depression
    - Two negative child RCT’s

*Not FDA approved for depression treatment <18*
<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>Equivalent Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>20 mg</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>20 mg</td>
</tr>
<tr>
<td>Sertraline</td>
<td>50-75 mg</td>
</tr>
<tr>
<td>Citalopram</td>
<td>20 mg</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>10 mg</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>100 mg</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>75 mg</td>
</tr>
</tbody>
</table>
But Aren’t SSRI’s Dangerous for Kids?

- FDA Black Box in 2004, based on 24 studies of both depression and anxiety
- For all diagnoses SSRI suicidality relative risk was 2.0 (95%CI=1.28-2.98) on medication versus placebo
Discussing the black box warning

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of PROZAC or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. PROZAC is approved for use in pediatric patients with MDD and Obsessive Compulsive Disorder (OCD).
### Other common SSRI side effects

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal distress</td>
<td>Typically self-resolves</td>
</tr>
<tr>
<td></td>
<td>Symptomatic care</td>
</tr>
<tr>
<td>Headache</td>
<td>Typically self-resolves</td>
</tr>
<tr>
<td></td>
<td>Symptomatic care</td>
</tr>
<tr>
<td>Appetite change</td>
<td>Counsel on healthy nutrition</td>
</tr>
<tr>
<td>Sedation</td>
<td>Administration at bedtime</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>Administration in morning</td>
</tr>
<tr>
<td></td>
<td>Counsel on sleep hygiene</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>No action if mild</td>
</tr>
<tr>
<td>Sexual side effects</td>
<td>Consider medication change</td>
</tr>
<tr>
<td>Activation (disinhibition, agitation, irritability, silly)</td>
<td>If persistent and significant, discontinue medication</td>
</tr>
<tr>
<td>Platelet dysfunction (rare)</td>
<td>Discontinue medication</td>
</tr>
</tbody>
</table>

If any symptoms are severe, prescriber may decrease medication dose or switch to another.
How I Make Sense of SSRI Suicidality

• Agitation/anxiety/activation is a potential SSRI side effect
  • Fairly common; typically happens early on
  • If it makes a depressed or anxious person even more anxious or irritable via uncomfortable sensations/feelings, it is logical to have “I can’t take this” thoughts

• SSRI-induced suicidal thoughts CAN happen, but they usually don’t
  • Recommend an early check in with patient about 1-2 weeks after starting medicine
    • Ask about activation, irritability, agitation, anxiety, restlessness, suicidality
Population Data Finds That SSRIs Are Suicide Preventative

• In the U.S: for every 1% increase in adolescent use of antidepressants, this correlates with a decrease of 0.23 suicides per 100,000

• 2 years after the black box warning:
  • Antidepressant use decreased 31%
  • Intentional drug poisonings increased 21%

Olfson, M et al, Relationship between antidepressant medication treatment and suicide in adolescents, 2003
Gibbons RD et al, Early evidence on the effects of regulators’ suicidality warnings on SSRI prescriptions and suicide in children and adolescents, 2007
Lu CY et al, Changes in antidepressant use by young people and suicidal behavior after FDA warnings and media coverage, 2014
SSRI Risks vs. Benefits

### TABLE 8

SSRI Benefit to Suicidal Risk Comparison

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number Needed to Treat</th>
<th>Number Needed to Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>10²</td>
<td>112</td>
</tr>
<tr>
<td>OCD</td>
<td>6</td>
<td>200</td>
</tr>
<tr>
<td>Non-OCD anxiety</td>
<td>3</td>
<td>143</td>
</tr>
</tbody>
</table>

- Data from ref 60. OCD, obsessive-compulsive disorder.
- $^{2}$ High number needed to treat likely secondary to high placebo response rate in pediatric depression studies (30% to 60% compared with 40% to 70% SSRI response rate). SSRI efficacy has been established, but pooled studies and this high number needed to treat underscore the importance of individualizing treatment.

Final consideration for benefits and risks for medication treatment for depression

• When considering the use of antidepressants in children and adolescents, the risk of antidepressant-related suicidality must be weighed against the benefits of treatment and the long-term risk of suicide in untreated depression.

• When considering this balance, the consensus among most mental health specialists is that the benefits of antidepressant therapy outweigh the risks. The ratio of response to suicidal events is approximately 11:1, and for remission to suicidal events is 4.5:1.
Where I see the role of SSRI in Child Depression

• Start with talk therapy alone if depression is not severe
• If mild depression not significantly better within 1-2 months, consider a medication trial
• If a moderate to severe depression, consider starting SSRI simultaneous with talk therapy
  • Explicit goal is to get better more quickly
Once things stabilize...

• Treatment should be continued for 6 to 12 months during the continuation phase
  • Patients typically should be seen at least monthly (or if doing well, every 3 months), depending on clinical status, functioning, support systems, environmental stressors, motivation for treatment, and the presence of comorbid psychiatric or medical disorders.

• General rule of thumb: the longer it takes to recover or the higher the # of recurrences, the longer the period of maintenance.
  • ≥ 2 episodes of depression, 1 severe episode, or chronic episodes should have maintenance treatment for > 1 yr.
Don’t know where to start?

• Call PAL to connect to a Psychiatrist
  • Can consult on patients up to age 19
  • 866-599-7257
Questions?
Other free resources, rating scales, parent handouts available at:

- http://www.seattlechildrens.org/PAL
Hope. Care. Cure.