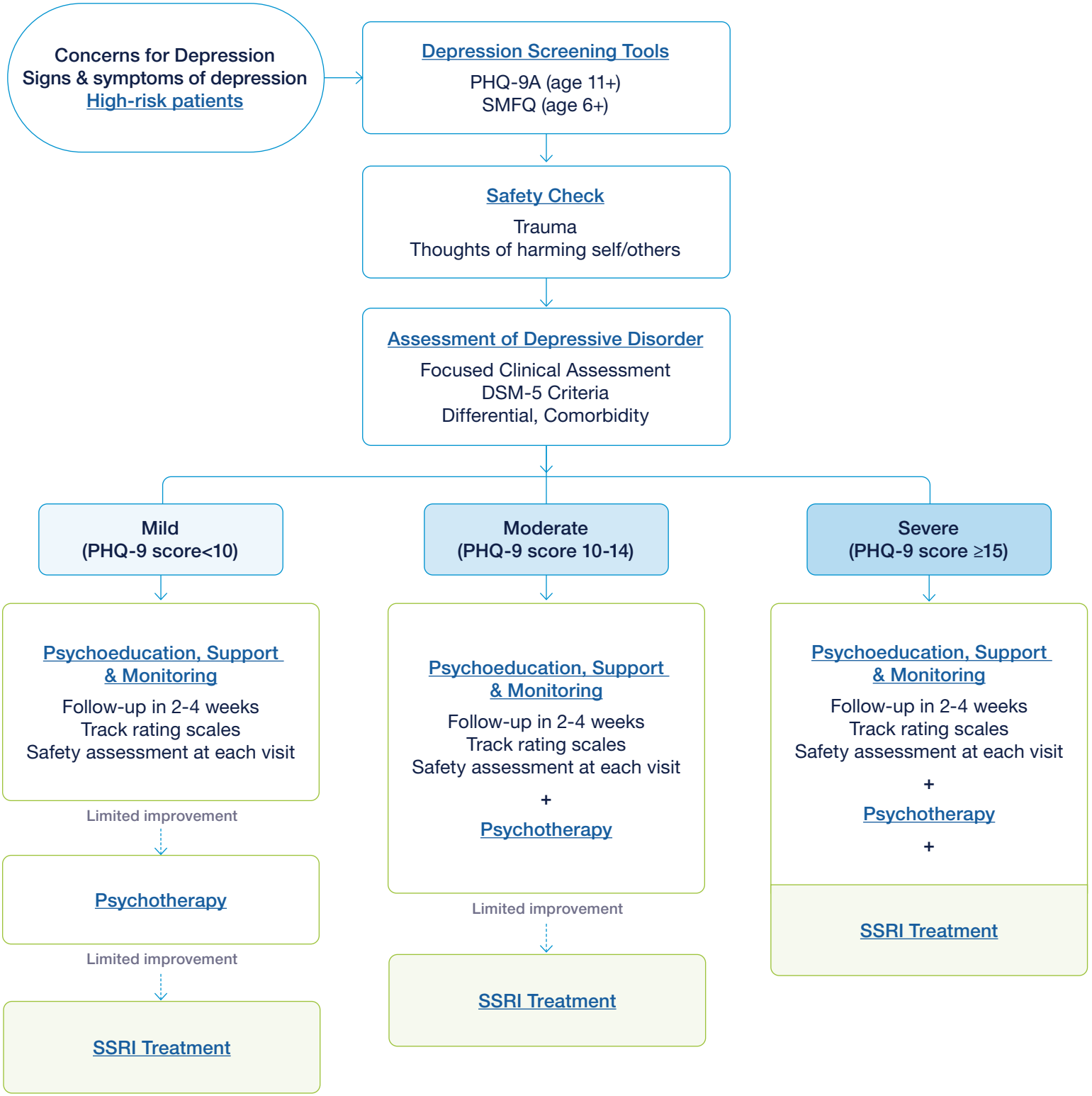
Clinical Work Pathway
Depression

UCSF Benioff Children's Hospitals | Child & Adolescent Psychiatry Portal



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Concerns for Depression

Common Signs and Symptoms of Depression in the pediatric population by age

Children	Adolescent
• Irritability • Somatic complaints • Boredom • Separation anxiety • Behavioral problems • Hallucinations	• Irritability • Behavioral problems • Sadness, change in mood • Atypical depression (increased sleep/appetite, mood reactive to positive response) • Suicidal ideation, attempts • Boredom • Premenstrual dysphoria

High risk patients should be identified and monitored closely

- Previous depressive episode
- Family history of mental health disorder
- Comorbid psychiatric diagnosis
- Substance use
- Trauma
- Psychosocial adversity
- Foster care, adoption
- Frequent somatic complaints

All youth age ≥12 should be routinely screened for depression at annual well child visits

Depression Screening Tools

Provider Resources-depression screening tool

- PHQ-9A
- SMFQ

Our rating scales they are displayed here:
https://capp.ucsf.edu/content/depression

Safety Check

Link to Safety evaluation algorithm

Assessment of Depressive disorder

Focused Clinical assessment (Clinical Pearls for History Taking)

Collateral history	• Gather collateral from family, teachers, school staff, other care takers, or after-school program • History may be obtained through rating scales, phone-calls, correspondence
Assess for functioning in multiple domains	• Family relationships • Peer relationships • School/Academic functioning; screen for learning disorders
Assess for acute stressors	• Acute stressors: stressors in family life, peer/social relationships, school/academic stressors etc
Assess for Trauma history, chronic stress	• Neglect, physical, sexual or emotional abuse • Screen for ACES
Longitudinal clinical hx of symptoms	• Onset of symptom presentation, developmental course • Behavioral concerns in earlier childhood years • Screen for developmental concerns (i.e. Developmental delay, Autism Spectrum Disorder)
Differential diagnosis and Comorbidities	• Children: Anxiety, Disruptive behavior disorders, ADHD • Teens: ADHD, Oppositional Defiant Disorder (ODD), Substance use • Physical disorders: Hypothyroidism, Mononucleosis, Anemia, certain cancers, Autoimmune disease, Premenstrual dysphoric disorder (PMDD), Chronic fatigue syndrome • Stressors: Bereavement, adjustment to stressors • Iatrogenic causes: stimulants, corticosteroids, contraceptives • May use general screeners: PSC-17 to assess for behavioral concerns- internalizing vs externalizing vs attention problems **and/or** • Symptom targeted screeners for Anxiety (SCARED, GAD-7), Substance use (CRAFFT)

DSM-5 Diagnostic Criteria

Presence of (1) depressed mood or (2) loss of interest or pleasure?
Presence 5 or more of the following symptoms during the same 2-week period?
Function impaired?

Depressed mood (e.g., feels sad, empty, hopeless) or observation by others (e.g., appears tearful) **In children and adolescents, can be irritable mood

Sleep changes: increase during day or decreased sleep at night

Interest (loss): of interest in activities that used to interest them

Guilt (worthless): depressed elderly tend to devalue themselves

Energy (lack): common presenting symptom (fatigue)

Concentration: reduced cognition &/or difficulty focusing

Appetite (wt. loss); usually declined, occasionally increased

Psychomotor: agitation (restlessness) or retardations (lethargic)

Suicidal ideation, plans or attempts

Psychoeducation, Support & Monitorings

Psychoeducational interventions

- Sleep hygiene
- Regular exercise
- Optimize self-care
- Journal positive events, mood changes
- Encourage behavioral activation

Monitoring symptoms

- Follow-up depressive symptoms in 2-4 weeks
- Track rating scales (PHQ-9A, SMFQ)
- Safety assessment at subsequent visits

Psychotherapy

Cognitive Behavioral Therapy (CBT)

CBT is a type of time-limited therapy based on the concept that thoughts, behaviors, and feelings all affect each other and that by changing our thoughts and behaviors, we can change how we feel. It is often the first choice for children and teens with depression, which ranges from 6-20 sessions. It is the psychotherapy with the most evidence for treatment of childhood anxiety disorders. It consists of five main parts:

1. Psychoeducation of kid and parents about anxiety disorders and CBT
2. Somatic management skills training
3. Cognitive restructuring
4. Exposures
5. Relapse prevention plans

Interpersonal psychotherapy (IPT) is a time-limited (12–16 sessions) individual psychotherapy for adolescents ages 12-18 with depression. It aims to identify life events that lead to depression and equips teens with interpersonal skills to interact with challenging situations positively.

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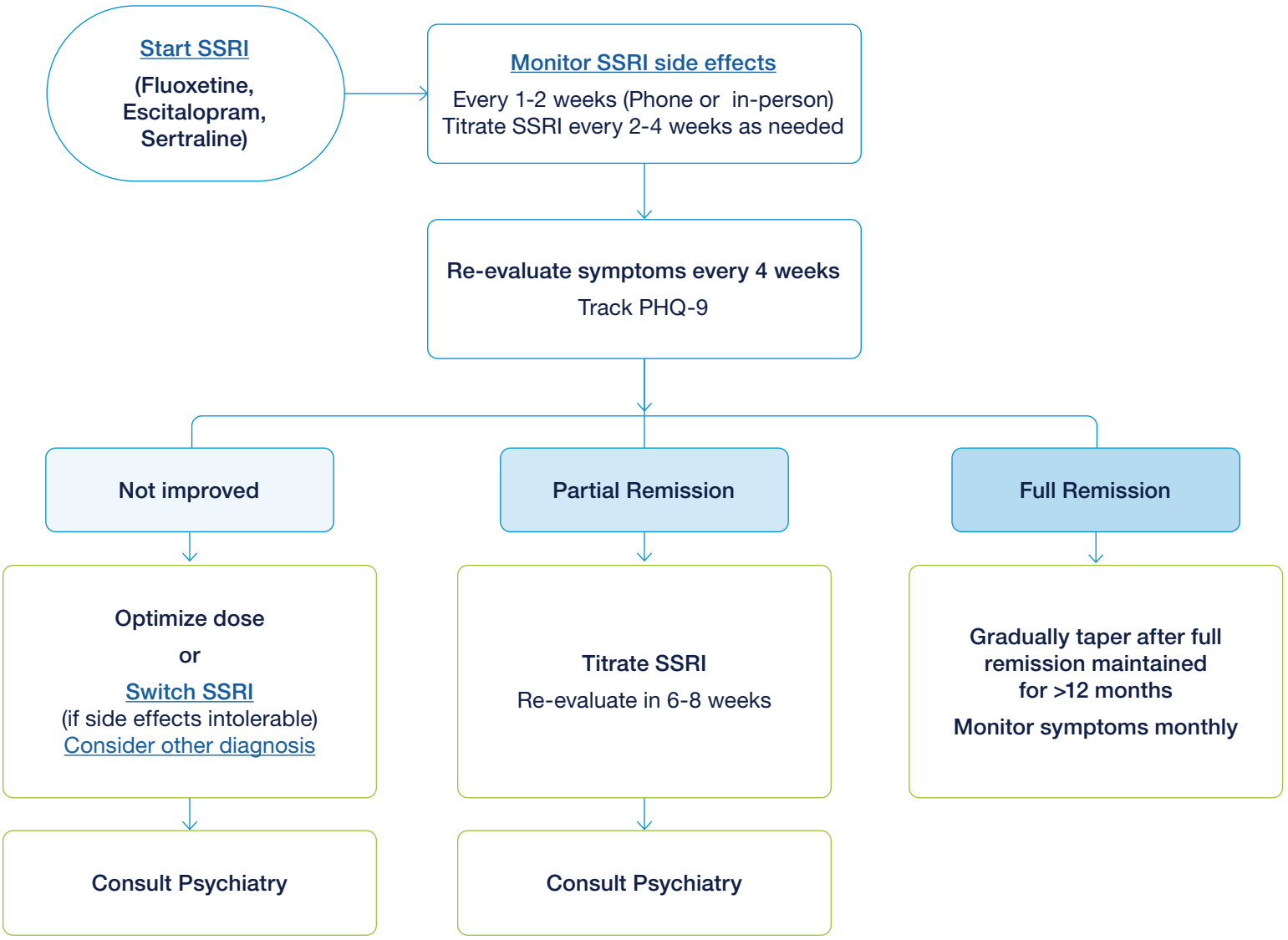
SSRI Treatment



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Partial Remission:
< 2-month period devoid of signs and symptoms of major depression
Full Remission:
2-month period or longer devoid of signs and symptoms of major depression
PHQ-9 score < 5 at 12 months (Kroenke, 2001)

HYPERBOXES from SSRI Treatment algorithm

SSRI

SSRI	Starting dose (mg/day)	Titration increment (mg)	Typical Dosage range (mg/day)	Comments	FDA approval
Escitalopram (Lexapro)	5-10	5	10-20	• Well tolerated • QTc prolongation; • less drug-drug interaction • Black-box warning • Indication for Depression (age ≥ 12), anxiety	MDD (age ≥ 12)
Fluoxetine (Prozac)	10-20	10	20-80	• Most activating • More drug-drug interactions • Least likely to cause discontinuation syndrome • QTc prolongation • Black-box warning • 1st line for Depression, Anxiety	MDD (age ≥ 8) OCD (age ≥ 7)
Sertraline (Zoloft)	25-50	25	100-200	• Somewhat activating • Black-box warning • Indication: Anxiety, Depression	OCD (age ≥ 6)

Adapted from San Francisco Health Network Behavioral Health Services Medication Use Improvement Committee (2019). Safer prescribing of Antidepressant medication 2017

What to Know About SSRIs

Most antidepressants take a few weeks to begin taking effect and take up to 6-8 weeks for the full effect. Consider SSRIs when an anxiety disorder is severe, interferes with participation in psychotherapy, or only partially responds to psychotherapy.

Start with fluoxetine (Prozac), escitalopram (Lexapro) or sertraline (Zoloft).

Start at a low dose and increase every 4 weeks.

Follow-up every 2-4 weeks while titrating the dose.

If good benefit, continue at minimal effective dose. If no or partial benefit and no significant side effects, continue increasing to max dose.

If significant side effects develop or there's a lack of benefit at max dose, try second SSRI.

If good benefit and no significant side effects, continue for a year and then try discontinuing by gradually tapering off the medication. Restart if they relapse.

Mild & Common Side Effects that tend to last only a few days:

- nausea (improved if the medication is taken with food)
- abdominal discomfort
- headache
- drowsiness or difficulty sleeping

More Serious & Rare Side Effects:

- increased restlessness
- increased irritability or aggression
- temporary increase in suicidal thoughts and behaviors for adolescents. The risk of increased suicidal thinking is very small (3.8% with medication compared to 2.2% with placebo). It doesn't happen suddenly. It is usually accompanied by general worsening of depressive symptoms, increased agitation, sometimes restlessness.

While rare, these more serious side effects are the **opposite** of the intended effect, so if they are feeling worse, please reach out by contacting us right away for an appointment

Other serious but very rare side effects:

- muscle rigidity, fever, excessive sweating, severe jaw clenching, tremors: these are signs of "serotonin syndrome", and require emergent medical evaluation

How to talk about Black-box warnings

Parent: Is my child/teen more likely to hurt and kill themself being on an antidepressant?

PCP: In 2004, FDA issued a black box warning that now includes all antidepressants based on 24 RCTs, due to the possible increased risk of suicidal thoughts and behaviors in young people up to age 25. There was a slightly increased risk (3.8% vs. 2.2% with placebo) of suicidal ideation and self-injury, however, **no actual increased risk of suicide found in these studies.**

The increased suicidal ideation may be related to "activation syndrome" secondary to antidepressants. With activation syndrome, people may feel more energized, agitated or restless (pacing or fidgeting). These symptoms may occur more often within the first 3 months of treatment.

Parent: Will the medication make my child/teen like a "zombie" or change their personality?

PCP: When taking and titrating as prescribed, SSRIs don't change one's personality. Rarely, at higher doses, blunted affect, apathy or "loss of emotions" could happen. Lowering the dose, augmenting with another medication, or switching to a different antidepressant (i.e. from SSRI to SNRI) may help.

Parent: Does that mean my child/teen would be better off not taking meds?

PCP: Since the black box warning issued by FDA, primacy care providers have understandably felt less comfortable prescribing these meds, and as the prescription rate went down, increased trend of child/teen depression and suicide was observed.

Depression is worth treating, and it is important to regularly follow up with me either in person or by phone to share anything about the medication that may be associated with your child/teen doing worse or better. Please feel free to contact me in this case so that we could discuss, or even consider stopping, as this is obviously the opposite of what we want.

Parent: Why is the antidepressant doing the opposite thing?

PCP: We believe that the suicidal thoughts and behaviors are still most likely associated with your child/teen's pre-existing depression. In the process of finding the right medication for their depression symptoms, we encourage your child/teen to also consider therapy. **Combining therapy with medication** can be helpful to allow patients and therapists to develop and build coping skills and language to express their thoughts and feelings, including the destructive and harmful ones.

SSRI Side effects and management strategies

Mild & Common Side effects (~10%)	Management Strategies
GI upset (Nausea, diarrhea, pain)	• Take with food. • Usually subsides within 2 weeks • Assess for other causes of eating disturbance
Headache	• Supportive care (hydration, Tylenol as needed) • Usually subsides within 1-2 weeks • Switch medication if symptoms persist and intolerable
Fatigue, low energy	• Administer at bedtime. • If symptoms persist and impairing, consider switching to different medication.
Difficulty sleeping	• Administer in AM • Discuss sleep hygiene, evaluate for other causes of sleep disorders
Less Common Side effects (<10%)	**Management Strategies**
↑ Agitation, Restlessness Anxiety	• Usually self-limiting within 2-4 weeks • May occur in 3-8% of patients • If persistent and symptoms are intolerable: • Decrease to lower dose • Switch to different medication
Sexual dysfunction	• Switch to different medication
Dry mouth	• Supportive care (sugarless gum, candy, hydrate)
Tremors	• If persists for longer than few weeks, and impairing switch to different medication
Rare & Uncommon Side effects (<1%)	**Management Strategies**
Black Box Warning **(↑ suicidal thoughts/behavior, thoughts of self-harm)**	Safety Assessment and Evaluation Consult with psychiatrist or mental health provider • FDA reviewed 24 studies with 9 different SSRIs (4,400 youth) • NO suicides in these studies • Adverse events of suicidal ideation and/or self-injurious behavior reported in 3.8% of patients on meds vs. 2.2% on placebo • No worsening or new suicidal ideation reported in 17/24 studies that inquired about SI
Increase in appetite	• Monitor weight, healthy diet
Increased bleeding time	• Medical evaluation, switch medication
Photosensitivity, SIADH	• Medical evaluation, switch medication
Serotonin Syndrome (Fever, flushing, muscle rigidity, jaw clenching, tremors, vital instability)	• Stop medications • Requires emergent medical evaluation (ER)

Switching antidepressants

Guide for switching antidepressants

Switching from	Switching to	Suggested approach
Fluoxetine	Other antidepressant	Taper -> stop -> start low, go slow with the new agent
SSRI	Other SSRI or SNRI	1. Direct switch to equivalent or lower doses 2. Cross-taper when higher doses of the initial antidepressants are used
SSRI or SNRI	TCA	1. Cross-taper for 1-2 weeks 2. Start with lower TCA doses if switching from an agent with CYP2D6** or CYP1A2*** inhibition
Any antidepressant (except MAOIs)	Mirtazapine or bupropion	Cross taper 1-4 weeks to minimize serotonin discontinuation syndrome
Bupropion	Other antidepressant	Cross taper over 1-3 weeks
Mirtazapine	Other antidepressant	Cross taper
TCA	Other antidepressant	Cross taper over 1-2 weeks

- ***When fluoxetine is involved, remember its active metabolite has long half-life of 9 days**
- ****CYP2D6 inhibition: fluoxetine, paroxetine, duloxetine. The inhibition may cause elevation of levels of medications metabolized by this pathway: TCAs, SSRIs, SNRIs, etc.**
- *****CYP1A2 inhibition: fluvoxamine**

Category of Antidepressants

Pediatric Antidepressants		Starting dose (mg/d)	Titration increment (mg)	Typical dose range (mg/d)	FDA-approved indications and age (years)
SSRI					
Citalopram	Celexa	10 - 20	10	20 - 40	—
Escitalopram	Lexapro	5 - 10	5	10 - 20	MDD (≥12)
Fluoxetine	Prozac	10 - 20	10	20 - 80	MDD (≥8), OCD (≥7)
Sertraline	Zoloft	25 - 50	25	100 - 200	OCD (≥6)
SNRI					
Venlafaxine	Effexor	37.5	75	150 - 225	—
Duloxetine	Cymbalta	20 - 30	20 - 30	40 - 60	GAD (≥7)
Desvenlafaxine	Pristiq	25	25	25 - 100	—
Atypical antidepressants					
Bupropion XL	Wellbutrin XL	150	150	150 - 450	—
Mirtazapine	Remeron	7.5 - 15	7.5-15	15 - 45	—
Vilazodone	Viibryd	Not studied			—
Vortioxetine	Trintellix	5	5	5 - 20	—
Tricyclic antidepressants					
Clomipramine	Anafranil	25	25	50 - 200	OCD (≥10)
Desipramine	Norpramin	25 - 50	25	50 - 200	—
Nortriptyline	Pamelor	10 - 50		30 - 50	—
Imipramine	Tofranil	10 - 25		50-100	Enuresis (≥7)

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Text Only Version of Main Flowchart

Title: "Clinical Work Pathway Depression"

1. First step is "**Concerns for Depression Signs & symptoms of depression** High-risk patients"
2. Then "Depression Screening Tools**:** PHQ-9A (age 11+); SMFQ (age 6+)"
3. Then "Safety Check**:** Trauma; Thoughts of harming self/others"
4. Then "Assessment of Depressive Disorder**:** Focused Clinical Interview; DSM-5 Criteria; Differential, Comorbidity"
5. Then stratify 3 actions steps
    - I. **Mild (PHQ-9 score<10)**: 1st line of treatment; Psychoeducation, Support & Monitoring **including:** Follow-up in 2-4 weeks; Track rating scales; Safety assessment at each visit): If limited improvement then 2nd line of treatment: Psychotherapy**.** If limited improvement then 3nd line of treatment: SSRI Treatment
    - II. **Moderate (PHQ-9 score 10-14)**: 1st line of treatment; Psychoeducation, Support & Monitoring **including:** Follow-up in 2-4 weeks; Track rating scales; Safety assessment at each visit) and Psychotherapy**.** If limited improvement then 2nd line of treatment: SSRI Treatment
    - III. **Severe (PHQ-9 score ≥15):** Psychoeducation, Support & Monitoring **including:** Follow-up in 2-4 weeks; Track rating scales; Safety assessment at each visit) and Psychotherapy **and** SSRI Treatment

Rev. 08/01/21

Text Only Version of SSRI Treatment Flowchart

Title: "SSRI Treatment"

1. First step is "Start SSRI: **(Fluoxetine, Escitalopram, Sertraline)**"
2. Then "Monitor SSRI side effects**:** Every 1-2 weeks (Phone or in-person); Titrate SSRI every 2-4 weeks as needed"
3. Then "**Re-evaluate symptoms every 4 weeks:** Track PHQ-9"
4. Then stratify 3 actions steps
    - I. **Not improved**: 1st line of treatment; **Optimize dose or** Switch SSRI (if side effects intolerable) Consider other diagnosis. Then **Consult Psychiatry**
    - II. **Partial Remission**: 1st line of treatment; **Titrate SSRI** Re-evaluate in 6-8 weeks. Then **Consult Psychiatry**
    - III. **Full Remission:** Gradually taper after full remission maintained for >12 months **Monitor symptoms monthly**

Rev. 08/01/21