

Using SSRIS in Pediatric Primary Care

- ▶ Abigail Schlesinger, MD
- ▶ TIPS Conference

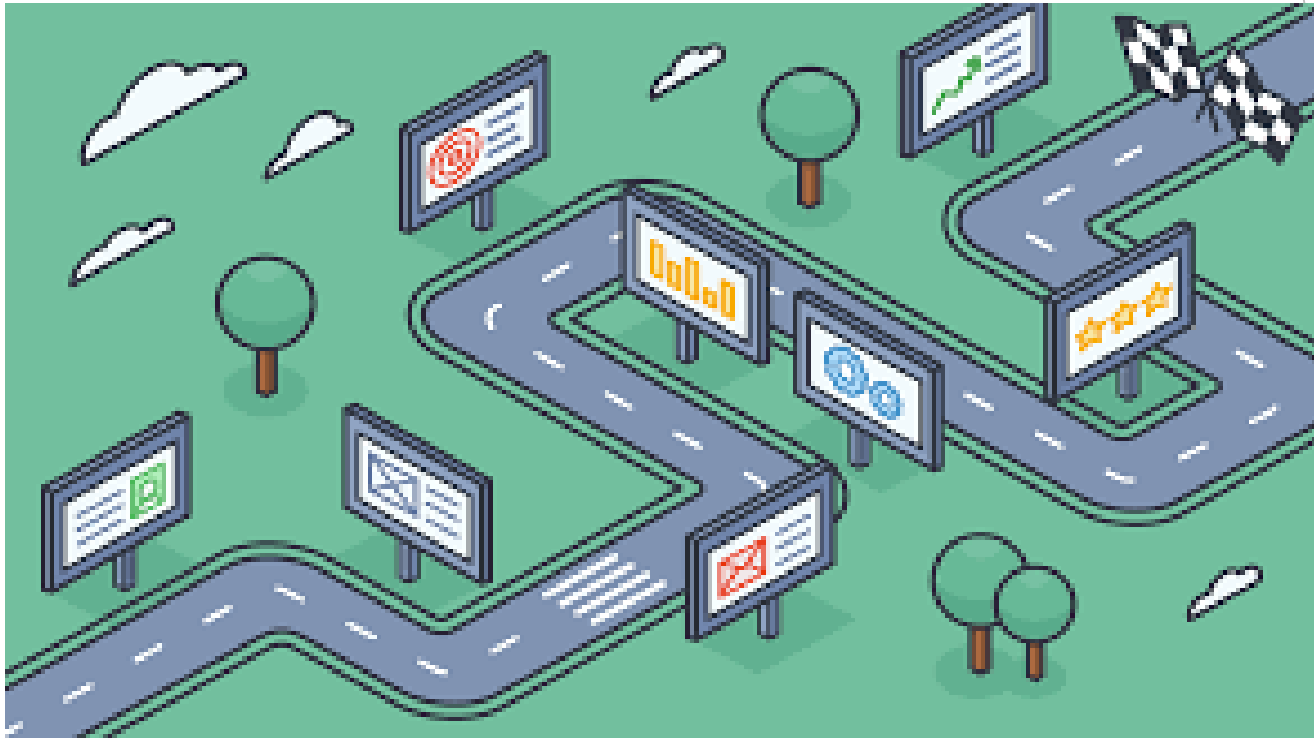
Objectives

- ▶ Be exposed to a primary-care based Selective Serotonin Reuptake Inhibitor(SSRI) Protocol for the treatment of anxiety and depressive disorders in children and adolescents.

Decision to start an SSRI

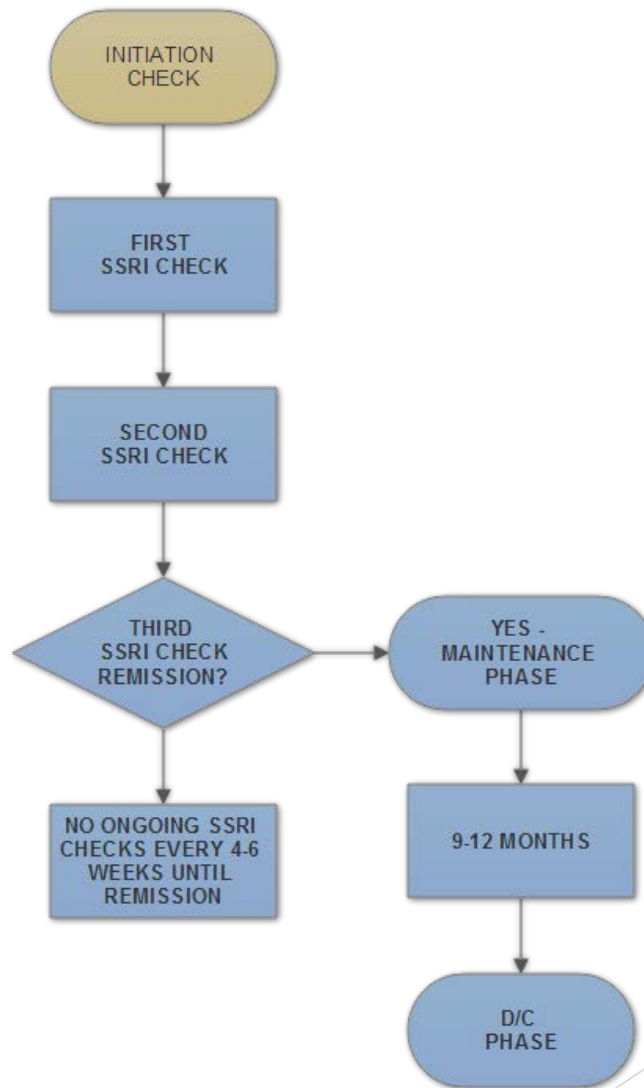
- ▶ Severity of diagnosable depressive or anxiety disorder
- ▶ Inability to respond to/engage in/or access therapy
 - ▶ A combination of therapy and medication is the evidence-based intervention for moderate-severe depression and Anxiety Disorders
 - ▶ Increasing intensity of treatment is always an option to “boost” response to treatment

The protocol is a road map



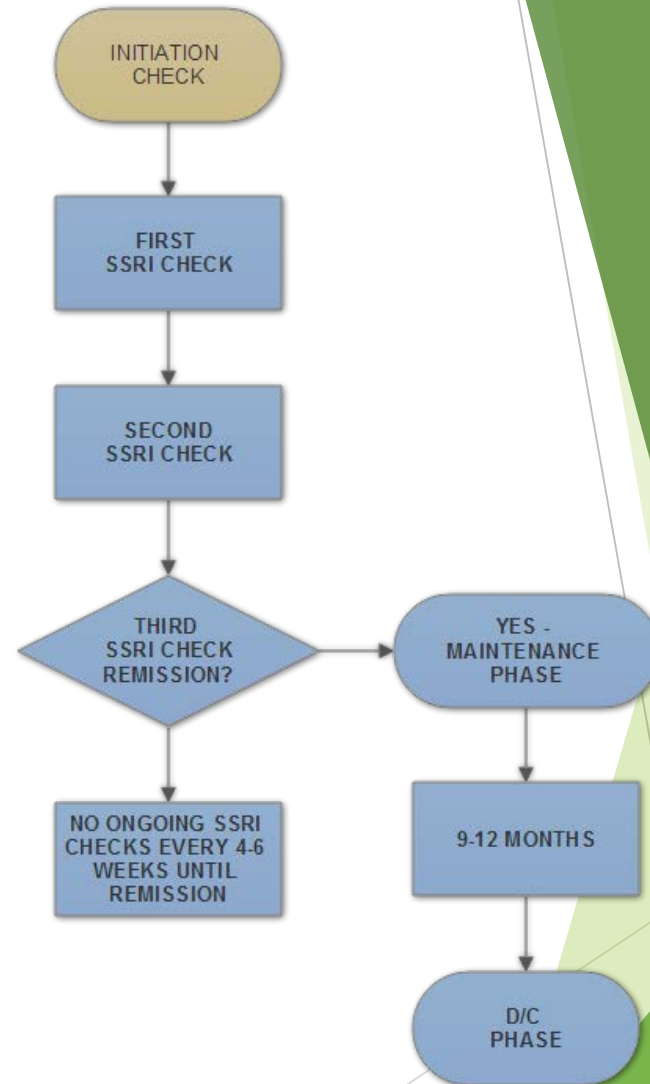
Your team can improve the trip.

OVERALL PROTOCOL



Initiation Check

1. Validate Diagnosis & Safety
2. Review Family History
3. Complete Consent/Assent
4. Clarify Goals/Expectations/Safety Plan
5. Start Medication
6. Schedule follow-up



1. Validate Diagnosis & Safety

- ▶ Review work-up - medical diagnosis & comorbid psychiatric
 - ▶ Confirm Diagnosis
 - ▶ Review Behavioral Scales
 - ▶ SCARED parent and child(7-18) or GAD-7(13 and over 18)
 - ▶ PHQ9(or PHQ9a)
 - ▶ Consider Comorbidities that can Complicate Treatment
 - ▶ ASSURE SAFETY



Consider Comorbidities that Could Complicate Treatment

- ▶ Bipolar Disorder
- ▶ Autistic Spectrum Disorder
- ▶ Trauma
- ▶ Substance Use
- ▶ Eating Disorder
- ▶ Suicidality
- ▶ ADHD & ODD
- ▶ Assess personal history
- ▶ Are ASD driving “anxiety behaviors”
- ▶ Acute or Chronic Trauma
- ▶ Consider Substance Screen
- ▶ Medication won’t work if you don’t have enough food to feed the brain
- ▶ Assess past and Current
- ▶ Consider Vanderbilts

Screening for Bipolar Disorder

- ▶ “Was there ever a period of time, for more than a few days, that you(or your child) didn’t need sleep, was on top of the world, and significantly different than usual”
- ▶ Note
 - ▶ This should be a clear change from baseline.
 - ▶ Child should be energetic during the day, ie not need a nap, not go to bed early
 - ▶ There is the most concern for bipolar disorder if the child was euphoric(more happy than normal) or grandiose(felt that they were special, had special powers etc) and there is no reason for it(ie it’s not the day before a holiday)

Safety

- ▶ Safety should be assessed in all children with depression and anxiety.

Depression & Suicide

- ▶ Untreated depression is the **number one** cause of suicide
- ▶ Over **90%** of children and teens who complete suicide have a **mental health diagnosis** (Mental Health: A Report of the Surgeon General)
- ▶ In 2015, H.S. students (CDC, 2016)
 - ▶ reported seriously contemplating suicide
 - ▶ **18%**
 - ▶ attempted at least once (in the preceding 12 months)
 - ▶ **9%**
- ▶ Suicide is the **#2** cause of death in the U.S. in those 10-24 years-old (NCHS)

Risk Assessment

- ▶ Begin with general questions: “Have you ever thought you would be better off dead....your family would be better off without you”
 - ▶ Death wish: 20% prevalence
- ▶ Progress to more specific questions: “Have you ever had a plan?” Means to carry out?
 - ▶ Much less common
 - ▶ Gave away possessions?
- ▶ **Normalize:**
 - ▶ Many times children who are feeling down or depressed describe having thoughts that they don't want to be alive. Have you ever felt that way?

2. Review Family History

- ▶ Bipolar Disorder
- ▶ Response to Antidepressants



3. Consent/Assent

- ▶ Parent should consent
- ▶ Adolescent (and preferably child) should assent



Consent/Assents

- ▶ Warn about side effects
 - ▶ More common that will probably go away if not too bothersome(if they even occur)
 - ▶ Rare and concerning
 - ▶ Suicidality
 - ▶ Mania
 - ▶ Serotonin Syndrome
 - ▶ Other
 - ▶ Activation - some kids get increased energy during the day, but have no trouble with sleep

SSRI Side Effects

- GI: nausea, abdominal pain, diarrhea, weight loss, weight gain
- Headaches
- Easier bruising
- Sweating
- Light-headedness/dizziness
- Nervousness/restlessness
- Sleep difficulties: sedation/insomnia, vivid dreams
- Sexual dysfunction
- Irritability/activation
- Potential risk for suicidal thinking
- Precipitation of mania

FDA Black Box Warning

- ▶ Based on a 2004 FDA review of reported adverse events in 23 clinical trials which involved 4300 children and adolescents, 9 different medications
- ▶ Studies used two different measures for suicidal thoughts and behavior
- ▶ FDA clumped both thoughts and behaviors as “suicidality”

FDA Black box

- ▶ First measure “event report”
- ▶ Second measure - 17 of 23 studies “standardized forms” questioned suicidality at each visit
- ▶ Second measure technique considered more accepted

FDA Black Box warning

- ▶ Studies that used event reporting noted that 2% who received placebo expressed increased suicidality compared to 4% on medication.
- ▶ Studied that used standardized forms that questioned suicidality at each visit demonstrated a slight reduction in suicidality for the medication group.

▶ THERE WERE NO
COMPLETED SUICIDES IN
THE 4300.

Black Box Warning

- ▶ “Less than 2% of kids who start an SSRI will see an increase in suicidality - often suicidal thoughts/ & thoughts about self-injury. I am recommending this medication because the benefits of treating this depression/anxiety far outweigh any risk associated with increased suicidality. But, because we take behavioral health seriously I will follow-up with you closer while starting medication to make sure that you are safe.”

4. Clarify Goals/ Expectations/Safety

▶ GOALS

- ▶ What does the family/child want to get out of treatment?
- ▶ Do you anticipate that this intervention will help?
- ▶ Are goals aligned with treatment

VALIDATE
DIAGNOSIS &
SAFETY

REVIEW
FAMILY HISTORY

COMPLETE
CONSENT/ASSENT

CLARIFY
EXPECTATIONS/
GOALS/SAFETY

START
MEDICATION



Clarify Expectations: Roles

- ▶ Providers in the practice
 - ▶ Help design & support the treatment plan that includes evidence-based intervention
 - ▶ Maintain confidentiality, with caveats
 - ▶ Help child/adolescent get better
- ▶ Parents & Patients
 - ▶ Participate in treatment
 - ▶ Help design and support the treatment plan
 - ▶ Speak up if things aren't going well



Expectations of Treatment

- ▶ Expectation of Treatment
 - ▶ Getting better takes time
 - ▶ SSRIS take time - 4-12 weeks at therapeutic dose
 - ▶ Dose may need to be adjusted over time
 - ▶ So response needs to be monitored
 - ▶ Treatment works better if you participate in therapy



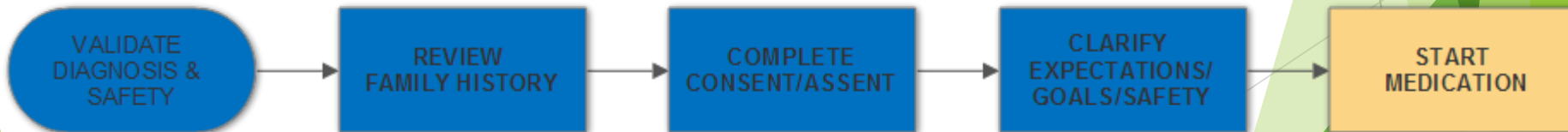
Safety Plan

1. Coping strategies
 2. Adult(s) who child will contact if distressed
 3. Emergency numbers
- ▶ Write the plan down
 - ▶ Share with the family



5. Start Medication

- ▶ You can increase medication weekly
- ▶ You can start at typical starting dose or low starting dose
 - ▶ We often start at low dose for kids with a lot of anxiety, somatic symptoms, young kids, or kids with developmental concerns



Choose a medication

- ▶ Factors to consider in choosing
 - ▶ Fluoxetine has the most data
 - ▶ Sertraline has more data for anxiety
 - ▶ If you have any concern about bipolarity don't use Prozac
 - ▶ Celexa has histaminergic properties - helps belly pain

SSRI Titration Schedule

Medication	Low Starting Dose	Typical Starting Dose	Typical Effective Dose	Typical Dose Range	Typical Escalation amount
Fluoxetine	5mg	10mg	20mg	60mg	10mg
Sertraline	25mg	50mg	100-150mg	200mg	25mg
Citalopram	5mg	10mg	20mg	40mg	10mg
Escitalopram	2.5mg	5mg	10mg	20mg	5mg

SSRI General Information

Medication	Typical Effective Dose	Typical Dose Range	Half-life	Half-life of Active Metabolites
Fluoxetine	20mg	60mg	2-3 days	2 weeks
Sertraline	100-150mg	200mg	Males - 22.4 hours females 32-36	NA
Citalopram	20mg	40mg	20-35 hours	NA
Escitalopram	10mg	20mg	20-35 hours	NA

Pediatric Approvals & data

Medication	FDA MDD	FDA OCD	FDA Enuresis	High quality RCT for Anxiety	High quality RCT for MDD
Fluoxetine	8-18	7-17			12-17
Sertraline		6-17		7-17	
Citalopram					
Escitalopram	12-17				
Fluvoxamine		8-18			
Clomipramine		10-17	10-17		
Imipramine			6-17		

Serotonin Syndrome

- ▶ Full blown serotonin syndrome is rare
 - ▶ But you do need to know what it is
- ▶ You can prescribe more than one serotonergic agent
 - ▶ But warn people(because if you don't the pharmacist will)
 - ▶ Tell parents/patients to call you if they are concerned about agitation or restlessness

Signs of Serotonin Syndrome

- ▶ Agitation or restlessness
- ▶ Confusion
- ▶ Rapid heart rate and high blood pressure
- ▶ Dilated pupils
- ▶ Loss of muscle coordination or twitching muscles
- ▶ Muscle rigidity and/or hyperreflexia
- ▶ Heavy sweating
- ▶ Diarrhea
- ▶ Headache
- ▶ Shivering
- ▶ Goose bumps

Severe Serotonin Syndrome

- ▶ High fever
- ▶ Seizures
- ▶ Irregular heartbeat
- ▶ Unconsciousness

Diagnosis

- ▶ Spontaneous clonus
- ▶ Inducible clonus PLUS agitation or diaphoresis
- ▶ Ocular clonus PLUS agitation or diaphoresis
- ▶ Tremor PLUS hyperreflexia
- ▶ Hypertonia PLUS temperature above 38°C PLUS ocular clonus or inducible clonus

Serotonin Syndrome

Symptoms	Management
Mild - hypertension, tachycardia, mydriasis, shivering, tremor, myoclonus, hyperreflexia	--Discontinue the offending agent(s) --Support via stabilizing vital signs, cooling measures --Mild agitation, fever, hypertension & tachycardia: benzodiazepine --Observe for at least 6 hours
Moderate - Above plus temperature of at least 40 deg C, hyperactive bowel sounds, ocular clonus, agitation, hypervigilance, pressured speech	--All of the above --Severe agitation & hyperthermia --5HT antagonist(cyproheptadine) --Admission to hospital for cardiac monitoring & observation
Severe - Above plus temperature greater than 41.1 deg C, dramatic swings in pulse, rate & blood pressure, delirium, muscle rigidity	--All of the above --Severe hypertension/tachycardia: esmolol or nitroprusside --Sedation & paralysis with a nondepolarizing agent & intubation/ventilation --Admission to ICU

QTC Prolongation

- ▶ Don't go over 40mg with celexa due to black box warning
- ▶ Be careful with drugs that have QTC interactions if using celexa - and warn parents

Drug-Drug Hepatic (CYP interactions)

- ▶ Go slow if using two medications that have CYP interactions.
- ▶ If EPIC tells you about an interaction consider what the interaction actually is...

- ▶ Citalopram is metabolized by CYP 3A4 & 2C19;
- ▶ Co-administration with a CYP2C19 inhibitor may increase the serum concentrations of citalopram and increase the risk of QT prolongation.
- ▶ The FDA recommends a maximum citalopram dose of 20 mg per day for patients taking concomitant CYP2C19 inhibitors.
- ▶ This interaction is largely theoretical based on the metabolic pathways of prescribed medications, and the clinical significance is unknown, especially with weak CYP2C19 inhibitors.

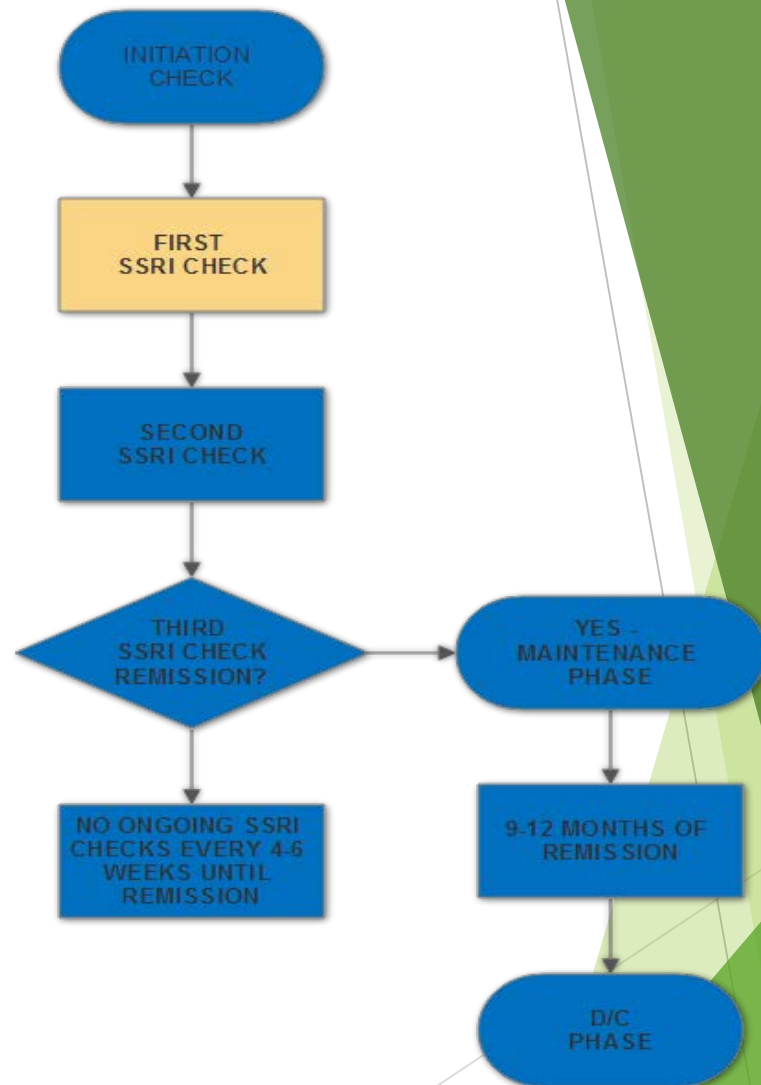
- ▶ For patients taking citalopram at 40 mg/d or less or escitalopram 20 mg/d or less and in combination with a PPI or an oral contraceptive, it is reasonable to continue the combination with the documentation of (1) no reported history of structural heart disease, (2) no personal or family history of sudden death or prolonged QT syndrome, and (3) a discussion with the patient regarding the risks and benefits of alternative therapies.
- ▶ Of note, recent FDA recommendations are that patients with hepatic dysfunction, those over 60 years of age, patients who are poor metabolizers of CYP2C19, and those who are taking another CYP2C19 inhibitor such as cimetidine (Tagamet) should not use citalopram at doses higher than 20 mg/d.7

FIRST SSRI CHECK

When

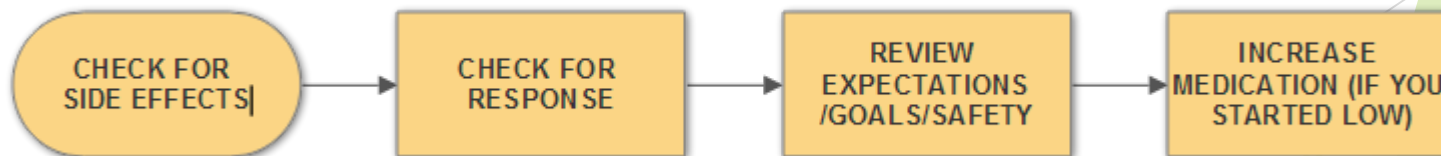
1-2 Weeks after starting medication

1. Check Side Effects
2. Check for Response
3. Review Expectations/Goals/Safety
4. Increase medication (if you started low)



FIRST SSRI CHECK

- ▶ We don't expect clinical response yet.
 - ▶ So condition may continue to worsen
- ▶ This check is predominantly to check
 - ▶ Side effects
 - ▶ Assure safety
 - ▶ Get medication to therapeutic dose
 - ▶ (Have a check in - in case it appears a higher level of care is needed)



FIRST SSRI Check

- ▶ Check side effects
 - ▶ “Are you concerned about side effects? Has anything changed that you are worried might be related to medication”
 - ▶ “Have you had any thoughts about hurting yourself or anyone else?”
- ▶ Check for response
 - ▶ “How are you doing?”
 - ▶ “On a scale of 1-10, 10 being as good as you could feel, how are you doing?”
- ▶ Review goals
 - ▶ “Are you still hoping to work on ____”
- ▶ Review safety plan
 - ▶ “Have you had to use your safety plan? Or How close have you come to using your safety plan? Do you still feel like you could use your safety plan”
 - ▶ “Could you repeat your safety plan?”
- ▶ Review expectations
 - ▶ “It’s early to see an impact of medication but you should see some positive response in 2-4 weeks.”
 - ▶ “We look forward to your next check-in in 1-2 weeks”
- ▶ Increase medication (if you started low)

First SSRI Check

1. Check Side Effects

- ▶ Are you concerned about side effects? Has anything changed that you are worried might be related to medication?”
- ▶ “Have you had any thoughts about hurting yourself or anyone else?”

2. Check for Response

- ▶ How are you doing?”
- ▶ “On a scale of 1-10, 10 being as good as you could feel, how are you doing?”

3. Review Expectations/Goals/Safety

4. Increase medication(if you started low)

First SSRI Check

1. Check Side Effects

2. Check for Response

3. Review goals

- ▶ “Are you still hoping to work on ____”

→ Review safety plan

- ▶ “Have you had to use your safety plan? Or How close have you come to using your safety plan? Do you still feel like you could use your safety plan”
- ▶ “Could you repeat your safety plan?”

→ Review expectations

- ▶ “It’s early to see an impact of medication but you should see some positive response in 2-4 weeks.”
- ▶ “We look forward to your next check-in in 1-2 weeks”

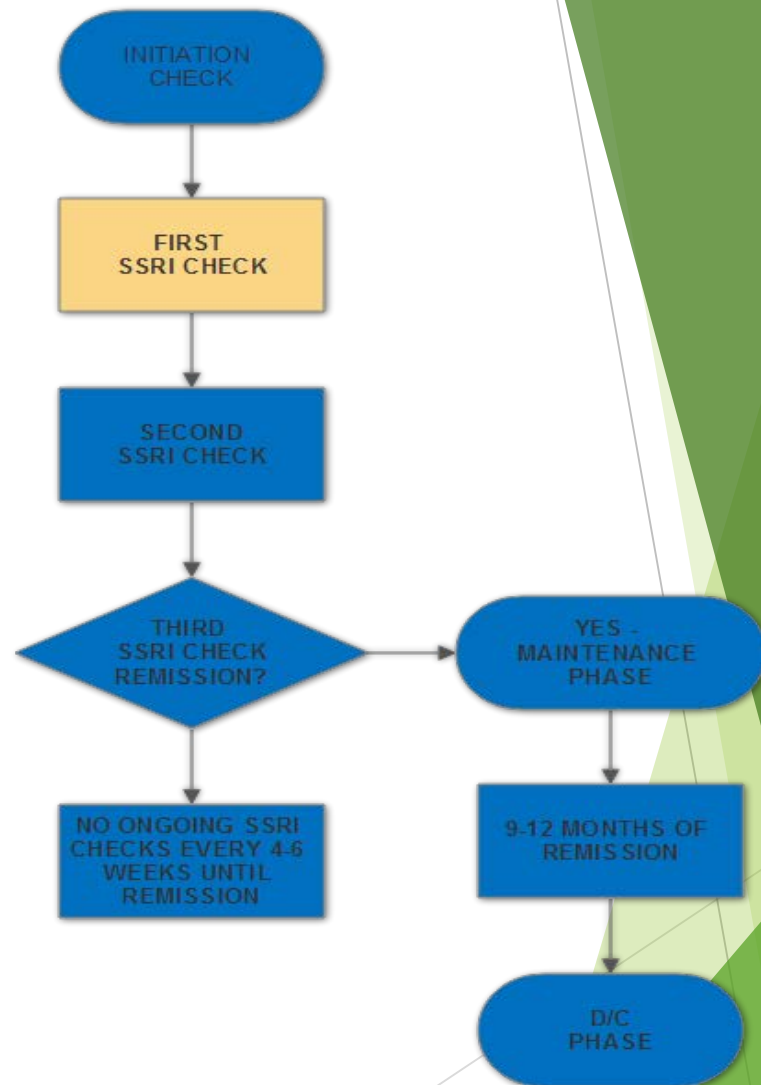
4.. Increase medication (if you started low)

FIRST SSRI CHECK

When

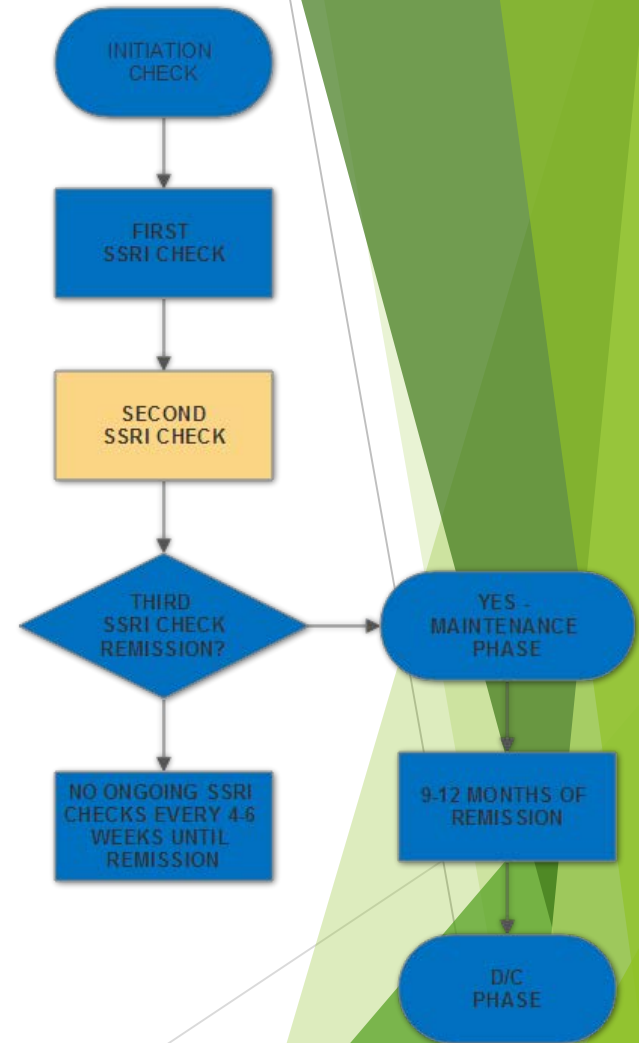
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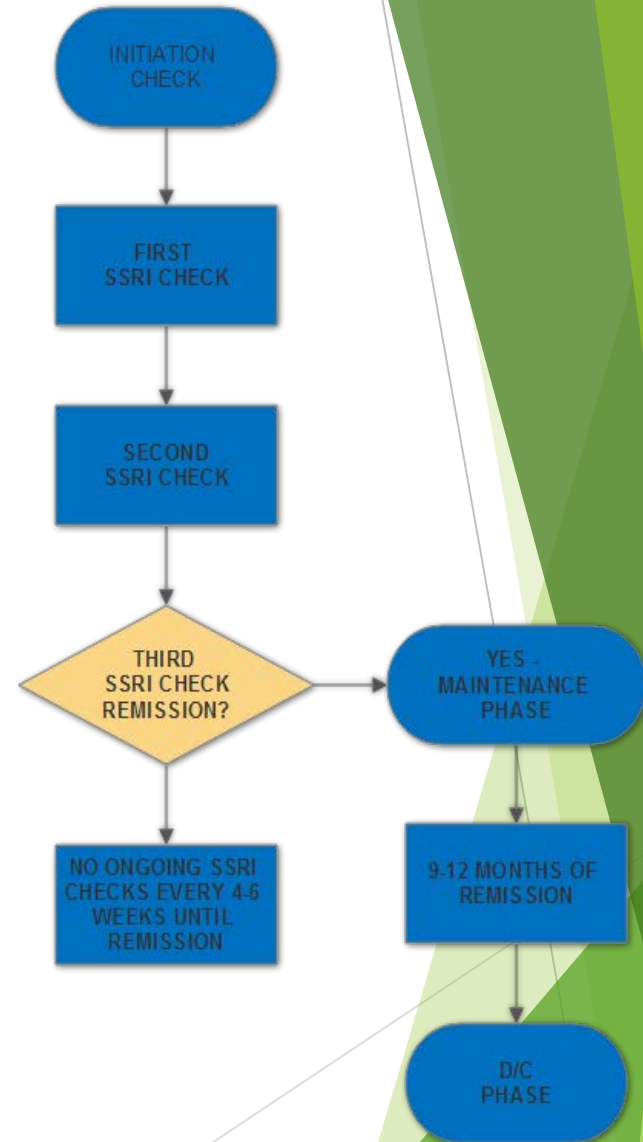
2ND SSRI Check

- ▶ When -
 - ▶ 2-4 weeks after 1st SSRI follow-up
 - ▶ (4-6 weeks after starting medication)
- 1. Assess Response
 - ▶ Ask how are you doing
 - ▶ Repeat original screens for target symptoms
- 2. Check for side effects
- 3. Review Expectations/goals/safety
- 4. Increase medication to therapeutic dose



3rd SSRI Check

- ▶ When -
 - ▶ 4-6 weeks after 2ndst SSRI follow-up
 - ▶ (8-12 weeks after starting medication)
- ▶ Assess response
 - ▶ Ask how are you doing?
 - ▶ Repeat original screens for target symptoms
- ▶ Check for side effects
- ▶ Review expectations/goals/safety plan
- ▶ Are they in remission?



Defining Full Remission

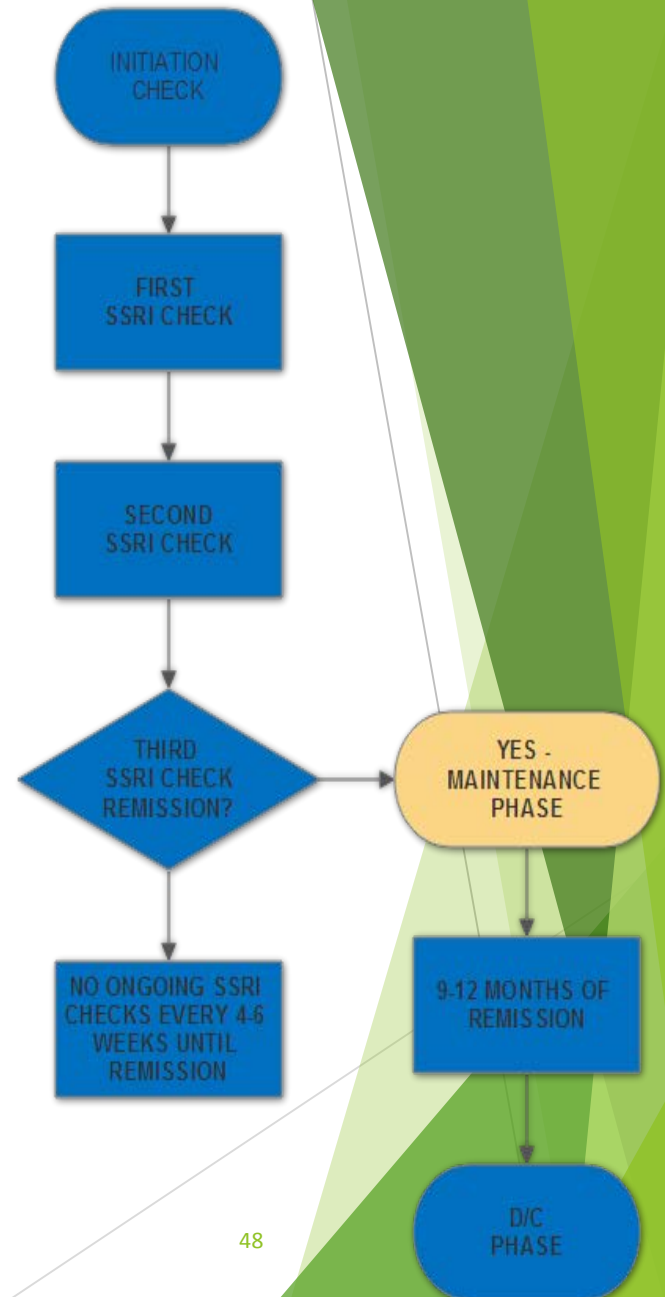
- ▶ Little or no evident impairment
 - ▶ May still be working on goals, but not getting stuck on them
- ▶ Anxiety
 - ▶ Overall SCARED < 13
 - ▶ GAD-7
- ▶ Depression- PHQ9 <10 and no impairment or <5

What to do if patient is not in remission

- ▶ Increase medication &/or therapy frequency
- ▶ Follow-up 4-6 weeks for SSRI check

Maintenance

- ▶ SSRI Check every 1-3 months
- ▶ Assess response
 - ▶ Ask
 - ▶ Repeat original screens for target symptoms
- ▶ Check side effects
- ▶ Review goals/expectations/safety plan
- ▶ Begin to discuss when discontinuation will occur

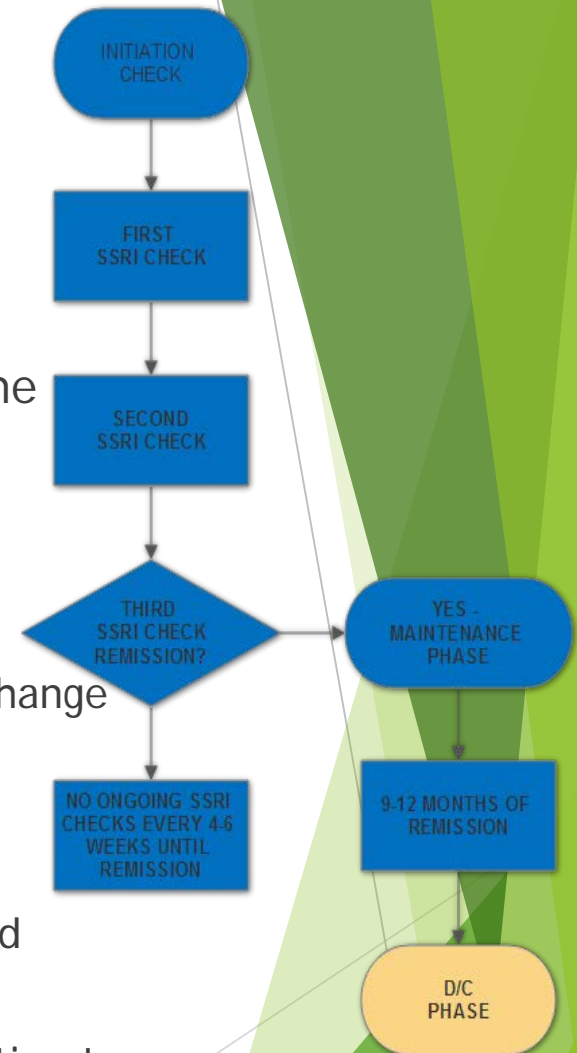


Length of Maintenance

- ▶ 1st episode 6-9 months of Full Remission
- ▶ 2nd episode 1 - 2 years
- ▶ 3rd episode - for life?

Discontinuation Phase: Stopping Medication

- ▶ Assure that maintenance occurred for enough time
- ▶ Consider increasing therapy while decreasing the medication
- ▶ Rules of thumb for when to stop
 - ▶ No - before or during time of great stress and/or change
 - ▶ Yes - if you've been in remission for 6-9 months
- ▶ How to stop
 - ▶ Best success by increasing frequency of therapy and decreasing medication slowly - weekly or less
 - ▶ But remember that it takes 4 half-lives for medication to get out of system and at least 4 weeks after that for recurrence



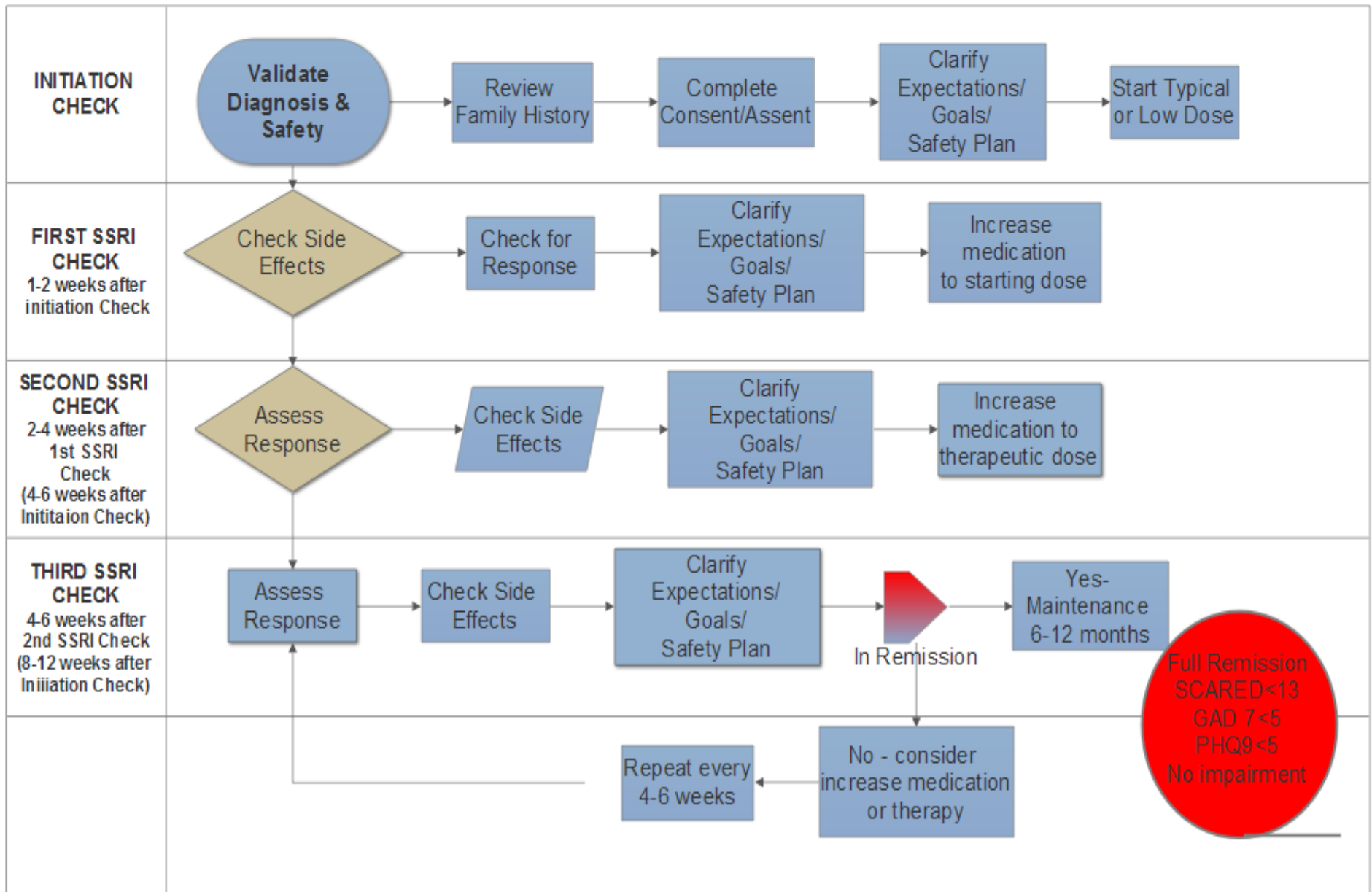
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Thank you

- ▶ PA Healthchoices - for supporting TIPS
- ▶ Gretchen Crum LCSW, Jennifer Chianese MD, Sheree Shafer and Via Winkeller MD for providing feedback and participating in original protocol training Sept 25 2017
- ▶ The providers and families who teach me new things everyday.
- ▶ My family
- ▶ UPMC Healthplan for supporting our expansion
- ▶ CHP - for supporting behavioral health

Selective Serotonin Reuptake Inhibitor(SSRI) Protocol



Selective Serotonin Reuptake Inhibitor(SSRI) Protocol

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1st SSRI CHECK SCRIPT

- ▶Check side effects
 - ▶"Are you concerned about side effects? Has anything changed that you are worried might be related to medication"
 - ▶"Have you had any thoughts about hurting yourself or anyone else?"
- ▶Check for response
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MANIA SCREEN

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