Depression and Anxiety

Practical Day of Pediatrics 2020

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Department of Pediatrics

Goals and Objectives

- Review DSM-5 criteria for each mood and anxiety disorder
- Review all medications used for mood and anxiety disorder
- Meet requirements to become a child and adolescent psychiatrist

Feelings, Thoughts, and Behaviors.

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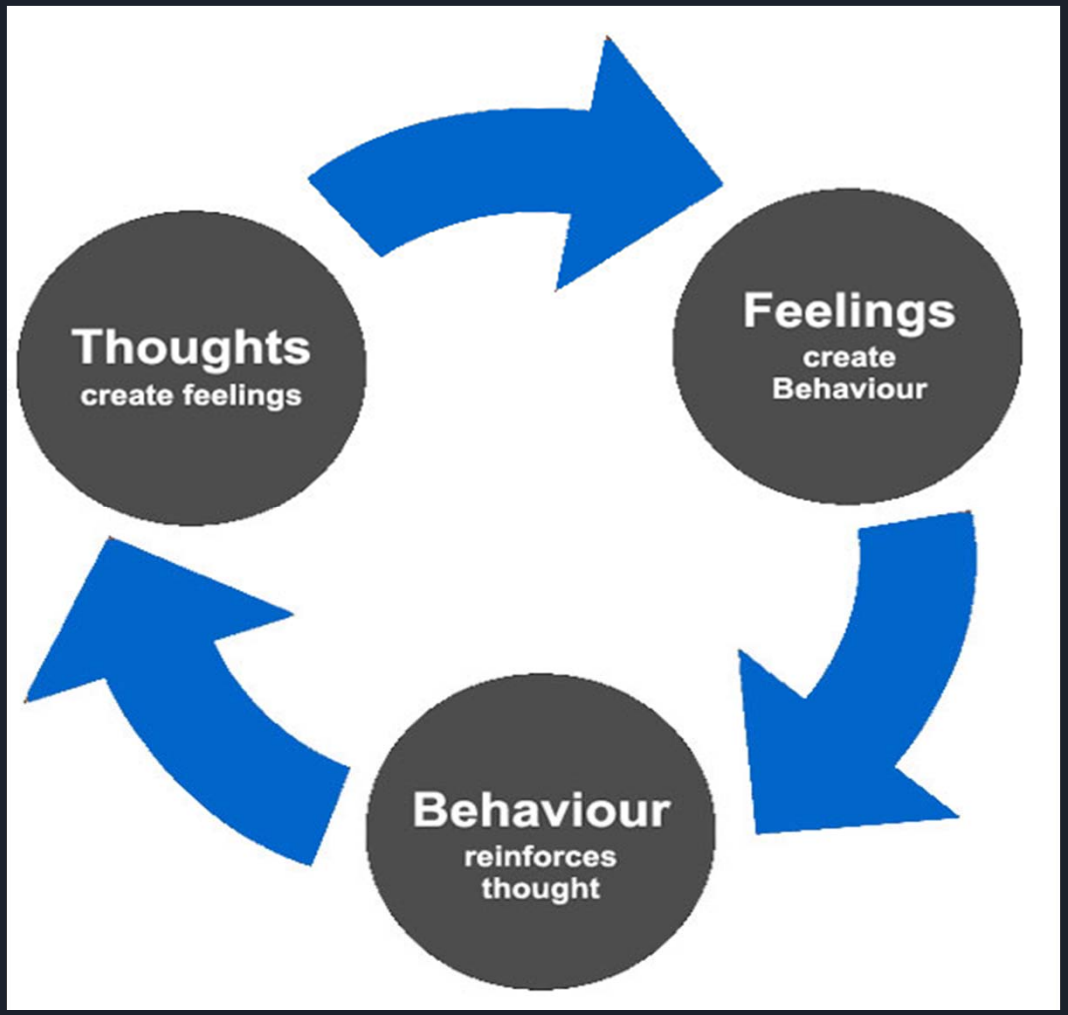
Department of Pediatrics

Goals and Objectives

- Review emotions in children, and discuss what is normal and what is “psychiatric”
- Review evidence based guidelines and treatment options
- Review local and additional resources


INSIDE OUT


DISGUST
SADNESS
JOY
ANGER
FEAR


Thoughts
create feelings
Feelings
create
Behaviour
Behaviour
reinforces
thought


DYSFUNCTION
JCT


DIAGNOSTIC AND STATISTICAL
MANUAL OF
MENTAL DISORDERS
FIFTH EDITION
DSM-5®

Bipolar and Related Disorders
Bipolar I Disorder
Bipolar II Disorder
Cyclothymic Disorder
Substance/Medication-Induced Bipolar and Related Disorder
Bipolar and Related Disorder Due to Another Medical Condition
Other Specified Bipolar and Related Disorder
Unspecified Bipolar and Related Disorder

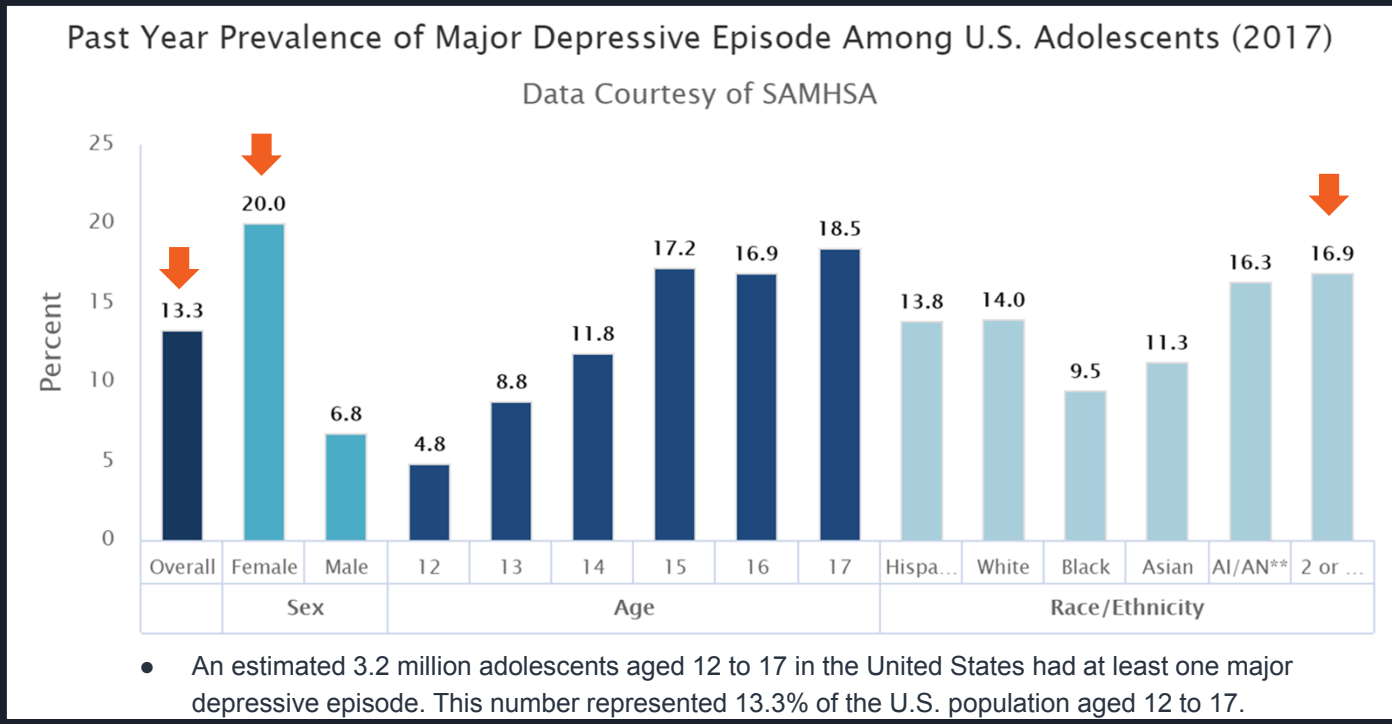
Depressive Disorders
Disruptive Mood Dysregulation Disorder
Major Depressive Disorder, Single and Recurrent Episodes
Persistent Depressive Disorder (Dysthymia)
Premenstrual Dysphoric Disorder
Substance/Medication-Induced Depressive Disorder
Depressive Disorder Due to Another Medical Condition
Other Specified Depressive Disorder
Unspecified Depressive Disorder

Trauma- and Stressor-Related Disorders
Reactive Attachment Disorder
Disinhibited Social Engagement Disorder
Posttraumatic Stress Disorder
Acute Stress Disorder
Adjustment Disorders
Other Specified Trauma- and Stressor-Related Disorder
Unspecified Trauma- and Stressor-Related Disorder

Anxiety Disorders
Separation Anxiety Disorder
Selective Mutism
Specific Phobia
Social Anxiety Disorder (Social Phobia)
Panic Disorder Panic Attack (Specifier)
Agoraphobia Generalized Anxiety Disorder
Substance/Medication-Induced Anxiety Disorder
Anxiety Disorder Due to Another Medical Condition
Other Specified Anxiety Disorder
Unspecified Anxiety Disorder

Obsessive-Compulsive and Related Disorders
Obsessive-Compulsive Disorder
Body Dysmorphic Disorder
Hoarding Disorder
Trichotillomania (Hair-Pulling Disorder)
Excoriation (Skin-Picking) Disorder
Substance/Medication-Induced Obsessive-Compulsive and Related Disorder Obsessive-Compulsive and Related Disorder Due to Another Medical Condition Other Specified Obsessive-Compulsive and Related Disorder Unspecified Obsessive-Compulsive and Related Disorder

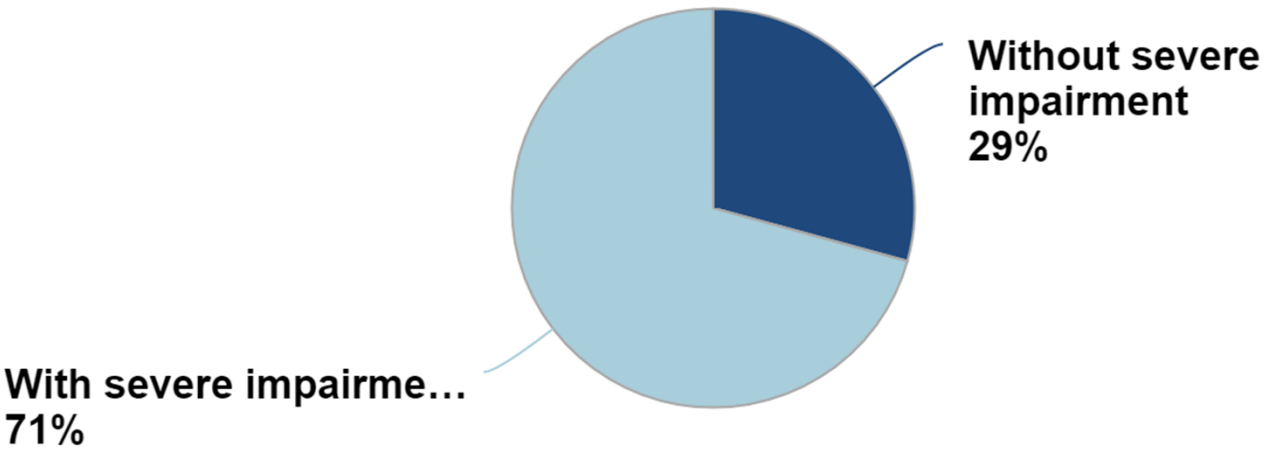
Prevalence of Major Depressive Episode



- An estimated 3.2 million adolescents aged 12 to 17 in the United States had at least one major depressive episode. This number represented 13.3% of the U.S. population aged 12 to 17.

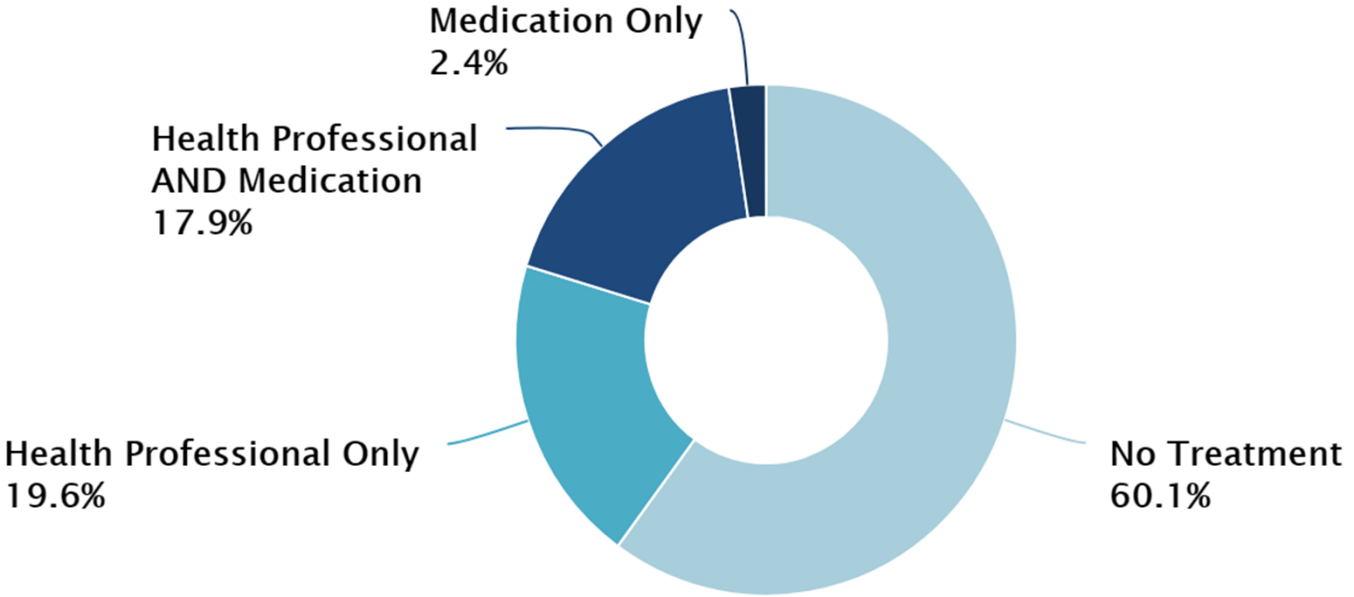
Past Year Severity of Major Depressive Episode Among U.S. Adolescents (2017)

Data Courtesy of SAMHSA



Past Year Treatment Received Among Adolescents with Major Depressive Episode (2017)

Data Courtesy of SAMHSA



17. According to the Substance Abuse and Mental Health Services Administration (SAMHSA), the prevalence of major depressive episode(MDE) among US adolescents in 2017 is:

A. 2.7%

B. 5.5%

C. 8.5%

D. 13.3%

E. 25.7%

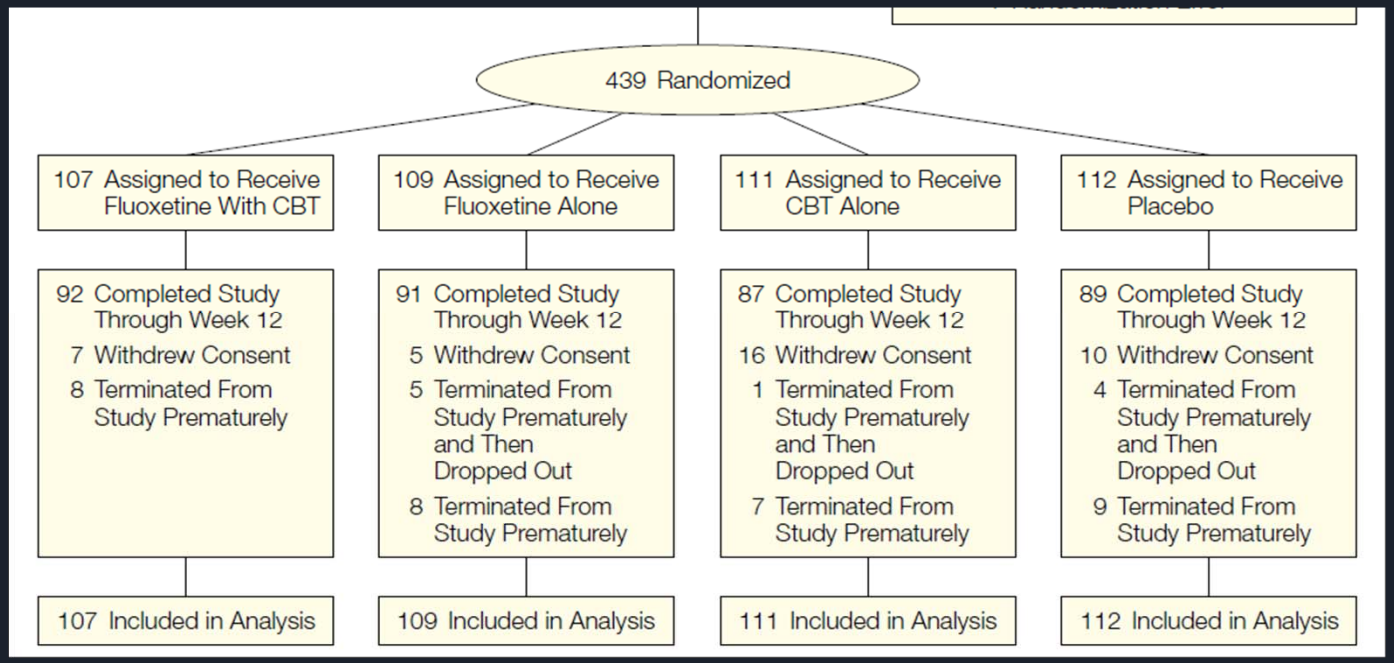

PSYCHIATRIC
HELP 5¢
THE DOCTOR
IS IN

Treatment for Adolescents with Depression Study (TADS)

Treatment for Adolescents with Depression Study (TADS)

- Multi-site clinical research study examining the short- and long-term effectiveness of an antidepressant medication and psychotherapy alone and in combination for treating depression in adolescents ages 12 to 17.
- Thirteen academic and community clinics across the country were involved in the $17 million trial.
- 439 participants ages 12 to 17 from various geographic regions in the United States who were diagnosed with major depression. Recruitment for the trial began in Spring 2000 and ended in Summer 2003

Treatment for Adolescents with Depression Study (TADS)



Treatment for Adolescents with Depression Study (TADS)

- At the end of the first 12 weeks, participants taking pills were informed if they were taking placebo or the active medication fluoxetine.
- Those taking the placebo who were not improved could choose to receive any one of the other three treatments in the study—fluoxetine alone, CBT alone, or combination therapy.
- Participants who did improve while taking placebo were followed by the researchers for up to 12 weeks and offered active treatment if their depression worsened during that time.

Treatment for Adolescents with Depression Study (TADS)

- Participants in any of the three active treatment groups (fluoxetine, CBT, or the combination treatment) who improved during the first 12 weeks continued with their assigned treatments for six more weeks (Stage 2).
- Participants who continued to do well in Stage 2 progressed to Stage 3, which lasted another 18 weeks for a total of 36 weeks of study participation.

Treatment for Adolescents with Depression Study (TADS)

TADS Study Results

Depression response rates at given study time:

	12 weeks	18 weeks	36 weeks
CBT and fluoxetine	**71%**	85%	86%
Fluoxetine alone	**61%**	69%	81%
CBT alone	43%	65%	81%
Placebo	35%		

Ref: March, JAMA (2004); March, Arch Gen Psych (2007)

Treatment for Adolescents with Depression Study (TADS)

- Suicidal thinking decreased substantially in all active treatment groups.
- Fluoxetine + CBT best in decrease of SI

18. According to the Treatment of Adolescents with Depression Study (TADS), which treatment has the best response in depression symptoms at 12 weeks?

A. Cognitive Behavioral Therapy (CBT) and fluoxetine

B. Fluoxetine alone

C. CBT alone

D. Placebo

The Impact of Antidepressant Dose and Class on Treatment Response in Pediatric Anxiety Disorders: A Meta-Analysis

Jeffrey R. Strawn, MD, Jeffrey A. Mills, PhD, Beau A. Sauley, MA, and Jeffrey A. Welge, PhD., J Am Acad Child Adolesc Psychiatry. 2018 Apr; 57(4): 235–244.e2.

SSRI v SNRI?

Does it really take “weeks” before it has effect?

Objective

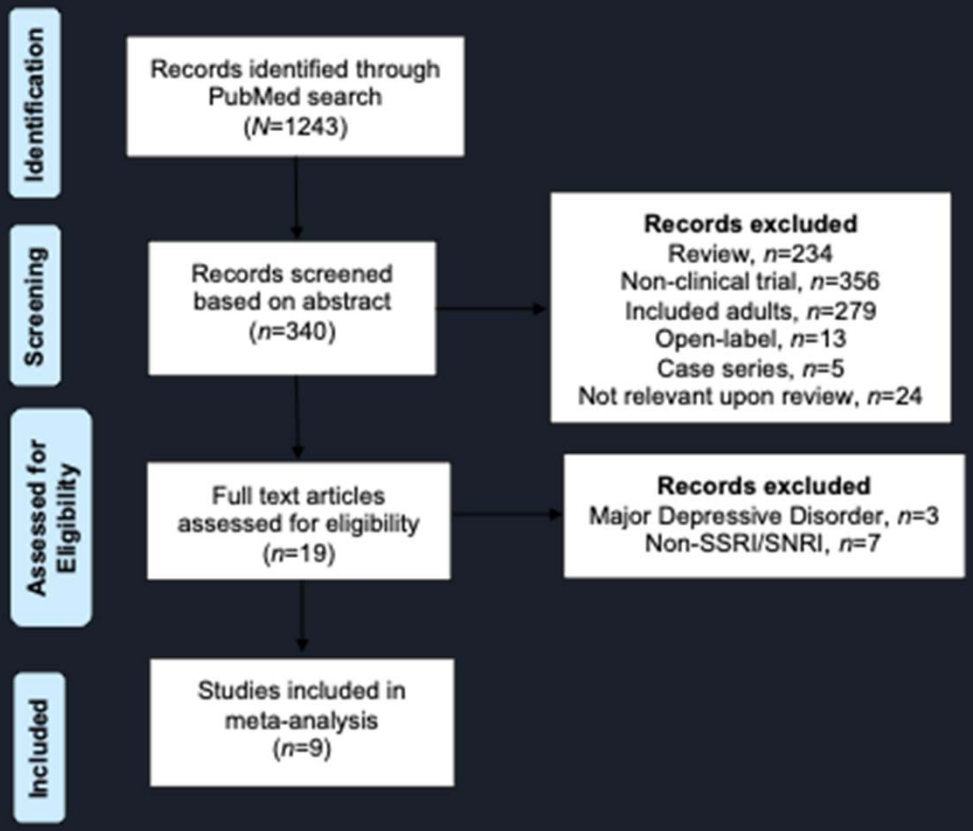
To determine the trajectory and magnitude of antidepressant response as well as the effect of antidepressant class and dose on symptomatic improvement in pediatric anxiety disorders.

Method

- Weekly **symptom severity data** were extracted from randomized, parallel group, placebo-controlled trials of SSRI and SNRI between 1966 and 2017 in pediatric anxiety disorders. (GAD, Social Anxiety Disorder, Separation Anxiety Disorder)
  - Integrated 9 double blind RCT (1,805 children, 8 antidepressants and placebo)
- **Treatment response** ; was modeled for the standardized change in continuous measures of anxiety using Bayesian updating.
- Change in symptom severity was evaluated as a function of time, class and, for SSRIs, standardized dose.

Statistical Methods

- Relative treatment effects were modeled using a Bayesian inferential approach
- Endpoint was typically week 8 to 12; except for two 16-week trials
- Low v High dose ; sertraline 120mg/d, fluvoxamine 100mg, paroxetine 20mg, fluoxetine 33mg

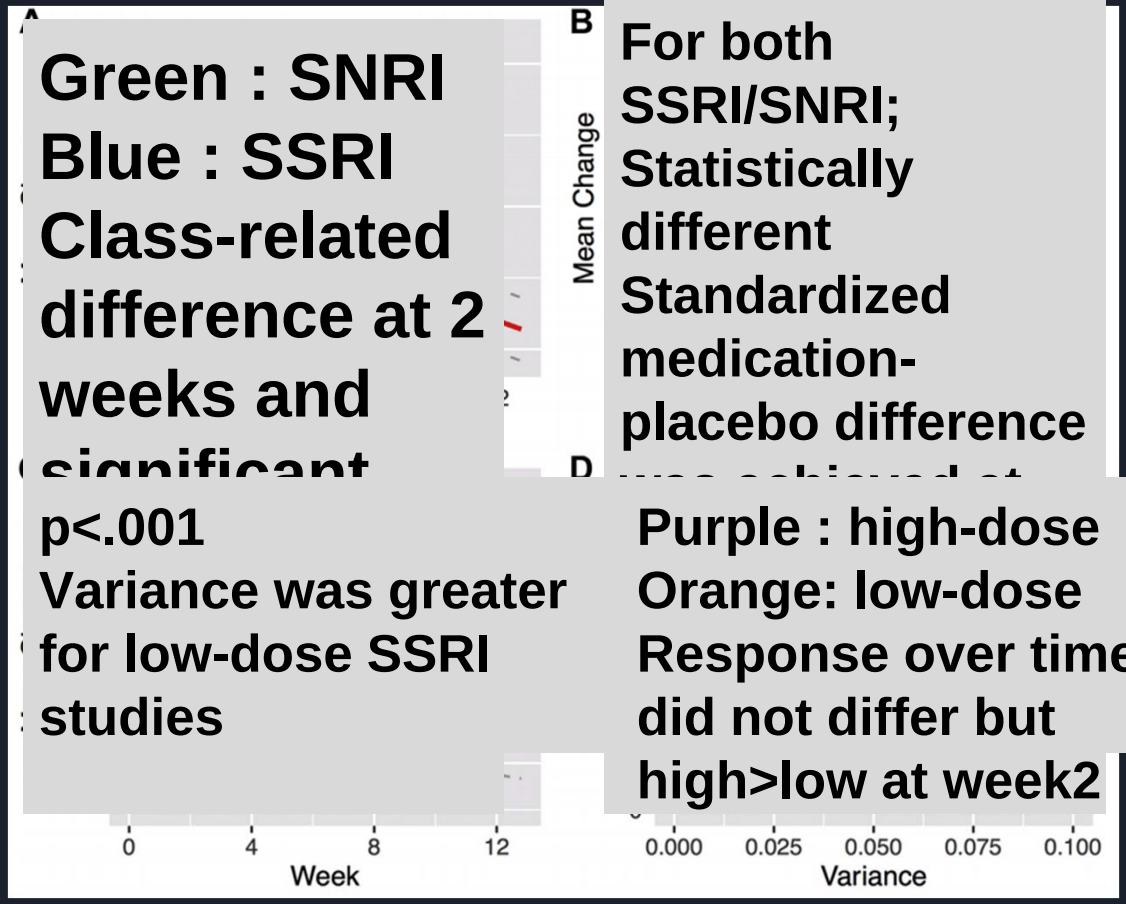

Identification
Records identified through PubMed search (N=1243)
Screening
Records screened based on abstract (n=340)
Records excluded
Review, n=234
Non-clinical trial, n=356
Included adults, n=279
Open-label, n=13
Case series, n=5
Not relevant upon review, n=24
Assessed for Eligibility
Full text articles assessed for eligibility (n=19)
Records excluded
Major Depressive Disorder, n=3
Non-SSRI/SNRI, n=7
Included
Studies included in meta-analysis (n=9)

Author	Publication Year	Recruitment Start Year	Funding	Group, n	Duration, wk	Sex, % male	Age Range, y	Medication	Outcome Measure	Endpoint Dose, mg/d	Maximum Dose, mg/d	High Dose SSRI	Medication–Placebo Attrition Difference
Rynn et al.[12]	2001	NR	Federal	11 11	9	67	5–17	Sertraline	HAM-A	50	50	No	9.1%
Birmaher et al.[17]	2003	1997	Federal	37 37	12	46	7–17	Fluoxetine	PARS	20	20	No	8%
RUPP[14]	2001	1997	Federal	63 65	8	51	6–17	Fluvoxamine	PARS	4.0±2.2[b]	300	Yes	6%
March et al.[13]	2007	2003	Industry	137 148	16[a]	44	8–17	Venlafaxine ER	SAS-CA	142	225	N/A	8.0%
Rynn et al.[11]	2007	2000	Industry	157 163	8	58	6–17	Venlafaxine ER	PARS	NR	225	N/A	1.6%
Walkup et al.[15]	2008	2003	Federal	133 76	12	53	7–17	Sertraline	PARS	133	200	Yes	1.4%
Wagner et al.[18]	2004	1999	Industry	163 156	16[a]	50	8–17	Paroxetine	PARS	32.6	50	Yes	9.4%
Strawn et al.[16]	2015	2010	Industry	135 137	10	47	7–17	Duloxetine	PARS	53.6	120	N/A	<1%
Geller et al.[42]	2007	2003	Industry	87 89	12	65	7–17	Atomoxetine	PARS	1.3[b]	120	N/A	1.7%

Note: *DBPCT = double blind, placebo-controlled trial; HAM-A = Hamilton Anxiety Rating Scale; PARS = Pediatric Anxiety Rating Scale; SAS-CA = Social Anxiety Scale for Children and Adolescents; pbo = placebo; NR = not reported.*

[a]*This was a 16-week trial, however, 12-week data were used for the analyses described herein.*

[b]*Dose is mg/kg/day, rather than mg/day.*



Green : SNRI
Blue : SSRI
Class-related difference at 2 weeks and significant

p<.001
Variance was greater for low-dose SSRI studies

For both SSRI/SNRI; Statistically different Standardized medication-placebo difference

Purple : high-dose
Orange: low-dose
Response over time did not differ but high>low at week2

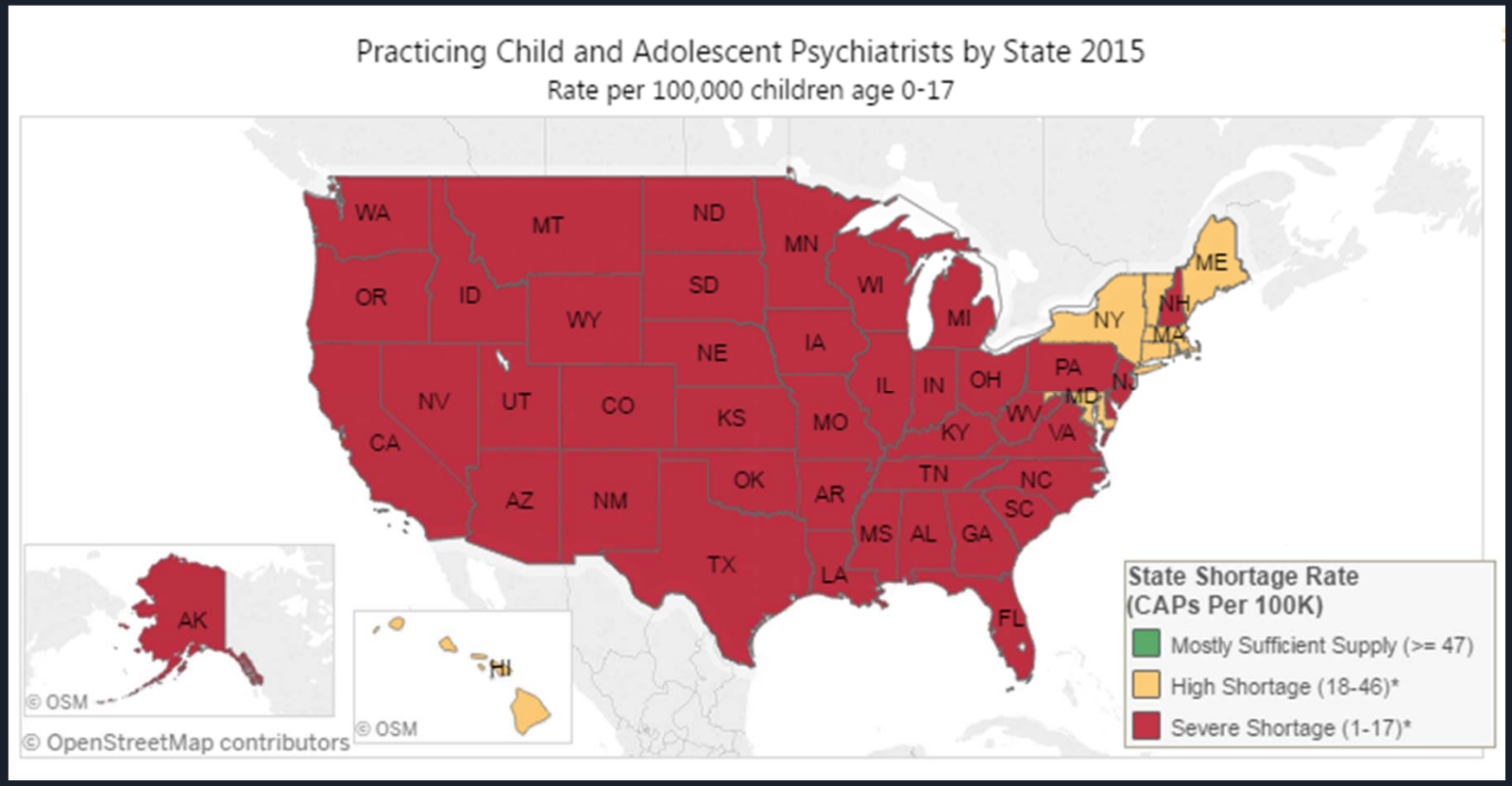
Summary

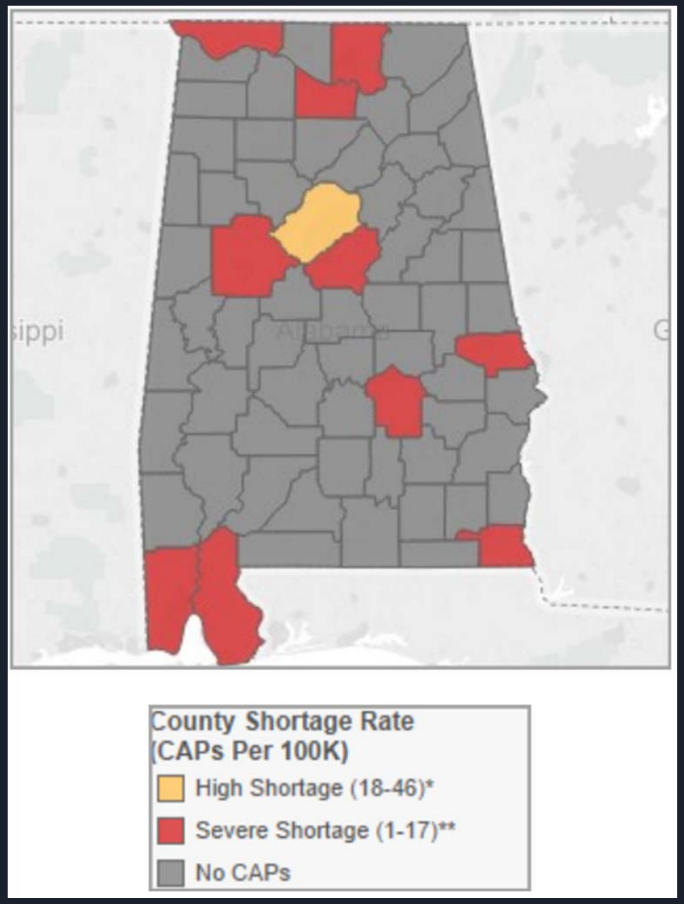
- Anxiety symptoms statistically separated from placebo as early as 2 weeks with clinically significant separation by 6 weeks.
- SSRI showed a larger response than SNRI
- Use SSRI as the first-line treatment for childhood anxiety

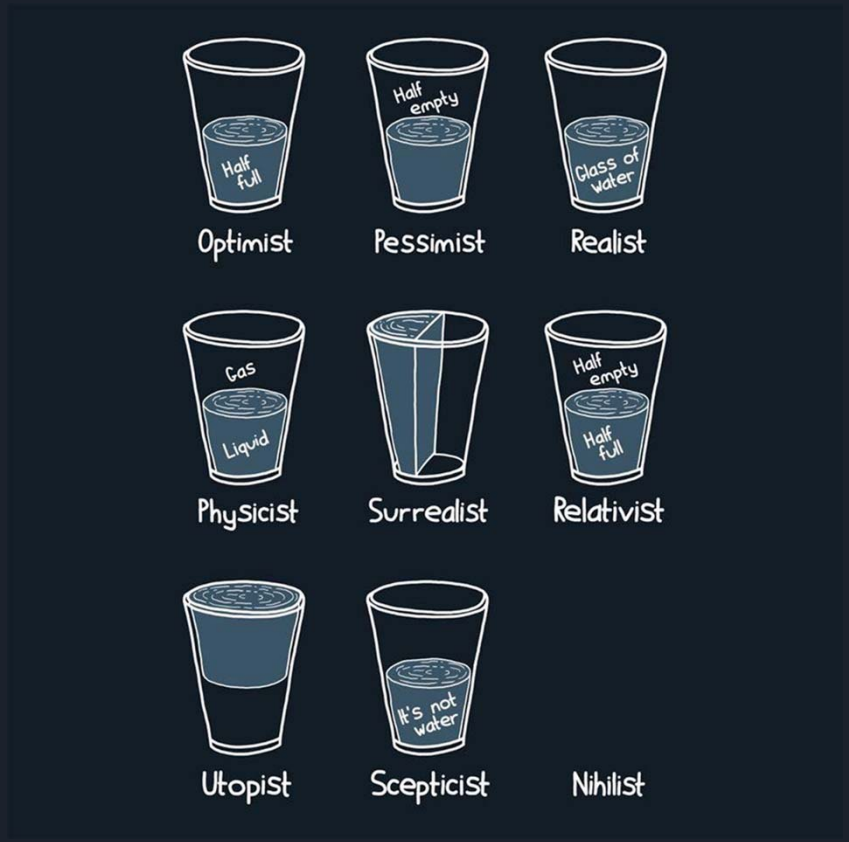
Great! I will refer patients to psychiatrist!

but...

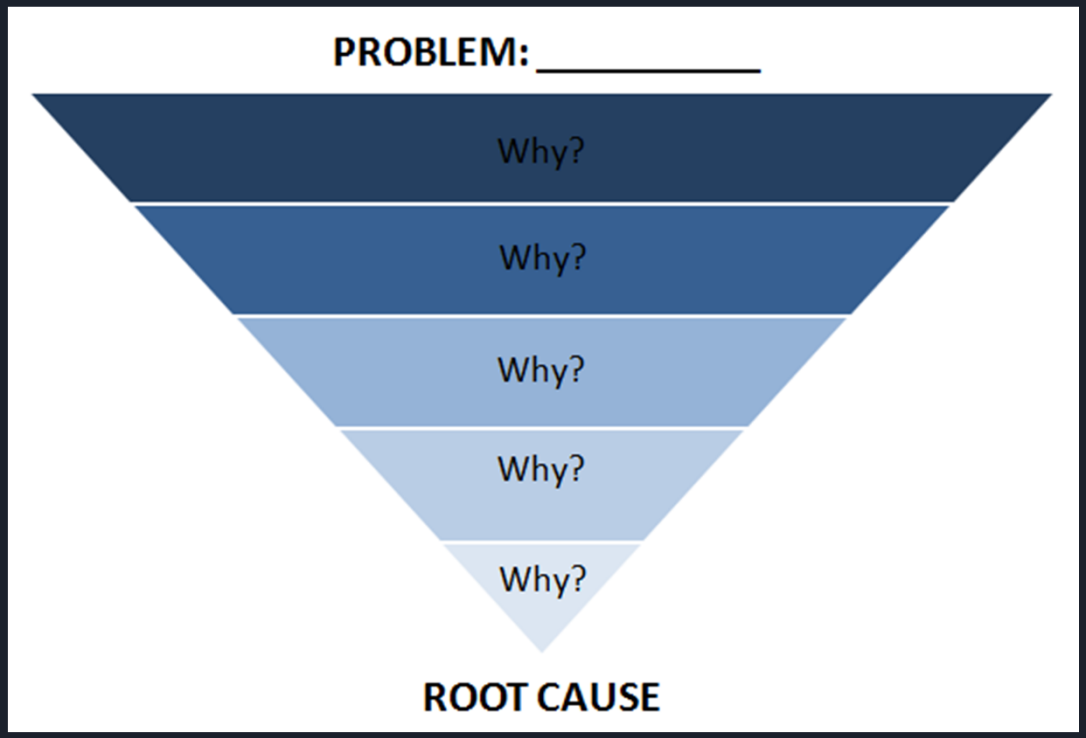

The Psychiatrist Population in the United States:
30K
60 Million Americans live with Mental Illness
To Treat Its Population, The US Needs
75K
Thousands more psychiatrists are needed
From 1995 - 2013 The US Population Grew
50


Practicing Child and Adolescent Psychiatrists by State 2015
Rate per 100,000 children age 0-17
WA
MT
ND
MN
OR
ID
SD
WI
MI
WY
NY
ME
NH
MA
NE
IA
PA
NJ
NV
UT
CO
KS
MO
IL
IN
OH
MD
WV
CA
KY
VA
AZ
NM
OK
AR
TN
NC
SC
MS
AL
GA
TX
LA
FL
AK
HI
© OSM
© OSM
© OpenStreetMap contributors
State Shortage Rate
(CAPs Per 100K)
Mostly Sufficient Supply (>= 47)
High Shortage (18-46)*
Severe Shortage (1-17)*


County Shortage Rate
(CAPs Per 100K)
High Shortage (18-46)*
Severe Shortage (1-17)**
No CAPs


Half full
Optimist
Half empty
Pessimist
Glass of water
Realist
Gas
Liquid
Physicist
Surrealist
Half empty
Half full
Relativist
Utopist
It's not water
Scepticist
Nihilist

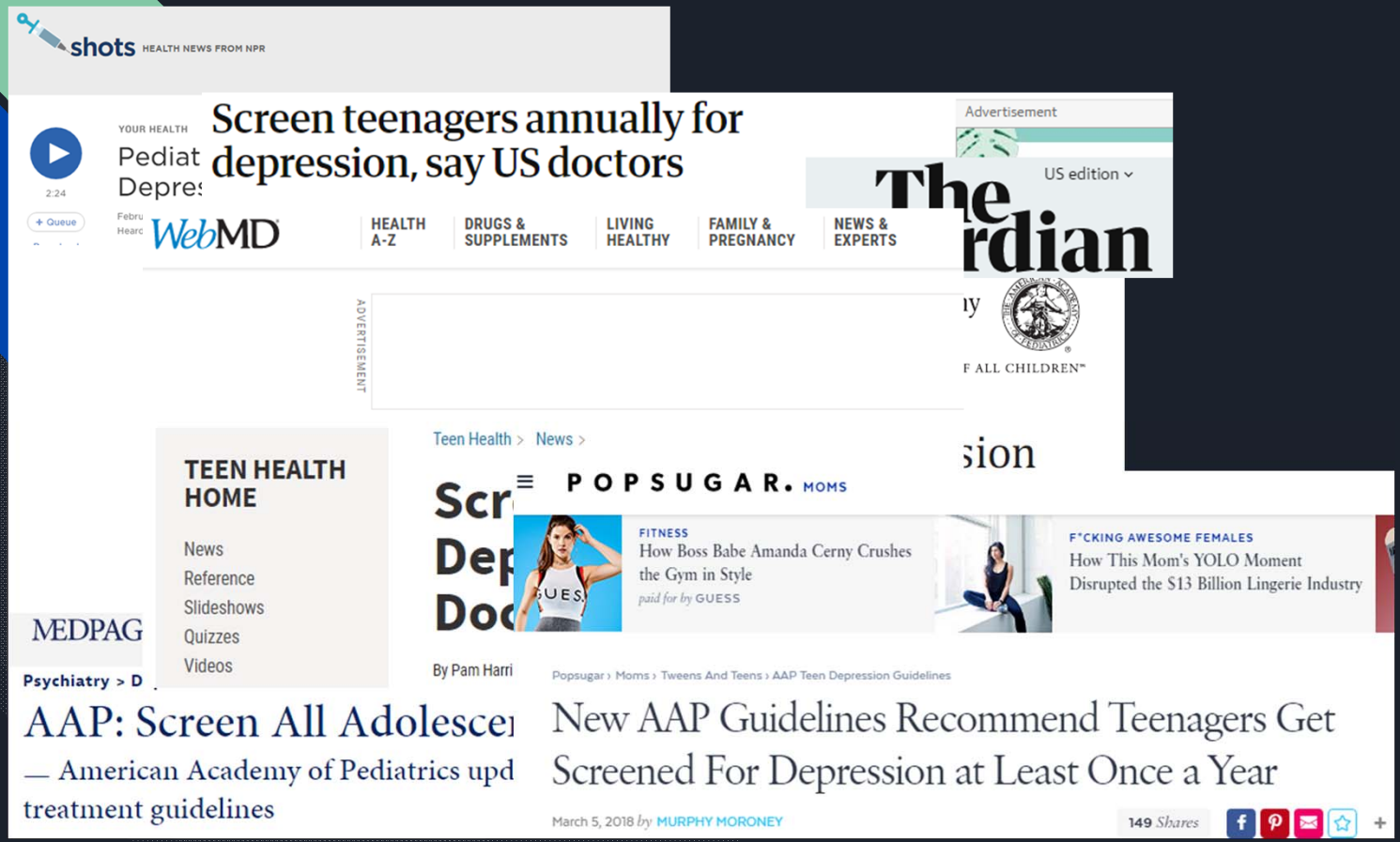

What
Can
I Do


PROBLEM: _____
Why?
Why?
Why?
Why?
Why?
ROOT CAUSE


Thoughts
create feelings
Feelings
create
Behaviour
Behaviour
reinforces
thought


THE AMERICAN ACADEMY OF PEDIATRICS

Guidelines for Adolescent Depression in Primary Care (GLAD-PC)


shots HEALTH NEWS FROM NPR
Screen teenagers annually for depression, say US doctors
Advertisement
US edition
WebMD
HEALTH A-Z
DRUGS & SUPPLEMENTS
LIVING HEALTHY
FAMILY & PREGNANCY
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TEEN HEALTH HOME
News
Reference
Slideshows
Quizzes
Videos
Teen Health > News >
POPSUGAR. MOMS
FITNESS
How Boss Babe Amanda Cerny Crushes the Gym in Style
paid for by GUESS
F*CKING AWESOME FEMALES
How This Mom's YOLO Moment Disrupted the $13 Billion Lingerie Industry
MEDPAG
Psychiatry > D
By Pam Harri
Popsugar › Moms › Tweens And Teens › AAP Teen Depression Guidelines
AAP: Screen All Adolesce
— American Academy of Pediatrics upd
treatment guidelines
New AAP Guidelines Recommend Teenagers Get Screened For Depression at Least Once a Year
March 5, 2018 by MURPHY MORONEY
149 Shares

Screening

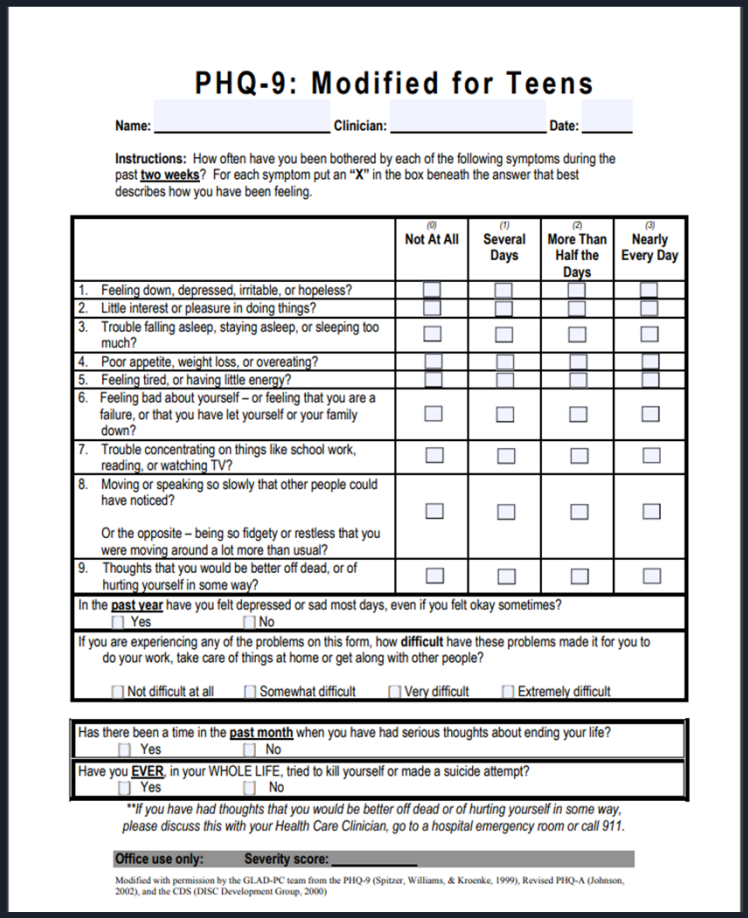
Identification

- Start at **12 years old**
- Use a **formal, self-report screening tool**
  - Can be paper or electronic
- High prevalence of adolescent depression
  - Lifetime prevalence ~20% by 20 years old
  - Can be persistent and is associated with significant problems as adults
- Only a fraction are identified in PC settings, even after USPSTF mandate on screening.
- Current guidelines suggest screening <u>at least</u> once a year.

PHQ-9
modified for teens

Available on aacap.org (free)

- PHQ-A has 2 questions asking about <u>suicidal ideation</u> and <u>attempt</u>
  - Has there been a time in the past month when you have had serious thoughts about ending your life?
  - Have you ever, in your life, tried to kill yourself or made a suicide attempt?



PHQ-9: Modified for Teens

Name: _____ **Clinician:** _____ **Date:** _____

Instructions: How often have you been bothered by each of the following symptoms during the past **two weeks**? For each symptom put an "**X**" in the box beneath the answer that best describes how you have been feeling.

	(0) Not At All	(1) Several Days	(2) More Than Half the Days	(3) Nearly Every Day
1. Feeling down, depressed, irritable, or hopeless?	☐	☐	☐	☐
2. Little interest or pleasure in doing things?	☐	☐	☐	☐
3. Trouble falling asleep, staying asleep, or sleeping too much?	☐	☐	☐	☐
4. Poor appetite, weight loss, or overeating?	☐	☐	☐	☐
5. Feeling tired, or having little energy?	☐	☐	☐	☐
6. Feeling bad about yourself – or feeling that you are a failure, or that you have let yourself or your family down?	☐	☐	☐	☐
7. Trouble concentrating on things like school work, reading, or watching TV?	☐	☐	☐	☐
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you were moving around a lot more than usual?	☐	☐	☐	☐
9. Thoughts that you would be better off dead, or of hurting yourself in some way?	☐	☐	☐	☐

In the **past year** have you felt depressed or sad most days, even if you felt okay sometimes?
☐ Yes ☐ No

If you are experiencing any of the problems on this form, how **difficult** have these problems made it for you to do your work, take care of things at home or get along with other people?
☐ Not difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult

Has there been a time in the **past month** when you have had serious thoughts about ending your life?
☐ Yes ☐ No

Have you **EVER**, in your WHOLE LIFE, tried to kill yourself or made a suicide attempt?
☐ Yes ☐ No

***If you have had thoughts that you would be better off dead or of hurting yourself in some way, please discuss this with your Health Care Clinician, go to a hospital emergency room or call 911.*

Office use only: **Severity score:** _____

Modified with permission by the GLAD-PC team from the PHQ-9 (Spitzer, Williams, & Kroenke, 1999), Revised PHQ-A (Johnson, 2002), and the CDS (DISC Development Group, 2000)

19. Which of the screening tools below screen for adolescent depression?

A. Ages and Stages Questionnaires (ASQ)

B. Patient Health Questionnaire(PHQ)-9 modified for teens

C. Screen for Child Anxiety Related Disorders (SCARED)

D. Bush-Francis Catatonia Rating Scale

Assessment

Assess for depression using DSM-5 diagnostic criteria;

- Having a **positive screen** on the formal screening tool
  - Either universal or targeted screening
- Presenting with any **emotional problem as the chief complaint**
- Those in whom **depression is highly suspected** despite a negative screening result

Grade of evidence: 3; strength of recommendation: VERY STRONG

- Refresher:
  - What are the DSM-5 criteria for depression?
    - Must have either **depressed mood** or **loss of interest/pleasure**
    - 5 of: SIG E CAPS
    - At least 2 wks duration
- **Adolescents may not clearly identify depressed mood as presenting complaint**! Be aware of common presenting symptoms that may signal MDD:
  - **Irritability**
  - **Fatigue**
  - **Insomnia or sleeping more**
  - **Weight loss/gain**
  - **Decline in academic functioning**
  - **Family conflict**

Assess depression via direct interviews with patients and families/caregivers…

- Obtain evidence of core symptoms from youth and families/caregivers separately.
  - Adolescents value their sense of privacy, confidentiality, and individuality
- Involvement of family is critical in all phases of management and should be part of the depressive disorder assessment.
  - If family involvement is determined to be detrimental, involve another responsible adult.
- Cultural backgrounds may impact presentation of core symptoms
- Collateral information from other sources (e.g. teachers) may also help.

…and include assessment of functional impairment

- Depression is associated with high rates of comorbid conditions. Assess for:
  - Substance use
  - Anxiety disorder
  - ADHD
  - Bipolar disorder
  - Physical abuse
  - Trauma
- Assess for impairment in key areas of functioning: school, home, peer settings.
- Evaluate subjective distress
- Regardless of diagnostic impression/treatment plan, always **make a safety assessment** (including for suicidality).

Treatment

Mild depression(PHQ9 <10)

- Active support and monitoring for 6-8 weeks q1-2 weeks
- Start with basics ; eat healthy, sleep well, regular exercise and leisure activities
- psychoeducation, supportive counseling, facilitate parental and patient self-management, refer for peer support, and regular monitoring of depressive symptoms and suicidality

If improved after 6-8 weeks

- cont to monitor for 6-24months with regular follow-up whether or not referred to mental health specialist
- maintain contact with mental health specialist if such treatment continues

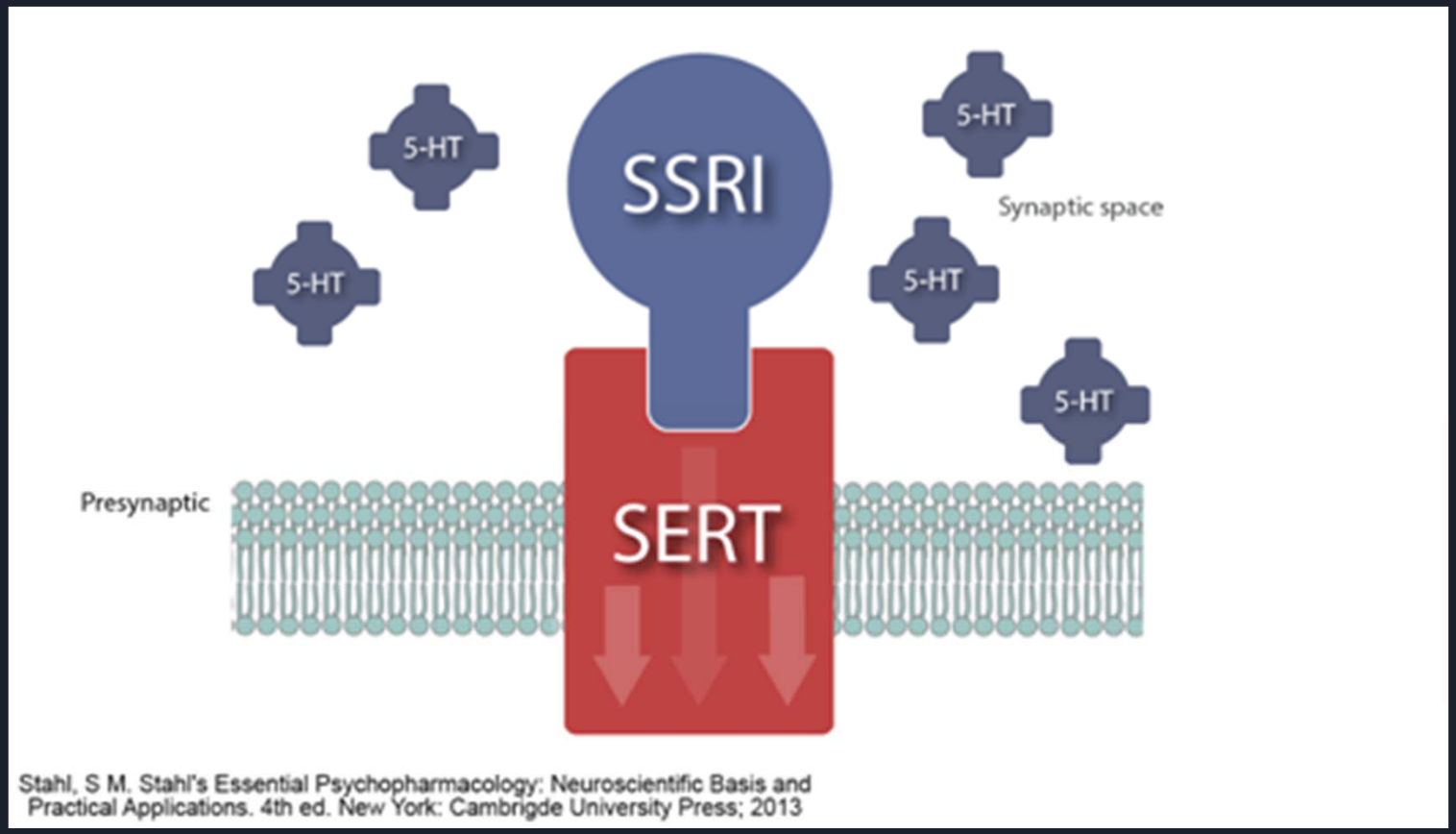
Moderate(PHQ9 10-14) to Severe Depression(>=15)

- Start with recommendations for mild depression
- Consider mental health consultation
- **Managing in Primary Care**

1. Initiate medication and/or therapy in primary care
    - **antidepressant** and/or **psychotherapy**

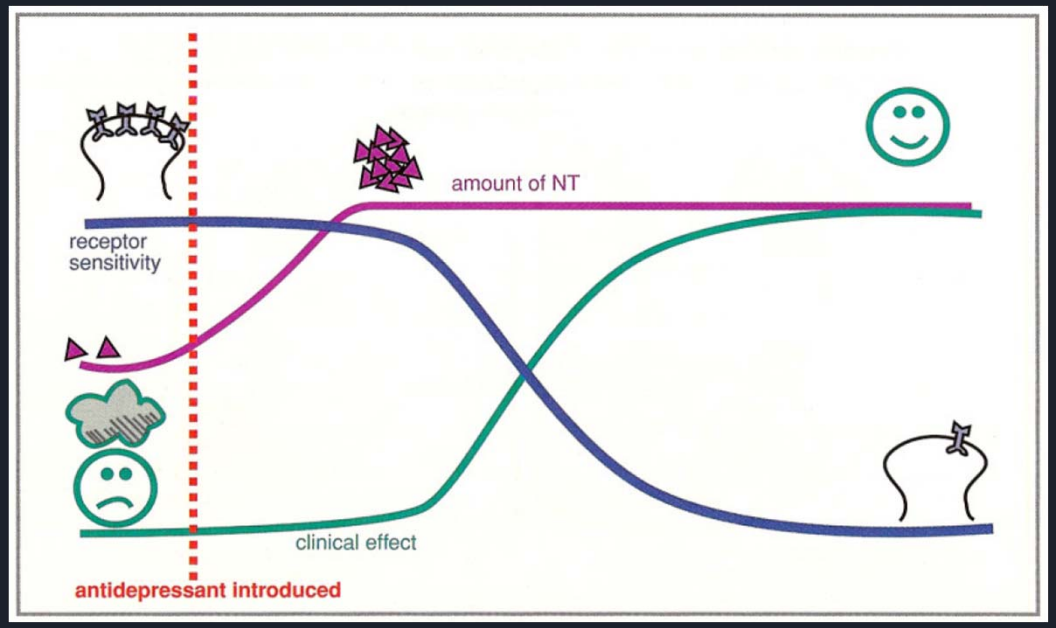
2. Monitor for symptoms and adverse events

    - increased suicidal ideation, agitation, or induction of mania

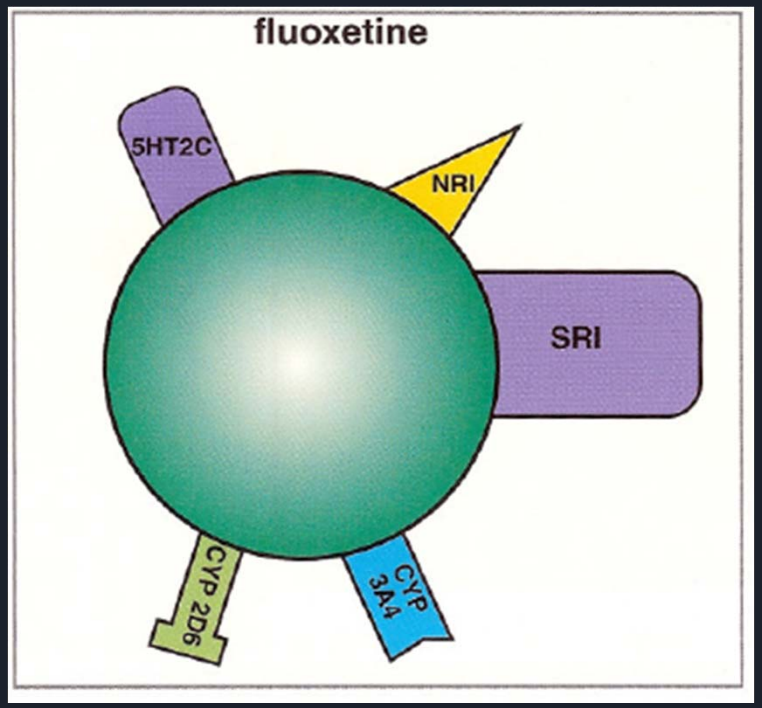


Stahl, S M. Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Applications. 4th ed. New York: Cambrigde University Press; 2013

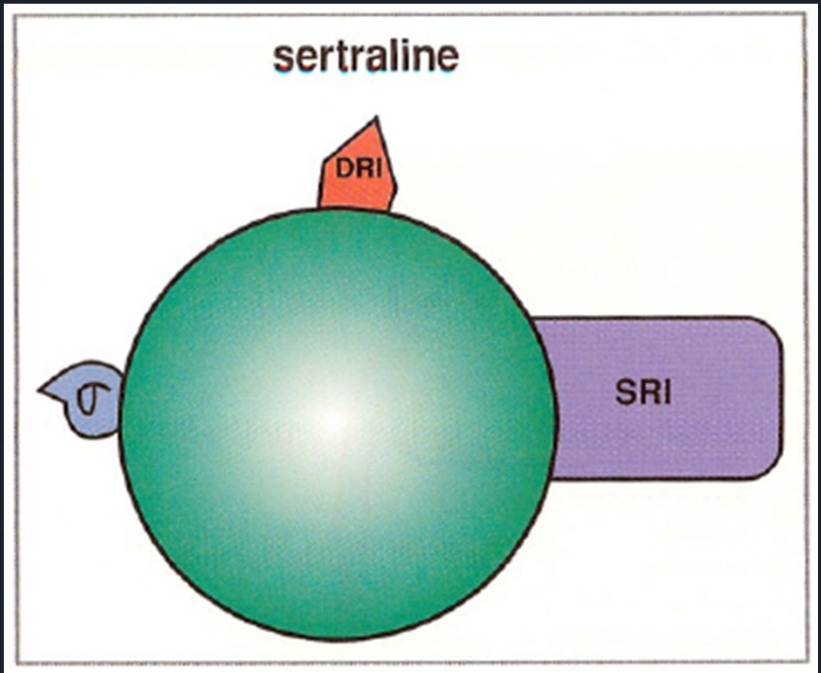
Time Course of Antidepressant effect



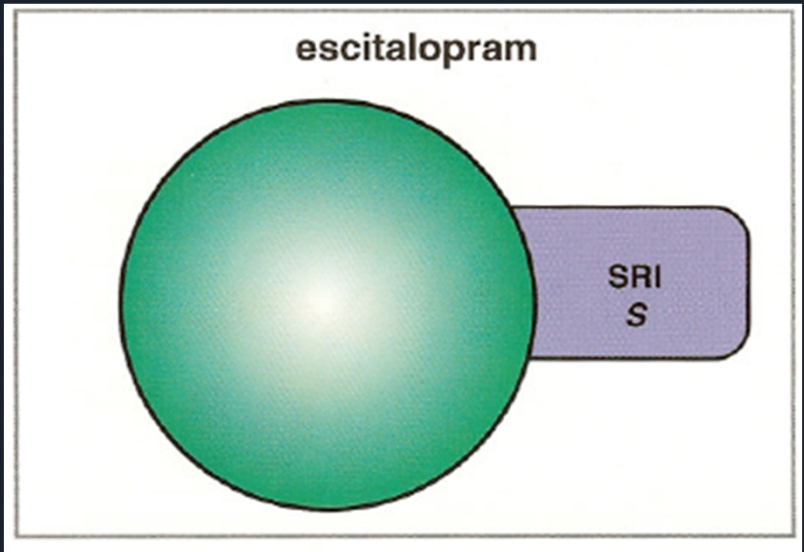
Stahl's Essential Psychopharmacology, Stahl 2013



- 5HT2C antagonist
  - Disinhibit NE and DA release
  - Activating, improves attention
  - Boost olanzapine when used together
- Weak NE reuptake inhibitor
  - At very high dose
- Inhibition of CYP450 2D6
  - Parent compound
  - Reduce withdrawl reaction
- Inhibition of CYP450 3A4
  - Active metabolite



- Dopamine transporter inhibition
  - Energy, motivation, concentration
  - Activating
- Sigma 1 receptor binding
  - ??
  - Anxiolytic effect
  - Antipsychotic
- ?CYP450 2D6 inhibitory properties
  - In high dose



- Removed unwanted R enantiomer from racemic citalopram(Celexa)
  - Antihistamine properties
  - Inhibition of CYP450 2D6
- Improve efficacy in lower doses
- Pure SERT inhibition
- Best-tolerated SSRI with fewer CYP450 mediated drug interaction

20. Which cytochrome p450 enzyme does fluoxetine inhibit?

A. CYP2C8

B. CYP2B6

C. CYP2D6

D. CYP2A6

FDA approved indication in children

Name	Duloxetine (Cymbalta)	**Escitalopram (Lexapro)**	**Fluoxetine (Prozac)**	**Sertraline (Zoloft)**	Olanzapine+ Fluoxetine (Symbyax)	Fluvoxamine (Luvox)	Clomipramine (Anafranil)
Diagnosis (age)	Generalized Anxiety Disorder	**Major Depressive Disorder (MDD)**	**MDD OCD**	**OCD**	Bipolar Depression	OCD	Obsessive Compulsive Disorder (OCD)
Age	7 and older	**12 and older**	**8 and older 7 and older**	**6 and older**	10 and older	8 and older	10 and older

Medication Dosing Guideline

Drug Name	Dosage Form	Usual starting dose for adolescent	Increase increment (after ~4 weeks)	RCT evidence in kids	FDA depression approved for children?	Editorial Comments
Fluoxetine (Prozac)	10, 20, 40mg 20mg/5ml	10 mg/day (60mg max)*	10-20mg**	Yes	Yes (Age ≥8)	Long 1/2 life, no side effect from a missed dose
Fluoxetine considered first line per the evidence base in children						
Sertraline (Zoloft)	25, 50, 100mg 20mg/ml	25 mg/day (200mg max)*	25-50mg**	Yes	No	May be prone to side effects when stopping
Escitalopram (Lexapro)	5, 10, 20mg 5mg/5ml	5 mg/day (20mg max)*	5-10mg**	Yes	Yes (Age ≥12)	The active isomer of citalopram.
Escitalopram and Sertraline considered second line per the evidence base in children						

21. Which Selective Serotonin Reuptake Inhibitor (SSRI) is approved by Food and Drug Administration(FDA) to treat major depressive disorder in a nine-year-old?

A. Fluvoxamine (Luvox)

B. Sertraline (Zoloft)

C. Escitalopram (Lexapro)

D. Fluoxetine (Prozac)

Evidence-based psychotherapy

- Cognitive Behavioral Therapy (CBT)
  - TADS trial showed combination of CBT and fluoxetine led to best result
  - Very little data comparing forms of psychotherapy in head to head trials

Safety Plans

- Restrict lethal means
- Engage a concerned 3rd party/assess for adequate adult supervision/support
  - Get agreement to help remove lethal means (e.g. meds, firearms) from area.
- Warn patients of disinhibiting effects of drugs/alcohol
- Develop an emergency communication mechanism
  - Develop with adolescent/families: includes list of persons/services they can contact if they deteriorate or are in acute crises (actively suicidal or danger to others)
  - Especially important during initial treatment, when safety concerns are highest
- Establish f/u within a reasonable period of time

Local crisis support/hospital services around UAB

- Anyone with a mental health question or concern regarding a child or adolescent is encouraged to contact the PIRC at **205-638-PIRC (7472)**
- PIRC is open seven days a week, year-round from 8 a.m. to 11 p.m.
- Anyone experiencing a crisis should call **911** or go to the nearest Emergency Room.
- Anyone experiencing suicidal thoughts should call the 24-hour, 7 day a week National Suicide Prevention Lifeline number at **1-800-273-TALK (8255)**.

Services provided by PIRC

- Access to a database of state agencies and services, linking patients and their loved ones to mental health services primarily in Jefferson, Shelby, St. Clair, Blount, and Walker counties
- Assess risk factors i.e., imminent danger
- Answer questions about mental health issues
- Provide community resource information
- Provide information about Emergency Room visits
- Safety Planning for future crises
- Follow up phone calls to confirm recommendations were followed

Services NOT provided by PIRC

- Over-the-phone diagnoses or psychiatric evaluations
- Over-the-phone scheduling or rescheduling of outpatient appointments
- Home visits
- Transportation
- Prescriptions or refills

Additional Resources

REACH Institute www.thereachinstitute . org

Child and Adolescent Psychology for PC www.cappcny. org

ADMSEP modules http://www.admsep.org

Seattle Children's Primary Care Principles for Child Mental Health

https://www.seattlechildrens.org/globalassets/documents/healthcare-professionals/pal/wy/wy-pal-care-guide.pdf

Thank you

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