Depression and Anxiety in Children and Adolescents: Earlier Identification, More Effective Treatment

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- No financial interest in any medications or products discussed in this presentation.
- Some medication uses discussed are not FDA-approved indications.
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Overview

- Principles appropriate across diagnoses
- Depression
  - Risk for Suicide
- Anxiety

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Early, Effective Treatment vs. "Watchful Waiting"

- Earlier intervention is central to improved outcomes in healthcare:

Myocardial infarction	- time to arrival at hospital
Stroke	- tPA within 3 hours
Cancer	- Outcomes in Stage I vs Stage IV

- Early treatment = Secondary Prevention.
  - Positive change in life-long health and function
- Early treatment modalities are low-risk.
  - Wellness. Sleep, exercise, social relationships
  - Improved family communication
  - Psychotherapy – individual and family

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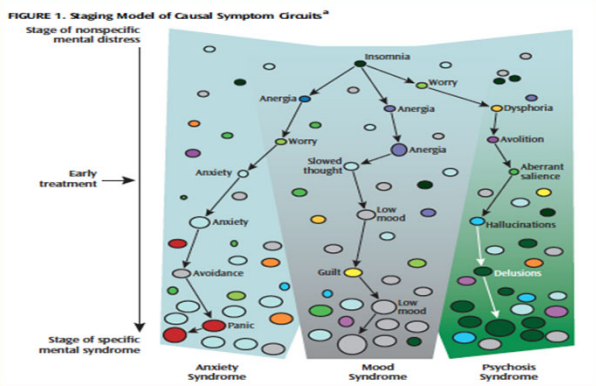
Many disorders progress from non-specific to more impairing stages. McGorry PD, et. al.



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Early treatment often requires that we start when the diagnosis is unclear.

- Diagnosis may help guide treatment, but interventions often have cross-diagnostic effects.
- Focus on symptoms that are impairing development and function, i.e.:
  - Family relationships
  - Peer relationships
  - Ability to learn
  - Positive sense of self

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Stages of Illness Development

Stage	Definition	Target Populations, Referral Sources
0	Increased risk, No symptoms	Possible family concerns
1a	Mild or non-specific symptoms. Mild functional decline	May be Identified by schools, primary care, family
1b	Moderate but sub-threshold symptoms. Moderate functional decline (e.g. GAF <70)	Referred by PCPs, schools, family, child welfare agencies, law enforcement
2	First Episode of full disorder Mod-Severe symptoms Serious functional decline	Primary Care, EDs, Mental Health Centers, Subst Abuse programs, Hospitals
3	Recurrent or Persistent Disorders	Mental health clinics, Psychiatric hospitals
4	Severe, Persistent, and Unremitting illness	Mental health clinics, Psychiatric hospitals

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Stepped Care and Stages of illness

Stage	Treatment	Site
0	Improved mental health literacy Family, Subst abuse education Brief cognitive skills training	Primary care, schools, other
1a	Mental health literacy/eHealth Problem solving and support Family psychoeducation Substance misuse reduction Exercise	Primary Care, Behavioral Health Integration
1b	Evidence-based psychotherapy Family psychoeducation Substance abuse reduction Medication as indicated (distress, impairment)	Mental health clinic or practice
2	Evidence-based psychotherapy Family psychoeducation Substance abuse reduction Medication as indicated	Mental health clinic or practice
3, 4	Comprehensive, intensive treatment	Intensive outpatient services, hospital

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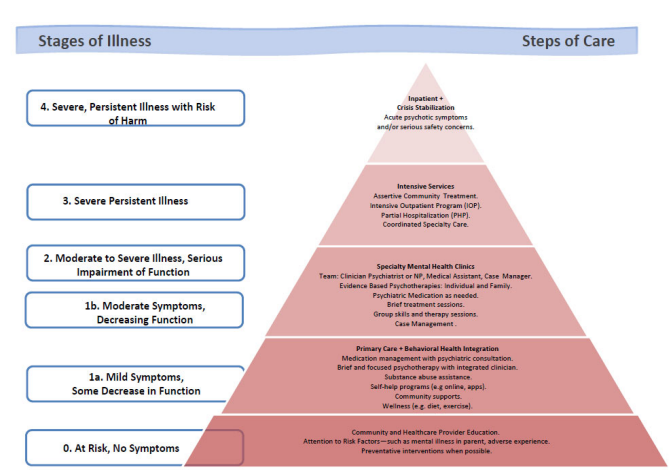
Maine Behavioral HealthCare



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Adverse Childhood Experience

- Traumatic experience and disrupted parenting relationships can:
  - Precipitate or exacerbate most mental illness, as well as physical illness (Obesity, COPD, Hepatitis…)
  - Can be factor in treatment-refractory mental illness
  - ACE score of >4:
    - 460% more likely depressed
    - 1,220% more likely to attempt suicide
  - https://www.childhealthdata.org/docs/default-source/cahmi/aces-resource-packet_all-pages_12_06-16112336f3c0266255aab2ff00001023b1.pdf

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Treatment for depression helps. We need to do better.

- Effective treatments: Over 70% respond to initial treatment.
  - Best: Combined Therapy and Medication:
    - Cognitive Behavioral Therapy plus SSRI
- But 30-40% of depressed adolescents do not respond to initial treatment.
- Response is often incomplete. Only one third achieve complete remission.
- Depression is a recurring illness.
  - Persisting symptoms = increased risk for recurrence.
  - At least ¼ of those improve will relapse within 5 years.

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Assessment

- Mood may be irritable rather than sad.
  - May present due to conflict with parents, peers, teachers.
- Somatic complaints are very common – e.g. headache, abdominal pain.
  - Depression magnifies perception of physical discomfort
- Drop in school performance due to poor concentration, loss of interest, pleasure, lower motivation.
- Decreased participation in sports, activities, social contacts.
  - Anhedonia, Low energy -
- In medically-ill, poor compliance with treatment.

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Assessment

- Multiple sources of information.
  - Interview child/adolescent alone.
    - Best source of subjective mood, thoughts of self-harm
  - Parent
    - Best source of information on behavioral changes, school function, withdrawal from peers, observed low energy
  - School report
    - Concentration, memory, level of interest (anhedonia), social interactions

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Rating Scales: Broad symptom surveys.

- Rating scales support, but do not make, a diagnosis.
- Clinical interview and history are key.
- Scales help monitor improvement.
  - Pediatric Symptom Checklist (PSC)
    - Public domain – free.
    - http://www.brightfutures.org/mentalhealth/pdf/professionals/ped_symptom_chklst.pdf
  - Behavior Assessment System for Children – (BASC-2). More detailed.
    - www.pearsonassessments.com
  - Child Behavior Checklist – (CBCL). Parent-, teacher-, and self-rated
    - www.aseba.org

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Rating Scales – Depression rating scales:

- PHQ-A Patient Health Questionnaire for depression, adapted to adolescents.

https://www.uacap.org/uploads/3/2/5/0/3250432/phq-a.pdf

- Free- Public domain
- Self-rated. Quick, easily scored.
- http://www.integration.samhsa.gov/images/res/PHQ%20-%20Questions.pdf

- Center for Epidemiological Studies – Depression (CES-D)
  - Free – Public domain
  - http://www.assessments.com/catalog/CES_D.htm
  - Self-rated . 10 minutes
  - 4 Factors: Depressed affect, Somatic, Positive affect, Interpersonal relationships

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Psychotherapy is under-used.

Best results if parents participate.
Limited effects of treatment if others in family are symptomatic.

Cognitive Behavioral Therapy (CBT)

- Focused on specific symptoms, functional impairment
- Relates Thoughts, Behaviors, and Feelings
- Specific strategies. Therapist as "Coach"

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Family Psychoeducation - Education for parents, Family Therapy

- Well-meaning families may miss symptoms, or become judgmental or irritated.
- Resources:
- Books
  - Raising a Moody Child: How to Cope with Depression and Bipolar Disorder. Mary Fristad and Jill Goldberg Arnold
  - Treating Child and Adolescent Depression. Joseph Rey and Boris Birmaher
- Web – Family Talk – William Beardslee
  - http://www.fampod.org/

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Family involvement is essential.

- CBT is effective, but not for adolescents with a currently depressed parent. (Garber J, et.al., 2009)
  - We must help the parent help the child.
- Mood disorders have high levels of heritability.
  - Very likely to find a parent with a mood or anxiety disorder, substance abuse.
- Avoid blaming parents, even if they complicate treatment.
  - They did not choose to be ill.
- Family transitions, losses, relationship difficulties – associated with onset of depression and with suicide.

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Substance Abuse worsens depression; decreases treatment effectiveness

- CRAFTT – Screening tool
  - A. Past 12 months, Any alcohol, cannabis, anything else to get high?
  - B: (2+ = further assessment)
    - In a Car?
    - Used to Relax, feel better about yourself, fit in?
    - Used Alone?
    - Ever Forget things while using?
    - Friends or Family ever said to cut down?
    - Ever got into Trouble while using?
- http://www.coloradohealthpartnerships.com/provider/care/CRAFFT.pdf
- Cannabis
  - Likely both self-medication and an exacerbating factor
  - Increases risk of mental illness in those with at risk
  - Decreases response to treatment
- Alcohol
- Increased risk of Opiate dependence and other drug abuse.

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Medications - SSRIs

- Fluoxetine - clearest evidence of efficacy (FDA).
  - Alone or with CBT decreases suicidal ideation. CBT + Flx decreases SI more than Flx alone.
  - Accelerates recovery in combination with CBT
  - CBT + Fluoxetine – fewer self-harm events
  - Effective relapse prevention
    (TADS, Emslie G et.al. 2004, 2007, 2008,2010,)
  - Challenge re: efficacy and safety – Cipriani A, et.al. Lancet 2016.
    - Questionable effectiveness of all but fluoxetine
- Likely similar effectiveness of Sertraline, Citalopram, Escitalopram, Fluvoxamine
  - Cochrane reports
  - No difference in effect between citalopram and escitalopram
  - Paroxetine – shorter half-life, more adverse effects.
    - Increased association with suicidal thinking or "harm-related" symptoms. But no assoc. with suicide
- No increased risk of suicide attempts in fluoxetine sertraline, citalopram, escitalopram, paroxetine, venlafaxine

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Medications - Other

- Buproprion (Wellbutrin)
  - Effective in ADHD
  - Open trial – effective in adolescents with MDD. (Davis, et.al., 2006)
- Venlafaxine (Effexor) – Effective in TORDIA study. Less rapid improvement than with SSRIs.
- Desvenlafaxine (Pristiq) – effective in adoles MDD. No comparison study vs venlafaxine
- Mirtazapine (Remeron) - no efficacy vs placebo in children and adolescents (Cheung AH, 2005, 2006)
- Duloxetine (Cymbalta) – inconclusive study in adolescents

- Overview –Garland EJ, et.al.,2016; 25(1): 4–10. Update on the Use of SSRIs and SNRIs with Children and Adolescents in Clinical Practice. J Can Acad Child Adoles Psychiatry.

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Fluoxetine – Practical guidelines

- Discuss adverse effects – Annoying, but not dangerous.
  - GI distress – minimal w. food and low starting dose
  - Activation/agitation. Can present as anxiety, irritability
  - Decreased libido. Patients may notice a change, and that it is temporary. Talk about it.
  - Black box warning re Suicide.
    - Minimal if any risk. SSRIs are protective against suicide.
- Discuss cannabis and other subst use.
  - Pros and Cons. Motivational interviewing, vs. lecture.
- Long-term use is safe for children and adolescents.
  - Not often needed.

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Fluoxetine – Practical guidelines - 2

- Dose:
  - Starting – 10 mg each AM x 1 week, then 20 mg x 2 weeks, 30 mg x 2 weeks, then 40 mg q d.
  - If adverse effects, slow down or back up.
    - Lower doses may be effective.
  - Slower titration for patients and parents more likely to be anxious about adverse effects.
    - Consider comorbid anxiety disorders
  - For relatively severe depression, faster titration,
    - e.g. 10 mg x 3 days, then 20 mg x 1 week, then 40 mg q d
  - Take in AM because activation can cause insomnia in some.

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Fluoxetine – Practical guidelines - 3

- Duration of treatment
  - Likely several days to 4 weeks for onset of effect
  - Expect to continue for several months or more
  - Goal of treatment is remission, not just improvement
  - Continue after remission for 4-6 months
- Discontinuation
  - Rare discontinuation symptoms with fluoxetine due to long half-life.
  - More common with Paroxetine (short half-life) and with Venlafaxine (Effexor) (SNRI)
  - Flu-like symptoms, hyperarousal, insomnia, nausea

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Inadequate response - Considerations

- Ineffective psychosocial treatment
  - Individual therapy, family therapy
- Substance abuse. Cannabis and alcohol.
- Possible latent bipolar disorder. Family Hx?
- Possible depression with psychosis. Depressive thinking can become delusional, or can take the form of auditory hallucinations
- If ineffective after good dose and duration:
  - Consider second SSRI. Citalopram or Sertraline

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Improvement is not Remission

- Treatment of Adolescent Depression Study (TADS)
  - Emslie, et. al. 2004, 2009
  - While response rates were robust with Fluoxetine and Fluoxetine plus CBT, remission rates were much lower – 37% with combined treatment and 23% with med alone.
  - At 36 weeks, Remission rates were similar for all treatments (55-64%) but approx 40% remained symptomatic.
  - Relapse in 30% of those improved, in following year

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Persistence:

- Educate and support parents and patients:
  The first treatment may not be effective.
  Patients may improve, but we want full recovery.
  We need to persevere until we find what works.
- Combined psychotherapy and SSRI medication
- Changes in medication may be necessary.
- Treat to full recovery. Residual symptoms increase risk of relapse.

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Suicide in Adolescents

- Increasing in Maine and nationally
- Guns – over 50% of teen suicides
- Impulsivity often.
  - Ready access to lethal means increases risk
- Unidentified pre-existing mental illness
- Substance Abuse
- Minimization of risk by adults

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Adolescent Suicide – Increasing in Maine

- https://www.maine.gov/suicide/docs/Youth-Data-Brief-2018.pdf
- https://www.maine.gov/suicide/docs/Maine-Suicide-and-Self-Injury-Databook-youth-2016.pdf

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Gun Violence – Our Responsibility

- NRA to Physicians: "Stay in your lane." Nov. 2018.
- " This is my lane!" - ED Physician
  - http://www.wbur.org/onpoint/2018/11/16/doctors-nra-gun-violence-stay-in-your-lane
- American College of Physicians, 2014, 2018. Ann. Int. Med.
  - "…firearm violence is not just a criminal justice issue, but also a public health threat that requires the nation's immediate attention."
  - 9 strategies:
  - http://annals.org/aim/fullarticle/2709820/reducing-firearm-injuries-deaths-united-states-position-paper-from-american
- NRA blocked CDC research on gun violence. – 1996.
  - https://www.npr.org/2018/04/05/599773911/how-the-nra-worked-to-stifle-gun-violence-research

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Suicide Risk - Assessment

- Direct, private interview with the adolescent. Essential.
- Increased risk with:
  - Symptoms of a major psychiatric disorder
    - Major Depressive Disorder, Bipolar Disorder, Schizophrenia, others
  - Substance abuse.
  - Family history of suicide
  - Recent awareness of suicide of peer, popular figure
- Columbia Suicide Severity Risk Scale (C-SSRS)
  - https://cssrs.columbia.edu/wp-content/uploads/C-SSRS_ChildBaseline_11.14.16.pdf
- Access to means increases risk. Guns. Automobiles.
  - Period of greatest risk of acting on suicidal impulse is often short.

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SSRIs and Suicide: Risks vs. Benefits

- Risk of suicide assoc w antidepressant meds is very small
  - No suicides in 27 studies of meds in 4500 depressed children and adolescents.
  - No emergence of suicidal symptoms with fluoxetine in TADS
  - Slight (2%) increased risk of suicidal thoughts or "harm-related behaviors" with meds vs. placebo.
- Autopsies of adolescent suicides in NY –
  - Only one of 31 on antidepressant medications – minimal blood level.
  - All untreated.
- Benefits of medication are considerable
  - Treatment – medication and/or therapy – decreases suicide rates
    - Treatment of Adolescent Depression Study (TADS), JAMA, Aug.18, 2004
    - Medications associated with lower number of suicide attempts in 24,000 adoles patients - Valuck, et.al, CNS Drugs Dec. 2004
- Untreated depression is associated with suicide. Not meds.

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Anxiety Disorders in Children and Adolescents

- Separation anxiety disorder
  - Normal sep. anxiety, approx ages 6-30 months
  - Persistence into older childhood
  - Excessive avoidance, school refusal
  - Decreased prevalence with age. May precede other anxiety disorders
- Specific phobias
  - Relatively common in early childhood
- Social phobia. Social anxiety
  - Selective Mutism

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Anxiety Disorders - continued

- Panic Disorder
  - Sudden onset, off-set
  - Prominent somatic symptoms
- Generalized Anxiety Disorder
  - Duration of over 6 months
  - Cognitive distortions. Overestimate likelihood of neg. consequences, danger
- Obsessive-Compulsive Disorder
- Post-Traumatic Stress Disorder
  - Complex PTSD
    - Recurrent or prolonged stressors
    - Re-experiencing trauma, avoidance, hyperarousal, somatic distress, insomnia, poor concentration, loss of trust in self or others

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Contributing factors

- Familial. Gene X Environment effects
  - Often prior shy, timid temperament in novel situations.
    - Jerome Kagan. Behavioral inhibition to the unfamiliar.
      If persistent – associated with anxiety disorders
    - Exacerbated by anxious parenting
- Adverse Childhood Experience – ACEs
- Social adversity.
- Bullying, Cyberbullying

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Assessment

- Multiple sources of information.
  - Symptoms may be greater in more challenging situations – home, vs. school, other unfamiliar places and relationships
  - Parents may have different experience with the same child. Not right vs. wrong
- Somatic symptoms are common:
  - GI, lethargy, tachycardia, rapid breathing, sweating
  - Not the same as malingering

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Importance of early treatment

Comorbidities:
In children and adolescents with GAD, only 13% had only one disorder.
- Depression – 62%
- ADHD -25-30%
- Oppositional behavior
- Comorbidities – more difficult to treat

Future risks
- Alcohol and other substance abuse.
- Adult anxiety disorders, Major Depressive Disorder, educational and vocational impairment
- Suicide attempts, Suicide

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Tools for assessment

- Screen for Child Anxiety Related Disorders (SCARED)
- http://www.midss.org/content/screen-child-anxiety-related-disorders-scared
- Child and Parent versions. Useful to compare

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Treatment – Psychosocial Considerations

- Support to family
  - Dilemmas in parenting an anxious child. Avoid blaming.
  - Support can become excessive accommodation, enabling.
- Identification of family members under stress
  - Note familial patterns, heritability
  - Avoid blaming.
- Stressful environments
  - Domestic conflict, violence
  - Peer environment. Bullying
  - Food insecurity

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Cognitive-Behavioral Therapy

- Exposure in supportive relationship
- Desensitization. "Baby steps". Positive reinforcement.
- Modeling alternative responses. Role playing
- Self-management cognitive strategies
  - Recognizing thinking patterns
  - Identifying somatic reactions
- RTC – 64% full remission after CBT. Gains maintained at one year. (Kendall, 1994)

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Family involvement

- Heritable. Possible anxiety disorders in parents.
- Patterns associated with anxiety in children:
  - Parent more intrusive, more negative, critical
    - Univ. ME Orono study. Jenga game
  - Parent perceived as less accepting, flexible
- Parenting style can be modified.
  - Support, modeling, and positive reinforcement

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Medications

- Selective Serotonin Reuptake Inhibitors (SSRIs)
  - Fluoxetine. 61% responders vs 35% on placebo
  - Fluvoxamine 76% response, vs 29% on placebo
  - Sertraline
- Tricyclic antidepressants – Fatal in overdose.
  - Clomipramine – effective with OCD, alone or as adjunct to SSRI
- Avoid benzodiazepines
  - Useful for time-limited stressors. Medical procedures.
  - Risk of dependency - adolescents

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Treatment goals

- Recovery, not just improvement
  - Persistence!
- Relapse prevention
  - Anticipate relapse!

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Obsessive-Compulsive Disorder

Etiology:

- Heritable component.
  - Familial links with Tourette's Disorder
- Hypothesis: Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infection (PANDAS); Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS)
  - Sudden onset, following Group A Beta-Hemolytic Strepococcal infection, or other infection
  - OCD symptoms not found to be associated with antibodies against strep. (Leckman, et.al., 2011; Murphy TK et.al., 2017)
  - Treatment with antibiotics – small n's, weak effects
  - Immunomodulation trials – IVIG, plasma electrophoresis, medications – not substantiated.
  - Review: Gilbert DL, et.al., J. Pediatrics, 2018.

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Obsessive-Compulsive Disorder

- Treatment:
  - Cognitive-Behavioral Therapy
  - SSRI medication

    (Franklin ME, et.al. (Pediatric OCD Treatment Study II (POTS II) 2011, JAMA)
- Request consultation for acute, fulminant cases, or those associated with severe delusions and other symptoms of psychosis.
- Monitoring tool. Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS)
  - https://iocdf.org/wp-content/uploads/2016/04/05-CYBOCS-complete.pdf

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Early treatment has Life-Long benefit

- Untreated anxiety and depression disorders are likely to become persistent, recurrent causes of disability.
- Early treatment, often in primary care, can have life-long positive effects.
- When in doubt, check it out.

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Resources

- Practice Parameter for the Assessment and Treatment of Children and Adolescents With Depressive Disorders
  - American Academy of Child and Adolescent Psychiatry
    - https://www.jaacap.org/article/S0890-8567(09)62053-0/pdf
- Practice Parameter for the Assessment and Treatment of Children and Adolescents with Anxiety Disorders
  - AACAP
    - https://www.jaacap.org/article/S0890-8567(09)61838-4/pdf
- Depression and Bipolar Support Alliance
    - https://www.dbsalliance.org/
  - Wellness Tracker
    - https://tracker.facingus.org/
- National Alliance on Mental Illness
  - https://www.nami.org/#
- Facts for Families - American Academy of Child and Adolescent Psychiatry
  - https://www.aacap.org/AACAP/Families_and_Youth/Facts_for_Families/AACAP/Families_and_Youth/Facts_for_Families/FFF-Guide/FFF-Guide-Home.aspx

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Resources

- MaineHealth Behavior Health Integration – Clinicians in Maine Health primary care practices.
- Maine Behavioral Healthcare
  - **844-292-0111**
  - **(207) 761-6644** or Toll Free (866) 857-6644
- D. Robbins MD
  - robbid@mainebehavioralhealthcare.org
  - 207 661-6618 – Maine Behavioral Healthcare
  - 207 405-7944

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