Depression: Treatment Considerations

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Pediatric Depressive Disorders. . .

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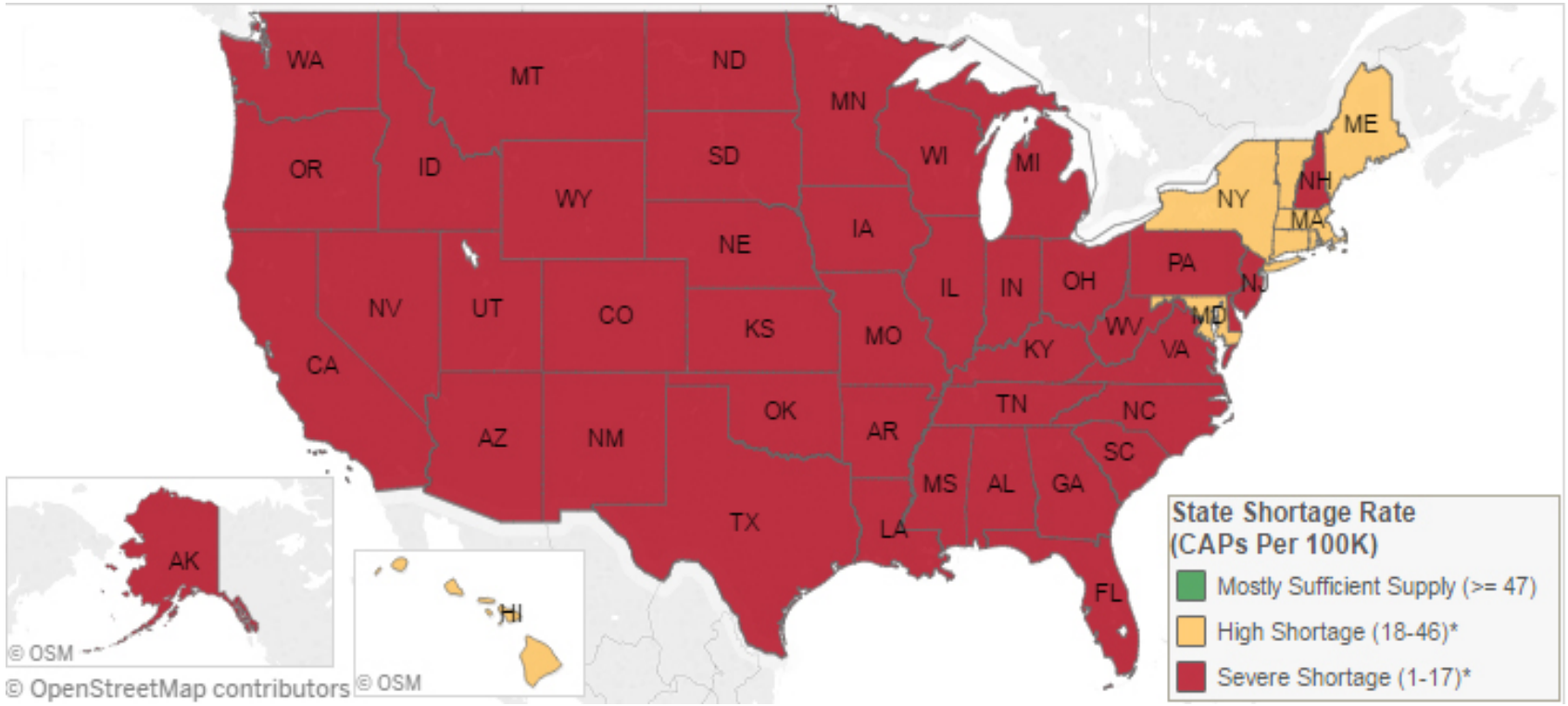
Child & Adolescent Psychiatrist Workforce Map by State (AACAP)



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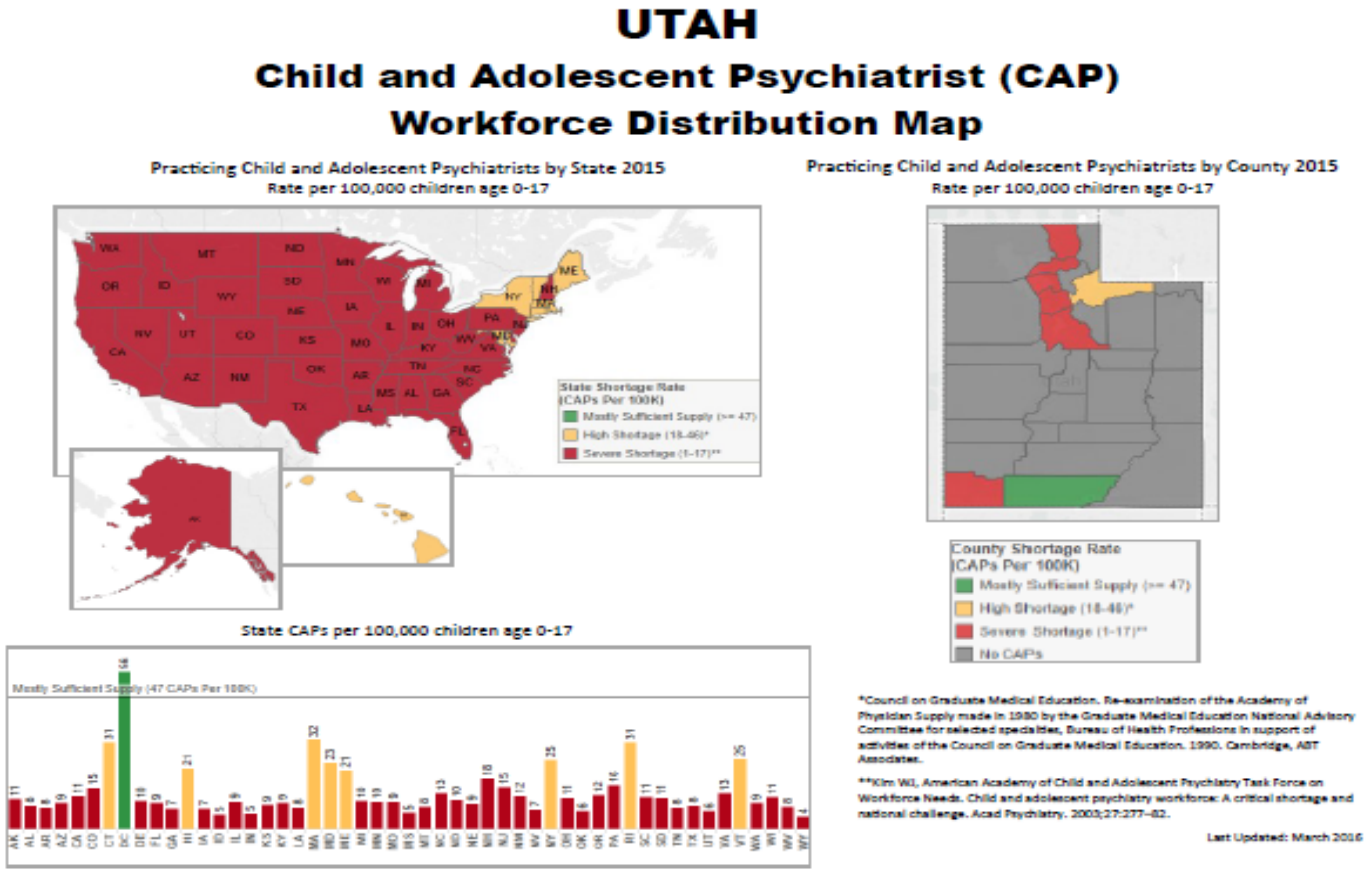
Utah Workforce Distribution (AACAP)



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Pediatric Depression Treatment

- Before starting specific interventions for mild to moderate depression, consider providing supportive clinical care for a few weeks, which may be enough to reduce depressive symptoms
  - Psychoeducation
  - Empathic listening
  - Reflecting
  - General problem solving about sleep hygiene, eating, staying active, IEP/School Support

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Pediatric Depression Treatment

- IF patient continues to have significant depressive symptoms after brief supportive care, consider more intensive therapy and/or medication management
  - Depends on clinical features of case
  - Which resources are available (medications vs therapy vs both)
  - Previous history/response to treatment
  - Patient/Family preference

Pediatric Depression Treatment

- SSRI's are 1st line treatment for moderate to severe depression
  - Fluoxetine, 8 years and above FDA approved
  - Escitalopram, 12 years and above FDA approved
  - Other SSRI's are also available . . .
    - Sertraline
    - Citalopram
    - Would avoid Paroxetine – not found to be effective for pediatric depression, concern for discontinuation syndrome, suicidal ideation and side effects
    - Monitor closely for suicidal ideation, black box warning. . .
    - FDA recommends weekly visits for 1st month and biweekly for 2nd month
      - Likely not always followed. . .

TADS Study – Treatment of Adolescent Depression Study (JAMA 2004)

- Sponsored by NIMH and Duke Clinical Research Institute
- Similar to real-life clinical samples in terms of co-morbidity
- Separate assessment tool for suicidal ideation
- Adverse Events separated: Harm-Related AE (e.g. cutting, worsening ideation without self-harm or any attempt or harm to others, aggression or violent ideation) Suicide-Related AE (worsening of suicidal ideation or attempt, but not cutting without suicidal intent)

TADS

Treatment Arms:

-Fluoxetine alone

-CBT alone

-Placebo alone with clinical management

-Combined Fluoxetine plus CBT

Initial 12 weeks; Fluoxetine plus cognitive-behavioral therapy produced the best success rate, CGI score of 1 or 2

-71% - Fluoxetine + CBT improved at the end of 12 weeks of treatment.

-61% - Fluoxetine alone improved

-43% - CBT alone improved

TADS

- Adverse Events. . .
  - Almost 30% of TADS participants had suicidal ideation at the start of the study
  - No suicides in the TADS study
  - Only 1.6% of patients (7 of 439) patients made a suicide attempt
  - Suicidality decreased substantially over 12 weeks in all treatment groups.
  - **Improvement in suicidal ideation is greatest** for the **combination** of Fluoxetine and CBT and least for Fluoxetine alone.

TADS and Adverse Events. . .

- CBT may protect against harm related events, adds new skills to deal with negative emotions
- During treatment, those taking Fluoxetine alone had higher rates of new suicidal ideation and behavior (15%) vs. Combo (8%) vs. Placebo (6%), particularly in the early stages of treatment

TADS at 36 weeks. . .

- At 18 weeks
  - Combo treatment was still the best with 85% response rate; 69% for Fluoxetine alone and 65% for CBT alone
- At 36 weeks
  - Combo treatment 86% response rate
  - Fluoxetine alone 81%
  - CBT alone 81%

TADS Take Home Points. . .

1. Teens with MDD should be identified and offered evidence-based treatments
2. Medication management of major depression should be made widely available, not discouraged
3. CBT plus meds improves outcomes and protects against suicidality; CBT should be readily available as part of comprehensive treatment for depressed adolescents
4. CBT alone eventually “catches up”, but is it worth waiting an additional 18 weeks? Start medications earlier than later for severe depression. . .

Treatment Resistant Depression

- 35%-40% of youth will not respond to the initial antidepressant
- Re-evaluate patient's clinical status and diagnosis, psychosocial circumstances
- Family, school, medication compliance?
- Assess for comorbid diagnosis, drug use
- Determine if psychotherapeutic interventions are helping/adequate

Treatment Resistant Depression

- TORDIA (Treatment of SSRI Resistant Depression in Adolescents)
  - 334 patients who had not responded to a SSRI.
  - Add another SSRI + CBT
  - Venlafaxine
  - Venlafaxine + CBT
  - CBT with either medication was associated with a higher response rate than medication alone
  - No response difference seen between SSRI and Venlafaxine
  - Among those with higher baseline SI, Venlafaxine had a higher rate of self-harm events.
  - ** adding CBT to another medication most effective

Other Augmentation Strategies . . .

- 2nd Generation Antipsychotics (metabolic issues, weight gain)
- Bupropion (dopamine effect, less sexual side effects, may lower seizure threshold)
- Duloxetine (SNRI, FDA approved for Generalized Anxiety,7-17 yrs of age)
- Mirtazapine (may help with sleep at lower doses, may cause weight gain)
- Trazodone (helps with sleep, be aware of priapism risk)
- Lithium (monitor blood levels, more long term complications, can reduce suicidal ideation)
- Thyroid Medication T3 (can be effective but rarely used)

SSRI's Warnings. . .

- Focus on Two Concerning Side Effects
  - Cardiotoxicity
  - Suicidality

Citalopram and Escitalopram

- Cardiotoxicity - FDA advisory warning in 2011 due to dose dependent risk of QTc prolongation
  - Assess for cardiovascular risk, especially children with known cardiac disease or family history, electrolyte issues due to bulimia/anorexia or potassium lowering diuretics.
  - Caution with concurrent use of medications which may prolong QTc (some 2nd generation antipsychotics such as Geodon and 1st generation Haldol)
  - If risk exists, check EKG and electrolytes before starting medication
  - Check EKG at doses higher than 40 mg daily of Citalopram or 20 mg daily of Escitalopram

Suicide Risk . . .

- Gained national attention in 2004 when FDA issued black box warning
- Warning extends to ALL medications used to treat depression and anxiety, not just SSRI's
- Paroxetine and Venlafaxine got most of the attention as raising risk for suicidal ideation and/or self harm behaviors. 2-3 % risk increase compared to placebo.
- Important to note: there were NO completed suicides in any of the analyzed clinical studies
- Risk was higher for those taking medication vs. those on placebo (4% to 2%)
- A total of 24 trials involving over 4,400 patients were included.
- The analysis showed a greater risk of suicidality during the first few months of treatment in those receiving antidepressants.

Disruptive Mood Dysregulation Disorder

- Main issue is the persistent irritability and mood dysregulation
- Focus on treating the main issue (mood? anxiety? ADHD? Defiance?)
- Assess overall functioning (home, school, extracurricular)
- Remember majority of these kids grow up to have traditional depression and anxiety symptoms. . .
- Cases where SSRI's work well. . .
- Cases where a mood stabilizer such as a 2nd generation antipsychotic medication or anti-epileptic is necessary to control agitation/aggression

Comorbid Issues . . .

- MDD with Psychotic Features; mild or vague, SSRI alone; if more severe, 2nd generation antipsychotic medication. . . upon resolution, slowly taper off the antipsychotic medication if possible
- Anxiety – SSRI for both disorders; augment with CBT
- ADHD – stimulants, Atomoxetine, monotherapy with bupropion
- Substance Abuse – therapy first to treat substance abuse (family therapy, motivational interviewing)
  - add SSRI if no response

Pediatric Depression

- Questions?
- Comments?

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