Treatment of Anxiety and Depression in Children and Adolescents

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Disclosure: John T. Walkup, MD

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Off Label Use

- Should consider all medication uses discussed as off label unless specifically noted otherwise

- Case example – details changed for confidentiality purposes
Introduction

- The issue of refractory anxiety
  - Problems with assessment
  - Problems with treatment implementation
  - Lack of adequate family preparation and involvement
  - Augmentation strategies
- The treatment of depression in teens
Anxiety, OCD and PTSD

- General changes
  - Anxiety Disorders, OCDDR, and Trauma- and Stressor-Related Disorders
  - Anxiety need not be experienced as excessive or unreasonable, just out of proportion ("All my patients with ......")
  - Duration criteria increased to 6 months
  - Some anxiety disorders removed from "Disorders First Diagnosed in Infancy, Childhood and Adolescence"
OCD and Related Disorders

- OCD
- Body Dysmorphic Disorder
- Trichotillomania (Hair Pulling Disorder)
- **Hoarding disorder**
- Excoriation (Skin-Picking) disorder
- Substance- or Medication-Induced
- **Due to Another Medical Condition**
- Other OCRD
- Unspecified OCRD
Anxiety Disorders in Children and Adolescents

- Specific Phobia
- Separation Anxiety Disorder
- Generalized Anxiety Disorder
- Social Anxiety Disorder
- OCD
- Acute Stress Disorder
- Post-traumatic stress disorder
- Panic Disorder
Ages of (Onset) Risk

- ASDs – 0-3 years or later for mild
- ADHD - 4-7 or later for mild, but differential is broader
- Anxiety – 6-12 years
- Depression – 13-16 years
- Bipolar and psychosis - > 16 years
- Disruptive behavior – almost anytime
Specific Phobia

- Animals, insects etc.
- Environmental - thunder, water, heights
- Blood, injection or other suspected painful event
- Situational - tunnels, bridges, elevators
- 70% have another anxiety disorder
Separation Anxiety Disorder

- Excessive concern regarding separation from home or from attachment figures
  - Bad things happening to parent and or child
  - Cannot be alone
  - Avoidance S, M, L, XL, XXL
  - Difficulty falling asleep or sleeping with loved ones
  - Physical aches and pains
  - Accommodation by adults S, M, L, XL, XXL
- Impairment or distress.
Generalized Anxiety Disorder

- Excessive worry and apprehensiveness
  - Restless, keyed-up or on edge.
  - Fatigued at end of school day
  - Concentration problems “choking on tests”
  - Sleep problems (falling asleep)
  - Tense and irritable

- Unable to control the worry

- Impairment or distress
Social Anxiety Disorder

- Fear of social or performance situations
- Social expercieved opportunity to be embarrassed or humiliated
  - Depersonalization or derealization in social settings
    - Specific
    - Generalized
Selective Mutism

- Ability to speak
- Not speaking in social situations
  - None
  - Limited voluntary speech – short answers to questions or low tone, (Walkup)
- Not part of another disorder
Acute Stress Disorder

- True stressful event – life threatening
- Re-experiencing the event
- Avoidance and numbing
- Increased arousal
- Negative thoughts, feelings and moods
- Time limited
Post-traumatic Stress Disorder

- True stressful event – life threatening
- Re-experiencing the event
- Avoidance and numbing
- Increased arousal
- Negative thoughts, feelings and moods
- Risks for enduring symptoms
  - Pre-existing mental disorder
  - Proximity
  - Post-traumatic environment
Panic Disorder

- Attacks of anxiety (Physical Symptoms)
  - Heart rate, pounding heart, palpitations
  - Hyperventilation, shortness of breath
  - Choking sensation
  - Chest discomfort or pain
  - Abdominal pain
  - Some psychological symptoms
- Worry about the next one
- Avoidance behavior related to the attacks
- Agoraphobia....
Obsessive Compulsive Disorder

- Prominent obsessions or compulsions
  - Dirt, germs, or other contamination
  - Ordering and arranging
  - Checking
  - Repetitive acts
- Impairing or time consuming
- More later
Subtypes of OCD

- Pure Obsessions
- Contamination
  - Least likely associated with other Axis I disorders
  - Lots of distress
- Symmetry/Order
  - Breeds true in families (with tic disorders)
  - Limited distress
- Hoarding
  - Breeds true in families
  - Poorer treatment response.
PANDAS

- Suspected cases
  - Throat culture
  - If positive – treat
    - Consider treating for extended period – 20 days vs. 10 (Murphy, personal communication)
- Not sure about getting titers
- Probably no role in non-research settings for other immunologically-based treatments
Anxiety Assessment Strategies

- Anxiety Disorder Interview Scale
- Multidimensional Anxiety Scale for Children (MASC) – J. March
- Screen for Child Anxiety Related Emotional Disorders Scale (SCARED) – B. Birmaher (search “U Pitt SCARED”)
- Achenbach Child Behavior Checklist (CBCL)
What to look for

- Hypervigilant
- Reactive to novel stimuli (triggered)
- Threat bias

- Avoidance coping
- Catastrophic reactions
- Parental accommodation, overprotection
- Mid line physical symptoms
Physical Symptoms – Provoked and Spontaneous

- Headache
- Stomachache – stomach and bowel problems
- Morning sickness
- Difficulty falling asleep
- Bladder and bowel urgency (constipation?)
- Shortness of breath
- Chest pain - tachycardia
- Sensitive gag reflex - fear of choking or vomiting
- Difficulty swallowing solid foods – growth inhibition?
- Dizziness, lightheaded
- Tension and tiredness – exhausted and irritable after a school day
- Derealization and depersonalization

- Avoidance to not experience the above
Other symptoms

- Strategies to maintain proximity to parents (SepAD)
- Excessive need for reassurance – lots of questions (GAD)
- Eating problems – over and under (all)
- Over studying (GAD)
- Inattention and poor performance at school (all)
- Explosive outbursts ala catastrophizing (not mania 😊)
- Easily overwhelmed
- Extremely sensitive, readily tearful
- Fears/preoccupation with death, dying
- Avoidance of outside and interpersonal activities – school, parties, camp, sleepovers, safe strangers
Epidemiology

- Very common
  - Current prevalence - 2-4%
  - 6-12 month prevalence - 10-12% (Costello, 2005)
  - Lifetime prevalence - 14-27%

- Early onset
  - SepAD ~ 7 years
  - SocAD ~ 13 years
  - GAD more variable but 9-11

- Under diagnosed - discounted as not meaningful
- Under treated – presume they will grow out of it
- Need to look for it – so common it is not discernible as pathological
Course of anxiety

- Onset in childhood -“Prepubertal affective illness”
- Adolescence - symptoms + accumulated disability
  - Intense symptoms “burn out” ..... sometimes
  - Generalized anxiety
  - Poor adaptation and coping – easily flooded and overwhelmed (pre-borderline)
  - Some morph to depression
  - School drop out (fade away)
- Young adulthood – symptoms + failure in major roles
  - Work inhibition
  - Fail to leave home or stay in college
  - Evolution into panic disorder
  - Substance abuse
Treatment of OCD
Serotonin Reuptake Inhibitors FDA Approvals

- Clomipramine - FDA approved to age 10 OCD
- Fluvoxamine - FDA approved to age 8 OCD
- Sertraline - FDA approved to age 6 OCD
- Paroxetine – effective for OCD and SoP
- Fluoxetine – effective for OCD; MDD to age 7
- Citalopram – No controlled trials in children
- Escitalopram – FDA approved to age 12 for depression
- Venlafaxine – Effective for SoP but + GAD
Pediatric OCD Treatment Study - POTS

- N = 112
- Ages 7-17 years
- 3 sites, 12 weeks
- CBT, Sertraline, COMB and placebo
CY-BOCS ITT Outcomes

Week 0  Week 12
PB\O  SER  CBT  COMB

COMB > SER = CBT > PBO

Pediatric OCD Study Team (2004)  *JAMA.*
Site x Treatment Interaction

Pediatric OCD Study Team (2004) *JAMA.*
## Types of Reinforcement

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| External Reinforcing | Attention and support (Redirect parents and others) | Avoidance (Re-engage, not escape) |
Treatment of Other Anxiety Disorders
Separation, Social, and Generalized Anxiety Disorder

- Pharmacotherapy
  - RUPP trial, 2001
  - Birmaher et al., 2003
  - CAMS, 2008
  - Industry trials

- Psychotherapy
  - Kendall, 1994
  - Kendall et al., 1997
  - Many others
Child/Adolescent Anxiety Multimodal Study (CAMS)

- NIMH-funded
- SAD, GAD and SoP
- N=488
- 12 weeks acute phase
- 6 month follow-up
- Results
  - COMBO 81%
  - CBT 60%
  - Sertraline 56%
  - PBO 24%
- Avg age 10-11
- Avg dose ~120-130 mg/day
Evaluation of Refractory

- Wrong diagnosis
- Wrong treatment choice
- Too short a duration or too limited a treatment
- Family/environmental factors
- Not prepared for treatment
- Half-hearted effort!
Wrong Diagnosis

- Look for anxiety driving behavior
- **Confusion re: repetitive behaviors**
  - Perseveration vs compulsions/obsessions
    - Stuck and can’t shift vs Distressed and trying to relieve distress
  - Tics vs compulsions
    - Motor movement and body sensation vs cognition and affective charge
  - Stereotypy vs. compulsion
    - Like perseveration
Assessment: Repetitive Thoughts

- Obsessions
- Ruminations
- Delusions
- Perseverative thoughts
- Cravings
- Over-valued ideas
- Flash-backs
Assessment: Repetitive Behaviors

- Compulsions
- Tics
- Stereotypies
- Perseverative behaviors
- Addictive behaviors
- Habits
Wrong Diagnosis

- Look for anxiety driving behavior
- Confusion re: repetitive behaviors
  - Perseveration vs compulsions/obsessions
    - Stuck and cant shift vs Distressed and trying to relieve distress
  - Tics vs compulsions
    - Motor movement and body sensation vs cognition and affective charge
  - Stereotypy vs. compulsion
    - Like perseveration
Wrong Diagnosis

- Goal-directed repetitive behaviors
  - Gratifying or + functional outcome
    - Drug use, shopping, fetishes, self-soothing
    - Lying, stealing, eating or starving, accumulating

- Inattentive subtype of ADHD, as opposed to anxiety

- ODD vs fear-based opposition

- Bipolar disorders instead of catastrophic reactions
Wrong Treatment Choice

- Supportive psychotherapy (Low PBO rates)
- CBT for severe anxiety
- Persist too long with monotherapy
- Fear of using antidepressants
  - Prior activation and fear of mania
  - Suicidality issues
- Antipsychotics and mood stabilizers for the activated dysregulated, overwhelmed
- Stimulants for inattention symptoms
- Reliance on benzos
Too limited treatment effort

- Patient/family not ready to change
- Passive approach to treatment engagement
- Non-exposure focused psychotherapy
  - Dynamic approaches may facilitate readiness
  - Dynamic approaches may also support child’s reintegration into family
- Capitulate to CBT resistance (child and parent)
- Poor quality CBT (aka supportive tx)
- Rote, not personalized CBT
- To heavy initial focus on exposures (flooding)
- Lack of a family approach or engagement
Too limited treatment effort

- Unable (unwilling) to engage family in a med trial – takes time, effort and capacity to persuade
- Don’t believe meds will work (too influenced media reports of med efficacy, and not the evidence base)
  - e.g. Mixed meta-analysis results especially with teen depression
  - Meta-analysis of SRIs and OCD hampered by inclusion of SSRI non-responsive OCD syndromes (i.e. tic-related OCD)
Too Limited a treatment effort

- No real plan for an effective trial – “see how it goes”
  - No target dose by a certain time frame
  - No target date to assess outcome
  - Uncertainty drives poor adherence and poor outcomes

- Start too slow, and stay too low
  - CAMS - SRT 200 mg week 8; Avg endpoint 120-130 mg at week 12
  - TADS - FXT 40 mg by week 12
  - TORDIA results

- Excessive sensitivity to adverse effects – i.e. suicidality

- Med changes before meds have a chance to work

- Confusion about adverse effects activation vs bipolar switch
Suicidality

- Risk Difference for Efficacy
  - MDD - 11.0% = NNT of 10 (NIH NNT = 3)
  - OCD - 19.8% = NNT of 5* (Heterogeneous subjects)
  - Non-OCD anxiety disorders - 37.1% = NNT of 3

- Risk Difference for Suicidality
  - Significant overall - .7% = NNH 0f 143
  - But not for individual disorders
    - MDD - 0.9%; NNH=100
    - OCD - 0.5%; NNH=200
    - non-OCD anxiety disorders - 0.7% NNH=140

Bridge et al., 2007
**Activation**

- Many other terms
- Activation implies no specific etiology
- Range of severity
  - Mental restlessness
  - Physical restlessness
  - Hyperactivity
  - Disinhibition (complex and goal directed behaviors)
Many medications cause activation

- Stimulants
  - During treatment and withdrawal
  - In certain patients – developmentally disabled

- Sedatives
  - Benzodiazepines
  - Antihistamines

- Tricyclic antidepressants

- SSRIs
Activation

- Clinical Implications
  - Common problem
  - Shortly after starting meds or a dose increase
  - Dose related
  - Reversible
  - **NO** long term prognostic implications
  - Differential diagnosis only an issue when activation becomes disinhibition
  - Younger children with minimal brain dysfunction?
  - Unknown relationship to suicidal ideation/behavior
Non-activating Antidepressants

- Mirtazapine (Remeron)
- Duloxetine (Cymbalta)
- Nefazadone* (Serzone)
- TCAs
  - Nortriptyline (Pamelor)
  - Clomipramine (Anafranil)
  - Desipramine (Norpramin)
Bipolar Switching

- Much more rare
  - Longitudinal studies
  - Large clinical trials
- Much more specific
  - Euphoria and grandiosity
  - Not just irritability
- Probably greater prognostic significance
  - First episode of bipolar disorder
Manic Episode: Hallmark Symptoms

Leibenluft et al., 2003

- Distinct period of abnormal elevated, expansive or irritable mood lasting > 7 days
- Three of the following if euphoric, four if irritable
  1) grandiosity
  2) decreased need for sleep
  3) distractibility
  4) pressured speech
  5) flight of ideas/ racing thoughts
  6) increased goal-directed activity or psychomotor agitation
  7) increased involvement in pleasurable activities with potential for painful consequences
Bipolar Switching

- Patient related, not drug related
  - High risk patients for bipolar disorder
    - Positive family history
    - Polysymptomatic and evolving presentations
- Not dose related, but duration of exposure
  - 2-4 weeks on stable dose
  - After a period of improvement
  - ? Association with receptor change
- Not so reversible with discontinuation
Family/Environment Factors

- Parental accommodation
- The “2X2 Square” of behavioral reinforcement
## Types of Reinforcement and Related Treatment Options

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## Mild Anxiety

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## Moderate to Severe Anxiety

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## Anxiety: Typical Functional Impairment

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## Anxiety; More Severe Functional Impairment

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- Anxiety and functional impairment are more severe when there is a combination of positive reinforcement and internally reinforcing factors, as indicated by the lack of shading in the corresponding cell.
Anxiety Provides some Gratification - rare

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Medication Augmentation Strategies

- Clomipramine
- Clonazepam
- Antipsychotics
- IV Clomipramine
- Buspirone
- Add second SSRI
- Lithium
- Stimulants
- Psychotherapy augmentation – d-cycloserine

Severe OCD

- Check EKG etc
- Start with clomipramine, not SSRI
- Check levels and EKG
  - Good levels consistent with good side effect management
- Check CMI:DCMI ratio
  - If >1 no problem
  - If <1 consider adding low dose fluvoxamine
- Add low dose fluvoxamine (Vendel et al. 1995)
  - Check levels to assure levels still in appropriate range
  - Check to see that CMI:DCMI ratio > 1
  - Check EKGs to make sure nothing changed significantly
- Repeat steps above until ....
Two SSRIs or SSRI and NSRI

- Partial response to one
- Cross taper to a second one (SSRI or NSRI)
- Looks good on two SSRIs (quickly)
- Next steps?
  - Don’t necessarily discontinue first SSRI
Add a Second SSRI

- Logical
- Pharmacokinetic and pharmacodynamic interaction
- Most will tolerate, but some will not
- Use short acting SSRIs
Switching SSRIs

- Discontinue med
- Start new med

Graph: OCD Control over Time

- Time

- OCD Control
Switching SSRIs – Stopping old med too soon

Discontinue old med here

Start new med

OCD Control

Time
Second drug offering improved benefit

Don’t cut old med dose

D’ C first med

Start new med

OCD Control

Time
Second drug augments first drug, but didn’t d’c first drug

- Don’t cut old med dose
- Didn’t D’C first med
- Start new med

OCD Control

Time
Risk for Serotonergic Side Effects by Combining SSRIS

- Don’t cut old med dose
- Didn’t D’C first med
- Start new med

Serotonergic Side Effect vs. Time
Lithium Augmentation

- No controlled trials
- Excellent for comorbid depression
- Good third drug
Buspirone Augmentation

- Lack of support from controlled trials
- Some clinicians swear by it
- High doses?
- Is there a small sub group of patients who respond?
Stimulants

- Good for SSRI-induced apathy
- Good for ADHD
- OK for mood disorders
D-cycloserine

- Partial NMDA agonist
- Facilitates extinction of learned fear in rats.
- Small positive studies for social anxiety disorder
- Lots to learn
  - Dose
  - Duration
  - Timing
N-Acetyl cysteine (Mucomyst)

- Involved in glutathione synthesis
- Glutathione is the predominant anti-oxidant in the cytoplasm
- Mucolytic properties as in its use in CF
- Glutathione is one of the detoxifiers of acetaminophen but in OD loss of glutathione results in cell death.
- NAC supplementation increase glutathione and its antioxidant properties
- Augment for OCD or trich etc..
Other Strategies

- Pindolol
- Inositol
- NAC

- Herbal
  - Kava?
  - But not St. John's wort, valerian, Sympathyl, or passionflower
Deep Brain Stimulation

- Indicated for Parkinson’s, tremor, pain
- Humanitarian exemption for OCD and dystonia
- Insertion of electrodes in candidate sites
- Connected by wires to “pacemaker” which is adjusted for maximum benefit
- Find sites for ablative procedures
Summary

- DSM-5 not much new
- SSRIs are the treatment of choice
- Others may work too
- Refractory means many different things
- Medication augmentation strategies
Introduction

- Evidence Base for Teen Depression
  - Short-term outcomes
  - Long-term outcomes
  - Suicidal behavior
Treatment of Depressed Teens

- Treatment for Adolescents with Depression Study (TADS)
- Treatment of Resistant Depression in Adolescents (TORDIA)
- ADAPT
- Treatment of Adolescent Suicide Attempters (TASA)
Teens and Depression

- 3-6% of teens suffer from depression at any point in time
- Up to 20% over a lifetime
- Most with depression do not get appropriately assessed or treated
- Depression is highly responsive to treatment
Treatment of Teen Depression

- Psychological treatments
  - Cognitive Behavioral Therapy (CBT)
  - Interpersonal Therapy (IPT)

- Medications
  - SSRIs and atypical antidepressants
  - TCAs and MAOIs

- Treatment of Adolescents with Depression Study (TADS)
Antidepressant Trials

- 2 NIMH-funded
  - Demonstrated efficacy
  - Low placebo response rates
  - Many quality indicators

- 15+ industry-funded
  - Multiple sites
  - High placebo rates
  - No quality indicators
  - FDAMA exclusivity
  - No investment in outcome
Placebo Response in C&A Antidepressant Trials

- Bridge et al. 2009
- 12 Studies – published and unpublished
- Placebo response correlated with number of sites
- Baseline severity inverse predictor of placebo response
- Younger subject had higher PBO response rate
e.g. Sertraline

- Wagner et al., 2003
- Pooled data of two multisite trials
- N=376 (Sites = 63)
- Ages 6-17 years
- 10 week, double-blind, placebo controlled trial
- Drug > placebo
- CDRS Responder 69% vs. 59%
- CGI-I Responder 63% vs. 53%
What is depression?

- Lets go back a step
- Normal human sadness
- Demoralization
- Sadness without cause
- Horwitz and Wakefield...Loss of Sadness
What is depression?

- Depression before DSM-III
  - Sadness with cause
  - Sadness without cause
    - Black bile
    - “Groundless despondency”
    - Melancholy

- Depression after DSM-III
  - Change in mood
  - Other depressed symptoms
  - Context and quality of mood irrelevant
Consequence of DSM-III

- All unhappiness with sufficient number of symptoms can be depression
  - Increase rates of depression
  - Increased psychological care
  - Increased medication use
  - Increased failure rates of conventional treatments
  - Maybe increased use of somatic treatments
What is depression?

- Normal human sadness
  - Common
  - Expectable reaction to certain events
  - Can be severe, if event is severe
  - Time limited, but not episodic - moving on is expected

- Can progress to an autonomous, excessive and disproportionate sadness
What is depression?

- Demoralization
  - Chronic unhappiness due to adverse circumstances
  - Depressive symptoms, but not anhedonia
  - Can be severe
  - Treated with a change in circumstances
What is depression?

- Sadness without cause
  - Depression with anhedonia
  - Many physical manifestations
  - Disproportionate and unexpected as to cause
  - Mood is distinct from normal sadness
- Autonomous course – unaffected by changes in life circumstances
The Depression Severity Assessment Dilemma

Depressive symptoms
The Depression Severity Assessment Dilemma

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Severity Threshold for Treatment

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Depressive symptoms
Impact on Clinical Trials
Who Should be Enrolled?

Potential Range of Severity for Treatment Trials

Depressive symptoms
Who Should be Enrolled?

Range of Severity for Treatment Trials

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Range of Severity for Treatment Trials

Depressive symptoms
Treatment of Adolescents with Depression Study (TADS)

- JAMA August 18, 2004
- N=439 teens at 13 sites
- Ages 12-17 years
- Treatment Comparisons
  - Meds (fluoxetine)
  - Cognitive-behavioral therapy (CBT)
  - Combination of medication + CBT
  - Medical Management with placebo
- Treatment duration - 12 weeks
TADS Response Rates

- COMB: 71%
- FLX: 61%
- CBT: > 43%
- PBO: 35%
Treatment for Adolescents with Depression Study (TADS)

- Longer term outcome
  - Week 18
    - COMB 85%
    - FXT 69%
    - CBT 65%
  - Week 36
    - COMB 86%
    - FXT 81%
    - CBT 81%
ADAPT Trial

- Goodyer et al. 2006
- N=249
- MDD to age 17 years
- Design
  - Brief intervention (n=164)
  - SSRI vs SSRI + CBT (n=208)
- Result wk 12
  - Brief intervention - 25%
  - SSRI 45%
  - SSRI+CBT 43%
ADAPT Longer Term Outcomes

- Total of approximately 80% responded
- Approx 20% no change or worse by endpoint
- Approx 10% persistently refractory
- Some new onset responders between 12-28 weeks
ADAPT Suicidal Adverse Events

- No increased events in either arm
- 15-20% had no baseline risk
- 45% had no risk at wk 6
- 65% had no risk at wk 28

- No between group differences
Treatment of SSRI-Resistant Depression in Adolescents (TORDIA) Trial

- 334 adolescents with major depression resistant to ≥ 8 weeks of SSRI treatment
- Randomized to one of four treatments:
  - Switch to alternate SSRI (Paroxetine then Citalopram)
  - Switch to alternate SSRI + CBT
  - Switch to venlafaxine
  - Switch to venlafaxine plus CBT
- 12 week trial
- Unique context

(Brent et al, JAMA 2008;299:901-913)
Results

- Antidep only - 50% response
- Combo – 60% response

Moderators

- Baseline - Lower depression, anxiety
- Week 12 – lower depression, suicidal ideation, anxiety and family problems
TORDIA Adherence

- Blood levels
  - Low and high did worse
  - Medium did better

- Pill Counts (>30% of pills remaining)
  - Adherent did better 63% vs. 47%
  - Some 51% had evidence of nonadherence
Week 12 Non-responders didn’t do more
- Less than half stayed on original med
- < 1/3 did something more with medication
- < ¼ switched to another med
- Very few switched to a non-SSRI/NSRI
- No Li or T3 Augmentation
- Non-response may require a special intervention to motivate participants for next steps.
Responders tailored their treatment even further between week 12 and 24.

Response breeds additional interest in treatment.
Treatment of Adolescent Suicide Attempters

- Brent et al., 2009
- N= 124
- Open trial
- Results
  - Depression – 72% responded
  - Suicidal events – 19%
  - Suicide attempts – 12%
  - Median time to event – 44 days
Summary of Studies

- Depression outcomes
- Moderators
- Suicidal behavior
- Role of psychotherapy
Longer Term Outcomes

- **TADS**
  - All active treatment converge – 80-85%

- **ADAPT**
  - Estimated 80+% responded; 10% persistently refractory

- **TASA**
  - 72% response

- **TORDIA**
  - 60% remitted

- **The earlier the response the better**
Moderators

- Severity
- Duration
- Comorbidity
- Family Issues
- Drugs and alcohol
- Adherence
Suicide Summary

- Treatment reduces risk
- Lack of response increases risk
  - Slow depression response
  - Predictors of poor response
- Only TADS had a finding supporting a relationship to SSRI treatment
Psychotherapy

- No additional benefit, if depression severe
  - TADS and ADAPT
- Small additional benefit in resistant dep
- Protective for suicidal behavior
  - Yes – TADS
  - No – TORDIA, ADAPT
Summary

- We have come a long way in the past 25 years!!
- Diagnosis, diagnosis, diagnosis
- Pick treatments to match the condition
- Early response breeds good outcomes and engagement in treatment
- Suicidal behavior risks and outcomes are better understood