Childhood OCD

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Question 1

Early onset OCD is characterized by:

A) Increased comorbid tic disorders

B) Decreased comorbid ADHD

C) Onset of OCD precedes tics by many years

D) Minimal genetic loading

Question 2

Common comorbid diagnoses with OCD include all of the following except:

A) ADHD and ODD
B) Major depression and anxiety
C) Somatoform disorders
D) Motor tics

Question 3

The following medications are effective in the treatment of OCD, except:

A) Clomipramine

B) Fluoxetine

C) Desipramine

D) Fluvoxamine

Question 4

The POTS trial in OCD found that the greatest reduction in CYBOCS scores results from:

A) Sertraline alone
B) CBT alone
C) Combined CBT+Sertraline
D) Family Therapy

Question 5

Criteria for diagnosing PANDAS include:

A) Motor and vocal tics

B) Obsessive and compulsive disorder of childhood onset

C) Tourette Disorder

D) Sudden onset of OCD after a streptococcal infection

Teaching Points

- Distinguish between normal rituals vs. OCD; young children may not recognize their rituals as unreasonable or excessive
- Most common obsessions: Concerns regarding contamination, self harm, doing the right thing (scrupulosity), reassurance or sexual thoughts
- SSRI+CBT may be the most efficacious treatment choice
- Look for PANDAS

Outline

- OCD vs. normal childhood rituals
- DSM-IV criteria
- OCD epidemiology and symptomatology
- Comorbidity of OCD
- Assessment of OCD
- Course of OCD
- Treatment options: CBT & Pharmacotherapy
- The POTS study
- Special issues: PANDAS

OCD vs. Normal rituals

- Obsessions: Persistent thoughts, images or impulses that are ego-dystonic & intrusive
- Compulsions: Repetitive, purposeful behaviors in response to an obsession, usually to relieve anxiety
- Young children may not recognize their rituals as unreasonable or excessive; Important for clinician to help recognize associated impairment

OCD vs. Normal rituals

- Normal developmental rituals may include avoiding stepping on cracks in sidewalks (rituals related to belief in power of wishing) & normal collecting behaviors including baseball cards
- Must distinguish vernacular “obsessive” and “compulsive” from clinical syndrome
- Look for severity of behaviors and functional impairment

DSM-IV criteria

A) Presence of either obsessions or compulsions

Obsessions:

1) Recurrent and persistent thoughts, impulses, or images that are experienced as intrusive and inappropriate and that cause marked worry or distress
2) Not simply excessive worries about real-life problems
3) Attempts to ignore or suppress them or neutralize them with some other thought or action.
4) Recognize they are a problem of ones own mind and not imposed from without (not children)

Compulsions:

1) Repetitive behaviors (hand washing, ordering, checking or mental acts (praying, counting, repeating words) one is driven to perform
2) Behaviors ward off distress or prevent dreaded situation (not children)

DSM-IV criteria

B) Is recognized as excessive or unreasonable (not children)

C) More than 1 hr a day, significant distress, or interfere with normal routine

D) Not part of another Axis 1 condition

E) Not caused by a substance or general medical condition

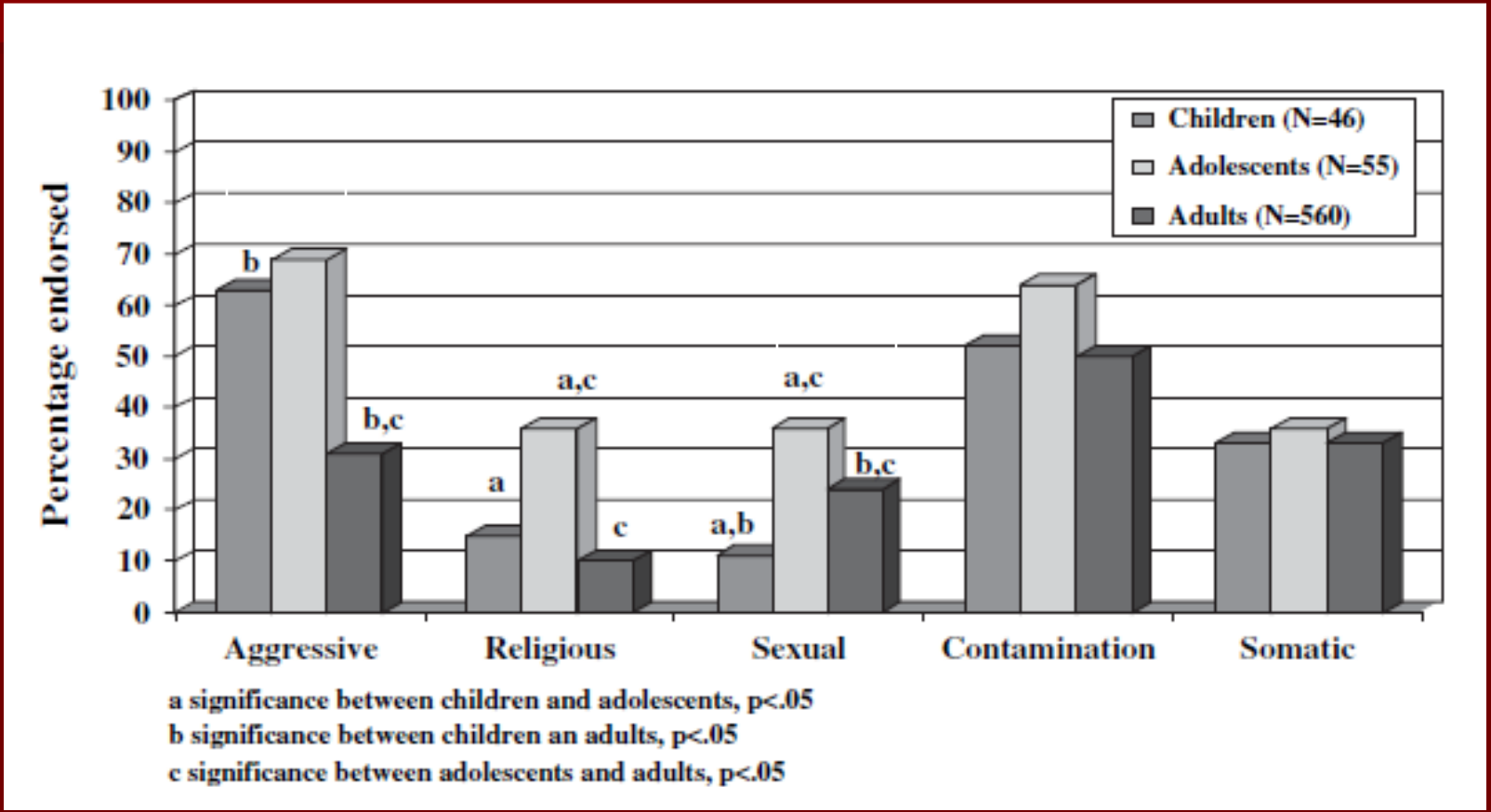
Common symptoms

- Excessive worries about danger, separation & contamination→ rituals of checking, hoarding & checking
- Most common obsessions: Concerns regarding contamination, self harm, doing the right thing (scrupulosity), reassurance or sexual thoughts
- Common compulsions: Washing, repeating, checking, counting, touching, arranging and hoarding
- Content of obsessions may be age dependent

Symptoms of Childhood OCD

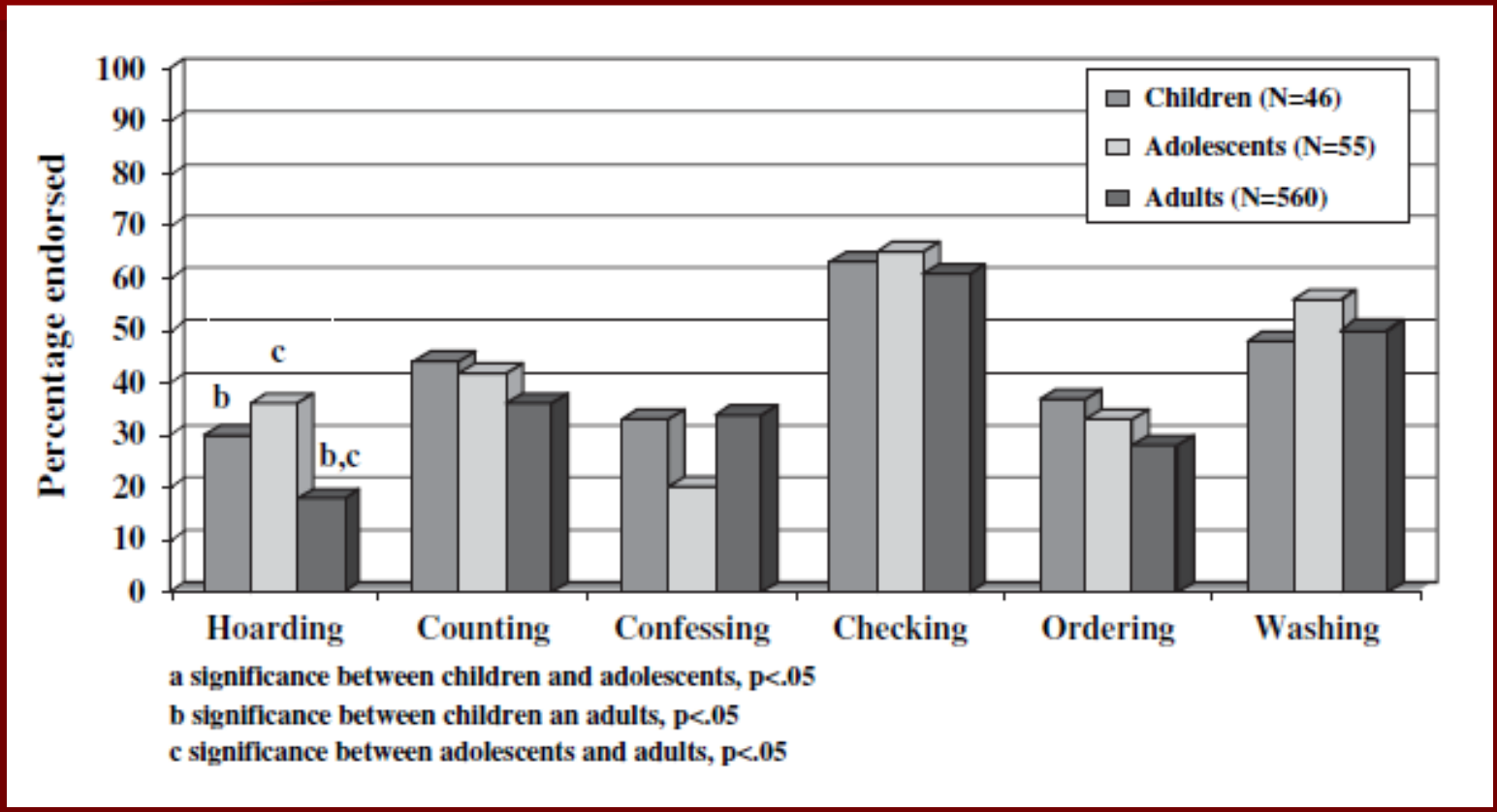
- Obsessive thoughts and washing- some times in 85%
- Repeating rituals in 50%: need to be perfect
- Checking in 46% (e.g., doors, windows, appliances)
- Ordering, arranging and symmetry in 17%,
- Scrupulosity in 13%
- Takes 4-6 months before parents aware of sxs, secretiveness can lead to long time before diagnosis (Leonard 1993)
- In teens, sexual and religious obsessions (Scahill et al 2003)
- Symptoms shift over time (Rettew et al 1992)

Obsessions over the Life Span



Geller et al, 1998

Compulsions over the Life Span



Geller et al, 1998

Symptoms: Cluster Analysis

- Aggressive/Checking* (55%)
- Sexual (10%)
- Contamination/Cleaning (36%)
- Ordering/Arranging (32%)
- Repeating, "Just Right" (*annoying*)* (45%)
- Health (35%)
- Misc: Confess, prevent, touch, blink* (60%)
- Magical, Superstitious (32%)
- Religious/Praying (18%)
- Hoarding (35%)

- Mental, Touch, Order (little cog content)
- Contamination/Cleaning
- Superstitious, repeating to prevent bad
- Obsessions (harm, relig, sex), w/ Confessing, Checking
- Somatic (illness)

N = 213; 96 F, 117 M

Ivarssaon et al, 2006

Epidemiology

- Point prevalence 0.8%; lifetime prevalence 1-4% (Keeley et al. 2007)
- Boys more likely with prepubertal onset; girls with pubertal onset
- Male/female ratio equalizes in adolescence
- Early-onset OCD: ↑ tic disorders; ↑ comorbid ADHD; onset of tics often precedes OCD by many years
- Early-onset OCD: Associated with stronger genetic loading
- One-third to one-half adults with OCD have childhood-onset

Etiology

- Genetic transmission- Twin studies show ‘genetic influences’: 45-65% (van Grootheest et al 2005)
- Higher rates of OCD in 1° relatives (Nestadt et al 2000); 30% of adolescents had 1° relatives with OCD (Lenane 1990)
- Areas of brain implicated: Basal ganglia
  - Functional deficits in cortico-striato-thalamo-cortical circuit underlie OCD (Saxena et al, 2000?; Fitzgerald et al, 2011)
  - Neurochemicals implicated: Serotonin, glutamate

Etiology

- Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) subgroup: Post streptococcal production of auto-antibodies which may cross-react with cellular components of basal ganglia

Differential Diagnosis (Leonard et al 2006)

- Depression and Anxiety disorders
- Eating disorders
- Tic disorders
- Body dysmorphic disorder
- Normal childhood rituals

OCD Comorbidity: 80%!

- Internalizing: ~60%
  - MDD: 40% child, 50 - 60% adolescts = adults
  - Separation anxiety: 50-60% child, 35% adolescts, 17% adults
  - Social anxiety, GAD, specific phobia, secondary panic
- Externalizing: ~30%
  - ADHD: 30-50% (more common in boys)
- Tics: up to 25% child, 9% adolescents, 6% adult
- PDD?
- "OC Spectrum Disorders"
  - trichotillomania, nail biting, skin picking, pathologic gambling, paraphilias, BDD, eating disorders
  - Less common in children and emerge more frequently in adolescence
  - Ego-syntonic, more difficult to treat

Assessment

- Use multiple sources of information
- Look for comorbidities
- Estimate extent of impairment
- Review developmental and family history
- Look for possible medical causes
- Utilize standardized instruments such as Children's Yale-Brown Obsessive Compulsive Scale (CYBOCS) (http://www.bpchildresearch.org/grand/grand_rounds.cfm?ID=24&page=YBOCS)

Symptoms: How to Assess

- CYBOCS
  - Obsessions: Contamination, Aggressive, Sexual, Religious, Superstitions (cracks, numbers), Need to Know/Remember/Tell, Hoarding (fears losing)
  - Compulsions: Cleaning, Checking, Praying, Superstitious Repeating & Rituals, "Just Right" Repeating (touch, tap, order, arrange, counting), Ordering/Arranging, Confessing/Telling, Reassurance-seeking, Mental Rituals
- How much time?
- Functional Impairment?
- Distress?
- Try to resist?
- Are you successful?

Assessment: Instruments (Merlo et al 2005)

- Semi-structured interviews (e.g. Anxiety Disorders Interview for Children): Clinician administered with parents and children interviewed separately for 45-60 mins or K-SADS with one of five subscales. These may be more appropriate for non-OCD anxiety disorders.
- Child's Leyton Obsessional Inventory: Cards sorted 3 times for type, resistance and interference (Berg 1988)
- Most often used scale in clinical trial to monitor response: C-YBOCS

Children's Yale Brown Obsessive Compulsive Scale (CYBOCS)

- Checklist of symptoms and 10 item clinician-driven questionnaire with 4 degrees of severity- 2 subscales Obsessions (20 points) and Compulsions (20 points)= 40 points; Integrate parent, child & clinician observations
- Total 0-7 subclinical
- Total 8-15 mild *10=remission
- Total 16-23 moderate
- Total 24-31 severe
- Total 32-40 extreme
- Good interrater reliability (Yucclen et al 2006)

Assessing response using CYBOCS

- CY-BOCS not extremely sensitive to change at highest severity
- A 25% or 35% decrease is generally taken as efficacy and a score of 10 indicates full remission

Childhood OCD with and without tics: Are there differences?

- Patients with OCD & comorbid tic disorder: Higher rates of symmetry, touching, rubbing, staring, blinking (Leckman 1994)
- Patients with OCD alone have more contamination and cleaning
- OCD comorbid with tics more familial, more common in boys and has early onset (Geller 2001)

OCD with comorbid ADHD

- In a survey of youth with OCD, 25% patients had co-morbid ADHD (Masi et al 2006)
- Comorbid ADHD can compromise school performance (Geller et al 2003); concentrating on school and homework common problems (Piacentini et al 2003)
- More problems in social functioning, school and depression (Sukhodolsky et al 2005)
- ADHD + OCD: Higher rate in males, an earlier onset of OCD, a greater psychosocial impairment, and a stronger co-morbidity with bipolar disorder, tic disorder, and oppositional defiant disorder/conduct disorder (Masi et al 2006)

Prognosis and long term outcome

- Meta-analysis by Stewart 2003:
  - ✓ 16 samples, n=521 children & adolescents with OCD: followed for 1-15 yrs
  - ✓ Pooled data: 41% had full OCD at follow-up, 60% full or sub-threshold OCD
  - ✓ Predictors of full OCD: Early age of onset, ↑ OCD duration & being inpatient; Comorbid psychiatric illness & poor initial treatment response were poor prognostic factors
- Long-term medication studies: Modest incremental improvement but not normalization over 52 weeks of SSRI treatment; relapse rate after SSRI discontinuation possibly high

Prognosis (continued)

- Recent longitudinal study by Bloch, 2009: 45 of 62 eligible children with OCD reassessed around 9 years later, in early adulthood.
- 44% of subjects had subclinical OC symptoms at the follow-up evaluation.
- Absence of a comorbid tic disorder & presence of prominent hoarding symptoms were associated with the persistence of OCD symptoms.
- Female gender, earlier age at childhood assessment, later age of OCD onset, more-severe childhood OCD symptoms, and comorbid oppositional defiant disorder also were associated with persistence of OCD symptoms into adulthood.

Cognitive Behavioral Therapy

- Hierarchy-based Exposure and Response Prevention (March 1994, Scahill 1996, Franklin 1998): 14 sessions over 12 wks with toolkit approach, self-monitoring, mindfulness (‘watch the Obsessions or Compulsions doing their own thing, not belonging to me’)- use of “fear” thermometer
- Imaginal exposure for obsessions: in vivo
- Habit reversal for “just-so” phenomena
- Cognitive restructuring for negative thoughts
- Self observation, extinction, operant conditioning, and modeling used in adolescence: Behavioral rewards
- Flooding, graded exposure, and response prevention (March et al 1994)
- Family and group forms of treatment are effective as well (Barrett et al 2004)

Pharmacotherapy

- FDA approval for youth:
  - ✓ Clomipramine >10 yrs
  - ✓ Fluoxetine >8 yrs
  - ✓ Fluvoxamine >8 yrs
  - ✓ Sertraline >6 yrs
- May need 10-12 weeks at highest tolerated doses
- Up to 30-40% reduction in OCD symptoms with pharmacotherapy alone
- Black Box warning for suicidality for all antidepressants in youth, regardless of disorder being treated

Pharmacotherapy: Important points

- All SSRIs appear equally effective
- Choice made on side effects, pharmacokinetic profiles and drug interactions
- Check for sexual side effects
- Go slow with upward titration
- 12 months of treatment better than 6 months
- Slow taper when discontinuing

Childhood OCD: Meta-analysis

- Meta-analysis of all DBPC medication trials in pediatric OCD including paroxetine (Geller et al 2003)
- 12 studies met inclusion criteria: 1044 children included; 8-12 weeks of treatment
- Overall effect size of 0.46 (modest effect)
- Clomipramine superior to each SSRI (which were indistinguishable from each other); this may however have resulted from its use (as the first such medication available) in non-refractory population

Clomipramine

- 3 studies support efficacy:
  - Flament et al 1985, 10wk DB cross-over of 23 youth 3mg/kg
  - DeVeaugh-Geis et al 1992 led to FDA approval
  - Leonard et al 1989 DB crossover between CMI 93-5mg/kg/dy and DMI
- Ask about sudden death in first-degree relatives
- In youth, CBC, LFTs, creatinine, EKG, BP and HR
- Start at 25mg and gradually increase by 25 mg every 10-14 days, get EKGs and at least one plasma level of CMI and desmethylCMI before next level and aim for 3mg/kg/day but not higher than 5mg/kg/day.
- Watch for anticholinergic, seizures, blood pressure and heart rate changes

Treatment Resistant OCD in Youth
(Reinblatt and Walkup 2005)

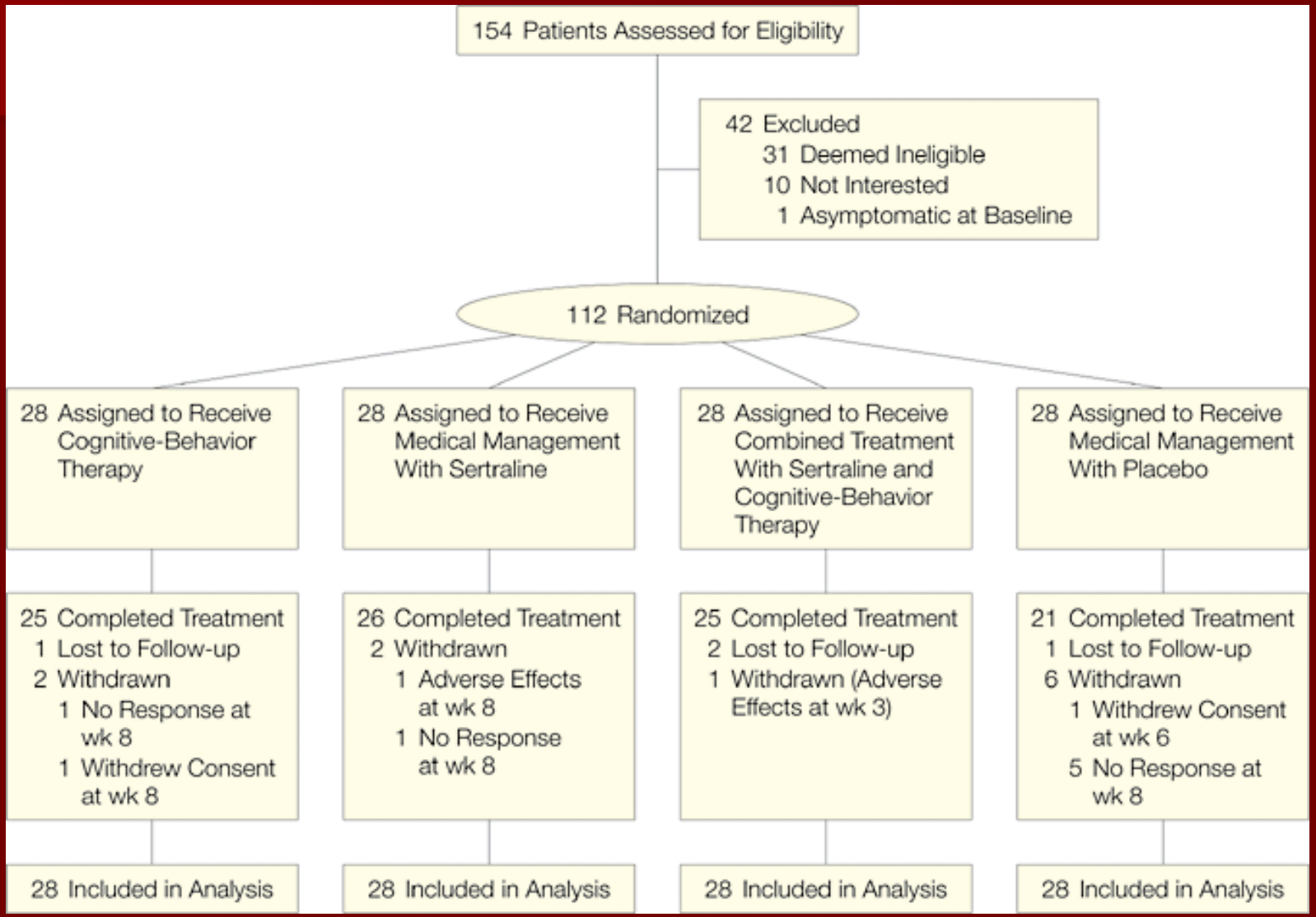
- If partial response, add CBT
- Switch SSRIs
- Augmentation with atypical antipsychotics, esp risperidone with schizotypy and tics
- Augmentation with Clomipramine, Buspirone, Li, Pindolol, another SSRI or SNRI, clonazepam, Lamotrigine
- SSRI and Clomipramine
- Memantine, Riluzole
- NAC, Inositol
- Psychosurgery

Pediatric OCD Treatment Study (POTS)

- Compared efficacy of 4 different treatment options: Sertraline alone, sertraline +CBT, CBT alone & placebo alone; n=112; 12 weeks
- Randomized parallel groups
- Entry criteria CYBOCS=16; Mean of 24.6 with only ADHD meds allowed
- Sertraline- Upward titration from 25→200 mg/d over 6 weeks
- Outcome measure of remission: CYBOCS <10

POTS

(Team POTS,JAMA 2004)



POTS
(Team POTS,JAMA 2004)

Table 2. Mean CYBOCS Score, by Treatment Group and Week (n = 28)

	CY-BOCS Score, Unadjusted Mean (SD)*			
Week	Cognitive-Behavior Therapy	Sertraline	Combined Treatment	Placebo
Baseline	26 (4.6)	23.5 (4.7)	23.8 (3.0)	25.2 (3.3)
4	20.6 (6.5)	18.5 (7.5)	18.1 (6.8)	22.4 (5.4)
8	18.1 (7.9)	16.9 (8.2)	14.4 (8.1)	22.5 (4.4)
12	14.0 (9.5)	16.5 (9.1)	11.2 (8.6)	21.5 (5.4)

Abbreviation: CY-BOCS, Children's Yale-Brown Obsessive-Compulsive Scale.
*Last observation carried forward used to impute missing values.

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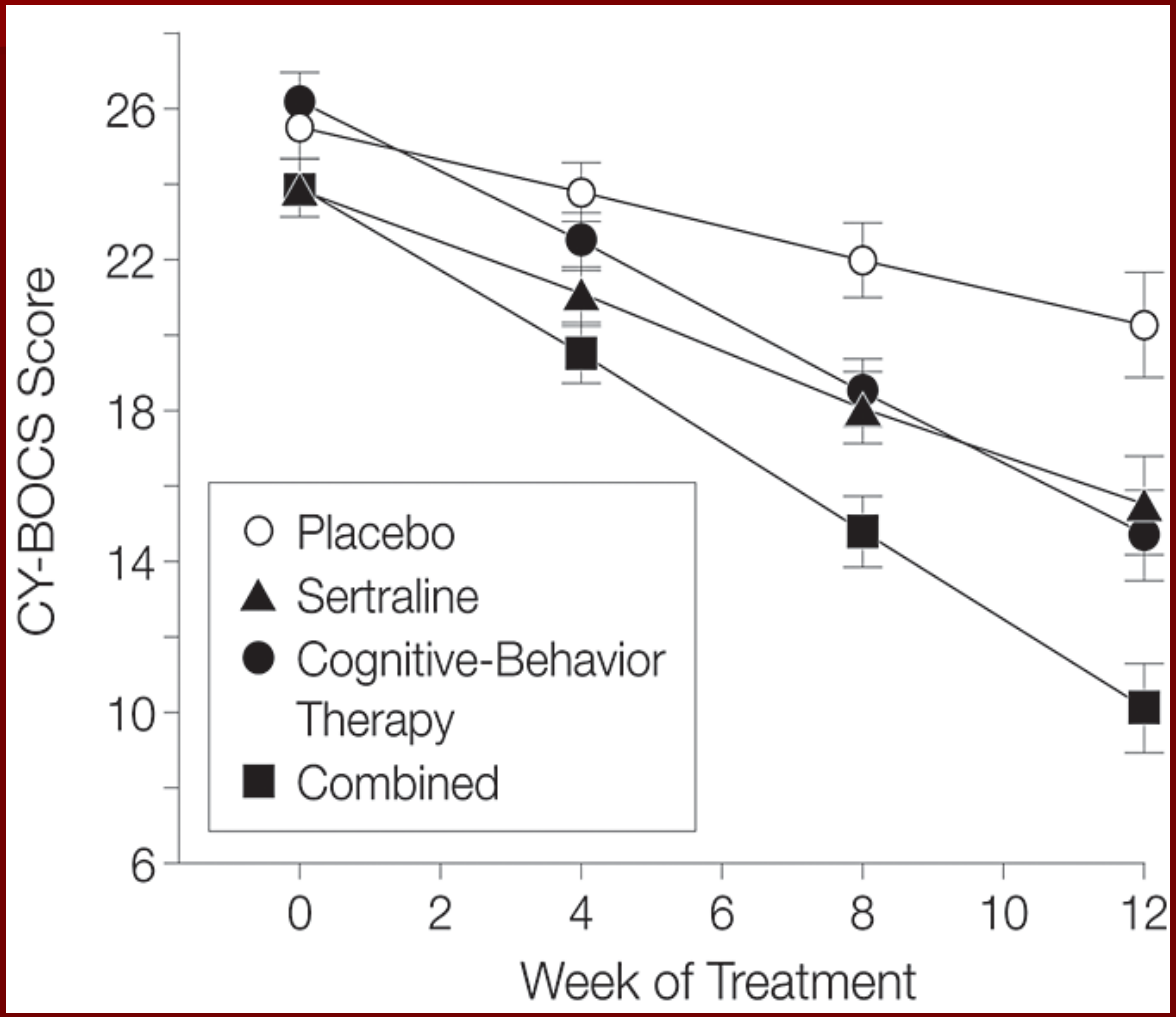
(Team POTS,JAMA 2004)



POTS

(Team POTS,JAMA 2004)

Table 3. Treatment-Emergent Adverse Events in Medication-Treated Patients*

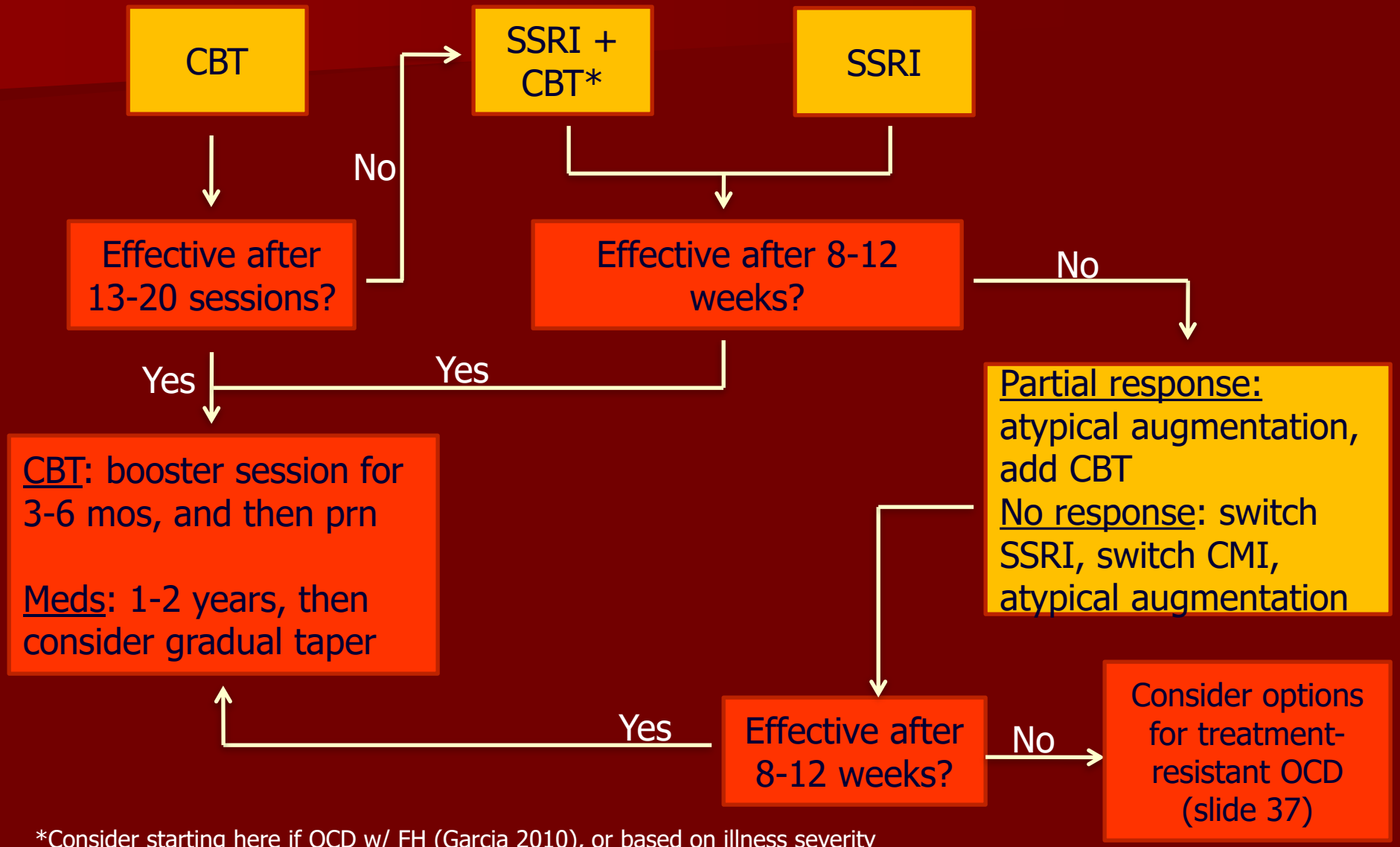
Adverse Event	No. (%)		
	Sertraline (n = 28)	Combined Treatment (n = 28)	Placebo (n = 28)
Decreased appetite	5 (18)	4 (14)	0
Diarrhea	6 (21)	0	1 (4)
Enuresis	2 (7)	2 (7)	0
Motor overactivity	1 (4)	6 (21)	1 (4)
Nausea	7 (25)	5 (18)	1 (4)
Stomachache	8 (29)	4 (14)	2 (7)

*Data are for events occurring in at least 5% of sertraline-treated patients and with an incidence of at least 2 times that seen in placebo-treated patients in either the sertraline-alone or the combined-treatment group. Medication-related adverse events were not recorded for patients treated with cognitive-behavior therapy alone.

POTS: Outcome

- Mean daily dose of sertraline
  - ✓ With combined treatment:133 mg/day
  - ✓ Sertraline alone: 176 mg/day
- Effect sizes:
  - ✓ CBT: 0.97
  - ✓ Sertaline alone: 0.67
  - ✓ Combined treatment:1.4
- Remission rates (CYBOCS=10) for combined 53.6%; CBT alone 39.3%; sertraline 21.4% and placebo 3.6%

Treatment algorithm



*Consider starting here if OCD w/ FH (Garcia 2010), or based on illness severity

POTS-II (Franklin et al, 2011)

- Examined the effects of augmenting SSRIs with CBT (or a brief form of CBT); instructions in CBT delivered in the context of medication management.

- 12-week RCT involving 124 outpatients (7-17 years old) with OCD as primary diagnosis and CYBOCS ≥16 despite adequate SRI trial (Franklin et al., JAMA 2011).

POTS II

- Randomly assigned to 1 of 3 treatment strategies that included 7 sessions over 12 weeks
  - a) 42 in the med. management only,
  - b) 42 in the med. management + instructions in CBT,
  - c) 42 in the med. management plus CBT.
- 68.6% in the ‘plus CBT’ group were responders, compared to 34.0% responders in the ‘plus instructions in CBT’ group and 30.0% in the ‘med. management only’ group.

POTS II (Franklin et al., 2011)

- The medication management plus CBT strategy was superior to the other 2 strategies on all outcome measures.
- Addition of CBT to medication (compared to medication alone) ⇒ significantly greater response rate; augmentation of medication management with the addition of instructions in CBT did not.

SSRI meta-analysis in OCD
(Bloch et al, 2009)

- Meta-analysis to determine differences in efficacy and tolerability between different doses of SSRIs in OCD.
- 9 randomized DBPC studies with 2268 subjects reviewed: Higher doses of SSRIs had improved treatment efficacy, using either Y-BOCS score or proportion of treatment responders as an outcome.
- SSRIs' dose not associated with the number of all-cause dropouts.
- Higher doses of SSRIs associated with significantly higher proportion of dropouts due to side-effects.

Cognitive-behavioral family treatment (O'Leary, 2009)

- Cognitive-behavioral family treatment (CBFT) for childhood obsessive-compulsive disorder: 38 participants (age 13-24 years) from a randomized controlled trial of individual or group CBFT for childhood OCD assessed 7 years post-treatment.
- 7 years after treatment: 79% participants from individual therapy & 95% from group therapy did not have a diagnosis of OCD.
- No significant differences found between treatment conditions except that depressive symptoms were more for individual treatment.
- CBFT for obsessive-compulsive disorder is effective 7 years post-treatment.

Pediatric Autoimmune Neuropsychiatric Disorders associated with Streptococcal infections (PANDAS)

- Five clinical criteria of the PANDAS subgroup:
  - Presence of OCD and/or tic disorder (using DSM-IV criteria)
  - Prepubertal symptom onset
  - Episodic course characterized by acute, severe onset and dramatic symptom exacerbations
  - Neurological abnormalities present during symptom exacerbations
  - Temporal relationship between GABHS infections & symptom exacerbations

Treatment Guidelines for PANDAS

(Swedo et al, 1998)

- Assess for GABHS infection by 48 hour culture in child with abrupt onset OCD/Tic D/O. Treat positive culture with 10-day course of antibiotics
- If abrupt onset of OCD/tics occurred 4-6 weeks before visit→ Check ASO & Anti-Dnase-B + 48 hr GABHS throat culture→ Do not treat with antibiotics if culture is negative (despite ↑ titers)
- Obtain throat cultures at the time of relapse of OCD symptoms
- Immunomodulatory treatment (Plasma exchange or IVIG) only used for most severely affected patients

Refutation of PANDAS hypothesis (Kurlan and Kaplan 2004)

(1) Level of severity of tics and OCD symptoms not defined

(2) Age of onset the same as ‘regular’ TS and OCD. Further, there has been a post pubertal case reported

(3) Abrupt onset not clinically specific since tics may not be identified gradually e.g. at least 2 studies show 38-50% of children with TS described as acute onset with no diagnosis of PANDAS

(4) Does presence of choreiform movement suggest that diagnosis is Sydenham's?

(5) GABHS as causative agent hard to show since a) carrier states b) infection worsens any tics. There is imprecision in the temporal course of PANDAS

Clinical implications: PANDAS (Kurlan and Kaplan 2004)

- Only get Streptococcal culture when there are clinical signs and symptoms (otherwise carrier state can be confusing)
- Antineuronal antibodies and D8/17 are NOT reliable indicators (even though elevated D8/17 on B lymphocytes is a susceptibility marker for Rh-F)
- Do not use prophylactic antibiotics and do not use plasma exchange and IV immunoglobulin

PANDAS

- Recent study by Leckman: At longitudinal follow up, those with presumed PANDAS were no more likely to have strep-related exacerbations of OCD than those children with regular OCD.

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Answers

1) A
2) C
3) C
4) C
5) D