Treatment Considerations for Teens

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Disclosure: John T. Walkup, MD

	Consultant	Advisory Board	Speaker's Bureau	Research Contract	Royalties	Support to Attend this Meeting
Pfizer				**X (2007) Drug and PBO**		
Abbott				**X (2005) Drug**		
Lilly				**X (2003) Drug and PBO**		
Hartwell Foundation				**X (current)**		
Tourette Syndrome Assoc.			**X (current)**	**X (current)**		
Oxford Press Guilford Press					**X (current)**	

Introduction

- Risk factors for suicide in teens
- Pharmacological treatment approaches
- Risks of antidepressant drugs
- Impact of the black box warning
- Managing antidepressant risk

Risk Factors for Teen Suicide

Model for Suicide with Implications for Prevention

Shaffer, 1998

ACTIVE DISORDER
e.g. Mood or anxiety,
Substance abuse

STRESS EVENT
e.g. In trouble with the law
or school, loss, humiliation

ACUTE MOOD CHANGE
e.g. anxiety-dread, hopelessness
anger, agitation

Inhibition

SOCIAL
Strong taboo
Available support,
Presence of others,
Lack of access to
method

MENTAL STATE
Slowed down

SURVIVAL

Facilitation

UNDERLYING TRAIT
Impulsive, intense

SOCIAL
Weak taboo
Available method
Being alone
Recent example

SUICIDE

Pharmacological Targets

- Impulsivity
- Rigidity
- Demoralization
- Anxiety
- Depression
- Psychosis

Impulsivity

- Stimulants (hyperactivity/impulsivity)
- Antidepressants (agitation and catastrophizing)
- Antipsychotics (dysregulated behavior)
- Mood stabilizers (poor control of upside mood)

Rigidity

- Antidepressants (obsessionality, rumination and catastrophizing)

Demoralization

- Address the demoralizing circumstances
- Antidepressants – “insurance” against the presence of co-occurring depression

Anxiety

- Antidepressants - “Syndromic” Anxiety
  - Separation, generalized and social anxiety disorders
  - OCD
- Benzodiazepines - Severe, but expectable and proportionate anxiety
  - Major dysruptive life events
  - Catastrophic reaction to major life events

Depression

- Antidepressants – depression but not for demoralization
- Augmentation strategies
  - Lithium
  - T_3
  - Antipsychotics
  - Other serotonergic agonist
  - Dopamine agonists

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)

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**

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

Psychosis

- Antipsychotics
- Antidepressants for psychotic depression
- Mood stabilizers for bipolar disorder

Treat the Underlying Condition

- Treating the underlying condition
  - Reducing risk completely
  - Has no impact on risk – suicidality tied to other risk factors
  - Treating the underlying condition worsens risk
- Successful treatment leads to risk for poor adherence

Treatment that Reduces Risk

- All suicidality is reduced with contact
  - TADS, TORDIA, TASA, ADAPT
- Anxiety disorders
- Major Depression
- Bipolar Disorder
- Psychoses

Treatment does not Reduce Risk

- Suicidality that is tied to other issues
  - Beliefs
  - Values
  - Imbedded in a coping strategy

Treatment Increases Risk

- Stabilization of mood and anxiety
- Increased capacity for action, but….
  - Poor premorbid adaptation and coping
  - Poor premorbid behavior control
  - High family conflict
  - Low family cohesion
  - High family blame

Black Box Warning (BBW)

Characteristics of BBWs

- Preventable adverse event from early detection and intervention
- Cohort for which the med is dangerous (25%)
- Adverse event worse than the benefit
- Dosing or drug interaction critical to safety (20%)
- Need for special prescriber training
- Need for exception care with use of the drug
- ~20% of drugs are withdrawn and get a BBW
  - 50% of withdrawals happen in the first 24 mos

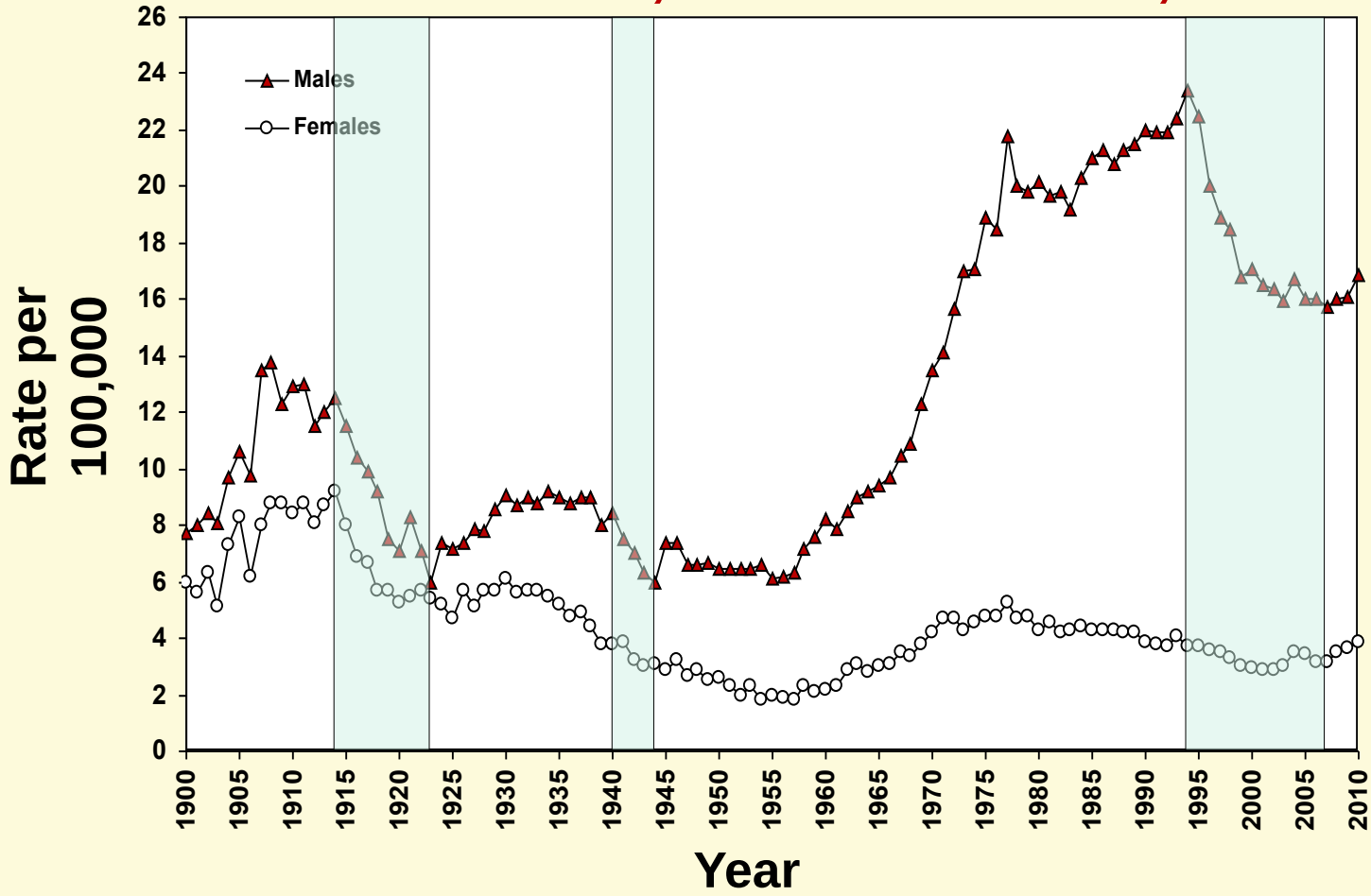
The Black Box

- Reduction in teen suicide rates from the comercialization of SSRIs to Black Box warning
- Change in prescribing practices
- Increased rates of suicide
- Efforts to repeal the BB warning

- The methodology doesn’t exist to address the issue

20TH- AND 21ST-CENTURY CHANGES IN YOUTH SUICIDE RATES BY GENDER

— UNITED STATES, AGES 15–24, 1900–2010 —



Anderson 2002; CDC, NCIPC 2005 (WISQARS) (cited 12/03/2012); CDC Wonder 2003; USDHEW 1956; Vital Statistics U.S. 1954–1978; prepared by David Shaffer and Ted Greenberg, Columbia University, Department of Psychiatry

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Case Study - Antidepressants

- Efficacy of antidepressants – “limited”
  - 2 NIMH trials - ****
  - 17+ industry trials ------
  - OCD trials ***
  - Non-OCD, non industry trials ****
- Chronology leading to the BBW re: suicide
  - European regulators
  - British regulators
  - U.S. regulators

Case Study - Antidepressants

- Down side of the BBW in 2004
  - Rates of dx of new MDD rose consistently from 1999 – 2004 then in 2005 declined to 1999 levels
  - Medical records suggest depression complaints rose, but diagnoses didn't rise after BBW
  - 47% decrease is use of antiD in new episodes of dep in 5-21 year olds from 2002-2006; rates stable in those currently on med (some controvery with this study)
  - Visit schedule – weekly for 4 weeks (didn't work)
  - Suicide and the BBW

Case Study - Antidepressants

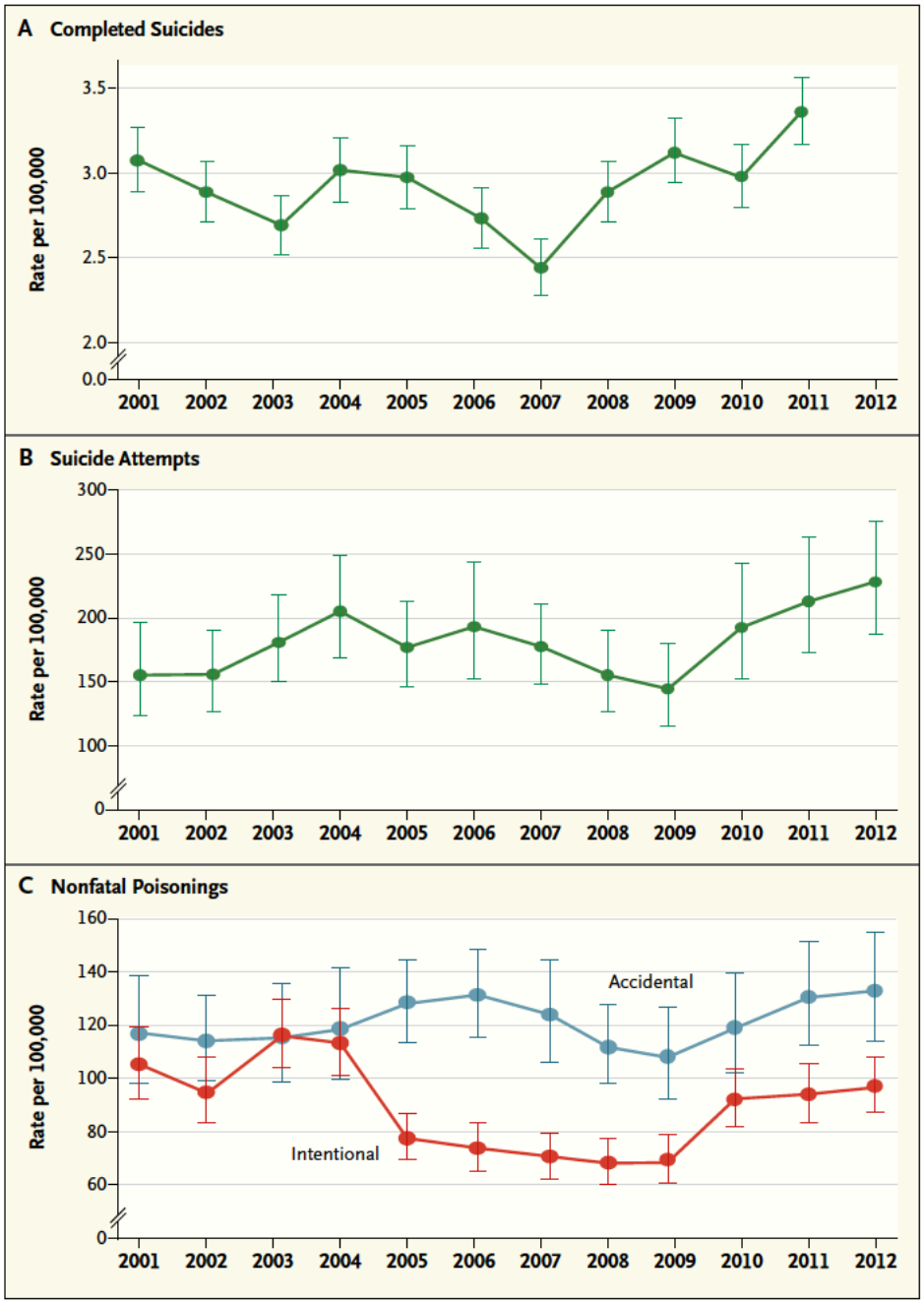
- Suicide and the BBW
  - Antidepressants Rx decreased for all age groups <60 years old
  - Decline in use of antidep associated with increased rates of suicide (after years of decline)
  - Additional meta-analyses
    - NNT and NNH

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

NNT: Number needed to treat; NNH: Number needed to harm

Bridge, et al. 2007.



Rates of Completed Suicides, Suicide Attempts, and Nonfatal Poisonings among Children and Adolescents 10 to 17 Years of Age in the United States, 2001–2012.

Data are from the Centers for Disease Control and Prevention.

Stone NEJM 2014

Managing Risk

- Do a good interview
- Focus on risk factors in the face of a negative interview
- Formulate how improvement in symptoms will either improve or worsen suicidality
  - Improve maladaptive coping
  - Energize maladaptive coping
- Adherence plan – short and long term

Summary

- Do good interviews
- Formulate causes of suicidality
- Medicate effectively
- Develop an adherence plan
- Be careful for those whose improvement might be associated with energized poor coping and adaptation.