Antidepressants and Suicide Risk and Prevention

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Disclosures

• My spouse has no relevant financial relationship with a commercial interest to disclose.”

• “I have the following relevant financial relationship with a commercial interest to disclose:”

  -- Publication of the book “Almost Depressed”
  By Harvard Health Publications

• Please note this presentation may include discussion of “off label” (Non-FDA approved) uses of medications
Excellent Recent Reviews

<table>
<thead>
<tr>
<th>Type of Self Harm</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suicidal Ideation</td>
<td>Thoughts of death, thoughts of one’s own death, with or without intent or a plan</td>
</tr>
<tr>
<td>Suicide Attempt</td>
<td>Self-destructive behavior with explicit or inferred intent to die</td>
</tr>
<tr>
<td>Nonsuicidal self harm</td>
<td>Self-destructive behavior with an aim to modify negative affect, punish self, or escape, but without any suicidal intent</td>
</tr>
<tr>
<td>Suicide</td>
<td>Suicide attempt that results in a fatality</td>
</tr>
<tr>
<td>Suicidal Event</td>
<td>New-onset or worsened suicidal ideation or suicidal behavior</td>
</tr>
</tbody>
</table>

Suicide rates in selected regions and countries

Suicide rates in individuals aged 15–24 years in selected countries

Relationship between Medications and Suicidal Behaviors

- Worldwide, there are about 1 million suicides annually.
- In the last 25 years, approximately 750,000 people committed suicide in the US, and suicides outnumber homicides by at least a 3 : 2 ratio.
- Deaths from suicide exceeded deaths from AIDS by 200,000 in the past 20 years, and
- Four times as many Americans died as a result of suicide than in the Vietnam war during the same time period.

a The solid red lines show the least squares linear regression, and the dotted red lines indicate the 95% confidence intervals for the regression.

A stress–diathesis model of suicide
Adapted from Mann 2003

Youth Suicide

- Male adolescents die by suicide at a rate 4 × higher than females
  - Of all suicide completions, 80% are male
  - 75% are white males
- Female adolescents attempt suicide at a rate 3 × higher than males
  - Asian-American females aged 14-24 years have the highest suicide rate (not attempts) of all females of ethnicity
- Gay, lesbian, bisexual, transgender, questioning have a 4 × greater risk of suicide attempts than heterosexuals

Available at: http://www.cdc.gov/ViolencePrevention/pdf/Suicide-DataSheet-a.pdf.
Risks and benefits of antidepressants by indication in youth.

Sociodemographic and Educational Risk Factors

- Gender (female for self-harm and male for suicide)—most countries*
- Low socioeconomic status*
- Lesbian, gay, bisexual, or transgender sexual orientation
- Restricted educational achievement*

Individual Negative Life Events and Family Adversity

• Parental separation or divorce*
• Parental death*
• Adverse childhood experiences*
• History of physical or sexual abuse
• Parental mental disorder*
• Family history of suicidal behavior*
• Marital or family discord
• Bullying
• Interpersonal difficulties*

Psychiatric and Psychological Factors

- Mental disorder*, especially depression, anxiety, attention deficit hyperactivity disorder
- Drug and alcohol misuse*
- Impulsivity
- Low self-esteem
- Poor social problem-solving
- Perfectionism
- Hopelessness*

Key risk factors for adolescent self-harm and suicide

“Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of [Drug Name] or any other antidepressant in a child or adolescent must balance this risk with the clinical need. Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. [Drug Name] is not approved for use in pediatric patients...”

**FDA approved treatments for MDD in Youth:**

1. Fluoxetine in patients 6-17 yo
2. Escitalopram in patients 12-17 yo
What do we know about the impact of age on the risk of suicidality?
Suicidal Ideation and Behavior in Subjects Taking Antidepressants for Psychiatric Reasons

Probability of Remaining Free of Deliberate Self-harm and Time Since Initiating High vs Modal-Dose Antidepressant Therapy, by Age Group

Risk of Mania and Antidepressant Treatment

What do other data tell us about the risk?
Ongoing Debate About Antidepressants and Suicidality

- Examined suicidality in 4582 cases in 24 controlled clinical trials on all antidepressants in pediatric patients
  - Text search with blind recoding
  - Risk ratio for depression trials, 1.66
  - Risk difference 0.02 (excess of 1-3 patients/100)
- No increase in suicidality on clinician rating scales
- Very few suicide attempts
- No patients committed suicide or seriously harmed self

Meta-Analysis of Overall Rate of Emergent Suicidality: All Types of Antidepressants

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number Needed to “Harm” (NNH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDD</td>
<td>112</td>
</tr>
<tr>
<td>OCD</td>
<td>200</td>
</tr>
<tr>
<td>Anxiety</td>
<td>143</td>
</tr>
</tbody>
</table>

OCD, obsessive compulsive disorder.
MDD, major depressive disorder.

Libby AM, Orton HD, Valuck RJ. Persisting decline in depression treatment after FDA warnings. Arch Gen Psychiatry 2009;66(6):635
Risk of Suicide Attempt Before and After Starting Treatment <25 Years

Autopsy Studies of Suicide Victims

- 151 youth suicides studied in Utah
  - Of 137 with toxicology, only 4 with detectable levels of AD, AP, or MS
- 41 youth suicides studied in NYC, 1999-2002
  - Of 36 with toxicology, only 1 AD detected
- 1419 adult suicides studied in NYC, 2002-2004
  - 13.9% of young adults (18-24 years) had AD present on toxicology

Ecological Studies in USA Comparing Trends in Suicide Rate and Antidepressant Prescribing

**Common finding**

Increases in SSRI prescribing associated with decreases in absolute suicide rates

**Caution!**

Cannot reach conclusion about causality

What do we know about the risk in recent studies of treatment of depression in youth using medications and psychosocial treatments?
Treatment for Adolescents with Depression Study (TADS): Two Central Findings

1. Fluoxetine alone, or in combination with CBT accelerates improvement of depression relative to CBT alone.

2. Adding CBT to fluoxetine therapy minimizes persistent suicidal ideation and treatment-emergent suicidal events.

The TADS Team, Arch Gen Psychiatry October 2007;64:1132-1143.
Predictors of Suicide Attempts and Nonsuicidal Self-Injury in the Adolescent Depression Antidepressants and Psychotherapy Trial (ADAPT)

TORDIA: Time to suicide attempts (SAs) and nonsuicidal self-injury (NSSI) during 24-wk trial

Baseline NSSI and Hopelessness predicted shorter time to SA
Baseline NSSI and/or abuse predicted shorter time to NSSI

Depressive symptoms and clinical status during the Treatment of Adolescent Suicide Attempters (TASA) Study

Child Depression Rating Scale-Revised Scores Over Time

What do we understand about some of the impact of the Black Box Warning?
National Trends in Prescribing Antidepressants Before and After an FDA Advisory on Suicidality Risk in Youths

Proportion of depression visits and antidepressant visits among all ambulatory visits by children ages 5 to 17 and adults, 1998–2007

Chen, S & Toh, S. Psychiatric Services 2011; 62:727-733
Suicide and antidepressants
Beware extrapolation from ecological data

Numbers of suicides per 100,000 in adolescents by year in the United States.

Hammad T A, Mosholder A D BMJ 2010;341:c6844
What do we know about how the risk of suicidality changes during various phases of treatment?
Adjusted Odds Ratios for Phases of Antidepressant Treatment

The dotted line at OR = 1.0 indicates the value of “equal risk” (equal odds of prior exposure to antidepressants for indicated group vs referent group); OR values higher than 1.0 indicate elevated risk, OR values lower than 1.0 indicate reduced risk.

Valuck RJ et al., J Clin Psychiatry 2009;70(8):1069–1077
Risk periods included in self-controlled case series analysis for attempted suicide, suicidal ideation and self-harm and suicide.

1=baseline; 2–5=1 month pre-exposure periods; 6=prescription day; 7–10=four 1 week exposure periods; 11=remainder of antidepressant exposure; 12–14=three 1-month washout periods.

A

Attempted suicide

B

Suicidal ideation

C

Intentional self-harm

Antidepressants, suicides, and drug regulation.

What do we know about the risk of specific antidepressant medications?
Risk of suicide attempt and completion associated with the use of individual antidepressants compared with no exposure

<table>
<thead>
<tr>
<th>Group; drug</th>
<th>No. of studies</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adolescents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>2</td>
<td>1.32 (0.41–4.29)</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>2</td>
<td>1.33 (0.38–4.58)</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>2</td>
<td>0.84 (0.26–2.73)</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>2</td>
<td>1.77 (1.05–2.99)</td>
</tr>
<tr>
<td>Sertraline</td>
<td>2</td>
<td>1.25 (0.49–3.21)</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>2</td>
<td>2.43 (1.47–4.02)</td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>2</td>
<td>0.87 (0.58–1.29)</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>2</td>
<td>0.83 (0.32–2.14)</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>2</td>
<td>1.39 (0.66–2.92)</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>2</td>
<td>0.91 (0.52–1.58)</td>
</tr>
<tr>
<td>Sertraline</td>
<td>2</td>
<td>0.46 (0.09–2.23)</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>2</td>
<td>1.32 (0.74–2.35)</td>
</tr>
</tbody>
</table>

Barbui C et al., CMAJ. 2009 Feb 3;180(3): 291-7
Comparative safety of antidepressant agents for children and adolescents regarding suicidal acts

Schneeweiss, S et al., Pediatrics 2010 May;125(5):876-88. Epub 2010 Apr 12
Risk for suicide attempt among children and adolescents who were current users of individual antidepressants compared with children and adolescents who were current users of fluoxetine

Where to from here?
Targets of Suicide Prevention

SUICIDAL BEHAVIOR

Stressful Life Event

Mood or Other Psychiatric Disorder

Suicidal Ideation

FACTORS INVOLVED IN SUICIDAL BEHAVIOR

Impulsivity

Hopelessness and/or Pessimism

Access to Lethal Means

Imitation

Suicidal Act

PREVENTION INTERVENTIONS

A Education and Awareness Programs
   Primary Care Physicians
   General Public
   Community or Organizational Gatekeepers

B Screening for Individuals at High Risk

Treatment

C Pharmacotherapy
   Antidepressants, Including Selective Serotonin Reuptake Inhibitors
   Antipsychotics

D Psychotherapy
   Alcoholism Programs
   Cognitive Behavioral Therapy

E Follow-up Care for Suicide Attempts

F Restriction of Access to Lethal Means

G Media Reporting Guidelines for Suicide

Mann, J. J. et al. JAMA 2005;294:2064-2074
Suicide Rates Reduced By:

- Educating Health Care Professionals about recognizing and treating depression.
- Restricting access to lethal methods.
- Other interventions need more evidence of efficacy.
- Ascertaining which components of suicide prevention programs are effective in reducing rates of suicide and suicide attempts is essential in order to optimize use of limited resources.

Mann, J. J. et al. JAMA 2005;294:2064-2074
Example of Adolescent Support Card

- Safety Plan (write together and rehearse)
- Doctor’s Number
- Therapist’s Number
- ER/Hospital Numbers
- Identified Support Network (Family, Pets, Friends, Church)
- National Adolescent Suicide Hotline
  800-621-4000
- [www.suicidehotlines.com/national.html](http://www.suicidehotlines.com/national.html)
Shneidman’s View...

• Suicide stems from psychological *pain*

• Psychological pain comes from frustrated psychological *needs* peculiar to each person
  
  — Can be related to early childhood assaults experiences

  “I tend to believe that, at rock bottom, the pains that drive suicide relate primarily not to the precipitous absence of . . . happiness in adulthood, but to the haunting losses of childhood’s special joys.”

  Shneidman, Edwin S.
  *The Suicidal Mind*. Oxford University Press, 1998
Five “Clusters” of Needs

- Thwarted *love*, acceptance, belonging
  - succorance, affiliation
- Fractured *control*, predictability, arrangement
  - achievement, autonomy, order, understanding
- Assaulted self-image and avoidance of *shame*
  - affiliation, defendance, shame-avoidance
- Ruptured key relationships and *grief*
  - affiliation, nurturance
- Excessive *anger*, rage, hostility
  - dominance, aggression, counteraction
Shneidman’s Cubic Model of Suicide (1987)

- Low to High Press (Stress)
- High to Low Perturbation/Agitation
- Low to High Psychache (Pain)

Completed Suicide
Psychache as Cause of Suicide

“The implications of this psychological view are quite extensive. For one thing, it means that our best route to understanding suicide is not through the study of the structure of the brain, nor the study of social statistics, nor the study of mental diseases, but directly through the study of human emotions described in plain English, in the words of the suicidal person.” (Shneidman, 1996, p.6)
Shneidman’s Two Questions

Where do you hurt?

How can I help?
David Jobes’ “Truisms”

- Most suicidal people **do not want an end to their biological existence**;
  - rather, they want an end to their psychological pain
- Most suicidal people **tell others** (including mental health professionals) that they are thinking about suicide as a compelling option for coping with their pain.
- Most suicidal people have **psychological problems, social problems, and poor methods for coping with pain** –
  - all things that mental health professionals are usually well trained to tackle.

“... I am passionately interested in providing a reasonable response to ending psychological pain without costing a patient his or her life. I have heard what my suicidal patients have said about their pain and suffering and I am dedicated to responding effectively to that pain and suffering. I am especially resolved to use my training and skills to fundamentally address psychological and social problems, creating whole new and better ways of coping with seemingly unbearable pain. ... Helping our patients find a way to choose life is the point of all our efforts in this most crucial of all clinical endeavors.”

Supports for Clinicians, Patients & Families

- American Psychiatric Association [www.psych.org]
- American Academy of Child and Adolescent Psychiatry [www.aacap.org]
- American Academy of Pediatrics
- American Society for the Prevention of Suicide [www.afsp.org]
- National Alliance for the Mentally Ill [www.nami.org]
- The American Association of Suicidology [www.suicidolgy.org]
- Mental Health Screening [www.mentalhealthscreening.org]
- [www.samaritains.org]
- **National Suicide Prevention Lifeline 1-800-273-TALK**
Extra Slides
Assessment of Suicidal Youth

• Characteristics of Suicidality
• Current and Lifetime Psychopathology
• Psychological Characteristics
• Family and Environmental Factors
• Availability of Lethal Means
• Use of Self-Report Instruments (e.g., Suicidal Ideation Questionnaire, Suicide Probability Scale) (Huth-Bocks et al., 2007)

SAFE-T
Suicide Assessment Five-step Evaluation and Triage

- Risk Factors
- Protective Factors
- Suicide Inquiry
- Determination of Risk Level/Intervention
- Documentation

Developed by Douglas Jacobs, MD
Screening For Mental Health
www.mentalhealthscreening.org
SAFE-T Continued

Suicide Assessment Five-step Evaluation and Triage

• Risk Factors
  – Current/Past Psychiatric Diagnoses,
  – Key Symptoms: anhedonia, impulsivity, hopelessness, panic, command hallucinations
  – History of prior attempts or Self-injurious behaviors
  – Precipitants/Stressors: humiliation, shame, despair, Medical Illness, Abuse, Neglect, Intoxication
  – Access to firearms

• Protective Factors
  – Internal: Ability to cope with stress, religious beliefs, frustration tolerance, absence of psychosis
  – External: responsibility for others, positive therapeutic relationship, social supports
SAFE-T Continued

Suicide Assessment Five-step Evaluation and Triage

- Suicide Inquiry
  - Ideation
  - Plan
  - Behaviors
  - Intent
  - Assess for homicidal ideation

- Determination of Risk Level/Intervention
  - Low: Modifiable risk factors, strong protective factors
  - Moderate: Multiple Risk Factors, Few Protective Factors
  - High: Comorbid, High Risk Diagnoses, Minimal Protective Factors
SAFE-T

Suicide Assessment Five-step Evaluation and Triage

- Documentation
  - Suicide Assessment
    - Conducted at first contact and for subsequent suicidal behavior ideation or pertinent clinical changes
  - Your impression at this time (and perhaps chronically) of level of risk,
  - Basis for determination,
  - Treatment plan to address/reduce current risk (e.g., Medication, Setting, ECT, Contact with others, Coping Skills, Consultation)
Risk Management in Treatment of Depressive Disorders in Youth

• Education is the foundation of successful treatment
  – Correct information about depression to patient, parents, educators and others involved in the development of child
    • Clinical manifestations
    • Course and Prognosis
    • Treatment(s): Importance of Adherence
  – Remove GUNS from home
  – Identify available supports and how to access
  – Together with parents (or guardians) and patient formulate and agree on a treatment plan (including a safety plan. Consider PRACTICING this plan)