25 Years of Research at Services for Teens at Risk: Prizes and Surprises

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Conflicts of Interest

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Objectives: To Review What We Have Learned About:

- Access to method and risk for suicide
- Psychiatric disorder and suicidal behavior
- Impact of exposure to suicide
- Familial contributors to suicidal behavior
- Treatment and prevention of depression
Case Study

- Greg was a 16 year old boy who came home intoxicated
- He pointed a gun at his mother and then killed himself.
- He told his best friend that he wanted to kill himself.
- He had been unsuccessfully treated for depression.
- Possible history of hypomania.
- Difficulty falling and staying asleep
- Father committed suicide as did an older brother, 8 months previously
- Mother was currently depressed and untreated
Questions that arose from this case

- Do guns in the home increase the risk of suicide?
- Do depression, bipolar disorder, and alcohol abuse play a role?
- Homicidal ideation and aggression—common?
- Do people who talk about suicide actually do it?
- Does suicide run in families? If so is it due to:
  - Imitation
  - Bereavement
  - Genetics
  - How do you help someone like this who would come for treatment?
Guns and Suicide*

* Brent, et al., 1991
Loaded Guns and Suicide

* Brent, et al., 1991
Guns and Suicide: A lethal mix

- If a gun is in the home, firearms is the method of choice for suicide (87.8% vs. 18.8%)
- The more guns in the home, the more likely the suicide victim will choose to use one.
- Intoxicated suicide victims were 5 times more likely to use a gun.
- Handguns are risk factor for urban areas; long guns in rural areas
- Other risk factors for suicide not associated with firearms ownership.
We talk, but do people listen..?

- Our conclusion was to insist that people remove guns if there is suicidal risk.
- When you ask parents of depressed kids to remove guns from the home, only ¼ of them did.
- **More likely** to remove the gun if the parent owns the gun, is a single parent.
- **Less likely** if the other parent owns the gun, is a substance abuser, and there are marital problems
- **Conclusion:** Talk with the gun owner. Don’t put the mom in the middle! Need to negotiate!
Back to the case...

- Availability of a gun increased his risk of suicide and use of a gun as a method.
- Intoxication made use of a gun more likely as well.
- He lived in a rural area, and used a long-gun to kill himself.
Clinical risk factors for suicide

- What is the role of mood disorder, specifically depression and bipolar disorder?
- What about the role of alcohol abuse?
- How are suicidal ideation, attempts, and completed suicide related?
- Are suicidal people more likely to be homicidal?
- Is there a relationship between suicide and aggression?
Risk Factors for Suicide and Suicidality*

*Brent, et al., 1988, 1993
Back to our case…

- Treatment resistant depression
- Possible bipolar spectrum disorder
- Planning for the attempt
- Prior communication of intent
- Homicidal ideation
- Sleep difficulties
- This person had several major risk factors, but..
- All of these problems can be clinically managed!
To prevent suicide in this case...

- Teach teens to “it is better to lose a friendship than a friend.”
- Teach parents and teachers to watch for warning signs
- Assess and treat alcohol abuse
- R/O bipolar disorder
- treat depression
- Address hopelessness (implied by high intent)
- Address sleep difficulties
Surprises

- In 1988, most experts doubted the bipolar finding.
- Now we know that early-onset bipolar disorder often presents with ultra-rapid cycling or a mixed state, hence often at high suicidal risk (up to 40% attempt).
- Kids who talk about suicide do commit suicide.
- Suicide is not just “aggression turned inward,” it is often turned outward as well.
When one sibling suicide follows another...

- Is it imitation?
- Is it grief?
- Is it genetic?
Youth Exposed to Suicide (YES)

Matched to unexposed controls taken at random from unexposed neighborhoods

- Suicide
- Sibling (~ 1)
- Close Friend (3)
- Acquaintance (3)
Pre-existing Vulnerabilities (%) Make Exposure to a Peer Suicide More Likely

*Brent et al. 1993
New Onset Psychiatric Disorder in Exposed & Unexposed Subjects (%) 6 Months After Exposure*

*Brent et al. 1993
Current & New-Onset Psychiatric Disorder in Exposed Siblings vs. Controls (n = 25)*

*Breent et al. 1996
Three-Year Cumulative Incidence of Suicide Attempts

- Raw rates: 2.3% vs. 2.8%, NS
- Adjusted OR = 0.5 (95% CI, 0.08 to 2.8) (Controlling for sibling conflict, discipline problems, age, family history, substance abuse)
Surprises

- After adjusting for prior risk of suicidal behavior, their risk was $\frac{1}{2}$ that of the unexposed controls!
- However, by seeing first hand the effects of suicide on a social network, they resolved never to engage in such behavior.
Could it be Complicated Grief?

- Bitterness
- Anger
- Numbness
- Difficulty “moving on”
- Preoccupation with the deceased
- Intrusive thoughts
- Guilt and blame
- Avoidance
Complicated Grief in Teens

- 14/76 (18.4%) had CG. Associated with 5-fold higher risk of suicidal ideation, even controlling for depression, **more than 6 years after death**

- **2011**: 10.4% of parentally bereaved youth have high CG scores. Predicted by history of depression, but also predicts onset of depression and functional impairment

- **Conclusion**: CG is real in youth, assess and treat!
Surprises about grief

• Siblings show a better resolution of depression and PTSF than friends, despite higher grief levels.
• Perhaps they had more external validation of their grief and more support.
• Complicated grief conveys an increased risk for suicidal ideation, depression, and even health problems above and beyond psychiatric disorder.
Does Suicide Run in Families?

- Familial tendency to suicidal behavior has been reported even in adoption studies.
- Monozygotic twins show greater concordance for suicidal behavior than dizygotic twins.
- No evidence of imitation in the bereaved friends or siblings of suicide victims.
Rates of Suicidal Behavior in First-Degree Relatives of Suicide Victims and Controls*

*Brent et al., 1996
Rates of Suicidal Behavior in First-Degree Relatives
Role of Proband Impulsive Aggressive Behavior

*Brent et al., 1996
Cumulative Proportion of Suicide Attempt Among Offspring of Attempters vs. Non-Attempters*

Generalized Savage: $\chi^2 = 7.89$, $p = .005$
OR = 6.2, 97.5% CI, 1.2 to 33.4

*Brent et al., 2002
Cumulative Proportion of Suicide Attempt Among Offspring of Concordant Attempters vs. Non-concordant Attempters vs. Non-attempters

Cumulative proportion

Age (years)

Concordant
Non-concordant
Non-attempters

Generalized Wilcoxon $x^2$: 10.1, df=2, p = .007
Kaplan Meier Survival Curve by Proband Attempt and Abuse
Parental Sexual Abuse & Offspring Suicide Attempt

*Brodsky, et al., 2008
Prizes and Surprises: Suicidal Behavior does run in families

- Familial transmission of suicidal behavior mediated by transmission of **impulsive aggression**.
- Suicide attempt and suicide are on the same **continuum**.
- Parental history of sexual abuse increased the risk for a child attempt as much as a family history of an attempt.
Back to this case…..

- **Imitation** is an unlikely explanation for his suicide.
- **Loss** of sibling could have precipitated a depression, or complicated grief.
- He was **genetically vulnerable** to suicide. Two first-degree relatives increase risk for suicide about 10-fold.
- BUT--the **vast majority** of people with a family history of suicidal behavior do **not** commit suicide.
Treatment and Prevention of Depression and Suicidal Behavior

- If mood disorders are the biggest risk factor for completed suicide, then better treatment of mood disorders should decrease the suicide rate
- **1997**: Pittsburgh Psychotherapy Study
- **2008**: Treatment of SSRI-Resistant Depression in Adolescents (TORDIA)
- **2009**: Prevention of Depression (with CBT)
- **2009**: Treatment of Adolescent Suicide Attempts (TASA)
Pittsburgh Psychotherapy Trial

- 107 depressed adolescents
- CBT, Family therapy (FT), or Supportive Therapy (ST)
- Outcome: no mood disorder and normal BDI (<9)
- CBT was more effective than FT or ST, but over time gap closed, in part due to open treatment
- No differential treatment impact on suicidality
Failure to Achieve Remission as a Function of Self-Reported Maternal Depression (BDI)*

* Brent et al., 1998
Depression can be prevented* ...

*Garber, et al., 2008
Prizes and Surprises

- **Prizes**: CBT superior to FT and ST
- **Surprises**: If the parent was depressed, CBT no better than supportive therapy
- Despite improving depression, CBT no better than the others on improving suicidality
Treatment of SSRI-Resistant Adolescent Depression (TORDIA)

- 334 depressed adolescents who did not respond to an SSRI
- CBT + switch to SSRI, CBT + switch to venlafaxine (VLX), SSRI, VLX
- moderate to severe depression, 58% suicidal, median length 2 years
- much or very much improvement + >50% improvement in symptoms
- CBT + Med>Med alone; Ven=SSRI, but more side effects
- by 6mos, the txs converged due to open treatment
Lessons from TORDIA

- We learned about some things we probably should NOT do…
- Use SSRI rather than Venlafaxine for suicidal youth
- Avoid use of benzos, trazodone
Increased Risk for Self-Harm in High Ideators treated with VLX

![Bar chart showing increased risk for self-harm in high ideators treated with VLX compared to SSRI (P=.75) and VLX (P=.02).]
SSRI vs. VLX: Impact on Suicidal Ideation*

LogTime: p<.001
Med: p=.36
Med*LogTime: p=.03

*Vitiello, et al., 2011
Benzodiazepines and Suicidal AE’s (%)+

* Significant even after controlling for ideation, family conflict and drug use

** Significant after controlling for ideation

+ Brent, et al., 2009
Sleep Meds and Response*

*Shamseddeen et al.
Lessons from TORDIA

- Add CBT, especially for comorbid cases
- Need adequate dose of CBT and medication
- Monitor concentration, adherence
- Watch out for alcohol and drug use
- Watch for subsyndromal BP?
- Need to accelerate early response to treatment
Moderation of CBT Response: Abuse and Comorbidity*

Abuse History

No CBT

CBT

Number of Comorbid Disorders

*Asarnow et al., 2009
Drug Plasma Concentration and Response*

*Sakolsky, et al., 2011
# Active ingredients in CBT (%)*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted Odds of Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;9 sess.</td>
<td>2.5</td>
</tr>
<tr>
<td>Social Skills</td>
<td>2.6</td>
</tr>
<tr>
<td>Problem Solving</td>
<td>2.3</td>
</tr>
</tbody>
</table>

*Kennard et al., 2009*
Alcohol/Substance Use and Treatment Response*

*Goldstein, et al., 2010
Adherence and Treatment Outcome in TORDIA*

Chi-sq tests for trend:
All: $\chi^2_1 = 3.72$, $p = .05$; SSRI: $\chi^2_1 = 4.19$, $p = .04$

* Woldu et al., in press
Importance of Early Response: Reduction in CDRS-R (Remitters vs. Non-Remitters)

LogTime: $p < .001$
Remission: $p = .06$
Remission*LogTime: $p < .001$
Slow or No Response and Bipolar Symptoms in TORDIA*

*Maalouf et al., in prep.
## Back to the case…

<table>
<thead>
<tr>
<th>Problem</th>
<th>Treatment Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Resistant MDD</td>
<td>Switch SSRI’s and add CBT</td>
</tr>
<tr>
<td>Uncertain if adherent or got adequate level</td>
<td>Monitor adherence and exposure to drug</td>
</tr>
<tr>
<td>Alcohol use/abuse</td>
<td>Push for abstinence</td>
</tr>
<tr>
<td>Maternal depression</td>
<td>Refer mom for treatment</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>Stronger case for CBT</td>
</tr>
<tr>
<td>Impulsive aggression</td>
<td>Problem-solving, emotion regulation</td>
</tr>
</tbody>
</table>
Treatment of Adolescent Suicide Attempters: TASA

- 124 depressed adolescent suicide attempters
- Treated with specific psychotherapy program designed to target vulnerabilities that led to suicide in the first place
- Rate of re-attempt/6 months is lower than expected from clinical reports (MR=0.12).
- Success associated with improvement in functioning, decrease in ideation
- Higher risk: greater number of previous attempts, high ideation, family conflict, lack of family cohesion
TASA: time to Suicidal Events & Attempts*

*Brent, et al., 2009
TASA: Surprises

- 40% of suicidal events occurred with 4 weeks of starting treatment
- Suggest need to frontload safety plan and early ER strategies.
What we can do

- Identify teens at risk for suicidal behavior
- Can develop a rational treatment plan
- Can treat depression, including treatment resistant depression
- Have identified some domains with which we can improve outcome further
What we can’t do

- Disseminate effective psychotherapies widely
- Treat the most severely depressed youth effectively
- Treat depression in younger children
- Treat complicated grief in youth
- Match treatment to patient
- Reduce the risk of suicide attempt
What the future will bring

- Brief Cognitive Behavior Therapy in primary care for depression and anxiety
- DBT for Pediatric Bipolar Disorder
- Family-based IPT, Contextual Emotion Regulation Therapy (CERT) for early onset depression
- Treatments for complicated grief in kids
- Test of TASA (CBT-SP) to prevent suicide re-attempts
ATRIUM (Accelerating Treatment Response in Unipolar Major Depression)

- CBT offers too low a dose of too many interventions and skills
- Better to identify what kids need and give them more of it so that they can learn it
- Areas of foci: problem-solving, cognitive bias, reward and positive affect, mindfulness
- Use of fMRI and EMA to monitor and shape treatment
To the cause that needs assistance
To the wrong that needs resistance
To the future in the distance
And the good that we can do

Mick Collins
Thank you for your attention!

- For copies of these slides, please email Robin Martin at martinrl2@upmc.edu
- These slides will also be posted on the STAR-Center web-site