Suicide Prediction and Prevention: A Practical Synthesis of the Evidence

Charles L. Rich, M.D.
UNIVERSITY OF SOUTH ALABAMA
Professor Emeritus of Psychiatry

DISCLAIMER

Dr. Rich does not have any industry relationships that would create a conflict of interest.

U.S. Suicide Rates, 1950–2003
(per 100,000 population)

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>All ages, age adjusted</td>
<td>13.2</td>
<td>13.2</td>
<td>13.2</td>
<td>13.2</td>
<td>12.5</td>
<td>11.6</td>
<td>10.4</td>
<td>10.7</td>
<td>10.5</td>
<td>10.8</td>
</tr>
<tr>
<td>Male, all ages</td>
<td>21.2</td>
<td>20.0</td>
<td>19.8</td>
<td>19.9</td>
<td>21.5</td>
<td>20.3</td>
<td>17.7</td>
<td>18.2</td>
<td>18.4</td>
<td>18.0</td>
</tr>
<tr>
<td>Female, all ages</td>
<td>5.6</td>
<td>5.6</td>
<td>7.4</td>
<td>5.7</td>
<td>4.8</td>
<td>4.3</td>
<td>4.0</td>
<td>4.2</td>
<td>4.2</td>
<td>4.2</td>
</tr>
</tbody>
</table>

Fluoxetine introduced in 1986
Suicide Prediction and Prevention: A Practical Synthesis of the Evidence

The Plan

1. Review Prediction Situation (briefly)
2. Develop an Accurate Suicide Model
3. Apply the Model to Prevention

Some Factors Correlated with Suicide

Correlations ≠ Predictions
Relationship Between Hopelessness and Ultimate Suicide: A Replication With Psychiatric Outpatients

Aaron T. Beck, M.D., Gary Brown, M.S., Robert J. Rushbeck, Ph.D., Bonnie L. Stewart, Ph.D., and Robert A. Yeser, R.D.O.

1958 patients evaluated from 1978-1985
1161 scored >9 on 20 point “hopelessness” scale
Included 16 of 17 suicides (high sensitivity)

\[
\frac{1145}{1161} = 98\% \text{ False Positive (low/no specificity)}
\]

Some Factors Correlated with Suicide

Stressors: Major events, financial, medical, legal
Precipitants: Trigger Events
Personality traits: Impulsivity, impulsivity, hopelessness, peer pressure
Genetics: Family history of suicide
External pressures: Police, medical, financial, moral, social
Diet: Alcohol, caffeine, tobacco
Demographics: Age, race, sex
Development: Early trauma, exposure to suicidal behavior

All of these correlates include too many false positives.

Suicide Prediction

Conclusion

No single correlate or combination can be used to predict an individual suicide with clinical (or legal) utility.
Some Factors Correlated with Suicide

Stressors: Personal, Financial, Medical, Legal
Precipitants: Triggers, Events
Personality Traits: Impulsivity, Rigidity, Hearsay, Under Self-Esteem
Genetic: Family History of Suicide
Existential Pressures: Loss, Failure, Isolation, Destabilization of Family, Loss of Community Ties
Brain Chemistry: Serotonin, Dopamine, GABA, Glutamate
Mental Disorders: Depression, Substance Abuse

Maybe we can put all of these together in a way that “explains” suicide and allows us to successfully intervene.

Suicide Prevention

GOAL
To devise a Representation (MODEL) of suicide
That is the most FACTUALLY COMPREHENSIVE
And CLINICALLY APPLICABLE
Substance Abuse and Suicide
The San Diego Study*

Charles L. Rich, M.D., Richard C. Fowler, M.D., and Deborah Young, M.D.

Mean Symptoms/Case

<table>
<thead>
<tr>
<th>Substance Abuse</th>
<th>Substance plus Affective Disorder</th>
<th>Affective Disorder</th>
<th>Other Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1</td>
<td>6.2</td>
<td>7.0</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Including low mood, decreased appetite, weight loss, sleep problems, agitation, withdrawal, decreased libido, low energy, worthlessness, guilt, thoughts of death, talk of suicide, suicide attempt.
The relative effect of particular stressors in a population can be estimated, but any individual’s response to a particular stressor at any given time is pretty much unpredictable.
Precipitants: "Why Now?"
1. Can’t always tell (<50% in SDSS)
2. Tend to be recurrent
3. Tend to be mundane
4. Tend to be…precipitous
5. Always determined after the fact
Therefore, not of much clinical utility
Psychoactive Substances in Suicides
Comparison of Toxicologic Findings in Two Samples

Dirk M. Dhossche, M.D., Charles L. Rich, M.D., and Göran Jarlsson, M.D., Ph.D.

<table>
<thead>
<tr>
<th></th>
<th>San Diego 1981-82</th>
<th>Mobile 1990-96</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td></td>
<td>143</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>198</td>
<td>41</td>
</tr>
<tr>
<td>+ Alcohol</td>
<td>30%</td>
<td>29%</td>
</tr>
<tr>
<td>+ Any IAS*</td>
<td>51%</td>
<td>65%</td>
</tr>
</tbody>
</table>

*IAS = Intoxicating Abusable Substance

Emergence of Intense Suicidal Preoccupation During Fluoxetine Treatment

Matthijs Tricoli, M.D., Ph.D., Carol Glool, R.N., M.S.C.S., and Jonathan O. Cole, M.D.

Six depressed patients free of recent serious suicidal ideation developed intense, violent suicidal preoccupation after 2–7 weeks of fluoxetine treatment. This state persisted for as little as 3 days to as long as 3 months after discontinuation of fluoxetine. None of these patients had ever experienced a similar state during treatment with any other psychotropic drug.

(Am J Psychiatry 1990; 147:207–210)

Suicide Rates in Clinical Trials of SSRIs, Other Antidepressants, and Placebo: Analysis of FDA Reports

Ali Khan, M.D., Seher Khan, Russell Kopel, Ph.D., Walter A. Brown, M.D.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of Patients Randomly Assigned to Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective serotonin reuptake inhibitors</td>
<td>26,109</td>
</tr>
<tr>
<td>Other antidepressants*</td>
<td>77,273</td>
</tr>
<tr>
<td>Placebo</td>
<td>4,895</td>
</tr>
</tbody>
</table>

Mainly short term studies
Subjects excluded for “suicidality”
So, any provocative effect should be seen – right?
Mainly short term studies
Subjects excluded for “suicidality”
So, any provocative effect should be seen – right?
The Suicide Risk of Discharged Psychiatric Patients

1. 1997-1999 – Hong Kong
2. 21,921 discharged patients >15 yo
3. 280 suicides in first year after discharge
4. 105 (38%) occurred in first 28 days
“We think the most likely explanation for this finding is that antidepressant treatment may not be immediately effective....”

“It is also possible that... patients [start] to take an antidepressant when their depression is at its worst....”

.........or maybe?

2/3 of people prescribed AD’s had negative toxicology

Utah Youth Suicide Study: Psychological Autopsy
Michelle Moskos, Ph.D., M.P.H.
Lenora Olson, M.A., Ph.D.
Sarah Haltern, B.S., M.P.H.
Trisha Keller, R.N., M.P.H.
Doug Gray, M.D.

- Phase 1 - 151 suicides age 13-21
- Phase 2 - 49 investigated thoroughly
  - 32 had been seen and diagnosed
  - 14 were prescribed medication
  - 0 positive on post mortem toxicology
LIFE

EXISTENTIAL PRESSURES

STRESSORS

DEPRESSION

SUBSTANCE

ABUSE

Other Mental Disorders:
- Mood Disorders
- Anxiety Disorders
- Personality Disorders

Suicide Protection Factor(s):
- Demographics
- Genetics
- Brain Chemistry
- Personality Traits
- etc.

Suicide

Defect(s):
- Demographics
- Genetics
- Brain Chemistry
- Personality Traits
- etc.

Protection Factor(s):
- Demographics
- Partner
- Children
- etc.

Precipitant(s):
- Time
- Place
- Method

Trends in Hanging and Firearm Suicide Rates in Australia: Substitution of Method?

Diego De Leo, MD, PhD, Jonathan Dwyer, PhD, David Fisen, and Kerren Neuling, B Biostat

Figure 4. Suicide deaths, by method and sex, United States, 1999 and 2014


“Our major clinical point, however, was and remains that suicidal individuals – be they old or young, urban or rural – cannot be considered out of harm’s way simply because they do not have access to a gun.”

Rich C, Amer J Psychiatry, Jan 1991

Suicide Prediction and Prevention: A Practical Synthesis of the Evidence

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3. Apply the Model to Prevention
Suicides and Antidepressant Sales

Summary of Pharmacoepidemiologic Studies

<table>
<thead>
<tr>
<th>Study Location</th>
<th>Year</th>
<th>Age Group</th>
<th>Methodology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isacsson - Sweden</td>
<td>1978-1996</td>
<td>All</td>
<td>All</td>
</tr>
<tr>
<td>Rihmer - Hungary</td>
<td>1984-1998</td>
<td>+</td>
<td>Positive</td>
</tr>
<tr>
<td>Joyce - New Zealand</td>
<td>1995-2000</td>
<td>Age 15-24</td>
<td>Neutral</td>
</tr>
<tr>
<td>Kelly - Northern Ireland</td>
<td>1985-1999</td>
<td>Older, Younger</td>
<td>Negative</td>
</tr>
<tr>
<td>Anthony - Mexico</td>
<td>1994-1997</td>
<td>Females, Males</td>
<td>Neutral</td>
</tr>
<tr>
<td>Hall - Australia</td>
<td>1991-2000</td>
<td>Older, Younger</td>
<td>Summary of Pharmacoepidemiologic Studies</td>
</tr>
<tr>
<td>Lodhi - England/Wales</td>
<td>1985-1996</td>
<td>Older Males</td>
<td>Neutral</td>
</tr>
<tr>
<td>Helgason - Iceland</td>
<td>1975-2000</td>
<td>Older, Younger</td>
<td>Neutral</td>
</tr>
<tr>
<td>Gilchrist - USA</td>
<td>1985-1999</td>
<td>Females</td>
<td>Neutral</td>
</tr>
<tr>
<td>Botler - Italy</td>
<td>1985-1996</td>
<td>Age 45</td>
<td>Neutral</td>
</tr>
<tr>
<td>Bramness - Norway</td>
<td>1996-2002</td>
<td>Males 55-74</td>
<td>Neutral</td>
</tr>
<tr>
<td>Kisikeda - Finland</td>
<td>1994-2001</td>
<td>All</td>
<td>Neutral</td>
</tr>
<tr>
<td>Thorsen - Norway</td>
<td>1980-2004</td>
<td>Males, Females</td>
<td>Neutral</td>
</tr>
<tr>
<td>Cappelletti - FVG Italy</td>
<td>1997-2004</td>
<td>All</td>
<td>Neutral</td>
</tr>
</tbody>
</table>

* indicates significant increase in suicides following SSRIs introduction.
Conclusions. This is the first meta-analysis suggesting antisuicidal effects of lithium in recurrent MDD, similar in magnitude to that found in bipolar disorders.


Lithium Treatment Reduces Suicide Risk in Recurrent Major Depressive Disorder

Francesca Giorgetti, M.D.; Leonardo Tondo, M.D.; Fiona Cenni Ferrero, M.D.; and Ross J. Baldessarini, M.D.

7 studies (10 reports) 1990-2012
(Texas, Japan, Austria, England, Greece)

5 Positive (higher lithium, lower suicides rates)
1 Neutral
1 ± Females

Lots of sampling and statistical issues

Known nephro- and thyrotoxic effects

Are you ready to have lithium put in your drinking water?
Call me old fashioned, but it’s not like flouride, is it?

NIMH Collaborative Study on the Psychobiology of Depression - 1978

954 depressed patients
10 years
32 suicides (3%) – 13 (41%) in 1st year

Time-Related Predictors of Suicide in Major Affective Disorder

*Am J Psychiatry* [1993]; 145:1189-1194

Jon Favret, M.D.; William A. Schotten, M.D.; Louis Fogg, Ph.D.; David C. Carl, Ph.D.; Michael A. Young, Ph.D.; Dan Hekler, Ph.D.; and Robert Gibbons, Ph.D.

NIMH Collaborative Study on the Psychobiology of Depression - 1978

954 depressed patients
10 years
32 suicides (3%) – 13 (41%) in 1st year
No studies confirm that treatment with sedatives/hypnotics reduces suicide risk

Acute Intoxication → Disinhibition (frequently)

Persistent Intoxication → Depression (infrequently)

The odds of completed suicide were greater among patients who received any anxiety medication, and were further increased among those who received high dose treatment.
100 consecutive suicides age 65+

“We found a four-fold increased suicide risk among elderly using sedatives and/or hypnotics....”

...alternatives to sedatives/hypnotics should be used if...early adjunctive treatment for anxiety...is thought to be indicated.”

Hydroxyzine
More sedating antidepressant?
Low dose second generation antipsychotic?

No data on actual suicide rates
“Emergent suicidality is a common occurrence [12%] in psychosocial treatment of adolescent depression, with rates similar to those reported in recent antidepressant trials.”

Suicide Prediction and Prevention

Clinical Conclusion

Growing evidence strongly supports the suicide preventive effect of antidepressant treatment.

Curious coincidence? or…….
Suicides Ages 10-19

"After the warning, suicide in this age group increased for 5 consecutive years (60.5%). The increase occurred among individuals not treated with antidepressants."

Thus, a treatment only approach to prevention has limited impact on national rates of suicide...."
A Public Health Approach

Prevention of Disease
- Healthy Living
- Healthy Environment
- Vaccination

Detection and Treatment of Disease
- Public Awareness of Diagnosis
- Accessibility to Treatment
- Encouragement of Treatment

“The program was successful in reducing suicide rates by 60%.”

“Prevention was successful for as long as the program was instituted.”

“Thus, a treatment only approach to prevention has limited impact on national rates of suicide…”

Treatment is what most of us do for a living, right?
Perspective

Antidepressants’ Black-Box Warning — 10 Years Later

Robert A. Freedman, M.D.

I would therefore argue that the FDA should consider removing the warning entirely.

Suicide Prediction and Prevention

Clinical Caveat

Because it occurs so rarely, we never know if we prevent an individual suicide.

Therefore: We must have faith in our best efforts.

But: We must also realize we can’t win them all.