DISCLAIMER

Dr. Rich does not have any industry relationships.
San Diego Suicide Study

A Decade of Digging
(with Apologies to Pathology)

CHARLES L. RICH, M.D.

Age Range

<table>
<thead>
<tr>
<th></th>
<th>&lt; 30</th>
<th>≥ 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>150</td>
<td>133</td>
</tr>
</tbody>
</table>

Drug Use

<table>
<thead>
<tr>
<th></th>
<th>59%</th>
<th>29%</th>
</tr>
</thead>
</table>

Clinical Investigation + Toxicology
CONCLUSIONS

1. Suicide is the fatal outcome of a small number of mental disorders (maybe only one)
2. The last straws in suicide are largely:
   a) unpredictable
   b) unpreventable

**ERGO:** The best way to prevent (or delay?) suicide is to effectively treat the potentially fatal illness(es)
That means: a) close monitoring
           b) long-term follow-up

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

- **Stressors**: Major life events, financial strain, health problems, legal issues
- **Personality**: Impulsivity, hopelessness, self-esteem
- **Act**: Methods, history of previous attempts
- **Genetics**: Family history of suicide
- **Existential Pressures**: Loss, major disaster, major life change, alienation, dissatisfaction of family
- **Mental Disorders**: Suicidal ideation, depression, substance abuse
- **Deprivation Status**: Socioeconomic status

Correlations ≠ Predictions

**Relationship Between Hopelessness and Ultimate Suicide: A Replication With Psychiatric Outpatients**

- 1958 patients evaluated from 1978-1985
- 1161 scored >9 on 20 point "hopelessness" scale
- Included 16 of 17 suicides (high sensitivity)
- \(1145/1161 = 98\%\) False Positive (low/no specificity)
Some Factors Correlated with Suicide

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 any degree of clinical (or legal) utility.

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 Profile (MODEL) that is the most FACTUALLY COMPREHENSIVE and CLINICALLY APPLICABLE.
Consecutive Cases
Systematic Database
Valid Diagnostic Criteria

8 Studies of Consecutive Suicides

Summary

<table>
<thead>
<tr>
<th>Disorder</th>
<th>MEAN %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Mental or Medical Disorder</td>
<td>5%</td>
</tr>
<tr>
<td>Medical Ill. Only</td>
<td>3%</td>
</tr>
<tr>
<td><strong>ANY MENTAL DISORDER</strong></td>
<td><strong>92%</strong></td>
</tr>
<tr>
<td>Any Depression</td>
<td>57%</td>
</tr>
<tr>
<td>Any Substance Abuse</td>
<td>38%</td>
</tr>
<tr>
<td>Depression &amp;/or Substance Abuse</td>
<td>69%</td>
</tr>
<tr>
<td>Adjustment Disorder</td>
<td>10%</td>
</tr>
</tbody>
</table>

≥ 80%

LIFE

DEPRESSION

SUBSTANCE (AB)USE

SUICIDE
Substance Abuse and Suicide
The San Diego Study*
Charles L. Rich, M.D., Richard C. Fowler, M.D., and Deborah Young, M.D.

<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
Emergence of Intense Suicidal Preoccupation During Fluoxetine Treatment

Marvin L. Trucker, M.D., Ph.D., Carol Gold, R.N., M.S.C.S., and Jonathan D. 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

Aqil Khan, M.D.
Shahid Khan
Russell Koff, 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</td>
<td>26,109</td>
</tr>
<tr>
<td>reuptake inhibitors</td>
<td></td>
</tr>
<tr>
<td>Other antidepressants</td>
<td>17,273</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?
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Subjects excluded for "suicidality"
So, any provocative effect should be seen – right?
The Suicide Risk of Discharged Psychiatric Patients

Ting-Pong Ho, M.D.
J Clin Psychiatry 2003; 64:702-707

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?

UK General Practice Research Database
159,810 Users of Antidepressants
1993-1999

APPA
4/21/2017
Charles L. Rich, M.D

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 Halbern, B.S., M.P.H.
Trisha Keller, R.N., M.P.H.
Doug Gray, M.D.
Suicide and Life Threatening Behavior
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
“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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### Suicides and Antidepressant Sales

#### Summary of Pharmacoepidemiologic Studies

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Positive</th>
<th>Neutral</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbui - Italy 1955-2000 (2005) &gt; age 45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Castelpietra - FVG Italy 1997-2008 (2008) all</td>
<td></td>
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</tbody>
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### Lithium Treatment Reduces Suicide Risk in Recurrent Major Depressive Disorder

**Francesca Guazzetti, M.D.; Leonardo Tonão, M.D.; Francescentorrino, M.D. and Ross J. Baldessarini, M.D.**

**Conclusions:** This is the first meta-analysis suggesting antisuicidal effects of lithium in recurrent MDD, similar in magnitude to that found in bipolar disorders.


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### Lithium in drinking water and suicide prevention: a review of the evidence

**Antonio Vita, Luca De Pori and Emilio Bacchetta**

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

*Teratogenicity*

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

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Short-Term Suicide Year 1</th>
<th>Long-Term Suicide Years 2-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hopelessness</td>
<td>0.463</td>
<td>0.007</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>0.029</td>
<td>0.372</td>
</tr>
<tr>
<td>Loss of interest or pleasure (anhedonia)</td>
<td>0.005</td>
<td>0.223</td>
</tr>
<tr>
<td>Psychic anxiety</td>
<td>0.012</td>
<td>0.879</td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>0.613</td>
<td>0.041</td>
</tr>
<tr>
<td>Suicide attempts</td>
<td>0.815</td>
<td>0.086</td>
</tr>
<tr>
<td>Obsessive-compulsive features</td>
<td>0.063</td>
<td>0.303</td>
</tr>
<tr>
<td>Indecisiveness</td>
<td>0.085</td>
<td>0.062</td>
</tr>
<tr>
<td>Diminished concentration</td>
<td>0.028</td>
<td>0.078</td>
</tr>
<tr>
<td>Global insomnia</td>
<td>0.011</td>
<td>0.785</td>
</tr>
</tbody>
</table>

No studies confirm that treatment with sedatives/hypnotics reduces suicide risk

Acute Intoxication ➔ Disinhibition (frequently)

Persistent Intoxication ➔ Depression (infrequently)
April 1, 1999 – September 30, 2004
887,859 Depressed veterans (92% males)
1,892 Suicides

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

Limited by what?
By the number of people getting the treatment, right?
Treatment is what most of us do for a living, right?

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

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

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

....and I agree completely!!
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

CONCLUSIONS
1. Suicide is the fatal outcome of a small number of mental disorders (maybe only one)
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ERGO: The best way to prevent (or delay?) suicide is to effectively treat the potentially fatal illness(s)
That means:
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   b) long-term follow-up