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Psychopharmacology for Suicide Prevention

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Disclosures
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Is a consultant to, or has collaborated in research with: Alkermes, Auritec, Biotrofix, IFI, Janssen, JDS, Lilly, Merck, NeuroHealing, Novartis, and Solvay Corporations

But has no speaker-panel or equity relationships with industrial organizations

"The medical treatment of the propensity to suicide, whether prophylactic or therapeutic, differs not from that which is applicable in cases of ordinary insanity"

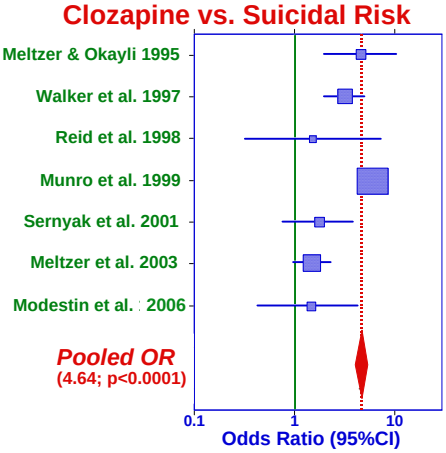
George M. Burrows, M.D.

[*Commentaries on the Causes, forms, Symptoms, Treatment, Moral and Medical, of Insanity*. London: Underwood, 1828]

Antipsychotics (APDs) vs. suicidal risk

- Only clozapine is FDA-approved (schizophrenia: 2003)–an historic precedent.
- Meta-analysis of the few studies of clozapine yield ≥4x reduction in risk of attempts or preparations, but little evidence of less mortality.
- Other antipsychotics and indictions remain to be studied.

Clozapine vs. Suicidal Risk



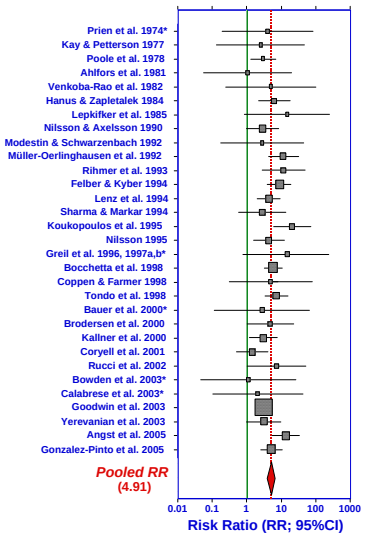
[Hennen & Baldessarini Schizophrenia Res 2005; 73: 139–145; Baldessarini 2006]

Mood-stabilizers vs. suicidal risk

- Lithium has strong and consistent evidence for reducing risks of both attempts & suicides by 4–5x, consistently in >30 studies, including 8 RCTs, in bipolar or "MDI" patients.
- Lithium may also limit risk of suicides and attempts in recurrent major depression.
- Discontinuing lithium, especially rapidly, markedly increases suicidal risk temporarily.
- Acute overdoses with lithium are uncommon & their mortal risk is similar to that of modern antipsychotics or SSRIs.
- Studies of possible antisuicidal effects of other mood-stabilizers are rare and limited to carbamazepine & divalproex, against which lithium was ca. 3x more effective.

Meta-Analysis: Lithium vs. Suicides & Attempts

[Baldessarini et al. 2006]



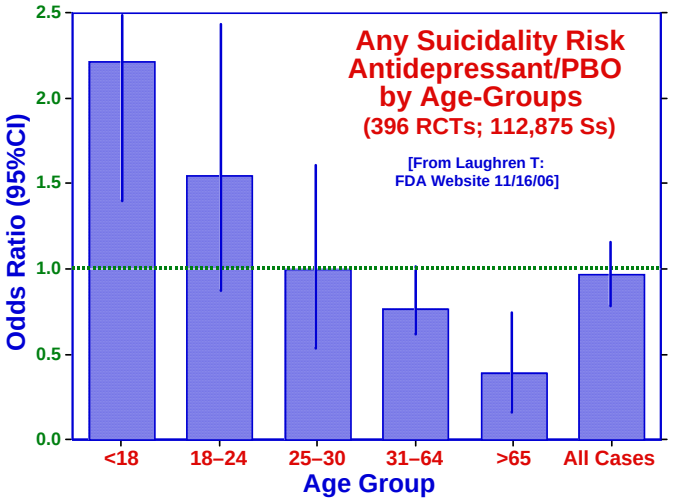
Anticonvulsants vs. Suicidal Risk

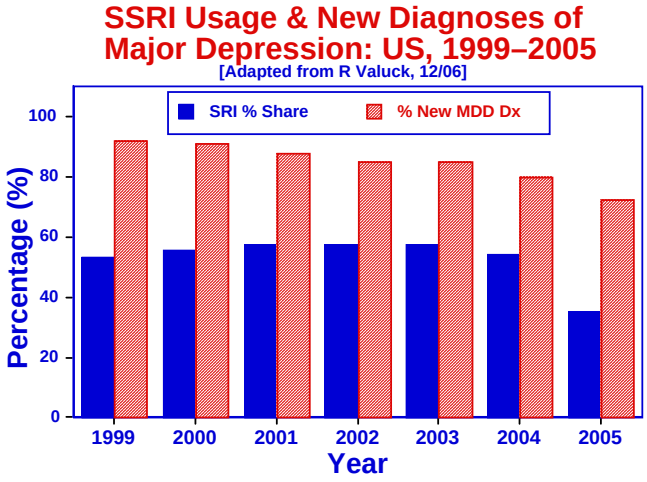
Study	Treatments (N)	Suicidal Risk (%/yr)
Thies-Flechtner et al. 1996	Lithium (189)	0.00
	Carbamazepine (142)	2.50
	Risk Ratio	>2.5
Goodwin et al. 2003	Lithium (28,894)	0.78
	Divalproex (24,138)	2.12
	Risk Ratio [CI]	2.7 [1.2–6.2]

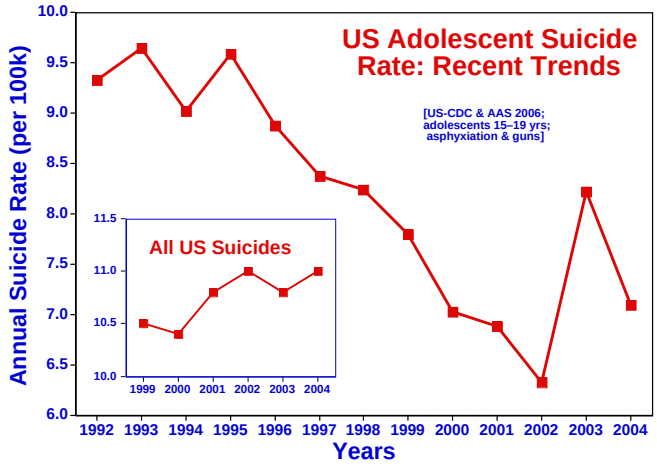
Risks = suicides + attempts or impending attempts.
a. Thies-Flechtner et al. Pharmacopsychiatry 1996; 29: 103–107;
b. Goodwin et al. JAMA 2003; 290: 1467–1473.

Antidepressants (ADs) vs. suicidal risk

- No. Amer. & No. Europe had slightly falling suicide rates with massively increased use of modern ADs in 1990–2000, largely anticipated in 1970–1990; whereas half the world experienced stable or rising rates.
- Suicide rates (US) are strongly associated with other indices of access-to-care, and no longer falling.
- Suicide & attempt rates are surprisingly high in AD RCTs, with *not*-lower, or even slightly greater *apparent* risks vs placebo.
- In RCTs, *spontaneously reported suicidal ideation* (not a valid index of suicidal risk) may be somewhat increased with ADs vs. placebo in RCTs at ages 5–25, but suicidality ratings in depression scales consistently fall with ADs > placebo in adult RCTs.
- Efficacy of ADs is weak in adolescent depression, poorly evaluated in children, and only moderate in adults.
- FDA-required "**black-box**" warnings since 2003 are associated with declining new diagnoses of major depression at all ages (mainly by non-psychiatrists), markedly declining SSRI sales, & rising suicide rates in adolescents.







Suicide prevention: Conclusions

- **Suicide: a major international public health challenge & highest source of liability-risk in psychiatry**
- **Risk commonly arises early, often well before diagnosis & systematic treatment program established**
- **Empirical therapeutic research: virtually unknown a decade ago**
- **Depression & bipolar disorders: major risk factors for suicide, esp. with comorbid substance abuse**
- **Access-to-care, rurality, economics: major risk factors**
- **Prevention requires comprehensive risk-assessment, patient-family collaboration, *ongoing* monitoring, intervention, treatment**
- ***Lithium*: strongest evidence for long-term antisuicide effectiveness, *clozapine* less, *antidepressants* & *anticonvulsants* none**
- **Psychosocial interventions: appropriately used clinically, despite very limited research support**
- **Recent practice patterns for managing depressed patients reflect excessive confidence in pills & little finanical support for time & "care"**