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# Global Mental Health: A growing problem and a downward spiral



# Depression is a Major Public Health Problem

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- 40K suicides/yr (vs. 13K homicides)      22  
veterans/day
- Bed days/mo 2<sup>nd</sup> only to heart disease. WHO:  
#1 cause of disability by 2020
- Depression increases mortality of the aged;  
e.g. death from MI 4x higher in patients with  
documented depression
- 1 of 6 worldwide has or will have depression

# Where is the Light

My mood is black. I've lost all hope.  
I've sunk into despair.  
The tentacles of gloom grip tight  
I must escape. But where

Am I to go? I've lost desire  
To live or love or laugh.  
I feel no pleasure, just dull pain.  
I see my epitaph,

Yet it is blank. This endless gloom  
From which I must escape  
Yields no promise of afterlife.  
I recognize no shape

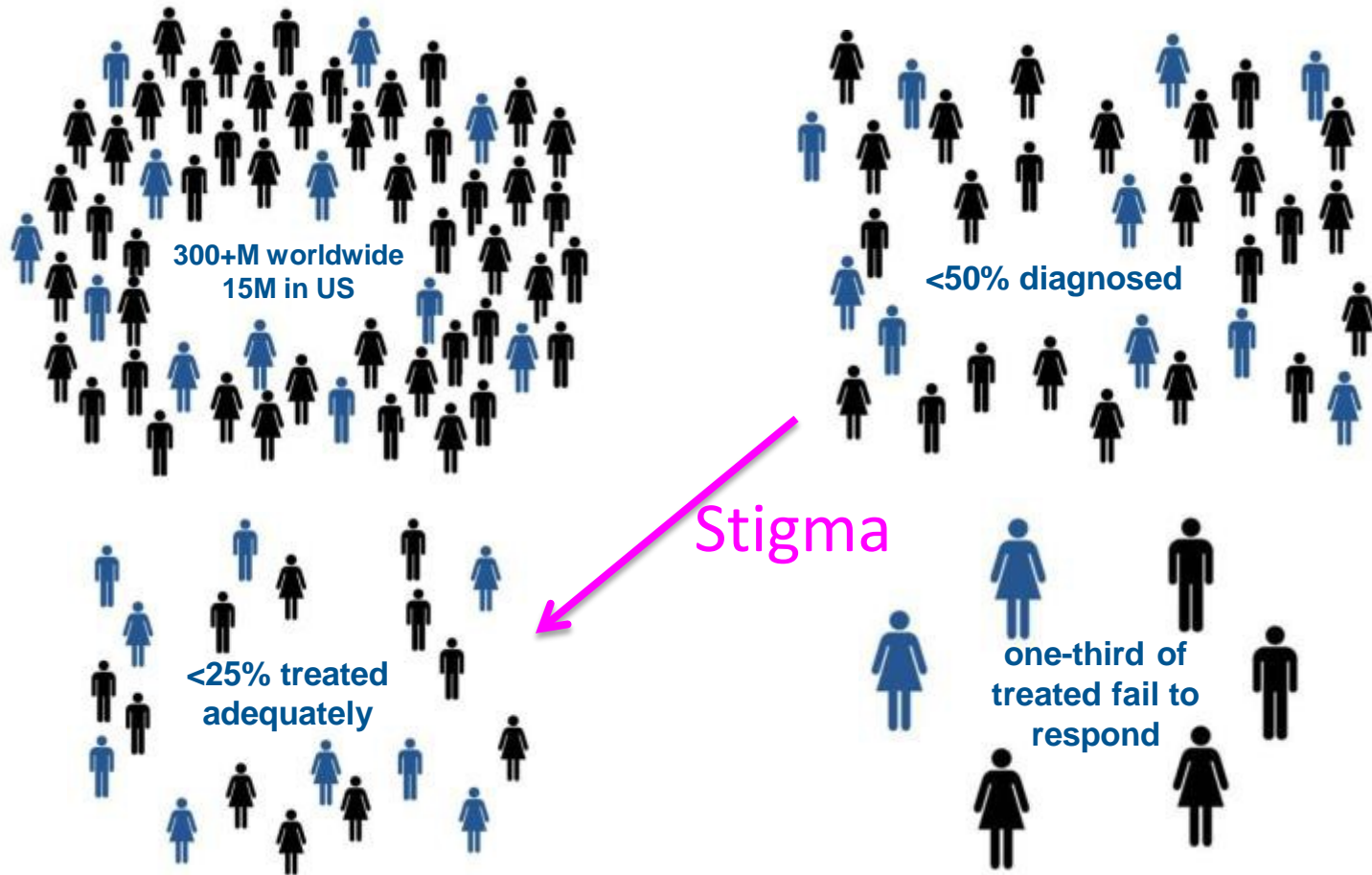
Nor color, taste, passion, joy;  
Just foul and acrid mood.  
I cannot work, I cannot play  
I lie in bed and brood .

Shall I end this worthless life?  
Have I the motivation?  
I guess I'll just maintain this state  
Of endless dissipation.

# Stressors

- Endogenous
- Financial
- Traumatic (violence, war, natural disasters)

# 1 OF EVERY 6 PEOPLE SUFFER DEPRESSION



**2013 US Annual Cost estimate--\$500B**

7/2/13 NYT

# Antidepressant Therapy

- Cognitive
- Direct Stimulation (ECT, TMS, AVS, DBS)
- MAO inhibitors (phenylzine, iproniazid)
- Tricyclics (amitriptyline, imipramine, chloipramine)
- SSRI (fluoxetine, sertraline, paroxetine, citalopram)
- Others (venlafaxine--DA uptake/5HT & NE antagonist)
- Combinations (as seen on TV)

# Are new antidepressants needed?

- Doesn't everybody get better with escitalopram?
- 30% respond well to any given treatment
- 40% have a partial response
- 30% do not respond
- Some of these are refractory to all treatment and are at risk of death from suicide



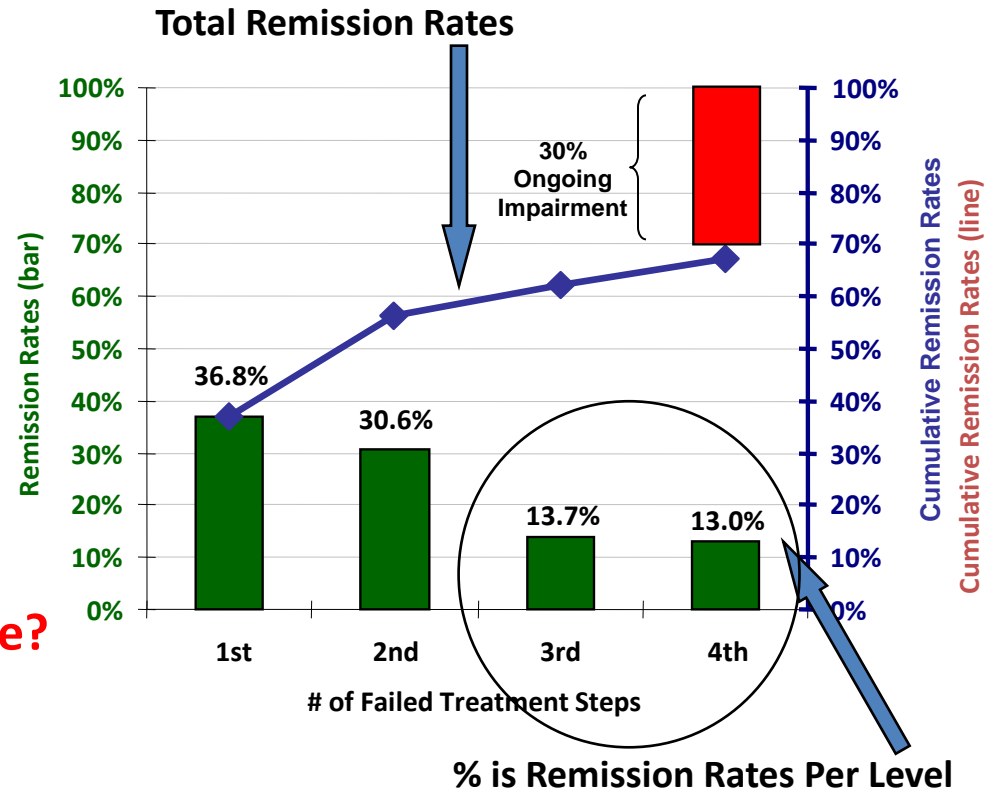
# Remission Harder To Achieve With Each Treatment Failure

## Significance of Moderate Levels of Prior Treatment Failure

With each level of treatment, remission rates decrease and relapse rates increase. An estimated 30% continue to experience significant impairment after 4 levels of treatment.

These people are at risk for suicide.

Is this the result of repeated failure?





## What's the problem?

- Stigma discourages many from seeking treatment
- Most current depression therapy requires 6-12 week lag before improvement of symptoms
- Settling for response rather than recovery.
- Designing new drugs based on existing drugs.

## What's the solution?

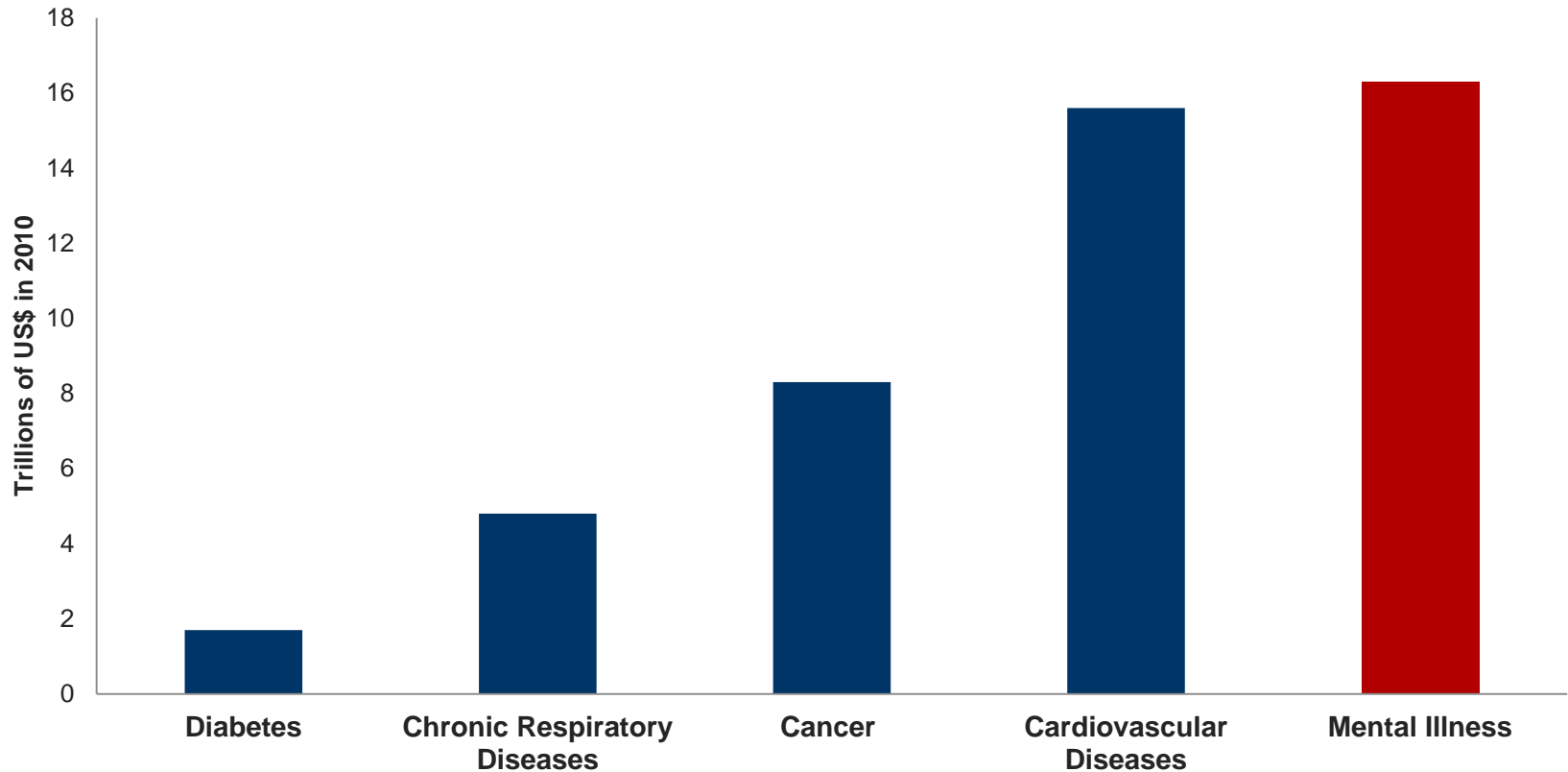
- Approaching depression and other psychiatric problems as a neurobiology issue (end stigma)
- Understanding the molecular/cellular basis of depression.
- Identifying clear, easily-obtainable biochemical/genetic hallmarks for diagnosis and treatment (biomarkers).

# Disability Adjusted Life Years (DALYs) in 2020: Depression #2 worldwide and #1 in developing world

Rank	Worldwide			Developed regions			Developing regions		
	Disease or injury	DALYs (×10 <sup>6</sup> )	Cum %	Disease or injury	DALYs (×10 <sup>6</sup> )	Cum %	Disease or injury	DALYs (×10 <sup>6</sup> )	Cum %
--	<b>All causes</b>	1388.8	--	<b>All causes</b>	160.5	--	<b>All causes</b>	1228.3	--
1	Ischaemic heart disease	82.3	5.9	Ischaemic heart disease	18.0	11.2	Unipolar major depression	68.8	5.6
2	Unipolar major depression	78.7	11.6	Cerebrovascular disease	9.9	17.4	Road-traffic accidents	64.4	10.8
3	Road-traffic accidents	71.2	16.7	Unipolar major depression	9.8	23.5	Ischaemic heart disease	64.3	16.1
4	Cerebrovascular disease	61.4	21.1	Trachea, bronchus, and lung cancers	7.3	28.0	Chronic obstructive pulmonary disease	52.7	20.4
5	Chronic obstructive pulmonary disease	57.6	25.3	Road-traffic accidents	6.9	32.3	Cerebrovascular disease	51.5	24.6
6	Lower respiratory infections	42.7	28.4	Alcohol use	6.1	36.1	Tuberculosis	42.4	28.0
7	Tuberculosis	42.5	31.4	Osteoarthritis	5.6	39.5	Lower respiratory infections	41.1	31.4
8	War injuries	41.3	34.4	Dementia and other degenerative and hereditary CNS disorders	5.5	43.0	War injuries	40.2	34.6
9	Diarrhoeal diseases	37.1	37.1	Chronic obstructive pulmonary disease	4.9	46.0	Diarrhoeal diseases	37.0	37.6
10	HIV	36.3	39.7	Self-inflicted injuries	3.9	48.4	HIV	34.0	40.4

86 % suicides and 75% global burden of neuropsychiatric disorders are in low and middle income countries

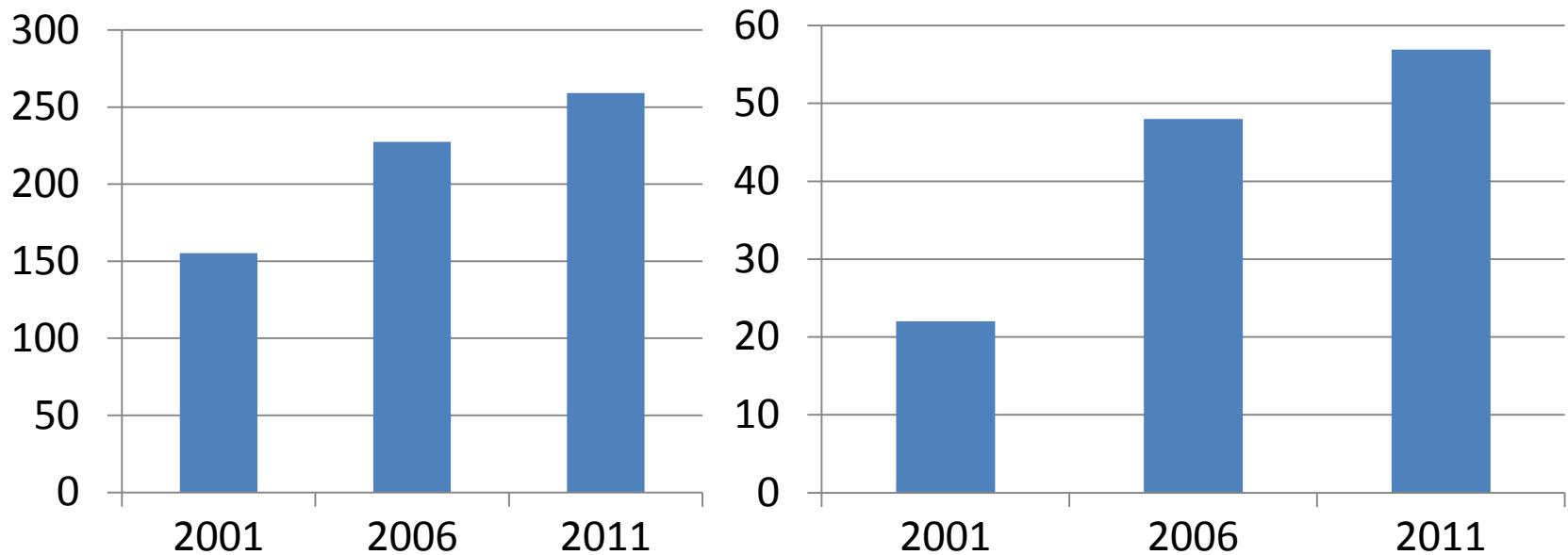
## Economic Burden of Noncommunicable Diseases 2011-2030



**US Annual Costs > \$300B for SMI (Insel, AJP, 2008)**  
**Global \$2.5T, 2010; \$6T, 2030**

Treatment has increased over the past decade

**A. Antidepressant prescriptions**   **B. Antipsychotic prescriptions**



(millions of prescriptions in US market – IMS Health)

## Inconvenient Truth #1

Increased treatment, worldwide, as measured by epidemiology, prescriptions, expense

No decrease and, in some areas, increase in morbidity and mortality

Explanations:

Effective treatments, but prevalence is increasing

Effective treatments, but delivery is inadequate

Current treatments are not effective enough to influence public health outcomes

## Inconvenient Truth #2

At a time of increased need, most Pharma companies have left CNS R&D.

U.S. federal funding has dropped 25% over past decade. No new targets

Explanations:

Market saturation w generics

Preclinical studies not predictive

Expensive Phase 3 failures

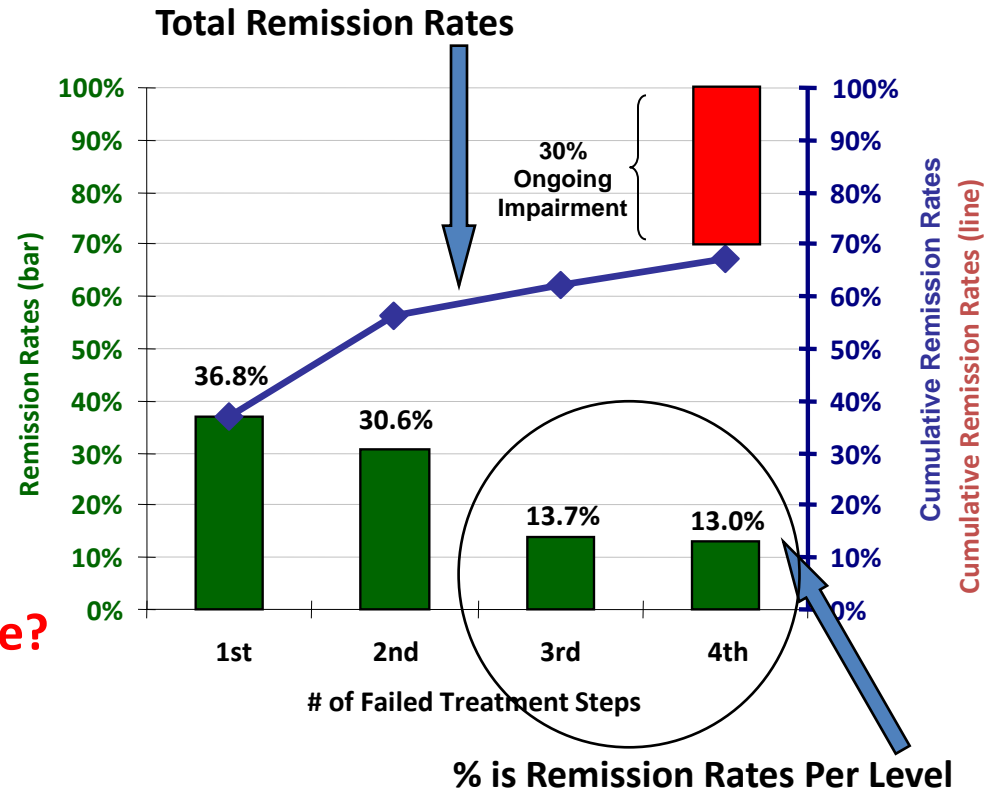
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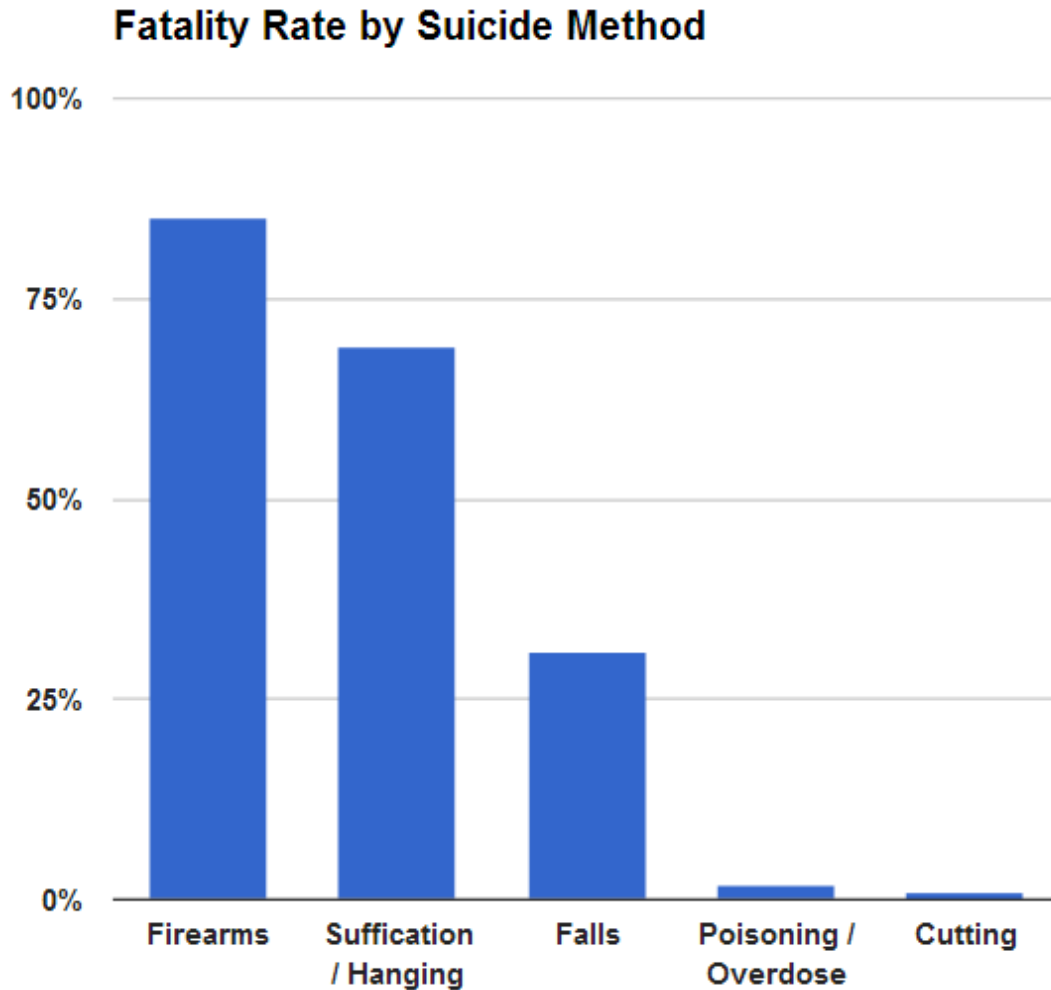




# Global Suicide Rates

Country	Year	Deaths per 100,000 People	Country	Year	Deaths per 100,000 People
Lithuania	2009	28.6	Germany	2010	8.8
South Korea	2009	26.3	Serbia	2010	8.8
Belarus	2009	24.0	El Salvador	2008	8.7
Kazakhstan	2009	23.5	Singapore	2009	8.1
Russia	2009	22.8	Netherlands	2010	8.0
China	2011	22.2	Bulgaria	2010	7.9
India	2010	22.0	Argentina	2008	7.5
Sri Lanka	2006	19.8	Australia	2006	7.4
Japan	2009	19.1	Mauritius	2010	7.4
Hungary	2009	19.0	Puerto Rico	2005	7.1
Latvia	2009	18.6	Ecuador	2009	7.0
Ukraine	2010	16.6	Portugal	2010	7.0
Moldova	2010	16.3	Costa Rica	2009	6.0
Slovenia	2009	16.2	United Kingdom	2010	6.0
Finland	2010	15.9	Panama	2008	5.7
Belgium	2006	15.2	Spain	2009	5.6
Poland	2009	14.3	Israel	2009	5.4
Uruguay	2004	14.3	Uzbekistan	2005	5.2
Montenegro	2009	13.6	Colombia	2007	5.1
Estonia	2010	13.5	Thailand	2006	5.0
France	2008	13.3	Brazil	2008	4.8
Switzerland	2007	13.3	Italy	2008	4.8
Croatia	2010	12.7	Albania	2004	4.7
New Zealand	2008	11.8	Guatemala	2008	4.2
Czech Republic	2010	11.4	Mexico	2008	4.2
Reunion	2008	11.4	Paraguay	2008	3.9
Austria	2010	11.3	Georgia	2009	3.6
Hong Kong SAR	2009	11.3	Venezuela	2007	3.5
Ireland	2009	11.3	Cyprus	2009	3.4
Chile	2007	10.8	Fiji	2009	3.3
Romania	2010	10.6	Greece	2009	2.7
Trinidad & Tobago	2006	10.3	Bahrain	2009	2.5
United States	2007	10.3	Philippines	2008	2.3
Canada	2004	10.1	Qatar	2009	2.3
Norway	2010	10.1	Armenia	2009	1.5
Sweden	2010	10.1	Kuwait	2009	1.3
Cuba	2008	9.9	South Africa	2008	1.0
Denmark	2006	9.3	Azerbaijan	2007	0.6
Kyrgyzstan	2009	9.1	Oman	2009	0.5
Slovakia	2009	9.0	Egypt	2010	0.1

# Completed Suicides by Method, USA



**Proportion of Firearm Suicides From 3 Data Points, Compared With Crude Suicide Rates and Proportions of Households Owning Firearms, by Country: 1983–2000**

Country <sup>a</sup>	Crude Suicide Rates (per 100 000 Population)			Proportion of Firearm Suicides, %			Proportion of Households Owning Firearms, %			
	~1983	~1993	~2000	~1983 <sup>b</sup>	~1993 <sup>b</sup>	~2000 <sup>b</sup>	1989	1992	1996	2000
United States	12.4 <sup>c</sup>	12.1 <sup>d</sup>	10.4 <sup>e</sup>	58.7	60.9	56.8	46.0	41.0	40.0	32.0
Switzerland	24.5 <sup>c</sup>	21.3 <sup>f</sup>	18.5 <sup>g</sup>	23.5	26.4	27.4	32.8	...	37.1	35.7
Finland	25.4 <sup>c</sup>	27.3 <sup>f</sup>	23.0 <sup>g</sup>	21.4	21.1	19.9	25.5	25.4	28.9	24.0
Norway	14.3 <sup>c</sup>	13.6 <sup>d</sup>	12.5 <sup>g</sup>	27.1	29.0	19.8	31.5	...	...	...
France	22.3 <sup>c</sup>	20.8 <sup>f</sup>	18.4 <sup>h</sup>	22.1	24.7	19.0	25.3	...	26.1	18.6
Canada	13.9 <sup>c</sup>	13.2 <sup>i</sup>	11.7 <sup>h</sup>	31.9	28.2	19.0	31.0	28.2	23.7	19.1
Austria	...	22.1 <sup>f</sup>	19.3 <sup>j</sup>	...	18.4	16.9	...	...	14.3	...
Sweden	18.2 <sup>k</sup>	15.8 <sup>d</sup>	13.3 <sup>g</sup>	11.6	13.3	12.2	...	16.8	16.9	16.9

# Availability of Treatment

- Psychiatrists/population:
  - Western Europe, 1:10,000
  - Central Africa, 1:400,000
  - But faith healers abound
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- Is there a fix?
  - More Psychiatrists?
  - More prisons?

# Global Strategy

- Will “throwing money at it” help?
- Psychiatrists not the answer
- Cultural competence
- Private funders
- Global mental health laboratory
- Family involvement ala Cuba