Approaches to Improve the Measurement of Suicide in Law Enforcement in the United States

Data Integration:
Combining Multiple Data Sources

Joel Greenhouse
Carnegie Mellon University
joel@stat.cmu.edu

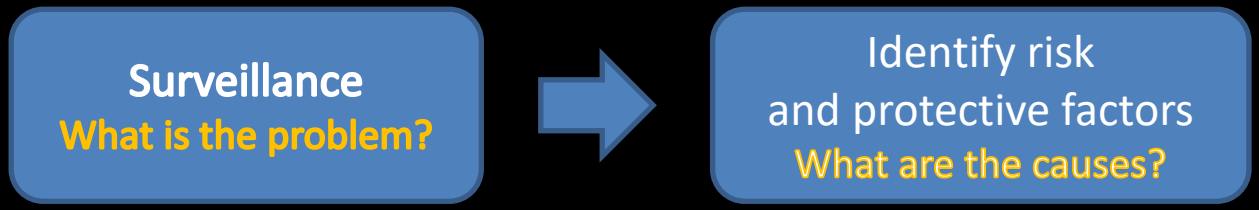
Why Measure Law Enforcement Suicide?

Surveillance and Stages of Information

Surveillance
What is the problem?

CDC, Center for Surveillance, Epidemiology, and Lab Services
https://slideplayer.com/slide/3477074/

Surveillance and Stages of Information



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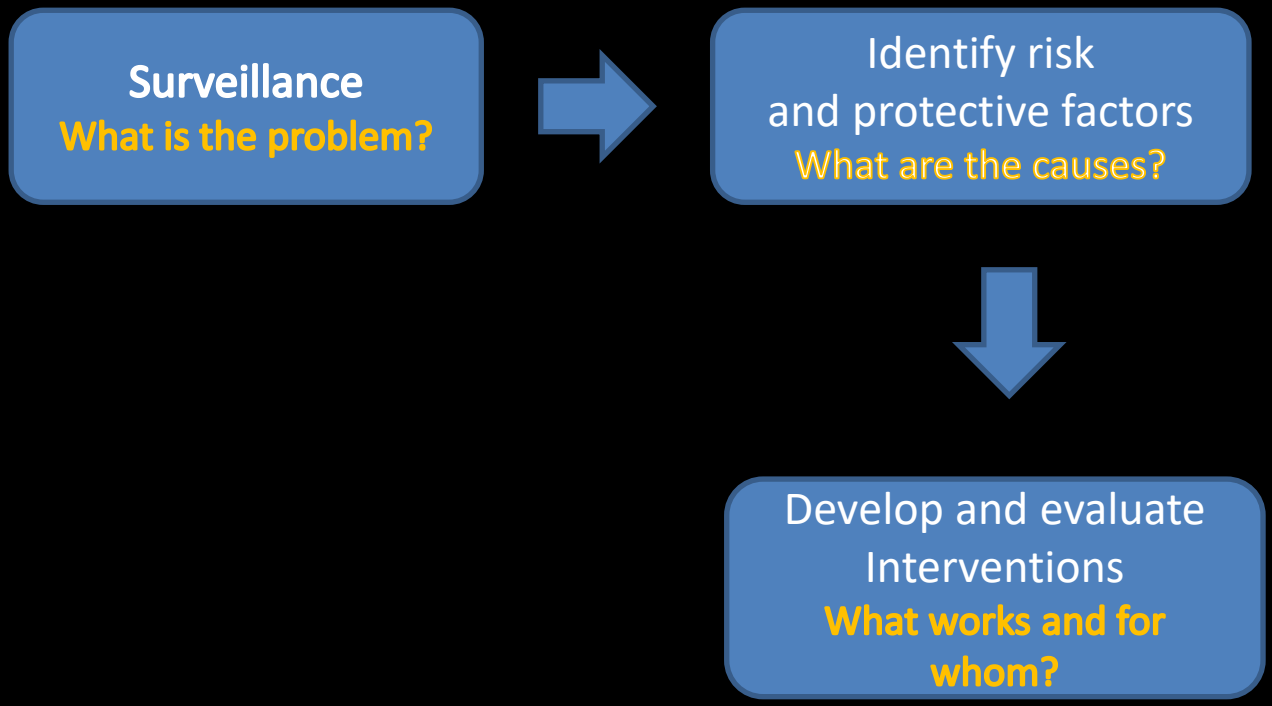
Surveillance and Stages of Information



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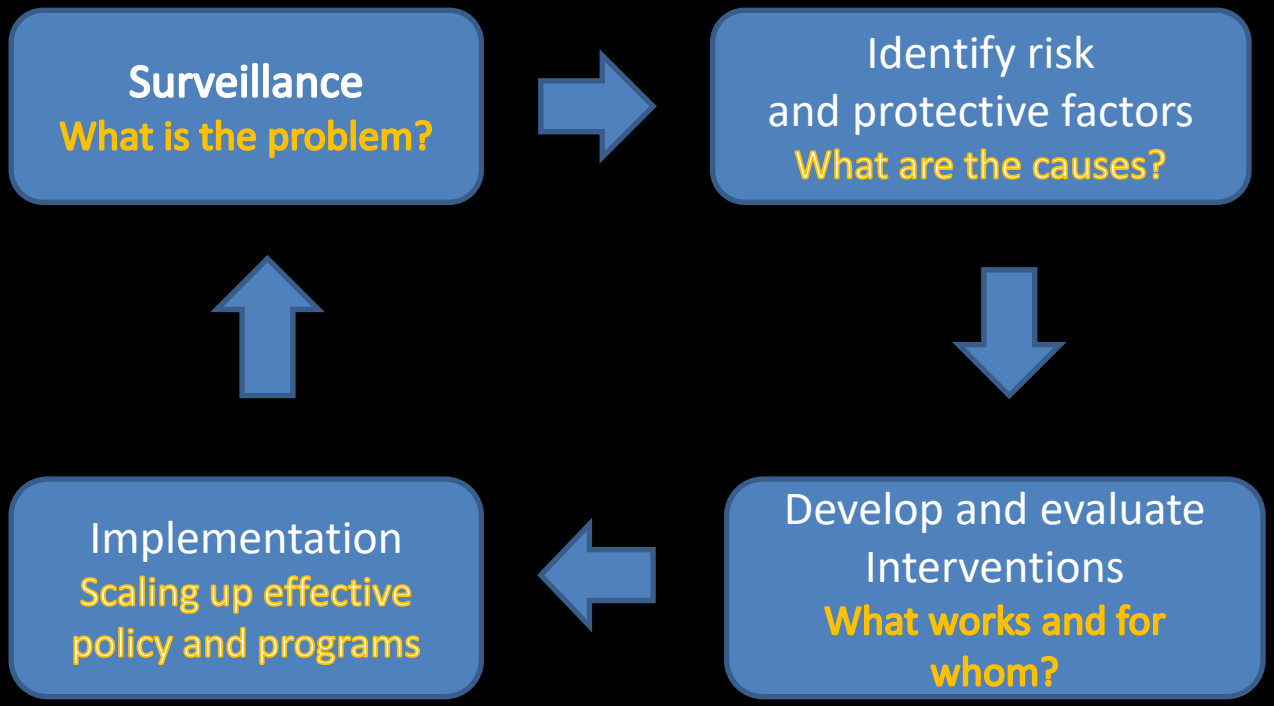

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Surveillance: Sources of Evidence

- Administrative government data systems
  - Eg. LESDC, NVDRS, DHS, Military
- Surveys
- Non-government data collection systems
  - Eg. Blue H.E.L.P.
- Investigator initiated studies

Multiple Sources of Evidence: Data Integration

"Combining information from disparate sources is a fundamental activity in both scientific research and policy decision making. The process of learning is one of combining information: we are constantly called upon to update our beliefs in the light of new evidence, which may come in various forms."

Committee on Applied and Theoretical Statistics, NRC (1992)
Combining Information: Statistical Issues and Opportunities for Research

Multiple Sources of Evidence: Data Integration

GAO (1992)
Cross-Design Synthesis: A New Strategy for Medical Effectiveness Research

- A Congressional study to develop a new strategy for evaluating the effectiveness and generalizability of medical interventions

- ***Cross-Design Synthesis*** uses evidence from complementary studies to help answer questions about what works for whom by capturing the strengths and minimizing the weaknesses of different study designs.

Multiple Sources of Evidence: Data Integration

Opportunities

- Improve the quality, timeliness and usefulness of evidence
- Provide evidence for important research questions
- Support evidence-based policymaking

21st Century Cures Act (Dec 2016)

- Allows the FDA to use Real World Data (RWD) to provide evidence about the effectiveness of drugs and medical devices where

  RWD are the data relating to patient health status and/or the delivery of care, for example:

  - Electronic health records
  - Claims data
  - Disease and device registries
  - Mobile health devices

- Real World Evidence (RWE) can be generated by different study designs or analyses, including RCTs and observational studies

FDA, https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence

Next Session

Towards a 21st Century National Data Infrastructure

Data Integration: Examples

Research Question	Linked Data Sources	Reference
How do risk factors for suicide compare among correction officers & police officers?	NVDRS + ACS	Zimmerman et al. (2023)
How do army suicide rates compare to suicide rates in the general population?	NVDRS + CPS	Griffen et al. (2020)
What is the relationship between suicide mortality and family structure and SES?	NHIS + Linked Mortality File	Denney et al. (2009)
	ACS – American Community Survey CPS – Current Population Survey NHIS – National Health Interview Survey	

Case Study:
Combining Multiple Data Sources

Antidepressants and Suicidality in Children and Adolescents

Background

Oct 2004: FDA issued a black box warning, the most severe regulatory action short of a total ban, regarding the use of antidepressants

> ``caution[ed] . . . about an increased risk of suicidal thinking and behavior in children and adolescents. . . who are taking antidepressant medication''

FDA Evidence: Data Source

- 24 Randomized Placebo-Controlled Trials
- 4 different indications – Depression, OCD, Anxiety, ADHD
- 9 different antidepressants
- 4,582 total children and adolescents studied

FDA Evidence:

- **No completed suicides**
- FDA defined new outcome:

  Suicidality = Suicidal Behavior or Ideation (n = 87)
- Adverse events - Assessed retrospectively
- Median Trial Length - 8 weeks

FDA Evidence: Meta-Analysis Results

Model	Relative Risk	95% Confidence Interval
Fixed Effect	**2.00**	**[1.3, 3.0]**

FDA Meta-Analysis: Conclusion

- FDA Scientific Advisory Committee (Leslie et al 2005)

  "There is a causal link between newer antidepressants and pediatric suicidality."

- FDA issued a **box warning** for the use of antidepressants in children and adolescents

FDA Meta-Analysis: **Issues**

- Outcome:
  - Suicidality = Suicidal Behavior + Suicidal Ideation
  - Retrospectively assessed
  - Rare events - sparse data
- Meta-Analysis
  - Observational study
- Selection Effects - e.g., **Exclusion of high risk patients**

What is the Effect of Excluding High Risk Patients?

Approach: Use Multiple Data Sources
(Real World Data/Real World Evidence)

Phase I – Study Population

- **New meta-analysis of FDA's RCTs**
  - Outcome: Suicide Attempt
  - Indication: Depression

Phase II – Target Population

- **Observational database**
  - Linked Health Insurance Claims Data

Phase III – Investigate the Effect of Exclusions

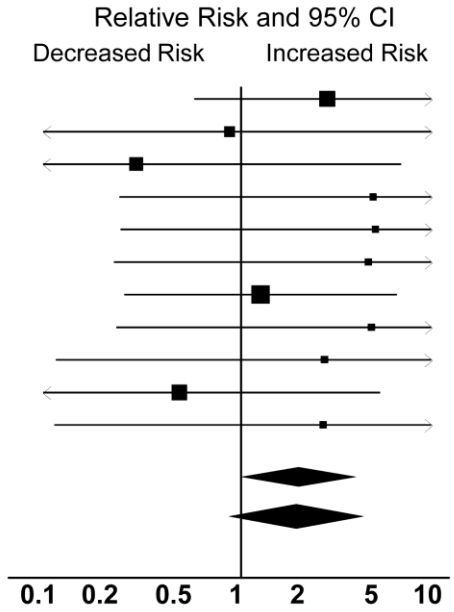
- **Restricted cohort/Simulated RCT**

Note: If the risk in the simulated sample is similar to the target population we are more confident in the generalizability of the results.

Phase I: FDA RCT Meta-Analysis

RCT Data: Phase I*

Study name	Relative Risk (95% CI)	Events / Total Treated	Placebo
Citalopram 94404	2.90 (0.60–14.10)	6/124	2/120
Citalopram CIT-MD-18	0.91 (0.06–14.39)	1/93	1/85
Fluoxetine HCCJ	0.30 (0.01–7.02)	0/21	1/19
Fluoxetine X065	5.00 (0.25–101.48)	2/48	0/48
Fluoxetine TADS	5.14 (0.25–105.78)	2/109	0/112
Paroxetine 329	4.73 (0.23–97.25)	2/93	0/88
Paroxetine 377	1.32 (0.26–6.67)	5/180	2/95
Paroxetine 701	4.90 (0.24–100.93)	2/104	0/102
Sertraline A0501001	2.82 (0.12–68.26)	1/97	0/91
Sertraline A0501017	0.51 (0.05–5.48)	1/92	2/93
Venlafaxine 384	2.77 (0.11–67.10)	1/102	0/94
Overall Fixed Effects	2.00 (1.01–3.96)		
Bayes	2.10 (0.96–4.12)**		



*The five RCTs that did not have events in either the treated or placebo study groups were excluded from the fixed-effects meta-analysis but were included in the Bayes analysis: Fluoxetine HCJE (0/109 [treated], 0/110 [placebo]); Nefazodone CN104-141 (0/95, 0/95); Nefazodone CN104-187 (0/184, 0/94); Mirtazapine 003-045 (0/170, 0/89); and Venlafaxine 382 (0/80, 0/85).

Studies: Depression (n=16) Outcome: Suicidal Behavior

RR_{MH} = 2.00 [95% CI: (1.01, 3.96)]

Phase II : Target Population

Administrative/Observational Data:

LifeLink Health Plan Claims Database

- Integrated medical + specialty + pharmacy claims
- > 95 managed care plans
- ~ 42 million covered lives
- Data are longitudinal

Phase II: Target Population

Case Identification:

1. **Diagnosis:** Depression based on ICD-9 codes

2. **Index Episode**
   - No antidepressant claim ≤ 90 days prior to episode
   - No depression-related dx ≤120 days prior to episode

3. **Age**: 5 -- 17 years

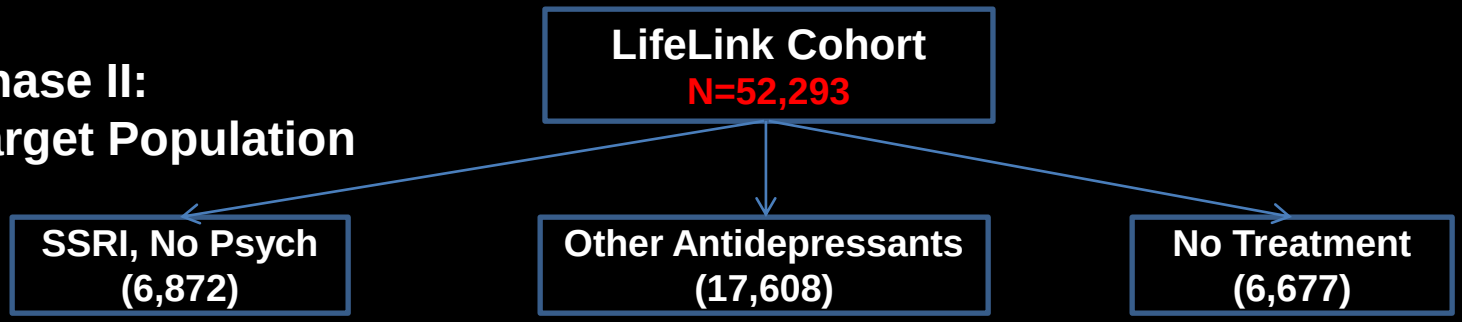
4. **Time Period**: January 1, 1999 -- June 30, 2008

5. **Eligible:** 12 months prior to index episode and 6 months following

Target population: LifeLink Cohort: N = 52,293

- **First Episode**
- **Outcome**: Suicide Attempt (CDC E-codes)
- **Follow-up**: 6 months post –index-episode

Phase II:
Target Population



Phase III: Restricted Cohort

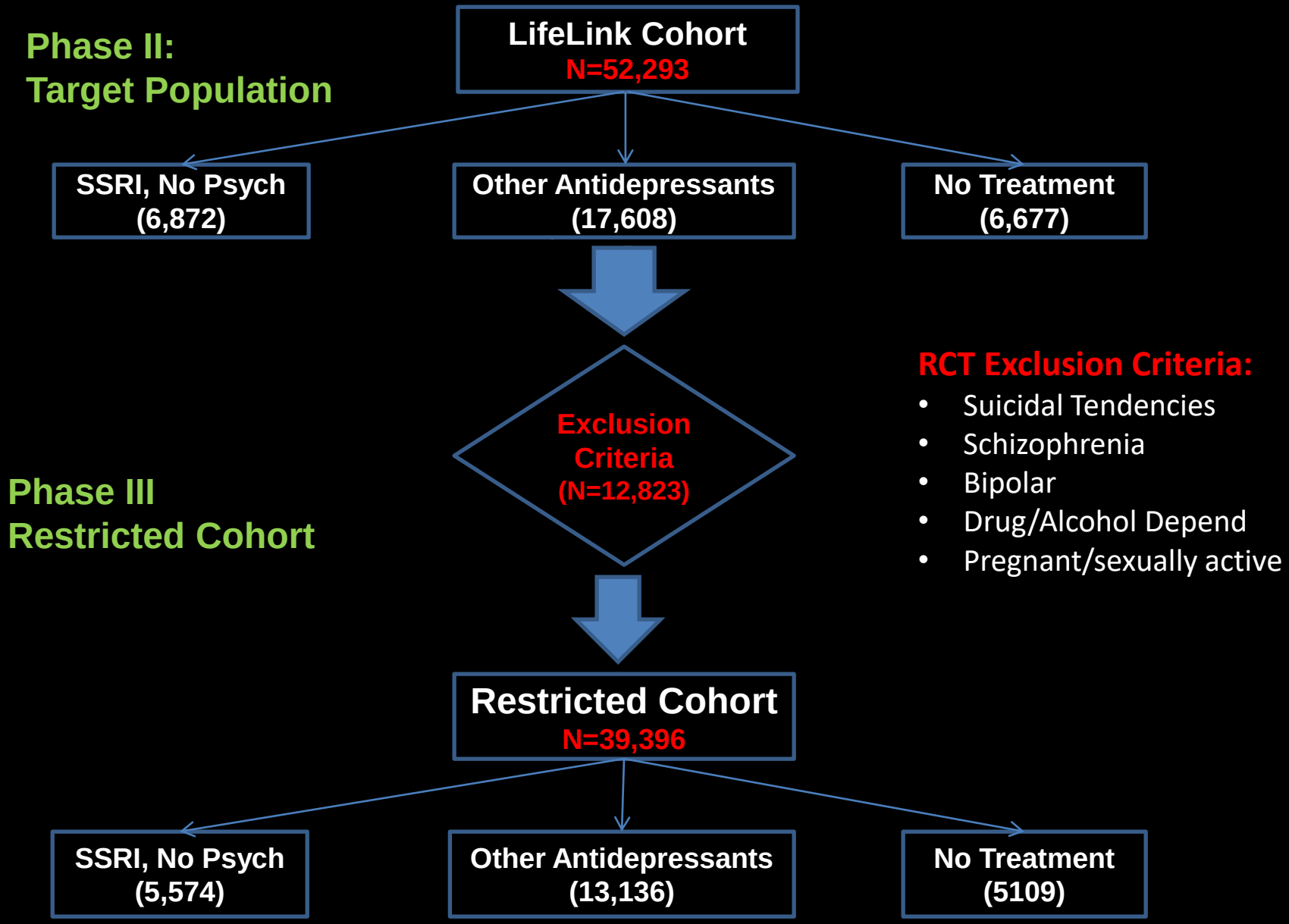
What is the effect of the RCT patient exclusion criteria?

We identified the most common patient **exclusion** criteria in the FDA RCT database:

- **High risk for suicidal behavior**
- **Current schizophrenia diagnosis**
- **Current or lifetime history of drug or alcohol dependence**
- **Current bipolar I or II diagnosis**
- **Currently pregnant or sexually active/no acceptable contraceptive use**

Patients who met any of these exclusion criteria were **not** included in the Restricted Cohort.

Study Population: Restricted Cohort: N = 39,396


Phase II:
Target Population
LifeLink Cohort
N=52,293
SSRI, No Psych
(6,872)
Other Antidepressants
(17,608)
No Treatment
(6,677)
Exclusion
Criteria
(N=12,823)
RCT Exclusion Criteria:
• Suicidal Tendencies
• Schizophrenia
• Bipolar
• Drug/Alcohol Depend
• Pregnant/sexually active
Phase III
Restricted Cohort
Restricted Cohort
N=39,396
SSRI, No Psych
(5,574)
Other Antidepressants
(13,136)
No Treatment
(5109)

Phase III: Restricted Cohort (con't)

What is the effect of the exclusion of high risk patients?

Analysis - simulate an RCT

- Balance treatment groups using propensity score
- Intent-to-treat analysis
- Estimate adjusted risk of suicide attempt

Phase II & III Results
Relative Risk: Antidepressant Monotherapy

[Phase I Meta-Analysis RCTs: 2.0 (1.0, 4.0)]

Treatment Group	Phase II TARGET POPULATION LifeLink Cohort Crude RR	N	Phase III SIMULATED Total # Events	RCT (restricted cohort) Adjusted* RR (95% CI)
SSRI	**2.7**	**5574**	**25**	**2.3 (1.1 – 5.1)**
Other Antidepressants	5.0	13136	107	4.5 (2.3 – 8.9)
No Treatment (ref)	1.0	5109	9	1.0

Figure 1. Relative Risk of Suicidal Behavior: Phases I-III

RCT Data: Phase I*

Study name	Relative Risk (95% CI)	Events / Total Treated	Placebo
Citalopram 94404	2.90 (0.60–14.10)	6/124	2/120
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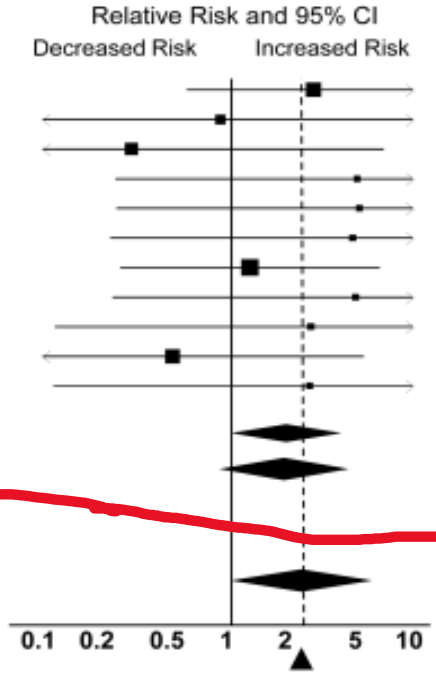

Observational Data: Phases II-III

Restricted Cohort	2.29 (1.10 – 5.10)
Lifelink Cohort = ▲	2.69

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**95% Credible Interval

Comments

- **Case Study**
  - Convergence of evidence for an increase risk of suicidal behavior among antidepressant users in depressed youth
  - Generalizable to youths who were excluded from RCTs
  - We still don’t know which subgroups of youth are at risk
- **General**
  - Use of multiple data sources, including RCTs and linked administrative claims data, provides a template for investigating the question of a selection effect.

Thank You

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