Sleeping with Buster, was like sleeping with a Vietnam vet, who suffered from PTSD...

New Yorker, 1-5-04
Post-Traumatic Stress Disorder, Drug Abuse and Suicidality*

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More specifically:

- Longitudinal patterns and associations of PTSD, substance abuse and suicidality.
- Potentially causative roles of PTSD and substance abuse on suicidality.
- Learning from the past to inform future research.
- How to capture situation-specific protective factors that mitigate already existing suicidal risk?
Acknowledgments*

- National Institute on Drug Abuse (K02DA00221, R01DA09281).
- Longer Life Foundation, Washington University School of Medicine and the Reinsurance Group of America.
- National Institute of Mental Health (R01MH60691).

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Background

- Three decades ago

Source: SAMHSA. The 1996 National Household Survey, Preliminary Results (1962-1995); the 2002 National Household Survey, Preliminary Results (1996-2001). The incidence rate of 1 is equivalent to 1,000 new users per year.
1971 - Thousands of American soldiers returning from Vietnam were addicted to narcotics. The White House initiated a study conducted by Washington University in 1972 and 1974.

1993 - Washington University began a follow-up study...

Washington University
Vietnam Era Study (VES)
VES Samples (Total Target N = 1,226)

1972
N = 898
- D+ Vet: 484
- D- Vet: 414
- Nonvet: 263
- Dead: 7

1974
N=855
- D+ Vet: 308
- D- Vet: 284
- Nonvet: 284
- Dead: 7
### VES Samples (Target N=1,226): Demographic Characteristics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Veterans</th>
<th>Non-veterans</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drug + (N = 511)</td>
<td>Drug - (N = 431)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>22.5 (3.2)</td>
<td>24.2 (4.9)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whites</td>
<td>59.9</td>
<td>81.7</td>
</tr>
<tr>
<td>Blacks</td>
<td>34.1</td>
<td>11.6</td>
</tr>
<tr>
<td>Hispanics</td>
<td>5.7</td>
<td>4.9</td>
</tr>
<tr>
<td><strong>Employment Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active duty in 1972</td>
<td>16.0(^1)</td>
<td>16.1(^1)</td>
</tr>
<tr>
<td>Not employed</td>
<td>31.3(^1)</td>
<td>15.7(^1)</td>
</tr>
</tbody>
</table>

1. 1972 status; among the interviewed.
2. 1974 status, the unemployed includes “laid-off.”
# Opiate Addiction before, in and after Vietnam

Table 1.—Drug Use Before, In, and After Vietnam

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Before Vietnam</th>
<th>In Vietnam</th>
<th>Since Vietnam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana, any</td>
<td>41%</td>
<td>69%†</td>
<td>45%</td>
</tr>
<tr>
<td>Any drug: narcotics, amphetamines, barbiturates</td>
<td>30%</td>
<td>45%</td>
<td>23%</td>
</tr>
<tr>
<td>Narcotics</td>
<td>11%</td>
<td>43%</td>
<td>10%</td>
</tr>
<tr>
<td>Addiction to narcotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By self-report</td>
<td>0.2%</td>
<td>20%</td>
<td>0.7%</td>
</tr>
<tr>
<td>By symptoms of dependence‡</td>
<td>0.4%</td>
<td>21%</td>
<td>1%</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>24%</td>
<td>25%</td>
<td>19%</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>14%</td>
<td>23%</td>
<td>12%</td>
</tr>
<tr>
<td>Combinations of drug types</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All 3: narcotics, amphetamines, barbiturates</td>
<td>4%</td>
<td>18%</td>
<td>6%</td>
</tr>
<tr>
<td>Amphetamines &amp; barbiturates</td>
<td>5%</td>
<td>0%</td>
<td>3%</td>
</tr>
<tr>
<td>Narcotics &amp; amphetamines</td>
<td>3%</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Narcotics &amp; barbiturates</td>
<td>2%</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>Narcotics only</td>
<td>2%</td>
<td>15%</td>
<td>1%</td>
</tr>
<tr>
<td>Amphetamines only</td>
<td>11%</td>
<td>2%</td>
<td>9%</td>
</tr>
<tr>
<td>Barbiturates only</td>
<td>2%</td>
<td>...§</td>
<td>2%</td>
</tr>
</tbody>
</table>

* Data from the interviewed general sample (N = 451).
† Estimate based on assumption that those who used marijuana before continued in Vietnam.
‡ Criteria given on p 957.
§ Less than 0.5%.

Opiate Use After Vietnam by Men First Addicted in Vietnam, Compared to NARA Patients

Narcotic use in eight to ten months after Vietnam by men first addicted in Vietnam. Narcotic Addict Rehabilitation Act indicated by NARA.

### Substance Use and Psychiatric Problems (%)

<table>
<thead>
<tr>
<th></th>
<th>Veterans</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drug-positive (D+)</td>
<td>Drug-negative (D-)</td>
<td>Nonveterans¹</td>
<td></td>
</tr>
<tr>
<td><strong>Pre-Vietnam</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opiate use</td>
<td>28.3</td>
<td>9.6</td>
<td>5.6</td>
<td></td>
</tr>
<tr>
<td>Heavy drinking²</td>
<td>47.7</td>
<td>40.8</td>
<td>32.0</td>
<td></td>
</tr>
<tr>
<td><strong>In-Vietnam/Interim</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opiate use</td>
<td>96.7</td>
<td>39.1</td>
<td>6.7</td>
<td></td>
</tr>
<tr>
<td>Amphetamines use</td>
<td>59.3</td>
<td>21.5</td>
<td>18.3</td>
<td></td>
</tr>
<tr>
<td>Barbiturate use</td>
<td>77.4</td>
<td>18.9</td>
<td>12.0</td>
<td></td>
</tr>
<tr>
<td>Heavy drinking²</td>
<td>19.2</td>
<td>41.3</td>
<td>33.5</td>
<td></td>
</tr>
<tr>
<td><strong>Post-Vietnam (1972-1974)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opiate use</td>
<td>36.9</td>
<td>14.9</td>
<td>6.0</td>
<td></td>
</tr>
<tr>
<td>Amphetamines use</td>
<td>55.0</td>
<td>27.9</td>
<td>16.6</td>
<td></td>
</tr>
<tr>
<td>Barbiturate use</td>
<td>36.3</td>
<td>13.4</td>
<td>7.8</td>
<td></td>
</tr>
<tr>
<td>Marijuana use</td>
<td>88.4</td>
<td>52.1</td>
<td>40.5</td>
<td></td>
</tr>
<tr>
<td>Heavy drinking²</td>
<td>67.0</td>
<td>58.0</td>
<td>36.6</td>
<td></td>
</tr>
<tr>
<td>Depressive syndrome³</td>
<td>26.2</td>
<td>17.9</td>
<td>10.2</td>
<td></td>
</tr>
</tbody>
</table>

¹. For nonveterans, the interim period corresponds to the date of induction of their matched veterans to two years prior to the 1974 survey.
². A 6-pack of beer, a bottle of wine, or 7 hard drinks in one day+/week.
³. Depressed mood, 4+ weeks, plus 2 out of 6 symptoms of depression.
Why A 95% Remission Rate?

- Military personnel are different from civilian addicts - less psychopathology.
- Later age of onset.
- “Setting” - extinguishing conditional response was easy after coming back to U.S. (Zinberg, Archive 1972).
- Lack of availability of drugs after return to U.S.
Something Was Puzzling

- Those young men were soaked in opiates!
- Weren’t they fighting a vicious war?
- Three-years were too short to see the long-term impact of drug abuse in Vietnam - they could have relapsed?
- Other signs of mal-adjustments have not been captured?
VES Samples (Total Target N = 1,226)

1974
N=855

D+ Vet: 263
D- Vet: 308
Nonvet: 284
Dead: 7

1996-7
N=841

D+ Vet: 323
D- Vet: 320
Nonvet: 198
Dead: 115

2002-4
(field closure)

D+ Vet: 132
D- Vet: 218
Nonvet: 38
Dead: 38
25-Year Follow-up: Three Steps

I. Feasibility
II. Instrumentation
III. Main Epidemiologic Study
   - Adult course of drug abuse.
   - Effects of war trauma on substance abuse.
   - Relationships among drug abuse, war trauma, PTSD and other psychopathology over time.
   - Impact of substance abuse and trauma on health care utilization.
## VES-III Field Final Status, 1997

<table>
<thead>
<tr>
<th>Field Status</th>
<th>D+ Veteran</th>
<th>D- Veteran</th>
<th>Non-veteran</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deceased during VES-III(^1)</td>
<td>24</td>
<td>10</td>
<td>5</td>
<td>39</td>
<td>3.6</td>
</tr>
<tr>
<td>Unlocated</td>
<td>21</td>
<td>8</td>
<td>3</td>
<td>32</td>
<td>2.9</td>
</tr>
<tr>
<td><strong>Contacted:</strong></td>
<td><strong>374</strong></td>
<td><strong>378</strong></td>
<td><strong>272</strong></td>
<td><strong>1024</strong></td>
<td><strong>93.5</strong></td>
</tr>
<tr>
<td>Interviewed</td>
<td>323</td>
<td>320</td>
<td>198</td>
<td>841</td>
<td>82.1</td>
</tr>
<tr>
<td>Final refusal(^2)</td>
<td>19</td>
<td>38</td>
<td>45</td>
<td>102</td>
<td>10.0</td>
</tr>
<tr>
<td>Other non-interviews(^2)</td>
<td>32</td>
<td>20</td>
<td>29</td>
<td>81</td>
<td>7.9</td>
</tr>
<tr>
<td><strong>Phase III Total Eligible</strong></td>
<td><strong>419</strong></td>
<td><strong>396</strong></td>
<td><strong>280</strong></td>
<td><strong>1095</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

1. New dead identified since December, 1993.
2. Percentage based on those contacted.
### VES-III Demographic Characteristics (N=839)\(^1\)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Veterans Drug + (N = 323)</th>
<th>Veterans Drug - (N = 319)(^1)</th>
<th>Non-veterans (N = 197)(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean Age in 1996 (SD)</td>
<td>46.5 (2.0)</td>
<td>48.0 (4.1)</td>
</tr>
<tr>
<td>Race</td>
<td>Whites</td>
<td>62.2</td>
<td>82.5</td>
</tr>
<tr>
<td></td>
<td>Blacks</td>
<td>28.5</td>
<td>9.4</td>
</tr>
<tr>
<td></td>
<td>Hispanics</td>
<td>5.3</td>
<td>5.3</td>
</tr>
<tr>
<td>Employment Status (%)</td>
<td>Active duty in 1972</td>
<td>16.1</td>
<td>16.0</td>
</tr>
<tr>
<td></td>
<td>Not employed in 1972/74(^2)</td>
<td>31.3</td>
<td>15.7</td>
</tr>
<tr>
<td></td>
<td>Not employed in 1996-97(^3)</td>
<td>26.8</td>
<td>16.9</td>
</tr>
</tbody>
</table>

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1. Excludes missing cases.
2. Veteran status as of 1972; nonveteran employment status as of 1974, including laid-off.
3. Includes those who were “between jobs,” housekeeping, disabled, retired and other.

* Pre-S (Pre-Service), In-S (In-Service), In-V (In-Vietnam), and Post-V (Post-Vietnam) up to the 1972 interview. Measures from the in-service period for veterans prior to their arrival in Vietnam were not used in the subsequent analyses.

Survival Curves for Drug-Positive Veterans, Drug-Negative Veterans and Nonveterans, 1972-1996 (N = 1,227)*

1974 - 1996 †

1971 - 1974 ‡

* Mortality information was available for the period of 1974-1996 for all three groups; for the period of 1971-1974, for the veterans only.
‡ The log-rank test between two groups for 1971-1974. D+ veterans vs. D- veterans: \( \chi^2 = .60, p = .44 \).
**Most Significant Early Risk Factors of Mortality Across Three Time Periods**

Veterans Interviewed in 1972 (n = 896)

<table>
<thead>
<tr>
<th></th>
<th>Conditional Risk Ratio</th>
<th>(95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (each year)</td>
<td>1.07</td>
<td>(1.02-1.11)</td>
</tr>
<tr>
<td>African-American</td>
<td>1.59</td>
<td>(1.06-2.40)</td>
</tr>
</tbody>
</table>

**Pre-Service**

<table>
<thead>
<tr>
<th></th>
<th>Conditional Risk Ratio</th>
<th>(95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Believed drank too much</td>
<td>2.91</td>
<td>(1.72-4.91)</td>
</tr>
</tbody>
</table>

**In-Vietnam**

<table>
<thead>
<tr>
<th></th>
<th>Conditional Risk Ratio</th>
<th>(95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEROS-positive status</td>
<td>2.57</td>
<td>(1.58-4.18)</td>
</tr>
<tr>
<td>Started drinking more</td>
<td>1.90</td>
<td>(1.21-2.96)</td>
</tr>
</tbody>
</table>

**Post-Vietnam**

<table>
<thead>
<tr>
<th></th>
<th>Conditional Risk Ratio</th>
<th>(95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disobeyed orders still in service</td>
<td>2.29</td>
<td>(1.13-4.65)</td>
</tr>
<tr>
<td>Knows where to buy opiates</td>
<td>1.86</td>
<td>(1.21-2.84)</td>
</tr>
<tr>
<td>Feelings of depression</td>
<td>1.51</td>
<td>(1.02-2.24)</td>
</tr>
</tbody>
</table>

-2 Log L = 74.78, d.f. = 8, P < .0001

Table continued on next slide
Most Significant Early Risk Factors of Mortality Across Three Time Periods* (con’t)

<table>
<thead>
<tr>
<th>Veterans and Nonveterans Interviewed in 1974 (n = 854)§</th>
<th>Conditional Risk Ratio</th>
<th>(95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>African-American</strong></td>
<td>1.96</td>
<td>(1.17-3.27)</td>
</tr>
<tr>
<td><strong>Pre-Service</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injected opiates</td>
<td>2.79</td>
<td>(1.24-6.24)</td>
</tr>
<tr>
<td><strong>Interim</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significant opiate withdrawal symptoms</td>
<td>3.09</td>
<td>(1.77-5.38)</td>
</tr>
<tr>
<td><strong>1972-1974</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not married in 1974</td>
<td>2.05</td>
<td>(1.24-3.39)</td>
</tr>
<tr>
<td>Depression with thought of death</td>
<td>2.14</td>
<td>(1.16-3.96)</td>
</tr>
<tr>
<td>Craving for opiates</td>
<td>2.34</td>
<td>(1.17-4.67)</td>
</tr>
</tbody>
</table>

-2 Log L = 74.78, d.f. = 8, P < .0001

* Significant predictors were chosen on the basis of the backward elimination criterion at the P = .05 level. The sample size for each Cox regression excludes missing cases.

§ 28 variables chosen as significant predictors of each time period using logistic regressions were entered to the final Cox regression.
Patterns and Predictors of Cumulative Mortality

- Drugs kill.
- A more malignant picture of the long-term impact of heroin use starting in Vietnam.
- Alcoholism and depression additional significant risk factors for premature death up to mid-40’s.
- Even a short-term intensive drug use appears to signal premature death.

* Price et al., Drug & Alc Dependence, 2001.*
Drug Abuse/Dependence Rate: 1972-1996

- **Marijuana Dep/abuse**
- **Cocaine Dep/abuse**
- **Any Illicit Drug Dep/abuse**
Alcohol Abuse/Dependence Rates: 1972-1996

Heavy Alcohol Use

Alcohol Dependence
Psychopathology Prevalence Rates (1972-1996)

- Adult ASP
- PTSD
- Depression
Long-Term Drug Use and Remission

- Relatively few relapse and remissions- the norm is no more than one relapse in adulthood.
- Marijuana showed the most stable pattern of use.
- Spontaneous remission appears a rule, not an exception.
- Considerable undermet needs for chronic drug users.

Long-Term Prognosis of “Vietnam Heroin Users”

- Characterized by polydrug use - alcohol and marijuana more problematic in adulthood.
- Gradually increasing abstinence (“narrowing of repertoire”) applies to most substances, except for cocaine.
- A majority remained symptomatic when considering a wide array of indicators of well-being (substance use, psychiatric and social indices).
Implications

- Even a short-term intensive drug use is a good predictor of long-term mortality and morbidity.
- Cessation from substance abuse is a long, complicated process.
- Substance abusers do recover over the long haul, but costs may be very high.
- Single-substance prevention and intervention policies do not make sense.
Limitations

- A long-term follow-up of a high risk sample is challenging even in the age of information overflow.
- Modest sample size from today’s population epidemiology standard.
- Generalizability limited.
- Impact of censoring by death unknown.
Life of Research

.. Is sometimes dictated by lives of research subjects
I can’t be around guns anymore...

I can’t clean game anymore because of the smell.
VES-III: Suicidal Behaviors Since Vietnam (%, OR)\(^1\)

Heroin Users

35% In Vietnam

Completed Suicide

1.4% (5.0)

Attempted

9.9% (10.7*)

Plan

12.4% (6.9*)

Frequent Thought

18.8% (3.9*)

VES III: Drug Use up to 1996-7

- **Heroin Users**: 35% in Vietnam
- **Dead**: 16.1%

- **Last 10 Years**
  - Marijuana: 50.8%
  - Cocaine: 29.4%
  - Opiates: 13.2%

- **Last 3 Months**
  - Marijuana: 27.7%
  - Cocaine: 10.2%
  - Opiates: 4.6%
VES-III: Post-Traumatic Stress Disorder (PTSD)

Heroin Users 35% in Vietnam

22.8% (2.1*) Originated in Vietnam

21.1% (1.9*) Originated Since 1972

Generality of 25-Year Followup
Suicidality Findings

- Are Vietnam veterans indeed at an increased risk of suicide?
  Estimates of suicide vary widely
  (4,000 ~ 20,000 ~ 100,000).

- Is war trauma a reason?
  “Most Vietnam veterans are just fine. And why shouldn’t they be? The majority didn’t see combat.” Collin Powell, USA Today, Nov., 2000.

- Is substance abuse a reason?
Objectives

- Cross-sectional prevalence rates of alcohol use disorders based on DSM-IV.
- Nationwide estimates.
- Large sample to allow detailed assessment of comorbidity among subgroups (e.g. gender, ethnicity).
- Longitudinal course: apparently not materialized.

Methods

- N=42,802, 18 years or older, non-institutionalized.
- Multi-stage sampling.
- Oversampling blacks, 18-29 years of age.
National Mortality Follow-Back Survey (NMFS, ‘93)

- One of a series of mortality surveys done by the National Center for Health Statistics -- arguably the largest incidence study of deaths in US.
- 1% of deaths in 1993 from a 10% drawing of death certificates (with oversampling of deaths from external causes).
- A large sample size of the deceased (N=22,957) with a sufficient number of suicide deaths.
- Used as “replication” of NCS results -- if suicide represents above threshold of the underlying distribution of suicidal behavior liability, most predictors should be similar.
- Measures obtained from death certificates and follow-back interviews with next-of-kins.
NMFS, NLAES, and VES-III: Suicide and suicide attempts

NMFS among males ages 40 to 60
- One out of four (25.6%) suicides were Vietnam veterans.
- But, one out of seven deaths (15.3%) were also Vietnam veterans.
- 3.4% of all deaths among Vietnam veterans were suicide. The risk is twice as high (OR = 1.98, CI, 1.24-3.17) compared to the civilian counterpart.

NLAES among males ages 40 to 60
- The lifetime suicidal attempts in this age group (2.0%) are not much higher than males as a whole (1.92%).
- Lifetime suicidal attempts among Vietnam veterans (2.67%) higher (OR = 1.62, CI, .99-2.66) than non-veterans.

VES-III (almost all ages 40 to 60)
- The lifetime suicide attempts among veterans is 8.7 times (CI, 2.95-30.59) higher than non-veterans.
- No suicide attempts were reported by non-veterans in the past year, compared to 4.2% among veterans.
- There was no completed suicide among non-veterans.
NMFS, NLAES, and VES-III: Predictors

- **Common predictors**
  - Age (metric)
  - Race (black = 1)
  - Education (HS = 1)
  - Employment (currently employed = 1)
  - Vietnam veteran
  - Other era veteran
  - Alcohol dependence\(^2\)
  - Drug use\(^3\)
  - Depression\(^4\)
  - Health problems\(^1\)

- **Unique predictors**
  - Adult ASP (4+ sxs)
  - Childhood ASP (4+ sxs)
  - PTSD (lifetime DSM-IV)
  - Combat (3+ combat experiences)

---

1. Not in NMFS93. 2. NMFS93 - 3+ sxs lifetime; NLAES-DSM-IV lifetime; VES-III; DSM-IV since 1972. 3. NMFS93 - more than occasional use, any past year; NLAES 12+ times any drug lifetime; VES-III- 5+ times any drug since 1972. 4. NMFS93- 8+ sxs past months; NLAES and VES-III, DSM-IV except suicidal behavior, lifetime.
<table>
<thead>
<tr>
<th>Suicidality (%)</th>
<th>MNFS Vietnam-era veteran (n=494)</th>
<th>MNFS Other (n=2,331)</th>
<th>NLAES Vietnam-era veteran (n=1,277)</th>
<th>NLAES Other (n=4,185)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed suicide (past yr)</td>
<td>5.6*</td>
<td>2.9*</td>
<td>- -</td>
<td>- -</td>
</tr>
<tr>
<td>Suicide attempt (lifetime)</td>
<td>- -</td>
<td>- -</td>
<td>2.7</td>
<td>1.8</td>
</tr>
<tr>
<td>Communication of suicide intent (past yr)</td>
<td>11.1</td>
<td>4.8</td>
<td>- -</td>
<td>- -</td>
</tr>
<tr>
<td>Suicidal thought (lifetime)</td>
<td>- -</td>
<td>- -</td>
<td>10.7*</td>
<td>8.4*</td>
</tr>
<tr>
<td>Expression of death wish (past yr, lifetime)</td>
<td>25.5</td>
<td>15.3</td>
<td>11.0</td>
<td>9.1</td>
</tr>
</tbody>
</table>

Source: Price et al. (under review). Prevalence rates were weighted with standard errors adjusted by the SUDAAN Taylor series method. * indicates $p<.05$ (Wald $\chi^2$) testing for an unadjusted logistic regression coefficient for Vietnam-era veterans compared to others (two-tail test). MNFS, past year; NLAES, lifetime.
### NMFS and NLAES: Common Predictors of Suicide and Suicide Attempts (Men Age 40-60)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>MNFS (completed suicide)</th>
<th>NLAES (attempted suicide)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vietnam-</td>
<td>Other</td>
</tr>
<tr>
<td></td>
<td>era veteran (n=494)</td>
<td>(n=2,331)</td>
</tr>
<tr>
<td>Age (50 years or older)</td>
<td>0.54</td>
<td>0.60</td>
</tr>
<tr>
<td>Race (African American)</td>
<td>0.20*</td>
<td>0.12*</td>
</tr>
<tr>
<td>Education (no highschool diploma)</td>
<td>0.53</td>
<td>1.43</td>
</tr>
<tr>
<td>Employment (cur. employed)</td>
<td>3.98*</td>
<td>2.01*</td>
</tr>
<tr>
<td>Marital status (currently married)</td>
<td>1.94</td>
<td>1.02</td>
</tr>
<tr>
<td>Living alone</td>
<td>3.42*</td>
<td>1.42</td>
</tr>
<tr>
<td>Alcohol problems ¹</td>
<td>4.90*</td>
<td>1.69</td>
</tr>
<tr>
<td>Drug use ¹</td>
<td>2.13</td>
<td>3.01*</td>
</tr>
<tr>
<td>Depression ¹</td>
<td>3.14*</td>
<td>0.88</td>
</tr>
<tr>
<td>Health problems ¹</td>
<td>0.10*</td>
<td>.25*</td>
</tr>
</tbody>
</table>

**Model fit**

- **F** = 5.07, **F** = 10.68, **F** = 6.05, **F** = 10.68
- **C** = 0.71, **C** = 0.66, **C** = 0.87, **C** = 0.82

---

Source: Price et al. (under review). The adjusted odd ratios (ORs); weighted with s.e.’s adjusted by the SUDAAN. *, p#.05 for beta’s for individual logistics. The underlined ORs indicate a significant difference of two OR’s between two samples within dataset (p<.10, two-tail test). 1. Alcohol problems and depression are close to meeting DSM-IV, drug use is experimental level, health problems are 2+. 
### VES-III: Predictors of Suicidal Attempts

#### VES-III: past year attempted suicide (n=831)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Common predictors only</th>
<th>Common &amp; unique predictors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (metric)</td>
<td>0.84</td>
<td>0.82</td>
</tr>
<tr>
<td>Race (African American)</td>
<td>0.79</td>
<td>0.86</td>
</tr>
<tr>
<td>Education (no high school diploma)</td>
<td>2.17</td>
<td><strong>3.03</strong>*</td>
</tr>
<tr>
<td>Employment (currently employed)</td>
<td><strong>0.29</strong>*</td>
<td>0.46</td>
</tr>
<tr>
<td>Marital status (currently married)</td>
<td>1.46</td>
<td>2.28</td>
</tr>
<tr>
<td>Living alone</td>
<td>0.87</td>
<td>1.14</td>
</tr>
<tr>
<td>Alcohol dependence (DSM-IV, 1972-96)</td>
<td>1.64</td>
<td>0.97</td>
</tr>
<tr>
<td>Illicit drug use (5+, 1972-96)</td>
<td>3.99</td>
<td>3.54</td>
</tr>
<tr>
<td>Depression (DSM-IV, 1972-96)¹</td>
<td><strong>3.23</strong>*</td>
<td>1.72</td>
</tr>
<tr>
<td>Physical illness (1+ of 15 major illnesses)</td>
<td><strong>2.95</strong>*</td>
<td>2.69</td>
</tr>
<tr>
<td>Adult antisocial personality (4+ sx)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>childhood conduct scale (4+)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSD (DSM-IV, lifetime)</td>
<td><strong>12.5</strong>*</td>
<td></td>
</tr>
<tr>
<td>Vietnam veteran</td>
<td>α</td>
<td>α</td>
</tr>
</tbody>
</table>

**Model fit**

- C = 0.91
- C = 0.93

---

Source: Price (unpublished). The adjusted odd ratios (ORs); unweighted with s.e.'s adjusted by a Huber-White sandwich estimator; *, p < .05 for beta's; α, quasi-complete separation (all suicide attempters were veterans). 1. Depression excludes suicidality questions.
Epidemiologic Evidence for Suicide and Suicidal Behavior in Middle Aged Men

- Common risk and protective factors across suicide and suicidal behaviors.
- Even occasional drug use signals an increased risk.
- Middle age men who are also Vietnam veterans are more vulnerable; however, the difference appears to be attributable to high levels of risk factors.
- PTSD appears to have a profound effect on suicidal behavior.
Role of Trauma in Suicide Behavior

People exposed to trauma are at higher risk for suicide and suicidal behavior

- sexual and physical abuse → adolescent suicidal behavior
- war trauma, rape → adult suicidal behavior

Mechanisms not well understood

- Trauma → PTSD → Suicidality
- Injury
  - Survivor guilt
  - Agent of killing

- Early Abuse → Trauma in Adult
  - Suicidal Behavior

PTSD
PTSD, SUDs & Suicidality

- Longitudinal patterns and associations of PTSD, substance abuse and suicidality.

- Self-reported narcotics dependence in 1971. Source: Price et al. (under review).
Length of Suicidal Ideation
Stratified by Concurrent PTSD
(n=120)

Length of Suicidal Ideation Stratified by Drug Dependence (n=120)

Logrank: \( p = .17 \)
Wilcoxon: \( p = .04 \)

PTSD, SUDs & Suicidality

- Potentially causative roles of PTSD and substance abuse on suicidality.
# PTSD, Substance Abuse and Other Psychopathology on Suicide Ideation: 1972-1996 (n=637)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Hazard Ratio</th>
<th>P</th>
<th>Risk Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol dependence</td>
<td>1.18</td>
<td>.343</td>
<td>.84 - 1.68</td>
</tr>
<tr>
<td>Major depression</td>
<td>3.21</td>
<td>&lt;.001</td>
<td>1.93 - 5.34</td>
</tr>
<tr>
<td>Adult antisocial personality</td>
<td>1.88</td>
<td>.002</td>
<td>1.25 - 2.81</td>
</tr>
<tr>
<td>PTSD</td>
<td>1.51</td>
<td>.339</td>
<td>.65 - 3.48</td>
</tr>
<tr>
<td>Drug dependence</td>
<td>2.06</td>
<td>.002</td>
<td>1.31 - 3.24</td>
</tr>
<tr>
<td>PTSD x log (time)</td>
<td>1.31</td>
<td>.049</td>
<td>1.00 - 1.70</td>
</tr>
</tbody>
</table>

Source: Price et al., Drug & Alc Dependence, 2004 (in press). 1. Time-dependent Cox regression analysis allowing for recurrence of suicidal ideation. A robust sandwich estimator applied to adjust the variances (data points n = 15,925). Age, race, enlistment status and education adjusted as covariates. 2. Depression measure excludes questions of suicidality. 3. Other interaction terms with log (time) were not significant.
PTSD, Drug Dependence and Suicidal Ideation: Path Analysis Model


- Paths with coefficient < .1 (approximately p <.05).
- Paths with coefficient > .1 (p < .001).
PTSD, Drugs and Suicidality

- PTSD most stable over time; drug dependence declines, but suicidal behavior increases over time to midlife.
- Associations become stronger over time.
- Alcohol dependence and antisocial personality not as strong as predictors of suicidal behavior.
- Drug dependence exacerbates PTSD and suicidal behavior; once the course is set, self-medication kicks in.

PTSD and Drugs

- Learning from the past to inform future research.
Coming Back in a Full Circle..

- Why a 95% remission? - Anomalous findings from a well-done study need to be explained.

- Endophenotypes - Following the fads or the research of the future?
24-Year Follow-up of California Addicts (Civil Commitment)

The natural history of narcotics addiction (N=581).

Brain Correlates of Chronic PTSD

- Amyglada
- Longitudinal Fissure
- Hippocampus
- Cingulate Cortex
HPA Paradox in Chronic PTSD

Extreme stress

Corticotropin-releasing hormone (CRH)

Adrenocorticotrophinc hormone (ACTH)

Cortisol release

HPA axis over-sensitization

Decreased basal cortisol level
Cortisol Levels, Hippocampus and Cognitive Functioning: Short- and Long-Term Feedback Loops

- Cognitive Function
- Hippocampus Anomaly
- Cortisol Levels
- Stress

Acute Toxicity

Short term effects

Long term effects
How about drugs?
Learning from Animal Research

Chronic exposure to morphine:

- Causes a marked increase in the number of corticosteroid-binding globulin (CBG) molecules in serum of adult male rats
- Decreases the amount of free, physiologically active, corticosterone in serum and brain.

[Note: Over 90% of cortisol is bound to CBG in human plasma].

One placebo or 75 mg morphine pellet was implanted into adult male rats and CBG was assayed at selected time intervals (Solid Line).

* indicates p < 0.05 versus the placebo group.

For data shown by the dashed lines, rats were implanted with an additional placebo or morphine pellet on day 7 to maintain elevated morphine levels in serum.

Free corticosterone in serum of unstressed adult male rats (zero time point) or rats mildly stressed by injection of physiological saline 7 days after implantation of 2 placebo or morphine pellets.

Free hormone levels were calculated using a modification of the mass equation, which takes into account total corticosterone and CBG levels and the binding affinity of CBG for corticosterone.

The Morphine-induced Upregulation of CBG Decreases the Amount of Physiologically Active Corticosterone in Brain

Two placebo or morphine pellets were implanted into adult male rats and free corticosterone in serum and brain was measured 7 days later.

ILLICIT OPIATE USE, STRESS & GLUCOCORTICOIDS*

Prolonged or Repeated Stress

Chronic HPA Activation & CBG Down-Regulation

Glucocorticoid Overexposure

Detrimental Physical and Mental Consequences

Morphine Usage as a Self-Medication

Persistent Glucocorticoid Deficiency

Compromises Ability to Cope with, Adapt to, and Recover from Everyday Challenges and Stressful Events and Conditions and Increases Vulnerability to PTSD

Contributes to Tolerance Development

Continuation and Escalation of Drug Use

Why A 95% Remission Rate?

- “Setting” - extinguishing conditional response was easy after coming back to U.S.

- Biological process(es) (e.g., bouncing back of cortisol level due to the sudden removal from a stressful environment) may have helped extinction process.
Why Do the Sick Get Sicker?

- Common biological processes affecting brain and HPA:
  - Hippocampal shrinkage?
  - Declined basal cortisol level?
  - Declined neurocognitive processing ability?

- Cumulative disadvantages in social, personal and occupational domains
  - Negative reinforcement
  - Increased stress
  - Decreased social and financial resources
Breaking the Cycle of Psychopathology

.. How can we do that?
How to capture situation-specific protective factors that mitigate already existing suicidal risk?
He is eager to hear my point of view.

...are finally listening.
VES-IV: “Suicide” Study

- Quasi case-control design to take advantage of the existence of concentrated suicidals.
- Episode-based interview to capture protective factors mitigating suicide risk.
- Quantitative-qualitative integration to examine the patterns of interactions between risk and protective factors.
The Surgeon General’s Call to Action to Prevent Suicide, 1999

The Public Health Approach Applied to Suicide Prevention

1. Defining the problem.

2. Identifying causes and protective factors.

The second step focuses on why. It addresses risk factors such as depression, alcohol and other drug use, bereavement or job loss. This step may be used to define groups of people at higher risk for suicide. Many questions remain, however, about the interactive matrix of risk and protective factors in suicide and suicidal behavior and, more importantly, how this interaction can be modified.
Capturing Protective Factors

- How to capture situation-specific protective factors that mitigate already existing suicidal risk?
  - How to gather the data needed?
  - How to analyze the data gathered?

- Approaches adapted from cognitive and cultural anthropology.
  - Integration of computational approaches.
Protective Factors

What Do They Mean?

- A category opposite of the category which is a risk factor (e.g. nonwhite).
- A characteristic which reduces the risk of a person who has it (e.g. religion).
- A characteristic or behavior which reduces the risk of a person in the presence of a risk factor (social support in presence of depression).
Protective Factors

What do we know?
- Married
- African-American
- Employed
- Religious commitment
- High level of social support
- Family cohesion

Effects that may be indirect or interactive
- Type of support (professional vs. family)
- Support in the presence of depression

The structure of protective factors not well understood.
- Findings are inconsistent
- Findings are not strong
VES-IV Sampling Design

In Target Sample (N=418)

Higher-Risk (N=168)

Projected = 49

Observed = 119

Not in Target Sample (N=224)

Medium Risk (N=223)

Lower-Risk (N=250)
## VES-III. Logistic Models Predicting Past-Year Suicidal Ideation

<table>
<thead>
<tr>
<th>Measures in VES-III</th>
<th>O.R.</th>
<th>Measures from VES-III</th>
<th>O.R.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depressive Symptoms</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressed mood</td>
<td>1.9</td>
<td>Two or more health problems</td>
<td>2.1</td>
</tr>
<tr>
<td>Lack of interest</td>
<td>1.8</td>
<td>Current health is poor</td>
<td>1.8</td>
</tr>
<tr>
<td>Diminished or increased appetite</td>
<td>1.0</td>
<td>Current health is worse than last year</td>
<td>1.5</td>
</tr>
<tr>
<td>Insomnia/hypersomnia</td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moving slowly/restlessness</td>
<td>.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue or lack of energy</td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feelings of worthlessness/guilt</td>
<td>4.7*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficulty in concentrating/confusion</td>
<td>1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoughts of suicide</td>
<td>Q</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Substance Use**

| Drug use<sup>3</sup> | .9  |
| Alcohol dependence<sup>4</sup> | .9  |

**Health Problems<sup>5</sup>**

| PTSD<sup>4</sup> | 3.1* |

**Antisocial Personality Syndrome**

| Four or more adult ASP symptoms | 1.2  |
| Four or more childhood ASP symptoms | 1.3  |

**Family History**

| Family member depressed | 1.0  |
| Family member w/ alcohol problems | .8  |
| Family member hospitalized for or drug problems | 1.5  |
| Family member commit suicide | .7  |

---

1. Based on the veteran sample only (n=641). The “Q” indicates the outcome and predictor variables were “quasi-separated”; the predictor was excluded from the results. All measures cover the period of 1972 to 1996/7, except childhood ASP. 2. Symptoms included in DSM-IV major depression. 3. Illicit drug 5+ or more use (sedative, stimulants, marijuana, opiates, cocaine, PCP, inhalants, or hallucinogens). 4. DSM-IV diagnosis. 5. Self-reported major diagnosed medical illnesses.
Suicidal Ideation Outcome in 2002-3 (n=348)

<table>
<thead>
<tr>
<th>“Predicted” from Scale up to 1997¹</th>
<th>Suicide Ideation Reported in 2002-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (N=213)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>92.2%</td>
</tr>
<tr>
<td>High (N=135)</td>
<td>51.2%</td>
</tr>
</tbody>
</table>

¹ Suicide risk scale was developed based on logistic regression of predictors up to 1996-7, including depressive symptoms, substance abuse, health problems, PTSD, ASP and family history. The medium risk group (n=223) not ascertained in VES-IV.
Process Model: Stressful Event and Coping

Etic - Basic Ideas

- Structural determinants underlying behavior patterns.
- Risk and protective factors: belief system, support system, psychopathology, substance abuse, etc.
- “Baseline” differences in risk and protective factors.
- Severity of event affecting the outcome.
- Coping: appraisal, management, etc.
Coping at the Time of Crisis

Emic - Basic Ideas

- “Coping” is a middle-class concept!
- Elasticity of human response.
- Time is the process.
- The process is “what they thought,” and “what they did.”
- Resource mobilization
  - “I found God” but “I’m not religious.”
  - “I called the VA...” but “VA killed my Dad.”
  - “I called my old buddy, he was sorry but wasn’t surprised” but “I don’t talk to nobody anymore.”
Process Model: Stressful Event and Coping

Structural Determinants

- Demographics
- SES
  - 
  - 
  - 
Process Model: “Normal” Stressful Event

Structural Determinants

Risk Factors
- Psycho-pathology
- Substance Abuse

Protective Factors
- Belief System
- Support System

General Coping Skills

Coping

Stressful Event
Process Model: Suicidal Episode

Structural Determinants

Risk Factors
- Psycho-pathology
- Substance Abuse

Protective Factors
- Belief System
- Support System

Very Stressful Event

Coping

General Coping Skills
Substance Abuse and Coping

“Risk” Elements
- Dependence symptoms
- Loss of rational thinking
- Impulse
- Anger

“Protective” Elements
- Self-medication
- Sedation
- Familiar milieu
Support System and Coping

**Informal Support**
- Family
- Friend
- Co-worker
- Church

**Formal Support**
- Health care system
- Professional Counseling
- Treatment
- Crisis Hotline
VES-IV Instrumentation

- Use of Life Chart throughout.
- Emphasis on respondent’s cognition.
- Use of probe sheets in qualitative sections to ask why and how.
- Multiple patterns of progression depending on the respondent’s response on recent suicidal ideation.
- Event-based, process-oriented assessment of suicidal behavior and reactions to stressful events.
- Structured risk assessment and triage plans using supplement sheets.
Qualitative-Quantitative Analysis Scheme

Data Input
Data Entry
- Transcription
- Coding
  - Assigns codes to words

Qualitative Analysis
- Description of themes
- Classification of themes
- Variability of themes

Data Transfer
Words changed to binary or scaled variables
- ASCII output
- SAS dataset
- S-Plus dataset

Qualitative-Quantitative Integration
Cluster Analysis
- Classifying individuals by codes
MDS
- Low-dimensional mapping
- Linking dimensions to family codes
Tree Regression
- Prediction of outcomes
- Interaction of risk and protective factors
Resource Mobilization at the Time of Crisis

Substance Use/Abuse

Frequency of “Quote” Mentions per Case*

- 0.4
- 0.2
- 0.2
- 0.6

- Substance Use Part of Trigger Event
- Used Drugs During Episode
- Used Alcohol During Episode
- Responded “No Substance Use”

* Scales of the horizontal axes are different, depending on frequencies.

- Blue: Responses from veterans who reported “Worst Negative Event” only (N=74).
- Light Blue: Responses for “Worst Negative Event” among veterans who responded to both (N=32).
- Red: Responses for “Worst Suicidal Event” among veterans who responded to both (N=32).
Resource Mobilization at the Time of Crisis

Belief System

Frequency of “Quote” Mentions per Case*

- Belief in God
- Pray to God
- “Mobilizing” God
- No Belief System

* Scales of the horizontal axes are different, depending on frequencies.

- **Blue** Responses from veterans who reported “Worst Negative Event” only (N=74).
- **Teal** Responses for “Worst Negative Event” among veterans who responded to both (N=32).
- **Red** Responses for “Worst Suicidal Event” among veterans who responded to both (N=32).
Resource Mobilization at the Time of Crisis

“Support” System
Frequency of “Quote” Mentions per Case*

- Friends
- Family Member or Relative
- VA and Other Government Services
- No Support Mentioned

* Scales of the horizontal axes are different, depending on frequencies.

- Responses from veterans who reported “Worst Negative Event” only (N=74).
- Responses for “Worst Negative Event” among veterans who responded to both (N=32).
- Responses for “Worst Suicidal Event” among veterans who responded to both (N=32).
Roles of trauma and substance abuse on suicidal behavior - Focus on war trauma among Vietnam veterans.

- Vietnam veterans are indeed at higher risk for suicide and suicidal behavior.
- PTSD appears to play a critical role in suicidal behavior in this population at least.
- PTSD, drug dependence and suicidality becomes part of “vicious cycle” over time.
- Both common biological mechanism and cumulative social disadvantage explanations may contribute to the cycle of psychopathology.
How to improve the knowledge of suicidal behavior in vulnerable populations such as Vietnam veterans with history of substance abuse and PTSD?

- Understanding protective factors is critical.
- Understanding the interaction among risk and protective factors is critical.
- Innovative assessment is needed to capture situation-specific protective factors.
- Innovative analytical techniques may be needed to capture the interaction of risk and protective factors.
Clinical Implications

Critical Intervention should be possible for most cases we studied.

- It is risk behaviors and loss of many protective factors that make Vietnam veterans at higher risk for suicidal behavior (data not shown).
- Role of physicians and professionals as “weak ties” who can save lives (data not confirmed).
- Listen carefully to what they say . . . In this age of medical advance, it is still language that is the best medium of communication.
- But also don’t forget - guns, guns, guns. . .
# VES-III & IV Collaborators

<table>
<thead>
<tr>
<th>Category</th>
<th>Collaborators</th>
</tr>
</thead>
<tbody>
<tr>
<td>WU Medicine</td>
<td>Rumi Kato Price, Edward Spitznagel, George Murphy, Collins Lewis, Lee Robins,</td>
</tr>
<tr>
<td>WU Social Work</td>
<td>Enola Proctor, Sally Haywood</td>
</tr>
<tr>
<td>St. Louis VA</td>
<td>Katherine Virgo, Seth Eisen</td>
</tr>
<tr>
<td>Readjustment Counseling Services (Vet Center)</td>
<td>Gary Collins, Rodney Haug, Robert Mathes</td>
</tr>
<tr>
<td>St. Louis Crisis Services Center</td>
<td>G. Lee Judy</td>
</tr>
<tr>
<td>Consultants</td>
<td>Bruce Goldberger, Gery Ryan</td>
</tr>
<tr>
<td>Contract Work</td>
<td>Research Triangle Institute, Psychemedics</td>
</tr>
</tbody>
</table>
A preventive war is an oxymoron . . . E. Morris