



Washington<sup>TM</sup>  
WASHINGTON · UNIVERSITY · IN · ST · LOUIS

# **Long-Term Trajectory of Substance Abuse and Psychiatric Comorbidity\***

**Rumi Kato Price, PhD, MPE**

**Washington University School of Medicine**

**St. Louis MO, USA**

**E-mail [price@rkp.wustl.edu](mailto:price@rkp.wustl.edu)**

**\* Prepared for NIDA Drug Abuse in 21st Century Meeting, 2004.**

## **Acknowledgments\***

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

**\* No financial conflicts exist with any of the above funding agencies; No consulting relationships; No stock equity over \$10,000; No involvement in a Speaker's Bureau.**

**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 School of Medicine**

# **Vietnam Era Study (VES)**

# **VES Long-Term Followups.**

## **Questions to Address:**

---

- **In what ways is long-term drug use harmful?**
- **Why do some drug users continue to abuse drugs so long?**
- **What areas do we expect problems will get worse?**

# **VES Long-Term Followups**

## **Mortality and Morbidity over 30 Years**

---

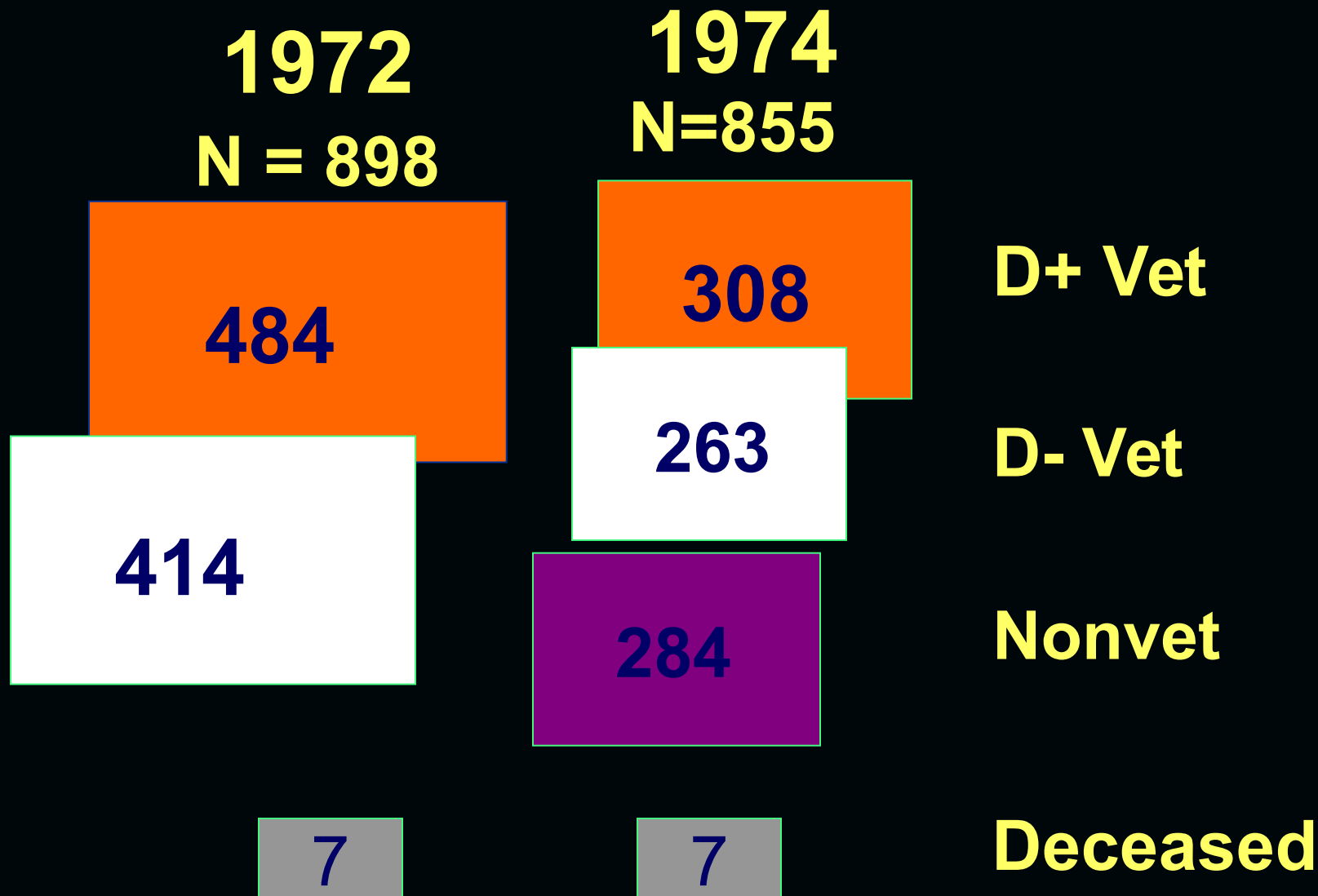
- **Mortality.**
- **Drug use transition patterns.**
- **Social and physical functioning.**
- **Psychiatric profiles over time.**
- **Drug abuse, PTSD and suicidality.**
- **Predictors of remission from drug abuse over time.**
- **Emerging drug use trends in middle age.**

# VES Long-Term Followups

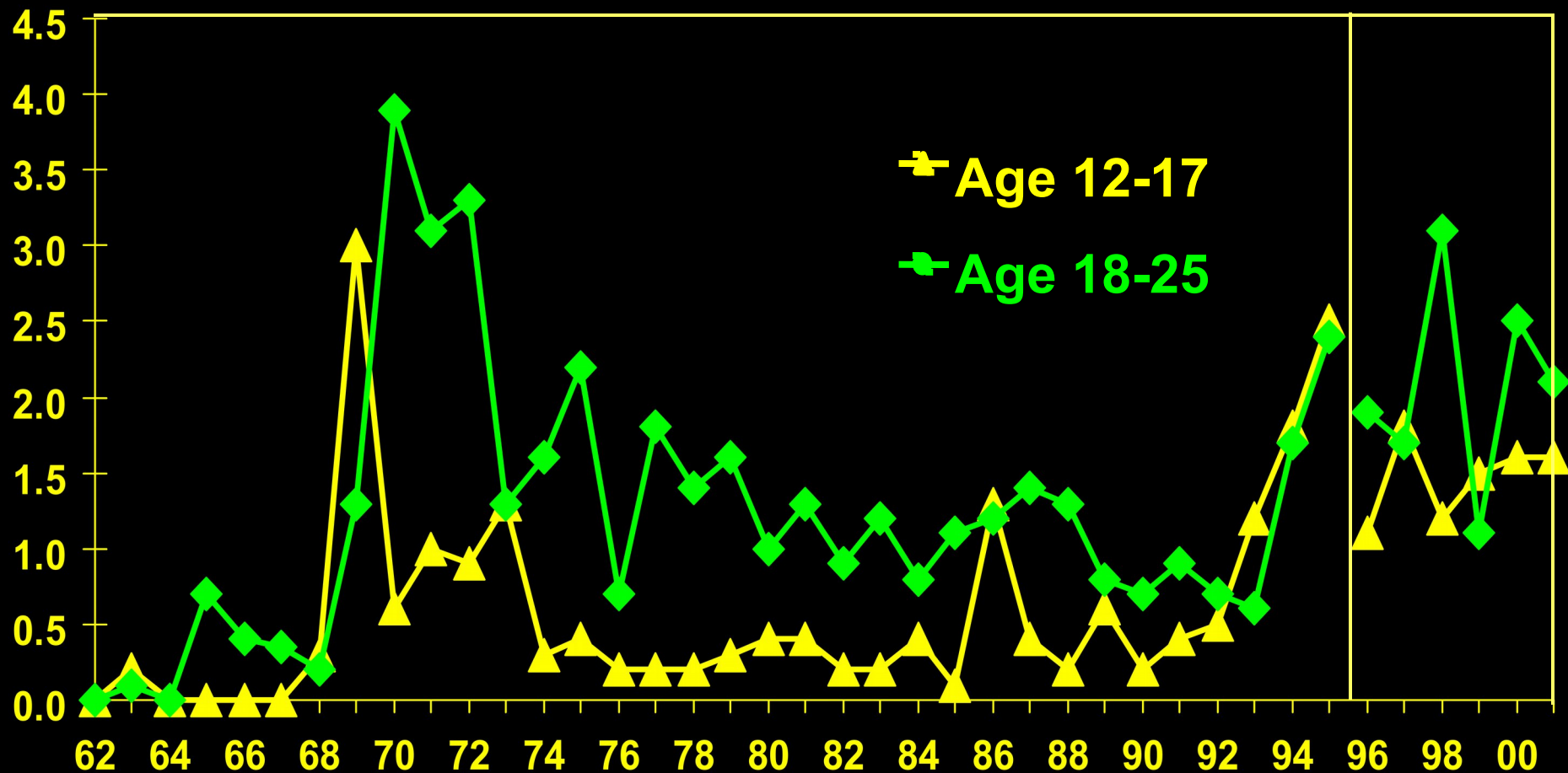
---

- **Background**

# VES Samples (Total Target N = 1,226)



# Initiation of Heroin Use: 1962-2001



**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.

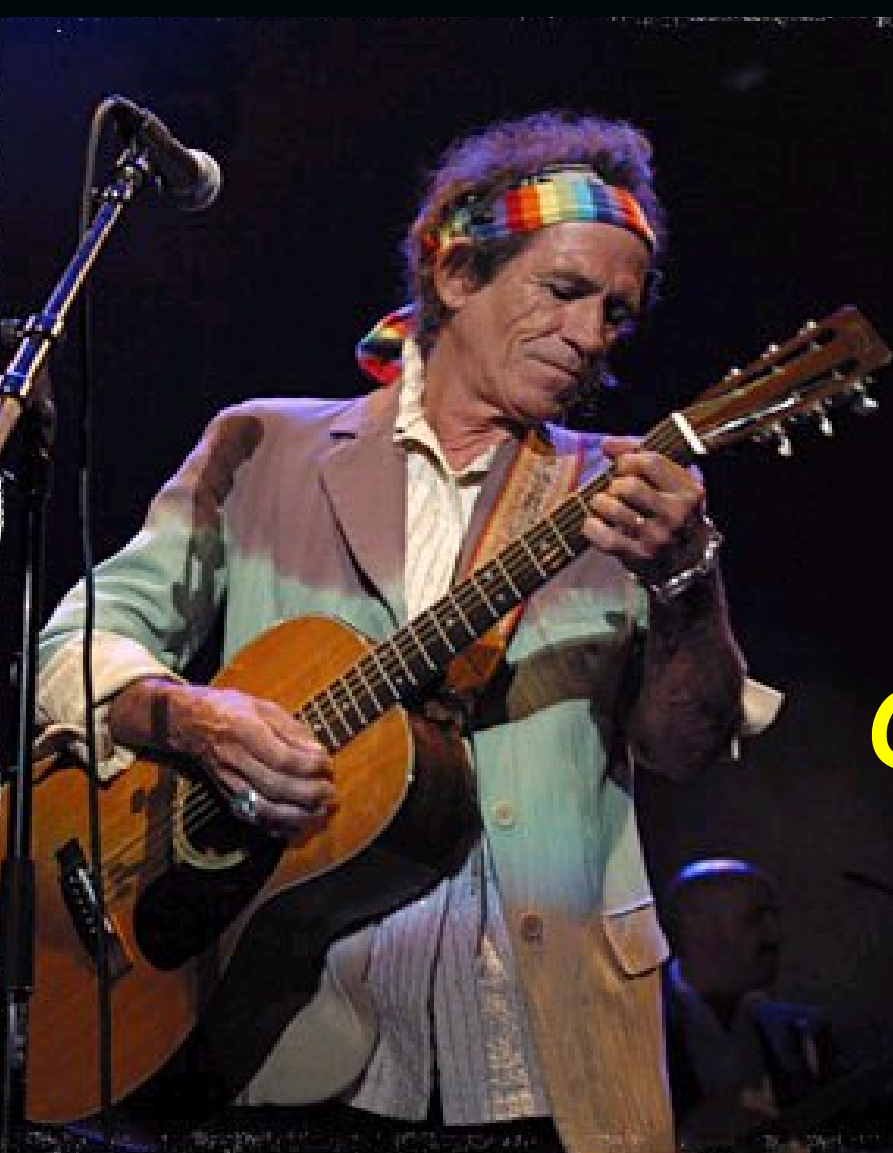


Heroin IS . . .



Deadly....

1994



|                                                                                  |                            |                                                 |                                                            |
|----------------------------------------------------------------------------------|----------------------------|-------------------------------------------------|------------------------------------------------------------|
| INQUIRIES, OR COMPLICATIONS WHICH CAUSED THE DEATH:                              |                            |                                                 | INTERVAL BETWEEN ONSET AND DEATH                           |
| A. Contact perforating shotgun wound to head                                     |                            |                                                 |                                                            |
| DUE TO, OR AS A CONSEQUENCE OF                                                   |                            |                                                 | BEST ONSET AND                                             |
| B. (mouth)                                                                       |                            |                                                 |                                                            |
| DUE TO, OR AS A CONSEQUENCE OF                                                   |                            |                                                 | TEN ONSET AND                                              |
| C.                                                                               |                            |                                                 |                                                            |
| DUE TO, OR AS A CONSEQUENCE OF                                                   |                            |                                                 | IN ONSET AND                                               |
| D.                                                                               |                            |                                                 |                                                            |
| LONG-CONDITIONS CONTRIBUTING TO DEATH BUT NOT PRECEDING                          |                            |                                                 | WAS CASE REFERRED TO MEDICAL EXAMINER OR CORONER (Y/N) Yes |
| 51. INQUIRY DATE (MM, Day, Yr)                                                   | 52. HOUR OF INQUIRY (24HR) | 57. DETECTION HOW INQUIRY OCCURRED              |                                                            |
| 4/5/1994                                                                         | 7PM                        | Self-inflicted shotgun wound                    |                                                            |
| 56. PLACE OF INQUIRY—AT HOME, FARM, STREET, FACTORY, OFFICE, BLDG, ETC (Specify) |                            | 58. LOCATION—STREET OR RD NO., CITY/TOWN, STATE |                                                            |
| Residence                                                                        |                            | Seattle King County Washington                  |                                                            |
| 59. REVIEWED BY                                                                  | DATE                       | 62. REVIEWER SIGNATURE                          | 63. DATE RECEIVED (MM, Day, Yr)                            |
|                                                                                  |                            | X                                               | APR 14 1994                                                |

Or,  
Just . . . Keeping  
The madness??

# VES Samples (N=1,227): Demographic Characteristics

| Demographics             |                     | Veterans            |                                  | Non-veterans           |
|--------------------------|---------------------|---------------------|----------------------------------|------------------------|
|                          |                     | Drug +<br>(N = 511) | Drug -<br>(N = 431) <sup>1</sup> | (N = 284) <sup>2</sup> |
| <b>Age</b>               | Mean Age in 1972    | 22.5                | 24.2                             | 22.6                   |
|                          | (SD)                | (3.2)               | (4.9)                            | (1.6)                  |
| <b>Race</b>              | Whites              | 59.9                | 81.7                             | 88.4                   |
|                          | Blacks              | 34.1                | 11.6                             | 6.3                    |
|                          | Hispanics           | 5.7                 | 4.9                              | 3.2                    |
| <b>Employment Status</b> |                     |                     |                                  |                        |
|                          | Active duty in 1972 | 16.0 <sup>1</sup>   | 16.1 <sup>1</sup>                | 0.0 <sup>2</sup>       |
|                          | Not employed        | 31.3 <sup>1</sup>   | 15.7 <sup>1</sup>                | 7.4 <sup>2</sup>       |

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

\* Data from the interviewed general sample (N = 451).

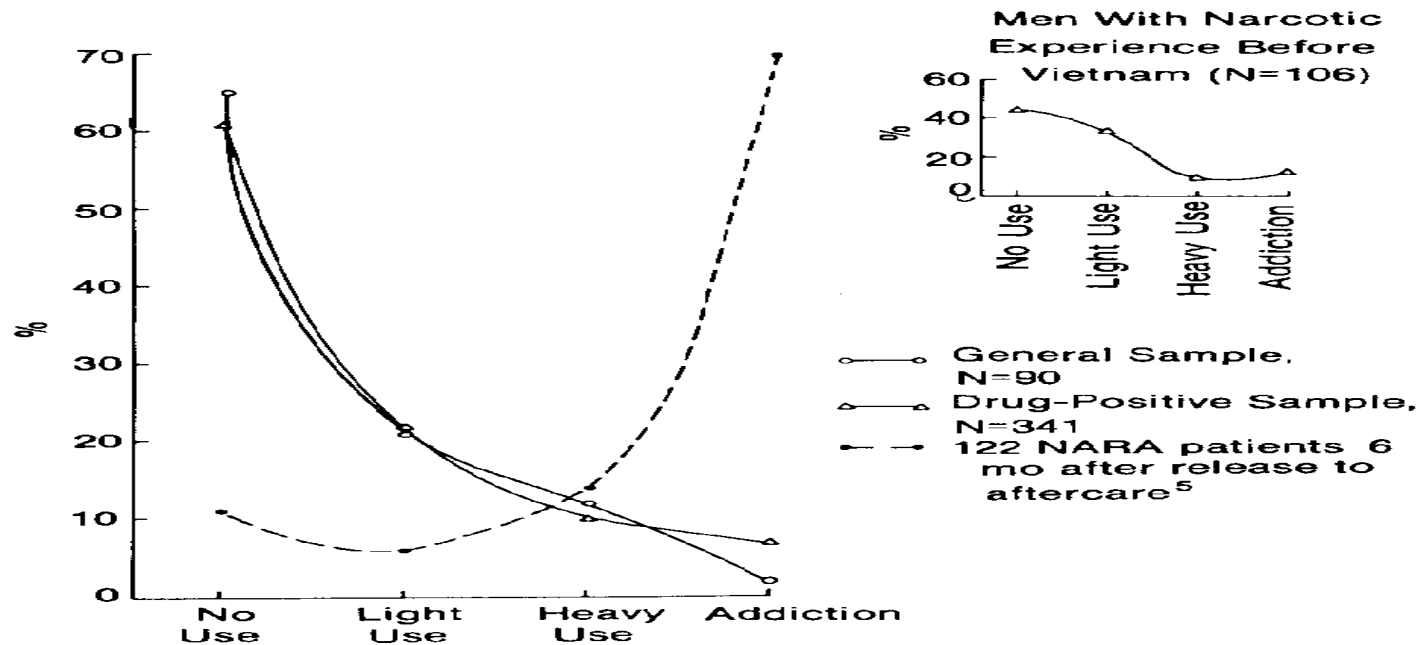
† Estimate based on assumption that those who used marijuana before continued in Vietnam.

‡ Criteria given on p 957.

§ Less than 0.5%.

Source: Robins LN, Helzer JE, Davis DH, Arch. Gen. Psychiatry, 1975

# 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 (%)

|                                        | Veterans              |                       | Nonveterans <sup>1</sup> |
|----------------------------------------|-----------------------|-----------------------|--------------------------|
|                                        | Drug-positive<br>(D+) | Drug-negative<br>(D-) |                          |
| <b><u>Pre-Vietnam</u></b>              |                       |                       |                          |
| Opiate use                             | 28.3                  | 9.6                   | 5.6                      |
| Heavy drinking <sup>2</sup>            | 47.7                  | 40.8                  | 32.0                     |
| <b><u>In-Vietnam/Interim</u></b>       |                       |                       |                          |
| Opiate use                             | 96.7                  | 39.1                  | 6.7                      |
| Amphetamines use                       | 59.3                  | 21.5                  | 18.3                     |
| Barbiturate use                        | 77.4                  | 18.9                  | 12.0                     |
| Heavy drinking <sup>2</sup>            | 19.2                  | 41.3                  | 33.5                     |
| <b><u>Post-Vietnam (1972-1974)</u></b> |                       |                       |                          |
| Opiate use                             | 36.9                  | 14.9                  | 6.0                      |
| Amphetamines use                       | 55.0                  | 27.9                  | 16.6                     |
| Barbiturate use                        | 36.3                  | 13.4                  | 7.8                      |
| Marijuana use                          | 88.4                  | 52.1                  | 40.5                     |
| Heavy drinking <sup>2</sup>            | 67.0                  | 58.0                  | 36.6                     |
| Depressive syndrome <sup>3</sup>       | 26.2                  | 17.9                  | 10.2                     |

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.**

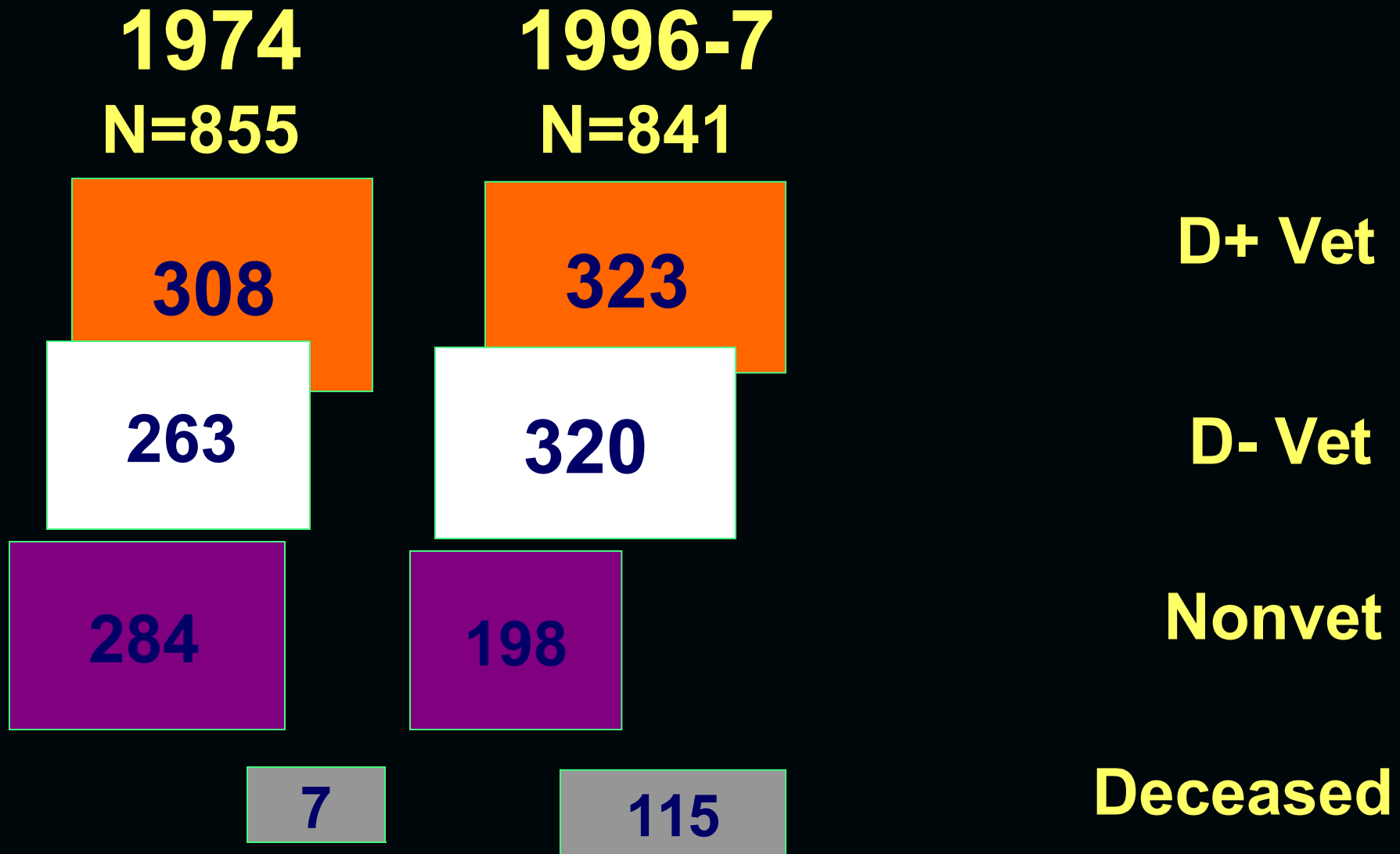
# **VES Long-Term Followups: Mortality and Morbidity over 25 Years**

---

- **Mortality.**

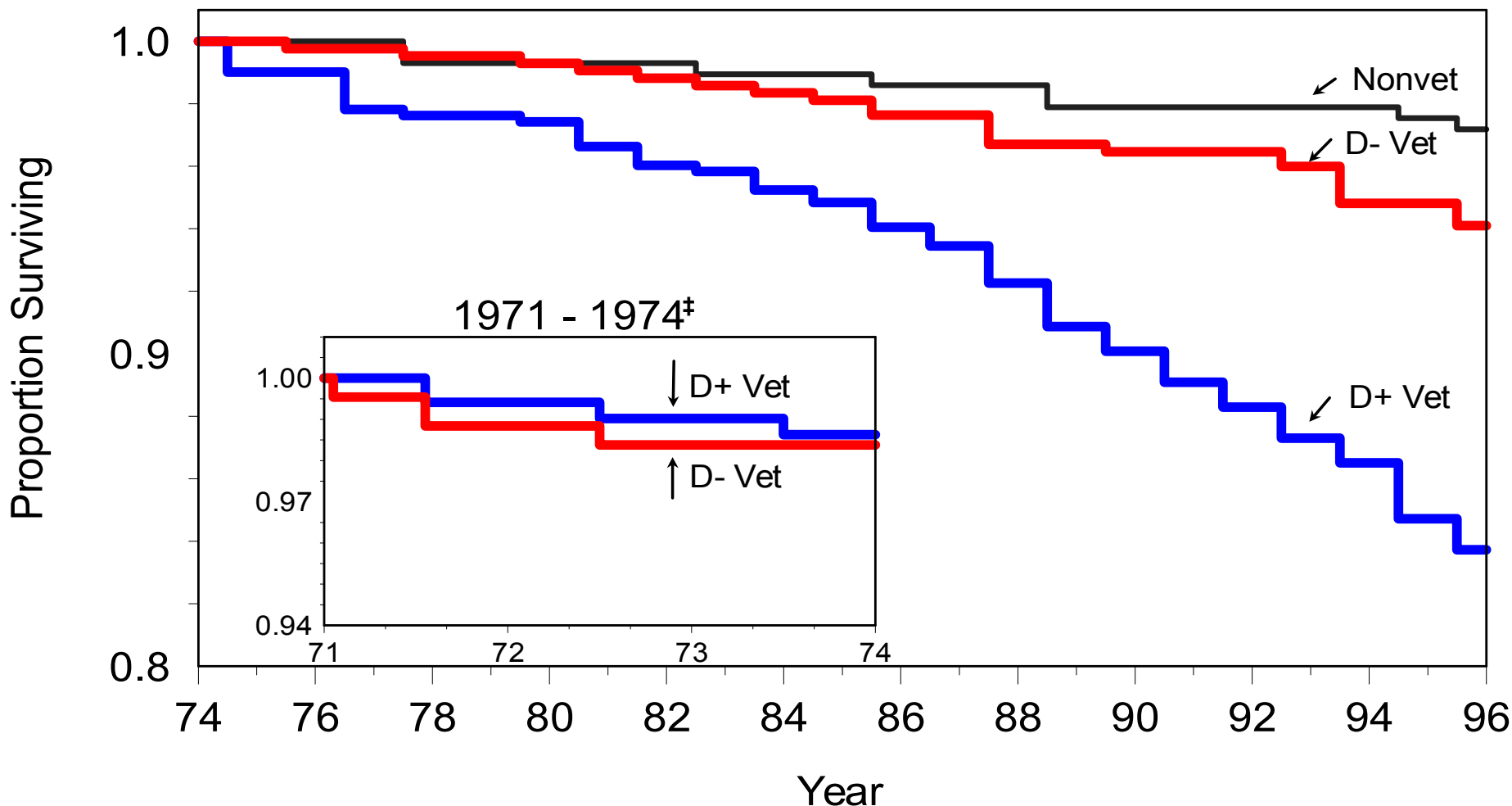


# VES Samples (Total Target N = 1,226)



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

1974 - 1996†



\* 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  $\chi^2$  score tests for the difference among three groups for 1974-1996. Nonveterans vs. D- veterans:  $\chi^2 = 3.59$ ,  $p = .06$ . D- veterans vs. D+ veterans:  $\chi^2 = 24.25$ ,  $p < .0001$ .

‡ The log-rank test between two groups for 1971-1974. D+ veterans vs. D- veterans:  $\chi^2 = .60$ ,  $p = .44$ .

# **Patterns and Predictors of Cumulative Mortality until Middle Age**

---

- **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.**

Source: Price et al., Drug & Alc Dependence, 2001.

# **VES-III.**

## **25-Year Followup**

---

- **Drug use transition patterns.**
- **Social and physical functioning.**
- **Psychiatric profiles over time.**
- **Drug abuse, PTSD and suicidality.**
- **Patterns of remission from drug abuse over time.**

# Annual Measures of Substance Abuse

|                                                 |                                                                 |
|-------------------------------------------------|-----------------------------------------------------------------|
| • <b>Alcohol</b>                                | <b>Heavy alcohol use<sup>1</sup><br/>Dependence<sup>2</sup></b> |
| • <b>Any illicit drug</b>                       | <b>Heavy use<br/>Dependence/abuse<sup>2</sup></b>               |
| • <b>Marijuana</b>                              | <b>Heavy use<br/>Dependence/abuse<sup>2</sup></b>               |
| • <b>Cocaine</b>                                | <b>Heavy use</b>                                                |
| • <b>Opiates</b>                                | <b>Heavy use</b>                                                |
| • <b>Illicit drugs other<br/>than marijuana</b> | <b>Heavy use<br/>Dependence/abuse<sup>2</sup></b>               |

1. Years (from onset and recency) R used alcohol most frequently, given meeting threshold criteria. 2. DSM-IV.

# Annual Measures of Socio-Environmental Covariates

- ▮ **Landmark events (negative or positive).**
- ▮ **Employment.**
- ▮ **Employment.**
- ▮ **Married or cohabitating.**
- ▮ **Number of children.<sup>1</sup>**
- ▮ **Number of important people (max = 4).<sup>1</sup>**
- ▮ **Number of important people who are regular alcohol/drug users (max = 4).<sup>1</sup>**

1. Constructed from onset/recency years.

# **Annual Measures of Psychiatric Comorbidity**

---

- **Posttraumatic stress disorder (PTSD) (based on traumatic event before or 1972 or after).<sup>1,2</sup>**
- **Major depression.<sup>1,2</sup>**
- **Adult antisocial personality (ASP).<sup>1,2</sup>**
- **Suicidal ideation.<sup>1</sup>**

1. Constructed from onset/recency years. 2. DSM-IV.

# **Time-Invariant Measures<sup>1</sup>**

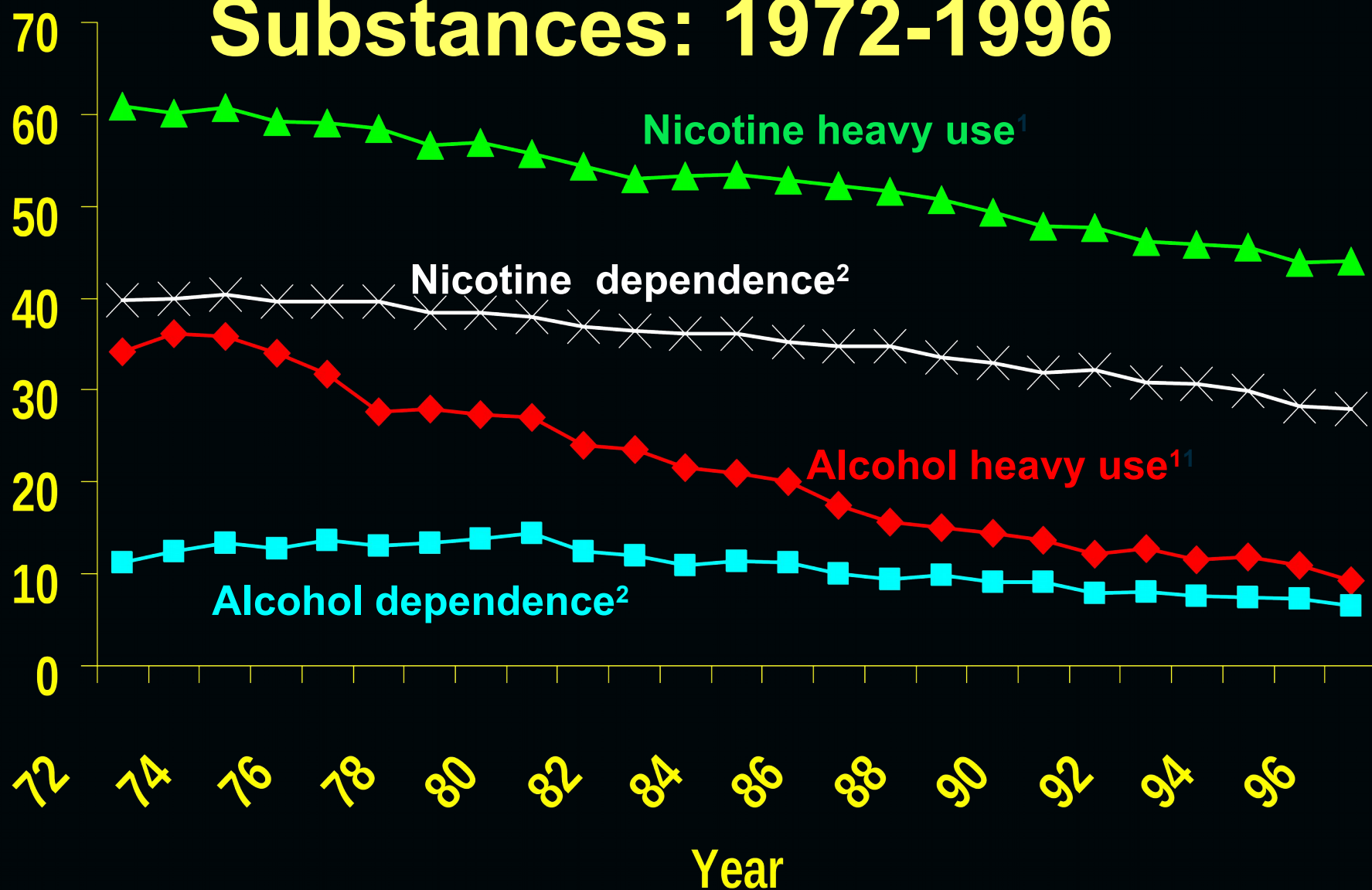
---

- **Sampling status (D+, D-, nonveteran).**
- **Enlistment status.**
- **Aptitude (military IQ test).**
- **Race.**
- **High school education.**
- **Age.**
- **Family psychopathology (depression, ASP symptoms, drinking problems, drug problems, hospitalization, life interference, suicide attempts).**

1. Not exhaustive list.



# Annual Prevalence Rates of Licit Substances: 1972-1996

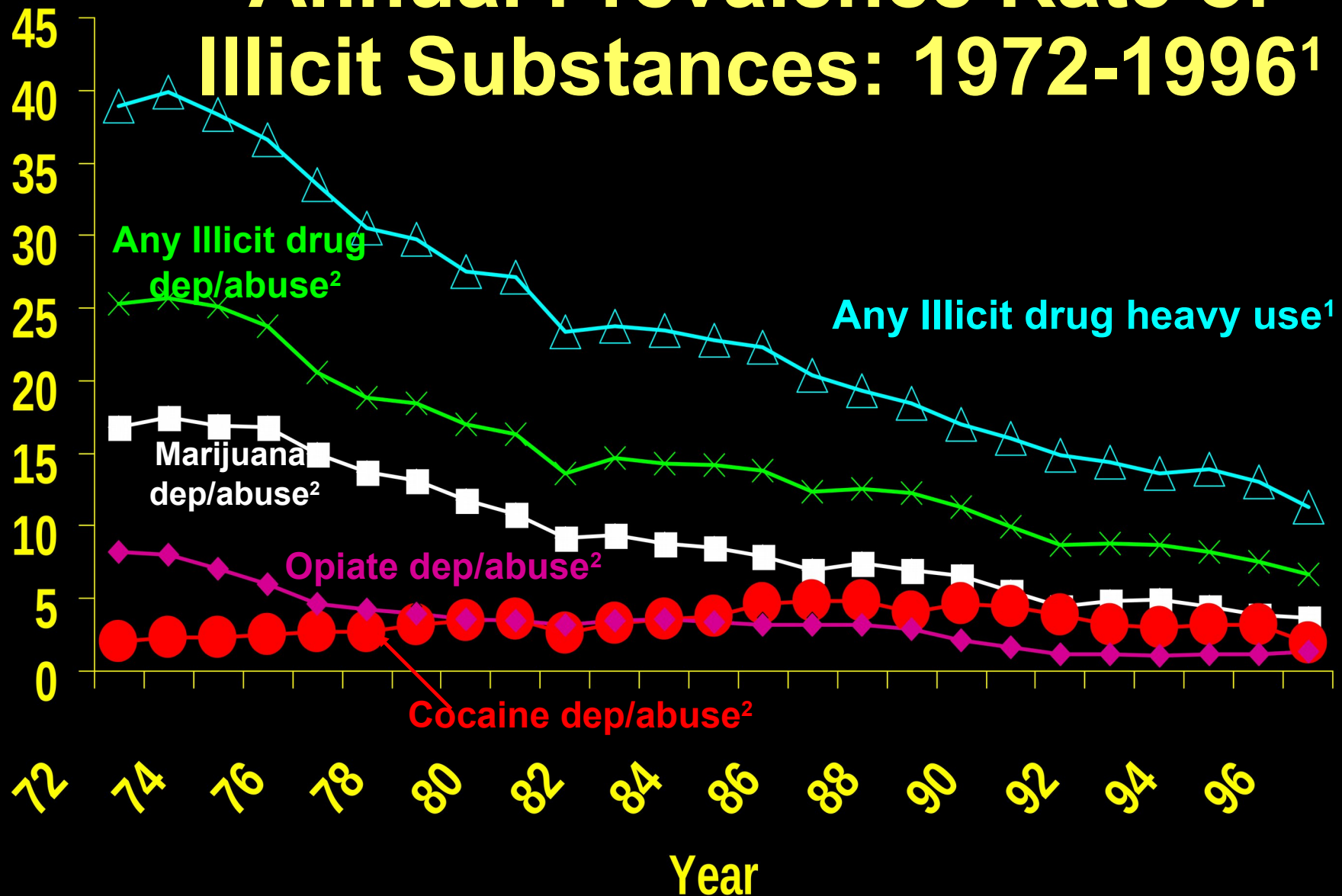


1. Years alcohol most frequently used, if meeting threshold criteria.

2. DSM-IV.

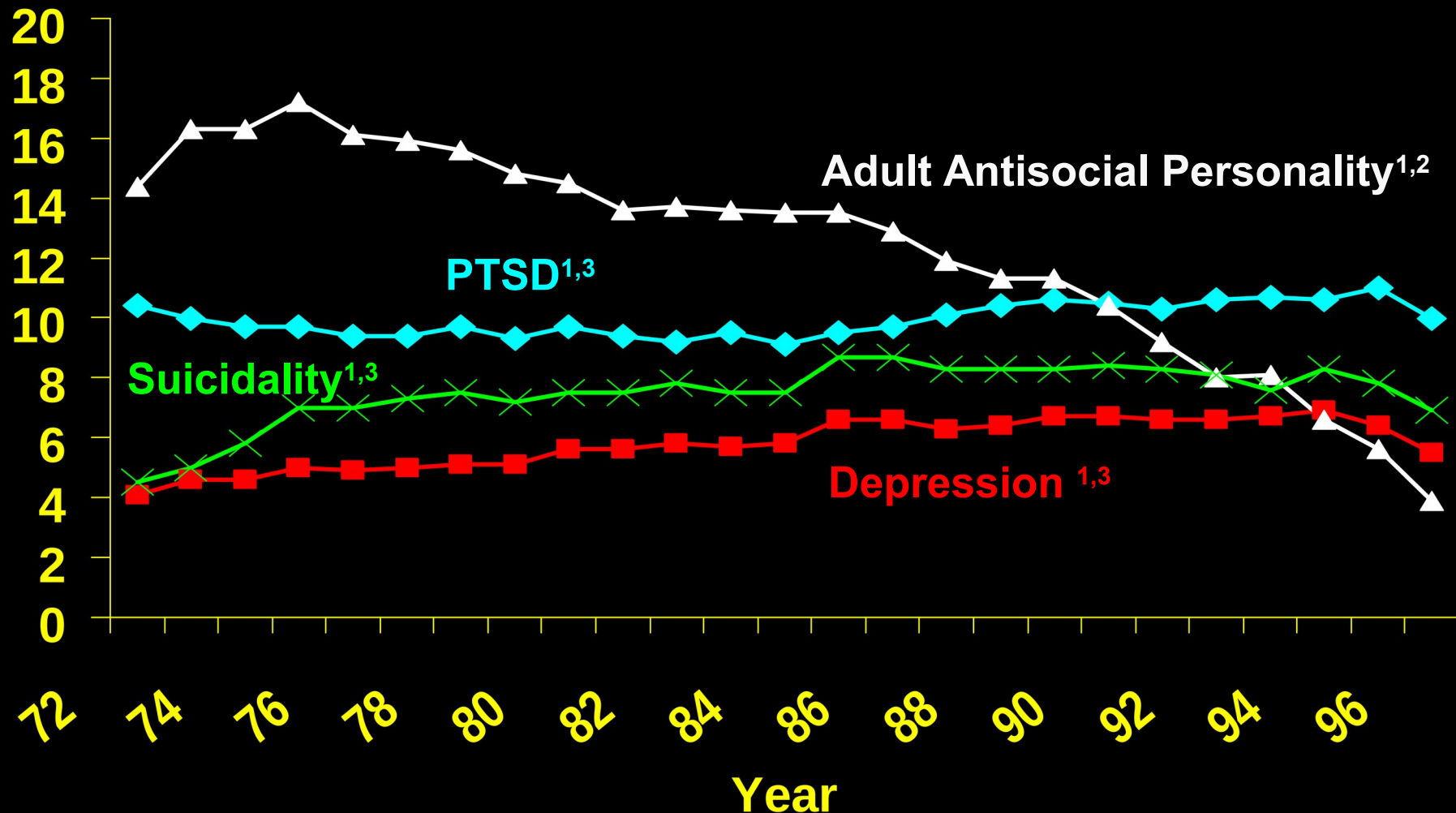
# Annual Prevalence Rate of Illicit Substances: 1972-1996<sup>1</sup>

Percentage



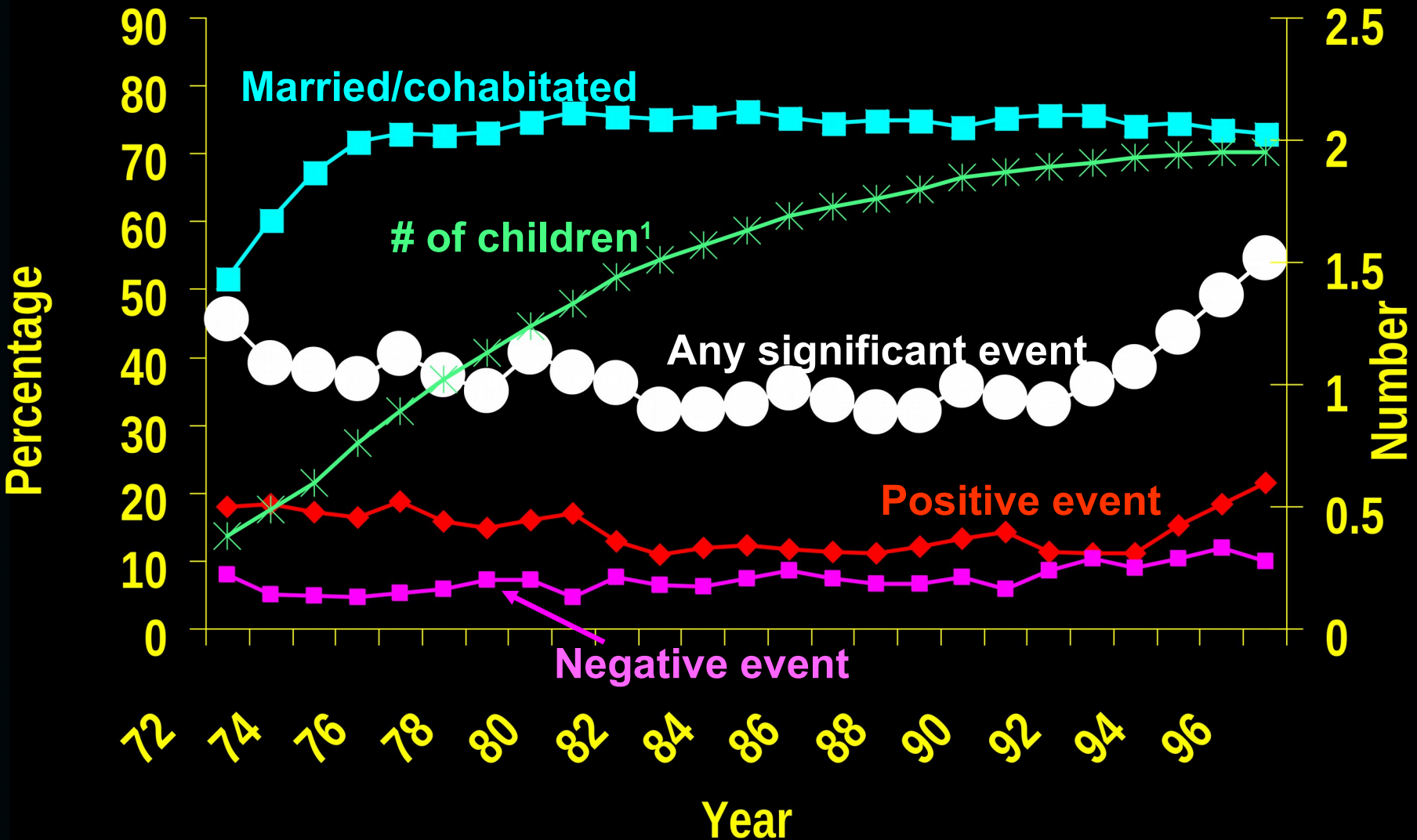
1. Years alcohol most frequently used, if meeting threshold criteria. 2. DSM-IV.

# Annual Prevalence Rates of Psychopathology: 1972-1996



1. Constructed from onset/recency years. 2. DSM-IV adult criteria only. 3. DSM-IV.

# Annual Endorsement Rates of Family and Life Events and: 1972-1996



1. Constructed from birthdates of children fathered.

# Yearly Size Social Circles: 1972-1996<sup>1</sup>



1. Variables are constructed from the respondents report on his four “most important friends ”

# **VES Long-Term Followups: Mortality and Morbidity over 30 Years**

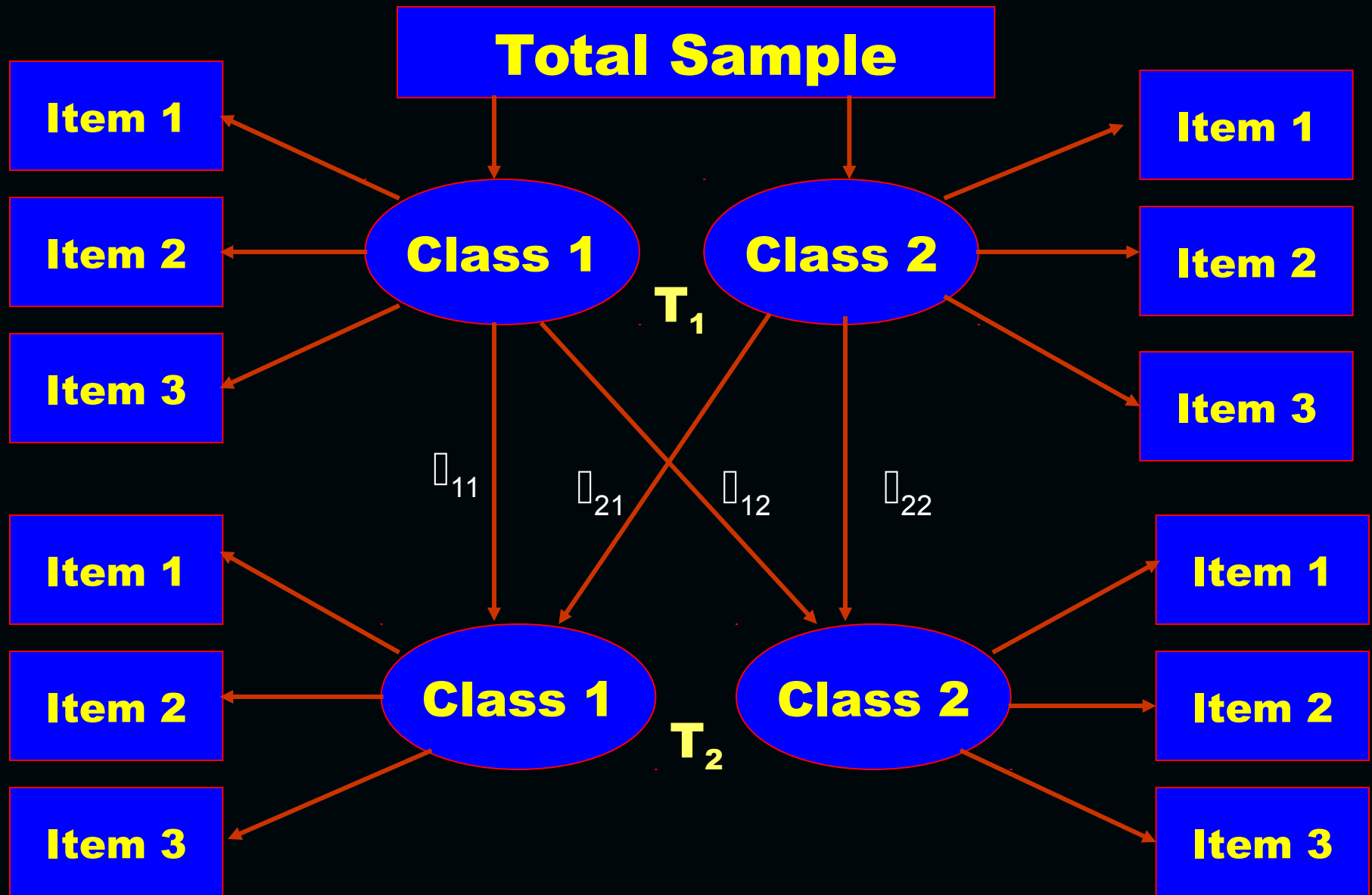
---

- **Drug use transition patterns.**

# **Dynamics of Polydrug Abuse Over Time**

- **What's the relationship between use of one drug and use of another drug over time?**
- **Is there evidence for switching from “harder” drug to a “softer” drug (“substitution” hypothesis)?**
- **Is there evidence for reducing the number of drugs abused (“unpiling” hypothesis)?**
- **Is there evidence for quitting all together at once (“rock-bottom” hypothesis)?**

# Basics of Latent Transition Analysis





# Latent Transition Analysis Estimation

- For 2 classes, 2 times, 3 endorsement items to endorse:

$$P(Y) = \sum_n \text{Ln} (\gamma_1 \pi_{111} \pi_{211} \pi_{311} T_{11} \pi_{112} \pi_{212} \pi_{312} \\ + \gamma_1 \pi_{111} \pi_{211} \pi_{311} T_{12} \pi_{122} \pi_{222} \pi_{322} \\ + \gamma_2 \pi_{121} \pi_{221} \pi_{321} T_{21} \pi_{112} \pi_{212} \pi_{312} \\ + \gamma_2 \pi_{121} \pi_{221} \pi_{321} T_{22} \pi_{122} \pi_{222} \pi_{322}).$$

$P(Y)$  - Total log likelihood.

$\gamma_i$  - Probability of starting in class  $i$ .

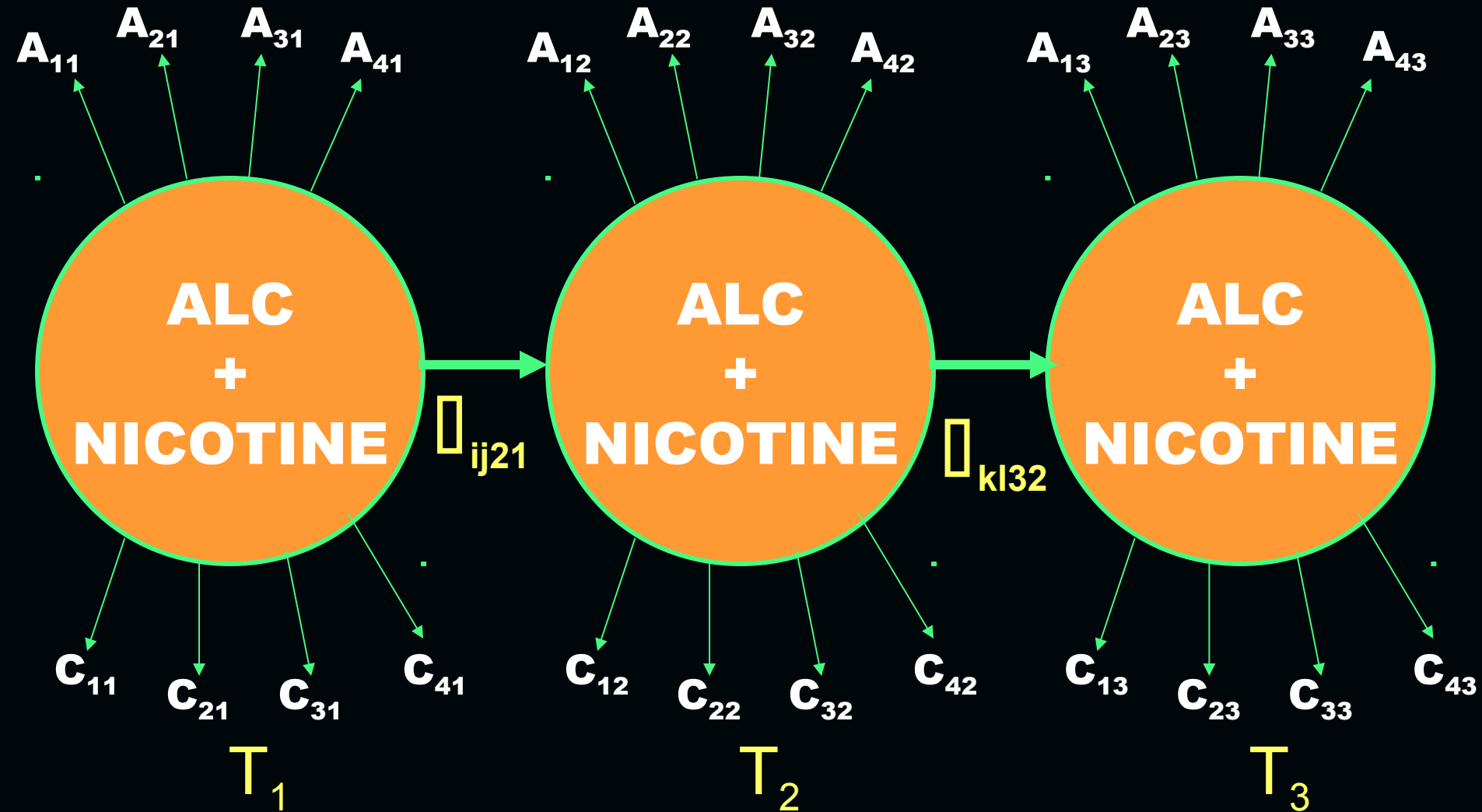
$T_{ij}$  - Transition probability.

$\pi_{kit}$  - Endorsement probability for item  $k$  if the observation is in class  $i$  at time  $t$ .

$n$  - Number of observations with the given pattern of endorsement.

- The EM algorithm to select parameters that maximize  $P(Y)$ .

# Latent Transition Model of Polydrug Abuse\*



\* i, j, k, l, indicates a class at each stage;  $\square_{[21]}$ ,  $\square_{[32]}$  indicate time periods involved. Source: Graham, Collins, et al., J Counsel Clin Psychol 1991; 59:48-57.

# LTA Hypothesis Testing for Transitions Rates ( $\tau$ )

| $T_1 \backslash T_2$ | None | ALC only | NIC only | ALC + NIC |
|----------------------|------|----------|----------|-----------|
| None                 |      |          |          |           |
| ALC only             | U    |          | S        |           |
| NIC only             | U    | S        |          |           |
| ALC + NIC            | R    | U        | U        |           |

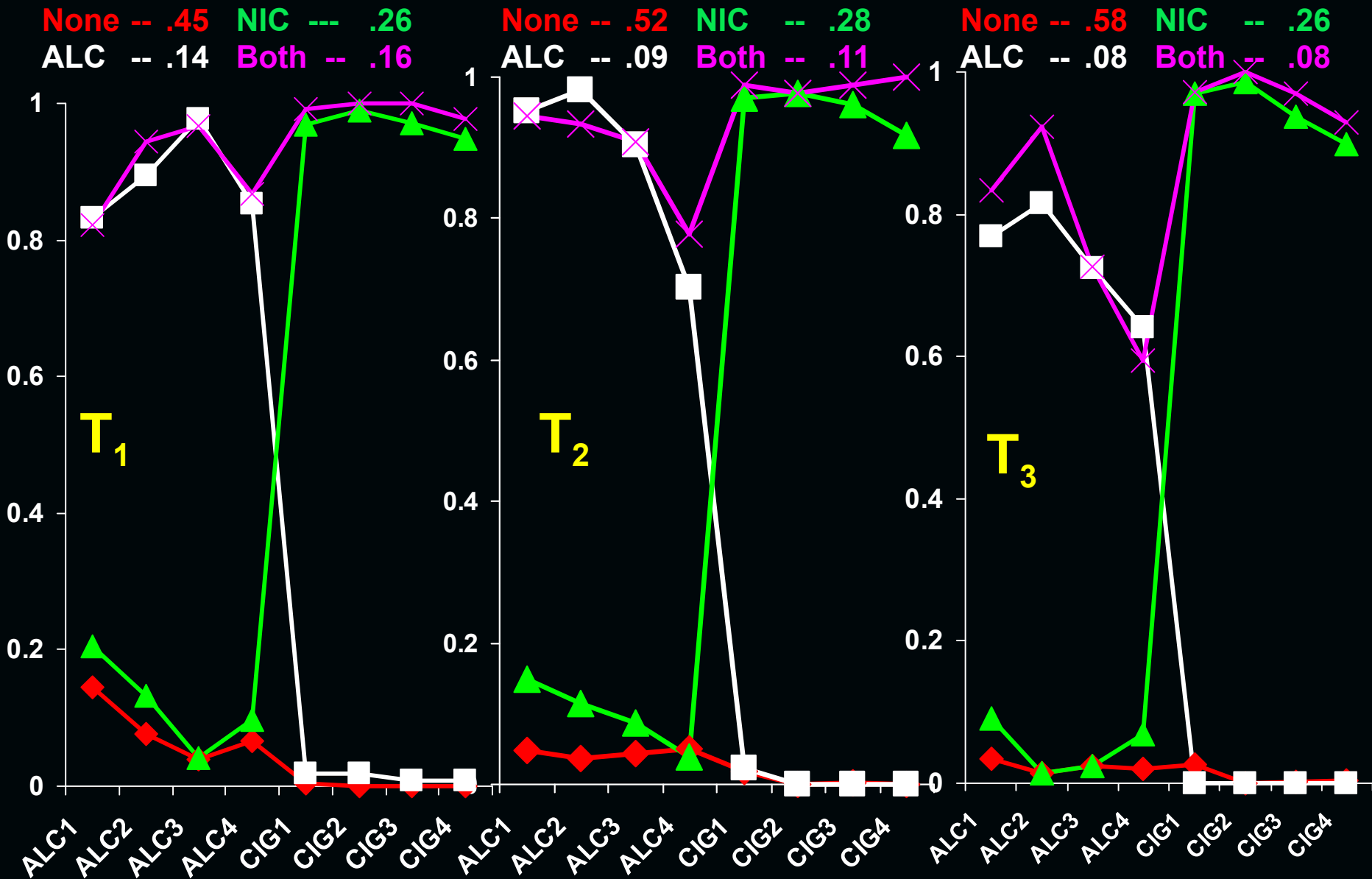
**S: Substitution hypothesis** - switch from one substance to another.

**U: Unpiling hypothesis** - quit one substance at a time

**R: Rock-bottom hypothesis** - quit substances altogether.

# LTA Endorsement Patterns:

## Alcohol + Nicotine - 4 classes, Unconstrained



# LTA Transitions Rates ( $\tau$ ) - 4 Class Model

Alcohol (Dependence) + Nicotine (Dependence)

$T_1 \rightarrow T_2$

$T_2 \rightarrow T_3$

|      | None | ALC | NIC | Both |
|------|------|-----|-----|------|
| None | .94  | .05 | .01 | .00  |
| ALC  | .47  | .52 | .01 | .00  |
| NIC  | .09  | .00 | .81 | .10  |
| Both | .04  | .02 | .41 | .53  |

|      | None | ALC | NIC | Both |
|------|------|-----|-----|------|
| None | .95  | .05 | .00 | .00  |
| ALC  | .43  | .57 | .00 | .00  |
| NIC  | .13  | .00 | .78 | .09  |
| Both | .06  | .01 | .38 | .55  |

## Hypothesis:

**Substitution**    **ALC**  $\xrightarrow{?}$  **NIC**    **NIC**  $\nrightarrow$  **ALC**    **ALC**  $\nrightarrow$  **NIC**    **NIC**  $\nrightarrow$  **ALC**  
**Unpiling**        **Both**  $\rightarrow$  **ALC**    **Both**  $\rightarrow$  **NIC**    **Both**  $\rightarrow$  **ALC**    **Both**  $\rightarrow$  **NIC**  
**Rock-Bottom**    **Both**  $\rightarrow$  **None**                            **Both**  $\rightarrow$  **None**

- $\rightarrow$  means constraining  $\tau = 0$  yielded a  $\chi^2$  (diff) above the cutoff at  $p = .05$ .
- $\xrightarrow{?}$  means some transition exists, but not at a significant level.
- $\nrightarrow$  no transition at all.

# **Dynamics of Poly-Substance Abuse Over Time**

---

- **Polydrug use is certainly common; however, substance abusers appear to have their “choice” of substance.**
- **Gradually increasing abstinence applies to most substances, except for cocaine.**
- **Switching of the main substance use is asymmetrical (MJ to ALC, OP to COC).**
- **“Narrowing of repertoire” occurs gradually over time.**

# **VES Long-Term Followups**

## **Consequences of Drug Abuse over 30 Years**

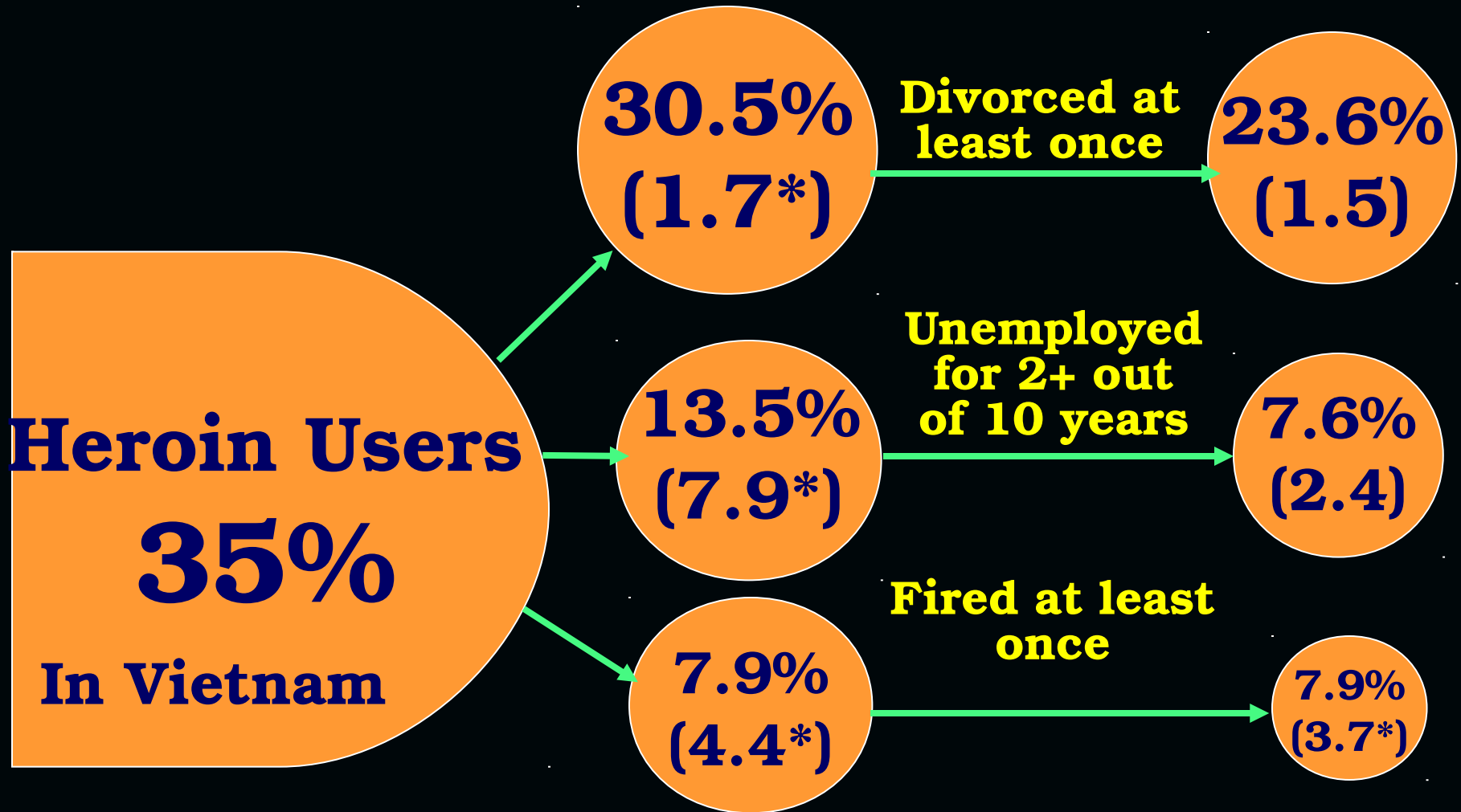
---

- **Social and physical functioning.**
- **Psychiatric profiles over time.**

# Marriage and Employment: 1972-1996<sup>1</sup>

First 10 Years

Last 10 Years

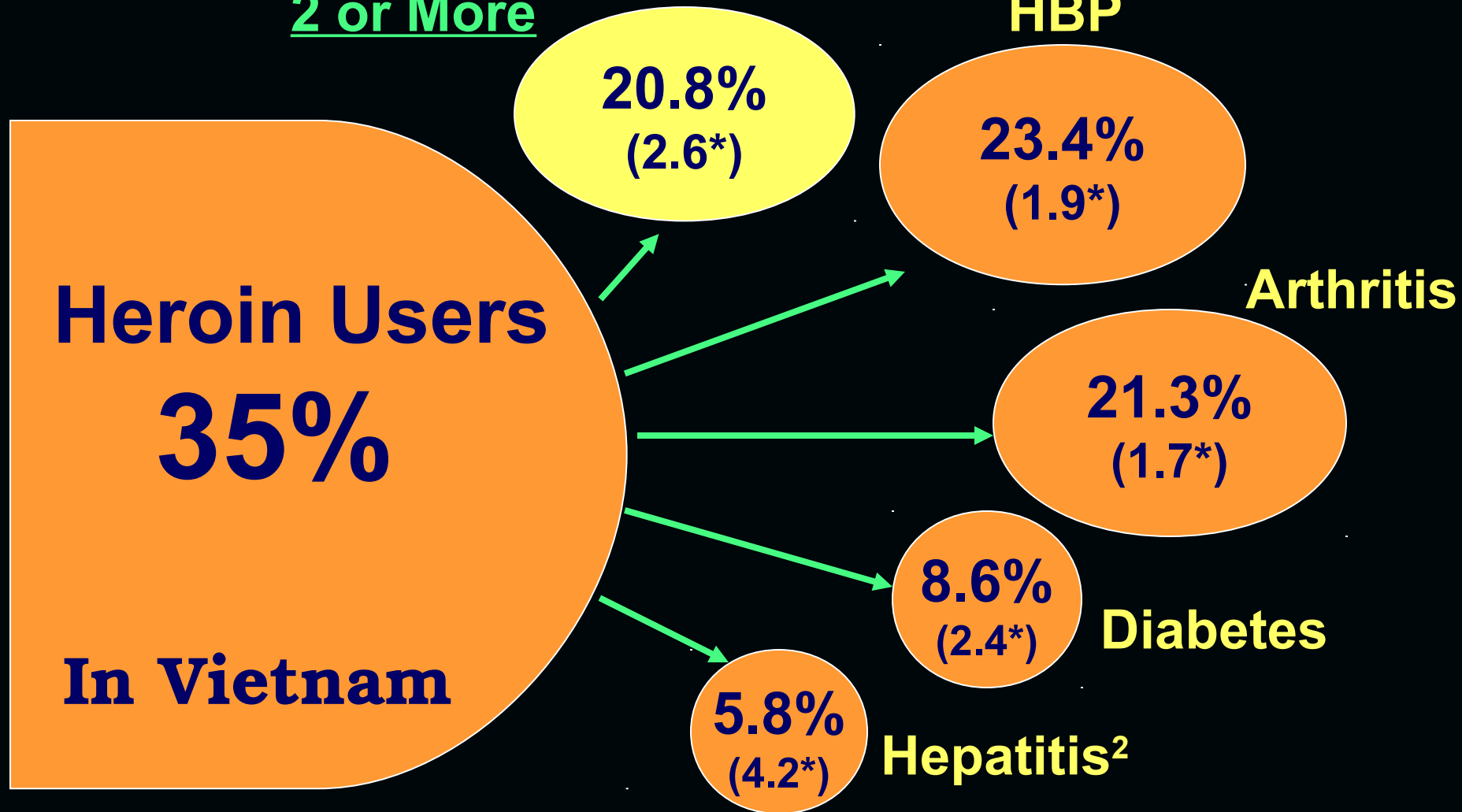


1. The weighted percentage of heroin users in Vietnam represents Sept. '71 returnees. The outcomes are unweighted encompassing up to 1996-7. Odds ratios are in comparison to nonveterans, adjusted for age and race; \*, significant. N=839.



# Health Problems in Past Year (1996-7)<sup>1</sup>

2 or More



1. The weighted percentage of heroin users in Vietnam represents Sept. '71 returnees. Health problem outcomes are unweighted encompassing up to 1996-7. Odds ratios are in comparison to nonveterans, adjusted for age and race; \*, significant. N=839. 2. Includes hepatitis due to both viral and alcohol use.

# **VES Long-Term Followups**

## **Consequences of Drug Abuse over 30 Years**

---

- **Drug abuse, PTSD and suicidality.**

# VES III. Drug Use: 1972 to 1996<sup>1</sup>

Last 10 Years

Last 3 Months

**Dead**

**16.1%**  
**(5.2\*)**

**51.5%**  
**(6.3\*)**

**27.7%**  
**(6.2\*)**

**Marijuana**

**Heroin Users**  
**35%**

**29.4%**  
**(4.7\*)**

**10.2%**  
**(6.9\*)**

**Cocaine**

**In Vietnam**

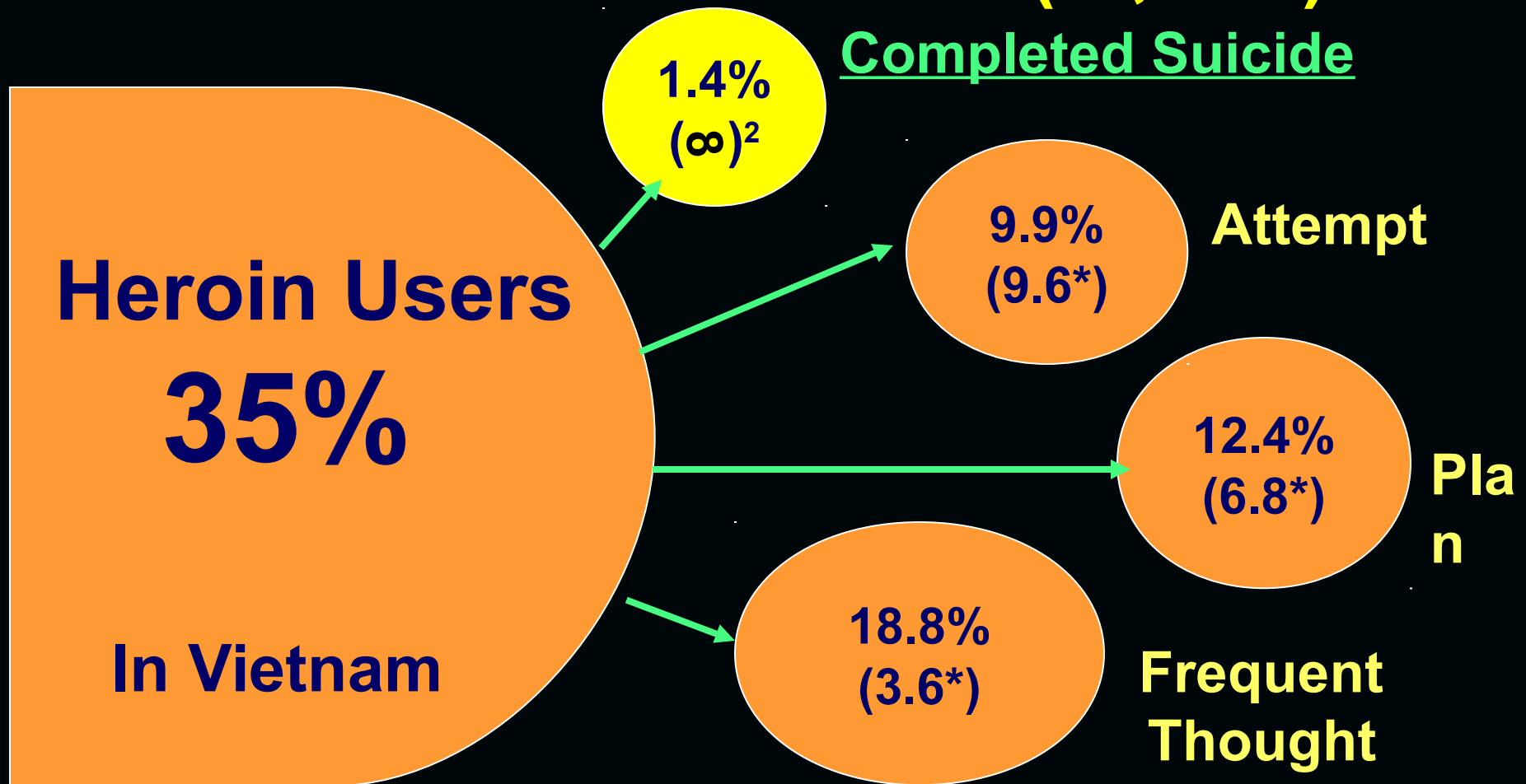
**13.2%**  
**(6.5\*)**

**Opiates**

**4.6%**  
**(4.8\*)**

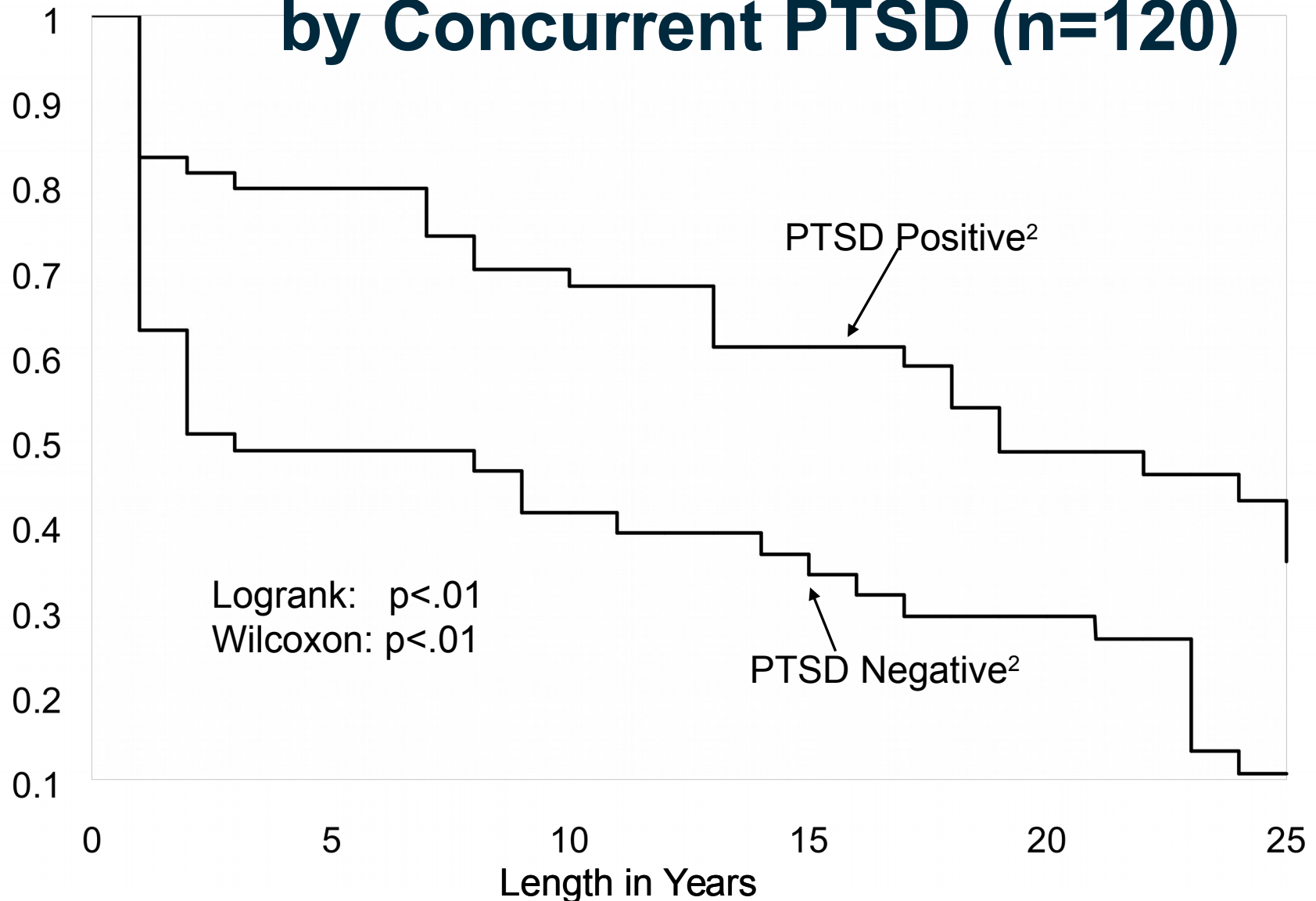
1. The weighted percentage of heroin users in Vietnam represents Sept. '71 returnees. Drug use outcomes are unweighted encompassing up to 1996-7. Odds ratios are in comparison to nonveterans, adjusted for age and race; \*, significant. N=839.

# VES-III. Suicidality: from Vietnam to 1996 (% , OR)<sup>1</sup>



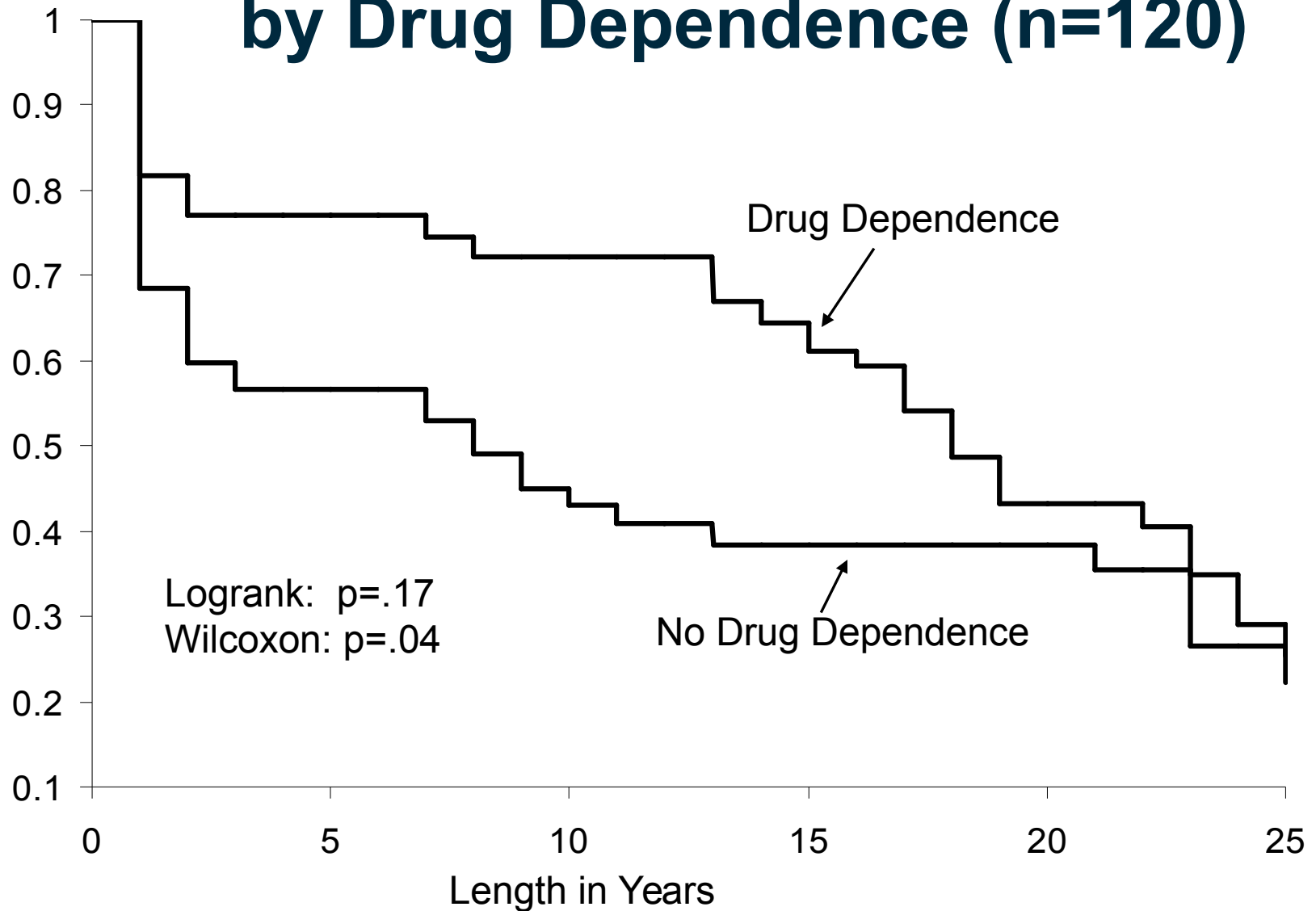
1. The weighted percentage of heroin users in Vietnam represents Sept. '71 returnees. The outcomes are unweighted encompassing up to 1996-7. Odds ratios are in comparison to nonveterans, adjusted for age and race; \*, significant. N=839. 2. No completed suicides were observed among nonveterans.

# Length of Suicidal Ideation Stratified by Concurrent PTSD (n=120)



**Source:** Price et al., Drug & Alc Dependence, 2004 (in press).

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



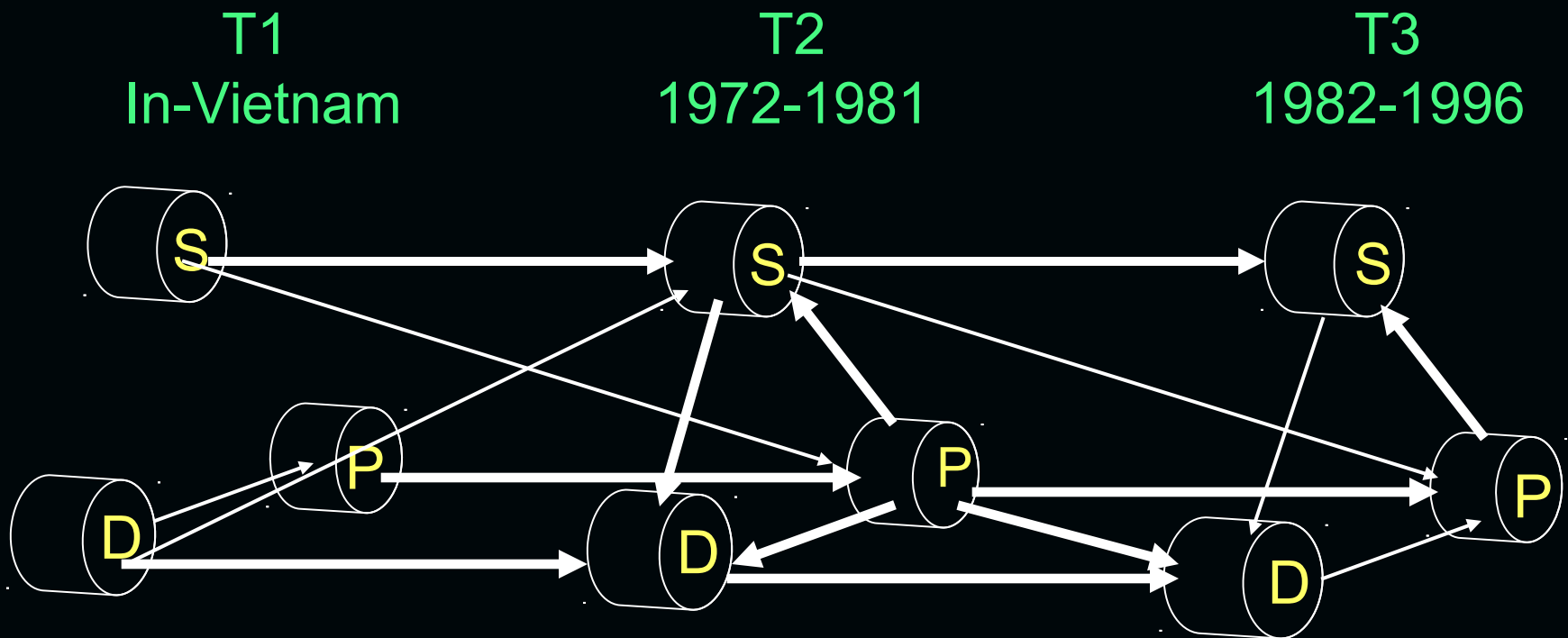
**Source:** Price et al., Drug & Alc Dependence, 2004 (in press).

# **PTSD, Substance Abuse and Other Psychopathology on Suicide Ideation: 1972-1996 (n=637)<sup>1</sup>**

|                                      | <b>Hazard ratio</b> | <b>P</b>        | <b>Risk limits</b> |
|--------------------------------------|---------------------|-----------------|--------------------|
| <b>Alcohol dependence</b>            | <b>1.18</b>         | <b>.343</b>     | <b>.84 - 1.68</b>  |
| <b>Major depression<sup>2</sup></b>  | <b>3.21</b>         | <b>&lt;.001</b> | <b>1.93 - 5.34</b> |
| <b>Adult antisocial personality</b>  | <b>1.88</b>         | <b>.002</b>     | <b>1.25 - 2.81</b> |
| <b>PTSD</b>                          | <b>1.51</b>         | <b>.339</b>     | <b>.65 - 3.48</b>  |
| <b>Drug dependence</b>               | <b>2.06</b>         | <b>.002</b>     | <b>1.31 - 3.24</b> |
| <b>PTSD x log (time)<sup>3</sup></b> | <b>1.31</b>         | <b>.049</b>     | <b>1.00-1.70</b>   |

**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



Source: Price et al, (in press). S: Suicidal Behavior (T3  $R^2=.41$ ) P:PTSD (T3  $R^2=.78$ ) D: Drug dependence (T3  $R^2=.58$ ). RMSEA=.23.

→ 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 ideation over time.**
- **Drug dependence exacerbates PTSD and suicidal ideation; once the course is set, self-medication kicks in.**

Source: Price et al., Drug & Alc Dependence, 2004 (in press).

# **VES Long-Term Followups: Mortality and Morbidity over 30 years**

---

- **Patterns of remission from drug abuse over time.**

# Patterns and Predictors of Remission

---

- Are the remission patterns stable over time?
- Are the remission patterns different across classes of substances?
- How common is spontaneous remission?
- Are the predictors of remission the same as covariates of long-term abuse?

# Use and Remission Measures: On-and-off Thresholds

- **A reasonable range of inclusion criteria beyond any use.**
  - **Alcohol - 7+ drinks/day, daily drinking 2+ weeks, 6+ drinks/day/per week for several weeks.**
  - **Nicotine - 20 cigarettes/day at least year.**
  - **Marijuana and other illicit drugs - 5+ times use.**
- **Abuse to remission threshold higher than occasional use, but lower than DSM level.**
  - **Alcohol: on - 7+ drinks/day when drinking most; off - quit attempt 3+ months.**
  - **Nicotine: on - 20 cigarettes/day usually; off - quit attempt 3+ months.**
  - **Marijuana other illicit drugs - “Most frequent” use; off - not “most frequent use.”**

# Use and Remission Patterns

| Class of Drugs <sup>1</sup>                                              | ALC                        | SED              | STIM             | MJ               | COC              | OP               |
|--------------------------------------------------------------------------|----------------------------|------------------|------------------|------------------|------------------|------------------|
| N                                                                        | 634 <sup>2</sup>           | 189 <sup>3</sup> | 226 <sup>3</sup> | 404 <sup>3</sup> | 215 <sup>3</sup> | 139 <sup>3</sup> |
| % Frequent use starting in 1972 or later <sup>4</sup>                    | 31.0                       | 32.8             | 28.8             | 13.6             | 35.4             | 6.6              |
| % Frequent use past yr.                                                  | 20.1                       | 6.4              | 5.4              | 17.8             | 9.0              | 8.8              |
| Mean duration (yrs.) of initiation to last remission (S.D.) <sup>5</sup> | 18.8<br>(9.0)              | 9.1<br>(7.3)     | 9.6<br>(7.4)     | 14.1<br>(8.8)    | 10.8<br>(8.0)    | 10.5<br>(8.7)    |
| Mean number of remissions (S.D.) <sup>5,6</sup>                          | 1.3 <sup>7</sup><br>(.8)   | 1.3<br>(0.6)     | 1.3<br>(0.6)     | 1.1<br>(0.7)     | 1.5<br>(0.6)     | 1.4<br>(0.6)     |
| Mean duration of remitted years (S.D.) <sup>5</sup>                      | 11.4 <sup>7</sup><br>(7.4) | 14.8<br>(6.5)    | 14.6<br>(6.2)    | 12.0<br>(7.7)    | 11.1<br>(5.5)    | 15.0<br>(7.2)    |

1. ALC = alcohol, SED = sedatives, STIM = stimulants, MJ = marijuana, COC = cocaine, OP = opiates.

2. 7+ drinks/one day, daily drinking 2+ weeks, or 6+ drinks/one day/week for several weeks since 1972.

3. 5+ times use since 1972.

4. Based on questions about most frequently used years. Comparable measures were used to eliminate cases starting frequent use prior to 1972.

5. Remission is defined as negative of years using most frequently.

6. Since 1972.

7. Meeting DSM-IV dependence/abuse.

**Source: Price et al., AJPH 2001.**

# “Spontaneous” Remission from Licit and Illicit Substance Abuse

| Class of drugs                                                                         | ALC           | SED           | STIM          | MJ            | COC           | OP            |
|----------------------------------------------------------------------------------------|---------------|---------------|---------------|---------------|---------------|---------------|
| N                                                                                      | 613           | 183           | 219           | 383           | 209           | 136           |
| % Attempted to quit at least once since 1971 (n) <sup>1</sup>                          | 60.4<br>(370) | 78.1<br>(143) | 77.2<br>(169) | 73.1<br>(280) | 74.6<br>(156) | 78.7<br>(107) |
| % Multiple quit attempts among those with quit attempts since                          | 38.1<br>(141) | 23.8<br>(34)  | 17.8<br>(30)  | 24.6<br>(69)  | 22.4<br>(35)  | 24.3<br>(26)  |
| % Last quit attempts were cold turkey (n) <sup>3</sup>                                 | 61.6<br>(228) | 84.6<br>(121) | 81.1<br>(137) | 82.5<br>(231) | 70.5<br>(110) | 55.1<br>(59)  |
| % Last cold turkey quit attempts associated with continuous remission (n) <sup>4</sup> | 71.5<br>(163) | 90.1<br>(100) | 95.4<br>(123) | 88.3<br>(188) | 95.0<br>(94)  | 96.3<br>(52)  |

Source: Price et al., AJPH 2001. 1. Intentional quit attempt lasting 3 months or longer. 2. Includes those who reported specific sequence of quit attempts, and those who reported "too many quit attempts to remember." 3. Of the most recent attempts of the multiple quit attempts, or single quit attempts, lasting 3 months or longer. 4. Includes those who remitted in the same year as the year of most recent quit attempt, and those who stopped using the drug frequently prior to the most recent quit attempt. The denominators are those who reported quitting cold turkey when attempting to quit most recently, excluding cases for which timing information was missing (marijuana, n = 213; opiates, n = 54).

# **VES Long-Term Followups: Mortality and Morbidity over 30 years**

---

- **Predictors of remission - Can we detect a symptom pattern that is likely to lead to remission?**

# **VES Long-Term Followups**

## **Symptom Patterns**

### **Predicting Remission**

---

- **Predictive power was in a good range when socio-environmental measures were included; better than DSM symptoms alone.**
- **Unique ANN weights capturing subtle changes? e.g., Hazardous use accompanied remission from cocaine heavy use and operated differently from severity symptoms (potentially a “make or break” role).**
- **Time-dependent logistic regression and on ANN weight structure analyses were inconsistent.**



# VES-IV: “Suicide” Study

- **Quasi case-control design to take advantage of the existence of a large number of 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.**

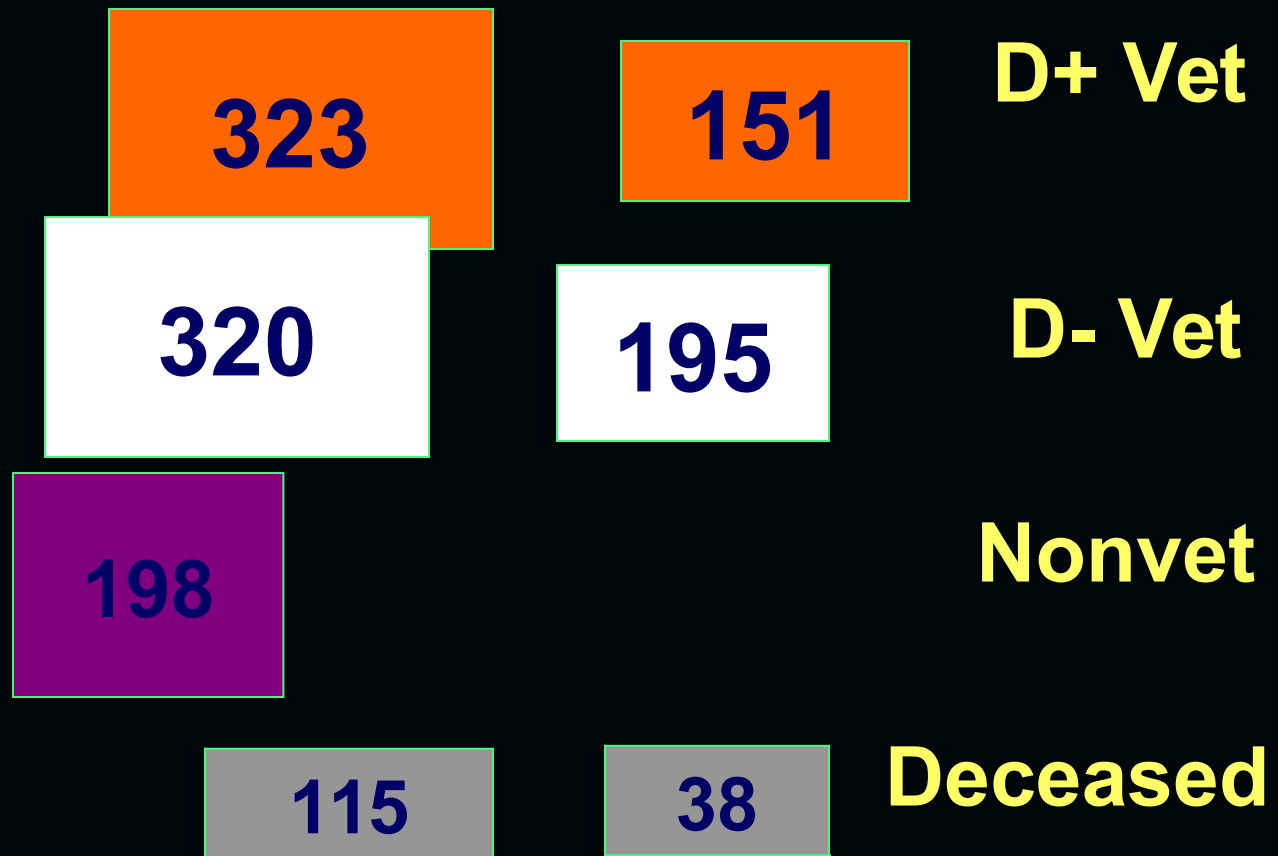
# VES Samples (Total Target N = 1,226)

**1996-7**

**N=841**

**2002-4**

**(n=346, in field)**



# **VES Long-Term Followups: Mortality and Morbidity over 30 years**

---

- **Emerging drug use trends in middle age.**

# Most Common Medicated Conditions: 1996/7-2002/4<sup>1</sup>

|                        | %    | # of mentions | Most popular medications |                        |                         |
|------------------------|------|---------------|--------------------------|------------------------|-------------------------|
| Physical conditions    |      |               |                          |                        |                         |
| HBP                    | 31.7 | 119           | Lisinopril               | Atenol                 | Verapamil               |
| Cholesterol            | 18.5 | 54            | Zocor <sup>2</sup>       | Lipitor <sup>3</sup>   | Lescol <sup>4</sup>     |
| Headaches/Pain         | 13.9 | 49            | Ibuprofen                | Hydrocodone            | Acetaminophen           |
| Heart Problems         | 9.4  | 52            | Nitroglycerin            | Aspirin                | Atenol                  |
| Diabetes               | 8.0  | 38            | Glyburide                | Glucotrol <sup>5</sup> | Glucophage <sup>6</sup> |
| Arthritis              | 6.3  | 19            | Acetaminophen            | Feldene <sup>7</sup>   | Vioxx <sup>8</sup>      |
| Psychiatric conditions |      |               |                          |                        |                         |
| Sleep disorders        | 11.2 | 34            | Trazadone                | Clonazepam             | Quetiapine              |
| Depression             | 11.2 | 43            | Sertraline               | Trazadone              | Fluoxetine              |
| Anxiety/nerves         | 9.4  | 31            | Diazepam                 | Clonazepam             | Lorazepam               |

1. VES-IV data, based on n=287 available for analysis to date. Average age is 54.6.  
 2. Simvastatin. 3. Atorvastatin. 4. Fluvastatin. 5. Glipizide. 6. Metformin. 7. Piroxicam. 8. Rofecoxib

# Common Treated Health Conditions (1996/7-2002/4) by Past Opiate Use<sup>1</sup>

| Measures of past opiate use      | Heroin use in Vietnam 1970-71 |                 | Opiate abuse/dep. 1972-96/7 |                 | Opiate use 1996/7-2002/4 |                 |
|----------------------------------|-------------------------------|-----------------|-----------------------------|-----------------|--------------------------|-----------------|
| Current condition                | %                             | OR <sup>2</sup> | %                           | OR <sup>2</sup> | %                        | OR <sup>2</sup> |
| Physical conditions <sup>3</sup> |                               |                 |                             |                 |                          |                 |
| Cholesterol                      | 13.3                          | 0.5*            | 4.7                         | 0.2*            | 8.7                      | 0.2             |
| Headaches/Pain                   | 19.9                          | 3.1**           | 23.3                        | 2.2             | 34.8                     | 3.9**           |
| Arthritis                        | 8.6                           | 2.5             | 16.3                        | 4.1**           | 21.7                     | 6.7**           |
| Psychiatric conditions           |                               |                 |                             |                 |                          |                 |
| Sleep disorders                  | 16.6                          | 3.7**           | 23.3                        | 3.1**           | 21.7                     | 2.4             |
| Depression                       | 13.9                          | 1.8             | 27.9                        | 4.3*            | 13.0                     | 1.2             |
| Anxiety/nerves                   | 13.3                          | 2.8*            | 16.3                        | 2.8             | 17.4                     | 2.3             |

1. VES-IV data, based on n=287 available for analysis to date. 2. Odds ratio's (OR's) referent group is negative for each past opiate use measure. 3. HBP, heart problems and diabetes had no significant differences. \*p<.05. \*\*P<.01.

# Illicit Oxycodone Use (1996/7-2002/4) by Other Drug Use Measures <sup>1</sup>

|                         | Heroin<br>use<br>in Vietnam<br>(n=346) | Opiate<br>abuse/dep.<br>1972-96<br>(n=346) | 90-day<br>opiate use<br>1996/7<br>(n=346) | 90-day<br>illicit drug<br>use 1996/7<br>(n=346) | Pain<br>medication in<br>2002/4<br>(n=287) |
|-------------------------|----------------------------------------|--------------------------------------------|-------------------------------------------|-------------------------------------------------|--------------------------------------------|
| % Drug/med.<br>positive | 54.0                                   | 13.8                                       | 3.4                                       | 18.4                                            | 13.9                                       |
| % Illicit oxy.<br>use   | 8.6                                    | 16.7                                       | 33.0                                      | 10.9                                            | 12.5                                       |
| OR <sup>2</sup>         | 4.9**                                  | 5.2**                                      | 10.6**                                    | 2.8*                                            | 5.6**                                      |

1. VES-IV data, based on n=346 available for analysis to date. 2. Odds ratio's (OR's) referent group is negative for each drug use/medication measure. \*p<.05. \*\*P<.01.

# VES Limitations

---

- **Special population: disadvantaged Vietnam veterans with high levels of trauma and opiate exposure.**
- **Cohort and gender specific population.**
- **Impact of censoring by death unknown.**
- **Yearly-assessed measures not available for some behaviors.**
- **Most yearly measured retrospective self-reports since 1972.**
- **Measures since 1996 still tentative.**

# **VES Followups Over 30 Years**

## **Summary (1)**

---

**In what ways is long-term drug use harmful?**

- **Drugs kill.**
- **Even a short-term intensive drug use is a good predictor of long-term mortality and morbidity.**
- **If drug abusers do not die, consequences are likely to show up in many areas: psychiatric, physical, social and occupational functioning are affected negatively.**
- **Substance abuse and psychiatric comorbidity take a cumulative toll.**



# VES Followups Over 30 Years

## Summary (2)

**Why do some drug users continue to abuse drugs so long?**

- **The maturing-out hypothesis hold for a majority of drug users in the community.**
- **Multiple pathways to eventual recovery - still the process if gradual.**
- **Life events and social resources may be more more malleable factors than psychiatric comorbidity.**
- **Crisis may be an ingredient for successful recovery.**

# VES Followups over 30 Years

## Summary (3)

---

**What areas do we expect problems will get worse?**

- **Substance abuse-psychiatric comorbidity is a twin evil.**
- **Consequences of aging are worse for those with substance abuse history - financial & occupational resources, health problems, and social resources are more detrimental than substance abuse per se.**

# VES-III & IV Collaborators

---

|                                               |                                                                                    |
|-----------------------------------------------|------------------------------------------------------------------------------------|
| WU Medicine                                   | Rumi Kato Price, Lee Robins,<br>Edward Spitznagel, George Murphy,<br>Collins Lewis |
| WU Social Work                                | Enola Proctor, Sally Haywood                                                       |
| St. Louis VA                                  | Katherine Virgo, Seth Eisen                                                        |
| Readjustment Counseling Services (Vet Center) | Gary Collins, Rodney Haug, Robert<br>Mathes                                        |
| St. Louis Crisis Services Center              | G. Lee Judy                                                                        |
| Consultants                                   | Bruce Goldberger, Gery Ryan                                                        |
| Contract Work                                 | Research Triangle Institute,<br>Psychemedics                                       |