PTEs and Postraumatic Stress Disorder: Mortality Risk and Treatment Success

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Presented at America Council of Life Insurers Medical Section Scientific Program
Charleston, South Carolina
February 24, 2020

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Overview of Presentation

- Why we should care about PTEs and PTSD.
- Definition of PTEs and PTSD.
- Epidemiology of PTE exposure, PTSD prevalence, and comorbid disorders with PTSD in adolescents and adults.
- Risk/protective factors for PTSD.
- ACE findings and value of adding PTE and PTSD assessment.
- Association of ACEs, PTEs, PTSD with risk of premature death.
- Treatment of PTSD
- Implications for assessment, treatment, and placing data on PTSD and mortality in perspective.

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Why We Should Care about PTEs and PTSD

- PTEs are "high end" subset of stressors; large literature showing that stressor exposure in childhood (e.g. Adverse Childhood Experiences; ACEs) increases risk of morbidity and mortality.
- Studying impact of PTEs across lifespan expands ACE findings re health risk behaviors, morbidity, mortality.
- Many PTE exposed individuals develop PTSD and related disorders.
- PTSD is prevalent, co-morbid with other disorders, increases health risk behaviors that risk of increase morbidity and mortality, and may directly increase morbidity and mortality.
- Effective assessments and treatments for PTSD exist, so we have tools to mitigate this major public health problem.

Definition of Potentially Traumatic Events (PTEs)

- **Defined as DSM-5 PTSD Criterion A Events**: Exposure to actual or threatened death, serious injury, or sexual violence through direct experience, witnessing it in person, learning that it happened to a family or friend, or vicarious exposure through work.
- Using the term, **potentially traumatic events,** instead of **traumatic events,** avoids confusion (e.g. trauma sometimes refers to **stressor stimuli** and sometimes to **responses** following exposure to stressors.
- More accurate to describe Criterion A stressors as potentially traumatic than as traumatic because not everyone exposed develops PTSD or related problems.

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DSM-5 Definition of PTSD

PTSD in new category of ***Trauma and Stressor-Related Disorders.*** PTSD defined as developing characteristic symptoms following exposure to PTEs:

- **Criterion A: Exposure to actual or threatened death, serious injury, or sexual violence.**
- **Criterion B: Intrusive symptoms** associated with the traumatic event(s).
- **Criterion C: Avoidance of stimuli** associated with traumatic event(s).
- **Criterion D: Negative alterations in cognition and mood.**
- **Criterion E: Changes in arousal and reactivity.**
- **Symptom Thresholds:** Must have at least one B symptom, one C symptom, two D symptoms, and two E symptoms.
- **Criterion F: Duration of symptoms more than 1 month.**
- **Criterion G: Clinically significant distress or functional impairment.**

Prevalence of PTEs and PTSD

- Population estimates of PTE exposure and PTSD cannot be obtained from clinical or service-seeking samples because many individuals with PTSD do not seek clinical or other services.
- Best estimates use probability samples, comprehensive assessment of PTEs, and careful assessment of PTSD symptoms in national probability samples.
- Will present DSM-IV prevalence estimates for U.S. adolescents and DSM-5 estimates for adults.

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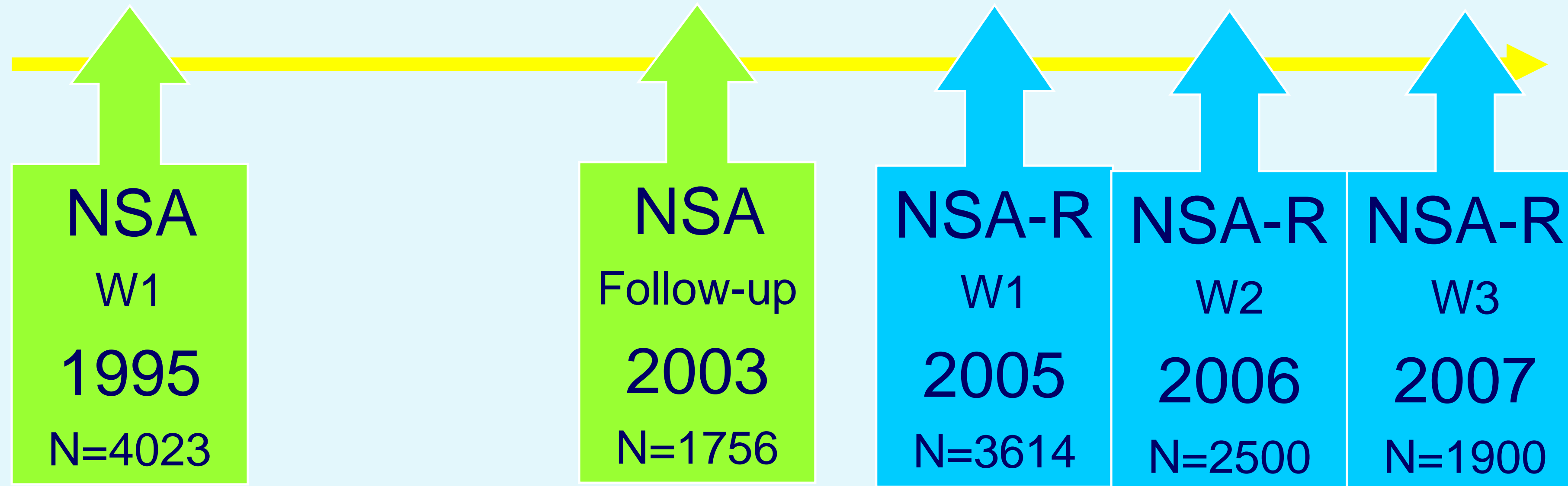
National Survey of Adolescents (NSA) and NSA Replication (NSA-R) Studies



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NSA and NSA-R Methodology

- Studies funded by CDC, NIJ, and NICHD.
- Nationally representative samples of 12-17 year old adolescents from telephone households interviewed about violence and other PTEs, PTSD, MD, and substance use disorders.
- RDD used to locate households; one parent interviewed briefly to obtain permission to interview adolescent; adolescent was interviewed.
- This presentation focuses primarily on NSA-R because findings are more recent.

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Lifetime Prevalence of Violence and Other PTEs among U.S. Adolescents: NSA-R

Violence Types	Lifetime Prevalence
Sexual Assault	7.8%
Physical Assault	22.0%
Witnessed Violence	41.1%
Any Violence	**49.2%**
No Violence	50.8%
Other PTE	44.7%
Any PTE	**68.8%**

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DSM-5: The National Stressful Events Survey (NSES)

- National Stressful Events Survey (NSES) sample (n= 2953) recruited from a national probability-based online panel of U.S. adults. Methodology and findings described in Kilpatrick et al (2013)
- Web survey was self-administered and mimicked structured clinical interview with follow-up questions.
- Measured all DSM-5 PTSD PTEs, all 20 DSM-5 PTSD symptoms, and distress/functional impairment.

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NSES: Prevalence of Exposure to PTEs

Event Type: DSM-5 Criterion A	N	%
Disaster	1429	48.3%
Accident/fire	1462	49.5%
Exposure to hazardous chemicals	462	15.6%
Combat or war zone exposure	233	7.9%
Physical or sexual assault	1523	51.6%
Witnessed physical /sexual assault	926	31.3%
Witnessed dead bodies/parts unexpectedly	649	22.0%
Threat or injury to family or close friend due to violence/accident/disaster	950	32.1%
Death of family/close friend due to violence/accident/disaster	1450	49.1%
Work exposure	318	10.8%
Any DSM-5 PTE	**2613**	**88.4%**
MORE THAN ONE PTE		73.3%

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Current Prevalence of PTSD, Depression, and Substance Abuse Among Adolescents: NSA-R

Disorder	Prevalence
Current PTSD[1]	3.8%
Current Depression[1]	6.2%
Current Substance Abuse[2]	11.3%

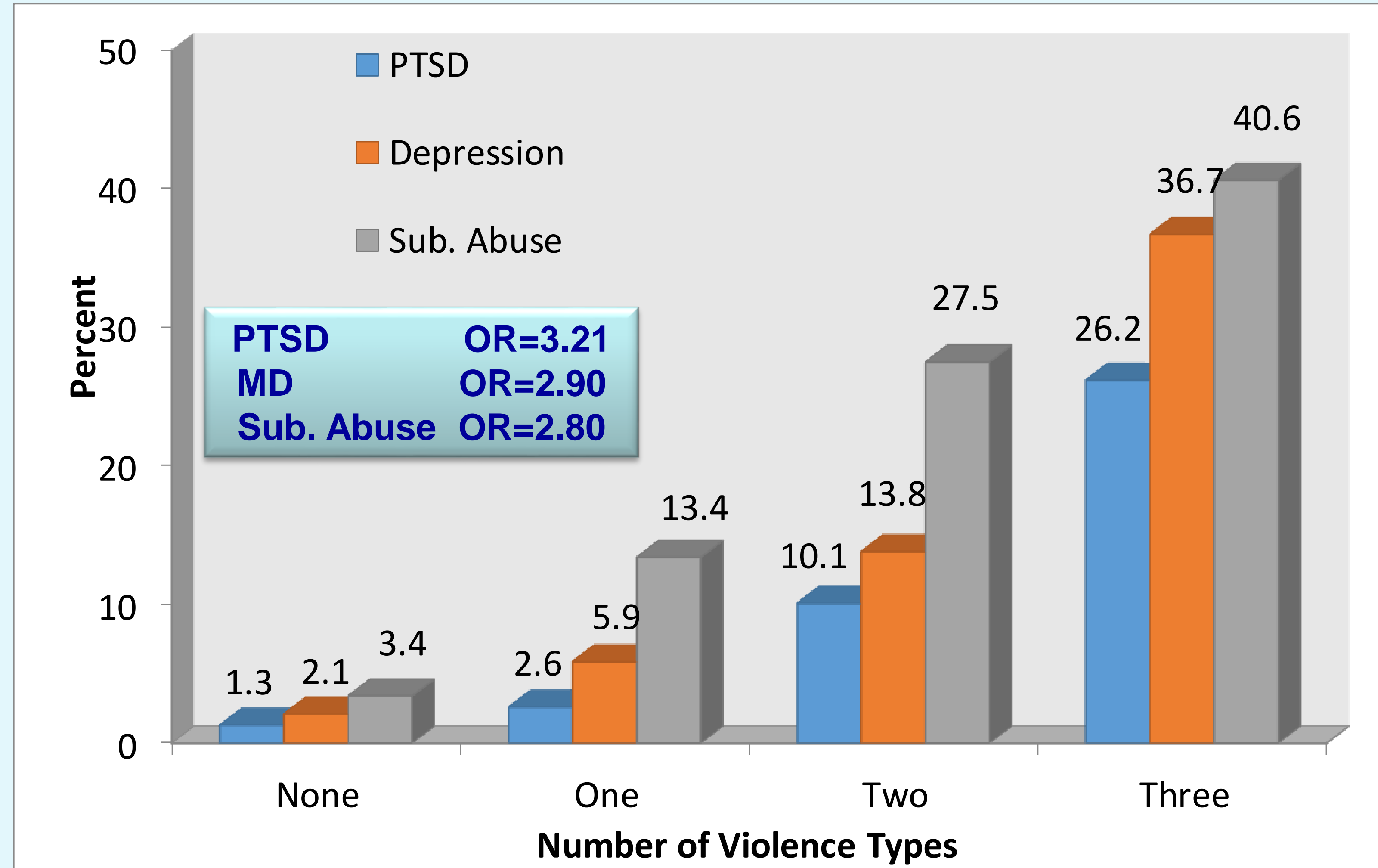
[1]Past 6 months

[2]Past year

Comorbid Prevalence of PTSD, Depression, and Substance Abuse Among Young Adults at Wave 2 of NSA

Disorder Pattern	Prevalence
Noncomorbid Prevalence	
PTSD Only	0.9%
Depression Only	4.7%
Substance Abuse Only	18.4%
Comorbid Prevalence	
PTSD + Depression	3.3%
PTSD + SA	1.2%
Depression + SA	1.9%
PTSD + Depression +SA	1.9%
No Disorder	66.5%

Risk of Lifetime Mental Disorders by Number of Violence Types : NSA-R



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DSM-5 PTSD: National Prevalence Estimates Among Adults

National prevalence estimates available from two studies:

- A paper from NESARC-3 (Goldstein et al, 2016) purports to provide national DSM-5 PTSD prevalence data, but skip outs and use of inaccurate symptom thresholds for Criteria D (n=3vs2) and E (n=3vs2) make these DSM-5 PTSD estimates inaccurate and too low.

  Lifetime PTSD: 6.1%; Past Year PTSD: 4.5%

- The National Stressful Events Survey (NSES; details to follow) found the following national DSM-5 PTSD prevalence estimates:

  Lifetime PTSD: 8.3%; Past Year PTSD: 4.7%

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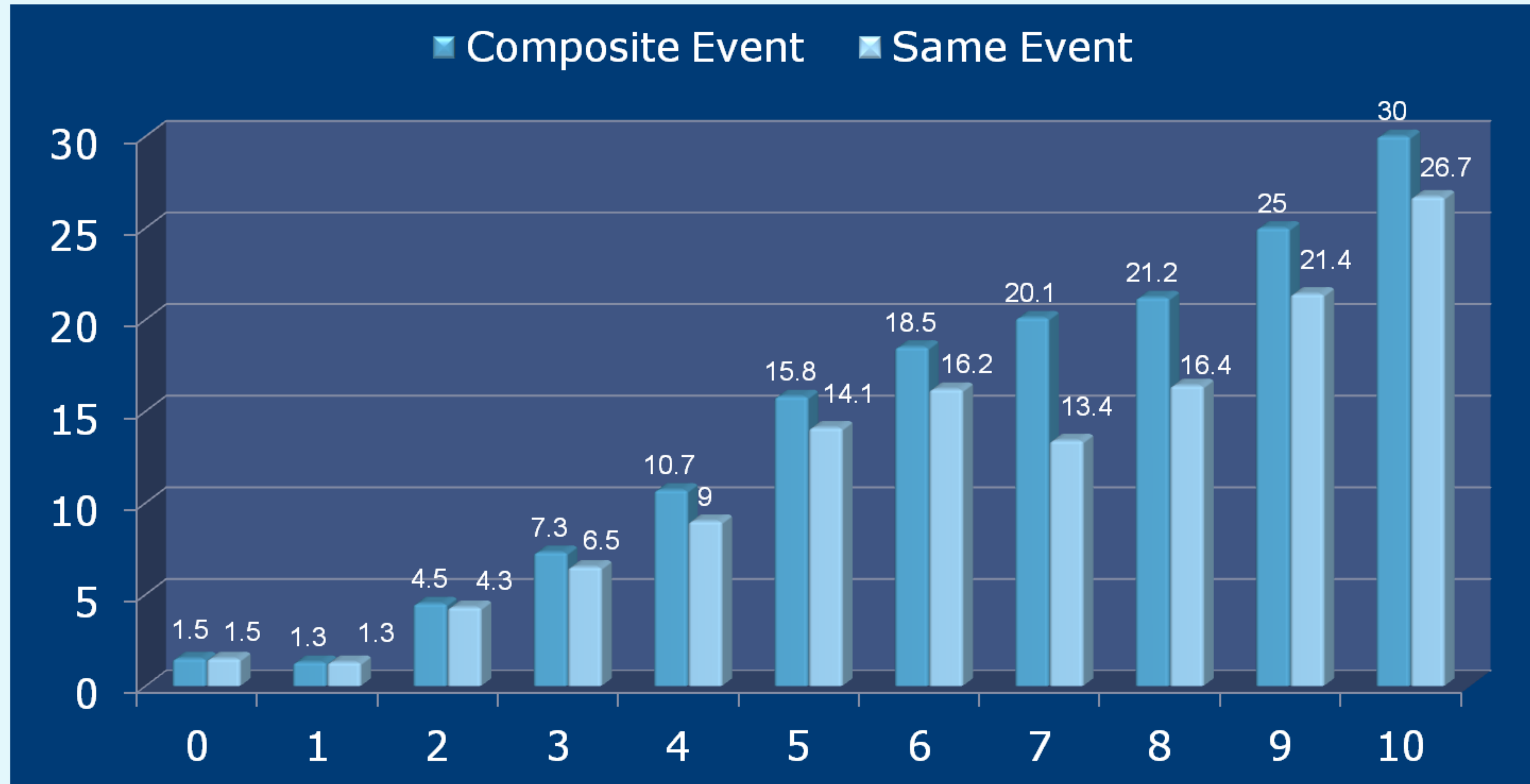
DSM-5 PTSD Lifetime Prevalence by Number of PTEs



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Summary of What We Know about PTE Exposure Across the Lifespan and PTSD

- PTE exposure not rare; having many PTEs is common.
- PTE exposure increases risk of MD and SUDs that are often comorbid with PTSD.
- Not everyone exposed to PTEs develops PTSD or other mental disorders; important to look for risk and protective factors for PTSD given PTE exposure.
- Risk factors for PTSD include age at time of exposure, sex, prior PTEs that involve IPV, PTEs involving IPV or perceived life threat, poverty, lack of social support pre-and post PTE, pre-event depression or PTSD.
- Protective factors include good social support, access to resources, and recovery environment.

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The Adverse Childhood Experiences Study

Method: Conducted at Kaiser Permanente San Diego Health Appraisal Clinic.

- Medical exams and questionnaire completed for 9508 adults.
- Measured ACEs before 18, health-related behaviors/problems and depression.

Outcomes: Risk factors for health problems, major diseases, and self-rated health.

Major findings: Number of ACEs associated with increased health risk behaviors, risk of diseases, and mortality

Research Article

Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults

The Adverse Childhood Experiences (ACE) Study

Vincent J. Felitti, MD, FACP, Robert F. Anda, MD, MS, Dale Nordenberg, MD, David F. Williamson, MS, PhD, Alison M. Spitz, MS, MPH, Valerie Edwards, BA, Mary P. Koss, PhD, James S. Marks, MD, MPH

Background: The relationship of health risk behavior and disease in adulthood to the breadth of exposure to childhood emotional, physical, or sexual abuse, and household dysfunction during childhood has not previously been described.

Methods: A questionnaire about adverse childhood experiences was mailed to 13,494 adults who had completed a standardized medical evaluation at a large HMO; 9,508 (70.5%) responded. Seven categories of adverse childhood experiences were studied: psychological, physical, or sexual abuse; violence against mother; or living with household members who were substance abusers, mentally ill or suicidal, or ever imprisoned. The number of categories of these adverse childhood experiences was then compared to measures of adult risk behavior, health status, and disease. Logistic regression was used to adjust for effects of demographic factors on the association between the cumulative number of categories of childhood exposures (range: 0–7) and risk factors for the leading causes of death in adult life.

Results: More than half of respondents reported at least one, and one-fourth reported ≥2 categories of childhood exposures. We found a graded relationship between the number of categories of childhood exposure and each of the adult health risk behaviors and diseases that were studied ($P < .001$). Persons who had experienced four or more categories of childhood exposure, compared to those who had experienced none, had 4- to 12-fold increased health risks for alcoholism, drug abuse, depression, and suicide attempt; a 2- to 4-fold increase in smoking, poor self-rated health, ≥50 sexual intercourse partners, and sexually transmitted disease; and a 1.4- to 1.6-fold increase in physical inactivity and severe obesity. The number of categories of adverse childhood exposures showed a graded relationship to the presence of adult diseases including ischemic heart disease, cancer, chronic lung disease, skeletal fractures, and liver disease. The seven categories of adverse childhood experiences were strongly interrelated and persons with multiple categories of childhood exposure were likely to have multiple health risk factors later in life.

Conclusions: We found a strong graded relationship between the breadth of exposure to abuse or household dysfunction during childhood and multiple risk factors for several of the leading causes of death in adults.

Medical Subject Headings (MeSH): child abuse, sexual, domestic violence, spouse abuse, children of impaired parents, substance abuse, alcoholism, smoking, obesity, physical activity, depression, suicide, sexual behavior, sexually transmitted diseases, chronic obstructive pulmonary disease, ischemic heart disease. (Am J Prev Med 1998;14:245–258) © 1998 American Journal of Preventive Medicine

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ACEs Before Age 18

- **Psychological/Emotional abuse**
- **Physical abuse**
- **Sexual abuse**
- **Five indicators of household dysfunction**: 1)substance abuse by household member, 2)mental illness or suicide attempt of household member, 3) intimate partner violence of mother or stepmother, 4) incarceration of household member, and 5) parental separation or divorce.
- **Note:** Some ACEs are PTEs; most are not; not all PTEs measured; and doesn't include PTEs occurring after age 17.

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ACEs, PTEs, PTSD and Mortality

Definitive national studies of potential impact of ACEs, PTEs, and PTSD on mortality difficult to conduct and hard to come by. Study design would require:

- Assembling large national probability birth cohort sample of U.S. population and conducting longitudinal follow-up assessments over 70 or 80 years to determine mortality status and cause of death.
- Repeated assessments of ACEs during childhood and PTEs across the lifespan.
- Repeated assessments of PTSD, related mental disorders, behaviors/circumstances that increase risks of numerous health problems, medical conditions contributing to risk of morbidity and mortality, and biomarkers associated with aging/death.
- Complex data analytic strategy to test direct effects of ACEs, PTEs, and PTSD on premature mortality as well as moderation/mediation models.

These studies don't exist, but more limited ones do provide some data.

ACE and PTE Data on Premature Mortality

Brown et al (2009):

- Mortality status obtained at end of 2006 for17,337 adults participating in original ACE study in 1995-97.
- 1539 deaths occurred from all causes
- People with 6 or more ACES died almost 20 years earlier than those with no ACEs (M= 60.6 yrs. vs 79.1 yrs.)

Elliot et al (2018):

- Obtained mortality data in 2015 on national probability sample of 7000 adults (ages 25-74 at Wave1 in1995) in Midlife Development in U.S. Study. At Wave 2 in 2004-2006, info on 12 "Lifetime Traumas" assessed consisting of 6 ACEs and 6 PTEs occurring throughout lifespan.
- Number of "Lifetime Traumas" (i.e. ACEs and PTEs) associated with increased risk of all cause mortality in dose response fashion (HR= 1.07).

PTSD and Mortality: Boscarino (2006)

- Study designed to examine associations between PTSD status and all-cause and specific-cause mortality among national probability sample (N=15,288) of U.S. Army Vietnam Era veterans initially assessed in 1985; mortality status determined as of 12/31/2000.
- Analyses controlled for several variables (e.g. volunteer status, race, Army entry and discharge ages, Army drug use, current age, IQ).
- Compared to veterans without PTSD, those with PTSD had higher risk of all-cause(HR=2.5; adjHR=2.1), CV (HR=1.7; adjHR=1.6), cancer (HR=1.8; adjHR=1.5), and external cause (HR=2.7; adjHR=2.3) deaths.
- Conclusion: Vets with PTSD at greater risk of death from numerous causes.

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ISTSS PTSD Prevention and Treatment Guidelines

- Methodology described on pages 2-11 of handout used systematic reviews of RCTs to evaluate strength of evidence supporting efficacy of PTSD treatments.
- Criteria for **Strong Effect Recommendations** included several well-controlled RCTs with large effect sizes for primary outcome of PTSD.
- **Three psychotherapy treatments for children, and five for adults, received strong recommendations.**
- **No strong recommendation pharmacological PTSD treatment for either children or adults!** Four drugs received low effect recommendations for adults: Fluoxetine, Paroxetine, Sertraline, and Venlafaxine.

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Strongly-Recommended PTSD Treatments for Children

- Cognitive Behavioral Therapy with Trauma Focus (TF-CBT) for Caregiver and Child
- Cognitive Behavioral Therapy with Trauma Focus (TF-CBT) for Child
- EMDR

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Strongly-Recommended PTSD Treatments for Adults

- Cognitive Processing Therapy
- Cognitive Therapy
- EMDR
- Individual Cognitive Behavior Therapy with a Trauma Focus
- Prolonged Exposure

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What About Marijuana and PTSD Treatment?

Steenkamp et al (2016) reviewed studies on MJ and other cannabinoids as treatments for PTSD. Major conclusions:

- Preclinical and clinical studies support biological plausibility of potential effects on some PTSD symptoms, but much variation in response.
- Few treatment outcome studies, and they are too poorly designed to yield good data on treatment outcome.
- MJ use linked to adverse psychiatric outcomes including substance misuse, depression, and psychosis.
- Bottom line: better research needed, but risks of MJ use outweigh unknown potential benefits as treatment for PTSD.

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Implications for Assessment and Treatment

- Screen comprehensively for PTE exposure because many individuals have multiple PTEs. Info about lifetime PTEs is important because it adds what we know from ACE studies.
- PTEs involving interpersonal violence, particularly those that occur during childhood, are important because they intensify the impact of subsequent PTEs that occur.
- Assess for risk and protective factors; social support really important.
- ACEs, PTE exposure, and PTSD all appear to increase risk of premature death, but better studies needed to confirm this finding in different populations, test mechanisms, and test impact of good PTSD treatments on addressing this increased risk.
- Effective treatments for PTSD exist! Use them!

Extra Slides: DSM-5 PTSD Criteria

DSM-5 PTSD Criterion A (i.e. PTEs)

A. **Exposure to actual or threatened death, serious injury, or sexual violence, in one or more of the following ways:**

1. Directly experiencing the traumatic event(s)
2. Witnessing, in person, the event(s) as it occurred to others.
3. Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.
4. Repeated or extreme exposure to aversive details of traumatic event(s); (e.g. first responders collecting human remains; police officers repeatedly exposed to details of child abuse).

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DSM-5 PTSD Criterion B

One or more intrusive symptoms associated with the traumatic event (s).

1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).
2. Recurrent distressing dreams in which the content and/or affect of dream is related to the event(s).
3. Dissociative reactions (e.g. flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring.
4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble aspect of the event(s).
5. Marked physiological reactions to internal or external cues that symbolize or resemble aspect of the event(s).

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DSM-5 PTSD Criterion C

Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of:

1. Avoidance or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
2. Avoidance or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the event(s)

DSM-5 PTSD Criterion D

Negative alterations in cognitions and mood associated with the traumatic event(s) as evidenced by two or more of the following :

1. Inability to remember important aspect of the traumatic event(s), typically due to dissociative amnesia and not due to other factors such as head injury, alcohol, or drugs.
2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world.
3. Persistent, distorted blame of self or others about the cause or consequences of the traumatic event(s).
4. Persistent negative emotional state.
5. Markedly diminished interest or participation in significant activities.

DSM-5 PTSD Criterion D (continued)

6. Feelings of detachment or estrangement from others.

7. Persistent inability to experience positive emotions (e.g. inability to experience happiness, satisfaction, satisfaction, or loving feelings).

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DSM-5 PTSD Criterion E

Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two or more of the following :

1. Irritable behavior and angry outbursts, typically expressed as verbal or physical aggression towards people or objects.
2. Reckless or self-destructive behavior.
3. Hypervigilance.
4. Exaggerated startle response.
5. Problems with concentration.
6. Sleep disturbance (e.g. difficulty falling or staying asleep, or restless sleep).

DSM-5 PTSD Criteria F and G

F. Duration of the disturbance (symptoms in Criteria B, C, D, and E) is more than one month.

F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of conditioning.

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