Understanding PTSD

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Conflict Disclosure Information

Diane McIntosh has received research support, spoken for, or sits on advisory boards for the following companies:

Lundbeck, Pfizer, Shire, Otsuka, BMS, Janssen-Ortho, Allergan

DSM-IV A1 Criteria

- …. experienced, witnessed, or was confronted with an event or events that involved **actual or threatened death or serious injury**, or a threat to the physical integrity of self or others
- The person's response involved **intense fear, helplessness, or horror**.

DSM-5 Changes

- **Outlines specific situations that might lead to PTSD**
  - Direct experience
  - Witness something happening to another
  - Learning trauma happened to someone close to you
  - Repeated, extreme exposure to details of trauma (first responders)
  - Does not include exposure over internet, TV , movies unless work –related

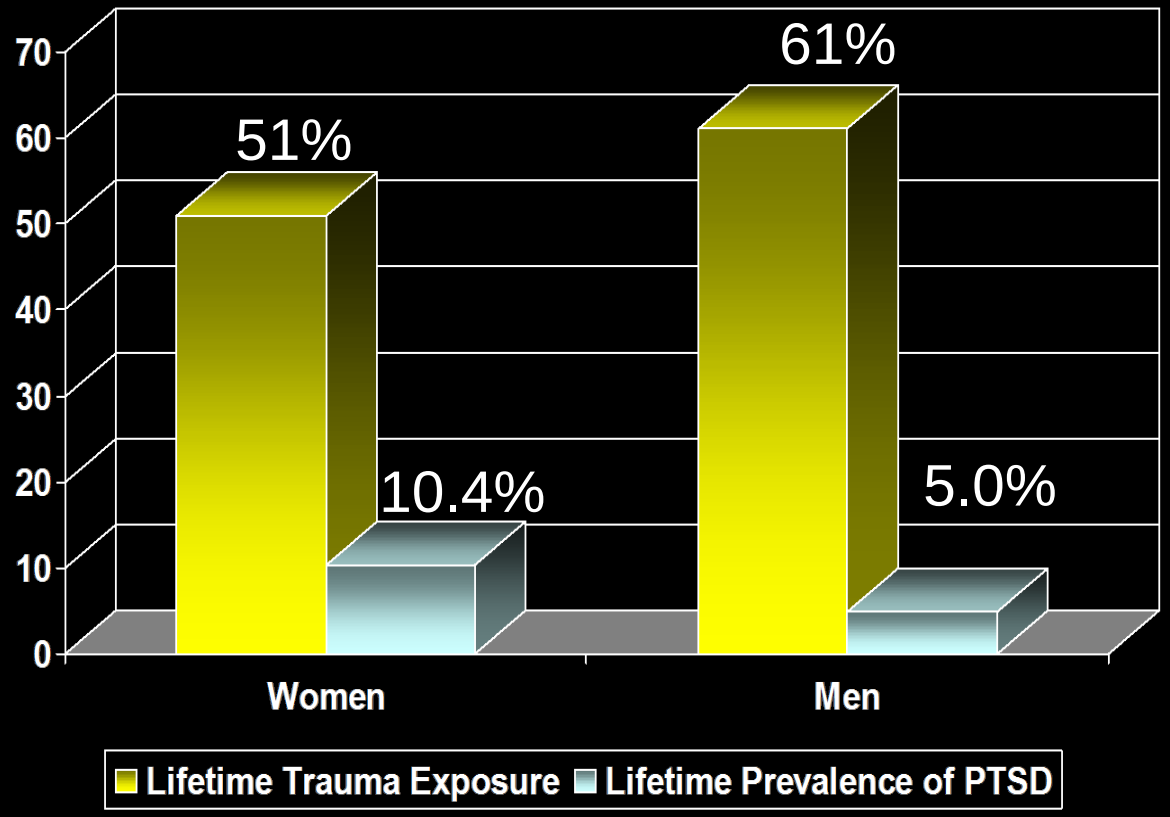
- **Some changes in the criteria**
- Negative alterations in cognition & mood associated with traumatic event
- **Dissociative symptom specifier**: Depersonalization, derealization
- **PTSD Criteria for children 6 and under**

Acute stress and PTSD

- Definition of trauma in both disorders:
  - Response involves intense fear, helplessness or horror.
  - Intrusive memories, negative mood, dissociative symptoms, avoidance and arousal symptoms
  - Clinically significant distress and impairment
  - Acute: Duration is 3 days to 1 month after trauma
- 70% of population experience at least one traumatic event meeting criterion A1.

Trauma Exposure and Lifetime Prevalence of PTSD in NCS

(n=5877, aged 15-54, DSM-III-R)



Trauma Vs PTSD

- Most people exposed to traumatic events recover
  - Breslau et al 1998- **90% had <u>one lifetime traumatic event</u> (average 4.8 traumas)** Community Epidemiology Study
  - PTSD symptoms in the acute phase are part of a normal reaction
- Exposure to trauma might lead to a number of disorders, not just PTSD
- Sexual assault carries the highest risk of PTSD; 60% males and 50% females

Reena

- 22-year old mother of 7 and 5-year-old
- Refugee from Iran
- Husband jailed and tortured
- She was sexually assaulted by judge while husband in jail
- Could tell no one because threatened with stoning; feared husband's response

Reena's Symptoms

- **Hyperarousal**
  - "I never sleep"
  - Irritability, frustrated with children
  - Children "walking on egg shells"
  - "I never feel safe. I can't be alone"
  - Fear generalized to all men.

Reena's Symptoms

- **Avoidance and Numbing**
  - "My life is over. I have hope my children will have a good life".
  - Negative valence of emotions
    - "I never feel happiness, only pain".
  - "I never stop moving. If I have a second to think I'm back in Iran"
  - Avoidance of all men, especially Persian men
  - "I cannot tell my husband my story"

Reena's Symptoms

- **Re-experiencing**
  - Nightmares, visual images, "flashbacks"(cued and un-cued)
  - Triggers included television, movies, being touched by her husband
  - Intense guilt and shame- worsened by husband who blames her
    - "Your kind of woman"

Pre-Trauma Risk Factors

- Female
- Personal and family psychiatric history
- Low SES, educational level
  - Increased vulnerability after the trauma
- Previous trauma and child abuse
- Cultural factors

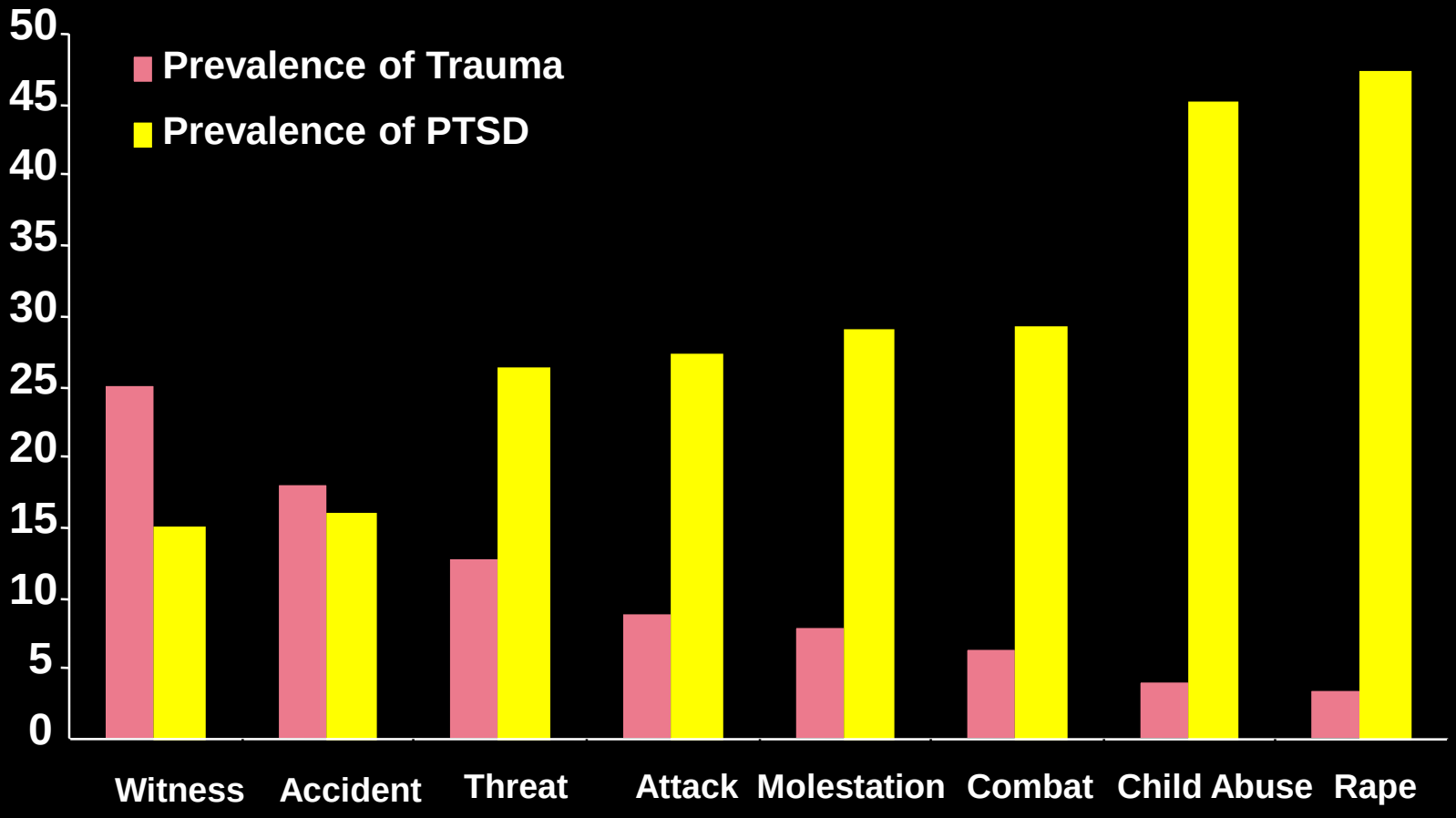
Brewin et al, J Consult Clin Psychol 2000

“It’s just body parts…”.

Peri-Traumatic Risk Factors

The type of trauma is an important risk factor

Prevalence of Trauma and PTSD



Violent assault carries the highest risk of developing PTSD

Kessler et al, Arch Gen Psychiatry 1995

Peri-Traumatic Risk Factors

- Personal
- Protracted
- Violent/ risk of death
- Sexual/ degrading
- Dissociation
- Perceived helplessness/ lack of control

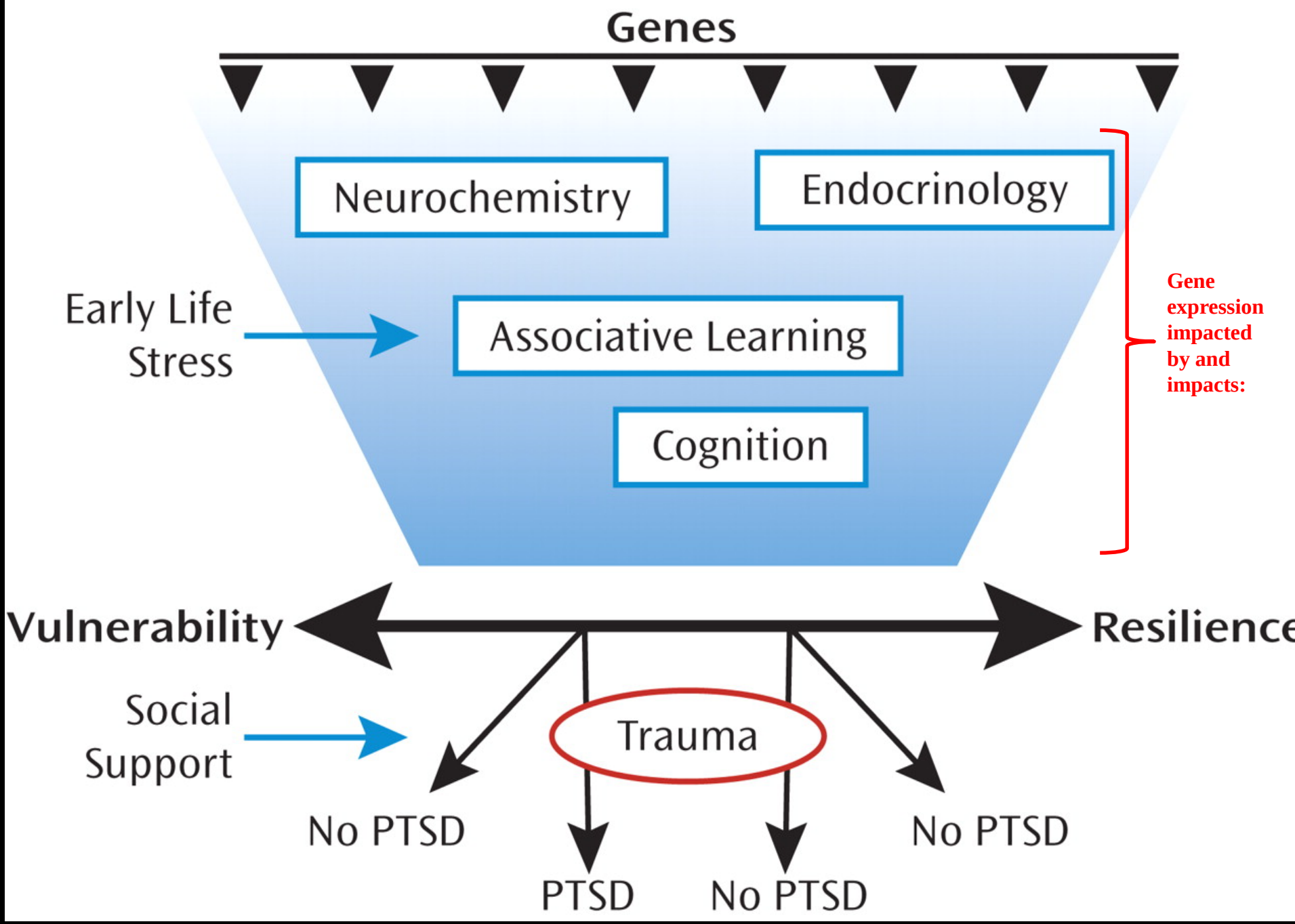
Adapted from Brewin et al, J Consult Clin Psychol 2000

Post-Trauma Risk Factors

- **Lack of social support**
- **Shame / guilt / self-doubt**
- **Ongoing life stressors**
- **Lack of appropriate early treatment or access to services**
- **Recovery-related secondary stressors like Stigma; Re-traumatization**

Yehuda et al, Biol Psychiatry1998

PTSD: The Power of Early Life Trauma



Tanja Jovanovic, Ph.D., and Kerry J. Ressler, M.D., Ph.D. Am J Psychiatry 2010; 167:648-662

UNESCO, Children and Trauma

UNITED NATIONS
Educational, Scientific, Cultural Organization

- Trauma is ubiquitous
- 50% of the world's children will be exposed to severe stress and adversity
- 230 million children living in countries affected by conflicts in 2014

Potential Impact of Poverty

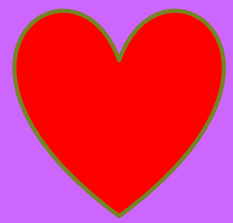
- **What we see**: Poverty ➡ maternal emotional distress ➡ impacts home environment ➡ school reports child has adaption difficulties
- **Behind the scenes**: Chronic stress alters gene expression ➡ **impacts hormones and neurotransmitters** ➡ emotional and behavioural consequences

Rat Love

- Rat moms: **“high lickers” or “low lickers”**
- A stable trait
- Environmental stress predicts the level of licking
- **Tactile stimulation of licking:**
  - promotes growth (regulates growth hormone)
  - suppresses catabolic glucocorticoids that inhibit growth.

Licking impacts:

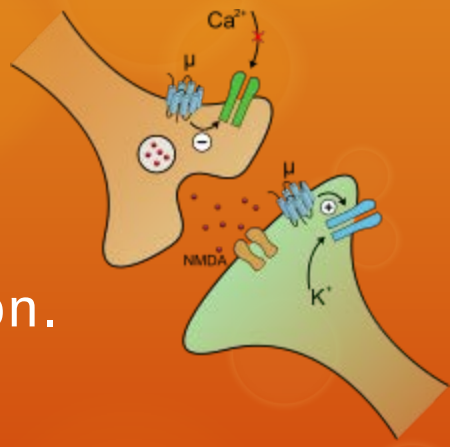
-stress responses
-neural development
-learning and memory
-metabolic function
-reproduction



Behav Neurosci 2014 Dec;128(6):736-48. Champagne and Meaney 2001, Lucassen et al 2013; Champagne et al 2003

The Hormone Connection

- The gene for the glucocorticoid receptor is **stably influenced by maternal care**
  - **High lickers: lots of glucocorticoid receptors** = good glucocorticoid regulation.
  - **Low lickers: fewer glucocorticoid receptors =** aberrant glucocorticoid regulation.



- The **good news**:
  - Low lick babes can be adopted to high licking moms: glucocorticoid levels normalized

Behav Neurosci 2014 Dec;128(6):736-48. doi: 10.1037/bne0000014. Epub 2014 Sep 22 AND 2013 Oct;127(5):628-36. doi: 10.1037/a0034186

A More Human Rat Model

- Don’t remove mum, but limit nesting material: maternal behavior less predictable, less time (“fragmented”)
- Period of emotional deprivation (stressed mum): **anhedonia**
- **Cognitive consequences** in middle age BUT also in adolescence when cognition tested under stressful conditions
- **Unpredictability and Fragmentation= enduring impairment**

T. Baram Neuropsychopharmacology 2015 Jun 24.; Molet et al 2014; Naninck et al 2015; Ivy et al 2008

Human Brain Maturation

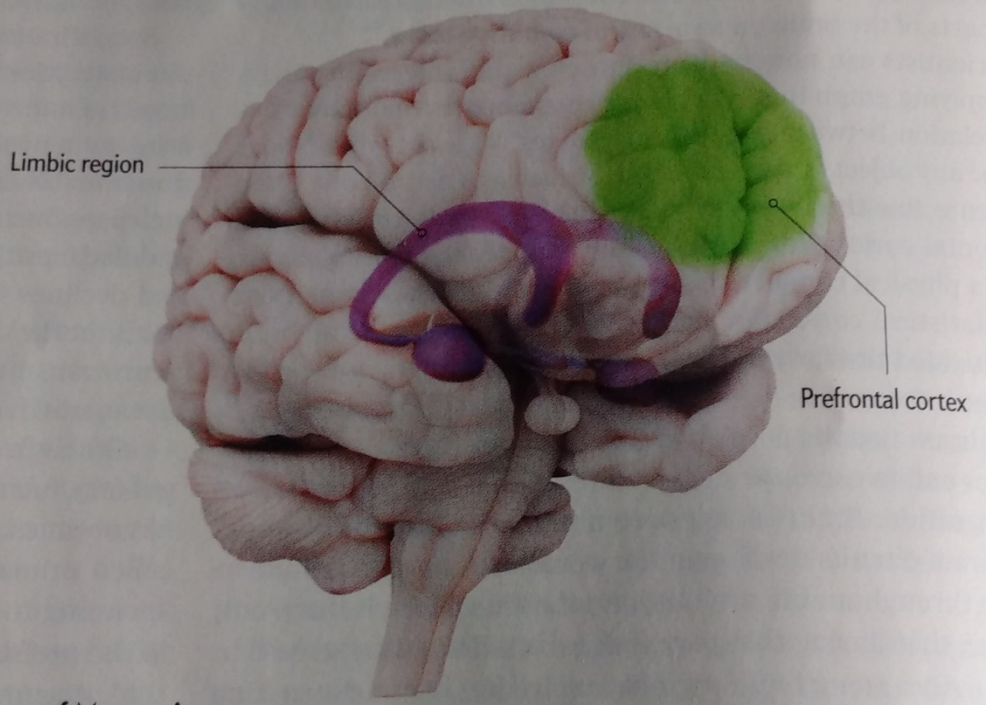
- Critical changes from **pre-natal period until mid to late 20s.**
  - Axonal and dendritic growth
  - stabilization of synapses
  - synaptic pruning

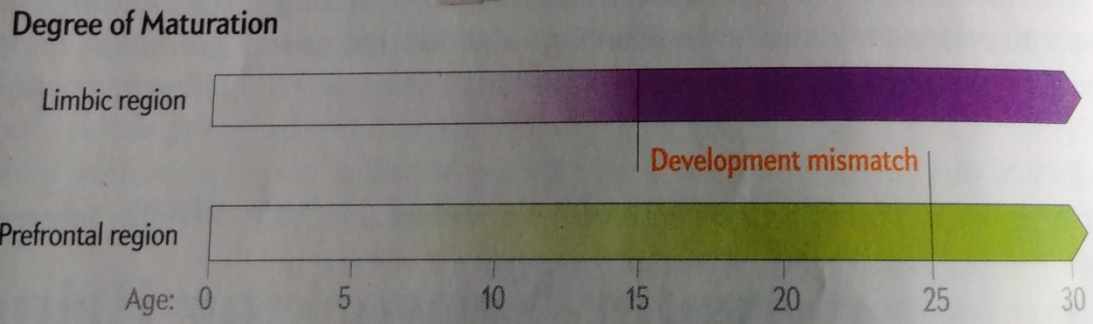
- **Perinatal period:** highly vulnerable to environment, with potentially permanent impact
  - Stress important but…how long? How severe? WHEN?
  - Context and nature of stress is important too.

Bale et al 2010; Regev and Baram 2014; Hoeijmakers et al 2015; Chen and Baram 2015; McEwan and Gianaros 2011; Maras et al 2014

Emotion vs. Control

Teenagers are more likely than children or adults to engage in risky behavior, in part because of a mismatch between two major brain regions. Development of the hormone-fueled limbic system (*purple*), which drives emotions, intensifies as puberty begins (typically between ages 10 to 12), and the system matures over the next several years. But the prefrontal cortex (*green*), which keeps a lid on impulsive actions, does not approach full development until a decade later, leaving an imbalance during the interim years. Puberty is starting earlier, too, boosting hormones when the prefrontal cortex is even less mature.

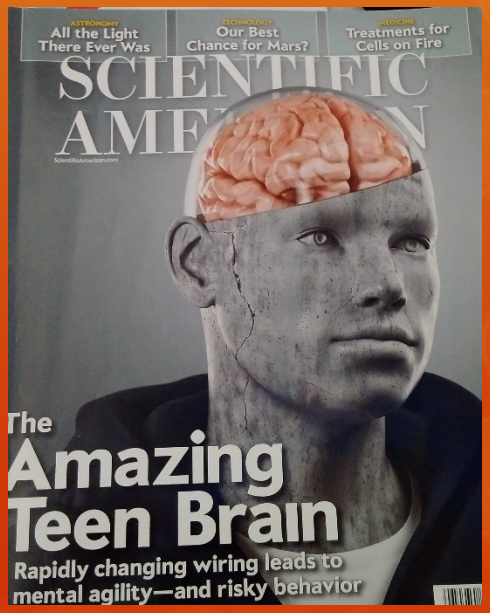




Teenage years:

-A time of **greater connectivity**

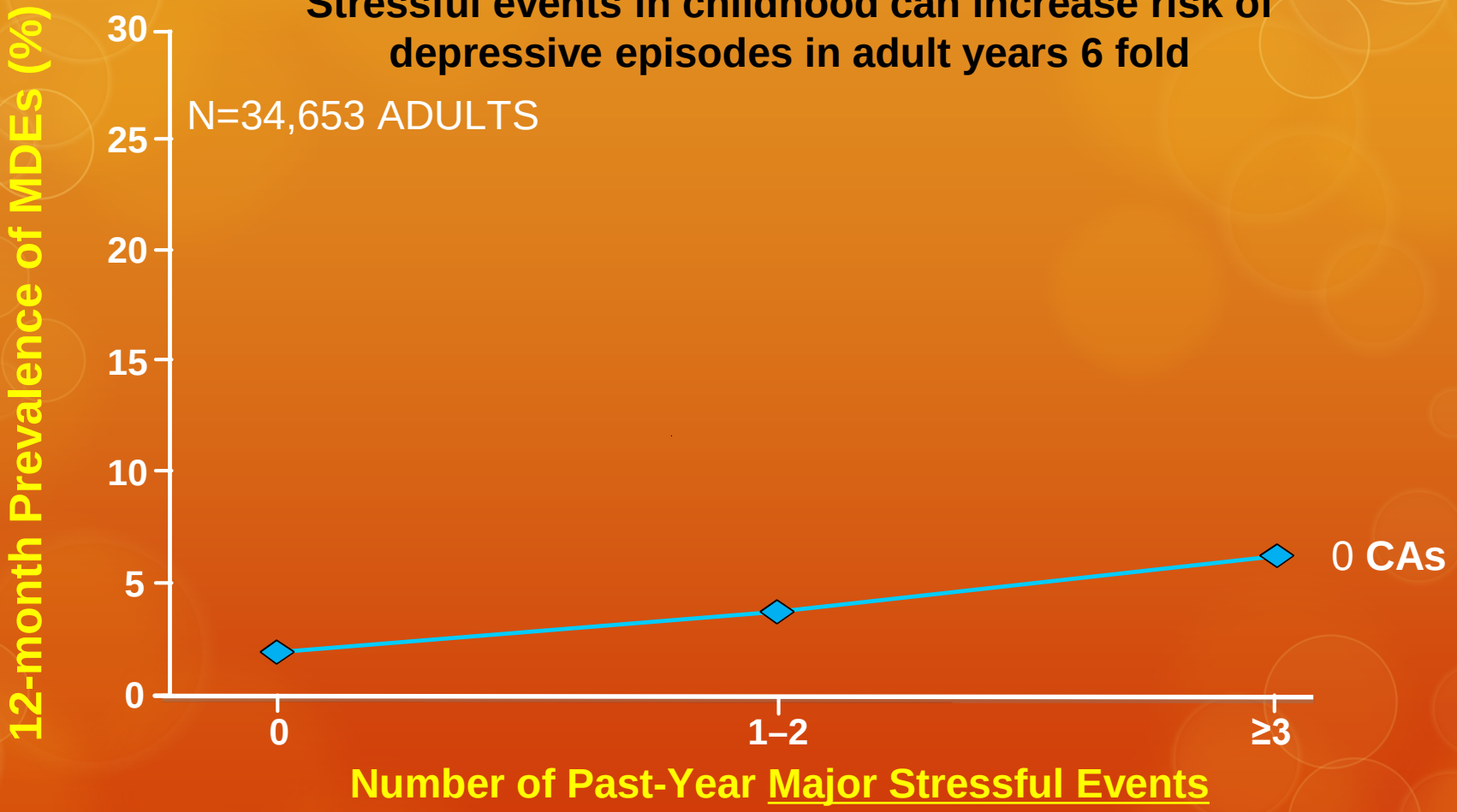
-Onset of mental illness



- **Not all stress is bad:** enhances memory and decision making.
  - It's adaptive to remember dangers.
- **Long-lasting or intense stress results in detrimental effects**

Childhood Adversity (CA) May Lead to Stress Sensitization

Stressful events in childhood can increase risk of depressive episodes in adult years 6 fold



CA= Childhood adversity (divorce, death, illness, abuse, neglect); Childhood adversity occurred in children <17 years old.

McLaughlin et al. *Psychol Med* 2009;17:1-12. [Epub ahead of print]

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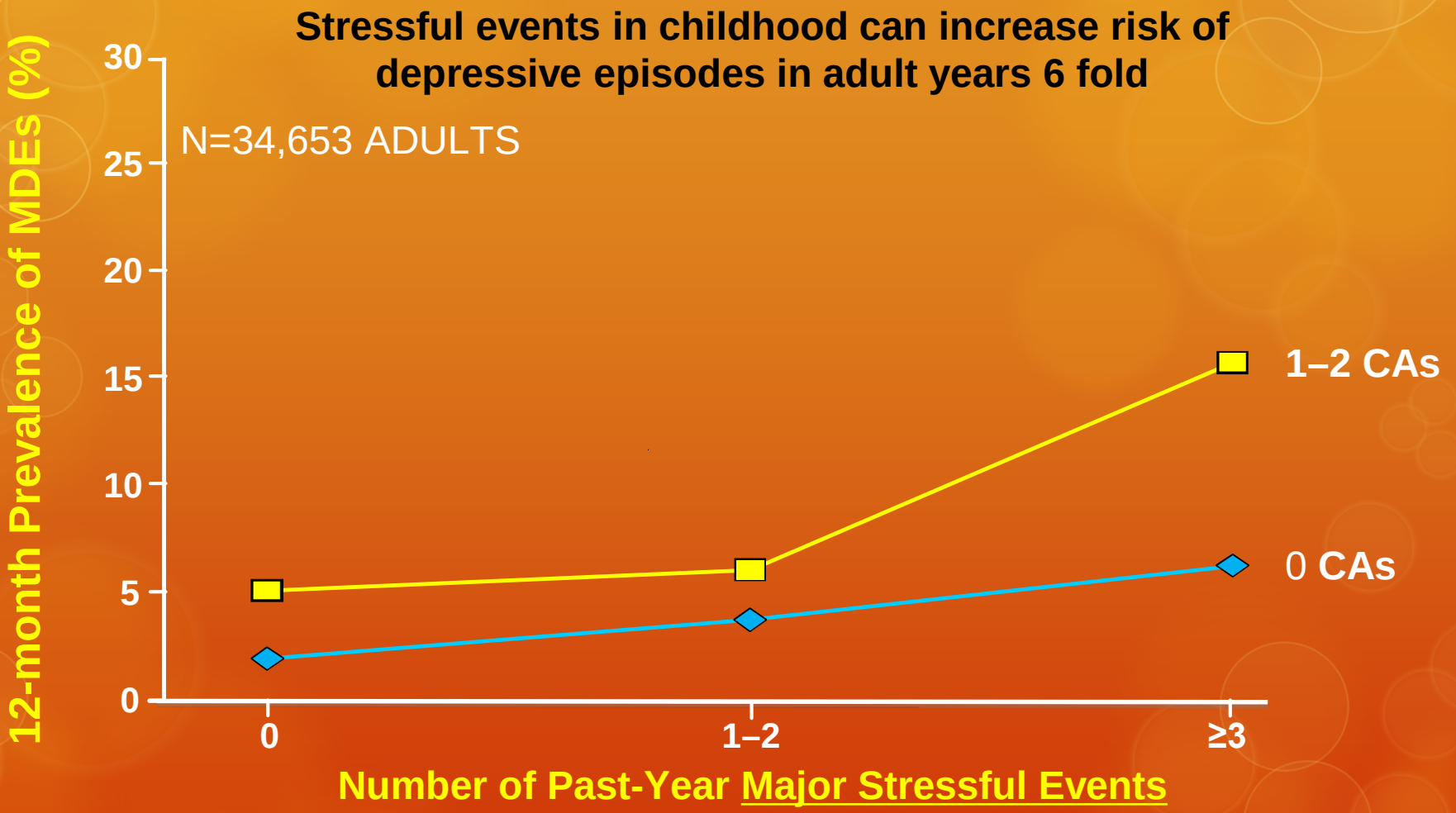

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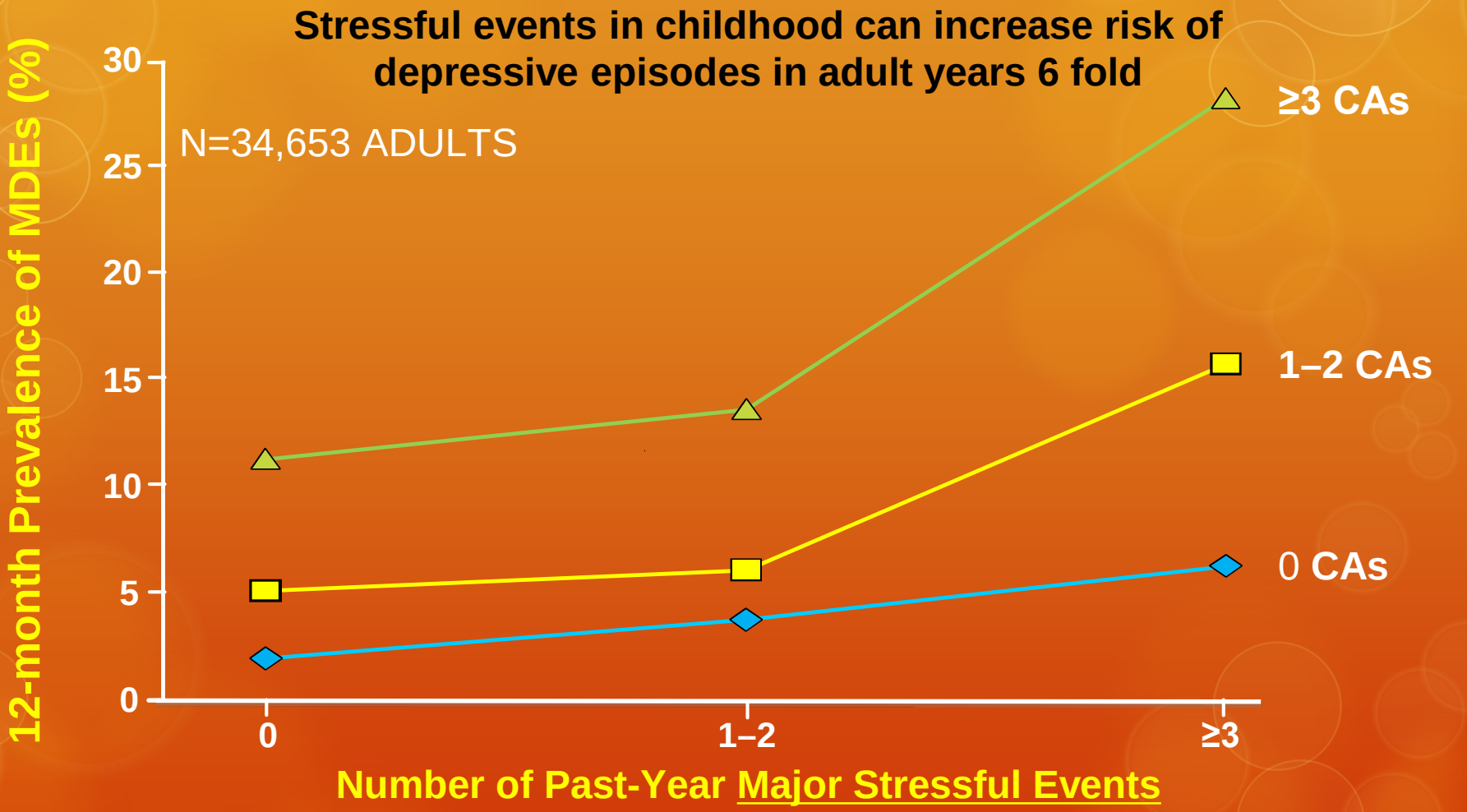

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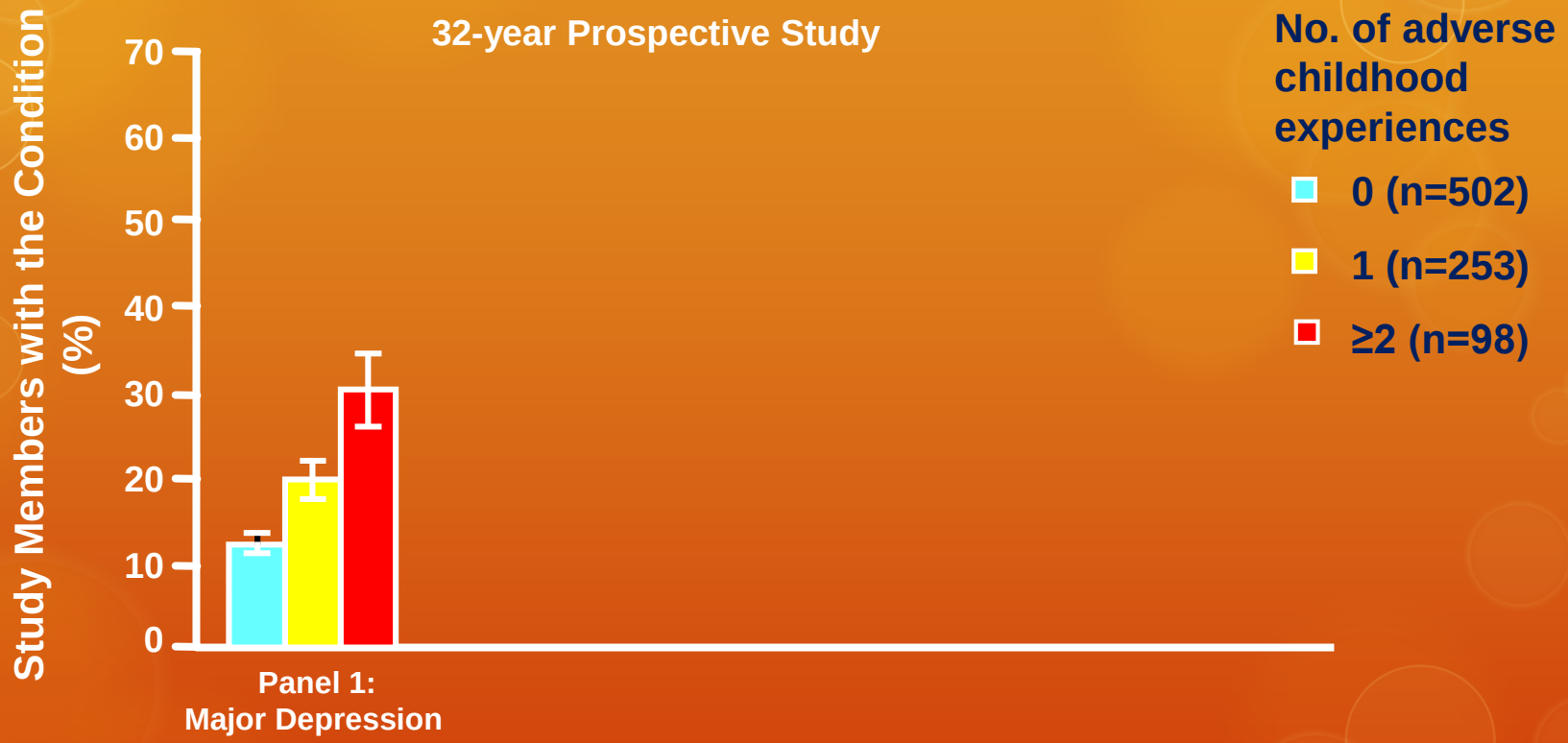
Childhood Adversity Represents a Risk for Adulthood Disease



Panel 1: z=4.94, p<0.001; hsCRP level >3 mg/L. Panel 2: z=3.24, p=0.001; clustering of metabolic risk markers. Panel 3: z=4.58, p<0.001; and ≥1 age-related disease risks. Panel 4: z=5.66, p<0.001.

CRP=C-reactive protein; hs=High-sensitivity.

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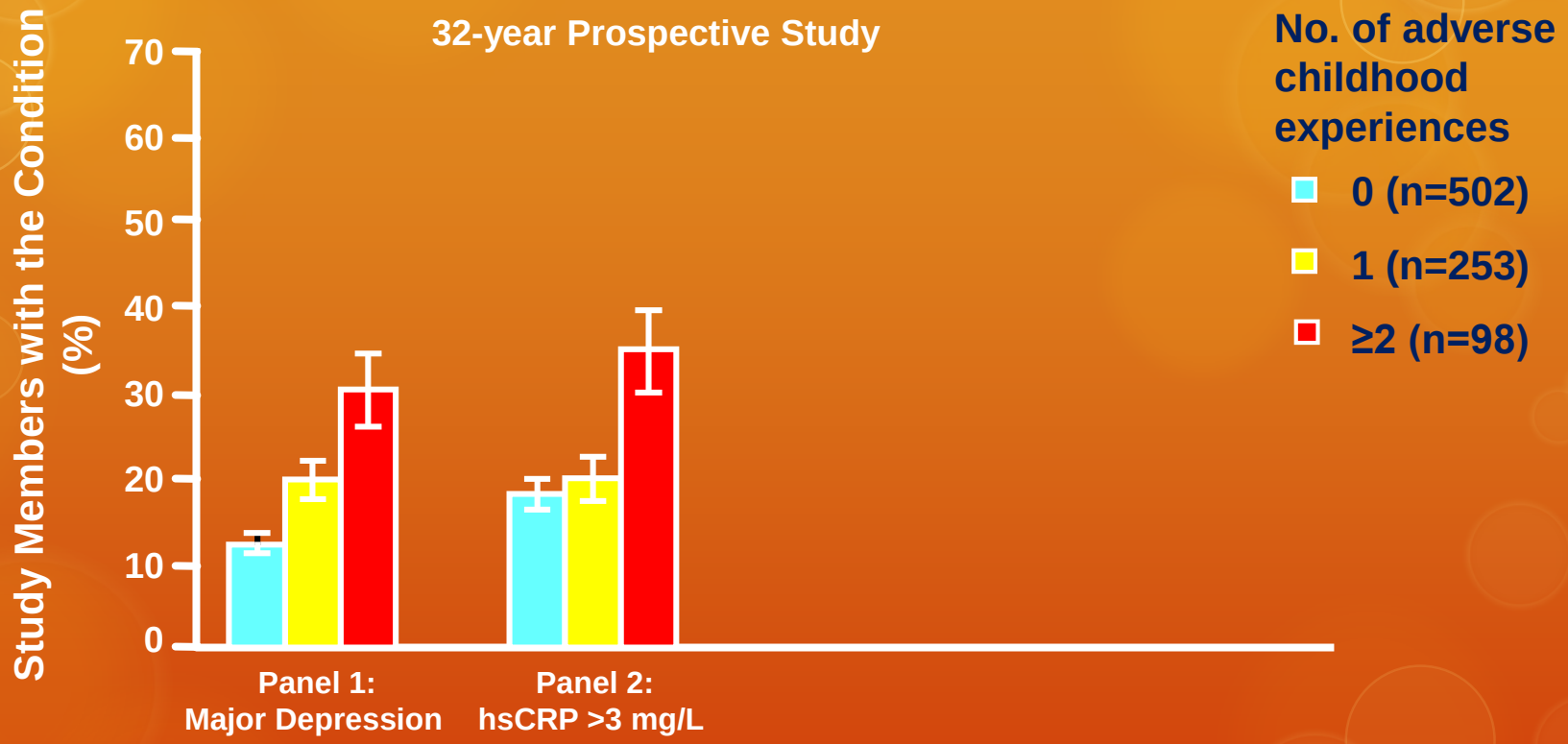

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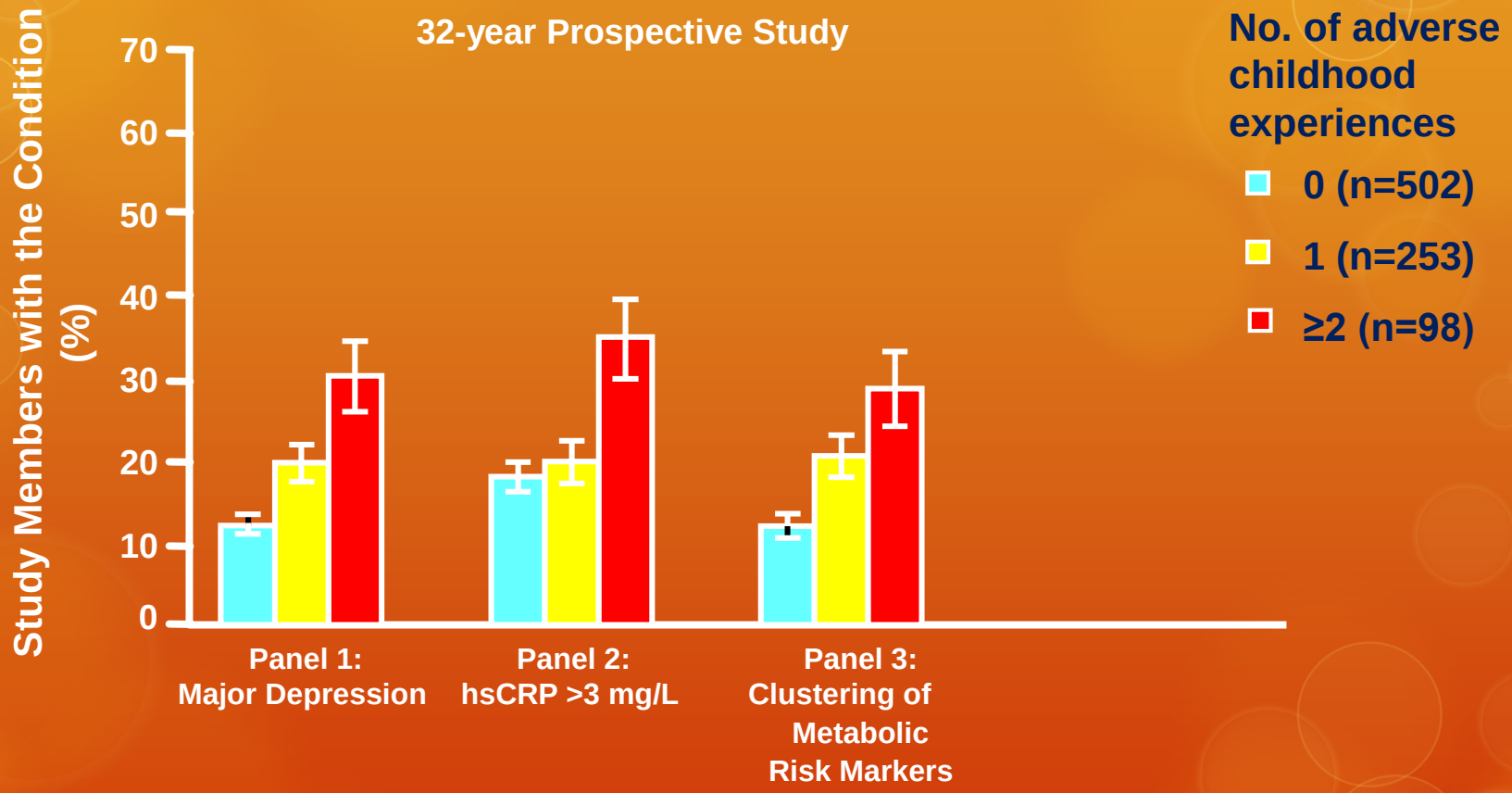

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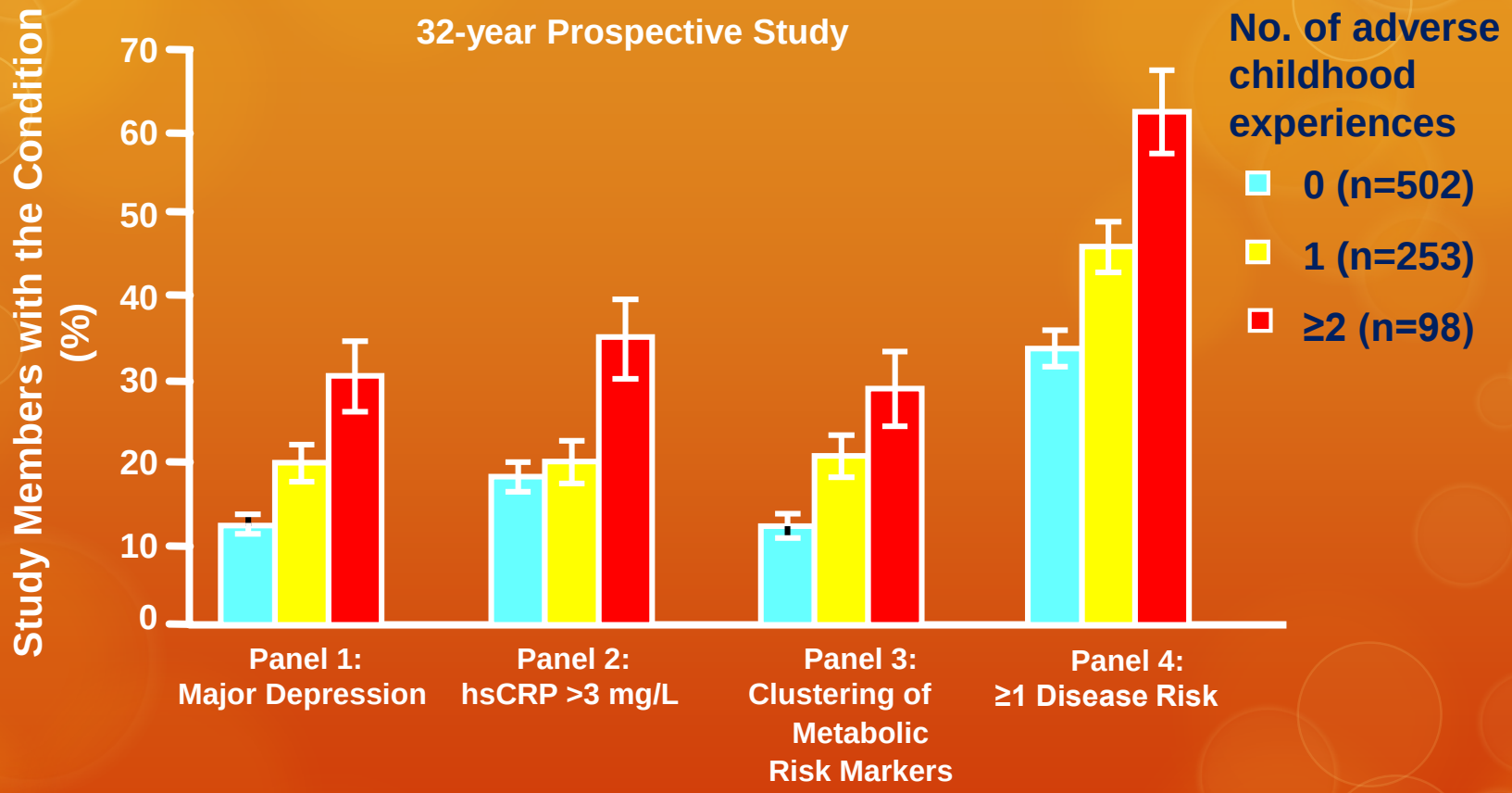

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Making the Diagnosis- PTSD

- Have you experienced, at any time during your life, physical, sexual or emotional abuse?
- Have you had any distressing events occur during your life that you don’t seem to be able to get over?
- Do you feel like you are reliving the event frequently, through vivid memories or dreams?
- Do you tend to avoid situations or places that remind you of the event?
- Are you jumpy or irritable, or is your sleep poor, particularly if you are reminded of the event?

Evidence-Based Treatment of Post-Traumatic Stress Disorder

JoAnn Difede, Megan Olden, and Judith Cukor
Department of Psychiatry, Weill Cornell Medical College, New York, New York 10065

Annu. Rev. Med. 2014. 65:319–32

Despite multiple studies documenting the lack of efficacy of a variety of agents used to treat PTSD, patterns of prescription persist

In light of the ongoing controversy regarding the evidence base for pharmacotherapy, and in the absence of strong evidence that medications offer a cure for PTSD, perhaps the most useful conceptualization of medication is as a means to offer symptom relief and improve daily functioning and quality of life.

Pharmacotherapy for PTSD

- 35 short-term (14 weeks or less) RCTs (N = 4597).
  - 17 trials Medication >> PBO (N = 2507)
  - 13 trials responder status superior with medication Vs PBO (N = 1272).
- Medication response 59.1% Vs PBO response 38.5%
- SSRIs best evidence of treatment efficacy
- Medication > PBO for severity of PTSD symptom clusters, comorbid depression and disability
- 3 maintenance trials suggested long term medication may be required.

Stein DJ Cochrane Database of Systematic Reviews 2006, Issue 1.

Recommendations for pharmacotherapy for core symptoms of PTSD

First-line	Fluoxetine, paroxetine, sertraline, venlafaxine XR
Second-line	Fluvoxamine, mirtazapine, phenelzine
Third-line	Amitriptyline, aripiprazole, bupropion SR, buspirone, carbamazepine, desipramine, duloxetine, escitalopram, imipramine, lamotrigine, memantine, moclobemide, quetiapine, reboxetine, risperidone, tianeptine, topiramate, trazodone
Adjunctive therapy	**Second-line:** eszopiclone, olanzapine, risperidone **Third-line**: aripiprazole, clonidine, gabapentin, levetiracetam, pregabalin, quetiapine, reboxetine, tiagabine **Not recommended**: bupropion SR, guanfacine, topiramate, zolpidem
Not recommended	Alprazolam, citalopram, clonazepam, desipramine, divalproex, olanzapine, tiagabine

SR = sustained release; XR = extended release.

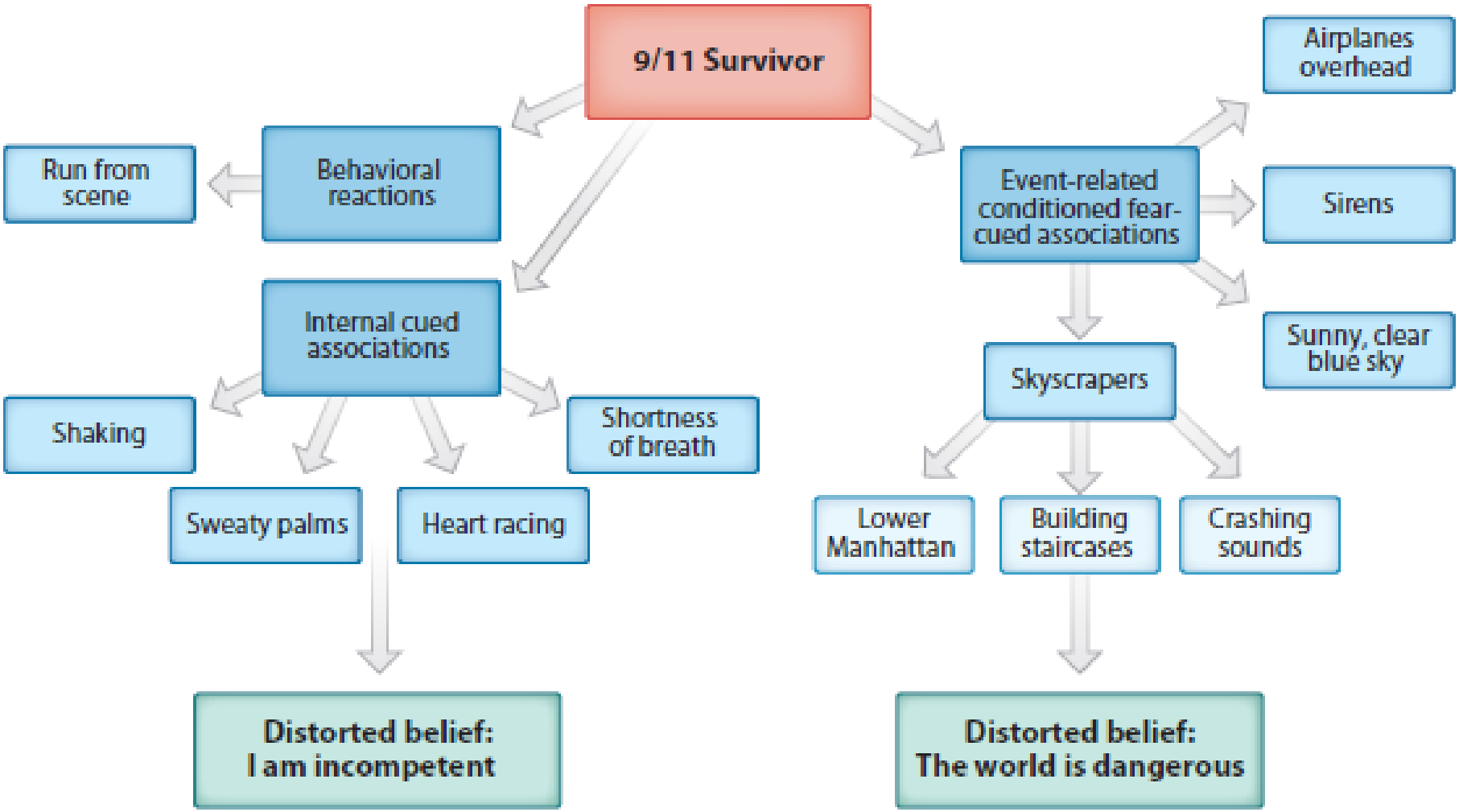


Figure 1

Fear structure and conditioned fear-cued associations after the 9/11 World Trade Center attacks.

Annu. Rev. Med. 2014. 65:319–32

Psychotherapy PTSD: CBT based

- **Exposure therapy**
  - Repeated intentional recall of traumatic memories
  - In vivo exposure to situations, objects
  - Relaxation, controlled breathing, information
- **Anxiety management therapies**
  - Stress inoculation training
- **Cognitive therapies**
  - Identification of trauma related exaggerated or inaccurate beliefs leading to challenging the thoughts
- **Eye movement desensitization and reprocessing**
  - Exposure to trauma related thoughts and feelings accompanied by oscillating eye movements, tapping etc

Psychotherapy: Cochrane Review 2009

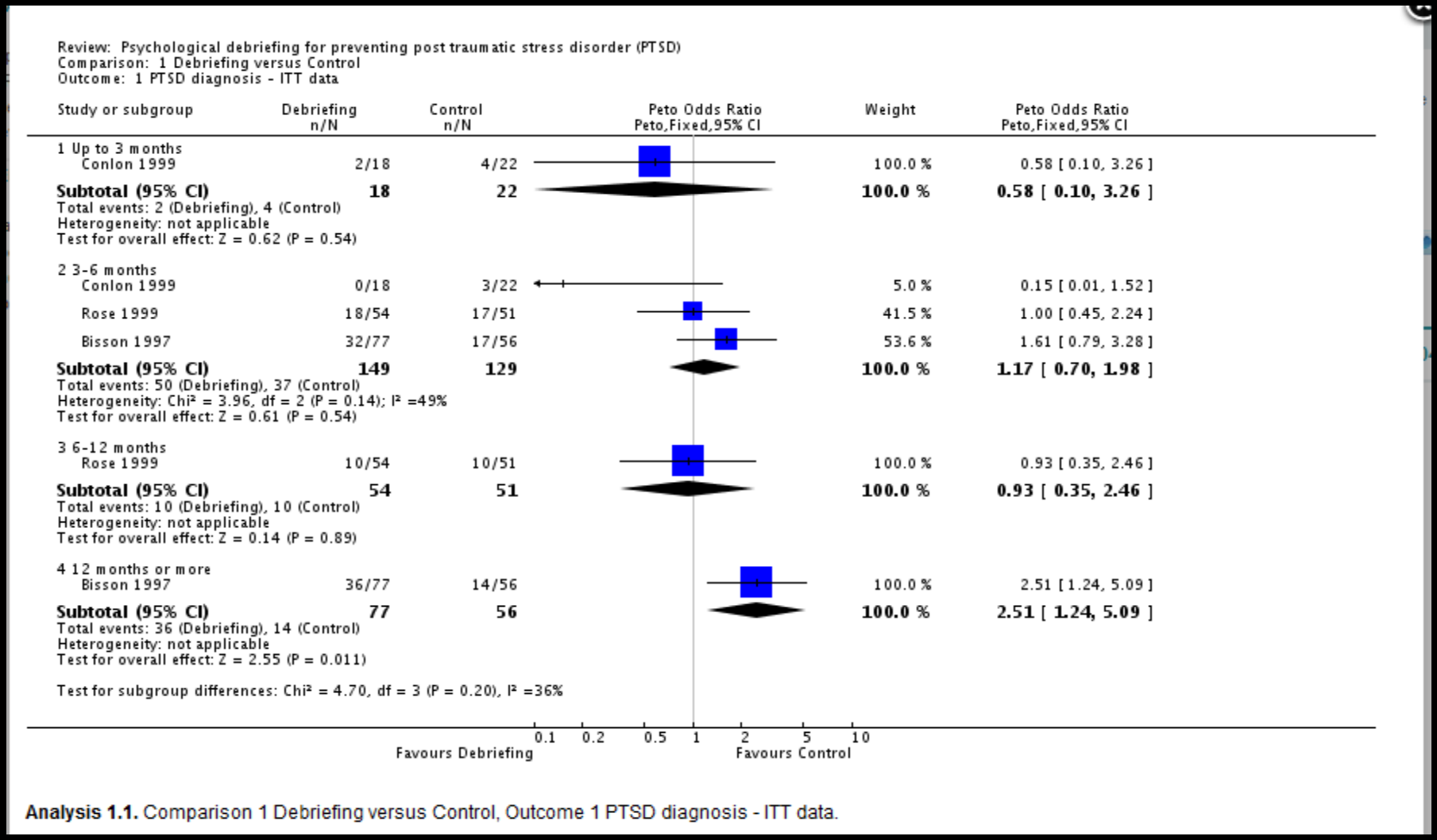
- **A U T H O R ‘S C O N C L U S I O N S:**

1. Psychological treatment can reduce traumatic stress symptoms in individuals with PTSD.

2. Trauma focused CBT and EMDR have the best evidence for efficacy at present and should be made available to PTSD sufferers

- Stress management and group TFCBT were also useful and non-trauma-focused therapy did not work (psychodynamic, hypnosis, mindfulness)

Psychological debriefing in trauma



Analysis 1.1. Comparison 1 Debriefing versus Control, Outcome 1 PTSD diagnosis - ITT data.

Rose SC et al 2009 Cochrane reviews

Rose SC et al 2009 Cochrane reviews

Psychological debriefing in trauma

Authors' conclusions:

- No evidence that single session debriefing is a useful treatment for the prevention of PTSD after traumatic incidents.
- Compulsory debriefing of victims of trauma should cease.
- A more appropriate response could involve a 'screen and treat' model

Rose SC et al 2009 Cochrane reviews

Stress De-Briefing

- Victims should not indiscriminately attend debriefing programs
  - Interferes with avoidance, which is part of the normal processing of a traumatic event
  - May act as a form of re-exposure without sufficient time for habituation (as seen in therapy)
  - May lead victim to bypass usual supports
  - Risk of story telling in a hyper-adrenergic state

McNally, Briant 2003; Rose, Bisson 2003; VanEmmerick et al 2002

PTSD Pearls

- PTSD is an abnormal response to a traumatic event- most common response to trauma is acute distress and recovery
- Many have previous/multiple trauma
- Personal, protracted, violent or sexual trauma is most likely to case PTSD
- PTSD is not the only MH outcome associated with trauma
- Trauma is subjective