

VA



U.S. Department
of Veterans Affairs



Women's Mental Health Across the Lifespan

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DISCLOSURES

No conflict of interest

No discussion of non-FDA-approved medications or devices

Case presentation is a composite with no personal identifiers

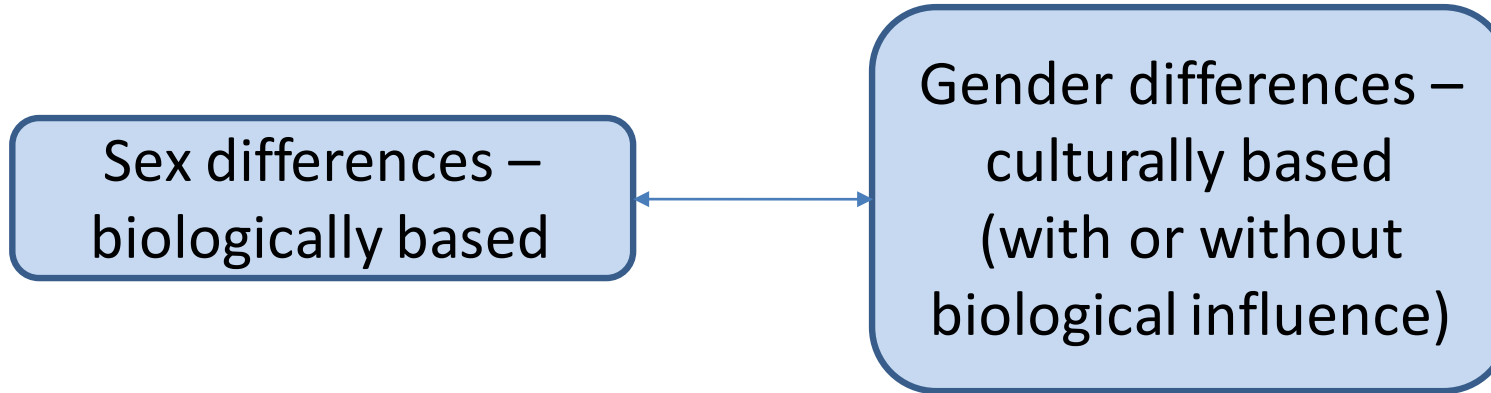


PURPOSE

- Sex and gender affect
 - The likelihood of developing mental health conditions
 - Course and treatment response
- This overview will highlight key influences on women's mental health throughout the lifespan, including
 - Genetics and epigenetics (environmental influences on how genes are expressed)
 - Gender-linked stresses and traumas
 - Reproductive cycle stages
- We'll see how these factors interact to influence mental health



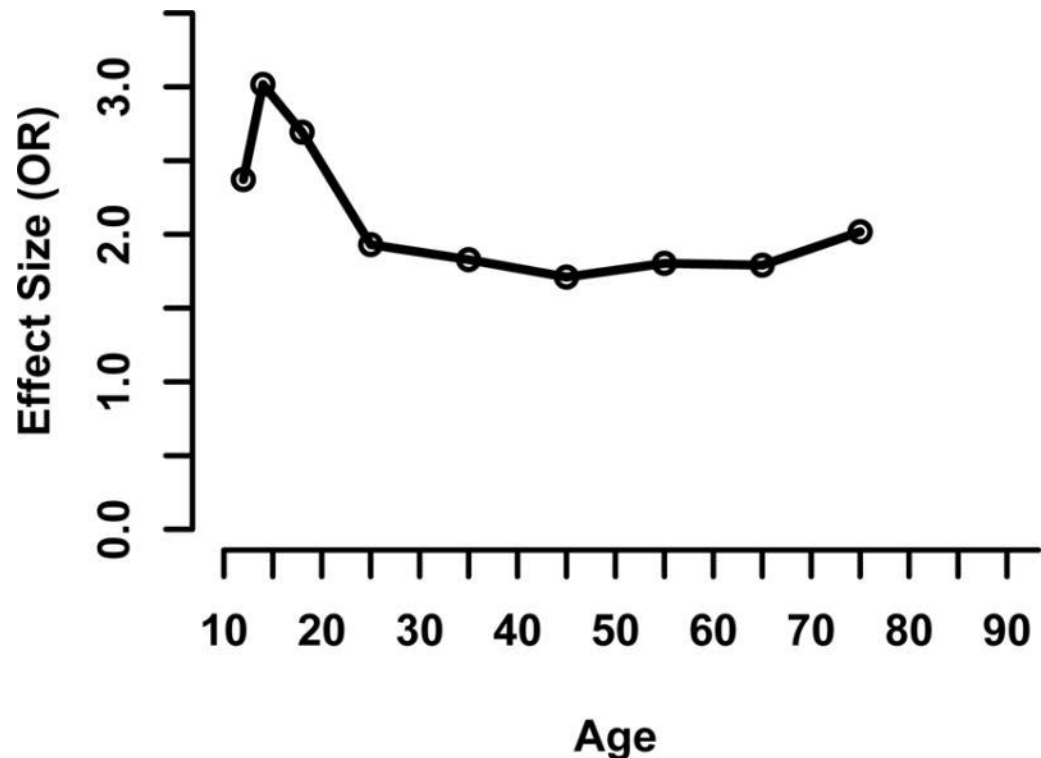
TERMINOLOGY



- Societal gender roles can amplify small sex differences
- These influences can accumulate across a lifetime
- “Biocultural” refers to the mutual influence of biology and culture



GENDER DIFFERENCES IN PREVALENCE OF DEPRESSION



Odds of major depression in women vs men (worldwide meta-analysis)

- Prevalence of major depressive disorder is almost doubled in women compared to men
- Gender divergence in depressive symptoms begins at age 12 and peaks at age 16

Salk RH et al: Psychol Bull 143(8):783-822, 2017



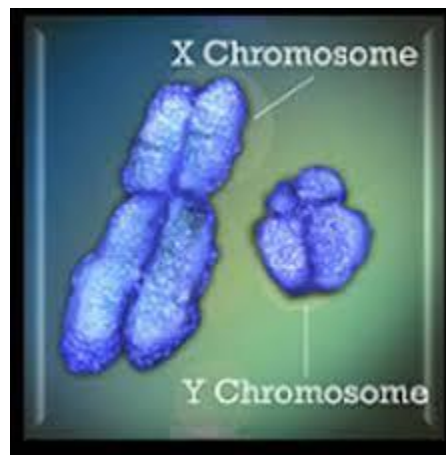
CASE EXAMPLE

Darinda is a 67 year old Army Veteran who comes to you with symptoms of major depression and post-traumatic stress disorder (PTSD). She's had depressive and anxiety symptoms on and off since adolescence. She's intermittently sought mental health treatment, but never sustained it. She's giving it another try because her symptoms have worsened since she retired 6 months ago.



GENETIC INFLUENCES ON MENTAL HEALTH

So let's start at the beginning to identify sex- and gender-linked influences on Darinda's mental health....



Darinda tells you that her mother, maternal grandmother and maternal aunt each had severe problems with depression and anxiety.



GENETIC SUSCEPTIBILITY TO STRESS

“Orchid” alleles more susceptible



“Cactus” alleles more resilient

When interacting with stress, “orchid” alleles confer more risk for depression and anxiety in females than in males

Perry LM et al: J Neurosci Res 95:737-62, 2017



CASE EXAMPLE: IN UTERO EXPOSURE TO STRESS



Darinda's mother was severely stressed and depressed throughout her pregnancy with Darinda.



PARTICIPANT POLL QUESTION

If a woman has severe distress throughout her pregnancy, do you think that could directly change how her fetus develops?

1. Yes
2. No



GOOD VERSUS BAD STRESS: FROM THE START

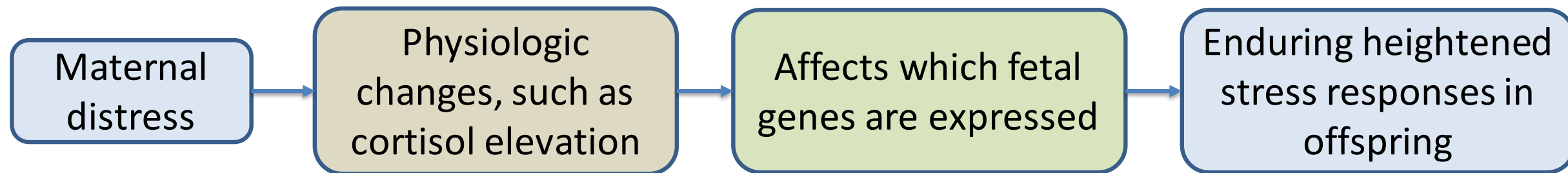
- When a pregnant woman intermittently experiences mild to moderate stress
 - Her fetus has a temporary increase in heart rate variability and reduced movement; these responses intensify as the fetus matures
 - This may help the fetus' stress response system develop normally – e.g. toddlers exposed to mild to moderate levels of maternal distress in the womb have improved motor development
 - A placental enzyme protects the fetus from excess maternal cortisol
- When a pregnant woman experiences severe, persistent distress
 - The fetus is no longer protected from excess cortisol
 - The fetal stress response system can develop as hypersensitive in an enduring way



DiPietro JA et al: Child Dev 77(3):573-87, 2006; DiPietro JA: Early Human Devel 74:125-38, 2003



EPIGENETICS AND FETAL PROGRAMMING



- A chronically reactive stress response system takes a health toll, physically and mentally, over time
- Societal disparities leading to maternal distress can affect her offspring's health from the start

Palma-Gudiel H et al: Epigenetics 10(10):893-902, 2015; Stonawski V et al: Dev Psychopathol Apr 2:1-13, 2018; Sutherland S, Brunwasser SM: Curr Psychiatr Rep 20(11):102, 2018



DO SEX AND GENDER MATTER IN FETAL PROGRAMMING?

- Study results vary, but most find that females are more responsive to stress signals in the uterine environment
- Female fetuses can adapt better (e.g. to malnutrition, inflammation), which increases survival compared to male fetuses
- However, this may result in increased vulnerability to subsequent mental health problems such as depression



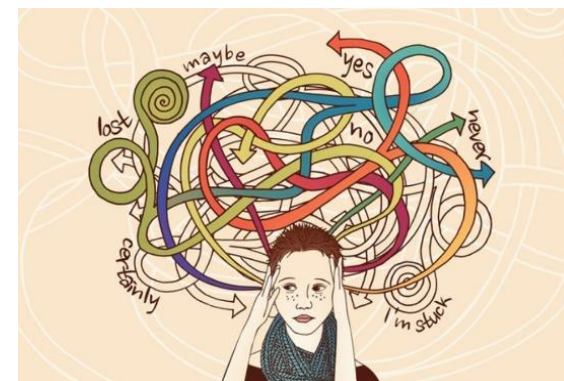
Sutherland S, Brunwasser SM: Curr Psychiatr Rep 20(11):102, 2018



GENDER INFLUENCE ON COPING STYLE

When Darinda was 6 years old, her mother married a man who wasn't her biological father. Darinda's mother and stepfather often fought, physically and verbally, in front of Darinda and her brother. Darinda tended to brood about this, and to overeat. Her brother usually distracted himself by playing video games.

- Rumination (directing attention toward negative feelings and thoughts) more common in girls
- Problem-solving and distraction more common in boys
- Ruminative style confers higher risk of depression



Gomez-Baya D et al: Cognitive Ther Res 41(2):289-303, 2017; Alloy LB et al: Clin Psychol Sci 4(5):867-81, 2016



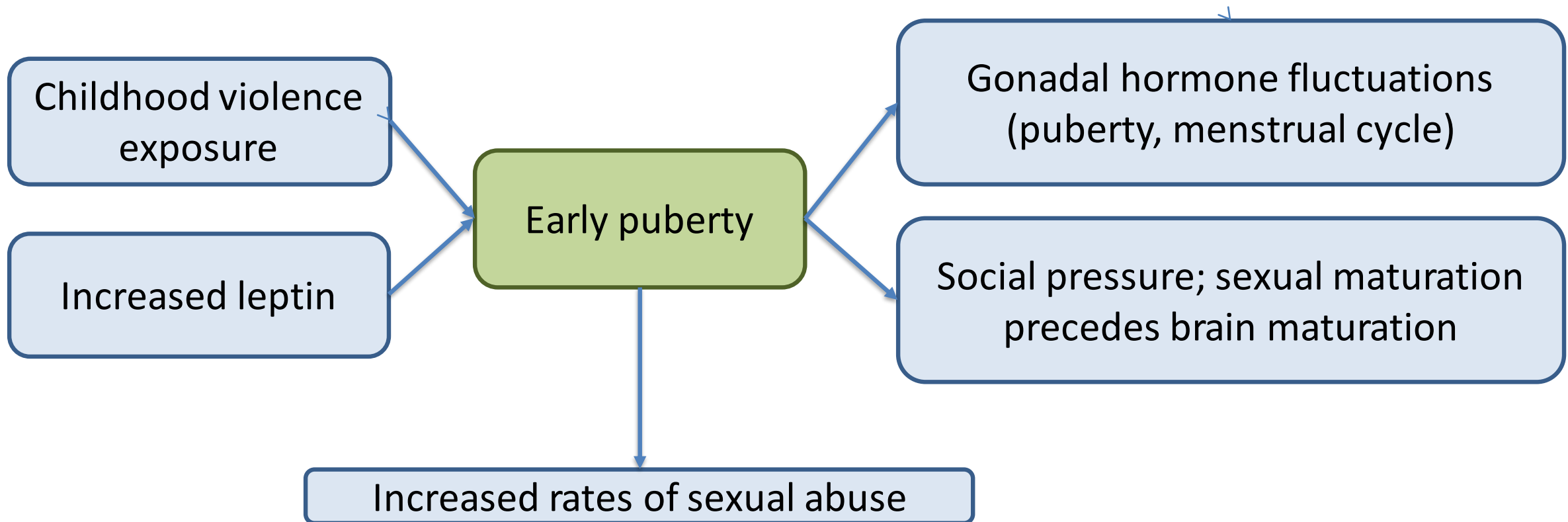
CASE EXAMPLE: EARLY PUBERTY

As a child, Darinda felt “fat and ugly”. She began showing breast development by age 9, with menarche at age 11. Boys started making sexual advances, sometimes aggressively. Darinda went through a period of promiscuity and binge alcohol drinking from age 12 – 18. In retrospect, this is when her depressive and anxiety symptoms began.



GENDER-LINKED INFLUENCES IN ADOLESCENCE

In adolescence, the prevalence of depression in girls rises to about twice that in boys



Colich NL et al: Psychol Bull doi.org/10.1037/bul0000270, 2020



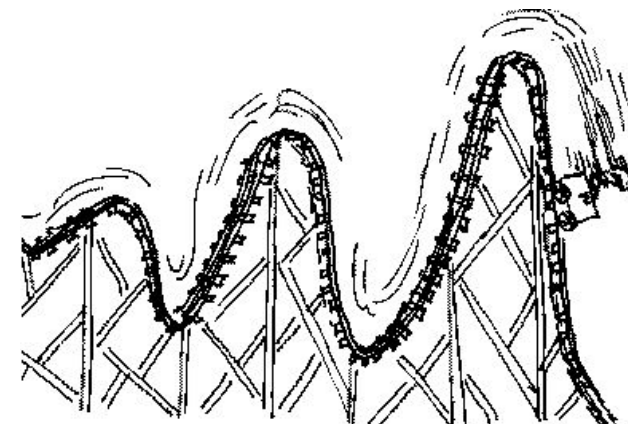
CASE EXAMPLE: PREMENSTRUAL EFFECTS

As a teenager, Darinda felt grouchy and emotional on and off, tending to snap at people and cry due to small slights. Her friend persuaded her to track her menstrual cycles and moods. She realized these symptoms always came about a week before her menstrual periods began.



REPRODUCTIVE STEROIDS AND BEHAVIOR

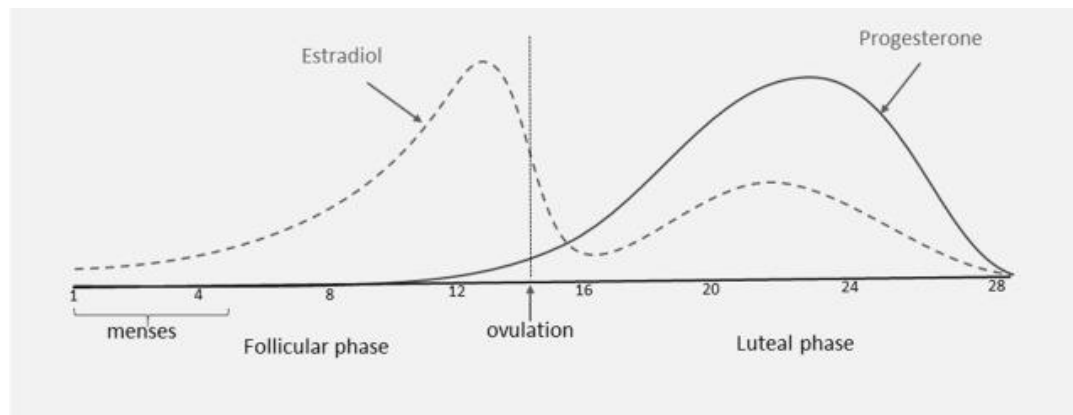
- Reproductive steroids regulate many neurologic functions (e.g. sexual and maternal behaviors, eating, sleep, cognition, impulse control)
- Changes in reproductive steroid levels during certain reproductive states (the premenstrual phase of the menstrual cycle, postpartum, the transition to menopause) can trigger mood dysregulation in a subset of women
- The degree of hormonal fluctuation, rather than absolute hormone levels, correlates with mood changes
- Hormonal flux interacts with stress to produce mental health symptoms



Schiller CE et al: Compr Physiol 6(3):1135-60, 2016



PREMENSTRUAL SYMPTOM PATTERNS

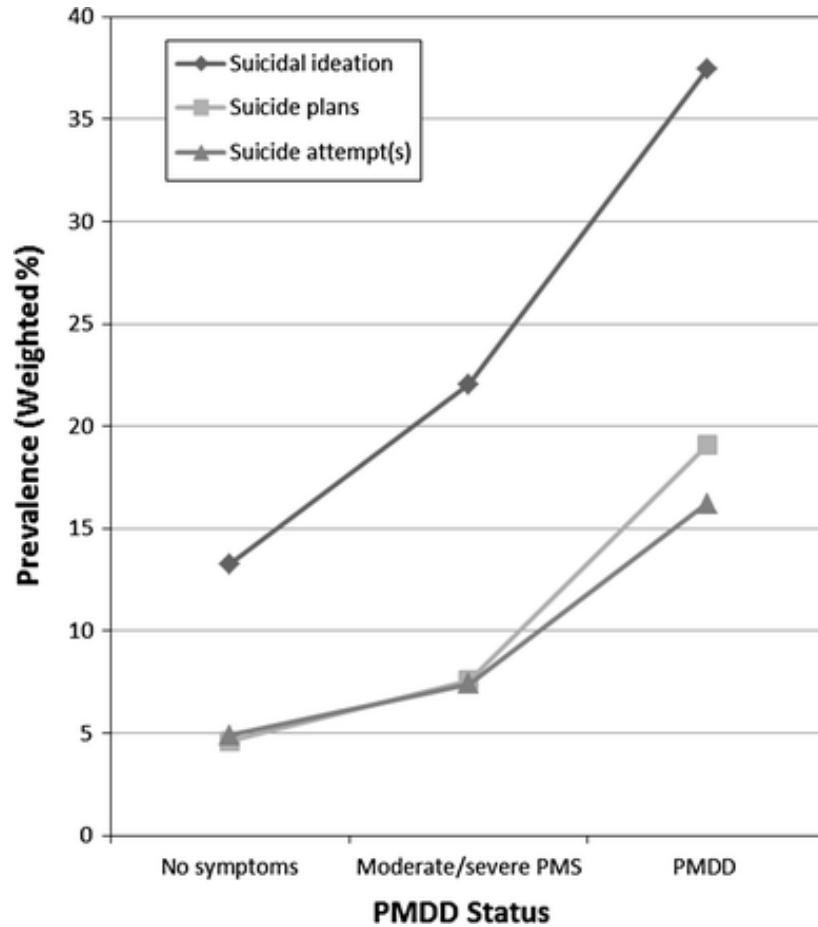


- Premenstrual syndrome (PMS)
 - Distress/impairment, but <5 symptoms; 12-18% of menstruating women
- Premenstrual dysphoric disorder (PMDD)
 - 1-8% of menstruating women
- Premenstrual exacerbation (PME)
 - A disorder that regularly worsens in the late luteal phase of the menstrual cycle

Potter J et al. *J Womens Health*. 2009;18(1):31-9; Halbreich U et al. *Psychoneuroendocrinol*. 2003;28(suppl 3):1-23; Gehlert S et al. *Psychol Med*. 2009;39(1):129-36; Takeda T et al. *Arch Womens Ment Health*. 2006;9(4):209-12; Wittchen HU et al. *Psychol Med*. 2002;32(1):119-32



PMDD AND SUICIDE RISK



PMDD is associated with increased suicidal thoughts, plans and attempts

Pilver CE et al 2013



CASE EXAMPLE: GENDER-LINKED STRESS AND TRAUMA



Darinda joined the Army at age 21. She performed well, but she endured insults and sexually suggestive comments from male peers. At age 24, Darinda was sexually assaulted by two men in her unit. She was intoxicated at the time, so she blamed herself and did not report this. She already felt stressed at that time because her mom was in the hospital.



PARTICIPANT POLL QUESTION

In addition to sexual harassment and assault, what are some other stresses and traumas that military women experience more often than military men?



GENDER-LINKED STRESSES AND TRAUMAS

Sexual

- Childhood sexual abuse
- Rape
- Sexual harassment
- Military sexual assault

Gender

- Harassment
- Inequities and discrimination
- Role stereotyping
- Intimate partner violence
- Chronic environmental strain

Reproductive

- Unintended pregnancy
- Perinatal loss
- Reproductive coercion



PRE-MILITARY STRESSORS IN MILITARY VS CIVILIAN WOMEN



Before serving in the military, military women significantly more often:

- Lived with someone mentally ill
- Lived with someone who abused alcohol or drugs
- Had parents who were separated or divorced
- Experienced childhood physical, verbal and/or sexual abuse

Katon JG et al: Am J Prevent Med 49(4):573-82, 2015



ACTIVE DUTY STRESSORS IN WOMEN VS MEN

Women > men

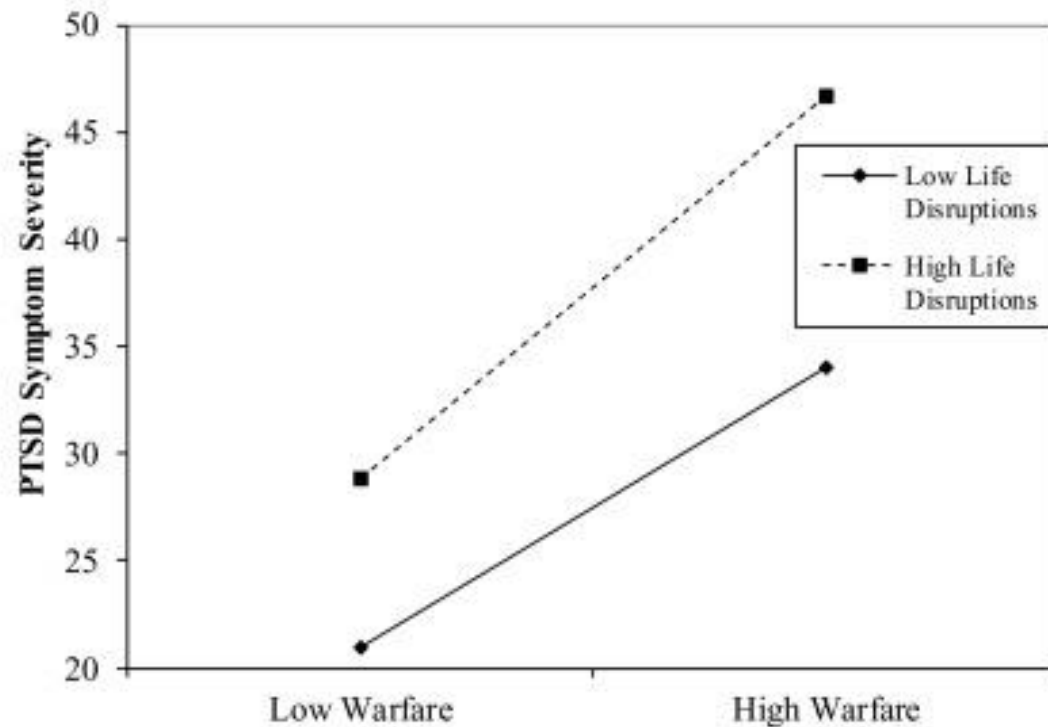
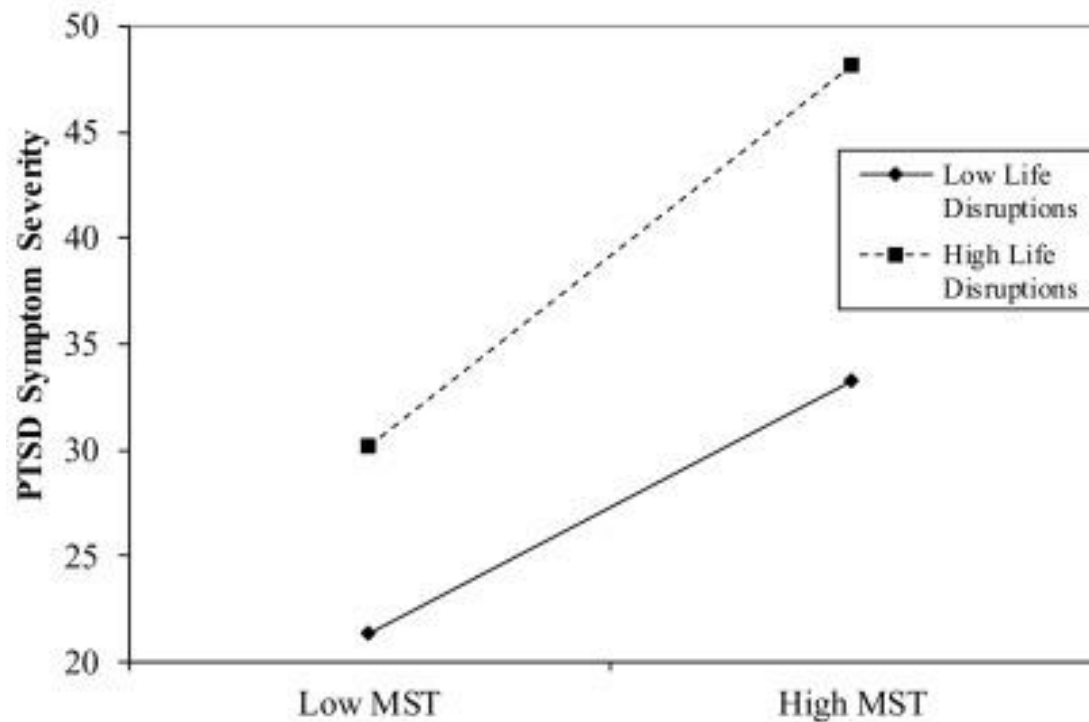
- Sexual harassment
- Sexual assault
- Gender harassment
- Lack of support from peers, supervisors (may be excluded from unit cohesion, a key influence on resilience)



Vogt D et al: J Abn Psychol 120(4):797-806, 2011; Street AE et al: Clin Psychol Rev 29(8):685-94, 2009; Vogt DS et al: J Trauma Stress 18(3):272-84, 2005; Kline A et al: Psychiatry 76(3):256-72, 2013



LIFE DISRUPTIONS AND MENTAL HEALTH RISKS



For women, life disruptions while deployed amplify the effect of sexual harassment, sexual assault and combat trauma on PTSD; this effect not found for men

Banducci AN et al: Addict Behav 2019 Nov;98:106032. doi: 10.1016



POST-MILITARY STRESSORS IN WOMEN VS MEN

- Compared to male Veterans, women Veterans are
 - 3 times more likely to be single parents if they have children
 - 5 times more likely to have a partner who is eligible for deployment
 - More likely to get divorced and remain divorced
- Gender-linked social challenges
 - Parenting transitions; attachment problems
 - Conflicting role expectations (woman/warrior)
 - Others have less understanding of their military identities and traumas upon homecoming



Street AE et al: Clin Psychol Rev 29(8):685-94, 2009



GOOD VERSUS BAD STRESS, CONTINUED

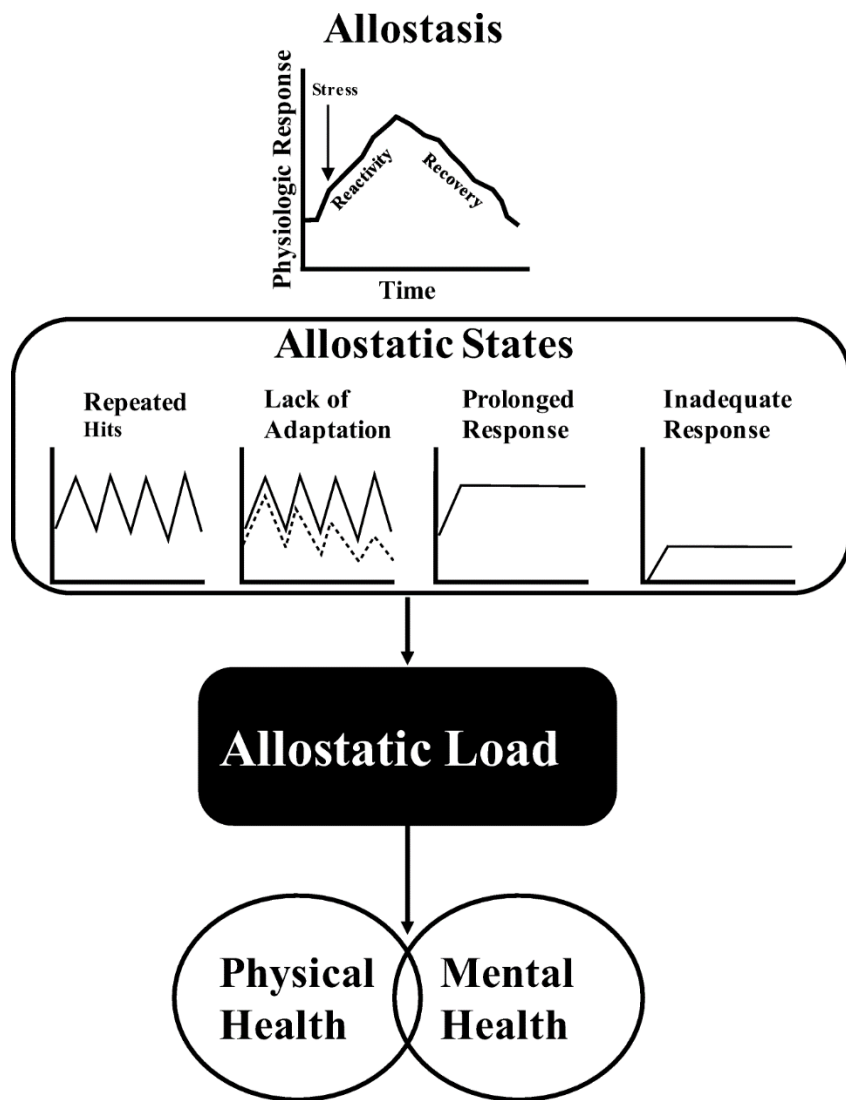
- Acute, intermittent stress
 - Sympathetic nervous system prepares the body for fight or flight by activating heart, blood vessels, muscles and stress hormones
 - The immune system is activated in anticipation of possible wounds or infection
 - These responses enhance immune function and overall health
- Severe and/or chronic stress
 - Sympathetic nervous system is over-activated, causing wear and tear
 - Immune function is suppressed, increasing vulnerability to disease



Dhabar FS: Immunol Res 58:193-210, 2014



ALLOSTATIC LOAD AND GENDER ROLES



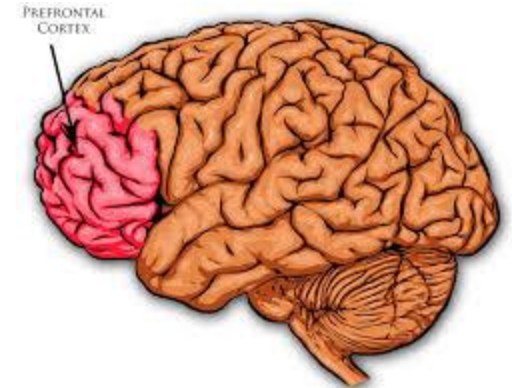
- **Allostasis** is the process of recalibrating physiology and behavior to handle stress
- **Allostatic load** is the wear and tear that comes from cumulative and/or chronic stresses that overwhelm this system
- Women in roles regarded as traditionally masculine (e.g. metal working, engineering, military service) may experience higher allostatic load
- Many women retain roles regarded as traditionally feminine (e.g. childrearing, homemaking) while also taking on traditionally masculine roles

Juster RP et al: Curr Psychiatry Rep 21(11):110, 2019



GENDER STEREOTYPING, PERFORMANCE & THE BRAIN

- Physiological stress from performing in a counter-stereotypical domain can impair a woman's ability to process information in the prefrontal cortex
 - She may be unable to fully attend to tasks because part of her brain is occupied with monitoring her performance and social acceptance
 - She may expend extra effort to suppress negative thoughts and emotions
- A woman may work harder to compensate for these cognitive and emotional demands, but can burn out
- A woman may also feel pressure to underperform in order to conform with others' gender expectations
- The cumulative effect of these pressures is that women's performance and health may suffer over time



Ellemers N: Annu Rev Psychol 69:275-98, 2018



CASE EXAMPLE: PREGNANCY AND POSTPARTUM

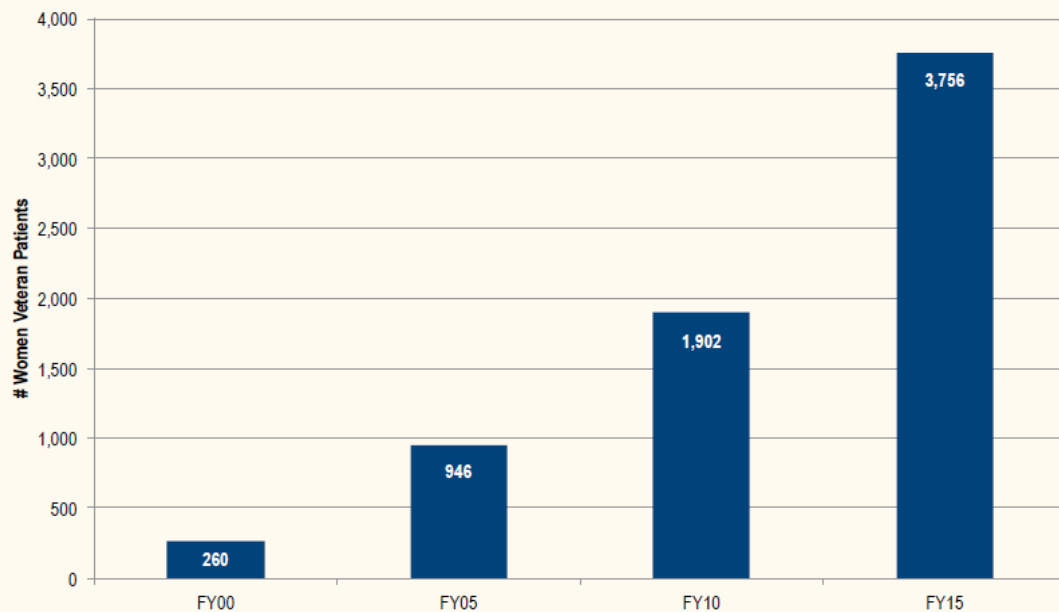
Darinda married a Navy Veteran. They had two children, the first unintended and the second planned. Darinda felt depressed for several months after the first birth.





THE PERINATAL PERIOD AND MENTAL HEALTH

Exhibit 2.Q. VHA-Covered Obstetric Deliveries Among Women Veteran VHA Patients, FY00-FY15



Key: FY – Fiscal Year; VHA – Veterans Health Administration
Notes: This Exhibit displays the number of women Veterans with at least one delivery through Purchased Care during the year being examined. Findings portray Veteran VHA patients, not the entire Veteran population. See Technical Appendix.
Cohort: Women Veteran VHA patients in each year. FY00: N=159,810; FY05: N=231,907; FY10: N=317,122; FY15: N=439,791.
Source: WHEI Master Database, FY00-FY15

- Pregnancy and the postpartum period pose unique mental health challenges
- Among Active Duty Service women, the prevalence of perinatal depression is 11 – 24% (7% - 20% in general population)
- Among women Veterans, there has been a more than 14-fold increase in pregnancies over 15 years
- A history of military sexual harassment or assault increases the risk of depressive symptoms and suicidal thoughts during pregnancy and postpartum

Klaman SL & Turner K: *Matern Child Health J* 20(Suppl 1): 52-65, 2016; Munk-Olsen T & Agerbo E: *Epidemiol* 26(1):79-84, 2015; Borrero S et al: *J Gen Intern Med* 32(8):900-8, 2017; Gross GM et al: *J Womens Health (Larchmt)* 2020 Jan;29(1):38-45. doi: 10.1089; O'Hara MW, Wisner KL: *Best Pract Res Clin Obstet Gynecol* 28(1):3-12, 2014; https://www.womenshealth.va.gov/WOMENSHEALTH/docs/WHS_Sourcebook_Vol-IV_508c.pdf



CASE EXAMPLE: PARENTING AND FAMILY STRESS

Darinda reports running her family “military-style”. In retrospect she thinks untreated PTSD symptoms led her to be too harsh in disciplining her children, because she was so anxious about their safety. Her husband cared for the children during Darinda’s deployments. She now feels that her strictness, harshness and absences when the children were young has strained her relationships with her adult children.



POST-DEPLOYMENT FAMILY STRESSORS

- Many women are stressed by simultaneous military and parenting roles and responsibilities
- Compared to civilian working parents, the main unique stressors relate to deployment absences and reunions, including challenges of resuming roles and reconnecting
- Among Active Duty Service members, PTSD is associated with
 - Less alliance with partner about parenting decisions
 - Inconsistent discipline (e.g. threatening a punishment but not delivering the punishment)
 - Harsher parenting
- Intimate relationships are 3x more likely to break down for military women than for military men



Giff ST et al: J Fam Psychol 33(2):166-75, 2019; Mankowski M & Everett JE: Nurse Educ Today 47:23-8, 2016; Creech SK et al: Prof Psychol Res Pr 45(6):452-64, 2014



CASE EXAMPLE: PERIMENOPAUSE AND MIDLIFE

Darinda left the Army at age 51 to help take care of her father, who had a stroke, and because she had developed chronic pain from fibromyalgia. After leaving active duty, Darinda spent more time around her husband, and noticed they had few interests in common. She had less interest in sex than before, which frustrated her husband. She was also having hot flashes, which often woke her from sleep. Her menstrual cycles had become irregular. She recalls feeling quite depressed at that time.

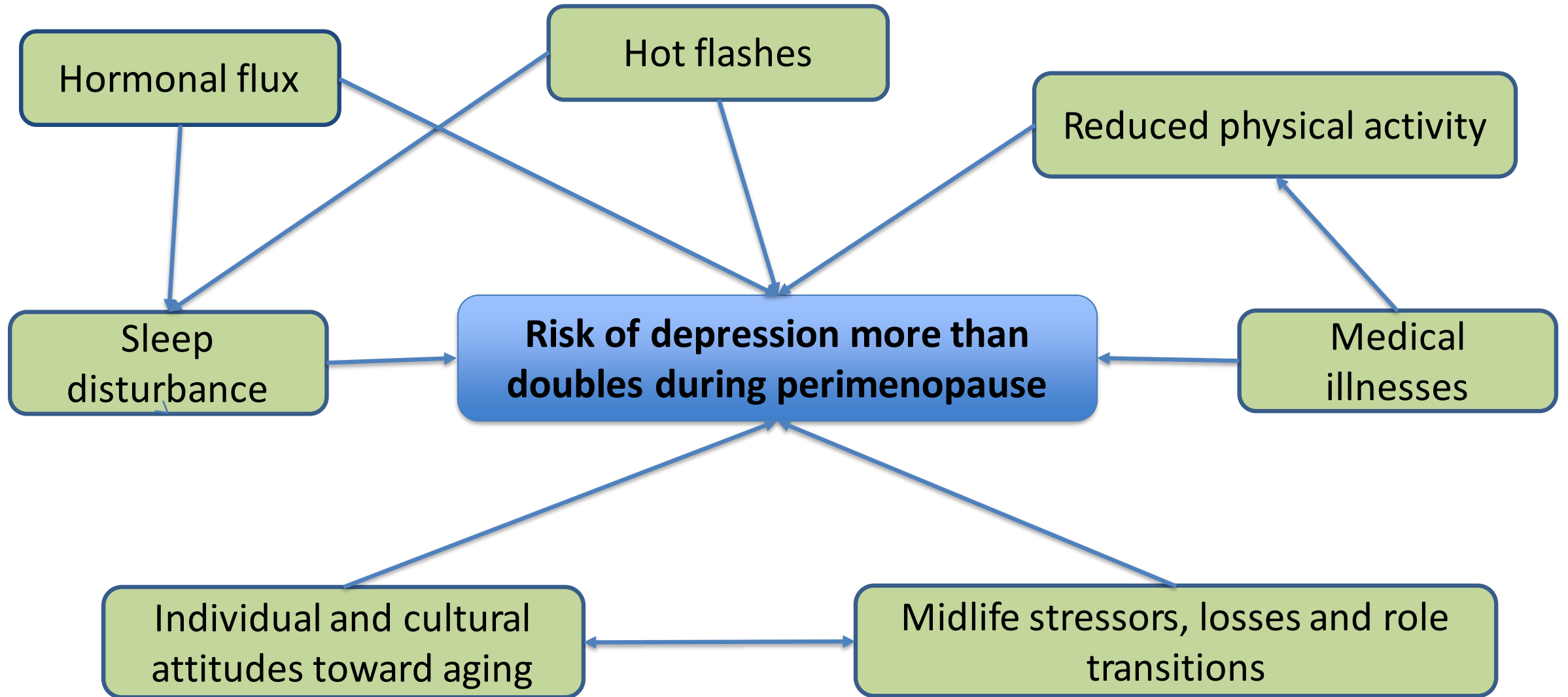


PARTICIPANT POLL QUESTION

What factors may contribute to women feeling more depressed at midlife?



INFLUENCES ON MENTAL HEALTH AT PERIMENOPAUSE





MIDLIFE, PERIMENOPAUSE AND SUICIDE RISK IN WOMEN

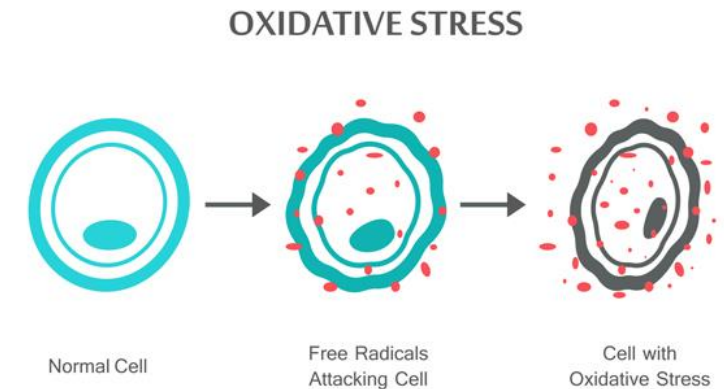
- From 1999 – 2010, suicide rates among U.S. middle-aged women increased by >30%, exceeding the relative increase among middle-aged men
- Suicidal ideation prevalence in a large epidemiologic study (2001 – 2003)
 - Pre-menopausal women: 1.1%
 - Perimenopausal women: 7.8%
 - Post-menopausal women: 1.0%
 - Middle-aged men: 1.0%
 - Older men: 0.6%

Usall J et al: J Affect Disord 116(1):144-7, 2009; Sullivan EM et al: MMWR Morb Mortal Wkly Rep 62(17):321-5, 2013



GOOD VS BAD STRESS: MIDLIFE WOMEN CAREGIVERS

- Cortisol (a key stress hormone)
 - Brief exposure mobilizes energy to handle stress, protects neurons and improves cell function
 - Long term exposure reduces cell function, promotes cell death
- “Free radicals” are reactive oxygen species that cause cell damage unless they are contained by antioxidants
 - Over time, accumulating oxidative damage contributes to chronic diseases and aging
- How these interact
 - Study comparing midlife women caregivers (chronic stress) to midlife women with healthy spouses (ordinary stress) found that chronic stress “primes” a rapid anticipatory cortisol response that leads to more oxidative damage



Aschbacher K et al: Psychoneuroendocrinol 38(9):1698-1708, 2013

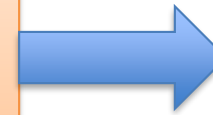


GOOD VERSUS BAD STRESS: “WEATHERING”

Ongoing social stressors (e.g. racism, gender discrimination)



- Chronic inflammation
- Oxidative damage
- Shortened telomere length (caps on chromosomes that shorten with age)



Chronic health problems



- “Weathering” is prolonged allostatic load over time; the physiologic link between intersectionality and health problems
- Found especially in women of color at midlife
- Explains chronic health conditions better than diet, exercise, smoking and low socioeconomic status

Simon RL et al: Devel Psychol 54(10):1993-2006, 2018



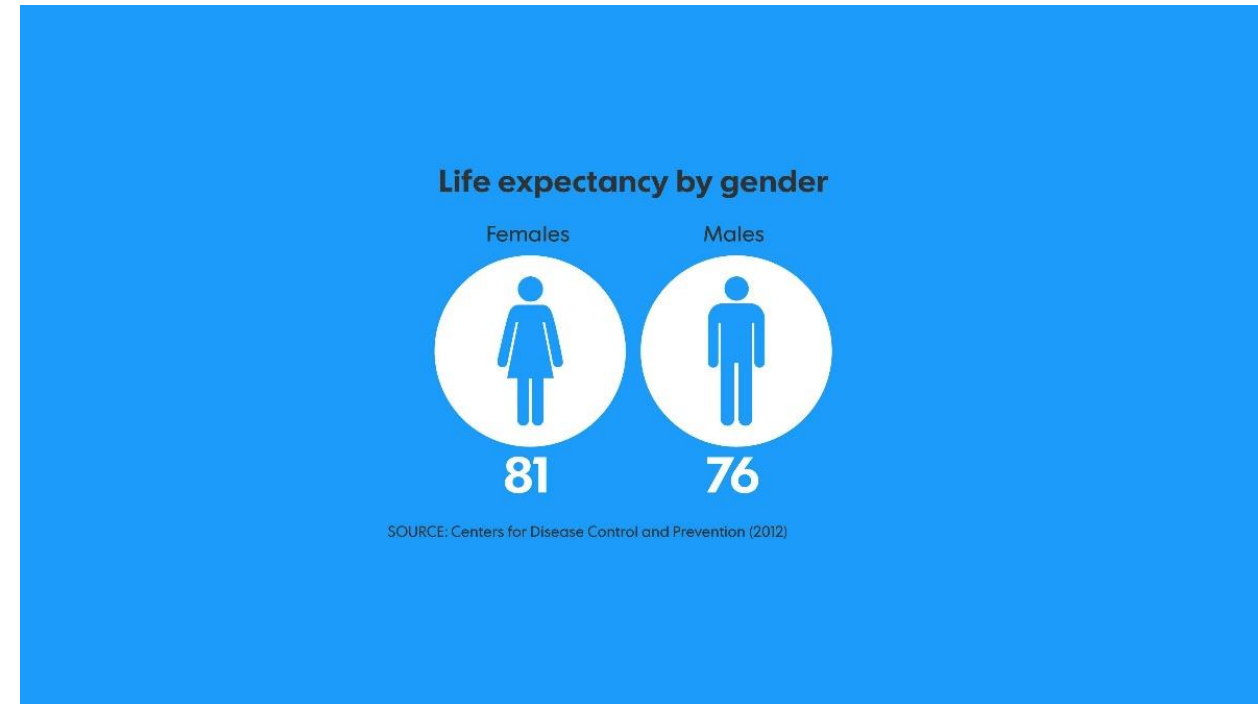
CASE EXAMPLE: AGING AND MENTAL HEALTH IN WOMEN

After her father had stabilized, Darinda worked as a civilian nurse until retiring 6 months ago, after her social security benefits maximized. At age 67, she is now widowed. Her two adult children are geographically and emotionally distant. She has chronic pain and is much less physically active than before. She feels quite depressed. Intrusive thoughts and nightmares about her military sexual assault have intensified.



GENDER EFFECTS ON AGING

- On average, women live longer than men
- Older women spend more years disabled, unpartnered, financially strained
- Compared to older women civilians, older women Veterans have
 - More impaired physical functioning
 - Less social support
 - Lower satisfaction with life, quality of life and sense of purpose



Acciai F & Firebaugh G: Soc Sci Med 190:174-80, 2017; LaCroix AZ et al: Gerontologist 56(Suppl 1):S14-26, 2016



AGING MAY REDUCE ACCESS TO COPING STRATEGIES

Coping Strategy	Changes with Aging
Keeping busy	Retirement, empty nest
Staying physically active	Pain, mobility limitations
Engaging with friends and relatives	Losses, inability to drive
Scanning the environment	Reduced visual and/or auditory acuity (hearing deficits more common in deployed military personnel)
Reframing anxious thoughts	Reduced cognitive abilities



RESILIENCE

Many older women Veterans have low levels of psychological distress despite having experienced high levels of trauma. This resilience is correlated with:



- Social connectedness
- Community integration (involvement in broader social networks)
- A sense of purpose in life
- Positive perceptions of the effects of military service on one's life



MILITARY SERVICE INFLUENCES RESILIENCE LIFELONG

Potential positive effects of military service

- Training and skill building
- Health behaviors
- Coping skills
- Maturity
- Hopefulness under extreme stress
- Self image
- Post-traumatic growth
- Access to health care and other benefits

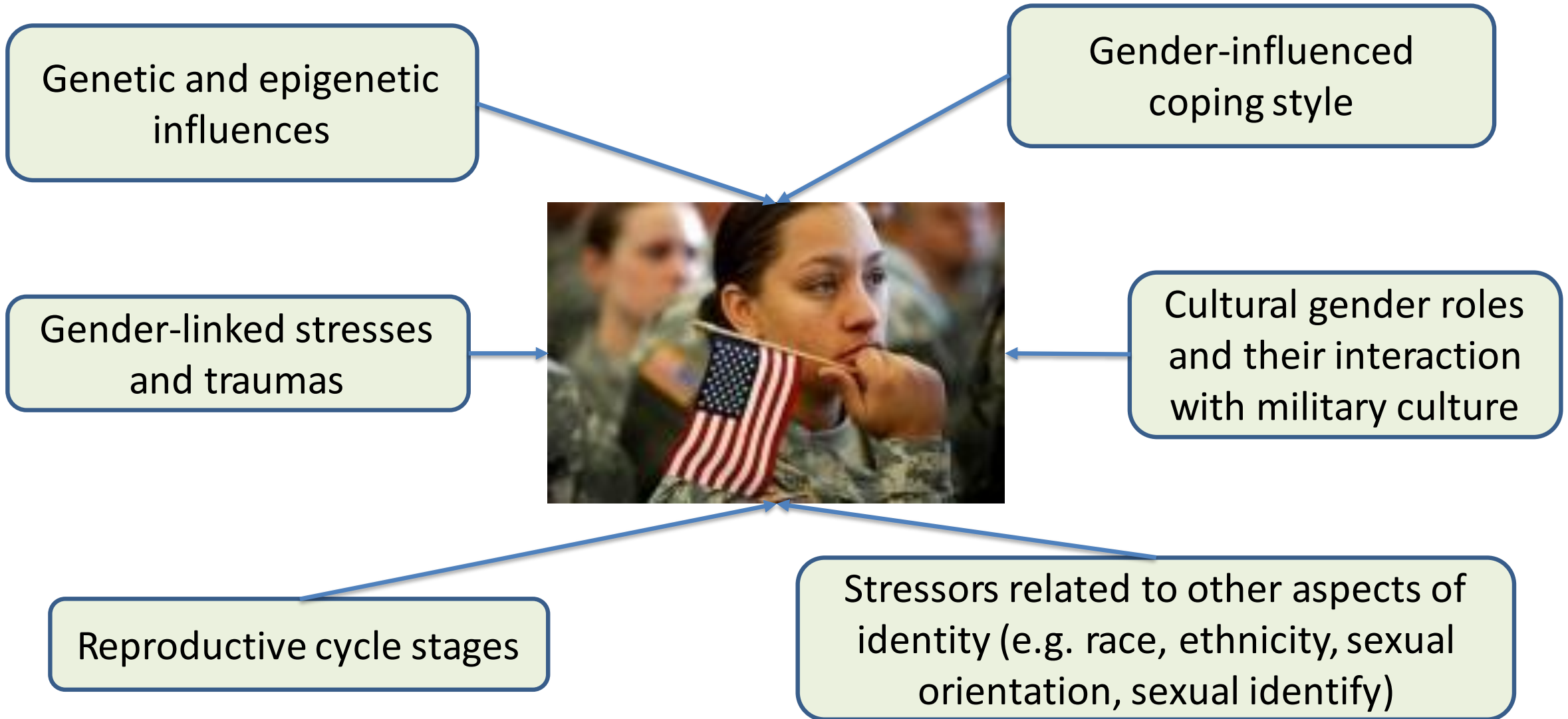
These effects can be amplified by

- Supportive social relationships in military and civilian life
- Sociohistorical context (how society regards women who serve in the military in different eras)
- Welcoming, respectful homecoming experiences; supportive transitions
- Economic opportunities

Spiro A et al: Gerontologist 56(1):5-13, 2016



INFLUENCES ON WOMEN'S VULNERABILITY AND RESILIENCE





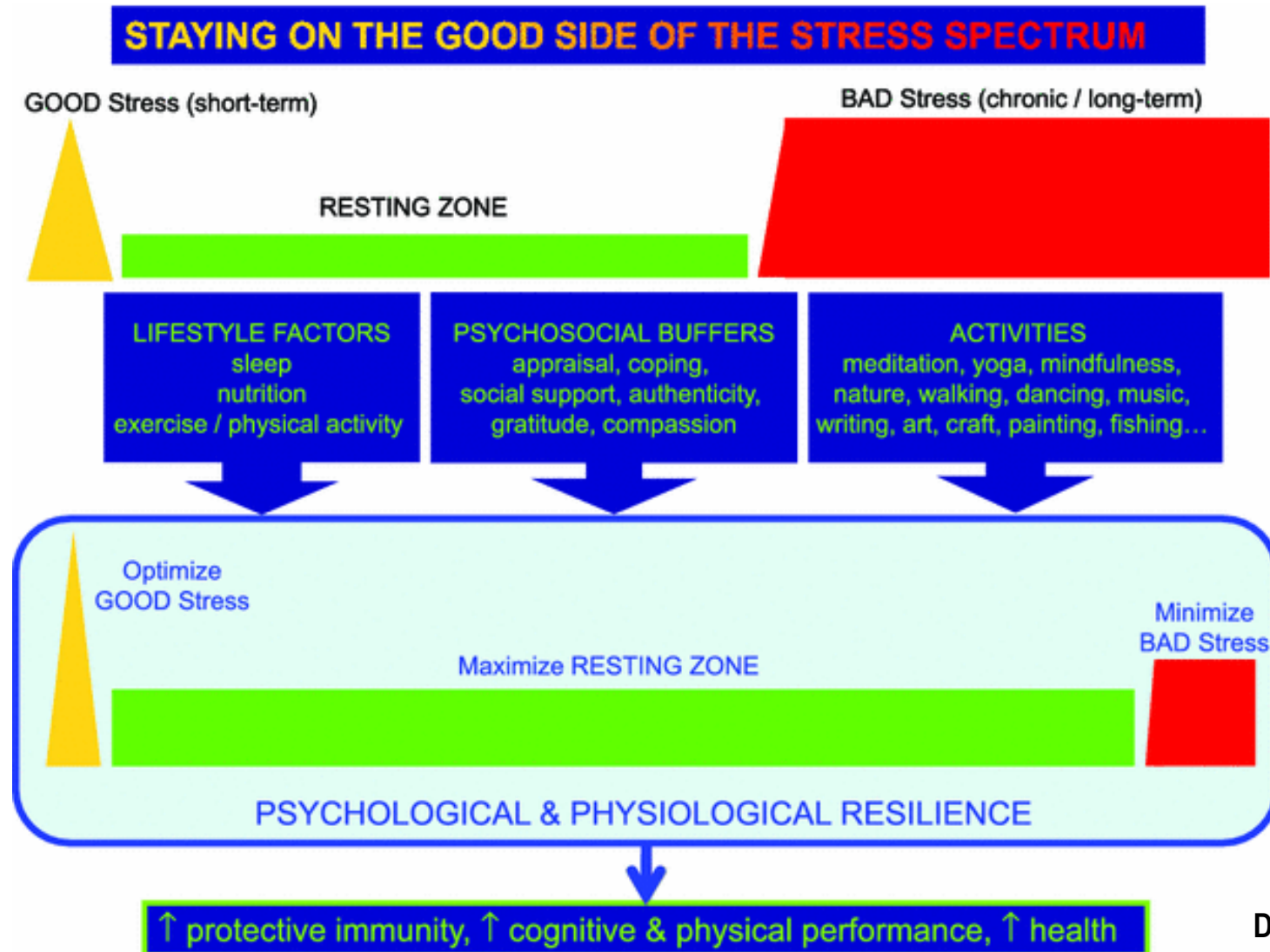
CLINICAL IMPLICATIONS OF A LIFE CYCLE APPROACH

- Understanding life-long influences on mental health helps a woman create a narrative of her strengths and vulnerabilities
- This can reduce self-blame and help women amplify their strengths
- Women who learn that they are genetically and/or epigenetically vulnerable to stress may be motivated to actively manage this
 - Physical activity
 - Healthy eating patterns and food choices
 - Social and spiritual support
 - Expanded repertoire of coping strategies





SELF-CARE IMPLICATIONS OF A LIFE CYCLE APPROACH



Dhabar FS: Immunol Res 58:193-210, 2014



TREATMENT IMPLICATIONS OF A LIFE CYCLE APPROACH

- Pharmacotherapy can be tailored to reproductive phases
 - Premenstrual
 - Perinatal
 - Perimenopausal
- Psychotherapy can target the most relevant influences and concerns, taking the whole life story into account





PRESENTER CONTACT INFORMATION

Thanks!!

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