Behavioral and Brain Sciences (forthcoming)

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Self-Protection as an Adaptive Female Strategy

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Keywords: emotions, immunity and illness, insomnia, longevity and survival, neuroticism, *pain* and injury, reproductive success, sex differences, social interactions, stress and threat

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Word count abstracts: 98/224
Word count main text: 13,999
Word count references: 7,467
Word count total: 21,465

Short Abstract

We extend Anne Campbell's "staying alive" theory by testing the hypothesis that human females produce stronger self-protective reactions than males not only to aggression but to threats in general. We found that females more than males tend to demonstrate heightened reactions to physical threats (e.g., immune activation, pain, nighttime awakenings, dangerous external stimuli); exert greater efforts to reduce social conflicts; exhibit a personality style geared more towards identifying danger; experience enhanced emotional reactions to threat; and develop threat-induced clinical conditions. Our findings suggest that human females have stronger self-protective reactions than males do, constituting an adaptive survival strategy.

https://doi.org/10.1017/S0140525X21002417

Long Abstract

Many male traits are well explained by sexual selection theory as adaptations to mating competition and mate choice, whereas no unifying theory explains traits expressed more in females. Anne Campbell's "staying alive" theory proposed that human females produce stronger self-protective reactions than males to aggressive threats because self-protection tends to have higher fitness value for females than males. We examined whether Campbell's theory has more general applicability by considering whether human females respond with greater self-protectiveness than males to other threats beyond aggression. We searched the literature for physiological, behavioral, and emotional responses to major physical and social threats, and found consistent support for females' responding with greater self-protectiveness than males. Females mount stronger immune responses to many pathogens; experience a lower threshold to detect, and lesser tolerance of, pain; awaken more frequently at night; express greater concern about physically dangerous stimuli; exert more effort to avoid social conflicts; exhibit a personality style more focused on life's dangers; react to threats with greater fear, disgust and sadness; and develop more threat-based clinical conditions than males. Our findings suggest that in relation to threat human females have relatively heightened protective reactions compared to males. The pervasiveness of this result across multiple domains suggests that general mechanisms might exist underlying females' unique adaptations. An understanding of such processes would enhance knowledge of female health and well-being.

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1.0 Introduction

Across diverse, contemporary human societies, numerous sex differences appear in physiology, behavior, and experiences that often vary in magnitude depending on the culture (Archer, 2019; Berenbaum & Beltz, 2021; Geary, 2021; Hyde, 2005; Wizeman & Pardue, 2001; Wood & Eagly, 2002; Zell et al., 2015). An evolutionary explanation for these differences relies on sexual selection theory.

Sexual selection occurs when one sex, usually the female, invests more in offspring, and the other sex, typically the male, invests more in mating competition (Darwin, 1871; Janicke et al., 2016; Trivers, 1972). When applied to humans, sexual selection theory has produced many explanations and testable predictions regarding the reproductive benefits of males' competitive strategies, including direct competition, physical aggression, risk-taking, showing off, impulsivity, sensation-seeking, and resource accumulation (Archer, 2009, 2019; Walter et al., 2020). Because such behaviors can improve males' ability to succeed in mating competition, they constitute part of an optimal strategy for fitness maximization even when they reduce survival. Mating competition thus accounts for many "male traits" (those that are expressed more in males than females).

In contrast to male traits, evolutionary theorists have tended to explain female traits in a more piecemeal manner. At least four theories related to sexual selection commonly have been applied to understanding female traits: mating competition, social selection, parental investment, and (in humans) "staying alive" theory.

The mating competition component of sexual selection theory explains female traits as adaptations for either defeating other females in conflicts over mates or being chosen as mates by males (Janicke et al., 2016). In humans, a high quality mate can enhance a woman's fitness through providing resources,

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protection, support, and/or good genes (Campbell, 2004). Human females' competitive strategies to attract high-quality males rarely involve direct competition, but instead rely more on self-promotion (Blake et al., 2018; Puts, 2010) and indirect tactics including denigration of competitors' reputations and social exclusion (Archer, 2004; Campbell, 2004; Hess et al., 2010; Reynolds, 2021).

Social selection theory applied to females emphasizes contests against other females for resources, territory, or allies (Clutton-Brock, 2007; Stockley & Bro-Jørgensen, 2010). Again, direct contests are relatively uncommon in humans (Campbell, 2004). Instead, human females frequently compete for resources and allies utilizing indirect tactics as in mating competition (Björkqvist, 1994; Burbank, 1987; Campbell, 2004; Jankowiak et al., 2005; Rucas, 2017).

Parental investment theory focuses on how adults, typically females, provide optimal levels of care for their young (Trivers, 1972). The theory examines adaptations that maximize production and survival of offspring independent of mating relationships, including optimizing interbirth intervals, manipulating sex ratios, and aborting embryos or infanticide (Hrdy, 1981; Trivers, 1974; Trivers & Willard, 1973). Parental investment theory has been applied fruitfully to humans to explain diverse patterns of mothering (Hrdy, 1999).

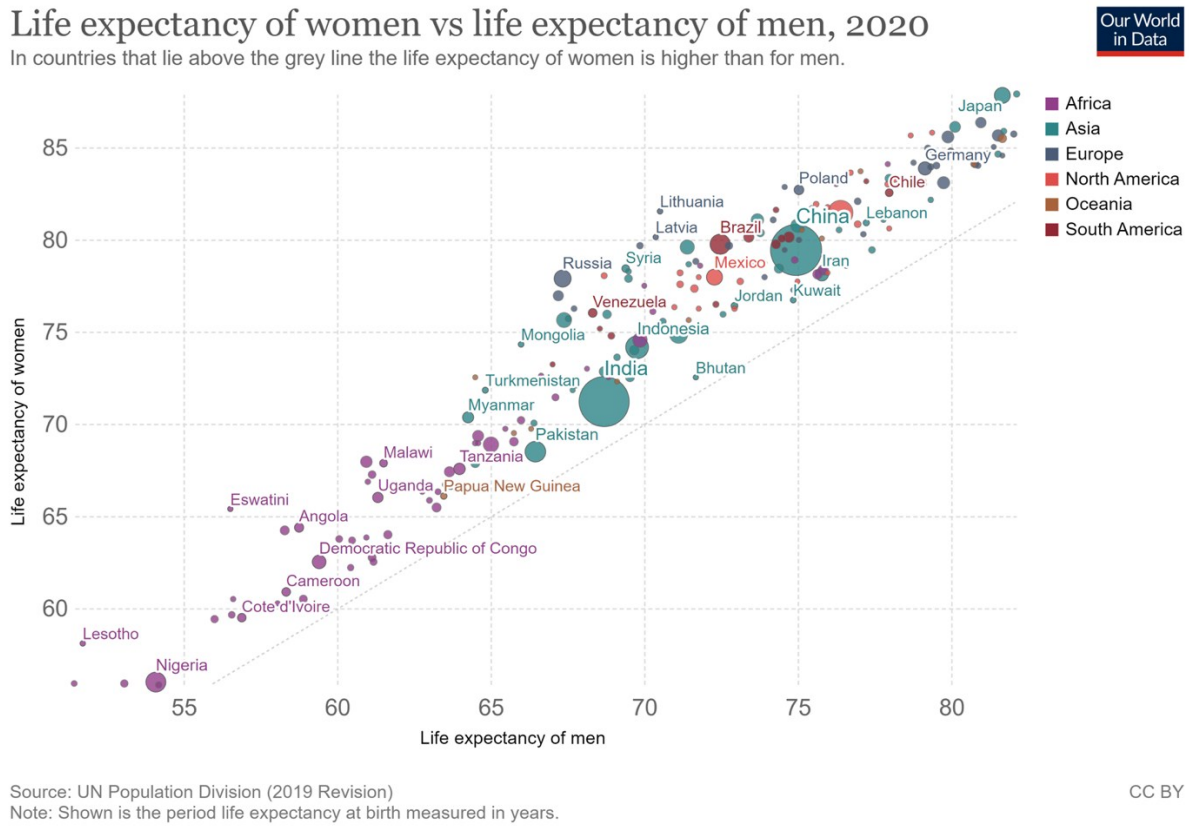
Building on parental investment theory, Anne Campbell (1999) proposed "staying alive" theory (SAT). She posited that survival is more fitness-enhancing for females than males, and therefore that human females more than males evolved to avoid physical aggression and invest in alternative traits. Campbell (1999) emphasized "that lower rates of aggression by women reflect not just the absence of male risk-taking but are part of a positive female adaptation driven by the critical importance of the mother's survival for her own reproductive success" (p. 204). Campbell focused on fear as the critical mechanism

https://doi.org/10.1017/S0140525X21002417

that protects females from injurious forms of aggression, and found that females indeed tend to be more fearful than males.

Here we examine whether Campbell's theory has more general applicability by considering the hypothesis that compared to males, human females respond with greater protectiveness to other threats beyond aggression. We define threat as anything potentially damaging to an individual's survival.

Campbell's (1999) assumption that survival is more fitness-enhancing for females than males predicts that females tend to outlive males. In support, despite large cultural variations, in virtually every country women outlive men as shown in Figure 1 for 2020 (Roser et al., 2013):



A similar tendency for females to live longer than males is found in mammals (Lemaître et al., 2020).

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SAT also predicts that the sex difference in longevity has evolved at least partly because of the benefits that offspring receive from female care, assuming that females contribute more than males to offspring survival. Studies of contemporary societies from hunter-gatherers to Western, Educated, Industrialized, Rich, and Developed (WEIRD) nations (Henrich, 2020) confirm females' greater investment in and contribution to offspring survival (Atrash, 2011; Hawkes et al., 2018; Sear & Mace, 2008). According to Wood and Eagly's (2002) analysis of 186 geographically and culturally diverse non-industrial societies from the Human Relations Area Files, "all of the cultures in our review revealed an alliance between men and women in a division of labor, which appeared to be organized primarily to enable mothers to bear children and nurse and care for infants" (p. 718). Mothers were the principal caregivers of infants in 92% of these societies (and simultaneously of young children in 26%-70% of these societies), whereas fathers and other men never were. Further, across six hunter-gatherer or horticulturalist societies, excluding nighttime co-sleeping, mothers took care of infants between 46-53% of the day and fathers between 0-6%, with older siblings, grandmothers, and others comprising the additional caregivers (Kramer, 2005).

Besides mothers, female kin, especially grandmothers and older daughters, most often helped mothers with childcare (Wood & Eagly, 2002). Grandmothers have been found to be particularly important for increasing grandchildren's survival, more so than grandfathers (Hawkes et al., 2018; Lahdenpera et al., 2004; Sear & Mace, 2008). A high adaptive value of grand-mothering is suggested by eight mammalian species in which females contribute to caring for their grand-offspring, because females' lifespans in those species averaged 43% longer than males, compared to only 8% longer in related species without grand-mothering (Péron et al., 2019).

Older daughters also help mothers (Bove et al., 2002; Kramer, 2005; Whiting et al., 1988). Across 13 traditional societies, girls were more likely than boys to assist in direct care for younger siblings (Whiting

et al., 1988). In six hunter-gatherer or horticulturalist societies, girls cared for younger siblings between 13-33% of the day, with boys childminding 1-14% of the day (Kramer, 2005). In WEIRD societies where children rarely care for younger siblings, girls more than boys cared for dolls [d=4.12] (Davis & Hines, 2020). In non-human primates, preadult females also attend to and hold infants more than males do (Benenson, 2019).

These data support the idea that the greater longevity of females than males is an evolutionary response to women's larger role in childcare, such that at all ages selection tends to favor female survival. Thus, females and males confront different life history tradeoffs, with the sex that cares for offspring investing more in survival (Hamilton, 1966; Kirkwood & Rose, 1991; Trivers, 1972; Williams, 1966). Preliminary evidence in mammals also links higher female longevity with greater female, relative to male, parental care (Allman et al., 1998).

To evaluate the applicability of Campbell's (1999) theory to threats beyond aggression, we searched for articles that analyzed sex differences in response to major threats to survival: internal and external physical dangers, social conflicts, personality styles, emotional reactions to threat, and threat-related clinical conditions. We surveyed highly cited reviews, meta-analyses, and articles that examined human sex differences with large samples from diverse countries, along with authoritative references such as the World Health Organization (WHO) and the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-V). We report sample sizes, effect sizes based on Hyde's (2005) cutoffs, and developmental effects when these were available. Because many fewer elderly men than women are alive thereby introducing confounds into sex-based comparisons, we focused on young and middle-aged adults. Further, because female investment in childcare increases sharply after puberty, we predicted increased magnitudes of sex differences following puberty and searched for evidence comparing children with

adolescents. We included only high-quality datasets for each kind of threat and searched for inconsistencies with other published findings. Following Campbell (1999), we included only self-protective reactions to threat, rather than reactions that *increase* the potential for harm, such as impulsivity, sensation-seeking, risk-taking, direct aggression, or homicide which are well-known to be less common in females than males (Archer, 2019). Additionally, we reviewed Hyde's (2005), Zell, Krizan, and Teeter's (2015), and Archer's (2019) meta-analytic summaries of sex differences to identify any additional protective reactions to threats or contrary findings. All sex differences we report were statistically significant unless otherwise stated.

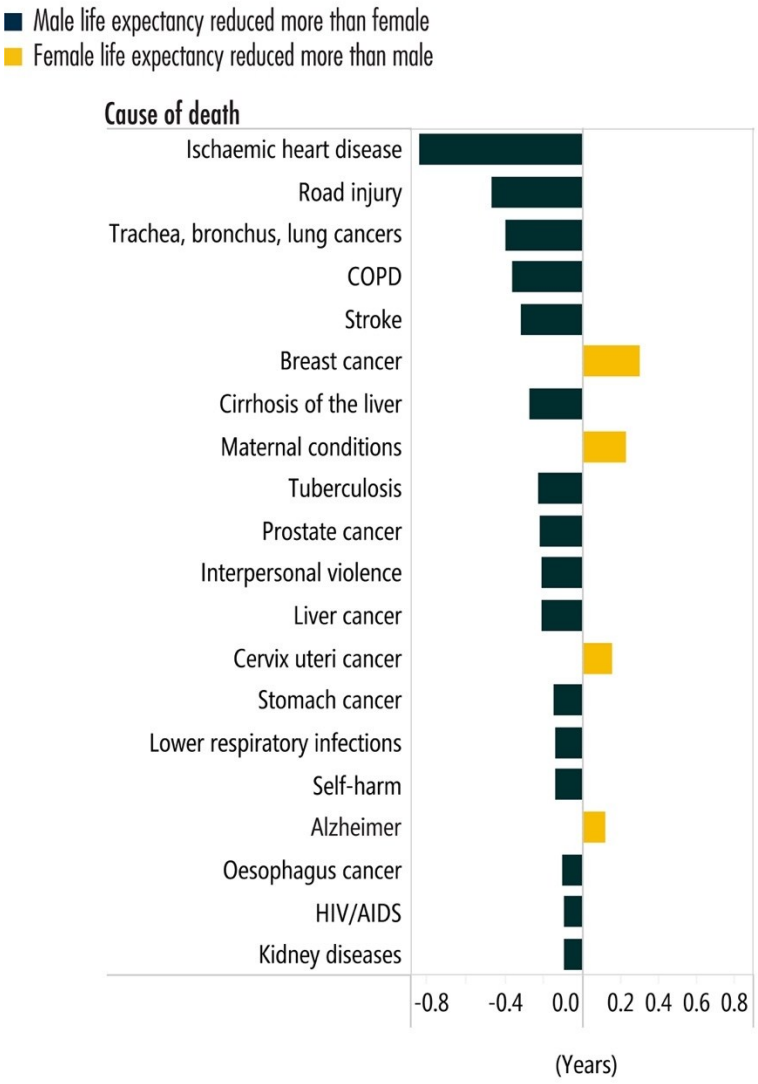
We recognize that human sex is a multidimensional construct influenced by the continuing interplay of biological and environmental components and that the studies we found are limited by including only binary comparisons (Berenbaum & Beltz, 2021; Eliot, 2009; Fausto-Sterling, 2019; Hyde et al., 2019). We also acknowledge that many sex differences in specific traits are small, so that sex stereotypes based on single traits mischaracterize the large overlap between the sexes (Hyde, 2005; Zell et al., 2015). Our goal is to suggest that many female-associated traits, which are often pathologized in comparison to male-related traits, can more appropriately be considered, like most evolved features, to enhance females' survival and reproductive success.

2. Protective Responses to Physical Threat

According to our extension of SAT, females should protect themselves more than males in response to all physical threats. We therefore tested the hypothesis that females exhibit stronger defenses than males against pathogens, bodily damage, and environmental dangers.

Recent cross-cultural evidence shows that females were less likely than males to die from disease at every age. The major causes of sex differences in mortality worldwide are shown in Figure 2 with disease the most common contributor (WHO, 2019):

Causes of death that most contribute to differences in life expectancy at birth globally for men and women, 2016



Sources: WHO (2018) *(2)* and see *(4)* for decomposition of life expectancy.

Excluding reproductive-related conditions, the fatal illnesses that contributed most to reducing life expectancy afflicted females less frequently or later in life than males (Austad, 2006; Verbrugge, 1985). Thus, females were less likely than males to develop many diseases, including malaria, leptospirosis,

schistosomiasis, brucellosis, rabies, leishmaniasis, pulmonary tuberculosis, hepatitis A, meningococcal and pneumococcal infections (Giefing-Kröll et al., 2015; Mihailova & Krams, 2018).

When females developed fatal diseases, they died later than males with small to moderate effect sizes. As examples, adjusting for age, worldwide in 2021 the odds of dying from lung [OR=.46], colorectal [OR=.68], and stomach [OR=.45] cancer were lower for women than men (WHO, 2021). In the USA in 2007, the age-adjusted odds of dying from cardiovascular disease (CVD) were lower for females than males [OR=.70] (Mosca et al., 2011). In the USA in 2010, females' age-adjusted death rate was lower than males' for 12 of the most frequent 15 diseases. Two were equal, while only Alzheimer's disease killed more women than men (Austad & Bartke, 2016). Mortality from the COVID-19 pandemic epitomizes the overall pattern: In 37/38 countries fewer women than men died (Scully et al., 2020) with an effect size [OR=.63] (Williamson et al., 2020). Sex differences in fatality rates from COVID-19 appeared even in mice (Scully et al., 2020). Overall, therefore, females are better protected than males from death by disease.

2.1. Immune defenses. Since immune activation is necessary for survival, SAT predicts that females should exhibit more effective immune responses than males. This prediction is upheld in vertebrates generally.

Across most vertebrate species, females are better able than males to defend themselves against a majority of environmental and vector-borne threats, including fungi, viruses, bacteria, parasites and allergens, as well as internal threats such as tissue damage and tumors (Giefing-Kröll et al., 2015; Klein, 2000; Klein & Flanagan, 2016; Oertelt-Prigione, 2012; Ortona et al., 2019). Females' immune systems also respond better than males' to trauma, sepsis, and shock (Angele et al., 2006; Angele et al., 2014). In

response to injury, estrogen administration has been shown to promote healing by upregulating the immune system and reducing morbidity and mortality (Angele et al., 2014; Bösch et al., 2018). The American National Health and Nutrition Examination Survey (n=38,000) from 1988-2006 of demographically representative adults showed that women exhibited a stronger immune response than men, as indicated by a higher inflammatory rate, with a large effect size [OR=4.17] (Yang & Kozloski, 2011).

The immune system functions in two waves (Roved et al., 2017). First, the general, continually active, costly, rapid, innate part of the immune system responds to a new infection or inflammation. Second, cytokines released by the innate immune system ramp up the adaptive immune system through increased cell-mediated T and humoral-situated B cells which are capable of remembering specific antigens, thereby creating longer-term protection. The type of adaptive immune response varies with T-helper (Th) cells, with one type (Th1, Th2, or Th17) increasing at the expense of another. Th1 immune cells typically produce pro-inflammatory responses that clear infections, whereas Th2 cells produce anti-inflammatory immune responses.

Part of the reason for female mammals' stronger immune response is that the X chromosome encodes more immune-related genes than the Y chromosome, and females have two X chromosomes while males have only one (Klein & Flanagan, 2016). Further, in females one X chromosome typically is randomly inactivated in each cell meaning that females are mosaics permitting increased transcription by both X chromosomes to contribute to immunity. Additionally, some X chromosomes escape inactivation also providing extra immunity (Takahashi & Iwasaki, 2021). In mice, experimentally adding an X chromosome to an XY individual to create an XXY individual increases longevity (Davis et al., 2019).

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Another reason for females' stronger immune defenses is their higher estrogen and lower androgen levels. Estrogens intricately regulate immunity by both stimulating and suppressing differing types of immune cells, while androgens generally reduce immune functioning (Foo et al., 2017; Klein & Flanagan, 2016; Roved et al., 2017). Differing concentrations of estrogens can regulate the balance between T-helper cells-2 (Th2) and Th1 and Th17 cells. In contrast, androgens reduce Th2 and Th17 immune processes.

Estrogen levels are not solely responsible for enhanced immunity however, because even pre-pubertal girls activated stronger innate responses than boys, though some sex differences did not appear until puberty (Klein & Flanagan, 2016). After puberty, more components of both the innate and adaptive immune systems were upregulated in women than in men.

Some of the clearest evidence for females' stronger inflammatory response comes from reactions to vaccinations. In response to most vaccinations including influenza, pneumonia, hepatitis A and B, tetanus, diptheria, measles, meningitis, rabies, yellow fever, and smallpox, especially after puberty, human females generally produced more antibodies, and experienced more side effects including fever, soreness, and redness, than males (Flanagan et al., 2017; Klein et al., 2010). Immune responses were more suppressed in older individuals, but the suppression developed more slowly in women than men. Immune response to vaccines were so much stronger in women than men that for a number of vaccines, half the dose of a vaccination in women caused the same level of antibodies as a full dose in men (Giefing-Kröll et al., 2015). While ceiling effects in vaccine efficacy obscure sex differences, when differences appeared, vaccines were more effective in females (Flanagan et al., 2017). However, when vaccine doses were too strong, females were more likely to die from the vaccine (Flanagan et al., 2011), as happened in some African infant inoculation campaigns (Aaby et al., 2020). Further, a higher

concentration of circulating estrogens was positively related to stronger responses to vaccines in humans and mice (Aaby et al., 2020). Figure 3 summarizes some of the human findings (Flanagan et al., 2017):

Sex differences in acceptance, immune responses, and adverse reactions to vaccines in humans

Target group	Vaccine	Gender difference in acceptance	Sex difference in immune response	Sex and gender difference in adverse reactions	Age (years)
Children	Hepatitis B	Not defined	Greater in females	Not defined	< 12
	Diphtheria	Not defined	Greater in females	Not defined	< 2
	Pertussis	Not defined	Greater in females	Not defined	< 2
	Pneumococcal	Not defined	Greater in females	Not defined	6–9
	Rabies	Not defined	Greater in females	Not defined	6–9
	Measles	Not defined	Greater in females or equivalent in both sexes	Increased in females	< 3
	Malaria (RTS,S)	Not defined	Greater in females	Increased in females	< 2
	Human papillomavirus	Less in males	Greater in females	Increased in females	5–17
Adults	Influenza	Less in females	Greater in females	Increased in females	18–49
	Hepatitis B	Not defined	Greater in females	Increased in females	18+
	Herpes virus	Not defined	Greater in females	Not defined	18+
	Yellow fever	Not defined	Greater in females	Increased in females	18+
	Rabies	Not defined	Greater in females	Not defined	18+
	Smallpox	Not defined	Greater in females	Not defined	18+
Aged adults	Influenza	Less in females	Greater in females	Increased in females	65+
	Td/Tdap	Less in females	Greater in males	Increased in females	65+
	Pneumococcal	Less in females	Greater in males	Increased in females	65+
	Shingles	Not defined	Not defined	Increased in females	65+

Results with mice demonstrated causality. In mice inoculated against H1N1, females produced more robust IgG and IgA antibodies and B cells and higher quality antibodies than males. When these mice were infected with H1N1, females became less sick, had a lower viral load in their lungs, and recovered more rapidly than males (Fink et al., 2018). Observations of people infected with COVID-19 similarly showed that women with higher antibody levels tended to be less sick (Takahashi et al., 2020).

Pregnancy illustrates the strength of the immune system in non-pregnant women. During pregnancy, myriad changes occur in the innate and adaptive immune systems that affect maternal and fetal responses to pathogens (Abu-Raya et al., 2020). A pregnant woman's immune system must find an

optimal way to balance ensuring survival of the genetically foreign fetus with protecting herself and the fetus from pathogens. One way this occurs is by downregulating Th1 cells producing pro-inflammatory cytokines. This switches the preponderance to Th2 cells producing anti-inflammatory cytokines. Sex hormones, including estrogens and progesterone, regulate the balance between Th1 and Th2 lymphocytes so that across pregnancy proinflammatory responses diminish and anti-inflammatory responses increase (Robinson & Klein, 2012).

The result is that pregnant women were more susceptible than non-pregnant women to, and/or suffer more severe, including fatal, reactions to infections from pathogens, including malaria, tuberculosis, influenza, hepatitis E, invasive pneumonia, herpes simplex virus, Ebola, and measles. In contrast, the severity of inflammatory diseases such as multiple sclerosis and arthritis were reduced (Abu-Raya et al., 2020). Increased maternal morbidity and mortality during pregnancy also occurred with recent severe acute respiratory viruses (H1N1, SARS and MERS) (Schwartz, 2020), including COVID-19 (Zambrano et al., 2020).

Stronger activation of non-pregnant females' immune system however has a downside labelled "the health-survival paradox." Despite their greater longevity, women felt sicker and were diagnosed with more illnesses than men across North America and Europe, and in Egypt, China, Indonesia, Mexico and the Tsimane of Bolivia (Alberts et al., 2014; Austad & Bartke, 2016; Christensen et al., 2009; Khadr & Yount, 2012; Macintyre et al., 1999; Mirowsky & Ross, 1995; Roved et al., 2017; Wheaton & Crimmins, 2016).

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Older women from culturally diverse societies including the Tsimane of Bolivia, Taiwan, Korea, Mexico, China, Indonesia, reported being sicker and weaker and were evaluated objectively by medical personnel and researchers to be in poorer health than men.

> "For instance, women in high-income countries are more likely than men to report difficulties in walking, climbing stairs, dressing, and other common activities. In low-income countries, women report greater difficulties than men in a wide range of common activities such as bending over, pumping water, or walking a specified distance. In addition, women make more doctor visits, spend more days hospitalized, and take more medications than do men …. Even in Russia, which has one of the largest sex differences in life expectancy in the world, with a male disadvantage of more than 10 years, males report better health and physical functioning at ages of 55 years and higher …." (Austad & Batke, 2015, p. 42).

In 20th century American nationwide statistics, at all ages women experienced fewer fatal conditions than men, but suffered from more frequent daily symptoms, and more acute (except for injuries) and chronic and disabling conditions as diagnosed by doctors and in hospitals. The sex difference was largest during young adulthood, even after all reproduction-related conditions were excluded. Women reported more daily symptoms, more days with symptoms, more days in bed, more disability days, more health problems across more bodily systems, more prescription drug use, more alternative care visits, and more frequent discussions about their health problems with family and friends (Verbrugge, 1976, 1985, 1986, 1989).

The sex difference in prevalence of immune activation increased at puberty but appeared by early childhood. In a large study of Norwegian adolescents (n=10,000, ages 17–19 years), 47% of girls versus 21% of boys [OR=3.34] reported at least one weekly health complaint (Myrtveit Sæther et al., 2018). Two weekly health complaints were reported by 30% of girls and 10% of boys [OR=3.86]. Employing the Health Behaviour in School-Aged Children (HBSC) scale, a WHO study in 32 countries in Europe and North America plus Israel (n=1,500 each nation at ages 11, 13, and 15 years, n>150,000) found that girls reported poorer general health than boys at ages 11 [OR=1.36], 13 [OR=1.68] and 15 years [OR=1.97]

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(Cavallo et al., 2006). Likewise in the Avon Longitudinal Study of Parents and Children (ALSPAC) (n>13,900), pregnant women in 1991-1992 in Southwestern England were recruited and later asked to report symptoms experienced by their 4-13 year-old children (Sweeting et al., 2017). From 4 years onwards, more girls than boys experienced colds, cold sores, tonsillitis, urinary infections, earaches, headaches, stomachaches, worm infections, head lice or scabies, constipation, and eczema. Beginning at age 7, more girls than boys experienced rashes, and by 10 years, more girls than boys developed fevers, ear and eye infections, and were struggling with poorer overall health. In contrast, in childhood boys were more likely than girls to suffer chest infections, breathlessness, wheezing, asthma, hay fever, pain in legs and joints, and diarrhea. After puberty, most of boys' excess health problems disappeared with girls then experiencing these problems equally or more frequently.

In summary, evidence supported the hypothesis that with the exception of pregnancy, human females mounted stronger and longer-lasting immune responses than males.

2.2. Preventing injury through the sensation of pain. Pain signals potential danger or actual damage typically following inflammation or trauma (Eisenberger & Lieberman, 2004). It therefore constitutes a critical self-protective warning mechanism and ongoing monitoring system that impels corrective action to protect an organism (Grahek, 2001). A heightened sensation of pain should reduce the prevalence of injury and repair damage from an already sustained injury by behaviorally removing or reducing pain-inducing stimuli, thereby enhancing survival. We therefore searched the literature to test the hypothesis that females experience greater pain than males.

Fillingim et al. (2009) reviewed clinical and experimental pain studies across diverse countries including rural Brazil, India, Nigeria, Turkey, as well as in European and North American nations. They found that in

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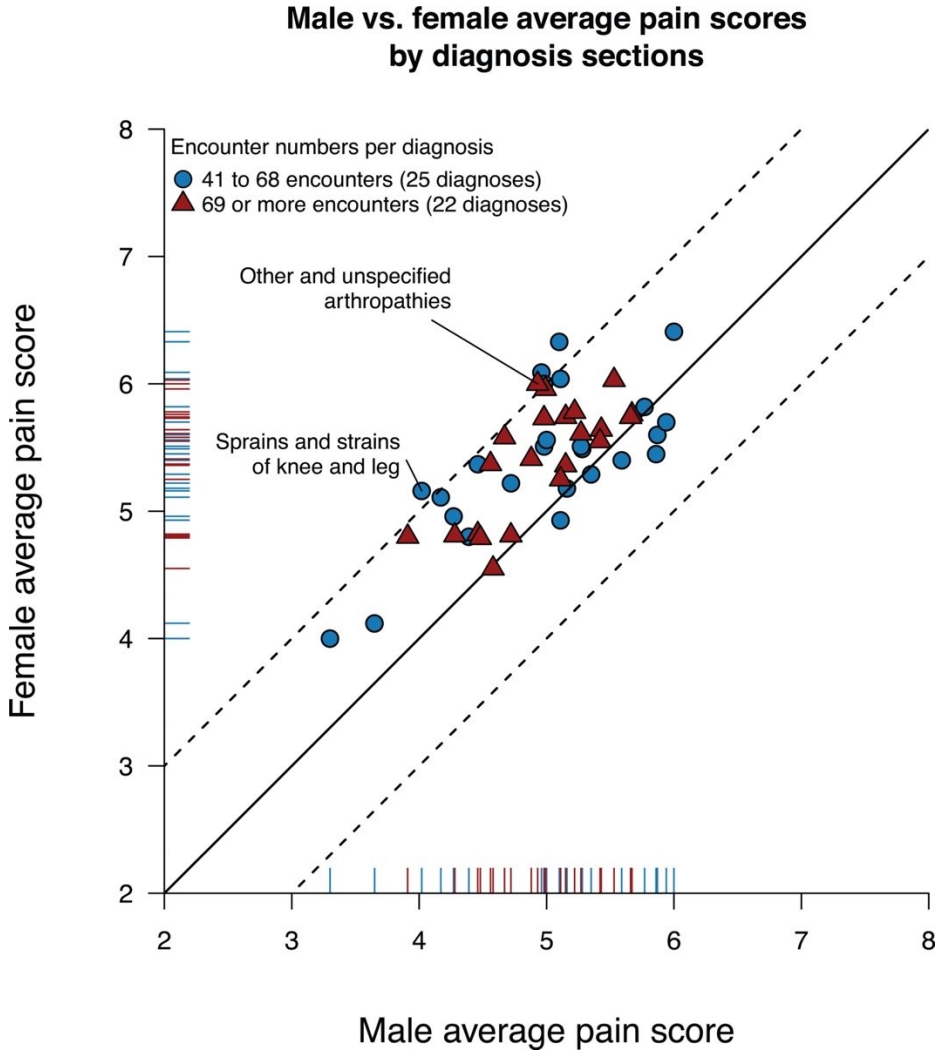
their daily lives, more women than men reported higher pain prevalence at all sites in the body in the prior week or day, including oral, abdominal, and head pain. Women experienced pain more than men from a variety of sources and across multiple bodily sites, including from cancer, neuropathic, musculoskeletal, and back pain. Likewise in a detailed study of 11,000 patients with 47 diagnoses in an American hospital, patient-reported or practitioner-rated pain scores were higher for women than men for the same diagnosis as pictured in Figure 4 (Ruau et al., 2012):



The same sex difference appeared also for chronic, widespread pain. Mansfield et al. (2016) reviewed studies of chronic widespread pain in diverse countries including North and South America, the Middle East, Europe, Oceania, and Asia. Chronic widespread pain was reported more frequently by women than men on average by a 2:1 margin with large variation across ages and cultures and female:male ratios ranging from 1.06-4.80.

Even during simple intramuscular injections, women experienced more pain than men (Fillingim et al., 2009). While this may be partially due to women's lower muscle density and tissue mass, even 5-year-old girls reported more pain than boys to venipuncture (Chambers et al., 1999).

Sex differences in pain emerge in childhood. The WHO HBSC study in 32 countries in Europe, North America, and Israel (n>150,000) found that more girls than boys experienced headaches at age 11 years, 13 years, and 15 years respectively [ORs=1.44, 1.88, 2.70], stomachaches [ORs=1.64, 2.00, 2.31], and backaches [ORs=1.16, 1.24, 1.28] (Cavallo et al., 2006). Likewise, the English ALSPAC study found that beginning with the youngest children in their study (age 4 years), girls reported more headaches, stomachaches and earaches than boys did (Sweeting et al., 2017). Chronic pain also was reported in childhood by females more than males (Fillingim et al., 2009).

Similar sex differences in responses to pain were found in mice and rats (Mogil, 2020). Rodent studies of the midbrain periaqueductal gray and the spinal cord showed that pain and analgesics are modulated differently in females than males (Shansky & Murphy, 2021).

In experimental studies that induce pain using identical stimuli, women consistently responded to bodily injury faster and endured it less long than men did across multiple bodily sites and modalities of inflicting

pain (Fillingim et al., 2009). In a meta-analysis of pain threshold (n>1,600) and pain tolerance (n>41,500) for pressure, heat, electrical shock, and ischemic induced pain, women endured pain at a lower stimulus intensity [d=.51] and for a shorter time period [d=1.17] than men, yielding moderate to large effect sizes (Riley et al., 1998). The sex difference in pain diminished in old age but never disappeared (Girotti et al., 2019).

In experimental tests with children, a meta-analysis showed few sex differences (Boerner et al., 2014). Overall, no sex differences were found in responses to pain intensity, and only 31% of studies found that girls exhibited lower pain thresholds than boys. Some specific types of pain, such as pain due to heat however, produced the same sex differences as in adolescents and adults.

In sum, adult females routinely experience greater pain than males. This suggests that a stronger experience of pain constitutes a female adaptation that functions to enhance survival through reducing injury. In support, the Global Burden of Disease findings showed that disability adjusted lost years (DALYs) from all types of injuries were typically lower for females than males for ages 15-49 years, as displayed in Figure 5 (Haagsma et al., 2016):

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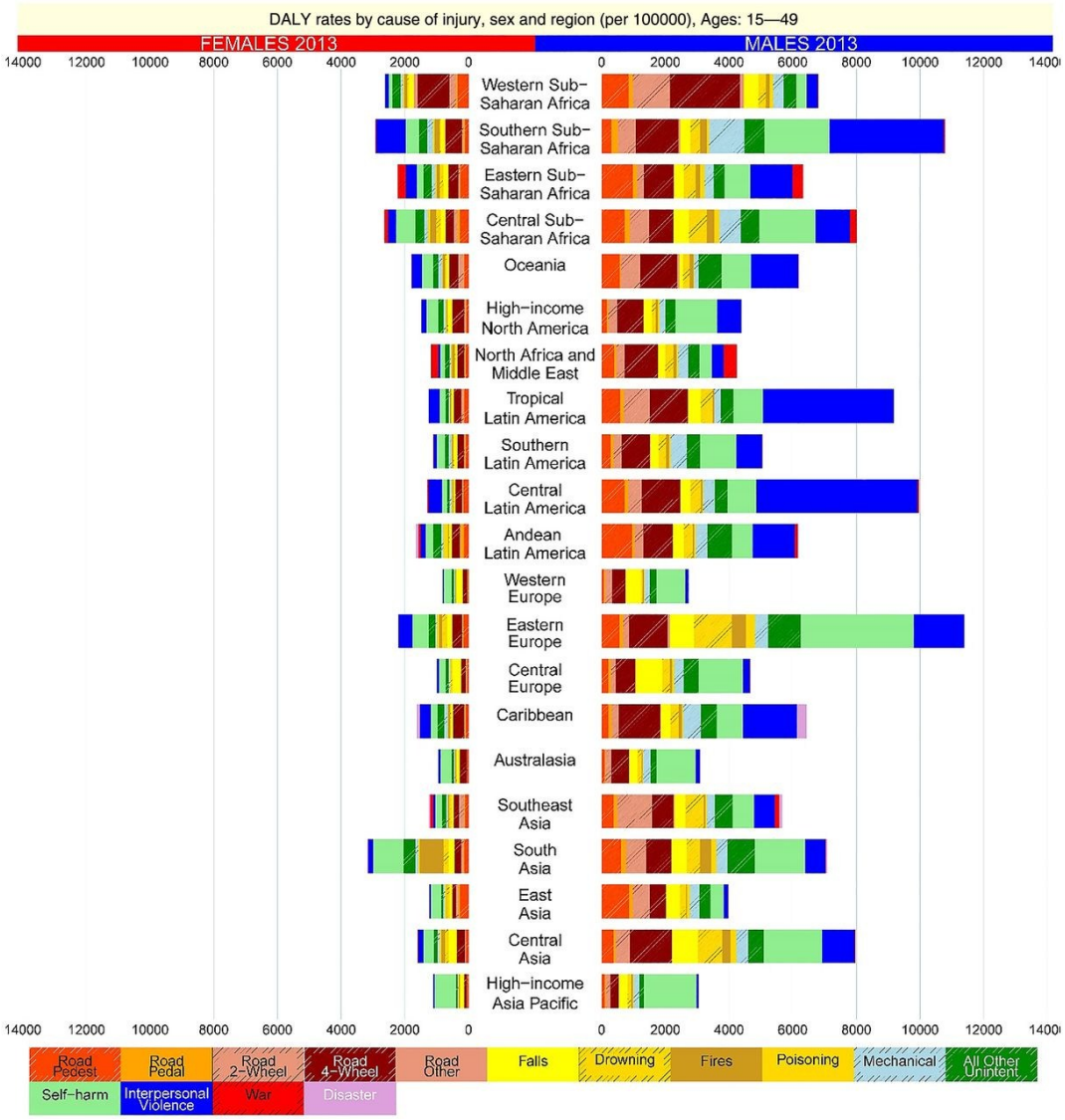

The sex difference was smaller but in the same direction for children 0-14 years. From 1990-2017, the same sex difference for adults in DALYs appeared globally for injuries from all causes except heat (James et al., 2020). Likewise, in the WHO HBSC study with 15-year-olds in 36 European and North American countries, girls reported fewer injuries overall than boys in the prior year and fewer physical fights (de Looze et al., 2019).

2.3. Countering nighttime threats through frequent awakening. Nighttime is a dangerous period because threats are not easily detected. Increased nighttime vigilance improves detection of physical and social threats, including intruders, predators, and fire, that could elude identification during sleep. Accordingly, we tested the prediction from SAT that females are more attuned than males to nighttime threats.

We found that worldwide women reported being awake at night more often than men did. The American Society for Women's Health Research concluded that women's sleep differed objectively and subjectively from men's (Mallampalli & Carter, 2014): women experienced more slow wave sleep and less non-REM sleep than men. Women also experienced longer sleep latency and reported feeling sleepier than men. Further, across humans, mice and rats, sex hormones affected females' more than males' sleep (Hajali et al., 2019; Mallampalli & Carter, 2014).

A meta-analysis (n>1.2 million, ages 15–103 years) from diverse countries of sex differences in sleep disturbances illustrated the findings: In 26 of 29 studies, at all ages women reported more frequent nighttime awakening than men [Risk Ratio=1.41] (Zhang & Wing, 2006). The Chinese Henan Rural Cohort Study (n>27,000, ages 18-79 years) employing the Pittsburgh Sleep Quality Index found that females experienced lower sleep quality than males with effect sizes ranging from negligible to small for subjective sleep quality [d = -.20], sleep latency [d=.21], sleep duration [d = -.03], sleep efficiency [d = -.13], sleep disturbance [d=.15], use of sleep medication [d=.08], daytime dysfunction [d=.08], and generally [d=.22] (Wang et al., 2019).

Globally, following puberty women had a 40% higher risk than men of developing insomnia during their lifetimes as depicted in Figure 6 (Mong & Cusmano, 2016):

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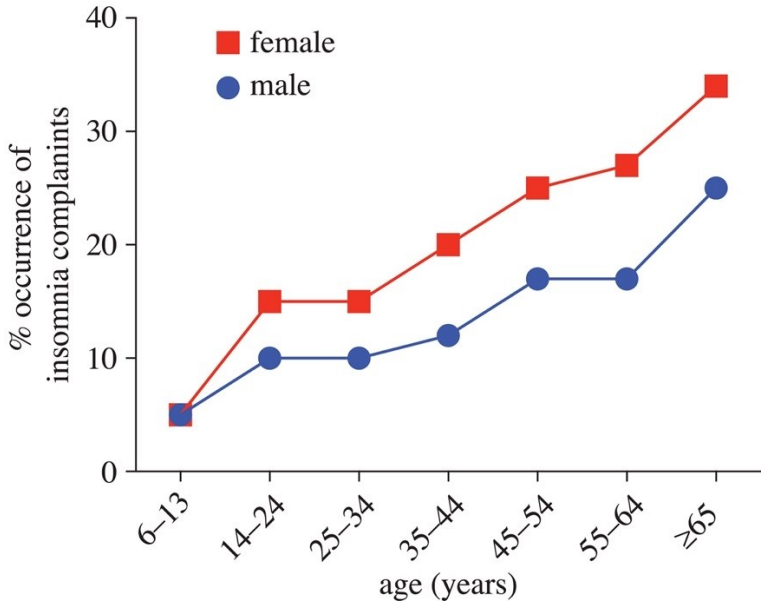
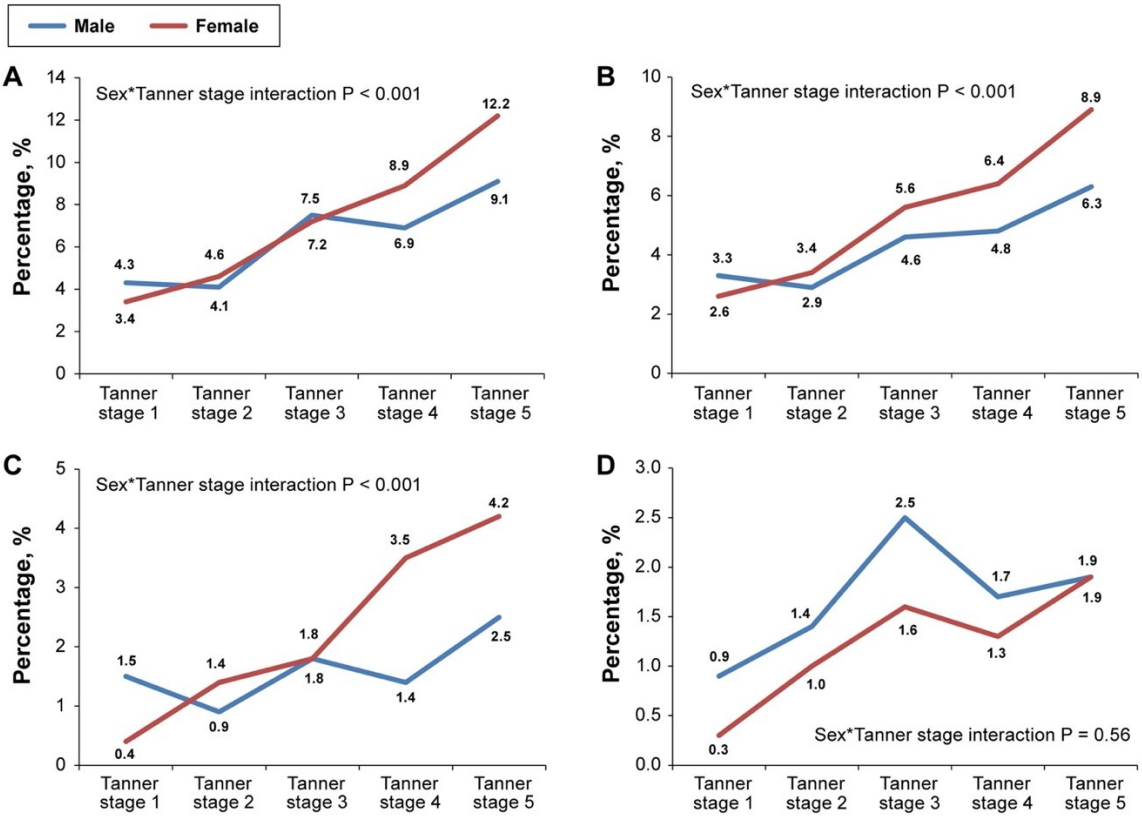


Furthermore, a meta-analysis (n>180,000) showed that more females than males experienced nightmares with negligible to small effect sizes in adolescents [Hedge's g=.22], young adults [g=.26], and in middle age [g=.15]. The sex difference was not significant for children [g=-.03], or >60 years [g=.10] (Schredl & Reinhard, 2011).

Although sex differences in nighttime awakenings were negligible to small for children, they increased with age and pubertal status. In the 32 country WHO HBSC survey, girls reported increasing sleep difficulties relative to boys at 11, 13, and 15 years of age [ORs=1.13, 1.36, 1.56, respectively] (Cavallo et al., 2006). A study in Hong Kong (n>7,500 ages 6–17 years) linked pubertal development to specific sleep disturbances (Zhang et al., 2016). Children and adolescents, and their caregivers, reported that girls developed more overall insomnia, difficulty initiating sleep, and difficulty maintaining sleep than boys as they entered pubertal stage 4 on the Tanner scale, although they already had experienced more difficulties with early morning awakening as displayed in Figure 7:



Overall, evidence supported the hypothesis that females experienced more nighttime awakenings than males. This is consistent with the hypothesis that nighttime awakenings constitute a female adaptation that enhanced self-protection during an interval of heightened vulnerability.

We also noted that women were less likely than men to suffer from severe, potentially fatal sleep disorders including narcolepsy, obstructive sleep apnea, and hypoventilation (Hajali et al., 2019; Lévy et al., 2015). Furthermore, laboratory studies of sleep indicated that length, depth, and efficiency of sleep, including enhanced slow wave sleep and slow wave activity, were higher in women than men (Hajali et al., 2019; Mong & Cusmano, 2016; Suh et al., 2018). While these observations are limited to Western

research, they suggest that females might compensate for their more frequent awakenings by maintaining a superior quality of sleep.

2.4. Miscellaneous physical threats. Innumerable external physical stimuli threaten survival. We tested the hypothesis, derived from SAT, that females would be more effective than males at avoiding or reducing such threats. We were able to locate evidence for three types of threat: hypothetical physical threats, long-term environmental degradation, and major disease outbreaks.

In the standardized International Affective Picture System (IAPS), participants evaluated the valence of photographs of non-human animals, scenes, and inanimate objects. In the US, Germany, Switzerland, and China, girls and women reported stronger aversion than their male counterparts to all represented threats, including accidents, illness, pollution, and dangerous animals (Bradley et al., 2001; Lang & Bradley, 2007) with moderate to large effect sizes in adults [d=.36] (Gomez et al., 2013), [d=.55] (Gong et al., 2018), [d=.43 and .80] (McManis et al., 2001), and in children [d=.64 and .67] (McManis et al., 2001).

Similar sex differences have been found in response to environmental dangers. In the International Social Survey Programme (ISSP) administered in 1993 and 2000 in 26 countries from Asia, Eastern and Western Europe, North and South America and Oceania (n>23,000), women expressed more concern about the state of the environment than men did (Franzen & Meyer, 2010). Between 2009-2011, an expanded ISSP in 32 nations in Africa, Asia, Europe, North and South America, and Oceania (n>45,000) showed that women exhibited more positive views than men towards protecting the environment, greater awareness of environmental problems, and more willingness to pay to correct environmental problems (Chan et al., 2019).

With regard to major outbreaks of disease, a review with Asian, European and North American participants (n>25,000, 12 countries) showed that during disease outbreaks women reported being more likely than men to adopt avoidant and protective measures, including handwashing, wearing a mask, and quarantining (Bish & Michie, 2010). Across eight OECD countries (n>20,000), women were more likely than men to have perceived COVID-19 as a serious health risk and to have complied with restraining public health rules (Galasso et al., 2020).

Nonetheless, women can be more reluctant than men to receive vaccines, most likely because of the more adverse side effects of vaccines in women than men (Flanagan et al., 2017). A review (37 studies, 15 diverse countries) of reactions to the 2009 strain of H1N1 influenza showed that both women in the general population and female health care professionals indicated they would be less likely than their male counterparts to be vaccinated (Bish et al., 2011). An explanation proposed by Bish et al. (2011) was that women tended to believe that the immediate negative effects of the vaccine outweighed its health benefits, consistent with greater side effects in women. A similar concern about negative effects might explain a meta-analysis (n=88 studies) with African, Asian, Australian, European, North and South American samples, which found that women were 50% more likely than men to have adopted non-pharmacological prevention and avoidant measures in reaction to respiratory pandemics (OR=1.49), whereas men were slightly more likely to take pharmaceutical protections (OR=.89) (Moran & Del Valle, 2016).

Overall, for the environmental threats we examined, women reacted more protectively than men with small to large effect sizes, consistent with a female adaptation for increasing longevity.

3. Protective Responses to Social Threat

Social threat includes at least two distinct types: conflicts and isolation. Social conflicts can be physically dangerous, potentially leading to fights, reputation denigration, ostracism, expulsion, and even capital punishment (Boehm, 1999; Wrangham, 2019). Social isolation predicts psychological and physical morbidity and mortality in young, middle-aged, and elderly adults in a dose-dependent manner (Hawkley & Cacioppo, 2010). A meta-analysis of longitudinal studies (n>3.4 million) showed that objective measures of both social isolation and feeling lonely predicted increased mortality [OR=1.26-1.83] (Holt-Lunstad et al., 2015). The longer the loneliness, the greater the risk. Even experimentally inducing feelings of loneliness increased stress and feelings of danger (Holt-Lunstad et al., 2015).

Conversely, it is well known that social ties increase survival. A meta-analysis of longitudinal findings from Asia, Australia, Europe, and North America in community and patient samples (n>300,000) showed that across sex, age, initial health status, and cause of death, social integration increased survival by 50%, and by 91% using multiple measures of integration (Holt-Lunstad et al., 2010). Similarly, in a large study in Asia, Europe, and North America (n>7.5 million), not being married increased all-cause mortality in both sexes, more for males [Risk Ratio=1.46] than females [Risk Ratio=1.22] (Wang et al., 2020).

SAT would predict that females tend to avoid conflicts and promote social ties more than males do. We found relevant evidence for four strategies that reduce negativity in interactions and facilitate positive connections, namely smiling, politeness, emotion identification, and avoidance of confrontations.

3.1. Smiling. Evidence indicates that women smile more than men with small to moderate effect sizes. A meta-analysis of 162 studies (n>100,000, 13 countries, 6 continents) reported greater smiling by women from adolescence through old age in every country [d=.41] (LaFrance et al., 2003). Sex differences were greater in same-sex pairs [d=.48] than mixed-sex pairs [d=.35]. Sex differences also were larger in

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contexts with greater social tension [d=.47] than little tension [d=.20], and when participants were unfamiliar [d=.45] rather than familiar [d=.24]. This suggested that an important function of smiling was to reduce threats from other individuals. Prior meta-analyses also concluded that women's smiles more than men's function to reduce social tension (Hall & Halberstadt, 1986).

Computerized coding likewise showed that women smiled more than men. Analyses of photographs of Asian, Black, and White New York City residents posted to Instagram and Twitter (n>15,000) demonstrated that the more females in a picture, the more smiling occurred as coded by automated software (Singh et al., 2017). Software similarly found that in Argentina, Brazil, China, Colombia, France, Germany, India, Japan, Mexico, Peru, Russia, the UK, and the USA (n>740,000), when watching television advertisements women smiled more than men (McDuff et al., 2017). Sex differences in smiling however were not found in children (Else-Quest et al., 2006).

3.2. Politeness. SAT would predict that females would be more likely than males to speak politely since this should reduce interpersonal conflicts. We tested the hypothesis that females more than males employed polite language.

Evidence indicated that females exhibited greater politeness than males with small to moderate effect sizes. In a meta-analysis in primarily WEIRD countries (n>3,500, 29 studies), women used more tentative language (hedges, expressions of uncertainty, intensifiers, and tag questions) than men [d=.23], which the authors interpreted as seeking the listener's consent (Leaper & Robnett, 2011). Ethnographic reports from Africa, Europe, North and South America, and Oceania also reported that girls and women used more tentative speech than boys and men by employing more qualifiers, euphemisms, and apologies, and speaking with less assertiveness, more agreement, higher numbers of softeners and compliments,

and greater supportiveness and modesty (Brown & Levinson, 1987; Coates, 2015; Guadagno & Cialdini, 2007; Haas, 1979; Holmes, 1989; Lakoff, 1975; Locke, 2011).

The same type of sex difference in use of language has regularly been found in early childhood. In a meta-analysis of speech forms in WEIRD cultures (46 studies, n>2,600), girls made more general affiliative comments [d=.26] than boys which was even stronger in unstructured contexts [d=.58] (Leaper & Smith, 2004). Ethnographic reports in 13 non-WEIRD societies likewise indicated in middle childhood girls use more prosocial and less egoistic dominance in their speech (Whiting et al., 1988).

3.3. Identification of others' emotions. Accurately identifying another's emotions facilitates interactions by enhancing understanding of the actor's emotional state. SAT would predict that females would be more likely than males to accurately identify another's emotions.

Studies utilizing primarily pictures or short videos of non-verbal facial, bodily, and vocal behavior consistently demonstrated that from early in life females detected social signals more accurately than males did with small to moderate effect sizes. A meta-analysis (75 studies, 1923-1978) with WEIRD and non-WEIRD societies showed that girls and women were better able than boys and men to accurately detect others' non-verbally expressed emotions [d=.40] (Hall, 1978). A follow-up review demonstrated that across cultures, ages, and target sex, girls and women were better able than boys and men to accurately detect the emotional valence of non-verbal facial and bodily behaviors, as well as verbal intonation and prosody [d=.41-.54] (Hall et al., 2000). A more recent meta-analysis showed that in 67% of 32 studies, women were more accurate than men in identifying the valence of emotions, whereas no sex differences occurred in the remainder (Forni-Santos & Osório, 2015). Similarly, an online study (n>7300, ages 18-75+ years) employing the Penn Emotion Recognition Test with happy, sad, angry, and

fearful faces showed that women more accurately identified emotions across the lifespan [d=.41] (Sasson et al., 2010).

Importantly, women were particularly proficient at detecting negative emotions, though the specific negative emotions were not always consistent across studies and the effect sizes were small. In a large meta-analysis (n>79,000), which encompassed several of the prior meta-analyses with children through adults in nations from Africa, East and Southeast Asia, Europe, North and South America, and including New Guinea, Taiwan, and Tibet, an overall female advantage was found in accurate recognition of emotional reactions to threat [d=.24] and of positive emotions [d=.19] (Thompson & Voyer, 2014). For specific emotions, the effect sizes were highest for anger [d=.25], sadness [d=.24], and fear [d=.22], then slightly lower for happiness [d=.18], disgust [d=.17], and surprise [d=.15], indicating that females were more accurate than males at all ages in decoding emotional signals of threat from non-verbal expressions.

In an Emotion Recognition Test (n>42,000, ages 11–78 years) conducted in seven South American nations, plus Mexico, Austria, Germany, Spain, Switzerland, and the USA, females were more accurate than males at identifying emotions [d=.22] (Merten, 2005). For specific emotions however, the sex difference was significant only for anger, fear, and sadness (not for disgust, joy, or surprise). In three online studies (n>1900) in which subjects rated static facial and dynamic bodily emotions in less than one second, women recognized disgust and sadness significantly more accurately than men did, but not anger, fear, or happiness (Connolly et al., 2019).

McClure (2000)'s meta-analysis of 58 studies of facial emotion processing in infancy through adolescence likewise demonstrated that girls were more accurate than boys at identifying emotions. The effect size

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was smaller in older children and adolescents [d=.18] than in infants [d=.70] however, which may be attributable to the earlier maturity of infant females than males (McClure, 2000).

Thus overall we found that females are reported to accurately identify others' emotions more than males.

3.4. Avoidance of confrontation. SAT would predict that females are more likely than males to avoid confrontations and facilitate positive interactions. We found two forms of confrontation with systematic evidence: direct competition and face-to-face aggression.

Evidence indicates that direct competition and aggression are less common in females than males with moderate to large effect sizes. Direct competition has been systematically examined both in economic games and sports. A standardized economic game was created in which individuals chose to either compete against others or work alone with equal expected payoffs (Niederle & Vesterlund, 2007). In WEIRD and non-WEIRD societies, across tasks, group size, and sex of opponents, two reviews concluded that girls and women were less likely than boys and men to compete against others (Klege et al., 2021; Sutter et al., 2019). Based on Klege et al. (2021), we calculated effect sizes for 33 studies with adults [d=.43] and 12 studies with children [d=.55].

Similar evidence came from sports. Throughout known history, cross-culturally women have participated less than men in competitive sports (Craig, 2002; Leibs, 2004). In a geographically and culturally diverse sample of 50 societies, of 248 sports documented, males participated in 95% of the sports and females in 20%, whereas no sex differences existed in participation in amusements (Deaner & Smith, 2013). In the detailed American Time Use Survey (2003-2010) of activities in the past 24 hours (n>112,000), 0.64% of

females and 2.69% of males [d=-.92] participated in team sports, and 1.29% of females and 4.45% of males participated in 1:1 sports [d=-.95], whereas no sex differences occurred in exercise (Deaner et al., 2012). Whether in the context of sports or simply informal interactions, ethnographic evidence from Africa, Canada, Europeans, Native Americans and in Oceania also described the less competitive and conflictual relationships of girls and women compared with boys and men (Locke, 2011).

Similar to findings on sex differences in direct competition, females were found to engage in less verbal [d=-.30] and physical [d=-.59] confrontation than males (Archer, 2019), with moderate effect sizes. Although most studies came from Asia, Europe, and North America, ethnographic reports provided the same conclusion. Despite large cultural variation, females engaged in less frequent and severe direct aggression than males did (Fry, 1998; Locke, 2011). The sex difference in direct aggression occurred across diverse cultures by age 2 years and continued through adolescence (Maccoby & Jacklin, 1974). In non-human primates as well, females typically engaged in less intense physical aggression than males (Sabbi et al., 2021; Smuts, 1987).

Thus evidence from smiling, politeness, emotion identification, and avoidance of direct confrontation indicated that females invested more than males in reducing social conflicts and protecting social bonds. This result is consistent with the finding from 70 countries with student and adult samples (n>75,000) that women evaluated the "preservation and enhancement of the welfare of people with whom one is in frequent personal contact" as more important than men did [d=.19-.36] (Schwartz & Rubel, 2005).

4. Personality Style as a Response to Threat

Neuroticism consists of a wide range of negative behaviors, moods, emotions, and thoughts. One component of neuroticism, focused on worry and feelings of vulnerability, has been associated with

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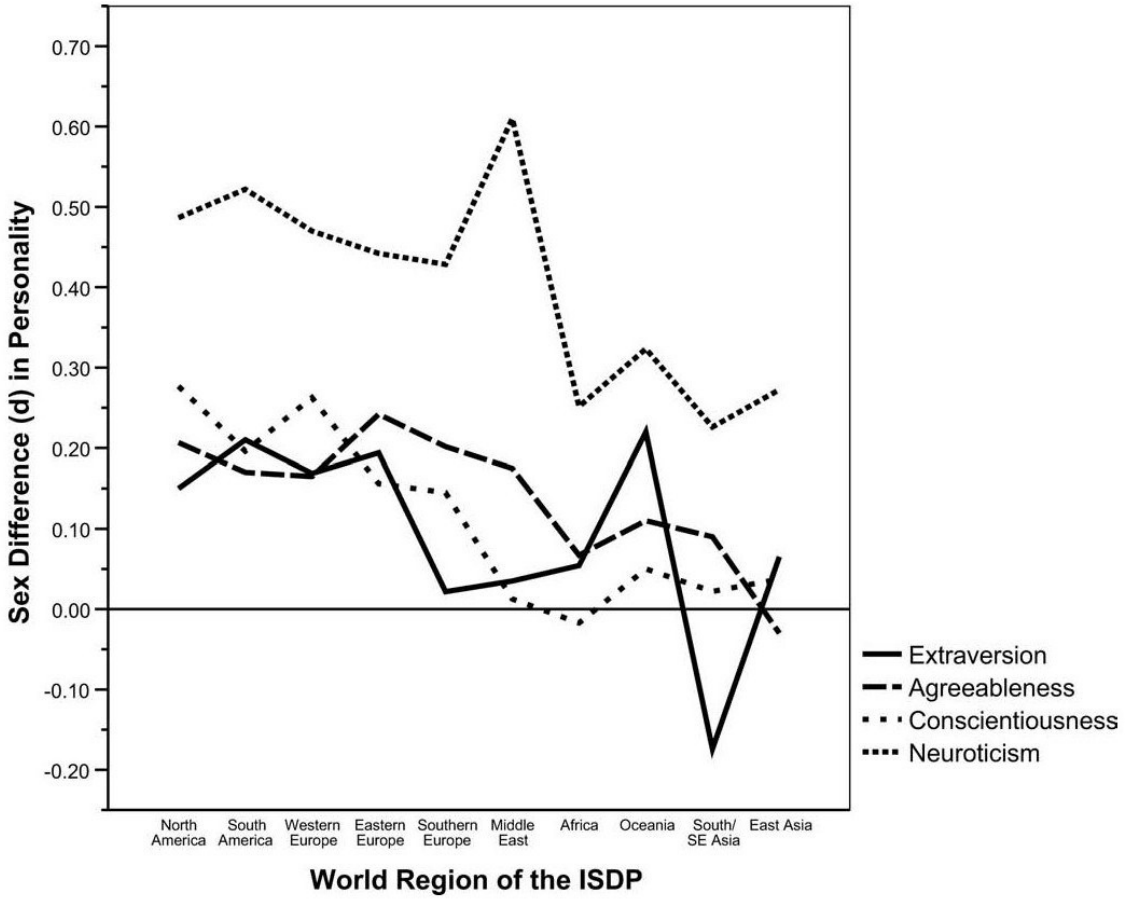
reduced morbidity and mortality (Weiss & Deary, 2020). Because worry and feeling vulnerable are consistent with promoting self-protective behaviors towards threats, we interpreted SAT as predicting that females should report higher neuroticism than males.

The conclusion from four large cross-cultural studies is that beginning in adolescence, women exhibit higher neuroticism than men. First, in a study of university students (n>17,500), neuroticism was defined as worrying, tension, nervousness, depression/blue, moodiness, uncalm in tense situations, easily upset, and not relaxed/handling stress poorly. In 49 of 55 countries, women reported more neuroticism than men did, whereas in no country did men report higher neuroticism than women [d=.40]. Figure 8 displays effect sizes for sex differences in personality styles from world regions with neuroticism showing small to moderate sex differences (Schmitt et al., 2008):



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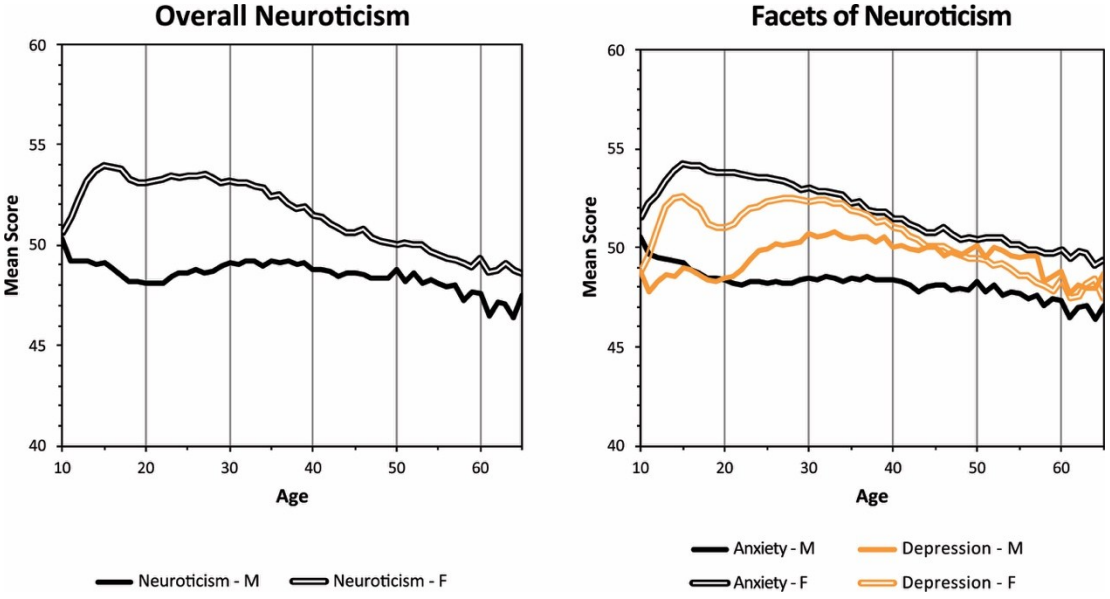
Second, in an online study with individuals primarily from Australia, Canada, Ireland, New Zealand, and the USA (n>1.2 million, ages 10–65 years, 70% Caucasian, 8% Asian, 6% African, 6% Hispanic), neuroticism was defined by worrying, not remaining calm in tense situations, being depressed/blue, and being moody (Soto et al., 2011). Overall neuroticism, and sub-clinical levels of anxiety and depression, differed by sex with females' rates increasing in early adolescence and remaining high during their peak reproductive years as displayed in Figure 9:



Third, a study of US adults (n>320,000) defined neuroticism as being anxious, angry, depressed, self-conscious, immoderate, and vulnerable. As before, women, particularly during their reproductive years, described themselves as more neurotic than men [d = .40] with the anxiety [d=.56] and vulnerability [d=.54] scores yielding the greatest sex differences (Kajonius & Johnson, 2018).

Finally, in a classic study of personality in 24 highly diverse countries with university students and adults, women rated themselves as more neurotic than men: more vulnerable [d=.28-.44], anxious [d=.32-.43], self-conscious [d=.22-.30], depressed [d=.17-.24], impulsive [d =.11-.23], and angry/hostile [d=.09-.19], although sex differences in angry/hostile were not always significant (Costa et al., 2001).

In childhood, as depicted above, sex differences in neuroticism began after age 10 years. Facets of neuroticism, particularly anxiety, however, demonstrated sex differences even earlier (Soto et al., 2011).

In summary, beginning in adolescence females consistently report higher neuroticism than males, with small to moderate effect sizes. The greater neuroticism of post-pubertal females conforms to the prediction from SAT, suggesting that neuroticism functions to protect females more effectively than males from a diversity of threats.

5. Emotions: Immediate Reactions to Threat

Emotional reactions to threat constitute critical signals that promote staying alive (Darwin, 1872; Ekman & Oster, 1979; Lazarus, 1991). Six basic emotions have been identified because they appear across diverse cultures, occur in other primates, and emerge in childhood (Ekman & Cordaro, 2011). Four of these (fear, disgust, sadness, and anger) are considered responses to threat, whereas two (joy and surprise) are not. Each basic emotion arising in response to a threat is believed to produce a unique aversive signal that promotes a defensive action aimed at removing or avoiding the threat.

Assuming that emotional responses to threat promote survival, SAT would predict that females should experience these emotions more than males. We therefore tested the hypothesis that females experience more fear, disgust, sadness, and anger than males.

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5.1. Fear. Fear enhances survival by motivating an individual to withdraw from potentially life-threatening danger (Ekman & Cordaro, 2011; Lazarus, 1991). Campbell (1999) predicated SAT on female's greater fear of physical aggression, while our extension of SAT predicts that females would exhibit greater fear than males to any threat.

Cross-cultural studies confirm that women tend to display greater fear than men. Archer's (2019) review reported greater fearfulness for adult females than males with small to large effect sizes [d=.07 to 1.16]. Additionally, when university students (n=5,000) from 11 countries were asked to rate the fearfulness of 52 stimuli organized into social, agoraphobic, bodily, and animal categories, women in every nation reported greater fearfulness to every category [d=.02-.90] (Arrindell et al., 2004). Further, in 1975-1980 when university students from 28 diverse countries were asked whether either sex was better described by various adjectives, women were characterized as more fearful than men in every country (Williams & Best, 1990).

In the International College Student Data (ICSD) survey (n>6,000, 39 countries), students reported how frequently and intensely they experienced different emotions. Women described more frequent and intense fear than men [d=.31] (Lucas & Gohm, 2000). In two studies, one with an Australian sample of students, kin, and friends (n>2,100), and a second with an international sample of students from 41 countries (n>6,500), women reported more frequent fear in the past month in Australia [d=.14] and in the international sample [d=.17] and more intense feelings of fear in the international sample [d=.26] (Brebner, 2003).

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A small effect has also been found in children. In a cross-cultural meta-analysis (n>4,500, 3 months-13 years), girls displayed greater fear than boys [d=.12] (Else-Quest et al., 2006).

5.2. Disgust. Like fear, disgust is believed to enhance survival by producing withdrawal from potentially life-threatening danger (Ekman & Cordaro, 2011; Lazarus, 1991). Classically, disgust arises in response to illness-causing objects, such as feces, vomit, mucous, signs of severe illness, rotting flesh, and other potentially contaminating stimuli. Additional, less well-known forms of disgust include sexual, animal, and moral disgust. Experiencing greater disgust or revulsion is directly linked with higher germ avoidance (Hartmann & Siegrist, 2018), immediately increased immune activation (Schaller et al., 2010; Stevenson et al., 2012), and disease avoidance (Curtis et al., 2004; Oaten et al., 2009). Since disgust acts as a mechanism for self-protection, SAT would predict that females would experience greater disgust than males.

We found that across varied disgust-producing stimuli, females experienced more disgust than males, with small to large effect sizes. In an online cross-cultural study (n>390,000, 67 countries), women were more distressed than men about lack of physical/spiritual purity and contamination (Atari et al., 2020). Likewise, on the BBC science website (n>39,000), children and adults evaluated which of two paired images evoked more disgust. Across ages and continents, females were more likely than males to rate the image designed to appear as if it could transmit disease as more disgusting than its disease-free twin (Curtis et al., 2004). In another online study (n>6,100, ages 20–69 years, 10 nations, 5 continents), researchers examined disgust ratings for animal flesh, poor hygiene, human contamination, mold, decaying fruits, fish, decaying vegetables, and living contaminants (Egolf et al., 2019). Across countries

women's disgust ratings were greater than men's [d=.12-.37]. Similarly, participants from Canada, England, and the USA (n>2,500, mean age 28 years) evaluated degree of disgust towards 5 targets. Women provided higher ratings than men for animal disgust [d=.82], sex disgust [d=.70], hygiene disgust [d=.48], food disgust [d=.44], and lesion disgust [d=.31] (Curtis & de Barra, 2018). Sexual stimuli produced some of the largest sex differences. Women experienced greater disgust than men to sexual stimuli [d=.60-1.54] (Al-Shawaf et al., 2018).

Sex differences in disgust appeared in childhood. As described in the large paired comparison study which began at age 7 years, even the youngest girls exhibited greater disgust than boys (Curtis et al., 2004).

5.3. Sadness. Sadness is believed to result from the loss of someone or something important to one's life (Ekman & Cordaro, 2011; Lazarus, 1991). Attachment theory posits that sadness or grief represents separation distress from a support figure (parent, spouse, ally) or from someone with close genetic ties (child, twin) (Archer, 2008; Bowlby, 1980). Loss of a relationship partner can threaten the bereaved's survival (Holt-Lunstad et al., 2015) or reproductive success (Archer, 2008) and often leads to withdrawal. Unlike with fear and disgust however, with sadness the loss often has already occurred, and withdrawal is gradual rather than sudden. Withdrawal is believed to protect the bereft individual who likely has lost a current or future ally, and to help elicit support from others (Lomas, 2018). On the assumption that sadness functions to reduce the impact of a threatening factor (the loss of a relationship partner), SAT would predict that females would experience greater sadness than males.

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Based on self-reports, females were found to exhibit more sadness than males, with small effect sizes. In the IAPS, standardized photographs depicting illness generated more sadness in women than men (Bradley et al., 2001). In the 39 nation ICSD survey, women reported more frequent and intense sadness than men did [d=.26] (Lucas & Gohm, 2000). Likewise, women reported more frequent sadness in Australia [d=.17] and the 41 country international sample [d=.16], and more intense feelings of sadness in Australia [d=.19] and the international sample [d=.28] (Brebner, 2003).

Higher self-reports of sadness could in theory be accounted for by women's greater willingness to report emotion. To examine this possibility, in 1990 researchers interviewed a demographically representative sample of Americans (n>2,000, ages 18–90 years) (Mirowsky & Ross, 1995). When asked the number of days in the prior week they felt sad, women reported more days of sadness than men. Then, participants were asked how much they hide their emotions. At every level of emotional reserve, women reported experiencing greater sadness than men, strongly suggesting that the sex difference in reported sadness was not due to a reporting bias.

Limited evidence suggests girls are sadder by adolescence. In a demographically representative American sample (n>21,000, ages 14-18 years), girls felt sadder than boys (Moeller et al., 2020). Likewise, when Swedish adolescents (n>1,000, ages 16–18 years) in 49 classrooms were asked how frequently they experienced sadness, 35% of the girls versus 8% of the boys reported feeling sad either "fairly often" or "very often" [OR=6.19] (Wiklund et al., 2012). In childhood, sex differences in sadness may not exist or are negligible. In a meta-analysis (n>2,300), in 11 of 16 studies in early and middle childhood exhibited girls greater sadness than boys, but the sex difference was not significant and negligible in size [d=.10] (Else-Quest et al., 2006).

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Evidence also indicated that females cry (weep) more than males, with moderate to large effect sizes. Crying is often associated with sadness, although it can also serve as a release from emotion and as a means of soliciting support (Rottenberg et al., 2008; Vingerhoets & Scheirs, 2000).

In the International Study of Adult Crying (ISAC) (n>5,500) conducted in 37 nations across six continents, university students were asked how easily and how frequently they had cried in the past month (Van Hemert et al., 2011). In every country, women reported crying more easily [d=1.11] and more recently [d=.94] than men. Another meta-analysis (15 studies) found that women reported crying more frequently, intensely, and for longer intervals than men across cultures, including Israel, Japan, and the USA (Vingerhoets & Scheirs, 2000). Similarly, across Australia, Croatia, the Netherlands, Thailand, and the United Kingdom (n>800, ages 18–40 years), women reported crying more frequently [d=.74] and intensely [d=.45] than men (Sharman et al., 2019). Ethnographic reports from diverse cultures similarly report that the loss of a relationship partner causes sadness and weeping, and more so in women than men (Palgi & Abramovitch, 1984). Sex differences in crying are not reported before adolescence (Vingerhoets & Scheirs, 2000).

5.4. Anger. Anger occurs after a personal goal has been obstructed, often by a specific perpetrator who purposefully wishes to harm a victim and/or her/his associates (Ekman & Cordaro, 2011; Lazarus, 1991). Unlike fear, disgust, and sadness however, anger activates approach, not withdrawal. A further contrast is that although anger-motivated responses can reduce a threat through avoidance, they can also increase the risk of being injured through approaching a perpetrator (Sell et al., 2009). This means that whether anger functions as self-protection will vary with the context. Anger should be more self-protective if it enhances avoidance of a perpetrator, but less self-protective if it motivates close

engagement or cycles of retaliation. Experiencing anger without approaching the perpetrator however should highlight the danger of future interactions with specific perpetrators, thereby enhancing survival.

SAT therefore would predict that females would feel angrier than males towards perpetrators, though only when approach was suppressed. Even though the prototype of an angry person is a man (Kring, 2000) most likely because larger individuals face lower likelihood and costs of retaliation (Sell et al., 2009), we tested the hypothesis that females feel angrier than males.

Evidence suggested at most a negligible effect size indicating females experienced more anger than males (Archer, 2004; Kring, 2000). However, no studies distinguished simple anger from anger tied to aggression. A meta-analysis of 11 countries found a non-significant effect for females to feel angrier than males [d=.04] (Archer, 2004). In the ICSD study, women reported more frequent anger than men [d=.08] (Lucas & Gohm, 2000). Likewise, in Brebner's (2003) Australian and international samples, women reported experiencing anger more frequently than men did both in Australia [d=.06] and the international sample [d=.05]. Women also reported greater intensity of anger in the international sample [d=.14]. In Mirowsky and Ross' (1995) American study, anger was defined as "feeling annoyed with things or people," "feeling angry," and "yelling at someone." Women reported feeling angrier than men, and "yelling at someone" more than men did. Sex differences in experiencing anger have not been found in children (Potegal & Archer, 2004).

In conclusion, evidence supported the hypothesis that females experienced more fear, disgust, and sadness than males did. Results did not support an overall sex difference in anger but anger could not be

separated from approaching a perpetrator. When a sex difference did arise however, women experienced more anger than men.

6. Clinical Conditions: Extreme Self-Protective Reactions to Threat

Some clinical conditions are believed to be non-adaptive exaggerations of normal adaptive reactions to stress (Del Giudice, 2018; Nesse, 2005). If self-protectiveness is an adaptive female strategy, then clinical conditions constituting extreme self-protectiveness to threats should be more prevalent in females than males. We therefore tested whether extreme forms of physical, social, emotional, and generalized reactions to threat occur more frequently in women than men.

6.1. Autoimmune diseases. As we reviewed above, non-pregnant women tend to exhibit stronger immune responses than men including enhanced Th2 reactions. Extrapolating from this result, we reasoned that more females than males would develop extreme immunoenhancing conditions. We therefore searched the literature to test the hypothesis that more females than males develop extreme immune reactions.

The prediction was supported by evidence that globally, women are more likely than men to develop systemic autoimmune diseases (AD) which are linked to proinflammatory responses with moderate effect sizes (Ji et al., 2016; Moroni et al., 2012; Purnamawati et al., 2018) and diminish in severity during pregnancy (Abu-Raya et al., 2020). Of 81 ADs identified worldwide, 47 afflict females more than males, 22 are more common in males, and 9 exhibit no sex difference (Hayter & Cook, 2012). Despite large cultural differences, overall 6.4% of females and 2.7% of males develop an AD [OR=2.46] with onset most common between 20-29 years. The more prevalent an AD, the higher the proportion of females who develop it, with women comprising 78% of those with ADs (Hayter & Cook, 2012). Whereas many

https://doi.org/10.1017/S0140525X21002417

female-preponderant ADs are believed due to enhanced Th2 responses, in male-preponderant ADs, Th1 reactions often are stronger (Fairweather et al., 2008). Precipitating factors for all ADs include infections or other types of diseases or trauma (Nielsen et al., 2016). Results therefore are consistent with a female adaptation that promotes immunoenhancing reactions to physical threat.

6.2. Pain disorders. Evidence reviewed above demonstrated that females experience more ordinary pain than males. According to the idea that clinical conditions are non-adaptive extensions of well-adapted responses, extreme pain reactions should be found more often in females than in males.

We found two examples for which cross-cultural evidence is available, migraine headaches and fibromyalgia, both of which were experienced by more females than males. The Global Burden of Diseases report finds that despite large national variations, worldwide 18.9% of women and 9.8% of men experienced migraine headaches [OR=2.15] with women ages 15-49 years most affected (Stovner et al., 2018). The most common precipitating factor was external stress, including odors, foods, weather, pain to the neck or head, or emotional trauma (Peroutka, 2014; Woldeamanuel & Cowan, 2017).

Fibromyalgia (FM) consists of chronic, severe, widespread pain in at least 11 of 18 points in the joints, muscles, and spine. Worldwide, 4.2% of females and 1.4% for males [OR=3.09] developed FM (Queiroz, 2013). Onset of FM typically followed a stressor, such as an accident, surgery, infection, or emotional trauma, and was accompanied by sleep disturbance, fatigue, memory and concentration problems, along with depression and anxiety (Galvez-Sánchez et al., 2019; Häuser et al., 2010). Prevalence ratios of migraine and FM showing moderate effect sizes were consistent with the hypothesis that a female adaptation exists for heightened experience of pain.

6.3. Sleep disorders. Prior evidence showed that females experienced more nighttime awakenings than males, which is plausibly an adaptive response. More extreme, non-adaptive nighttime awakenings were therefore also expected to occur more often in females than in males. We therefore tested whether more females than males developed conditions with severe nighttime awakening.

In line with this prediction, we found that more women than men experienced severe sleep disturbances with small to moderate effect sizes. Although no sharp distinction separates nighttime awakenings from a severe sleep disorder (Suh et al., 2018), analyses of major DSM-V clinical conditions showed a female:male prevalence ratio of 1.4 for insomnia disorder and 1.5-2 for restless leg syndrome, which disrupts sleep, as well as a higher female prevalence for nightmare disorder (Hartung & Lefler, 2019). A meta-analysis (n>18,500) further confirmed a female preponderance for restless leg syndrome [OR=1.63-2.22] (Ohayon & Roth, 2002). Additionally, a detailed study in Hong Kong (n>8,500) found women were more likely than men to experience nightmares $\geq$3 times/week [OR=2.10] (Li et al., 2010).

Furthermore, major sleep disruptions including day-night reversals were associated with clinical conditions with a female preponderance (Lashley, 2003). These included responses to infections, many autoimmune conditions (systemic lupus erythematosus, multiple sclerosis, rheumatoid arthritis), pain-related disorders (migraine, fibromyalgia), and as described below, anxiety disorders, major depression, post-traumatic stress disorder, and chronic fatigue syndrome. Prevalence ratios of severe sleep disruption were consistent with the thesis that because a female adaptation exists for being especially attuned to nighttime threats, females were also vulnerable to having extreme responses that are likely maladaptive.

6.4. Separation disorder. We have presented evidence that females were more likely than males to avoid social confrontations and to become more distressed about relationship partners' well-being. A more extreme version of this response would consist of becoming extremely distressed about the loss of relationship partners. We therefore tested whether more females than males develop conditions characterized by excessive concern for maintenance of relationships. We found one condition with cross-cultural evidence that clearly fit this criterion: separation anxiety disorder. Separation anxiety disorder includes severe distress at being away from an attachment figure along with persistent worry about negative events befalling attachment figures.

Examining 18 DSM-IV mental disorders (n>72,000, across Africa, the Americas, Asia, Europe, the Middle East, and the Pacific), the WHO World Mental Health Survey (WMHS) study found that lifetime prevalence of separation anxiety disorder was more common in females than males with a small effect size [OR=1.6], whereas the reverse was true for antisocial disorders (Seedat et al., 2009). Similarly, in analyses of the DSM-V categories, separation anxiety disorder was more common in females than males, while males suffered more from antisocial disorders (Hartung & Lefler, 2019; Holthausen & Habel, 2018; Shear et al., 2006). A demographically representative survey in the USA (n>14,000) likewise showed that by the end of early childhood and throughout life females were more likely than males to have experienced separation anxiety disorder [OR=2.2] (Shear et al., 2006). Reported rates of separation disorder are thus consistent with a heightened female adaptation for maintaining relationships.

6.5. Anxiety disorders. Evidence reviewed above demonstrated that females of all ages were more likely than males to experience fear in response to threats. More persistent and intense fear reactions would accordingly be expected to develop in females than males. We therefore tested whether more females than males developed conditions characterized by severe fear.

Anxiety disorders are specific or generalized worries and fears about potential threats often accompanied by unpleasant physical sensations, including increased heart rate and shaking. The worldwide WHO WMHS study showed a higher prevalence for females than males of anxiety disorders with small effect sizes, including panic disorder (OR: 1.9), generalized anxiety disorder (OR: 1.7), agoraphobia (OR: 2.0), social phobia (OR: 1.3), specific phobia (OR: 2.0), separation anxiety disorder (OR: 1.6) as mentioned, and any anxiety disorder (OR: 1.7) (Seedat et al., 2009). Other estimates of the female:male ratio of global prevalence of anxiety disorders were 1.9 (Remes et al., 2016) with the DSM-V analysis finding a ratio of 2:1 (Hartung & Lefler, 2019). Thus, anxiety disorders conform to the hypothesis that they represent exaggerated versions of responses that would be adaptive if produced at an appropriate level.

6.6. Major depression and suicide attempts. Earlier we showed evidence that females were more likely than males to experience sadness. Extrapolating from this produces the prediction that more females than males should develop an extreme form of sadness: depression. We tested this hypothesis.

Major depression consists of an array of uncomfortable emotional and physical symptoms including sadness, feelings of worthlessness, reductions in activity and energy levels, changes in appetite and sleep, and difficulty thinking. In 80% of cases, depression is precipitated by stress (LeMoult, 2020). A meta-analysis of sex differences in major depression across six continents (n>1.7 million, ages 12–70+ years) showed a higher female prevalence with a moderate effect size [OR=1.95] (Salk et al., 2017). The DSM-V analysis reported depression to be 1.5-3 times more common in women than men (Hartung & Lefler, 2019).

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Major depression likely plays a role in suicide attempts. Suicide attempts however may be not only an exaggeration of depression, but also an adaptive request for help across diverse societies (Syme et al., 2016). Although cross-culturally women were less likely than men to commit suicide (Alothman & Fogarty, 2020; WHO, 2014b), women were more likely than men to attempt suicide, beginning in early adolescence (Freeman et al., 2017; Lenz et al., 2019; WHO, 2014b). Maximal rates of non-fatal self-injuries for females occurred between 10-24 years [OR=1.72]. Females were still more likely than males to attempt suicide between 25-44 years [OR=1.29], but the sex difference became negligible at older ages (Nock et al., 2008). A meta-analysis of suicide attempts by 12–26-year-olds further found that in 23 of 24 studies girls were more likely than boys to attempt suicide [OR=1.96] (Miranda-Mendizabal et al., 2019). Effect sizes range from small to moderate. The higher rates of depression and lower success of female suicide attempts can be interpreted as females being more invested in self-protection, in line with SAT.

6.7. Psychiatric disorders incorporating disgust. We found previously that females were more likely than males to experience disgust in response to potentially contaminating stimuli. We therefore tested the idea that more extreme forms of disgust would also be more common in females than males.

We found that disgust is integral to three psychiatric illnesses: animal phobias, contamination-related obsessive-compulsive disorders with continual washing (OCD), and blood-injection-injury (BII) phobia which can include fainting. All three of these illnesses were more common in women than men (Arrindell et al., 1999; Davey, 2011; Mathis et al., 2011; Olatunji et al., 2010; Wani & Ara, 2014). Disgust has also been associated with other serious psychiatric problems that are more prevalent in women than men, including eating disorders, agoraphobia, and female sexual dysfunction (Hartung & Lefler, 2019). In all cases, specific threats were the focus. In contrast, most hypersexual-related psychiatric illnesses were

more frequent in men than women. Thus, evidence supported the idea that extreme forms of disgust were experienced by more females than males.

6.8. Threat-induced conditions. Given evidence that females reacted more self-protectively than males to threats, it would be expected that conditions having well-established associations with threat should develop in more females than males. We therefore searched for conditions in which identifiable threats constituted clear precipitating factors, to test whether more females than males developed these conditions. We found two conditions known to be caused by stress: Post-Traumatic Stress Disorder (PTSD) and Chronic Fatigue Syndrome also known as Myalgic Encephalomyelitis (CFS/ME).

Both PTSD and CFS/ME demonstrate a female preponderance. PTSD follows trauma and consists of intense, long-lasting emotional and physical symptoms, typically flashbacks, hypervigilance, and nightmares, as well as major depression, anxiety, and sleep disorders. In a WHO WMHS study in 15 diverse societies (n>72,900), females experienced PTSD more than males (OR=2.6) (Seedat et al., 2009).

Sex differences in experience of PTSD however must control for the nature of the precipitating stimulus. A detailed meta-analysis (290 studies) of types of trauma producing PTSD in primarily WEIRD societies showed that for every type of trauma except childhood sexual abuse, more females than males developed PTSD [OR=1.98] (Tolin & Foa, 2006). Further detail came from a Nordic study (n>5,200) in which approximately twice as many women (25.6%) as men (13.2%) were categorized as having PTSD (Ditlevsen & Elklit, 2012). Using a continuous measure of PTSD, females experienced stronger PTSD than males with effect sizes varying from small to large based on type of trauma: disasters and accidents [d=.84], loss [d=.47], non-malignant disease [d=.47], chronic disease [d=.39], violence [d=.27], and overall [d=.60].

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While the female preponderance of PTSD could be due to more females than males experiencing severe trauma, current evidence disputed this. In the meta-analysis in WEIRD countries, fewer females than males confronted severe traumas [OR=.77] (Tolin & Foa, 2006). Likewise, globally, females were less likely than males to die from fatal injuries (WHO, 2014a) or become disabled due to injuries (Haagsma et al., 2016).

CFS/ME is a debilitating, often life-long condition. Along with extreme exhaustion and weakness, the most common symptoms include immune activation (flu-like symptoms), intense pain (often migraines), severe sleep disturbance, depression or anxiety, concentration problems, and adverse reactions to chemicals (Chu et al., 2019; Friedman, 2019; Natelson, 2019). Based on a review of 13 Asian, Australian, North and South American studies, despite varying national prevalence rates, after puberty women were 3-4 times more likely than men to develop CFS/ME (Son, 2012) with a large effect size in an American study [OR=4.51] (Reyes et al., 2003). Onset typically occurred between ages 20-45 years following a specific threat: an infective illness (64% of cases), a major aversive life event (emotional stressor in the family or at work in 39% of cases), and a reaction to environmental toxins such as vaccines (20% of cases), with multiple precipitating stressors for some individuals. CFS/ME is not believed to be a disease in the typical sense, but rather a systemic reaction to stress (Cortes Rivera et al., 2019). Prevalence rates of both PTSD and CFS/ME thus supported the prediction that more females than males exhibited extreme self-protective reactions to threats.

In conclusion, eight types of threat-related clinical condition, although maladaptive, may reasonably be interpreted as extreme self-protective reactions, and were more prevalent in females than males.

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7. Discussion

7.1. Sex differences in self-protective responses. Our goal was to evaluate whether Campbell's (1999) "staying alive" theory applied not merely to physical aggression but more generally to all threats. By searching the literature for cross-cultural evidence with large samples, we tested the hypothesis that females demonstrate more self-protective reactions than males to major threats. We found that females exhibited stronger self-protective reactions than males to important biological and social threats; a personality style more geared to threats; stronger emotional responses to threat; and more threat-related clinical conditions suggestive of heightened self-protectiveness. That females expressed more effective mechanisms for self-protection is consistent with females' lower mortality and greater investment in childcare compared with males. Table 1 summarizes our major findings. As our hypothesis would predict, the magnitudes of sex differences in self-protective reactions were largest for the most potent threats to life- including heightened antibody production, reduced endurance of pain, and greater avoidance of direct competition, with fear, disgust, and crying sometimes also producing large effect sizes.

Our test of Campbell's extended SAT is limited by our inability to examine every conceivable kind of threat, and by the incomplete availability of cross-cultural data. Nevertheless, we found evidence from many large samples and diverse cultures. Strikingly, despite intense searching, we failed to find large studies or meta-analyses that showed sex differences in the opposite direction to those expected from SAT. We conclude that the tendency for females to show more self-protective physiology, social interactions, personality styles, emotional reactions, and threat-related clinical conditions than males provides a strong first test for the extension of Campbell's SAT.

Many additional potential examples of greater female self-protectiveness occur in important areas that we excluded due to limited cross-cultural evidence. As examples, females more than males exhibit a lower threshold for detecting many sensory stimuli (Velle, 1987); remain closer to home (Ecuyer-Dab & Robert, 2004); overestimate the speed of incoming stimuli, discuss threats and vulnerabilities more frequently, find punishment more aversive, demonstrate higher effortful control, and experience deeper empathy (Archer, 2019); express greater concern over friend's (Hall, 2011) and romantic partner's (Carpenter, 2012) loyalty; and seek more frequent help (Möller-Leimkühler, 2002; Tamres et al., 2002; Whiting & Whiting, 1975).

Developmental evidence generally supported the prediction that females would exhibit greater self-protective reactions than males throughout life, but that the magnitude of the sex difference would increase following puberty when females can reproduce. Sex differences in immune functioning, pain, and nighttime awakenings appeared in childhood, but increased post-pubertally. Sex differences in politeness, emotional identification, and avoidance of confrontations emerged by early childhood, but in smiling only after puberty. Sex differences in neuroticism arose only after puberty, but girls displayed some components of neuroticism more than boys pre-pubertally. Girls experienced greater fear and disgust than boys pre-pubertally, but not sadness, for which the sex difference only clearly arose post-pubertally.

We did not systematically examine sex differences in children's clinical conditions due to lack of cross-cultural evidence. However, sex differences in some conditions, such as anxiety (Rescorla et al., 2007) and depression (Salk et al., 2017), emerge only after puberty, whereas in others, such as immune functioning, shifts occur from childhood to puberty (Klein & Flanagan, 2016).

7.2. Complexities in interpreting sex differences. That numerous sex differences conform to SAT is consistent with the thesis that self-protective reactions constitute a series of evolved female adaptations. If sex differences are to be fully understood however, additional factors must be included.

First, sex/gender is a multidimensional construct resulting from the continuing interplay between biological and environmental factors (Berenbaum & Beltz, 2021; Eliot, 2009; Fausto-Sterling, 2019; Hyde et al., 2019). Further, some of its important components and related constructs, including epigenetic configurations, hormonal balances, reproductive capacity, gender identity, gender roles, and sexuality, often fluctuate over the lifespan. Thus, menarche and menopause typically produce diverse changes for human females. Males too undergo transitions. Testosterone diminishes in bachelors who marry and even further after they father children (Gettler, McDade, Feranil, & Kuzawa, 2011; Gray, Kahlenberg, Barrett, Lipson, & Ellison, 2002). Because the studies we found do not define sex/gender and treat it as binary, we cannot specify which characteristics of sex/gender relate to self-protection. More precise structural, epigenetic, cellular, hormonal, cultural, social, emotional, cognitive and behavioral indices will greatly improve understanding of the relation between self-protection and sex/gender.

Second, the magnitude of sex differences in self-protectiveness depends on local threats and safeguards which may differentially affect females and males. For example, in matrilineal societies where females receive greater protection from kin (Smuts, 1992), girls and women appear to be as directly competitive as their male counterparts in economic games (Klege et al., 2021). Likewise, when women's rights are protected by laws, the normally higher rates of men physically battering their female partners (WHO, 2014a) can disappear (Archer, 2006). In impoverished societies that provide infants with both nutritional supplementation and breastmilk, females' immune systems are strengthened more than males' (Khulan et al., 2012; Osrin et al., 2005). Prevalence of physical illness itself varies depending on gender identity,

role, and status (Mauvais-Jarvis et al., 2020) and societal kinship structure (Reynolds et al., 2020). Even sex differences in mortality are influenced by societal factors, including patients', physicians', and researchers' belief systems (Mauvais-Jarvis et al., 2020); rates of female infanticide, sexual abuse of and violence against women (Solotaroff & Pande, 2014; WHO, 2014a); and men's willingness to seek help (Verbrugge, 1989).

More individual factors also likely regulate the magnitude of sex differences in self-protective reactions. For example, grandmothers typically invest more in daughters' than sons' young children, thereby tending to maximize their own fitness (Sear & Mace, 2008). The extent of a particular grandmother's investment, however, should regulate her daughter's self-protective reactions. Similarly, although worldwide mothers care for infants (Wood & Eagly, 2002), a particular family's norms regarding exclusivity of maternal responsibility for childcare likely influences maternal self-protective reactions. As another example, females may have lower thresholds than males to even perceive physical symptoms, social conflicts, or other threats, as extrapolation from research on pain would suggest (Riley et al., 1998). Nevertheless, the degree to which members of an individual's social network reward or punish females' versus males' expressions of vulnerability should regulate sex differences in even recognizing threats (Jansz, 2000).

Third, more research is necessary to understand the societal impact of gender equality, measured by women's participation and power in public life, on self-protectiveness. Greater gender equality is associated with even fewer women than men committing suicide (Alothman & Fogarty, 2020); and increased proportions of women than men expressing concerns about environmental degradation (Chan et al., 2019), reporting neuroticism (Costa et al., 2001; Schmitt et al., 2008), and experiencing depression (Salk et al., 2017). These somewhat paradoxical findings require further inquiry. Gender equality

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however is intertwined with other ecological and cultural variables (Kaiser, 2019) and may not adequately capture the realities of life of people in non-WEIRD societies (Markus, 2021).

Fourth, a large overlap exists between the sexes in many self-protective reactions as is found in many studies of sex differences (Eliot, 2009; Hyde et al., 2019; Zell et al., 2015). Consequently, a particular self-protective response cannot be predicted simply from knowing an individual's binary sex. Our evidence merely demonstrates that there is a population-wide tendency in the direction predicted by Campbell's theory.

Distinct self-protective responses, however, frequently co-occur. Myriad studies report links among somatic, social, neurotic, emotional and clinical responses (Okur Güney et al., 2019; Yunus, 2007). This suggests that aggregating self-protective reactions could more accurately describe the effect of greater self-protectiveness on females' than males' lives than simply comparing the sexes on only one self-protective response at a time. Thus, multivariate statistical techniques could provide a more qualitative distinction between the sexes (Del Giudice, 2021).

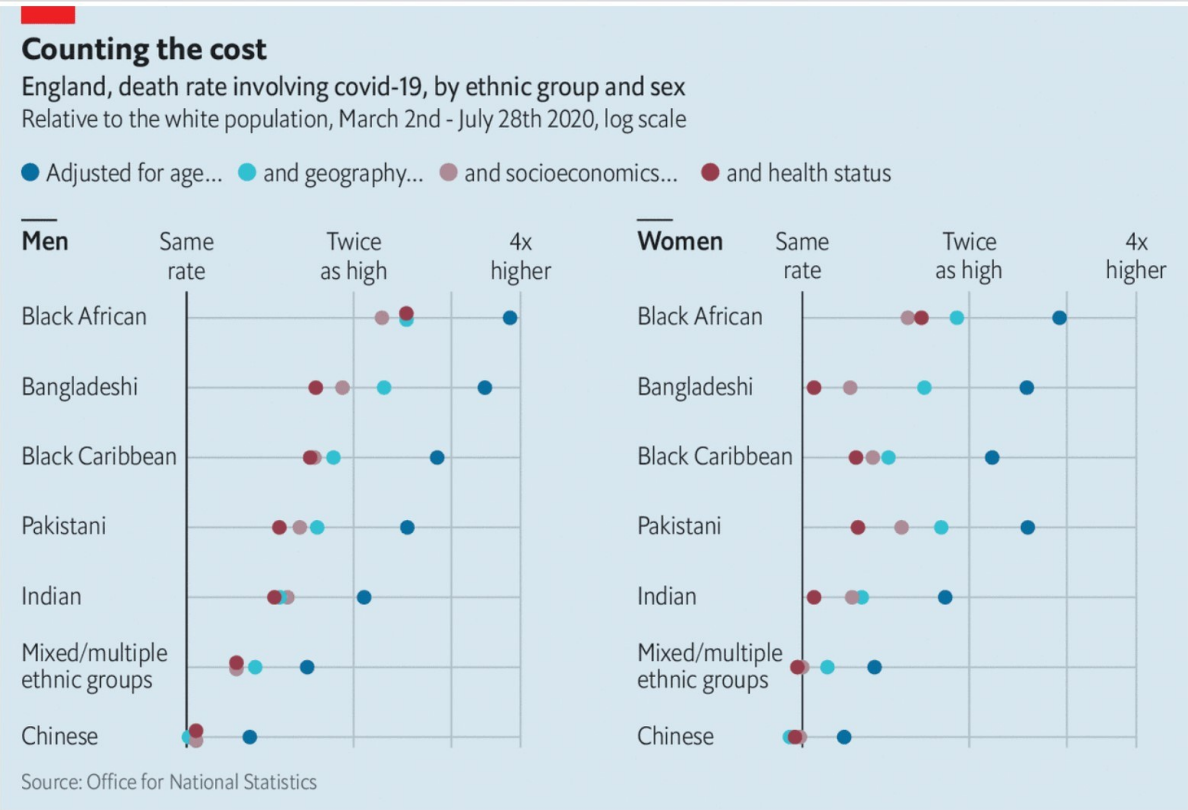
Fifth, many female-prevalent illnesses and clinical conditions could impede women's ability to care for their children, thereby reducing their fitness. An adaptive approach however suggests that the benefits accrued from women's greater longevity outweigh the costs of chronic illness (Del Giudice, 2018; Nesse, 2005).

Overall, considering the diversity of our evidence, the consistency of our findings is striking. Accordingly, we regard sex differences in self-protective responses as important to investigate not only for theoretical

https://doi.org/10.1017/S0140525X21002417

reasons but also for practical value related to medical and psychological health (Clayton, 2016; Shansky & Murphy, 2021).

An analysis of rates of COVID-19 illustrates how sex differences can vary widely in magnitude without undermining their significance. Both absolute frequencies and sex differences vary markedly by ethnicity, age, geographical location, socioeconomic status, and baseline health status even within the same country, as depicted in Figure 10 for England (Economist, 2020):



Despite this variation, women are almost always less likely than men to die within each demographic group. Thus, sex constitutes an important biological variable that can enhance causal understanding of a phenomenon which varies on many factors (Clayton, 2018).

Finally, further research is necessary to understand whether some threats elicit stronger self-protective reactions in men than women. Examples include male concerns over status and warfare. Current evidence however indicates no sex differences in the desire to attain status (Anderson et al., 2015), even though the sexes may choose different strategies to achieve it (Benenson & Abadzi, 2020). Whether men are more concerned than women about imminent military attacks has not been investigated.

7.3. Complementary explanations. Our findings provide support for self-protective responses as a female adaptation. Alternative, but potentially compatible, explanations however could also apply.

First, males' higher levels of androgens, larger body size, more negative social interactions, greater risk-taking, and other sexually selected characteristics related to mate competition are expected to partially explain why males exhibit lower self-protectiveness than females (Dunsworth, 2020; Klein, 2000; Kruger & Nesse, 2006; Zuk, 2009). Individual and population variation among males in their optimal strategies and biological constraints will therefore contribute to explaining their lower self-protectiveness. Nevertheless, it is not simply degree of mate competition that produces sex differences in self-protectiveness. Rather, females invest in costly self-protective mechanisms, including immune functioning and conflict reduction measures, that elevate the probability of survival. Independent selective pressures on both male and female traits influence the nature and degree of sex differences in self-protectiveness.

Unquestionably, women's smaller size and muscle mass enhances their self-protectiveness with men. Nonetheless, sex differences in size and strength alone cannot explain all self-protective reactions. For example, in children where sex differences in size and muscularity are minimal, girls often exhibit more

self-protective reactions than boys, including greater pain to vaccines (Chambers et al., 1999) or politer language (Leaper & Smith, 2004; Whiting et al., 1988).

Second, a "trauma hypothesis" might suggest that traumas specific to women increase their self-protectiveness. Worldwide, one in three women suffers domestic or sexual violence; 20% of girls are sexually abused; and reproductive-related morbidity and mortality are more frequent where women have fewer rights (WHO, 2014a). However, universally more men than women are exposed to lethal threats (WHO, 2014a). If trauma alone were responsible for greater self-protectiveness, then men should exhibit stronger self-protective responses than women in some areas, such as in response to violent social interactions or accidents which affect men more (WHO, 2014a), but they do not (Ditlevsen & Elklit, 2012). Many of the sex differences we reviewed therefore are not explicable by the trauma hypothesis.

Third, women's greater self-protectiveness could result from the high costs of pregnancy and lactation which could render women less physically, socially, emotionally, and clinically functional than men. This view is commonly held by medical and psychological professionals who perceive "self-protective" reactions as maladaptive or compensatory (Chesler, 1972; Cleghorn, 2021). If reproduction itself were the only critical factor however, sex differences in self-protective reactions would be highest during pregnancy and lactation, but this is not the case. Some sex differences in self-protectiveness appear by infancy (e.g., immune functioning, fear); others arise at puberty (e.g., smiling, sadness); some are maximal throughout the reproductive years (e.g., neuroticism, migraine); and others increase with age (e.g., insomnia).

Fourth, worldwide men tend to hold higher status than women, particularly in the public sphere (Fiske et al., 2016; Rosaldo & Lamphere, 1974). This difference almost certainly heightens females' self-protective

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reactions compared to when females hold power such as within the confines of families or in matrilineal societies (Smuts, 1992). Status differences do not readily explain other socially self-protective reactions, however, such as females' greater fearfulness (Else-Quest et al., 2006) or more accurate emotional identification (McClure, 2000) from infancy onwards.

In sum, the evolutionary explanation offered by "staying alive" theory complements other accounts of women's greater responses to threats by integrating divergent domains. Further, it views females' strategies as evolved adaptive functions, rather than being constrained features that are sub-optimal compared to those of males. It also helps resolve many apparent paradoxes in which women are *less* likely than men to die from pathogens, injuries, social conflicts, and suicide, yet *more* likely to experience physical symptoms, pain, sleep disturbances, avoidance of social conflicts, generalized worry, fear, disgust, and sadness, and make suicide attempts. SAT posits that stronger self-protective reactions to threat enhance survival, rendering females less vulnerable than males. Furthermore, SAT would predict that individuals who assume primary responsibility for children's well-being will increase their self-protective reactions so as to enhance their own survival.

7.4. Conclusion. Girls' and women's heightened responsiveness to physical and social threats, neuroticism, emotional reactions to threats, and related clinical conditions are often pathologized, that is, attributed to hysteria, mental health disorders, or other abnormalities, because men are the reference point (Chesler, 1972; Cleghorn, 2021). Our extension of Campbell's "staying alive" theory suggests, by contrast, that females' "sensitivity" should be construed not as a constrained weakness or compromise enforced by reproductive biology but as a strategic approach to counteracting threats. Male traits, equivalently, that are often seen as the norm, are suboptimal for enhancing survival, but serve to maximize men's fitness given the constraints that they confront (Seager, 2019). Thus, independent

consideration of each sex, along separate dimensions, is necessary for understanding the ways in which each sex's traits are optimized. Had the evidence existed, we would have compared the reproductive success of females who varied in their degree of reactions to threats, and not included males at all.

A richer understanding of the adaptive nature of female self-protection ultimately will depend on discovering its underlying mechanisms and how they may have co-evolved. Promising mechanisms undergirding self-protectiveness include sex chromosomes (Schurz et al., 2019), sex hormones (Klein & Flanagan, 2016), centralized reactivity (Yunus, 2007), support of attachment figures (Archer, 2008; Bowlby, 1980) and the larger community (Smuts, 1992), and degree of responsibility for offspring survival (Allman et al., 1998).

In conclusion, in response to a wide diversity of threats, human females exhibit greater self-protective responses than males. This finding suggests an opportunity for researchers and clinicians to better understand the adaptive nature of diverse female traits, both in humans and other species.

Acknowledgements. The authors sincerely thank Dr. Barbara Finlay and the six reviewers for their excellent recommendations which greatly improved the manuscript.

Funding Statement. This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflicts of Interest. None

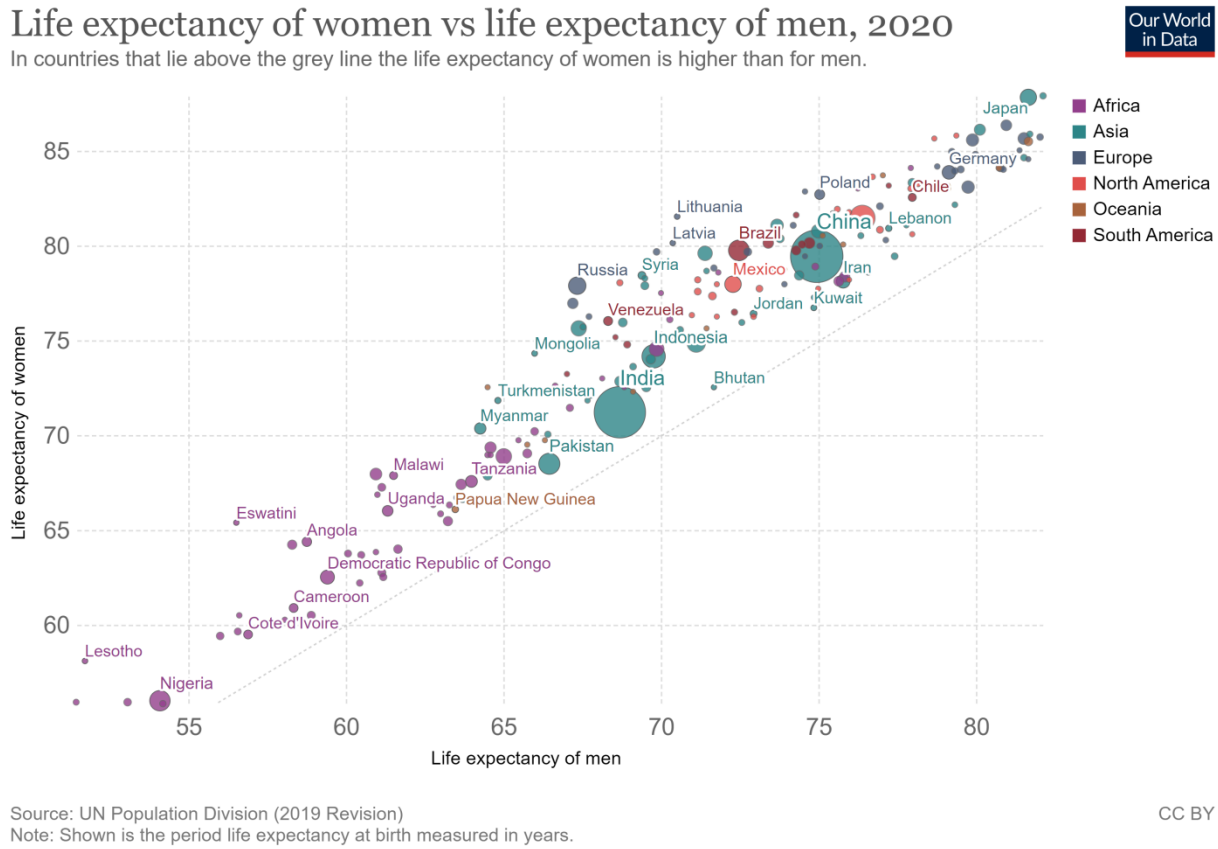
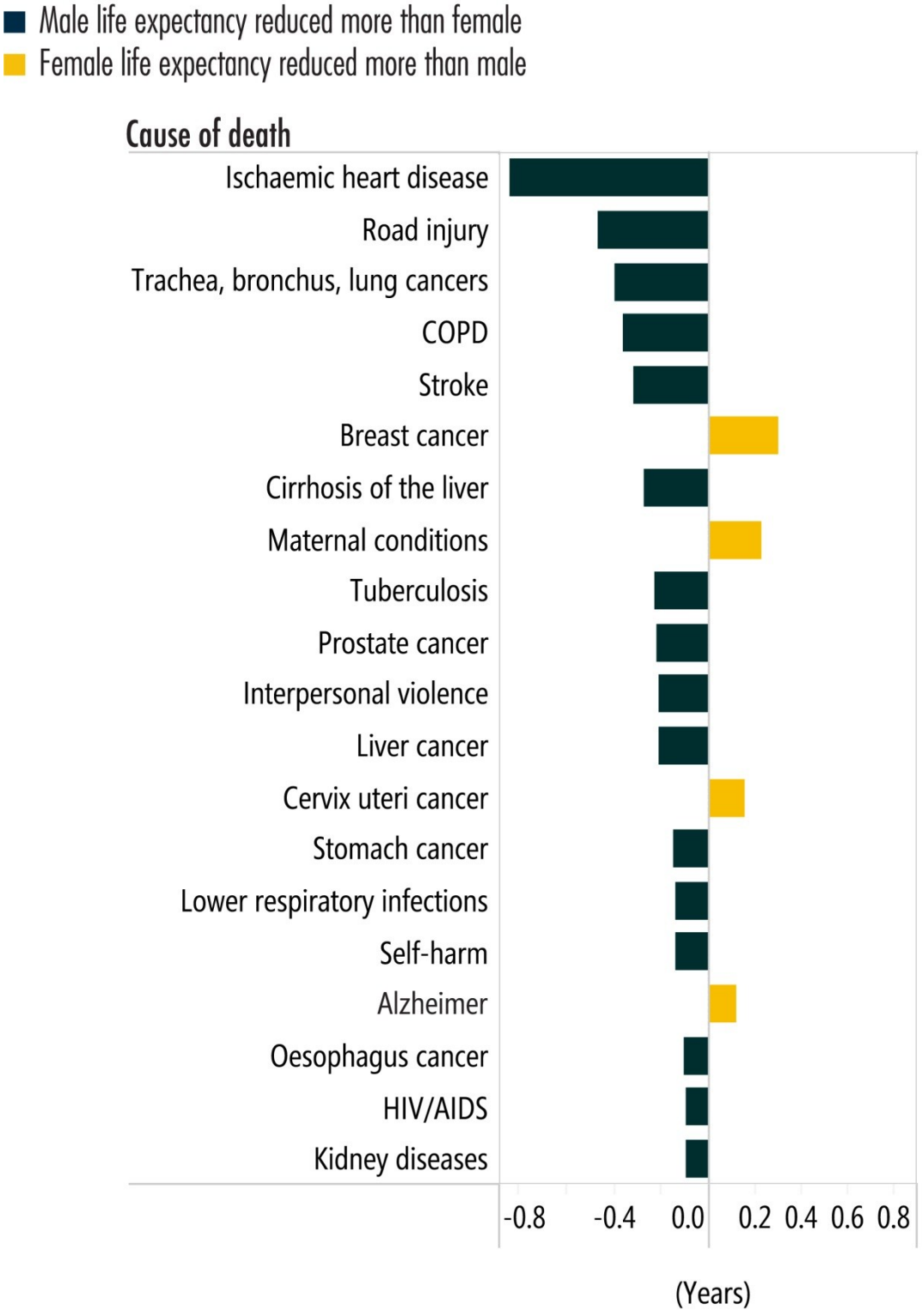


Figure 1. United Nations data for life expectancy by sex for 2020.

Causes of death that most contribute to differences in life expectancy at birth globally for men and women, 2016



Sources: WHO (2018) *(2)* and see *(4)* for decomposition of life expectancy.

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Figure 2. Sex differences in diseases that are major causes of death worldwide from the World Health Organization.

Sex differences in acceptance, immune responses, and adverse reactions to vaccines in humans

Target group	Vaccine	Gender difference in acceptance	Sex difference in immune response	Sex and gender difference in adverse reactions	Age (years)
Children	Hepatitis B	Not defined	Greater in females	Not defined	< 12
	Diphtheria	Not defined	Greater in females	Not defined	< 2
	Pertussis	Not defined	Greater in females	Not defined	< 2
	Pneumococcal	Not defined	Greater in females	Not defined	6–9
	Rabies	Not defined	Greater in females	Not defined	6–9
	Measles	Not defined	Greater in females or equivalent in both sexes	Increased in females	< 3
	Malaria (RTS,S)	Not defined	Greater in females	Increased in females	< 2
	Human papillomavirus	Less in males	Greater in females	Increased in females	5–17
Adults	Influenza	Less in females	Greater in females	Increased in females	18–49
	Hepatitis B	Not defined	Greater in females	Increased in females	18+
	Herpes virus	Not defined	Greater in females	Not defined	18+
	Yellow fever	Not defined	Greater in females	Increased in females	18+
	Rabies	Not defined	Greater in females	Not defined	18+
	Smallpox	Not defined	Greater in females	Not defined	18+
Aged adults	Influenza	Less in females	Greater in females	Increased in females	65+
	Td/Tdap	Less in females	Greater in males	Increased in females	65+
	Pneumococcal	Less in females	Greater in males	Increased in females	65+
	Shingles	Not defined	Not defined	Increased in females	65+

Figure 3. Sex differences in immune responses and adverse reactions to vaccinations over the lifespan.

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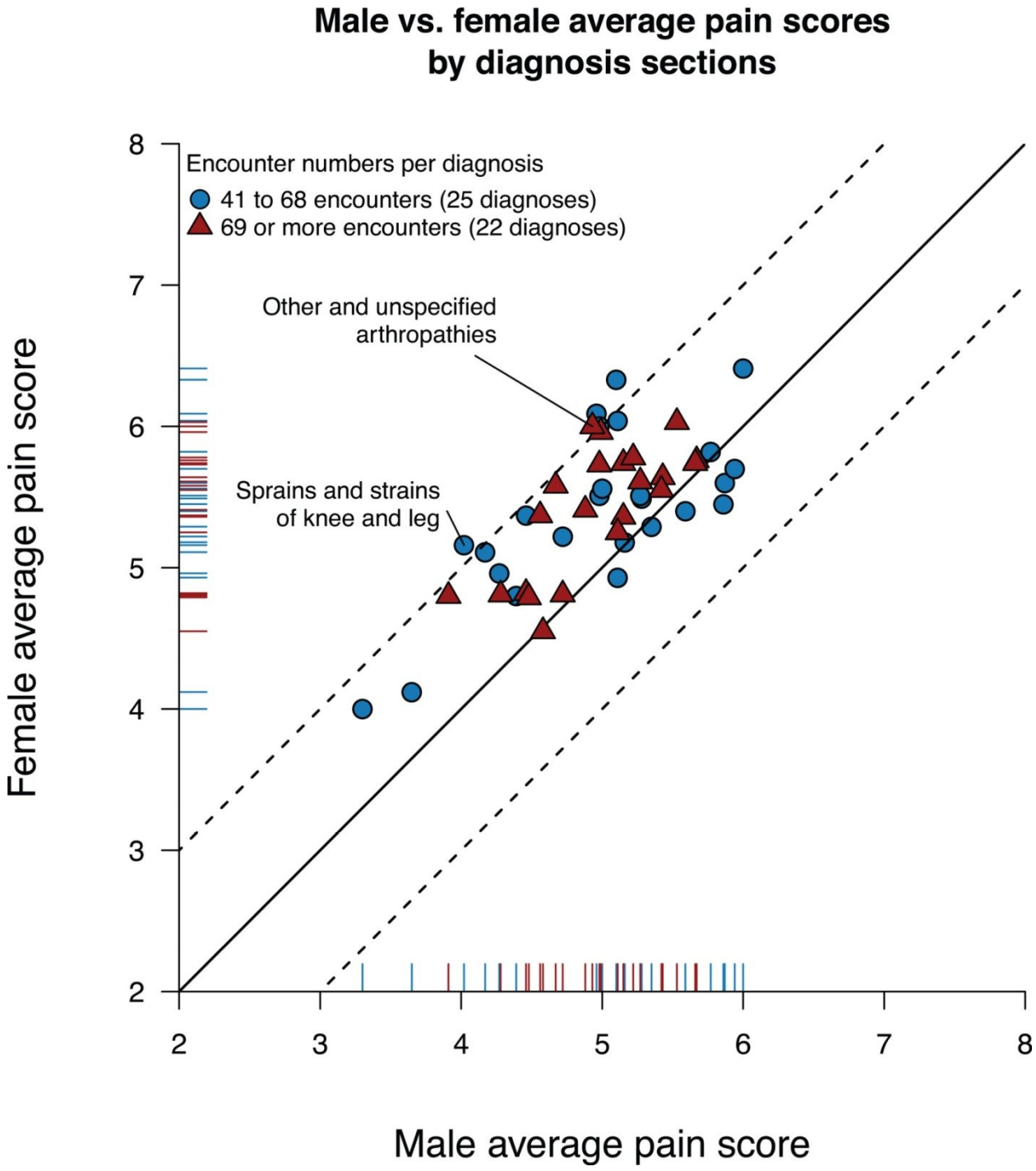

Figure 4. Average pain scores by sex for 47 conditions from one American hospital.

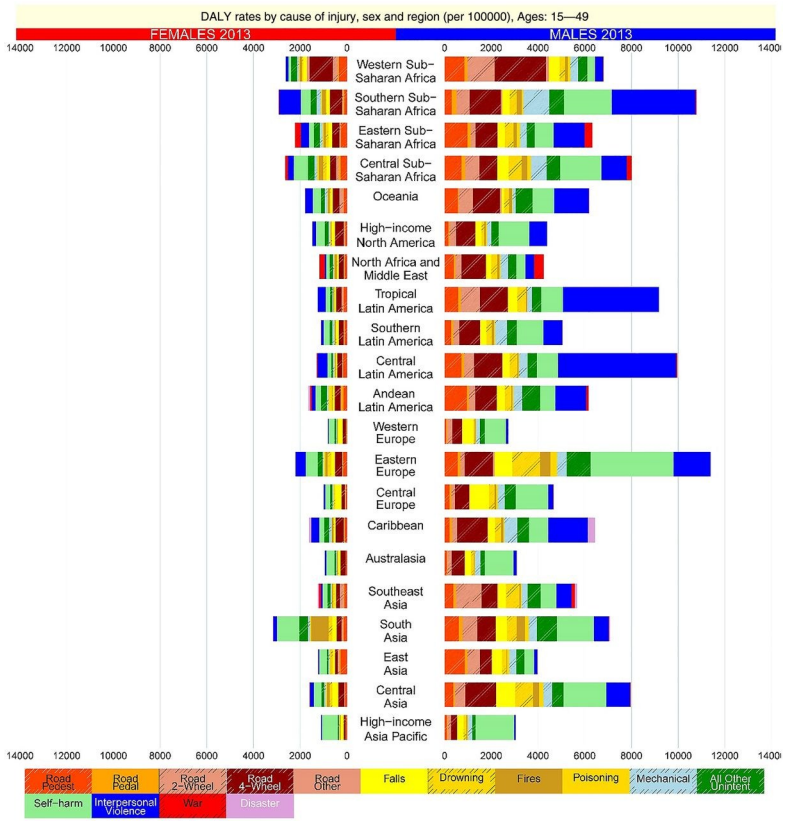

Figure 5. Disability-adjusted life year (DALY) by injury, sex, and region for ages 15-49 years from the Global Burden of Disease project.

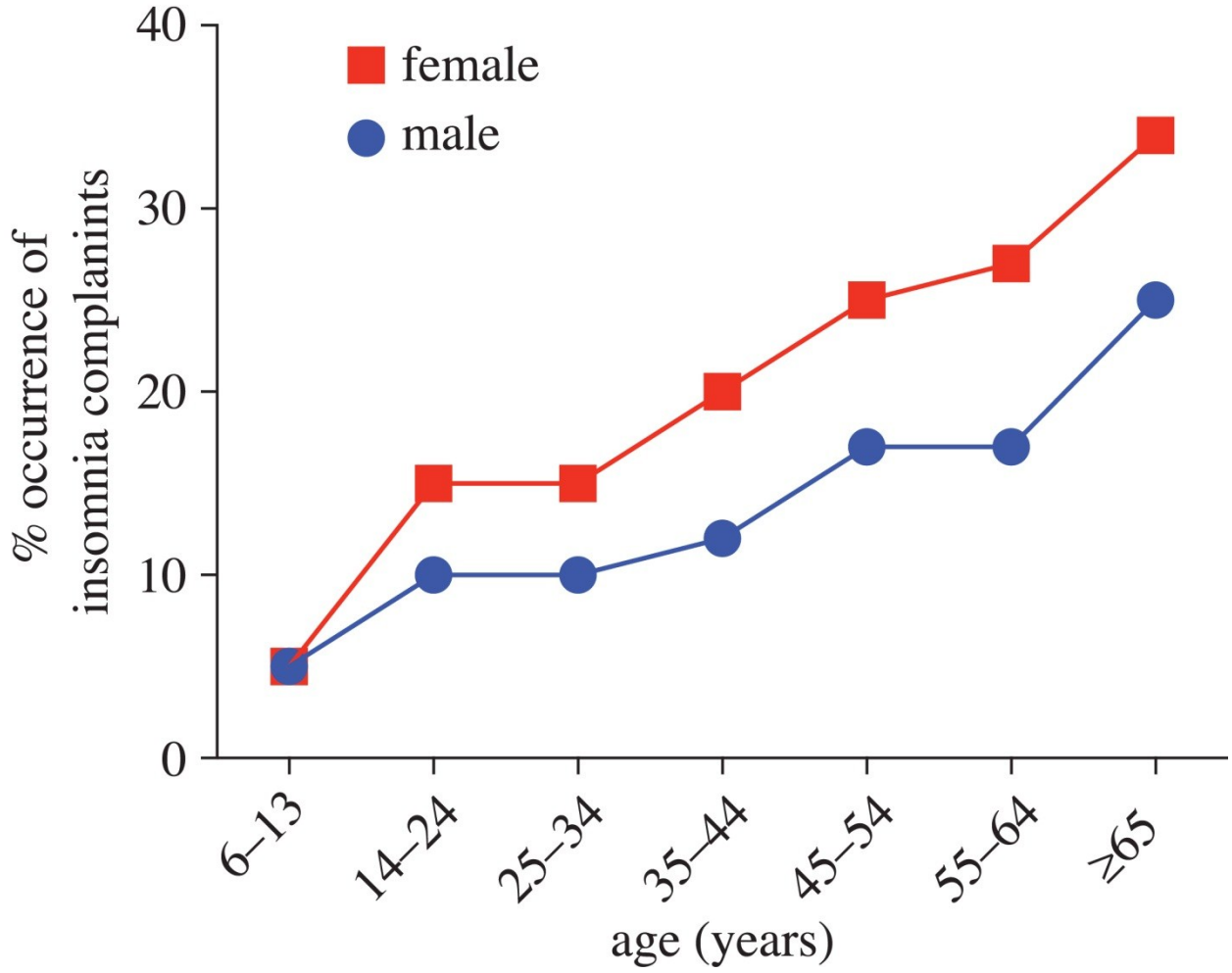

Figure 6. Prevalence of insomnia by sex and age.

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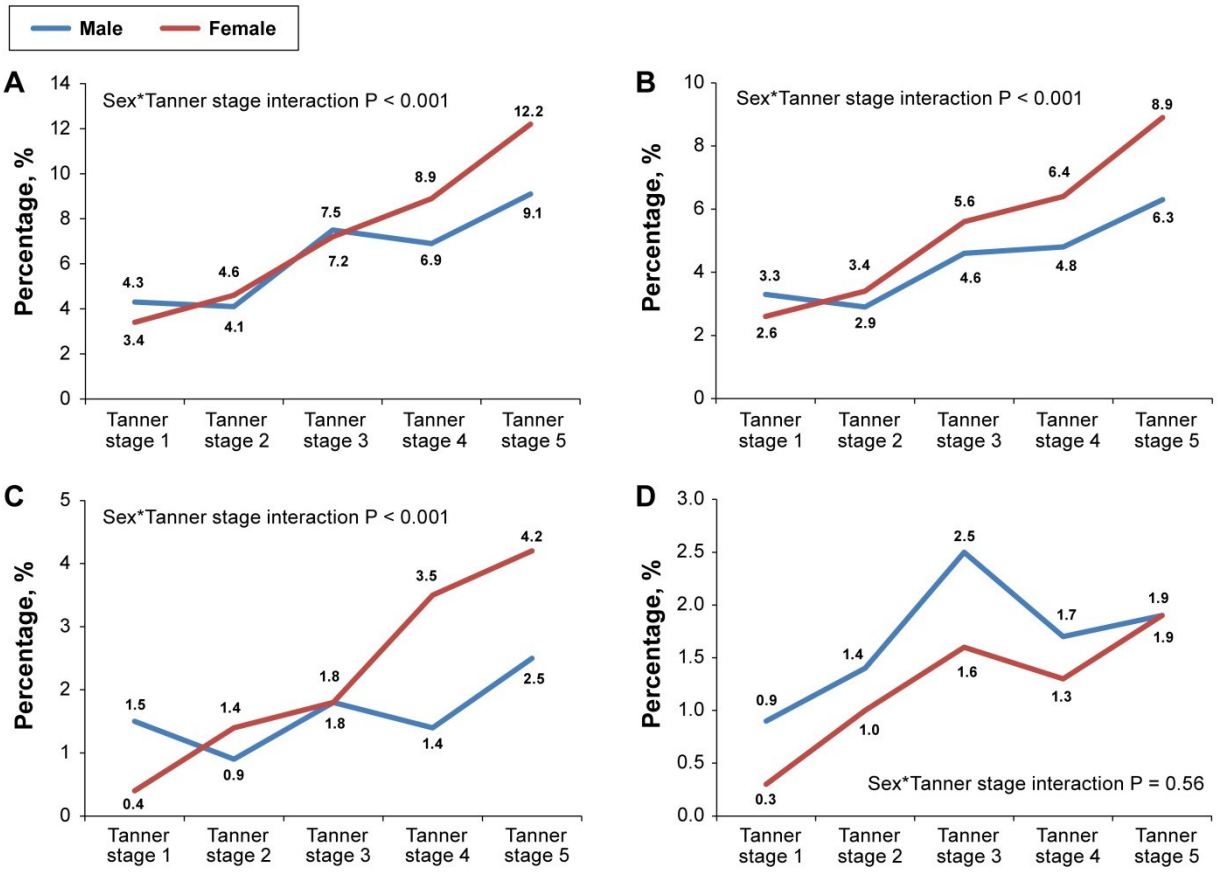

Figure 7. Rates of insomnia in Hong Kong by sex and Tanner stage for A) overall insomnia symptoms B) difficulty initiating sleep C) difficulty maintaining sleep and D) early morning awakening.

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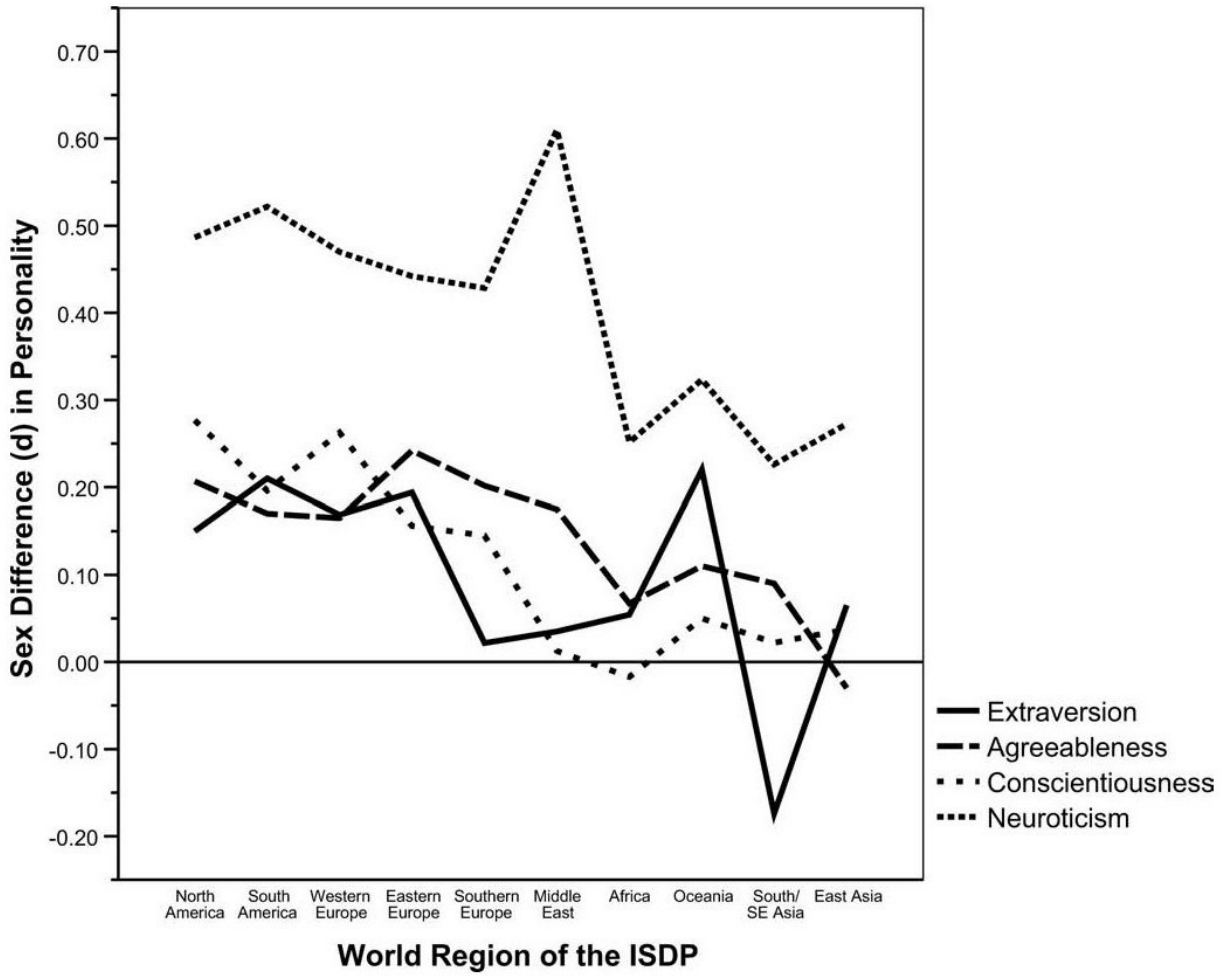

Figure 8. Magnitudes of sex differences in neuroticism by world region based on the International Sexuality Description Project.

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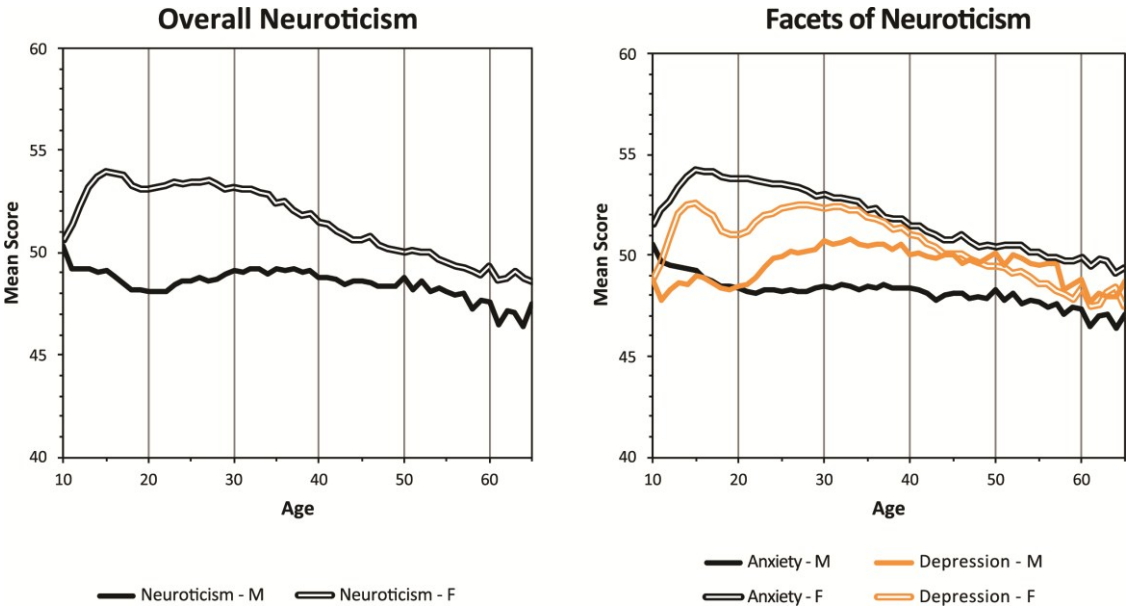

Figure 9. Sex differences in neuroticism by age in a large English-speaking sample.

Figure 10. Sex differences in frequency of COVID-19 infections across varied demographic factors in England.

https://doi.org/10.1017/S0140525X21002417

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Table 1. Threats, Self-Protective Responses, Extreme Protective Reactions, and Fatal Conditions with Estimates of Adult Female:Male Odds Ratios [OR]*.

Threat	Protective Response	Extreme Protective Reaction	Fatal Conditions Overall Mortality [.66][l]
External pathogens and internal pathologies	Antibody Production [4.17][a]	Autoimmune Disease [2.46][aa]	CVD [.70][ll] Cancer [.45-.68][lll] COVID-19 [1.59][lV]
	Non-pharmacological [1.49][b] and Pharmacological [.89][b] Preventive Behaviors to Pandemics		
Bodily damage	Adverse Reactions to Pictured Environmental Threats [1.92-4.27][c] Lower Threshold for Pain [2.52][d] Shorter Endurance of Pain [8.35][d]	Migraine [2.15][bb] Fibromyalgia [3.09][cc]	Accidental Injuries[V] Road Traffic [.37] Drowning [.43] Poisoning [.57] Fire-related [.95]
Nighttime Threats	Sleep Disturbances [1.06-1.46][e] Nightmares [.94-1.60][f]	Insomnia Disorders [RR=1.41][dd] Nightmare Disorder [2.10][ee] Restless Leg Syndrome [1.63-2.22][ff]	Obstructive Sleep Apnea[VI] [.27-.43]
Reduction of Social Threats and Facilitation of Social Bonds	Smiling [2.10][g] Politeness [1.52][h] Emotion Identification [1.36-2.67][i] Direct Competition [.19-.46][j] Direct Aggression [.34-.58][k]	Separation Anxiety Disorder [1.60][gg] Major Depression [1.95][hh] Suicide Attempt [1.29-1.96][ii]	Suicide [.52][V] Victim of Homicide [.23][V]
Personality Style	Neuroticism [2.07][l]		
Emotional Reactions	Fear [1.04-8.20][m] Disgust [1.24-16.33][n] Sadness [1.34-1.66][o] Crying [2.26-7.45][p] Anger [1.08][q]	PTSD [2.60][gg] CFS/ME [4.51][jj] Anxiety Disorder [1.70][gg]	

*Odds ratios >1 indicate higher prevalence in females than males and <1 indicate higher prevalence in males than females.

[a]Yang & Kozloski 2011 antibodies [b]Moran and Del Valle 2016 pandemic prevention [c]Bradley et al. 2001; Gong et al. 2018; Gomez et al. 2013; Lang & Bradley 2007; McManis et al. 2001 adverse reactions to photographs of environmental threat [d]Riley et al. 1998 pain [e]Wang et al. 2019 sleep disturbances [f]Schredl & Reinhard 2011 Hedge's g nightmares [g]LaFrance et al. 2003 smiling [h]Leaper & Robnett 2011 politeness [i]Connolly et al. 2019; Hall, 1978; Hall et al. 2000; Sasson et al. 2010; Thompson & Voyer 2014 emotion identification [j]Klege et al. 2021; Deaner & Smith 2012 direct competition [k]Archer 2019 direct

https://doi.org/10.1017/S0140525X21002417

aggression [l]Kajonius & Johnson 2018; Schmitt et al. 2008 neuroticism [m]Archer 2019; Arrindell et al. 2004; Brebner 2003 fear [n]Al-Shawaf et al. 2018; Atari et al. 2020; Curtis & de Barra 2018; Egolf et al. 2019 disgust [o]Brebner 2003; Lucas & Gohm 2000 sadness [p]Sharman et al. 2019; van Hemert et al. 2011 crying [q]Archer 2004 anger

[aa]Hayter & Cook 2012 Autoimmune Disorder [bb]Stovner et al. 2018 migraine [cc]Queiroz 2013 Fibromyalgia [dd]Zhang & Wing 2006 Risk Ratio insomnia disorder [ee]Li et al. 2010 Hong Kong ≥3 nightmares/week [ff]Ohayon & Roth 2002 restless leg syndrome [gg]Seedat et al. 2009 separation anxiety disorder, PTSD, anxiety disorder [hh]Salk et al. 2017 major depression [ii]Nock et al. 2008 non-fatal self-injury; Miranda-Mendizabal et al. 2019 [jj]Reyes et al. 2003 CFS in USA

[I]GBD, 2018 mortality [II]Mosca et al. 2011 cardiovascular disease [III]WHO 2021 cancer mortality [IV]Williamson et al. 2020 [V]WHO 2014a for deaths from injuries, suicides, and homicides (we calculated ORs based on graph). We assume being a victim of homicide can be avoided to some extent through self-protective reactions. [VI]Lévy et al. 2015 obstructive sleep apnea

https://doi.org/10.1017/S0140525X21002417