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Gender-based violence and trauma in marginalized populations of women: Role of biological embedding and toxic stress

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Abstract

Gender-based violence (GBV) and trauma can dysregulate and recalibrate environmentally sensitive physiological (i.e. central nervous, endocrine, and immune) systems placing survivors at risk for multiple health problems. The researchers build the case that the effects of GBV are likely to be particularly high impact and contribute to health disparities for marginalized survivors of GBV. Further, the researchers underscore a need for a multi-level bio-socio-ecological model that deciphers, characterizes, and explains individual differences in these effects and the need to establish an evidence base from which to derive interventions that address biological effects of toxic stress among marginalized survivors of GBV.

Introduction

In recent decades, due to growing recognition of the interconnections between brain, behavior and environment (McEwen, 2017), there has been renewed research interest in the effects of stress and adversity on health and human development (Shonkoff, 2016). Contemporary theoretical approaches are highly interdisciplinary and are largely grounded in conceptual models focused on predicting individual differences in risk versus resilience (Rutter, 2012, 2013). These theoretical approaches explain the impact of risk and resilience factors interacting across multiple levels of analysis. The structural components of these models also include concepts from the social-ecological framework which emphasizes the impact of social forces within and between families, communities, cultures and societies

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(Southwick, Bonanno, Masten, Panter-Brick, & Yehuda, 2014). Recently, researchers have also included biological levels of analyses both as outcomes and mechanisms translating environmental events into divergent outcomes (Boyce, 2016; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van Ijzendoorn, 2011; McEwen, 2017; Shonkoff, 2016). The application of these models has significantly advanced our understanding of the short- and long-term consequences of childhood poverty, homelessness, prenatal drug exposure, prematurity, child maltreatment, and childhood exposure to violence/trauma. Surprisingly, few researchers have applied these models to advance our understanding of the effects of gender-based violence (GBV) and trauma on women (Lemieux, Coe, & Carnes, 2008; Leserman & Drossman, 2007; Levandowski et al., 2013; Meston & Lorenz, 2013; Moog et al., 2016; Woods et al., 2005), and almost none have focused attention specifically on GBV among women from marginalized groups (Gill, 2007). By definition, and through social exclusion, marginalized women are systematically blocked or denied full access to various rights, opportunities and resources that are fundamental to social integration and observance of human rights (Nigam, 2014). For these reasons, the effects of GBV are likely to be particularly high impact on marginalized women's health and well-being. In this paper, the authors bring these contemporary models of the effects of toxic stress to the attention of the national research agenda on health disparities in women. The authors present GBV as a global public health and human rights problem, review current theoretical models, then synthesize and integrate relevant literature, and conclude by outlining programmatic research goals to address the effects of biological embedding and toxic stress on the health of marginalized women.

GBV: A global public health and human rights problem

GBV is a public health and human rights problem. It refers to the "violence that occurs as a result of the normative role expectations associated with each gender, along with the unequal power relationships between the two genders, within the context of a specific society" (Bloom, 2008, p. 14). Since women are disproportionally victimized by GBV, the term is mostly used to describe violence against women. The examples include physical/ sexual violence, murder, forced prostitution, and genital mutilation (Heise, Ellsberg, & Gottmoeller, 2002). Globally, 35% of women have experienced either physical and/or sexual intimate partner violence (IPV) or nonpartner sexual violence (World Health Organization (WHO), 2013). In the WHO multi-country study, 15–71% of women experienced physical or sexual violence (Ellsberg et al., 2008). In a systematic review on prevalence of GBV in multiple countries, 10–50% of women reported lifetime physical IPV (Watts & Zimmerman, 2002). In the US, >27% of women have experienced sexual violence, physical violence, and/or stalking by an intimate partner in their lifetime (Black et al., 2011).

The impact of GBV is seen in the form of both fatal and nonfatal outcomes for women. Fatal outcomes include homicide, suicide, maternal mortality, and AIDS-related deaths. Nonfatal outcomes include health issues such as chronic pain, PTSD, unwanted pregnancy, and HIV/ STIs (Heise et al., 2002). At the family level, GBV can threaten family structures leading to inability to carry out daily activities (United States Agency for International Development (USAID), 2012). Children witnessing GBV suffer from poor mental health, poor academic performance and accept violence as a means of conflict resolution/communication and often

become perpetrators themselves (United Nations Children's Fund (UNICEF), 2006; USAID, 2012). Thus, GBV has a negative impact on women, and families with ripple effects throughout communities. At the societal level, GBV is associated with economic costs such as inability to work and loss of income (USAID, 2012).

Women exposed to toxic stress of GBV over the life span are at increased risk for a variety of poor health outcomes (Blanch, Shern, & Steverman, 2014; Scott-Storey, 2011). Stress is a physiological and psychological response to an external threat that individuals feel that they do not have the resources to deal with (Lazarus & Folkman, 1984; McLeod, 2010; Schneiderman, Ironson, & Siegel, 2005). Toxic stress refers to prolonged, frequent, and/or severe or extreme activation of the stress response due to exposure to adverse life experiences (Johnson, Riley, Granger, & Riis, 2013; Shern, Blanch, & Steverman, 2014) such as violence, trauma, and lack of social support (Johnson et al., 2013). Violence, as a chronic stressor (Pavlish, Noor, & Brandt, 2010) can negatively impact health via dysfunctional stress response and immune system (Bevans, Cerbone, & Overstreet, 2008; De Bellis et al., 1994; Robertson Blackmore et al., 2016). Chronic stress poses multiple health risks such as poor mental health (Sundermann, Chu, & DePrince, 2013) and HIV/STIs (Haydon, Hussey, & Halpern, 2011; Hillis, Anda, Felitti, Nordenberg, & Marchbanks, 2000). For instance, higher rates of HIV/STIs have been reported among some marginalized groups (e.g., immigrants) relative to the general US population (Kerani et al., 2008) which may relate to chronic stress or trauma in their lives. Further, women are more vulnerable than men to the development of posttrauma symptoms and take longer to recover from them (Meewisse, Reitsma, de Vries, Gersons, & Olff, 2007; Silove et al., 2017). Specific psychobiological reactions to trauma such as more sensitized HPA axis (i.e., which is a body's central stress response system that is responsible for effective adaptation to external demands) with lower cortisol levels (i.e., hormone that regulates stress), peri-traumatic disassociation, and use of avoidant coping strategies may contribute to higher risk for PTSD among women (Meewisse et al., 2007). Under certain conditions, women's typical responses to stress are more marked by a pattern of "tend and befriend" than "fight-or-flight." Tending involves nurturant activities that protect them from harm and befriending process involves affiliation with social networks to reduce risk (Taylor et al., 2000). Marginalized women who lack resources may be less able to benefit from the "befriend" response, which could protect them from poor health outcomes of toxic stress.

Discrimination, marginalization, and gender inequality

The impact of GBV can be more profound on women that face discrimination, marginalization and gender inequality. Intersectionality describes the intersecting effects of race, class, gender, and other marginalizing characteristics that contribute to social identity and affect health (Seng, Lopez, Sperlich, Hamama, & Reed Meldrum, 2012, p. 2437). The negative impact on health occurs via discrimination and other forms of inequalities (Seng et al., 2012). "Minority stress" refers to the experience of stress in negative or undesirable situations due to the individual's membership in a stigmatized social group, that is, a group that is the target of discrimination and prejudice (Arbona & Jimenez, 2014). Minorities' location at the intersection of disadvantaged gender, race and class background and associated social inequality is a central aspect of stress in their lives (Perry, Harp, & Oser,

2013). Stress related to living in a volatile environment with limited resources, financial insecurities, and uncertainty about future can place women at risk for multiple health problems. Inability to resolve uncertainty creates a chronic situation, burdening individuals with “allostatic load.” Uncertainty can create a vicious cycle of altered brain architecture and systemic pathophysiology, leading to further damage of an individual’s ability to cope with uncertainty (Peters, McEwen, & Friston, 2017). This in turn, places individuals at risk for health issues such as depression, and stroke (McEwen, 1998; Peters et al., 2017). Marginalized women, are therefore, at high risk for health outcomes associated with toxicity of stress.

From an intersectional viewpoint, marginalized women face worse outcomes of GBV due to multiple stressors related to their position in society. For instance, immigrant women’s stress comes from multiple sources of vulnerability such as undocumented status and reluctance to seek care because of concerns about mistreatment (Derose, Escarce, & Lurie, 2007). Acculturation is an additional source of stress with symptoms such as poor mental health, heightened psychosomatic symptom levels and identity confusion (Berry, Kim, Minde, & Mok, 1987). US-born minority women (i.e., women of color), are also disproportionately impacted by GBV and its negative effects (Sabri et al., 2013). GBV, perceived as chronic psychological stressor (Jun, Rich-Edwards, Boynton-Jarrett, & Wright, 2008), is associated with adverse health outcomes, but under-utilization of services (Himle, Baser, Taylor, Campbell, & Jackson, 2009; Sabri et al., 2013). Minority women’s marginalization and their multiple intersecting identities may extenuate stress related to GBV and amplify its adverse effects.

Biological embedding of GBV

Exposure to stressors at multiple contextual levels (societal, community, and interpersonal; Heise, 1998) significantly impacts health. Stress is a physiological and psychological response to an external threat that individuals feel that they do not have the resources to deal with (Lazarus & Folkman, 1984; McLeod, 2010; Schneiderman et al., 2005). Physiologically, the stress response rapidly and pervasively adjusts the body to manage and adapt to an external threat (Chrousos, 1998). The perception or evaluation of threat by the brain and execution of physiological responses are fundamentally shaped by individual differences in constitutional (genetics, development, and experience), behavioral (strategies of coping), and historical (e.g., traumatic experiences) factors. These factors ultimately determine individuals’ resiliency to stress (Juster, McEwen, & Lupien, 2010; McEwen, 1998). Brief or day-to-day naturalistic stressors do not impose a health burden, especially among healthy people with good coping responses. However, strong and persistent stressors take the form of toxic stress, especially among biologically vulnerable individuals due to factors such as age, genetics (Schneiderman et al., 2005), and maladaptive coping. Toxic stress refers to prolonged, frequent, and/or severe or extreme activation of the stress response due to exposure to adverse life experiences (Johnson et al., 2013; Shern et al., 2014) such as violence or trauma, and lack of social support (Johnson et al., 2013).

The long-term effects of toxic stress on a person differ based on his or her stage of brain development when he or she is exposed to stress. Exposure to toxic stress early in life (i.e.,

prenatal and early childhood) has the broadest impact, causing long term changes in the brain's structure, through a process referred to as the "biological embedding of experience" (Johnson et al., 2013; Shern et al., 2014). Biological embedding is "the process by which individuals' previous experiences and environments systematically alter their health and functioning across the life span (Hertzman, 1999; Johnson et al., 2013, p. 320). In early years of life, the nervous system is growing, and the brain structure is being developed. In this stage, toxic stress negatively impacts an individual's ability to learn and his or her memory. Exposure to toxic stress in later childhood and adolescence leads to problems related to attention, impulse and emotional control. In late adolescence or early adulthood, toxic stress results in heightened fear response and hyper-reactivity to stressful stimuli. Toxic stress during adulthood intensifies the ageing process and affect emotions, memory and cognition (Shern et al., 2014). Lifetime exposure to toxic stress can shorten the life span (Epel & Lithgow, 2014). Other health effects of toxic stress are adult-onset diabetes, cardiovascular disease, hypertension, osteoporosis, reproductive decline, and immune suppression (Sapolsky, 2004). These conditions become common with increasing age (Sapolsky, 2004). Thus, efforts are needed to identify risk and protective factors for toxic stress and prevent negative outcomes of toxic stress. Efforts are particularly needed towards preventing negative health effects of toxic stress among populations at high risk such as marginalized women exposed to lifetime violence/trauma.

Environmental stress triggers activation of many physiological mechanisms including the autonomic nervous system (ANS) and the hypothalamic– pituitary–adrenal (HPA) axis. The ANS is made up of the sympathetic nervous system (SNS), the parasympathetic nervous system and the enteric nervous system. The sympathetic–adrenal–medullary (SAM) axis connects the brain directly to the adrenal medulla via SNS. On exposure to stress, both SAM and the HPA axis are the two major interconnected systems that manage the stress response. These SAM and the HPA axis also influence the immune system and regulate inflammation (Sturmberg & Martin, 2013).

The HPA axis is primarily responsible for regulation of the stress response and maintenance of homeostasis. The HPA axis comprise of three endocrine glands (glands that release hormones): the hypothalamus, the pituitary gland and the adrenal medulla. When a situation is perceived as stressful by the brain, the hypothalamus (part of the brain in charge of the stress response) is activated. At triggering of a stress response, the hypothalamus sends signals to the pituitary gland and the adrenal medulla. The pituitary gland secretes adrenocorticotropic hormone (ACTH). The ACTH stimulates the adrenal glands to signal the release of glucocorticoid hormone (i.e., cortisol) (Lundberg, 1999; McLeod, 2010).

When a stress response is triggered, the hypothalamus along with the SNS also stimulates the adrenal medulla, activating the SAM axis to produce the catecholamines: epinephrine (adrenaline), and norepinephrine (noradrenaline), into the blood stream, preparing the body for battle (Glaser & Kiecolt-Glaser, 2005; Lundberg, 1999; McLeod, 2010; Romeo, 2013). Both catecholamines and cortisol stress hormones work together to increase available sources of energy by promoting lipolysis (breaking down fats into usable sources of energy) and the conversion of glycogen into glucose (i.e., blood sugar) (Schneiderman et al., 2005). Catecholamines and cortisol increase in response to stress, preparing the body for action to

fight against the stress. Two features make these stress responses adaptive. First, the release of stress hormones makes energy stores available for the body's immediate use. Second, energy is diverted to areas such as the skeletal muscles, the brain, activation of the immune system, with suspension of less critical activities such as digestion (Schneiderman et al., 2005). These physiological changes co-occur with elevated inflammatory cytokines and the response of the parasympathetic nervous system, which counterbalances both sympathetic activation and inflammatory responses (Shonkoff et al., 2012).

The activation of stress regulatory systems mobilizes the body to confront or flee from the stressor (the fight or flight response). The fight or flight response, as a short-term rapid stress response is regulated by the SAM axis, with long-term stress and related slower stress response regulated by the HPA axis (Glaser & Kiecolt-Glaser, 2005; Lundberg, 1999; McLeod, 2010; Romeo, 2013). The stress response mechanisms provide support over the short term for behavioral action or coping. However, repeated activation of the stress systems over the long term, compromise their functioning and lead to poor health or diseases (Cohen, Gianaros, & Manuck, 2016; Taylor, 2010).

Frequent or chronic activation of stress responses can result in dysregulation of physiological mechanisms leading to a chronic "wear and tear" effect on multiple organs of the body including the brain (Shonkoff et al., 2012). The process of "wear and tear" the body experiences because of cumulative, stress induced burden, is referred to as the "allostatic load"(Juster et al., 2010; Shonkoff et al., 2012). Allostatic load is the price paid by the body for "being forced to adapt to adverse psychosocial or physical situations, and it represents either the presence of too much stress or the inefficient operation of the stress hormone response system, which must be turned on and then turned off again after the stressful situation is over" (McEwen, 2000, p. 111). Allostatic load occurs due to (a) repeated "hits" from multiple novel stressors (e.g., child abuse); (b) Inability to manage the hormonal stress response (failure to habituate to repeated stressors of the same kind); (c) Prolonged response due to delayed shut down (failure to turn off each stress response efficiently such as prolonged elevation of blood pressure); and (d) hormonal stress response being inadequate to the needs of the individual genotype, resulting in increased levels of inflammatory cytokines that are normally controlled by elevated levels of cortisol and catecholamines (McEwen, 2000). Allostatic load has negative consequences for health. For instance, excessive discharge of epinephrine and norepinephrine can lead to the suppression of the immune system, abnormal heart rhythms, and neurochemical imbalances that may lead to mental health disorders. Prolonged cortisol secretion can destroy neurons in the hippocampus and lead to metabolic and immune changes potentially prognostic for developing chronic illnesses (Taylor, 2010). Thus, over-activation of the stress-regulating systems in the context of repeated/chronic adversity leads to alterations in their regulation (Shonkoff et al., 2012).

Toxic stress can also lead to accelerated aging and early diseases via shorter telomere length. Telomeres, the DNA-protein caps at the ends of chromosomes, delay ageing by protecting genetic material from degradation (Puterman et al., 2016; Stacy, 2014). Whenever a cell divides, some telomeres are lost. The telomerase enzyme can replenish it, but toxic stress can decrease the supply of telomeres. The telomere if too diminished can kill the cells or

make them pro-inflammatory, thus accelerating the aging process and ageing-related health risks (Stacy, 2014). Adverse life experiences such as childhood abuse have been associated with higher inflammation and shorter telomeres among adults (Epel et al., 2010; Kiecolt-Glaser, Jaremka, Derry, & Glaser, 2013). Shorter telomeres have been associated with multiple health issues such as depression and enhanced risk for infections (Epel et al., 2010; Kiecolt-Glaser et al., 2013; Lin, Epel, & Blackburn, 2012).

Psychological consequences of toxic stress influence the nature and direction of the HPA axis response. Research suggests that psychological factors such as emotions or perceived uncontrollability of stress are powerful determinants of HPA activity (Miller, Chen, & Zhou, 2007). For instance, traumatic experiences and subsequent PTSD has been related to low levels of cortisol (hypocortisolism). Individuals experiencing uncontrollable stress may have diminished HPA activity, which may explain their withdrawn and disengagement behaviors (Miller et al., 2007). Thus, cortisol and HPA activity play a role in mental and behavioral health. These mechanisms also play a role in physical health. For instance, hypocortisolism may lead to somatic disorders (Heim, Ehlert, Hanker, & Hellhammer, 1998). The immunosuppressive action of cortisol prevents toxic effects of body defensive mechanisms that are activated in response to stress. Thus, a persistent lack of cortisol in individuals exposed to trauma/toxic stress might place them at increased risk for autoimmune disorders, inflammation, chronic pain, allergies, and asthma (Heim et al., 1998; Munck, Guyre, & Holbrook, 1984).

Bio-psycho-socio-ecological model and life course perspective: Risk and resilience

Components of the social-ecological model have been used to understand the interplay of person variables and social factors that combine to cause GBV (Heise, 1998; Heise et al., 2002; Sabri, 2014) and shape health. The social-ecological perspective focuses on interdependence of risk factors at multiple levels in the environment that contribute to health disparities. The biopsychosocial perspective posits that health is best understood in terms of a combination of biological, psychological and social/environmental factors (Borrell-Carrio, Suchman, & Epstein, 2004) and health concerns result from a disruption in the balance of body, mind and environment (Warshaw, Sullivan, & Rivera, 2013). For instance, chronic or repeated stress from the environment over time results in a pattern of HPA hyperactivity and immune-dysregulation leading to poor health (Lu & Halfon, 2003). Per the life course approach, biological, behavioral, and psychosocial processes that operate across an individual's life course influence health and hence may account for health disparities (Kuh, Ben-Shlomo, Lynch, Hallqvist, & Power, 2003). A life course perspective is a person-in-context view of how an individual goes through unique developmental pathways shaped by individual, and environmental factors. For instance, factors at multiple contextual levels increase risk for GBV and related health risks. The examples of environmental/societal-level factors include socio-cultural norms and beliefs that promote GBV (Heise, 1998; Heise et al., 2002; Krug, Dahlberg, Mercy, Zwi, & Lozano, 2002; Sabri, 2014). The community-level factors include level of support from formal and informal institutions such as the police. The relationship-level factors include partner's behaviors such as control of wealth in the family. At the individual level is the biological and personal history that a woman brings to her behavior in relationships (Heise et al., 2002) such as dependence on the partner. Protective

factors are those contextual factors that buffer against the risk for GBV. Protective factors such as social support at the community level (Sabri, Simonet, & Campbell, 2018) and laws and regulations against GBV at the societal level may protect against risk and negative impact of GBV (Figure 1).

Chronic exposure to GBV can result in allostatic load and its pathophysiological consequences. However, GBV victims may differ in the vulnerability and resilience to the development of psychopathological or pathophysiological outcomes such as alterations in the endocrine system (Blasco-Ros, Herbert, & Martinez, 2014). The differences in effects of GBV can be explained by risk and resiliency factors. Risk factors directly lead to psychopathology. Resilience factors known as “personal psychological and biological variables or “strengths” protect against the development of psychopathology in the face of trauma” (Hoge, Austin, & Pollack, 2007, p. 139). Risk and resilience is influenced by the interactions between genetic variations and environmental experiences (Rutter, 2006). Since the genetic variant is not a risk or protective factor alone, research shows there is little or no effect on psychopathology in the absence of the environmental risk factors (Rutter, 2006). The diathesis-stress perspective stipulates that underlying predisposition/vulnerability (i.e., due to genetics or biological factors) place some individuals at higher risk than others (Hartman & Belsky, 2016; Zuckerman, 1999). The environment interacts with the diathesis to trigger negative responses to toxic stress. In contrast, differential susceptibility perspective asserts that individuals more susceptible to adverse life experiences are, simultaneously, most likely to benefit from a supportive environment because they are more developmentally plastic (Hartman & Belsky, 2016; Zuckerman, 1999). This could be a case with more severe stressors such as GBV. Research on abused children (Cicchetti & Rogosch, 2012) showed that children with the greatest genetic susceptibility had the poorest level of functioning when abused but had the highest level of functioning when not abused. Conversely, less genetically susceptible children showed no effect of abuse on their functioning (Cicchetti & Rogosch, 2012; Hartman & Belsky, 2016). Thus, women victimized by GBV may be most vulnerable to its negative health effects. However, they may benefit the most from social support, as they may generally be more environmentally responsive and developmentally plastic (Hartman & Belsky, 2016; Zuckerman, 1999).

Natural biological resiliency variables for stress include DHEA(S), Neuropeptide Y (NPY), a 36 amino-acid peptide, allopregnanolone (Hoge et al., 2007). Psychological variables such as greater internal locus of control (belief one can generally influence one’s life circumstances), actionoriented coping, ability to use and sustain social support, self-efficacy, mastery, and optimism have been identified as resiliency factors among survivors of violence/trauma (Hoge et al., 2007). Resiliency factors may confer biological benefits via pathways such as social support. Social support may influence health, at least in part, by modulating neural reactivity to stress and consequent neuroendocrine responses such as lower dorsal anterior cingulate cortex (a brain region related to monitoring threat) activity and lower cortisol responses, suggesting lower levels of experienced stress. Individuals with positive beliefs (i.e., optimism, self-esteem, and mastery) who are exposed to stressors have been found to be able to successfully manage stress by cortical regulation of amygdala reactivity and consequent lower downstream neuroendocrine responses (Taylor, 2010). Thus,

women exposed to GBV who possess more resiliency factors are less likely to have high allostatic load than women who are more vulnerable to negative effects of GBV.

GBV as toxic stress

GBV is a prototypical example of toxic stress due to characteristics such as unpredictability, uncontrollability, severity, and long-lasting nature. Exposure to toxic or traumatic stress (Heim et al., 1998) including GBV (Pico-Alfonso, Garcia-Linares, Celda-Navarro, Herbert, & Martinez, 2004; Trickett, Noll, & Putnam, 2011) may result in chronic or prolonged activation of the HPA axis leading to symptoms such as PTSD (Chrousos, 2009; Heim et al., 1998). Research supports HPA axis dysregulation among women exposed to GBV and those with comorbid PTSD, depression and anxiety symptoms (Inslicht et al., 2006; Pico-Alfonso et al., 2004). Both recent and lifetime histories of violence can lead to dysregulated HPA axis or stress responses among women (Basu, Levendosky, & Lonstein, 2013; Rellini, Hamilton, Delville, & Meston, 2009; Shenk, Noll, Putnam, & Trickett, 2010). For instance, GBV survivors have shown lower levels of morning cortisol levels (Basu et al., 2013; Blasco-Ros et al., 2014; Seedat, Stein, Kennedy, & Hauger, 2003) and higher levels of evening cortisol levels (Blasco-Ros et al., 2014; Pico-Alfonso et al., 2004). In a systematic review of 37 studies, significantly lower cortisol levels were found among women with PTSD, and those with PTSD due to violence when compared to the controls. Specifically, in the afternoon, people with PTSD had lower levels of cortisol than those in the control group (Meewisse et al., 2007). GBV also negatively impact the immune system (Garcia-Linares, SanchezLorente, Coe, & Martinez, 2004) placing women at risk for a range of health problems such as reproductive health problems and HIV (Ghosh, Rodriguez-Garcia, & Wira, 2013).

Future directions

Here, we have reviewed information from various fields in an effort to encourage women's health researchers to apply these models and ideas to advance our understanding of the causes and consequences of GBV in marginalized women. The gaps in knowledge are large and filling those gaps is key to developing implications for policy and practice. We searched the following five electronic data bases to identify articles on GBV, trauma, and biological outcomes of stress: the PubMed, CINAHL, PsychINFO, Academic Search Complete, and Embase. The GBV-related terms such as "Violence Against Women," "GBV, were combined using Boolean connector "OR." Using Boolean connector "OR" we combined stress-related terms such as "Toxic Stress," "Physiological Stress." The GBV and stress terms were combined using the Boolean connector "AND." After removing four duplicates, the search resulted in 226 articles which were subsequently screened for relevance. Only 27 articles focused on GBV among women. The findings show a gap in the literature in terms of studies on the biological effects of GBV on adult women, particularly marginalized women. To begin to address those gaps we make the following recommendations. First, we see a need for building, testing, and refining mid-level multi-level bio-socio-ecological models of this phenomenon. Second, there is a need to establish an evidence base for GBV interventions that include biological measures and are designed to address biological effects of toxic stress. Studies could examine the role of biological differences in moderating the effects of GBV interventions and in impacting the outcomes of the interventions. This could help

determine the degree to which biological changes are reversible. Third, we underscore the need to generate descriptive or comparative data that focuses on marginalized groups with appropriate comparison groups, so we can describe how these interacting factors may function differently in the context of socially excluded marginalized women. Fourth, studies are needed that integrate biological processes as mechanisms that translate individual differences in exposure to individual differences in outcomes. Finally, studies are needed that focus on GBV as a global phenomenon and evaluate the cultural and societal forces that both enable and could be harnessed to reduce prevalence/incidence. To accomplish these recommendations will require that careful attention is paid to developing best practices to recruit and retain marginalized women's involvement in the research enterprise.

Conclusions

This paper highlights the need for multilevel bio-socio-ecological models to examine effects of biological embedding and toxic stress as contributors of health disparities among women survivors of GBV, particularly those that belong to marginalized populations. Unfortunately, as long as there are familial, cultural, and political conflicts, marginalized women survivors of GBV will be systematically blocked or denied full access to various rights, opportunities and resources that are fundamental to social integration and observance of human rights. GBV is a global public health and human rights problem. The world needs a much more sophisticated understanding of the effects of toxic stress on marginalized women's health.

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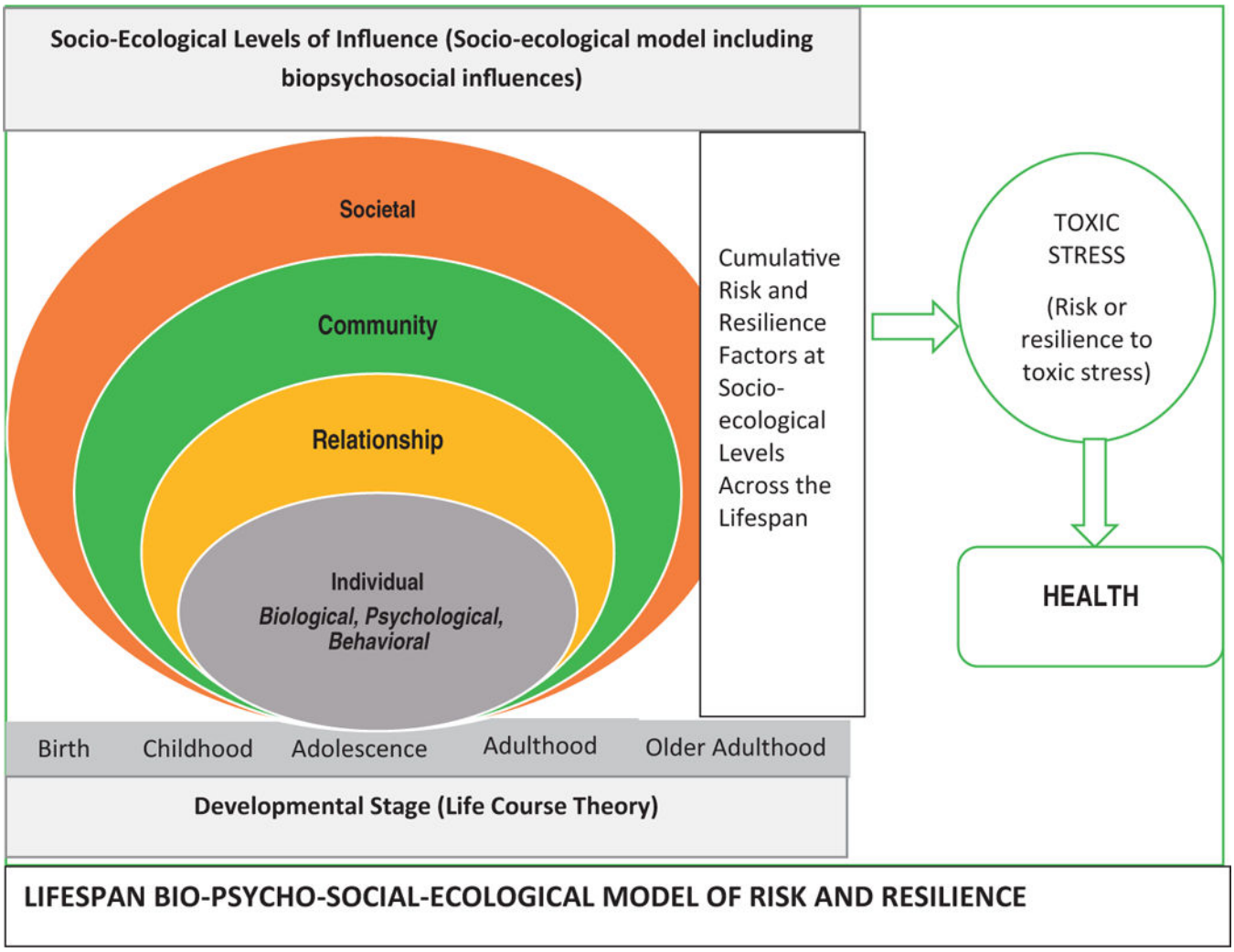

Figure 1.
Lifespan bio-psycho-social-ecological model of risk and resilience.