Lived experience and allostatic load among transmasculine people living in the United States

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ABSTRACT

Background: Transgender and gender diverse people face significant stigma that can adversely affect their physical and mental health. However, the psychobiological link between lived experience and health has been underexplored in this population. We thus examine perceived distress, mental health, and physiological ‘wear and tear’ by indexing allostatic load (AL) and assess associations with a range of contextual and experiential factors from transmasculine people living in the United States.

Methods: Sixty-five people who identified as transgender men or along a transmasculine spectrum, living in Massachusetts, Vermont, and Rhode Island participated in The Transition Experience Study (age: M = 31.8, range 18–55), which examines lived experience of social and medical transition and embodied gender minority/marginalization stress among a sample of transmasculine people. Based on in-depth in-person interview and survey data and inspired by an ecological systems model, we created indices representing (1) perceived progressive geopolitical climate; (2) socio-demographic advantage; (3) social support and resources; (4) gender minority and marginalization stressors; and (5) health behaviors. The Perceived Stress Scale and psychological symptoms (depression, anxiety, insomnia) were also assessed. AL indexed 10 neuroendocrine, immune, cardiovascular, and metabolic biomarkers.

Results: Regressions revealed that perceived stress and psychological symptoms were negatively correlated with progressive geopolitical climate (respectively B = 1.47, p = 0.19; B = 0.77, p < 0.001) and positively correlated with gender minority and marginalization stressors (respectively B = 1.51, p < .001; B = 0.38, p = .005). AL was negatively associated with perceived progressive geopolitical climate (B = −0.55, p = .007) and socio-demographic advantage (B = −3.2, p = .001).

Discussions: These findings underline the importance of assessing geopolitical context and indexing lived experiences and life domains along with biomarker sampling. Together, these enable the identification of psychological pathways to better nuance multi-level contributors to health and well-being and understand embodied inequalities. These analyses of embodied stigma inclusive of AL biomarkers thus provide a model to further research centering transgender people’s health from youth through old age.

1. Introduction

Transgender and gender diverse (TGD) people (i.e., people whose gender identity differs from those typically associated with their sex assigned at birth) face significant mental and physical health disparities in the U.S. and globally (Bradford et al., 2013; Reisner et al., 2016; Winter et al., 2016). These include heightened rates of distress, depression, anxiety (Boekting et al., 2013a; Budge et al., 2013; Puckett et al., 2020), insomnia (Butler et al., 2020), and alarmingly high rates of attempted suicide with estimates ranging from 26% to 45% compared to 2–9% in the general population (James et al., 2016; Nock et al., 2008; Perez-Brumer et al., 2015). Importantly, psychosocial stress experienced from stigma and discrimination is recognized as a major driver of health disparities among sexual and gender minority people (Williams and Mann, 2017). Though effects of stigma on mental health have been relatively well-established, the physiological and potential long-term

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health effects (e.g., via allostatic load) of stigma are relatively less examined and have yet to be explored among TGD people. Moving forward, data driven models of embodied stigma inclusive of physiological pathways are needed to further support TGD people’s health from youth through old age.

Stigma and adversity are pernicious and can come from several spheres of one’s environment to shape their lived experience. To conceptualize this across multiple levels, we consider Bronfenbrenner’s ecological systems model (Bronfenbrenner, 1977, 1994, 1995) that situates individuals within layers of reciprocally interacting systems. These interdependent forces consist of the individual and their immediate environment (micro-system), the interconnections among several individuals (meso-systems), the indirect influence of social structures and settings (exo-system), and finally the current overarching cultural and sub-cultural patterns (macro-system) at a given time (chrono-system). This model is helpful to situate the multiple levels whereby stigma influences health of TGD people. Drawing on qualitative data obtained through in-depth in-person interviews and survey data collected as part of The Transition Experience Study, analyses presented here index micro-level (perceived geopolitical climate), exo-level (e.g., socio-demographics), meso-level (e.g., gender marginalization stressors and social support), and micro-level (e.g., health behaviors) domains collectively to represent the lived experiences of a sample of transmasculine people and assesses these in association with indicators of health and wellness.

Our rationale for this study is rooted in recognition that stigma experienced by TGD people, spanning from the micro-level to the macro-level, contributes to experiences of marginalization and gender minority stress. This refers to the unique stress experienced by TGD people above and beyond those experienced as general life stressors (Brooks, 1981; Meyer, 1995, 2003). More recently, minority stress is also referred to as “marginalization stress” to emphasize the role of stigma and oppression over minority status (e.g., Puckett et. al, 2021). Although originally developed for cisgender (i.e., not transgender) sexual minority people (e.g., lesbian, gay and bisexual; LGB), adaptations of the minority stress model (Hendricks and Testa, 2012) recognize the high levels of discrimination and stigma experienced by TGD people and the negative effects these have on health (White Hughto et al., 2015).

Collectively, sexual and gender minority stress models (Rockting et al., 2013b; Brooks, 1981; Meyer, 1995, 2003) focus on two key stress processes. First, proximal minority stress processes refer to individual-level experiences (e.g., micro-level) like internalized transphobia and concealment of one’s minority identity (Herek, 2009). Second, distal minority stress processes refer to stressors like discrimination and violence experienced at the interpersonal level (e.g., meso- and exo-levels). This also includes structural stigma, the societal-level (e.g., macro-level) conditions, cultural norms, and institutional policies that constrain the opportunities, resources, and well-being of the stigmatized (Hatzenbuehler et al., 2013). Further understanding of lived experiences of gender minority and marginalization stress (Puckett et al., 2021) and other experiential and contextual factors that drive subsequent health disparities is much needed among TGD populations (IOM, 2011). Moreover, the physiological pathways mapping the embodiment of these stressors and their impact on chronic and long-term health remain largely under-explored.

To date, research focused on TGD health and well-being have characterized several gender marginalization stressors but have yet to examine sufficiently how these may become embodied, impacting health and disease risk. For example, impactful stressors include experiences of misgendering (McLemore, 2015) (e.g., enacted stigma of using an incorrect gender pronoun), identity concealment (e.g., to avoid stigma-related mistreatment and stress) and relatedly, passing/blending or being perceived as cisgender (Rood et al., 2017). Additional gender marginalization stressors identified through The Transitioning Experience Study, include “transitioning identity stress” (e.g., socially ‘juggling’ a public gender identity that varies or is in flux) (DuBois et al., 2017) and more broadly, the stress associated with the use of gender-specific public bathrooms (DuBois et al., 2017; Herman, 2013).

Social stigma and inequality are endured by TGD people in large part due to sociopolitical and cultural “enforcement” of rigid binary gender/sex categories and associated norms (DuBois and Shattuck-Heidorn, 2021). These may be particularly impactful in rural compared to urban areas in the U.S. in part due to the relative homogeneity of populations living in those areas and decreased access to communities of supportive and other resources. In terms of impact, when compared to TGD people living in urban areas, those living in rural environments in particular have been found to have higher levels of anxiety and depression, lower self-esteem (Horvath et al., 2014), and are less likely to be out as transgender in their personal networks compared to cisgender LGBT peers (Whitehead et al., 2016). As social determinants of health, these sociocultural, placed-based lived experiences can become embodied and can consequently harm health on multiple levels. Though understudied, subsequent physical health disparities and chronic disease risk specifically are increasingly recognized as urgent areas in TGD health more broadly (Downing and Przedworski, 2018; Rich et al., 2020; Witten, 2014).

Despite recognition of the important health effects of sociocultural and geopolitical context, sexual and gender marginalization stress models have generally been employed in studies using self-report experiential measures without identifying how these may become embodied. Far less attention has been placed on biomarker measures of embodied stress and related pathophysiological processes impacting health and wellness among TGD people (DuBois et al., 2021a). Moreover, the majority of marginalization stressors characterized in the literature focus on impacts on mental health with far less consideration of physical health and disease risk, including physiological profiles such as those related to the stress hormone cortisol (Parra et al., 2016) or inflammatory pathways (Doyle and Molix, 2016). Inflammatory processes in particular are likely to exert important effects that should be examined further, especially in regards to aging processes. (Diamond et al., 2021).

1.1. The Transition Experience Study

Toward addressing these gaps in knowledge, The Transition Experience Study (DuBois, 2012a) integrates data reflecting lived experience (e.g., self-report measures and in-depth, in person interviews) with data obtained through minimally invasive biomarker sampling to assess a number of biological systems (DuBois et al., 2021a). The aim of this study was to examine lived experience of gender affirmation/transition (social and medical) and embodied stress among a sample of transmasculine people, all who were accessing testosterone therapy to affirm their gender. As a cross-sectional study of transition experience, the sample included participants reflecting a broad age range (18-55 years) and included those early in medical transition - 1 week through 14 years on testosterone therapy. This single investigator study (PI DuBois, an out transgender man) focused in on the transitional experiences of those on testosterone therapy in respectful recognition of the complexities a broader diversity of gender-identities and exogenous hormonal regimens would bring to the project. A study conducted by a larger team of researchers that is inclusive of trans women/trans feminine and a greater number of non-binary participants would be worthwhile and is much needed in the future. Notwithstanding, here we draw on these data to develop our model of embodied inequality and health among TGD people.

1.2. Allostatic load among sexual and gender diverse people

Central to our analysis is the concept of allostatic load (AL), which represents the multi-systemic ‘wear and tear’ of chronic stress that is synergized by health behaviors (McEwen and Stellar, 1993) like poor diet, sleep problems, and physical inactivity. In nearly 300 studies to
date and counting (Guidi et al., 2021), AL has been indexed using a comprehensive battery of stress-related biomarkers (McEwen and Stellar, 1993; Seeman et al., 1997), presumably representing the experiences of the general population without regard for gender identity. AL indices predict numerous physical, mental, and cognitive outcomes better than traditional biomedical approaches because algorithms ascribe sub-clinical thresholds for several biomarkers attaining pre-clinical cut-offs (Juster et al., 2010). Over the last 25 years or so, AL has been consistently associated with accelerated aging (Crimmins et al., 2003), socio-economic inequalities (Crimmins et al., 2009), and race/ethnic disparities (Merkin et al., 2009a). AL in turn is associated with numerous health outcomes like cardiovascular disease, physical decline, metabolic problems, psychiatric symptoms, and all-cause mortality (Sabbah et al., 2008).

The AL model has recently been used to study health disparities among people representing sexual diversity (Juster et al., 2013; Mays et al., 2018; Walubita et al., 2021). To summarize, results are mixed with sub-group differences detected only among presumed cisgender men. Specifically, cisgender bisexual men show high AL compared to straight cisgender men. A possible explanation is that bisexual people often experience greater alienation and stigma from people in both straight and LGB communities (Balsam and Mohr, 2007; Persson et al., 2014). On the other hand, gay men showed lower AL than cisgender straight men. This might be explained by sub-group socio-cultural drivers among gay men (e.g., high endorsement of muscular physique (Calzo et al., 2013; Kaminski et al., 2005), disordered eating (Russell and Keel, 2002; Yelland and Tiggemann, 2003), body dissatisfaction and/or even resilience pathways (e.g., health behaviors, social support) that have yet to be elucidated. In stark contrast to findings among cisgender men as a function of sexual orientation, sexual minority cisgender women (e.g., lesbian, bisexual cisgender women) show no differences in AL (Juster et al., 2013; Mays et al., 2018; Walubita et al., 2021), a perplexing result to be further explored in relation to intersectionality and health behaviors (Desjardins et al., 2021).

Findings to date among sexual diverse people who are presumably cisgender are mixed and point to sub-group differences that highlight the importance of disaggregating analyses according to sex assigned at birth and gender. While sexual minority stress has been indirectly assessed in these novel AL studies among LGB cisgender sub-groups, we know of no published research examining AL among TGD people. Here we draw on qualitative and quantitative data to examine AL in relation to lived experience among a sample of transmasculine people accessing testosterone therapy to affirm their gender. Based on the methodologies developed for this study, we propose a model (Fig. 1) for understanding embodied experience and stress that can be used in research focused on health and well-being among TGD people more broadly.

1.3. Specific aims and hypotheses

Despite recognition of the impact of stigma and gender marginalization stress, this study is the first to apply analyses inclusive of multiple levels of lived experience that also incorporates physiological measures among TGD people. Details of The Transition Experience Study have been published previously (DuBois, 2012a,b; DuBois et al., 2017; DuBois et al., 2021b). Compared to trans women and transfeminine people, trans men and transmasculine people have received considerably less health research attention (IOM, 2011), especially in the context of any gender-affirming transition experience. To address this, The Transition Experience Study was a cross-sectional, mixed-methods study that aimed to (1) understand lived experiences and identify specific minority stressors experienced by transmasculine people who are affirming their gender in part through testosterone therapy, and (2) examine how experiences become embodied and influence health using minimally invasive biomarker samples, thus enabling data collection outside of.

Fig. 1. Conceptual model of lived experience combining gender minority and marginalization stress processes (top half) embedded within ecological systems (bottom half) spanning the micro-level (immediate environment), meso-level (interconnections among several individuals), exo-level (the indirect influence of social structures and settings), macro-level (current overarching cultural and sub-cultural patterns, and chrono-level (time period). In parallel, stress processes and stigma are experienced at individual (e.g., self-stigma, disclosure), interpersonal (e.g., abuse, rejection, discrimination, community (e.g., marginalization), and structural (e.g., state policies, institutional practices) levels through history. These gender minority stressors depict in the top half can be considered as compounding and in addition to those experienced everyday by many people.
clinical settings. Drawing on these data, we here generate indices developed from multiple biomarker samples along with in-depth interview and survey data to assess perceived distress, mental health, and AL in relation to contextual and experiential domains among this sample of transmasculine people.

Framed in close correspondence to ecological systems theory (Fig. 1), we index specific domains representing levels of geopolitical progressiveness, sociodemographic advantage, social support, gender marginalization stressors, and health behaviors. In our analyses of these indices of lived experience, we hypothesized that living (1) in more progressive geopolitical climates, (2) with greater socio-demographic advantage, (3) with greater social support and resources, (4) with less exposure to stressors related to gender-based stigma and marginalization, and (5) with more engagement in health behaviors, would be associated with less perceived distress, better mental health, and lower embodied stress as measured via AL.

2. Methods

2.1. Participants

Participants in The Transition Experience Study included 65 people who identified as trans men and/or along a transmasculine spectrum aged 18–55 years old who were living in the states of Massachusetts, Vermont, and Rhode Island in 2009–2012. The study aimed to understand stress exposure reflecting gender marginalization and stigma and explore physiological pathways through which these stressors might impact health among trans men and/or transmasculine people accessing testosterone therapy to affirm their gender. Eligibility criteria required each participant be over 18-years of age, assigned a female sex designation at birth, identify as a man/transgender man/along the transmasculine spectrum, and be administering testosterone to affirm their gender. Participants were ineligible if they were taking medications for any cardiovascular or immune-related conditions due to the biomarkers measured in the study to assess stress and calculate AL. Information about steroid-based cold or allergy medications were ascertained but participants were otherwise free of any acute illness or injury within 2 weeks of participation.

The study was conceptualized and conducted by a transgender man (LZD) who is trained as a biocultural anthropologist. Beyond the conceptualization of the study, this proved relevant to enabling community access, participant recruitment and retention, development of biomarker sampling protocols, and collection of multiple samples for biomarker measurement (detailed below). In fact, many participants indicated the importance of the aims of the study and that it was being conducted by a trans-identified researcher in their decision to participate. Targeted recruitment efforts included online TGD supportive list-servs, LGBTQIA+ health clinics, area support groups, community organizations, social media (e.g., Facebook) and snowball sampling techniques. Although the final sample is predominately white, it is quite diverse in terms of age (18–55 years), duration of time on testosterone (1 week to 14 years), and sexual and gender identities (see Table 1 for Sample Characteristics).

Given the social stigma TGD individuals endure, efforts to protect the privacy and safety of study participants included conducting interviews in participants’ homes or supportive LGBT clinics, area support groups, community organizations, social media (e.g., Facebook) and snowball sampling techniques. Although the final sample is predominately white, it is quite diverse in terms of age (18–55 years), duration of time on testosterone (1 week to 14 years), and sexual and gender identities (see Table 1 for Sample Characteristics).

Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, M (SD)</td>
<td>31.8 (9.1)</td>
</tr>
<tr>
<td><strong>Self-identified race/ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>White, n (%)</td>
<td>48 (73.8)</td>
</tr>
<tr>
<td>Jewish, n (%)</td>
<td>7 (10.8)</td>
</tr>
<tr>
<td>Latino/a, n (%)</td>
<td>4 (6.2)</td>
</tr>
<tr>
<td>Black/African American, n (%)</td>
<td>3 (4.6)</td>
</tr>
<tr>
<td>Asian, n (%)</td>
<td>2 (3.1)</td>
</tr>
<tr>
<td>Mixed race/ethnicity, n (%)</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td><strong>Gender identity (within transmasculine spectrum)</strong></td>
<td></td>
</tr>
<tr>
<td>Man or guy, n (%)</td>
<td>32 (49.2)</td>
</tr>
<tr>
<td>Trans man, n (%)</td>
<td>20 (30.8)</td>
</tr>
<tr>
<td>Genderqueer/queer, n (%)</td>
<td>7 (10.8)</td>
</tr>
<tr>
<td>Transfeminine, n (%)</td>
<td>4 (6.2)</td>
</tr>
<tr>
<td>Not female, n (%)</td>
<td>2 (3.1)</td>
</tr>
<tr>
<td><strong>Sexual Identity</strong></td>
<td></td>
</tr>
<tr>
<td>Heterosexual/Straight, n (%)</td>
<td>15 (23.1)</td>
</tr>
<tr>
<td>Gay (prefers cis and/or trans men), n (%)</td>
<td>9 (14.5)</td>
</tr>
<tr>
<td>Queer (prefers cis and/or trans women), n (%)</td>
<td>16 (24.6)</td>
</tr>
<tr>
<td>Queer (flexible/bisexual), n (%)</td>
<td>25 (38.5)</td>
</tr>
<tr>
<td><strong>Current Job Status</strong></td>
<td></td>
</tr>
<tr>
<td>Works full-time, n (%)</td>
<td>34 (52.3)</td>
</tr>
<tr>
<td>Works part-time, n (%)</td>
<td>16 (24.6)</td>
</tr>
<tr>
<td>Unemployed/ laid off, n (%)</td>
<td>15 (23.1)</td>
</tr>
<tr>
<td>Monthly Income, M (SD)</td>
<td>$1986 ($1039)</td>
</tr>
<tr>
<td><strong>Financial Status</strong></td>
<td></td>
</tr>
<tr>
<td>Makes less than needs/seeks work, n (%)</td>
<td>30 (46.9)</td>
</tr>
<tr>
<td>Makes exactly what needed/ no wage gap, n (%)</td>
<td>13 (20.3)</td>
</tr>
<tr>
<td>Makes just enough to be comfortable, n (%)</td>
<td>16 (25)</td>
</tr>
<tr>
<td>Makes plenty/can be generous, n (%)</td>
<td>5 (7.8)</td>
</tr>
<tr>
<td>Accrued medical debt from transition costs</td>
<td>20 (31)</td>
</tr>
<tr>
<td><strong>Gender Affirming/Transition-Related Care</strong></td>
<td></td>
</tr>
<tr>
<td>Years on testosterone therapy, M (SD)</td>
<td>3.3 (3.4)</td>
</tr>
<tr>
<td>Top surgery, n (%)</td>
<td>40 (61.5)</td>
</tr>
<tr>
<td>Hysterectomy, n (%)</td>
<td>15 (23.1)</td>
</tr>
<tr>
<td><strong>Psychosocial</strong></td>
<td></td>
</tr>
<tr>
<td>Perceived Stress Scale, M (SD)</td>
<td>16.4 (6.7)</td>
</tr>
<tr>
<td>Victimized due to gender presentation</td>
<td></td>
</tr>
<tr>
<td>Yes, before starting testosterone, n (%)</td>
<td>12 (18.5)</td>
</tr>
<tr>
<td>Yes, before and after starting testosterone, n (%)</td>
<td>7 (10.8)</td>
</tr>
<tr>
<td>Yes, after starting testosterone, n (%)</td>
<td>17 (26.2)</td>
</tr>
<tr>
<td><strong>Gender Minority &amp; Marginalization Stressors</strong></td>
<td></td>
</tr>
<tr>
<td>Reports Transitioning-identity stress, n (%)</td>
<td>29 (44.6)</td>
</tr>
<tr>
<td>Reports stress associated with ‘coming out’, n (%)</td>
<td>29 (44.6)</td>
</tr>
<tr>
<td>Levels of stress using gender specific public bathrooms, M (SD)</td>
<td>4.2 (3.1)</td>
</tr>
<tr>
<td><strong>Relationship status &amp; history</strong></td>
<td></td>
</tr>
<tr>
<td>Single, n (%)</td>
<td>15 (23.1)</td>
</tr>
<tr>
<td>Dating/in a relationship, n (%)</td>
<td>15 (23.1)</td>
</tr>
<tr>
<td>Partnered/married, n (%)</td>
<td>35 (53.8)</td>
</tr>
<tr>
<td>Lives with partner, n (%)</td>
<td>32 (49.2)</td>
</tr>
<tr>
<td>Current relationship preceded starting testosterone</td>
<td>23 (36.9)</td>
</tr>
<tr>
<td><strong>Health Behaviors</strong></td>
<td></td>
</tr>
<tr>
<td>Medications for allergies or colds, n (%)</td>
<td>14 (21.2)</td>
</tr>
<tr>
<td>Smoker, n (%)</td>
<td>13 (20)</td>
</tr>
<tr>
<td>Consumes alcohol ever, n (%)</td>
<td>53 (82.8)</td>
</tr>
<tr>
<td>Exercises regularly, n (%)</td>
<td>44 (66.8)</td>
</tr>
</tbody>
</table>

2.2. Data collection

Each participant completed an in-person semi-structured interview and orally administered demographic and background health questionnaires designed for this study. Additionally, a series of minimally invasive biomarker sampling methods were employed to assess stress and AL (see DuBois et al., 2021a for an overview of these methodologies). Biomarker sampling included anthropometric (height, weight, triceps skinfolds), bioimpedance (% lean muscle and fat), 24 h ambulatory blood pressure, salivary cortisol and testosterone, and C-reactive protein (CRP) and Epstein-Barr virus antibodies (EBVab) obtained from a dried blood spot. Participants also completed compliance and experiential diaries during sample collections (i.e., during 3-day salivary and 24 h blood pressure collections) as detailed below. To ensure minimal burden to the participant and facilitate data analyses, all biomarker...
samples were collected during the interview and within the 2-week period following the interview and tailored around each individual’s testosterone administration schedule.

2.3. Interview and survey data

Each participant engaged in a 2–4 h in-person interview which was audio recorded with participant consent. A semi-structured interview guide developed through pilot research for this study (by LJD), included topical sections focused on overall gender experience and identity; gender-based stigma and minority stress experience; experiences of inequality and marginalization, gender embodiment, expression and bodily satisfaction (DuBois et al., 2021); social treatment, relationships, access to resources, and social support. Additionally, participants were asked questions about their overall health and health background and completed a demographic questionnaire also developed for this study (see DuBois, 2012a for details and appendices for questionnaires). Each of these were administered verbally during the in-person interview or completed in writing prior and reviewed in-person for completion and accuracy. The indices used in our analyses (detailed below) were then developed from the data obtained from these interviews, questionnaires, and surveys. Variables were created from answers to structured survey questions or from open-ended interview questions coded by two independent coders.

2.4. Minimally invasive biomarker sampling

Minimally invasive biomarkers enable biological samples to be collected effectively outside of clinical settings while reducing participant burden and enabling participant agency and involvement. Details of the development and validation of these methods (Ice and James, 2007; Mccade et al., 2007b) and recommendations for adaptation and application among TGD people (DuBois et al., 2021a) have been published elsewhere. For this study, participants self-collected salivary samples for measuring salivary cortisol over three consecutive days at five time-points (for findings related to cortisol, see DuBois et al., 2017): (1) upon awakening (while still in bed), (2) thirty minutes post-waking, (3) mid-morning (approximately 4 h post waking, avoiding mealtime), (4) mid-afternoon (approximately 8 h post-waking, avoiding meal time), and (5) at bedtime (prior to brushing teeth).

Study PI (LJD) sent each participant text message reminders for all mid-morning and mid-afternoon samples to improve compliance and collection times were confirmed using a paper–pen diary completed with each sample. Participants were provided in-person and written instruction to collect their saliva using the “passive-drool” technique, with a straw and polypropylene vial. Each participant was instructed to refrain from brushing their teeth, smoking, or consuming dairy, alcohol, or caffeine 30 min prior to sample collection.

For measurements of inflammation (CRP) and immune function (EBVab), whole blood spots were collected from participants who reported no symptoms of illness, injury, or infection in the past two weeks. Drops were obtained from a single finger prick with a sterile disposable lancet and collected on standardized Whatman filter paper (903). Samples were dried for 24 h at room temperature then frozen in a –80 freezer until shipped to the Laboratory for Human Biology Research at Northwestern University. Concentrations of CRP and EBVab (mg/L) were determined using enzyme-linked immunosorbent assay (ELISA) protocols (McDade et al., 2004, 2007a).

Cardiovascular biomarkers included 24-h ambulatory measures of heart rate and systolic and diastolic blood pressure (DuBois, 2012b). Measures were taken every 20-min during waking hours and every 30 min while sleeping (as tolerated) using the Oscaro2 ambulatory oscillometric monitor which has been validated for use in clinical research (Jones et al., 2004). Methodological details and analyses of this measure have been published previously.

Metabolic biomarkers included body mass index (BMI), percent body fat, lean muscle, and triceps skinfold measures. BMI was calculated from weight (kg)/height (m²) based on weight measured using a portable Tanita scale and height measured using a free-standing portable titanium anthropometer. Triceps skinfold measurements were taken to the nearest .5 mm using Lange calipers. Percentage of lean muscle and body fat was calculated using a Maltron bio-impedance monitor. Note that here, the average standardized percentages based on readings using algorithms for both “male” and “female” categories on the monitor were used; however, the utility of these measures and this type of solution will need to be considered carefully and respectfully in future research (DuBois et al., 2021a). This issue is now also being recognized in clinical settings (Kidd et al., 2019).

2.5. Indexing lived experience

Indices of major life and health domains were derived from information collected as part of in-depth, in-person interviews. Specifically, these indices were coded so that higher scores represented protective factors (progressive geopolitical climate, sociodemographic advantage, and social support) as well as potential risk factors (gender minority stressors and health behaviors). This approach of indexing multiple domains was inspired by similar indexing of major life stressors and cumulative health behaviors by Puterman and Epel’s research group (Puterman et al., 2015) as well as cumulative risk scores from Evan’s group assessing AL in youth (Evans, 2003). The following represents the variables we include in our study that we encourage future studies to further explore.

2.5.1. Progressive geopolitical climate

Progressive geopolitical climate was indexed as the sum of the following: geographical location (1 = rural/suburban, 2 = urban/college town) and participant’s perceived political inclination of the community (0 = generally conservative, 1 = generally progressive). This was assessed at 3 time points including retrospectively for residence prior to starting gender affirming testosterone therapy, when beginning testosterone therapy, and at time of interview. Higher indices represent more progressive geopolitical climate based on the differential health impacts of rural to urban residence.

2.5.2. Socio-demographic advantage

Socio-economic advantage was indexed as the sum of the following: employment status (0 = unemployed/laid off, 1 = part-time, 2 = full-time), educational attainment (1 = some high-school, 2 = high-school diploma, 3 = some college, 4 = Bachelors, 5 = Masters, 6 = Doctoral), monthly income (1 = <$1200, 2 $1201–$2400, 3 = > $2401), home ownership (0 = rent, 1 = own), persons per number of bedrooms in home ratio, and subjective financial status (1 = makes less than needs/seeks more work, 2 = makes exactly what needs/no wiggle room, 3 = just enough to be comfortable, 4 = plenty/enough to be generous), financial debt from transition costs (0 = yes, 1 = no), and finally the privilege of white race/ethnicity (0 = non-European decent, 1 = European decent). Higher indices represent more socio-demographic advantage.

2.5.3. Social support

Social support was indexed as the sum of the following variables: relationship status (0 = single/dating, 1 = partnered/married), romantic partner cohabitation (0 = no, 1 = yes), partnership precedes transition/starting testosterone therapy (0 = no, 1 = yes), partner generally supportive (0 = no, 1 = yes), family support (0 = no, 1 = yes), workplace support (0 = no, 1 = yes), religious belief (0 = no, 1 = yes), sense of community (0 = no, 1 = yes), loneliness (0 = sometimes/often, 1 = hardly ever feels lonely), social isolation (0 = sometimes/often, 1 = hardly ever), and sense of community (0 = no, 1 = yes). Higher indices represent more social support.
2.5.4. Gender minority and marginalization stressors

Stressors related to gender and marginalization were measured based on data obtained through the in-person interviews. These data were analyzed and coded as described below. Overall, these stressors reflect challenging experiences stigmatizing social treatment (e.g., misgendering) and marginalizing processes (e.g., legal name changes and barriers to accessing affirming care). These are then indexed as the sum of the following variables based on participants’ current stress experience: gender specific public bathroom stress (scale ranging from 0 to 10 median split as 0 <=4 and 1 = 5 +), testosterone injection stress (scale ranging from 0 to 10 median split as 0 <=2 and 1 = 3 +), stress associated with chest binding/packing (0 = no, 1 = yes), and “passing” stress (0 = no, 1 = yes). Note that “passing” stress reflects participants’ own word choice to describe the stress of being read as transgender (and thus not “passing” as cisgender) within a sociopolitical context in which transgender people experience violence, stigma and inequality. The language used to characterize the gender marginalization stressor related to “passing” thus reflects language used by study participants themselves at that time (2009-2012) and could also be understood in the context of related misgendering experience. Today, however, the term “passing” is less used.

In addition, “coming out” stress (reports current stress related to the process of “coming out” as transgender, 0 = no/infrequent, 1 = frequent/always), transitioning identity stress (stress related to “juggling” social identities in flux during social and/or medical gender transition; two judge consensus (kappa = 0.75) coded as 0 = no/low or 1 = high), misgendering stress (stress of being misgendered or not being treated respectfully by others in terms of gender identity; 0 = most of the time or always, 1 = never or seldom), age-based treatment stress (stress due to perceived age, for instance being misperceived as younger with testosterone administration; 0 = no, 1 = yes), stress related to interactions or treatment by health professionals including psychotherapist, endocrinologist, physician (obstetric, gynecologist, general practitioner), and/or surgeon (0 = no, 1 = yes) and legal name change related stress (0 = no, 1 = yes) and/or work/school human resource related stress (0 = no, 1 = yes). Higher indices represent more lived experiences of gender minority and marginalization stressors.

2.5.5. Health behaviors

Behaviors that may negatively impact or reflect poorer health were indexed as the sum of the following variables: tobacco smoker (0 = no, 1 = yes), excessive alcohol consumption (0 = 0–7 drinks per week, 1 = 8+ drinks per week), sleep quantity (0 <=7 h, 1 = 7+ hours), physical inactivity (0 = no, 1 = yes), medication use (number of prescribed medications for asthma, allergies, and/or for mental health purposes), and infrequent medical check-ups (0 = more frequent check-ups, 1 = less frequent check-ups). Higher indices represent those that may have more negative impacts on health.

2.6. Perceived distress

The 14-item Perceived Stress Scale (Cohen et al., 1983) measures perceived distress using a 5-point Likert-scale from 0 (never) to 4 (very often). Upon reverse coding of positive items, scores are summed for all items (e.g., In the last month, how often have you been upset because of something that happened unexpectedly?). Original psychometric properties revealed strong internal consistency (mean α = .85), test-retest reliability (mean r = .85), and evidence of concurrent validity with depression (mean r = .71) and physical complaints (mean r = .59) among young students. Interestingly and consistent with theory, this measure of perceived stress was only mildly correlated with number (rs between .17 and .20) and impact (rs between .24 and .30) of negative life events (Cohen et al., 1983) in the original study.

2.7. Mental health symptoms

Mental health symptoms were indexed to represent the presence or absence of depression, anxiety, and insomnia at the time of interview. This could range from 0 to 3.

2.8. Allostatic load

AL indices were calculated based on the following 10 biomarkers representing neuroendocrine (cortisol awakening response and systemic HPA-axis output from mid-morning until bedtime), immune (C-reactive protein, Epstein-Barr virus antibodies), cardiovascular (heart rate, systolic and diastolic blood pressure), and metabolic (body mass index (BMI), percent body fat, and triceps skinfold measurement) functioning. All biomarkers have been previously incorporated in the existing AL literature (Juster and Lupien, 2012; Juster et al., 2010; Kerr et al., 2020). Note that we do not include testosterone as a biomarker in the AL index but rather ran a supplemental correlation among testosterone and AL indices exploratorily as requested by reviewers but is not explored further as it is not a biomarker normally included in AL studies.

Table 2 lists all individual biomarker information and the cut-off(s) used to calculate AL indices. Individuals’ values were coded with respect to biomarker ranges for the sample as opposed to clinical cut-offs or binary sex-based formulations common in the literature. As traditionally done in the count-based quartile system (Seeman et al., 1997), percentiles were calculated and values falling within the highest 75th percentile were scored as “1” while those falling normally below the 75th percentile were scored as “0”. Because hypo- and hyper-cortisolism are both potentially deleterious (Fries et al., 2005, Juster et al., 2011), a two-tailed alternative formulation (Sepulaki et al., 2005) set at the 12.5th and 87.5th percentiles were used for diurnal cortisol measures. In sum, AL indices were operationally defined as the total number of dysregulated biomarkers that could theoretically range from 0 to 10 (M = 2.42, SE = .235).

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>M (SE)</th>
<th>Cut-Off (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol Awakening Response (-30 min minus Awakening)</td>
<td>2.98 (0.77)</td>
<td>&lt; -4.27 or &gt;10.14</td>
</tr>
<tr>
<td>Cortisol Mid-Morning to Bedtime (AUCg)</td>
<td>8.71 (0.39)</td>
<td>&lt; .541 or &gt;12.05</td>
</tr>
<tr>
<td>C-Reactive Protein</td>
<td>1.50 (0.35)</td>
<td>&gt; 1.44</td>
</tr>
<tr>
<td>Epstein-Barr Virus</td>
<td>122.33 (8.00)</td>
<td>&gt; 162.15</td>
</tr>
<tr>
<td>Heart Rate (BPM)</td>
<td>77.14 (1.19)</td>
<td>&gt; 83.09</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>129.62 (1.37)</td>
<td>&gt; 138.00</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>78.44 (1.01)</td>
<td>&gt; 85.00</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>30.22 (0.83)</td>
<td>&gt; 33.60</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>33.82 (0.97)</td>
<td>&gt; 39.63</td>
</tr>
<tr>
<td>Triceps Skin-fold measures (mm)</td>
<td>23.36 (1.06)</td>
<td>&gt; 29.00</td>
</tr>
</tbody>
</table>
Three multiple regressions were employed to assess dimensions associated with (1) perceived distress, (2) mental health symptoms, and (3) allostatic load. The independent variables included indices coded to represent progressive geopolitical climate, socio-demographic advantage, social support, transgender-specific stressors, and health behaviors. Following convention, multicollinearity was deemed acceptable if variance inflation factors were < 5. In the following, multicollinearity was negligible as indicated with variance inflation factors ranging between 1.03 and 1.15. We report all key statistics in Table 3 and summarize the results in-text. The Statistical Package for the Social Sciences Version 25 was used for statistical analyses.

3. Results

3.1. Perceived distress

The regression model was statistically significant ($F_{(5,59)} = 4.33, p = .002$) and accounted for approximately 27% of the variance explaining perceived distress as predicted significantly by trans-specific stress and geopolitical climate. Specifically, experiencing more gender minority or marginalization stress and living in a less progressive geopolitical climate was associated with more perceived distress (Table 3A).

3.2. Mental health

The regression model was statistically significant ($F_{(5,59)} = 5.08, p = .001$) and accounted for approximately 30% of the explained variance predicted significantly by gender minority and marginalization stressors and geopolitical context. Specifically, experiencing more stressors reflective of gender-based stigma and marginalization and living in a less progressive geopolitical climate was associated with more mental health symptoms (Table 3B).

3.3. Allostatic load

The regression model was statistically significant ($F_{(5,59)} = 5.21, p = .001$) and accounted for approximately 31% of the explained variance predicted significantly by geopolitical climate and socio-demographic experiences. Specifically, living in a less progressive geopolitical climate and with less socio-demographic advantage was associated with higher allostatic load (Table 3C).

Supplemental analyses revealed that neither age ($r = .021, p = .869$), years on testosterone therapy ($r = -.100, p = .426$), nor salivary testosterone concentrations ($r = -.145, p = .347$) were significantly correlated with AL indices.

4. Discussion

Transgender people continue to endure high rates of marginalization, discrimination, and distress that adversely affect their physical and mental health (IOM, 2011; Anon, 2020). Our overall aim in this study was to assess the physiological mechanisms whereby challenging life experiences become embodied, contributing to poor health and health disparities among TGD people (Fig. 1). To do this, we used an ecological systems perspective of lived experience to study AL among a sample of transmasculine people accessing gender-affirming testosterone therapy. To summarize, we found that living in less geopolitically progressive places and experiencing more gender marginalization stressors was related to more perceived distress as well as more symptoms of depression, anxiety, and insomnia. Crucially, we also found that living in less geopolitically progressive places and having less sociodemographic advantage was related to higher AL as indexed from 10 biomarkers previously used in the growing AL literature (Juster et al., 2010; Kerr et al., 2020). This is the first study to apply the concept of “wear and tear” using the AL model to examine embodied experience among TGD people and more specifically the lived experiences of transmasculine people accessing testosterone therapy to affirm their gender. We offer the following discussion in the hopes of informing future research on psychosocial and physiological functioning and the health and well-being of TGD people more broadly.

By creatively combining qualitative and quantitative data, we contribute a mixed-method approach to index key lived experiences that could prove useful in future biobehavioral research, particularly with sexual and gender minority people. This approach is like previous work indexing developmental risk factors, major life stressors and behaviors impacting health (Evans, 2003; Puterman et al., 2015). Our approach was further inspired by ecological systems models (Fig. 1) that are useful for expanding gender marginalization stress frameworks (Canoy et al., 2019; Edwards et al., 2019; Paceley et al., 2020). In addition to a focus on stigma and inequality that can negatively impact health and well-being, aspects of resilience (e.g., social support, health supporting behaviors, community resources) are important buffers against the negative effects of stigma and gender marginalization processes that can negatively affect both mental and physical health (Meyer and Frost, 2013).
Our study clearly shows the benefits of socio-demographic advantage and perceived geopolitical progressiveness on AL. While only at trend level, note that AL was positively correlated with perceived distress (r = .222, p = .080) and negative mental health symptoms (r = .227, p = .069). Despite non-significance, this supplemental analysis indicates that mental health correlates marginally with physiological dysregulation that could negatively affect long term health. As health research has only begun to address the role of stigma in health disparities of TGD people, we want to highlight the importance of capturing nuanced sources of stress as well as of resilience that are specific to TGD people along with other key domains reflective of lived experience spanning the micro-level to the macro-level (Fig. 1).

Here we also draw on place-based research on health and well-being (Oswald and Wu, 2011) which points to the importance of assessing contextual level factors specifically as socio-spatial determinants of health among sexual and gender minority populations (Davies et al., 2018). Urban and rural classifications have been used in several AL studies (Glei et al., 2007; Merkin et al., 2009b; Zhu et al., 2021), but generally merely as a sample characteristic or as a covariate rather than a way to examine distal or structural levels of minority stress. But place of residency impacts health and well-being in several ways, including as a social environment in which people live their lives and should be drawn on to contextualize lived experiences in future research.

Sociopolitical attitudes and policies vary at regional, state, and neighborhood levels and early studies document the impacts of these on minority stress and mental health among sexual minority people (Everett, 2014; Hatzenbuehler, 2010; Hatzenbuehler et al., 2009). Differential exposure to minority stressors are apparent, for example, among LGB people living in rural and small towns endure greater exposure to enacted stigma including homophobic statements and employment and housing discrimination, compared to those living in urban areas in the United States (Swank et al., 2013). However, “rural” categorization should not be interpreted simply as a proxy for “politically conservative.” Indeed, factors impacting health and well-being need to be examined at multiple levels within these varying environments (e.g., Sinnard et al., 2016). In addition to urban and rural stratifications, it is critical to also consider perceptions regarding local political and sociocultural climates as these enable a sense of the degree to which rural/urban location contributes to experiences of stigma and discrimination people feel on a day-to-day basis (Oswald et al., 2018).

Models of sexual and gender minority stress have drawn on conceptualizations of stigma and the processes by which people become socially discredited and discriminated against (Fig. 1). In fact, many of these processes are damaging because they are attributed with characteristics deemed undesirable such as negative stereotypes (Brewis and Wutich, 2020; Link and Phelan, 2001). Our findings align with the few conducted among TGD populations and are similar to studies that recognize geographic location as impacting mental health among LGB people. These include an online exploratory study of mental health among TGD people that found geographic location influences psychological distress, including exacerbating anxiety and depression in this population (Sinnard et al., 2016). A qualitative community-based study among mid-western TGD youth, that also draws on ecological systems theory, also highlights the importance of including analyses of perception and experience of “climate” across multiple levels (Faceley et al., 2020).

Our findings point to the need that geopolitical context be recognized as a socialcontext determinant of health for TGD people. Although advances are being made in terms of visibility and positive representations of TGD people (e.g., in the media, entertainment industry), it is only recently that progress has been made toward providing legislative protections against discrimination at the federal level (e.g., Bostock, 2020 and Equality Act). In many states, this progress has been met with significant political backlash. By May of 2021 months into the Biden administration, 17 American states had already enacted anti-LGBTQ measures into law with the majority of these targeting TGD people in ways specifically harmful to TGD youth (e.g., banning TGD youth from sports) (Anon, 2021; Ronan, 2021).

Currently, many American states lack any protections inclusive of gender identity or TGD people specifically. A study of the effects of state non-discrimination laws on the health and well-being of TGD people reflects the importance of these protections. Gleason and colleagues’ showed that participants living within states that lacked protections reported higher levels of perceived community stigma which were in turn associated with increased likelihood of experiencing lifetime victimization, discrimination, and attempted suicide (Gleason et al., 2016). Another study of TGD people revealed that protective state policies moderated the association between minority stress experiences of victimization and discrimination with suicide attempts (Rabasco and Andover, 2020). These findings are particularly relevant as many states in the U.S. continue to introduce discriminatory anti-transgender bills such as those criminalizing the provision of gender affirming care for transgender youth. Our findings indicate that these forms of structural stigma are actually damaging to TGD people’s health via increased AL.

The main take-home finding shows that geopolitical climate ‘gets under the skin and skull’ of transmasculine people living even in states generally considered politically “progressive.” This reflects the importance of assessing the impact of individual-level perception of local context in addition to state and structural level policies and protections. These will need to be investigated further over time as legislation changes, but our finding provides compelling evidence for place-based effects on AL.

4.1. Strengths and limitations

Our study has several strengths and limitations as they relate to measuring gender minority and marginalization stress, stigma, indexing AL, and respectfully representing TGD people in health research. Stigma experienced by marginalized groups (e.g., focused on childhood racism, lifetime and everyday discrimination, and weight discrimination) have been linked to higher AL (Miller et al., 2021). To date, however, stigma has never been directly measured in the existing AL literature on sexual and gender minority health. Instead, stigma is indirectly assumed to differ at the group-level (Juster et al., 2019). This is a major limitation of the pre-existing literature that we partially addressed by indexing numerous stressors reflecting gender marginalization among TGD people.

Ignoring stigma measures is especially problematic for under-represented sub-groups (e.g., older TGD people) and TGD people more broadly who face the highest rates of health disparities among sexual and gender diverse populations (IOM, 2011) that are further compounded by intersecting identities (Crenshaw, 1989). For example, TGD individuals age 50 and older have higher rates of self-reported disability, distress, and depression than LGB people of the same age (Freidken-Goldsen et al., 2014). It is important to note that our sample was primarily white and may not generalize to more diverse race/ethnic minority TGD people. In addition to our index approach, the selection of validated questionnaires that allow for multiple stigmatized identities to be represented would be an asset to include in future AL research. Here, we wish to note that many validated questionnaires commonly used were developed without consideration of gender identity. This, along with an aim of generating in-depth discussion, was the rationale for why we created new items in our semi-structured interview. Moving forward, psychometric validation with consideration of gender diverse populations and other marginalized groups for social support, perceived stress, and numerous other commonly used constructs is highly encouraged.

Measuring AL is riddled by heterogeneity in operational approaches that requires careful considerations among TGD populations and minority populations more broadly (Rodriguez et al., 2019). The use of cut-offs derived from our sample is the most traditional way of calculating the original count-based AL index. In addition, we opted not to use...
clinical cut-offs (Juster et al., 2011) due to poor representation of normative data among TGD people. We also avoided cut-offs based on sex assigned at birth (Juster et al., 2016) that could be an inaccurate metric and are not aligned with TGD participants identities. Moreover, TGD people may not want to be categorized according to biomarker references that are based on binary sex categories, which themselves are recognized as problematic in human biology (DuBois and Shattuck-Heidorn, 2021). This presented itself as a challenge in our study for example when assessing body fat, of which using an average for males and females was our solution. But there are other problematic biomarkers like body mass index and other anthropometrics that have not been adequately considered in relation to TGD populations (Kidd et al., 2019). It is our hope that this first study is one among many that respectfully represents TGD people in the growing AL literature.

4.2. Conclusions

Inspired by an ecological systems model (Bronfenbrenner, 1977, 1994, 1995), the current study assessed a range of relevant contextual and experiential domains among a sample of transmasculine people residing in relatively progressive states in the United States. Even so, those living in less geopolitically progressive areas of these states experienced poorer mental health and higher AL. In addition to geopolitics, stressors related to gender marginalization were strongly associated with more perceived distress and symptoms of poor mental health. Unfortunately, research that identifies pathways for embodied inequalities that impact both mental well-being and physical health of TGD people is lacking in the AL literature (Fig. 1). Our study therefore provides a preliminary step towards research that nuances biobehavioral mechanisms of sexual and gender minority and marginalization stress (Diamond et al., 2021). This will be complimented with future research that is able to further nuance socio-cultural and geopolitical sources of stigma that impact TGD people and communities.

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Declaration of Competing Interest

Neither author declares any conflicts of interest.

References


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CRedit authorship contribution statement

L. Zachary DuBois: Conceptualization, Methodology, Investigation, Formal analysis, Writing – original draft, Funding acquisition. Robert-Paul Juster: Conceptualization, Methodology, Formal analysis, Writing – original draft.

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