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Inflammation and minority stress: A moderated mediation model of childhood adversity and mental health in young men who have sex with men

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ABSTRACT

Rationale: Adverse childhood experiences (ACEs) are linked to later anxiety and depression, and inflammation has been implicated as a mediating mechanism. Black and Latinx men who have sex with men (MSM) face higher prevalences of ACEs, anxiety, and depression compared to White, heterosexual peers. Understanding the links between ACEs and mental health is crucial to addressing these disparities.

Methods: This study used structural equation modeling to test moderated mediation models examining inflammation as a mediator of the relationship between ACEs and symptoms of anxiety/depression and minority stress as a moderator on the path between ACEs and inflammation. Data was from a community sample of Black and Latinx MSM (n = 246; mean age = 22.6).

Results: ACEs were significantly associated with symptoms of anxiety (B = 0.414; p < 0.001) and depression (B = 0.346; p < 0.001), but inflammation did not show a significant mediating effect. Additionally, the interaction between ACEs and minority stress had no significant indirect effect on anxiety/depression.

Conclusions: These findings underscore the possibility that inflammation may not represent the global perturbations of stress processes after ACEs at younger ages, particularly among a relatively healthy sample of emerging adults.

1. Introduction

1.1. Anxiety and depression in MSM

Depression and anxiety significantly impact wellbeing and life opportunity by impairing function across social, occupational, and physical health related domains of life (McKnight et al., 2016; McLaughlin, 2011). Depression, in particular, has been ranked as a leading cause of disability worldwide (Friedrich, 2017) and suicidality is one of the most serious comorbidities associated with depression (Orsolini et al., 2020).

The impacts of both anxiety and depression are a critical issue for men who have sex with men (MSM), including gay, bisexual, or other sexual identities, who face heightened risks. Population studies have demonstrated that gay men have 2.91 greater odds and bisexual men have 2.41 greater odds of experiencing depression compared to heterosexual men after controlling for socioeconomic and demographic factors (Gonzales and Henning-Smith, 2017). MSM with racially minoritized identities (e. g., Black, Latinx) may be at even greater risk for anxiety, depression, and mental distress compared to White MSM (Graham et al., 2011; Lee et al., 2017). These disparities, coupled with evidence linking depression to

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suicidality and documented higher rates of suicidal ideation and attempts among MSM than heterosexual men, underscore a critical public health concern (Malik et al., 2023; Orsolini et al., 2020). Addressing these risks through research and intervention is vital for advancing health equity and social justice for MSM communities (Bränström and van der Star, 2013; Mustanski and Macapagal, 2023).

1.2. Adverse childhood experiences (ACEs), anxiety, depression, and course of illness

ACEs are a critical factor in the development of depression and anxiety as the links between ACEs and these mental health outcomes are well established. ACEs include traumatic events before age 18, such as abuse, neglect, household dysfunction, bullying, as well as environmental factors such as community violence (Cronholm et al., 2015; Felitti et al., 1998; Finkelhor et al., 2013). ACEs have been consistently linked to increased risks for anxiety and depression in adulthood (Chapman et al., 2004; McCutchen et al., 2022; Merrick et al., 2017; Whitaker et al., 2021). Population studies have demonstrated that individuals with three or more ACEs are up to 3.05 (95 % CI: 2.06-4.51) times more likely to report an anxiety disorder and 2.34 (95 % CI; 1.67–3.28) times more likely to report major depression compared to those with no ACEs (Whitaker et al., 2021). These findings are particularly relevant for those who identify as Black or Latinx and those with sexual minority identity, who report higher ACE exposures than populations of White and heterosexual individuals (Merrick et al., 2018). Higher ACE exposures have been documented among MSM compared to heterosexual groups, with one study on a nationally representative dataset finding that 30 % of gay and bisexual men reported four or more ACEs compared to 15 % of heterosexual men (Dosanjh et al., 2023). A study of MSM indicated that approximately 80 % of participants reported at least one ACE (Bernstein et al., 1997), compared to 63.9 % in the general population (Swedo et al., 2023). Notably, this is consistent with a recent study of a community sample of Black and Latinx MSM wherein 72 % of participants reported at least one ACE (Wiss et al., 2023). This pattern of elevated exposure underscores the pressing need to consider the role of ACEs as a contributing factor to mental health disparities among Black and Latinx MSM.

The higher prevalence of depression, anxiety, and ACEs among Black and Latinx MSM populations represents an accumulation of critical risk factors. Of further concern is research highlighting a more severe course of illness and reduced effectiveness of treatment for those with anxiety or depression and a history of ACEs compared to those without ACEs (Bruce et al., 2011; Lippard and Nemeroff, 2022; Nanni et al., 2012; Widom et al., 2007). These adults often present with a more complicated symptom profile including earlier age of onset, more severe symptoms, lifetime suicide attempts, and psychiatric related inpatient admissions (Giampetruzzi et al., 2023; Lähdepuro et al., 2019). Treatment outcomes are often worse for individuals with a history of ACEs, including slower remission rates, higher treatment dropout rates, and reduced treatment efficacy (Bruce et al., 2011; Nanni et al., 2012). These findings highlight the need to identify modifiable treatment targets for Black and Latinx MSM with depression or anxiety and a history of ACEs, to inform the development of tailored and effective interventions for this population.

1.3. ACEs and inflammation

Identification of the processes linking ACEs to mental health outcomes may provide clues to guide future interventions for Black and Latinx MSM with symptoms of anxiety and/or depression and a history of ACEs. A robust body of science has established that ACEs disrupt the hypothalamic-pituitary-adrenal axis (HPA), which is involved in the endocrine response to stressors and plays a critical role in modulating inflammatory processes involved in immune function (Ridout et al., 2018a,b; Smith and Vale, 2006; Straub and Cutolo, 2016). Dysregulation of the HPA axis has been linked to increased inflammation, which in turn

has been associated with depression and anxiety in adults (Costello et al., 2019; Moriarity et al., 2020; Ridout et al., 2018a,b). Inflammation has therefore been identified as a potential mechanism linking ACEs to later anxiety and depression (Danese & Lewis, 2017; Lippard and Nemeroff, 2020, 2022; Ridout et al., 2018a,b).

Research supporting inflammation as a potential mechanism between ACEs and anxiety or depression has primarily focused on isolated pairwise associations, such as relationships between ACEs and inflammation (Baumeister et al., 2016; Coelho et al., 2014) and inflammation and anxiety (Costello et al., 2019; Salim et al., 2012) or depression (Danese and Baldwin, 2017; Howren et al., 2009; Miller and Raison, 2016). Few studies have tested indirect effects. Two recent review studies (Dosanjh et al., 2025; Maayan and Maayan, 2024) together identified only nine mediation studies on inflammation and ACE-related depression with adult samples (where inflammatory variables were measured after age 18), six of which found significant effects. However, this evidence was limited by predominantly middle-aged and older (40+), White, higher-income samples, with no data on sexual orientation or gender identity, highlighting a gap in knowledge regarding the role of inflammation in Black and Latinx MSM populations. Additionally, there is a gap in understanding how systemic sources of inequity and stress may contribute to inflammation and anxiety and/or depression after ACEs in this population. The evaluation of population specific additive stressors during the life course is crucial to develop inclusive and effective interventions for young, Black or Latinx MSM with mental health symptomatology and a history of ACEs.

1.4. Theory and current work

This research is framed by the allostatic load and energy models, which explain how chronic activation of stress responses can lead to biological wear and tear, ultimately resulting in disease (Bobba-Alves et al., 2022; McEwen, 2017; Sterling, 2012). While allostatic processes are initially adaptive, their prolonged activation depletes a finite energy budget, diverting resources from growth, maintenance, and repair to prioritize survival (Bobba-Alves et al., 2022; McEwen, 2017). ACEs can lead to either heightened or blunted stress reactivity which is reflected in the function of the HPA axis (Ellis and Del Giudice, 2019; Shonkoff and Garner, 2012). These alterations impact cortisol receptivity and/or production, thereby increasing inflammation; over time these processes cause wear and tear and elevate risk for depression and anxiety (Danese and Baldwin, 2017; Moriarity et al., 2020; Ridout et al., 2018a,b; Straub and Cutolo, 2016). These explanations support a model where inflammation has an indirect effect on the relationship between ACEs and depression and/or anxiety. Life course perspectives (Jones et al., 2019), the minority stress model (Meyer, 2003), and intersectionality (Shangani et al., 2020) further extend this framework. Life course frameworks emphasize the need to examine developmental processes and cumulative exposure to stressors across the life span. The minority stress model identifies the chronic stressors associated with sexual minority identity - such as harassment, discrimination, victimization, anticipation of rejection, internalization of homophobia and stress associated with concealment - that have been associated with inflammation, anxiety, and depression (Flentje et al., 2020; Meyer, 2003). Intersectionality further acknowledges that sexual minority and racial minority identity may compound experiences of stigma and minority stress (Shangani et al., 2020). Together, these frameworks support the possibility that when occurring after ACEs, sexual orientation and race related minority stressors may intensify physiological dysregulation and amplify the risk for inflammation, anxiety and depression in Black and Latinx MSM. The role of minority stress as an additional factor is also supported by research demonstrating that minority stress is associated with anxiety and depression (Meyer, 2003) and dysregulation of biological systems involved in stress processes, including elevated inflammation (Flentje et al., 2020).

In the current study, two a priori hypotheses were tested in

moderated mediation models. Each model hypothesized that: 1) inflammation would mediate the relationship between ACEs and anxiety or depression; and 2) minority stress would moderate the mediation effect. Mediation analysis is a statistical procedure that can test indirect pathways between variables (Fiedler et al., 2011; Hayes, 2009). We tested whether the effect of ACEs on anxiety and/or depression operated through, or was explained by levels of inflammation. We hypothesized that the relationship between ACEs and anxiety and depression would be explained by inflammatory processes. Tests of statistical moderation can detect the conditions (ie. for whom and when) variables are associated (Wu and Zumbo, 2008). In this moderated mediation model, we tested whether higher levels of exposure to minority stress magnified and increased the strength of the relationship between ACEs and inflammation, thereby leading to increased symptoms of anxiety or depression. This work addresses previous gaps by testing these hypotheses in a sample of Black and Latinx MSM. We incorporate minority stress a moderator of indirect effects to account for the way systemic inequities intersect with biological stress processes to influence mental health. By addressing these factors, this work stands to generate insights to inform inclusive and effective interventions for Black and Latinx MSM with anxiety and/or depression and a history of ACEs.

2. Methods

2.1. Sample

Data for this study comes from the Healthy Young Men's Cohort Study (HYM) (Kipke et al., 2019), which is a longitudinal study examining HIV prevention services engagement among a cohort of predominantly Black and Latinx young adult MSM. Data was collected in Los Angeles in two waves per year between 2017 and 2021. Please see the work by Kipke and colleagues (2019) for a full description of the study protocol. Notably, only blood draws from participants who provided samples in two waves (either wave two, four, or six) were assessed for inflammatory cytokines. The analytic sample (n = 246) was comprised of participants who provided data on ACEs in wave two, minority stress in wave three, depression and anxiety in wave five, and provided a blood draw in wave four. Participant ages were between 18 and 25. Almost all (96.3 %) identified as male. The majority (78.0 %) identified as gay and 17.1 % as bisexual. The largest proportion of participants reported their race as Latinx (58.9 %), followed by Black (22.4 %), and mixed race (18.7 %). Approximately 65 % of participants reported some college education, a bachelors, or graduate degree, and 30.8 % had a high school diploma or less education. The distribution of employment status was 28.5 % full time, 40.7 % part time, and 29.7 % unemployed. In the wave two data collection, approximately half (55 %) of the participants reported running out of money for basic needs such as for rent, food, or utilities at least once in the previous three months.

2.2. Measures

2.2.1. Adverse childhood experiences

ACEs were measured through the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 1997), which has shown robust internal consistency with racially diverse lesbian, gay, and bisexual adults ($\alpha=0.86\text{-}0.94$) (Balsam et al., 2010) and men who have sex with men ($\alpha=0.84\text{-}0.96$) (Noor et al., 2020). This 25-item retrospective screener assesses childhood maltreatment across emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect, with responses ranging from 1 ("never true") to 5 ("very often true"). Dichotomous variables were created, coding exposure as "1" and no exposure as "0". Items were summed and total ACEs scores range from 0 to 25. Subscales for specific maltreatment types including physical, emotional, and sexual abuse, and emotional and physical neglect were formed (with scores ranging from 0 to 5).

2.2.2. Minority stress

Minority stress was captured using two scales (Díaz et al., 2004; Flores et al., 2009). Questions related to experiences of gay and race related discrimination, harassment, or violence came from Díaz and colleagues (2004) while items on internalized homophobia came from Flores and colleagues (2009). The scale developed by Díaz and colleagues (2004) emphasizes discrimination, however, several items align with other dimensions of minority stress as identified by Meyer (2003), including expectations of rejection and stress associated with concealment. Both scales demonstrated robust internal consistency with the original study samples. Díaz et al. (2004) demonstrated high levels of internal consistency in both the homophobia ($\alpha = 0.75$) and racism ($\alpha =$ 0.82) subscales. The four items from Flores and colleagues (2009) demonstrated robust internal consistency with racially diverse MSM (α = 0.87). Díaz's scale asked respondents to report how frequently they experienced events (ie. "how often have you had to pretend to be straight) while Flores and colleagues' scale asked about agreement with internalized homophobia statements (ie. "sometimes I wish I were not sexually attracted to men"). Responses were scored on a 4- point Likert scale (1 "never" or "strongly disagree" to 4 "many times" or "strongly agree"). A total of 20 items were coded dichotomously (responses of 2-4=1, 1=0). Subscales were summed for homophobia, race-based discrimination, and internalized homophobia. Total scores for all minority stress experiences range from 0 to 20.

2.2.3. Inflammation

Blood samples were collected annually for three years (waves 2, 4, 6) approximately 12 months apart) between 10:56 a.m. and 14:52 p.m. to account for diurnal variation in pro-inflammatory cytokines (Izawa et al., 2013). Samples were centrifuged, aliquoted, and stored at -80 °C until all biomarker data were collected and analyzed in a single batch. They were shipped overnight in dry ice to the Immune Assessment Core at UCLA Immunogenetics Center for Luminex panel assay. Pro-inflammatory cytokines IL-6, IL-1B, IFN-y, TNF-a, and anti-inflammatory IL-10 from wave four were used in this analysis based on previous research linking these cytokines to ACEs and/or depression or anxiety (Miller and Raison, 2016; O'Shields et al., 2022; Soares et al., 2021). Inflammation was categorized using the 75th percentile to create a high-risk dichotomy (Bonaccio et al., 2016; Juster et al., 2010) with IL-10 included due to its positive association with pro-inflammatory cytokines (Madhurantakam et al., 2023). A total inflammation variable was created by summing the number of high-risk markers for each participant, with scores ranging from 0 to 5. This variable represents the cumulative burden of immune dysregulation including pro and anti-inflammatory activation across several markers.

2.2.4. Anxiety and depression

Symptoms of anxiety and depression were measured through the Brief Symptom Inventory (BSI-18) (Meijer et al., 2011). The BSI-18 has three subscales: depression, anxiety, and somatization, with depression and anxiety subscales used in this study. The BSI-18 has been tested widely in patients with varying psychological and physical health diagnoses (Franke et al., 2017) and showed high internal consistency in previous research with HYM study participants (depression, $\alpha=0.83$; anxiety, $\alpha=0.83$) (Parra et al., 2023). Respondents rated their distress over symptoms in the past seven days on a 5-point Likert scale (1 "not at all" to 5 "extremely"). Items were dichotomized (symptoms reported =1 and "not at all" =0) and summed scores for the depression and anxiety subscales range from 0 to 6.

2.2.5. Descriptive variables

Several demographic and socioeconomic variables were documented in order to characterize the sample. Those included: age, sexual orientation (gay, bisexual, pansexual, or questioning), gender identity (male or non-binary/unspecified), race/ethnicity (Black, Latinx, or mixed race), highest level of education (high school/GED or less, vocational

school, some college or associates, bachelors, graduate school), employment status (full time, part time, unemployed), and experiences of running out of money for basic needs such as for rent, food, or utilities in the previous three-month period (did not run out, ran out once/month or less, ran out more than once/month).

2.3. Data analysis

Structural equation modeling (SEM) was employed to test the study's hypotheses through a multi-step process. Descriptive analyses characterized the sample, and tests for outliers, multivariate skewness, and kurtosis assessed data normality (Mardia, 1970). Only severe non-normality, defined as skewness > |2| and kurtosis > |6|) was addressed (Kim, 2013), and the few identified outliers were not removed, given the robust performance of maximum likelihood with robust standard errors (MLR), and weighted least squares mean and variance adjusted (WLSMV) estimators under moderate non-normality (Li, 2016; Sardeshmukh and Vandenberg, 2017). Measurement models for the latent constructs were evaluated through confirmatory factor analysis (CFA) and the structural models were tested through SEM. Intrinsic to the use of WLSMV and MLR estimators, missing data in these analyses were handled using pair-wise deletion in the CFAs and full information maximum likelihood (FIML) in the structural models. FIML is a robust method that leverages all available data to produce unbiased parameter estimates, therefore sample size was not reduced in SEM analyses (Dong and Peng, 2013). The sample (n = 246) was assessed for adequate power following Boomsma (1985) who suggests a minimum sample size of 100-200 cases and Nunnally (1975) who indicates that 10 cases per variable is adequate. The dataset was further assessed for the smallest detectable effect sizes through the inverse square root method as proposed by Kock and Hadaya (2018), which estimates the smallest detectable effect size based on the standard error derived by sample size. Using a conservative range of 200-2011 participants, and assuming 80 % power, the model was expected to detect effects in the range of 0.18-0.19 (Kock and Hadaya, 2018).

In the CFA analyses, ML was used for total ACEs, while WLSMV was employed for constructs with categorical indicators (e.g., threat- and deprivation-based ACEs, minority stress, inflammation, anxiety, and depression) due to its distributional robustness (Gazeloglu and Greenacre, 2020). Model fit was assessed using common thresholds: SRMSR <0.05, CFI/TLI \ge 0.95, RMSEA <0.06 (Hooper et al., 2008) and

 $\gamma^2/df < 3$ (Kline, 2016). Standardized factor loadings >0.4 were considered acceptable (Stevens, 1992), and modifications were applied where necessary following MacCallum (1986). As presented in Figs. 1 and 2, the study's two a priori hypotheses were tested through an index of moderated mediation examining: 1) whether inflammation mediated the relationship between ACEs and depression or anxiety; and 2) whether this mediation was moderated by minority stress, such that the relationship between ACEs and inflammation varied depending on levels of minority stress. Model one examined depression and model two examined anxiety as outcome variables. To ensure the robustness of findings, two sensitivity analyses were performed. The first examined outcomes when ACEs were scored according to experiences of threat and deprivation, in alignment with the dimensions of maltreatment framework (McLaughlin, 2011). Simple mediation was also planned (without minority stress moderation) in the event that no moderated mediation effects were observed. To provide additional context for interpreting the results of the SEM analyses, bivariate correlations among the latent variables included in the structural model were also examined including ACEs, minority stress, inflammation, depression, and anxiety. Model parameters were estimated using MLR. Significance was set at p < 0.05(Concato and Hartigan, 2016), with indirect and moderated mediation effects assessed via bias-corrected 95 % confidence intervals using 10, 000 bootstraps to correct for the non-normal distribution of indirect effects (Hayes, 2015). Main analyses were conducted using Mplus (v. 8.1) (Muthén & Muthén, 1998-2021) and R (R Core Team, 2023) with sample characteristics analyzed in IBM SPSS Statistics (version 28).

3. Results

3.1. Data and sample characteristics

Data was assessed for normality and all summed scales demonstrated acceptable values for skewness (<|2|) and kurtosis (<|6|). As presented in Table 1, the largest proportion of the sample experienced emotional neglect (87 %), followed by emotional abuse (74 %), physical abuse (69 %), physical neglect (67 %), and sexual abuse (28 %). Notably, 53 % of the sample reported experiences in either four or five of these ACE categories while 24 % reported three, and 14 % reported two categories. Across all 25 ACE items the sample reported an average of 9.5 exposures. The average number of inflammatory markers in the high-risk range (75th percentile) was 1.3 in this sample. This sample reported an

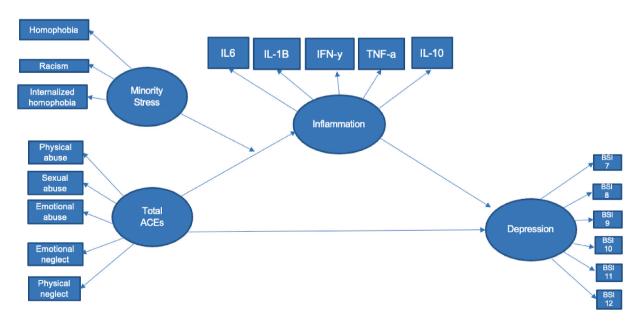


Fig. 1. Hypothesized Moderated Mediation Model 1: Depression. Note. ACEs = adverse childhood experiences.

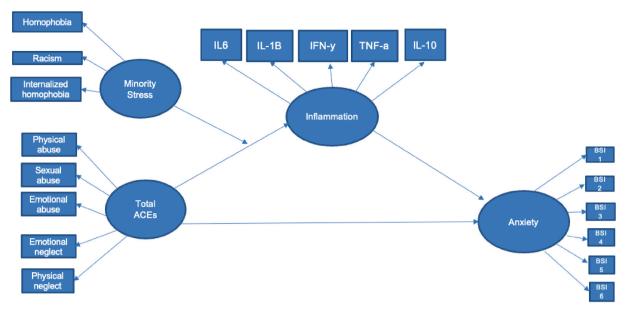


Fig. 2. Hypothesized Moderated Mediation Model 2: Anxiety. Note. ACEs = adverse childhood experiences.

average of 5.5 experiences related to minority stress. The average number of symptoms reported in this sample was 1.9 for depression and 1.7 for anxiety.

3.2. Measurement models

All latent constructs estimated by CFA demonstrated acceptable fit. The sexual abuse subscale was removed from the total ACEs construct, resulting in a model with strong fit ($\chi^2 = 0.275$ [df = 1; p = 0.59], RMSEA = 0.00, CFI = 1.00, TLI 1.00, SRMR = 0.004). The latent construct for threat-based ACEs retained questions related to physical, emotional, and sexual abuse, showing good fit ($\chi^2 = 78.310$ [df = 35; p] = 0.00], RMSEA = 0.072, CFI = 0.968, TLI 0.958, SRMR = 0.083). Similarly, the deprivation-based ACEs construct retained questions related to physical and emotional neglect and achieved acceptable fit $(\chi^2 = 30.108 \ [df = 20; p = 0.068], \text{RMSEA} = 0.046, \text{CFI} = 0.994, \text{TLI}$ 0.992, SRMR = 0.052). For the inflammation construct, all items were retained except IL-10, which was excluded to improve fit ($\chi^2 = 1.349$ [df = 2; p = 0.51], RMSEA = 0.00, CFI = 1.00, TLI 1.00, SRMR = 0.023). The minority stress construct retained items reflecting: 1) discrimination, harassment, or violence related to sexual or racial minority identity; and 2) expectations of rejection. However, items related to internalized homophobia and concealment stress were removed due to poor fit. The final solution demonstrated acceptable fit($\chi^2 = 70.514$ [df =35; p=0.003], RMSEA=0.065, CFI=0.961, TLI 0.950, SRMR=0.114). Both depression and anxiety constructs retained all original items without requiring modifications. Depression achieved acceptable fit $(\chi^2 = 16.028 [df = 9; p = 0.066], RMSEA = 0.057, CFI = 0.996, TLI =$ 0.993, SRMR = 0.047), as did anxiety: $(\chi^2 = 4.825) [df = 9; p = 0.849]$, RMSEA = 0.00, CFI = 1.00, $TLI \ 1.00$, SRMR = 0.019). Sample sizes for these analyses varied due to pairwise deletion of missing data, with the number of cases ranging from 211 to 244.

3.3. Structural models

As presented in Table 2, the moderated mediation model was not significant in either depression or anxiety models. The interaction between ACEs and minority stress did not significantly predict inflammation and inflammation did not significantly predict depression or anxiety. However, ACEs were a significant predictor of both anxiety and depression. Total ACEs were positively associated with depression ($B = \frac{1}{2}$)

0.346, p < 0.001) in model one and anxiety (B = 0.414, p < 0.001) in model two. As presented in Tables S1 and S2, sensitivity analyses showed that when ACEs were scored according to the dimensions of threat and deprivation, the results were very similar. Deprivation-based ACEs were positively associated depression (B = 0.255, p < 0.001) and anxiety (B = 0.321, p < 0.001), and threat-based ACEs also positively predicted depression (B = 0.300, p < 0.001) and anxiety (B = 0.350, p < 0.001). However, neither threat or deprivation-based ACEs were associated with inflammation and the interaction between each dimension of ACEs and inflammation did not associate with inflammation. Simple mediation analyses without minority stress as a moderator also demonstrated that inflammation had no indirect effect on the relationship between ACEs (total ACEs, deprivation, or threat) and anxiety or depression, as presented in Table S3.

3.4. Correlation of latent variables

To further examine relationships between latent variables, a correlation analysis was derived from the analysis of the structural models. As presented in Table 3, total ACEs were related to all latent variables except inflammation. The correlations between total ACEs and depression, anxiety, and minority stress were statistically significant (p < 0.01). Inflammation demonstrated no statistically significant relationships with the other variables. Depression, anxiety, and minority stress were all related to one another (p < 0.05). Notably, the correlations between ACEs and depression (r = 0.471) and ACEs and anxiety (r = 0.528) were the highest in this sample.

4. Discussion

The current study extends prior research by examining two moderated mediation models where inflammation was considered as a mediator of the relationship between ACEs and depression and anxiety, and minority stress was hypothesized as a moderator on the path between ACEs and inflammation in a sample of young Black and Latinx MSM. Contrary to the hypotheses guiding this study, we did not detect an indirect effect of inflammation on the relationship between ACEs and depression or anxiety, and we did not detect evidence that minority stress moderated the hypothesized mediation. However, findings demonstrated that ACEs, regardless of scoring practices, were significantly related to anxiety and depression.

Table 1 Descriptive characteristics of study sample (n = 246).

Descriptive characteristics of study sa	inple (ii = 1)		
	n	%	M(SD)
Sexual orientation	100	70.0	
Gay	192 42	78.0 17.1	
Bisexual		4.9	
Other (pansexual, questioning) Gender	12	4.9	
Male	237	06.2	
	9	96.3 3.7	
Non-binary or unspecified Race	9	3./	
Black	55	22.4	
Latinx	145	58.9	
Mixed	46	18.7	
Highest Level of Education	40	10.7	
High School/GED or less	76	30.8	
Vocational School	9	3.7	
Some College or Associates	108	43.9	
Bachelors	49	19.9	
Graduate School	3	1.2	
Employment Status	3	1.2	
Full Time	70	28.5	
Part time	100	40.7	
Unemployed	73	29.7	
Money for Basic Needs	73	29.7	
Did not run out of money	110	44.7	
Ran out once/month or less	87	35.3	
Ran out more than once/month	48	19.4	
Number and Type of ACE Categories	10	17.1	
0	3	1.2	
1	16	6.7	
2	33	13.8	
3	59	24.7	
4 or 5	128	53.5	
Physical abuse	169	68.7	
Emotional abuse	193	78.5	
Sexual abuse	70	28.5	
Physical neglect	164	66.7	
Emotional neglect	215	87.4	
		Range	M (SD)
Participant Age		18–25	22.6 (1.8)
Total ACEs Exposure		0–25	9.5 (5.9)
ACE Category Exposure		0–5	3.4 (1.2)
Total Inflammation		0–5	1.3 (1.2)
Minority Stress		0–20	5.5 (3.8)
Depression		0–6	1.9 (1.9)
Anxiety		0–6	1.7 (1.9)
			(1,2)

Note. Number of ACEs = number of ACE categories (i.e. physical, emotional, and sexual abuse, emotional and physical neglect). Total ACEs Exposure = number of items on 25-point scale reported by participants. Total Inflammation = number of inflammatory markers in the high-risk 75th percentile range.

4.1. Indirect effects of inflammation

The lack of detected indirect effect of inflammation on ACEs and anxiety or depression may point to important considerations regarding aging and time. Research has established that low-grade, chronic inflammation is strongly associated with aging and it is considered to be a hallmark of the aging process itself (Campisi et al., 2019; Franceschi et al., 2000; Li et al., 2023). Although numerous studies have identified associations between ACEs and inflammatory activity during early development (Huffhines et al., 2021; Soares et al., 2022), findings have been mixed and meta-analytic work suggests that these associations may become more consistent and widespread later in the lifespan. A meta-analysis evaluating these associations in children and adolescents (mean ages: 1.5-19.5 years) across 27 studies found that ACEs had an overall small but statistically significant association with c-reactive protein (CRP) (z = 0.07; 95 % CI = 0.04-0.10), but not with interleukin-6 (IL-6) (Kuhlman et al., 2020). In contrast, a meta-analysis of these variables in 25 studies of adults (mean ages: 26-65 years) found that ACEs were significantly associated with CRP (z = 0.10; 95 % CI = 0.05–0.14), IL-6 (z = 0.08; 95 % CI = 0.03–0.14), and TNF-a (z = 0.23; 95 % CI = 0.14-0.32) (Baumeister et al., 2016). While both studies

Table 2 Path estimates for models 1 and 2: Total ACEs (n = 246).

Variables	В	SE	Two tailed p	95 % bootstrapped CI
Model 1 - Total ACE and	Depression			
Depression on				
Total ACEs	0.346	0.075	0.000	
Inflammation	-0.075	0.105	0.475	
Inflammation on				
Total ACEs	0.169	0.104	0.104	
Minority Stress	-0.144	0.122	0.239	
Total ACEs*Minority	-0.005	0.120	0.968	
Stress				
Model 2 - Total ACEs and	l Anxiety			
Anxiety on				
Total ACEs	0.414	0.076	0.000	
Inflammation	-0.046	0.098	0.640	
Inflammation on				
Total ACEs	0.166	0.103	0.108	
Minority Stress	-0.139	0.121	0.252	
Total ACEs*Minority	-0.010	0.119	0.931	
Stress				
Index of Moderated	b	SE		95 % bootstrapped
Mediation				CI
IMM1 -Total ACEs and	0.001	0.028		[-0.6609, 0.6508]
depression				
IMM2- Total ACEs and	0.002	0.025		[-0.6391, 0.6275]
anxiety				

Note. IMM1 = index of moderated mediation model 1; IMM2 = index of moderated mediation model 2; B = standardized estimates; SE = standard error; b = unstandardized estimates; CI = confidence intervals from 10,000 bootstraps.

Table 3 Estimated correlation matrix for latent variables (n = 246).

Variables	1	2	3	4
1 Total ACEs	_	_	_	_
2 Inflammation	0.106	_	_	_
3 Depression	0.471**	-0.022	_	_
4 Anxiety	0.528**	0.056	0.249*	_
5 Minority Stress	0.285**	0.030	0.134*	0.207*

Note. *statistically significant at p < 0.05; **statistically significant at p < 0.01.

identified positive associations between ACEs and CRP, the effect size was slightly larger in adults. Notably, the association between ACEs and IL-6 was not significant in children and adolescents, but emerged as significant in the adult samples. Comparisons of findings between these two meta-analyses suggest the possibility that the inflammatory consequences of ACEs may accumulate or become more detectable with age.

The young age of the current sample may offer one possible explanation for the lack of detected associations between inflammation and the other variables in the study. This sample was younger (18-25 years) than the adult samples (26-65) analyzed in Baumeister and colleagues (2016) where significant association were found between ACEs and three inflammatory markers. The current sample demonstrated relatively low levels of inflammatory activity as the mean number of markers in the high risk 75th percentile was only 1.3 out of a possible five. While our sample reported high ACEs (53 % reported 4+ exposures) and moderate effect sizes were found on the paths linking ACEs to anxiety and depression, there was no detectable evidence that inflammation was associated with any other variables or that it had an indirect effect on these relationships. Given the established association between aging and inflammation, it is possible that the lack of variability in the inflammatory markers (and thus lack of detected indirect effects of inflammation on the ACEs to anxiety and/or depression link) in this sample was due to differences in how the effects of ACEs manifest physiologically across the life course. Previous review studies have highlighted a small repository of research demonstrating statistically

significant indirect effects of inflammation on relationships between ACEs and depression (Dosanjh et al., 2025; Maayan and Maayan, 2024), however, the ages of the adult samples were predominantly middle-aged and older (40+). This interpretation is consistent with the results of another study of 3931 participants from the Avon Longitudinal Study of Parents and Children (a prospective population-based cohort study). Iob and colleagues (2022) examined ACEs and group-based trajectories of inflammation and depression where inflammatory data was measured before the age of 18 and depression between the ages of 18-23 years. Only two types of ACEs were related to inflammation, inflammation was unrelated to depression, and inflammation did not mediate associations between ACEs and depression. The findings of the current study mirror those of Iob and colleagues (2022), however, this research extends Iob's findings by replicating them in a community sample of young Black and Latinx MSM. Together, these studies point to the possibility that at younger ages, dysregulation of stress related biological processes following ACE exposure may not yet be consistently reflected in detectable variations in inflammatory activity.

The possibility that low-grade chronic inflammation may not consistently represent biological stress processes or serve as a mediator between ACEs and mental health issues in younger individuals aligns with the allostatic load model (Sterling, 2012), the energy model (Bobba-Alves et al., 2022), and life course perspectives. The energy model and the allostatic load model explain how allostasis, while adaptive, can cause physiological wear and tear. These models highlight that during chronic stress, energy is diverted from growth and repair toward immediate survival needs, resulting in a trade-off that can compromise health over time (Bobba-Alves et al., 2022). However, these frameworks do not specify the exact timeline for this wear and tear to manifest as disease. Life course frameworks expand on this by emphasizing that cumulative stress effects often begin early in life, with their impacts compounding over decades and midlife has been identified as a developmental point where key physiological systems are weakened, resulting in disease (Jones et al., 2019). These frameworks point to questions regarding time and long-term trajectories of health and inflammation after ACEs. Studies on ACEs in middle-aged and older adults have demonstrated that individuals with higher levels of ACEs are more likely to experience age-associated functional impairments (Lee et al., 2023), accelerated epigenetic aging (as measured through DNA methylation and aging clocks) (Kim et al., 2023; Klopack et al., 2022), and inflammation (Lacey et al., 2020). The low levels of inflammatory processes in this young sample, paired with data showing accelerated aging in middle-aged and older adults after ACEs supports the possibility that individuals between the ages of 18 and 25 years may not consistently manifest the effects of physiological dysregulation, such as chronic inflammation after ACEs. Future longitudinal research is needed to monitor biological markers of dysregulated stress physiology over time to refine understanding of developmental timelines for the onset of chronic inflammation and other stress related markers and to identify suitable measures for capturing the effects of ACEs at earlier developmental time points.

4.2. Minority stress

One of the main hypotheses of this research was that the interaction between minority stress and ACEs would demonstrate a positive association with inflammation, which would in turn positively influence levels of depression and anxiety. Contrary to this hypothesis, the interaction between ACEs and minority stress did not have a detectable indirect effect on depression through inflammation. Previous evidence has supported the fundamental tenant of Meyer's (2003) minority stress model which postulates that repeated experiences of stigma, discrimination, victimization, and the psychological responses to these events heighten vulnerability to mental health problems over the life course (Diamond and Alley, 2022). Experiences of minority stress have furthermore been linked to heightened biological stress processes,

resulting in wear and tear and disease (Flentje et al., 2020). It is also important to recognize that inflammation was not found to mediate the relationship between ACEs and anxiety or depression, and by extension, possibly does not accurately represent the dysfunction of stress response systems after ACEs. For this reason, this research endeavor was not able to assess whether minority stress magnified the physiological dysregulation and depressive and anxiety symptoms after ACEs. It is possible that in the presence of a more accurate biological measure of HPA axis dysfunction, minority stress may still play a significant role. This area represents an important future direction for continued research with populations of Black and Latinx MSM.

4.3. ACEs, depression, and anxiety

This sample reported remarkably high levels of ACE exposures that exceed previous population statistics on sexual minority populations. Population studies have shown that 22.4 % of U.S. adults have experienced four or more ACEs (Aslam et al., 2024) while 30 % of gay men have reported four or more ACEs (Dosanjh et al., 2023). A study comparing ACE prevalence by race found that 14.8 % of Black youth and 13.2 % Hispanic youth reported four or more ACEs (Mersky et al., 2021). A study examining average ACE exposure by race and sexual orientation using the BRFSS (a nationally representative dataset) found that gay Black men reported an average of 1.63 ACEs, gay White men reported 1.99, and gay Hispanic men reported 2.59 average ACEs (Giano et al., 2023). In contrast, over 50 % of the sample in the current study - primarily gay men of Black or Hispanic race - reported four or more ACEs with an average of 3.4 ACEs. This aligns with Mersky and colleagues (2021) who demonstrated that ACEs cluster in the presence of interlocking social categories related to minoritized identity and low socioeconomic status. The participants in this sample were gay, bisexual, or pansexual men with racially minoritized identity. Only 28 % were employed full time, 55 % reported financial hardship, and 37 % reported experiences of food insecurity in the last year. These findings support Mersky's (2021) work, suggesting that gay men with racially minoritized identity may experience several overlapping stressors and cumulative burdens that often cluster with ACEs.

While expanded ACE scales recognize the impacts of community sources of adversity (Cronholm et al., 2015), this study measured only five types of ACEs. Despite this limitation, ACEs were ubiquitously related to anxiety and depression in all models. Although the relationship between ACEs and later anxiety and depression are well established in the scientific literature (Hughes et al., 2017), this finding contributes to a scarce literature on these variables in Black and Latinx MSM. We are aware of only one other similar study. Wiss and colleagues (2023) conducted a study with 321 Black and Latinx men who have sex with men. They found that participants with five or more ACEs had significantly higher odds of anxiety and depression, though no dose response relationship was observed (Wiss et al., 2023). The current study replicates and extends this work by confirming dose response relationships in a sample of Black and Latinx MSM. Furthermore, Wiss and colleagues (2023) investigated ACEs as predictors of anxiety and depression in a design where anxiety and depression were assessed six years prior to the collection of ACEs data. The current study examined the relationship between ACEs measured at time point two and anxiety and depression measured at time point five, utilizing a more robust longitudinal approach that strengthened evidence for temporal associations. The current study therefore represents a notable contribution to the repository of knowledge on these variables in Black and Latinx MSM.

4.4. Limitations

While this study offers several novel insights into the relationships between ACEs, minority stress, inflammation, depression, and anxiety, it is important to acknowledge limitations that may impact interpretation of findings. One key consideration is the sample size and corresponding statistical power. Although the sample size met the lower bound of recommendations for SEM analyses (Boomsma, 1985; Nunnally, 1975), it may have limited the ability to detect small effects in these mediation and moderated mediation analyses. As established by the inverse square root analysis, this study was powered to detect effects of approximately 0.18 or larger. In contrast, the coefficients for the indirect effects were extremely small in magnitude (close to zero), suggesting that if any true effects were present, they were likely smaller than our detection threshold and negligible in practical terms. The lack of influential effect of inflammation in the structural models is also mirrored in the correlation analysis of latent variables, where all variables were analyzed using the same sample size and estimator, with sufficient power to detect significant associations among ACEs, depression, anxiety, and minority stress, though none emerged for inflammation. Therefore, the near-zero values representing the indirect effects of minority stress and inflammation on the relationships between ACEs and depression and anxiety, suggest a very limited or even absent influence. While larger samples increase power and sensitivity to detect smaller effects (Cohen, 1988), it is important to note that sample size and effect sizes are independent (Sullivan and Feinn, 2012). A larger sample would not necessarily produce larger effects, only more precise estimates of any effects that may actually be present. Nonetheless, it is still important to consider the possibility that increased power could have detected statistically significant effects in the range of these very low values.

Further limitations include constraints related to the sample participants, who were recruited through convenience and snowball sampling methods, therefore the results of this study are not generalizable. Additionally, inflammatory data was only available for participants who provided at least two blood samples at waves two, four, or six, suggesting the possibility of non-random attrition bias which may have led to underestimation of inflammatory activity. Further methodological challenges included a limited set of ACE items, assessment of inflammatory markers at one time-point rather than across time, the use of limited types of minority stress experiences in the minority stress latent variable, and lack of data availability regarding participants' use of antiinflammatory medications, chronic diseases, and other lifestyle factors. Future research endeavors with Black and Latinx MSM should address these limitations through more robust sampling strategies, larger sample sizes, collection of broad data regarding health and medication use, and implementation of measurement instruments that offer a more comprehensive assessment of ACEs and minority stress.

4.5. Future directions and conclusion

This research provides novel contributions by analyzing inflammation as a mediator of the relationship between ACEs and anxiety and depression in a sample of Black and Latinx MSM – a population that has been historically harder to reach in research (Ellard-Gray et al., 2015). To our knowledge, this is the first study to test relationships between these variables in this population. Further contributions include the analysis of minority stress as potential magnifier of the effect of ACEs on inflammatory processes and by extension, depression and anxiety. The variables examined in the moderated mediation analysis represent the intersecting influences of biological systems and social inequities processes that influence development and mental health disparities in MSM populations. By addressing these factors, this work aimed to generate insights to inform inclusive and effective interventions for Black and Latinx MSM with anxiety and/or depression and a history of ACEs. The findings of this work suggest that inflammation may not capture stress related dysregulation after ACEs in younger individuals, highlighting the need for future research using alternative biological markers that may better capture this dysregulation at earlier developmental time points. Future work in this area could inform more targeted interventions addressing both biological systems and social determinants of mental health in Black and Latinx MSM populations.

Further research is needed before knowledge regarding the

biological processes linking ACEs to anxiety and depression can be translated into targeted interventions, however, pressing concerns related to the mental health needs of young, Black and Latinx MSM can be addressed immediately through policy and community level services. Given the known associations between ACEs and anxiety and depression (Chapman et al., 2004; McCutchen et al., 2022; Merrick et al., 2017; Whitaker et al., 2021) and the higher prevalence of ACE exposures and mental health symptomatology among Black and Latinx MSM compared to White MSM and heterosexual peers (Gonzales and Henning-Smith, 2017; Graham et al., 2011), policies that promote and expand existing mental health services for this population are crucial. We recommend support for policies that would fund organizations that support these communities. Counseling interventions that are trauma-informed to address the impact of ACEs and culturally tailored to account for the unique strengths and socially embedded stressors faced by this population can be implemented to provide more effective and accessible mental health care. These immediate measures, along with continued research on the biological processes linking ACEs to depression and anxiety can together contribute to dismantling the systemic health disparities seen in young, Black and Latinx MSM communities.

CRediT authorship contribution statement

Laura H. Dosanjh: Writing - review & editing, Writing - original draft, Methodology, Formal analysis, Conceptualization. Cynthia Franklin: Writing - review & editing, Writing - original draft, Supervision, Methodology, Conceptualization. Yessenia Castro: Writing review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. Bridget Goosby: Writing - review & editing, Writing – original draft, Supervision, Methodology, Conceptualization. Fiona N. Conway: Writing - review & editing, Writing original draft, Supervision, Methodology, Conceptualization. Frances A. Champagne: Writing - review & editing, Writing - original draft, Supervision, Methodology, Conceptualization. Luis A. Parra: Writing review & editing, Writing - original draft, Project administration, Methodology, Formal analysis, Data curation. Jeremy T. Goldbach: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization. Michele D. Kipke: Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Conceptualization.

IRB

The current study is a secondary data analysis and was determined to be 'non-human subjects' research by the University of Texas at Austin's IRB.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.socscimed.2025.118119.

Data availability

The authors do not have permission to share data.

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