The Queer Health Study: Protocol for a Longitudinal Feasibility Study Examining Links between Minority Stress, Allostatic Load, and Drug and Alcohol Use in Sexual Minorities

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Abstract

Background: Substance use rates among sexual minorities are disproportionately greater than that of their heterosexual counterparts. Minority stress theory posits that one explanation for disproportionate substance use in sexual minority populations is a result of increased social stress associated with holding a minoritized identity. This minority stress has been linked to a myriad of negative mental health outcomes, including alcohol and drug use. In addition, emerging research has begun to demonstrate links between minority stress and stress physiology dysregulation. While animal and human models have demonstrated links between stress physiology dysregulation and substance use outcomes, to date, no studies have examined the role that stress physiology plays within a minority stress framework in predicting substance use among sexual minorities. The Queer Health Study was designed to explore the longitudinal links between minority stress, stress physiology (specifically, allostatic load, the cumulative “wear and tear” on the body and brain as a result of chronic stress), and substance use.

Objective: The aims of this feasibility study are to assess feasibility of collecting longitudinal data to explore the temporal links between minority stress processes, allostatic load, and drug and alcohol use, as well as to obtain estimates of effect size to determine the appropriate sample size necessary to conduct a fully-powered longitudinal study.

Methods: This feasibility study is a three-wave longitudinal design consisting of a self-report survey, researcher-assisted Timeline Followback to assess for drug and alcohol use, and blood and anthropometric data collection to measure allostatic load at each of the time points. A total of 40 ethically/racially-diverse sexual minority adult participants (aged 18-60) will be enrolled.

Results: The study received University of Houston IRB approval on July 31, 2023 (STUDY00004277). Recruitment began in June 2024. As of February 2025, the initial sample of 46 participants completed the Time 1 visit, and Time 2 visits are ongoing. We estimate that all study activities will be completed by July 2025.

Conclusions: Results can inform the development of targeted prevention and treatment interventions. In addition, this research will provide an innovative framework for exploring diverse risk and resilience factors impacting addiction in this at-risk population. Ultimately, results have important implications for public health and have the potential to reduce the many dire economic and health consequences of drug use and addiction.

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Keywords:

sexual and gender minorities; allostatic load; substance use; minority stress; biomarkers; LGBTQ+; health disparity

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Introduction

Sexual minority (SM) adults disproportionally use drugs and are at greater risk for substance use disorders (SUDs) than their heterosexual counterparts. National data revealed that SM adults were more than twice as likely as heterosexuals (39.1% versus 17.1%) to have used drugs in the past year[1]. Likewise, SM women (60.8% versus 24.3%) and SM men (65.0% versus 49.9%) are more likely to have a lifetime SUD compared to heterosexuals[2] Drug use is estimated to cost society over $193 billion annually[3,4]. Given the documented disparity in drug use and SUDs among SM adults, it is critical to understand the factors that mediate risk and resilience for drug use and abuse.

One explanation for high rates of drug use and SUDs among SMs is that increased stress related to being a SM confers risk for drug use. This social stress has been termed minority stress[5, 6] and has been linked—primarily in cross-sectional research—to a variety of negative mental health outcomes[7] and alcohol and drug use[8,9].

Nascent research has begun to demonstrate that minority stress is related to stress physiology dysregulation[10]. This research demonstrated that SMs who had disclosed their sexual orientation had lower concentrations of the stress hormone cortisol than those who had not disclosed[10]. Related, Doyle et al.[11] found that gay men who experienced more discrimination had higher levels of the inflammatory cytokine interleukin-6. Another study found that SM young adults who were raised in highly stigmatizing environments demonstrated a blunted cortisol response to a social stressor[12].

In addition to limited studies linking minority stress processes to individual markers of stress physiology, research has revealed that SMs, compared to heterosexuals, demonstrate different stress physiology patterns. For example, Juster et al.[13] showed that SM men had lower allostatic

load (AL) than heterosexual men. Also, SM women displayed higher cortisol reactivity than heterosexual women; SM men, on the other hand, showed lower cortisol reactivity than heterosexual men. Mays et al.[14] found that bisexual men had significantly higher AL than heterosexual men but gay men had lower AL than heterosexual men.

Currently only a handful of studies exist that examine minority stress constructs in the context of stress physiology. However, no studies to date have examined the link between stress physiology and drug use in SM samples. Research in other populations suggests that stress physiology dysregulation—specifically, the concept of AL—may be a promising avenue for understanding drug use vulnerability and trajectory.

AL refers to the cumulative "wear and tear" on the body and brain due to repeated activation of allostatic responses resulting from chronic stress[15]. Prolonged secretion of stress hormones—through the HPA and SAM axes—results in strain on interdependent systems and subsequent physiological dysregulation. Moreover, AL confers risk for accelerated aging, worsened disease trajectories, and all-cause mortality[16]. In both animal and human research, chronic stress, subsequent HPA axis dysregulation, and allostatic states—including AL—are linked to both the initiation of and trajectories of drug use[17] and addiction[18]. Indeed, stress and addiction neurocircuitry are intertwined[19].

At a theoretical level, drug addiction fits within an allostatic model in that it challenges the brain circuits involved in emotional regulation to exacerbate addiction cycles of binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation[18]. Under conditions of chronic drug abuse and relapse, reward and stress pathways become dysregulated and contribute to allostatic states and AL via the HPA-axis and downstream effects[20]. For example, Wand et al.[21] found that stress-induced cortisol was positively correlated with both

amphetamine-induced mesolimbic dopamine and the subjective positive effects of amphetamine, both risk factors for drug use initiation and addiction. Moreover, AL has been implicated in the transition from drug use to addiction, and the AL framework helps to explain the biological mechanisms undergirding both initial use and subsequent addiction[22,23].

No published research to date has explored the link between AL and drug use in SM adults. Given that SM adults face unique, chronic stressors—which are linked to AL—and are more likely than their heterosexual counterparts to use drugs and be diagnosed with SUDs, there is an urgent need to explore the mechanisms underlying drug use outcomes in this at-risk population. In addition, limited research has measured AL repeatedly over time (in any population) to explore the link between AL change and subsequent health outcomes. The limited data suggest that AL variability over time may be an important predictor of health[24]. Thus, more research is needed to understand the longitudinal links between changes in AL and health outcomes.

The Proposed Research. To date, no studies have comprehensively measured minority stress (i.e., discrimination, internalized homonegativity, concealment, expected rejection[5]) in research examining SM biomarkers. Moreover, most research examines single markers of stress physiology. Next, the majority of research is cross-sectional. Thus, there is a need to fully explore the impact of minority stressors on a comprehensive measure of stress physiology dysregulation using longitudinal methods. Finally, no research exists to examine the links between stress physiology and drug use in SM adults, a population with demonstrated drug use and SUD disparities. Thus, the current research proposes that minority stressors resulting from minority sexual orientation lead to allostatic states and increased AL, which in turn confers risk for drug use. See Figure 1 (adapted from Juster[25]) for an overview of our conceptual model.

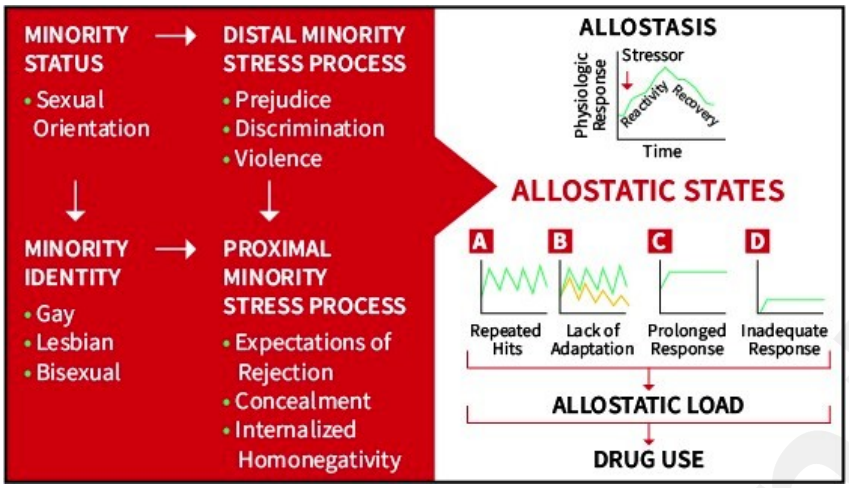

Figure 1. Conceptual model

Objective

The aim of the proposed study is to examine the feasibility of collecting longitudinal data to examine the relationships between minority stress, AL, and drug use, following a sample of SM adults over the course of 1 year. This innovative study will be the first to explore the links between AL and drug use in this population, which has demonstrated drug-use health disparities.

This protocol proposes three aims:

1. *Assess the feasibility of collecting longitudinal data to explore the links between minority stress processes, allostatic load, and drug use*. It is hypothesized that participants will find the study procedures acceptable, there will be minimal attrition over time, there will be minimal missing data, and the target sample size will be successfully recruited.

2. *Obtain estimates of effect size.* Pilot data will be used to obtain estimates of effect sizes between minority stress and AL, AL and drug use, and minority stress and drug use over 3 repeated-measures time points. These effect sizes will be used to determine the necessary sample size to conduct a fully-powered longitudinal study over a longer time period (e.g., 6 time points over 2 years).

3. *Explore the temporal links between minority stress, AL, and drug use.* Because

physiological dysregulation has been linked to the initiation of drug use, and drug use has been linked to subsequent physiological dysregulation, an *exploratory aim* (given the limited sample size) of this research is to test 2 competing models: 1. Minority stress → AL → drug use versus 2. Minority stress → drug use → AL.

Methods

Overview and Design. In order to test proof of concept and feasibility, we will conduct a prospective longitudinal design with 3 time points over the course of 1 year (i.e., every 4 months). These 3 time points were chosen to reduce participant burden while maximizing our ability to examine change over time.

A total of 40 ethnically/racially-diverse SM adult participants (aged 18-60) will be targeted. A sample of 40 participants is consistent with sample size recommendations for pilot feasibility studies[26,27] To address potential attrition, the first time point will over enroll by approximately 20% (~48 participants to be enrolled at Time 1). Participants will be limited to age 18-60 because of the impact of natural aging on AL[16]. This age range was chosen because AL steadily increases from 25 to 60 and then plateaus[28]. Limiting to adults <61 will allow us to target the age group that shows the greatest shifts in AL, maximizing chances of detecting meaningful change.

We expect to have equal proportions of female-assigned-at-birth and male-assigned-at-birth participants. Trans individuals who also identify as SMs will be included. The racial/ethnic makeup of the sample is expected to mirror that of Houston, which includes non-Hispanic Whites (24.4%), Black/African Americans (22.6%), Asian/Asian Americans (6.8%), and Latine/ Hispanic (45.0%)[29].

Participants will be recruited in the metropolitan Houston, TX, area through advertisements and events in community venues. Advertisements will include flyers in SM-inclusive bars,

restaurants, and retail shops; in print/electronic advertisements (e.g., Facebook/Instagram, Grindr); and at SM community events, such as the annual Houston pride celebration (700,000 attendees annually).

Inclusion/Exclusion Criteria include: (1) self-identification as lesbian, gay, bisexual, queer, or other non-heterosexual identity; (2) aged 18-60; (3) willingness to complete study tasks; (4) valid email address (for maintaining contact, such as sending appointment reminders); and (5) proficient in English. Failure to meet any inclusion criterion will result in study exclusion.

Design

The current study involves a prospective longitudinal design with 3 time points over the course of 1 year (i.e., every 4 months). Participants come to the laboratory every 4 months over the course of 1 year to provide biomarkers and self-report data. At each visit, participants will complete computer-administered (Qualtrics) self-report measures and a researcher-assisted Timeline Followback to assess for drug and alcohol use. Participants will provide blood samples to assess biomarkers, and have anthropometric data collected to assess for adiposity and blood pressure.

Participants will be compensated in retail gift cards (i.e., Tango; tangocard.com) for completion of specific portions of the study. They will receive $50 for completing each of 3 in-person assessment visits ($150 total); and an additional $50 for the completion of all 3 in-person assessments. In total, a participant can receive up to $200 in retail gift cards for participating in the study.

Method. Interested participants will complete an initial phone screening to assess for inclusion criteria. Those meeting all inclusion criteria will be given a scheduled time to come to the laboratory. Eligible participants will then complete blood draw, anthropometric

measurements, and self-report measures.

Measures. At each of 3 timepoints, participants will complete self-report questionnaires (via Qualtrics), containing a demographic questionnaire and the measures below. All measures have good reliability and validity, and have been used with SM samples.

Self-report measures.

Demographics will assess sexual orientation, sex assigned at birth, current gender identity, race and ethnicity, age, income, education, employment, occupation, relationship status, and current medications.

Internalized homonegativity will be measured using Theodore et al.'s Internalized Homophobia Scale [30,31].

Discrimination will be measured using Szymanski's Heterosexist Harassment, Rejection, and Discrimination Scale[32].

Anticipated discrimination will be measured using Pachankis's Gay-Related Rejection Sensitivity Scale[33,34].

Sexual orientation concealment will be measured using Mohr and Jackson's Sexual Orientation Concealment Scale[35].

Intersectional stress will be measured by Mereish's Everyday Identity Stress Scale[36].

Participant acceptability will be measured using quantitative and qualitative questions from the Theoretical Framework of Acceptability[37,38].

Study feasibility will be assessed via participant recruitment, enrollment, and attrition, which will be tracked following CONSORT guidelines[39]. In addition, we will track how long it takes to recruit the sample and calculate the proportion of: missing data, useable biomarker data, participants eligible after screening, participants consented, and participants retained at each time

point.

Drug and alcohol abuse consequences will be assessed via the Drug Abuse Screening Test (DAST-10)[40] and the Alcohol Use Disorders Identification Test (AUDIT)[41].

Depression will be measured by the Center for Epidemiological Studies Depression Scale[42.]

Anxiety will be measured by the GAD-7[43].

Sleep quality will be measured using the Pittsburgh Sleep Quality Index[44].

Belongingness will be measured using the General Belongingness Scale[45].

Drug/alcohol use frequency will be assessed using 120-day Timeline Followback (TLFB)[46] for the following substances: Alcohol, Cannabis, Cocaine, PCP, Opiates, Methamphetamine (including Ecstasy/MDMA), Hallucinogens, Methadone, Heroin, Amphetamines, Barbiturates, Benzodiazepines, Inhalants, and synthetic cannabinoids.

Smoking will be measured using standard questions from the National Health Interview Survey[47]. Vaping will be measured by the Penn State Electronic Cigarette Dependence Index[48].

Physiologic and Anthropometric Measures. Biomarkers will include immune functioning (interleukin (IL) 1β, 6, and 8, tumor necrosis factor alpha (TNF-α), C-reactive protein (CRP), serum amyloid A (SAA), vascular cell adhesion molecule 1 (VCAM-1), and intercellular cell adhesion molecule 1 (ICAM-1)), metabolic functioning (glycosylated hemoglobin (HbA1c), HDL/LDL cholesterol, and triglycerides), adiposity (BMI, body fat percent, waist-to-hip ratio), and blood pressure.

Blood Collection and Assaying. A total of 10 mL of blood will be collected via venipuncture at University of Houston by a certified phlebotomist. Samples will be centrifuged, and plasma will be extracted and aliquoted into cryovials for storage at -80°C until assaying. All samples will be tested in duplicate; samples from the same participant will be assayed on the same plate

within the same run. Validated V-PLEX Viral Panel 1 kits (i.e., IL-1β, IL-6, IL-8, TNF-α) and Vascular Injury Panel 2 kits (i.e., CRP, SAA, VCAM-1, ICAM-1) from Meso Scale Discovery will be used to assay these biomarkers using the MESO QuickPlex SQ 120. HbA1c will be measured using a Siemens DCA Vantage Analyzer. HDL/LDL cholesterol and triglycerides will be measured using CardioChek Plus, a standard point-of-care device.

Adiposity. Weight, percent body fat, muscle mass, bone mass, and percent body water will be measured using a Tanita DC-430U dual frequency total body composition analyzer. Height will be measured using a Seca (model 217) stadiometer. Body mass index (BMI) will be calculated using the standard formula. Body fat percent will be calculated using sex-specific formulas (for trans participants, the average of the male and female ranges will be used). Waist-to-hip ratio will be measured with an ergonomic Seca (model 201) measuring tape, measured in cm, dividing waist by hip circumference.

Blood Pressure. Blood pressure will be measured using an electronic sphygmomanometer (Omron model BP785N). The average of 3 systolic and 3 diastolic resting readings—taken while sitting—will be computed.

Allostatic Load. AL will be calculated using an established count-based approach[10,49,50]: for each measure, a clinical cutoff will be utilized such that those falling above the cutoff will score 1, while those falling below will score 0; scores will be summed to calculate AL index. This approach to AL index calculation has been utilized in previous studies of SM adults[10]. As an alternative to the most-commonly-used count-based AL index, we also will calculate a z-score AL index that represents the sum of an individual's obtained z-scores for each biomarker based on the sample's distribution of biomarker values, allowing the relative weight of each biomarker to be different depending on its deviation from the sample's mean[21].

Data Analytical Plan. To address Aim 1, we will track how long it takes to recruit the sample and calculate proportion of: missing data, useable biomarker data, participants eligible after screening, participants consented, and participants retained at each time point. Measures of central tendency and of dispersion will be calculated for acceptability measures. Open-ended acceptability data will be analyzed via content analysis.

To address Aim 2 and exploratory Aim 3, we will first examine the missing data pattern and apply imputation procedures for the missing responses following dropout, such as multiple imputation, in which each missing value is replaced with several plausible values[51]. Next, field and range checks will be conducted. Distributional characteristics will be assessed and outliers will be checked. Prior to inferential procedures, extensive descriptive statistical analyses of the outcome and predictor variables will be conducted. Standard descriptive statistics including means, standard deviations, ranges, box plots, histograms, and frequencies will be calculated. Normalizing transformations will be explored as appropriate. For Aim 2, estimates of effect size will be calculated via Pearson correlations (or Spearman correlations, depending on distribution).

For exploratory Aim 3, a longitudinal path modeling using a fully cross-lagged design[52] will be used to explore whether 1. minority stress impacts AL, which in turn impacts drug use or 2. minority stress impacts drug use, which in turn impacts AL. Because minority stress and AL will be measured at the same time, the casual directions between them cannot be established. Therefore, we will use a cross-lagged design—a special case of structural equation modeling[53]—to estimate autoregressive and cross-lagged paths, allowing us to address reciprocal influences of minority stress and AL simultaneously. Because of the longitudinal model, the autoregressive effects are modeled as lags where baseline measures are predictors of post-1 measures and post-1 measures are predictors of post-2 measures; thus, the temporal order is preserved. Given the

small sample size and exploratory nature of the analysis, the model will be underpowered. Nonetheless, we will be able to observe trends in the data. All analyses will be conducted using SAS 9.4[54] and Mplus 8.4[55].

Results

The study received University of Houston IRB approval on July 31, 2023 (IRB ID: STUDY00004277). Funding for the study was approved by the National Institute of Minority Health and Health Disparities on August 1, 2023. Recruitment began in June 2024. As of February 2025, an initial sample of 46 participants completed the Time 1 visit. Time 1 was oversampled to account for anticipated attrition with the goal of achieving a total sample size of 40 that completes all time points. Approximately half of the initial sample has completed the Time 2 visit, and assessments are ongoing. We estimate that all study activities will be completed by July 2025.

Conclusion

It is expected that the protocol will be feasible with high participant satisfaction. The results will also provide estimates of effect size, which we will use to develop a fully-powered study to be conducted over a longer time period (e.g., six visits over two years). More important, the results will provide novel insights into the mechanisms and trajectories of drug addiction in an at-risk population and provide a useful framework for examining the role of stress physiology dysregulation in other populations at-risk for drug use disparities.

This innovative protocol is the first to propose a longitudinal study of sexual minority biopsychosocial determinants of substance use. As the only research to date that explores the interplay of neurobiological and psychosocial risk factors in drug use outcomes among SM adults—a population with demonstrated disparities in drug use and SUDs—the proposed

research will provide an innovative framework for future research to explore diverse risk and resilience factors impacting addiction in this at-risk population. As such, this research addresses a critical health disparity.

Moreover, the outcomes of this research will provide important insights into the potential mechanisms of action for substance use trajectory and addiction, as well as offer implications for development of interventions to reduce and prevent substance use. If results support the longitudinal links between minority stress and substance use through stress physiology dysregulation, researchers will be provided with novel insights into the mechanisms driving substance use in this population.

In addition, such results will provide clear direction for intervention development. For example, the results can influence the development of tailored interventions to directly target AL among SMs. Indeed, reducing AL has been demonstrated to be beneficial. Research in older adults has revealed that reductions over time in AL are protective against all-cause mortality, with a mortality rate of 15% for those whose AL increased over 2.5 years but only 5% for those whose AL decreased over the same time period[24]. In addition, research has revealed that behavioral interventions can reduce AL. For example, stress-reduction interventions such as transcendental meditation and yoga have demonstrated effects on reductions in AL-related variables such as blood pressure[56] and cortisol[57]. Thus, results from the proposed study can be used to develop tailored, interdisciplinary interventions that target multiple, modifiable risk factors for addiction.

Next, the methodological framework developed and tested in the research has the potential to serve as a model for exploring factors influencing addiction in other underrepresented populations with health disparities (see, for example, research on links between physiological

dysregulation and drug use in African American young adults[58]). As noted, the results can also be used to develop innovative prevention, early detection, and treatment efforts to reduce drug use and addiction (in this and other populations) based on understanding how the interactions of biological and psychosocial factors influence drug use trajectories.

Ultimately, the research described in this protocol has the potential to reduce the many dire economic and health consequences of drug use and addiction. Moreover, the research represents a critical step in eliminating health disparities that reduce quantity and quality of life and increase healthcare costs.

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Supplementary Files

Figures

Conceptual Model.