DETECTING, EXPLAINING, AND REDUCING SUBSTANCE USE, MENTAL HEALTH, AND VIOLENCE INEQUITIES FOR SEXUAL AND GENDER MINORITY YOUTH AND EMERGING ADULTS

by

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DETECTING, EXPLAINING, AND REDUCING

SUBSTANCE USE, MENTAL HEALTH, AND VIOLENCE INEQUITIES

FOR SEXUAL AND GENDER MINORITY YOUTH AND EMERGING ADULTS

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ABSTRACT

This dissertation extended the existing scientific literature concerning the detection, explanation, and reduction of substance use, mental health, and violence victimization inequities for sexual and gender minority (SGM) youth and emerging adults (people aged less than 18 years and 18-25 years, respectively). This dissertation aimed to: (1) estimate sexual-orientation differences in longitudinal alcohol use trajectories (AUTs) and alcohol use disorders (AUDs) during emerging adulthood, and test whether AUTs mediated sexual-orientation differences in AUDs; (2) investigate sexual-orientation differences in typologies of familial and non-familial warmth during childhood and adolescence, and test whether these differences mediated sexual-orientation differences in AUTs and AUDs during emerging adulthood; and (3) systematically review the peer-reviewed scientific literature on interventions and their efficacy in preventing or reducing substance use, mental health problems, and violence victimization among SGM youth. In Aim 1, this dissertation found that several sexual-minority subgroups had higher odds of belonging to heavier AUTs than completely heterosexuals. These differences partially explained the higher risk of AUDs among sexual-minority women but not among sexual-minority men. In Aim 2, sexual-minority women were less likely to report having familial and non-familial warmth during childhood and adolescence, which partially explained why they have greater risk

of AUDs. However, there were fewer sexual-orientation differences in warmth for men, and these did not explain the sexual-orientation differences in AUTs and AUDs for men. In Aim 3, this dissertation found that 6 interventions were evaluated among SGM youth for reducing mental health problems, 1 for substance use, and 0 for violence victimization in the extant scientific literature. In conclusion, this dissertation used the life-course perspective to advance research concerning the detection and explanation of sexual-orientation inequities in AUTs and AUDs during emerging adulthood. This dissertation also found significant gaps in intervention research for SGM youth. Without more evidence-based interventions, SGM youth and emerging adults will likely continue to experience health inequities in substance use, mental health, and violence victimization across the life course. Despite the major advances in public health research on SGM populations, intervention research is sorely lacking—but essential—for SGM youth and emerging adults to achieve health equity.

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PREFACE

I am grateful to everyone who supported me throughout the conceptualization and execution of this dissertation, including BRH, KJC, RSC, CLG, CLK, CLW, RDS, CFM, NM, AJS, MRF, ALH, JEE, SMK, HLC, HJJ, NLT, JPC, KE, BLF, BMC, EM, DES, DDM, JRB, ALB, SM, LAB, CJC, DK, LMB, MCV, CP, ADG, MLK, GUTS, and NIH.

1.0 DISSERTATION INTRODUCTION

Sexual and gender minority youth and emerging adults (people aged less than 18 years and 18-25 years, respectively) experience substantial inequities in health compared with their heterosexual cisgender peers, especially in substance use, mental health concerns, and violence victimization.[1-56] In 2011, the landmark Institute of Medicine (IOM) report[1] on health inequities among sexual and gender minority (SGM) people (gay/lesbian, bisexual, transgender, and gender-nonconforming people; people with same-gender attractions or sexual behaviors; and people whose gender identity does not match their assigned sex at birth) documented these disparities and identified related research gaps—and the following gaps will be directly addressed in this dissertation. The IOM report[1] highlighted the scant longitudinal research on SGM populations, which limits knowledge of how SGM populations' health and inequities change as people age. Furthermore, the IOM report[1] recommended that future research examine the social influences on the health of SGM populations. Such research can identify how SGM populations' social ecologies positively and negatively affect their health, highlighting mechanisms (e.g., support, stigma) to be targeted and modified by intervention programs and policies. Intervention research was also a research priority in the IOM report.[1] Interventions can help mitigate SGM health inequities, thereby providing equal health to all populations regardless of sexual orientation, gender identity, and gender expression.

The IOM report[1] also recommended that SGM health research priorities be informed by multiple cross-cutting perspectives, including the life-course perspective,[57] which is a theoretical orientation that is both multidimensional and multitheoretical, and guided by the following 5 principles[57]:

1. Human development is a lifelong process. In general, health develops via dynamic processes throughout a lifetime and is not only an artifact of events that occurred last week, month, or year.
2. Individuals are social beings, both interdependent and linked to other humans. Social networks impact individuals' well-being.
3. Events, transitions, and patterns impact people, and their consequences may depend on the developmental period of the life course in which they occur. Timing of events is incredibly important in a life-course perspective.
4. Historical and geographical context shapes individuals' life courses. This refers to how both socio-historical context and geographical location can directly shape the opportunities and constraints placed on populations, and consequently have great influence on public health.[58] Historical and geographical location can also interact with factors and characteristics found at other social ecological levels to impact health.
5. Human, proxy, and collective agency can impact public health. Agency refers to how individuals and communities can act as change agents to impact social structures and their own lives, including their health.

This dissertation will use the life-course perspective[57] as a theoretical orientation to investigate innovative descriptive, explanatory, and intervention-related research questions among SGM youth and emerging adults.

Finally, this dissertation will advance research on health inequities for SGM youth and emerging adults in each of the 3 primary "generations" or "phases" of the public health inequities research agenda.[59,60] The first generation of research involves detecting health inequities.[59,60] Detection of health inequities is accomplished through rigorous epidemiologic research. This process involves defining and sampling study populations, measuring health problems, and selecting appropriate study designs. The second generation of research involves explaining the determinants of health inequities.[59,60] Like the first generation of research, epidemiologic research is well-poised to test determinants of health inequities in the second generation of research, and multidisciplinary theoretical frameworks often guide this research. The third generation of research involves reducing health inequities.[59,60] This includes designing, implementing, and evaluating intervention programs and policies aimed at reducing health inequities. These three generations of research can work together to help propel SGM populations towards health equity.[59,60]

1.1 DISSERTATION AIMS

The purpose of this dissertation is to extend the research about the health of SGM populations in three distinct areas: detecting, explaining, and reducing health inequities. In Chapter 2, this dissertation detects sexual-orientation differences in alcohol use trajectories and alcohol use disorders during emerging adulthood. In Chapter 3, this dissertation investigates how sexual-

orientation differences in warmth during childhood and adolescence mediate sexual-orientation differences in alcohol use trajectories and alcohol use disorders during emerging adulthood. In Chapter 4, this dissertation systematically reviews existing intervention research about preventing and reducing substance use, mental health concerns, and violence victimization among SGM youth.

2.0 SEXUAL-ORIENTATION DIFFERENCES IN ALCOHOL USE TRAJECTORIES AND DISORDERS IN EMERGING ADULTHOOD: RESULTS FROM A LONGITUDINAL COHORT STUDY IN THE UNITED STATES

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2.1 ABSTRACT

Aims: We estimated sexual-orientation differences in longitudinal alcohol use trajectories during emerging adulthood, and tested whether alcohol use trajectories mediated sexual-orientation differences in alcohol use disorders (AUDs).

Design: Prospective survey data from the Growing Up Today Study cohort.

Setting: United States.

Participants: Longitudinal data from 12,493 participants aged 18-25 during the 2003, 2005, 2007, or 2010 surveys.

Measurements: Stratified by gender, longitudinal latent class analyses estimated alcohol use trajectories (using self-reported alcohol use items: past-year frequency, quantity, and heavy episodic drinking; measured from 2003-2010). Multinomial logistic regression tested differences in trajectory class membership by sexual orientation (comparing completely heterosexuals to sexual-minority subgroups: mostly heterosexuals; bisexuals; and gays/lesbians). Modified Poisson regression and mediation analyses tested whether trajectories explained sexual-orientation differences in AUDs (past-year DSM-IV abuse or dependence; measured in 2010).

Findings: Six alcohol use trajectory classes emerged for women and five emerged for men: these included heavy, moderate, escalation-to-moderately-heavy, light (for women only), legal

(drinking onset at age 21), and non-drinkers. Compared with completely heterosexual women, mostly heterosexual and bisexual women had higher odds of being heavy, moderate, escalation-to-moderately-heavy, and light drinkers versus non-drinkers (odds ratios: 2.01-3.26; p-values: <0.0001-0.0403). Compared with completely heterosexual men, mostly heterosexual men had higher odds of being heavy, moderate, and legal drinkers versus non-drinkers (odds ratios: 2.16-3.22; p-values: 0.0001-0.0032). Mostly heterosexual men and women, bisexual women, and gays/lesbians had higher risk of AUDs in 2010 than their same-gender completely heterosexual counterparts (risk ratios: 1.35-2.19; p-values: <0.0001-0.0037). Alcohol use trajectory groups mediated sexual-orientation differences in AUDs for women (proportion of effect mediated: 18.6-30.5%; p-values: <0.0001-0.0383) but not for men.

Conclusions: Throughout emerging adulthood, several sexual-minority subgroups had higher odds of belonging to heavier alcohol use trajectories than completely heterosexuals. These differences partially explained the higher risk of alcohol use disorders among sexual-minority women but not sexual-minority men.

2.2 INTRODUCTION

Alcohol use and heavy episodic drinking (HED; i.e., consuming at least 4 drinks for women or 5 drinks for men on one occasion) in the United States is highest during the emerging adulthood period (i.e., ages 18-25).[61-66] Nevertheless, emerging adults have diverse alcohol use trajectories. This diversity is often characterized using statistical approaches well-suited for identifying homogenous subgroups of alcohol use trajectories.[67-69] A recent systematic review of longitudinal alcohol use throughout emerging adulthood found common trajectories, such as

consistently heavy drinkers, escalation drinkers, and non-drinkers.[70] Importantly, consistently heavy or escalating alcohol use trajectories place emerging adults at greater risk for acquiring alcohol use disorders,[71-74] which are associated with great morbidity and mortality as well as severe economic burden.[75-77]

Alcohol use and alcohol use trajectories are not equal across all populations of emerging adults. For example, some sexual-minority subgroups (e.g., lesbian, gay, bisexual, and those who describe their sexual orientation as "mostly heterosexual") have higher alcohol use than their completely heterosexual peers, according to both cross-sectional[30,38,39,42-45,47] and longitudinal[19,31,40,41,46,78] research. These studies show that sexual-minority women are at greater risk of alcohol use and HED than completely heterosexual women.[19,30,38-44,78] On the other hand, findings among men are mixed: most studies found no sexual-orientation differences in the prevalence of alcohol use or HED[30,38-42,45,46]; some studies found higher prevalence of drinking and HED for sexual-minority versus heterosexual men[14,40,44,46,78]; while others found lower prevalence of heavy drinking among sexual-minority men.[30,42,43,47] With few exceptions,[19,31,78] much of the prior research on sexual-orientation differences in emerging adulthood has largely used data from college-based samples,[79] calling for additional research using data from participants sampled outside of college settings. Additionally, there is little information about how sexual orientation is related to membership in different alcohol use trajectory groups throughout emerging adulthood, which is a focus of the current study and has been identified as a priority by researchers and the Institute of Medicine.[1,79]

Sexual-minority adults are also at higher risk than heterosexual adults for having alcohol use disorders (AUDs; i.e., abuse or dependence).[48-50] Scant research suggests this is also true during emerging adulthood,[51] when people in the U.S. are at greatest risk for AUDs.[80] Generally,

the development of AUDs is positively associated with earlier or concurrent high alcohol use trajectories[70,81,82]; therefore, sexual-orientation differences in alcohol use trajectories may partially explain sexual-orientation differences in subsequent AUDs. Support for this hypothesis would suggest that interventions reducing sexual-orientation differences in alcohol use trajectories may also be able to decrease differences in AUDs.

2.3 AIMS

This paper addressed gaps in knowledge about how sexual orientation is related to alcohol use trajectories and disorders using data from an ongoing prospective cohort study. First, we estimated longitudinal alcohol use trajectories during the emerging adulthood period. We hypothesized that there would be different trajectory groups characterized by higher and lower alcohol use. Second, we tested for sexual-orientation differences in alcohol use trajectory memberships. We hypothesized that sexual-minority populations would be more likely to be members of high alcohol use trajectory groups than completely heterosexuals, and these sexual-orientation differences would be larger among women than men. Third, we estimated sexual-orientation disparities in AUDs in late emerging adulthood, and tested for the presence of mediation of these disparities by longitudinal alcohol use trajectories. We hypothesized that sexual-minority populations would be more likely to have AUDs in late emerging adulthood, and longitudinal alcohol use trajectories throughout emerging adulthood would mediate these disparities. The results of this study can help identify sexual-orientation subgroups at risk for having heavy alcohol use trajectories and AUDs, and will show whether reducing sexual-

orientation differences in alcohol use trajectories can reduce sexual-orientation disparities in AUDs.

2.4 METHODS

Study Design and Population

We analyzed data from participants in the Growing Up Today Study (GUTS), which began in 1996. GUTS initially enrolled 16,875 participants aged 9-14 years who were children of women participating in the Nurses' Health Study II—a cohort study of 116,430 registered nurses from 14 U.S. states begun in 1989. Additional information about GUTS is reported elsewhere.[19,83] Brigham and Women's Hospital Institutional Review Board (IRB) approved original study procedures.

The current study included participants who provided information on sexual orientation and who were 18-25 years old when they responded to at least 1 alcohol use item during the 2003, 2005, 2007, or 2010 survey waves. We selected these waves because they assessed alcohol use and contained the age range that was the focus of this analysis. Our analytic sample included 12,493 participants (7,465 women; 5,028 men), representing 74.0% of the cohort. Compared to cohort participants excluded from our analyses, participants in our analytic sample were more likely to be female (35.8% versus 59.8%, respectively; $p<0.001$) and to live in the Western region of the U.S. at baseline (14.7% versus 11.5%, respectively; $p<0.001$). Participants included versus excluded in our analytic sample did not differ by race/ethnicity ($p=0.838$) or age at baseline ($p=0.094$). Participants' mean age in our analytic sample was 18.8 years in 2003 and 25.2 years in 2010. Among participants in our analytic sample, 84.2% responded to the 2003

survey, 83.3% in 2005, 78.1% in 2007, and 68.2% in 2010. Overall, 53.3% responded to all 4 waves, 19.7% responded to 3 waves, 14.6% responded to 2 waves, and 12.5% responded to 1 wave.

Measures

Alcohol Use

Three indicators assessed alcohol use in 2003, 2005, 2007, and 2010. These indicators were non-normally distributed, hence we coded and modeled them as ordinal variables. We assessed *past-year average frequency*: "On average, in the past year, how often did you drink beer, wine, or liquor?" Response options included: don't drink; less than once a month; less than once a week; 1-2 days per week; 3-5 days per week; almost every day; and daily. We combined daily and almost every day because of small cell sizes, and coded this variable from 0 ("don't drink") to 6 ("daily or almost every day"). We assessed *past-year average quantity*: "When you drink alcohol, how much do you usually drink at one time?" Response options included: don't drink; less than 1; 1; 2; 3; 4; 5; and 6 or more drinks. We coded this variable from 0 ("don't drink") to 7 ("6 drinks"). We assessed *past-year HED*: "Over the past year, how many times did you drink 4 (for women) or 5 (for men) or more alcohol drinks over a few hours?" Response options included: none; 1; 2; 3-5; 6-8; 9-11; and 12 or more times. We coded this from 0 ("none") to 6 ("12 or more times").

Alcohol Use Disorders

We measured criteria for probable AUD during the past 12-months for the first time in 2010 with items assessing symptoms based on the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV),[84] adapted from the National Survey on Drug Use and Health [85]. The DSM-IV described two distinct disorders, alcohol abuse and alcohol dependence,

prevalence among participants was 10.1% and 10.6%, respectively. If participants met criteria for alcohol abuse or dependence, we coded them as having a probable AUD, creating a single binary variable. We made this analytic decision based on prior research[48,86,87] and because the DSM-5[88] integrates abuse and dependence into a single disorder. We conducted sensitivity analyses with the original DSM-IV categorizations, which yielded results (not shown) similar to results using the single binary AUD variable.

Sexual Orientation

Adapted from the Minnesota Adolescent Health Survey,[89] the following question assessed sexual orientation at each survey wave included in this analysis: "Which one of the following best describes your feelings?" Response options included: completely heterosexual (attracted to persons of the opposite sex); mostly heterosexual; bisexual (equally attracted to men and women); mostly homosexual; completely homosexual (attracted to persons of the opposite sex); and unsure. We classified sexual orientation based on participants' last report. As has been done previously,[19] we combined mostly and completely homosexual into a single group (henceforth referred to as lesbian/gay) to increase statistical power; we removed participants who were "unsure" of their sexual orientation because of small sample size.

Covariates

We controlled for variables previously associated with sexual orientation and alcohol use (i.e., potential confounding variables).[21,90-94] These included race/ethnicity (White vs. non-White; measured at baseline), region of residence (West vs. Midwest, Southwest, and Northeast; measured in 2010), and age (we used age in 2010 when used as a covariate). We assessed college attendance in 2010 using the following item adapted from the National Survey of Family Growth[95]: "What is the highest grade of school you have completed or the highest degree you

have received?" There were 8 response options, which we dichotomized into any college attendance versus none (i.e., high/trade/vocational school graduate or less). We prospectively assessed lifetime pregnancy (yes/no) from 1999-2010 for women. We used the missing indicator method[96] for college attendance and pregnancy, which creates an additional "missing" category for each variable, allowing us to analyze all available data and preserve statistical power.

Analyses

Following Masyn's guidelines,[69] we used a classify-analyze approach to characterize longitudinal alcohol use trajectory classes and estimate predictors and outcomes associated with these classes.

Alcohol Use Trajectory Classes

We estimated alcohol use trajectories using longitudinal latent class analyses in Mplus version 7.2 (Los Angeles, CA), which allows for the estimation of subgroup populations who differ across multiple indicators of alcohol use over time. We estimated the unconditional model (i.e., no covariates) with the three ordinal alcohol use variables at each participant's age using a cohort-sequential design.[97,98] We used Full Information Maximum Likelihood estimation, allowing all available observations to be used without imputing data or deleting observations with missing data.[67,99] We accounted for the non-normality of alcohol use variables by using the robust maximum likelihood estimator.[100,101] We employed the complex survey analysis procedure in Mplus to account for non-independence of sibling clusters.[99]

We estimated the trajectory classes separately by gender because men drink higher quantities of alcohol on average than women.[102-105] Our approach was to keep models separate by gender if results yielded a different number of best-fitting classes for men and women. If number of classes estimated was the same for men and women, we would combine genders into

a single model and test for measurement invariance by gender.[106,107] We estimated 1- through 9-class solution models for women, and 1- through 7-class solution models for men. To determine the best-fitting number of classes, we examined several fit statistics, including Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), the Bayes Factor (BF), the correct model probability (cmP), and the Vuong-Lo-Mendell-Rubin adjusted likelihood ratio test.[69,99,108,109] We considered the best fitting model to have the lowest BIC, BF>10, the greatest cmP, and highest interpretative validity.[69,101,108] We examined entropy and other classification qualities (i.e., average posterior probabilities [AvePP] and odds of correct classification [OCC]).[69,110] We considered good latent class separation and assignment as classes with AvePP>0.7 and OCC>5.[110] We assigned participants to the class for which they had the highest posterior probability of membership.

Disparities in Alcohol Use Trajectory Class Membership

Using SAS version 9.4 (Cary, NC), we used Rao-Scott chi-squared tests[111] adjusting for sibling clusters to examine the bivariate associations of trajectory groups with sexual orientation and covariates. We fit multinomial logistic regression models to test for sexual-orientation differences in trajectory class membership (polytomous variables), controlling for covariates, using generalized estimating equations (GEE) to account for the non-independence of sibling clusters. Reference groups in the models were non-drinkers (versus other trajectory classes) and completely heterosexuals (versus sexual-minority subgroups).

Alcohol Use Disorders

Because AUD prevalence was greater than 10%, we fit modified Poisson regression models (i.e., log-link with Poisson distribution) using GEE.[112] First, we estimated sexual-orientation differences in AUDs, controlling for covariates. Second, we estimated the effects of

sexual orientation and alcohol trajectory classes on AUD, controlling for covariates. Subsequently, we tested whether the alcohol use trajectory classes mediated sexual-orientation differences in AUDs using the publicly available %MEDIATE macro.[113]

2.5 RESULTS

Overall, 81.1% of women identified as completely heterosexual, 15.0% as mostly heterosexual, 2.3% as bisexual, and 1.5% as lesbian (Table 2-1). Among men, 90.4% identified as completely heterosexual, 6.0% as mostly heterosexual, 0.7% as bisexual, and 2.9% as gay.

From ages 18-25 years, participants completed data for 28,825 alcohol frequency items, 28,698 alcohol quantity items, and 31,197 HED items. We selected the 6-class model for women and the 5-class model for men based on the fit indices (Table 2-2). These classes had good separation and adequate assignment (all AvePP>0.77 and OCC>11).

Figure 2-1 depicts the latent classes for women. *Non-drinkers* (7.0%) mostly abstained from drinking. *Heavy drinkers* (23.5%) used 1-2 days/week, consumed 4-5 drinks/occasion, and 55-80% of them engaged in monthly HED. *Moderate drinkers* (31.8%) increased their frequency slightly from ages 18-21 to 1-2 days/week, and then plateaued until age 25. Their average quantity increased slightly from ages 18 to 19 at 3 drinks, and decreased to 2 drinks by age 25. Their HED increased slightly from 18-21 to 6-8 times/year, and then plateaued until age 25. *Legal drinkers* (11.1%) abstained from alcohol use from ages 18-20, and nearly all of them drank alcohol from ages 21-25. *Escalation-to-moderately-heavy drinkers* (9.7%) abstained from drinking at age 18, and escalated to moderately heavy use by age 21, plateauing thereafter. *Light*

drinkers (17.0%) consumed 2 drinks/occasion less than once a month and engaged in one HED episode/year, on average, from ages 18-25.

Figure 2-2 depicts the latent classes for men. *Non-drinkers* (9.1%) mostly abstained from drinking. *Heavy drinkers* (36.9%) consumed alcohol 1-2 days/week at age 18, which increased slightly to age 21, plateauing thereafter. Most heavy drinkers consumed 6 drinks/occasion at age 18, decreasing slightly from ages 19-25. Fifty percent of heavy drinkers engaged in monthly HED at age 18, and 75-95% engaged in monthly HED from ages 19-25. *Moderate drinkers* (26.4%) increased their frequency slightly from ages 18-21 to 1-2 days/week and then plateaued until age 25. Their quantity was 3-4 drinks/occasion from ages 18-22, decreasing slightly thereafter. Their HED remained consistent from ages 19-25 around 3-5 HED episodes/year. *Legal drinkers* (15.7%) largely abstained from alcohol use from ages 18-20, and nearly all of them drank from ages 21-25. *Escalation-to-moderately-heavy drinkers* (12.0%) abstained from drinking at age 18, and escalated to moderately heavy use by age 20, plateauing thereafter.

As shown in Table 2-3, sexual orientation and all covariates were associated with alcohol use trajectory classes. Table 2-4 shows the multivariable results for sexual-orientation differences in alcohol use trajectory class membership. For women, mostly heterosexual and bisexual participants had significantly higher odds (odds ratios [ORs] range: 2.01-3.26; p-values range: <0.0001-0.0403) than completely heterosexual participants of being heavy, moderate, escalation-to-moderately-heavy, and light drinkers versus non-drinkers. For men, mostly heterosexual participants had significantly higher odds (ORs range: 2.16-3.22; p-values range: 0.0001-0.0123) than completely heterosexual participants of being heavy, moderate, and legal drinkers versus non-drinkers. Gay men had 3.30 times the odds (p-value=0.0032) of completely heterosexual men of being moderate drinkers versus non-drinkers.

Among women, sexual-minority subgroups were 2.04-2.19 times more likely (p-values<0.0001) than completely heterosexuals to meet criteria for probable AUD in 2010, adjusting for covariates (Table 2-5; multivariable model 1). Heavy, moderate, and escalation-to-moderately-heavy drinkers were more likely than non-drinkers to evidence AUD (risk ratios [RRs] range: 11.76-29.55; p-values<0.0001; multivariable model 2). Alcohol use trajectory classes mediated sexual-orientation differences in AUD (mediated proportions range: 18.6-30.9%; p-values range: <0.0001-0.0383). After controlling for alcohol use trajectory classes, mostly heterosexual, bisexual, and lesbian women remained more likely than completely heterosexual women to evidence AUD (RRs range: 1.73-1.81; p-values range: <0.0001-0.0009).

Compared with completely heterosexual men, mostly heterosexual men were 1.35 times more likely (p=0.0037), and gay men were 1.56 times more likely (p=0.0003) to evidence AUD, adjusting for covariates (Table 2-5; multivariable model 1). Heavy, moderate, legal, and escalation-to-moderately-heavy drinkers were more likely than non-drinkers to meet criteria for AUD (RRs range: 5.67-39.21; p-values range: <0.0001-0.0035; multivariable model 2). Alcohol use trajectory classes did not mediate sexual-orientation differences in probable AUD for men. After controlling for alcohol use trajectories, mostly heterosexual (RR=1.41; p=0.0001) and gay men (RR=1.68; p<0.0001) were more likely than completely heterosexual men to meet criteria for AUD.

2.6 DISCUSSION

In our first study aim, we found distinct alcohol use trajectory groups for women and men: this includes heavy, moderate, escalation-to-moderately-heavy, legal, light (for women only), and

non-drinkers. While our trajectories were similar to previous research,[70] our study extended previous literature by simultaneously modeling three separate indicators of alcohol use for each year of the emerging adulthood period, providing rich descriptions of alcohol use across these years. Heavy and moderate drinkers comprised the largest classes for both men and women, suggesting that 55-63% of adults sustain moderate to heavy levels of alcohol use from ages 18-25. Chronic heavy and moderate alcohol use have myriad short-term and long-term negative consequences, such as AUDs, reduced neurocognitive functioning, alcohol-impaired driving, injuries, sexual violence, high-risk sexual behaviors, cardiovascular diseases, and cancers.[44,114-131] Non-drinkers were the smallest class; and we found a small class of legal drinkers, which to our knowledge only emerged in a study conducted in Sweden.[132] These findings suggest that minimum legal drinking age laws in the U.S. (which greatly reduce alcohol-related problems[133]) may deter 18-27% of people from drinking before age 21, highlighting the need for increased enforcement (e.g., penalizing alcohol outlets for selling to minors) as well as effective alcohol and harm reduction interventions for emerging adults.

In our second aim, we found several sexual-minority subgroups had greater odds of being in higher alcohol use trajectory groups than completely heterosexuals, and these disparities were larger for women than men. Our longitudinal study extends prior research[19,30,31,38-47,78] by showing that certain sexual-minority subgroups have greater odds of having higher alcohol use trajectories across the entire emerging adulthood period. This likely places sexual-minority emerging adults at greater risk than completely heterosexuals for numerous alcohol-related problems.[44,114-131] Additionally, long-term problems may be particularly heightened among sexual-minority populations because they begin drinking alcohol at earlier ages than completely heterosexuals.[19,21]

In our third aim, we found several sexual-minority subgroups to be at greater risk than completely heterosexuals for probable AUDs. While AUDs are usually higher among sexual-minority adults,[48-50] we corroborated the scant research[51] quantifying sexual-orientation differences in AUDs during the emerging adulthood period. Furthermore, we added novel contributions by examining whether sexual-orientation differences in AUDs were mediated by longitudinal alcohol use trajectories. We found that longitudinal alcohol use trajectories explained 19.7-30.8% of sexual-orientation disparities in AUDs for women, but did not explain any of the associations for men. These findings suggest that decreasing sexual-minority populations' alcohol use may help to reduce some of the burden of AUDs in sexual-minority women, but not among sexual-minority men.

Social ecological factors may be critical determinants of sexual-orientation disparities in alcohol use trajectories and disorders. Prior research shows minority stress—internalized, interpersonal, or structural stigma—may influence sexual-orientation disparities in alcohol use and disorders.[12,21,48,87,134-142] For example, sexual-minority populations face chronic and acute stressors because of their minority sexual orientation, which can lead to drink alcohol as a coping mechanism.[134] While previous research investigating how minority stress impacts alcohol use has largely been cross-sectional, a life-course perspective[58,143-145] can be useful in elucidating how risk and protective factors (e.g., adult support, abuse) from earlier periods of the life-course influence sexual-orientation disparities in alcohol use and disorders during emerging adulthood. Longitudinal cohort studies, like GUTS, are well-poised to examine predictors from earlier in the life course. Additionally, sexual-minority stressors and cultural norms (e.g., gay bar attendance) may interact with alcohol use to place sexual-minority populations at greater risk for AUDs, as posited by differential vulnerability models of health.[146,147] Alternatively, sexual-minority

populations may be more likely than completely heterosexuals to report AUD symptoms because they are more likely to be in mental health treatment,[148] thereby increasing their awareness about how alcohol negatively impacts their well-being.

Our study has limitations. GUTS participants were non-probabilistically sampled from the U.S., were predominantly non-Hispanic White, and were children of mothers who were Nurses' Health Study II participants; therefore, our results may not generalize to more globally, racially, ethnically, or socioeconomically diverse populations. Attrition bias may also be present if nonresponse was differentially related to sexual orientation, alcohol use trajectory classes, or AUD; however, the extent of this bias is unknown. Additionally, sexual orientation was measured using each participant's last report of sexual identity/attraction; thus, our findings may not be generalizable to other operationalizations of sexual orientation (e.g., sexual behavior, sexual orientation trajectories). We also removed the few people who reported being "unsure" of their sexual orientation (limiting our knowledge of this subgroup), and had few bisexual men in our study (limiting statistical power). We measured past-year AUD using self-reported items (not clinical assessments) based on the DSM-IV criteria and not DSM-5, which slightly revised the definition of AUD.[84,88] We may have measurement error in our longitudinal latent classes; however, we expect this to be similar across sexual-orientation groups and within gender, resulting in non-differential misclassification. We may also have residual confounding, despite controlling for several covariates.

Overall, our study extended the extant literature by investigating sexual-orientation differences in alcohol use trajectories and disorders in emerging adulthood, and our findings can inform future intervention and epidemiologic studies. Given the sexual-orientation disparities shown in our study, sexual-minority emerging adults should be a priority target population for

interventions aimed at reducing alcohol use and preventing AUDs. However, there is scant research on interventions aimed at reducing alcohol use and disorders among sexual-minority populations.[1] Sexual-orientation disparities in AUDs were partially explained by alcohol use trajectories for women but not for men, thus highlighting the need for research testing additional causal mechanisms. Additional epidemiologic and intervention research can help understand and eliminate sexual-orientation disparities in alcohol use trajectories and AUDs, thereby fostering health equity for sexual-minority populations.

2.7 ACKNOWLEDGEMENTS

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2.8 TABLES AND FIGURES

Table 2-1. Characteristics of the sample by sexual orientation, stratified by gender: Growing Up Today Study, 2003-2010

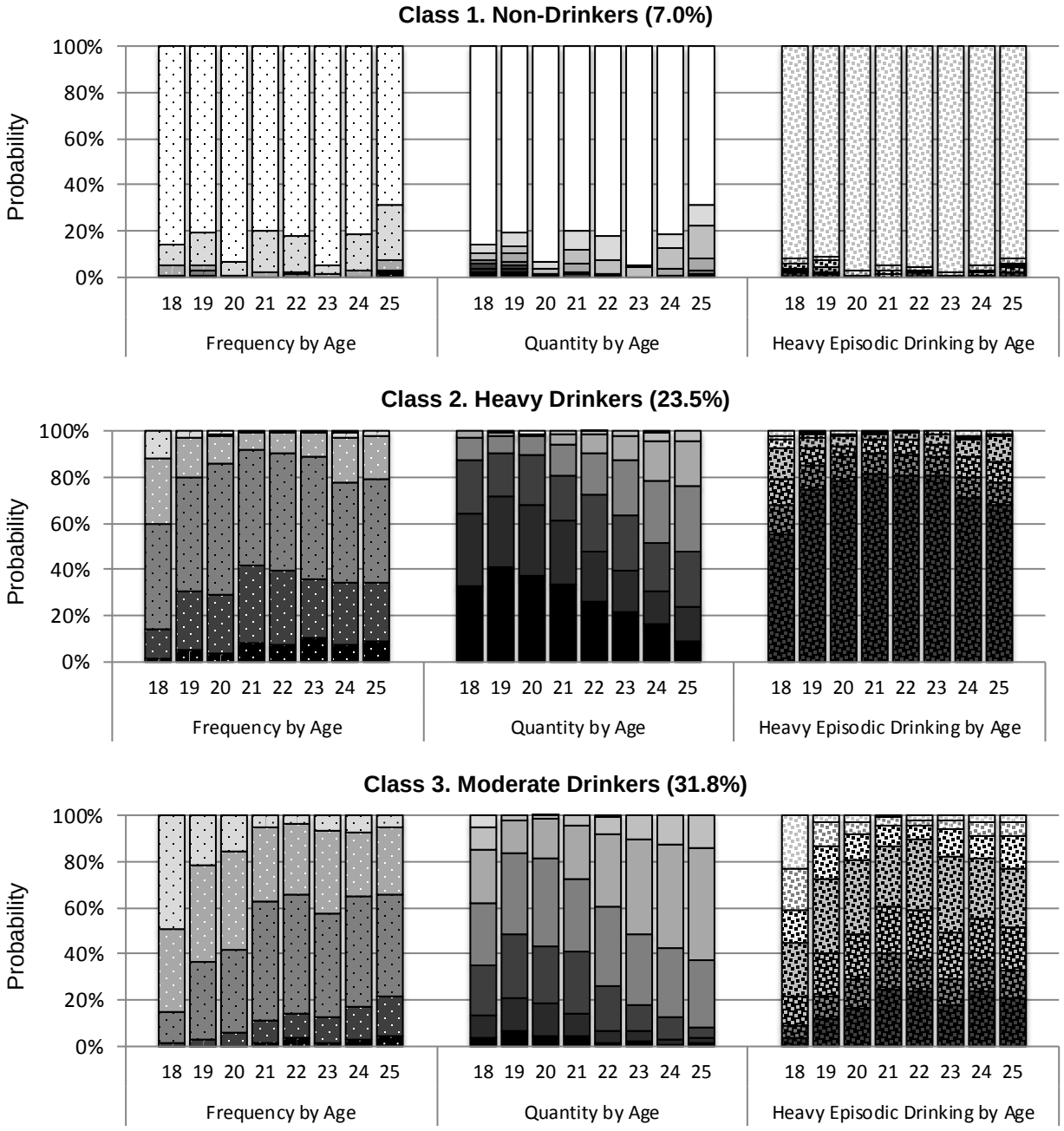
	Sexual Orientation										
	Completely Heterosexual		Mostly Heterosexual			Bisexual			Gay/Lesbian		
	n	*(%)*	*n*	*(%)*	*p-value*	*n*	*(%)*	*p-value*	*n*	*(%)*	*p-value*
WOMEN											
Total, *row percentage*	6,057	(81.1)	1,121	(15.0)		174	(2.3)		113	(1.5)	
Race/ethnicity											
White	5,691	(94.0)	1,026	(91.5)	0.0065	156	(89.7)	0.0661	105	(92.9)	0.6707
Non-White	366	(6.0)	95	(8.5)		18	(10.3)		8	(7.1)	
Region											
West	898	(14.8)	247	(22.0)	<.0001	31	(17.8)	0.2348	20	(17.7)	0.1907
Midwest	2,039	(33.7)	296	(26.4)		46	(26.4)		27	(23.9)	
South	1,092	(18.0)	179	(16.0)		32	(18.4)		21	(18.6)	
Northeast	2,028	(33.5)	399	(35.6)		65	(37.4)		45	(39.8)	
College Attendance											
Never Attended	119	(2.7)	36	(4.2)	0.0397	14	(9.6)	0.0059	2	(2.2)	0.7270
Attended	4,316	(97.3)	817	(95.8)		132	(90.4)		91	(97.8)	
Lifetime Pregnancy											
No	3,515	(77.5)	666	(75.8)	0.2603	104	(68.9)	0.0245	84	(88.4)	0.002
Yes	1,018	(22.5)	213	(24.2)		47	(31.1)		11	(11.6)	
Age in 2010, *mean (sd)*	25.3	(1.6)	25.2	(1.6)	0.5648	25.3	(1.6)	0.9518	25.5	(1.7)	0.1537
MEN											
Total, *row percentage*	4,547	(90.4)	301	(6.0)		34	(0.7)		146	(2.9)	
Race/ethnicity											
White	4,255	(93.6)	262	(87.0)	0.0017	33	(97.1)	0.2431	129	(88.4)	0.0538
Non-White	292	(6.4)	39	(13.0)		1	(2.9)		17	(11.6)	
Region											
West	751	(16.5)	69	(22.9)	0.0543	5	(14.7)	0.2664	24	(16.4)	0.3276
Midwest	1,533	(33.7)	94	(31.2)		10	(29.4)		41	(28.1)	
South	765	(16.8)	46	(15.3)		3	(8.8)		23	(15.8)	
Northeast	1,498	(32.9)	92	(30.6)		16	(47.1)		58	(39.7)	
College Attendance											
Never Attended	121	(4.7)	5	(2.2)	0.0251	1	(4.8)	0.9865	4	(3.5)	0.5239
Attended	2,463	(95.3)	218	(97.8)		20	(95.2)		109	(96.5)	
Age in 2010, *mean (sd)*	25.1	(1.6)	25.2	(1.7)	0.9186	24.8	(1.6)	0.2998	25.2	(1.6)	0.5754

Note. Using completely heterosexuals as the referent, p-values were derived using Rao-Scott chi-squared tests for categorical variables and univariable models with generalized estimating equations for age, both of which adjusted for sibling clusters. Missing data for college attendance and pregnancy were excluded from this table, including the Rao-Scott chi-squared tests. sd = standard deviation.

Table 2-2. Class enumeration fit indices and qualities for longitudinal latent class analyses, stratified by gender: Growing Up Today Study, 2003-2010

Classes	Free parameters	Log-Likelihood	AIC	BIC	SSA-BIC	Entropy	BF	cmP	AWE	VLMR LRT p-value
WOMEN										
1	144	-99,373	199,035	200,031	199,573	n/a	<1	0.00	201,895	n/a
2	289	-87,488	175,554	177,553	176,635	0.875	<1	0.00	181,296	0.76
3	434	-83,383	167,634	170,637	169,258	0.848	<1	0.00	176,256	0.76
4	579	-81,446	164,049	168,055	166,215	0.828	<1	0.00	175,553	0.77
5	724	-80,440	162,328	167,337	165,036	0.817	<1	0.00	176,712	0.82
6	**869**	**-79,627**	**160,992**	**167,004**	**164,243**	**0.798**	**>10**	**1.00**	**178,257**	**0.76**
7	1,014	-79,024	160,076	167,091	163,869	0.779	>10	0.00	180,222	0.80
8	1,159	-78,516	159,350	167,369	163,686	0.777	>10	0.00	182,376	0.83
9[a]	1,304	-78,045	158,698	167,720	163,576	0.778	n/a	0.00	184,605	0.87
MEN										
1	144	-55,321	110,929	111,869	111,411	n/a	<1	0.00	113,791	n/a
2	289	-48,430	97,438	99,323	98,405	0.860	<1	0.00	103,180	0.58
3	434	-45,869	92,606	95,437	94,058	0.838	<1	0.00	101,228	0.76
4	579	-44,784	90,726	94,504	92,664	0.818	<1	0.00	102,229	0.78
5	**724**	**-44,104**	**89,656**	**94,380**	**92,079**	**0.779**	**>10**	**1.00**	**104,040**	**0.77**
6	869	-43,555	88,849	94,518	91,757	0.762	>10	0.00	106,113	0.79
7	1,014	-43,155	88,338	94,953	91,731	0.754	n/a	0.00	108,484	0.76

Note. Models were estimated with samples of 7,470 women and 5,033 men. Boldface indicates the model we selected for each gender. AIC = Akaike information criterion; BIC = Bayesian information criterion; SSA-BIC = Sample size-adjusted Bayesian information criterion; BF = Bayes factor; cmP = Correct model probability; AWE = Approximate weight of evidence criterion; VLMR LRT = Vuong-Lo-Mendell-Rubin likelihood ratio test; n/a = not applicable. The likelihood ratio chi-square goodness-of-fit tests could not be computed in Mplus because the latent class indicator model was too large. Bootstrap likelihood ratio test could not be estimated because we employed the COMPLEX command in Mplus to adjust for non-independence within sibling clusters. [a] = model was not well-identified.


Class 1. Non-Drinkers (7.0%)
Probability
100%
80%
60%
40%
20%
0%
18 19 20 21 22 23 24 25
Frequency by Age
18 19 20 21 22 23 24 25
Quantity by Age
18 19 20 21 22 23 24 25
Heavy Episodic Drinking by Age
Class 2. Heavy Drinkers (23.5%)
Probability
100%
80%
60%
40%
20%
0%
18 19 20 21 22 23 24 25
Frequency by Age
18 19 20 21 22 23 24 25
Quantity by Age
18 19 20 21 22 23 24 25
Heavy Episodic Drinking by Age
Class 3. Moderate Drinkers (31.8%)
Probability
100%
80%
60%
40%
20%
0%
18 19 20 21 22 23 24 25
Frequency by Age
18 19 20 21 22 23 24 25
Quantity by Age
18 19 20 21 22 23 24 25
Heavy Episodic Drinking by Age

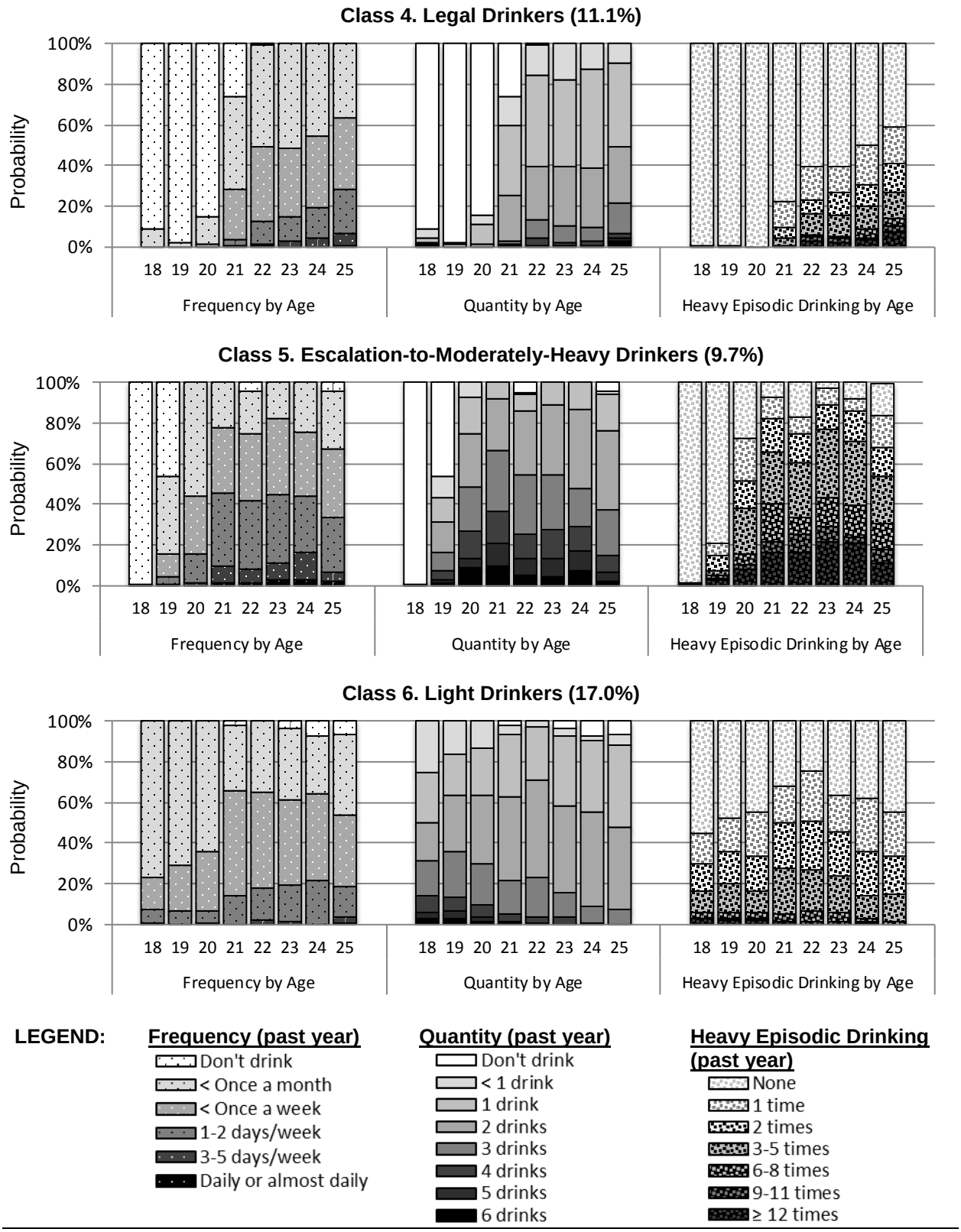
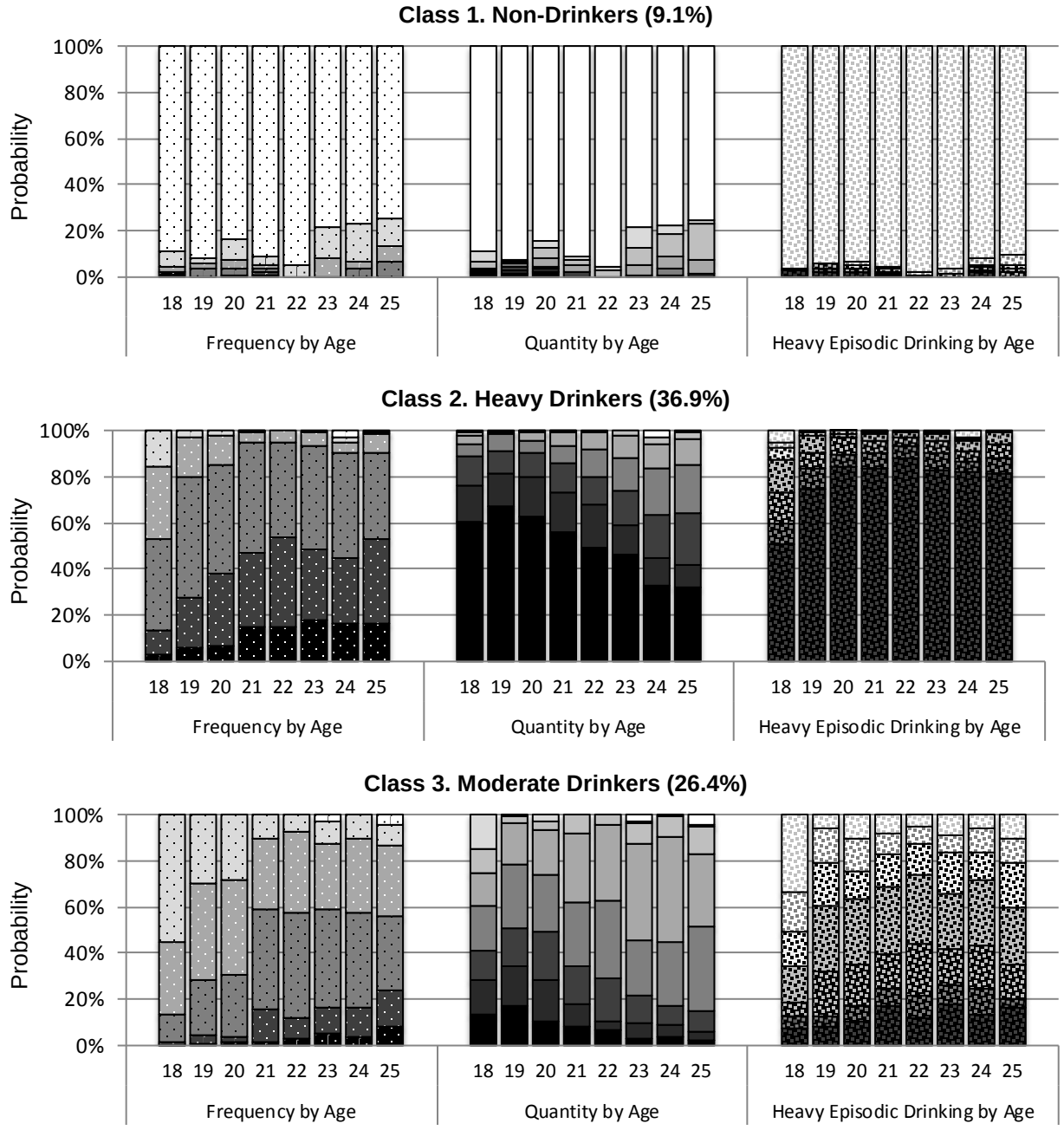


Figure 2-1. Longitudinal latent class analysis profile plots for past-year alcohol frequency, quantity, and heavy episodic drinking from ages 18 to 25 among women: Growing Up Today Study, 2003-2010


Class 1. Non-Drinkers (9.1%)
Probability
100%
80%
60%
40%
20%
0%
18 19 20 21 22 23 24 25
Frequency by Age
18 19 20 21 22 23 24 25
Quantity by Age
18 19 20 21 22 23 24 25
Heavy Episodic Drinking by Age
Class 2. Heavy Drinkers (36.9%)
Probability
100%
80%
60%
40%
20%
0%
18 19 20 21 22 23 24 25
Frequency by Age
18 19 20 21 22 23 24 25
Quantity by Age
18 19 20 21 22 23 24 25
Heavy Episodic Drinking by Age
Class 3. Moderate Drinkers (26.4%)
Probability
100%
80%
60%
40%
20%
0%
18 19 20 21 22 23 24 25
Frequency by Age
18 19 20 21 22 23 24 25
Quantity by Age
18 19 20 21 22 23 24 25
Heavy Episodic Drinking by Age

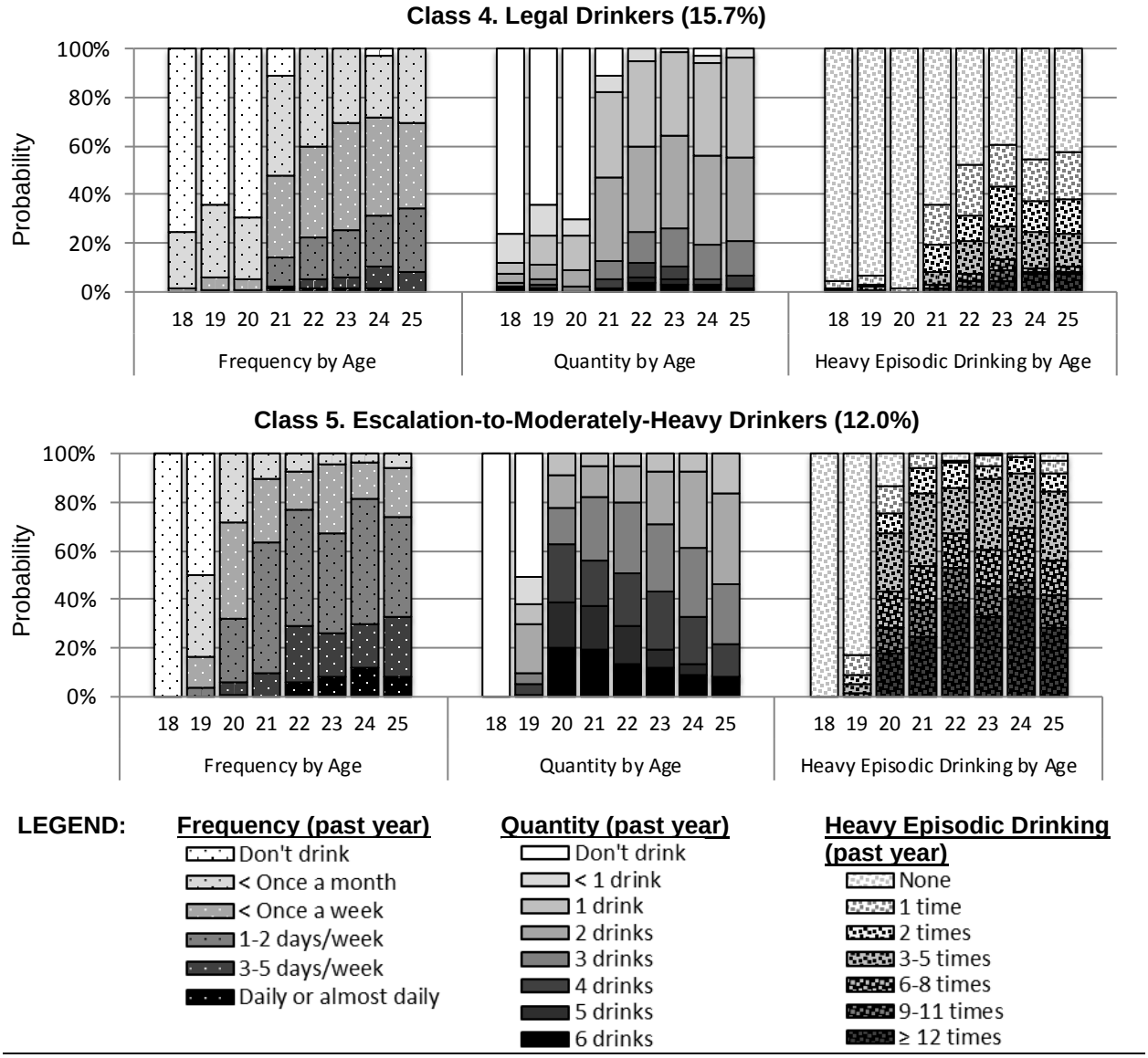


Figure 2-2. Longitudinal latent class analysis profile plots for past-year alcohol frequency, quantity, and heavy episodic drinking from ages 18 to 25 among men: Growing Up Today Study, 2003-2010

Table 2-3. Bivariate sociodemographic characteristics of longitudinal alcohol use trajectories, stratified by gender: Growing Up Today Study, 2003-2010

	Alcohol Use Trajectory Groups											
	Class 1. Non-Drinkers		Class 2. Heavy Drinkers		Class 3. Moderate Drinkers		Class 4. Legal Drinkers		Class 5. Escalation-to-Moderately-Heavy Drinkers		Class 6. Light Drinkers		
	n	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*p-value*
WOMEN													
Total	521	(7.0)	1,754	(23.5)	2,373	(31.8)	830	(11.1)	723	(9.7)	1,264	(17.0)	
Sexual Orientation													
Completely Heterosexual	467	(7.7)	1,337	(22.1)	1,903	(31.4)	738	(12.2)	580	(9.6)	1,032	(17.0)	<.0001
Mostly Heterosexual	43	(3.8)	339	(30.2)	379	(33.8)	74	(6.6)	109	(9.7)	177	(15.8)	
Bisexual	7	(4.0)	50	(28.7)	55	(31.6)	12	(6.9)	19	(10.9)	31	(17.8)	
Lesbian	4	(3.5)	28	(24.8)	36	(31.9)	6	(5.3)	15	(13.3)	24	(21.2)	
Race/ethnicity													
White	480	(6.9)	1,670	(23.9)	2,228	(31.9)	763	(10.9)	675	(9.7)	1,162	(16.7)	0.0038
Non-White	41	(8.4)	84	(17.3)	145	(29.8)	67	(13.8)	48	(9.9)	102	(20.9)	
Region													
West	102	(8.5)	258	(21.6)	378	(31.6)	157	(13.1)	100	(8.4)	201	(16.8)	<.0001
Midwest	183	(7.6)	536	(22.3)	757	(31.4)	305	(12.7)	231	(9.6)	396	(16.5)	
South	123	(9.3)	255	(19.3)	412	(31.1)	145	(11.0)	135	(10.2)	254	(19.2)	
Northeast	113	(4.5)	705	(27.8)	826	(32.6)	223	(8.8)	257	(10.1)	413	(16.3)	
College Attendance													
Never Attended	36	(21.1)	36	(21.1)	34	(19.9)	19	(11.1)	16	(9.4)	30	(17.5)	<.0001
Attended	383	(7.2)	1,227	(22.9)	1,704	(31.8)	606	(11.3)	545	(10.2)	891	(16.6)	
Missing	102	(5.3)	491	(25.3)	635	(32.8)	205	(10.6)	162	(8.4)	343	(17.7)	
Lifetime Pregnancy													
No	280	(6.4)	1,030	(23.6)	1,424	(32.6)	509	(11.7)	450	(10.3)	676	(15.5)	<.0001
Yes	156	(12.1)	250	(19.4)	349	(27.1)	131	(10.2)	125	(9.7)	278	(21.6)	
Missing	85	(4.7)	474	(26.2)	600	(33.2)	190	(10.5)	148	(8.2)	310	(17.2)	
MEN													
Total	458	(9.1)	1,854	(36.9)	1,326	(26.4)	788	(15.7)	602	(12.0)			
Sexual Orientation													
Completely Heterosexual	437	(9.6)	1,697	(37.3)	1,148	(25.3)	716	(15.8)	549	(12.1)			<.0001
Mostly Heterosexual	13	(4.3)	105	(34.9)	104	(34.6)	49	(16.3)	30	(10.0)			
Bisexual	1	(2.9)	12	(35.3)	15	(44.1)	3	(8.8)	3	(8.8)			
Gay	7	(4.8)	40	(27.4)	59	(40.4)	20	(13.7)	20	(13.7)			
Race/ethnicity													
White	422	(9.0)	1,739	(37.2)	1,248	(26.7)	715	(15.3)	555	(11.9)			0.0288
Non-White	36	(10.3)	115	(33.0)	78	(22.4)	73	(20.9)	47	(13.5)			
Region													
West	105	(12.4)	290	(34.2)	232	(27.3)	132	(15.6)	90	(10.6)			<.0001
Midwest	145	(8.6)	608	(36.2)	430	(25.6)	285	(17.0)	210	(12.5)			
South	89	(10.6)	251	(30.0)	233	(27.8)	158	(18.9)	106	(12.7)			
Northeast	119	(7.2)	705	(42.4)	431	(25.9)	213	(12.8)	196	(11.8)			
College Attendance													
Never Attended	26	(19.9)	35	(26.7)	39	(29.8)	23	(17.6)	8	(6.1)			<.0001
Attended	245	(8.7)	1,010	(35.9)	706	(25.1)	471	(16.8)	378	(13.5)			
Missing	187	(9.0)	809	(38.8)	581	(27.8)	294	(14.1)	216	(10.4)			

Note. P-values were derived using Rao-Scott chi-squared tests for categorical variables and adjusted for sibling clusters.

Table 2-4. Results of multinomial logistic regression models predicting longitudinal alcohol use trajectory class membership, stratified by gender: Growing Up Today Study, 2003-2010

	Heavy Drinkers versus Non-Drinkers		Moderate Drinkers versus Non-Drinkers		Legal Drinkers versus Non-Drinkers		Escalation-to-Moderately-Heavy Drinkers versus Non-Drinkers		Light Drinkers versus Non-Drinkers	
	OR (95% CI)	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*
WOMEN										
Sexual Orientation										
Completely Heterosexual	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)	
Mostly Heterosexual	**3.06 (2.15, 4.35)**	**<.0001**	**2.39 (1.69, 3.38)**	**<.0001**	1.17 (0.78, 1.76)	0.4483	**2.23 (1.51, 3.29)**	**<.0001**	**2.01 (1.39, 2.89)**	**0.0002**
Bisexual	**3.26 (1.43, 7.43)**	**0.0050**	**2.52 (1.12, 5.68)**	**0.0260**	1.34 (0.52, 3.47)	0.5460	**2.68 (1.10, 6.54)**	**0.0296**	**2.40 (1.04, 5.55)**	**0.0403**
Lesbian	2.35 (0.80, 6.90)	0.1191	2.11 (0.73, 6.13)	0.1691	0.91 (0.25, 3.32)	0.8872	2.84 (0.93, 8.70)	0.0671	2.70 (0.92, 7.96)	0.0712
Race/ethnicity										
White	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)	
Non-White	**0.64 (0.42, 0.98)**	**0.0397**	0.82 (0.56, 1.21)	0.3231	1.10 (0.72, 1.67)	0.6615	0.93 (0.59, 1.47)	0.7464	1.09 (0.73, 1.63)	0.6848
Region										
West	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)	
Midwest	1.24 (0.91, 1.69)	0.1750	1.19 (0.89, 1.60)	0.2382	1.13 (0.82, 1.57)	0.4482	1.40 (0.98, 1.99)	0.0658	1.18 (0.86, 1.61)	0.3160
South	0.87 (0.62, 1.21)	0.4042	0.95 (0.69, 1.31)	0.7704	0.79 (0.56, 1.13)	0.2047	1.20 (0.81, 1.76)	0.3660	1.10 (0.78, 1.54)	0.5987
Northeast	**2.40 (1.73, 3.31)**	**<.0001**	**1.94 (1.42, 2.64)**	**<.0001**	1.26 (0.89, 1.79)	0.1843	**2.33 (1.61, 3.38)**	**<.0001**	**1.87 (1.34, 2.61)**	**0.0002**
College Attendance										
Never Attended	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)	
Attended	**3.02 (1.81, 5.03)**	**<.0001**	**4.28 (2.56, 7.13)**	**<.0001**	**2.54 (1.38, 4.69)**	**0.0028**	**2.97 (1.59, 5.55)**	**0.0006**	**2.83 (1.68, 4.77)**	**<.0001**
Missing	**2.78 (1.38, 5.60)**	**0.0044**	**4.44 (2.27, 8.68)**	**<.0001**	**2.90 (1.29, 6.50)**	**0.0099**	**3.03 (1.33, 6.88)**	**0.0082**	**3.00 (1.50, 5.98)**	**0.0019**
Lifetime Pregnancy										
No	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)	
Yes	**0.48 (0.37, 0.62)**	**<.0001**	**0.47 (0.37, 0.61)**	**<.0001**	**0.48 (0.36, 0.64)**	**<.0001**	**0.53 (0.39, 0.72)**	**<.0001**	**0.78 (0.60, 1.02)**	**0.0652**
Missing	1.63 (0.92, 2.89)	0.0969	1.31 (0.77, 2.24)	0.3198	1.06 (0.56, 1.99)	0.8628	1.04 (0.56, 1.96)	0.8957	1.40 (0.80, 2.48)	0.2397
MEN										
Sexual Orientation										
Completely Heterosexual	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)			
Mostly Heterosexual	**2.16 (1.19, 3.91)**	**0.0111**	**3.22 (1.78, 5.82)**	**0.0001**	**2.22 (1.19, 4.16)**	**0.0123**	1.77 (0.91, 3.44)	0.0948		
Bisexual	2.88 (0.37, 22.39)	0.3131	5.55 (0.73, 42.38)	0.0984	1.85 (0.18, 18.54)	0.6028	2.30 (0.23, 22.89)	0.4783		
Gay	1.46 (0.65, 3.28)	0.3623	**3.30 (1.49, 7.30)**	**0.0032**	1.66 (0.69, 3.98)	0.2552	2.11 (0.88, 5.05)	0.0938		
Race/ethnicity										
White	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)			
Non-White	0.89 (0.59, 1.33)	0.5599	0.76 (0.49, 1.16)	0.2017	1.32 (0.87, 2.01)	0.1952	1.15 (0.72, 1.85)	0.5491		
Region										
West	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)			
Midwest	**1.51 (1.12, 2.03)**	**0.0072**	1.32 (0.97, 1.80)	0.0762	**1.67 (1.20, 2.32)**	**0.0023**	**1.77 (1.23, 2.53)**	**0.0019**		
South	1.03 (0.74, 1.44)	0.8437	1.20 (0.85, 1.69)	0.2979	**1.49 (1.04, 2.14)**	**0.0312**	1.45 (0.98, 2.17)	0.0652		
Northeast	**2.12 (1.56, 2.89)**	**<.0001**	**1.60 (1.16, 2.20)**	**0.0046**	**1.51 (1.06, 2.13)**	**0.0213**	**1.99 (1.37, 2.90)**	**0.0003**		
College Attendance										
Never Attended	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)			
Attended	**2.93 (1.72, 4.98)**	**<.0001**	**1.81 (1.06, 3.08)**	**0.0284**	**2.14 (1.20, 3.83)**	**0.0102**	**4.91 (2.18, 11.06)**	**0.0001**		
Missing	**3.08 (1.80, 5.26)**	**<.0001**	**2.06 (1.20, 3.52)**	**0.0084**	1.77 (0.98, 3.20)	0.0590	**3.68 (1.62, 8.36)**	**0.0018**		

Note. Models were estimated with samples of 7,466 women and 5,028 men. OR = odds ratio; CI = confidence interval.

Table 2-5 Mediational effects of longitudinal alcohol use trajectory classes on sexual-orientation differences in alcohol use disorders, stratified by gender: Growing Up Today Study, 2003-2010

	Alcohol Use Disorder						
	Univariable		Multivariable Model 1		Multivariable Model 2		Proportion Mediated
	%	*p-value*	*RR (95% CI)*	*p-value*	*RR (95% CI)*	*p-value*	*% (p-value)*
WOMEN							
Sexual Orientation							
Completely Heterosexual	14.0	<.0001	1.00 (referent)		1.00 (referent)		
Mostly Heterosexual	30.8		**2.19 (1.92, 2.49)**	**<.0001**	**1.78 (1.58, 2.02)**	**<.0001**	**30.9 (<.0001)**
Bisexual	29.5		**2.10 (1.58, 2.80)**	**<.0001**	**1.81 (1.41, 2.32)**	**<.0001**	**18.6 (0.0383)**
Lesbian	29.3		**2.04 (1.45, 2.88)**	**<.0001**	**1.73 (1.25, 2.38)**	**0.0009**	**30.5 (0.0137)**
Alcohol Use Trajectory Classes							
Non-Drinkers	1.3	<.0001			1.00 (referent)		
Heavy Drinkers	40.3				**29.55 (12.24, 71.31)**	**<.0001**	
Moderate Drinkers	17.4				**13.03 (5.38, 31.54)**	**<.0001**	
Legal Drinkers	3.4				2.61 (0.98, 6.93)	0.0538	
Escalation-to-Moderately-Heavy Drinkers	16.3				**11.76 (4.79, 28.86)**	**<.0001**	
Light Drinkers	3.4				2.54 (0.99, 6.56)	0.0533	
MEN							
Sexual Orientation							
Completely Heterosexual	26.7	0.0015	1.00 (referent)		1.00 (referent)		
Mostly Heterosexual	36.7		**1.35 (1.10, 1.65)**	**0.0037**	**1.41 (1.18, 1.68)**	**0.0001**	not mediated
Bisexual	38.9		1.49 (0.84, 2.65)	0.1772	1.53 (0.85, 2.74)	0.1564	not mediated
Gay	41.4		**1.56 (1.23, 1.97)**	**0.0003**	**1.68 (1.38, 2.04)**	**<.0001**	not mediated
Alcohol Use Trajectory Classes							
Non-Drinkers	1.3	<.0001			1.00 (referent)		
Heavy Drinkers	50.9				**39.21 (12.83, 119.81)**	**<.0001**	
Moderate Drinkers	19.2				**13.98 (4.53, 43.12)**	**<.0001**	
Legal Drinkers	7.6				**5.67 (1.77, 18.17)**	**0.0035**	
Escalation-to-Moderately-Heavy Drinkers	29.6				**22.34 (7.24, 68.99)**	**<.0001**	

Note. Models were estimated with samples of 5,122 women and 2,511 men. Univariable p-values were derived using Rao-Scott chi-squared tests for categorical variables and adjusted for sibling clusters. Multivariable models were adjusted for race/ethnicity, age, region, and lifetime college attendance (yes/no). Models for women were also adjusted for lifetime pregnancy (yes/no).

3.0 MEDIATIONAL EFFECTS OF FAMILIAL AND NON-FAMILIAL WARMTH DURING CHILDHOOD AND ADOLESCENCE ON SEXUAL-ORIENTATION DISPARITIES IN ALCOHOL USE TRAJECTORIES AND DISORDERS DURING EMERGING ADULTHOOD

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3.1 ABSTRACT

Purpose—We investigated sexual-orientation differences in typologies of familial and non-familial warmth in childhood (before age 11 years) and adolescence (ages 11-17). Subsequently, we tested whether differences in warmth typologies explained sexual-minority populations' heightened odds of having heavier alcohol use trajectories (AUTs) and risks for alcohol use disorders (AUDs) in emerging adulthood (ages 18-25) compared to completely heterosexuals.

Methods—Using self-reported data from the US-based Growing Up Today Study cohort, latent class analyses identified typologies of familial and non-familial warmth during childhood and adolescence. Multinomial logistic regression tested differences in warmth typologies by sexual orientation (comparing completely heterosexuals to sexual-minority subgroups: mostly heterosexuals; bisexuals; and gays/lesbians). Multinomial logistic and modified Poisson regression tested whether warmth typologies explained sexual-orientation differences in AUTs (longitudinal latent classes derived from 4 survey waves) and AUDs (past-year DSM-IV abuse or dependence) in emerging adulthood.

Results—Six warmth classes emerged, and, within each warmth class, familial and non-familial warmth were generally stable across developmental periods (childhood and adolescence). The warmth classes were: High-High (i.e., high familial and high non-familial warmth, respectively;

18.5%); High-Moderate (23.3%); Moderate-Moderate (19.4%); Moderate-Occasional (20.6%); Occasional-Occasional (14.1%); and Low-Low (4.1%). Among women, mostly heterosexuals and bisexuals had higher odds than completely heterosexuals of being in the Moderate-Moderate, Moderate-Occasional, and Occasional-Occasional versus the High-High warmth class (adjusted odds ratios [AORs] range: 1.38-2.25; p-values: <0.0001-0.0066). Lesbians and mostly heterosexual men had higher odds than their same-gender completely heterosexual peers of being in the Occasional-Occasional versus the High-High warmth class (AOR=1.76-2.96; p-value=0.0044-0.0242). Lower warmth classes (versus the High-High warmth class) were generally associated with greater AUDs, and mediated heightened disparities in AUDs for mostly heterosexual and bisexual women compared with completely heterosexual women (4.0-7.8% mediated). Warmth did not mediate sexual-orientation disparities in AUDs among men. Additionally, warmth classes were generally not associated with AUTs, and did not mediate sexual-orientation differences in AUTs.

Conclusions—Warmth during childhood and adolescence was significantly associated with AUDs—but not AUTs—in emerging adulthood, thereby suggesting that lower warmth is associated with greater alcohol-related problems, but not alcohol use itself. Additionally, warmth explained a small proportion of the heightened disparities in AUDs for sexual-minority women—but not for men.

3.2 INTRODUCTION

Having warmth from adults during childhood and adolescence is associated with healthy development.[149-154] Warmth refers to demonstrations and expressions of praise, closeness, love, and affection,[155,156] and can be provided by family members (e.g., parents) as well as non-family members (e.g., teachers, community leaders). Unfortunately, some youth populations may experience less warmth than others: for example, sexual-minority youth (SMY; e.g. gay/lesbian, bisexual, and mostly heterosexuals) may be less likely to experience warmth than heterosexual youth because their minority sexual orientation is often stigmatized.[157] Research has found mixed results for sexual-orientation differences in familial warmth: most studies show that SMY have lower familial warmth than heterosexual youth[23,24,158-160]; but other research found no differences in familial warmth by sexual orientation.[161,162] Fewer studies have examined sexual-orientation differences in non-familial warmth; nevertheless, existing studies show that the presence of non-familial warmth is lower among SMY subgroups than heterosexual youth.[23,24] Research also suggests that boys report less warmth than girls[35,37,163]; but to our knowledge it remains unknown whether gender modifies sexual-orientation differences in warmth, despite evidence that gender modifies sexual-orientation differences in many experiences for youth (e.g., victimization, substance use).[2,4,15,16,21,137] Additionally, warmth can vary across time[164-167] (e.g., maternal warmth usually decreases from childhood to adolescence[166,167]), but few studies have investigated sexual-orientation differences in warmth across multiple developmental time points. By identifying certain periods of the life-course when warmth differs by sexual orientation, researchers can target interventions to developmental periods where warmth is lacking and to

subgroups of young people who may be at risk for poorer outcomes because they lacked warmth during these developmental periods.

Providing warmth to children and adolescents can foster healthy coping mechanisms and self-regulation (i.e., guiding one's own cognitive, emotional, and behavioral processes to achieve goals), as well as decrease pro-substance use norms, which can reduce youths' consumption of alcohol.[168-171] As a result, a growing body of research has examined the associations between warmth and alcohol use.[172] Empirical studies of adolescents show that having familial and non-familial warmth is cross-sectionally associated with lower alcohol use.[149,173-179] However, during emerging adulthood (i.e., ages 18-25 years[61]), cross-sectional analyses found mixed results for the associations between familial warmth and alcohol use: one study found null associations,[180] and another found protective associations for certain subgroups (i.e., White but not Asian populations).[181] Furthermore, longitudinal studies found that familial and non-familial warmth from earlier periods in the life-course were directly and indirectly associated with lower alcohol use in later periods, including emerging adulthood.[169,182,183] Yet, it remains unknown whether familial and non-familial warmth in childhood and adolescence are associated with alcohol use trajectories throughout emerging adulthood. Common alcohol use trajectories for emerging adults include consistently heavy drinkers, moderate drinkers, escalation drinkers, and non-drinkers.[70] If lower warmth is associated with heavier alcohol use trajectories (AUTs), then interventions that increase warmth during childhood and adolescence may reduce the likelihood of having heavy AUTs throughout emerging adulthood. Such interventions may also reduce the many short- and long-term negative consequences[44,114-131] of chronic heavy and moderate alcohol use.

One problematic consequence positively associated with heavy alcohol use is alcohol use disorder (AUD; e.g., abuse or dependence).[70,81,82] However, few studies have examined the effects of warmth on AUDs. One study found that low maternal warmth during adolescence was associated with increased odds of having comorbidity of AUDs and mental health disorders at age 21 years.[184] Yet most studies found that familial warmth was not associated with AUD or AUD-comorbidity (e.g., joint AUD and mental health disorders) in adolescence[185,186] and emerging adulthood.[187] However, previous studies have examined the effects of familial warmth from a single developmental period on AUD, thereby limiting knowledge about how warmth from multiple contexts (e.g., familial and non-familial) and during multiple developmental time periods (e.g., childhood and adolescence) are associated with AUDs in emerging adulthood. Such a study would provide a richer description of how warmth from earlier periods is linked with AUDs in emerging adulthood.

Prior research among emerging adults, including in the Growing Up Today Study, has shown that sexual-minority emerging have greater risk of alcohol use, heavy AUTs, and AUDs than their heterosexual peers, especially among women.[19,28,30,31,42-44,51,159] These differences may be partially explained by the existence of sexual-orientation differences in warmth during childhood and adolescence. Support for this hypothesis would suggest that increasing warmth for SMY would mitigate sexual-orientation disparities in AUTs and AUDs, thereby informing future intervention studies and prevention efforts.

3.3 AIMS

This paper sought to address the aforementioned gaps in research on warmth and alcohol outcomes across the first three decades of the life-course using data from the Growing Up Today study. First, we estimated latent classes of self-reported familial and non-familial warmth during childhood and adolescence. We hypothesized there would be different warmth classes characterized by high and low warmth. Second, we tested for sexual-orientation differences in warmth class memberships, and whether these differences varied by gender. We hypothesized that sexual-minority populations would be more likely to be members of classes exemplifying less warmth. Third, we examined the effects of warmth classes on AUTs and AUDs in emerging adulthood, and tested whether warmth classes mediated the sexual-orientation disparities in AUTs and AUDs. We hypothesized that lower warmth classes will be associated with heavier AUTs and greater risk of AUDs, and that warmth classes would mediate the sexual-orientation differences in AUTs and AUDs.

3.4 METHODS

Study Design and Population

We analyzed data from participants in the longitudinal Growing Up Today Study (GUTS), which began in 1996. GUTS initially enrolled 16,875 participants aged 9-14 years who were children of women participating in the Nurses' Health Study II—a cohort study of 116,430 registered nurses from 14 U.S. states begun in 1989. Additional information about GUTS is reported elsewhere.[19,83]

The current study included participants who provided information on sexual orientation and at least 1 of the 4 familial or non-familial warmth items, which were measured in the 2007 survey wave. Our analytic sample included 9,096 participants (5,783 women; 3,313 men), representing 53.9% of the cohort. Comparisons of participants included versus excluded in our analytic sample showed that they did not differ by race/ethnicity ($p=0.9812$) or age at baseline ($p=0.9729$), but did significantly differ by gender ($p<0.001$) and region of residence ($p<0.001$). Compared to cohort participants excluded from our analyses, participants in our analytic sample were more likely to be female (63.6% versus 41.8%, respectively) and to live in the Western region of the U.S. (15.5% versus 12.1%, respectively), and less likely to live in Northeast region at baseline (34.5% versus 37.4%, respectively). Participants' mean age in our analytic sample was 22.7 years (range: 19-27 years) in 2007. Brigham and Women's Hospital Institutional Review Board (IRB) approved original GUTS data collection procedures. University of Pittsburgh's IRB deemed the current study exempt because they study used previously collected data.

Measures

Warmth

Warmth was assessed on the 2007 questionnaire with 4 items adapted from the Childhood Trauma Questionnaire (CTQ).[188,189] The original CTQ item assessed familial warmth, and GUTS adapted an item to assess non-familial warmth. We also adapted the items to assess 2 developmental time periods—childhood (before age 11 years) and adolescence (11-17 years of age). For example, we assessed childhood familial warmth using the following question: "When you were a child (before age 11) how often did someone in your family make you feel that you were important or special?" We modified this item to measure childhood non-familial warmth

(by stating "someone who was NOT a family member"), teenage familial warmth (by stating "when you were a teenager (ages 11–17)"), and teenage non-familial warmth. We ordinally coded all 4 items' response options: never; rarely; sometimes; often; and very often.

Sexual Orientation

The following question assessed sexual orientation at each survey wave from 1999-2010: "Which one of the following best describes your feelings?" Response options included: completely heterosexual (attracted to persons of the opposite sex); mostly heterosexual; bisexual (equally attracted to men and women); mostly homosexual; completely homosexual (attracted to persons of the opposite sex); and unsure. We classified sexual orientation based on participants' last report. As has been done previously,[19] we combined mostly and completely homosexual into a single group (henceforth referred to as lesbian/gay) to increase statistical power; we also removed participants who were "unsure" of their sexual orientation because of small sample size (n=6).

Alcohol Use Trajectory Classes

AUT classes were derived using longitudinal latent class analyses (LLCA) in Chapter 2 of this dissertation. We conducted LLCA on data from the emerging adulthood period from ages 18-25, with 3 indicators of alcohol use, including past-year average frequency of drinking, past-year average quantity of drinking per episode, and number of times engaging in heavy episodic drinking in the past year. Six AUT classes emerged for women, and five emerged for men: these included heavy, moderate, escalation-to-moderately-heavy, light (for women only), legal (drinking onset at age 21), and non-drinkers.

Alcohol Use Disorders

We measured criteria for probable AUD for the first time in 2010 (when participants' mean age was 25.3 years) with items assessing symptoms based on the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV),[84] as adapted by the National Survey on Drug Use and Health.[85] The DSM-IV described two distinct disorders, alcohol abuse and alcohol dependence, which were present in 9.9% and 10.3% of participants, respectively. If participants had either alcohol abuse or dependence, we coded them as having a probable AUD (20.1% prevalence), creating a single binary variable. We made this analytic decision based on prior research[48,86,87] and because the DSM-5[88] integrates abuse and dependence into a single disorder.

Demographics

We assessed gender (natal female versus male; measured at baseline), race/ethnicity (White vs. non-White; measured at baseline), region of residence (West vs. Midwest, Southwest, and Northeast; measured in 2007), and age in years (calculated based on participant's birthdate and date of the 2007 questionnaire return).

Covariates

In analyses of AUT and AUD outcomes, we controlled for variables that may confound the associations between sexual orientation and these outcomes.[21,90-94] We assessed college attendance in 2010 using the following item adapted from the National Survey of Family Growth[95]: "What is the highest grade of school you have completed or the highest degree you have received?" There were 8 response options, which we dichotomized into any college attendance versus none (i.e., high/trade/vocational school graduate or less). We prospectively assessed lifetime pregnancy (yes/no) from 1999-2010 for women. We used the missing indicator

method[96] for college attendance and pregnancy, which creates an additional "missing" category for each variable, allowing us to analyze all available data and preserve statistical power.

Analyses

Warmth Classes

Following Masyn's guidelines,[69] we used a classify-analyze approach to characterize latent classes of familial and non-familial warmth and estimate predictors and outcomes associated with these classes. First, we estimated warmth trajectories using latent class analyses in Mplus version 7.2 (Los Angeles, CA), which allows for the estimation of subgroup populations who differ across multiple indicators of warmth. We estimated the unconditional model (i.e., no covariates) with the 4 ordinal warmth variables. We used Full Information Maximum Likelihood estimation, allowing all available observations to be used without imputing data or deleting observations with missing data.[67,99] We adjusted for the non-normality of warmth variables by using the robust maximum likelihood estimator.[100,101] We employed the complex survey analysis procedure in Mplus to account for non-independence of sibling clusters.[99]

We estimated 1- through 8-class solution models. To determine the best-fitting number of classes, we examined several fit statistics, including Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), the Bayes Factor (BF), the correct model probability (cmP), and the Vuong-Lo-Mendell-Rubin adjusted likelihood ratio test (VLMR LRT).[69,99,108,109] We considered the best fitting model to have a low BIC, a significant improvement in fit over the previous model (based on VLMR LRT), and the highest interpretative validity.[69,101,108] We examined entropy and other classification qualities (i.e., average posterior probabilities [AvePP] and odds of correct classification [OCC]).[69,110] We considered good latent class separation and

assignment as classes with AvePP>0.7 and OCC>5.[110] We also examined class patterns separately by gender but results were similar; therefore, we reported results from the total sample. We assigned participants to the class for which they had the highest posterior probability of membership.

Differences in Warmth Class Membership

Using SAS version 9.4 (Cary, NC), we used Rao-Scott chi-squared tests[111] adjusting for sibling clusters to examine the bivariate associations of warmth classes with sexual orientation. We then fit multinomial logistic regression models to test for sexual-orientation and gender differences in warmth class membership (which was a polytomous variable), controlling for demographics, using generalized estimating equations (GEE) to account for the non-independence of sibling clusters. We then added sexual-orientation-by-gender interaction terms to test effect modification of sexual orientation by gender.

Associations with AUTs and AUDs

We engaged in a two-step model building process to examine whether warmth mediates sexual-orientation differences in AUTs and AUDs. The first model contained the main effects of sexual orientation on the outcome (controlling for demographics and covariates); and the second model added the main effects of warmth class on the outcome to the first model. When warmth was significantly associated with sexual orientation and the outcome, we conducted a formal test of mediation using the publicly available %MEDIATE macro.[113] We stratified all analyses by gender, given previous research showing that AUTs differed by gender (see first dissertation paper) and AUD disparities were larger for women than men in prior research.[51]

For AUTs, we fit multinomial logistic regression models to test for associations with trajectory class membership (which was a polytomous variable), controlling for demographics

and covariates, using GEE in SAS to account for the non-independence of sibling clusters. Reference groups in the models were non-drinkers (versus other trajectory classes). For the binary AUD variable, we fit modified Poisson regression models (i.e., log-link with Poisson distribution) using GEE in SAS because AUD prevalence was greater than 10%.[112]

3.5 RESULTS

Overall, 80.3% of women identified as completely heterosexual, 15.8% as mostly heterosexual, 2.4% as bisexual, and 1.6% as lesbian (Table 3-1). Among men, 88.5% identified as completely heterosexual, 7.2% as mostly heterosexual, 0.7% as bisexual, and 3.7% as gay. Compared to completely heterosexual women: mostly heterosexual women were less likely to be White, live in the Midwestern region of the U.S., and have attended college; bisexual women were less likely to have attended college; lesbian women were less likely to ever have been pregnant. Compared to completely heterosexual men, mostly heterosexual and gay men were less likely to be White.

We selected the 6-class model for familial and non-familial warmth in childhood and adolescence based on interpretability and the fit indices (Table 3-2). There was significant improvement in model fit from the 5- to 6-class model (VLMR LRT $p<0.0001$), but a non-significant improvement from the 6- to 7-class model (VLMR LRT $p=0.7639$). The final model had highest entropy, and the 6 classes had good separation and adequate class assignment (all AvePP>0.9 and OCC>39). Figure 3-1 depicts the 6 latent classes of warmth. Based on visual inspection, there was more within-class variation by context (familial versus non-familial) than across developmental periods (childhood versus adolescence). The high familial and high non-

familial (henceforth, High-High) warmth class comprised 18.5% of participants. The high familial and moderate non-familial (henceforth, High-Moderate) warmth class comprised 23.3% of participants. The moderate familial and moderate non-familial (henceforth, Moderate-Moderate) warmth class comprised 19.4% of participants. The moderate familial and occasional non-familial (henceforth, Moderate-Occasional) warmth class comprised 20.6% of participants. The occasional familial and occasional non-familial (henceforth, Occasional-Occasional) warmth class comprised 14.1% of participants. The low familial and low non-familial (henceforth, Low-Low) warmth class comprised 4.1% of participants.

Differences in Warmth Class Membership

Table 3-3 shows the percentages of membership in each warmth class by sexual orientation for women and men separately.

Main Effects

Multivariable models including main effects of gender and sexual orientation on warmth class membership (adjusting for demographics) showed that men had higher odds than women of being in the High-Moderate (OR=1.45; $p<0.0001$), Moderate-Moderate (OR=1.95; $p<0.0001$), Moderate-Occasional (OR=3.20; $p<0.0001$), Occasional-Occasional (OR=2.68; $p<0.0001$), and Low-Low (OR=1.96; $p<0.0001$) warmth classes versus the High-High warmth class. Mostly heterosexuals had higher odds than completely heterosexuals of being in the Moderate-Moderate (OR=1.37; $p=0.0037$), Moderate-Occasional (OR=1.62; $p<0.0001$), and Occasional-Occasional (OR=2.18; $p<0.0001$) warmth classes than the High-High warmth class. Bisexual participants had higher odds than completely heterosexual participants of being in the Moderate-Moderate (OR=1.98; $p=0.0171$), Moderate-Occasional (OR=2.75; $p=0.0003$), and Occasional-Occasional (OR=2.79; $p=0.0005$) warmth classes versus the High-High warmth class. The odds for bisexual

and mostly heterosexual participants did not significantly differ from the odds for completely heterosexual participants of being in the High-Moderate (ORs range: 1.05-1.34; p-values: 0.3141-0.6291) or Low-Low (ORs range: 0.98-1.03; p-values: 0.9277-0.9608) warmth classes versus the High-High warmth class. There were no significant differences in warmth class memberships for lesbian/gay versus completely heterosexual participants (ORs range: 0.71-1.49; p-values: 0.1098-0.8102).

Gender-Specific Effects

Multivariable models including the interactions between gender and sexual orientation (adjusting for demographics) showed that one-third of the interaction effects were statistically significant. All effect estimates trended in the same direction with sexual-orientation differences in warmth class membership being larger for women than men. Therefore, we presented final models stratified by gender.

Among women (Table 3-4), mostly heterosexuals had higher odds than completely heterosexuals of being in the Moderate-Moderate, Moderate-Occasional, and Occasional-Occasional warmth classes than the High-High warmth class (ORs range: 1.38-2.25; p-values: <0.0001-0.0066). Bisexual women had higher odds than completely heterosexuals of being in the Moderate-Moderate, Moderate-Occasional, and Occasional-Occasional warmth classes than the High-High warmth class (ORs range: 2.07-3.49; p-values: <0.0001-0.0188). Lesbians had higher odds than completely heterosexuals of being in the Occasional-Occasional warmth classes than the High-High warmth class (OR=2.96; p-value=0.0044).

Among men (Table 3-4), mostly heterosexuals had higher odds than completely heterosexuals of being in the Occasional-Occasional warmth classes than the High-High warmth

class (OR=1.76; p-value=0.0242). There were no significant differences in warmth class memberships for gay and bisexual men compared with completely heterosexual men.

Unadjusted Associations for Alcohol Use Trajectories and Disorders

Table 3-5 shows the unadjusted associations of sexual orientation and warmth on AUTs and AUDs stratified by gender. Sexual orientation was significantly associated with AUTs and AUDs. Warmth was significantly associated with AUDs but not AUTs.

Multivariable Models for Alcohol Use Trajectories

Among women, mostly heterosexual (ORs range: 1.99-2.87; p-values range: <0.0001-0.0006) and bisexual (ORs range: 2.66-3.14; p-values range: 0.0129-0.0490) participants had higher odds than completely heterosexual participants of being heavy, escalation-to-moderately-heavy, and light drinkers versus non-drinkers (Table 3-6; Model 1). Mostly heterosexuals had 2.35 times the odds ($p<0.0001$) of completely heterosexuals of being moderate drinkers versus non-drinkers. Warmth classes were not significantly associated with AUTs (Model 2; controlling for sexual orientation, demographics, and covariates), thereby they did not mediate sexual-orientation differences in AUTs for women.

Among men, mostly heterosexual participants had higher odds than completely heterosexual participants of being heavy (OR=2.07; p=0.0281) and moderate (OR=3.14; p=0.0005) drinkers versus non-drinkers (Table 3-6; Model 3). Gay men had 3.45 times the odds (p=0.0039) of completely heterosexual men of being moderate drinkers versus non-drinkers (Model 3). A few warmth classes were significantly associated with AUTs (Model 4). Men in the High-Moderate warmth class had higher odds than men in the High-High warmth class of being heavy drinkers versus non-drinkers (OR=2.11; p=0.0451). Men in the Moderate-Occasional warmth class had higher odds than men in High-High warmth class of being heavy, moderate,

and escalation-to-moderately-heavy drinkers versus non-drinkers (ORs range: 1.67-2.00; p-values range: 0.0020-0.0276). However, warmth did not mediate sexual-orientation differences in AUTs because the sexual-orientation effects were not attenuated (instead, most were accentuated) from Models 3 to 4.

Multivariable Models for Alcohol Use Disorders

Among women, mostly heterosexual, bisexual, or lesbian participants were 1.80-2.05 times more likely (p-values range: <0.0001-0.0040) than completely heterosexual participants to meet criteria for probable AUD (Table 3-7; Model 1). Moderate-Occasional, Occasional-Occasional, Low-Low warmth classes were 1.44-1.56 times more likely (p-values range: <0.0001-0.0154) to report probably AUDs than High-High warmth class participants (Model 2). Warmth classes mediated sexual-orientation differences in AUD for mostly heterosexuals and bisexuals compared to completely heterosexuals (mediated proportions range: 4.0-7.8%; p-values range: 0.0070-0.0087). After controlling for warmth classes, mostly heterosexual, bisexual, and lesbian women remained more likely than completely heterosexual women to evidence AUD (Model 2; RRs range: 1.74-2.00; p-values range: <0.0001-0.0054).

Among men, mostly heterosexual and gay participants were 1.36-1.60 times more likely (p-values range: 0.0002-0.0064) than completely heterosexual participants to meet criteria for probable AUD in 2010 (Table 3-7; Model 1). Moderate-Moderate and Moderate-Occasional warmth classes were 1.31-1.32 times more likely (p-values range: 0.0302-0.0327) to report probable AUDs than High-High warmth class participants (Model 2). Warmth classes did not significantly mediate sexual-orientation differences in AUD for men. After controlling for warmth classes, mostly heterosexual and gay men remained more likely than completely

heterosexual men to evidence AUD (Model 2; RRs range: 1.35-1.61; p-values range: 0.0002-0.0075).

3.6 DISCUSSION

We found distinct typologies of familial and non-familial warmth across childhood and adolescence, and membership in these typologies differed by gender and sexual orientation. Our study adds unique contributions to the literature by simultaneously examining latent classes of warmth from multiple contexts (familial and non-familial) and multiple developmental periods (childhood and adolescence). Overall, warmth classes had more within-class variation by context than across developmental period, substantiating previous studies that suggested warmth from earlier time points was associated with warmth at later time points.[164,165,167] Additionally, men were more likely to be in lower warmth classes than women, corroborating previous research on warmth.[35,37,163] Our analyses also extended previous literature[23,24,158-162] by formally testing gender-by-sexual orientation interactions in warmth class membership by using multivariable models. Specifically, among women, we found that several sexual-minority subgroups were more likely to be in lower warmth classes compared with completely heterosexuals; among men, sexual-orientation differences in warmth were minimal. These results align with the bivariate results from prior research that shows that sexual-orientation differences in warmth were slightly smaller for males than females.[24,158,159]

Strong theoretical and empirical foundations explaining these gendered sexual-orientation differences in warmth are lacking. Nevertheless, stigma as a "fundamental cause" of health disparities is one theory that can inform these findings.[157,190,191] Because sexual minorities,

especially bisexuals, are stigmatized,[192] SMY may experience lower familial and non-familial warmth. Why this may occur among women more than among men remains unknown and under-theorized. Nevertheless, these differences are likely derived from bidirectional gender-specific processes involving both child-level factors (e.g., gender nonconformity), as well as adult-level factors (e.g., attitudes towards gay/lesbian and bisexual populations).[35,37,193] Since a constellation of factors likely influences these findings, qualitative interviews with youth and adults may provide insight and theoretical foundations can help to explain our results.

Our study also found that warmth during childhood and adolescence was significantly associated with alcohol use disorders—but not alcohol use trajectories—in emerging adulthood. Alcohol use is highest in emerging adulthood,[62-66] and heavy and moderate drinking trajectories are normative during this developmental period.[70] Our results suggest that emerging adults will engage in heavy and moderate alcohol use trajectories regardless of warmth provided in earlier periods. On the other hand, lower warmth was positively associated with probable AUDs, suggesting that greater warmth may ameliorate some negative consequences of alcohol use in emerging adulthood. Though our study's findings of negative associations between warmth and AUD confirm some research,[184] it contradict others.[185-187] However, our study was unique in that it examined AUD as an outcome separate from other comorbidities (e.g., mental health disorders) and measured warmth across developmental periods, which may explain our novel findings. Furthermore, prior research suggests that warmth can help youth develop self-regulation,[170,171] which may help emerging adults avoid alcohol-related problems captured by measures of AUD (e.g., having alcohol use interfere with job duties). Our results also suggest that having warmth may lower the negative physiological side effects of alcohol use (e.g., withdrawal). While warmth can positively affect other biological outcomes, such as lower

cortisol secretion in response to stress[165,194] and delayed pubertal onset,[195-197] more research is needed to examine the biological implications of warmth on the physiological symptoms of AUDs.

Additionally, warmth explained a small albeit statistically significant proportion of the sexual-orientation differences in AUDs for women—but not for men. This has implications for future epidemiologic and intervention research. Warmth may serve as a resiliency factor[198-201] that buffers the numerous minority stressors faced by SMY, thereby making them less likely to have problematic alcohol use despite facing adversity. Additionally, other factors related to adult–youth relationships, especially parent–child relationships, may influence sexual-orientation differences in AUTs and AUDs. Such factors include monitoring, rejection, and psychological control, which have been shown to be related to alcohol use and AUDs.[172] Increasing warmth should not necessarily be the only mechanism through which interventions aim to reduce sexual-orientation disparities in AUTs or AUDs. Instead, interventions can target warmth in addition to other underlying mechanisms.

There are limitations to our study. GUTS participants were non-probabilistically sampled from the U.S., were predominantly non-Hispanic White, and were children of mothers who were Nurses' Health Study II participants; therefore, our results may not generalize to more globally, racially, ethnically, or socioeconomically diverse populations. Our study may be prone to recall bias. On average, participants were 23 years of age when they reported on warmth from childhood and adolescence. Despite the recall period, previous research has validated adult responses to childhood and adolescent experiences for other measures.[163] Attrition bias may also be present if nonresponse was differentially related to warmth, sexual orientation, AUTs, or AUD; the extent of this bias is unknown. Additionally, we measured sexual orientation using

each participant's last report of sexual identity/attraction; thus, our findings may not generalize to other ways of operationalizing sexual orientation (e.g., sexual behavior, sexual orientation trajectories, extent to which one was "out"). We measured past-year AUD using self-reported items (not clinical assessments) based on the DSM-IV criteria and not DSM-5, which slightly revised the definition of AUD. Single items measured familial and non-familial warmth during each developmental period, which may not capture all important information (e.g., the number and kinds of people who provided warmth). We may also have residual confounding, despite controlling for several covariates.

Conclusions

Our paper addressed one of the recommendations put forth by the Institute of Medicine report[1] about lesbian, gay, bisexual, and transgender health: to use a life-course approach[57] to examine how early life experiences influence health disparities for sexual-minority populations later in life. Compared to completely heterosexual women, sexual-minority women report having lower familial and non-familial warmth in childhood and adolescence, which mediated a small proportion of their elevated risk of AUDs. However, warmth did not mediate sexual-orientation disparities in AUDs for men. Warmth also had little effect on alcohol use trajectories for all emerging adults. Future epidemiologic research can consider the role warmth plays in combination with other factors that influence AUTs and AUDs in emerging adulthood. Warmth is also protective against many other health problems, including other substance use, sexual risk taking, anxiety, and depression.[149,151-153] Since these health problems also disproportionately burden SMY,[2,3,202] research can test if warmth helps to explain sexual-orientation disparities in these health areas, especially for women.

3.7 ACKNOWLEDGEMENTS

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3.8 TABLES AND FIGURES

Table 3-1. Characteristics of the sample by sexual orientation, stratified by gender: Growing Up Today Study

	Sexual Orientation										
	Completely Heterosexual		Mostly Heterosexual			Bisexual			Lesbian/Gay		
	n	*(%)*	*n*	*(%)*	*p-value*	*n*	*(%)*	*p-value*	*n*	*(%)*	*p-value*
WOMEN											
Total, *row percentage*	4,642	(80.3)	912	(15.8)		139	(2.4)		90	(1.6)	
Race/ethnicity											
White	4,362	(94.0)	833	(91.3)	0.0091	125	(89.9)	0.1179	84	(93.3)	0.8113
Non-White	280	(6.0)	79	(8.7)		14	(10.1)		6	(6.7)	
Region											
West	708	(15.3)	190	(20.8)	<.0001	30	(21.6)	0.0984	15	(16.7)	0.0602
Midwest	1,634	(35.2)	256	(28.1)		37	(26.6)		19	(21.1)	
South	793	(17.1)	150	(16.5)		23	(16.6)		20	(22.2)	
Northeast	1,507	(32.5)	316	(34.7)		49	(35.3)		36	(40.0)	
College Attendance											
Never Attended	95	(2.4)	31	(4.2)	0.0259	13	(10.4)	0.0046	2	(2.5)	0.9560
Attended	3,859	(97.6)	712	(95.8)		112	(89.6)		78	(97.5)	
Lifetime Pregnancy											
No	3,158	(78.8)	584	(76.2)	0.1249	91	(72.2)	0.1036	73	(88.0)	0.0154
Yes	849	(21.2)	182	(23.8)		35	(27.8)		10	(12.1)	
Age, *mean (sd)*	22.7	(1.7)	22.7	(1.7)	0.5504	22.6	(1.6)	0.3334	22.9	(1.6)	0.2233
MEN											
Total, *row percentage*	2,931	(88.5)	238	(7.2)		23	(0.7)		121	(3.7)	
Race/ethnicity											
White	2,749	(93.8)	208	(87.4)	0.0040	23	(100.0)	n/a	106	(87.6)	0.0444
Non-White	182	(6.2)	30	(12.6)		0	(0.0)		15	(12.4)	
Region											
West	498	(17.0)	55	(23.1)	0.1251	2	(8.7)	0.3946	19	(15.7)	0.2288
Midwest	1,037	(35.4)	75	(31.5)		7	(30.4)		33	(27.3)	
South	434	(14.8)	36	(15.1)		3	(13.0)		22	(18.2)	
Northeast	962	(32.8)	72	(30.3)		11	(47.8)		47	(38.8)	
College Attendance											
Never Attended	85	(4.0)	4	(2.1)	0.1086	1	(5.3)	0.8009	4	(4.0)	0.9983
Attended	2,059	(96.0)	184	(97.9)		18	(94.7)		97	(96.0)	
Age, *mean (sd)*	22.6	(1.7)	22.6	(1.6)	0.5371	22.5	(1.6)	0.7315	22.6	(1.7)	0.9383

Note. Column percentages are presented throughout the table except where noted otherwise. Using completely heterosexuals as the referent, p-values were derived using Rao-Scott chi-squared tests for categorical variables and univariable models with generalized estimating equations for age, both of which adjusted for sibling clusters. Missing data for college attendance and pregnancy were excluded from this table, including the Rao-Scott chi-squared tests. sd = standard deviation. n/a = not applicable because there was a zero cell for bisexuals. Sexual orientation was based on participants' last self-report from 1999-2010; gender and race/ethnicity were assessed in 1996 at baseline; region was assessed in 2007; college attendance was assessed in 2010; lifetime pregnancy was assessed prospectively from 1999-2010; age was assessed in 2007.

Table 3-2. Class enumeration fit indices and qualities for latent class analyses for familial and non-familial warmth during childhood and adolescence among total sample: Growing Up Today Study

Classes	Free parameters	Log-Likelihood	AIC	BIC	SSA-BIC	χ^2 model fit	χ^2 df	χ^2 p-value	Entropy	BF	cmP	AWE	VLMR LRT p-value
1	16	-46,607	93,246	93,360	93,310	10,123.11	600	<0.0001	n/a	<1	0.00	93,554	n/a
2	33	-40,254	80,575	80,810	80,705	7,680.45	583	<0.0001	0.889	<1	0.00	81,209	<0.0001
3	50	-37,879	75,857	76,213	76,054	6,079.23	571	<0.0001	0.849	<1	0.00	76,820	<0.0001
4	67	-36,923	73,979	74,456	74,243	5,052.32	555	<0.0001	0.852	<1	0.00	75,269	<0.0001
5	84	-35,939	72,047	72,644	72,377	4,505.35	538	<0.0001	0.908	<1	0.00	73,662	<0.0001
6	**101**	**-35,336**	**70,874**	**71,592**	**71,271**	**3,662.29**	**520**	**<0.0001**	**0.932**	**<1**	**0.00**	**72,816**	**<0.0001**
7	118	-35,066	70,368	71,208	70,833	3,212.82	503	<0.0001	0.907	<1	0.00	72,637	0.7639
8	135	-34,832	69,935	70,895	70,466	2,658.99	486	<0.0001	0.908	n/a	1.00	72,530	0.7604

Note. Models were estimated with a sample of 5,786 women and 3,316 men. Warmth was assessed in 2007. Boldface indicates the model we selected. AIC = Akaike information criterion; BIC = Bayesian information criterion; SSA-BIC = Sample size-adjusted Bayesian information criterion; BF = Bayes factor; cmP = Correct model probability; AWE = Approximate weight of evidence criterion; VLMR LRT = Vuong-Lo-Mendell-Rubin likelihood ratio test; df = degrees of freedom; n/a = not applicable. Bootstrap Likelihood Ratio Test could not be estimated because we employed the COMPLEX command in Mplus to adjust for non-independence within sibling clusters.

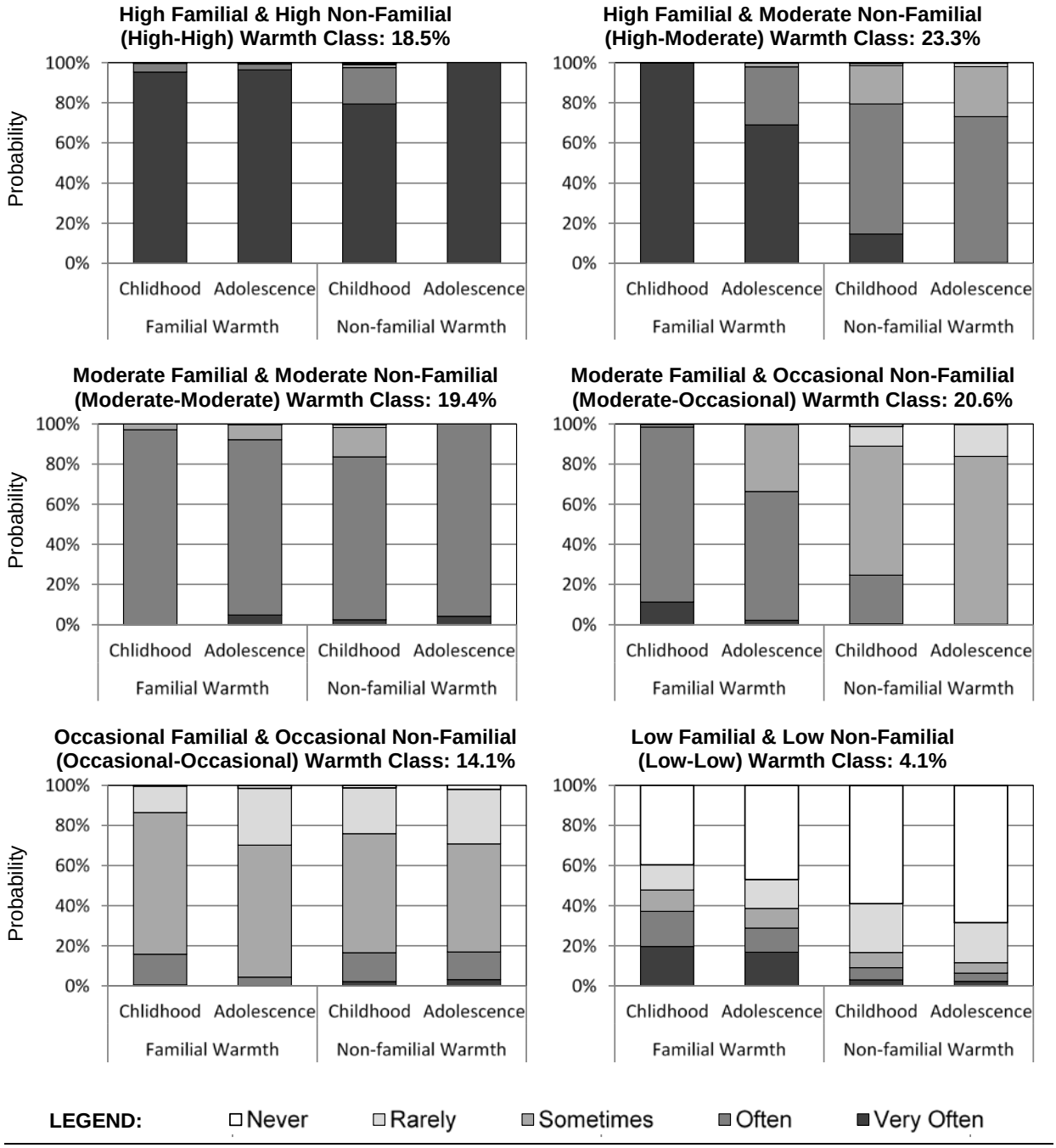

Figure 3-1. Latent class analysis profile plots for familial and non-familial warmth in childhood and adolescence: Growing Up Today Study

Table 3-3. Bivariate associations between sexual orientation and warmth classes, stratified by gender: Growing Up Today Study

	Warmth Classes												
	High Familial & High Non-Familial (High-High)		High Familial & Moderate Non-Familial (High-Moderate)		Moderate Familial & Moderate Non-Familial (Moderate-Moderate)		Moderate Familial & Occasional Non-Familial (Moderate-Occasional)		Occasional Familial & Occasional Non-Familial (Occasional-Occasional)		Low Familial & Low Non-Familial (Low-Low)		
	n	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*p-value*
WOMEN													
Total	1,285	(22.2)	1,466	(25.4)	1,109	(19.2)	966	(16.7)	726	(12.6)	231	(4.0)	
Sexual Orientation													
Completely Heterosexual	1,098	(23.7)	1,218	(26.2)	888	(19.1)	729	(15.7)	515	(11.1)	194	(4.2)	<.0001
Mostly Heterosexual	158	(17.3)	196	(21.5)	174	(19.1)	183	(20.1)	170	(18.6)	31	(3.4)	
Bisexual	17	(12.2)	28	(20.1)	28	(20.1)	39	(28.1)	24	(17.3)	3	(2.2)	
Lesbian	12	(13.3)	24	(26.7)	19	(21.1)	15	(16.7)	17	(18.9)	3	(3.3)	
MEN													
Total	401	(12.1)	657	(19.8)	651	(19.6)	907	(27.4)	556	(16.8)	141	(4.3)	
Sexual Orientation													
Completely Heterosexual	352	(12.0)	599	(20.4)	576	(19.7)	804	(27.4)	468	(16.0)	132	(4.5)	0.0234
Mostly Heterosexual	25	(10.5)	32	(13.5)	49	(20.6)	68	(28.6)	59	(24.8)	5	(2.1)	
Bisexual	3	(13.0)	3	(13.0)	6	(26.1)	4	(17.4)	6	(26.1)	1	(4.4)	
Gay	21	(17.4)	23	(19.0)	20	(16.5)	31	(25.6)	23	(19.0)	3	(2.5)	

Note. Row percentages are presented throughout the table. P-values were derived using Rao-Scott chi-squared tests adjusting for sibling clusters. Sexual orientation was based on participants' last self-report from 1999-2010; gender was assessed in 1996 at baseline; warmth was assessed in 2007.

Table 3-4. Results of multinomial logistic regression models testing sexual-orientation differences in warmth class memberships, stratified by gender: Growing Up Today Study

	High-Moderate versus High-High Warmth Class		Moderate-Moderate versus High-High Warmth Class		Moderate-Occasional versus High-High Warmth Class		Occasional-Occasional versus High-High Warmth Class		Low-Low versus High-High Warmth Class	
	OR (95% CI)	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*
WOMEN										
Sexual Orientation										
Completely Heterosexual	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)	
Mostly Heterosexual	1.11 (0.89, 1.39)	0.3675	**1.38 (1.09, 1.74)**	**0.0066**	**1.75 (1.39, 2.22)**	**<.0001**	**2.25 (1.77, 2.86)**	**<.0001**	1.11 (0.73, 1.68)	0.6233
Bisexual	1.47 (0.80, 2.70)	0.2152	**2.07 (1.13, 3.81)**	**0.0188**	**3.49 (1.96, 6.22)**	**<.0001**	**2.94 (1.56, 5.53)**	**0.0008**	0.99 (0.29, 3.42)	0.9923
Lesbian	1.78 (0.89, 3.57)	0.1052	1.98 (0.95, 4.10)	0.0673	1.89 (0.86, 4.15)	0.1150	**2.96 (1.40, 6.23)**	**0.0044**	1.40 (0.39, 5.06)	0.6053
MEN										
Sexual Orientation										
Completely Heterosexual	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)	
Mostly Heterosexual	0.76 (0.44, 1.31)	0.3290	1.20 (0.73, 1.96)	0.4778	1.19 (0.74, 1.92)	0.4710	**1.76 (1.08, 2.87)**	**0.0242**	0.52 (0.20, 1.41)	0.2002
Bisexual	0.61 (0.13, 2.95)	0.5368	1.25 (0.31, 5.03)	0.7570	0.60 (0.13, 2.67)	0.5007	1.54 (0.38, 6.15)	0.5440	0.90 (0.09, 8.74)	0.9256
Gay	0.66 (0.36, 1.22)	0.1856	0.59 (0.31, 1.11)	0.1013	0.65 (0.37, 1.16)	0.1447	0.82 (0.44, 1.51)	0.5251	0.38 (0.11, 1.26)	0.1133

Note. Boldface indicates statistical significance (p<0.05). Models were estimated with samples of 5,784 women and 3,313 men. Models adjusted for race/ethnicity (assessed in 1996 at baseline), age (assessed in 2007), and region (assessed in 2007). Sexual orientation was based on participants' last self-report from 1999-2010; gender was assessed in 1996 at baseline; warmth was assessed in 2007. High-High = High familial & high non-familial warmth; High-Moderate = High familial & moderate non-familial warmth; Moderate-Moderate = Moderate familial & moderate non-familial warmth; Moderate-Occasional = Moderate familial & occasional non-familial warmth; Occasional-Occasional = Occasional familial & occasional non-familial warmth; Low-Low = Low familial & low non-familial warmth; OR = odds ratio; CI = confidence interval.

Table 3-5. Alcohol use trajectories and disorders by sexual orientation and warmth classes, stratified by gender: Growing Up Today Study

	Alcohol Use Trajectory Classes from Ages 18-25							Alcohol Use Disorder	
	Non-Drinkers	Heavy Drinkers	Moderate Drinkers	Legal Drinkers	Escalation-to-Moderately-Heavy Drinkers	Light Drinkers		Past-Year Prevalence	
	%	%	%	%	%	%	*p-value*	%	*p-value*
WOMEN									
Total	7.4	22.9	31.3	11.0	10.4	17.0		16.8	
Sexual Orientation									
Completely Heterosexual	8.2	21.6	30.9	12.0	10.3	17.0	<.0001	14.0	<.0001
Mostly Heterosexual	4.2	28.8	34.0	6.5	10.3	16.2		28.7	
Bisexual	4.3	26.6	29.5	8.6	11.5	19.4		28.0	
Lesbian	3.4	23.6	30.3	6.7	14.6	21.4		25.7	
Warmth Classes									
High-High	7.7	23.4	30.5	10.8	9.6	18.0	0.2071	13.5	<.0001
High-Moderate	6.8	23.5	32.0	10.0	11.9	15.8		15.6	
Moderate-Moderate	6.7	22.7	32.5	13.3	9.9	14.9		15.0	
Moderate-Occasional	7.9	21.1	32.6	10.6	10.2	17.5		20.5	
Occasional-Occasional	8.7	22.2	29.1	10.4	10.0	19.6		22.4	
Low-Low	7.4	26.5	27.4	10.0	9.6	19.1		19.7	
MEN									
Total	9.2	35.3	25.4	16.6	13.5			27.3	
Sexual Orientation									
Completely Heterosexual	9.8	35.8	23.9	16.9	13.6		<.0001	25.8	0.0023
Mostly Heterosexual	4.6	33.8	34.2	16.0	11.4			36.0	
Bisexual	4.4	30.4	39.1	13.0	13.0			38.9	
Gay	5.0	26.7	41.7	10.8	15.8			40.9	
Warmth Classes									
High-High	11.5	31.8	24.0	19.5	13.3		0.2804	23.4	0.0086
High-Moderate	9.0	36.9	26.5	15.0	12.7			24.7	
Moderate-Moderate	9.2	34.5	25.8	16.7	13.8			30.8	
Moderate-Occasional	7.4	38.1	24.1	16.1	14.4			30.8	
Occasional-Occasional	10.3	30.9	27.5	17.9	13.4			26.0	
Low-Low	11.4	40.4	22.7	13.5	12.1			17.1	

Note. Row percentages are presented throughout the table. Univariable p-values were derived using Rao-Scott chi-squared tests ajusting for sibling clusters. Sexual orientation was based on participants' last self-report from 1999-2010; gender was assessed in 1996 at baseline; warmth was assessed in 2007; alcohol use trajectories were derived using longitudinal latent class analyses from participants' past-year alcohol frequency, quantity, and heavy episodic drinking from 2003-2010 when they were aged 18-25 years (the light drinker class only emerged among women); past-year alcohol use disorders were assessed in 2010. For alcohol use trajectories, we analyzed data from 5,754 women and 3,285 men. For alcohol use disorders, we analyzed data from 4,620 women and 2,159 men. High-High = High familial & high non-familial warmth; High-Moderate = High familial & moderate non-familial warmth; Moderate-Moderate = Moderate familial & moderate non-familial warmth; Moderate-Occasional = Moderate familial & occasional non-familial warmth; Occasional-Occasional = Occasional familial & occasional non-familial warmth; Low-Low = Low familial & low non-familial warmth.

Table 3-6. Results of multinomial logistic regression models testing the associations of sexual orientation and warmth classes on longitudinal alcohol use trajectories, stratified by gender: Growing Up Today Study

	Heavy drinkers versus Non-drinkers		Moderate drinkers versus Non-drinkers		Legal drinkers versus Non-drinkers		Escalation-to-Moderately-Heavy drinkers versus Non-drinkers		Light drinkers versus Non-drinkers	
	OR (95% CI)	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*	*OR (95% CI)*	*p-value*
WOMEN										
Model 1: Controlling for Demographics										
Sexual Orientation										
Completely Heterosexual	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)	
Mostly Heterosexual	**2.87 (1.96, 4.21)**	**<.0001**	**2.35 (1.61, 3.42)**	**<.0001**	1.14 (0.73, 1.79)	0.5579	**2.12 (1.40, 3.22)**	**0.0004**	**1.99 (1.34, 2.95)**	**0.0006**
Bisexual	**3.14 (1.27, 7.73)**	**0.0129**	2.40 (0.99, 5.85)	0.0532	1.68 (0.61, 4.63)	0.3116	**2.66 (1.00, 7.06)**	**0.0490**	**2.69 (1.08, 6.68)**	**0.0327**
Lesbian	2.66 (0.76, 9.26)	0.1254	2.38 (0.69, 8.19)	0.1701	1.43 (0.34, 5.97)	0.6214	3.48 (0.96, 12.62)	0.0577	3.16 (0.91, 10.92)	0.0697
Model 2: Controlling for Demographics and Warmth Classes										
Sexual Orientation										
Completely Heterosexual	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)	
Mostly Heterosexual	**2.97 (2.02, 4.38)**	**<.0001**	**2.40 (1.64, 3.51)**	**<.0001**	1.16 (0.74, 1.81)	0.5271	**2.18 (1.43, 3.32)**	**0.0003**	**2.02 (1.36, 3.00)**	**0.0005**
Bisexual	**3.24 (1.33, 7.93)**	**0.0099**	2.41 (1.00, 5.81)	0.0512	1.66 (0.61, 4.52)	0.3215	**2.69 (1.02, 7.09)**	**0.0451**	**2.71 (1.09, 6.69)**	**0.0311**
Lesbian	2.72 (0.78, 9.54)	0.1173	2.42 (0.70, 8.36)	0.1634	1.45 (0.35, 6.04)	0.6093	3.52 (0.97, 12.83)	0.0560	3.21 (0.92, 11.17)	0.0665
Warmth Classes										
High-High	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)	
High-Moderate	1.14 (0.82, 1.57)	0.4409	1.20 (0.88, 1.64)	0.2600	1.07 (0.74, 1.54)	0.7274	1.41 (0.98, 2.04)	0.0627	0.99 (0.71, 1.39)	0.9713
Moderate-Moderate	1.07 (0.75, 1.53)	0.6955	1.20 (0.85, 1.68)	0.3009	1.43 (0.97, 2.11)	0.0673	1.15 (0.77, 1.72)	0.5024	0.91 (0.63, 1.32)	0.6320
Moderate-Occasional	0.84 (0.59, 1.20)	0.3349	1.04 (0.74, 1.46)	0.8382	1.02 (0.68, 1.52)	0.9249	1.04 (0.69, 1.56)	0.8681	0.93 (0.64, 1.34)	0.6834
Occasional-Occasional	0.80 (0.54, 1.18)	0.2662	0.84 (0.58, 1.22)	0.3619	0.92 (0.60, 1.43)	0.7264	0.92 (0.59, 1.43)	0.6981	0.91 (0.61, 1.35)	0.6224
Low-Low	1.14 (0.62, 2.08)	0.6732	0.91 (0.50, 1.65)	0.7651	0.96 (0.48, 1.94)	0.9185	1.00 (0.50, 2.01)	0.9967	1.06 (0.57, 1.98)	0.8489
MEN										
Model 3: Controlling for Demographics										
Sexual Orientation										
Completely Heterosexual	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)			
Mostly Heterosexual	**2.07 (1.08, 3.97)**	**0.0281**	**3.14 (1.64, 6.00)**	**0.0005**	1.98 (1.00, 3.94)	0.0517	1.77 (0.86, 3.65)	0.1192		
Bisexual	1.71 (0.21, 14.22)	0.6190	3.44 (0.43, 27.59)	0.2443	1.70 (0.17, 17.45)	0.6543	2.03 (0.20, 20.61)	0.5485		
Gay	1.46 (0.61, 3.49)	0.4007	**3.45 (1.47, 8.10)**	**0.0045**	1.21 (0.46, 3.22)	0.6982	2.23 (0.88, 5.64)	0.0908		
Model 4: Controlling for Demographics and Warmth Classes										
Sexual Orientation										
Completely Heterosexual	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)			
Mostly Heterosexual	**2.11 (1.10, 4.06)**	**0.0254**	**3.14 (1.64, 6.02)**	**0.0006**	1.95 (0.98, 3.89)	0.0578	1.76 (0.85, 3.64)	0.1264		
Bisexual	1.81 (0.22, 15.22)	0.5836	3.51 (0.44, 28.09)	0.2375	1.72 (0.17, 17.45)	0.6468	2.09 (0.21, 21.08)	0.5322		
Gay	1.52 (0.63, 3.66)	0.3540	**3.55 (1.50, 8.37)**	**0.0039**	1.22 (0.46, 3.24)	0.6930	2.29 (0.90, 5.83)	0.0819		
Warmth Classes										
High-High	1.00 (referent)		1.00 (referent)		1.00 (referent)		1.00 (referent)			
High-Moderate	**1.57 (1.01, 2.46)**	**0.0451**	1.53 (0.96, 2.41)	0.0719	1.00 (0.62, 1.63)	0.9890	1.29 (0.77, 2.16)	0.3345		
Moderate-Moderate	1.41 (0.90, 2.21)	0.1332	1.39 (0.88, 2.22)	0.1617	1.07 (0.66, 1.74)	0.7862	1.33 (0.79, 2.24)	0.2893		
Moderate-Occasional	**2.00 (1.29, 3.11)**	**0.0020**	**1.67 (1.06, 2.65)**	**0.0276**	1.34 (0.84, 2.14)	0.2250	**1.83 (1.11, 3.02)**	**0.0184**		
Occasional-Occasional	1.12 (0.70, 1.78)	0.6380	1.28 (0.80, 2.06)	0.3091	1.05 (0.64, 1.71)	0.8562	1.20 (0.70, 2.04)	0.5086		
Low-Low	1.32 (0.69, 2.53)	0.4076	1.02 (0.50, 2.06)	0.9618	0.71 (0.34, 1.52)	0.3806	0.95 (0.43, 2.09)	0.9067		

Note. Boldface indicates statistical significance (p<0.05). Light drinkers were only present among women. Models were estimated with samples of 5,764 women and 3,285 men. All models adjusted for race/ethnicity (assessed in 1996 at baseline), age (assessed in 2007), region (assessed in 2007), and lifetime college attendance (assessed in 2010). Models for women also adjusted for lifetime pregnancy (assessed prospectively from 1999-2010). Sexual orientation was based on participants' last self-report from 1999-2010; gender was assessed in 1996 at baseline; warmth was assessed in 2007; alcohol use trajectories were derived using longitudinal latent class analyses from participants' past-year alcohol frequency, quantity, and heavy episodic drinking from 2003-2010 when they were aged 18-25 years. The light drinker class only emerged among women. High-High = High familial & high non-familial warmth; High-Moderate = High familial & moderate non-familial warmth; Moderate-Moderate = Moderate familial & moderate non-familial warmth; Moderate-Occasional = Moderate familial & occasional non-familial warmth; Occasional-Occasional = Occasional familial & occasional non-familial warmth; Low-Low = Low familial & low non-familial warmth; OR = odds ratio; CI = confidence interval.

Table 3-7. Mediational effects of warmth classes on sexual-orientation differences in alcohol use disorders, stratified by gender: Growing Up Today Study

	Alcohol Use Disorder				
	Model 1: Controlling for Demographics		**Model 2: Model 1 + Warmth Classes**		**Proportion Mediated for Model 1 vs 2**
	RR (95% CI)	*p-value*	*RR (95% CI)*	*p-value*	*% (p-value)*
WOMEN					
Sexual orientation					
Completely Heterosexual	1.00 (referent)		1.00 (referent)		
Mostly Heterosexual	**2.05 (1.78, 2.37)**	**<.0001**	**2.00 (1.73, 2.30)**	**<.0001**	**4.0 (.0070)**
Bisexual	**2.04 (1.50, 2.77)**	**<.0001**	**1.96 (1.43, 2.68)**	**<.0001**	**7.8 (.0087)**
Lesbian	**1.80 (1.21, 2.68)**	**0.0040**	**1.74 (1.18, 2.56)**	**0.0054**	1.6 (.3567)
Warmth Classes					
High-High			1.00 (referent)		
High-Moderate			1.16 (0.95, 1.41)	0.1576	
Moderate-Moderate			1.07 (0.86, 1.33)	0.5428	
Moderate-Occasional			**1.44 (1.17, 1.77)**	**0.0005**	
Occasional-Occasional			**1.56 (1.25, 1.95)**	**<.0001**	
Low-Low			**1.48 (1.08, 2.04)**	**0.0154**	
MEN					
Sexual orientation					
Completely Heterosexual	1.00 (referent)		1.00 (referent)		
Mostly Heterosexual	**1.36 (1.09, 1.70)**	**0.0064**	**1.35 (1.08, 1.69)**	**0.0075**	not mediated
Bisexual	1.54 (0.87, 2.72)	0.1349	1.54 (0.88, 2.71)	0.1303	not mediated
Gay	**1.60 (1.25, 2.06)**	**0.0002**	**1.61 (1.25, 2.06)**	**0.0002**	not mediated
Warmth Classes					
High-High			1.00 (referent)		
High-Moderate			1.07 (0.82, 1.40)	0.6233	
Moderate-Moderate			**1.32 (1.02, 1.71)**	**0.0327**	
Moderate-Occasional			**1.31 (1.03, 1.67)**	**0.0302**	
Occasional-Occasional			1.08 (0.82, 1.43)	0.5766	
Low-Low			0.74 (0.44, 1.24)	0.2512	

Note. Boldface indicates statistical significance (p<0.05). Models 1 and 2 were estimated with 4,591 women and 2,156 men. Models 3 and 4 were estimated with 4,586 women and 2,145 men. All models adjusted for race/ethnicity (assessed in 1996 at baseline), age (assessed in 2007), region (assessed in 2007), and lifetime college attendance (yes/no; assessed in 2010). Models for women also adjusted for lifetime pregnancy (yes/no; assessed prospectively from 1999-2010). Sexual orientation was based on participants' last self-report from 1999-2010; gender was assessed in 1996 at baseline; warmth was assessed in 2007; alcohol use trajectories were derived using longitudinal latent class analyses from participants' past-year alcohol frequency, quantity, and heavy episodic drinking from 2003-2010 when they were aged 18-25 years; past-year alcohol use disorders were assessed in 2010. High-High = High familial & high non-familial warmth; High-Moderate = High familial & moderate non-familial warmth; Moderate-Moderate = Moderate familial & moderate non-familial warmth; Moderate-Occasional = Moderate familial & occasional non-familial warmth; Occasional-Occasional = Occasional familial & occasional non-familial warmth; Low-Low = Low familial & low non-familial warmth; RR = relative risk; CI = confidence interval.

4.0 INTERVENTIONS FOR PREVENTING, REDUCING, AND TREATING SUBSTANCE USE, MENTAL HEALTH PROBLEMS, AND VIOLENCE VICTIMIZATION FOR SEXUAL AND GENDER MINORITY YOUTH: A SYSTEMATIC REVIEW

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4.1 ABSTRACT

Importance: Sexual and gender minority youth have significantly greater risk than their cisgender heterosexual peers for experiencing substance use, mental health problems, and violence victimization.

Objective: We systematically reviewed the scientific literature on interventions and their efficacy in preventing, reducing, or treating substance use, mental health problems, and violence victimization among sexual and gender minority youth.

Evidence Review: We included peer-reviewed studies from PubMed, PsycINFO, and ERIC databases published from January 1, 2000 through 2016. We included studies that examined intervention efficacy for substance use, mental health problems, and violence victimization outcomes among sexual and gender minority youth. We included randomized and non-randomized studies with pretest and posttest data. We appraised each study's methodological rigor using the Quality Assessment Tool for Quantitative Studies.

Findings: This review identified 6 interventions for mental health, 1 for substance use, and 0 for violence. These studies evaluated data from 593 sexual or gender minority participants whose average age at baseline being 15.4 years. Three studies evaluated interventions tailored to transgender youth, and three studies evaluated interventions tailored to sexual minority youth. Among the sexual-minority-specific interventions, 1 evaluated a therapist-administered family-based intervention to reduce mental health problems, 1 evaluated a self-administered computer-based intervention to reduce mental health problems, and 1 study evaluated a self-administered online intervention to reduce substance use and stress. All the transgender-specific interventions examined transition-related medical care interventions—puberty suppression, cross-sex hormones, gender reassignment surgery, or psychological support. All interventions improved mental health outcomes, and one study reduced other drug use for participants; however, the results of these studies should be interpreted cautiously due to less than optimal methodological quality.

Conclusions and Relevance: The small collection of diverse evidence-based interventions identified in this review is likely insufficient to mitigate the substantial population-level inequities present among sexual and gender minority youth in substance use, mental health problems, and violence. Existing epidemiologic and intervention research can inform future interventions to help bring health equity to sexual and gender minority youth.

4.2 INTRODUCTION

More than two decades of research consistently show that sexual-minority youth (i.e., gay/lesbian and bisexual youth, and youth with same-gender attractions or sexual behaviors) are

at greater risk than heterosexual youth of experiencing substance use, mental health problems, and violence.[2-24] Meta-analyses have shown that on average, compared with heterosexuals, sexual minority youth had: 123-623% higher odds of lifetime substance use (i.e., alcohol, cigarette, marijuana, and other drug use)[2]; 82-317% higher odds of mental health problems (i.e., depressive symptoms, suicidality)[3]; and 20-280% higher odds of experiencing violence victimization (i.e., school victimization, sexual abuse, parental physical abuse).[4] These sexual-orientation disparities were even larger for certain subgroups (i.e., bisexuals for all outcomes[2-4]; males for violence[4]; and females for substance use[2]). Epidemiologic data also show that gender minority youth (e.g., youth whose gender identity does not match their assigned sex at birth, and transgender and gender-nonconforming youth) have greater risk than cisgender youth (e.g., youth whose gender identity matches their assigned sex at birth) for substance use, mental health problems, and violence victimization.[25-27] For example, compared with cisgender youth, gender minority youth had: 42-80% higher odds of lifetime substance use;[25]; 470-1130% higher odds of depressive symptoms and suicidality[26,27]; and 90-350% higher odds of violence victimization.[25,26] These substantial health inequities suggest that sexual and gender minority (SGM) youth be a priority population for research focused on preventing, reducing, and treating substance use, mental health problems, and violence.

There are many reasons why it is important to mitigate SGM inequities during childhood and adolescence. First, experiences of substance use, mental health problems, and violence prior to age 18 place individuals at greater risk of experiencing these same issues later in the life-course.[203-209] Therefore, mitigating health inequities for SGM populations during childhood and adolescence may help diminish SGM health inequities later in the life-course. Second, substance use, mental health problems, and violence victimization are bidirectionally associated with each

other,[210-213] suggesting that reducing one of these health problems could reduce the others. Third, reducing these problems may in turn reduce their myriad negative health consequences, including sexually transmitted infections, cardiovascular disease, and even mortality.[204,205,214] Fourth, from a health equity perspective,[215] health is a fundamental right of all individuals and populations, including SGM youth. Finally, numerous U.S. agencies and organizations have called for mitigating health inequities for SGM youth.[1,216,217]

Theoretical perspectives and epidemiologic research have identified many risk factors associated with substance use, mental health, and violence inequities experienced by SGM youth. Stigma theory[218,219] posits that SGM populations experience stigma in multiple forms (i.e., internalized, interpersonal, and structural) because they have a minority sexual orientation or gender identity. Because it is a "fundamental cause of health inequities,"[157,191] stigma increases SGM populations' prevalence of risk factors and decreases their access to health-promoting resources (e.g., knowledge, beneficial social connections).[157,191] According to minority stress theory,[134] experiences of stigmatization cause elevated levels of chronic and acute stress among SGM populations; if this stress exceeds one's ability to cope, individuals may develop mental health problems or use substances to cope. Furthermore, syndemics theory[220,221] suggests that stressors, such as violence victimization, can cause co-occurring and interacting health problems, such as depression and substance use, which exacerbates health problems among populations. These theories have been supported in a robust body of empirical studies among SGM populations.[25,33,34,48,87,135,141,142,222-231]

Despite the theoretical and epidemiologic research on SGM health inequities, there remains limited knowledge about the efficacy of interventions aimed at preventing, reducing, or treating health problems among SGM youth. In 2011, the Institute of Medicine report on SGM

populations identified few interventions for SGM youth.[1] Nevertheless, there exist many interventions targeting substance use, mental health problems, and violence for youth in general.[232-235] Consequently, one of the five major recommendations of the Institute of Medicine report was to develop, implement, and evaluate interventions for SGM populations.[211] However, interventions do exist for SGM adults. Numerous treatment interventions exist for reducing alcohol and substance use among sexual minority men (see reviews[236,237]). There are also many smoking cessation interventions for SGM adults (see review[238]); however, most of them lacked outcome evaluations.[238] Regarding mental health interventions, only 1 of 232 randomized controlled trials for anxiety and depression have measured sexual orientation;[239] none assessed gender minority status.[239]

4.3 AIMS

Systematically documenting whether any universal or targeted interventions are efficacious for SGM youth can provide a rigorous assessment of the current state of the field. Therefore, the purpose of this paper is to systematically review the state of the scientific literature on interventions and their efficacy in preventing, reducing, or treating substance use, mental health problems, and violence among SGM youth. This review will highlight current strengths in and future opportunities for intervention research, both of which can inform future public health research and practice aimed propelling SGM youth towards achieving health equity.

4.4 METHODS

We used systematic review methods recommended by the *Cochrane Handbook for Systematic Reviews of Interventions.*[240] Our protocol was approved in PROSPERO prior to any data extraction.[241]

Criteria for Considering Studies for this Review

Types of Studies

We included both randomized controlled trials and non-randomized study designs; we included the latter because not all LGBT-relevant interventions (e.g., federal policies) are conducive to randomization. However, non-randomized studies are more likely to be biased than randomized trials,[242] and to limit potential biases we only included studies that had both pre- and post-intervention data from participants, as recommended by Cochrane.[243] Such designs include controlled before-after studies, interrupted time series studies, and repeated measures studies. We excluded cross-sectional studies and case report studies.

Types of Participants

We included studies that examined participants aged less than 18 years at baseline. We selected this because having any of our outcomes (i.e., substance use, mental health problems, violence victimization) before age 18 are associated with the similar outcomes later in life. [203-209] Because studies sometimes enroll populations both under and over 18 years of age, we included studies with a minority (<25%) of adult participants (≥18 years old) or studies that reported results separately for child/adolescent participants versus adult populations, as has been done in previous Cochrane reviews.[244,245]

We included studies if they assessed sexual or gender minority status based on the prior reviews.[1,238] We defined sexual minority populations as lesbian, gay, bisexual, queer, and other

sexual-minority identities, as well as youth who have same-gender sexual behavior or attractions. We defined gender minority populations as transgender people (e.g., those who identify as transgender, or whose current gender identity does not match assigned sex at birth) or people with other gender nonconforming identities (e.g., genderqueer).

Types of Interventions

We included any type of intervention that was a "purposeful action by an agent to create change"[246] or a "process of intervening on people groups, entities or objects."[247] Therefore, this review potentially included behavioral, psychological, educational, pharmacological, medical, and policy interventions.

Types of Outcomes

We included studies that examined substance use, mental health problems, or violence as outcomes. We included youth outcomes as reported by any entity (i.e., self-, parent-, teacher-, school-, or therapist-reported). Substance use included licit and illicit drug use, such as alcohol, tobacco, marijuana, prescription drug misuse, heroin, hallucinogens, methamphetamine, ecstasy, and cocaine. Mental health problems included stress, anxiety, depressive symptoms, suicidality (thoughts, plans, or attempts), internalized homo/bi/transphobia, and self-injury (or self-harm). Violence outcomes included experiences or threats of bullying, cyberbullying, aggression, violence with weapons, harassment, discrimination, sexual assault, sexual abuse, physical abuse, and emotional abuse from all types of perpetrators (e.g., peers, parents, siblings).

Search Methods for Identifying Potential Studies

We conducted a search of electronic databases with a research librarian (B.F.), who developed, piloted, and executed the search strategies. We searched PubMed, PsycINFO, and ERIC databases for studies published from January 1, 2000 through a date in 2016 (see Figure 1

for exact dates for each database). The search strategies used a combination of text words and medical subject headings (e.g., MeSH terms) adapted for each database. The search strategy included the following concepts: sexual or gender minority status (adapted from this review[248]); youth; substance use, mental health problems, or violence; study design and intervention terms; human research; and studies in the English language. We excluded animal studies, as well as meta-analyses, systematic reviews, news, editorials, and commentaries. We had no geographical restrictions.

Data Collection and Analysis

Selection of Studies

First, we identified potentially relevant studies by reviewing the titles and abstracts of all articles retrieved from our searches. We considered studies with insufficient information in the title or abstract as potentially relevant articles for further assessment. Second, we reviewed the full text of potentially relevant studies for final inclusion or exclusion in our study. Two of five investigators (R.W.S.C., J.E.E., S.K., M.R.F., and K.E.), independently screened each record, and had substantial agreement for title and abstract screening (κ=0.70) and full text screening (κ=0.79).[249] The first author resolved any disagreements. We tracked all screening results in DistillerSR (Evidence Partners, Ottawa, Canada).

Data Extraction and Management

We conducted a narrative synthesis for each study. Using a standardized form, two of four investigators (R.W.S.C., J.E.E., S.K., and M.R.F.) independently extracted data from each included study. We extracted data on each study's intervention, evaluation design, sampling and recruitment procedures, inclusion/exclusion criteria, sample characteristics, outcome measures, and main findings. One investigator placed all extracted data in tabular format, and another

investigator reviewed the table for accuracy and completeness. The two investigators discussed any discrepancies until they reached consensus.

Methodological Quality

We selected the Quality Assessment Tool for Quantitative Studies (QATQS) checklist to assess methodological rigor because this tool assesses characteristics of both randomized and non-randomized studies.[250] Two independent raters evaluated each study; raters discussed any discrepancies until they reached consensus. Raters assessed 6 characteristics for each study: selection bias; study design; confounders; blinding; data collection method; and withdrawals and dropouts. Based on the ratings from these 6 characteristics, each study received a global rating. Possible ratings for each study characteristic and global rating included weak, moderate, and strong (ranging from least to most methodologically rigorous).

4.5 RESULTS

Searches identified 4090 unique studies, of which 308 studies were potentially relevant for inclusion in this review (Figure 1). After full-text screening, 6 studies met the inclusion criteria.[251-256]

Intervention Descriptions

Three studies evaluated interventions tailored to transgender youth,[251-253] and three studies evaluated interventions tailored to sexual-minority youth[254-256] (Table 1). All the transgender-specific interventions examined transition-related medical care interventions—puberty suppression, cross-sex hormones, gender reassignment surgery, and psychological support following the Standards of Care of the World Professional Association for Transgender

Health (WPATH).[251-253,257] Two studies[251,252] examined the effects of puberty suppression (i.e., the provision of gonadotropin-releasing hormone analogues that delay the physical changes associated with puberty[257]) on mental health. Specific criteria must be met to receive puberty-suppressing hormones.[251,252,257] Should those criteria not be met, youth receive psychological support as standard of care; therefore, one study[251] had a two-group design: comparing the effects of psychological-only intervention to psychological-and-puberty-suppression intervention. The other study[252] had a one-group design, following only youth who received puberty suppression. The third transgender-specific study[253] examined the effects of cross-sex hormones and gender reassignment surgery on mental health using a subset of participants from the previous study.[252] None of the transgender-specific intervention studies explicitly stated the dosage of intervention provided to participants, but they followed WPATH standards of care[257] and all participants received ongoing medical or psychological care from baseline through final posttest assessment.[251-253]

Among the sexual-minority-specific interventions, 1 evaluated a therapist-administered family-based intervention to reduce mental health problems,[254] 1 evaluated a self-administered computer-based intervention to reduce mental health problems,[255] and 1 study evaluated a self-administered online intervention to reduce substance use and stress.[256] Both the self-administered interventions[255,256] were shorter in duration and smaller in dosage than the therapist-administered intervention.[254] The self-administered interventions used 3 14-minute modules delivered during a 1-month period[256] or 7 30-minute modules delivered during a 2-month period.[255] The therapist-administered intervention had between 8 and 16 one-hour weekly in-person sessions.[254] All these interventions had theoretical underpinnings.[254-256] One intervention incorporated input from youth during development,[255] and 1 used input from clinicians.[254]

Evaluation Designs

One study used a randomized controlled study design[256]; 1 used a nonrandomized comparison group design[251]; and 4 used a one-group design.[252-255] Two studies had a pretest-posttest design[252,256]; 1 had a pretest-posttest-posttest design[255]; 2 had a pretest-midtest-posttest design[253,254]; and 1 had pretest-posttest design with multiple posttests.[251] Average length between baseline and final posttest was longer for the transgender-specific studies (range: 1.5-7.1 years[251-253]) than for sexual-minority-specific studies (range: 0.0-0.5 years[254-256]). Two of the sexual-minority-specific interventions used 3-month follow-up periods as the final posttest.[255,256]

Sampling, Recruitment Procedures, and Inclusion Criteria

All studies sampled transgender or sexual minority populations[251-256]; none sampled cisgender heterosexual populations. All studies used various forms of convenience sampling: the transgender-specific studies[251-253] recruited participants from clinics; for the sexual-minority-specific interventions, 1 study recruited from clinics,[254] 1 from Facebook,[256] and 1 from high schools, a local LGBT organization, and LGBT media.[255] The transgender-specific interventions were conducted in Europe,[251-253] with 1 in England[251] and 2 in the Netherlands[252,253]; two of the sexual-minority-specific interventions were conducted in the United States[254,256] and 1 was in New Zealand.[255] The transgender-specific studies only included youth who had a gender identity disorder diagnosis.[251-253] In the sexual-minority-specific studies, 1 study only included youth with significant suicidal ideation,[254] 1 study only included youth with depressive symptoms,[255] and 1 study did not have any eligibility criteria related to mental health.[256]

Sample Characteristics

The included studies had 593 total participants, ranging from 10[254] to 236[256] participants. The average age of participants at baseline was 15.36 years (ranging from 11 to 19).[251-256] Four

samples included only youths less than 18 years at baseline.[251-253,256] All studies reported participants' gender identity or assigned natal sex.[251-256] Four studies reported participants' sexual orientation[252,254-256]—all four reported sexual attractions,[252,254-256] and 1 study also reported sexual identities.[254]

Outcome Measures

All studies examined mental health outcomes[251-256]: 4 studies examined depressive symptoms[252-255]; 3 examined anxiety symptoms[252,253,255]; 2 examined internalizing and externalizing symptoms[252,253]; 2 examined psychosocial functioning[251,253]; 1 examined hopelessness[255]; 1 examined perceived stress[256]; and 1 examined suicidal ideation.[254] Mental health outcomes were assessed using reports from participants, parents, clinicians, and researchers.[251-256] One study examined self-reported substance use outcomes,[256] which examined alcohol, cigarette, marijuana, and other drug use. Zero studies examined violence outcomes.

Intervention Results

Transgender-specific Studies

A one-group pretest-posttest study suggested that initiation of pubertal suppression reduced depressive, internalizing, and externalizing symptoms, but not anxiety symptoms.[252] De Vries, et al., also conducted a follow-up study using data from a subset of these participants as they initiated cross-sex hormones and gender reassignment surgery.[253] Using a one-group pretest-midtest-posttest study across 7.1 years, participants were assessed at baseline (before initiating puberty suppression), mid-intervention (just prior to initiating cross-sex hormones), and post-intervention (1-year after gender reassignment surgery).[253] Over time, psychosocial functioning increased linearly, while internalizing and externalizing symptoms from the Child/Adult Behavior Checklist decreased linearly.[253] Depressive symptoms and internalizing

symptoms from the Youth/Adult Self-Report decreased from baseline to mid-intervention, but increased slightly at post-intervention.[253] For both measures of internalizing symptoms and externalizing symptoms from the Child/Adult Behavior Checklist, the percentage of participants in the clinically significant range decreased over time.[253] While the aforementioned results were similar for transmen and transwomen, some results were moderated by gender: anxiety and externalizing symptoms from the Youth/Adult Self-Report decreased linearly for transmen, but increased after gender reassignment surgery for transwomen.[253]

Costa, et al., compared transgender youth who received a psychological-only intervention to those who received a psychological-and-puberty-suppression intervention.[251] Results showed that the two nonrandomized groups did not significantly differ in average psychosocial functioning at any assessment point (i.e., baseline, 6-, 12-, and 18-month follow-ups).[251] Within-group analyses revealed that for participants in the psychological-only intervention group, average psychosocial functioning improved after initiating the psychological intervention and plateaued thereafter.[251] For participants in the psychological-and-puberty-suppression intervention group, average psychosocial functioning did not improve after initiation of the psychological intervention, but did significantly improve after initiating puberty suppression.[251]

Sexual-minority-specific Studies

Youth who participated in the in-person family-based therapy intervention had significant decreases in average depressive symptoms and suicidal ideation symptoms across pretest-midtest-posttest.[254] Youth who participated in the computerized cognitive behavioral therapy intervention also had significant decreases in average depressive symptoms (across three different measures), anxiety symptoms, and hopelessness from baseline to immediate post-

intervention.[255] Average depressive symptoms plateaued from immediate post-intervention to 3-month post-intervention.[255]

According to a randomized controlled trial, the online intervention aimed at reducing substance use showed that, compared to control participants, intervention participants had significantly lower perceived stress and past-month frequency of other drug use at 3-month follow-up.[256] However, there were no significant differences between intervention and control groups in past-month frequency of alcohol, cigarette, or marijuana use at 3-month follow-up.[256]

Risk of Bias

Table 2 shows the methodological quality of the studies rated across several dimensions as conceptualized by the QATQS.[250] All studies received a weak global rating,[251-256] since they each had two or more weak ratings across the individual dimensions. Regarding selection bias, all studies were weak because their samples were not necessarily representative of their target populations or they had low or unreported participation rates.[251-256] Nevertheless, study designs ranged from moderate to strong.[251-256] The one study with a strong rating was a randomized controlled trial,[256] and the others were longitudinal study designs with one or two groups.[251-255] Regarding confounders, all studies were weak because they only reported unadjusted associations.[251-256] Blinding procedures (i.e., blinding data collectors to participants' intervention status; and blinding participants to the study's primary research question) were moderate across all studies.[251-256] Data collection methods were strong in 5 studies because they used valid and reliable measures.[251-255] One study had weak data collection methods because it was unclear if they used valid and reliable measures.[256] Withdrawals and dropouts were strong in 3 studies that had greater than or equal to 80% of participants complete the final study assessment.[254-256] The 3 remaining studies were rated as weak because of substantial attrition.[251-253]

4.6 DISCUSSION

This systematic review identified the scarcity of interventions for SGM youth evaluated in peer-reviewed scientific literature. Specifically, we found 6 interventions for mental health problems,[251-256] 1 for substance use,[256] and 0 for violence. While these interventions made significant improvements in mental health problems and substance use,[251-256] their results should be interpreted cautiously due to less than optimal methodological quality as appraised by the Quality Assessment Tool for Quantitative Studies.[250] For example, the lack of a comparison/control groups threatens validity because the intervention may not have improved health outcomes; instead, participants' improvements may be attributable to maturation or history.[258] These are salient concerns for SGM adolescents, given the many developmental changes throughout adolescence[259] and the ever-changing political and social climates for SGM populations.[260-262] Overall, this small collection of diverse evidence-based interventions is likely insufficient to mitigate the substantial population-level inequities present among SMG youth in substance use, mental health problems, and violence.

Our review, however, is not without limitations. It was impossible to include intervention evaluations still under review at scientific journals or evaluations still underway. This review also does not capture interventions without evaluations or those with evaluations published outside of the peer-reviewed scientific literature. Conducting and publishing evaluations in the scientific peer-reviewed literature is important for both understanding intervention efficacy and dissemination. For example, without a peer-reviewed publication of evaluation results, interventions cannot be included in national intervention registries (e.g., the National Registry of Evidence-Based Programs and Practices[235]), thereby hampering the widespread implementation of potentially efficacious interventions. We also did not examine interventions for intersex

populations. Finally, bias towards publishing only significant efficacious results[263] may have limited the number of studies included in this review, potentially limiting our knowledge about inefficacious interventions.

Nevertheless, there are many ways to advance the field of SGM intervention research for reducing substance use, mental health problems, and violence. Investigators can: (1) examine the efficacy of existing interventions (e.g.,[264-266]) that included youth in their studies but failed to meet our Cochrane-informed[244,245] age eligibility criteria; (2) evaluate the efficacy of interventions designed and implemented by community-based organizations (e.g.,[267]); (3) conduct outcome evaluations for interventions currently only examined via process evaluations (e.g.,[268]); (4) conduct natural experiments and quasi-experimental studies for policy changes, which is becoming more feasible given better epidemiologic data being collected on SGM youth (e.g., Youth Risk Behavior Surveillance System[269]); (5) adapt existing interventions to incorporate SGM-specific content (e.g.,[254,255]); (6) test whether interventions targeting all youth (e.g.,[232-235]) are efficacious specifically among SGM youth; and (7) develop, implement, and evaluate new interventions specifically tailored for SGM youth (e.g., [256]). Importantly, integrating the target populations' perspectives into intervention development can increase the intervention's relevance and protect participants' rights.[270] Additionally, interventions are more efficacious when their development utilizes theoretical foundations of behavior change.[271,272] Finally, researchers and review boards will contend with ethical dilemmas, including issues of parental consent which could potentially "out" SGM youth.[273]

Interventions also can incorporate knowledge from the extant epidemiologic research. For example, interventions can target SGM in myriad contexts: SGM youth usually live with families—though living in homelessness is heightened among SGM youth[274]—and they also

attend schools, after-school programs, community-based organizations, sports programs, churches, and medical clinics. Since SGM youth often comprise a relatively small proportion of youth[275] and most youth use the Internet,[276] Internet-based intervention methods may be a particularly effective way to reach SGM. Prevention interventions may also benefit from targeting SGM youth as early as possible in life-course because: across all youth, bullying victimization is more prevalent at younger ages[13,277,278]; and sexual minority youth have earlier substance use initiation than heterosexuals.[15,19] The needs of bisexual youth also deserve particular attention, since this is the largest sexual minority subgroup,[12] and they often have worse health outcomes than their gay/lesbian counterparts.[2-4,12] Additionally, the needs of racial/ethnic minority SGM populations warrant careful consideration, since many health outcomes and risk factors vary by race/ethnicity among SGM youth.[15,16,21,279]

Future interventions can target and enhance protective and resilience factors to improve health among SGM youth.[201,280] For example, research shows that adult support and warmth is associated with lower substance use, mental health problems, and violence, but adult support is generally lower among sexual minority youth compared with their heterosexual peers.[10,11,23,24,158-160,281-284] These support structures are also less protective against certain health problems, such as suicidality, for sexual minority youth.[10] Other potential health promoting factors include SGM-affirmative school climates, curricula, and policies (e.g., SGM-inclusive anti-bullying policies), gay-straight alliances, and supportive peers.[12,34,281,282,284-295] Interventions may benefit from incorporating some of these factors into their design.

Finally, because stigma and discrimination are the primary driving forces behind SGM youth health inequities in substance use, mental health problems, and violence,[157,296] developing interventions that reduce stigma and discrimination may be critical. Stigma and discrimination

are multidimensional influences, existing at multiple levels—individual, interpersonal, organizational, and structural levels—and in multiple forms (i.e., covert and overt biases).[297] Reducing and eliminating stigma and discrimination for SGM youth will require multilevel, multipronged approaches.[201,298-301] Otherwise, interventions may be less efficacious.[302] Prior systematic reviews highlight numerous strategies for reducing stigma and discrimination for other stigmatized populations (e.g., racial/ethnic minority people, people living with mental health disorders), including: group-based therapy interventions to reduce internalized stigma[303]; educational, cooperative learning, media, reading, and motivational interviewing interventions to reduce interpersonal stigma[303-305]; contact-based training and educational programs to reduce organizational stigma[303]; and anti-discrimination policies and legal cases to reduce structural stigma.[262,306] However, the most efficacious methods for reducing stigma and discrimination remain unknown because less than optimal methods evaluated the aforementioned interventions.[303-305] Reducing stigma and discrimination for SGM will be no easy feat, especially given that in the United States SGM protections are currently being taken away and threatened (e.g., the current president removed protections for transgender students in public schools[260]).

Conclusions

With few efficacious interventions for SGM youth, inequities in substance use, mental health problems, and violence for SGM youth are likely to persist. Existing epidemiologic and intervention research can inform future interventions to help bring health equity to SGM youth.

4.7 ACKNOWLEDGEMENTS

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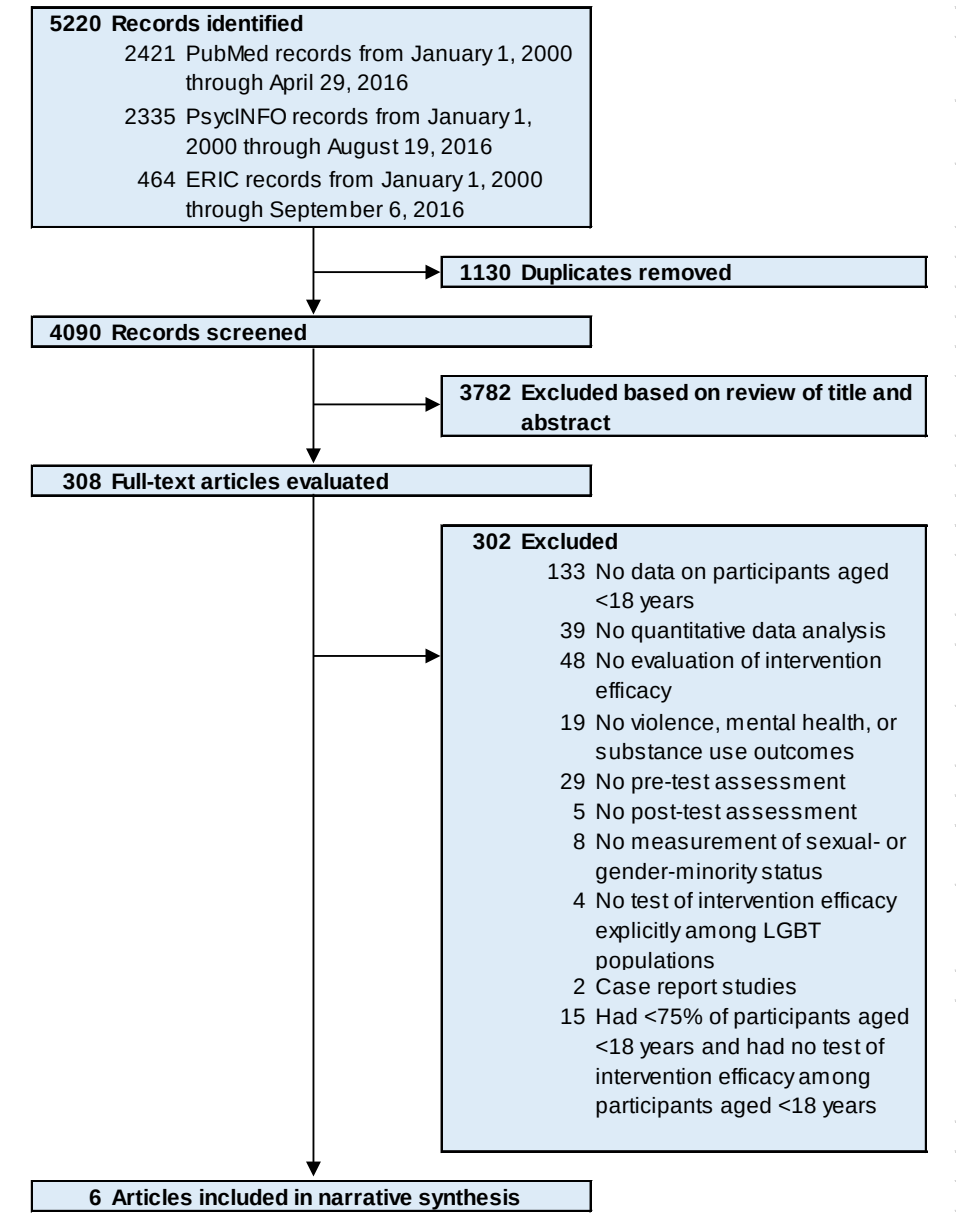
4.8 TABLES AND FIGURES



Note. The specific reasons for exclusion of records at the title and abstract screening level were not recorded.

Figure 4-1. Flow diagram of literature searches and review process results

Table 4-1. Summaries of studies included in this review

Source	Intervention Description	Intervention Length	Evaluation Design	Sampling and Recruitment	Inclusion Criteria	Sample Characteristics	Outcome Measures	Results
Costa et al. (2015)	Aimed at relieving distress associated with puberty development in adolescents with gender dysphoria, this study examined the effects of psychological-only and psychological-and-puberty-suppression interventions on youths' psychosocial functioning. These interventions were delivered following guidelines set by the World Professional Association for Transgender Health Standards of Care. Psychological support was provided to youth and their families (both together and separately) to support them through the early recognition and non-judgmental acceptance of youths' gender identities, and ameliorate any behavior, emotion, or relationship problems. A variety of psychotherapeutic approaches were used, and sometimes included social and educational interventions. Puberty suppression was provided using gonadotropin-releasing hormone analogs.	Immediately following baseline assessment, all youth received psycho-logical support during the entire duration of the study at least once per month. Nine months (on average) after baseline assessment, puberty suppression was initiated for the psycho-logical-and-puberty-suppression intervention group.	Nonrandomized comparison group pretest-posttest design using multiple posttests. Youths were assessed at baseline, 6, 12, and 18 months (corresponding to Time 0 through 3). At Time 0, no intervention had taken place. At Time 1, all participants had received psychological support. At Times 2 and 3, some participants had received only the psychological intervention (i.e., the psychological-only intervention group); and some participants had received psychological and puberty suppression interventions (i.e., the psychological-and-puberty-suppression intervention group). Participants were placed in the psychological-and-puberty-suppression intervention group if they had: a presence of gender dysphoria from early childhood on; an increase in gender dysphoria after their first puberty changes; an absence of psychiatric comorbidity that interferes with the diagnostic work-up or treatment; adequate psychological and social support during treatment; and a demonstration of knowledge and understanding of the effects of puberty suppression, cross-sex hormone treatment, surgery, and the social consequences of sex reassignment. Otherwise, participants were placed in the psychological-only intervention group.	Youth were recruited from a population of gender dysphoric youth who were referred to a gender identity clinic in London, England from 2010-2014. All youth who completed the standard-of-care diagnostic assessments (around 6 months after entry into the clinic) were invited to take part in the study.	At baseline, all participants were diagnosed with Gender Identity Disorder (per the DSM-IV-TR criteria). Youths and their parents gave informed consent.	Total sample contained 201 youth; 101 youth were in the psychological-only intervention group; and 100 youth were in the psychological-and-puberty-suppression intervention group. The two intervention groups did not differ with regards to natal sex, age, living arrangement, and education. <u>Total Sample (n=201)</u> Age (mean): 15.52 years at baseline (range: 12-17 years). Assigned Birth Sex: 62.2% female; 37.8% male.	<u>Psychosocial Functioning</u> Children's Global Assessment Scale	In the total sample, compared to Time 0 (57.73), psychosocial functioning significantly improved at Time 1 (60.68; $p<0.001$), Time 2 (63.31; $p<0.001$), and Time 3 (64.93; $p<0.001$). The psychological-only intervention group did not significantly differ from the psychological-and-puberty-suppression intervention group in psychosocial functioning at any time point (*p-values* range: 0.14-0.73). Among the psychological-only intervention group, compared to Time 0 (56.63), psychosocial functioning significantly improved at Time 1 (60.29; $p=0.05$), Time 2 (62.97; $p=0.005$), and Time 3 (62.53; $p=0.02$). However, psychosocial functioning was not significantly different for Time 1 versus 2 ($p=0.22$), Time 1 versus 3 ($p=0.37$), or Time 2 versus 3 ($p=0.88$). Among psychological-and-puberty-suppression intervention group participants, compared to Time 0 (58.72), psychosocial functioning did not significantly differ at Time 1 (60.89; $p=0.19$), but was significantly higher at Time 2 (64.70; $p=0.003$) and Time 3 (67.40; $p<0.001$). While psychosocial functioning significantly improved from Time 1 versus 3 ($p=0.001$), there were not significant differences for Time 1 versus 2 ($p=0.07$), and Time 2 versus 3 ($p=0.35$).

Table 4-1. Continued

Source	Intervention Description	Intervention Length	Evaluation Design	Sampling and Recruitment	Inclusion Criteria	Sample Characteristics	Outcome Measures	Results
de Vries et al. (2011)	Aimed at enabling gender dysphoric youths to explore their gender identity without the distress of physical puberty development, this intervention used puberty suppression via gonadotropic-releasing hormone analogues.	Puberty suppression was conducted for 1.9 years (on average).	One-group pretest-posttest design. Youths were assessed at baseline and post-intervention, which was 3.0 years on average after baseline (prior to the start of cross-sex hormones). Puberty suppression was initiated 1.1 years, on average, after baseline assessment.	From 2000-2008, 140 of 196 referred youth were considered eligible for medical intervention at a gender identity clinic in Amsterdam, Netherlands. Of the 140 youth, 111 youths were given the intervention. Participants of this study were the first 70 youth who had subsequently started cross-sex hormone treatment.	Adolescents were eligible for puberty suppression when they: were diagnosed with gender identity disorder; have shown persistent gender dysphoria since childhood; live in a supportive environment; and have no serious comorbid psychiatric disorders that may interfere with the diagnostic assessment. Youths and their parents gave informed consent.	Total sample contained 70 youths. Total Sample (n=70) Age (mean): 13.56 years at baseline (range: 11-17 years). Assigned Birth Sex: 52.9% female; 47.1% male. Sexual Orientation: 88.6% same-natal-sex attractions; 8.6% had both-natal-sex attractions; 2.8% reported something else.	<u>Depressive Symptoms</u> Beck Depression Inventory-II <u>Anxiety Symptoms</u> State-Trait Anxiety Inventory <u>Internalizing Symptoms</u> Youth Self-Report Child Behavior Checklist <u>Externalizing Symptoms</u> Youth Self-Report Child Behavior Checklist	Depressive symptoms decreased significantly from baseline to post-intervention (8.31 versus 4.95; $F(1,39)=9.28$; $p=0.004$). Anxiety symptoms did not significantly decrease from baseline to post-intervention (39.43 versus 37.95; $F(1,39)=1.21$; $p=0.276$). Internalizing symptoms decreased significantly from baseline to post-intervention (56.04 versus 49.78; $F(1,52)=15.05$; $p<0.001$). The percentage of youths scoring in the clinical range for internalizing symptoms significantly decreased from baseline to post-intervention (29.6% versus 11.1%; $\chi^2(1)=5.71$; $p=0.017$). Internalizing symptoms decreased significantly from baseline to post-intervention (61.00 versus 54.46; $F(1,52)=22.93$; $p<0.001$). Externalizing symptoms decreased significantly from baseline to post-intervention (53.30 versus 49.98; $F(1,52)=7.26$; $p=0.009$). Externalizing symptoms decreased significantly from baseline to post-intervention (58.04 versus 53.81; $F(1,52)=12.04$; $p=0.001$).

Table 4-1. Continued

Source	Intervention Description	Intervention Length	Evaluation Design	Sampling and Recruitment	Inclusion Criteria	Sample Characteristics	Outcome Measures	Results
de Vries et al. (2014)	Aimed at providing high-quality clinical care to youths with gender dysphoria, this intervention included puberty suppression, cross-sex hormones, and gender reassignment surgery. Puberty suppression was provided using gonadotropin-releasing hormone analogs. Cross-sex hormones were provided. Gender reassignment surgery included vaginoplasty for transwomen, and mastectomy and hysterectomy with ovariectomy for transmen.	Participants started puberty suppression at mean age 14.8 years (range: 11.5-18.5 years), cross-sex hormones at mean age 16.7 years (range: 13.9-19.0 years), and gender reassign-ment surgery at mean age 19.2 years (range: 18.0-21.3 years).	One-group pretest-midtest-posttest design. Youths were assessed at baseline (Time 0), during intervention (Time 1; approximately 3.1 years after baseline; after initiation of puberty suppression and before initiation of cross-sex hormones), and post-intervention (Time 2; approximately 7.1 years after baseline; and 1 year after gender reassignment surgery).	Participants were recruited from the first cohort of 70 youths who had gender dysphoria, who were prescribed puberty suppression in Amsterdam, Netherlands, and who continued with gender reassignment surgery between 2004 and 2011.	Youths were eligible for puberty suppression, cross-sex hormones, and gender reassignment surgery at the respective ages of 12, 16, and 18 years if they had: a history of gender dysphoria; no psychosocial problems; adequate family or other support; and good comprehension of the impact of medical interventions. At post-intervention, from 2008-2012, young adults were eligible if they were ≥1 year past their gender reassignment surgery. Puberty suppression started after youths entered the first stages of puberty (Tanner stages 2-3). At baseline and Time 1, youths and their parents provided consent. At Time 3, only participants provided consent.	Total sample contained 55 participants. Total Sample (n=55) Age (mean): 13.6 years at baseline (range: 11.1-17.0 years). Gender: 40.0% transwomen; 60.0% transmen.	Depressive Symptoms Beck Depression Inventory Anxiety Symptoms State-Trait Anxiety Inventory Psychosocial Functioning Children's Global Assessment Scale Internalizing Symptoms Child/Adult Behavior Checklist Youth/Adult Self-Report Externalizing Symptoms Child/Adult Behavior Checklist Youth/Adult Self-Report	Depressive symptoms had significant quadratic trends over time (p=0.04), decreasing from baseline (7.89) to Time 1 (4.10), and increasing at Time 2 (5.44). Trends were similar by gender. Anxiety symptoms did not have linear (p=0.42) or quadratic (p=0.47) trends over time. However, the linear trends were different by gender (p=0.05): for transmen, symptoms decreased over time (44.41 at baseline; 41.59 at Time 1; and 39.20 at Time 2); for transwomen, average symptoms were lower at baseline and Time 1 (31.87 and 31.71) than at Time 2 (35.83). Psychosocial functioning increased linearly over time (p<0.001). Psychosocial functioning was 71.13 at baseline, 74.81 at Time 1, and 79.94 at Time 2. Trends were similar by gender. Internalizing symptoms linearly decreased over time (p<0.001). Average internalizing symptoms were 60.83 at baseline, 54.42 at Time 1, and 50.45 at Time 2. Trends were similar by gender. Overall, prevalence of clinical levels of internalizing symptoms significantly decreased from baseline to Time 1 (30.0% vs. 12.5%), plateauing at Time 3 (10.0%). Internalizing symptoms had quadratic trends over time (p=0.008), decreasing from baseline to Time 1 (55.47 to 48.65), and increasing Time 2 (50.07). Trends were similar by gender. Overall, prevalence of clinical levels of internalizing symptoms significantly decreased from baseline to Time 1 (30.0% versus 9.3%), but Time 2 prevalence (11.6%) was similar to both prior time points. Externalizing symptoms decreased linearly over time (p<0.001; 57.85 at baseline, 53.85 at Time 1, and 47.85 at Time 2). Trends were similar by gender. Overall, the prevalence of clinical levels of externalizing symptoms was not significantly different from baseline to Time 1 (40.0% versus 25.0%), but was significantly lower at Time 2 (2.5%). Externalizing symptoms did not have linear (p=0.14) or quadratic (p=0.09) trends. But linear trends differed by gender (p=0.005): for transmen, there were linear decreases (57.16 at baseline; 52.64 at Time 1; and 50.24 at Time 2); for transwomen, symptoms were lower at baseline and Time 1 (46.00 and 44.71) than at Time 3 (50.24). Overall, prevalence of clinical levels of externalizing symptoms did not significantly change (21.0% at baseline, 11.6% at Time 1, 7.0% at Time 2).

Table 4-1. Continued

Source	Intervention Description	Intervention Length	Evaluation Design	Sampling and Recruitment	Inclusion Criteria	Sample Characteristics	Outcome Measures	Results
Diamond et al. (2012)	Aimed at reducing suicidal ideation and depressive symptoms among sexual-minority youth, this intervention tested a form of Attachment-Based Family Therapy specifically tailored to the needs of sexual-minority youth and their families. Attachment-Based Family Therapy is an empirically informed, manualized family-based treatment, but this specific intervention was adapted by researchers and clinicians who had experience working with sexual-minority youth. All therapy sessions were delivered in-person by a PhD-level clinical psychologist. Sessions were provided to an adolescent by themselves, parent(s) by themselves, and an adolescent and their parent(s) together. This intervention was guided by attachment theory, structural family therapy, multidimensional family therapy, and emotion-focused therapy.	Completing at least 8 sessions was considered a full intervention dosage. The number of sessions per participant ranged from 8 to 16, with an average of 12 sessions per family. Sessions were ~60 minutes in length and were conducted on a weekly basis.	One-group pretest-midtest-posttest design. Research assistants naïve to the study purpose administered assessments at baseline, 6 weeks later (halfway through intervention), and 12 weeks later (post-intervention).	Patients were recruited from two private psychiatric hospitals in Philadelphia, Pennsylvania, United States, where participants had been admitted for suicidal ideation or attempts. Social work staff employed by the hospitals screened potential participants one week before their discharge, and youths endorsing significant levels of suicidal ideation (per a score ≥ 31 on the Suicidal Ideation Questionnaire-Junior) were referred to the study.	Youths had to self-identify as gay/lesbian or bisexual and had to report significant levels of suicidal ideation as evidenced by a score ≥ 31 on the Suicidal Ideation Questionnaire-Junior. Youths were excluded if they had current psychosis or mental retardation. Youths and their parents gave informed consent.	Total sample contained 10 youths. Regarding parental participation, 40% of youths completed the intervention with two parents, and 60% completed the intervention with their mother only. <u>Total Sample (n=10)</u> Age (mean): 15.10 years at baseline (range: 14-18 years). Gender: 80% female; 20% male. Sexual Orientation: 30% identified as exclusively gay or lesbian; 10% identified as primarily gay and also attracted to females; 60% identified as primarily lesbian and also attracted to males. Race/Ethnicity: 20% White; 50% African American; 20% Multiracial; 10% other.	<u>Depressive Symptoms</u> Beck Depression Inventory-II <u>Suicidal Ideation Symptoms</u> Suicidal Ideation Questionnaire-Junior	Average depressive symptoms decreased over the course of treatment ($F(2,18)=4.59$; $p=0.03$; $d=0.90$). Average suicidal ideation decreased over the course of treatment ($F(2,18)=18.78$; $p=0.001$; $d=2.10$).

Table 4-1. Continued

Source	Intervention Description	Intervention Length	Evaluation Design	Sampling and Recruitment	Inclusion Criteria	Sample Characteristics	Outcome Measures	Results
Lucassen et al. (2015)	Aimed at reducing depressive symptoms for sexual-minority youth, this intervention used a 7-module computerized cognitive behavioral therapy intervention delivered via CD-ROM on personal computers and using a paper-based user notebook. This intervention used the medium of a fantasy world, where the user's avatar is faced with a series of challenges to rid a virtual world of gloom and negativity. Based on Cognitive Behavioral Therapy theories and adapted from an efficacious intervention (SPARX), this intervention was tailored to the needs of sexual-minority youth by having them contribute to the adaptation process. Participants could choose whether to complete the program at home, at a youth-led organization for sexual minority youth, at a selected high school, or on a dedicated computer where the study was based.	Each of the 7 modules took ~30 minutes to complete. Participants were instructed to complete one or two modules per week and to finish all modules within two months.	One-group pretest-posttest-posttest design. Youths completed questionnaires at baseline, immediately post-intervention, and 3 months post-intervention.	One youth-led organization for sexual-minority youth and four high schools promoted the study in Auckland, New Zealand. The study was also advertised and endorsed by the sexual-minority media.	Youth had to be: attracted to the same sex, both sexes, or not sure of their sexual attractions; 13-19 years old; have depressive symptoms (i.e., Child Depression Rating Scale – Revised raw score ≥30) at baseline; and living in Auckland, New Zealand. Sexual-minority youth with severe depressive symptoms, at risk of suicide or self-harm were eligible, if they reported receiving support from a school guidance counselor, therapist, or general practitioner. Those receiving antidepressant medication or other relevant therapies were able to take part; these additional treatments were documented at the pre-intervention assessment. For youths <16 years, youths and their parents gave informed consent. For youths ≥16 years, only youths gave informed consent.	Total sample contained 21 youths. <u>Total Sample (n=21)</u> Age (mean): 16.5 years at baseline (range: 13-19 years). Gender: 47.6% female; 52.3% male. Sexual Orientation: 47.6% had same-sex attractions; 47.6% had both-sex attractions; 4.8% were not sure. Race/Ethnicity: 71.4% New Zealand European; 9.5% Māori; 4.8% Pacific Ethnicity; 14.3% Asian.	<u>Depressive Symptoms</u> Children's Depression Rating Scale – Revised Reynolds Adolescent Depression Scale Mood and Feelings Question-naire <u>Anxiety Symptoms</u> Spence Children's Anxiety Scale <u>Hopeless-ness</u> Kazdin Hopeless-ness Scale for Children	Depressive symptoms decreased significantly from baseline to immediate post-intervention (mean change=-7.43; 95% CI: -10.79, -4.07; p<0.0001; d=1.01). Depressive symptoms remained similar from immediate post-intervention to 3-month post-intervention (mean change=-0.62; 95% CI: -5.82, 4.58; p=0.81). Depressive symptoms decreased significantly from baseline to immediate post-intervention (mean change=-7.90; 95% CI: -12.17, -3.64; p=0.001; d=0.84). Depressive symptoms remained similar from immediate post-intervention to 3-month post-intervention (mean change=-0.86; 95% CI: -5.41, 3.70; p=0.70). Depressive symptoms decreased significantly from baseline to immediate post-intervention (mean change=-6.19; 95% CI: -11.13, -1.25; p=0.02; d=0.57). Depressive symptoms remained similar from immediate post-intervention to 3-month post-intervention (mean change=0.67; 95% CI: -5.58, 6.92; p=0.83). Anxiety symptoms decreased significantly from baseline to immediate post-intervention (mean change=-7.86; 95% CI: -11.62, -4.10; p<0.0001; d=0.95). Anxiety symptoms were not assessed 3 months post-intervention. Hopelessness scores decreased significantly from baseline to immediate post-intervention (mean change=-1.43; 95% CI: -2.43, -0.43; p=0.008; d=0.65). Hopelessness was not assessed 3 months post-intervention survey.

Table 4-1. Continued

Source	Intervention Description	Intervention Length	Evaluation Design	Sampling and Recruitment	Inclusion Criteria	Sample Characteristics	Outcome Measures	Results
Schwinn et al. (2015)	Aimed at reducing sexual-minority youths' substance use via an online intervention, this intervention had an animated young adult narrator guide youths through interactive games, role-playing, and writing activities. Activities focused on skills for identifying and managing stress, making decisions, addressing drug use rates, and teaching drug refusal skills. This intervention was guided by a social competency skill-building strategy and minority stress theory.	3 sessions were completed throughout a 4-week period. Youths completed each session in 14 minutes, on average.	Randomized controlled trial using pretest-posttest design. Youths completed online questionnaires at baseline, immediately post-intervention, and 3-months post-intervention. Youths completed follow-up questionnaires approximately 1 month and 4.5 months after baseline. Authors only reported baseline and 3-month post-intervention results.	Youths were recruited from across the United States through Facebook ads posted to the pages of 15- and 16-year-olds. Six ads ran for 9 days in the spring of 2014.	Youths were included if they were 15 or 16 years of age, a United States resident, had access to a personal computer, and identified as gay, lesbian, bisexual, transgender, or questioning. Youths had to correctly answer a five-question quiz on study procedures to participate. This study had a waiver of parental permission.	Total sample contained 236 youth. Intervention and control groups did not differ by demographics at baseline. Intervention Arm (n=119) Age (mean): 16.05 years at baseline (range: 15-16 years). Gender: 32.1% male; 49.6% female; 18.3% queer/fluid/other. Sexual Orientation: 39.4% had same-sex attractions; 49.5% had both-sex attractions; 5.5% had opposite-sex attractions; 5.6% were unsure. Race/Ethnicity: 66.1% White; 12.8% Hispanic; 7.3% Black; 6.4% Asian; 7.4% other. Control Arm (n=117) Age (mean): 16.10 years at baseline (range: 15-16 years). Gender: 33.3% male; 52.2% female; 4.5% queer/fluid/other. Sexual Orientation: 37.9% had same-sex attractions; 49.1% had both-sex attractions; 6.9% had opposite-sex attractions; 6.1% were unsure. Race/Ethnicity: 58.1% White; 13.7% Hispanic; 12.0% Black; 8.5% Asian; 7.7% other.	Alcohol Use Number of times drank in past 30 days Cigarette Smoking Number of times smoked in past 30 days Marijuana Use Number of times used in past 30 days Other Drug Use Number of times used in past 30 days Perceived Stress Scores ranged from 1 (low) to 5 (high)	At baseline, there was not a significant difference for intervention versus control groups (p=0.09). At 3-month follow-up, there was not a significant difference for intervention versus control groups in mean alcohol use frequency (1.29 versus 1.10; $p \geq 0.05$; $t=0.66$). At baseline, there was not a significant difference for intervention versus control groups (p=0.82). At 3-month follow-up, there was not a significant difference for intervention versus control groups in mean cigarette smoking frequency (0.72 versus 0.90; $p \geq 0.05$; $t=0.59$). At baseline, there was not a significant difference for intervention versus control groups (p=0.51). At 3-month follow-up, there was not a significant difference for intervention versus control groups in mean marijuana use frequency (1.63 versus 1.74; $p \geq 0.05$; $t=0.41$). At baseline, there was not a significant difference for intervention versus control groups (p=0.31). At 3-month follow-up, intervention group participants had significantly lower mean other drug use frequency than control group participants (1.03 versus 1.09; $p<0.05$; $t=2.16$; $d=0.34$). At baseline, there was not a significant difference for intervention versus control groups (p=0.72). At 3-month follow-up, intervention group participants had significantly lower mean perceived stress than control group (3.05 versus 3.33; $p<0.05$; $t=2.27$; $d=0.34$).

Table 4-2. Summary of methodological quality ratings by study

Source	Global Rating	Selection Bias	Study Design	Confounders	Blinding	Data Collection Method	Withdrawals and Dropouts
Costa et al. (2015)	Weak	Weak	Moderate	Weak	Moderate	Strong	Weak
de Vries et al. (2011)	Weak	Weak	Moderate	Weak	Moderate	Strong	Weak
de Vries et al. (2014)	Weak	Weak	Moderate	Weak	Moderate	Strong	Weak
Diamond et al. (2012)	Weak	Weak	Moderate	Weak	Moderate	Strong	Strong
Lucassen et al. (2015)	Weak	Weak	Moderate	Weak	Moderate	Strong	Strong
Schwinn et al. (2015)	Weak	Weak	Strong	Weak	Moderate	Weak	Strong

Note. Methodological assessments were determined according to the Quality Assessment Tool for Quantitative Studies (QATQS) checklist.

5.0 DISSERTATION DISCUSSION

When I entered the PhD program 5 years ago, I wanted my research to straddle the public health fields of epidemiology and intervention research. This dissertation reflects the current culmination of my work in these areas, and highlights opportunities for me to pursue future research agendas in both epidemiologic and intervention research concerning SGM youth and emerging adults.

5.1 SUMMARY OF DISSERTATION FINDINGS

Six years ago, the Institute of Medicine[1] recommended that additional epidemiologic and intervention research be conducted using the life-course perspective[57] to examine the health of SGM populations. This dissertation addressed these goals by extending three distinct "generations" of public health research for SGM youth and emerging adults: detection, explanation, and reduction of health inequities.[59,60]

First, this dissertation found that there are distinct sexual-orientation disparities in alcohol use trajectories and alcohol use disorders during emerging adulthood. Several sexual-minority subgroups had higher odds of belonging to heavier alcohol use trajectories than completely heterosexual populations. These differences partially explained the higher risk of alcohol use disorders among sexual-minority women but not among sexual-minority men.

Second, this dissertation found that sexual-minority women were less likely to report having familial and non-familial warmth during childhood and adolescence, which partially explained why they had greater risk of alcohol use disorders. However, there were fewer sexual-orientation differences in warmth for men, which did not explain the sexual-orientation differences in alcohol use trajectories or disorders for men.

Third, this dissertation examined the extant literature on interventions for preventing, reducing, and treating substance use, mental health concerns, and violence victimization among SGM youth. Overall, 6 interventions were evaluated among SGM youth for reducing mental health problems, 1 for substance use, and 0 for violence victimization in the extant scientific literature.

5.2 FUTURE DIRECTIONS

The research conducted within this dissertation offers future directions for both epidemiologic and intervention research pertaining to the health of SGM youth and emerging adults.

Epidemiologic Research

Epidemiologic research can be extended to examine additional study populations. The quantitative data examined in this dissertation were derived from the children of nurses in the United States, who were primarily White. However, prior research has found that alcohol use trajectories and alcohol use disorders differ by race/ethnicity[307] and socioeconomic status,[308] and across countries.[309] Therefore, race/ethnicity, socioeconomic status, and nationality may modify the effects of sexual-orientation differences in alcohol use trajectories and disorders. For example, cross-sectional research on youth has shown that race/ethnicity moderates sexual-

orientation differences in alcohol use.[21] Future research can explore these potential effect modifiers by using methods inclusive of more racially, ethnically, socioeconomically, and globally diverse populations. Additionally, this dissertation did not examine alcohol use trajectories or disorders among transgender populations—despite extant research suggesting that transgender youth and emerging adults experience higher risk of alcohol use[25] and heavy episodic drinking.[28] The lack of longitudinal studies measuring transgender populations impedes knowledge about the development of health outcomes for these populations who are particularly vulnerable to poor health because they often live in unsupportive and harmful social ecologies.[299,310]

Additionally, the etiologies of alcohol use trajectories and disorders are complex.[311,312] This dissertation advanced the research on one hypothesized factor—warmth—but other factors at multiple social ecological levels also influence alcohol use and disorders.[311,312] For example, internalized, interpersonal, and structural stigma and discrimination are associated with increased risk of alcohol use and disorders for SGM populations.[12,18,21,48,87,136-142,226,228,313-315] Alternatively, some factors, such as social support,[158,283,316] are associated with decreased risk of alcohol use and disorders; such factors may also buffer the effects of stigma and discrimination, thereby serving as resiliency factors among SGM populations.[198,201,317] Additional empirical and theoretical research is needed to more holistically investigate the complex causes of SGM inequities in alcohol use trajectories and alcohol use disorders.

More intensive longitudinal observation studies and computational simulation modeling can help address research questions about the complex multilevel factors contributing to SGM inequities in health. Though this dissertation examined how warmth from specific developmental periods influenced alcohol use trajectories and disorders, warmth is not consistent across every

day, month, year, and developmental period. An intensive longitudinal observational study method, such as ecological momentary assessments,[318] can repeatedly measure factors—such as warmth—across smaller periods of time, allowing for more robust estimation of acute and cumulative effects of factors on health for SGM populations compared to their non-SGM peers. Additionally, agent-based modeling[319,320] is a computational simulation technique that allows for the modeling of multilevel influences on health using simulated populations across both time and geographical space. Upon calibration, agent-based models can test hypothetical intervention mechanisms and measure how they change SGM health inequities (e.g.,[321]). Together, ecological momentary assessments and agent-based models can provide nuanced information about how social ecological factors and processes affect alcohol use, thereby illuminating specific modifiable mechanisms during specific developmental periods to be targeted by future interventions.

Intervention Research

Intervention research for SGM youth is truly in its infancy. This dissertation's review of the peer-reviewed scientific research found the existence of 6 interventions designed to reduce mental health problems and 1 to reduce substance use among SGM youth. These intervention studies, however, had less than optimal methodological rigor. Furthermore, no interventions aimed to reduce violence victimization among SGM, which is particularly concerning given that violence victimization experienced during youth has ill effects on health later in the life course.[204] The current lack of interventions evaluated among SGM populations highlights the need for rigorous evaluations of structural, organizational, interpersonal, and individual level interventions for substance use, mental health concerns, and violence victimization for SGM youth. Multilevel interventions (i.e., interventions that target factors at multiple social ecological

levels) may also be particularly useful.[201,298-301] Overall, more methodologically rigorous studies evaluating diverse interventions are necessary to effectively reduce population-level SGM health inequities.

Interventions aimed at reducing SGM health inequities during emerging adulthood are also warranted because SGM emerging adults experience health inequities in substance use, mental health, and violence victimization.[1,28-30,38-47,51-56,322,323] Given the stricter human protections requirements for implementing interventions with people under versus over 18 years, there likely exist more interventions for SGM emerging adults than youth, but a systematic review of interventions for SGM emerging adults has yet to be conducted. Nevertheless, a systematic review of sexual assault interventions showed that there were no interventions for SGM populations,[324] despite their higher risk of being victimized.[28,29,52-56] This exemplifies the existence of important gaps in—and opportunities for—intervention research for SGM emerging adults as well.

There are numerous ways to advance the field of intervention research for SGM youth and emerging adults. Investigators can:

1. Evaluate the efficacy of interventions designed and implemented by community-based organizations (e.g.,[267]);
2. Conduct outcome evaluations for interventions currently only examined via process evaluations (e.g.,[268]);
3. Conduct natural experiments and quasi-experimental studies for policy changes, which is becoming more feasible given better epidemiologic data being collected on SGM youth (e.g., Youth Risk Behavior Surveillance System[269]);
4. Adapt existing interventions to incorporate SGM-specific content (e.g.,[254,255]);

5. Test whether interventions targeting all youth (e.g.,[232-235]) are efficacious specifically among SGM youth; and
6. Develop, implement, and evaluate new interventions specifically tailored for SGM youth (e.g., [256]).

All these methods can bolster the existing portfolio of intervention research to help mitigate health inequities for SGM youth and emerging adults.

5.3 DISSERTATION CONCLUSIONS

Greater than 2 decades of research has identified great health inequities for SGM youth and emerging adults compared with their heterosexual cisgender peers,[1-56] exemplifying great strides in the first generation of research concerning the detection of health inequities. Epidemiologic research has also identified many explanatory determinants of these inequities, helping to meet the goals of the second generation of research. However, the largest gaps in knowledge exist in the third generation of research: the reduction of health inequities. Without more evidence-based interventions, SGM youth and emerging adults will likely continue to experience great health inequities in substance use, mental health problems, and violence victimization. Furthermore, SGM populations will likely continue to experience great health inequities across the life course. Despite the major advances in public health research on SGM populations, intervention research is sorely lacking—but essential—for SGM youth and emerging adults to achieve health equity.

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