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Characterizing the hierarchical depression phenotype in sexually diverse individuals

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Abstract

Introduction: Sexual diverse individuals are at high risk for internalizing psychopathologies, such as depression. Understanding how symptom profiles of heterogeneous psychiatric disorders such as depression differ for sexually diverse vs. heterosexual individuals is thus critical to advance precision psychiatry and maximize our ability to effectively treat members of this population. Research has failed to consider the possibility of hierarchical phenotypes, wherein sexual orientation status may be uniquely and simultaneously associated with both depression broadly and with individual symptoms.

Method: To address these issues, we conducted a moderated nonlinear factor analysis in Wave IV of the Add Health study, using sexual diversity status as a predictor of (a) latent depression, (b) factor loadings, and (c) individual symptoms, with and without controlling for race.

Results: Sexual diversity status was positively and simultaneously associated with latent depression, concentration difficulties, and happiness.

Discussion: These findings suggest that sexually diverse populations not only face greater depression, broadly defined, but are disproportionately more likely to experience concentration difficulties and be happier compared to heterosexual counterparts. Methodologically, these models indicate that the CES-D is scalar noninvariant as a function of sexual diversity status (i.e., identical scores on the CES-D may represent different manifestations of depression for sexually diverse

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CRediT authorship contribution statement

Jenna C. Alley: Writing – review & editing, Writing – original draft, Project administration, Conceptualization. **Daniel P. Moriarity:** Writing – review & editing, Formal analysis. **Matthew B. Figueroa:** Writing – review & editing. **George M. Slavich:** Writing – review & editing, Supervision.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpsychires.2024.03.005>.

and heterosexual participants). Studies examining disparities in depression across heterosexual and sexually diverse samples should thus consider depression broadly as well as specific symptoms. Further, it is critical to examine whether these relations function via different mechanisms.

Keywords

Diversity; Depression; Symptoms; Phenotyping; Precision psychiatry

1. Introduction

Depression is a highly heterogeneous disorder, both with respect to risk factors and variability in symptom profiles (Fried, 2017; Fried et al., 2014). This fact has inspired researchers to characterize which specific symptoms in the depression syndrome are associated with specific risk factors (i.e., a phenotype) (Hilland et al., 2019; Moriarity et al., 2021; van Loo et al., 2018). Clarifying specific risk factor—psychopathology associations is, in turn, critical to advancing precision psychiatry insofar as it can enable the selection of treatments based on a person's symptom profile. For example, knowing that a certain group is more likely than other groups to have a symptom profile characterized by concentration difficulties can lead a mental health care provider to prioritize concentration-oriented therapies to maximize effectiveness. This work is also important to ensure the rigor of future research because characteristics that are differentially associated with symptoms within a syndrome cause an issue called measurement noninvariance when testing said characteristic as a predictor of symptom scores (e.g., sum score, latent variable) (Putnick and Bornstein, 2016; Moriarity et al., 2022). Briefly, measurement noninvariance is when a measure quantifies a construct differently across different groups. In this situation, standard analytic options (i.e., mean comparison) will not suffice because standard scoring procedures will not be equally valid for all groups. Therefore, phenotyping research is necessary both to maximize the translatability psychiatric research and enhance the measurement validity of assessments in diverse populations (Bauer, 2023).

Research examining individuals at high risk of developing depression has found that sexually diverse adults and youth experience depression at much higher rates than their heterosexual counterparts (Argyriou et al., 2021; Bostwick et al., 2010; Chakraborty et al., 2011; King et al., 2008; Pakula and Shoveller, 2013; Ploderl and Tremblay, 2015; Wittgens et al., 2022). However, across studies, the strength of this association is quite variable. For example, Marshal et al. (2011) conducted a meta-analysis of studies examining depression and suicidality in sexually diverse youth, and found that although sexually diverse youth consistently have higher rates of depression and suicidality, the strength of these associations varied across depression assessment methods (e.g., using a one item scale vs. a widely validated multi-item measure, such as the Center for Epidemiologic Studies–Depression Scale (CES-D) (Radloff, 1977). Although variability in the strength of findings is clearly impacted by the scale used to measure depression, we can also see variability due to the ways in which scholars use specific scales. For example, studies can test differences in depression symptoms as a singular diagnostic construct (e.g., total or latent symptom scores) or can test differences in individual symptoms to characterize symptom-specific phenotypes. These two approaches can yield very different conclusions. Careful consideration of how

measures are used is particularly important for widely used scales like the CES-D, including how these scales might function differently across populations.

Research that takes a symptom-level approach, and that examines how individual constructs and items differ across groups, can provide far more specificity in our understanding of depression in specific populations as compared to simply examining latent scores. For example, Radusky et al. (2021) used the 20-item CES-D scale to investigate differential item functioning in a sample of diverse men with and without HIV. They found that regardless of HIV status, sexually diverse men were less likely to endorse factors “people were unfriendly” and “I felt like people disliked me,” and more likely to endorse the factor “I did not feel like eating,” than their heterosexual counterparts. This finding contradicts the theoretical prediction that those who face more stigma should have more negative interpersonal experiences (Meyer, 2003), and it highlights that sexually diverse men might be more prone to appetite suppression and malnourishment than non-sexually diverse peers. To date, however, Radusky et al. (2021) is one of—if not the only—study to have examined the differential functioning of individual items of the CES-D in sexually diverse populations.

Critically, the findings articulated above may not generalize to the larger sexually diverse population given that their sample was only men and was focused on assessing the impact of HIV status as well as sexual orientation. Therefore, research using more representative samples is needed. Additionally, the statistical techniques chosen were exclusively symptom-specific, failing to consider that sexual diversity might be simultaneously and uniquely associated with both depression generally and individual symptoms in a “hierarchical phenotype” (Moriarity et al., 2023). Without modeling both levels of depression measurement, it is impossible to falsify theories about whether sexual diversity is associated with depression and/or individual symptoms. To address these concerns, we leverage moderated nonlinear factor analysis (MNLFA) to explore the possibility of sexual diversity-centered hierarchical phenotypes of depression symptoms (i.e., that sexual diversity might be simultaneously and uniquely associated with depression generally as well as individual symptoms) in a diverse sample of 5065 adults.

2. Method and materials

Design and population:

Data were derived from the National Longitudinal Study of Adolescent to Adult Health (Add Health). The initial Add Health sample was drawn from 80 high schools and 52 middle schools throughout the United States (Harris, 2013; Bradley et al., 2010; Irwin et al., 1999). A subsample of students ($n = 20,747$) were asked to complete additional in-home interviews and were contacted for follow-up interviews between 2001 and 2002 (Wave III) and 2007–2008 (Wave IV). Between 2016 and 2018 (Wave V), respondents were contacted again for follow-up interviews. The present article uses data from Wave IV, which has a response rate of 80.3% for the full sample. For the purpose of the present analysis, we only used the publicly available data from Wave IV, which gave us an analytic sample of 5114 adults, ranging in age from 25 years to 34 years ($M = 29$), about 14% of which were sexually diverse. For this study the only exclusion criteria we implemented was pertaining to sexual orientation, specifically we excluded participants who didn't report their sexual orientation

($n = 49$) all other data and participants were retained in the full sample which gives us a full sample ($N = 5065$). Since we analyzed publicly available pre-collected data, this study was IRB exempt.

Sexual diversity status:

Wave IV of the Add Health dataset assessed sexual orientation with the following question “Please choose the description that best fits how you think about yourself” participants were given the options of “100% heterosexual (straight)”, “mostly heterosexual (straight) but somewhat attracted to people of your own sex”, “bisexual that is attracted to men and women equally,” “mostly homosexual (gay) but somewhat attracted to people of the opposite sex”, “100% homosexual”, “not sexually attracted to either males or female”, “refuse” and “don’t know”. For the purpose of the present analysis, we created a binary variable with 100% heterosexual as our reference group and all other options (excluding refuse and don’t know; $n = 49$) as the sexually diverse group.

Depression Criteria:

Wave IV of the Add health dataset used a modified 10-item version of the Center for Epidemiologic Studies Depression CES-D-10. This scale has acceptable reliability and validity among adolescents and adults (Bradley et al., 2010; Irwin et al., 1999). Across waves 1, 2, 3 and 4, participants were asked about their frequency of symptoms related to depression across the past week on a scale from 0 (*rarely*) to 3 (*most of the time or all the time*). Specifically, the scale addresses the following symptoms of depression; being bothered by things, not being able to shake off the blue, felt as good as others, trouble concentrating, felt depressed, felt tired, felt happy, enjoyed life, felt sad, and felt disliked. The scale also shows good internal consistency ($\alpha = .92$; Irwin et al., 1999) ($\alpha = .85$; Bradley et al., 2010). Specific wording of the scale can be found in Table 1.

Statistical Analyses:

Models were estimated in Mplus 8 (Radusky et al., 2021), and model execution and result summaries were facilitated using the MplusAutomation package (Hallquist and Wiley, 2018) in R 3.6.2 (Team, 2013). All models accounted for relevant survey weights as dictated by the Add Health data use guidelines. An initial model fit single factor confirmatory factor analyses (CFAs) to the CES-D using the robust weighted least squares estimator (WLSMV) (Flora and Curran, 2004). The Comparative Fit Index (CFI) (Bentler, 1990), and Root Mean Square Error of Approximation (RMSEA) (Steiger, 1990) were used to evaluate model fit. We report chi-square values for completeness, but this metric is typically oversensitive at the sample sizes used here (Bollen, 1989). According to conventional standards, excellent fit will be indicated by CFI $.95$ and RMSEA values $.05$ and acceptable fit is indicated by CFI $>.90$ and RMSEA = $.05$ -. 10 .

Moderated nonlinear factor analyses (MNLFA) were estimated using maximum likelihood with robust standard errors (MLR). Symptom-specific MNLFA models simultaneously tested sexual diversity as a predictor of (a) an individual symptom intercept, (b) the factor loading of that symptom onto latent depression, and (c) latent depression. Sexual diversity was mean-centered. All parameters were estimated at $\alpha = .05$. Effect sizes and p -values

between sexual diversity and latent depression represent the average effects across all nine symptom-specific modeling iterations. If measurement noninvariance was found, MNFLA models would be re-estimated to extract depression scores corrected for measurement invariance to result in sexual diversity-phenotyping informed depression scores. Specifically, MNLFA models would be re-estimated with sexual diversity as a predictor of both the factor loading and symptom intercept of any items that had either (a) loading or (b) intercept predicted by sexual diversity in the original model (i.e., if sexual diversity predicts the factor loading for depressed mood and the item intercept for concentration difficulties in the original models, the new MNFLA models will include sexual diversity as a predictor of both the factor loading and item intercept for both depressed mood and concentration difficulties). Latent depression values from the sexually diverse phenotype informed models were extracted using Mplus and compared to depression values estimated without accounting for sexual diversity using both Pearson and Spearman correlations (to quantify the continuous and rank-order associations, respectively) and a paired samples *t*-test. Finally, the bivariate correlations between (a) sexual diversity and each latent variable (Spearman) and (b) both latent variables (Pearson) were compared (Steiger, 1980) to test if the strength of association differs as a function of whether sexual identity-based measurement noninvariance is accounted for when generating a latent variable. All supplemental materials, including code, data, and output, are available at <https://osf.io/mzwg3/>.

3. Results

3.1 Confirmatory factor analysis

The unidimensional confirmatory factor analysis for the CES-D had acceptable fit according to the (CFI = .936), but an RMSEA that indicated nonideal fit (RMSEA = .123; 90% CI = .119-.127). The chi-square test was significant ($\chi^2(2729.651)$, $df = 35$, $p < .001$), but, as referenced above, this is unsurprising with sample sizes this large.

3.2 Moderated nonlinear factor analyses

All result can be found in Tables 2 and 3. Non-heterosexual individuals had higher latent depression in all models compared to heterosexual individuals (range of average r s = .111-.120, all p s < .001). Non-heterosexual individuals also reported significantly more concentration difficulties ($r = .043$, $p = .002$) and happiness ($r = .030$, $p = .032$) relative to heterosexual individuals. Sexual orientation was not a significant predictor of factor loadings (all p s > .05).

3.3 Comparison of measurement noninvariance adjusted latent depression to standard latent depression

The latent depression values extracted from the measurement noninvariance-adjusted models were highly correlated with the latent values extracted from the unadjusted CESD model (Pearson $r = .994$, $p < .001$, Spearman $r = .993$, $p < .001$). Paired sample *t*-tests comparing the two found that, on average, the unadjusted latent depression scores were moderately higher than the measurement noninvariance adjusted scores (Cohen's $d = .405$, 95% CI = .376 - .433, $p < .001$). Correlations between sexual diversity and the measurement noninvariance adjusted depression scores was stronger than the correlation between sexual

diversity and the unadjusted depression scores (Spearman $r = .160, p < .001$ and Spearman $r = .133, p < .001$, respectively), a difference that was statistically significant ($Z = 16.448, p < .001$). Therefore, failure to account for sexual diversity-associated measurement noninvariance in CESD depression scores might result in meaningfully different scores and could attenuate effect sizes between sexual diversity and depression.

3.4 Secondary analysis

Given evidence suggesting that racially and ethnically diverse individuals are more likely than their White counterparts to experience chronic, prolonged depression (Bailey et al., 2019), we conducted a follow-up analysis where we ran the same moderated non-linear factor analysis described above while controlling for race. The results revealed that sexually diverse individuals had higher latent depression in all models compared to heterosexual individuals (range of average r s = .112-.122, all p s $< .001$). Sexually diverse individuals reported significantly more concentration difficulties ($r = .042, p = .002$) and happiness ($r = .030, p = .030$) relative to heterosexual individuals. Sexual diversity was not a significant predictor of factor loadings. Given that controlling for race did not meaningfully alter the findings, we do not interpret these specific results any further.

4. Discussion

These results show that sexually diverse individuals in the Add Health dataset exhibit significantly greater latent depression scores compared to heterosexual individuals. Furthermore, sexual diversity is simultaneously, and uniquely, associated with symptom-level differences: namely, greater concentration difficulties and higher happiness in what has been described as a “hierarchical phenotype” (Moriarity et al., 2023). These results thus suggest that standard tests of sexual diversity differences in depression summary scores (e.g., means or latent values) obscure symptom-level nuances in how depression presents in sexually diverse vs. heterosexual patients. Methodologically, this finding underscores that the CESD-10 is *scalar noninvariant* as a function of sexual diversity, contraindicating mean-difference testing that does not incorporate these item-level differences (Putnick and Bornstein, 2016).

It is important to note that because sexual diversity was simultaneously associated with both latent depression and individual symptoms this reflects the unique ways in which sexually diverse individuals’ depression manifests. Unlike studies examining latent depression and symptom-level associations with biological predictors like CRP (Moriarity et al., 2023), the present results—which focus on a social identity as the focal predictor—do not exactly show that identifying as sexually diverse increases one’s depression risk but more likely speaks to how the experiences that sexually diverse individuals face impact depression across multiple levels. Specifically, it is not simply identifying as a sexually diverse individual that puts one at increased risk of depression and concentration difficulties, but it may be that the experiences of marginalization and discrimination faced by those who identify as sexually diverse is more likely the mechanism. For example, discrimination and victimization are important considerations in the association between sexual diversity and depression (Argyriou et al., 2021).

Not all of the present findings suggest that sexually diverse individuals have poorer mental health. Specifically, we also found that sexually diverse individuals reported being happier than their heterosexual counterparts, which may be perplexing given the literature documenting higher depression rates among sexually diverse individuals (Argyriou et al., 2021). However, the nuanced statistical approach used here enables us to disaggregate variance that is shared between the different symptoms (i.e., “latent depression”) and the symptom-specific variance not explained by the latent variable in a way prior studies have not. Indeed, most studies examining depression in sexually diverse populations simply examine latent or summed depression scores, ignoring potential symptom-level effects.

One possible explanation for this unexpected finding is that we did not measure one of the largest protective factors in this population—namely, social support and inclusion in the community. Research has shown that sexual diversity is indirectly associated with depression, anxiety, and happiness via lower levels of safety and belonging (Wilson and Liss, 2022). Therefore, the present results pertaining to happiness may reflect unmeasured characteristics of our sample such that the individuals in this specific dataset may have particularly high social support or may be in better integrated in their sexually diverse communities, which can significantly impact individual symptoms within the overarching construct of depression such as happiness, but may not be strong enough to buffer larger societal issues and stigma (Thomeer and Reczek, 2016) therefore retaining significant differences in latent depression scores. Although it is an important area for future research to address social support, we chose not to measure these variables in the present model given that the measures of social support used in Wave IV of the Add Health dataset set do not assess the specific type of social support (e.g., parental and caretaker support, and romantic relationship functioning and quality) we hypothesize is most relevant for bolstering resilience in sexual diverse individuals (Diamond and Alley, 2022; Slavich, 2020, 2022; Slavich et al., 2023). Future research should thus consider testing the impact of social support in a similar model using more community specific measures of social support such as identity integration, connection to community, and LGBT acceptance and safety.

4.1 Strengths and limitations

Several strengths of this study should be noted. First, we used advanced moderated nonlinear factor analyses (MNLFA) to examine how sexual diversity as a predictor impacted (a) latent depression scores, (b) factor loadings, and (c) individual symptoms as measured by the CES-D in a large openly available dataset that is widely used to examine both heterosexual and sexually diverse well-being and experiences. Second, this approach showed that the CES-D functions differently for sexually diverse individuals and heterosexual individuals within the Add Health dataset, which is critical information for scholars who wish to use the Add Health to characterize the mental health of sexually diverse individuals. Finally, we offer in depth discussion of what these results suggest in terms of implications for future research and offer suggestions for future studies that can help clarify any limitations we have in the existing approach.

Several limitations should also be noted. First, the present analysis used cross-sectional data, which cannot test directionality of sexual diversity related associations with latent

depression or individual symptoms. Although the current dataset does have multiple waves, there is currently no longitudinal extension of MNLFA (our statistical approach). Second, longitudinal data are necessary to explore whether the timescales or mechanisms of the sexual diversity → latent depression differ from the sexual diversity → symptom effects. Third, the abbreviated 10-item CES-D might miss nuance from a more comprehensive measure. For example, Marshal et al. (2011) found strong associations between sexual diversity and suicidality; however, the 10 item CES-D does not assess suicidality, a critical area of further investigation given the high rates in this population.

Fourth, we did not measure protective factors such as relationship status or social support, which may have affected participants' depression scores (Thomeer and Reczek, 2016; Wilson and Liss, 2022). Although doing such analyses (mediation examinations with social support, community connection and safety) as articulated above should be goals for future research, the scales available in Add health do not permit a quality test of these issues and therefore are outside of the scope of the current analysis. Finally, we combine all sexually diverse individuals into one category given the relatively small amount of sexually diverse individuals in the data, which did not enable us to examine differences in depression within the sexually diverse population. This is a limitation given evidence suggesting that there is significant variability in depression within the sexually diverse population (Borgogna et al., 2019). Future work should thus consider re-running such analyses using a sample with a better distribution across heterosexual and sexually diverse categories to provide more specificity.

5. Conclusion

In conclusion, the present study demonstrates that sexual diversity is associated with both latent depression as well as concentration difficulties and happiness, as measured using the 10-item CES-D included in the Add Health dataset, which is a commonly used dataset to study sexually diverse specific experiences, health, and behavior. The findings thus provide important information for scholars investigating depression in sexually diverse populations and shed light on how depression symptoms may differentially manifest in sexually diverse populations. Further, these findings are critically important for those examining depression and or sexually diverse mental health in Add Health and more clearly describe what may be underlying differences in latent depression scores across heterosexual and sexually diverse participants. Future research should consider conducting similar analyses in other datasets with more comprehensive measures of depression to better understand the range of sexual diversity-based depression phenotypes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Item Descriptions

All items begin with “During the past seven days”.

Felt Sad: “You felt sad”
Felt Disliked: “You felt that people disliked you”
Enjoyed Life: “You enjoyed life”
Felt Happy: “You felt happy”
Felt Tired: “You felt that you were too tired to do things”
Felt Depressed: “You felt depressed”
Trouble concentrating: “You had trouble keeping your mind on what you were doing”
Felt as good as others: “You felt you were just as good as others”
Shake Blues: “You could not shake off the blues, even with help from your family and your friends”
Bothered: “You were bothered by things that don’t usually bother you”

Table 2

Latent and Symptom-level Associations with sexual diversity and CES-D items.

Latent Depression ^a	Bothered	Concentration Difficulty	Felt Disliked	Enjoyed Life	Felt Depressed	Felt as Good as Others	Felt Happy	Felt Sad	Shake Blues	Felt Tired
$r = .115$	$r = .005$	$r = .043$	$r = .016$	$r = .021$	$r = .021$	$r = .007$	$r = .030$	$r = .007$	$r = .016$	$r = .013$
$p < .001$	$p = .721$	$p = .002$	$p = .252$	$p = .135$	$p = .144$	$p = .620$	$p = .032$	$p = .601$	$p = .242$	$p = .366$

* = significant results; r = converted correlation coefficient; p = p -value.

^aStatistics for "Latent Depression" represent mean results across all 9 item-level models.

Table 3

Factor Loading Relations with sexual diversity status and CES-D items.

	Bothered	Trouble Concentrating	Felt Disliked	Enjoyed Life	Felt Depressed	Felt as Good as Others	Felt Happy	Felt Sad	Shake Blues	Felt Tired
<i>r</i>	.007	.014	.012	.009	.004	.002	.021	.010	.007	.017
<i>p</i>	.614	.325	.383	.522	.764	.871	.110	.466	.611	.233

r = converted correlation coefficient; *p* = *p*-value.