



## REVIEW

# Transgender and Gender-Diverse Minority Stress and Substance Use Frequency and Problems: Systematic Review and Meta-Analysis

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### Abstract

The goal of this preregistered study was to systematically review and meta-analyze quantitative research examining relationships between minority stress (distal stress, expectations of gender-based rejection, concealment of gender identity, and internalized transphobia) and substance use (alcohol use frequency and problems, and drug use frequency and problems) in transgender and gender-diverse (TGD) samples. Searches of PsycInfo, MEDLINE, Gender Studies, and LGBTQ+ Source databases were conducted for quantitative articles that included effect sizes for cross-sectional associations between TGD-based minority stress and substance use outcomes. Random-effects meta-analyses were used to compute effect sizes for 16 minority stressor-substance use variable pairs. Moderator analyses were conducted for publication year and proportion of the sample assigned female sex at birth, identified as Black, Indigenous, or people of color (BIPOC), or identified as a sexual minority. Thirty-six studies with 76 effect sizes were included. Significant correlations were observed for relationships between distal stress and alcohol use frequency ( $r=0.13$ ; 95% confidence interval [CI]=0.06 to 0.20) and problems ( $r=0.09$ ; 95% CI=0.03 to 0.14), and drug use frequency ( $r=0.16$ ; 95% CI=0.11 to 0.21) and problems ( $r=0.14$ ; 95% CI=0.05 to 0.23). No associations for proximal minority stress-substance use variable pairs were significant. Effect sizes for associations between distal stress and alcohol use frequency were higher in samples with more BIPOC participants ( $z=4.27$ ,  $p<0.001$ ,  $R^2=0.740$ ). Findings indicate that distal, but not proximal, minority stress was significantly associated with drug and alcohol use frequency and problems. Theoretical and clinical implications are discussed.

**Keywords:** meta-analysis; minority stress; substance use; transgender

### Introduction

*Minority stress theory* proposes that sexual and gender minority populations exhibit disproportionate rates of mental health problems owing to unique psychosocial stressors that are related to their actual or perceived sexual and gender identity, rather than from their sexual or gender identity in itself.<sup>1–3</sup> Minority stress theory conceptualizes four types of minority stressors. *Distal* stressors include “those external events that occur in the [transgender or gender-diverse (TGD)] individual’s environment and are related to either knowledge or perception of the individual’s minority status,” (p. 462).<sup>1</sup> They can comprise a wide range of gender identity-based

prejudice events, including physical violence, harassment, and discrimination in a variety of social contexts (family, school, workplace, health care providers, etc.).

In addition, there are three categories of *proximal* stressors, all of which can be broadly conceptualized as internal psychological processes related to one’s gender identity or expression. These categories are expectations of rejection or discrimination based on gender identity or expression, concealment of one’s gender identity, and internalized transphobia or gender-related stigma.<sup>1</sup>

Transgender and gender-diverse (TGD) people commonly experience minority stress during their

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everyday lives.<sup>4,5</sup> They are more likely than their cis-gender peers to be subjected to general interpersonal stressors, including physical and sexual violence,<sup>6,7</sup> intimate partner violence,<sup>8</sup> bullying and peer victimization,<sup>9,10</sup> and cyberbullying.<sup>11</sup> They also experience disproportionately high rates of adverse childhood experiences<sup>12,13</sup> and child abuse,<sup>14,15</sup> with many also being rejected by their families of origin<sup>16</sup> and forced into homelessness<sup>17</sup> or the foster care system.<sup>18</sup>

Previous research has amassed overwhelming evidence that minority stress is significantly associated with poor mental health outcomes in TGD populations, including depression and suicide.<sup>19–22</sup> Furthermore, prior systematic reviews have found consistent associations between experiences of minority stress and substance use in TGD populations.<sup>23</sup> However, it is unclear whether substance use is most associated with different types of minority stress or whether minority stress is more strongly associated with specific types of substance use (frequency of use vs. use problems, alcohol vs. drugs, etc.). Therefore, this study will systematically review and meta-analyze the cross-sectional associations between minority stress and substance use frequency and problems in TGD individuals.

## Methods

Methods for the current meta-analysis were largely derived from a previous meta-analysis on minority stress, depression, and suicidality in TGD populations.<sup>19</sup> The present meta-analysis was preregistered in PROSPERO (CRD42022296027) and follows Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>24,25</sup> Institutional review board review was not required for this study. The PsycInfo, MEDLINE, Gender Studies Database, and LGBTQ+ Source databases were searched for dissertations and peer-reviewed articles published between January 1, 2000 and October 29, 2022. The search string (Supplementary Appendix SA1) was created from keywords relating to minority stress and substance use, and was partially derived from previous meta-analyses on TGD populations.<sup>19,26</sup>

### Eligibility and coding

The current meta-analysis included quantitative research examining the association between TGD minority stress constructs and substance use and problems in TGD samples. Included studies must have met the following criteria: (1) published in English; (2) sample either consists entirely of TGD participants or provides

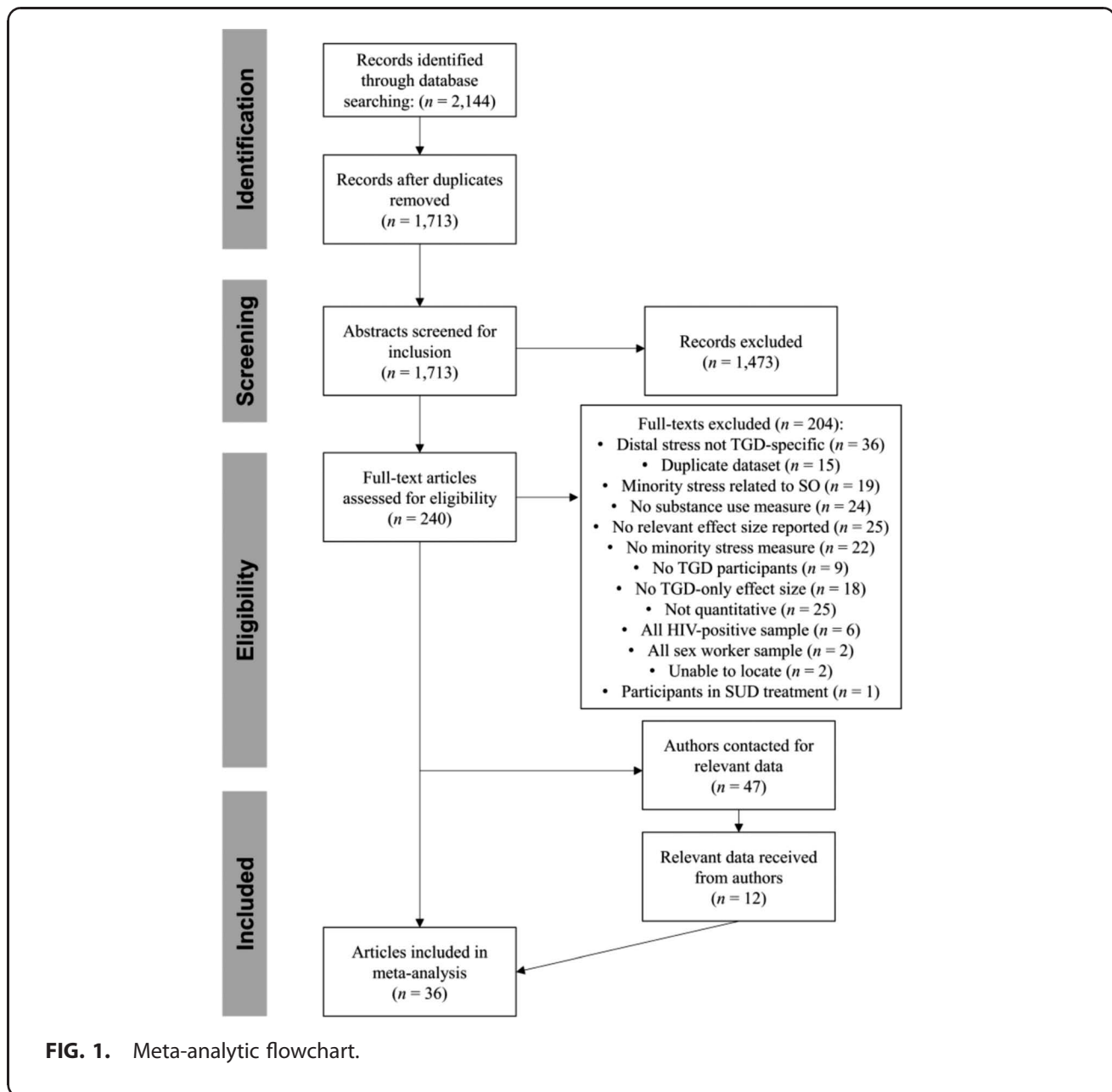
an effect size for TGD subsample(s); (3) uses at least one measure of minority stress (i.e., distal stress, internalized transphobia, concealment, expectations of rejection); (4) uses at least one measure of substance use frequency or problems; and (5) reported an effect size for the cross-sectional association between minority stress and substance use frequency or problems. The current meta-analysis was *a priori* limited to cross-sectional research because of the paucity of longitudinal research on TGD minority stress.<sup>19</sup>

Samples that were entirely composed of HIV+ participants were excluded owing to unique stigma processes associated with HIV and the high comorbidity between HIV and substance use.<sup>27</sup> Likewise, samples composed entirely of sex workers were also excluded because of their unique stigma experiences<sup>28</sup> and high rates of substance use.<sup>29</sup>

The meta-analytic flowchart is given in Figure 1. The search yielded 2144 records (1713 with duplicates removed). The first author reviewed titles and abstracts for all nonduplicate records, of which 240 were selected for full-text review. The first author then reviewed these full texts for inclusion based on the inclusion/exclusion criteria described previously. One-fourth of these full texts were also reviewed by the second author, with disagreement resolved through discussion (percent agreement = 77.0%). In cases where studies included measures of substance use and minority stress but no relevant effect size was reported ( $k = 47$ ), corresponding authors were contacted to request effect size and sample demographic information. Authors provided 19 additional effect sizes from 12 samples.<sup>30–41</sup> Thus, the final meta-analytic sample included 36 studies with 76 effect sizes. All study data were extracted and coded by the first author, and 25% of included articles were independently double coded by the second author, with disagreement resolved through discussion.

### Analytic plan

Meta-analyses were conducted in R<sup>42</sup> using the meta<sup>43</sup> and metafor<sup>44</sup> software packages. Pooled correlation coefficients were calculated for 16 minority stress–substance use pairs, consisting of four types of minority stress (i.e., distal stress, internalized transphobia, expectations of TGD-based rejection, and concealment of gender identity) paired with four types of substance use (i.e., alcohol use frequency, alcohol use problems, drug use frequency, and drug use problems). Item content was determinative in categorizing substance use measures as assessing substance use frequency (e.g.,



“In the past six months, have you used any of the following non-prescription drugs?”<sup>40</sup> versus substance use problems (e.g., the drug abuse screening test).<sup>45</sup> When multiple relevant effect sizes were reported within a study for a single stress-substance use pair (multiple measures of distal stress, measures of individual drug types, etc.), the mean of these effect sizes was used.

Odds ratios and Cohen’s  $d$  were converted to correlation coefficients using formulas specified by Borenstein et al.<sup>46</sup> Standardized regression coefficients were converted to correlation coefficients using the imputa-

tion formula proposed by Peterson and Brown,<sup>47</sup> and chi-square values were converted to correlation coefficients using the formula proposed by Rosenberg.<sup>48</sup>

Because meta-analyses are frequently subject to between-study heterogeneity, and thus an identical true effect size should not be assumed across studies,<sup>49</sup> random effects meta-analyses were conducted. Both the  $Q$  statistic and  $I^2$  were used to quantitatively assess between-study heterogeneity. A significant  $Q$  statistic indicates the presence of significant heterogeneity in effect sizes across studies,<sup>50</sup> whereas  $I^2$  was used to

quantify “the percentage of total variation across studies that is due to heterogeneity rather than chance,” with 25%, 50%, and 75% indicating low, medium, and high proportions of heterogeneity, respectively.<sup>51</sup>

Several study-level variables were extracted from the included articles to conduct moderator analyses using meta-regression. These variables include publication year, sample country, mean age of the sample, proportion of the sample identifying as Black, Indigenous, or people of color (BIPOC), proportion of the sample assigned female sex at birth, and proportion of the sample that identified as a sexual minority (i.e., non-heterosexual). Based on suggestions by previous researchers,<sup>52,53</sup> moderator analyses were only conducted on those minority stress-substance use variable pairs in which  $k \geq 10$ . First, each moderator variable was individually tested for significant moderation using meta-regression. If more than one moderator was found to be significant, then all significant moderators were then simultaneously entered into the meta-regression model.

#### Publication bias

Several methods were used to not only assess, but also reduce the likelihood of publication bias in the current meta-analysis. First, master's theses and doctoral dissertations were included in the search strategy (by searching in the ProQuest Dissertations database) and several ( $k = 4$ ) were included in analyses.<sup>54–57</sup> Second, funnel plots were used to assess for publication bias, both through visual inspection and Egger's regression test of funnel plot asymmetry.<sup>58</sup> This test could only be conducted for minority stress-substance use variable pairs with at least  $k \geq 3$ . Finally, fail-safe  $N$  was used to determine the robustness of the current meta-analysis to hypothetical subsequent nonsignificant results.<sup>59</sup> A cutoff of  $N_{fs} > 5k + 10$  was used to determine if results were robust to publication bias.<sup>59</sup>

#### Study quality

Study quality was determined using the Appraisal Tool for Cross-Sectional Studies (AXIS).<sup>60</sup> AXIS contains 20 items that assess the methodological quality of cross-sectional research studies based on components such as study sampling methods, examination of nonresponses, clarity of research and quantitative analysis procedures, and conformity to ethical best practices for research. The first author independently reviewed each of the included studies for adherence to each of the 20 AXIS items, assigning ratings based on whether the item requirements were met (+), unmet (–), or unknown (?).

## Results

In total, 36 studies with 76 effect sizes were included in the current meta-analysis (see Table 1 for study characteristics and effect sizes and Supplementary Appendix SA2 for additional information about included studies).<sup>30–41,54–57,61–80</sup> Included studies were published between 2010 and 2023, with a median publication year of 2018. Sample sizes of included studies ranged from 6 to 27,715 (mean = 1767.25, standard deviation = 5110.62). The vast majority of included studies derived their samples from the United States or Canada ( $k = 32$ , 88.89%).

Pooled effect sizes for each minority stress-substance use pair are given in Table 2. Small but significant pooled bivariate correlations were observed between distal stress and alcohol use frequency ( $r = 0.13$ ; 95% confidence interval [CI] = 0.06 to 0.20,  $k = 15$ ), alcohol use problems ( $r = 0.09$ ; 95% CI = 0.03 to 0.14,  $k = 8$ ), drug use frequency ( $r = 0.16$ ; 95% CI = 0.11 to 0.21,  $k = 24$ ), and drug use problems ( $r = 0.14$ ; 95% CI = 0.05 to 0.23,  $k = 4$ ). No significant pooled correlations were observed between internalized transphobia and alcohol use frequency ( $r = 0.01$ ; 95% CI = –0.11 to 0.12,  $k = 3$ ), alcohol use problems ( $r = 0.06$ ; 95% CI = –0.02 to 0.13,  $k = 5$ ), drug use frequency ( $r = 0.05$ ; 95% CI = –0.04 to 0.14,  $k = 6$ ) or drug use problems ( $r = 0.01$ ; 95% CI = –0.10 to 0.12,  $k = 1$ )<sup>79</sup>

Similarly, no significant pooled correlations were observed between expectations of TGD-based rejection and alcohol use frequency ( $r = 0.05$ ; 95% CI = –0.06 to 0.17,  $k = 1$ ),<sup>71</sup> alcohol use problems ( $r = 0.04$ ; 95% CI = –0.10 to 0.17,  $k = 3$ ), drug use frequency ( $r = 0.05$ ; 95% CI = –0.06 to 0.17,  $k = 1$ ),<sup>57</sup> or drug use problems ( $r = 0.07$ ; 95% CI = –0.04 to 0.18,  $k = 1$ ).<sup>79</sup> Finally, no significant pooled correlations were observed between concealment of TGD identity and alcohol use frequency ( $r = 0.01$ ; 95% CI = –0.01 to 0.02,  $k = 1$ ),<sup>69</sup> alcohol use problems ( $r = 0.06$ ; 95% CI = –0.06 to 0.19,  $k = 2$ ), or drug use frequency ( $r = –0.05$ ; 95% CI = –0.15 to 0.06,  $k = 1$ ).<sup>57</sup> No included studies reported an effect size for the relationship between concealment and drug use problems.

#### Moderator analyses

Moderator analyses were conducted for the relationship between distal stress, alcohol use frequency, and drug use frequency (because, for these variable pairs,  $k \geq 10$ ). Tested study-level moderator variables included publication year, mean age, proportion of sample assigned female sex at birth, proportion of sample identified as sexual minority, and proportion of sample

**Table 1. Included Studies and Selected Information**

| Author(s) (year) <sup>Ref.</sup>         | n      | Country              | Age  | % AFAB | % SM  | % BIPOC | Predictor | Outcome           | r     |
|------------------------------------------|--------|----------------------|------|--------|-------|---------|-----------|-------------------|-------|
| Coulter et al. (2018) <sup>30</sup>      | 2338   | United States        | 14.7 | 39.5   | 89.1  | 78.3    | DIST      | Alcohol frequency | 0.31  |
| Drazdowski et al. (2016) <sup>31</sup>   | 30     | United States        | 26.2 | —      | 86.7  | 100.0   | DIST      | Drug frequency    | 0.09  |
|                                          |        |                      |      |        |       |         | IT        | Drug frequency    | 0.43  |
| Kassing et al. (2021) <sup>32</sup>      | 41     | United States        | 31.4 | 56.9   | 70.7  | 22.4    | DIST      | Alcohol problems  | 0.10  |
|                                          |        |                      |      |        |       |         | DIST      | Drug problems     | 0.20  |
| McGraw et al. (2021) <sup>33</sup>       | 750    | United States        | 15.1 | —      | 13.4  | 37.2    | DIST      | Drug frequency    | 0.15  |
| Pachankis et al. (2020) <sup>34</sup>    | 25     | United States        | 24.3 | 88.0   | 100.0 | 4.0     | DIST      | Alcohol problems  | 0.26  |
|                                          |        |                      |      |        |       |         | DIST      | Drug problems     | −0.14 |
| Phillips et al. (2020) <sup>35</sup>     | 94     | United States        | 18.8 | 100.0  | 98.9  | 71.3    | DIST      | Drug frequency    | 0.07  |
| Puhl et al. (2019) <sup>36</sup>         | 9674   | United States        | —    | —      | —     | —       | DIST      | Alcohol frequency | 0.07  |
|                                          |        |                      |      |        |       |         | DIST      | Drug frequency    | 0.09  |
| Ruben et al. (2019) <sup>37</sup>        | 6      | United States        | 60.7 | 0.0    | 100.0 | 16.7    | DIST      | Alcohol frequency | 0.17  |
| Walls et al. (2010) <sup>38</sup>        | 16     | United States        | 15.6 | —      | 84.6  | 38.5    | DIST      | Alcohol frequency | 0.38  |
|                                          |        |                      |      |        |       |         | DIST      | Drug frequency    | 0.27  |
| Wolfe et al. (2021) <sup>39</sup>        | 530    | United States        | 31.3 | 64.8   | —     | 18.6    | DIST      | Drug frequency    | 0.27  |
| Xavier Hall et al. (2022) <sup>40</sup>  | 91     | United States        | 22.8 | 0.0    | 80.2  | 76.9    | DIST      | Alcohol problems  | 0.24  |
|                                          |        |                      |      |        |       |         | DIST      | Drug frequency    | 0.13  |
|                                          |        |                      |      |        |       |         | DIST      | Drug problems     | 0.22  |
| Yamasaki and Le (2022) <sup>41</sup>     | 48     | United States        | 23.9 | 83.3   | 97.9  | —       | IT        | Alcohol frequency | 0.17  |
| Hingston (2019) <sup>54</sup>            | 93     | United States        | 20.3 | 86.6   | 94.8  | 12.5    | DIST      | Alcohol problems  | 0.00  |
|                                          |        |                      |      |        |       |         | DIST      | Drug frequency    | 0.18  |
| Sapareto (2018) <sup>55</sup>            | 29     | United States/Canada | 40.2 | 58.6   | 86.2  | 10.3    | DIST      | Alcohol problems  | 0.12  |
|                                          |        |                      |      |        |       |         | DIST      | Drug frequency    | 0.12  |
|                                          |        |                      |      |        |       |         | IT        | Alcohol problems  | −0.11 |
|                                          |        |                      |      |        |       |         | IT        | Drug frequency    | −0.02 |
| Staples (2017) <sup>56</sup>             | 237    | United States        | 28.0 | 64.8   | 85.3  | 26.3    | DIST      | Alcohol problems  | 0.10  |
|                                          |        |                      |      |        |       |         | IT        | Alcohol problems  | −0.01 |
| Wilson (2013) <sup>57</sup>              | 342    | International        | 35.0 | 79.8   | 85.6  | 18.4    | CONC      | Alcohol problems  | 0.00  |
|                                          |        |                      |      |        |       |         | CONC      | Drug frequency    | −0.05 |
|                                          |        |                      |      |        |       |         | ER        | Alcohol problems  | 0.05  |
|                                          |        |                      |      |        |       |         | ER        | Drug frequency    | −0.10 |
|                                          |        |                      |      |        |       |         | IT        | Alcohol problems  | 0.06  |
|                                          |        |                      |      |        |       |         | IT        | Drug frequency    | −0.07 |
| Arayasirikul et al. (2017) <sup>61</sup> | 149    | United States        | 46.1 | 0      | —     | 74.5    | DIST      | Alcohol frequency | 0.30  |
| Beckman et al. (2018) <sup>62</sup>      | 221    | United States        | 48.8 | 13.6   | —     | 11.8    | DIST      | Alcohol frequency | 0.09  |
|                                          |        |                      |      |        |       |         | DIST      | Drug frequency    | 0.05  |
| Benotsch et al. (2013) <sup>63</sup>     | 155    | United States        | 31.9 | 32.9   | —     | 62.3    | DIST      | Drug frequency    | 0.21  |
| Bradford et al. (2013) <sup>64</sup>     | 350    | United States        | 37.1 | 34.6   | 79.1  | 38.3    | DIST      | Alcohol problem   | 0.08  |
|                                          |        |                      |      |        |       |         | DIST      | Drug frequency    | 0.08  |
| Brennan et al. (2012) <sup>65</sup>      | 151    | United States        | 21.0 | 0.0    | —     | 95.0    | DIST      | Drug frequency    | 0.15  |
| Gonzalez et al. (2017) <sup>66a</sup>    | 530    | United States        | 24.0 | 100.0  | 79.2  | 23.2    | DIST      | Alcohol frequency | −0.04 |
|                                          |        |                      |      |        |       |         | DIST      | Drug frequency    | 0.02  |
|                                          |        |                      |      |        |       |         | IT        | Alcohol frequency | −0.08 |
|                                          |        |                      |      |        |       |         | IT        | Drug frequency    | −0.02 |
| Gonzalez et al. (2017) <sup>66b</sup>    | 680    | United States        | 37.0 | 0.0    | 69.7  | 20.4    | DIST      | Alcohol frequency | 0.02  |
|                                          |        |                      |      |        |       |         | DIST      | Drug frequency    | 0.02  |
|                                          |        |                      |      |        |       |         | IT        | Alcohol frequency | 0.05  |
|                                          |        |                      |      |        |       |         | IT        | Drug frequency    | 0.09  |
| Hearld et al. (2019) <sup>67</sup>       | 291    | Dominican Republic   | 26.0 | 0.0    | —     | —       | DIST      | Alcohol frequency | 0.05  |
| Hughto et al. (2021) <sup>68</sup>       | 558    | United States        | 31.3 | —      | —     | 18.1    | DIST      | Drug frequency    | 0.00  |
|                                          |        |                      |      |        |       |         | IT        | Drug frequency    | 0.18  |
| Kcomt et al. (2020) <sup>69</sup>        | 27,715 | United States        | 32.7 | 34.9   | 76.1  | 34.1    | CONC      | Alcohol frequency | 0.01  |
|                                          |        |                      |      |        |       |         | DIST      | Alcohol frequency | 0.05  |
| Kidd et al. (2019) <sup>71</sup>         | 286    | United States        | 34.6 | 51.1   | —     | 54.6    | DIST      | Alcohol frequency | 0.05  |
|                                          |        |                      |      |        |       |         | ER        | Alcohol frequency | 0.05  |
| Kidd et al. (2021) <sup>70a</sup>        | 11,005 | United States        | 36.9 | 0.0    | —     | 19.5    | DIST      | Drug frequency    | 0.33  |
| Kidd et al. (2021) <sup>70b</sup>        | 15,684 | United States        | 26.3 | 100.0  | —     | 15.1    | DIST      | Drug frequency    | 0.24  |
| Klein et al. (2018) <sup>72</sup>        | 5981   | United States        | 36.7 | 41.2   | —     | 22.2    | DIST      | Drug frequency    | 0.25  |
| Lindley et al. (2021) <sup>73</sup>      | 297    | International        | 28.0 | —      | 89.3  | 16.0    | CONC      | Alcohol problems  | 0.13  |
|                                          |        |                      |      |        |       |         | ER        | Alcohol problems  | 0.15  |
|                                          |        |                      |      |        |       |         | IT        | Alcohol problems  | 0.17  |
| Operario et al. (2014) <sup>74</sup>     | 191    | United States        | 37.9 | 0.0    | —     | 84.3    | DIST      | Alcohol frequency | 0.08  |
|                                          |        |                      |      |        |       |         | DIST      | Drug frequency    | 0.09  |
| Peitzmeier et al. (2019) <sup>75</sup>   | 150    | United States        | 27.5 | 100.0  | 88.0  | 24.8    | DIST      | Alcohol frequency | 0.07  |
| Reisner et al. (2014) <sup>76</sup>      | 191    | United States        | 36.3 | 0.0    | —     | 84.3    | DIST      | Drug frequency    | 0.01  |

(continued)

Table 1. (Continued)

| Author(s) (year) <sup>Ref.</sup>      | <i>n</i> | Country       | Age  | % AFAB | % SM | % BIPOC | Predictor | Outcome           | <i>r</i> |
|---------------------------------------|----------|---------------|------|--------|------|---------|-----------|-------------------|----------|
| Rowe et al. (2015) <sup>77</sup>      | 292      | United States | 21.0 | 0.0    | —    | 63.0    | DIST      | Alcohol frequency | 0.27     |
|                                       |          |               |      |        |      |         | DIST      | Drug frequency    | 0.26     |
| Shah et al. (2018) <sup>78</sup>      | 189      | Pakistan      | 29.0 | —      | —    | —       | DIST      | Drug frequency    | 0.35     |
| Tebbe and Moradi (2016) <sup>79</sup> | 335      | United States | 25.2 | 53.1   | 93.7 | 18.2    | DIST      | Alcohol problems  | 0.05     |
|                                       |          |               |      |        |      |         | DIST      | Drug problems     | 0.13     |
|                                       |          |               |      |        |      |         | ER        | Alcohol problems  | −0.09    |
|                                       |          |               |      |        |      |         | ER        | Drug problems     | 0.07     |
|                                       |          |               |      |        |      |         | IT        | Alcohol problems  | 0.02     |
|                                       |          |               |      |        |      |         | IT        | Drug problems     | 0.01     |
| Vance et al. (2023) <sup>80</sup>     | 252      | United States | —    | 65.0   | —    | 100.0   | DIST      | Alcohol frequency | 0.35     |
|                                       |          |               |      |        |      |         | DIST      | Drug frequency    | 0.40     |

<sup>a</sup>sample 1. <sup>b</sup>sample 2.

AFAB, assigned female sex at birth; BIPOC, Black, Indigenous, or people of color; CONC, concealment; DIST, distal stress; ER, expectations of rejection; IT, internalized transphobia; SM, sexual minority.

identified as Black, Indigenous, or as a person of color (BIPOC). Proportion of the sample identified as BIPOC significantly moderated the relationship between distal stress and alcohol use frequency ( $z=4.27$ ,  $p<0.001$ ,  $R^2=0.740$ ,  $k=13$ ), such that effect sizes for this relationship were larger in samples with a greater proportion of self-identified BIPOC participants. No other moderators were found to be significant (all  $p>0.05$ ).

#### Heterogeneity

Measures of between-study heterogeneity are given in Table 2. Based on the *Q* statistic, significant heterogeneity was observed for the relationship between distal stress and alcohol use frequency [ $Q(14)=214.21$ ,  $p<0.001$ ] and drug use frequency [ $Q(32)=475.64$ ,  $p<0.001$ ]. Likewise, significant heterogeneity was also observed for the relationships between internalized transphobia and alcohol

use frequency [ $Q(2)=6.32$ ,  $p=0.042$ ], expectations of rejection and alcohol use problems [ $Q(2)=9.24$ ,  $p=0.010$ ], and internalized transphobia and drug use frequency [ $Q(4)=16.68$ ,  $p=0.005$ ]. No other minority stress-substance use pairs had significant *Q* statistics (all  $p>0.05$ ).

Between-study heterogeneity was also indicated by medium to high  $I^2$  values. Large  $I^2$  values (i.e.,  $\sim 75\%$  or higher)<sup>51</sup> were observed for relationships between distal stress and alcohol use frequency ( $I^2=93.5$ ) and drug use frequency ( $I^2=95.2$ ), internalized transphobia and alcohol use frequency ( $I^2=68.4$ ) and drug use frequency ( $I^2=70.0$ ), expectations of rejection and alcohol use problems ( $I^2=78.4$ ), and concealment and alcohol use problems ( $I^2=62.8$ ). Meanwhile, low heterogeneity was observed for associations between distal stress and alcohol use problems ( $I^2=0.0$ ), as well as internalized transphobia and alcohol use problems ( $I^2=34.4$ ).

Table 2. Pooled Effect Sizes and Measures of Heterogeneity for Relationships Between Minority Stress and Substance Use Variables

| Predictor   | Outcome           | <i>k</i> | <i>N</i> | Effect size           |          |          | Heterogeneity |          |          |
|-------------|-------------------|----------|----------|-----------------------|----------|----------|---------------|----------|----------|
|             |                   |          |          | <i>r</i> (95% CI)     | <i>z</i> | <i>p</i> | $I^2$         | <i>Q</i> | <i>p</i> |
| Distal      | Alcohol frequency | 15       | 42,791   | 0.13 (0.06 to 0.20)   | 3.58     | <0.001   | 93.5          | 214.21   | <0.001   |
| IT          | Alcohol frequency | 3        | 1258     | 0.01 (−0.11 to 0.12)  | 0.10     | 0.917    | 68.4          | 6.32     | 0.042    |
| ER          | Alcohol frequency | 1        | 286      | 0.05 (−0.06 to 0.17)  | 0.88     | 0.381    | —             | —        | —        |
| Concealment | Alcohol frequency | 1        | 27,715   | 0.01 (−0.01 to 0.02)  | 1.00     | 0.318    | —             | —        | —        |
| Distal      | Alcohol problems  | 8        | 1194     | 0.09 (0.03 to 0.14)   | 3.03     | 0.002    | 0.0           | 4.21     | 0.755    |
| IT          | Alcohol problems  | 5        | 1240     | 0.06 (−0.02 to 0.13)  | 1.49     | 0.136    | 34.4          | 6.10     | 0.192    |
| ER          | Alcohol problems  | 3        | 974      | 0.04 (−0.10 to 0.17)  | 0.52     | 0.605    | 78.4          | 9.24     | 0.010    |
| Concealment | Alcohol problems  | 2        | 639      | 0.06 (−0.06 to 0.19)  | 0.97     | 0.330    | 62.8          | 2.69     | 0.101    |
| Distal      | Drug frequency    | 24       | 47,732   | 0.16 (0.11 to 0.21)   | 6.00     | <0.001   | 95.2          | 475.64   | <0.001   |
| IT          | Drug frequency    | 6        | 2169     | 0.05 (−0.04 to 0.14)  | 1.16     | 0.245    | 70.0          | 16.68    | 0.005    |
| ER          | Drug frequency    | 1        | 342      | −0.10 (−0.20 to 0.01) | −1.85    | 0.065    | —             | —        | —        |
| Concealment | Drug frequency    | 1        | 342      | −0.05 (−0.15 to 0.06) | −0.92    | 0.357    | —             | —        | —        |
| Distal      | Drug problems     | 4        | 492      | 0.14 (0.05 to 0.23)   | 3.09     | 0.002    | 0.0           | 2.51     | 0.473    |
| IT          | Drug problems     | 1        | 335      | 0.01 (−0.10 to 0.12)  | 0.18     | 0.855    | —             | —        | —        |
| ER          | Drug problems     | 1        | 335      | 0.07 (−0.04 to 0.18)  | 1.28     | 0.201    | —             | —        | —        |
| Concealment | Drug problems     | 0        | 0        | —                     | —        | —        | —             | —        | —        |

CI, confidence interval.

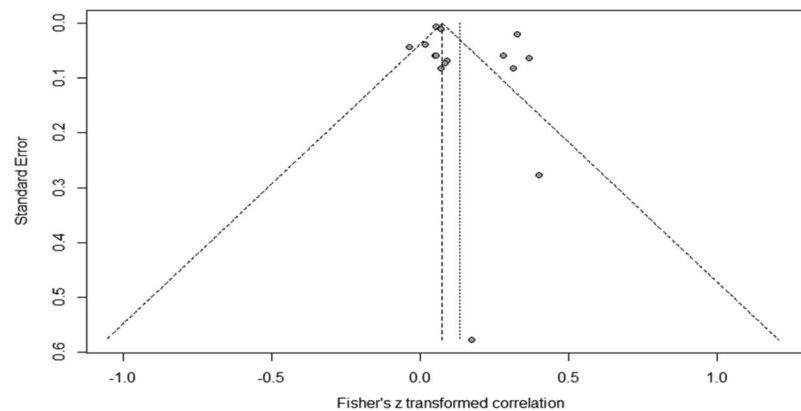


**FIG. 2.** Funnel plot for studies assessing the relationship between distal stress and alcohol use frequency.

#### Publication bias

Funnel plots for the relationship between distal stress and alcohol use frequency, as well as distal stress and drug use frequency, are given in Figures 2 and 3, respectively. Egger's test did not find any significant funnel plot asymmetry for all minority stress-substance use variable pairs for which  $k \geq 3$  (all  $p > 0.05$ ). Results of fail-safe  $N$  indicate that effect sizes for the relationship between distal stress and alcohol use frequency, alcohol use problems, and drug use frequency were robust to publication bias, whereas all other minority stress-substance use variable pairs were not.

#### Study quality

AXIS quality assessment ratings for included studies are given in Supplementary Appendix SA3. Similar to findings from a previous meta-analysis of transgender mi-

nority stress,<sup>19</sup> several criteria on the AXIS assessment were not met by the majority of included studies. Most studies used convenience, snowball, or other purposive sampling methods, potentially because of the relatively low prevalence of TGD identities in the general population and the difficulty in identifying and recruiting TGD participants.<sup>81</sup> Nevertheless, utilizing such sampling techniques may limit the generalizability of the findings to the broader TGD population. Most included studies were also limited by lack of sample size justification and classification or description of nonresponders.

#### Discussion

The findings in the current meta-analysis indicate that experiences of TGD-based distal minority stress are significantly associated with alcohol use frequency, alcohol use problems, drug use frequency, and drug use

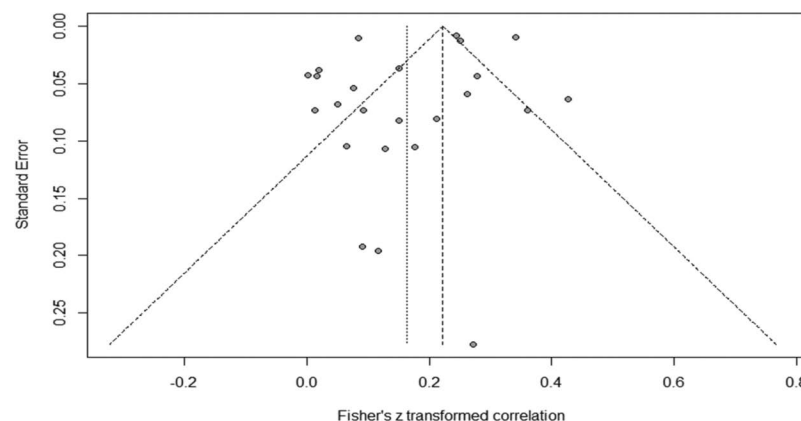


**FIG. 3.** Funnel plot for studies assessing the relationship between distal stress and drug use frequency.

problems. These results provide further evidence for minority stress theory, particularly for the relationship between distal stressors and adverse psychological and behavioral outcomes,<sup>1,3</sup> and signals that experiences of such prejudice events may help to explain substance use disparities in TGD populations.<sup>6,23,82</sup> Significant pooled effect sizes for the relationship between distal minority stress drug and alcohol use frequency imply that TGD individuals may engage in substance use to cope with prejudice events.

Post-traumatic stress disorder (PTSD) and substance use are highly comorbid,<sup>83,84</sup> and substance use is significantly associated with a variety of traumatic victimization events, including adverse childhood experiences,<sup>85</sup> childhood sexual abuse,<sup>86</sup> bullying,<sup>87</sup> intimate partner violence,<sup>88</sup> and sexual assault.<sup>89</sup> Many use substances to cope with these traumatic experiences,<sup>90,91</sup> and many marginalized groups report using substances to cope with prejudice events, including people of color,<sup>92</sup> sexual minorities,<sup>93,94</sup> and TGD people.<sup>95,96</sup>

It is noteworthy that the current meta-analysis did not find significant bivariate associations between measures of proximal minority stress (i.e., internalized transphobia, expectations of gender-based rejection, and concealment of gender identity) and substance use outcomes. This finding conflicts with minority stress theory, which proposes that there are direct associations between proximal minority stressors and mental health outcomes.<sup>1,3</sup> Research on other outcomes (i.e., depression, suicidal ideation, and suicide attempt) have even found *larger* effect sizes for some proximal stress constructs (i.e., internalized transphobia and expectations of gender-based rejection) compared with distal stress.<sup>19</sup> Yet, more recent research has found similar results to the current meta-analysis; distal minority stress, but not proximal stress, was associated with greater concurrent substance use in daily diary paradigms.<sup>97,98</sup> These findings indicate that components of minority stress may differentially impact internalizing and externalizing psychopathology, with the former more strongly associated with proximal stress and the latter more strongly associated with distal stress.

Results of moderator analyses demonstrate that effect sizes for the relationship between distal minority stress and alcohol use frequency were larger in samples with a greater proportion of self-identified BIPOC participants. This finding may be best understood through the lens of *intersectionality*,<sup>99,100</sup> which posits that the minority stress experiences of individuals with multiple marginalized identities cannot be adequately under-

stood from looking at each of those identities in isolation (e.g., looking at race/ethnicity and gender identity alone). Rather, these identities need to be viewed as intersecting and combinatory to fully grasp how prejudice impacts the lives of those who hold them. For example, intersectionality suggests that the discrimination experiences of a woman of color cannot be understood merely through the lens of her racial or gender identity alone, but rather, can only be understood completely as the unique intersection between racism and sexism.<sup>99,101</sup>

For the current meta-analysis, intersectionality would propose that the minority stress experiences of TGD BIPOC cannot be understood merely through their race or gender in isolation,<sup>102</sup> and this conclusion is supported by the observed significant moderation of race on distal stress and alcohol use frequency.

Existing research supports an intersectional conceptualization of minority stress for TGD BIPOC. Although the current results demonstrate that distal minority stress is associated with alcohol use in TGD individuals, and other research shows that the same is true for BIPOC,<sup>103,104</sup> looking at race/ethnicity and gender identity in isolation does not uncover how these identities intersect. Among the TGD population, TGD BIPOC display disproportionately high rates of adverse childhood experiences,<sup>105</sup> psychological distress,<sup>106</sup> physical health problems,<sup>107</sup> suicide attempts,<sup>108</sup> polyvictimization,<sup>109</sup> intimate partner violence,<sup>110</sup> homicide victimization,<sup>111</sup> and gender-based discrimination<sup>106</sup> compared with their White TGD peers, and among BIPOC, TGD BIPOC likewise exhibit significantly higher rates of nonsuicidal self-injury,<sup>108</sup> psychological distress,<sup>112</sup> sexual assault victimization,<sup>113</sup> and homelessness<sup>114</sup> compared with their cisgender BIPOC peers. TGD BIPOC also exhibit higher rates of depression and suicidality,<sup>115</sup> sexual assault victimization,<sup>116</sup> and substance use<sup>117</sup> compared with their White cisgender peers.

Furthermore, TGD BIPOC experience unique forms of prejudice as a result of their combined TGD and racial/ethnic minority identities,<sup>118–120</sup> which in turn can lead to adverse outcomes, including HIV,<sup>121</sup> substance use,<sup>122</sup> and poor mental health outcomes.<sup>123,124</sup>

High levels of between-study heterogeneity were observed in the present meta-analysis, which can be explained by the methods used to assess variables of interest. For one, there was a notable lack of consistency in the assessment of minority stress and substance use across studies. Measures of substance use differed

across several dimensions, including the substances included in measurement (e.g., some studies assessed use of multiple substances in a single measure, whereas others only assessed use of a single substance per measure) and the number of items assessing use. Similarly, there were differences in minority stress measures across studies regarding the operationalization of concealment (i.e., concealment vs. disclosure of gender identity), context of distal stress (e.g., health care discrimination vs. family rejection vs. peer victimization), inclusion of sexual orientation minority stress in assessment (i.e., experiencing minority stress because of your TGD vs. LGBTQ+ identity), and number of items assessing stress (e.g., dichotomous vs. continuous).

Studies also differed in their sampling methods. Many utilized convenience samples recruited from online and offline TGD communities,<sup>39</sup> whereas others were derived from larger population-based samples.<sup>33</sup> It is possible that subjects may substantively differ across samples in their experiences of minority stress and psychopathology (e.g., those receiving treatment at a gender clinic likely have better mental health than their nontreatment-seeking peers).<sup>125</sup>

One final study-level variable warrants discussion: the striking lack of geographic diversity across samples. The vast majority of included studies were from the United States or other Western nations, although this may be at least partially a result of limiting search results only to publications written in English.<sup>126</sup> Researchers have consistently critiqued psychological science for its disproportionate focus on samples that are “WEIRD” (i.e., Western, educated, industrialized, rich, and democratic)<sup>127</sup> and TGD research is not immune to this critique. This paucity of global TGD research may be masking cross-cultural differences in the impact of minority stress on health outcomes. For instance, whereas the vast majority of the population of some nations believe that TGD people “should be allowed to have surgery so their body matches their identity” (e.g., in Argentina),<sup>128</sup> the opposite is true for other countries (e.g., Malaysia).<sup>129</sup>

### Limitations

Several methodological limitations of this study should be noted, which provide avenues for further research. Decisions made by researchers undoubtedly impact the results of systematic reviews, including creation of search strings, selection of databases, and placing of limits on included search results.<sup>130</sup> Despite using search terms from previous systematic reviews on mi-

nority stress and substance use, inclusion of more specific related terms in the string (stigma, MDMA, etc.) may have yielded relevant studies that were missed by the search terms used in this review. Similarly, although the year 2000 was selected *a priori* as a starting date for the search because of the relatively recent development of minority stress theory,<sup>3</sup> particularly as it related to TGD individuals,<sup>1</sup> and the relative dearth of research on TGD mental health before 2010,<sup>131,132</sup> an earlier selection date may have yielded additional results.

As stated previously,<sup>19</sup> although the classification of minority stress in this study is based on minority stress theory as originally conceptualized,<sup>1-3</sup> this method of categorization has some notable limitations. First, distal stress is conceptualized broadly to include “those external events that occur in the [TGD] individual’s environment and are related to either knowledge or perception of the individual’s minority status” (p. 462).<sup>1</sup> This definition was chosen to be inclusive of a wide variety of distal stress experiences (e.g., from microaggressions to gender-based physical or sexual violence). Yet, it is possible that this comprehensive definition contributed to observed between-study heterogeneity. Multidimensional assessments of distal minority stress in TGD samples indicate that effect sizes for the relationship between distal stress and mental health differ based on the specific type of distal stress assessed (e.g., identity nonaffirmation may be more associated with internalizing symptoms when compared with overt discrimination).<sup>133,134</sup> However, research examining differential effects of specific types of distal stress on substance use outcomes in TGD populations is relatively sparse, and future research in this area is needed.

Similarly, although the operationalization of substance use (i.e., alcohol and drug frequency and problems) in this meta-analysis mirrors previous meta-analyses on substance use,<sup>135,136</sup> this method of categorizing substance use prevents a more nuanced examination of the role of minority stress on use of specific substance types. It is possible that effect sizes may differ across distinct substances subsumed under the broader “drugs” category (e.g., cannabis vs. methamphetamine), because these substances have very different psychosocial consequences and potential for harm or problematic use.<sup>137</sup> Furthermore, substances may differ in their motives for use,<sup>138</sup> which may have ramifications for how these substances are used to cope with experiences of minority stress.<sup>139</sup> Further research should examine whether TGD populations are more likely to use some substances over

others in response to minority stress, and whether minority stress is more likely to lead to problematic substance use for certain substances compared with others.

This study is further limited by its conceptualization of gender diversity. Because of inconsistencies across studies in measurement of gender identity, all TGD identities were included under a single umbrella. This ignores the potential presence of disparities in minority stress and substance use between TGD subgroups. Occasional differences in minority stress have been observed between binary and nonbinary TGD populations, but the overall findings have thus far been equivocal. Whereas some research has found that binary TGD individuals experience greater levels of distal stress compared with nonbinary peers,<sup>140</sup> others have reported the opposite finding.<sup>141</sup> Likewise, rates of substance use and other poor mental health outcomes may differ between binary and nonbinary TGD people, but these differences have also been equivocal across studies.<sup>142–144</sup> Future meta-analytic studies would benefit from greater consideration of these subgroups to determine the unique effects of minority stress on these subpopulations.

Moderator analyses were also limited in their conceptualization of race/ethnicity. The racial/ethnic composition of the sample was operationalized as the proportion of the sample that identified as BIPOC. This binary operationalization was chosen owing to the heterogeneous categorization of race/ethnicity across studies. However, this dichotomization of White versus BIPOC not only incorrectly places Whiteness as the default category to which other groups must be compared,<sup>102</sup> but also prevents examination of important differences between BIPOC racial/ethnic groups that may be differentially marginalized. These limitations could also be applied to the binary measurement of sexual orientation; it centers heterosexuality as the default category and precludes probing subgroup differences (lesbian/gay vs. bisexual vs. questioning, etc.). Future research would benefit from examining whether the effect of minority stress on TGD populations differ based on these subgroups, and how TGD-based minority stress interacts with other forms of minority stress on substance use outcomes.

Finally, the current meta-analysis was limited to cross-sectional effect sizes, limiting its ability to draw causal inferences about relationships between TGD minority stress and substance use outcomes. Analyses were limited to cross-sectional effect sizes because of

the limited amount of longitudinal research on TGD minority stress,<sup>19</sup> as well as the inherent heterogeneity that results from combining longitudinal effect sizes that utilize different time intervals.<sup>145</sup> Although existing longitudinal research indicates that minority stress (particularly distal stress) is associated with substance use in TGD populations,<sup>146–148</sup> additional research is needed before a longitudinal meta-analysis would be feasible.

### Clinical implications

This study found that distal minority stress, but not proximal minority stress (i.e., expectations of gender-based rejection, concealment of gender identity, and internalized transphobia), was associated with substance use frequency and problems. This finding provides further evidence for coping with distal minority stress as an important point of intervention for mental health professionals working with TGD populations. Indeed, adapted psychotherapeutic interventions that focus on minority stress have been shown to lead to reductions in depression, anxiety, and alcohol use in sexual and gender minority populations.<sup>149</sup> Use of these tailored interventions may provide TGD clients with strategies that are more effective and less harmful than substance use to cope with experiences of distal minority stress. The lack of significant findings regarding proximal minority stress in the present meta-analysis suggest that, although both types of stressors are important, in clinical work focusing on reducing substance use in TGD clients, exploration of previous experiences of and responses to distal stress may be more productive than an emphasis on proximal minority stressors like expectations of rejection, concealment, and internalized transphobia.

These results also provide directions for advocacy for practitioners working with TGD populations. Psychologists have long noted that they occupy an important position of power in advancing the rights of their marginalized clients<sup>150</sup> and public policy that protects their vulnerable clientele.<sup>151</sup> This advocacy is necessary in a political and legal landscape that remains fraught with opposition toward TGD people and their rights and difficulty in obtaining TGD-related health care.<sup>152,153</sup> For example, although the majority of Americans support TGD rights,<sup>154</sup> >100 bills were proposed in 2021 to limit rights for TGD Americans.<sup>155</sup> Some of these bills, like those that restrict access to life-saving gender-related health care,<sup>156</sup> cite popular misinformation from nonscientists about gender dysphoria and

gender-affirming interventions<sup>157,158</sup> to support legislation that will lead to increased levels of distal<sup>5</sup> and proximal stress in TGD individuals.<sup>159</sup> This need for advocacy is not limited to the United States; internationally, TGD individuals confront legal barriers to gender-affirming care,<sup>160</sup> lack of support or acceptance among the general public,<sup>128</sup> lack of legal protections against gender-motivated violence,<sup>161,162</sup> restrictions on freedom of expression,<sup>163,164</sup> and restrictions on legal recognition of TGD identities.<sup>165</sup> Clinicians should further help reduce distal stress for their TGD clients by using their advanced subject matter expertise to advocate against these anti-TGD policies and promote legislation that codifies legal protections for TGD people.

## Conclusion

The current meta-analysis provided further evidence for some aspects of minority stress theory, finding that distal stress, but not proximal stress, is associated with alcohol and drug use frequency and problems in TGD samples. Results further demonstrated that minority stress may disproportionately impact alcohol use among TGD BIPOC, identifying TGD BIPOC as uniquely vulnerable to negative mental health effects of distal minority stress. These findings highlight the core role that distal minority stress plays in the mental health of TGD individuals and the potential protective effect of institutional policies that protect this population from TGD-based discrimination.

## Authors' Contributions

M.J.P.: conceptualization, methodology, software, formal analysis, investigation, writing—original draft, writing—review and editing, project administration. M.E.Q.: investigation, writing—review and editing. J.A.C.: conceptualization, methodology, writing—review and editing, supervision.

## Author Disclosure Statement

The authors have no conflicts of interest to declare.

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## Supplementary Material

Supplementary Appendix SA1  
Supplementary Appendix SA2  
Supplementary Appendix SA3

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### Abbreviations Used

AFAB = assigned female sex at birth  
 AXIS = Appraisal Tool for Cross-Sectional Studies  
 BIPOC = Black, Indigenous, or people of color  
 CI = confidence interval  
 CONC = concealment  
 DIST = distal stress  
 ER = expectations of rejection  
 IT = internalized transphobia  
 SM = sexual minority  
 TGD = transgender and gender-diverse