Title

Response to a letter to the editor about eating disorder (ED) symptoms among transgender and gender diverse (TGD) youth seeking gender-affirming care.

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Author(s) in a letter to the editor (LTE et al., 2024), highlight the importance of clarity and methodological rigor for the advancement of research on eating disorders (ED) among transgender and gender diverse (TGD) youth. LTE et al. (2024) shared specific aspirations for Kramer et al. (2024) to a) clarify how gender-affirming hormones were defined, b) explain why only a sample of TGD youth were included, and c) address how missing data were handled in the manuscript "Eating disorder (ED) symptoms among transgender and gender diverse (TGD) youth seeking gender-affirming care." As research demonstrates gender affirmative care enhances quality of life (Allen et al., 2019; Call et al., 2021; Hughto et al., 2020), reduces ED symptoms (Jones et al., 2018; Nowaskie et al., 2021), and may mitigate experiences of marginalization and minority stress (Mezza et al., 2024) among TGD individuals, the authors wish to clarify methodology to bolster research efforts related to TGD youth and clarify concerns noted by LTE et al. (2024).

First, LTE et al. (2024) state that gender-affirming hormones can refer to gonadocorticoids (e.g., sex steroids as in estrogen and testosterone), pubertal suppressants, and anti-androgens. The authors of the letter to the editor (LTE et al., 2024) asked Kramer et al. (2024) to clarify how they defined gender-affirming hormone use. In this instance, Kramer et al. (2024) only assessed gonadocorticoid use (estrogen and testosterone) and did not have access to specific dosages of gonadocorticoids prescribed (due to how data were pulled) or whether TGD youth received pubertal suppressants or anti-androgens. Authors can clarify that each individual receiving gonadocorticoids was given doses based on their individual medical history in line with WPATH standards of care (Coleman et al., 2022). At the time of the study, TGD youth assigned male at birth and identifying as female were typically prescribed Estradiol (a gonadocorticoid) and given Spironolactone (a testosterone blocker that may be considered an

anti-androgen) or, on rare occasions, Finasteride (an alpha-reductase inhibitor) instead of Spironolactone. For TGD youth assigned male at birth and identifying as female, testosterone (a gonadocorticoid) was prescribed. For children who were starting puberty, medications to pause puberty (Leuprolide and Histraline) were offered. Further, there was no indication for how long TGD youth were taking gonadocorticoids, which is another limitation; it may take months to see the full effects of these medications. At the time of writing and submission, Kramer et al. (2024) noticed that minimal research had explored the association between any form of gender-affirming hormone use and ED symptoms among TGD youth seeking gender-affirmative care. Therefore, Kramer et al. (2024) wanted to present preliminary associations even if a full assessment of gender-affirmative interventions and the causal link between gonadocorticoids and ED symptoms could not be established.

A confound not unique to the study by Kramer et al. (2024) is that gender-affirmative care may look vastly different and take different lengths of time for individuals to complete (given age at assessment, social support, country of residence (i.e., different regulations for when to start puberty suppression and other gender-affirmative interventions), and availability of interventions). Some adolescents may not be seeking medical interventions such as gender-affirming hormones or gender-affirming genital surgery, may focus on other forms of gender-affirmative support, or may not experience gender dysphoria or seek interventions at all. Thus, it is not only an issue of understanding if TGD youth receive pubertal suppressants, gonadocorticoids, and anti-androgens and the length of time they have taken each. It is also essential to understand what gender-affirmative care TGD youth are receiving beyond just medical care (e.g., social, psychological) and how many interventions someone has received compared to what they are hoping to receive. That is, one TGD youth may receive pubertal

suppressants, then testosterone, and will not seek anything more, while another has received the same interventions but also seeks "top surgery" (gender-affirming;k mastectomy) and phalloplasty. It is also beneficial to understand the impact of discrimination and minority stress TGD youth may face; these experiences may explain psychological outcomes in research (Witcomb et al., 2019).

LTE et al. (2024) also share concerns about the binary definition of gender identity used by Kramer et al. (2024). Participants in our study self-identified as transgender male, transgender female, and non-binary, and groups were thus operationalized based on self-determined labels. Given that only two individuals identified as non-binary, we were not adequately powered to include this group in analyses. Kramer et al. (2024) agrees that a more nuanced assessment of gender identity is imperative and that previous comparisons of gender using a binary approach may be biased (conceivably individuals identifying as cisgender may not be cisgender in older studies). Individuals identifying as non-binary are unfortunately excluded or also missed when researchers assess gender identity and TGD in a binary manner (de Graaf et al., 2021; Scandurra et al., 2019; Schudson & Morgenroth, 2022).

The second clarification request relates to the lack of comparison groups in the Kramer et al. (2024) manuscript (LTE et al., 2024). Kramer et al. (2024) are grateful for this comment since a sample of youth diagnosed with ED as a comparison group was initially included in the manuscript, but prior reviewers suggested removing the sample diagnosed with ED. The sample of youth with ED were adolescents (*Mage* = 15.82) starting interdisciplinary ED treatment with Adolescent Medicine and psychologists at the same institution as TGD youth seeking gender-affirmative care. When the age-matched ED sample was included (see Table 1 and Table 2), analyses indicated that youth with ED scored higher on the Global EDE-Q compared to TGD

youth ($p < .001$, Cohen's $d = 1.19$). While youth with ED endorsed higher frequency of self-induced purging, subjective and objective binge episodes, and compensatory exercise, it was notable that TGD youth and youth with ED did not endorse different frequency of laxative use (χ^2 (1) = 0.001, $p = .98$, $OR = 1.01$, 95% CI [0.43, 2.40]) which is concerning since laxative use has been associated with ED development (Hazzard et al., 2021) and severity (Bryant-Waugh et al., 2006).

Given that prior research has established that TGD youth endorse higher levels of ED symptoms compared to community samples (Coelho et al., 2019), Kramer et al. (2024) were less inclined to compare data with community samples initially and submitted their manuscript prior to the publication by Hallward et al., (2023). Kramer et al. (2024) agree that this would have been an added strength and have taken the liberty to look at this now. We compared groups using Mond et al. (2014) because age ranges in that sample were more aligned with our TGD sample compared to Hallward et al. (2023) and Whitcomb et al. (2015). Comparing the current sample to the Hallward et al. (2023) data was also more difficult because Hallward et al. (2023) further separated groups by sexual orientation and did not provide a combined total for comparison. However, comparisons between Kramer et al. (2024) sample and Mond et al. (2014) indicated that Global EDE-Q was not significantly different among TGD females and cisgender females (t (78) = -1.57, $p = .121$, Cohen's d = 0.19) but was significantly different between TGD males and cisgender males (t (249) = 7.71, $p < .001$, Cohen's d = .77) using Welch's t-test given unequal variances. When comparing TGD males to cisgender males on ED behaviors, a greater portion of TGD males reported having at least one instance of subjective binge eating (Z = 5.39, $p < .001$), objective binge eating (Z = 4.56, $p < .001$), laxative use (Z = 4.24, $p < .001$), and compensatory exercise (Z = 2.82, $p = .005$) compared to cisgender males. A greater portion of TGD females

endorsed at least one subjective binge eating episode ($Z = 14.42$, $p < .001$), objective binge eating episode ($Z = 9.96$, $p < .001$), self-induced vomiting ($Z = 8.96$, $p < .001$), and laxative use ($Z = 14.74$, $p < .001$), compared to cisgender females. A smaller portion of TGD females reported any compensatory exercise ($Z = -6.97$, $p < .001$) compared to cisgender females.

Kramer et al. (2024) agree that it is essential to be transparent and account for missing data when running analyses to reduce bias. For clarity, among the sample of TGD youth, no Global EDE-Q score was missing (0%), and ED behavior data were also complete (e.g., 0% missing data). There was missing data for gonadocorticoid use among 63 TGD youth (24%). Missing data occurred at random due to errors in data pull. Kramer et al. (2024) did control for missing data, although they did not explicitly state how they did so in the manuscript. When conducting zero-inflated negative binomial regressions and negative binomial regressions, authors addressed missing data using Full Information Maximum Likelihood (FIML) using the Mplus estimator=ml command. It uses all data available and works to minimize bias under the missing at random (MAR) assumption (Enders & Gottschall, 2011; Little & Rubin, 2019). For ANCOVAs, listwise deletion was used when examining the association between gonadocorticoids and Global EDE-Q scores.

We are grateful for the opportunity to clarify that we specifically looked at gonadocorticoid use versus other hormonal agents based on the request by LTE et al. (2024). The additional opportunity to respond to comparison group questions allowed us to demonstrate that TGD youth were experiencing significantly greater ED symptoms and more likely to report ED behaviors compared to cisgender peers, except self-induced vomiting among TGD males and cisgender males. While youth with ED generally endorsed greater ED severity and were more likely to report ED behaviors, TGD youth endorsed similar levels of laxative use compared to the

sample of youth with EDs, suggesting assessment of laxative use among TGD youth may be particularly important (Hazzard et al., 2021).

In summary, there are several ways that studies of ED symptoms among TGD youth can be strengthened. For one, research should thoroughly assess and report which kind of gender-affirmative hormones are used (i.e., puberty suppressants, gonadocorticoids, anti-androgens) and what gender-affirmative care TGD youth are receiving (i.e., medical, psychological, and social). Further, it is crucial to consider the degree of gender-affirmative care someone has received compared to what they are seeking and TGD youths' access to care, which is particularly relevant given restrictions against gender-affirmative care in much of the United States. Thoughtful assessment of gender identity is also essential to understand research findings and for replication. While cross-sectional studies support associations between variables, longitudinal studies are warranted to demonstrate causality and support the benefits of gender-affirmative care among TGD youth at high risk for ED development. The degree of gender affirmation, minority stress, and discrimination TGD youth experience are also essential considerations when concluding findings (Call et al., 2021; Mezza et al., 2024). We are grateful for the opportunity to address the LTE and hope our clarifications help to bolster future research.

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Table 1. Descriptive and Demographic Breakdown of ED and TGD sample

	Transgender Males (n = 181)		Transgender Females (n = 70)		TGD Youth (n = 251)		Females With ED (n = 77)		Males With ED (n = 13)		Youth with ED (n = 90)	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Age‡	16.77	(2.74)	17.79	(3.12)	17.06	(2.87)	15.96	(2.02)	15.16	(2.24)	15.84	(2.06)
BMI§	26.87	(7.88)	25.05	(6.49)	26.28	(7.55)	18.15	(3.42)	17.75	(2.35)	18.10	(3.30)
EDE-Q¶	1.34	(1.17)	1.55	(1.50)	1.39	(1.27)	3.02	(1.65)	3.08	(1.89)	3.02	(1.67)
	N (%)		N (%)		N (%)		N (%)		N (%)		N (%)	
Ethnicity												
Non-Hispanic	130	(96.3)	43	(97.7)	173	(96.6)	64	(98.5)	12	(100.0)	76	(98.7)
Hispanic	5	(3.7)	1	(2.3)	6	(3.4)	1	(1.5)	0	(0.0)	1	(1.3)
Race												
White	122	(89.7)	40	(90.9)	162	(90.0)	61	(93.8)	11	(91.7)	72	(93.5)
Black	3	(2.2)	3	(6.8)	6	(3.3)	0	(0.0)	1	(8.3)	1	(1.3)
Asian	3	(2.2)	1	(2.3)	4	(2.3)	1	(1.5)	0	(0.0)	1	(1.3)
Other†	8	(100.0)	0	(0.0)	9	(4.4)	3	(4.6)	0	(0.0)	3	(3.9)

BMI = Body Mass Index, EDE-Q = Global Eating Disorder Examination-Questionnaire Score, †As listed in Electronic Medical Record, ‡ TG females age was significantly higher than TG males ($p < .05$), §TGD sample BMI was statistically higher than ED sample ($p < .05$), ¶ED sample had higher EDE-Q scores than TGD sample ($p < .05$).

Table 2: Descriptives of Behavioral Items

	Transgender Males	Transgender Females	Females With ED	Males With ED
Subjective Binge Episodes				
% endorsed	15.6	23.2	45.5	41.7
Mean (SD)	1.14 (4.71)	2.82 (8.15)	3.71 (7.10)	5.33 (10.69)
Minimum – Maximum	0 – 28	0 – 38	0 – 28	0 – 28
Objective Binge Episodes				
% endorsed	17.6	23.6	37.7	33.3
Mean (SD)	0.80 (3.21)	2.40 (6.32)	2.29 (5.10)	7.25 (12.93)
Minimum – Maximum	0 – 28	0 – 28	0 – 28	0 – 30
Self-Induced Vomiting				
% endorsed	1.4	9.1	22.1	7.7
Mean (SD)	0.11 (0.96)	0.22 (0.76)	2.09 (5.11)	0.08 (0.29)
Minimum – Maximum	0 – 10	0 – 4	0 – 25	0 – 1
Laxatives				
% endorsed	6.4	15.3	5.2	30.8
Mean (SD)	0.01 (0.08)	0.58 (3.81)	0.42 (2.99)	2.53 (5.88)
Minimum – Maximum	0 – 1	0 – 28	0 – 25	0 – 20
Compensatory Exercise				
% endorsed	16.2	12.9	63.2	38.5
Mean (SD)	1.23 (4.08)	0.91 (4.00)	7.68 (9.20)	9.00 (12.34)
Minimum – Maximum	0 – 35	0 – 28	0 – 26	0 – 28

% endorsed = percent of group reporting a frequency of 1 or greater of variable.