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ORIGINAL ARTICLE

Subjective and objective binge episodes in relation to eating disorder and depressive symptoms among middle-aged women

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Abstract

Purpose Evidence suggests loss of control over eating may be the driving component of binge eating, a transdiagnostic symptom of eating disorders and highly comorbid with depressive symptoms. Prior studies have evaluated eating disorder and depressive symptoms across types of binge episodes among adolescent and young adult samples, yet no studies have focused on middle-aged women who may be particularly vulnerable to both binge eating and depressive symptoms. The goal of this study was to compare eating disorder symptoms and depressive symptoms across different types of binge eating episodes among middle-aged women.

Methods Women ($N = 347$), ages 40–63, completed an online survey about both objective (OBE) and subjective binge episodes (SBE), eating disorder symptoms, and depressive symptoms. Participants were categorized as OBEs only, SBEs only, both OBEs and SBEs, and no binge eating.

Results Controlling for group differences, results showed middle-aged women who experienced SBEs only reported greater levels of anorexia nervosa attitudes and behaviors compared to all other groups, and greater dietary restraint compared to those who experienced only OBEs and those with no binge eating. Middle-aged women who experienced any type of binge eating reported greater levels of body image concerns and depressive symptoms compared to those who reported no binge eating.

Conclusions Findings suggest that loss of control is more clinically relevant in terms of associations with eating disorder and depressive symptoms in middle-aged women.

Level of evidence Level V based on descriptive studies.

Keywords Subjective binge eating · Objective binge eating · Eating disorder · Depressive symptoms · Middle-aged women

Introduction

Evidence suggests binge eating is transdiagnostic across eating disorders, and associated with significant forms of psychopathology including depressive symptoms [1–3]. Several studies have compared different types of binge episodes across key markers of psychopathology in adolescents and adults [2, 4, 5]; however, no research has evaluated types of binge episodes focusing exclusively on middle-aged women, who research suggests may experience increased vulnerability for eating disorder and depressive symptoms related to the perimenopausal transition [6–10]. Epidemiological data across the lifespan suggests that although the highest rate of eating disorder symptoms seems to occur prior to age 24, symptoms may dip between ages 25 and 35, followed by a resurgence to a second peak around ages 45 through 55 [11]. For middle-aged women, evidence suggests there may be a higher risk of binge eating in comparison to other eating disorder symptoms (i.e., significantly low weight, purging, etc.), with as many as 10% of women experiencing binge episodes without meeting full diagnostic criteria for an eating disorder [7]. Despite this evidence, no data has

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examined the different types of binge episodes specifically among middle-aged women. It is essential to understand the psychopathology of binge episodes, as well as related comorbidities, to effectively develop age-relevant treatment and prevention programs for middle-aged women.

Currently, the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) defines a binge episode as having two components: (1) consuming an objectively large amount of food in a discrete period of time, *and* (2) experiencing a sense of loss of control over eating [12]. Although DSM-5 places clinical importance on both components, research suggests that loss of control over eating may be the more important component of a binge episode in comparison to the amount of food consumed [4, 5, 13]. As a result, two types of binge episodes have been conceptualized: *objective* binge episodes (OBEs), characterized as both experiencing loss of control over eating and consuming an objectively large amount, and *subjective* binge episodes (SBEs), conceptualized as experiencing the sense of loss of control but without having consumed an objectively large amount [14].

In contrast to DSM-5, the International Classification of Diseases (ICD-11) [15] emphasizes only the loss of control component and has removed the criterion related to size of the binge episode. Evidence suggests the current ICD-11 diagnostic guidelines outperform the previous ICD-10 (which defined a binge episode by both size and loss of control) in distinguishing eating disorders and has greater clinical utility and global applicability [16].

This change in diagnostic conceptualization of a binge episode reflects data which demonstrate no significant differences between OBEs and SBEs across a variety of outcomes. For example, among women ages 18–42 with bulimia-type disorders, women with only SBEs reported similar levels of dietary restraint, and eating and body image concerns [17] in addition to comparable levels of depressive symptoms [18], compared to women with only OBEs. Brownstone et al. [4] demonstrated no significant differences between OBEs and SBEs for eating pathology or negative affect among adult females ages 18–65 with threshold or subthreshold bulimia nervosa. Similar results have been found among community samples of adolescents, young adults, and adult women [5, 13, 19]. Furthermore, there is some evidence that adults who experience SBE experience greater dietary restriction, body shame, and depressive symptoms compared to adults who experience only OBEs [20]. Although several of these studies have included women of middle-age in their samples [4, 17, 19], only one was a community sample [19], and none exclusively focused on middle-age as a developmental period.

Overall, the pattern of findings across these studies indicates the objectively large size component of a binge episode is not characteristic of greater distress or increased severity in psychopathology compared to loss of control over eating. Furthermore, individuals who experience loss of control over eating but do not consume objectively large amounts of food seem to be experiencing significant levels of distress related to binge eating [19], negative affect, and global eating pathology [4], on par with individuals who experience OBEs, even though those with loss of control over eating only would not currently meet diagnostic thresholds for an eating disorder according to DSM-5 standards.

Given the changes in ICD-11, removing the clinical distinction between OBEs and SBEs, it is important to test this conceptualization among middle-aged women who are vulnerable to binge eating [21], dietary restriction [22], and depressive symptoms [10] associated with the menopausal transition.

Therefore, the goal of the current study was to evaluate eating disorder and depressive symptoms across different types of binge eating episodes among middle-aged women. We hypothesized that middle-aged women who experienced any type of binge episode (OBEs only, SBEs only, or both OBEs and SBEs) would report significantly greater levels of eating disorder symptoms and depressive symptoms compared to middle-aged women who experienced no binge episodes. In addition, given the overall pattern of data suggesting there are no significant differences between binge episode types among samples not focused on middle-age [2, 18], we predicted there would be no significant differences in eating disorder and depressive symptoms for middle-aged women who engage in only OBEs and those who engage in only SBEs.

Methods

Participants

We recruited participants to take part in a study of body image and disordered eating among three generations of women: college students (young adult women), their mothers (middle-aged women), and their maternal grandmothers (older women). Young adult women were recruited through introductory psychology courses at a large, public, southeastern university, and their mothers (the middle-aged women who are the focus of this study) were recruited via contact information provided by their daughters. Daughters were not penalized or excluded if their mothers were not interested in participating. The current data on the middle-aged cohort represent secondary data analyses from the larger study.

In total, 364 of these mothers (ages 35–68) completed the study out of 369 potential mothers contacted, representing a total of 98.6% of the sample. In accordance with prior studies of middle-aged women setting a lower age limit of 40 years [7, 22, 23] and an upper age limit of 64 [24],

15 women were excluded from current analyses for being under 40 or over 64 years in addition to two participants with missing age data. Therefore, the final sample consisted of 347 middle-aged women with a mean age of 50.13 years (SD = 4.64; range 40–63 years). In terms of race, approximately 80% identified as White ($n = 276$), 9% as Asian ($n = 32$), 7% as Black ($n = 25$), and 2% as biracial or multiracial ($n = 6$). Mean body mass index (BMI) was 25.92 kg/m^2 ($SD = 5.97$; range 17.72–51.76 kg/m^2), and, as an indication of socioeconomic status, they completed an average of 16.18 years of education, the equivalent of about a 4-year college degree ($SD = 2.29$; range 9–21 years).

Procedure

Participants were emailed a link to complete an online survey and received a recruitment phone call when phone number was available. Participants provided electronic consent before completing a series of questionnaires. As compensation, they had the option of entering into a drawing for ten $15 gift cards; the opportunity to help their daughters earn course credit was an additional incentive for participation. The study was approved by the institutional review board of the University of North Carolina at Chapel Hill.

Measures

Demographics

Self-reported demographic data for age, highest level of education, race, ethnicity, and height and weight (used to calculate BMI) were collected via a set of questionnaires created for this study.

Binge episodes

OBEs and SBEs were assessed using the Eating Disorder Examination-Questionnaire-4 (EDE-Q-4) [25, 26] to measure the frequency of both OBEs and SBEs in the past 28 days using three items. The first two capture OBEs: "*Over the past 28 days, how many times have you eaten what other people would regard as an unusually large amount of food (given the circumstances)?*"; (2) "*…On how many of these times did you have a sense of having lost control over your eating (at the time that you were eating)?*" To count as an OBE, participants needed to give a response of 1 or greater to the second question. A single item assessed SBEs: "*Over the past four weeks (28 days), how many episodes of eating have you had in which you have had a sense of having lost control and eaten too much, but have not eaten an unusually large amount of food given the circumstances?*" To count as an SBE, participants needed to give a response of 1 or greater. The EDE-Q is validated for use among adult women [27].

Participants were sorted into mutually exclusive binge eating categories based on their responses. Those in the OBE only group experienced at least one OBE and zero SBEs. Those in the SBE only group experienced zero OBEs and at least one SBE. In the both OBE and SBE group, participants had to have reported at least one episode of each type. In addition, those in the no binge category indicated zero to all binge eating items.

Eating disorder symptoms

Participants completed three measures of eating disorder symptoms to capture breadth across forms of eating pathology which are related to yet distinct from binge eating. The Eating Attitudes Test-26 (EAT-26) [28] was used to measure a broad range of anorexia nervosa (AN) attitudes and behaviors: "*I think about burning up calories when I exercise."* The EAT-26 has been validated for use among samples of adult women [28]. Coefficient alpha for the current sample was 0.80.

The EDE-Q-4 Restraint subscale [25] assessed dietary restraint via the frequency of engaging in restrictive dieting behaviors in the past 28 days: *"Have you been deliberately trying to limit the amount of food you eat to influence your shape or weight (whether or not you have succeeded)?"* As this measure was added after the initial wave of recruitment, the first 60 (17%) participants did not complete this questionnaire. Coefficient alpha for the current sample was 0.80.

The Weight Concern and Shape Concern subscales of the EDE-Q-4 [25] measured participants' body image concerns over the past 28 days in terms of frequency of thoughts reflecting concerns about weight and shape: "*How dissatisfied have you been with your weight?"* Consistent with past research [29], weight and shape concern were evaluated together as a single construct in the current study. Coefficient alpha for the current sample was 0.92.

Depressive symptoms

Depressive symptoms were measured with a modified version of the Patient Health Questionnaire (PHQ-9) [30, 31]: *"For the last two weeks, how often have you felt bothered by feeling down, depressed, or hopeless?"* For the current study, one item related to suicidality was omitted for ethical reasons due to lack of follow-up. The PHQ-9 is reliable and valid for use among adults [30, 31]. Coefficient alpha for the current sample was 0.90.

Data analytic plan

Original values for each measure were reviewed to identify potential errors in data entry. All values fell within expected ranges for each measure. All participants were included in analyses with no cases deleted from the data set. Analysis of variance (ANOVA) and Chi-square analyses compared participants in each mutually exclusive binge type group (OBEs only, SBEs only, both OBEs and SBEs, and no binge eating) on demographic variables. Correlations between demographic and outcome variables were also performed. Any demographic variable that both differed by group and was significantly correlated with an outcome variable was used as a covariate in analyses for that outcome.

To compare eating disorder and depressive symptoms across binge episode groups, multivariate analysis of variance (MANOVA) was used for the set of eating disorder symptoms dependent variables (AN attitudes and behaviors, dietary restraint, and body image concerns), and analysis of variance (ANOVA) was used to evaluate depressive symptoms as the dependent variable. A significant MANOVA finding was followed up with ANOVAs, and all significant ANOVAs were followed up with Tukey's tests for pairwise comparisons. The Benjamini–Hochberg procedure was used to correct for multiple comparisons setting a false discovery rate of 0.05 [32, 33]. All statistical analyses were conducted using IBM SPSS Statistics version 26.

Results

Examination of binge eating reports per the EDE-Q yielded the following groups: OBEs only ($n=38$), SBEs only ($n=29$), both OBEs and SBEs ($n=76$), and no binge eating ($n=204$). Participants who experienced only OBEs reported on average about 9 such episodes in the past month ($M=8.84$, SD = 15.55, range 1–75); those who experienced only SBEs had on average about 5 such episodes in the past month ($M=4.62$, SD = 4.21, range 1–15). Participants who experienced both OBEs and SBEs reported on average about 15 binge episodes in the past month ($M=14.72$, SD = 19.56, range 2–70).

Evaluations of demographic variables as potential covariates are presented in Table 1. BMI was the only indicator to significantly differ by group with participants who engaged in only OBEs or both OBEs and SBEs reporting a significantly higher BMI compared to participants who experienced no binge episodes ($p=0.001$). Groups did not significantly differ on age, race, ethnicity, or level of education ($ps \geq 0.370$).

BMI was also significantly correlated with three outcome variables: dietary restraint ($r=0.21$, $p<0.001$), body image concerns ($r=0.49$, $p<0.001$), and depressive symptoms ($r=0.21$, $p<0.001$). Therefore, it was considered as a covariate with the set of eating disorder dependent variables (i.e., MANCOVA) and with the single dependent variables of dietary restraint, body image, and depressive symptoms (i.e., ANCOVAs).

The MANCOVA model comparing binge episode groups across eating disorder symptoms revealed significant group

Table 1 Descriptive statistics and group comparisons of demographic variables

	Objective binge episodes only ($n=38$)	Subjective binge episodes only ($n=29$)	Both objective and subjective binge episodes ($n=76$)	No binge episodes ($n=204$)	ANOVA	Chi-Square
Age (years)	49.21 (3.62)	51.10 (4.95)	50.38 (4.70)	50.06 (4.59)	$F(3, 343)=1.05$, $p=.370$, partial $\eta^2=.01$	–
Race (% identifying as white)	81.6%	79.3%	73.7%	81.5%	–	X^2 (3, $N=347)=2.12$, $p=.548$
Ethnicity (% identifying as Latina)	0.0%	6.9%	5.3%	5.4%	–	X^2 (3, $N=347)=2.33$, $p=.506$
Highest level of education (years)	16.21 (2.28)	16.24 (2.68)	16.07 (2.35)	16.21 (2.23)	$F(3, 343)=0.08$, $p=.969$, partial $\eta^2=.001$	–
Body mass index (kg/m^2)	28.28 (6.60)	25.98 (5.63)	27.37 (6.24)	24.92 (5.58)	$F(3, 340)=5.58$, $p=.001$, partial $\eta^2=.05$	–

Descriptive statistics are presented as means (standard deviations) or percentages. Highest level of education presented in years (12 = high school graduation, 16 = 4-year college, 21 = PhD or MD)

differences after controlling for BMI ($F(9,679) = 9.09$, $p < 0.001$, partial $\eta^2 = 0.09$). A follow-up ANOVA indicated middle-aged women who experienced only SBEs reported significantly higher levels of AN attitudes and behaviors compared to all other groups ($ps < 0.016$) (see Table 2). Those who experienced both OBEs and SBEs reported greater AN attitudes and behaviors compared to participants who experienced no binge episodes ($p = 0.001$).

Regarding dietary restraint, after controlling for BMI, participants who experienced only SBEs reported significantly more dietary restraint than those who only experienced OBEs ($p = 0.012$) and those who had no binge episodes ($p < 0.001$) (see Table 2). Those who experienced both OBEs and SBEs reported more dietary restraint than those with no binge eating ($p < 0.001$).

Regarding body image concerns, participants who experienced any binge episode (only OBE, only SBE, or both) had significantly more body image concerns than those who reported no binge episodes, after controlling for BMI ($ps < 0.001$). There were no significant differences in body image concerns between individuals who experienced only OBEs, only SBEs, or both OBE and SBEs ($ps > 0.158$; see Table 2).

Finally, results indicated significant group differences for depressive symptoms after controlling for BMI. Participants who experienced any binge episodes had significantly greater depressive symptoms compared to participants who reported no binge episodes ($ps < 0.01$). There were no significant differences in depressive symptoms between individuals who experienced only OBEs, only SBEs, or both OBE and SBEs ($ps > 0.349$; see Table 2).

Discussion

Results comparing AN attitudes and behaviors and dietary restraint across types of binge episodes were mixed. For example, participants who self-reported only SBEs reported significantly greater anorexia-like attitudes and behaviors compared to all other groups and greater dietary restraint than those with only OBEs and those with no binge eating. Participants who self-reported only OBEs did not differ on these constructs when compared to those with no binge eating. Participants who reported both SBEs and OBEs reported greater AN attitudes and behaviors and dietary restraint compared to participants who experienced no binge eating episodes. This is in contrast to data demonstrating no differences in drive for thinness or dietary restraint between adolescents who experienced OBEs only and those who experienced SBEs only [5], suggesting the experience of loss of control in the absence of a large consumption of food may be associated with greater eating disorder symptoms associated with restriction for middle-aged women.

Finally, our findings of no differences between OBEs and SBEs for body image concerns and depressive symptoms are consistent with prior literature among adolescents [5], and adult women ages 18–42 [17].

Table 2 Descriptive Statistics and Group Comparisons of Eating Disorder and Depressive Symptoms According to Types of Binge Episodes

	Objective binge episodes only ($n = 38$)	Subjective binge episodes only ($n = 29$)	Both objective and subjective binge episodes ($n = 76$)	No binge episodes ($n = 204$)	ANOVA/ANCOVA
Anorexia nervosa attitudes and behaviors	6.37 (5.04)[a,c]	12.62 (11.80)[b]	8.74 (7.01)[c]	5.67 (4.25)[a]	$F(3, 346) = 14.21$, $p < .001$, partial $\eta^2 = .11$
Dietary restraint	1.38 (1.23)[a,b]	2.07 (1.61)[c]	1.71 (1.28)[b,c]	1.00 (1.07)[a]	$F(3, 287) = 8.20$, $p < .001$, partial $\eta^2 = .08$
Body image concerns	2.80 (1.31)[a]	2.81 (1.62)[a]	3.00 (1.41)[a]	1.59 (1.19)[b]	$F(3, 344) = 24.12$, $p < .001$, partial $\eta^2 = .18$
Depressive symptoms	14.00 (5.37)[a]	13.03 (4.82)[a]	14.03 (4.70)[a]	10.70 (3.51)[b]	$F(3, 339) = 13.21$, $p < .001$, partial $\eta^2 = .11$

Descriptive statistics presented as means (standard deviations). For anorexia nervosa attitudes and behaviors, an ANOVA model was evaluated. ANCOVA models for dietary restraint, body image concerns, and depressive symptoms controlled for BMI. Anorexia nervosa attitudes and behaviors was measured by the Eating Attitudes Test-26 (possible range: 0–78). Dietary restraint was measured by the Restraint subscale of the Eating Disorder Examination-Questionnaire-4 (possible range: 0–6). Body image concerns were calculated from a combined score of the Weight Concern and Shape Concern subscales of the Eating Disorder Examination-Questionnaire-4 (possible range: 0–6). Depressive symptoms were measured by the depression module of the Patient Health Questionnaire (possible range: 0–24). For all constructs, higher scores reflect greater levels. Different superscript letters indicate significant group differences at $p < .05$ for outcome variables covarying for body mass index, where appropriate, and after applying the Benjamini–Hochberg procedure (Benjamini-Hochberg, 1995) which controlled for multiple comparisons by controlling the false discovery rate

Although some of the current findings are inconsistent with prior data indicating SBEs and OBEs are associated with similar levels of eating pathology [4, 5], they are consistent with prior data among adolescents with subthreshold or threshold bulimia nervosa showing SBEs explained a significantly greater proportion of unique variance of dietary restraint compared to OBEs [2]. Furthermore, given the EAT-26 captures a variety of anorexia-specific attitudes and behaviors [28], it may be that smaller amounts of food lead to feeling out of control (SBEs) for individuals with more rigid and controlled attitudes toward eating in terms of food restriction. Similarly, it is possible the finding that self-reported SBEs only was more related to dietary restraint than OBEs only can potentially be understood within a conceptualization of individuals highly invested in food restriction being more likely to have a sense of loss of control over "normal" or small amounts of food. This finding also supports prior literature among patients in a residential eating disorder treatment center, where SBEs were more highly correlated with dietary restraint than OBEs [34].

It was somewhat surprising that middle-aged women with self-reported OBEs only did not differ significantly from those with no binge eating in terms of AN attitudes and behaviors or dietary restraint. Given the no binge eating group was not a true control group absent of any eating pathology, it is possible individuals with anorexia nervosa restrictive subtype were captured in this group which could explain this finding. In addition, 29% ($n=11$) of participants in the OBEs only group reported only one binge episode in the past 28 days. Therefore, it is possible the large number of individuals reporting low frequencies of binge episodes was driving the lack of differences in AN attitudes and behaviors and dietary restraint between the OBEs only group and the no binge eating group.

Strengths and limitations

Strengths of the current study include the large sample size representing an understudied, yet vulnerable, population: middle-aged women. Limitations of the current study include the high proportion of educated white women in the sample, and the study design targeting recruitment of middle-aged women through their college-aged daughters, both of which limit generalizability to more diverse populations. For example, the study did not have alternative options for daughters without mothers, daughters who thought their mothers may not be interested in participating, or daughters who did not want their mothers to participate. In addition, the cross-sectional study design limits our ability to evaluate changes of these variables across time in middle age. Another limitation of this study is the lack of a true control group absent of any eating pathology. It is possible the no binge group captured participants with anorexia nervosa restricting subtype which could have biased results. Furthermore, although OBEs and SBEs were assessed using the EDE-Q, a well-validated measure [26, 27, 29] that is highly correlated with the EDE clinical interview [35], and depressive symptoms were assessed using the PHQ-9 (the most widely used screener for depressive symptoms which has clinical utility comparable to psychiatric interview [30]), the self-report nature of both the EDE-Q and PHQ-9 may not exactly reflect what a trained clinician or researcher would conclude from an interview. In addition, although psychometric evaluations of the EDE-Q subscales have revealed different factor structures than the original four factors theorized [36–38], there seems to be general agreement that a body dissatisfaction (i.e., weight and shape concerns) factor and a factor capturing dietary restraint exist [36–38] which supports the use of the EDE-Q in the current study.

Future research should compare types of binge episodes in samples of middle-aged women with a full-threshold eating disorder (e.g., binge eating disorder) and middle-aged women who do not meet full-threshold criteria for an eating disorder to further examine which women may be ignored or left out of clinical care based on the current DSM-5 criteria.

What is already known about this subject?

The DSM-5 conceptualizes a binge episode (a transdiagnostic symptom of eating disorders and highly comorbid with depressive symptoms) as having two components (loss of control over eating and consumption of an objectively large amount of food) [12]. However, the ICD-11, which requires only loss of control over eating [15], seems to have greater clinical utility than the DSM-5 which suggests the DSM-5 criteria may be too restrictive and exclude potential cases from clinical care. Data suggest loss of control over eating may be the more relevant component of a binge episode [1–5]. For women, middle-age is a particular window of vulnerability for eating disorder and depressive symptoms [6–9, 21]; however, no prior study has evaluated eating pathology and depressive symptoms according to different components of a binge episode with a specific focus on middle-aged women.

What this study adds?

These data suggest key symptoms of eating disorders and depression occur in middle-aged women who experience loss of control over eating irrespective of binge episode size. Importantly, the current study provides support for the change in diagnostic criteria of binge eating in the ICD-11 which removed the episode size requirement. In

contrast, by including the episode size requirement for binge eating in the DSM-5, the DSM-5 may be excluding middle-aged women who report loss of control over eating not in conjunction with objectively large amounts of food, yet experience potentially greater eating disorder symptoms and equivalent depressive symptoms compared to middle-aged women who experience loss of control when consuming objectively large amounts of food. Clinicians working with middle-aged women should consider screening for loss of control over eating rather than size of eating episodes. For both researchers and clinicians, prevention and intervention programs, which have been tested almost exclusively in adolescents and young adults [39, 40], should consider including and targeting loss of control over eating in middle-aged women.

Overall, this study extends prior literature demonstrating that experiences of loss of control over eating may be the more relevant component of binge eating associated with eating pathology and depressive symptoms in middle-aged women. In addition, there may be something unique about SBEs that is associated with greater levels of AN attitudes and behaviors and dietary restraint compared to the experience of only OBEs.

Author contributions Authors ABC designed the study and wrote the protocol. KAT, AAD, CNG, and JK conducted literature searches, provided summaries of previous research studies, and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

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Availability of data and materials The data sets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Code Availability Analyses were performed using SPSS version 26.

Declarations

Conflict of interest All of the authors declare that they have no conflicts of interest.

Ethical statement This research was conducted using human subjects and in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). This manuscript is in line with the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals. The study was approved by the Institutional Review Board of the University of North Carolina at Chapel Hill, and informed consent was obtained from all participants.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication The authors affirm that human research participants provided inform consent for publication of the data.

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