Menstrual disorders in adolescents and young adults with eating disorders

Nadia Saldanha, MD,* and Martin Fisher, MD

Although amenorrhea is no longer a specific criterion required to make the diagnosis of anorexia nervosa (AN), the relationship between restrictive eating and menstrual status remains important in the diagnosis, treatment, and consequences for patients with eating disorders. Clinicians should understand the relationship between menstrual irregularities and malnutrition due to eating disorders, as it may be possible to intervene sooner if the diagnosis is made earlier. Treatment of AN (in those who are underweight) and atypical AN (in those who are not underweight) is aimed at cessation of restrictive thoughts and behaviors, restoration of appropriate nutrition and weight, and normal functioning of the body. While eating disorder thoughts and behaviors are helped by both therapy and nutrition, regular functioning of the body, including regular menstruation, is linked to both appropriate nutrition and weight. Patients who are not underweight based on their body mass index (BMI) may still have oligo/amenorrhea due to their caloric restriction; thus any patient who has irregular menses should have a detailed dietary evaluation as part of their workup. Timely diagnosis and treatment of patients with eating disorders and amenorrhea is important due to the impact on bone mass accrual for adolescents who have prolonged amenorrhea. Menstrual abnormalities may also be seen in patients with bulimia nervosa (BN).

Curr Probl Pediatr Adolesc Health Care 2022; 52:101240

Eating disorders are a common diagnosis among adolescents and young adults, impacting 0.3F1.6% of adolescents[1] in the United States, depending on eating disorder subtype; and there has been an increase in eating disorder behaviors and diagnoses during the COVID-19 pandemic.[2,3] While patients may present with a clear history of intentional weight loss and dietary restriction, oftentimes patients do not disclose their behaviors due to feelings of guilt or not wanting anyone to know about their eating disorder behaviors. Vital sign changes and physical examination findings, such as bradycardia or hypotension, may indicate the presence of an eating disorder, but often these abnormalities are only present when the malnutrition is more severe.[4]

One of the key findings for many patients with malnutrition is the absence of regular periods. This amenorrhea may even occur before any weight loss as was noted in approximately 20% of patients with anorexia nervosa (AN) in one study.

One of the key findings for many patients with malnutrition is the absence of regular periods. This amenorrhea may even occur before any weight loss as was noted in approximately 20% of patients with anorexia nervosa (AN) in one study.

For this reason, it is important for clinicians to understand the relationship between menstrual irregularities and malnutrition due to eating disorders, as it may be possible to intervene sooner if the diagnosis is made earlier.

Patients with restrictive eating disorders will primarily carry the diagnosis of AN, atypical AN, or Avoidant Restrictive Food Intake Disorder (ARFID). The Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) (DSM-5)

From the Division of Adolescent Medicine, Cohen Children's Medical Center, Northwell Health, 410 Lakeville Road, Suite 108, New Hyde Park, New York 11042, USA; andDonald and Barbara Zucker, School of Medicine at Hofstra / Northwell, Hempstead, New York, USA.
*Corresponding author.
E-mail: NSaldanh12@northwell.edu

Curr Probl Pediatr Adolesc Health Care 2022;52:101240
1538-5442/$ - see front matter

https://doi.org/10.1016/j.cppeds.2022.101240

currently defines AN as a disorder in which restriction of energy intake relative to a person's requirements leads to a significantly low weight or, specifically in adolescents, a weight that is less than what is minimally expected. Other features include an intense fear of gaining weight despite being at a low weight and a lack of recognition of the severity of the illness. Notable in the current definition is the absence of amenorrhea.[5] In previous versions of the DSM, amenorrhea was required to make the diagnosis of AN. The removal of amenorrhea as a requirement for the diagnosis of AN was done in part to broaden the group of patients who could be diagnosed with AN—those who despite being at a low weight continue to have regular periods and otherwise meet the criteria of AN, and in part became amenorrhea is now acknowledged to be a physiologic response to the weight loss rather than a core psychological aspect of the condition.[4] AN and atypical AN have a similar pathophysiology, with the main difference being that patients with atypical AN do not lose to a weight that makes them underweight based on age and height percentiles, but those patients can and do have the same degree of medical compromise as patients with typical AN based on the amount and/or rapidity of their weight loss.[6,7] Patients with ARFID, who tend to be younger than those with AN and atypical AN and thus may present earlier in their pubertal course, restrict their diet due to anxiety or avoidance of a particular food or fear of inciting a particular event, such as vomiting, choking, an allergic reaction, or abdominal pain, among others. Due to the restricted caloric intake for patients with AN, atypical AN or ARFID, in addition to the psychological stress related to fears about eating or weight gain, these patients can develop irregular menses or amenorrhea. It is important to note that patients who are not underweight based on their body mass index (BMI) may still have oligo/amenorrhea due to their caloric restriction; thus any patient who has irregular menses or amenorrhea should have a detailed dietary evaluation as part of their workup.

Amenorrhea in patients with eating disorders is generally classified as functional hypothalamic amenorrhea, which is amenorrhea not attributed to another organic cause and is instead related to stress, inadequate caloric intake, or, in some cases, excessive exercise.

Patients with malnutrition may have primary or secondary amenorrhea—primary amenorrhea defined as the absence of menarche by age 15 years in someone with otherwise normal growth and development, and secondary amenorrhea defined as the absence of menses for three consecutive months in someone who has achieved menarche.

Amenorrhea in patients with eating disorders is generally classified as functional hypothalamic amenorrhea, which is amenorrhea not attributed to another organic cause and is instead related to stress, inadequate caloric intake, or, in some cases, excessive exercise.

The timing of the malnutrition as it relates to pubertal development will determine whether the amenorrhea is primary, as the patient may present with delayed puberty, but more often patients will present with secondary amenorrhea.[8]

In functional hypothalamic amenorrhea, gonadotrophin releasing hormone (GnRH) drive is reduced, leading to a reduction in lutenizing hormone (LH) pulses and follicular stimulating hormone (FSH) levels, which cause ovulatory dysfunction.[9] The follicular phase becomes prolonged, and without adequate stimulation, ovulation and the luteal phase may not occur. The impact of stress and malnutrition is mediated on the hypothalamic-pituitary-ovarian (HPO) axis by a combination of hormonal and neuroendocrine changes. The mechanism of this suppression involves neurotransmitters, including leptin, corticotropin releasing hormone (CRH), norepinephrine, beta-endorphins and dopamine, as each are involved in the regulation of GnRH. The energy depletion of weight loss and exercise are thought to exert their effects on the HPO axis through leptin, while stress and exercise may exert their effects through the hypothalamic-pituitary-adrenal (HPA) axis, norepinephrine, beta-endorphins, and CRH.[10]

The HPA axis is directly impacted by insufficient nutrition. Caloric restriction activates the HPA axis, which leads to a decrease in LH pulsatility. The HPA axis is also activated by psychological stress.[9] Stress results in the release of norepinephrine and CRH, which leads to increased levels of glucocorticoids, which in turn suppress pituitary release of LH and

ovarian release of estrogen and progesterone. Corticotropin-releasing hormone is also found in ovarian tissue and other reproductive organs, having a direct effect on all aspects of reproductive function. Higher levels of CRH directly inhibit GnRH pulsatility and indirectly inhibit GnRH through the activation of endorphins, which then further inhibits GnRH.[10]

Leptin is secreted in proportion to the amount of adipose tissue and is an indicator of the amount of energy reserves the body has.

Leptin has been well-studied with regard to malnutrition and amenorrhea, as leptin levels have been shown to be a marker of energy stores in fat and changes in caloric intake.

Leptin has been well-studied with regard to malnutrition and amenorrhea, as leptin levels have been shown to be a marker of energy stores in fat and changes in caloric intake.

Lower levels of leptin are believed to be an adaptive response to an energy-deficient state, as leptin decreases appetite, so in a malnourished state leptin levels are lowered in order to prevent the body from being susceptible to its appetite suppressant effects. In women who are normal weight and have hypothalamic amenorrhea, leptin levels have also been found to be low. In a study by Bruni et al. that looked to differentiate patients with functional hypothalamic amenorrhea from those with amenorrhea due to eating disorders, they found that leptin was lower in those with eating disorders, although it was lower than normal in both groups.[11] In an older study of women with a BMI less than 17.5 kg/m2, those who had amenorrhea also had lower leptin levels than those women who had periods but were at a low weight.[12] Because of this, studies have looked at a possible therapeutic effect of leptin on patients with amenorrhea and eating disorders and have found that administration of recombinant leptin led to LH pulsatility and ovulation in patients with hypothalamic amenorrhea.[13,14] Clinically, however, treatment for resumption of menses has been focused on improved nutrition and not by providing leptin replacement in patients with eating disorders.

Treatment of AN and atypical AN is aimed at cessation of restrictive thoughts and behaviors, restoration of appropriate nutrition and weight, and normal functioning of the body. While eating disorder thoughts and behaviors are helped by both therapy and nutrition, the regular functioning of the body, including regular menstruation, is linked to both appropriate nutrition and weight. One area that has been studied, but still remains unclear, is what weight best predicts the resumption of menses in patient with restrictive eating disorders. Identifying a weight range in which resumption of menses can be expected is an important part of treatment as it often provides clinicians and patients with a target to work towards; but identifying the weight range is not uniform and needs to take into account multiple factors. In an older study of 127 adolescents with AN and secondary amenorrhea, the weight at which menstruation resumed was closely related to the weight at which menstruation was lost.[15] Weight gain is necessary for resumption of menses, as androgens are converted to estrogen in fat tissue. Because of this, there has also been discussion as to whether it is just weight that helps predict resumption of menses or if body composition also plays a role. Ghoch et al. found in their study of adult women with AN who had weight restored to a normal body weight, those who had resumed menses had significantly higher total body fat percentage.[16] In another study of adult women, those who resumed menstruation also had a significantly higher body fat percentage than whose who remained amenorrheic. The authors also found that total fat mass and lean mass were less strong predictors of resumption of menses compared to fat percentage.[17] When counseling patients, it is important for them to understand, therefore, that weight alone is not the only metric to determine resumption of menses, as many patients will be reluctant to gain more weight once reaching their presumed goal weight, but it may be that they need to also regain body fat.

Prospective studies to address multiple factors that contribute to resumption of menses in patients with restrictive eating disorders are limited. Golden et al. followed patients with anorexia nervosa for two years. During that time, in addition to measuring weight and percent body fat, they also measured several hormones, including estradiol, lutenizing hormone and follicular stimulating hormone. In their sample of 100 adolescents with anorexia nervosa, 86% had resumption of menses within six months of reaching 90% of standard body weight. In their study, percent body fat did not predict resumption of menses. Those that did have resumption of menses had an estradiol of at least

30 pg/mL. The authors also found that a weight of approximately 2 kg above the weight at which the patient last had menses was necessary for resumption of menses in most of their patients.[18] More recently, Castellini et al. performed a similar study that followed patients with anorexia nervosa for four years. In addition to measuring estradiol, LH, FSH, and BMI at study enrollment, they also included two self-administered eating disorder questionnaires, the Symptom Checklist-90 and the Eating Disorder Examination Questionnaire. In their sample of 50 patients, 29 had resumption of menses during the study period. Those who had resumption of menses earlier had a shorter duration of illness and the binge-eating/purging subtype of AN.[19] This study highlights the importance of early diagnosis, as those with a shorter eating disorder course had resumption of menses sooner.

In another study of adolescents and young adults with anorexia nervosa, resumption of menses occurred on average at 95% of expected body weight, which the authors suggested means that previous goal weights set at a lower percentage may be insufficient for resumption of menses.

In the same study, about one third of patients who did not have resumption of menses did achieve at least 95% of expected body weight, indicating that average expected body weight may not be a high enough goal weight for all patients.[20]

It is important to note that for patients with atypical AN, whose weight may have always been above the expected body weight for age, a goal weight at what would ordinarily be the expected body weight for height and age is likely too low for them to have resumption of menses and resolution of their eating disorder. In practice, using an individual patient's own growth curve is often the most useful tool to identify the growth trajectory for that patient in order to project where she needs to be to have periods return. In a study of 163 adolescents with anorexia nervosa and secondary amenorrhea, Seetharaman et al. found that the amount of weight gain needed for resumption of menses was somewhat different for patients whose pre-morbid weight was normal as for those who were overweight. Those who were at a normal weight prior to weight loss needed to gain to approximately 94% of the weight at the 50th percentile BMI for those patients while those who were overweight needed to gain to approximately 106% of the weight at the 50th percentile BMI for those patients.[21] When setting the goal treatment weight for resumption of menses, therefore, it is necessary to use estimated average body weight for height and age, weight at last menstrual period, and the patient's own growth history.

A primary concern for patients with eating disorders who develop amenorrhea is the impact of amenorrhea on their bone health. Unlike an adult who has already achieved peak bone mass and then develops an eating disorder, adolescents are at risk of impacting both their bone growth and mineralization.

A primary concern for patients with eating disorders who develop amenorrhea is the impact of amenorrhea on their bone health. Unlike an adult who has already achieved peak bone mass and then develops an eating disorder, adolescents are at risk of impacting both their bone growth and mineralization.

Risk of osteoporosis is related to accrual of bone mineral density; thus, if adolescents have suboptimal bone mineral density they are at risk of developing osteoporosis and fractures even after they achieve weight restoration, with long term studies suggesting this risk persists for at least 10 years after the eating disorder diagnosis is made.[10] Even in patients with subclinical eating disorders, there may be loss of bone mineral density, highlighting the need for early diagnosis.[22] High estrogen levels impact bone growth via IGF-1 by stimulating the growth spurt and playing a role in the accrual and maintenance of bone mineral density.[23]

In another study of adolescents and young adults with anorexia nervosa, resumption of menses occurred on average at 95% of expected body weight, which the authors suggested means that previous goal weights set at a lower percentage may be insufficient for resumption of menses.

Given the impact of secondary amenorrhea on bone growth, it has been theorized that estrogen replacement would be a beneficial treatment to manage the

effects of amenorrhea. Multiple studies have shown, however, that weight gain is necessary to raise estrogen levels in these patients and that administration of estrogen via oral contraceptive pills does not help improve bone mineral density. This is believed to result from the lowering of IGF-1 caused by the estrogen in oral contraceptive pills. IGF-1 enhances bone formation through its action on mature osteoblasts, and circulating levels of IGF-1 are necessary for the preservation of cortical bone mass. Physiologic estrogen replacement at doses higher than what is found in oral contraceptive pills does increase bone accrual rates in those with AN. In a study by Misra et al. of 150 girls with AN, those who were given estrogen via a transdermal patch twice a week containing 100 microgram of estrogen did show an increase in their bone mineral density Z-scores of the spine and hip when compared to those who did not receive estrogen.[24] An increase in bone mineral density in these patients may result in maintenance of bone mineral density depending on the duration of amenorrhea and where the patient is in their skeletal development and thus catch-up for existing losses may not occur, likely because of the effect of other hormones.[25,13,26] Clinically many providers will start patients on calcium and vitamin D to help improve bone health, but studies have not shown an improvement in bone mineral density in those with anorexia nervosa who are given these vitamins for supplementation.[27] Because of the potential long term impact of the malnutrition and hypogonadal state, it is important to highlight for patients why the resumption of menses is such a key marker of progress in treatment.

Another concern of many patients and families is the impact of amenorrhea on future fertility. Some studies have shown higher rates of fertility problems and increased rates of obstetric complications in those who have had anorexia nervosa, while others have shown no difference in rate of pregnancy or need for infertility treatment.[28] In a large cohort study, women with a history of AN were more likely to seek medical care for concerns of a fertility issue than those without AN, but did not require fertility treatment more than others in the cohort.[29] In a study by Linna et al., patients with eating disorders were less likely to have children and had lower pregnancy rates compared to controls.[30] Whether this is due to fertility issues, or a desire to not get pregnant due to persistent body image concerns, is unclear. In a recent study, Pitts et al. measured Anti-Mullerian hormone (AMH) as a marker of ovarian reserve in adolescents and young adults with eating disorders, hypothesizing that these patients would have lower levels of Anti-Mullerian hormone due to their malnutrition. Prior studies have shown that AMH is a marker of ovarian reserve and is not affected by the activity of the hypothalamic-ovarian axis.[31] Interestingly they found that the levels of AMH were higher in those with anorexia nervosa when compared to healthy study participants and published normative data, concluding that AMH could be measured to identify ovarian reserve in patients with anorexia nervosa.[32]

In a systematic review of studies of women who had recovered from AN and were followed-up over the long term, Chaer et al. found that weight gain and weight restoration lead to the normalization of reproductive function.[33] Patients can generally be counseled that with appropriate treatment of their eating disorder, their fertility will return to that which was expected prior to their malnutrition and amenorrhea.

In a systematic review of studies of women who had recovered from AN and were followed-up over the long term, Chaer et al. found that weight gain and weight restoration lead to the normalization of reproductive function.[33] Patients can generally be counseled that with appropriate treatment of their eating disorder, their fertility will return to that which was expected prior to their malnutrition and amenorrhea.

While the menstrual abnormalities are more common among patients with restrictive eating disorders compared to those with bulimia nervosa (BN), patient with bulimia or purging behaviors can also see disruptions in regular menstrual function. BN is defined by recurrent binge eating episodes that include a lack of control over eating during the binge episode. Binge eating occurs in a discrete amount of time and involves consuming a larger amount of food than what most people would eat. In addition to the binge episode there is a compensatory mechanism to prevent weight gain, which may include vomiting, laxative or diuretic use, or excessive exercising.[5]

In a study of adolescent girls, those reporting vomiting as a weight control behavior 1 to 3 times per month were 1.5 times more likely than those without vomiting to have irregular menses, and girls vomiting more than once per week were 3 times more likely to have irregular menses after adjustment for body mass index (BMI), age, and race,

In a study of adolescent girls, those reporting vomiting as a weight control behavior 1 to 3 times per month were 1.5 times more likely than those without vomiting to have irregular menses, and girls vomiting more than once per week were 3 times more likely to have irregular menses after adjustment for body mass index (BMI), age, and race,

Including only those with a normal BMI.[34] This is important, as patients may present with irregular menses and not amenorrhea to their primary care doctor, and in those patients an eating disorder should be considered. In a sample of adult women, secondary amenorrhea was more common in those with restrictive eating disorders, but 8.7% of patients with BN reported secondary amenorrhea, which suggests that other stressors, in addition to weight loss, can have an impact on the HPO axis.[35] Menstrual abnormalities can be seen in patients with binge eating, but those are similar to what is seen in patients with an elevated BMI, as discussed in a separate article in this review.

In summary, menstrual abnormalities can be seen in patients with all subtypes of eating disorders but absence of menses is most commonly seen in those with malnutrition due to a restrictive eating disorder. Patients with eating disorders often do not want to disclose their eating disorder behaviors and thoughts and may present to their primary care doctor or gynecologist for menstrual concerns well before they are seen by an eating disorder specialist. Thus, for any patient with irregular menses it is important to take a brief dietary history, assess for changes in weight, and ask about body image concerns. The shorter the duration of illness the less likely it is for amenorrhea to develop and the faster it is for menses to resume. This is important given the impact on bone mass accrual for adolescents who have prolonged amenorrhea. The best treatment for amenorrhea in patients with eating disorders is weight gain to at least where menses stopped, or possibly to a higher weight depending on the patient's previous growth trajectory. Fortunately, with appropriate treatment, adolescents with amenorrhea due to their eating disorder are not likely to develop future fertility issues, which may provide some comfort during what can be a challenging illness and treatment course.

Declaration of Competing Interest

The authors do not have any conflicts to declare.

References

1. Hornberger LL, Lane MA. Committee on adolescence. identification and management of eating disorders in children and adolescents. *Pediatrics* 2021;147:e2020040279.
2. Robertson M, Duffy F, Newman E, et al. Exploring changes in body image, eating and exercise during the COVID-19 lockdown: a UK survey. *Appetite* 2021;159:105062.
3. Reed J, Ort K. The rise of eating disorders during COVID-19 and the impact on treatment. *J Am Acad Child Adolesc Psychiatry* 2021 Nov 12:S0890-8567(21)01976-6.
4. Attia E, Roberto CA. Should amenorrhea be a diagnostic criterion for anorexia nervosa? *Int J Eat Disord* 2009;42:581–9.
5. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.
6. Peebles R, Hardy K, Wilson J, et al. Medical compromise in eating disorders not otherwise specified: are diagnostic criteria for eating disorders markers of medical severity? *Pediatrics* 2010;125:e1193–201.
7. Sawyer S, Whitelaw M, Le Grange D et al. Physical and psychological morbidity in adolescents with atypical anorexia nervosa. Pediatrics. 2016 137: pii: e20154080
8. Jamieson M. Disorders of menstruation in adolescent girls. *Pediatr Clin N Am* 2015;62(9):43–961.
9. Gordon CM, Ackerman KE, Berga SL, et al. Functional hypothalamic amenorrhea: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2017;102:1413–39.
10. Saldanha N, Carmine L. Endocrine abnormalities in patients with eating disorders. *Adolesc Med* 2015;26:393–410.
11. Bruni V, Dei M, Morelli C, et al. Body composition variables and leptin levels in functional hypothalamic amenorrhea and amenorrhea related to eating disorders. *J Pediatr Adolesc Gynecol* 2011;24:347–52.
12. Gendall K, Joyce P, Carter F, et al. The psychobiology and diagnostic significance of amenorrhea in patients with anorexia nervosa. *Fertil Steril* 2006;85:1531–5.
13. Warren MP. Endocrine manifestations of eating disorders. *J Clin Endocrinol Metab* 2011;96:333–43.

14. Singhal V, Misra M, Kilbanski A. Endocrinology of anorexia nervosa in young people: recent insights. *Curr Opin Endocrinol Diabetes Obes* 2014;21:64–70.
15. Swenne I. Weight requirements for return of menstruations in teenage girls with eating disorders, weight loss and secondary amenorrhea. *Acta Paediatr* 2004;93:1449–55.
16. Ghoch ME, Calugi S, Chignola E, et al. Body fat and menstrual resumption in adult females with anorexia nervosa: a 1-year longitudinal study. *J Hum Nutr Diet* 2016;29:662–6.
17. Winkler LA, Frolich JS, Schulpen M, et al. Body composition and menstrual status in adults with a history of anorexia nervosa—at what fat percentage is the menstrual cycle restored? *Int J Eat Disord* 2017;50:370–7.
18. Golden NH, Jacobson MS, Schebendach J, et al. Resumptions of menses in anorexia nervosa. *Arch Pediatr Adolesc Med* 1997;151:16–21.
19. Castellini G, Rossi E, Cassioli E, et al. Predictors of resumption of menses in anorexia nervosa: a 4-year longitudinal study. *Psychosomat Med* 2020;82:782–6.
20. Faust JP, Goldschmidt AB, Anderson KE, et al. Resumption of menses in anorexia nervosa during a course of family-based treatment. *J Eat Disord* 2022;1:12.
21. Seetharaman S, Golden NH, Halpern-Felsher B, et al. Effect of a prior history of overweight on return of menses in adolescents with eating disorders. *J Adolesc Health* 2017;60:469–71.
22. Nieves JW, Ruffing JA, Zion M, et al. Eating disorders, menstrual dysfunction, weight change, and DMPA use predict bone density change in college-aged women. *Bone* 2016; 84:113–9.
23. Emmanuelle NE, Marie-Cécile V, Florence T, et al. Critical role of estrogens on bone homeostasis in both male and female: from physiology to medical implications. *Int J Mol Sci* 2021;22:1568.
24. Misra M, Katzman D, Miller KK, et al. Physiologic estrogen replacement increases bone density in adolescent girls with anorexia nervosa. *J Bone Miner Res* 2011;10:2430–8.
25. Swenne I, Stridsberg M. Bone metabolism markers in adolescent girls with eating disorders and weight loss: effects of growth, weight trend, developmental and menstrual status. *Arch Osteoporos* 2012;7:125–33.
26. Misra M, Kilbanski A. Anorexia Nervosa and Bone. *J Endocrinol* 2014;221:R163–76.
27. Foo JP, Hamnvik OP, Mantzoros CS. Optimizing bone health in anorexia nervosa and hypothalamic amenorrhea: new trials and tribulations. *Metabolism* 2012;61:899–905.
28. Kimmel MC, Ferguson EH, Zerwas S, Bulik CM, Meltzer-Brody S. Obstetric and gynecologic problems associated with eating disorders. *Int J Eat Disord* 2016;49:260–75.
29. Easter A, Treasure J, Micali N. Fertility and prenatal attitudes towards pregnancy in women with eating disorders: results from the avon longitudinal study of parents and children. *BJOG* 2011;118:1491–8.
30. Linna MS, Raevuori A, Haukka J, et al. Reproductive health outcomes in eating disorders. *Int J Eat Disord* 2013 Dec 46:826–33.
31. Luisi S, Ciani V, Podfigurna-Stopa A, et al. Serum anti-mullerian hormone, inhibin B, and total inhibin levels in women with hypothalamic amenorrhea and anorexia nervosa. *Gynecolog Endocrinol* 2012;28:34–8.
32. Pitts S, Dahlberg SE, Gallagher JS, et al. Is ovarian reserve impacted in anorexia nervosa? *J Pediatr Adolesc Gynecol* 2021;34:196–202.
33. Chaer R, Nakouzi N, Itani L, et al. Fertility and reproduction after recovery from anorexia nervosa: a systematic review and meta-analysis of long-term follow-up studies. *Diseases* 2020;8:46.
34. Austin SB, Ziyadeh NJ, Vohra S, et al. Irregular menses linked to vomiting in a nonclinical sample: findings from the national eating disorders screening program in high schools. *J Adolesc Health* 2008;42:450–7.
35. Martini MG, Solmi F, Krug I, et al. Associations between eating disorder diagnoses, behaviors, and menstrual dysfunction in a clinical sample. *Arch Womens Ment Health* 2016;19:553–7.