

# Depression, Anxiety, and Pubertal Timing

## CURRENT RESEARCH AND FUTURE DIRECTIONS

ABIGAIL G. RICHBURG, DOMINIC P. KELLY, AND PAMELA E. DAVIS-KEAN

The current review synthesizes the literature regarding the effects of early and late pubertal timing on adolescent depression and anxiety. Early pubertal timing has been consistently shown to increase the risk of depression and anxiety in adolescents, particularly adolescent girls. Late pubertal timing has yielded more mixed results, with some research suggesting an increased risk of depression and anxiety in adolescent boys, indicating the need for future research specifically examining potential late pubertal timing effects on adolescent mental health disorders. Future research should examine the interactions between pubertal timing and pubertal status, as well as focus on diversifying samples to explore the pubertal experiences of many different groups, such as adolescent boys, low-SES adolescents, racial and ethnic minorities, and LGBTQ+ adolescents.

#### **Keywords**

pubertal timing, early pubertal timing, adolescence

#### Introduction

Throughout recent decades, the rate of child and adolescent mental disorder diagnoses has risen significantly. A 2015 meta-analysis evaluating the prevalence of child and adolescent mental disorders in 27 countries from across the world estimated that 13.4% of children and adolescents are affected by mental disorders. A 2019 analysis of the National Survey of Children's Health, a nationally representative sample from the United States, found that among children between the ages of 3–17 years, 3.2% and 7.1% had current depression and anxiety problems, respectively. Although these disorders can occur in children,

Contact: Abigail G. Richburg

they often first appear during adolescence, and adolescents are at heightened risk for diagnosis.<sup>4–8</sup>

Some theories suggest that adolescence may be a risky period for mental health disorders due to the varied effects of puberty on development. Although puberty itself is universal biological transition, the experience of puberty can differ dramatically between individuals depending on a complex interplay between multiple biological and social factors. One such factor is the effect of pubertal timing, defined here as the timing of the onset of puberty in relation to the timing of puberty for same-gender and same-age peers. Pubertal timing has been thought to affect the prevalence of depression and anxiety in adolescents. Given that we know that the age of onset of puberty is decreasing in both boys and girls worldwide, understanding the effects of earlier pubertal timing on mental health outcomes is urgent.

Due to the important consequences of mental health disorders during adolescence and their downstream effects across the lifespan, greater comprehension is needed of the effects of pubertal timing on the development of depression and anxiety. Therefore, this review serves two purposes: first, to examine the existing research on the relationship between early and late pubertal timing on adolescent depression and anxiety; and second, to identify the unanswered questions and future directions required for this crucial line of research.

#### Mental Health Disorders and Adolescence

Globally, depression and anxiety are the most common mental health disorders in total.4, 16-17 Depression affects many facets of a person's life, including, but not limited to, daily functioning, mood, interests, appetite, cognition, and energy levels. 18-20 Likewise, anxiety has been shown to affect concentration, sleep, mood, and academic performance.21-23 In general, depression is understood to be a collection of symptoms related to negative affect or an inability to feel pleasure, 6, 18, 24 while anxiety is understood to be a state of negative emotional arousal with an intense focus on the future.<sup>23, 25</sup> Theoretical work on depression and anxiety suggests that both disorders involve issues with downregulation of negative affect, but depression also involves issues with regulation of positive affect.<sup>7, 26</sup> Approximately 6% and 4–7% of adults worldwide suffer from Major Depressive Disorder and Generalized Anxiety Disorder, respectively. 19, 23 However, the two disorders frequently co-occur, and their symptoms often overlap.<sup>27</sup> Furthermore, it is important to note that many people experience symptoms of depression and anxiety without being diagnosed with either condition.<sup>20-21</sup> Data suggest that female depression and anxiety rates are higher than male depression rates throughout the lifespan.<sup>28–30</sup>

41

For adolescents, depression and anxiety are the most prevalent mental health disorders.<sup>31–33</sup> While mental health disorders can occur in children, they often first appear during adolescence.<sup>4, 6, 8</sup> Depressive symptoms are related to a range of potential problem behaviors during adolescence, including drug and alcohol use, <sup>34–35</sup> risky sexual behaviors, <sup>36–37</sup> and suicidal behaviors.<sup>6, 38–39</sup> Likewise, anxiety may lead to harmful outcomes during adolescence, including worse academic achievement, <sup>22, 43</sup> less peer acceptance, <sup>44–45</sup> more peer victimization, <sup>44–46</sup> and the development of depressive symptoms. <sup>47</sup> Adolescent depression has also been shown to negatively impact downstream outcomes in adulthood, including impaired educational attainment, <sup>40</sup> difficulty with interpersonal relationships, <sup>31, 41</sup> substance abuse, <sup>31</sup> and mental health issues throughout the lifespan. <sup>31, 42</sup> Similarly, adolescents who experience anxiety may experience downstream effects of their condition in adulthood, including decreased life satisfaction, <sup>48</sup> poor family relationships, <sup>49</sup> worse employment and income outcomes, <sup>50</sup> and mental health issues. <sup>49, 51, 52</sup>

## Mental Health Disorders and Pubertal Timing

Puberty marks a time of significant biological and social maturation<sup>9, 53</sup> Biological maturation refers to hormonal changes, such as increased testosterone and estrogen, and resulting physical changes in the body, such as deepened voice for males and development of breasts in females.<sup>54</sup> Social maturation refers to the fact that puberty marks a social milestone that is influenced by gender-specific societal views and expectations.<sup>55</sup> The pubertal transition takes place throughout three to four years and involves complex interplay between these biological and social factors.<sup>9</sup> Globally, data suggest that the onset of puberty is becoming earlier.<sup>13</sup>

The timing of a child's pubertal onset is the result of biological and environmental factors and the interplay between them. Pubertal timing is a highly heritable trait;<sup>57–59</sup> an estimated 50–80% of the variation in pubertal timing is thought to be genetically determined.<sup>57</sup> Some environmental factors thought to affect pubertal timing include chronic psychological stress, father absence, and parental conflict.<sup>55, 60–61</sup> Evidence indicates that children who live in low socioeconomic status (SES) households, particularly girls, experience earlier pubertal timing on average than their peers who live in middle or high SES households.<sup>55, 62, 63</sup> Furthermore, pubertal timing seems to be influenced by childhood diet.<sup>64–66</sup> Various facets of childhood diets may differentially impact pubertal timing in boys and girls; for example, research has linked higher vegetable and lean protein consumption at the age of three to delayed breast development in girls and higher processed meat and refined grain consumption at the age of three to advanced testicular development in boys.<sup>65</sup> Inversely, higher processed and high-fat food consumption tends to trigger the onset of puberty earlier, particularly for girls.<sup>66</sup>

Another cause is speculated to be exposure to endocrine-disrupting chemicals that are often found in plastics and other materials.<sup>14, 56</sup>

The consequences of offset pubertal timing are broad; for example, earlier pubertal timing has been associated with worsened body image and beliefs for girls,<sup>67</sup> earlier and riskier adolescent sexual behavior for boys and girls,<sup>68</sup> and adolescent substance use for boys and girls.<sup>69</sup> Some of the most extensive work has been on the effects of pubertal timing on depression and anxiety, especially the differing effects of early and late pubertal timing.

Theories. Three commonly cited hypotheses attempt to explain the relationship between offset pubertal timing and increased risk of mental health disorders: the maturational disparity, social deviance, and gendered deviation hypotheses.<sup>5</sup> The maturational disparity hypothesis posits that early pubertal timing is detrimental to both boys and girls due to the disparity between their advanced physical development and their relatively lagging cognitive and emotional development.5 Specifically, the mismatch between advanced development in the limbic system and gradual development in the prefrontal cortex may place early-developing adolescents at a higher risk for mental health disorders. 5, 53, 55 The social deviance hypothesis postulates that offset pubertal timing, be it early or late, leads to an increased risk of mental health disorders.<sup>5</sup> This may be due to the social consequences of being unlike one's peers, such as the stress of feeling different or misunderstood.55 The gendered deviation hypothesis suggests that early-developing girls and late-developing boys are each at increased risk of mental health disorders.<sup>5</sup> This elevated risk occurs at the intersection of within- and across-gender comparisons, as early maturing girls and late maturing boys constitute the most extreme ends of the entire peer group.<sup>5</sup> While the maturational disparity hypothesis has received much empirical attention and support,5,70 late pubertal timing is generally less understood and less studied,5,53 and boys are generally underrepresented in puberty research,71 indicating the need for further research in order to better establish the veracity of these three theories.

Early pubertal timing. Adolescents who experience the onset of puberty earlier than their same-gender and same-age peers have been shown to be at a higher risk for mental health disorders.<sup>5, 9, 70</sup> This relationship has been observed in adolescent samples throughout the world.<sup>5, 72, 73</sup> Both cross-sectional and longitudinal data support the negative correlation between pubertal timing and risk for mental health disorders.<sup>74–75</sup> Furthermore, these effects have been shown to persist into adulthood.<sup>11, 53</sup>

Early pubertal timing has been shown to be an especially significant risk factor for mental health disorders in females, an effect that has been consistently replicated.<sup>5, 53, 55</sup> For example, a 2013 analysis of 3,648 girls from a U.K. birth cohort found a strong relationship between early menarche and increased depressive symptoms in early to mid-adolescence.<sup>76</sup> In general, pubertal timing

research has focused more on female adolescents, and the detrimental effects of early pubertal timing appear to be stronger for females.<sup>5, 55</sup> Because females are two times more likely than males to develop mental health disorders during puberty,<sup>5, 77</sup> the abundance of research regarding mental health in this population may be due to the relative prevalence of those disorders in this gender.

However, some studies have also demonstrated that early pubertal timing is also a strong risk factor for depression and anxiety in boys.<sup>5, 55, 78</sup> A 2017 meta-analysis found that sex did not moderate the small but significant association found between early pubertal timing and mental health disorders, meaning that this relationship did not depend on sex.<sup>5</sup> Some posit that although the magnitude of direct effects of pubertal timing on mental health disorders is similar for boys and girls, there is still reason to believe that the mechanisms that cause this effect may vary by sex.<sup>5</sup> For example, psychosocial mechanisms may include the social and interpersonal skills required to navigate relationships during the pubertal transition. Boys and girls may differ in the extent to which they display such skills, but some researchers suggest that future research is needed to examine possible sex differences.<sup>5</sup>

Four mechanisms have commonly been proposed to explain the relationship between early pubertal timing and increased risk of mental health disorders: hormonal influence, maturation disparity, contextual amplification, and accentuation.<sup>70</sup> First, the hormonal influence hypothesis proposes that the hormonal changes associated with puberty place early-developing adolescents at risk for poor mental health outcomes either due to greater sensitivity to pubertal hormones or because they are exposed to greater amounts of them.<sup>79–80</sup> Second, the maturation disparity hypothesis states that the relationship between early pubertal timing and mental health disorders is a result of the disparity between physical and psychosocial maturity in early-developing adolescents.<sup>70, 80</sup> Third, the contextual amplification hypothesis states that the biological changes associated with puberty interact with stressful environments and amplify environmental stressors, such as peer pressure.<sup>70, 78</sup> Finally, the accentuation hypothesis states that pre-existing emotional and behavioral issues, such as increased negative affect, become amplified due to the stress and uncertainty associated with early pubertal timing.<sup>5, 70, 74, 78</sup>

Late pubertal timing. Compared to the findings on early pubertal timing, research findings related to late pubertal timing are more mixed.<sup>5, 53</sup> Much of the literature seems to agree that late pubertal timing does not appear to make mental health disorders more likely for girls.<sup>5, 81</sup> In fact, some studies have pointed to potential protective effects of late pubertal timing on mental health disorders for girls,<sup>5</sup> and some studies of female adolescents have found a positive correlation between late pubertal timing and factors related to psychological functioning, such as academic achievement.<sup>53, 82</sup>

However, in line with the gendered deviation hypothesis, there is some research that suggests that late pubertal timing has a negative impact on boys. <sup>57</sup> <sup>10, 55, 83–84</sup> For example, a 2009 study found that depression was associated with early pubertal timing in girls and late pubertal timing in boys. <sup>83</sup> Another 2010 study supported the gendered deviation hypothesis in its finding that under high peer stress, both early-developing girls and late-developing boys were at the highest risk for maladjustment. <sup>84</sup> However, in contrast, a 2017 meta-analysis found no significant association between late pubertal timing and mental health disorders for either boys or girls. <sup>5</sup> This disparity is potentially due to the relative lack of research examining late pubertal timing and mental health disorders. Generally, there is a much larger body of literature examining early pubertal timing as opposed to late pubertal timing, <sup>5</sup> and given the lack of research that could be included in the aforementioned meta-analysis, more research is needed on the effects of late pubertal timing to be more confident of its effects.

**Measurement.** Pubertal timing can be measured using a wide variety of methodologies, which can be split into two categories: one, concerning the timing of milestones of puberty, or two, using self- or parent-reports of pubertal onset.

First, pubertal timing can be measured by determining the onset of certain events associated with pubertal status for an individual. Pubertal status refers to an adolescent's stage of pubertal development, regardless of the onset of puberty.<sup>9, 11</sup> Health providers or researchers typically conduct these assessments of pubertal status.<sup>85</sup> While there is considerable variation in the methodologies used to assess pubertal status,54 the most commonly used method is the fivestage scales for the development of secondary sexual characteristics throughout puberty known as the Tanner stages.<sup>86–88</sup> Pubertal timing can therefore be indexed by standardizing the measurement of an indicator of pubertal status, e.g. age at menarche, and categorizing the standardized scores of an individual as early, on time, or late. However, there is not necessarily widespread agreement on either what the best milestone to measure pubertal timing is or where the category boundaries should be.54 Therefore, instead of using categories of onset to measure pubertal timing, some researchers use the residuals from regressing pubertal stage on age in order to conceptualize pubertal timing as a continuous measure in terms of pubertal status, but this method also suffers from the lack of agreement on norms.<sup>54</sup> In particular, pubertal timing in boys suffers from a lack of consensus on methods.<sup>55</sup> Some studies use self-report of age at spermarche, or the onset of sperm emission, as an analogous event to self-report of age at menarche, but researchers disagree concerning whether this is a reliable indicator. 50, 60, 89 Some argue that the most valid indicator of pubertal onset in boys is testicular volume,<sup>54</sup> but this measurement can be perceived as invasive.<sup>55</sup>

Second, subjective measures are also frequently used to measure pubertal timing, such as self-reports and parent reports.<sup>54, 85</sup> These measures are similar to the objective measures discussed above, but they differ in that they are reported by adolescents or parents as opposed to assessed by health providers or researchers.<sup>85</sup> For example, the Pubertal Development Scale allows individuals to disclose the timing of certain pubertal milestones, such as menstruation in females, voice changes in males, and so on.<sup>54, 90</sup> The retrospective report of puberty instrument is similar, but is designed to be reliably used even after the pubertal transition has ended.<sup>91</sup> These methods also suffer from the same lack of consensus on the best milestones to use, particularly for boys.<sup>54</sup>

**Summary.** Pubertal timing results from the interactions between biological and environmental factors.<sup>9</sup> Offset pubertal timing has been linked to increased risk of developing adolescent mental health disorders.<sup>5</sup> Three generally acknowledged hypotheses offer explanations for this relationship: maturational disparity, social deviance, and gendered deviation<sup>70</sup> Research examining the effects of offset pubertal timing on adolescent mental health disorders has yielded more consistent results for early as opposed to late pubertal timing.<sup>5</sup> Many gaps remain in the literature, including, but not limited to, the effects of late pubertal timing and the most representative and predictive ways of measuring pubertal timing.

#### **Future Directions**

The body of research related to puberty has significantly increased in the past decade, particularly in regard to pubertal timing<sup>14, 85</sup> However, much research has tended to focus on the effects of early pubertal timing in adolescent girls.<sup>5</sup> There remains a need to examine the possible effects of late pubertal timing for both boys and girls, to parse pubertal timing and status, and to explore the pubertal experiences of understudied populations.

First, additional research is necessary to further examine the effects of late pubertal timing on adolescent depression and anxiety. Much of the existing pubertal timing research focuses on early as opposed to late pubertal timing, and there are fewer cross-sectional and longitudinal studies on the effects of late pubertal timing on adolescent depression and anxiety. The lack of research related to late pubertal timing may be in part due to the widespread popularity of the aforementioned maturational disparity hypothesis, which only focuses on the detrimental effects of early pubertal timing on adolescent mental health. Widespread acceptance of this idea may discourage research related to late pubertal timing. The lack of research on the effects of late pubertal timing on adolescent depression and anxiety makes it difficult to understand the extent to which this may or may not be a risk factor.

Second, more research is needed on the complex interplay between pubertal timing and pubertal status. Relatively few studies have directly compared pubertal timing and pubertal status.<sup>11</sup> One such study found an association between early pubertal timing and depressive symptoms in girls at age 14, but not at ages 17 or 19,92 indicating that early-developing girls were more likely to develop depressive symptoms earlier on in the pubertal transition. Because females who experienced early pubertal timing will also be at a more advanced pubertal stage at the age of 14, and research has demonstrated an association between advanced pubertal stage in females and depressive symptoms, status in this example therefore may be the more important contributing factor to these depressive symptoms.<sup>11</sup> While it is difficult to parse pubertal timing and status,<sup>54</sup> such research is needed in order to determine the unique effects of each aspect of puberty on adolescent mental health disorders. Although a large-scale meta-analysis exists on the relationship between pubertal timing and adolescent mental health disorders,<sup>5</sup> no such meta-analysis on the effects of pubertal status exists. Such a comprehensive review may be illuminating, as some research suggests that progression through pubertal stages is a more reliable indicator than pubertal timing of depression in girls.<sup>9, 93</sup>

Finally, further research is needed to evaluate the pubertal experiences of traditionally less studied groups, particularly adolescent boys, low-SES adolescents, racial and ethnic minorities, and LGBTQ+ adolescents.

Adolescent boys: Adolescent boys are greatly underrepresented in puberty research.<sup>71</sup> Some have speculated that the gender disparity in research may be related to the difficulty and uncertainty surrounding the measurement of pubertal timing in boys.<sup>55</sup> There is less consensus on pubertal timing measures for boys than for girls.<sup>54</sup> Furthermore, given that many of the mainstream pubertal timing theories reference gender differences (i.e. the maturational disparity hypothesis and the gendered deviation hypothesis), more research is needed to further examine these hypotheses.

Socioeconomic status: Low-SES adolescents are also understudied in puberty research.<sup>85</sup> Low-SES females often experience puberty earlier than their higher-SES peers.<sup>55, 62–63</sup> Menarche is thought to be related to nutrition and increased body fat,<sup>94</sup> and low-SES girls are at increased risk for obesity due to decreased access to healthy foods.<sup>62, 95</sup> Therefore, more research is needed to better understand the pubertal and mental health experiences of this at-risk population.

Racial and ethnic minorities: In addition, racial and ethnic minorities are also understudied in puberty research.<sup>85, 96</sup> Given that early pubertal timing is more frequently seen in minority groups such as African American and Latino adolescents,<sup>85, 97</sup> more research is needed to better understand the pubertal experiences of racial and ethnic minorities.

*LGBTQ*+: Lesbian, gay, bisexual, transgender, and queer (LGBTQ+) adolescents are also underrepresented in puberty research.<sup>96, 98</sup> Given that LGBTQ+ adolescents often experience emotional distress as a result of peer discrimination and coming out,<sup>99–100</sup> an increased focus on this population may illuminate the unique experiences of puberty of LGBTQ+ adolescents. In particular, transgender adolescents may have particularly unique experiences with mental health disorders during puberty due to emotional distress resulting from physical development that conflicts with their gender identity.<sup>98, 101</sup>

### Conclusion

Adolescent mental health disorders, specifically depression and anxiety, are a prevalent issue in psychology and society. Puberty involves a myriad of complex process, including pubertal timing, which have been shown to be related to increased risk for adolescent depression and anxiety. This review examined the existing evidence for the differential impacts of early and late pubertal timing on adolescent depression and anxiety. This discussion is especially urgent, as pubertal timing is decreasing globally among boys and girls. While stronger evidence exists implicating early pubertal timing in adolescent depression and anxiety, particularly for girls, more research is needed to clarify the mixed findings regarding late pubertal timing. Future pubertal timing research might want to focus on further exploring the potential effects of late pubertal timing on adolescent depression and anxiety, parsing pubertal status and timing, and diversifying samples to better understand the pubertal experiences of understudied groups, such as adolescent boys, low-SES adolescents, racial and ethnic minorities, and LGBTQ+ adolescents.

#### References

- 1. Olfson, M.; Blanco, C.; Wang, S.; Laje, G.; Correll, C. U. National Trends in the Mental Health Care of Children, Adolescents, and Adults by Office-Based Physicians. *JAMA Psychiatry*. **2014**, *71*, 81–90.
- Polanczyk, G. V.; Salum, G. A.; Sugaya, L. S.; Caye, A.; Rohde, L. A. Annual Research Review: A Meta-Analysis of the Worldwide Prevalence of Mental Disorders in Children and Adolescents. *J. Child Psychol. Psychiatry.* 2015, 56, 345–365.
- 3. Ghandour, R. M.; Sherman, L. J.; Vladutiu, C. J.; Ali, A. M.; Lynch, S. E.; Bitsko, R. H.; Blumberg, S. J. Prevalence and Treatment of Depression, Anxiety, and Conduct Problems in US Children. *J. Pediatr.* **2019**, 206, 256–267.
- 4. Kessler, R. C.; Berglund, P.; Demler, O.; Jin, R.; Merikangas, K. R.; Walters, E. E. Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication. *JAMA Psychiatry*. 2005, 62, 593–602.

- 5. Ullsperger, J. M.; Nikolas, M. A. A Meta-Analytic Review of the Association Between Pubertal Timing and Psychopathology in Adolescence: Are There Sex Differences in Risk? *Psychol. Bull.* **2017**, *143*, 903–938.
- 6. Werner-Seidler, A.; Perry, Y.; Calear, A. L.; Newby, J. M.; Christensen, H. School-Based Depression and Anxiety Prevention Programs for Young People: A Systematic Review and Meta-Analysis. *Clin. Psychol. Rev.* **2017**, *51*, 30–47.
- 7. Young, K.; Sandman, C.; Craske, M. Positive and Negative Emotion Regulation in Adolescence: Links to Anxiety and Depression. *Brain Sci.* **2019**, *9*, 76.
- 8. Zdebik, M. A.; Boivin, M.; Battaglia, M.; Tremblay, R. E.; Falissard, B.; Côté, S. M. Childhood Multi-Trajectories of Shyness, Anxiety and Depression: Associations with Ddolescent Internalizing Problems. *J. Appl. Dev. Psychol.* **2019**, *64*, 1–12.
- 9. Copeland, W. E.; Worthman, C.; Shanahan, L.; Costello, E. J.; Angold, A. Early Pubertal Timing and Testosterone Associated with Higher Levels of Adolescent Depression in Girls. *J. Am. Acad. Child Adolsec. Psychiatry.* **2019**, *58*, 1197–1206.
- Graber, J. A.; Lewinsohn, P. M.; Seeley, J. R.; Brooks-Gunn, J. Is Psychopathology Associated with the Timing of Pubertal Development? *J. Am. Acad. Child Adolsec.* Psychiatry. 1997, 36, 1768–1776.
- Lewis, G.; Ioannidis, K.; Van Harmelen, A. L.; Neufeld, S.; Stochl, J.; Lewis, G.; Jones, P. B.; Goodyer, I.; Schooling, C. M. The Association Between Pubertal Status and Depressive Symptoms and Diagnoses in Adolescent Females: A Population-Based Cohort Study. PLOS ONE. 2018, 13(6), e0198804.
- Winer, J. P.; Parent, J.; Forehand, R.; Breslend, N. L. Interactive Effects of Psychosocial Stress and Early Pubertal Timing on Youth Depression and Anxiety: Contextual Amplification in Family and Peer Environments. J. Child Fam. Stud. 2016, 25, 1375–1384.
- 13. Brix, N.; Ernst, A.; Lauridsen, L. L. B.; Parner, E.; Støvring, H.; Olsen, J.; Henriksen, T. B.; Ramlau-Hansen, C. H. Timing of Puberty in Boys and Girls: A Population-Based Study. *Paediatr Perinat. Epidemil.* **2019**, *33*, 70–78.
- 14. Mendle, J. Beyond Pubertal Timing: New Directions for Studying Individual Differences in Development. *Curr. Dir. Psychol. Sci.* **2014**, 23, 215–219.
- 15. Pierce, M.; Hardy, R. Commentary: The Decreasing Age of Puberty—As Much a Psychosocial as Biological Problem? *Int. J. Epidemiol.* **2012**, 41, 300–302.
- 16. Walsh, L. M.; Roddy, M. K.; Scott, K.; Lewis, C. C.; Jensen-Doss, A. A Meta-Analysis of the Effect of Therapist Experience on Outcomes for Clients with Internalizing Disorders. *Psychother. Res.* 2019, 29, 846–859.
- 17. Gilbert, P. Introduction: Controversies Old and New. In *Depression: The Evolution of Powerlessness*, 1st ed; Routledge, Taylor & Francis Group; London; 2017; pp 3–22.
- 18. Fried, E. I.; Nesse, R. M. Depression Sum-Scores Don't Add Up: Why Analyzing Specific Depression Symptoms Is Essential. *BMC Med.* **2015**, *13*, 72–82.
- 19. Otte, C.; Gold, S. M.; Penninx, B. W.; Pariante, C. M.; Etkin, A.; Fava, M.; Mohr, D. C.; Schatzberg, A. F. Major Depressive Disorder. *Nat. Rev. Dis. Primers.* **2016**, *2*, 16065.
- Vandeleur, C. L.; Fassassi, S.; Castelao, E.; Glaus, J.; Strippoli, M. P. F.; Lasserre, A. M.; Rudaz, D.; Gebreab, S.; Pistis, G.; Aubry, J. M.; Angst, J.; Preisig, M. Prevalence and Ccorrelates of DSM-5 Major Depressive and Related Disorders in the Community. *Psychiatry Res.* 2017, 250, 50–58.
- 21. Llorca, A.; Malonda, E.; Samper, P. Anxiety in Adolescence. Can We Prevent It? *Medicina Oral Patología Oral y Cirugia Bucal*. 2016, e70–e75.

- Nail, J. E.; Christofferson, J.; Ginsburg, G. S.; Drake, K.; Kendall, P. C.; McCracken, J.T.; Birmaher, B.; Walkup, J. T.; Comptom, S. N.; Keeton, C.; Sakolsky, D. Academic Impairment and Impact of Treatments Among Youth with Anxiety Disorders. *Child Youth Care Forum.* 2015, 44, 327–342.
- 23. Robichaud, M.; Koerner, N.; Dugas, M. J. Cognitive Behavioral Treatment for Generalized Anxiety Disorder: From Science to Practice, 2nd ed.; Taylor & Francis Ltd: New York; 2019.
- 24. Ho, N.; Sommers, M. Anhedonia: A Concept Analysis. *Arch. Psychiatr. Nurs.* 2013, 27, 121–129.
- 25. Mathews, B. L.; Koehn, A. J.; Abtahi, M. M.; Kerns, K. A. Emotional Competence and Anxiety in Childhood and Adolescence: A Meta-Analytic Review. *Clin. Child Fam. Psychol. Rev.* **2016**, *19*, 162–184.
- 26. Werner-Seidler, A.; Banks, R.; Dunn, B. D.; Moulds, M. L.; An Investigation of the Relationship Between Positive Affect Regulation and Depression. *Behav. Res. Ther.* **2013**, 51, 46–56.
- 27. McElroy, E.; Fearon, P.; Belsky, J.; Fonagy, P.; Patalay, P. Networks of Depression and Anxiety Symptoms Across Development. *J. AM. Acad. Child Adolesc. Psychiatry.* **2018**, *57*, 964–973.
- 28. Altemus, M.; Sarvaiya, N.; Epperson, C. N. Sex Differences in Anxiety and Depression Clinical Perspectives. *Front Neuroendocrinol.* **2014**, *35*, *320–330*.
- 29. Copeland, W. E.; Angold, A.; Shanahan, L.; Costello, E. J. Longitudinal Patterns of Anxiety from Childhood to Adulthood: The Great Smoky Mountains Study. *J. AM. Acad. Child Adolesc. Psychiatry.* **2014**, 53, 21–33.
- 30. Piccinelli, M.; Wilkinson, G. Gender Differences in Depression: Critical Review. *Br. J. Psychiatry.* **2000**, *177*, 486–492.
- 31. McLeod, G. F. H.; Horwood, L. J.; Fergusson, D. M. Adolescent Depression, Adult Mental Health and Psychosocial Outcomes at 30 and 35 Years. *Psychol. Med.* **2016**, 46, 1401–1412.
- 32. Merikangas, K. R.; He, J.; Burstein, M.; Swanson, S. A.; Avenevoli, S.; Cui, L.; Benjet, C.; Georgiades, K.; Swendsen, J. Lifetime Prevalence of Mental Disorders in US Adolescents: Results from the National Comorbidity Study-Adolescent Supplement (NCS-A). J. AM. Acad. Child Adolesc. Psychiatry. 2010, 49, 980–989.
- 33. Sun, M.; Rith-Najarian, L. R.; Williamson, T. J.; Chorpita, B. F. Treatment Features Associated with Youth Cognitive Behavioral Therapy Follow-Up Effects for Internalizing Disorders: A Meta-Analysis. *J. Clin. Child Adolesc. Psychol.* **2019**, 48, S269–S283.
- 34. Edlund, M. J.; Forman-Hoffman, V. L.; Windser, C. R.; Heller, D. C.; Kroutil, L. A.; Lipari, R. N.; Colpe, L. J. Opioid Abuse and Depression in Adolescents: Results from the National Survey on Drug Use and Health. *Drug Alcohol Dependence*. **2015**, 152, 131–138.
- Pedrelli, P.; Shapero, B.; Archibald, A.; Dale, C. Alcohol use and Depression During Adolescence and Young Adulthood: A Summary and Interpretation of Mixed Findings. Curr. Addiction Rep. 2016, 3, 91–97.
- 36. Braje, S. E.; Eddy, J. M.; Hall, G. C. N. Comparison of Two Models of Risky Sexual Behavior During Late Adolescence. *Arch. Sex. Behav.* **2016**, 45, 73–83.
- 37. Khan, M. R.; Kaufman, J. S.; Pence, B. W.; Gaynes, B. N.; Adimora, A. A.; Weir, S. S.; Miller, W. C. Depression, Sexually Transmitted Infection, and Sexual Risk Behavior Among Young Adults in the United States. *JAMA Pediatr.* 2009, 163, 644–652.

- 38. Thapar, A.; Collishaw, S.; Pine, D. S.; Thapar, A. K. Depression in adolescence. *Lancet*. **2012**, 379, 1056–1067.
- 39. Turecki, G.; Brent, D. A. Suicide and Suicidal Behaviour. *The Lancet.* **2016**, *387*, 1227–1239.
- 40. Fletcher, J. M. Adolescent Depression and Educational Attainment: Results Using Sibling Fixed Effects. *Health Econ.* **2012**, *19*, 855–871.
- 41. O'Connor, M.; Sanson, A. V.; Toumbourou, J. W.; Norrish, J.; Olsson, C. A. Does Positive Mental Health in Adolescence Longitudinally Predict Healthy Transitions in Young Adulthood? *J. Happiness Stud.* **2017**, *18*, 177–198.
- 42. Johnson, D.; Dupuis, G.; Piche, J.; Clayborne, Z.; Colman, I. Adult Mental Health Outcomes of Adolescent Depression: A Systematic Review. *Depress. Anxiety.* **2018**, 35, 700–716.
- 43. Weidman, A. C.; Augustine, A. A.; Murayama, K.; Elliot, A. J. Internalizing Symptomatology and Academic Achievement: Bi-Directional Prospective Relations in Adolescence. *J. Res Pers.* **2015**, *58*, 106–114.
- 44. Erath, S. A.; Flanagan, K. S.; Bierman, K. L. Social Anxiety and Peer Relations in Early Adolescence: Behavioral and Cognitive Factors. *J. Abnorm. Child Psychol.* **2016**, *35*, 405–416.
- 45. Oberle, E.; Schonert-Reichl, K. A.; Thomson, K. C. Understanding the Link Between Social and Emotional Well-Being and Peer Relations in Early Adolescence: Gender-Specific Predictors of Peer Acceptance. *J. Youth Adolesc.* **2010**, *39*, 1330–1342.
- 46. McLaughlin, K. A.; Hatzenbuehler, M. L.; Hilt, L. M. Emotion Dysregulation as a Mechanism Linking Peer Victimization to Internalizing Symptoms in Adolescents. *J. Consult Clin Psychol.* **2009**, **77**, 894–904.
- 47. Starr, L. R.; Stroud, C. B.; Li, Y. I. Predicting the Transition from Anxiety to Depressive Symptoms in Early Adolescence: Negative Anxiety Response Style as a Moderator of Sequential Comorbidity. *J. Affect Disord.* **2016**, *190*, 757–763.
- 48. Fergusson, D. M.; McLeod, G. F. H.; Horwood, L. J.; Swain, N. R.; Chapple, S.; Poulton, R. Life Satisfaction and Mental Health Problems (18 to 35 years). *Psychol. Med.* **2015**, 45, 2427–2436.
- 49. Essau, C. A.; Lewinsohn, P. M.; Olaya, B.; Seeley, J. R. Anxiety Disorders in Adolescents and Psychosocial Outcomes at Age 30. *J. Affect Disord.* **2014**, *163*, 125–132.
- 50. Swan, A. J.; Kendall, P. C. Fear and Missing Out: Youth Anxiety and Functional Outcomes. *Clin Psychol (New York)*. **2016**, 23, 417–435.
- 51. Costello, E. J.; Copeland, W. E.; Angold, A. Trends in Psychopathology across the Adolescent Years: What Changes When Children Become Adolescents, and When Adolescents Become Adults? J. Child Psychol Psychiat. 2011, 52, 1015–1025.
- 52. Woodward, L. J.; Fergusson, D. M. Life Course Outcomes of Young People with Anxiety Disorders in Adolescence. *J. Am. Acad. Child Adolesc. Psychiat.* **2001**, 40, 1086–1093.
- 53. Graber, J. A. Pubertal Timing and the Development of Psychopathology in Adolescence and Beyond. *Horm. Behav.* **2013**, *64*, 262–269.
- 54. Dorn, L. D.; Dahl, R. E.; Woodward, H. R.; Biro, F. Defining the Boundaries of Early Adolescence: A User's Guide to Assessing Pubertal Status and Pubertal Timing in Research with Adolescents. *Appl. Dev. Sci.* **2006**, *10*, 30–56.
- 55. Mendle, J.; Ferrero, J. Detrimental Psychological Outcomes Associated with Pubertal Timing in Adolescent Boys. *Dev. Rev.* **2012**, *32*, 49–66.

- 56. Lee, Y.; Styne, D. Influences on the Onset and Tempo of Puberty in Human Beings and Implications for Adolescent Psychological Development. *Horm. Behav.* **2013**, *64*, 250–261.
- 57. De Sanctis, V.; Soliman, A. T.; Elsedfy, H.; Soliman, N. A.; Elalaily, R.; Di Maio, S. An Update of the Genetic Basis of Pubertal Timing: A Mini Review. *Rivista Italiana di Medicina dell' Adolescenza*. **2016**, 14, 5–14.
- 58. Howard, S.; Lyon, France, 18–21 May 2019; ECE conference proceedings; 21st European Congress of Endocrinology.
- 59. Wohlfahrt-Veje, C.; Mouritsen, A.; Hagen, C. P.; Tinggaard, J.; Mieritz, M. G.; Boas, M.; Petersen, J. H.; Skakkebæk, N. E.; Main, K. M. Pubertal Onset in Boys and Girls Is Influenced by Pubertal Timing of Both Parents. *J. Clin. Endocrinol Metab.* **2016**, *101*, 2667–2674.
- 60. Acacio-Claro, P. J.; Koivusilta, L. K.; Doku, D. T.; Rimpelä, A. H. Timing of Puberty and Reserve Capacity in Adolescence as Pathways to Educational Level in Adulthood—A Longitudinal Study. *Ann Hum Biol.* **2019**, *46*, 35.
- 61. Belsky, J.; Steinberg, L. D.; Houts, R. M.; Friedman, S. L.; DeHart, G.; Cauffman, E.; Roisman, G. I.; Halpern-Felsher, B. L.; Susman, E. Family Rearing Antecedents of Pubertal Timing. *Child Dev.* 2007, 78, 1302–1321.
- 62. Deardorff, J.; Abrams, B.; Ekwaru, J. P.; Rehkopf, D. H. Socioeconomic Status and Age at Menarche: An Examination of Multiple Indicators in an Ethnically Diverse Cohort. *Ann. Epidemiol.* **2014**, *24*, 727–733.
- 63. Obeidallah, D.; Brennan, R. T.; Brooks-Gunn, J.; Earls, F. Links Between Pubertal Timing and Neighborhood Contexts: Implications for Girls' Violent Behavior. *J. Am. Acad. Child Adolesc. Psychiat.* **2004**, *43*(12), 1460–1468.
- 64. Günther, A. L. B.; Karaolis-Danckert, N.; Kroke, A.; Remer, T.; Buyken, A. E. Dietary Protein Intake throughout Childhood Is Associated with the Timing of Puberty. *J. Nut.* **2010**, **140**, 565–571.
- 65. Jansen, E. C.; Zhou, L.; Perng, W.; Song, P. X.; Rojo, M. M. T.; Mercado, A.; Peterson, K. E.; Cantoral, A. Vegetables and Lean Proteins–Based and Processed Meats and Refined Grains –Based Dietary Patterns in Early Childhood Are Associated with Pubertal Timing in a Sex-Specific Manner: A Prospective Study of Children from Mexico City. *Nut Res.* 2018, 56, 41–50.
- 66. Soliman, A.; De Sanctis, V.; Elalaily, R. Nutrition and Pubertal Development. *Indian J. Endocrinol Metab.* **2014**, *18*, S39–S47.
- 67. Grower, P.; Ward, L. M.; Beltz, A. M. Downstream Consequences of Pubertal Timing for Uoung Women's Body Beliefs. *J. Adolesc.* **2019**, 72, 162–166.
- 68. Baams, L.; Dubas, J. S.; Overbeek, G.; Van Aken, M. A. G. Transitions in Body and Behavior: A Meta-Analytic Study on the Relationship detween Pubertal Development and Adolescent Sexual Behavior. *J. Adolesc Health.* **2015**, *56*, 586–598.
- 69. Stumper, A.; Olino, T.; Abramson, L. Y.; Alloy, L. B. Pubertal Timing and Substance Use in Adolescence: An Investigation of Two Cognitive Moderators. *J. Abnorm. Child Psychol.* **2019**, 47, 1509–1520.
- 70. Ge, X.; Natsuaki, M. N. In Search of Explanations for Early Pubertal Timing Effects on Developmental Psychopathology. *Curr. Dir. Psychol Sci.* **2009**, *18*, 327–331.
- 71. Mendle, J.; Moore, S. R.; Briley, D. A.; Harden, K. P. Puberty, Socioeconomic Status, and Depression in Girls: Evidence for Gene × Environment Interactions. *Clin. Psychol. Sci.* **2016**, *4*, 3–16.

- 72. Deardorff, J.; Cham, H.; Gonzales, N. A.; White, R. M. B.; Tein, J. Y.; Wong, J. J.; Roosa, M. W. Pubertal Timing and Mexican-Origin Girls' Internalizing and Externalizing Symptoms: The Influence of Harsh Parenting. *Dev. Psychol.* **2013**, *49*, 1790–1804.
- 73. Kaltiala-Heino, R.; Marttunen, M.; Rantanen, P.; Rimpelä, M. Early Puberty Is Associated with Mental Health Problems in Middle Adolescence. *Soc. Sci. Med.* **2003**, *57*, 1055–1064.
- 74. Crockett, L. J.; Carlo, G.; Wolff, J. M.; Hope, M. O. The Role of Pubertal Timing and Temperamental Vulnerability in Adolescents' Internalizing Symptoms. *Dev. Psychopathol.* **2013**, 25, 377–389.
- 75. Hamlat, E. J.; Stange, J. P.; Abramson, L. Y.; Alloy, L. B. Early Pubertal Timing as a Vulnerability to Depression Symptoms: Differential Effects of Race and Sex. *J. Abnorm. Child Psychol.* **2014**, 42, 527–538.
- 76. Joinson, C.; Heron, J.; Araya, R.; Lewis, G. Early Menarche and Depressive Symptoms from Adolescence to Young Adulthood in a UK Cohort. *J. Am. Acad. Child Adolesc. Psychiat.* **2013**, 52, 591–598.
- 77. Zahn-Waxler, C.; Shirtcliff, E. A.; Marceau, K. Disorders of Childhood and Adolescence: Gender and Psychopathology. *Ann. Rev. Clin. Psychol.* **2008**, *4*, 275–303.
- 78. Rudolph, K. D.; Troop-Gordon, W. Personal-Accentuation and Contextual-Amplification Models of Pubertal Timing: Predicting Youth Depression. *Dev. Psychopathol.* **2010**, 22, 433–451.
- 79. Ibáñez, L.; Potau, N.; Zampolli, M.; Street, M. E.; Carrascosa, A. Girls Diagnosed with Premature Pubarche Show an Exaggerated Ovarian Androgen Synthesis from the Early Stages of Puberty: Evidence from Gonadotropin-Releasing Hormone Agonist Testing. *Fertil. Steril.* 1997, 67, 849–855.
- 80. Pauldine, M. R. Pubertal Timing and Internalizing Psychopathology of Adolescent Females: Evaluating the Maturation Disparity Hypothesis. Thesis, Wichita State University: Wichita, KS, 2017.
- 81. Benoit, A.; Lacourse, E.; Claes, M. Pubertal Timing and Depressive Symptoms in Late Adolescence: The Moderating Role of Individual, Peer, and Parental Factors. *Dev. Psychopathol.* **2013**, 25, 455–471.
- 82. Graber, J. A.; Seeley, J. R.; Brooks-Gunn, J.; Lewinsohn, P. M. Is Pubertal Timing Associated with Psychopathology in Young Adulthood? *J. Am. Acad. Child Adolesc. Psychiat.* **2004**, *43*, 718–726.
- 83. Conley, C. S.; Rudolph, K. D. The Emerging Sex Difference in Adolescent Depression: Interacting Contributions of Puberty and Peer Stress. *Dev. Psychopathol.* 2009, 21, 593–620.
- 84. Sontag, L. M.; Graber, J. A.; Clemans, K. H. The Role of Peer Stress and Pubertal Timing on Symptoms of Psychopathology During Early Adolescence. *J. Youth Adolesc.* **2011**, *40*, 1371–1382.
- 85. Mendle, J.; Beltz, A. M.; Carter, R.; Dorn, L. D. Understanding Puberty and Its Measurement: Ideas for Research in a New Generation. *J. Res. Adolesc.* **2019**, *29*, 82–95.
- 86. Marshall, W. A.; Tanner, J. M. Variations in Pattern of Pubertal Changes in Girls. *Arch. Dis. Child.* **1969**, 44, 291–303.
- 87. Marshall, W. A.; Tanner, J. M. Variations in the Pattern of Pubertal Changes in Boys. *Arch. Dis. Child.* **1970**, 45, 13–23.
- 88. Tanner, J. M. *Growth at adolescence; with a general consideration of the effects of hereditary and environmental factors upon growth and maturation from birth to maturity,* 2nd ed.; Blackwell Scientific Publications: Oxford, 1962.

- 89. Hirsch, M.; Lunenfeld, B.; Modan, M.; Ovadia, J.; Shemesh, J. Spermarche—The Age of Fnset of Sperm Emission. *J. Adolesc. Health.* **1985**, *6*, 35–39.
- 90. Brooks-Gunn, J.; Warren, M. P.; Rosso, J.; Gargiulo, J. Validity of Self-Report Measures of Girls' Pubertal Status. *Child Development*. **1987**, *58*, 829–841.
- 91. Beltz, A. M.; Berenbaum, S. A. Cognitive Effects of Variations in Pubertal Iiming: Is Puberty a Period of Brain Organization for Human Sex-Typed Cognition? *Horm. Behav.* **2013**, 63, 823–828.
- 92. Sequeira, M. E.; Lewis, S. J.; Bonilla, C.; Smith, G. D.; Joinson, C. Association of Timing of Menarche with Depressive Symptoms and Depression in Adolescence: Mendelian Randomization Study. *Br. J. Psychiatry.* **2017**, 210, 39–46.
- 93. Angold, A.; Costello, E.; Erkanli, A.; Worthman, C. M. Pubertal Changes in Hormone Levels and Depression in Girls. *Psychol. Med.* **1999**, 29, 1043–1053.
- 94. Blum, W. F.; Englaro, P.; Hanitsch, S.; Juul, A.; Hertel, N. T.; Ller, J. M.; Skakkeb, N. E.; Heiman, M. L.; Birkett, M.; Attanasio, A. M.; Kiess, W.; Rascher, W. Plasma Leptin Levels in Healthy Children and Adolescents: Dependence on Body Mass Index, Body Fat Mass, Gender, Pubertal Stage, and Testosterone. *J. Clin. Endocrinol. Metab.* 1997, 82, 2904–2910.
- 95. Hemmingsson, E. Early Childhood Obesity Risk Factors: Socioeconomic Adversity, Family Dysfunction, Offspring Distress, and Junk Food Self-Medication. *Curr. Obes. Rep.* **2018**, **7**, 204–209.
- 96. Deardorff, J.; Hoyt, L. T.; Carter, R.; Shirtcliff, E. A. Next Steps in Puberty Research: Broadening the Lens Toward Understudied Populations. *J. Res. Adolesc.* **2019**, *29*, 133–154.
- 97. Herman-Giddens, M. E.; Steffes, J.; Harris, D.; Slora, E.; Hussey, M.; Dowshen, S. A.; Wasserman, R.; Serwint, J. R.; Smitherman, L.; Reiter, E. O. Secondary Sexual Characteristics in Boys: Data From the Pediatric Research in Office Settings Network. *Pediatrics*. 2012, 130, 1058–1068.
- 98. Crockett, L. J.; Deardorff, J.; Johnson, M.; Irwin, C.; Petersen, A. C. Puberty Education in a Global Context: Knowledge Gaps, Opportunities, and Implications for Policy. *J. Res. Adolesc.* **2019**, *29*, 177–195.
- 99. Almeida, J.; Johnson, R. M.; Corliss, H. L.; Molnar, B. E.; Azrael. D. Emotional Distress Among LGBT Youth: The Influence of Perceived Discrimination Based on Sexual Orientation. *J. Youth Adolesc.* **2009**, *38*, 1001–1014.
- 100. Kosciw, J. G.; Palmer, N. A.; Kull, R. M. Reflecting Resiliency: Openness About Sexual Orientation and/or Gender Identity and Its Relationship to Well-Being and Educational Outcomes for LGBT Students. Am. J. Community Psychol. 2015, 55, 167–178.
- Vance, S. R.; Ehrensaft, D.; Rosenthal, S. M. Psychological and Medical Care of Gender Nonconforming Youth. *Pediatrics*. 2014, 134, 1184–1192.