

# Sleep Problems in Children with Attention Deficit/Hyperactivity Disorder: Current Status of Knowledge and Appropriate Management

Ming-Horng Tsai<sup>1,2</sup> · Jen-Fu Hsu<sup>2,3,4</sup> · Yu-Shu Huang<sup>2,3,5</sup>

Published online: 29 June 2016  
© Springer Science+Business Media New York 2016

**Abstract** Attention deficit hyperactivity disorder (ADHD) affects approximately 5 % of children and adolescents, and sleep problems are common in these patients. There is growing evidence informing the significant importance of sleep problems in youth with ADHD. The sleep problems in children with ADHD include specific sleep disorders and sleep disturbances due to comorbid psychiatric disorders or ADHD medications. The specific sleep disorders of ADHD children include behaviorally based insomnia, sleep-disordered breathing, and restless legs syndrome/periodic limb movement disorder. Current practices on the management of sleep problems for ADHD children are based mostly on expert consensus, whereas more evidence-based literature can be found only recently. Assessment of the sleep conditions in ADHD children before initiation of pharmacotherapy is the currently recommended guideline, and good sleep hygiene can be considered as the first-line treatment option. In addition to modifying the dose regimens, formulation, or alternative stimulants when

sleep problems are encountered in ADHD children, atomoxetine, once daily guanfacine extended release, and melatonin are potential choices for ADHD children with more severe sleep problems. In this review, we aimed to provide the most updated information, preferably based on meta-analyses, systemic review, and randomized controlled trials published in the latest 3 years, in order to be clinically useful for practitioners and clinicians.

**Keywords** Sleep disorders · Attention deficit hyperactivity disorder · Children · Melatonin · Insomnia

## Introduction

Attention deficit/hyperactivity disorder (ADHD) and sleep disorders can have similar symptoms and influence on daily functioning, social attendance, and quality of life, and these two problems can affect each other [1, 2, 3]. Sleep disorders are ubiquitous among children and adolescents with ADHD, probably due to the shared neurobiological pathways involving areas of the cortex responsible for regulation and arousal, the medication effects of stimulants for ADHD, and presence of comorbid mental health disorders [2, 4, 5]. ADHD-associated disrupted behaviors may influence nighttime sleep with symptoms of insomnia, bedtime struggles, poor sleep quality, or insufficient sleep duration [2, 4]. Conversely, primary sleep disorders, such as obstructive sleep apnea (OSA), restless legs syndrome (RLS), and periodic limb movement disorder (PLMD), cause daytime neurobehavioral problems which resemble those of ADHD, especially in children.

This article aims to review new developments and present a useful updated overview of the most relevant studies on the prevalence, etiologies, pathophysiology, and treatment strategies of sleep problems in children with ADHD. Furthermore,

---

This article is part of the Topical Collection on *Sleep Disorders*

✉ Yu-Shu Huang  
hu1109s@yahoo.com.tw

- <sup>1</sup> Division of Pediatric Neonatology and Hematology/Oncology, Department of Pediatrics, Chang Gung Memorial Hospital, Yunlin, Taiwan
- <sup>2</sup> College of Medicine, Chang Gung University, Taoyuan, Taiwan
- <sup>3</sup> Sleep Center and Child Psychiatry Department, Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan
- <sup>4</sup> Division of Neonatology, Department of Pediatrics, Chang Gung Memorial Hospital, Taoyuan, Taiwan
- <sup>5</sup> Department of Child Psychiatry and Sleep Center, Chang Gung Memorial Hospital, 5, Fu-Shing St., Kwei-Shan, Taoyuan 333, Taiwan

we aimed to provide evidence- or consensus-based recommendations concerning the assessment and management of sleep problems in pediatric ADHD patients.

### Relationship of Sleep Disorders and ADHD

The prevalence of ADHD is reported to be around 3.5–7.1 % of children and adolescents [6–8] and persists into adulthood in approximately two thirds of patients [9, 10]. Inattention, hyperactivity, and impulsiveness are the major ADHD symptoms based on the diagnostic criteria of *Diagnostic and Statistical Manual of Mental Disorders (DSM), Fifth Edition (American Psychiatric Association)* [11] and *International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10)* (World Health Organization). The prevalence of sleep disturbances in individuals with ADHD is reported to be in the range of 35–70 % and differs as a function of gender, age, ADHD subtype, psychiatric comorbidities, and medication use [1, 5, 8, 12–15].

The relationship between sleep problems and ADHD is multifaceted and complex. Sleep problems in children and adolescents with ADHD include specific sleep disorders, ADHD medication-related, and those related to comorbid psychiatric disorders. Sleep disturbances may aggravate ADHD symptoms and also mimic ADHD in individuals referred for ADHD-like symptoms [16], that is, potentially resulting in misdiagnosis [17]. Around 55–87 % of children or adolescents with ADHD have at least one comorbidity and up to 20 % have three or more comorbid conditions, including Tourette syndrome, bipolar disorder, depression, autism, conductive disorder, post-traumatic stress disorder, and obsessive compulsive disorder [18–20]. These comorbidities are often associated with sleep problems [21]. Furthermore, ADHD children are prescribed psychostimulant medications, which impair sleep in these patients and may further complicate the interrelationship with sleep problems [21, 22, 23]. It is important to consider the interactions of psychiatric comorbidities, ADHD medications, and sleep problems together when managing patients.

### Treatment Strategies for Specific Sleep Disorders in Children With ADHD

#### Insomnia

Behavioral interventions are the major non-medical methods for ADHD children with insomnia and include sleep hygiene and cognitive behavioral therapy [24, 25]. The effectiveness of cognitive behavioral therapy for insomnia in both young children and adolescents with ADHD has been evaluated [16, 26]. Sleep hygiene includes establishment of consistent behavior surrounding bedtime to promote productive and restful sleep, a stable bedtime, and regular wake time [26]. Cognitive

behavioral therapy includes a combination of relaxation training, stimulus control therapy, sleep restriction, and cognitive therapies [26]. Cortese et al. recommended behavioral interventions as the first-line treatment for children with ADHD and insomnia in a critical review in 2013, even if the sleep complaints are thought to be medication-related, but pointed to the need for more research [2, 27]. In 2015, a randomized controlled trial demonstrated that a brief behavioral sleep intervention modestly improves the severity of ADHD symptoms, leads to substantial benefits for their families, and also improves the children's sleep, quality of life, and functioning, with most benefits sustained to 6 months post-intervention [28]. For children who are in pharmacological treatment but still had persistent symptoms, Vidal et al. demonstrated the efficacy of group cognitive behavioral therapy in reducing ADHD symptoms and functional impairment in another randomized controlled trial [29]. However, follow-up study is still warranted to determine long-term benefits and healthcare costs or savings.

Re-evaluating ADHD medications is an important step in managing ADHD-associated insomnia. Because higher stimulant dose is usually associated with reduced sleep duration and later sleep start time [30], the relative impacts of different medications on specific aspects of sleep should be considered on an individual basis. If both sleep hygiene and cognitive behavioral therapy do not work after some weeks, during which time the negative effect of medication on sleep may be spontaneously decrease, alternative dosages, adjusting dose regimen, formulations, or alternative ADHD medications are recommended [2, 22, 31].

For children without improvement after both behavioral interventions and adjusting primary ADHD medications, the use of a sleep-promoting medication could be considered. Approximately one in five children with ADHD take sleep medications [15], most common being melatonin and clonidine [32]. However, neither are approved by the American Food and Drug Administration (FDA). Melatonin has been increasingly used for ADHD children in recent years [33, 34], and about half of the young children stay on melatonin treatment for several years [33], because a previous study showed that children with ADHD and sleep-onset insomnia exhibit a delayed evening increase in endogenous melatonin levels and melatonin is effective in advancing the sleep-wake rhythm [35, 36]. Current data suggest that melatonin is a well-tolerated and efficacious treatment option for pediatric patients with chronic sleep-onset insomnia and ADHD [32, 37]. However, melatonin is found to be associated with earlier waking times in a randomized, double masked placebo-controlled trial [38]. In a long-term follow-up study, discontinuation of melatonin treatment usually leads to a relapse of sleep-onset insomnia and in resuming melatonin treatment [39].

Clonidine is an FDA-approved, effective, and safe monotherapy or adjunctive treatment to psychostimulants in the management of ADHD in children and adolescents [40]. The use of clonidine in the treatment of ADHD-related sleep disturbances has been investigated since more than two decades ago [41, 42], which showed adequate efficacy and safety. An increased percentage of children with ADHD, regardless of whether they are receiving stimulants, are treated frequently with clonidine in an off-label manner [43, 44]. Somnolence and/or related symptoms, such as fatigue, sedation, and hypersomnia, are the most commonly reported adverse events [43]. Zolpidem, another commonly prescribed medication for the treatment of insomnia, failed to reduce the latency to persistent sleep in 6- to 17-year-old ADHD children and produced significant adverse events of dizziness and headache at a dose of 0.25 mg/kg/day [44].

In conclusion, behavioral strategies are highly recommended as the first-line therapy for ADHD children with sleep-onset insomnia, and adjustments of stimulants for ADHD should be considered simultaneously. If both are ineffective, the sleep-promoting agents, including melatonin and  $\alpha$ 2-adrenoceptor agonists, can be considered as the alternative choice.

#### *Sleep-Disordered Breathing*

Sleep-disordered breathing (SDB) includes a wide spectrum of upper airway resistance syndrome, obstructive hypoventilation, and the most severe OSA. An elevated incidence of SDB was reported recently, ranging from 25 to 57 % among children and adolescents with ADHD [45, 46, 47]. The relative higher hypercapnia, hypoxia, and increased production of free radicals, inflammatory cytokines, and oxidative stress in SDB patients may cause neurological dysfunction, which consequently lead to inattention, hyperactivity, or impulsivity symptoms [48]. Removal of the hypertrophic adenotonsillar tissues, the most common cause of OSA, can cause symptom resolution in more than 85 % of children with OSA [49]. Therefore, adenotonsillectomy can result in a significant decrease of the ADHD symptoms [49, 50, 51]. In a recent meta-analysis, a medium relationship between ADHD and SDB was noted, and a medium improvement in ADHD symptoms following adenotonsillectomy (ES = 0.43) was concluded [51].

#### *Restless Legs Syndrome and Periodic Limb Movement Disorder*

Pediatric RLS occurs in only 1.9 % of the general population between 8 and 18 years of age [52], but a reported prevalence of 33–52 % is noted in children and adolescents with ADHD [53, 54]. RLS is characterized by unpleasant sensations mainly in the lower limbs between the ankle and the knee [55].

PLMD is a frequent comorbid diagnosis in RLS. The non-pharmacologic management of patients with RLS can be used alone or combined with pharmacologic options [56]. In mild cases of RLS, good sleep hygiene, a regular sleep schedule, mentally alerting activities, physical exercise, and avoiding alcohol or certain medications (e.g., neuroleptics, antihistamines, or selective serotonin reuptake inhibitors) are beneficial [57].

The pharmacological treatments for RLS/PLMD include non-ergot dopaminergic agonist, calcium channel  $\alpha$ -2- $\delta$  ligand, iron supplementation, high-potency opioids, or a combination of the above medications [57, 58]. Weinstock et al. reported that 43 % of RLS-associated conditions are associated with systemic iron deficiency [59]. A recent meta-analysis identified an increased prevalence of RLS only in iron deficiency and kidney disease [60]. Although the underlying mechanism between iron deficiency and RLS remains unclear, both oral and intravenous iron supplementation (ferric carboxymaltose or iron sucrose) have been proven effective and safe in childhood-onset RLS, as well as in pregnant women with RLS [61–64]. Low iron stores contribute to ADHD symptoms [65]; however, only one small clinical trial has documented the effectiveness of oral iron treatment (ferrous sulfate) for RLS in children with ADHD [66].

Levodopa, a dopaminergic agent, can effectively reduce the symptoms of RLS/PLMD in children [67] but not significantly modify the leg movement time structure during sleep [68]. Although RLS is significantly common in children and adolescents with ADHD, only a few studies reported the effectiveness of other dopaminergic agents, including pergolide, ropinirole, and levetiracetam, for treatment of children with ADHD and RLS [69–71]. Long-term treatment (more than 6 months) options which have been established as effective for RLS include pregabalin (up to 1 year), pramipexole, and rotigotine (up to 6 months) and gabapentin enacarbil, pramipexole, and ropinirole (ranging from 1 to 5 years) [72]. However, long-term treatment with dopaminergic agents may be complicated by the development of reversed increase in the severity and frequency of RLS/PLMD and loss of efficacy [58]. There are no data regarding the long-term use of these medications for children with ADHD and RLS/PLMD and deserve further investigation in the future.

#### **Management of Sleep Problems in Children With ADHD and Comorbid Psychiatric Disorders**

Most children with ADHD have psychiatric comorbidities, including conduct disorder, oppositional defiant disorder (ODD), anxiety, and/or depression [73]. The sleep problems in these children are strongly associated with the psychiatric comorbidities. Becker et al. found sleep problems significantly predicted greater ODD symptoms, general externalizing behavior problems, and depressive symptoms in a 1-year

follow-up study of 81 ADHD children [74•]. In turn, an increase in sleep problems over time can also be predicated by a diagnostic cluster that includes ODD, generalized anxiety disorder, and depression [75•].

For the treatment of sleep problems in ADHD children with comorbid psychiatric disorders, the expert consensus from a recent review suggests to review the medications, which may be the potential cause of sleep disorder and prioritize whether this drug should be used for the psychiatric disorder, or modified because of severe sleep problems [76•]. The alternative options are behavioral interventions, including good sleep hygiene and cognitive behavioral therapy [28•, 77, 78]. In cases of poor response to the above interventions, the clinicians can try sleep-promoting medications, such as melatonin, antihistamine, clonidine, benzodiazes, or trazodone [76•].

### Management of the Sleep Problems due to Adverse Effects of ADHD Medications

#### *Effects of ADHD Medications on Sleep*

Psychostimulants are the drug most often prescribed to treat children and adolescents with ADHD but, despite the emergence of newly developed drugs, they are associated with adverse events of sleep problems [79•, 80•]. The first-line FDA-approved medications, including methylphenidate, amphetamine, dextroamphetamine, and pemoline, are known to cause sleep problems in short- or long-term clinical trials [23, 81–83]. Difficulty falling asleep, night awakenings, shorter sleep duration, sleep-onset delay, and difficulty getting up in the morning are the commonly reported adverse effects [84]. The impact of ADHD medications on sleep varies and differs depending on the age, gender, dosage, presence of comorbidity, whether stimulant naïve, and duration of treatment [83, 85–88]. Sleep disturbance in children with ADHD may also occur during the psychostimulant titration stage (i.e., increase over baseline values in ADHD symptoms when the medication wears off) [76•, 84], and dopamine-releasing agents, e.g., amphetamine, are reported to have rebound hypersomnolence in the first few hours following wake [89]. A recently approved drug in Europe, lisdexamfetamine, although well tolerated in children and adolescents with ADHD and seems better response than methylphenidate, is found to have similar or even higher rate of sleep disturbance (e.g., insomnia) or headache in children and adolescents with ADHD [90, 91, 92•].

The common adverse event of insomnia caused by psychostimulants can be solved by switching to non-stimulant medications, such as atomoxetine [93], which has been reported to have better quality of sleep than methylphenidate [94]. In a recent meta-analysis of double-blind randomized controlled trials for atomoxetine treatment in pediatric

ADHD [95•], Schwartz et al. found sleep-onset insomnia was not significantly higher in children treated with atomoxetine compared to placebo and rarely caused discontinuation of treatment. Other non-CNS stimulants, including guanfacine extended release and clonidine extended release, are found to have effective effects on ADHD core symptoms and well-tolerated adverse effects of sleep in recent clinical trials and meta-analyses [96, 97•, 98–100].

#### *Management of Sleep Problems Caused by ADHD Medications*

Since children with ADHD may have sleep disturbance due to ADHD medications or ADHD per se, a baseline assessment of sleep conditions should be done before initiation of ADHD medications, as the European ADHD Guidelines Group (EAGG) has suggested [101]. The baseline children's Sleep Habits Questionnaire (CHSQ) [102], as well as a sleep diary completed by parents or adolescent patients, is suggested as the basic screening tool. Baseline polysomnography is the choice of objective screening tool for sleep-breathing disorder, episodic nocturnal phenomena, RLS, or limb movements [84].

Clinical experience suggests that ADHD medications negatively impact sleep, but the effects vary considerably from one patient to another. Therefore, reviewing the nature and effects of ADHD medications when sleep problems are encountered in ADHD children is recommended. For treatment of medication-related sleep disturbance in ADHD children, sleep hygiene is recommended as the first-line option by Cortese et al. [76•] and has been proven as effective and safe treatment when combined with melatonin for initial insomnia in a subgroup of ADHD children on stimulants [103]. In a recent randomized controlled trial, Hiscock et al. found brief behavioral sleep intervention modestly improves the severity of ADHD symptoms, as well as improved sleep conditions in a community sample of children with ADHD, most of whom were taking stimulant medications [28•]. While sleep hygiene is in progress, the clinicians may consider decreasing the medication on sleep simultaneously.

The European ADHD Guidelines Group for the management of adverse events during treatment with ADHD drugs recommends adding small (5 mg) doses of methylphenidate intermediate release in the evening if rebound effect with psychostimulants is documented [101, 104]. If psychostimulant is the current treatment and sleep-onset difficulty is not related to rebound effect, we may consider reducing the total dose, changing the dose regimen or formulation of the stimulants [76•, 101, 104]. For example, osmotic-release oral system methylphenidate (OROS-MPH) was found to have a low proportion of adverse events of insomnia (only 7.7 to 18 %) [105], a decrease in the number of nighttime awakenings, and an increase in the percentage of stage 2

sleep, compared with pretreatment baseline [106]. Otherwise, an option is to consider switching to a different stimulant (e.g., use methylphenidate from amphetamine or vice versa).

Switching to a non-stimulant (e.g., atomoxetine, guanfacine extended release, or bupropion) and adding an  $\alpha 2$  agonist are the alternative choices [76, 101, 104]. Guanfacine extended release has been found effective whether administered in the morning or evening as once daily monotherapy for ADHD [107, 108]. The treatment-related adverse events are only mild or moderate in severity [107, 108]. Another placebo-controlled trial found the somnolence adverse events of guanfacine extended release emerged within the first 2 weeks of dosing and generally resolved later [109]. We may consider giving atomoxetine once daily in the evening because this schedule is less associated with somnolence than morning dosing [110]. Furthermore, in cases of sleep-onset delay, atomoxetine should be considered since it is more commonly associated with somnolence rather than insomnia [111, 112]. Administration of melatonin along with methylphenidate was found to partially improve symptoms of sleep disturbance in a recent randomized controlled trial [113]. Adding an antihistamine has been tried in some studies with appropriate effects solving the sleep-onset insomnia in children with ADHD [84, 114].

## Conclusion

We have presented and discussed the most updated, peer-reviewed clinical trials or meta-analyses regarding the common adverse events of sleep in children and adolescents with ADHD, due to ADHD medications, the associated comorbidities of ADHD, or ADHD per se, which we hope will be helpful for clinicians.

In conclusion, optimized managements of sleep problems in ADHD children include reviewing the ADHD medications and ruling out differential diagnosis according to baseline screening of initial sleep conditions, accurate identification of ADHD-related specific sleep disorders, and comorbid psychiatric disorders. Initiating good sleep hygiene and behavioral therapy remain the first-line therapy, and adjusting the ADHD medications, including decreasing the dose regimens and switching to other formulation, another stimulants, non-stimulants,  $\alpha 2$ -adrenergic agonists, or antihistamine, can be the alternative choice. The available evidence-based pieces of information regarding both non-pharmacological and pharmacological treatment for sleep problems of ADHD children, while on ADHD medications, are still limited by small size and short duration. Therefore, further randomized controlled trials are urgently needed to investigate the optimized treatment strategies for ADHD patients with sleep disorders.

**Acknowledgments** This material is the result of work supported with resources and the use of facilities at the Yunlin Chang Gung Memorial Hospital, Yunlin, Taiwan, Republic of China.

## Compliance with Ethical Standards

**Conflict of Interest** Ming-Horng Tsai, Jen-Fu Hsu, and Yu-Shu Huang declare that they have no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

## References

Papers of particular interest, published recently, have been highlighted as:

- Of importance,
- Of major importance

1. Sung V, Hiscock H, Sciberras E, Efron D. Sleep problems in children with attention-deficit/hyperactivity disorder: prevalence and the effect on the child and family. *Arch Pediatr Adolesc Med.* 2008;162:336–42.
2. Um YH, Jeong JH, Hong SC, Kim TW, Lim HK, Seo HJ, et al. Association between sleep parameters and cognitive function in drug-naïve children with attention-deficit hyperactivity disorder: a polysomnographic study. *Sleep Med.* doi:10.1016/j.sleep.2015.11.016. **This study documented the relationship between sleep parameters and cognitive function in drug-naïve children with ADHD, while most subjects in previous studies were on medication, which is a potent confounding factor.**
3. Mulraney M, Giallo R, Lycett K, Mensah F, Sciberras E. The bidirectional relationship between sleep problems and internalizing and externalizing problems in children with ADHD: a prospective cohort study. *Sleep Med.* 2016;17:45–51.
4. Katzman MA, Sternat T. A review of OROS methylphenidate (Concerta®) in the treatment of attention-deficit/hyperactivity disorder. *CNS Drugs.* 2014;28:1005–33.
5. Becker SP, Piffner LJ, Stein MA, Burns GL, McBurnett K. Sleep habits in children with attention-deficit/hyperactivity disorder predominantly inattentive type and associations with comorbid psychopathology symptoms. *Sleep Med.* 2015;11:S1389–9457.
6. Canals J, Morales-Hidalgo P, Jané MC, Doménech E. ADHD prevalence in Spanish preschoolers: comorbidity, socio-demographic factors, and functional consequences. *J Atten Disord.* 2016. doi:10.1177/1087054716638511.
7. Yallop L, Brownell M, Chateau D, Walker J, Warren M, Baillis D, et al. Lifetime prevalence of attention-deficit/hyperactivity disorder in young adults: examining variations in the socioeconomic gradient. *Can J Psychiatry.* 2015;60:432–40.
8. Wang KY. Updated findings on neurodevelopmental disorders in Taiwan: impact of the institutionalized national healthcare system on prevalence and health outcomes. *Curr Opin Psychiatry.* 2016;29:144–8.
9. Aquirre Castaneda RL, Kumar S, Voigt RG, Leibson CL, Barbaresi WJ, et al. Childhood attention-deficit/hyperactivity disorder, sex, and obesity: a longitudinal population-based study. *Mayo Clin Proc.* 2016;91:352–61.

10. van Lieshout M, Luman M, Twisk JW, van Ewijk H, Groenman AP, Thissen AJ, et al. A 6-year follow-up of a large European cohort of children with attention-deficit/hyperactivity disorder-combined subtype: outcomes in late adolescence and young adulthood. *Eur Child Adolesc Psychiatry*. 2016. doi:10.1007/s00787-016-0820-y.
11. Casas M, Rösler M, Sandra Kooij JJ, Ginsberg Y, Ramos-Quiroga JA, Heger S, et al. Efficacy and safety of prolonged-release OROS methylphenidate in adults with attention-deficit/hyperactivity disorder: a 13-week, randomized, double-blind, placebo-controlled, fixed-dose study. *World J Biol Psychiatry*. 2013;14:268–81.
12. Rönnlund H, Elovainio M, Virtanen I, Matomäki J, Lapinleimu H. Poor parental sleep and the reported sleep quality of their children. *Pediatrics*. 2016. doi:10.1542/peds.2015-3425.
13. Kronholm E, Puusniekka R, Jokela J, Villberg J, Urrila AS, Paunio T, et al. Trends in self-reported sleep problems, tiredness and related school performance among Finnish adolescents from 1984 to 2011. *J Sleep Res*. 2015;24:3–10.
14. Hysing M, Pallesen S, Stormark KM, Lundervold AJ, Sivertsen B. Sleep patterns and insomnia among adolescents: a population-based study. *J Sleep Res*. 2013;22:549–56.
15. Efron D, Lycett K, Sciberras E. Use of sleep medication in children with ADHD. *Sleep Med*. 2014;15:472–5.
16. Corkum P, Davidson F, MacPherson M. A framework for the assessment and treatment of sleep problems in children with attention-deficit/hyperactivity disorder. *Pediatr Clin N Am*. 2011;58:667–83.
17. Cortese S, Lecendreux M, Mouren MC, Konofal E. ADHD and insomnia. *J Am Acad Child Adolesc Psychiatry*. 2006;45:384–5.
18. Mitchison GM, Njardvik U. Prevalence and gender differences of ODD, anxiety, and depression in a sample of children with ADHD. *J Atten Disord*. 2015. doi:10.1177/1087054715608442.
19. Lee MJ, Yang KC, Shyu YC, Yuan SS, Yang CJ, Lee SY, et al. Attention-deficit hyperactivity disorder, its treatment with medication and the probability of developing a depressive disorder: a nationwide population-based study in Taiwan. *J Affect Disord*. 2016;189:110–7.
20. Spruyt K, Gozal D. Sleep disturbances in children with attention-deficit/hyperactivity disorder. *Expert Rev Neurother*. 2011;11:565–77.
21. Sciberras E, Lycett K, Efron D, Mensah F, Gerner B, Hiscock H. Anxiety in children with attention-deficit/hyperactivity disorder. *Pediatrics*. 2014;133:801–8.
22. Kidwell KM, Van Dyk TR, Lundahl A, Nelson TD. Stimulant medications and sleep for youth with ADHD: a meta-analysis. *Pediatrics*. 2015;136:1144–53. **This is a recent published meta-analysis of stimulant medication regarding its effects of longer sleep latency, worse sleep efficiency, and shorter sleep duration.**
23. Santisteban JA, Stein MA, Bergmame L, Gruber R. Effect of extended-release dexamethylphenidate and mixed amphetamine salts on sleep: a double-blind, randomized, crossover study in youth with attention-deficit hyperactivity disorder. *CNS Drugs*. 2014;28:825–33.
24. LeBourgeois MK, Giannotti F, Cortesi F, Wolfson AR, Harsh J. The relationship between reported sleep quality and sleep hygiene in Italian and American adolescents. *Pediatrics*. 2005;115:257–65.
25. Meltzer LJ, Brimeyer C, Russell K, Avis KT, Biggs S, Reynolds AC, et al. The children's report of sleep patterns: validity and reliability of the sleep hygiene index and sleep disturbance scale in adolescents. *Sleep Med*. 2014;15:1500–7.
26. Weiss MD, Salpekar J. Sleep problems in the child with attention-deficit/hyperactivity disorder: defining etiology and appropriate treatments. *CNS Drugs*. 2010;24:811–28.
27. Sciberras E, Fulton M, Efron D, Oberklaid F, Hiscock H. Managing sleep problems in school aged children with ADHD: a pilot randomized controlled trial. *Sleep Med*. 2011;12:932–5.
28. Hiscock H, Sciberras E, Mensah F, Gerner B, Efron D, Khano S, et al. Impact of a behavioral sleep intervention on symptoms and sleep in children with attention-deficit/hyperactivity disorder, and parental mental health: randomized controlled trial. *BMJ*. 2015;350:h68. **This study providing evidence-based information using RCT documenting the effect of behavior sleep intervention on ADHD children with sleep problems.**
29. Vidal R, Castells J, Richarte V, Palomar G, Garcia M, Nicolau R, et al. Group therapy for adolescents with attention-deficit/hyperactivity disorder: a randomized controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2015;54:275–82. **This study is the latest and an important RCT documenting the effect of group therapy for adolescents with ADHD.**
30. Santisteban JA, Stein MA, Bergmame L, Gruber R. Effect of extended-release dexamethylphenidate and mixed amphetamine salts on sleep: a double-blind, randomized, crossover study in youth with attention-deficit hyperactivity disorder. *CNS Drugs*. 2014;28:825–33. **This study highlights that higher stimulant doses are associated with reduced sleep duration and later sleep start times, regardless of medication class.**
31. Bock DE, Roach-Fox E, Seabrook JA, Rieder MJ, Matsui D. Sleep-promoting medications in children: physician prescribing habits in Southwestern Ontario. *Canada Sleep Med*. 2016;17:52–6.
32. Golmirzaei J, Mahboobi H, Yazdanparast M, Mushtag G, Kamal MA, Hamzei E. Psychopharmacology of attention-deficit hyperactivity disorder: effects and side effects. *Curr Pharm Des*. 2016;22:590–4.
33. Furster C, Hallerback MU. The use of melatonin in Swedish children and adolescents—a register-based study according to age, gender, and medication of ADHD. *Eur J Clin Pharmacol*. 2015;71:877–81.
34. Dalsgaard S, Nielsen HS, Simonsen M. Five-fold increase in national prevalence rates of attention-deficit/hyperactivity disorder medications for children and adolescents with autism spectrum disorder, attention-deficit/hyperactivity disorder, and other psychiatric disorders: a Danish register-based study. *J Child Adolesc Psychopharmacol*. 2013;23:432–9.
35. van der Heijden KB, Smits MG, Van Someren EJ, Gunning WB. Idiopathic chronic sleep onset insomnia in attention-deficit/hyperactivity disorder: a circadian rhythm sleep disorder. *Chronobiol Int*. 2005;22:559–70.
36. van Geijlswijk IM, Korzilius HP, Smits MG. The use of exogenous melatonin in delayed sleep phase disorder: a meta-analysis. *Sleep*. 2010;33:1605–14.
37. Bendz LM, Scates AC. Melatonin treatment for insomnia in pediatric patients with attention-deficit/hyperactivity disorder. *Ann Pharmacother*. 2010;44:185–91.
38. Gringras P, Gamble C, Jones AP, Wiggs L, Williamson PR, Sutcliffe A, et al. Melatonin for sleep problems in children with neurodevelopmental disorders: randomized double masked placebo controlled trial. *BMJ*. 2012;345:e6664.
39. Hoebert M, van der Heijden KB, van Geijlswijk IM, Smits MG. Long-term follow-up of melatonin treatment in children with ADHD and chronic sleep onset insomnia. *J Pineal Res*. 2009;47:1–7.
40. Sallee F, Connor DF, Newcorn JH. A review of the rationale and clinical utilization of  $\alpha$ 2-adrenoceptor agonists for the treatment of attention-deficit/hyperactivity and related disorders. *J Child Adolesc Psychopharmacol*. 2013;23:308–19.
41. Prince JB, Wilens TE, Biederman J, Spencer TJ, Wozniak JR. Clonidine for sleep disturbances associated with attention-deficit hyperactivity disorder: a systemic chart review of 62

- cases. *J Am Acad Child Adolesc Psychiatry.* 1996;35:599–605.
42. Wilens TE, Biederman J, Spencer T. Clonidine for sleep disturbances associated with attention-deficit hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry.* 1994;33:424–6.
  43. Jain R, Segal S, Kollins SH, Khayrallah M. Clonidine extended-release tablets for pediatric patients with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry.* 2011;50:171–9.
  44. Blumer JL, Findling RL, Shih WJ, Soubrane C, Reed MD. Controlled clinical trial of zolpidem for the treatment of insomnia associated with attention-deficit/hyperactivity disorder in children 6 to 17 years of age. *Pediatrics.* 2009;123:e770–6.
  45. Sedky K, Carvalho K, Lippmann S. Attention deficit hyperactivity disorder and sleep disordered breathing in children. *J Pediatr Biochem.* 2013;3:61–7.
  46. Gruber R, Xi T, Frenette S, Robert M, Vannashin P, Carrier J. Sleep disturbances in prepubertal children with attention deficit hyperactivity disorder: a home polysomnography study. *Sleep.* 2009;32:343–50.
  47. Amiri S, AbdollahiFakhim S, Lotfi A, Bayazian G, Sohrabpour M, Hemmatjoo T. Effect of adenotonsillectomy on ADHD symptoms of children with adenotonsillar hypertrophy and sleep disordered breathing. *Int J Pediatr Otorhinolaryngol.* 2015;79:1213–7. **This study documented the significant effect of adenotonsillectomy on ADHD children with sleep disordered breathing.**
  48. Mostofsky SH, Cooper KL, Kates WR, Denckla MB, Kaufmann WE. Smaller prefrontal and premotor volumes in boys with attention-deficit/hyperactivity disorder. *Biol Psychiatry.* 2002;52:785–94.
  49. Song SA, Tolisano AM, Cable BB, Camacho M. Neurocognitive outcomes after pediatric adenotonsillectomy for obstructive sleep apnea: a systemic review and meta-analysis. *Int J Pediatr Otorhinolaryngol.* 2016;83:205–10. **This study documented the significant effect of adenotonsillectomy on obstructive sleep apnea, which leads to improved neurocognitive outcomes.**
  50. Huang YS, Guilleminault C, Li HY, Yang CM, Wu YY, Chen NH. Attention-deficit/hyperactivity disorder with obstructive sleep apnea: a treatment outcome study. *Sleep Med.* 2007;8:18–30.
  51. Sedky K, Bennett DS, Carvalho KS. Attention deficit hyperactivity disorder and sleep disordered breathing in pediatric populations: a meta-analysis. *Sleep Med Rev.* 2014;18:349–56.
  52. Picchetti MA, Picchetti DL. Advances in pediatric restless legs syndrome: iron, genetics, diagnosis and treatment. *Sleep Med.* 2010;11:643–51.
  53. de Weerd A, Arico I, Silvestri R. Presenting symptoms in pediatric restless legs syndrome patients. *J Clin Sleep Med.* 2013;9:1077–80.
  54. Oner P, Dirik EB, Taner Y, Caykoylu A, Anlar O. Association between low serum ferritin and restless legs syndrome in patients with attention deficit hyperactivity disorder. *Tohoku J Exp Med.* 2007;213:269–76.
  55. Paulo Daubian-Nose P, Frank MK, Esteves AM. Sleep disorders: review of the interface between restless legs syndrome and iron metabolism. *Sleep Sci.* 2014;7:234–7.
  56. Sharon D. Nonpharmacologic management of restless legs syndrome (Willis-Ekbom Disease): myths or science. *Sleep Med Clin.* 2015;10:263–78.
  57. Silber MH, Becker PM, Earley C, Garcia-Borreguero D, Ondo WG, Medical Advisory Board of the Willis-Ekbom Disease Foundation. Willis-Ekbom Disease Foundation revised consensus statement on the management of restless legs syndrome. *Mayo Clin Proc.* 2013;88:977–86.
  58. Rinaldi F, Galbiati A, Marelli S, Ferini Strambi L, Zucconi M. Treatment options in intractable restless legs syndrome/Willis-Ekbom Disease (RLS/WED). *Curr Treat Options Neurol.* 2016;18:7.
  59. Weinstock LB, Walters AS. Restless legs syndrome is associated with irritable bowel syndrome and small intestinal bacterial overgrowth. *Sleep Med.* 2011;12:610–3.
  60. Trenkwalder C, Allen R, Högl B, Paulus W, Winkelmann J. Restless legs syndrome associated with major diseases: a systematic review and new concept. *Neurology.* 2016;86:1336–43. **This article provides the latest updated information regarding restless legs syndrome being as a continuous spectrum with a major genetic contribution and a major comorbid disease of other entities.**
  61. Allen RP, Adler CH, Du W, Butcher A, Bregman DB, Earley CJ. Clinical efficacy and safety of IV ferric carboxymaltose (FCM) treatment of RLS: a multi-centred, placebo-controlled preliminary clinical trial. *Sleep Med.* 2011;12:906–13.
  62. Schneider J, Krafft A, Manconi M, Hübner A, Baumann C, Werth E, et al. Open-label study of the efficacy and safety of intravenous ferric carboxymaltose in pregnant women with restless legs syndrome. *Sleep Med.* 2015;16:1342–7.
  63. Grim K, Lee B, Sung AY, Kotagal S. Treatment of childhood-onset restless legs syndrome and periodic limb movement disorder using intravenous iron sucrose. *Sleep Med.* 2013;14:1100–4.
  64. Tilma J, Tilma K, Norregaard O, Ostergaard JR. Early childhood-onset restless legs syndrome: symptoms and effect of oral iron treatment. *Acta Paediatr.* 2013;105:e221–6.
  65. Konofal E, Lecendreux M, Arnulf I, Mouren MC. Iron deficiency in children with attention-deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med.* 2004;158:1113–5.
  66. Konofal E, Lecendreux M, Deron J, Marchand M, Cortese S, Zaim M, et al. Effects of iron supplementation on attention deficit hyperactivity disorder in children. *Pediatr Neurol.* 2008;38:20–6.
  67. England SJ, Picchetti DL, Couvadelli BV, Fisher BC, Siddigui F, Wagner ML, et al. L-Dopa improves restless legs syndrome and periodic limb movements in sleep but not attention-deficit/hyperactivity disorder in a double-blind trial in children. *Sleep Med.* 2011;12:471–7.
  68. Ferri R, Bruni O, Novelli L, Picchetti MA, Picchetti DL. Time structure of leg movement activity during sleep in attention-deficit/hyperactivity disorder and effects of levodopa. *Sleep Med.* 2013;14:359–66.
  69. Walters AS, Mandelbaum DE, Lewin DS, Kugler S, England SJ, Miller M. Dopaminergic therapy in children with restless legs/periodic limb movements in sleep and ADHD. Dopaminergic Therapy Study Group. *Pediatr Neurol.* 2000;22:182–6.
  70. Konofal E, Arnulf I, Lecendreux M, Mouren MC. Ropinirole in a child with attention-deficit hyperactivity disorder and restless legs syndrome. *Pediatr Neurol.* 2005;32:350–1.
  71. Gagliano A, Arico I, Calarese T, et al. Restless leg syndrome in ADHD children: levetiracetam as a reasonable therapeutic option. *Brain Dev.* 2011;33:480–6.
  72. Garcia-Borreguero D, Kohonen R, Silber MH, Winkelmann JW, Earley CJ, Högl B, et al. The long-term treatment of restless legs syndrome/Willis-Ekbom disease: evidence-based guidelines and clinical consensus best practice guidance: a report from the international restless legs syndrome study group. *Sleep Med.* 2013;14:675–84.
  73. Cuffè SP, Visser SN, Holbrook JR, Danielson ML, Geryk LL, Wolraich ML, et al. ADHD and psychiatric comorbidity: functional outcomes in a school-based sample of children. *J Atten Disord.* 2015. doi:10.1177/1087054715613437.
  74. Becker SP, Langberg JM, Evans SW. Sleep problems predict comorbid externalizing behaviors and depression in young adolescents with attention-deficit/hyperactivity disorder. *Eur Child Adolesc Psychiatry.* 2015;24:897–907. **This article highlights the importance of sleep problems as the important predictor**

- of externalizing behavior and depression in ADHD adolescents.**
75. Shanahan L, Copeland WE, Angold A, Bondy CL, Costello EJ. Sleep problems predict and are predicted by generalized anxiety/depression and oppositional defiant disorder. *J Am Acad Child Adolesc Psychiatry*. 2014;53:550–8. **This is the first study documenting sleep problems can predict and be predicted by generalized anxiety/depression and oppositional defiant disorder.**
  76. Cortese S, Brown TE, Corkum P, Gruber R, O'Brien LM, Stein M, et al. Assessment and management of sleep problems in youths with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2013;52:784–96. **This is the expert consensus and meta-analysis regarding the latest assessment and management of sleep problems in youths with ADHD.**
  77. Papadopoulos N, Sciberras E, Hiscock H, Mulraney M, McGillivray J, Rinehart N. The efficacy of a brief behavioral sleep intervention in school-aged children with ADHD and comorbid autism spectrum disorder. *J Atten Disord*. 2015. doi:10.1177/1087054714568565.
  78. Sciberras E, Mulraney M, Anderson V, Rapee RM, Nicholson JM, Efron D, et al. Managing anxiety in children with ADHD using cognitive-behavioral therapy: a pilot randomized controlled trial. *J Atten Disord*. 2015. doi:10.1177/1087054715584054.
  79. Storebø OJ, Ramstad E, Krogh HB, Nilausen TD, Skoog M, Holmskov M, et al. Methylphenidate for children and adolescents with attention deficit hyperactivity disorder (ADHD). *Cochrane Database Syst Rev*. 2015;11:CD009885. **This is the latest systemic review and meta-analysis regarding the stimulant effects on children with ADHD.**
  80. Storebø OJ, Krogh HB, Ramstad E, Moreira-Maia CR, Holmskov M, Skoog M, et al. Methylphenidate for attention-deficit/hyperactivity disorder in children and adolescents: Cochrane systematic review with meta-analyses and trial sequential analyses of randomized clinical trials. *BMJ*. 2015;351:h5203. **This study focusing on whether methylphenidate beneficial or harmful for treatment of ADHD children concludes caution regarding the use of methylphenidate, since it is associated with an increased risk of non-serious adverse events.**
  81. Huang YS, Tsai MH. Long-term outcomes with medications for attention-deficit hyperactivity disorder: current status of knowledge. *CNS Drugs*. 2011;25:539–54.
  82. Becker SP, Froehlich TE, Epstein JN. Effects of methylphenidate on sleep functioning in children with attention-deficit/hyperactivity disorder. *J Dev Behav Pediatr*. 2016;37(5):395–404.
  83. Wang LJ, Chen CK, Huang YS. Gender differences in the behavioral symptoms and neuropsychological performance of patients with attention-deficit/hyperactivity disorder treated with methylphenidate: a two-year follow-up study. *J Child Adolesc Psychopharmacol*. 2015;25:501–8.
  84. Konofal E, Lecendreux M, Cortese S. Sleep and ADHD. *Sleep Med*. 2010;11:652–8.
  85. Wang LJ, Chen CK, Huang YS. Neurocognitive performance and behavioral symptoms in patients with attention-deficit/hyperactivity disorder during twenty-four months of treatment with methylphenidate. *J Child Adolesc Psychopharmacol*. 2015;25:246–53.
  86. Lecendreux M, Lavault S, Lopez R, Inocente CO, Konofal E, Cortese S, et al. Attention-deficit/hyperactivity disorder (ADHD) symptoms in pediatric narcolepsy: a cross-sectional study. *Sleep*. 2015;38:1285–95.
  87. Coghill DR, Banaschewski T, Lecendreux M, Soutullo C, Zuddas A, Adeyi B, et al. Post hoc analyses of the impact of previous medication on the efficacy of lisdexamfetamine dimesylate in the treatment of attention-deficit/hyperactivity disorder in a randomized, controlled trial. *Neuropsychiatr Dis Treat*. 2014;10:2039–47.
  88. Simonoff E, Taylor E, Baird G, Bernard S, Chadwick O, Liang H, et al. Randomized controlled double-blind trial of optimal dose methylphenidate in children and adolescents with severe attention deficit hyperactivity disorder and intellectual disability. *J Child Psychol Psychiatry*. 2013;54:527–35.
  89. Gruner JA, Marcy VR, Lin YG, Bozyczko-Coyne D, Marino MJ, Gasior M. The roles of dopamine transport inhibition and dopamine release facilitation in wake enhancement and rebound hypersomnolence induced by dopaminergic agents. *Sleep*. 2009;32:1425–38.
  90. Roskell NS, Setyawan J, Zimovetz EA, Hodgkins P. Systemic evidence synthesis of treatments for ADHD in children and adolescents: indirect treatment comparisons of lisdexamfetamine with methylphenidate and atomoxetine. *Curr Med Res Opin*. 2014;30:1673–85.
  91. Coghill DR, Caballero B, Sorooshian S, Civil R. A systemic review of the safety of lisdexamfetamine dimesylate. *CNS Drugs*. 2014;28:497–511.
  92. Dittmann RW, Cardo E, Nagy P, Anderson CS, Adeyi B, Caballero B, et al. Treatment response and remission in a double-blind, randomized, head-to-head study of lisdexamfetamine dimesylate and atomoxetine in children and adolescents with attention-deficit hyperactivity disorder. *CNS Drugs*. 2014;28:1059–69. **This study compared the efficacy and side effects of lisdexamfetamine dimesylate and atomoxetine in children with ADHD.**
  93. Warrer P, Thomsen PH, Dalsgaard S, Hansen EH, Aagaard L, Wallach Kildemoes H, et al. Switch in therapy from methylphenidate to atomoxetine in children and adolescents with attention-deficit/hyperactivity disorder: an analysis of patient records. *J Child Adolesc Psychopharmacol*. 2016;26(4):354–61.
  94. Prasad S, Steer C. Switching from neurostimulant therapy to atomoxetine in children and adolescents with attention-deficit hyperactivity disorder: clinical approaches and review of current available evidence. *Pediatr Drugs*. 2008;10:39–47.
  95. Schwartz S, Correll CU. Efficacy and safety of atomoxetine in children and adolescents with attention-deficit/hyperactivity disorder: results from a comprehensive meta-analysis and metaregression. *J Am Acad Child Adolesc Psychiatry*. 2014;53:174–87. **This study using meta-analysis documented the efficacy and safety of atomoxetine, and concluded it as the alternative choice for children and adolescents with ADHD.**
  96. Hervas A, Huss M, Johnson M, McNicholas F, van Stralen J, Sreckovic S, et al. Efficacy and safety of extended-release guanfacine hydrochloride in children and adolescents with attention-deficit/hyperactivity disorder: a randomized, controlled, phase III trial. *Eur Neuropsychopharmacol*. 2014;24:1861–72.
  97. Stein MA, Sikirica V, Weiss MD, Robertson B, Lyne A, Newcorn JH. Does guanfacine extended release impact functional impairment in children with attention-deficit/hyperactivity disorder? Results from a randomized controlled trial. *CNS Drugs*. 2015;29:953–62. **This updated RCT documented guanfacine extended release treatment is associated with reductions in ADHD symptoms, and has tolerable adverse events.**
  98. Dittmann RW, Cardo E, Nagy P, Anderson CS, Bloomfield R, Caballero B, et al. Efficacy and safety of lisdexamfetamine dimesylate and atomoxetine in the treatment of attention-deficit/hyperactivity disorder: a head-to-head, randomized, double-blind, phase IIIb study. *CNS Drugs*. 2013;27:1081–92.
  99. Daviss WB, Patel NC, Robb AS, McDermott MP, Bukstein OG, Pelham Jr WE, et al. Clonidine for attention-deficit/hyperactivity disorder: II. ECG changes and adverse events analysis. *J Am Acad Child Adolesc Psychiatry*. 2008;47:189–98.
  100. Ming X, Mulvey M, Mohanty S, Patel V. Safety and efficacy of clonidine and clonidine extended-release in the treatment of



- children and adolescents with attention deficit and hyperactivity disorders. *Adolesc Health Med Ther*. 2011;2:105–12.
101. Graham J, Banaschewski T, Buitelaar J, Coghill D, Danckaerts M, Dittmann RW, et al. European guidelines on managing adverse effects of medication for ADHD. *Eur Child Adolesc Psychiatry*. 2011;20:17–37.
102. Owens JA, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. *Sleep*. 2000;23:1043–51.
103. Weiss MD, Wasdell MB, Bomben MM, Rea KJ, Freeman RD. Sleep hygiene and melatonin treatment for children and adolescents with ADHD and initial insomnia. *J Am Acad Child Adolesc Psychiatry*. 2006;45:512–9.
104. Cortese S, Holtmann M, Banaschewski T, Buitelaar J, Coghill D, Dittmann RW, et al. Practitioner review: current best practice in the management of adverse events during treatment with ADHD medications in children and adolescents. *J Child Psychol Psychiatry*. 2013;54:227–46.
105. Hvolby A. Associations of sleep disturbance with ADHD: implications for treatment. *Atten Defic Hyperact Disord*. 2015;7:1–18.
106. Kim HW, Yoon IY, Cho SC, Kim BN, Chung S, Lee H, et al. The effect of OROS methylphenidate on the sleep of children with attention-deficit/hyperactivity disorder. *Int Clin Psychopharmacol*. 2010;25:107–15.
107. Wilens TE, Bukstein O, Brams M, Cutler AJ, Childress A, Rugino T, et al. A controlled trial of extended-release guanfacine and psychostimulants for attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2012;51:74–85.
108. Newcorn JH, Stein MA, Childress AC, Youcha S, White C, Enright G, et al. Randomized, double-blind trial of guanfacine extended release in children with attention-deficit/hyperactivity disorder: morning or evening administration. *J Am Acad Child Adolesc Psychiatry*. 2013;52:921–30.
109. Sallee FR, McGough J, Wigal T, Donahue J, Lyne A, Biederman J, et al. Guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder: a placebo-controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2009;48:155–65.
110. Block SL, Kelsey D, Coury D, Lewis D, Quintana H, Sutton V, et al. Once-daily atomoxetine for treating pediatric attention-deficit/hyperactivity disorder: comparison of morning and evening dosing. *Clin Pediatr*. 2009;48:723–33.
111. Cortese S, Panei P, Arcieri R, Germinario EA, Capuano A, Margari L, et al. Safety of methylphenidate and atomoxetine in children with attention-deficit/hyperactivity disorder (ADHD): data from the Italian National ADHD Registry. *CNS Drugs*. 2015;29:865–77.
112. Shang CY, Pan YL, Lin HY, Huang LW, Gau SS. An open-label, randomized trial of methylphenidate and atomoxetine treatment in children with attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol*. 2015;25:566–73.
113. Mohammadi MR, Mostafavi SA, Keshavarz SA, Eshraghian MR, Hosseinzadeh P, Hosseinzadeh-Attar MJ, et al. Melatonin effects in methylphenidate treated children with attention deficit hyperactivity disorder: a randomized double blind clinical trial. *Iran J Psychiatry*. 2012;7:87–92.
114. Kratochvil CJ, Lake M, Pliszka SR, Walkup JT. Pharmacological management of treatment-induced insomnia in ADHD. *J Am Acad Child Adolesc Psychiatry*. 2004;44:499–501.