Aims and objectives. The aim of this review was to explore the literature to determine what is known about adolescent sleep, the causes and consequences of disturbed sleep in adolescence and the implications this has for nursing practice.

Background. Sleep disorders are relatively common in young people. Disturbed sleep can be both a cause and a result of ill health and if recognised can indicate psychosocial, psychological or physical difficulties.

Design. Literature review.

Methods. Searching of key electronic databases.

Results. Disturbed sleep in adolescents has several potential consequences, including daytime sleepiness, reduced academic performance and substance use/abuse. However, despite its significance and frequency, sleep disturbance is an area of adolescent health that is almost entirely unaddressed within the nursing literature.

Conclusion. Nursing has a role to play in assisting adolescents and their families to recognise the importance of sleep to the general health and well-being of young people.

Relevance to clinical practice. There is a need for nursing to develop tools to assess sleep in adolescent clients and non-pharmaceutical interventions to assist adolescents achieve optimum sleep and rest. Nurses may also contribute to educating adolescents and their families regarding the importance of good sleep hygiene.

Key words: adolescent health, adolescents, literature review, nursing education, sleep, sleep disturbance

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Introduction

Sleep is essential to the healthy development of children and adolescents and to the maintenance of all bodily processes (Stoer 2001). Adolescence is a time of rapid growth and physical and neurological development that is highly sensitive to environmental and biological factors. Sufficient quantity and quality of sleep is essential for the challenges that these rapid changes present. There is a growing body of literature regarding adolescent sleep and sleep disturbance.

Paediatric and adolescent sleep disorders are common and may have serious consequences to both physical and mental health (Grunstein & Grunstein 2001, Cukrowicz et al. 2006). Ohayon et al. (2000) estimate that 25% of adolescents report symptoms of insomnia and 4% have sleep disturbances severe enough to warrant the diagnosis of a sleep disorder using DSM-IV criteria. Although specialist adolescent nurses and mental health nurses may be familiar with issues pertaining to sleep disturbance in adolescents, nurses from a more generalist background may be
unfamiliar with the potential significance of sleep disturbance in young people.

Aims
The purpose of this study is to review the literature related to adolescent sleep, to explore the causes and consequences of disturbed sleep in adolescence and to discuss the implications this has for nursing practice.

Methods and objectives
Databases used in this literature search included Blackwell Synergy, CINAHL, Journals@Ovid, PsychINFO, Medline/PubMed and Sciencedirect. Search terms used singly or in combination included: adolescent, sleep, health and nursing. Database searches were limited to English and to capture the range and diversity of relevant literature, papers published in the years 1990–2007 were selected for inclusion. The University of Western Sydney’s library catalogue was also used for books published on the topics of adolescent health and sleep. The objective of this review was to examine published literature about adolescent sleep with a particular focus on nursing perspectives.

Results
Findings revealed that the literature can be classified under the broad headings of: sleep and sleep disorders; physiological factors affecting adolescent sleep; adolescent sleep disorders; adolescent sleep and mental health issues; consequences of disturbed sleep in adolescence and nursing and adolescent sleep disturbance. Findings will be discussed under these broad headings.

Discussion
Sleep and sleep disorders
Sleep is a state of rest normally occurring in a recumbent position, quietly with little movement, during which consciousness and responsiveness are decreased. This state is reversible by external stimulation or internal satiation (Stores 2001). Sleep is organised into two broad categories, rapid eye movement (REM) and non-REM sleep. It is during REM that most dreaming occurs. Despite a loss of muscle tone, REM is very similar to an awake state and sleepers are easily roused (Dahl & Lewin 2002). Non-REM sleep occurs in four stages, with stages 1 and 2 considered light sleep and stages 3 and 4 [slow wave sleep (SWS)], the deepest stages of sleep. Slow wave sleep increases proportionally with hours spent awake and is more difficult to arouse a sleeper from. This stage of sleep is associated with restoration, increases in secretion of growth hormone and immune function changes (Dahl & Lewin 2002).

There are two intrinsic biological processes thought to control patterns of sleep and waking. These are the circadian rhythm regulated by the suprachiasmatic nucleus (SCN) of the hypothalamus, which is influenced by cues such as daylight, mealtimes, hunger and temperature and the homeostatic process, which responds to time (Dahl & Lewin 2002, Jenni & Carskadon 2004, Jenni et al. 2005) spent awake by increasing sleep pressure (the urge to sleep) (Jenni & Carskadon 2004, Jenni et al. 2005). Hormonal secretion also contributes to sleep timing. Dim light melatonin from the pineal gland initiates sleep onset and cortisol from the SCN governs the sleep wake rhythm (Stores 2001, Dahl & Lewin 2002).

Sleep disorders are diagnosed when sleep is disturbed over a period of time, usually more than one month, and when the disturbance causes significant disruption to daytime activity (American Psychiatric Association 2000). Sleep disorders can be classified into four groups: parasomnias, dyssomnias, sleep disorders associated with mental, neurological or other medical disorders and proposed sleep disorders (American Academy of Sleep Medecine (AASM) 2001). Parasomnias are disorders of arousal and sleep-stage transition, that includes sleepwalking, sleep talking, night terrors and nightmares. Dyssomnias, describe difficulty that occurs with either going to sleep or remaining asleep and include insomnia, narcolepsy, obstructive sleep apnoea syndrome (OSAS), upper airway resistance syndrome (UARS), restless legs syndrome (RLS) and delayed sleep phase syndrome (DSPS) (AASM 2001). Sleep disorders associated with neurological or mental disorders, are disorders occurring secondary to other conditions (AASM 2001).

Physiological factors affecting adolescent sleep
Sleep in adolescence undergoes changes that are brought about by both biological and psychosocial factors, including changes to hormonal secretion, brain maturation and the homeostatic process. These factors conspire to allow adolescents to stay awake later. To determine if older adolescents had a later biological sleep pressure than younger adolescents, Taylor et al. 2005 examined dim light melatonin secretion in saliva and sleep onset drive during a period of extended wakefulness, in nine prepubertal and 11 postpubertal adolescents. They found that older adolescents’ melatonin secretion in dim light commenced approximately one
hour later than in the younger adolescents. Furthermore, they found that older adolescents had reduced sleep pressure (compared to the younger adolescents) as they passed their conditioned bedtime. This occurred despite still physically requiring the same amount, if not more sleep than younger adolescents.

This finding was confirmed by Jenni et al. in a sleep deprivation study of seven prepubertal and six mature adolescents: sleep pressure, measured by polysomnography, built much more slowly in the mature adolescents. Although Taylor et al. (2005) and Jenni et al. (2005) found that younger adolescents had a greater tendency to fall asleep earlier, a longitudinal study by Laberge et al. (2001) of over 1000 children aged 10–13 years, found a large proportion of younger adolescents had difficulty falling asleep This is comparable to similar results from a European study by Tynjala et al. (1993), Laberge et al. (2001) attribute this to a transitory increase of sleep disturbance related to puberty onset and acknowledge the need for further large studies to compare objective sleep measurement with hormonal status.

Several studies have assessed whether there is an association between sleep patterns and pubertal status. Knutson (2005) analysed survey data from adolescents and their parents on two occasions approximately one year apart. In the first survey, 1270 females and 1069 males between the ages of 12–16 years participated and in the second, 1135 females and 932 males. Findings suggest that there is a gender difference in sleep difficulties with increasing pubertal development, with females having an increased risk of insomnia and tiredness on waking than males.

Children who have enforced early bed times (when they are not tired), may develop sleep disturbances because of their engagement with activities closely linked to arousal, such as watching television and listening to music (Meijer et al. 2005). Laberge et al. (2001) studied the development of sleep habits in an equal number of boys and girls (n = 588) for whom mothers completed annual sleep questionnaires when the children were aged 10–13 years. Nocturnal sleep times decreased with age, which correlates with findings by Knutson (2005) who suggests that duration of sleep decreases with increasing pubertal status and Taylor et al. (2005), who found that during extended waking, sleep pressure was lower in more mature adolescents. While examining EEG markers of sleep homeostasis to evaluate the presence of maturational changes to explain altered sleep patterns across puberty, Carskadon et al. (2004) found some changes that may explain later bedtimes in adolescents. However, these authors also suggest that adolescents experience circadian rhythm changes, which can result in delayed sleep onset and later arousal times. This in turn increases the risk of excessive sleepiness, mood regulation difficulties, impaired learning and academic performance and school absenteeism.

Adolescent sleep disorders

Adolescents frequently suffer from daytime sleepiness. Daytime sleepiness has been reported in 20% of adolescents in a large study (n = 1125) from four European countries: France, Great Britain, Germany and Italy (Ohayon et al. 2000). A survey of adolescents conducted in four cities in Argentina (n = 2884) indicated that insufficient sleep was common (Perez-Chada et al. 2007). Laberge et al. 2000 examined the development of parasomnias from childhood to early adolescence to find sleepwalking (24%) and night terrors (6%), while diminishing from childhood levels, still occurred in adolescence. Night terrors differ from nightmares and begin with a frightening scream, generally within the first hour of sleep in non-REM sleep and are rarely recollected. In contrast, nightmares occur later in the sleep cycle in REM sleep and are usually remembered by the individual (AASM 2001). If recurrent, nightmares could be indicative of a range of other sleep disorders or psychological stress.

Insomnia in adolescents is a symptom rather than a diagnosis (Owens 2006). Once an adolescent has difficulty falling asleep, they can develop anxiety when going to bed that heightens arousal, decreasing their ability to fall asleep (Owens 2006). This can lead to irregular sleeping patterns with adolescents staying up late each night and sleeping in on weekends to compensate (sleep lag) (Curcio et al. 2006). Sleep lag has been described as a form of jetlag that can arise for adolescents during the shift between weekend and weekday sleep schedules (Dahl & Lewin 2002). According to Curcio et al. (2006), sleep lag contributes to the development of DSPS, as well as waking difficulties. DSPS is a circadian rhythm disorder that affects 5–10% of adolescents and prevents them from falling asleep at a time that would allow them the 8.5–9.5 hours needed for restoration (Givan 2004, Meltzer & Mindell 2004, 2006). Sleep in DSPS is typically delayed although normal once initiated. If adolescents attempt to go to bed earlier they will suffer from insomnia until their normal delayed sleep time is reached. Delayed sleep phase syndrome has ramifications for daytime functioning, behaviour problems, depression and academic performance (Meltzer & Mindell 2004, 2006).

Narcolepsy in adolescence most often presents as daytime sleepiness that will evolve to include cataplexy, hypnagogic hallucinations, sleep paralysis and broken sleep, as the adolescent ages into adulthood (Meltzer & Mindell 2006). It is estimated that 0.2% of children suffer from
narcolepsy (Givan 2004). However, adolescent narcolepsy is difficult to diagnose as symptoms may be vague or confused with other sleep disorders (Meltzer & Mindell 2006). The sense that sleep disorders may be indistinguishable from normal adolescent sleep behaviour affects knowledge of true prevalence of sleep disorders in adolescents.

Overweight and obese youth are prone to snoring, UARS and OSAS, as there can be an ‘increase in soft tissue structures surrounding the upper airways, size of the tongue, soft palate and lateral pharyngeal walls’ (Carotenuto et al. 2006). UARS can also appear in children of average weight, but is normally corrected by adenotonsillectomy (Givan 2004). Restless Leg Syndrome manifests as ‘…creepy-crawly or tingling feeling, most commonly in the legs that can be alleviated temporarily with movement’ (Meltzer & Mindell 2006) and can make it difficult for adolescents to get comfortable enough to fall asleep (Stores 2001).

Buda et al. (2006) found that RLS is commonly under diagnosed in adolescents. Strongly associated with Attention Deficit Hyperactivity Disorder (ADHD), RLS affects 2% of adolescents (Picchietti et al. 2007). Restless Leg Syndrome manifests as ‘…creepy-crawly or tingling feeling, most commonly in the legs that can be alleviated temporarily with movement’ (Meltzer & Mindell 2006) and can make it difficult for adolescents to get comfortable enough to fall asleep (Stores 2001).

Adolescent sleep and mental health issues

Sleep disturbance in adolescents has been linked to a range of mental illnesses (AASM 2001, Roberts et al. 2001, Stores 2001, Meltzer & Mendell 2006). Roberts et al. (2001) surveyed 5423 North American middle school children to examine the association between suicidal ideation and sleep disturbance. They concluded that disturbed sleep in adolescents is associated with psychiatric, psychosocial and somatic disorders.

Anxiety and depression are both linked with sleep disturbance (Breslau et al. 1996, Signoretta et al. 2005, Cukrowicz et al. 2006). Insomnia is a significant predictor of depression and suffering nightly insomnia for two or more weeks may be an indicator of pending major depression (Breslau et al. 1996). Nightmares and disturbing dreams have been identified as predictive of depression and a significant predictor of suicidal ideation and suicide risk (Cukrowicz et al. 2006). Signoretta et al. (2005) in a retrospective study of 1010 students, found a link between specific temperaments, sleep disturbances and anxiety behaviours that may indicate a predisposition to major mental illnesses.

In a study of sleep disturbances in 61 medication-free patients with childhood-onset schizophrenia (COS), Mattai et al. 2006 noted that poor sleepers (average duration of sleep approximately four hours), showed significantly greater and more severe positive psychotic symptoms, such as hallucinations and delusions and negative symptoms, such as anergia and withdrawal. However, although there is a definite relationship between sleep and psychotic symptoms, it is difficult to determine which precedes the other. The importance of detecting the onset of sleep disturbance in adolescents with an existing psychiatric disorder has been recognised, as it is a sensitive indicator that relapse is occurring (Stores 2001, Mattai et al. 2006).

The consequences of disturbed sleep in adolescence

Daytime sleepiness

Sleepiness, which is defined as a propensity to fall asleep (Fallone et al. 2002), is one of the most common consequences of disturbed sleep in adolescence and is indicated as a factor in poor academic performance, depressed mood and behavioural problems (Carskadon & Acebo 2002, Owens 2006), use of psychoactive substances (Giannotti & Cortesi 2002), injury and adolescent motor vehicle accidents (Givan 2004, Grunstein & Grunstein 2001). Daytime sleepiness can be caused by lack of sleep, poor quality sleep or conditions that abnormally increase the need for sleep such as narcolepsy, drug use or some infections (Givan 2004). Mercer et al. (1998) found that 63% of a sample of American high school students (n = 612) felt they required more sleep on school nights to be able to complete schoolwork and avoid feeling sleepy in the daytime.

Reduced academic performance

Sleep disturbance in adolescents can impair academic performance by interfering with the consolidation of memory and the learning process that occurs during sleep (Curcio et al. 2006). Decreased SWS combined with other stage related delays and social impingements on sleep quality and total sleep time, have implications for an adolescent’s ability to store and process academic knowledge (Curcio et al. 2006). Poor academic results have been associated with higher daytime sleepiness, increased use of psychoactive substances, sleep disturbances, later bedtimes and lowered mood (Giannotti & Cortesi 2002). Similarly, Perez-Chada et al. (2007) found that daytime sleepiness, snoring and sleep apnoea are independent predictors of poor academic performance, with those adolescents who had apnoeic episodes
having the most severe effect on academic performance. A study of North American high school children ($n = 3120$) found that, while morning rise times remained constant across the age range (13–19 years), bedtimes were progressively later in older adolescents with 40% of those surveyed reporting going to bed after 11 pm on school nights (Wolfson & Carskadon 1998, 2003). Over a quarter of the sample reported sleeping < 6.5 hours on weekdays and there were average sleep lag times of 110 minutes. When comparing these results to academic performance, students who reported less sleep, irregular sleep or increased sleep lag, were more likely to be performing poorly (C grades or below). The authors hypothesise that better rested students are more able to concentrate on learning than those disabled by daytime tiredness. The authors caution however that the results should not be considered definitive as some students will succeed academically on limited sleep and that the results do not consider extraneous factors such as ‘coping strategies, family rules, class schedules and type of academic work’ (Wolfson & Carskadon 1998).

Buboltz et al. 2001 used a questionnaire to gather information regarding the sleep behaviours of 191 American college students. Similar to other research (such as Breslau et al. 1996), sleep disturbance was common, affecting more females than males. Buboltz et al. (2001) propose that educational institutions recognise that sleep disturbances in their students have the potential to pose significant problems that may be minimised with the implementation of education and appropriate interventions. Further to this, Buboltz et al. (2001) suggest that sleep difficulties may be exacerbated by inappropriate scheduling as well as living environments. Hansen et al. 2005 agree that early morning start times negatively impact on school performance and contribute to sleep deprivation among adolescents.

In a study that explored the effects of sleep deprivation on psychological variables related to college students’ cognitive performance, Pilcher & Walters 1997 found that participants who were sleep deprived performed significantly worse than those who had approximately eight hours sleep. However, those that were sleep deprived rated their performance, ability to concentrate and effort as significantly greater than those who had slept did, indicating the lack of awareness regarding the negative impact that sleep deprivation can have on ability to perform cognitive tasks (Pilcher & Walters 1997).

Substance use
The literature suggests that disturbed sleep in adolescents can contribute to daytime tiredness and increased use of psychoactive substances (Bootzin & Stevens 2005). Adolescents experiencing sleep disturbance may self medicate with substances either to increase alertness or facilitate going to sleep. Vice versa, those adolescents who abuse substances may develop sleep disturbance as some substances like alcohol, while correcting short-term insomnia, contribute to daytime tiredness (Bootzin & Stevens 2005).

A nation-wide survey of Finnish adolescents ($n = 4000$) found that 30% of the older adolescents reported feeling tired almost every day (Tynjala et al. 1997). Correlations were drawn between daytime sleepiness, sleep disruption and substance abuse in 26% of 15-year-old males and 12% of 15-year-old females. The male students in this group were more likely than the females to abuse alcohol, to stay up late and have disrupted sleep, while the girls were more likely to exhibit somatic illness and had a predilection for tobacco use (Tynjala et al. 1997). Higher levels of tobacco use in adolescent females has also been associated with depressive disorders (Coelho et al. 2002). In the Finnish study, coffee consumption was not excessive among either sex (Tynjala et al. 1997). Contrary to this, the National Sleep Foundation Sleep and Teens Task Force 2000 found that 75% of American adolescents polled, used drinks containing caffeine to stay alert.

Bootzin and Stevens (2005) reviewed literature pertaining to substance abuse and mental health issues. Further, they examined the relationship between substance abuse and sleep disturbance in 55 adolescents with histories of substance abuse and who complained of sleep disturbances. Interventions that were designed to improve both substance abuse and sleep disturbance in adolescents were both described and evaluated. Interventions consisted of a six-session multi-component small group treatment, which included a mixture of cognitive and physical therapies as well as education. Those who completed treatment noted substantial improvement in sleep time and sleep quality (Bootzin & Stevens 2005).

Nursing and adolescent sleep disturbance
Most of the literature on adolescent sleep is drawn from medicine with nursing having scant literature in the area. However, Mindell and Owens (2003) recognised that despite the prevalence of sleep disturbance in the paediatric patient population, it was an undertreated area of paediatric health and so surveyed 317 paediatric nurses to ascertain their practises in relation to screening for sleep in children. Nurses surveyed cited time constraints and competing priorities as the reason sleep disturbance were under diagnosed. Screening for sleep disturbance declined in line with the child’s age with just 35.3% of the sample responding that they were ‘very
likely to screen patients over the age of 13 (Mindell & Owens 2003). Despite the most common adolescent sleep disorder being circadian or phase delay related (Vignau et al. 1997) only 2·1% of those surveyed by Mindell and Owens (2003, p. 327) were likely to screen for a circadian disorder and only 4·3% of the sample was ‘very confident’ in their ability to deal with the problem. Other results indicated that the majority of respondents had received no formal training in dealing with paediatric sleep disorders (Mindell & Owens 2003).

Although the nursing literature highlights the importance for nurses to have knowledge of sleep, because of their position as primary caregivers to those whose sleep is disturbed (Cohen et al. 1992) education of healthcare professionals and nurses in particular neglects sleep and sleep disturbance (Cohen et al. 1992, Stores 2001). Cohen et al. 1992 found that most undergraduate nursing courses had one hour or less of sleep related content and there is no evidence that this has increased in the intervening years. Stores (2001) attributes the neglect of addressing sleep disturbance to the fact that sleep crosses the boundaries of many disciplines, yet is claimed by none. Furthermore, as curricula are constrained by time and money and have to include an understanding of rapidly increasing technology, sleep remains an area considered familiar and less important than other health issues (Stores 2001).

Relevance to clinical practice

There is abundant evidence that sleep disturbance in adolescence can be indicative of a range of physical, mental and behavioural problems and may be both a cause and effect of a variety of disorders (Signoretta et al. 2005, Carotenuto et al. 2006, Mattai et al. 2006). However, despite the plethora of evidence as to the significance of sleep and sleep disturbance, there is little to suggest that nurses conduct routine sleep assessment with adolescent patients/clients (Mindell & Owens 2003). This lack of routine assessment, coupled with the difficulty discerning sleeping difficulties from normal adolescent behaviour that is highlighted in the literature (Meltzer & Mindell 2006) makes prevalence difficult to estimate. While some sleep disorders would have a higher prevalence than others in adolescents, nurses need an awareness of the range of disorders to provide optimal care. However, findings by Cohen et al. (1992) suggested that sleep is generally overlooked in nursing curricula and more recent findings suggest that this oversight transfers into the practice arena (Mindell & Owens 2003).

Clearly, as sleep is so important for adolescent health, nurses should be alert to the importance of sleep when obtaining health history from adolescent patients/clients and their family members. Accurate and detailed information about sleeping patterns should be gathered, as should any sleep related difficulty, such as nightmares, sleep walking and talking, difficulty settling to sleep or night waking. Kotagal and Pianosi (2006) suggest that assessment should consider the sleep hygiene factors, such as the significance of night-sleep and inappropriate arousal at bedtime. In the event of disturbances in sleep pattern and sufficiency being identified, primary central nervous system disorders, breathing disturbances, substance use and psychiatric symptomatology need to be ruled out (Kotagal & Pianosi 2006, p. 332).

The onset of mental illness such as depression is common in adolescence (Patton et al. 2000) and sleep disturbance may be the first indicator of more serious underlying problems. Therefore, assessment of sleep that uncovers problems should be followed by a mental health assessment with a focus on early symptoms of psychosis and depression. In addition, should such difficulties be identified, it is useful to explore other activities of daily living such as leisure activities or other factors that could be affecting sleep. There is a need for knowledge of the processes for assessing the quality and quantity of sleep, a range of interventions that may assist in improving sleep in adolescents and skills in identifying when judicious referral needs to be made in relation to sleep problems.

Several questionnaires and sleep assessment tools have been designed for research and clinical application (Chervin et al. 2000, Spilsbury et al. 2007). Many assessment tools are designed for adults or for infant and child sleep disturbance, rather than adolescents and some are useful for extensive assessment (such as the ‘BEARS’) after initial identification of a sleep disturbance is made (Owens & Dalzell 2005). The ‘BEARS’ assessment includes domains of Bedtime problems, Excessive Sleepiness, Awakenings, Regularity of Sleep and Sleep-disordered breathing (Owens & Dalzell 2005). Lee and Ward (2005) suggest several domains that should be covered in an initial assessment: use of medications or substances for sleep; time of bedtime and wakening; awakening during night (identify causes including snoring) and daytime sleepiness. The maintenance of a sleep log over several weeks that identifies sleep times, use of caffeine, activities such as exercise and television watching, daytime snoozing or napping and use of medications may be useful to raise awareness of sleep activity.

Rest and sleep are positioned among the key activities of daily living that concern nurses and so we need to develop a robust research base to inform our knowledge and practices in the area of sleep. Specifically, there is a need to develop and
implement age appropriate brief sleep screening processes, as part of a general health assessment, with more detailed assessment being initiated if problems are identified. Furthermore, nursing interventions for sleep problems and disorders need to be investigated. There is a need to explore a range of non-pharmaceutical interventions to enhance sleep in young people experiencing disturbed sleep. Non-pharmaceutical interventions can be used alone or to augment the efficacy of medication where pharmaceutical intervention for adolescent sleep disturbance is warranted.

The need for early recognition of sleep disturbance is particularly strong for adolescents, who are vulnerable to the development of mental health difficulties and may attempt to self medicate for sleep disturbance through the use of recreational and illicit substances. Nurses have a role in patient education and are ideally placed to be able to educate both adolescents and parents about the importance of sleep, the significance and implications of sleep disturbance and interventions that may assist sleep. Such information can be delivered to patients/clients and their families via printed leaflets, web-based media or in face-to-face consultation settings.

Conclusion

This review of the literature reveals that sleep disturbance in adolescence can potentially act as a sensitive indicator of psychosocial, psychological or physical difficulties and yet, it is an important area of adolescent health almost entirely unaddressed by nursing. Nursing has a role to play in assisting adolescents and their families to recognise the importance of sleep to the general health and well-being of young people.

Contributions

Study design: TV, KP, DJ, LOB; data collection and analysis: TV, KP, DJ, LOB and manuscript preparation: TV, KP, DJ, LOB.

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