The bidirectionality of the relationship between insomnia, anxiety and depression in adolescents: A longitudinal study

Pasquale K Alvaro
Bachelor of Psychology (Hons)

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School of Psychology
Faculty of Health Sciences
University of Adelaide

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Declaration

I hereby declare this submission is my own work and that, to the best of my knowledge and belief, it contains no material that has been accepted for the award of any other degree or diploma of a university or other institute of higher learning, except where due acknowledgement is made in the body of the text. All work contained in the submission was initiated, undertaken, and prepared within the period of candidature. In addition, I certify that no part of this work will, in the future, be used in a submission in my name for any other degree or diploma in any university of other tertiary institutions without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint award of this degree. I give consent to this copy of my thesis when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968. The author acknowledges that copyright of published works contained within this thesis (as listed below) resides with the copyright holder(s) of those works.


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X

Pasquale Alvaro
PhD Candidate
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Abstract

Bidirectionality refers to whether variable $x$ predicts and/or is predicted by variable $y$. This thesis identified and accounted for gaps within the literature on the bidirectionality of the relationship between insomnia, depression, and anxiety during adolescence. Namely, bidirectionality was assessed across different subtypes of anxiety, using continuous variables. The independent effect of chronotype on the bidirectionality of the relationship between insomnia and depression, and insomnia and subtypes of anxiety were also considered.

Study one systematically reviewed the literature of the bidirectional associations between sleep disturbances, anxiety and depression across all age groups. In total, the systematic review contained nine independent studies. Best available evidence indicates that insomnia is bidirectionally related to anxiety and depression. The limited data available suggests that bidirectionality may extend beyond insomnia to other sleep disturbances, although additional research is needed to further clarify this notion.

Study two assessed the cross-sectional independent relationships between insomnia and depression, and insomnia and various subtypes of anxiety during adolescence. The predictive effect of chronotype on insomnia, depression, and subtypes of anxiety was also assessed. Baseline data from 318 South Australian high school students in grades 7 to 11 (age range 12-18, mean 14.96 ± 1.34) were collected. Insomnia, depression, subtypes of anxiety and chronotype were assessed by validated self-report questionnaires. Insomnia predicted depression and panic disorder (PD) after controlling for confounders, although the latter was not considered clinically significant. Depression and generalised anxiety disorder
(GAD) predicted insomnia after confounders were controlled. Insomnia was not significantly associated with other subtypes of anxiety once depression was controlled. Eveningness uniquely predicted insomnia and depression, but was not associated with any anxiety subtype.

Study three investigated the bidirectionality of the relationship between insomnia and various subtypes of anxiety, and insomnia and depression; and the independent predictive effects of chronotype on insomnia, depression, and each subtype of anxiety during adolescence. The study was longitudinal, with a 6-month follow-up. Two-hundred and fifty-five high school students completed self-report questionnaires at baseline and follow-up. Once depression was controlled, insomnia predicted depression and GAD after controlling for other variables, and vice-versa, but was not related to other anxiety subtypes in either direction. An evening chronotype predicted insomnia once other variables were controlled, but did not predict depression or subtypes of anxiety once insomnia was controlled.

Together, the results suggest that insomnia is bidirectionally related to depression and GAD, and related to other subtypes of anxiety through a common factor, depression. Furthermore, chronotype predicts the development of insomnia, and is related to depression and anxiety subtypes through the common factor of insomnia. Chronotype, then, may be a risk-factor for the development of insomnia, which may subsequently contribute to depression or GAD, which in turn may create a vulnerability to other anxiety disorders. Ultimately, these findings may significantly enhance prevention and treatment. Chronotype, depression and GAD should be considered while implementing insomnia interventions, insomnia may be important to address in the treatment of depression and GAD, and
depression should be assessed and considered for all sleep and anxiety disorder presentations.
Chapter 1: Introduction

1.1. Brief overview of thesis and chapter

This thesis is focussed on the bidirectionality of the relationship between insomnia and depression, and insomnia and different subtypes of anxiety during adolescence, as well as the effects of chronotype on these relationships. Although this thesis concerns adolescents, discussions about literature based on adult samples are included when there was insufficient evidence in the adolescent literature. Chapter 1 introduces key concepts, such as adolescence, sleep, adolescent sleep, insomnia, depression, and anxiety. Chapter 1 then discusses the existing literature on the relationship between insomnia, depression and anxiety during adolescence, including the bidirectionality of these relationships. Methodological problems and the significance of chronotype to this topic are then discussed, followed by the aims, significance and contribution of this thesis. Chapter 1 is a precursor to studies 1, 2 and 3. Therefore, an attempt was made to avoid as much overlap between chapter 1 and the introductions of the studies as possible. The author sincerely apologises in advance where overlap is present.

1.2. Adolescence

Adolescence refers to an age range from 12 to 18, and is characterised by physical and sexual maturation (Malina & Bouchard, 1991); psychosocial (Blakemore, 2008), emotional (Larson, Moneta, Richards, & Wilson, 2002), and behavioural (Spear, 2000) change; and substantial development in brain structures and functional organisation (Casey, Jones, & Hare, 2008; Ernst, Pine, & Hardin, 2006; Paus, Keshavan, & Giedd, 2008). Such changes, both individually and when interacting, have been found to increase the vulnerability to mental
health disorders following puberty. For example, Brand and Kirov (2011) note that various psychological functions such as emotional processing and executive control undertake considerable and rapid change during adolescence, and these changes have been associated with maladaptive decision making and actions; significant distress; and increased incidence of unintentional injuries, homicide, suicide attempts, and substance abuse. Furthermore, Teunissen and colleagues’ (2011) well-designed longitudinal study found that an interaction between early pubertal development and low levels of popularity (rather than the former alone) predicted future depressive symptoms. Unsurprisingly, then, a rapid increase of prevalence rates in mental health disorders from childhood to adolescence has been widely reported (Green, 2005; Kessler, Avenevoli, & Merikangas, 2001; Saluja et al., 2004), and the median of lifetime risk for first onset of mental health disorders is age 14 (Kessler et al., 2005). Together, the evidence portrays a clear picture that adolescence is a vulnerable period for the development of mental health disorders, although prospective and longitudinal research identifying the age of initial onset would further strengthen this argument.

The physical, neuronal, psychological and behavioural markers of adolescence are associated with changes to the sleep-wake cycle, sleep timing, sleep duration, and sleep architecture (Brand & Kirov, 2011; Crabtree & Williams, 2009; Laberge et al., 2001; O'Brien & Mindell, 2005; Roffwarg, Muzio, & Dement, 1966; Tarokh & Carskadon, 2010). Such changes may lead to sleep patterns that eventually resemble those observed in adults, and result from the maturation of sleep regulatory mechanisms within the brain during adolescence; synaptic reorganisation typical of adolescence (Roffwarg, et al., 1966; Tarokh & Carskadon, 2010; Taylor, Jenni, Acebo, & Carskadon, 2005); and/or the adaptation of the sleep-wake cycle.
cycle to increased social, academic, familial or environmental pressures (Kaneita et al., 2009; Laberge, et al., 2001; O’Brien & Mindell, 2005; Petersen & Leffert, 1995; Peterson, 2004). Adolescence is therefore an extremely vulnerable period for the development of sleep disturbances and mental disorders (Graber, Brook-Gunn, & Petersen, 1996; Kessler, et al., 2005). This thesis, then, focuses specifically on adolescents.

1.3. Sleep

Sleep is a reversible, recurring and active state of reduced consciousness that consolidates learning and memory, and promotes growth, repair and restorative processes throughout the brain and body (Benington, 2000; Diekelmann & Born, 2010; Krueger & Obal Jr, 2003; Peigneux, Laureys, Delbeuck, & Maquet, 2001; J. M. Siegel, 2009; Tononi & Cirelli, 2006). Normal sleep contains two distinct phases, non-rapid eye movement (NREM) and rapid eye movement (REM). NREM sleep can be divided into three stages, NREM stage 1 – 3 (Kryger, Roth, & Dement, 2005).

Sleep usually begins with a brief period of stage 1 NREM sleep, where alpha waves that are present during wakefulness fade (Colten & Altevogt, 2006). Stage 2 NREM sleep then follows (Colten & Altevogt, 2006), which is characterised by sleep spindles (spurts of rhythmic activity that last for 1-2 seconds) and k-complexes (short negative high-voltage complex, followed by slower positive peaks of rhythmic activity and a final negative complex) (Rechtschaffen & Kales, 1968). Sleep then progresses into stage 3 NREM (formerly classified as stages 3 and 4), where deeper phases or slow-wave-sleep (SWS) occurs, blood pressure and body temperature decline and electroencephalograms (EEGs) commonly display slow, high-voltage delta waves (Colten & Altevogt, 2006). SWS is typically proceeded by a short period of stage 2 NREM sleep, after which a short phase of REM occurs (Brand &
Kirov, 2011). REM sleep is characterised by the sudden movement of eyes under closed eyelids (Colten & Altevogt, 2006), EEG activation akin to that seen during wakefulness, muscle atonia (inhibition) and irregular heart rate and respiration (Aserinsky & Kleitman, 1953; Kryger, et al., 2005; Rechtschaffen & Kales, 1968).

The above process is equivalent to one sleep cycle, and usually takes approximately 90 minutes to complete (Brand & Kirov, 2011). Five or more sleep cycles typically occur during normal human sleep, depending on sleep need (Rechtschaffen & Kales, 1968; Sinton & McCarley, 2000). The first half of the night contains an increased proportion of SWS, whereas the second half predominately contains REM and stage 2 NREM sleep (Brand & Kirov, 2011).

The NREM and REM stages describe the physiological mechanisms that underlie sleep, but ignore the processes that regulate sleep and wakefulness. The following subsection describes a model of sleep regulation, then discusses how this model can explain the initiation, maintenance and termination of sleep, along with the maintenance of wakefulness.

1.3.1. Sleep regulation: a two-process model

Sleep is believed to be regulated via an interaction of two independent processes; process S and process C (Achermann & Borbény, 1994). Process S, the homeostatic regulation of sleep, represents the propensity of an individual to fall asleep. Although its neurobiology is unclear (Carskadon, Acebo, & Jenni, 2004), process S is known to accumulate during wakefulness and diminish during sleep (Borbény, 1982). Accordingly, the propensity for sleep is determined by the amount of prior wakefulness and sleep (Carskadon, et al., 2004).
Therefore, the peak of homeostatic sleep propensity occurs just before sleep onset, and the nadir at sleep termination following adequate sleep.

Process C is the circadian timing system of sleep propensity (Carskadon, 2011) that changes over the course of 24 hours (Tononi & Cirelli, 2006). The circadian sleep propensity is regulated by the suprachiasmatic nucleus (SCN) (Klein, Moore, & Reppert, 1991), and is hence independent from prior waking and sleep (Dijk & Czeisler, 1995). The SCN neuronal firing rate decreases in late day/early evening, stimulating sympathetic activity and resulting in the production of melatonin by the pineal gland (Moore, 2007). Melatonin chemically induces drowsiness and heat loss (Kräuchi, Cajochen, Pache, Flammer, & Wirz-Justice, 2006), lowers core body temperature (Cagnacci, Kräuchi, Wirz-Justice, & Volpe, 1997), further inhibits the firing of SCN neurons, and in turn promotes sleep propensity and reduces the circadian drive for arousal (Moore, 2007). Melatonin production, along with sleep propensity, rises until it peaks at approximately 2am to 4am (Brzezinski, 1997; Dijk & Czeisler, 1995). Melatonin levels and sleep propensity then drop rapidly during the waking day, which is likely to be at least partially due to the inhibiting effects of bright light on the production of melatonin (Brainard et al., 2001). Therefore, the nadir of melatonin production and circadian sleep propensity occurs in the late afternoon/early evening, rendering sleep during this period unlikely (Dijk & Czeisler, 1995).

Homeostatic and circadian processes seem to function as corresponding systems to promote sleep initiation and termination. The sleep systems simultaneously contribute to increased likelihood of sleep nearing the typical bedtime, and promote termination of sleep nearing the typical rise time. In contrast, the homeostatic and circadian processes function as opposing systems to maintain sleep and wakefulness. The decline in homeostatic sleep
propensity coincides with an increase in circadian sleep propensity during the night to maintain sleep, whereas the rising homeostatic propensity for sleep throughout the waking day coincides with the decline of circadian sleep propensity to maintain wakefulness (Carskadon, et al., 2004).

1.4. Adolescent sleep

Adolescent sleep is characterised by declines in the amplitude and proportion of Delta waves and a decrease in NREM sleep from childhood (Baker, Turlington, & Colrain, 2012; Tarokh & Carskadon, 2010). In particular, SWS decreases by 40% during adolescence. This finding may reflect a loss of cortical synaptic density that occurs with age (Feinberg, 1983). REM sleep occupies approximately 20 to 25% of adolescent sleep (Carskadon & Dement, 2011). Ultimately, the adolescent sleep architecture closely resembles that described in section 1.3.

A delayed sleep phase is also a feature of adolescent sleep (Giannotti, Cortesi, Sebastiani, & Ottaviano, 2002). Adolescents become more evening-orientated with age due to circadian rhythm and environmental changes (Crowley, Acebo, & Carskadon, 2007), suggesting that older adolescents prefer later bed and rise times. The delayed sleep phase is more apparent on non-school nights (weekends and vacations) than school nights (Carskadon, 1990; Giannotti, et al., 2002; Wolfson & Carskadon, 1998) (see Carskadon, Acebo & Jenni, 2004, for a review), although evidence suggests that adolescents often prefer later bedtimes even on school nights (Carskadon, Wolfson, Acebo, Tzischinsky, & Seifer, 1998). These findings, paired with the enforced early starts for school, often result in sleep deprivation during the week, and therefore highlight the importance of effective sleep management strategies in adolescents.
1.5. Insomnia

Insomnia refers to sleeplessness that results from troubles with sleep initiation (falling asleep), sleep maintenance (remaining asleep without enduring nocturnal awakenings), sleep duration (awaking early in the morning), and/or non-restorative sleep (waking up feeling unrefreshed despite adequate sleep opportunity) (Johnson, 2006; Poceta & Mitler, 1998). According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013), insomnia symptoms meet the criteria for insomnia disorder when the aetiology of sleeplessness is not attributable to other disorders, presents independently from other causal factors for at least three nights a week for three months despite adequate opportunity for sleep, and causes impairment in social, occupational, educational, academic, behavioural or other important areas of functioning. Insomnia symptoms and disorders have historically been referred to as secondary insomnia when the aetiology of sleeplessness is attributable to other disorders or causal factors (Lipton, Becker, & Kothare, 2008). Accordingly, insomnia disorder and secondary insomnia have different risk-factors. The following section describes the risk-factors that are related to insomnia disorder and secondary insomnia. Note that insomnia disorder was labelled ‘primary insomnia’ in the previous DSM (American Psychiatric Association, 2000), and therefore was used extensively in previous literature. The following section will retain the original terminology when used in the studies presented, and hence will use ‘primary insomnia’ and ‘insomnia disorder’ interchangeably.

1.5.1. Risk-factors for insomnia disorder and secondary insomnia

The risk-factors for insomnia disorder are best categorised as biological factors, physiological traits, and psychosocial stressors. Regarding biological risk-factors, work from
Gehrman et al. (2011), Gregory, Rijsdijk, Lau, Dahl, and Eley (2009), and Barclay, Gregory, Eaves, and Silberg (In Press) suggest that insomnia is at least moderately heritable. In particular, Barclay and colleagues’ (In Press) longitudinal twin study reported that genetic vulnerability at age 8 significantly predicted the development of clinically significant insomnia disorder at ages 10, 14 and 15. Furthermore, Gregory and colleagues’ (2009) longitudinal study reported a genetic predisposition for chronic paediatric sleep problems. Together, these studies suggest that genetic factors may contribute to the development and maintenance of insomnia disorder and other sleep problems. However, as noted by Ohayon (2002) and Roberts, Roberts, and Chan (2008), the genetics of primary insomnia and other sleep disorders are still largely unknown, and, as Tafti, Maret, and Dauvilliers (2005) stated, genetic factors of primary insomnia are highly likely to be complex. Future research could aim to identify the genes that interact with environmental factors and in turn contribute to the development of insomnia disorder.

Regarding the physiological risk-factors, trait hyperarousal and hyperactivity have been associated with the development of insomnia across various studies. Riemann et al. (2010) reviewed a wide range of autonomic, neuroendocrine, neuroimmunological, neuroimaging, and electrophysiological studies that demonstrate increased day and night time arousal in those with primary insomnia. In addition, Bonnet and Arand’s (2010) extensive literature review demonstrated a large amount of research depicting elevated whole body and brain metabolic activation, and increased heart rate and sympathetic nervous system activation during sleep in patients with primary insomnia. Indeed, both Riemann, et al. (2010) and Bonnet and Arand (2010) argue that the evidence strongly suggests high physiological arousal and activity levels across the 24-hour sleep cycle can predispose individuals to the
development of primary insomnia, which seems accurate given their rigorous and systematic review of the literature.

Interestingly, Riemann, et al. (2010) state that primary insomnia is likely to result from an interaction between predisposing factors such as genetic and physiological traits, and psychosocial/medical stressors. This theory, labelled the stress-diathesis model of insomnia (Spielman, Caruso, & Glovinsky, 1987), is widely endorsed (Bonnet & Arand, 2003; Perlis, Giles, Mendelson, Bootzin, & Wyatt, 1997), and argues that along with genetics and trait hyperactivity and hyperarousal, psychological predisposing factors such as a tendency for stress, worry or rumination may interact with precipitating factors such as psychosocial stressors (i.e., negative life events), and in turn trigger acute episodes of primary insomnia symptoms and eventually lead to chronic primary insomnia. Most recently, a longitudinal study of over 2,300 adults demonstrated that premorbid trait sleep reactivity interacts with stressful life events and stress-induced cognitive intrusion to further increase the risk of developing insomnia disorder two years later (Drake, Pillai, & Roth, 2014). The authors suggest that trait sleep reactivity interacts with stressful life events and stress-induced cognitive intrusion to trigger the development of insomnia (Drake, et al., 2014). This statement seems probable given the amount of endorsement the stress-diathesis model for primary insomnia has received from respected scholars (Bonnet & Arand, 2003; Perlis, et al., 1997; Riemann, et al., 2010; Spielman, et al., 1987), but empirical evidence is limited, and therefore definitive conclusions cannot be made.

Perhaps the most common theory of the development of chronic primary insomnia from acute symptoms stems from the International Classification of Sleep Disorders’ [Second Edition (ICSD-2)] notion of psychophysiological insomnia (American Academy of Sleep
Acute episodes of primary insomnia are theorised to become sub-chronic when reinforced by maladaptive coping strategies, such as excessive time spent in bed, and remaining awake while in bed (Perlis, et al., 1997; Spielman, et al., 1987). Both maladaptive strategies may reinforce one another: individuals with insomnia often retire before sleepy to increase the opportunity for sleep, yet remain awake while in bed (Perlis, et al., 1997; Spielman, et al., 1987); and wakefulness in bed often leads to increased time in bed to increase sleep opportunity (Spielman, et al., 1987). The consequence is wakefulness in bed for an excessive period of time, and in turn an experience of physiological, cognitive and somatic arousal (e.g., excessive worry and rumination about sleeplessness, and physiologically hyperarousal before sleep onset). Sub-chronic insomnia is thought to become chronic when physiological, cognitive and somatic arousal are conditioned to the sleep environment (Bonnet & Arand, 2010; Perlis, et al., 1997) rather than pre-sleep de-arousal that is seen in good sleepers (Robertson, Broomfield, & Espie, 2007), hence, obstructing the sleep onset process. However, psychophysiological insomnia has been removed from the newest edition of the International Classification of Sleep Disorders (ICSD-3) diagnostic manual, because it was not considered to be reliably reproducible in clinical practice (American Academy of Sleep Medicine, 2014). Nevertheless, the mechanisms of psychophysiological insomnia have been supported in the literature (Bastien, St-Jean, Morin, Turcotte, & Carrier, 2008; Broman & Hetta, 1994; Perlis, et al., 1997; Robertson, et al., 2007), and therefore may still have important implications for theories of primary insomnia.

Early explanations for insomnia considered it primarily as a symptom or consequence of other disorders, particularly depression (Morin & Benca, 2012), but such a distinction is now thought to oversimplify the notion of insomnia. The term secondary insomnia, then,
was adopted to differentiate primary insomnia from sleeplessness that is attributed to risk-factors, such as social factors, other sleep disorders, medication, medical conditions (e.g., asthma), neurological disorders, psychiatric disorders and substance abuse (Lipton, et al., 2008). Research is moving towards an understanding of the possible development of primary insomnia processes even in the presence of contributing or triggering comorbidities (Jansson-Fröjmark & Lindblom, 2008). Secondary insomnia, therefore, is now often referred to as comorbid insomnia.

1.5.2. Epidemiology of insomnia

Insomnia is the most common sleep problem reported by or diagnosed within the general population (Bixler, Kales, Soldatos, Kales, & Healy, 1979). However, prevalence rates in adolescents have ranged widely, from 2 to 38% (Abdel-Khalek, 2004; Johnson & Breslau, 2001; Roberts, Ramsay Roberts, & Ger Chen, 2002), which likely results from the differing methodologies, definitions, symptom severity, and symptom duration of insomnia used across studies (Johnson, 2006). However, there is also a wide range of frequencies reported within studies. For example, the prevalence of any insomnia symptom during adolescence using a 30 day period without a severity criteria is approximately 30% (range from 23 to 40%), and 11% (range from 7.2 to 40%) for those using a severity criteria (Johnson, 2006). Furthermore, the only four studies that have used diagnostic criteria in adolescents report rates of 4% (Ohayon, Roberts, Zulley, Smirne, & Priest, 2000), 2% (Ohayon & Roberts, 2001) 10.9% (Dohnt, Gradisar, & Short, 2012) and 11% (Johnson, Roth, Schultz, & Breslau, 2006). Therefore, regardless of the criteria used to identify insomnia, an accurate single estimate of prevalence rates seems difficult to achieve. Range estimates may provide a more reliable source of information.
In a review of over 50 epidemiological studies of children, adolescents and adults, Ohayon (2002) investigated the prevalence of insomnia according to the following four categories; (1) insomnia symptoms; (2) insomnia symptoms accompanied by daytime consequences; (3) dissatisfaction with sleep quantity or quality; and (4) insomnia diagnosed according to the DSM-IV or International Classification of Sleep Disorders (ICSD) criteria. The prevalence rates for insomnia symptoms alone ranged from 30 to 48%, compared to 12 to 16% when frequency criteria were added (e.g., at least 3 nights per week, or often/always). Prevalence rates ranged from 10 to 28% when a severity criterion was added (e.g., moderate to extreme levels of insomnia). The prevalence rates of insomnia symptoms accompanied with daytime consequences was approximately 10% and ranged from 9 to 15%. Eight to 18% of the general population were identified with insomnia based on dissatisfaction with sleep quality and quantity. Finally, the prevalence of insomnia based on the DSM-IV or ICSD criteria was approximately 6%, ranging from 4.4 to 6.4% (Ohayon, 2002). Collectively, the evidence above suggests that insomnia is highly prevalent, but the frequency rates vary greatly with definition and severity, and therefore can be difficult to estimate.

1.5.2.1. Epidemiology of insomnia and gender

Most studies have found higher rates of insomnia in females than males (L. Hale et al., 2009; Kirmil-Gray, Eagleston, Gibson, & Thoresen, 1984; Mellinger, Blater, & Uhlenhuth, 1985; Ohayon, 2002; Roth, 2005; Sivertsen, Krokstad, Øverland, & Mykletun, 2009; Yang, Zuo, & Eaton, 1987). Ohayon (2002) demonstrated that the gender effect remains irrespective of the severity and definitions (e.g., symptoms to disorder continuum) that are used to assess insomnia, with a female/male ratio for insomnia symptoms of approximately 1.4:1 and a ratio for insomnia diagnosis of 2:1. Furthermore, Manni and colleagues (1997)
found a significant association between chronic poor sleep (symptoms of insomnia) and the female gender. A recent meta-analysis found a female:male risk ratio of 1.41 (95% confidence interval: 1.28-1.55), which progressively increased across age (Zhang & Wing, 2006).

Evidence suggests the gender effect may partially result from biological factors. Johnson, Roth, Schultz and colleagues (2006) reported a 2.75-fold increased risk for females of insomnia diagnosed by the DSM-IV criteria following onset of menses in adolescents, but no association between insomnia and maturational development in boys. The retrospective nature of the variables that were used for the analyses of these findings provide a good platform to suggest that a biological aspect of the gender effect may be the onset of puberty, but prospective and longitudinal studies are necessary to provide more definitive conclusions.

Alternatively, but not necessarily independently, Stattin and Magnusson (1990) argued that increased social pressures following the onset of puberty are more prevalent for girls than boys, and hence may contribute to the gender effect. However, this argument was made regarding the gender effect of depression in adolescents and thought potentially relevant to insomnia by Johnson and colleagues (2006), because few (if any) studies have been conducted in this area concerning insomnia (see section 1.6.2.1. for the discussion about depression and the gender effect in adolescents). Future studies should assess the different social pressures faced by prepubescent boys and girls and adolescent males and females, along with the association between each type of social pressure and insomnia.
1.5.2.2. Epidemiology of insomnia during adolescence and chronicity

Even after the onset of puberty, studies that assess the effects of age on the prevalence of insomnia have suggested that prevalence rates increase during adolescence. For example, Siomos et al. (2010) found that 8% of 14 year olds reported insomnia symptoms compared to 21.1% of 15 year olds, and Liu and colleagues (2002) reported a higher overall prevalence rate of insomnia for adolescents aged 18 (23.3%) than those aged 12 (10.2%). The increase in prevalence of insomnia across adolescence is likely to at least be partially attributable to the decreased amount of sleep that often occurs during adolescence (Liu & Zhou, 2002; Siomos, et al., 2010). Indeed, a recent meta-analysis of 41 adolescent studies reported a strong correlation between age and total sleep times worldwide ($r = -0.66$) (Gradisar, Gardner, & Dohnt, 2011).

Insomnia during adolescence is also likely to be of a chronic nature. Roberts, Roberts, and Duong (2008) found that 46% of adolescents who met the criteria for primary insomnia at baseline maintained their diagnostic status after one year. Moreover, Johnson, Roth, and Breslau (2006) reported that 88% of adolescents with a history of insomnia show ongoing chronic insomnia symptoms (i.e. not naturally remitting). Finally, two studies found that 50% of adolescents who report at least one symptom of insomnia at baseline report the same symptom(s) two and four year later (Morrison, McGee, & Stanton, 1992; Patten, Choi, Gillin, & Pierce, 2000). Therefore, it seems that disorders and even symptoms of insomnia during adolescence can persist for years after onset without intervention.

The evidence presented in this section suggests that insomnia symptoms and disorders frequently develop during adolescence, and are likely to persist across time. Efforts towards insomnia prevention and treatment may most effectively target adolescents, and prevent
future negative outcomes that are associated with insomnia. The following section discusses the concurrent and longitudinal associations of adolescent insomnia.

1.5.3. Concurrent and longitudinal associations with insomnia during adolescence

Studies have reported a relationship between insomnia and neurocognitive impairment. Fernández-Mendoza and colleagues (2009) reported that perceived concentration and memory was significantly poorer in adolescents and young adults with insomnia complaints than those without (24.2% vs 14.9% and 32.2% vs 22.9%, respectively). The same study reported a significant association between insomnia complaints, and poorer perceived concentration and memory after controlling for Delayed Sleep Phase Syndrome (DSPS), suggesting that insomnia symptoms are related to subjective concentration and memory beyond DSPS in adolescents and young adults (Fernández-Mendoza, et al., 2009). Insomnia has also been associated with adult objective memory performance in overnight sleep laboratory studies that used polysomnography to formally assess sleep, specifically declarative and procedural memory (Backhaus et al., 2006; Nissen et al., 2006). Finally, poor sleep and sleep deprivation, both of which have been related to insomnia (according to Johnson et al., 2006), are risk-factors for impaired declarative and procedural memory consolidation (Walker & Stickgold, 2004) during adolescence (Curcio, Ferrara, & De Gennaro, 2006), which Curcio and colleagues (2006) argues in a review of over 100 research articles (including experimental sleep manipulation studies) can affect learning. Therefore, although causal inferences cannot be made with certainty, the methodological rigour of the above studies allows for a strong suggestion that sleeplessness may directly impact neurocognitive performance. Indeed, Curcio et al., (2006) suggest that the neurocognitive dysfunction
associated with sleeplessness may be explained by the vulnerability of the prefrontal cortex to sleep loss.

Insomnia has also been related to compromised academic achievement. Paavonen et al. (2000) found an association between children who reported sleep complaints (mainly problems with sleep onset and night awakenings) and poorer academic grades as reported by teachers. Furthermore, a non-experimental study of Greek adolescents reported a significant association between academic performance and insomnia (multiple linear regression beta = -0.390) that was higher in females than males (Lazaratou, Dikeos, Anagnostopoulos, Sbokou, & Soldatos, 2005). Studies have also inferred an association between poorer academic achievement and other sleep problems [for a detailed review see Curcio et al., (2006)]. The association between insomnia and poorer academic achievement is likely to at least partially be explained by the fact that insomnia is considered a risk-factor for neurocognitive deficits, as discussed above.

Insomnia also precipitates various behavioural and psychological problems during adolescence. A recent longitudinal study found that adolescents with symptoms or diagnoses of chronic insomnia were more likely to report problems at home, school and with peers, poorer life satisfaction and perceived mental health, depressed mood, and alcohol/drug use at 12-month follow up than those without insomnia (Roberts, Roberts, & Duong, 2008). Similarly, a longitudinal study by Johnson and Breslau (2001) found that insomnia at baseline predicts the use of cigarettes, alcohol and any illicit drug after adjusting for age, gender, ethnicity, family income, and internalising (depression and anxiety) and externalising (deviance and aggression) problems. These findings suggest that insomnia predicts substance use independently from demographic factors and psychiatric problems.
Indeed, Bootzin and Stevens (2005) found that treatment leading to improved sleep also lead to a reduction of substance abuse problems in adolescents at 12-month follow-up, suggesting a potential causal factor between insomnia and substance abuse. Regarding other behavioural and psychological problems, Kirmil-Gray, et al. (1984) reported an association between poor sleep and depression, low energy levels, tenseness, mood alternations and irritability. Insomnia is also a risk-factor for conduct problems, delinquent and aggressive behaviour, anger, irritability, fearfulness, tenseness, social problems, risk-taking behaviour, withdrawal, emotional instability, and suicide attempts and ideation (Choquet, Kovess, & Poutignat, 1993; Gau, 2000; Liu & Zhou, 2002; Morrison, et al., 1992; O'Brien & Mindell, 2005; Tynjälä, Kannas, & Valimaa, 1993; Vignau et al., 1997; Wolfson & Carskadon, 1998).

Of all the associations with mental health problems, perhaps the strongest are between insomnia and depression, and insomnia and anxiety (Liu & Zhou, 2002). The following two sections discuss depression and anxiety in more detail.

### 1.6. Depression

A depressed mood is characterised by sadness, low mood, or reduced pleasure in previously enjoyable activities; with or without feelings of guilt, hopelessness, low self-esteem or low self-regard (Parker, 1979). It is considered as pathological when symptoms are sustained and cause clinically significant distress or impaired functioning in social, academic, occupational or other important areas of life (American Psychiatric Association, 2013). Depressive symptoms may be attributable to a major depressive episode/disorder when a depressive or irritable mood, or loss of interest is experienced most days for at least two weeks and accompanied by at least four additional symptoms. Such symptoms include:
significant changes in appetite or weight (a change of more than 5% of body weight in a month), sleep (insomnia or hypersomnia), or psychomotor activity; fatigue or decreased energy most days; feelings of worthlessness or excessive, inappropriate guilt most days; difficulty thinking, concentrating, or making decisions; and recurrent thoughts of death, suicidal ideation, plans, or attempts (American Psychiatric Association, 2013).

According to the diathesis-stress model, depression develops as a consequence of an interaction between stressful life events, such as child neglect or the death of a loved one, and various risk-factors (Monroe & Simons, 1991). An increased amount of risk-factors reduces the stressors required to trigger the onset of depression, and vice-versa. Consequently, the degree of predisposition for the development of depression varies according to the amount of risk-factors and stressors. The following section describes neurological, biological and psychosocial risk-factors of adolescent depression, and makes references to studies that assess the interaction between risk-factors and stressful/traumatic life events.

1.6.1. Risk-factors for depression

Various neurological and biological factors have been associated with the development of depression during adolescence. M. J. Owens and Nemeroff (1998) proposed a chemical imbalance of neurotransmitters such as dopamine, and serotonin as a risk-factor for adolescent depression, a theory that has been both supported and contradicted across adolescent and adult studies (Angold & Costello, 2006; Dunlop & Nemeroff, 2007; Eley et al., 2004; Risch et al., 2009). Furthermore, abnormal brain structures may also serve as risk-factors for the development of depression during adolescence as suggested by well-designed and widely cited research. Studies have reported increased pituitary gland and frontal grey
matter volume, decreased brain and frontal white matter volumes, and a significant trend towards increased cerebrospinal fluid in adolescents with major depressive disorder relative to healthy controls (MacMaster & Kusumakar, 2004; Steingard et al., 2002). A recent meta-analysis reported the same abnormalities in adult brains, along with lateral ventricle enlargement, increased cerebrospinal fluid volume and decreased volumes of the hippocampus, frontal lobe and basal ganglia in patients with depression relative to health controls (Kempton et al., 2011). Depression is also proposed to be at least partially heritable, as Thapar and Rice (2006) reported in a comprehensive review a 30 to 50% genetic risk for the development of depression during adolescence.

Various psychosocial factors have also been associated with the development of depression during adolescence, including low socio-economic status (Goodman, Huang, Wade, & Kahn, 2003), childhood poverty, high maternal anxiety and depression, distressed parental relationships, divorce/separation (Spence, Najman, Bor, O'Callaghan, & Williams, 2002), and negative inferential styles (Alloy et al., 2006). Poorer coping styles, less social support, and ongoing stressful life events have been proposed as some underlying risk-factors for depression in those with lower socio-economic status (Turner & Lloyd, 1999). Furthermore, a recent study found that childhood maladaptive schemas is related to depression during early, middle and late adolescence, but only reported an interaction with stressful life events in older adolescents (Braet, Vlierberghe, Vandevivere, Theuwis, & Bosmans, 2013). Braet, et al.’s finding suggests that the diathesis-stress model in its current state may be insufficient to explain all aspects of the development of adolescent depression, although replications of such findings is necessary for more definitive conclusions.
Interestingly, stressful life events that are related to the onset of adolescent depression may differ across age. Braet, et al. (2013) found that stress induced by paternal and particularly maternal rejection strongly predicts depressive symptoms in younger adolescents, weakly during middle adolescence, and not at all in older adolescence, whereas peer rejection becomes a more important predictor with age. Furthermore, studies have shown that stressful life events more strongly predict initial onset rather than relapse of depression in adolescents, whereas dysphoric mood and dysfunctional thinking are stronger predictors of the onset of recurrent rather than initial depressive episodes (Daley, Hammen, & Rao, 2000; Lewinsohn, Allen, Seeley, & Gotlib, 1999; Post, 1992). Lewinsohn, et al. (1999) proposed that the more depressive episodes experienced by an adolescent, the more the episode becomes independent of the stressful event, and hence the less a psychosocial stressor is required for the reoccurrence of an episode. Indeed, studies have provided support for this theory (Ma & Teasdale, 2004), although additional evidence is required for further consolidation.

Thapar, Collishaw, Pine, and Thapar (2012) argued that an interaction between genetic factors and psychosocial events can increase the risk of depression during adolescence. Indeed, Caspi et al. (2003) reported findings that suggested people with the S allele gene are more likely to suffer from depression if (and only if) they also experienced stressful or traumatic life events such as childhood maltreatment. Subsequent studies have reported inconsistent findings, with two meta-analyses suggesting that the serotonin transporter genotype does not increase the risk of depression when interacting with stressful life events (Munafò, Durrant, Lewis, & Flint, 2009; Risch, et al., 2009). However, Karg, Burmeister, Shedden, and Sen (2011) note that both meta-analyses have received widespread criticism.
for the limited number of studies that were included in the analyses (n= 5 in Munafò, et al., 2009; 14 in Risch, et al., 2009), excluding studies that assessed an interaction with other psychosocial variables (e.g., childhood maltreatment), and the lack of relevant data that was obtained from the original studies or follow-up emails [for example, Munafò & associates (2009) excluded ten studies that met the inclusion criteria due to an inability to obtain primary data]. Taking such criticisms into account, Karg and colleagues’ (2011) meta-analysis of 54 studies found that the S allele gene strongly moderates the relationships between depression and childhood maltreatment and depression and specific medical conditions, and marginally moderates the relationship between depression and stressful life events. Therefore, it seems that the S allele gene predisposes an individual to the development of depression via an interaction with a range of psychosocial factors, but the magnitude of the interaction ranges across psychosocial factors. In any case, the sensitivity to stressful and traumatic life events has been argued to intensify as a result of the hormonal and maturational changes during adolescence, hence further predisposing individuals to depression (Thapar, et al., 2012).

Finally, depression may be precipitated by other health-related factors, such as a lack of exercise (Brand et al., 2010), quality of diet (Jacka et al., 2010), disabilities and chronic illnesses (Camhi, Morgan, Pernisco, & Quan, 2000), drug and alcohol use (Bootzin & Stevens, 2005), and sleep disturbances such as insomnia (Fergusson & Woodward, 2002). Regarding sleep disturbances, a recent meta-analysis of adults has indicated that insomnia at baseline is related to the development of depression at follow-up (Baglioni et al., 2011). A discussion about the mechanisms that underlie the relationship between insomnia and depression can be found in studies 1, 2 and 3.
1.6.2. Epidemiology of depression

Like those for insomnia, the findings from epidemiological studies of adolescent depression have varied as a function of the definitions used by researchers. In general, point prevalence estimates for major depressive disorder during adolescence range from 1% (Fergusson, Horwood, & Lynskey, 1993) to 7% (Garrison et al., 1997), whereas 6 and 12-month estimates range from 2% (McGee et al., 1990; Velez, Johnson, & Cohen, 1989) to 13% (Feehan, McGee, Raja, & Williams, 1994). Lifetime prevalence estimates are higher still, ranging from 4% (Whitaker et al., 1990) to 24% (Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993). A meta-analysis found that after controlling for the effects of time-frame, taxonomy [(e.g., DSM vs International Classification of Disease ICD)], and measurement instrument, the prevalence rate for a depressive disorder during adolescence is approximately 5.6% (Costello, Erkanli, & Angold, 2006).

The prevalence rates of pathological depressive symptoms also vary considerably. Myers and Troutman (1993) reported a range from 10 to 40% in a review of youth depression. More recently, large epidemiological studies of adolescent depression symptoms have found prevalence rates from approximately 18 to 28% (Rothon et al., 2010; Rushton, Forcier, & Schectman, 2002; Saluja, et al., 2004). Furthermore, in an epidemiological study of 13, 568 adolescents, Rushton, et al. (2002) found that 19% of adolescents reported mild symptoms of depression, while 9% reported moderate or severe symptoms. Therefore, depressive disorders, along with clinically significant symptoms of depression at different spectrums of a severity continuum, are common during adolescence.
1.6.2.1. Epidemiology of depression and gender

Studies have consistently depicted higher rates of depression in females than males following puberty (Hankin et al., 1998; Hyde, Mezulis, & Abramson, 2008; Nolen-Hoeksema & Girgus, 1994). This phenomenon is unlikely the result of differences in help-seeking or symptom reporting, as the gender effect has been found in healthy and clinical samples (Thapar, et al., 2012), across different grades (Saluja, et al., 2004) and methods of assessment (Thapar, et al., 2012). Adolescent depression was thought to be mainly associated with post-pubertal changes to hormones and brain structures, and more closely related to female hormonal development than chronological age (Thapar, et al., 2012). Indeed, Brooks-Gunn and Warren (1989) found an association between depressive affect and the fastest rise of oestradiol levels in girls aged 10 to 14, yet no association between depressive affect and age.

Nevertheless, evidence suggesting that oestrogen and other gonadal hormones are the main individual predictors of the development of depression is limited. The involvement of neuroendocrine changes in the development of depression was mainly presumed because of the sharp increase in depression that occurs over the five years following puberty onset (Weller, Kloos, Kang, & Weller, 2006). Furthermore, some studies have found that psychosocial factors such as undesirable life events explain more variance of depressive affect than hormonal factors [8% vs 4% (Brooks-Gunn & Warren, 1989)]. Together, this evidence suggests a lack of empirical evidence for the notion that gonadal hormones are the main individual predictor of the development of depression following puberty, and that psychosocial factors are stronger predictors of post-pubertal depression. Therefore, oestrogen and gonadal hormones are unlikely to be the main mechanism that underlies the
gender effect. Indeed, various psychosocial factors have been associated or theorised to be associated with the gender effect, including emotion-focused coping strategies [which is associated with femininity (Washburn-Ormachea, Hillman, & Sawilowsky, 2004)] and large changes to social roles, school environments, and parental, peer and romantic relationships (Cyranowski, Frank, Young, & Shear, 2000).

However, it seems that an interaction between genetic and psychosocial factors have a greater association with the gender effect in adolescents than either individually. Brooks-Gunn and Warren’s (1989) study found that an interaction between negative life events and oestrogen change accounted for 17% of the variance in depressive affect, as opposed to the 8% and 4% of variance that the individual constructs accounted for respectively. More recently, Natsuaki et al. (2009) found that an interaction between physical development and severe responses to interpersonal stressors were associated with more internalising problems in young girls than either construct individually. Indeed, various researchers have suggested that hormonal changes are more likely to indirectly predict the onset of depression through sensitising the brain to the effects of stress or other psychosocial factors than directly contribute to the depression of depression in teenagers (Angold & Costello, 2006; Goodyer, Tamplin, Herbert, & Altham, 2000; Hyde, et al., 2008), although further research may help solidify such an argument. Nevertheless, the current evidence suggests that biological and psychosocial factors that change following puberty, both individually and when interacting, are likely to explain the gender effect found in adolescent depression. Future research could identify more specific biological and psychosocial factors that interact to further consolidate this notion.
1.6.2.2. Epidemiology of depression and age

The prevalence rate of depression tends to rise substantially from childhood to adolescence (Green, 2005; Kessler, et al., 2001). Saluja, et al. (2004) reported prevalence rates of 10% in grade 6, 20.4% in grade 8 and 24.5% in grade 10. Such a substantial increase in frequency may result from the maturation of the social information processing network (brain structures include the amygdala and prefrontal cortex; associated with reward and danger) and psychosocial changes (e.g., increased subjective stress levels) that occur during adolescence (Nelson, Leibenluft, McClure, & Pine, 2005; Thapar, et al., 2012). Abnormal development of the social information processing network may render adolescents more susceptible to a depressive episode in reaction to a social stressor. Indeed, Thomas et al. (2001) reported functional abnormalities in amygdala responsiveness to particular social stimuli in depressed and anxious adolescents. It could also be a mismatch in the maturation of particular brain structures (Blakemore, 2008). Nelson, et al. (2005) proposed that the slower development of the prefrontal cortex (involved in impulse inhibition and goal-setting behaviour, i.e., executive functioning) relative to brain structures involved in detecting social stimuli and emotional-awareness leads to the onset of depression during adolescence, depending on psychosocial stimuli (e.g., rejection by romantic partners). In any case, it seems that an interaction between biological and psychosocial risk-factors also explains the heightened prevalence rates of depression in adolescents relative to children.

1.6.3. Concurrent and longitudinal associations with depression during adolescence

Depression during adolescence is related to present and future morbidity. A cross-sectional study found that adolescent depression was associated with issues such as
absenteeism, smoking, and suicidal ideation after controlling for socio-demographic variables, life events, sexual abuse, physical abuse and exposure to violence (Glied & Pine, 2002). Regarding future morbidity, adolescent depression has been found to predict adult psychiatric problems, such as suicidal ideation (2.3:1 odds ratio) (Fergusson, Horwood, Ridder, & Beautrais, 2005), and agoraphobia without panic (4.3:1 odds ratio) (W. E. Copeland, Shanahan, Costello, & Angold, 2009), all of which were found after controlling for comorbid adolescent mental health problems and other factors. Adolescent depression also predicts other future health related outcomes, such as health status ($\beta = .16$), self-health perception ($\beta = 1.10$), medical care use ($\beta = 1.26$), physical impairment at work ($\beta = .38$) (Keenan-Miller, Hammen, & Brennan, 2007), and the presence of disease and functional impairment (Lewinsohn, Seeley, Hibbard, Rohde, & Sack, 1996). Together, these studies suggest that adolescent depression is a risk-factor for current and future psychological, behavioural, and physical health problems.

The extent to which adolescent depression predicts negative outcomes in adults is particularly evident in females. A study found that adolescent depression in girls predicted tobacco dependence and more medical problems at age 21 above and beyond prior health status issues (Bardone et al., 1998). Adolescent girls with depression are more likely to smoke, attain lower levels of education, report lower self-worth, and higher levels of body dissatisfaction and eating problems during young adulthood than adolescents without depression (Franko et al., 2005). Another study of adolescent girls found that depression predicted higher rates of marriage during young adulthood and subsequent marital dissatisfaction above and beyond the presence of adolescent non-affective psychiatric disorders (Gotlib, Lewinsohn, & Seeley, 1998). Therefore, prevention and treatment efforts
for various negative psychosocial outcomes in adult women should target depression in adolescent females.

Depression during adolescence is also a risk-factor for future depression (Thapar, et al., 2012). Fergusson, et al. (2005) found that depression at 17 and 18 years of age predicts depression at 25 years of age (2.4:1 odds ratio), and G. Fava, Ruini and Belaise’s (2007) review article suggested that adults often fail to completely recover between depressive episodes. Furthermore, although longitudinal community and clinical studies have found that 60-90% of depressive episodes during adolescence remit within a year (V. Dunn & Goodyer, 2006; March, 2004), follow-up studies suggest that 50-70% of these adolescents suffer from further depressive episodes within five years (V. Dunn & Goodyer, 2006; Lewinsohn, Rohde, Seeley, Klein, & Gotlib, 2000). Together, the evidence strongly suggests that depression during adolescence is often chronic and/or relapsing, and can persist into adulthood.

1.7. Anxiety

Anxiety is a natural reaction to a stressor (i.e., safety threat) involving the sympathetic nervous system, that is characterised by cognitive, affective and physiological symptoms such as acute stress, tension, discomfort, worry, an increased heart rate, and excessive fears about future negative events (Evans, Foa, & Gur, 2005; Kaplan & Sadock, 1998). An anxiety response is classified as clinically significant when symptoms arise in the absence or in excess of objectively-threatening stimuli (Evans, et al., 2005), and is diagnosed as a disorder when symptoms become intrusive, are experienced amid tension and excess apprehension, and cause substantial distress or functional impairment more often than not for at least 6 months (American Psychiatric Association, 2013).
According to the DSM-5 (American Psychiatric Association, 2013), anxiety disorders can manifest in various ways, including excessive worry over separation from home or loved ones [separation anxiety disorder (SAD)]; excessive and persistent fear of embarrassment or negative evaluation during social situations or performances [social phobia (SP)]; distinct episodes of unexpected intense fear, distress, or physiological reactions such as palpitations, sweating, a sense of imminent danger, an urge to escape, or a fear of dying [panic disorder (PD)], that is sometimes accompanied by an avoidance of situations that may trigger panic (agoraphobia); excessive and persistent fear of objectively non-threatening stimuli such as animals, the natural environment or medical procedures (phobias); and excessive and often uncontrollable worry accompanied by physiological anxiety [generalised anxiety disorder (GAD)]. Obsessive-compulsive disorder (OCD), defined as severe recurrent time-consuming obsessions or compulsions, was originally classified as an anxiety disorder in the DSM-IV, but has a separate category in the DSM-5.

Like depression, the diathesis-stress model has been used to explain the development of anxiety during adolescence (Mineka & Zinbarg, 2006; Rapee, Schniering, & Hudson, 2009). The following section describes various risk-factors that have been associated with the development of anxiety problems.

1.7.1. Risk-factors of anxiety

It seems reasonable to assume that the development of anxiety disorders contains a genetic component. In a study of 1,162 twin pairs and 426 siblings, Ehringer, Rhee, Young, Corley, and Hewitt (2006) found evidence indicating genetic influences for attention deficit hyperactivity disorder, GAD, SAD, and major depressive disorder. Various other studies have reported similar findings across different anxiety disorders (Stevenson, Batten, & Cherker,
1992; Thapar & McGuffin, 1995; Topolski et al., 1997), along with an overlapping genetic component with depression (Eley, 1997; Gregory & Eley, 2007).

Environmental factors are also known vulnerabilities for the development of anxiety disorders during adolescence. Ehringer, et al. (2006) suggested that environmental factors are stronger predictors of lifetime GAD and major depressive disorder than genetic factors, although this may have been the result of insufficient statistical power. They also note that environmental influences shared between siblings (twins and singletons) are associated with GAD, but not SAD, whereas non-shared environmental factors were associated with both (Ehringer, et al., 2006). Shared environmental influences predicting the development of anxiety disorders include negative or overcritical and particularly overprotective or over-controlling parenting styles (Bögels & Brechman-Toussaint, 2006; McLeod, Wood, & Weisz, 2007; Rapee, 1997; Wood, McLeod, Sigman, Hwang, & Chu, 2003), and non-shared environmental factors include peers, hobbies, parental treatment, and social support (J. Dunn & Plomin, 1990; La Greca & Lopez, 1998).

Personality factors also increase the risk of anxiety during adolescence. Meeus, Van de Schoot, Klimstra, and Branje (2011) found that an over-controlling personality style was associated with future anxiety, whereas resilience appeared to have a protective effect against future anxiety. Furthermore, Prior, Smart, Sanson, and Oberklaid (2000) reported an association between shy-inhibited temperament persisting from childhood to adolescence and adolescent anxiety. Prinzie, van Harten, Deković, van den Akker, and Shiner (2014) reported a similar finding, with shyness, irritability and altruism during childhood predicting more problematic adolescent anxiety and depression. The same study also found that energy, optimism, compliance and trait anxiety during childhood predicted adolescent
anxiety symptoms, but shyness, irritability and compliance were moderated by over-reactive parenting (Prinzie, et al., 2014). Therefore, it seems that an interaction between certain personality and environmental factors during childhood may further increase the risk of developing anxiety during adolescence.

Finally, various disorders, such as insomnia, have been associated with the development of anxiety (Jansson-Fröjmark & Lindblom, 2008). A discussion about the mechanisms that underlie the relationship between insomnia and anxiety can be found in studies 1, 2 and 3.

1.7.2. Epidemiology of anxiety

Anxiety disorders are the most prevalent mental health problems experienced during adolescence (Beesdo, Knappe, & Pine, 2009). Beesdo, et al. (2009) argues that estimates of prevalence rates vary because of differences in assessment instruments (e.g., Composite International Diagnostic Interview, and Kiddie-Schedule for Affective Disorders), information source (e.g., self-report, parent/teacher report), method of data aggregation (from multiple information sources or multiple assessment waves), diagnostic criterion (e.g., DSM-III-R, DSM-IV, and ICD-10), definitions (e.g., any anxiety disorder), and strictness of symptom severity (e.g., impairment required or not) used across studies. Nevertheless, a recent meta-analysis found that 11% of adolescents aged 13 – 18 suffer from any anxiety disorder, 6.7% suffer from specific phobias, 5.0% from SP, 2.3% from SAD, 1.9% from GAD, and 1.1% from PD (Costello, Egger, Copeland, Erkanli, & Angold, 2011).
1.7.2.1. Epidemiology of anxiety and gender

Similarly to insomnia and depression, females report higher rates of anxiety than males across all anxiety disorders (Beesdo, et al., 2009). Gender differences tend to increase during adolescence to approximately 2:1 – 3:1 (Pine, Cohen, Gurley, Brook, & Ma, 1998; Wittchen, Nelson, & Lachner, 1998). As with insomnia and depression, the gender effect is likely to be associated with biological and psychosocial factors, namely post-pubertal changes to hormones and brain structures, female hormonal development, increased social issues for girls relative to boys, and a combination of all. Nevertheless, more research is needed to further identify the risk-factors that are relevant to adolescent girls for the development of anxiety problems.

1.7.2.2. Epidemiology of anxiety and age

Prevalence rates of anxiety disorders remain constant after puberty for some disorders but increase for others. In their review, Beesdo, et al. (2009) note that the prevalence rates for SAD, and specific and social phobia are similar in children and adolescents, but are higher in adolescents for PD. The meta-analysis conducted by Costello et al. (2011) found similar results. The causes of the increase in prevalence rate in PD are likely to be similar to those for insomnia and depression, such as post-pubertal changes to hormones and brain structures, and increased social, academic and familial pressures from childhood to adolescence.
1.7.3. Concurrent and longitudinal associations with anxiety during adolescence

Anxiety can impact the school life of adolescents. Various studies have suggested that anxiety disorders during childhood and adolescence are associated with premature withdrawal from school and difficulties with concentration and motivation, both of which can compromise school performance and impact the quality of relationships with peers and family (Stein & Kean, 2000; Van Ameringen, Mancini, & Farvolden, 2003; Varley & Smith, 2003). Because anxiety is often chronic in nature (see below), the transitional process from childhood to adolescence can be impaired by the consequent feelings of worthlessness and low self-esteem (Varley & Smith, 2003). Indeed, SAD has been associated with victimisation at school (R. S. Siegel, La Greca, & Harrison, 2009), which could further disrupt the transitional process and hence impact on academic achievement and quality of life at school.

Longitudinal data suggests that anxiety symptoms and disorders consistently present during adolescence. Adolescent anxiety disorders have been found to predict anxiety disorders in the short and long term (Lewinsohn, Zinbarg, Seeley, Lewinsohn, & Sack, 1997; Woodward & Fergusson, 2001). Furthermore, various studies have reported that GAD, OCD, SP, and specific phobias during adolescence predict the same disorders 1.3 to 15 years later (Berg et al., 1989; Bittner et al., 2004; W. Hale, Raaijmakers, Muris, Van Hoof, & Meeus, 2008; Merikangas, Avenevoli, Acharyya, Zhang, & Angst, 2002; Pine, et al., 1998; Stein et al., 2001). Therefore, like insomnia and depression, anxiety disorders are likely to be chronic, and/or relapsing conditions that persist well into adulthood.

Anxiety during adolescence is considered a risk-factor for other health and psychological outcomes. Berg, et al. (1989) showed that 56% of adolescents with OCD
developed other anxiety and mood disorders at 2-year follow-up. Studies have also shown an association between anxiety at ages 14 – 16 and other subtypes of anxiety, depression, illicit drug dependence, and failure to attend university at ages 16 – 21 after controlling for various covariates (Essau, Conradt, & Petermann, 2002; Woodward & Fergusson, 2001). Furthermore, anxiety disorders in adolescent females have been associated with more medical problems in young adulthood, including anaemia, arthritis, cancer, hepatitis, diabetes, serious back trouble, heart trouble, kidney and bladder infections, epilepsy, acne, colitis, menstrual problems, and migraines (Bardone, et al., 1998). Finally, Johnson, Roth, and Breslau (2006) found that prior anxiety predicts insomnia during adolescence. Together, the evidence suggests that anxiety problems during adolescence are risk-factors for a number of psychological, behavioural, and medical problems, including insomnia and depression. The following section discusses the association between insomnia, anxiety and depression in adolescents.

1.8. The relationship between insomnia, depression and anxiety

Studies investigating the relationship between insomnia, depression and anxiety have defined the latter two as either a single variable (Gregory & O’Connor, 2002; Kaneita, et al., 2009), or two separated constructs (Liu & Zhou, 2002). Regarding the former, Gregory and O’Connor (2002) found a correlation between sleep problems and depression/anxiety at age 15 ($r= 0.52$). Moreover, Kaneita, et al. (2009) reported an association between the Japanese version of the Pittsburgh Sleep Quality Index (PSQI) overall score, which is highly sensitive in detecting primary insomnia in Japanese adolescents (Doi et al., 2000), and mental health status as measured by the Japanese version of the 12-item General Health Questionnaire
which contains a depression/anxiety subscale. The same authors subsequently validated the GHQ-12 in Japanese adolescents and found that current subjective insomnia symptoms were associated with both the depression/anxiety and loss of positive emotions subscales (Suzuki et al., 2011). In addition, Liu and Zhou (2002) found that Chinese adolescents who reported experiencing insomnia symptoms ‘often’ within the past month also reported higher levels of anxiety/depressive symptoms than those who did not report experiencing insomnia symptoms (25.4% vs 9.9% respectively). Given the above studies have been conducted in different countries, the association between insomnia and depression/anxiety seems to be present irrespective of culture.

Interestingly, the magnitude of the association between sleep problems and depression/anxiety may be affected by developmental changes overtime (Gregory & Sadeh, 2011). Gregory and O’Connor (2002) found a positive correlation between sleep problems and depression/anxiety, which significantly increased from \( r = .39 \) at age 4 to \( r = .52 \) at age 15. Furthermore, Johnson, Chilcoat, and Breslau (2000) reported a greater association between troubles sleeping and depression/anxiety at age 11 (OR= 9.7) than at age 6 (OR= 4.7). These findings may be explained by the physical and social changes experienced during adolescence that can impact on the development of insomnia, anxiety and depression, such as increased autonomy and psychosocial (e.g., peer groups), familial, and educational demands (Kaneita, et al., 2009; Lipton, et al., 2008).

Various studies have also reported an association between insomnia and depression, and insomnia and anxiety. Kirmil-Gray and associates (1984) found that 66.7% of adolescents who reported insomnia symptoms at least once a week also reported pathological depressive symptoms, whereas 36% of those who slept well reported depressive symptoms
(p < 0.05). Also, Ohayon et al., (2000) demonstrated that 76.5% of adolescents aged 15 – 18 with an anxiety disorder and 67.6% with a depressive disorder reported at least one current symptom of insomnia. Furthermore, Roane and Taylor (2008) found that adolescents aged 12 – 18 with clinically significant insomnia symptoms were 3.27 times more likely to display clinically significant depression symptoms than those without clinically significant insomnia symptoms. Regarding anxiety subtypes, Alfano, Zakem, Costa, Taylor, and Weems (2009) reported that sleep disturbances are associated with clinically significant symptoms of GAD, PD/agoraphobia, and SP, but not OCD or SAD in adolescents. Considering the evidence, it seems that a relationship between insomnia and depression, and insomnia and anxiety (assessed as an overall construct) during adolescence is consistently reported across definitions and severity criteria, but not subtypes of anxiety.

1.8.1. Potential mechanisms that underlie the relationship between insomnia, depression and anxiety

There are various mechanisms that may underlie the consistently reported associations between insomnia and depression, and insomnia and anxiety. These disorders may arise due to common risk-factors, or there may be a causal relationship. Both mechanisms are likely to underlie the relationship between insomnia, depression and anxiety, although to what extent is unclear. The following section describes common risk-factors and causality in more detail.

1.8.1.1. Common risk-factors

Common risk-factors have been theorised to explain the relationship between disorders in two ways. Neale and Kendler (1995) proposed that common risk-factors, all independent and of small effect, are alternative forms of the same disorder, suggesting that
a disorder may manifest in different ways (e.g., via insomnia or depression). In contrast, Staner (2010) notes that such risk-factors may result in two distinctive yet associated disorders if risk-factors are common to both conditions.

Although both theories have merit, the evidence seems to contradict the prior theory and support the latter theory when considering the relationships between insomnia and depression. Various studies have reported a predictive relationship between insomnia and depression after controlling for covariates (i.e., common risk-factors) (Baglioni, et al., 2011; Jansson-Fröjmark & Lindblom, 2008; Meijer, Reitz, Deković, van den Wittenboer, & Stoel, 2010), suggesting that the disorders are separate constructs even when considering common risk-factors. Furthermore, cross-sectional and longitudinal studies have reported that anxiety and other covariates (e.g., age and gender) partially account for the relationship between insomnia and depression, suggesting that although insomnia and depression are separate disorders, comorbid insomnia and depression is at least partially due to common risk-factors (i.e., anxiety, age and gender) (Alfano, et al., 2009; Gregory, et al., 2009; Jansson-Fröjmark & Lindblom, 2008). Therefore, the current evidence indicates that common risk-factors are a mechanism that underlies the relationship between insomnia and depression, but other factors are also likely to explain this relationship.

The relationship between insomnia and anxiety, however, is less clear. Cross-sectional and longitudinal studies have reported mixed findings, where covariates (e.g., depression, gender and age) have been found to completely account for the relationship between insomnia and anxiety in some studies (Alfano, et al., 2009), and partially account for this relationship in other studies (Jansson-Fröjmark & Lindblom, 2008; Meijer, et al., 2010). One reason for the contrast in results could be that anxiety is often assessed as an overall...
variable (i.e., the different anxiety disorders are grouped as one), and studies have reported that the relationship between insomnia and anxiety differs across anxiety subtypes (Alfano, Ginsburg, & Kingery, 2007). Even so, it seems safe to assume that insomnia and anxiety disorders are separate constructs given the different symptoms, diagnostic criteria and recommended treatments for each disorder (although some do overlap) (American Psychiatric Association, 2013). Therefore, the above evidence likely indicates that the mechanisms underlying the relationship between insomnia and anxiety are either partially or entirely explained by common risk-factors.

1.8.1.2. Cause-effect relationship

Insomnia, depression and anxiety may also have a causal relationship, where the development of an insomnia disorder results in the development of a depressive or anxiety disorder, or vice-versa. Although the notion of causality is difficult to ascertain, Hill (1965) proposed a widely used criteria that focuses on nine aspects of a relationship by which causal inferences can be made. Such aspects of the relationship include the magnitudes of the effect-sizes that are reported in studies, the consistency of a significant effect across different studies and cultures, the specificity of the observed association (is it limited to a particular population or circumstance?), the bidirectionality of the relationship, the dose-response linear relationship of two variables, the biological plausibility (are there biological mechanisms that can explain the relationship?), coherence (correspond with the known facts of the disorder), the experimental evidence available, and analogy (can a judgment be made in similar circumstances?) (Hill, 1965).

Hill (1965) notes that these criteria do not bring irrefutable evidence for a cause-effect relationship. In fact, the specificity, dose-response linear relationship, biological plausibility
and analogy criteria are features he argues cannot be demanded. Rather, such criteria aim to assist in determining whether or not there is a more logical explanation than a cause-effect relationship. With this in mind, the findings of the relationships between insomnia and depression and insomnia and anxiety largely satisfy Hill’s (1965) criteria. Studies across many cultures have consistently reported a wide range of dose-linear associations, with varying effect-sizes, and have not seriously conflicted with the known facts about insomnia, depression or anxiety (Gregory & O'Connor, 2002; Gregory, et al., 2009; Jansson-Fröjmark & Lindblom, 2008; Kaneita, et al., 2009; J. M. Kim et al., 2009). Such studies have often control for potential covariates, and hence further strengthen the notion of a cause-effect relationship. There has also been experimental evidence based on treatment studies (Alfano, et al., 2007; Manber et al., 2008), and various biologically plausible explanations (see Chapters 3, 4 and 5).

The bidirectionality of the relationships between insomnia and depression, and insomnia and anxiety has also been assessed (Gregory & O'Connor, 2002; Jansson-Fröjmark & Lindblom, 2008). Bidirectionality refers to whether insomnia predicts or is predicted by anxiety and depression. The following section introduces the topic of bidirectionality, describes the research within this area of study, and highlights the methodological issues within this literature.

1.9. The bidirectionality of the relationship between insomnia, depression and anxiety

Research that assesses the bidirectionality of the relationship between insomnia, depression and anxiety aims to explore the potential overlapping developmental courses of these problems. Anxiety may be a risk factor for insomnia, and insomnia may be a risk factor
for depression (Johnson, Roth, & Breslau, 2006), or each may be associated with the development of the other (Jansson-Fröjmark & Lindblom, 2008). Such research can help identify key aetiological factors for insomnia, depression and anxiety, establish whether the onset of one is a risk-factor for the others, and inform public health campaigns and clinical interventions for each disorder (Jansson-Fröjmark & Lindblom, 2008; Johnson, Roth, & Breslau, 2006; Kaneita, et al., 2009). Bidirectionality can only be established by considering whether insomnia is associated with the development of depression or anxiety, and whether depression or anxiety is associated with the development of insomnia, in subsequent analyses. A recent meta-analysis of longitudinal studies found that baseline insomnia predicts follow up depression, but did not establish directionality because the association between baseline depression and follow-up insomnia was not assessed simultaneously (Baglioni, et al., 2011).

Recent evidence on bidirectionality has been limited and contentious. After controlling for gender, race, and prior disorders of insomnia, anxiety or major depressive disorder, Johnson, Roth, and Breslau (2006) reported significant associations between prior anxiety disorders and onset of insomnia disorder [Hazard Ratio=3.5; the hazard in an exposed group divided by the hazard in an unexposed group (Hernán, 2010)], and prior insomnia disorder and onset of major depressive disorder (Hazard Ratio=3.8). However, a significant relationship was not found between prior insomnia disorder and onset of an anxiety disorder, or prior major depressive disorder and onset of insomnia disorder. Similarly, Ohayon and Roth (2003) found that adults with current but no previous history of any anxiety disorder presented with insomnia symptoms simultaneously and after the anxiety disorder more often than before (38.6%, 43.5% and 18% respectively), whereas those
without a history of mood disorders presented with insomnia symptoms more often before mood disorders than simultaneously or after (41%, 29.4% and 28.9% respectively). These studies suggest the possibility of two separate cause-effect relationships (Figure 1), where anxiety leads to insomnia (Figure 1a) and insomnia leads to depression (Figure 1b) (Johnson, Roth, & Breslau, 2006), but not vice-versa. Consequently, insomnia, depression, and anxiety are thought to have distinct natural courses of development during adolescence, from anxiety to insomnia and insomnia to depression (Johnson, Roth, & Breslau, 2006). Therefore, the relationship between insomnia, depression, and anxiety may predominately follow a pathway from anxiety to insomnia to depression (Figure 1c) (Johnson, Roth, & Breslau, 2006).

In contrast, Jansson-Frojmark and Lindblom (2008) demonstrated an association between symptoms of anxiety and depression, and new episodes of insomnia at 1-year follow-up (OR=4.27 and 2.28, respectively). They also reported an association between symptoms of insomnia, and new cases of anxiety (OR=2.30) and depression (OR=3.51) at 1-year follow-up. Similarly, after controlling for predictor variables at baseline, Morphy and

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Figure 1. Aetiologically exclusive relationships between insomnia, anxiety and depression.

(1a) Anxiety leads to insomnia (1b) Insomnia leads to depression (1c) Anxiety leads to insomnia, which leads to depression

In contrast, Jansson-Frojmark and Lindblom (2008) demonstrated an association between symptoms of anxiety and depression, and new episodes of insomnia at 1-year follow-up (OR=4.27 and 2.28, respectively). They also reported an association between symptoms of insomnia, and new cases of anxiety (OR=2.30) and depression (OR=3.51) at 1-year follow-up. Similarly, after controlling for predictor variables at baseline, Morphy and
colleagues (2007) reported a relationship between symptoms of anxiety and depression at baseline, and symptoms of insomnia at 12-month follow-up, and vice-versa. Among adolescents, Kaneita and associates (2009) found a significant relationship between poor sleep quality present at baseline and follow-up, and mental health status (depression/anxiety symptoms) at follow-up (OR=5.81) in participants who did not display poor mental health at baseline. Poor mental health status present at baseline and follow-up also predicted poor sleep quality at follow-up (OR=6.9) in participants who did not display poor sleep quality at baseline. Gender, baseline sleep quality or mental health status, and baseline lifestyle and contentment with daily life were used as covariates in each analysis (Kaneita, et al., 2009). These studies suggest a bidirectional relationship between insomnia, depression, and anxiety, where each contribute to the development of one another (Jansson-Fröjmark & Lindblom, 2008; Kaneita, et al., 2009; Morphy, et al., 2007) (Figure 2). Consequently, insomnia, depression and anxiety are thought to have overlapping courses of development rather than two distinct associations, which may be facilitated by familial, social and environmental stressors (Kaneita, et al., 2009) or abnormalities to neurotransmitters associated with the sleep wake cycle, anxiety and depression such as dopamine, hypocretin-1 and serotonin (Holmes, 2003; Nestler & Carlezon, 2006; Peroutka, 1998; Tseng & O’Donnell, 2007; Yoshioka, Matsumoto, Togashi, & Saito, 1996).

Figure 2. A bidirectional relationship between insomnia, anxiety and depression.
1.9.1. Methodological variations across studies

The inconsistent nature of the evidence may relate to variations in the type of methodologies employed to date. Studies that support the model depicted in Figure 1 have used cross-sectional designs and retrospective reports (Johnson, Roth, & Breslau, 2006; Ohayon & Roth, 2003). Cross-sectional designs assess variables at a single time-point rather than over a period of time, and retrospective reports often display recall bias (poor recall of past events), rounding (participants excessively report ages ending with 0 or 5) and telescoping effects (onset of disorders are often reported more recently or less recently than in reality), thus compromising the accuracy of memory (Golub, Johnson, & Labouvie, 2000). Cross-sectional designs and retrospective reports cannot separate cause-effect relationships from associations and hence are unsuitable for accurate investigations of bidirectionality. Conversely, studies supporting the bidirectional theory have used longitudinal designs and prospective reports (Jansson-Fröjmark & Lindblom, 2008; Kaneita, et al., 2009; Morphy, et al., 2007), resulting in more power to suggest (but not assume) causality and reliability to assess the bidirectionality of the relationship between insomnia, anxiety and depression over time. They have also accounted for the baseline covariates, which is essential in establishing bidirectionality (Chilcoat & Breslau, 1998). However, the study that investigated adolescents used a combined depression/anxiety variable, which could mask the different relationships between insomnia and depression, and insomnia and anxiety. Therefore, inferences cannot be suggested about the developmental pathways of insomnia, depression and anxiety during adolescence.

The inconsistent populations and variables that have been investigated in the literature is another important variation. Some studies have assessed sleep quality in
adolescents (Kaneita, et al., 2009), while others have assessed insomnia in adults (Jansson-Fröjmark & Lindblom, 2008). The related yet slightly inconsistent variables used across studies may contribute to the contradictory findings.

1.9.2. Overlapping methodological issues within the literature

The supporting studies of both theories also contain overlapping methodological issues (Jansson-Fröjmark & Lindblom, 2008; Johnson, Roth, & Breslau, 2006; Kaneita, et al., 2009; Morphy, et al., 2007; Ohayon & Roth, 2003). Firstly, the effects of different types of anxiety subtypes on the bidirectionality of the relationship between insomnia, depression and anxiety have not been considered. Johnson et al., (2006) suggested that insomnia may present more often in adolescents with OCD and less with simple phobias than with other forms of anxiety disorders and major depressive disorder and depression during adolescence, although this was not tested specifically tested by the authors. Also, Alfano, Ginsburg, and Kingery (2007) found that youths aged 6 to 17 who suffered from GAD or SAD were more likely to experience insomnia than youths who did not, but did not find a significant difference between youths who suffered from SP and youths who did not. Therefore, it may be that bidirectionality may differ across anxiety subtypes.

Secondly, the bidirectionality of the relationship between insomnia, depression, and anxiety has only been assessed using categorical variables, assuming that each disorder as present or absent. However, symptoms of insomnia, depression, and anxiety can differ in severity, and the relationship between these symptoms likely in part depends on severity levels. That is, the more severe the insomnia symptom, the more severe the depression or anxiety symptom. Indeed, youth studies have reported positive correlations between sleep problems and depression (Alfano, et al., 2009), and insomnia and anxiety (Alfano, et al.,
Furthermore, a study that performed two meta-analyses reported the reliability and validity of measures of psychopathology increase by 15% and 37% respectively when assessed as continuous variables compared to categorical variables (Markon, Chmielewski, & Miller, 2011). Therefore, assessing bidirectionality using continuous variables will allow for the consideration of symptom severity, and is potentially a more reliable and valid method to assess insomnia, depression and anxiety.

1.9.2.1. Chronotype

Finally, the impact of chronotype on the relationships between insomnia and depression, and insomnia and anxiety has not been considered in previous studies. Chronotype refers to a circadian rhythm position indicator that categorises individuals according to both their body clock position relative to the 24 hour day (Roenneberg et al., 2004) and the time he/she prefers to engage in cognitively and physically demanding activities (Ferraz, Borges, & Vianna, 2008). People who wake and sleep earlier are classified as morning types, whereas those who wake and sleep later are classified as evening types.

As noted in section 1.4., adolescents become more evening orientated with age during adolescence (Crowley, et al., 2007). Such a phenomenon may be problematic, as studies have suggested that a preference for evenings is associated with insomnia, depression and anxiety during adolescence. Giannotti, et al. (2002) found that an evening chronotype at age 14 – 16 predicted anxiety/depression at age 16.1 – 18.6. Eveningness was also associated with insomnia at ages 14 – 16 and 16.1 – 18.6. Furthermore, Randler, Bilger, and Diaz-Morales (2009) reported that adolescents with an evening chronotype have longer sleep onset latencies that are indicative of sleep onset insomnia, and Gau et al. (2007) found that eveningness is more predictive of anxious/depressive symptoms than morningness.
Therefore, the developmental relationship between insomnia, depression and anxiety may be affected by chronotype rather than exclusively unidirectional or bidirectional. Indeed, people with sleep-onset insomnia exhibit a phase delay pattern in body temperature rhythm (Morris, Lack, & Dawson, 1990) that, coupled with retirement before sleepiness, could lead to prolonged wakefulness in bed and hence present an opportunity for hyperarousal and rumination as per psychophysiological insomnia. Regarding depression and anxiety, homeostatic, circadian and personality factors (particularly low self-control) have been hypothesised to underlie the association between an eveningness chronotype and poor mental and physical health (Saxvig, Pallesen, Wilhelmsen-Langeland, Molde, & Bjorvatn, 2012). Furthermore, Gaspar-Barba et al. (2009) argue that the association between depression, anxiety disorders and eveningness may be related to corticotropin-releasing factor (Arborelius, Owens, Plotsky, & Nemeroff, 1999).

Nevertheless, the effects of chronotype on the bidirectionality of the relationship between insomnia, depression and anxiety during adolescence is unclear. That is, whether eveningness predicts insomnia after accounting for depression and anxiety; depression after accounting for insomnia and anxiety; and anxiety subtypes after controlling for insomnia and depression; or accounts for the relationship between these variables is still unknown. The evidence above suggests that eveningness predicts insomnia, depression and anxiety. However, depression and anxiety were not controlled in the previous studies when the relationship between chronotype and insomnia was assessed, nor was insomnia controlled when the relationships between chronotype and depression, and chronotype and anxiety were assessed. Furthermore, the analyses that assessed the relationship between insomnia and chronotype were cross-sectional, meaning an educated guess about the effects of
eveningness on the development of insomnia is difficult to make based on the current literature. Eveningness would be a risk factor for the development of insomnia should it predict insomnia at follow-up after controlling for depression and anxiety at baseline, and therefore appear chronologically before insomnia. Similarly, eveningness would be considered as a risk factor for the development of depression and/or anxiety should it predict these variables at follow-up after controlling for insomnia, and depression or anxiety at baseline, and therefore appear chronologically before depression and/or anxiety. In contrast, eveningness would account for the relationships between insomnia and depression, or insomnia and anxiety, should these associations no longer be significant in any direction once chronotype was controlled.

1.10. Aims of the thesis

There were two aims of the thesis. Firstly, this thesis investigated the bidirectionality of the relationship between insomnia, depression and different subtypes of anxiety during adolescence, and secondly, the independent effect of chronotype on these relationships.

Three studies were conducted that contributed to the investigation of these aims. Study 1 intended to identify the inferences that can be made about the bidirectionality of the relationship between insomnia, depression and anxiety based on previous studies. A systematic review was conducted that focused on the differences in results according to the sleep variables that were assessed, as various studies have discussed and compared the results of different sleep variables. Study 1, therefore, primarily assessed the first aim.

Study 2 aimed to investigate the independent cross-sectional relationships between insomnia and depression, and insomnia and subtypes of anxiety during adolescence, and the
independent effect of chronotype on these relationships. The anxiety subtypes that were assessed in study 2 included GAD, OCD, PD, SAD, and SP. Continuous variables were used to indicate the severity of symptoms for insomnia, depression and subtypes of anxiety. The results of this study contributed to the research of both aims, by providing a base to predict the findings of study 3.

Study 3 assessed both aims, and hence was the main study of this thesis. The methodology was longitudinal and prospective, with two data collection points (one baseline and one follow-up assessment six months apart). This study investigated the bidirectionality of the relationship between insomnia and depression, and insomnia and subtypes of anxiety during adolescence after chronotype and other covariates were controlled, along with the independent predictive power of chronotype on insomnia, depression and anxiety subtypes after controlling for baseline anxiety subtypes, depression, and/or insomnia. Continuous variables were also used to indicate the severity of symptoms for insomnia, depression and subtypes of anxiety.

1.1. Significance/Contribution to the discipline

This thesis will contribute to the understanding of the aetiological relationship between and hence prevention of insomnia, depression and anxiety during adolescence. Unidirectionality would suggest that subtypes of anxiety are related to the development of insomnia, and insomnia is related to the development of depression, but not vice-versa. The treatment of anxiety subtypes or insomnia may then prevent the development of subsequent insomnia or depression, respectively (Johnson, Roth, & Breslau, 2006). Bidirectionality would suggest that insomnia is a risk-factor for the development of depression and subtypes of anxiety, and vice-versa. The presence of insomnia, anxiety or
depression that is preceded by key contributing symptoms may indicate targets for most
effective/efficient therapy (e.g. target prior insomnia rather than current depression).
Therefore, the successful treatment of primary insomnia may prevent the onset or
exacerbation of subsequent depression or anxiety disorders, and vice-versa (Kaneita, et al.,
2009).

An examination of the cross-sectional effects and longitudinal predictive power of
chronotype on the relationships between insomnia and depression, and insomnia and
subtypes of anxiety would identify potential underlying mechanisms of these relationships.
Chronotype (most likely eveningness) would be considered a risk-factor for the development
of insomnia, depression or subtypes of anxiety should eveningness (or morningness) predict
either variable after controlling for baseline covariates (insomnia, depression or subtypes of
anxiety). In contrast, chronotype would be considered a risk factor for the interaction
between insomnia, subtypes of anxiety and depression during adolescence should
chronotype partly account for these relationships. Consequently, prevention and treatment
strategies could target chronotype to limit the development or exacerbation of these
problems. Similarly, insomnia, subtypes of anxiety and/or depression would not be
considered as aetiologically related should the association between these variables no
longer be significant once chronotype has been controlled. Such a finding would suggest that
insomnia, depression and subtypes of anxiety do not directly impact on the development of
each other. Instead, the relationship between these variables would mainly result from a
certain chronotype, which, if targeted by public health campaigns and treatment efforts,
could reduce the relationship between insomnia, depression and subtypes of anxiety.
This research project offers the possibility for an improvement in the identification of symptoms of insomnia, depression and subtypes of anxiety, along with an enhanced understanding of the relationship between these symptoms in the adolescent population. The consequent treatment of insomnia, depression and subtypes of anxiety may also prevent the development or reduce the risk of unhealthy behaviours during adolescence. For instance, Johnson and Breslau’s (2001) longitudinal study found an association between the use of cigarettes, alcohol and any illicit drug, and adolescents’ report of sleep disturbances after adjusting for age, sex, race and family income. Controlling for internalising (depression and anxiety) and externalising (deviance and aggression) problems reduced this association, suggesting that the relationship between insomnia and unhealthy behaviours is partially attributable to psychological problems.
Chapter 2: Exegesis

Chapter 1 presented the definitions of major concepts such as adolescence, sleep, adolescent sleep, insomnia, depression, anxiety and chronotype. An examination of the epidemiology and consequences of insomnia, anxiety and depression during adolescence, past research of the bidirectionality of the relationship between insomnia, depression and anxiety, and methodological issues within the bidirectionality research were also presented. Finally, chapter 1 discussed the significance and contribution of the thesis and studies in detail.

Chapter 2 presents an exegesis aimed to explain additional information about the thesis and each study that goes beyond the scope of the manuscripts or that was excluded from the manuscripts because of the journal word limit. In particular, this exegesis outlines the reasons why each study was conducted, the methodological overlap and differences between each paper, and provides explanations about important decisions that were made.

2.1. The thesis

The concept of this thesis was conceived from a desire to understand potentially important theories of and relationships between mental health problems, sleep disturbances, and other factors that are not common knowledge. Assessing the birectionality of the relationship between insomnia, depression and anxiety was considered after reading a paper (Johnson, Roth, & Breslau, 2006) that was recommended by Dr Jodie Harris (co-supervisor). Following several meetings with Dr Rachel Roberts (primary supervisor) and Dr Jodie Harris, the topic of this thesis was developed.
I decided to use self-report methods due to funding restrictions. Standardised questionnaires were chosen that assessed insomnia, depression, generalised anxiety disorder (GAD), obsessive compulsive disorder (OCD), panic disorder (PD), separation anxiety disorder (SAD), social phobia (SP) and chronotype. Various potential covariates were also assessed, such as chronotype, total sleep time, total time in bed, academic achievement, exercise, caffeine intake, amount of time spent on homework, amount of time spent working (occupation) outside of school hours, and alcohol and drug use. The decision to include chronotype was based on previous research (Giannotti, et al., 2002; Randler, et al., 2009). The decision to include the other variables was also based on previous research, which showed an association between each construct and insomnia, anxiety and depression (Benvegnù, Fassa, Facchini, Wegman, & Dall'Agnol, 2005; Bootzin & Stevens, 2005; Brand, et al., 2010; Curcio, et al., 2006; Fergusson & Woodward, 2002; Kovacs & Devlin, 1998).

Although chronotype was assessed, other potential covariates were excluded from the analyses for studies 2 and 3. Total sleep time and time in bed were used to tabulate data on delayed sleep phase syndrome (see study 2). Academic achievement was not deemed to have been measured reliably, as only two participants at baseline and one at follow-up reported lower than average grades. The distributions were extremely skewed and the amount of outliers exceeded 25% for exercise, caffeine intake, amount of time spent on homework, amount of time spent working (occupation) outside of school hours, and alcohol and drug use. These results are likely due to the decision to develop only one or two items for the assessment of each variable that were not based on empirically validated questionnaires. The decision to use few and non-validated items rather than empirically validated questionnaires was based on a request from the Department for Education and
Child Development to limit the amount of questions that were asked to the adolescents. Furthermore, the above variables were not the main focus of the thesis.

There was approximately 11% of data missing for the drug and alcohol use variables, as the Department for Education and Child Development would only grant ethics committee approval if students from public schools received a copy of the questionnaire without the drug and alcohol items. Of those who answered the questions, approximately 90% and 98% stated they have never consumed alcohol or illicit drugs, respectively. The lack of identification of alcohol and illicit drug consumption may have resulted from a caveat that was placed on the information sheets stating the following: “the information regarding drug and alcohol use collected in this study could in principle be obtained by court order: that is, it could be required to be handed over to the police and used as evidence in a court of law against your child. However, this is unlikely, and the researchers will make every effort to ensure that any information gathered will remain confidential”. The Human Research Ethics Committee of the University of Adelaide would only grant ethics approval if this caveat was on the information sheets.

The above caveat was a rollover effect of a request from the Human Research Ethics Committee and the requirement of Australian psychologists who conduct research with at-risk populations to identify and follow-up participants with potential mental health disorder. Drs Rachel Roberts and Jodie Harris are both registered clinical psychologists, and adolescents are considered an ‘at-risk’ population. The participants were required to write their names on the top of the questionnaire, and were informed (along with their parents) of the reasons for this. Once data was collected, each questionnaire was locked in a secure location, and data was de-identified as soon as possible.
Adolescents were identified as at risk and requiring identification of follow-up if they reported clinically significant scores in the questionnaire that assessed depression and subtypes of anxiety AND reported thinking about death often or always (the RCADS, see methods section of studies 2 and 3 for specific details regarding how the scores were tabulated). Parents were contacted when students were identified as at risk. They were informed of the findings, and sent a resources sheet containing various treatment options and information sources via email or mail. The treatment options on each resources sheet were based on the sector of Adelaide/South Australia the adolescent resided (e.g., north, south, east, west or central).

2.2. Study 1 - A Systematic Review Assessing Bidirectionality between Sleep Disturbances, Anxiety, and Depression

Study 1 was conducted to give an overview of the current literature, along with the shortcomings and potential future directions of research. Such a study was deemed a useful introductory paper for this thesis, and lead into assessing the bidirectionality of the relationship between insomnia, depression, and anxiety.

Participants of any age and variables of any sleep disturbance were included in study 1, as only one study assessed bidirectionality between insomnia, anxiety and depression during adolescence (Johnson, Roth, & Breslau, 2006), and five independent studies assessed insomnia in various age groups (Buysse et al., 2008; Hasler et al., 2005; Jansson-Fröjmark & Lindblom, 2008; Johnson, Roth, & Breslau, 2006; J. M. Kim, et al., 2009; Morphy, et al., 2007). Another study was originally included in the systematic review that assessed the place of chronic insomnia in the course of development of anxiety and depressive disorders,
and vice-versa (Ohayon & Roth, 2003). However, this study did not use significance testing, and, after a discussion between all authors, was deemed not to adequately assess bidirectionality.

The terms *sleep disturbance* encompassed any variable that was indicative of disrupted sleep, including clinically significant and diagnosed disorders. The terms *sleep problems* portrayed an overall variable consisting of items representing more than one sleep disturbance that was assessed by a study included in the systematic review. For example, a questionnaire that contained items about insomnia and nightmares would be considered as *sleep problems*. Sleep problems was consistently referred to as *childhood sleep problems*, as each sleep problem variable was assessed in children. *Sleep quality* was reflected by variables that assessed how well an individual slept, and often contained insomnia items. *Insomnia* was defined as troubles with sleep initiation, sleep maintenance, night-time awakenings, and sleep latency following night-time awakenings. Some articles that assessed insomnia also assessed daytime functioning. Although not specifically a sleep disturbance variable, *time in bed* was included in the systematic review, as lower amounts of time in bed suggests sleep loss.

### 2.3. Study 2 – The Independent Relationships between Insomnia, Depression, Subtypes of Anxiety, and Chronotype during Adolescence

Study 2 was a cross-sectional study of 318 high school students that used self-report measures. There were two main aims; firstly, to assess the relationship between the main variables of the thesis at baseline; and secondly, to discover whether or not chronotype predicts insomnia, depression and subtypes of anxiety once covariates are controlled.
Chronotype was deemed to potentially predict insomnia, depression and subtypes of anxiety, as previous studies have found that chronotype was correlated to each variable during adolescence (Ferber, 1990; Giannotti, et al., 2002; Randler, et al., 2009; Russo, Bruni, Lucidi, Ferri, & Violani, 2007). Study 2 originally assessed the mediation effects of chronotype on the relationship between insomnia and depression above and beyond anxiety, and insomnia and each subtype of anxiety above and beyond depression. However, a reviewer for study 2 suggested that such an investigation lacked theoretical support, and hence suggested that moderation or prediction be assessed. The authors decided on prediction to be consistent with study 3 and the overall aim of the thesis.

The decision to use generalised linear equations to analyse the aims of study 2 was based on the recommendation of a statistician at the University of Adelaide (statistical justifications can be found in the methods section of the study). Furthermore, although outliers were found, the 5% trimmed mean for insomnia, depression, subtypes of anxiety and chronotype subscales were very similar to the actual means (differences ranged from .09 to .26), suggesting the outliers would have a minimal effect on the results. Indeed, sensitivity analyses showed this to be the case. Therefore, these data were retained (Pallant, 2011).

Less than 2% of the data from study 2 was missing for the insomnia, depression, subtypes of anxiety and chronotype scales. Although some evidence suggests that missingness may have been non-random, the sample size was large and the missing values were very small. Therefore, on the recommendation of Tabachnick and Fidell (2007), participants with missing data were only excluded for the analyses that assessed the
variables containing their missing data and retained for the analyses where all data was present.

2.4. Study 3 – Bidirectional relationships between insomnia and depression, and insomnia and subtypes of anxiety during adolescence: does chronotype effect these relationships?

Study 3, a longitudinal report of 255 high school students, was the main paper for this thesis. The aims were to investigate the bidirectionality of the association between insomnia, depression and subtypes of anxiety, and the effects of chronotype on these relationships. Chronotype was used as a predictor for study 3.

Bootstrap step-wise regression analyses were used rather than generalised linear equations in study 3 after consulting a statistician. Different analyses were needed, as study 3 was longitudinal and study 2 was cross-sectional. The statistician noted that because mediation analyses were not conducted for study 3, deciding on the statistical analysis to use should be based on whether cluster variables (schools in this case) have a large enough effect on the outcome variables. He recommended not accounting for clustering if schools explain less than 5% of the outcome variables, but if they did, further tests were to be conducted. The amount of variance explained by schools for each outcome variable was below 4%, with most below 2%, therefore suggesting minimal clustering.

The amount of missing data for study 3 was a little higher than that of study 2, but still below 3% for depression, each anxiety subtype and chronotype, and below 7% for insomnia (approximately 6.6%). The evidence suggested that missing data was random, while the
sample size was large and the amount of missing values was very low. Therefore, participants with missing data were only excluded from the analyses when they had missing data for all major variables (i.e., insomnia, anxiety subtypes, depression and chronotype) (Tabachnick & Fidell, 2007).

Outliers were also found in study 3, and the 5% trimmed means for the outcome variables were slightly higher than those found in study 2. However, as suggested by Pallant (2011), the outliers were retained, as the differences between the 5% trimmed means and original means were still very low (ranging from 0.12 to 0.45). These findings, paired with the sensitivity analyses, suggested that the outliers had a negligible impact on the results.

Originally, there was a debate regarding the length of time between baseline and follow-up for study 3. Bidirectionality studies have typically used 12 or 24 month intervals between baseline and follow-up (Jansson-Fröjmark & Lindblom, 2008; Kaneita, et al., 2009; J. M. Kim, et al., 2009; Meijer, et al., 2010), but the current study used a six month interval. This makes for a more reliable study, as potential confounders such as schools, classrooms, friends and lifestyle (e.g., driving and dating) is more likely to remain constant. It could be argued that seasonal affective disorders are more likely to bias the results when using a six month follow-up, as baseline and follow-up would occur at opposing seasons. However, studies have found low prevalence rates of winter seasonal affective disorders within Australia [3.65% (Kasof, 2009), 1.7% (Morrissey, Raggatt, James, & Rogers, 1996), 0.7% and 0.5% (Murray, 2004)], suggesting that seasonal affective disorders are not expected to greatly impact the results. Furthermore, such prevalence rates are likely to be exaggerated; the Seasonal Pattern Assessment Questionnaire was used by each study to assess seasonal affective disorders, which has been found to overestimate the prevalence rate of seasonal
affective disorders compared to clinical assessments (for a discussion see Mersch, Middendorp, Bouhuys, Beersma, & Van Den Hoofdakker, 1999). Finally, summer seasonal affective disorders are likely to occur in tropical climates (Morrissey, et al., 1996) and therefore should not affect the study population, because South Australian weather resembles a Mediterranean climate.

The choice of a 6-month follow-up had a repercussion on the statistical analyses. Although study 1 argued that outcome variables must be controlled at baseline to accurately assess bidirectional relationships, it was deemed inappropriate to control for baseline outcome variables due to the 6-month follow-up. Firstly, symptoms and disorders of insomnia, depression and subtypes of anxiety are often chronic (see chapter 1 for a review of the chronicity of each disorder). Secondly, 6 months is unlikely to be enough time for many new cases of clinically significant insomnia and mental health problems to develop either independently or as a result of one another, although some new cases may arise. Indeed, Pearson’s correlation analyses between baseline and follow-up variables showed $r$ values that ranged between .66 and .78 for insomnia, depression, generalised anxiety disorder, separation anxiety disorder, and chronotype, and an $r$ value of .61 for obsessive compulsive disorder and .59 for panic disorder. Furthermore, paired samples $t$-tests did not find a significant difference between baseline and follow-up insomnia, depression or anxiety subtypes, except for PD. However, the Cohen’s $d$ statistic was small in magnitude ($d= 0.12$) (Cohen, 1992), suggesting the change was unlikely to be meaningful. Moreover, Baglioni, et al. (2011) stated that a long-term evaluation of the relationship between insomnia and depression should have a follow-up of no less than a 12 month. Thirdly, a minimum criterion of GAD is the presentation of symptoms more often than not for at least 6 months. The
current thesis did assess clinically significant symptoms of GAD, but this assessment was based on, and has been validated against (see chapters 4 and 5 for a review of the validation literature) the DSM-IV diagnostic criteria (American Psychiatric Association, 2000). Therefore, the development of clinically significant GAD symptoms is likely to reflect the development of GAD that is diagnosed according to the DSM-IV diagnostic criteria. Indeed, Mathyssek et al. (2013) psychometric evaluation of the Revised Children’s Anxiety and Depression Scale (RCADS, the inventory that was used to assessed symptoms of anxiety subtypes in this research project) suggests that measured stability or changes of anxiety symptoms over time are highly indicative of true stability or changes in anxiety levels over time. Nevertheless, the authors recognise the validity of the argument for controlling baseline outcome variables, and have therefore presented such the results in an appendix in chapter 7.

2.5. Sample size rationale for studies 2 and 3

Tabachnick and Fidell (2007) recommended the following equation to attain a sample size that would yield adequate power ($\alpha = .05$, $\beta = .20$), as dependent variables were expected to be skewed (which was the case) and possibly small in magnitude:

$$N \geq \left( \frac{8}{f^2} \right) + (m - 1)$$

Where $f^2 = R^2/(1 - R^2)$, and $m$ = number of predictors.

An examination of the recent literature found that effect sizes ($f^2$) generated by studies that assessed the bidirectionality of the relationship between anxiety, depression and sleep disturbances ranged from 0.02 - 0.33 (Gregory & O'Connor, 2002; Gregory, et al., 2009; Jansson-Fröjmark & Lindblom, 2008; Kaneita, et al., 2009; J. M. Kim, et al., 2009), with the
majority between .04 and .08. An $f^2$ statistic of .03, considered to be a small effect size (Cohen, 1992), was used to calculate the target sample size to be conservative.

$$N \geq \left( \frac{8}{.03} \right) + (4 - 1)$$

$$N \geq 228.57 + 3$$

$$N \geq 231.57$$

Therefore, approximately 232 participants were needed at follow up to achieve adequate power. A further 25% was added to the target sample size at baseline to account for dropouts. Therefore, the target sample size was 290 at baseline.

2.6. Summary

The current chapter described information that was important to but beyond the scope of the manuscripts due to journal word limits. The reasons for conducting each study were discussed, along with the methodological overlap and differences between the manuscripts, and reasons for important decisions such as sample size.

The next chapter presents the first study entitled ‘A systematic review assessing bidirectionality between sleep disturbances, anxiety and depression’. It follows a normal structure for a systematic review, which begins with an abstract, followed by an introduction, methods, results and discussion. The main difference between the structure of a systematic review and an original article is in the methods section, where a systematic review outlines the assessment of quality for each study that is included in the analyses.
Chapter 3: Study 1

A Systematic Review assessing Bidirectionality between Sleep Disturbances, Anxiety and Depression.

Alvaro, P.K., Roberts, R.M., & Harris, J.K.

School of Psychology, University of Adelaide

Published: 2013, Sleep, 36 (7), 1059 – 1068.

Pasquale Alvaro (PhD Candidate)

I collected data, performed each synthesis, interpreted data, wrote the manuscript and acted as the corresponding author. I also made the decisions on what data and arguments to present in this paper. I later made the revisions to the paper based on the reviewers’ comments.

Date: 25/08/14
Rachel Roberts (Co-Author)

I was the primary supervisor for the research project that led to this paper, so was involved in the design of the study described in the paper and discussions of results, particularly in the case of adolescent literature. Mr Alvaro was responsible for writing the paper, and I was responsible for providing editorial comments and advice on making changes following review. I hereby give my permission for this paper to be included in Mr Alvaro’s submission for the degree of PhD at the University of Adelaide.

Date: 25/08/14

Rachel Roberts
Co-author

Jodie Harris (Co-Author)

I was the co-supervisor for the research project that led to this paper. I was involved in the design of the study described in the paper and discussions of results, particularly where the sleep variables were concerned. I also provided editorial comments and advice on making changes following review. I hereby give my permission for this paper to be included in Mr Alvaro’s submission for the degree of PhD at the University of Adelaide.

Date: 25/08/14

Jodie Harris
Co-author
Sleep, v. 36(7), pp. 1059-1068

NOTE: 
This publication is included on pages 66-92 in the print copy of the thesis held in the University of Adelaide Library. 

It is also available online to authorised users at: 

http://doi.org/10.5665/sleep.2810
Chapter 4: Study 2

The independent relationships between insomnia, depression, subtypes of anxiety, and chronotype during adolescence.

Alvaro, P.K., Roberts, R.M., & Harris, J.K.

School of Psychology, University of Adelaide

Published: 2014, Sleep Medicine, 15 (8), 934 – 941.

Pasquale Alvaro (PhD Candidate)

I collected data, performed each analysis, interpreted data, wrote the manuscript and acted as the corresponding author. I also made the decisions on what data and arguments to present in this paper. I later made the revisions to the paper based on the reviewers’ comments.

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X
Jodie Harris
Co-author
Date: 25/08/14
4.1. Abstract

4.1.1. Objectives

This study investigated the independent effects of depression and subtypes of anxiety on insomnia, and vice-versa, and the independent effect of chronotype on insomnia, depression and subtypes of anxiety.

4.1.2. Methods

Three-hundred and eighteen South Australian high school students from grades 7 to 11 (age range 12-18, mean 14.97 ± 1.34) participated in this cross-sectional study. Validated self-report questionnaires were used to assess insomnia, depression, subtypes of anxiety and chronotype.

4.1.3. Results

After confounder variables were controlled, insomnia predicted depression and panic disorder PD, whereas insomnia was predicted by depression and generalised anxiety disorder (GAD). Obsessive compulsive disorder (OCD), separation anxiety (SAD) and social phobia (SP) were not significantly related to insomnia. Eveningness predicted the models where depression and PD predicted insomnia and vice-versa. Eveningness also predicted the models when insomnia was predicted by OCD, SAD and SP.

4.1.4. Conclusions

Insomnia independently predicts depression and is predicted by depression and GAD, but not other forms of anxiety. The independent prediction of insomnia on panic disorder
(PD), is unlikely to be clinically significant. Chronotype independently predicts insomnia and depression, but not subtypes of anxiety. Theoretical and clinical implications are discussed.

4.2. Introduction

Insomnia is a very common sleep problem in the general population, with a lifetime prevalence rate of approximately 11% in adolescents aged 13 to 16 (Johnson, Roth, Schultz, et al., 2006). Recent studies have consistently found an association between insomnia and depression, and insomnia and anxiety disorders in adolescent populations (Gregory & O’Connor, 2002; Johnson, Roth, & Breslau, 2006), which is expected given that the presence of insomnia is a possible criteria for the diagnosis of depression and various anxiety disorders, and these disorders contain overlapping neurobiological, psychological and social risk-factors (Casey, et al., 2008; Holmes, 2003; Kaneita, et al., 2009; Lipton, et al., 2008; Nestler & Carlezon, 2006; Peroutka, 1998; Tseng & O’Donnell, 2007; Yoshioka, et al., 1996). Insomnia comorbid with anxiety or depression can further intensify the problematic outcomes associated with each disorder, such as alcohol and drug abuse during adolescence (Johnson & Breslau, 2001).

Despite their well-documented association, various aspects and mechanisms of the relationships between insomnia and anxiety, and insomnia and depression are unclear. Firstly, the significance of the relationship between insomnia and anxiety may differ across anxiety disorders. A recent study found an association between insomnia and separation anxiety disorder, and insomnia and generalised anxiety disorder, but not between insomnia and social anxiety disorder (Alfano, et al., 2007). Indeed, some associations between sleep difficulties and anxiety disorders (generalised anxiety disorder) are expected given the symptom overlap for diagnosis. Another study found that youths with generalised anxiety
disorder reported higher rates of trouble sleeping overall than youths with separation anxiety disorder, social phobia, and obsessive compulsive disorder (Alfano, Pina, Zerr, & Villalta, 2010). Secondly, the mediated and independent effects of insomnia on anxiety or depression, and vice-versa, remain unclear. Anxiety may mediate the relationship between insomnia and depression, while depression may mediate the relationship between insomnia and anxiety due to the common underlying neurobiological, psychological and social factors mentioned above. Finally, chronotype, defined as an individual’s natural inclination for mornings (morningness) or evenings (eveningness), could uniquely predict insomnia, anxiety and depression. Recent studies suggest that an eveningness chronotype predicts higher levels of insomnia, anxiety and depression during adolescence (Ferber, 1990; Giannotti, et al., 2002; Randler, et al., 2009; Russo, et al., 2007). These studies, however, have yet to demonstrate whether eveningness predicts insomnia beyond depression and anxiety, anxiety beyond insomnia and depression, or depression beyond insomnia and anxiety. Such findings would suggest that eveningness is an independent risk factor for insomnia, anxiety and depression. These findings would be particularly important, because adolescents tend to develop a preference for evenings due to circadian rhythm and environmental changes (Crowley, et al., 2007), which sometimes develops into and is the main symptom of delayed sleep phase syndrome (American Academy of Sleep Medicine, 2005). This syndrome affects approximately 8% of adolescents (Saxvig, et al., 2012), and has been associated with insomnia, anxiety and depression (Reid et al., 2012).

This study, therefore, adds to the previous literature by investigating in one study the independent effect of depression and various types of anxiety on insomnia, and vice-versa, and the effect of chronotype on insomnia, depression and subtypes of anxiety that is
independent from other predictors. The anxiety subtypes assessed in the current study include Generalised Anxiety Disorder (GAD), Obsessive Compulsive Disorder (OCD), Panic Disorder (PD), Separation Anxiety Disorder (SAD) and Social Phobia (SP). It was hypothesised that insomnia will be independently related to some but not other mental health problems, in particular, to depression, GAD and SAD, but not SP. It was also hypothesised that chronotype will independently predict insomnia, depression, and subtypes of anxiety above and beyond other predictors. The independent effect was defined as the amount of variance of a dependent variable (Y) that is explained by an independent variable (X) after controlling for confounder variables (C). Insomnia, anxiety subtypes and depression were used as predictor and outcome variables, as recent studies have suggested that insomnia, anxiety and depression are bidirectionally related (Alvaro, Roberts, & Harris, 2013). Understanding the pathways of the relationship between insomnia and anxiety subtypes, and insomnia and depression can inform public health campaigns and clinical interventions for each disorder, and also enhance the understanding of the interaction between these disorders.

4.3. Method

4.3.1. Participants

Three-hundred and eighteen South Australian secondary school students aged 12–18 (M= 14.96, SD= 1.34) participated in the study. One-hundred and sixty-four (51.6%) students were male and 154 (48.4%) were female. Nine students were in grade 7, 102 were in grade 8, 66 in grade 9, 52 in grade 10 and 89 in grade 11. The study was voluntary, and required student and parental consent for participation. Participants were eligible for this study if their parents consented, were in grades 7 to 11, and were fluent in English. This study was approved by the Human Research Ethics Committee (HREC) from the University of Adelaide,
the Department for Education and Child Development (DECD), and Catholic Education South
Australia (CESA).

4.3.2. Measurements

A questionnaire composed of several inventories was used to assess adolescent sleep
and mental health. Demographic questions include date-of-birth, gender, and
socioeconomic status as assessed by postcode (Australian Bureau of Statistics, 2008b).
Personal questions such as previous sleep or mental-health problems, previous therapy for
sleep or mental health problems, previous or current disabilities/chronic illnesses (e.g.,
asthma, diabetes, deafness, etc), current medications that may affect sleep or mental health
and the frequency of drug and alcohol consumption were adaptations from the School Sleep
Habits Survey (SSHS) (Wolfson & Carskadon, 1998). Total Sleep time, bed time and rise time
on weekdays and weekends were also reported, the latter two of which were used to
calculate total bed time. These questions were asked to give an account of the general
characteristics of the sample.

Insomnia was measured by the Insomnia Severity Index (ISI) (Morin, 1993), a 7-item
inventory that assesses the severity of subjective symptoms and consequences of insomnia
based on the DSM-IV (American Psychiatric Association, 2000). Each item was scored on a 0
to 4 Likert scale. Total scores were calculated by the sum of each item and ranged from 0 to
28. Higher scores indicate more severe insomnia. Morin (1993) provides a scoring guideline:
0–7 no clinically significant insomnia, 8–14 subthreshold insomnia, 15–21 moderate clinical
insomnia, and 22–28 severe clinical insomnia. The symptoms assessed included difficulty
falling sleep, difficulty staying asleep, and problems waking up too early, while the
consequences assessed included impaired quality of life, worry/distress about current sleep
patterns, and perceived interference of sleep problems with daily life. Although designed for adults, the ISI has been widely used in the adolescent population (Brand et al., 2011; Luo, Zhang, & Pan, 2012; Short, Gradisar, Lack, & Wright, 2013). Furthermore, a recent study has validated the ISI in an adolescent population, reporting significant correlations with clinical ratings of insomnia, the Sleep-Wake Habits Questionnaire, General Mental-Health Questionnaire, Epworth Sleepiness Scale, smoking habits, alcohol use, number of naps per week, and academic performance (Chung, Kan, & Yeung, 2011). A Cronbach’s alpha of 0.83, and a 2-week test-retest reliability of 0.79 for the ISI in an adolescent population (Chung, et al., 2011) were also reported.

The Morningness-Eveningness Scale for Children (MES) (Carskadon, Vieira, & Acebo, 1993), a 10-item adaptation of the Composite Scale of Morningness (Smith, Reilly, & Midkiff, 1989), was used to assess adolescents’ orientation towards Morning and Evening chronotypes. Seven items are scored on a Likert scale from 1 to 4, while 3 items are scored on a Likert scale from 1 to 5. Total scores are calculated by the sum of each item and range from 10 to 42. Lower scores indicate a tendency towards eveningness. The MES successfully discriminates between morningness and eveningness in adolescents (Díaz-Morales, De León, & Sorroche, 2007). In accordance with previous research (Giannotti, et al., 2002; Russo, et al., 2007), evening and morning-types were defined as below the 10th and above the 90th percentile, respectively, and scores in between were identified as neither types (cut-off scores were below 20 for eveningness and above 33 for morningness). Previous studies have reported good internal consistency, with Cronbach’s \( \alpha \) of 0.73 (Giannotti, et al., 2002), 0.82 (Díaz-Morales, et al., 2007), and 0.82 (Warner, Murray, & Meyer, 2008) in Italian, Spanish, and Australian adolescents respectively. Good test-retest reliability (0.78) (S. Kim, Dueker,
Hasher, & Goldstein, 2002) and external validity have been reported (Díaz-Morales, et al., 2007), and the MESC has been shown to predict daytime functioning, academic achievement and various behavioural outcomes in adolescents (Giannotti, et al., 2002; Warner, et al., 2008). Two items were altered to keep the language consistent with the Australian population and the age of the sample. First, the phrase “gym class” was changed to “Sports class”. Second, the item “Your parents have decided to let you set your own bed time. What time would you pick?” was changed to “What time would you prefer to go to bed?”

Adolescents who met the following criteria were deemed to likely suffer from delayed sleep phase syndrome (Johnson, Roth, Schultz, et al., 2006; Sivertsen et al., 2013); a minimum of 1-hour shift in bed and rise times from weekdays to the weekend; moderate, severe or very severe complaints of difficulty falling asleep; no or mild complaint of difficulty maintaining sleep; AND not at all easy to wake up in the morning.

Subtypes of anxiety and depression were assessed by the Revised Child Anxiety Depression Scale (RCADS) (Chorpita, Yim, Moffitt, Umemoto, & Francis, 2000), a 47-item self-report questionnaire that is an adaption of the Spence Children’s Anxiety Scale (Spence, 1997) and corresponds to diagnostic categories of DSM-IV. Each item is scored on a 0 to 3 Likert scale, with higher scores corresponding to more severe depression or anxiety. Subscales are provided for Generalised Anxiety Disorder (GAD, 6 items, scores ranging from 0 to 18), Panic Disorder (PD, 9 items, scores ranging from 0 to 27), Obsessive Compulsive Disorder (OCD, 6 items, scores ranging from 0 to 18), Separation Anxiety Disorder (SAD, 7 items, scores ranging from 0 to 21), Social Phobia (SP, 9 items, scores ranging from 0 to 27), and Major Depressive Disorder (MDD, 10 items, scores ranging from 0 to 30). An overall scale for anxiety (37 items, scores ranging from 0 to 111) is also provided. Scales are
calculated by the sum of each item. The RCADS users guide [available on the University of California, Los Angeles website (Chorpita, 2011)] converted raw scores into standardised T scores, where T scores between 65 and 69 indicate borderline clinical threshold and T scores ≥ 70 indicate above clinical threshold. A recent study reported the following Cronbach’s α in Hawaiian adolescents: SP, α=0.81; PD, α=0.85; GAD, α=0.80; MDD, α=0.76; SAD, α=0.78; and OCD, α=0.71 (Chorpita, et al., 2000). The same study provided strong support for the structural, convergent and discriminant validity of the RCADS. The RCADS has also been validated in Australian adolescents; De Ross and colleagues (2002) provided support for the internal consistency for MDD, and anxiety overall, and anxiety subscales. Good convergent validity was also demonstrated (2002) with moderate to strong correlations between the subscales of RCADS with scores on the Revised Manifest Anxiety Scale (RCMAS) (Reynolds & Richmond, 1985) and the Children’s Depression Inventory (CDI) (Kovacs, 1981). Indeed, the RCADS has been extensively used in the adolescent population (Austin & Chorpita, 2004; Weems & Costa, 2005), including in studies that have assessed the relationship between sleep problems, anxiety and depression (Alfano, et al., 2009).

4.3.3. Procedure

Every secondary school within a 40km radius of the Adelaide CBD that was listed by the Department for Education and Child Development (DECD) in South Australia or in the 2010 Annual Report of the Advisory Committee on Non-Government Schools in South Australia (n= 71 within catchment area) was approached to participate in the study. Each principal was sent a letter that invited the school to participate and outlined the study details, along with the relevant documents including the questionnaire, information letters to students and parents, and consent forms. Principals who did not respond to the letter
received a follow-up phone call or email. Once principals agreed to participate, information letters and consent forms for the students and parents were given to each student in selected grades. Students were asked to return consent forms to their home-group teachers, and those who did not were unable to participate. Questionnaires were completed in class time under the supervision of teachers. Eight secondary schools in South Australia participated in the current study.

4.3.4. Statistical analyses

Descriptive statistics were reported using means and standard deviations, or numbers and percentages. Spearman’s rho (Spearman, 1910) was used to calculate correlations to account for the slightly skewed data. Direct effects were assessed when a predictor variable was correlated with an outcome variable.

Two analyses were conducted to assess the independent effect of insomnia on depression or subtype of anxiety, and vice-versa, and the unique effect of chronotype on insomnia, depression and subtypes of anxiety. One analysis used insomnia, chronotype, and depression, an anxiety subtype or anxiety overall as the predictor variables, and an anxiety subtype or depression as the outcome variable (Figure 5). The other analysis used insomnia as the outcome variable, and depression or an anxiety subtype, chronotype and anxiety overall or depression as predictor variables (Figure 5). When anxiety subtypes were analysed, chronotype and depression were assessed as predictors. When depression was analysed, chronotype and an anxiety overall variable were used as predictors. The overall anxiety variable was used to control for all anxiety symptoms.
Figure 5. Steps for analyses.
Generalised Estimating Equations (GEE) were used to assess the above analyses. GEE accounts for clustered and skewed data (Galbraith, Daniel, & Vissel, 2010) that commonly occur when data are collected from schools. GEE also produces regression coefficients (β) and confidence intervals (CI). β represents the magnitude of the effects of X on Y, and is used to generate the coefficients of each unique independent effect. The independent effect of X on Y is represented by the β that is calculated after each predictor is accounted for CIs are used for significance testing, where CIs that contain 0 fail to reject the null hypothesis.

Sample size analysis for the GEE was based on multiple regression, as both apply to the class of generalised linear models and produce β coefficients. The difference between GEE and multiple regression is that GEE generates robust standard errors that account for clustered data (Galbraith, et al., 2010), and hence should have more power to detect an effect when analysing clustered data.

4.4. Results

4.4.1. Descriptive statistics

Tables 6, 7 and 8 report descriptive statistics for demographic information, sleep and mental health variables, and frequencies of clinically significant and sub-threshold mental health and insomnia cases. Approximately 25% of adolescents reported suffering from past sleep or mental health problems, while approximately 17% reported previous treatment for sleep or mental health problems. Approximately 20% reported other medical issues, while 14% reported previous or ongoing treatment for such issues. Insomnia was the most frequently identified clinically significant problem (11.19%), whereas MDD was the most common mental health problem (8.39%).
<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Self-report past mental health symptoms</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Depression</td>
<td>22</td>
<td>6.9</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>21</td>
<td>6.6</td>
<td></td>
</tr>
<tr>
<td>Sleep problems</td>
<td>25</td>
<td>7.9</td>
<td></td>
</tr>
<tr>
<td>Depression, Anxiety</td>
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<td>1.3</td>
<td></td>
</tr>
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<td>Depression, Anxiety and Insomnia</td>
<td>5</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
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<td>8</td>
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<td></td>
</tr>
<tr>
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<td>233</td>
<td>73.3</td>
<td></td>
</tr>
<tr>
<td><strong>Self-report past treatment for symptoms of</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>depression, anxiety, sleep problems</td>
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<td></td>
<td></td>
</tr>
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<td>11</td>
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<td></td>
</tr>
<tr>
<td>Counsellor</td>
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<td>7.5</td>
<td></td>
</tr>
<tr>
<td>GP</td>
<td>5</td>
<td>1.6</td>
<td></td>
</tr>
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<td></td>
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<td><strong>Permanent disabilities or illnesses</strong></td>
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<td></td>
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<tr>
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</tr>
<tr>
<td>None</td>
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<td>80.2</td>
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</tr>
<tr>
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<td>No</td>
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</tr>
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<td>Asthma medication e.g., Ventolin puffer</td>
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<tr>
<td>ADHD medication</td>
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<tr>
<td>Sleep medication</td>
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</tr>
<tr>
<td>Prescribed antidepressants</td>
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<td>0</td>
<td></td>
</tr>
<tr>
<td>Non-prescribed antidepressants or sleep medication</td>
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<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>12</td>
<td>3.7</td>
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<td><strong>Alcohol use</strong></td>
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<td><strong>Drug use</strong></td>
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<td></td>
</tr>
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<td>1.6</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>279</td>
<td>87.7</td>
<td></td>
</tr>
<tr>
<td>Missing data</td>
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<td>10.7</td>
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</tr>
<tr>
<td><strong>Subjective sleep sufficiency</strong></td>
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<td></td>
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</tr>
<tr>
<td>Too little sleep</td>
<td>143</td>
<td>44.9</td>
<td></td>
</tr>
<tr>
<td>Enough sleep</td>
<td>170</td>
<td>53.4</td>
<td></td>
</tr>
<tr>
<td>Too much sleep</td>
<td>5</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td><strong>Frequency of sufficient sleep</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Never</td>
<td>7</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Rarely</td>
<td>50</td>
<td>15.7</td>
<td></td>
</tr>
<tr>
<td>Sometimes</td>
<td>112</td>
<td>35.2</td>
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</tr>
<tr>
<td>Usually</td>
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<td>41.8</td>
<td></td>
</tr>
<tr>
<td>Always</td>
<td>16</td>
<td>5.0</td>
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</tr>
<tr>
<td><strong>Chronotype</strong></td>
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<td></td>
</tr>
<tr>
<td>Eveningness</td>
<td>37</td>
<td>11.64</td>
<td></td>
</tr>
<tr>
<td>Neither</td>
<td>252</td>
<td>79.25</td>
<td></td>
</tr>
<tr>
<td>Morningness</td>
<td>26</td>
<td>8.18</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>3</td>
<td>0.94</td>
<td></td>
</tr>
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</table>
Table 7

Descriptive statistics for sleep and mental health variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Missing data</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
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</thead>
<tbody>
<tr>
<td>Insomnia</td>
<td>312</td>
<td>6</td>
<td>7.63</td>
<td>5.28</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>Major Depressive Disorder</td>
<td>314</td>
<td>4</td>
<td>7.62</td>
<td>4.69</td>
<td>0</td>
<td>28</td>
</tr>
<tr>
<td>Generalised Anxiety Disorder</td>
<td>314</td>
<td>4</td>
<td>5.63</td>
<td>3.2</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Obsessive Compulsive Disorder</td>
<td>313</td>
<td>5</td>
<td>4.36</td>
<td>3.01</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>314</td>
<td>4</td>
<td>6.55</td>
<td>4.37</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td>Separation Anxiety</td>
<td>314</td>
<td>4</td>
<td>3.68</td>
<td>3.15</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Social Phobia</td>
<td>314</td>
<td>4</td>
<td>6.69</td>
<td>4.4</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>Morningness-Eveningness</td>
<td>315</td>
<td>3</td>
<td>27.17</td>
<td>5.41</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>Total Sleep Time weekday</td>
<td>313</td>
<td>5</td>
<td>8.31</td>
<td>1.27</td>
<td>4</td>
<td>11.5</td>
</tr>
<tr>
<td>Total Sleep Time weekend</td>
<td>314</td>
<td>4</td>
<td>9.43</td>
<td>1.72</td>
<td>4.5</td>
<td>15</td>
</tr>
<tr>
<td>Total Time in Bed weekday</td>
<td>316</td>
<td>2</td>
<td>8.7</td>
<td>1.1</td>
<td>4</td>
<td>11.5</td>
</tr>
<tr>
<td>Total Time in Bed weekend</td>
<td>311</td>
<td>7</td>
<td>9.67</td>
<td>1.48</td>
<td>3.5</td>
<td>13.5</td>
</tr>
</tbody>
</table>

Table 8

Number and frequency of clinically significant cases

<table>
<thead>
<tr>
<th></th>
<th>Depression</th>
<th>GAD</th>
<th>OCD</th>
<th>PD</th>
<th>SAD</th>
<th>SP</th>
<th>Insomnia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical case frequency</td>
<td>29</td>
<td>21</td>
<td>7</td>
<td>14</td>
<td>17</td>
<td>15</td>
<td>39</td>
</tr>
<tr>
<td>Total case frequency</td>
<td>314</td>
<td>314</td>
<td>313</td>
<td>314</td>
<td>314</td>
<td>314</td>
<td>312</td>
</tr>
<tr>
<td>Clinical frequency</td>
<td>9.24%</td>
<td>6.69%</td>
<td>2.24%</td>
<td>4.46%</td>
<td>5.41%</td>
<td>4.78%</td>
<td>12.50%</td>
</tr>
</tbody>
</table>

GAD= Generalised Anxiety Disorder, PD= Panic Disorder, OCD= Obsessive Compulsive Disorder, SAD= Separation Anxiety Disorder, SP= Social Phobia.

Correlations are reported in Table 9. ISI was moderately to highly correlated with each subscale from the RCADS. The results also depicted small to medium correlations between chronotype and each subscale from the RCADS, except for GAD, where no significant correlation was found. The difference between total sleep time on weekends and weekdays was significantly correlated with an eveningness chronotype, insomnia, depression, PD, OCD, and SP.

Table 9

Spearman's rho correlations between anxiety, subtypes of anxiety, depression, insomnia and chronotype

<table>
<thead>
<tr>
<th>Anxiety overall</th>
<th>Depression</th>
<th>GAD</th>
<th>PD</th>
<th>OCD</th>
<th>SAD</th>
<th>SP</th>
<th>Insomnia</th>
<th>CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety overall</td>
<td>1</td>
<td>0.744**</td>
<td>0.790**</td>
<td>0.800**</td>
<td>0.797**</td>
<td>0.843**</td>
<td>0.866**</td>
<td>0.580**</td>
</tr>
<tr>
<td>Depression</td>
<td>1</td>
<td>0.484**</td>
<td>0.683**</td>
<td>0.693**</td>
<td>0.578**</td>
<td>0.659**</td>
<td>0.672**</td>
<td>0.414**</td>
</tr>
<tr>
<td>GAD</td>
<td>1</td>
<td>0.537**</td>
<td>0.573**</td>
<td>0.649**</td>
<td>0.590**</td>
<td>0.414**</td>
<td>0.030</td>
<td></td>
</tr>
<tr>
<td>PD</td>
<td>1</td>
<td>0.637**</td>
<td>0.643**</td>
<td>0.593**</td>
<td>0.503**</td>
<td>0.218**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OCD</td>
<td>1</td>
<td>0.619**</td>
<td>0.597**</td>
<td>0.457**</td>
<td>-0.193**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAD</td>
<td>1</td>
<td>0.659**</td>
<td>0.447**</td>
<td>0.178**</td>
<td>-0.222**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SP</td>
<td>1</td>
<td>0.496**</td>
<td>0.447**</td>
<td>0.178**</td>
<td>-0.222**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
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<td>-0.438**</td>
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<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**. Correlation is significant at the 0.01 level (2-tailed).

GAD= Generalised Anxiety Disorder, PD= Panic Disorder, OCD= Obsessive Compulsive Disorder, SAD= Separation Anxiety Disorder, SP= Social Phobia.
Generalised estimation equations were run with and without participants who were identified with delayed sleep phase syndrome tendencies (complete data available for 300 participants, n= 18, percentage= 6%). No differences were found, and therefore all available data were retained.

4.4.2. Depression and Insomnia

The depression scale contained an item similar to insomnia, which was thought to possibly inflate the regression coefficients of the relationship between insomnia and depression. The overall pattern of results remained the same when analyses were conducted with and without the insomnia-based MDD item. Therefore, the original MDD scale was retained.

The analyses of depression and insomnia included 302 participants. Depression had a significant independent effect on insomnia (β= 0.526, 95% CI= 0.406 - 0.645), and vice-versa (β= 0.3767, 95% CI= 0.276 - 0.477). Chronotype and anxiety uniquely predicted insomnia (chronotype β= -0.210, 95% CI = -0.306 – -0.113; anxiety β= 0.040, 95% CI = 0.0017 – 0.063) and depression (chronotype β = -0.103, 95% CI = -0.169 – -0.036; anxiety β= 0.167, 95% CI= 0.137 – 0.196).

4.4.3. GAD and Insomnia

Three-hundred and seven participants were included in the analyses for the relationship between GAD and insomnia. Chronotype and GAD were not associated before potential confounders were controlled. Therefore, chronotype was not used to predict GAD.

Significant independent effects were found when GAD predicted insomnia (β= 0.258, 95% CI= 0.025 - 0.336) but not when insomnia predicted GAD (β= 0.116, 95% CI= -0.005 -
Chronotype and depression predicted insomnia (chronotype β = -0.227, 95% CI = 0.030 - 0.124; depression β = 0.522, 95% CI = 0.385 – 0.659), and depression predicted GAD (depression β = 0.245, 95% CI = 0.158 – 0.345).

4.4.4. OCD and Insomnia

The analyses for the relationship between OCD and insomnia contained 303 participants. A significant independent effect was not found when OCD predicted insomnia (95% CI = -0.117 – 0.080) nor when insomnia predicted OCD (95% CI = -0.050 – 0.034). Depression and chronotype predicted insomnia (depression β = 0.618, 95% CI = 0.499 – 0.738; chronotype β = -0.194, 95% CI = -0.286 – -0.103), whereas depression but not chronotype uniquely predicted OCD (depression β = 0.400, 95% CI = 0.351 – 0.449; chronotype 95% CI = -0.041 – 0.096).

4.4.5. Panic Disorder and Insomnia

The sample size for the analyses of the relationship between PD and insomnia contained was 304. An independent significant effect was found when insomnia predicted PD (independent β = 0.064, 95% CI = 0.007 – 0.121) but not when PD predicted insomnia (95% CI = -0.003 – 0.201). Depression and chronotype predicted insomnia (depression β = 0.562, 95% CI = 0.463 – 0.661; chronotype β = -0.199, 95% CI = -0.290 – -0.108), but depression and not chronotype predicted PD (depression β = 0.464, 95% CI = 0.395 – 0.532; chronotype 95% CI = -0.010 – -0.081).

4.4.6. Separation Anxiety and Insomnia

Three hundred and three participants were used for the analyses of the relationship between SAD and insomnia. A significant independent effect was not found when SAD
predicted insomnia (95% CI= -0.028 – 0.276), nor when insomnia predicted SAD (95% CI= -0.016 – 0.113). Depression and chronotype predicted insomnia (depression $\beta= 0.581$, 95% CI= 0.479 – 0.684; chronotype $\beta= -0.200$, 95% CI= -0.294 – -0.106), whereas depression but not chronotype uniquely predicted SAD (depression $\beta= 0.239$, 95% CI= 0.161 – 0.318; chronotype 95% CI= -0.058 – 0.061).

4.4.7. Social Phobia and Insomnia

The sample size for the analyses of the relationship between SP and insomnia was 304. The results failed to show a significant independent effect when SP predicted insomnia (95% CI= -0.048 – 0.143), and vice-versa (95% CI -0.065 – 0.191). Depression and chronotype uniquely predicted insomnia (depression $\beta= 0.578$, 95% CI= 0.481 – 0.676; chronotype $\beta= -0.197$, 95% CI= -0.285 – -0.109), whereas depression but not chronotype predicted SP (depression $\beta= 0.663$, 95% CI= 0.522 – 0.804; chronotype 95% CI= -0.051 – 0.168).

4.5. Discussion

The first aim of the study was to investigate the independent relationship between insomnia and depression, and insomnia and different subtypes of anxiety. The results were consistent with previous adolescent studies that reported a positive association between insomnia and depression (Gregory & O'Connor, 2002; Johnson, Roth, & Breslau, 2006), insomnia and GAD, but not between insomnia and SP (Alfano, et al., 2007). The current study, however, adds to these findings by showing that insomnia is related to depression and GAD after chronotype and anxiety or depression (respectively) are controlled for. Higher levels of insomnia were significantly predicted by higher levels of depression, and
conversely, higher levels of insomnia significantly predicted higher levels of depression and GAD.

The relationships observed between insomnia, GAD and depression may be at least partially explained by abnormalities to neurotransmitters and brain structures such as dopamine, hypocretin-1, serotonin, the brainstem and thalamus, which are associated with the sleep-wake cycle, anxiety and depression (Casey, et al., 2008; Holmes, 2003; Nestler & Carlezon, 2006; Peroutka, 1998; Tseng & O’Donnell, 2007; Yoshioka, et al., 1996). Consequently, insomnia, anxiety and depression may have overlapping courses of development, and hence contribute to the development of and result from one another (Jansson-Fröjmark & Lindblom, 2008; Kaneita, et al., 2009; Morphy, et al., 2007). Psychological and social factors that are common during adolescence such as increased autonomy, and psychosocial (e.g., peer groups), familial and educational stressors (Kaneita, et al., 2009; Lipton, et al., 2008) may also predispose adolescents to the development of insomnia, anxiety and depression.

This study also showed that while associations between insomnia, OCD, SAD and SP were evident, the relationships were no longer significant when depressive symptoms were controlled for. In contrast, a previous study reported an association between insomnia and SP (Alfano, et al., 2007), and suggested that depression has a large yet partial mediation effect when social phobia predicts insomnia (Buckner, Bernert, Cromer, Joiner, & Schmidt, 2008). These studies used different methodologies; the items used in the current study, as opposed to the other (Buckner, et al., 2008), are based on DSM-IV (American Psychiatric Association, 1994) criteria and hence may better represent the symptoms that are assessed for a clinical diagnosis of insomnia, depression and subtypes of anxiety. Furthermore, the
previous study used an overall sleep construct that assessed insomnia via one item (Alfano, et al., 2007), whereas the current study used a validated 7-item instrument that is specific to insomnia. An explanation for the current study’s findings could be that symptoms of depression and GAD may lead to significant and persistent distress and cognitive arousal at night, whereas symptoms of PD, SAD and SP are triggered by particular stimuli that may not be present nocturnally (American Psychiatric Association, 1994).

The findings from this study also suggest that depression has a stronger role in either the development or maintenance of sleep and anxiety symptoms than insomnia. Depression and not insomnia (or chronotype) predicted each anxiety variable. Furthermore, insomnia predicted each anxiety subtype before but not after depression was entered into the models, suggesting that depression may explain the relationship between insomnia and anxiety subtypes. Nevertheless, this study improves upon current clinical theories by indicating that insomnia has a stronger relationship with depression than anxiety subtypes, insomnia is independently related to some but not other anxiety subtypes, and depression may be a mediating factor between insomnia and subtypes of anxiety. Such findings, paired with the high correlations between insomnia and all anxiety subtypes before covariates were controlled further consolidate the notion of a complex and intertwined relationship between insomnia, anxiety and depression (Jansson-Fröjmark & Lindblom, 2008).

The second aim of this study was to investigate the effect of chronotype on insomnia, depression, and subtypes of anxiety that is unique from other predictors. The current study found that an evening chronotype predicted insomnia and depression after controlling for other predictors, which replicates the findings from previous studies that reported an association between chronotype and sleep problems, and chronotype and depression.
(Ferber, 1990; Giannotti, et al., 2002; Randler, et al., 2009; Russo, et al., 2007). However, in contrast to previous research (Ferber, 1990; Giannotti, et al., 2002; Randler, et al., 2009; Russo, et al., 2007), chronotype did not predict OCD, PD, SAD and SP. This result is likely due to the effect of insomnia, as chronotype was significantly correlated with OCD, PD, SAD and SP, but did not predict either anxiety subtype after insomnia was controlled for. Also, the results regarding PD may better reflect the large sample size, as the effect size was small and confidence intervals approached zero. Together, these results suggest that chronotype may have a more direct association with insomnia and depression than with anxiety subtypes, and that the relationship between chronotype and anxiety subtypes may be largely due to the presence of insomnia.

The independent effect of chronotype on insomnia and depression may be explained by symptoms that are common to depression, insomnia and an evening preference during adolescence such as persistent sleep deprivation, sleep displacement, difficulty adjusting to social constraints and an alternating lifestyle are also related to poor sleep and mental health (Giannotti, et al., 2002). Carskadon (Carskadon, et al., 2004) and Kaneita (Kaneita, et al., 2009) suggested that daily pressures of life accumulate during adolescence and hence promote later bedtimes, poorer sleep and more mental health problems in older adolescents. Furthermore, Russo and colleagues (Russo, et al., 2007) found that later bed and rise times occur with older age on the weekends, indicating that rise times are dictated by school schedule. Consequently, total sleep time on school nights decreases with age but remains constant on the weekend, suggesting that sleep deprivation may occur during the week (Russo, et al., 2007). The results of this study showed a similar pattern.
The current study has public health and clinical implications. Given that depression and GAD independently predict insomnia, prevention and treatment plans for insomnia may also focus more broadly on depression and GAD. Similarly, given that insomnia independently predicts depression, prevention and treatment plans for depression might also consistently focus on improving sleep. Eaton, Badawi and Melton (Eaton, Badawi, & Melton, 1995) estimated that 47% of cases of depression could have been prevented had sleep problems been successfully treated one year prior. Furthermore, Ohayon and Roth found that insomnia was a precursor for relapse of anxiety and depression (Ohayon & Roth, 2003). Also, given that chronotype and anxiety predicted insomnia and depression, prevention and treatment plans for depression and insomnia could simultaneously focus on anxiety and the eveningness chronotype. Finally, given the importance of depression, prevention and treatment plans for various subtypes of anxiety disorders should also consider depression. Therefore, interventions that focus on mental health, sleep and circadian rhythms could prevent the development or help alleviate symptoms of insomnia, depression and the subtypes of anxiety.

4.5.1. Limitations

The current study contained some limitations. First, directionality could not be inferred due to the cross-sectional methodology used, and knowledge about the aetiological aspect of the relationship between these problems remains unclear. This is particularly relevant to the finding that GAD predicted insomnia, but insomnia did not predict depression. Such a finding can only infer a relationship, and longitudinal studies are needed for a clearer understanding of the direction of this relationship. Future studies, then, could assess the longitudinal relationships between insomnia and subtypes of anxiety, and insomnia and
depression after accounting for potential covariates, thereby expanding the current knowledge base of the direction and hence aetiological relationship between these problems.

Second, this study is based on self-reported sleep and mental health symptoms rather than methods that allow a clinical diagnosis. Regarding mental health problems, comprehensive interviews are required to detect the presence of other disorders that may confound the results, such as adjustment or conduct disorder. Nevertheless, the RCADS has been extensively used in the adolescent population (Austin & Chorpita, 2004; Weems & Costa, 2005), including in studies that have assessed the relationship between sleep problems, anxiety and depression (Alfano, et al., 2009). Furthermore, recent studies have shown inconsistencies between subjective and objective reports of poor sleep in paediatric populations diagnosed with Major Depressive Disorder (Bertocci et al., 2005; Forbes et al., 2008) and anxiety disorders (Forbes, et al., 2008). The same studies also showed that objective and subjective reports of sleep were more similar in the general population than in youths diagnosed with anxiety or depression (Bertocci, et al., 2005; Forbes, et al., 2008). Indeed, the current study assessed the general population, and prevalence rates of clinically significant insomnia, depression and SP were similar to those found in other studies using the general population (Australian Bureau of Statistics, 2008a; Costello, et al., 2011; Johnson, Roth, & Breslau, 2006). The RCADS and ISI are also measures of mental health disorders and insomnia that are based on the DSM-IV diagnostic criteria (American Psychiatric Association, 1994). Future studies could use objective measures and/or clinical methods of assessment for insomnia, depression and subtypes of anxiety.
Moreover, other sleep problems were not assessed. However, disorders such as obstructive sleep apnoea are unlikely to confound the results due to the relatively low prevalence rates [range from 0.4% (Johnson & Roth, 2006) - 2.9% (Sánchez-Armengol et al., 2001)] in paediatric populations. In any case, future studies could use polysomnography and sleep diaries to detect other sleep disorders, and even assess biological measures that are directly relevant to chronotype and therefore could better detect delayed sleep phase syndrome such as core body temperature and dim light melatonin onset.

4.5.2. Conclusions

In conclusion, this study adds to the current literature by assessing the independent relationship between insomnia and depression, and insomnia and anxiety across subtypes of anxiety, while investigating the effects of chronotype on insomnia, anxiety and depression above and beyond potential confounders. The general adolescent population was the targeted sample, and psychometrically sound measures based on the DSM-IV (American Psychiatric Association, 1994) criteria for insomnia, subtypes of anxiety and depression were used. The results suggested that insomnia is independently related to symptoms of depression and GAD, but not the other subtypes of anxiety. Furthermore, an evening preference uniquely predicted insomnia and depression, but not GAD, PD, OCD, SAD or SP. Prevention and treatment efforts for insomnia and depression should potentially consider and concurrently focus on mental health, sleep and the eveningness chronotype, whereas prevention and treatment efforts for anxiety subtypes may consider also focussing on insomnia and depression.
Acknowledgements

Dr Stewart Howell contributed to the statistical analyses.
Chapter 5: Study 3

Bidirectional relationships between insomnia and depression, and insomnia and subtypes of anxiety during adolescence: does chronotype affect these relationships?

Alvaro, P.K., Roberts, R.M., Harris, J.K., & Bruni, O.

School of Psychology, University of Adelaide

Prepared for submission

Pasquale Alvaro (PhD Candidate)

I collected data, performed each analysis, interpreted data, wrote the manuscript and acted as the corresponding author. I also made the decisions on what data and arguments to present in this paper.

Date: 25/08/14
Rachel Roberts (Co-Author)

I was the primary supervisor for the research project that led to this paper, so was involved in the design of the study described in the paper and discussions of results, particularly in the case of adolescent literature. Mr Alvaro was responsible for writing the paper, and I was responsible for providing editorial comments. I hereby give my permission for this paper to be included in Mr Alvaro’s submission for the degree of PhD at the University of Adelaide.

X
Rachel Roberts
Co-author
Date: 25/08/14

Jodie Harris (Co-Author)

I was the co-supervisor for the research project that led to this paper. I was involved in the design of the study described in the paper, the write up of the introduction, and discussions of results, particularly where the sleep variables were concerned. I hereby give my permission for this paper to be included in Mr Alvaro’s submission for the degree of PhD at the University of Adelaide.

X
Jodie Harris
Co-author
Date: 25/08/14
Oliviero Bruni (Co-Author)

I was responsible for Pasquale Alvaro during his academic visit to La Sapienza University of Rome. As a co-author of this paper, I was heavily involved in editing the write-up, and statistical analyses. I also contributed to the design of the study, the introduction, and the discussions of results, particularly where the adolescent sleep research was concerned. I hereby give my permission for this paper to be included in Mr Alvaro’s submission for the degree of PhD at the University of Adelaide.

X
Oliviero Bruni
Co-author

Date: 20/08/14
5.1. Abstract

5.1.1. Study Objectives

To assess (1) the bidirectionality of the relationship between insomnia and various subtypes of anxiety, and insomnia and depression after controlling for confounders; (2) the independent predictive effects of chronotype on insomnia, depression, and each subtype of anxiety during adolescence.

5.1.2. Design

Prospective, longitudinal study with a 6-month follow-up. Assessment of insomnia, subtypes of anxiety, depression and chronotype was made via self-report questionnaires.

5.1.3. Settings

Community sample from eight high schools in Adelaide, South Australia.

5.1.4. Participants

The study was completed at baseline and follow-up by 255 high-school students aged 12 – 18 (M= 14.96, SD= 1.34), attending school grades 7 to 11 at baseline.

5.1.5. Measurement and Results

Participants completed the Insomnia Severity Index, the Revised Child Anxiety and Depression Scale to assess subtypes of anxiety and depression, and the Morningness-Eveningness Scale to assess chronotype. After accounting for covariates, insomnia was bidirectionally related to depression (covariates were baseline age, gender, chronotype and anxiety overall) and Generalised Anxiety Disorder (GAD, covariates were baseline age,
gender, chronotype and depression), but was not related to other subtypes of anxiety (covariates were baseline age, gender, chronotype and depression). Chronotype predicted insomnia after accounting for covariates (baseline age, gender, depression and anxiety), but not depression (covariates were baseline age, gender, insomnia and anxiety overall) or any anxiety subtypes (covariates were baseline age, gender, insomnia and depression).

5.1.6. Conclusion

Evidence suggests that insomnia is related to depression and GAD above and beyond other factors, and vice-versa, but not to other anxiety subtypes. An eveningness chronotype independently predicts the development of insomnia above and beyond other factors, but not depression or anxiety subtypes. Eveningness, then, predisposes an individual to the development of insomnia, which is a risk-factor for depression or GAD.
5.2. Introduction

Insomnia, anxiety and depression are common disorders during adolescence, with prevalence rates of 10.7% (Johnson, Roth, & Breslau, 2006), 17% (Johnson, Roth, & Breslau, 2006), and 5.6% (Costello, et al., 2006) respectively. In adolescents, symptoms of insomnia, anxiety and depression have been associated with various problematic outcomes, such as reduced satisfaction with life (Roberts, Roberts, & Duong, 2008), poor academic achievement (Paavonen, et al., 2000; Varley & Smith, 2003), suicidal ideation (Choquet, et al., 1993; Glied & Pine, 2002), excessive use of tobacco, alcohol and drugs (Johnson & Breslau, 2001), and various medical and psychiatric problems in adulthood (Bardone, et al., 1998; Franko, et al., 2005). Insomnia is also often comorbid with anxiety and depression, perhaps partly attributable to insomnia being a possible criterion for anxiety and depressive disorders, but also to the overlapping neurobiological, psychological and social risk-factors (Casey, et al., 2008; Holmes, 2003; Kaneita, et al., 2009; Lipton, et al., 2008; Nestler & Carlezon, 2006; Peroutka, 1998; Tseng & O'Donnell, 2007; Yoshioka, et al., 1996). Such comorbidity can exacerbate the consequences associated with each disorder, particularly the use of tobacco, alcohol and illicit drugs (Johnson & Breslau, 2001). These findings, paired with the increased risk of developing insomnia, anxiety and depression following puberty (Beesdo, et al., 2009; Johnson, Roth, & Breslau, 2006; Thapar, et al., 2012), highlight the importance of understanding the relationship between these disorders during adolescence.

A recent systematic review has suggested that insomnia and anxiety, and insomnia and depression are bidirectionally related (Alvaro, et al., 2013). That is, insomnia is related to the development of anxiety and depression, and anxiety and depression are related to the
development of insomnia (Jansson-Fröjmark & Lindblom, 2008; Kaneita, et al., 2009; Morphy, et al., 2007).

However, various uncertainties remain about the nature of these bidirectional relationships. One study in teenagers aged 13 to 15 found that prior anxiety predicted insomnia and prior insomnia predicted depression, but prior depression did not predict insomnia and prior insomnia did not predict anxiety (Johnson, Roth, & Breslau, 2006). However, this study was retrospective, and longitudinal adolescent studies have depicted bidirectional relationships between other sleep and mental health problems (Kaneita, et al., 2009; Meijer, et al., 2010).

Moreover, a recent adolescent study found significant associations between insomnia and Separation Anxiety Disorder (SAD), and insomnia and Generalised Anxiety Disorder (GAD), but not between insomnia and Social Anxiety Disorder (Alfano, et al., 2007). Although such findings are expected given the symptom overlap for diagnosis, the bidirectionality of the relationship between insomnia, anxiety and depression during adolescence, particularly for different anxiety disorders, remains unclear.

Finally, recent studies have reported an association between an evening chronotype (chronotype refers to a circadian rhythm position indicator that categorises individuals according to both their body clock position relative to the 24 hour day (Roenneberg, et al., 2004) and the time he/she prefers to engage in cognitively and physically demanding activities (Ferraz, et al., 2008)) and insomnia, anxiety and depression during adolescence (Ferber, 1990; Giannotti, et al., 2002; Randler, et al., 2009; Russo, et al., 2007). Such relationships are important, because adolescents tend to become more evening-orientated (i.e., become evening stimulus seeking and exhibit delayed bedtimes) with age due to
circadian rhythm and environmental changes that are experienced during adolescence (Crowley, et al., 2007). In some cases, eveningness tendencies predispose adolescents to the development of delayed sleep phase syndrome (American Academy of Sleep Medicine, 2005), which affects approximately 8% of adolescents (Saxvig, et al., 2012), and has been associated with insomnia (Reid, et al., 2012), anxiety (Reid, et al., 2012; Saxvig, et al., 2012), depression (Saxvig, et al., 2012), smoking (Saxvig, et al., 2012), alcohol use (Saxvig, et al., 2012), and poor academic achievement (Saxvig, et al., 2012) during adolescence. Nevertheless, the independent predictive effect of an evening chronotype on insomnia after accounting for depression and anxiety; on depression after accounting for insomnia and anxiety; and on anxiety subtypes after controlling for insomnia and depression are still unknown. An evening chronotype may be a predisposing, precipitating or perpetuating factor in depressive, anxiety and/or insomnia symptoms during adolescence.

The current study, therefore, investigated the bidirectionality of the longitudinal relationships between insomnia and subtypes of anxiety [Generalised Anxiety Disorder (GAD), Obsessive Compulsive Disorder (OCD), Panic Disorder (PD), Separation Anxiety Disorder (SAD) and Social Phobia (SP)], and insomnia and depression during adolescence. Note that although OCD was removed from the anxiety disorders category in the current Diagnostic and Statistical Manual of Mental Disorders (DSM 5) (American Psychiatric Association, 2013), it was included in the current study because of the strong associations reported with insomnia, depression and other subtypes of anxiety in adolescents (Johnson, Roth, & Breslau, 2006).

This study also considered the predictive effect of chronotype on insomnia once depression and anxiety were controlled, on depression once insomnia and anxiety were
controlled, and on anxiety subtypes once insomnia and depression were controlled. It was hypothesised that insomnia would be bidirectionally related to depression and some anxiety subtypes, but not others, and that an evening chronotype will predict insomnia, depression and subtypes of anxiety. Such an investigation will add to the current knowledge of the potential pathways of insomnia, depression and subtypes of anxiety, inform public health campaigns and clinical interventions for each problem, and enhance the understanding of the interaction between each problem.

5.3. Methods

5.3.1. Participants

Three-hundred and eighteen South Australian secondary school students aged 12 – 18 (M= 14.96, SD= 1.34) volunteered to participate in the study at baseline. Of these, 255 completed the study by returning the questionnaire at follow up (approximately 20% attrition rate; M age = 15.49, SD= 1.32). One-hundred and forty (54.90%) were male and 115 (45.10%) were female. At follow up, 68 students were in grade 8, 39 in grade 9, 76 in grade 10, 29 in grade 11 and 42 in grade 12. Participants were eligible if their parents consented, they completed the questionnaires at baseline and follow-up, were in grades 7 to 11 at baseline, and were fluent in English.

Attrition was not found to be related to baseline insomnia, depression, GAD, OCD, SAD, SP or chronotype. However, there was a significant difference in mean severity of panic disorder symptoms \[t(313)= 3.21, p<.01\] between adolescents who dropped out (M= 5.20, SD= 5.36) and those who completed the study (M= 3.89, SD= 3.61). Nevertheless, Cohen’s effect size was of small magnitude \(d= 0.35\) (Cohen, 1992), suggesting that the symptoms of
PD in those who dropped out were only marginally more severe than those who completed the study.

5.3.2. Measures

The demographic questionnaire contained items about personal history of mental health and sleep problems, medical history, treatment for mental health, sleep or medical problems, chronic illnesses, alcohol use and drug use; sleep duration, variability and sufficiency (defined as how often the adolescent thought they had sufficient sleep); and total sleep time on weeknights and weekends. The questionnaire also contained measures of insomnia, chronotype, depression and subtypes of anxiety.

5.3.2.1. Insomnia

The Insomnia Severity Index (ISI) (Bastien, Vallières, & Morin, 2001) was used to assess insomnia. The ISI is a 7-item self-report inventory that assesses the severity of subjective symptoms and consequences of insomnia based on the DSM-IV (American Psychiatric Association, 2000). Each item is scored on a 0 to 4 Likert scale, and total scores are calculated by summing each item (total score range 0 to 28). Higher total scores denote more severe insomnia. Scores between 0–7 indicate no clinically significant insomnia, 8–14 indicates subthreshold insomnia, 15–21 indicates moderate clinical insomnia, and 22–28 indicates severe clinical insomnia (Morin, 1993). Items include questions assessing difficulty falling sleep, difficulty staying asleep, problems waking up too early, satisfaction with current sleep patterns, worry/distress about current sleep patterns, and perceived interference of sleep problems with daily life. The ISI has been widely used (Brand, et al., 2011; Luo, et al., 2012; Short, et al., 2013) and also validated in the adolescent population (Chung, et al.,
A recent study reported significant correlations between the ISI and clinical diagnosis of insomnia, the Sleep-Wake Habits Questionnaire, General Mental-Health Questionnaire, Epworth Sleepiness Scale, smoking habits, alcohol use, number of naps per week, and academic performance during adolescence (Chung, et al., 2011). Furthermore, a Cronbach’s alpha of 0.83, and a 2-week test-rest reliability of 0.79 for the ISI in an adolescent population (Chung, et al., 2011) were reported. In the current study, a Cronbach’s alpha of 0.86 and 0.84 were obtained for baseline and follow-up, respectively.

5.3.2.2. Chronotype

The Morningness-Eveningness Scale (MES) (Carskadon, et al., 1993) was used to assess adolescents’ chronotype. It is a 10-item adaptation of the Composite Scale of Morningness (Smith, et al., 1989). Seven items are scored on a 1 to 4 Likert scale, and 3 items are scored on a 1 to 5 Likert scale. Total scores range from 10 to 42 and are calculated by summing each item. Higher scores indicate a tendency towards morningness. The MES can differentiate morningness from eveningness in adolescents (Díaz-Morales, et al., 2007). Extreme evening and morning-types were defined as below the 10th and above the 90th percentile, respectively, and scores in between were identified as neither types (cut-off scores were 20 and below for eveningness and 34 and above for morningness) (Giannotti, et al., 2002; Russo, et al., 2007). Recent studies have reported Cronbach’s α of 0.73 (Giannotti, et al., 2002), 0.82 (Díaz-Morales, et al., 2007), and 0.82 (Warner, et al., 2008) in Italian, Spanish, and Australian adolescents. Good external validity and high test-retest reliability (0.78) (S. Kim, et al., 2002) have been reported (Díaz-Morales, et al., 2007). The MES can also predict daytime functioning, academic achievement and various behavioural outcomes in adolescents (Giannotti, et al., 2002; Warner, et al., 2008), and successfully discriminate
morningness from eveningness in adolescents (Díaz-Morales, et al., 2007). Two items were altered. First, the phrase “gym class” was changed to “sports class” to keep the language relevant to the Australian population. Second, the item “Your parents have decided to let you set your own bed time. What time would you pick?” was changed to “What time would you prefer to go to bed?” to be more age-appropriate for the sample. Cronbach’s alpha for the MES in the current study was 0.80 and 0.82 for baseline and follow-up, respectively.

5.3.2.3. Depression and subtypes of anxiety

Depression and subtypes of anxiety were assessed by the Revised Child Anxiety and Depression Scale (RCADS) (Chorpita, et al., 2000). The RCADS is a 47-item adaption of the Spence Children’s Anxiety Scale (Spence, 1997) that corresponds to the DSM-IV (American Psychiatric Association, 1994) diagnostic criteria for Major Depressive Disorder (MDD; 10 items), Generalised Anxiety Disorder (GAD; 6 items), Panic Disorder (PD; 9 items), Separation Anxiety Disorder (SAD; 7 items), Obsessive Compulsive Disorder (OCD; 6 items) and Social Phobia (SP; 9 items). Each item is scored on a 0 to 3 Likert scale with higher scores indicating more severe depression or subtype of anxiety. Total scores are calculated by the sum of each item for each scale. MDD scores range from 0 to 30, GAD ranges from 0 to 18, PD ranges from 0 to 27, SAD ranges from 0 to 21, OCD ranges from 0 to 18, and SP ranges from 0 to 27. An overall 37-item scale for anxiety is also provided, with scores ranging from 0 to 111. A recent study reported Cronbach’s alphas in Hawaiian adolescents for each subscale: SP, alpha=0.81; PD, alpha=0.85; GAD, alpha=0.80; MDD, alpha=0.76; SAD, alpha=0.78; and OCD, alpha=0.71 (Chorpita, et al., 2000). The majority of Cronbach’s alphas for each subscale at baseline and follow-up in the current study ranged from 0.80 to 0.90, with OCD at baseline (alpha= 0.76), and SAD at baseline (0.68) and follow-up (0.73) falling below this range. This
study also reported good support for the structural, convergent and discriminant validity of the RCADS. Furthermore, internal consistency for MDD, anxiety subscales and overall anxiety has been found in Australian adolescents (De Ross, et al., 2002). Good convergent validity was also demonstrated (De Ross, et al., 2002) via moderate to strong correlations between the subscales of RCADS with scores on the Revised Manifest Anxiety Scale [RCMAS (Reynolds & Richmond, 1985)] and the Children’s Depression Inventory [CDI (Kovacs, 1981)]. Standardised T scores converted from raw scores are used to indicate the clinical significance of each variable. Scores between 65 and 69 indicate borderline clinical threshold and T scores ≥ 70 indicate above clinical threshold (Chorpita, 2011).

5.3.3. Procedure

All principals of high schools within a 40km radius of the Adelaide CBD that were listed with the Department for Education and Child Development in South Australia (Department for Education and Child Development, 2012) or in the 2010 Annual Report of the Advisory Committee on Non-Government Schools in South Australia (Government of South Australia, 2011) (n= 71 within catchment area) were approached. Each school principal received a package via mail that contained an invitation to participate in the study, a copy of the questionnaire, information letters for students and parents, and consent forms. The schools that did not respond to the letter received a follow-up phone call or email. Eight schools agreed to participate in the study. Information letters and consent forms for the students and parents were then given to each student in grades that were selected by the school. Questionnaires were completed in class time under the supervision of teachers at baseline and six months later. Baseline data was collected from May 2012 until August 2012, while follow-up data was collected from October 2012 to February 2013 follow-up range 5 – 7
months. This study was approved by the Human Research Ethics Committee from the University of Adelaide, the Department for Education and Child Development, and Catholic Education South Australia.

5.3.4. Statistical Analyses

The analysis of missing data was based on the recommendations of Tabachnick and Fidell (2007). Less than 2% of the baseline data was missing for the insomnia, depression, subtypes of anxiety and chronotype scales. Some evidence suggests that missingness at baseline may have been non-random, as the missing data group had a significantly higher SAD symptom severity score than those without missing data. However, the missing data group for this analysis only contained one participant, which is not enough to adequately represent the remaining participants with missing data. Furthermore, the evidence suggested that missing data at follow-up was random, as no significant differences were found in predictor or outcome variables between those with and without missing data. In any case, a large the sample size was retained after attrition and the amount of missing values was very low (below 3% for measures of depression, anxiety subtype and chronotype, and 6.6% for the insomnia measure). Therefore, on the recommendation of Tabachnick and Fidell (2007), participants with missing data at baseline and/or follow-up were only excluded for the analyses that assessed the variables containing their missing data.

Means, standard deviations, and frequencies were used to report descriptive statistics. Paired samples t-tests were used to assess significant differences between baseline and follow-up mean symptom severity. Statistics of frequencies for chronotype groups (evening-types, morning-types and neither-types) according to those who were and were not
identified with sub-threshold and clinically significant insomnia were also reported. Pearson’s $r$ was used to calculate correlations.

Two sets of step-wise regression analyses (Pallant, 2011) were conducted to investigate the bidirectionality of the relationship between insomnia and subtypes of anxiety, and insomnia and depression during adolescence, along with the effect of chronotype on these relationships. Insomnia and chronotype at baseline were used to predict depression or anxiety subtypes at follow-up for the first analysis, while depression or anxiety subtypes and chronotype at baseline was used to predict insomnia at follow-up for the second analysis.

Four steps were used to assess the hypotheses. Firstly, the predictor variable was regressed on the outcome variable at follow-up. Secondly, chronotype at baseline was added as a predictor when correlated with the predictor and outcome variable. Thirdly, anxiety overall or depression was added as a predictor to statistically control these variables. Finally, age at baseline and gender were added as a predictor and hence statistically controlled for to impart control for physical development of adolescents (see Figure 6). Bidirectionality is indicated if insomnia predicted depression or an anxiety subtype at the fourth step, and vice-versa. Chronotype is suggested to independently predict insomnia, depression, or an anxiety subtype should it predict an outcome variable at step 4.

Bootstrapping, a technique that is used when outcome variables are skewed, produces confidence intervals based on resampling with replacement. Bootstrapping was used to calculate correlations and hierarchical regression analyses, as the skewed coefficients and an inspection of the histograms for each variable suggested that the data may be slightly skewed. Based on Preacher and Hayes’ (Preacher & Hayes, 2008) recommendations, 5000
resamples were used for final reporting, and bias-corrected and accelerated (BCa) 95% confidence intervals were calculated.
Figure 6. Steps for regression analyses
5.4. Results

Demographic information, personal history and subjective sleep variables are reported in Table 10. Descriptive statistics for symptoms of insomnia, depression and anxiety subtypes at baseline and follow-up were reported in Table 11. A significant difference was not found between baseline and follow-up mean scores for insomnia, depression and each anxiety subtype, except PD. However, Cohen’s $d$ was of small magnitude ($d=0.12$), suggesting a small increase in PD symptom severity across the two waves. Adolescents slept longer on the weekends than weekdays at baseline (9 hours and 25 minutes vs. 8 hours and 17 minutes respectively) and follow-up (9 hours and 19 minutes vs. 8 hours and 10 minutes).

Frequencies for sub-threshold and clinically significant mental health and insomnia, and circadian preferences were reported in Table 12. Insomnia was the most common clinically significant problem at baseline and follow-up (11.60% and 10.08%), whereas OCD at baseline (2.79%) and OCD and GAD (4% each) at follow-up were the least common clinically significant problems. Furthermore, at baseline and follow-up, respectively, approximately 12.60% and 7.87% of participants reported one clinically significant problem, 3.94% and 6.69% reported two clinically significant problems, and 7.09% and 4.72% reported three or more clinically significant problems. The distribution of chronotypes in participants with sub-threshold and clinically significant insomnia showed a higher prevalence of evening type at baseline and follow-up (Table 13).

Table 14 shows the bootstrapped correlations involving baseline and follow-up variables. Correlations were found between all variables at baseline. Insomnia, depression, and subtypes of anxiety at baseline and follow-up were correlated with insomnia, depression, subtypes of anxiety at follow-up. Chronotype at baseline was associated with
insomnia, depression, GAD and PD at follow-up, but not with OCD, SAD or SP. Therefore, chronotype at baseline was not entered into the models that predicted OCD, SAD or SP.
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<th>Follow-up</th>
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<td><strong>Mean (SD)</strong></td>
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<td><strong>Number (%)</strong></td>
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<td><strong>Past treatment depression, anxiety, insomnia</strong></td>
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<td>Counsellor and other</td>
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<td><strong>Subjective opinion on amount of sleep</strong></td>
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<td></td>
</tr>
<tr>
<td>Too little sleep</td>
<td>113 (44.5)</td>
<td>105 (41.3)</td>
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<tr>
<td>Enough sleep</td>
<td>137 (53.9)</td>
<td>146 (57.5)</td>
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<tr>
<td>Too much sleep</td>
<td>4 (1.6)</td>
<td>2 (0.79)</td>
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Table 10 cont...

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Follow-up</th>
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<tr>
<td>Subjective opinion of sufficient sleep</td>
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<tr>
<td>Never</td>
<td>4 (1.57)</td>
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<td>Rarely</td>
<td>40 (15.74)</td>
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<tr>
<td>Sometimes</td>
<td>87 (34.25)</td>
<td>92 (36.22)</td>
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<tr>
<td>Usually</td>
<td>110 (43.30)</td>
<td>103 (40.55)</td>
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<td>Always</td>
<td>13 (5.12)</td>
<td>18 (7.09)</td>
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Table 11

Descriptive statistics for sleep and mental health symptoms at baseline and follow-up

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<th>Significance</th>
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<td>Range</td>
<td>Mean (SD)</td>
<td>Range</td>
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<td>0-25</td>
<td>7.45 (5.22)</td>
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<tr>
<td>Depression</td>
<td>0-24</td>
<td>6.68 (3.25)</td>
<td>0-24</td>
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<td>GAD</td>
<td>1-19</td>
<td>5.63 (3.20)</td>
<td>0-18</td>
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<tr>
<td>OCD</td>
<td>0-17</td>
<td>3.92 (3.13)</td>
<td>0-18</td>
</tr>
<tr>
<td>PD</td>
<td>0-18</td>
<td>3.42 (3.64)</td>
<td>0-26</td>
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<tr>
<td>DAD</td>
<td>0-14</td>
<td>3.00 (2.72)</td>
<td>0-14</td>
</tr>
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<td>SP</td>
<td>0-25</td>
<td>9.65 (5.44)</td>
<td>0-26</td>
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<td>Chronotype</td>
<td>10-40</td>
<td>27.19 (5.29)</td>
<td>13-39</td>
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<tr>
<td>TST WD</td>
<td>4-11.50</td>
<td>8.28 (1.23)</td>
<td>3-13.17</td>
</tr>
<tr>
<td>TST WE</td>
<td>4.5-15</td>
<td>9.41 (1.73)</td>
<td>4-13.00</td>
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</tbody>
</table>

GAD= Generalised Anxiety Disorder, PD= Panic Disorder, OCD= Obsessive Compulsive Disorder, SAD= Separation Anxiety Disorder, SP= Social Phobia, TST WD= Total sleep time weekday, TST WE= Total sleep time weekend

Table 12

Amount of cases of clinically significant and sub-threshold insomnia, subtypes of anxiety and depression, and morningness, neutral and eveningness chronotype at baseline and follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
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<td></td>
<td>Sub-threshold n (%)</td>
<td>Clinically significant n (%)</td>
</tr>
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<td>Insomnia</td>
<td>80 (32.00)</td>
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<tr>
<td>Depression</td>
<td>11 (4.37)</td>
<td>23 (9.16)</td>
</tr>
<tr>
<td>GAD</td>
<td>16 (6.32)</td>
<td>17 (6.72)</td>
</tr>
<tr>
<td>OCD</td>
<td>12 (4.78)</td>
<td>7 (2.79)</td>
</tr>
<tr>
<td>PD</td>
<td>12 (4.76)</td>
<td>11 (4.37)</td>
</tr>
<tr>
<td>SAD</td>
<td>20 (7.97)</td>
<td>17 (6.77)</td>
</tr>
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<td>SP</td>
<td>10 (3.97)</td>
<td>12 (4.76)</td>
</tr>
<tr>
<td>Morningness</td>
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<td>N/A</td>
</tr>
<tr>
<td>Neither</td>
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<td>N/A</td>
</tr>
<tr>
<td>Eveniningness</td>
<td>N/A</td>
<td>N/A</td>
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</table>

GAD= Generalised Anxiety Disorder, PD= Panic Disorder, OCD= Obsessive Compulsive Disorder, SAD= Separation Anxiety Disorder, SP= Social Phobia, subthreshold insomnia= Insomnia Severity Index scores between 8 – 14, clinically significant insomnia= Insomnia Severity Index scores ≥15, subthreshold mental health variables= Revised Children’s Anxiety and Depression Scale standardised T scores between 65 and 69, clinically significant mental health variables= Revised Children’s Anxiety and Depression Scale standardised T scores ≥70, Eveningness= Morningness-Eveningness Questionnaire scores ≥20, Neither= Morningness-Eveningness Questionnaire scores between 21 – 33, Morningness= Morningness-Eveningness Questionnaire scores ≥34.
<table>
<thead>
<tr>
<th></th>
<th>Eveniness n (%)</th>
<th>Morningness n (%)</th>
<th>Neither n (%)</th>
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<tbody>
<tr>
<td><strong>Baseline</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Without clinically significant insomnia</td>
<td>14 (10.07)</td>
<td>25 (17.99)</td>
<td>100 (71.94)</td>
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<td>12 (15.19)</td>
<td>8 (10.13)</td>
<td>59 (74.68)</td>
</tr>
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<td>Clinically significant insomnia</td>
<td>14 (50.00)</td>
<td>1 (3.57)</td>
<td>13 (46.43)</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
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<tr>
<td>Without clinically significant insomnia</td>
<td>9 (6.92)</td>
<td>33 (25.39)</td>
<td>88 (67.69)</td>
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<tr>
<td>Subthreshold insomnia</td>
<td>20 (24.10)</td>
<td>7 (8.43)</td>
<td>56 (67.47)</td>
</tr>
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<td>Clinically significant insomnia</td>
<td>12 (50.00)</td>
<td>2 (3.57)</td>
<td>10 (46.43)</td>
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</tbody>
</table>

Without clinically significant insomnia= Insomnia Severity Index scores between 0 – 7.  
Subthreshold insomnia= Insomnia Severity Index scores between 8 – 14  
Clinically significant insomnia= Insomnia Severity Index scores ≥15  
Eveniness= Morningness-Eveningness Questionnaire scores ≤20  
Morningness= Morningness-Eveningness Questionnaire scores ≥34  
Neither= Morningness-Eveningness Questionnaire scores between 21 – 33
Table 14

**Correlations involving baseline and follow-up depression, subtypes of anxiety, insomnia and chronotype**

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<th>OCD</th>
<th>PD</th>
<th>SAD</th>
<th>SP</th>
<th>Insomnia</th>
<th>Chronotype</th>
<th>Follow-up</th>
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<th>GAD</th>
<th>OCD</th>
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</tbody>
</table>

Note. Bootstrapped correlations between baseline data (n= 245 – 252) are presented in the top left hand corner, bootstrapped correlations between baseline and follow-up (n= 234 – 249) are presented in the bottom left hand corner, and bootstrapped correlations between follow-up data (n= 232 – 250) are presented in the bottom right hand corner.  GAD= Generalised Anxiety Disorder, PD= Panic Disorder, OCD= Obsessive Compulsive Disorder, SAD= Separation Anxiety Disorder, SP= Social Phobia, ** = Significant correlation according to the confidence intervals
5.4.1. Step-wise regression analyses

Insomnia at baseline predicted depression and GAD in steps 1, 2, 3, and 4, and depression and GAD predicted insomnia across each step. Insomnia did not predict other subtypes of anxiety once depression was entered into the model (i.e., step 3). Similarly, other subtypes of anxiety did not predict insomnia once depression was entered into the model (i.e., step 2 or 3, depending if chronotype was assessed as a predictor). Chronotype predicted insomnia in steps 1, 2, 3, and 4 across each analysis, but did not predict depression or subtypes of anxiety. Age at baseline predicted follow-up depression, but no other outcome variables. Gender did not predict any outcome variables. Table 15 reports the final step of the regression analyses where insomnia was used as the outcome variable, while Table 16 reports the final step of the regression analyses where insomnia was used as a predictor variable. The full step-wise regression analyses can be found in the appendix.¹

¹ Note there are two separate appendices, one in section 5.5 and one in section 7. The former is a part of the third study that will be submitted for publication, so we decided to keep it in the same section. The latter adds information that is beyond the scope of study 3. Therefore, we decided to separate the two appendices.
Table 15
Regression analyses with insomnia as the outcome variable

<table>
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<tr>
<th>Model</th>
<th>Predictor</th>
<th>β (Bootstrap)</th>
<th>CI Lower</th>
<th>CI Upper</th>
<th>$R^2_{\text{adjusted}}$</th>
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</thead>
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<td>1</td>
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<td>Gender</td>
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<tr>
<td>2</td>
<td>GAD</td>
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<td>0.43</td>
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<td>-0.23</td>
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a. Dependent Variable: Insomnia
* β= regression co-efficient, CI= Bca 95% Confidence Interval, GAD= Generalised anxiety disorder, OCD= Obsessive compulsive disorder, PD= Panic disorder SAD= Separation anxiety disorder, SP= Social phobia
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*GAD= Generalised anxiety disorder, OCD= Obsessive compulsive disorder, PD= Panic Disorder, SAD= Separation anxiety disorder, SP= Social phobia, CI= Bca 95% Confidence Interval
5.5. Discussion

This study supported previous research that has found a bidirectional relationship between insomnia and depression, (Alvaro, et al., 2013; Jansson-Fröjmark & Lindblom, 2008) and extended upon this research by depicting a bidirectional relationship after controlling for chronotype, anxiety and age in adolescents. Whereas previous studies have reported a bidirectional relationship between insomnia and anxiety as an overall construct (Jansson-Fröjmark & Lindblom, 2008; Morphy, et al., 2007), the current study clarified a bidirectional relationship between insomnia and GAD during adolescence. In contrast, a previous adolescent study found that anxiety predicted the development of insomnia and insomnia predicted the development of depression, but not vice-versa (Johnson, Roth, & Breslau, 2006). This study, however, was retrospective, and other longitudinal adolescent studies have depicted bidirectional relationships between sleep and mental health problems (Kaneita, et al., 2009; Meijer, et al., 2010). Therefore, it seems likely that insomnia and depression, and insomnia and GAD are bidirectionally related during adolescence.

Several factors may explain the bidirectional associations between insomnia, depression and GAD during adolescence, all of which may coexist. Firstly, these disorders may involve overlapping neurobiological underpinnings such as abnormal levels of dopamine, hypocretin-1 and serotonin (Holmes, 2003; Nestler & Carlezon, 2006; Peroutka, 1998; Tseng & O’Donnell, 2007; Yoshioka, et al., 1996). Secondly, as Batterham and colleagues (2012) note, biological factors such as increased inflammatory dysregulation in response to sleep disturbances (Patel, et al., 2009) are also associated with anxiety (Maes, et al., 1998) and depression (Müller, et al., 2011). Also, various psychosocial changes in an adolescent’s life are triggers for the onset of insomnia, depression and GAD, such as increased autonomy, and peer group, familial and educational stressors (Kaneita, et al.,
2009; Lipton, et al., 2008). Indeed, insomnia, depression and GAD may be related, where only the order of appearance of symptoms may alter, or be independent but mutually influencing disorders (Kaneita, et al., 2009).

Interestingly, the results failed to depict a significant relationship between insomnia and OCD, PD, SAD or SP once controlling for chronotype (in the case of PD), depression and age. These findings are unlikely to be the result of a bias towards more severe PD symptoms in those who dropped out of the study, as the effect-size was small and therefore unlikely to greatly affect the results. Rather, it seems that depression completely accounted for the relationships between insomnia and OCD, PD, SAD and SP, as these relationships were no longer significant when depression was the sole variable that was controlled. Furthermore, the largest $r^2$ increase occurred after depression was entered into each model of anxiety subtype from both directions. Together, these results suggest that the relationship between insomnia and OCD, PD, SAD and SP may be better explained by a common association with depression. Therefore, the course of development for insomnia may be bidirectionally related to depression and GAD but not to OCD, PD, SAD or SP, and the significance of the relationship between insomnia and anxiety differs across subtypes of anxiety. Symptoms of depression and GAD (American Psychiatric Association, 1994) may result in substantial nocturnal distress and cognitive arousal, contributing to insomnia, whereas symptoms of PD, SAD and SP are specific to certain objectively non-threatening stimuli that are likely to be absent at night (American Psychiatric Association, 1994).

Previous studies have reported an association between an eveningness chronotype and insomnia, anxiety and depression during adolescence (Ferber, 1990; Giannotti, et al., 2002; Randler, et al., 2009; Russo, et al., 2007). In particular, eveningness significantly predicted depression/anxiety after controlling for insomnia and various other variables
(Giannotti, et al., 2002). However, this finding may be a function of the sample size from the former study (742 evening-types, 1005 morning-types) given that eveningness only explained 1% of the variance after all other variables were controlled (Giannotti, et al., 2002). Indeed, the current study found that once age, depression, and anxiety were controlled, eveningness significantly predicted insomnia, but once insomnia was controlled, eveningness did not depression or anxiety subtypes. These findings suggest that insomnia accounts for the relationships between chronotype and depression, chronotype and subtypes of anxiety. Therefore, eveningness is not a direct predisposing factor for future depression or anxiety subtypes during adolescence, but rather a risk-factor for the development of insomnia, which predisposes adolescents to the development of depression or GAD. Should depression present following insomnia, it may in turn contribute to the development of OCD, PD, SAD or SP. Nevertheless, further research is needed for more definitive conclusions about this possible pathway.

Various studies have also reported an association between eveningness and insomnia during adolescence (Adan, Fabbri, Natale, & Prat, 2006; Fernández-Mendoza, et al., 2009; Ong, Huang, Kuo, & Manber, 2007). In particular, one study of adolescents and young adults found that eveningness predicted insomnia complaints after controlling for age, gender and various sleep variables (Fernández-Mendoza, et al., 2009). These results, paired with those found in the current study suggest that a preference for evenings may contribute to the development of insomnia during adolescence and early adulthood above and beyond depression, anxiety, and other sleep parameters.

Various mechanisms may explain the independent predictive effect of eveningness on insomnia. Firstly, factors associated with an evening preference such as sleep-wake irregularity may contribute to the development and maintenance of insomnia (Adan, et al.,
Similarly, adolescents may experience symptoms of sleeplessness and sleep deprivation induced by an evening preference and an enforced school schedule. Teenagers often become more evening-orientated with age due to various circadian rhythmic and environmental changes, yet often rise early during the week for school and sleep later on weekends (Crowley, et al., 2007). Consequently, total sleep time on school nights decreases with age but remains constant on weekends (Russo, et al., 2007). The results of this study showed a similar pattern at baseline and follow-up, in that total sleep time on school nights was negatively correlated with age but remained constant on the weekend.

5.5.1. Clinical implications

The results of this study have prevention and treatment implications for symptoms and disorders of insomnia, depression and anxiety. The bidirectional relationship between symptoms of insomnia and depression, and insomnia and GAD suggests prevention and treatment plans for insomnia disorder that also consider symptoms of depression and/or GAD may prevent or alleviate the primary insomnia disorder, and vice-versa. Alternatively, prevention and treatment programs may focus on symptom overlap and processes that mutually contribute to the development of clinically significant (or even disordered) insomnia, depression and GAD. For example, excessive worry is common to GAD, depression, and insomnia disorder (American Psychiatric Association, 2013; Harvey & Greenall, 2003; Jansson-Fröjmark & Linton, 2006a), and hence may be one of many underlying processes that is key to efficiently and effectively address bidirectionality and comorbidity between these disorders. Indeed, Danielsson, Harvey, MacDonald, Jansson-Fröjmark, and Linton (2013) found that catastrophic worry partially mediates the relationship between sleep disturbances and depression in adolescents, and a study
reported symptom improvements in adolescents diagnosed with GAD after cognitive-behavioural therapy that focussed on excessive worry (Leger, Ladouceur, Dugas, & Freeston, 2003). Future research is needed to further consolidate this notion, and could investigate the mediation effects of excessive worry on the relationship between symptoms of insomnia disorder and GAD, or the efficacy of treatment for insomnia disorder and depression in adolescents that focusses on excessive worry.

The chronotype construct may be useful for identifying a cohort of adolescents who are at increased risk for developing an insomnia disorder. At baseline and follow-up, half of the adolescents who were identified with clinically significant insomnia reported an evening chronotype. Similarly, Giannotti, et al. (2002) found higher prevalence rates of clinically significant sleep onset insomnia symptoms in evening-type adolescents relative to morning-types. Together, the results suggest that clinically significant insomnia and an evening chronotype are likely to co-present, and therefore, a large cohort of adolescents with insomnia will also report a delayed sleep phase. Early clinical assessment, then, could aim to detect delayed sleep phases in adolescents by assessing chronotype preference, and in turn identify at risk cohorts or individuals before more severe insomnia symptoms (and perhaps insomnia disorder) develop. Future research could consolidate this notion by aiming to further improve the identification processes of insomnia disorder. In particular, research could also randomly assign adolescents with an evening circadian preference who are not diagnosed with an insomnia (or sleep) disorder to a control group or treatment/prevention/education group that aims to stabilise circadian rhythms, and compare the longitudinal outcomes across treatment groups. A larger prevalence rate of insomnia disorder in the control group would suggest that early assessment of insomnia disorder should aim to identify adolescents with a delayed sleep phase.
Given the research discussed above and the predictive effect of baseline eveningness on insomnia severity at six month follow-up, prevention and treatment plans for insomnia that also consider evening tendencies could lead to improved outcomes in the cohort of adolescents with a delayed sleep phase. Furthermore, such prevention and treatment plans for this adolescent cohort could also improve clinically significant symptoms of depression, OCD, PD, SAD and SP, given that baseline insomnia predicted follow-up depression, and baseline depression completely accounted for the relationships between insomnia and OCD, PD, SAD and SP. Indeed, Golden and colleagues’ (2005) meta-analysis found high efficacy for bright light therapy when treating seasonal affective disorder and nonseasonal depression, although the included studies used adult samples.

Nevertheless, the small magnitude of the predictive effect of baseline eveningness on follow-up insomnia suggests that for the majority of adolescents with clinically significant insomnia (or an insomnia disorder), alternative treatments are likely to be more efficacious than treatments that only focus on circadian rhythms for the majority of adolescents. An integrated approach that focuses on the various potential underlying processes of the relationship between insomnia, depression, anxiety subtypes and chronotype may be the best form of intervention. For example, early intervention for maintaining school attendance (i.e., addressing school refusal) is likely to maximise social and educational functioning, and in turn improve sleep, mood and anxiety symptoms (Egger, Costello, & Angold, 2003). Furthermore, stress management programs may reduce stress levels that are associated with disorders of insomnia, depression and anxiety (Hammen, 2005; McEwen, Eiland, Hunter, & Miller, 2012; Morin, Rodrigue, & Ivers, 2003). Moreover, emotional literacy programs could aim to improve social support, a known preventative barrier for insomnia, depression, and anxiety disorders (Dumont & Provost, 1999; La Greca & Harrison, 2005;
Roberts, et al., 2002), by creating an environment that allows for open and honest discussions about mental health symptoms. Finally, large scale and individual based interventions (e.g., bright light therapy, behavioural sleep scheduling, pharmacotherapy); and education for adolescents, parents and teachers about delayed sleep phases, circadian rhythm disorders, sleep, mental health, and the importance of understanding (and hence not pathologising) symptoms that are likely to be a normal part of the transition to adulthood may play an important role in improving the awareness of clinically significant symptoms and disorders of insomnia, depression, subtypes of anxiety; circadian rhythms; and their impact on emotional well-being. Such an integrated approach could help reduce the social and educational impact of DSM disorders, and also prevent the onset of later insomnia, depression and anxiety disorders.

5.5.2. Limitations

Self-report questionnaires were used to assess symptoms of insomnia, depression and anxiety subtypes, which arguably does not accurately represent DSM diagnoses of insomnia, depression and anxiety disorders. Indeed, some studies have reported inconsistencies between data that derives from self-report paediatric measures of symptoms and data that derives from measures considered the gold standard of paediatric sleep and mental health disorders, namely clinical assessments of DSM disorders and objective methods of sleep parameters (Bertocci, et al., 2005; Forbes, et al., 2008). Nevertheless, while a perfect reflection may be impossible, standardised and well validated psychometric inventories can be very good indicators DSM disorders. Wolpert, Cheng, and Deighton’s (In Press) review article of four patient reported outcome measures found that the RCADS has the most empirical support for sensitivity to change over time in paediatric populations, and Mathyssek, et al. (2013) found that changes to symptoms of anxiety disorders over time as
assessed by the RCADS most likely reflects true changes to anxiety disorders. Furthermore, studies have shown that the RCADS is a valid screening tool for depression and anxiety disorders in paediatric populations (Chorpita, Moffitt, & Gray, 2005; Esbjørn, Sømhovd, Turnstedt, & Reinholdt-Dunne, 2012; Mathyssek, et al., 2013), which is expected given that psychometric measures of depression, anxiety and even insomnia symptoms yield similar results to objectively or clinically assessed diagnoses in the general adolescent population (Bertocci, et al., 2005; Forbes, et al., 2008). Indeed, the prevalence rates of clinically significant insomnia, depression and SP at baseline and follow-up in this study were similar to those found in the general population (Australian Bureau of Statistics, 2008a; Costello, et al., 2011; Johnson, Roth, & Breslau, 2006). Together, the evidence suggests that well-validated psychometric measures of symptoms can accurately reflect DSM disorders, and therefore, studies assessing symptoms are applicable to diagnoses.

Other psychiatric, medical and sleep disorders, as well as potential genetic or neurobiological vulnerabilities that may confound the results were not assessed in the current study. For example, delayed sleep phase syndrome is common in adolescents and may contribute to insomnia, depressive and anxiety symptoms (Reid, et al., 2012). Nevertheless, although approximately 11% of students were identified as having an evening chronotype, the insomnia construct in the current study is likely to be a valid measure of primary insomnia given the results remained the same when those with clinical indicators of delayed sleep phase syndrome were excluded from the analyses [see (Alvaro, Roberts, & Harris, 2014) for details of the procedure]. Regarding genetic or neurobiological vulnerabilities, an increased sensitivity to natural or experimental alterations of the serotonergic system has been associated with and hence may contribute to the development of depression and sleep (Jans, Riedel, Markus, & Blokland, 2006). Future
studies could replicate the current study but use objective measures and/or clinical assessments for insomnia, depression and subtypes of anxiety, assess other sleep and psychiatric disorders, and consider genetic and neurobiological vulnerabilities.

5.5.3. Conclusions

This study added to the literature by assessing the bidirectional relationship between insomnia and subtypes of anxiety, and insomnia and depression during adolescence after circadian preference is controlled for, and the independent predictive effect of chronotype on insomnia, depression and different subtypes of anxiety. Insomnia was bidirectionally related to depression and GAD, but not to OCD, PD, SAD, nor SP. An evening chronotype predicted insomnia, but not any mental health problem once insomnia was statistically controlled. Eveningness during adolescence may lead to insomnia, which may result in depression or GAD, and depression could in turn contribute to the development of other anxiety subtypes. Prevention and treatment efforts for insomnia should potentially consider and concurrently focus on depression, GAD and circadian rhythm dysregulation, whereas prevention and treatment efforts for depression and GAD may consider also focussing on insomnia. Finally, prevention and treatment plans for OCD, PD, SAD and SP should concurrently focus on depression.
### 5.5. Appendix

#### Appendix a

Stepwise regression analyses with insomnia as the outcome variable

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a. Dependent Variable: Insomnia

* CI = Bias-corrected and accelerated confidence interval, GAD= Generalised anxiety disorder, OCD= Obsessive compulsive disorder, PD= panic disorder, SAD= separation anxiety disorder, SP= social phobia
### Appendix b
Baseline insomnia, chronotype, anxiety and age regressed on follow-up depression

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* CI= Bias-corrected and accelerated confidence interval, GAD= Generalised anxiety disorder, OCD= Obsessive compulsive disorder, PD= panic disorder, SAD= Separation anxiety disorder, SP= social phobia
Chapter 6: Discussion

Chapter 1 defined and reviewed the literature of the major concepts of the thesis. Chapter 1 also presented a literature review about the bidirectionality of the relationship between insomnia, depression and anxiety. The literature review depicted inconsistent findings from the studies that have assessed the direction of the relationship between insomnia, depression and anxiety, with one-way and bidirectional models as the two most supported hypotheses. It was argued that these inconsistencies are the result of different methodologies employed by previous studies, and overlapping methodological issues within the literature should be addressed. In particular, chronotype had not been considered in previous research. These arguments formed the basis of the two main research aims addressed in this thesis, which were to investigate:

1. The bidirectionality of the relationship between insomnia, depression and different subtypes of anxiety;
2. The independent effect of chronotype on these relationships.

Aim 1 was assessed by studies 1 and 3, whereas aim 2 was assessed by study 3, and study 2 contributed to the research base of both aims. Study 1 systematically reviewed the current literature on the bidirectionality of the relationship between insomnia, depression and anxiety. Study 2 investigated the cross-sectional independent relationships between insomnia and depression, and insomnia and subtypes of anxiety, along with the independent effects of chronotype on insomnia, depression, and subtypes of anxiety. Study 3 assessed the bidirectionality of the relationship between insomnia and depression over time, and insomnia and subtypes of anxiety during adolescence after chronotype and other covariates were controlled. This study also assessed the independent predictive power of chronotype.
on insomnia, depression and anxiety subtypes after controlling for baseline anxiety subtypes, depression, and/or insomnia.

The current chapter summarises the results of each paper, then discusses these results according to the aims stated above, with an attempt to avoid as much overlap with the three studies as possible. Some overlap was unavoidable, and the author again apologises for the instances where overlap is present.

This chapter also expands on the discussions provided in the above studies with information that could be not included because of word restrictions. Section 6.2 focuses on the bidirectionality of the relationships between insomnia and depression, and insomnia and subtypes of anxiety, and section 6.3 discusses the independent effect of chronotype on these problems. Additional inferences about the aims are made from considering the results of studies 1, 2 and 3. Section 6.4 discusses the theoretical implications of the results, while section 6.5 focusses on the clinical implications of the results. Section 6.6 discusses the limitations and future research that are directly relevant to the thesis but beyond the scope of the studies.

6.1. Summary of the results from Studies 1, 2 and 3

Study 1 found that the bidirectionality of the relationship between sleep disturbances and depression, and sleep disturbances and anxiety differs across sleep variables. Childhood sleep problems predicted higher levels of depression and a combined depression/anxiety variable, but not vice-versa. A one-way relationship was also found where anxiety predicted excessive daytime sleepiness, but excessive daytime sleepiness was not associated with depression. Insomnia and sleep quality were bidirectionality related to anxiety and depression, and depression/anxiety, respectively. Definitive conclusions about
bidirectionality were not made in study 1 for excessive daytime sleepiness, childhood sleep problems and sleep quality due to the small number studies, the heterogeneity of samples across studies, and the overall nature of the sleep and mental health variables used that may mask potentially differences between different sleep and mental health variables. Nevertheless, best available evidence supports the bidirectional theory of the relationship between insomnia, depression and anxiety.

Study 2 reported prevalence rates of 12.50%, 9.24%, 6.69%, 2.24%, 4.46%, 5.41% and 4.78% for clinically significant insomnia, depression, GAD, OCD, PD, SAD and SP, respectively, which were similar to prevalence rates reported in previous studies (Myers & Troutman, 1993; Ohayon, 2002). Correlations between insomnia and each mental health variable before controlling for covariates were also reported. After covariates were controlled, insomnia predicted depression, whereas insomnia was predicted by depression and GAD. Interestingly, OCD, SAD and SP were not significantly related to insomnia once depression was entered into the model, suggesting depression may be the factor underlying these relationships. Eveningness uniquely predicted insomnia and depression once all covariates were controlled. Eveningness was correlated with each anxiety subtype (except GAD) before covariates before but not after insomnia was controlled, suggesting insomnia may account for these relationships. Although insomnia independently predicted panic disorder (PD), the effect was not likely to be clinically significant.

Prevalence rates for study 3 at follow-up were similar to those reported at baseline in study 2, except SAD was more prevalent in study 3 than study 2 (9.68% vs 6.77%). In any case, the prevalence rates reinforce the frequency and importance of sleep and mental health problems in adolescents. Study 3 also reported correlations between insomnia and each mental health variable before covariates were controlled. After accounting for
covariates, insomnia was bidirectionally associated with depression and GAD. However, after controlling for baseline depression, insomnia did not significantly predict other subtypes of anxiety, and vice-versa. Baseline chronotype predicted insomnia at follow-up after accounting for covariates, but not depression or any anxiety subtype after controlling for baseline insomnia. Insomnia was interpreted as associated with the development of depression and GAD above and beyond other factors, and vice-versa. The relationship between insomnia and other anxiety subtypes was suggested to be the result of a confounding effect of depression. An eveningness chronotype was interpreted to independently predict the development of insomnia above and beyond other factors, but not depression or anxiety subtypes. The relationship between chronotype and mental health problems was suggested to be the result of a common association with insomnia.

6.2. The Bidirectionality of the relationships between insomnia and depression, and insomnia and subtypes of anxiety

The additional inferences discussed in section 6.2 include the consistency of bidirectionality across age groups, cultures, methods of assessment, follow-up time-periods, and anxiety subtypes over a period of time. Underlying mechanisms of the relationships between insomnia, depression and GAD are also discussed.

6.2.1. Bidirectionality across various age groups and cultures

The evidence from studies 1 and 3 support the theory of a bidirectional relationship between insomnia, depression and anxiety. Whereas study 3 assessed adolescents from Australia, study 1 identified large population studies that found bidirectional relationships in young adults (Buysse, et al., 2008; Hasler, et al., 2005), adults (Jansson-Fröjmark & Lindblom,
2008; Morphy, et al., 2007), and the elderly (J. M. Kim, et al., 2009) across European (Buysse, et al., 2008; Hasler, et al., 2005; Morphy, et al., 2007) and Asian cultures (J. M. Kim, et al., 2009). Studies that have assessed the longitudinal associations between insomnia and depression, or insomnia and anxiety from one direction (e.g., longitudinal association between baseline insomnia and follow-up depression, or baseline anxiety and follow-up insomnia) have also found significant relationships across various ages and cultures (Baglioni, et al., 2011; Jansson-Fröjmark & Linton, 2006b). Indeed, an association between insomnia and depression, and insomnia and anxiety (overall and subtypes) have been reported across age and cultures in cross-sectional studies (Alfano, et al., 2009; Cheung & Wong, 2011), including study 2.

Together, the studies above can be interpreted in various ways. Firstly, the relationship between insomnia and depression remains bidirectional from adolescence to older adulthood. Neurobiological and psychological factors that are likely to maintain this relationship, such as abnormal dopamine secretion and familial stressors, may be constant throughout life, particularly without treatment. Secondly, the relationship between insomnia and depression remains bidirectional across cultures. This explanation may support the notion of a genetic component of the relationship between insomnia and depression, or similar neurobiological factors and psychological stressors may be experienced across cultures. Indeed, studies have reported overlapping genetic components of insomnia, depression and anxiety in youths (Gehrman, et al., 2011). Thirdly, insomnia is likely to be bidirectionally related to at least some anxiety problems across age and culture, for the same reasons stated above. Fourthly, insomnia and GAD are more likely to be directly associated than other subtypes of anxiety during adolescence (an explanation of this was given in study 3). Finally, the relationships between insomnia and depression, insomnia and
an overall construct of anxiety, and insomnia and GAD are also stable across age and cultures, both longitudinally and cross-sectionally.

6.2.2. Bidirectionality across different methods of assessment

Bidirectionality has also been reported across different methods of assessment. Of the studies identified in the systematic review that reported bidirectional relationships between insomnia and depression, and/or insomnia and anxiety, two used self-report questionnaires (Jansson-Fröjmark & Lindblom, 2008; Morphy, et al., 2007), two studies that assessed the same sample used semi-structured interviews (Buysse, et al., 2008; Hasler, et al., 2005), and one used structured interviews (J. M. Kim, et al., 2009). The study that found a one-way relationship was conducted using structured interviews, but was retrospective. This consistency is in contrast to previous non-bidirectional insomnia and mental health studies that have reported different results across different methods of assessment (Bertocci, et al., 2005; Forbes, et al., 2008). Therefore, although a limitation, the use of self-report questionnaires to investigate bidirectionality may be less problematic than when used in non-bidirectional studies. The findings that the reliability and validity of measures of psychopathology increase by 15% and 37% respectively when assessed as continuous variables compared to categorical variables (Markon, et al., 2011) further support the use of self-report questionnaires.

6.2.3. Bidirectionality and follow-up time-periods

The studies that have reported bidirectional relationships between insomnia and depression, and insomnia and anxiety have used different time-periods between baseline and follow-up. Study 3 used a six-month follow-up period, whereas two studies included in the systematic review used a one-year follow-up (Jansson-Fröjmark & Lindblom, 2008;
Morphy, et al., 2007), one study used a two-year follow-up (J. M. Kim, et al., 2009), and the two studies that assessed the same sample used two-year, five-year and six-year follow-up periods (Buysse, et al., 2008; Hasler, et al., 2005). These findings indicate a rapid development (i.e. within six months) and chronic nature (i.e., at least 6 years) of the bidirectional relationship between insomnia and depression, and insomnia and anxiety problems across the life-span.

Such a relationship can be both rapidly developing and chronic in nature even during adolescence. The adolescent studies in the systematic review that assessed sleep quality (a variable that overlaps greatly with insomnia) found bidirectional relationships with depression/anxiety variables after one (Meijer, et al., 2010) and two-year follow-ups (Kaneita, et al., 2009). Therefore, a bidirectional relationship between insomnia and depression, and insomnia and certain subtypes of anxiety may develop within six-months (as suggested by study 3) and last for at least 2 years during adolescence.

Together, the above evidence suggests the rapid development of subsequent sleep or mental health issues following insomnia, depression or GAD, which in turn highlights the importance of prompt identification and treatment of each problem. A discussion about prevention and treatment for insomnia, depression and subtypes of anxiety can be found in section 6.5. below.

6.2.4. Bidirectionality and time-period across subtypes of anxiety

Study 3 reported a bidirectional relationship between insomnia and GAD after controlling for chronotype and other covariates. The results of study 2 were similar to the results of study 3 in that both reported relationships between insomnia and GAD once chronotype and other covariates were statistically controlled. Furthermore, insomnia was
related to OCD, SAD and SP before but not after depression was controlled. Together, these results suggest that the nature of the relationship between insomnia and GAD, OCD, SAD and SP remains constant over a 6 month period.

The results regarding anxiety subtypes support Alfano, et al.’s (2009) finding of a cross-sectional association between sleep problems and GAD, but not the findings of cross-sectional relationships between sleep problems and PD, and sleep problems and SP (Alfano, et al., 2009). Alfano, et al. (2009) used the RCADS to assess the anxiety subtypes, but assessed depression using the Child Depression Scale, which may account for the differences in results. Also, Alfano, et al. (2009) assessed sleep problems as an overall construct, whereas insomnia was assessed as a single variable in the current thesis. The natures of the relationships are likely to differ between subtypes of anxiety and sleep problems, and even depression and various sleep problems. Such a premise is further supported by the findings of study 1. Previous studies did not assess the longitudinal associations between insomnia and specific subtypes of anxiety.

It must be noted that GAD predicted insomnia in study 2, but not vice-versa, whereas a bidirectional relationship was found between insomnia and GAD in study 3. The longitudinal methodology of study 3 allows for reliable directional inferences, whereas the cross-sectional methodology of study 2 allows only for associational inferences.

6.2.5. Potential mechanisms of the relationship between insomnia, depression and GAD

Studies 1, 2 and 3 suggested various common mechanisms, risk-factors or processes that may underlie the bidirectionality of the relationships between insomnia and depression, and insomnia and GAD, such as neurobiological (Holmes, 2003; Nestler & Carlezon, 2006;
Peroutka, 1998; Tseng & O'Donnell, 2007; Yoshioka, et al., 1996), psychological and social factors (Kaneita, et al., 2009; Lipton, et al., 2008). In addition, the diathesis-stress model (Monroe & Simons, 1991) proposes that stressors may trigger the development of disorders (e.g., insomnia, depression or GAD) in genetically predisposed or otherwise vulnerable individuals. Taylor, Lichstein, et al. (2005) infer that insomnia induced stress may precipitate the development, or trigger the relapse of depression or anxiety, and vice-versa. Those with sleep initiation problems often spend nocturnal awakenings ruminating about past failures or worry about future issues, thus resulting in depression or anxiety (Taylor, Lichstein, et al., 2005). Conversely, daytime stress associated with ruminations regarding past failures or worry about future issues usually extend to bedtime, increasing psychological and physiological arousal, and therefore causing insomnia (Taylor, Lichstein, et al., 2005). Nevertheless, such theories are mostly speculation, and more research is needed to support or refute such notions. This section will discuss common risk-factors and a potential cause-effect relationship between symptoms and disorders of insomnia, depression, GAD and other subtypes of anxiety.

6.2.5.1. Common risk-factors

Neale and Kendler (1995) propose that common risk-factors, all independent and of small effect, actually reflect alternative forms of the same disorder, suggesting that the same disorder may manifest in different ways (e.g., via insomnia or depression). In contrast, Staner (2010) notes that such risk-factors may result in two distinctive yet associated disorders if risk-factors are common to both conditions. The results of studies 2 and 3 support the latter theory regarding the relationships between insomnia and OCD, PD, SAD and SP, where depression was found to be the common link. Previous studies have suggested that hopelessness, a maladaptive core belief and symptom of depression, is
strongly correlated with insomnia in young adults (Ribeiro et al., 2012) and anxiety during adolescence (Thompson, Mazza, Herting, Randell, & Eggert, 2005). An adolescent with depression may contain a hopelessness core belief that may trigger or contribute to the development of concurrent episodes of insomnia and anxiety. In any case, together, the results from this thesis and the studies above suggest that depressive symptoms, such as hopelessness, are the common link between insomnia and various subtypes of anxiety.

Common maladaptive coping strategies may also underlie the developmental overlap between insomnia, depression and anxiety subtypes. Emotional coping strategies have been associated with insomnia, depression and anxiety (Morin, et al., 2003; Plancherel & Bolognini, 1995). Examples of emotional coping strategies include seeking comfort and support from others, avoiding stress triggers, writing about deep emotions, relaxation techniques, emotional suppression, self-criticism, and wishing the problem will go away (Compas, Connor-Smith, Saltzman, Thomsen, & Wadsworth, 2001; Folkman, 1984). For example, an examination period may trigger physiological anxiety and excessive, uncontrollable worry in adolescents who fear failure, leading to the avoidance of studying, which can precipitate the development of depressive symptoms (e.g., hopelessness) and further physiological arousal, and thus result in sleep initiation problems. Alternatively, nocturnal insomnia episodes may provide opportunities for excessive rumination about problems or worry, all of which are likely to exacerbate poor sleep, depressed mood, and anxiety. Substance abuse has been associated with insomnia, depression and anxiety during adolescence (Johnson & Breslau, 2001; Kaneita et al., 2006), and hence may represent another common mechanism that underlies the relationship between these variables. Depressive or anxious symptoms may precipitate substance use (adolescents often report alcohol or marijuana use as a coping mechanism for depression), which can precipitate the
development of insomnia and anxiety (Shibley, Malcolm, & Veatch, 2008). Conversely, an adolescent with sleep initiation problems may consume excessive amounts of alcohol or marijuana to assist with sleep, which may precipitate or exacerbate symptoms of depression and anxiety.

Attentional biases towards threatening stimuli may also underlie the relationship between insomnia, depression and anxiety. Hankin, Gibb, Abela, and Flory (2010) reported that adolescents with depression are more likely to have an attentional bias towards sad facial expressions rather than happy or angry, whereas youths with anxiety are more likely to focus on angry facial expressions. Interestingly, youths with comorbid anxiety and depression are more likely to have an attentional bias towards angry and sad facial expressions, and avoided happy faces. These findings suggest an attentional bias towards cues that resemble adolescents’ internalising problems. Moreover, Mor and Winquist’s (2002) meta-analysis of children, adolescents and adults reported an association between self-focused rumination and negative affect (depression, anxiety and negative mood). The same study found that private self-focus (self-motivated goals that do not require the consideration of others) was more strongly related to depression and GAD, whereas public self-focus (goals that require the consideration of others) was more strongly associated with SAD (Mor & Winquist, 2002). Therefore, an adolescent may have a self-focused attentional bias towards, which may lead to rumination about a threat or hopelessness, and in turn contribute to sleeplessness or depression.

6.2.5.2. Cause-effect relationship

Finally, Insomnia, depression and GAD may be bidirectionally and causally related, where the development of an insomnia disorder results in the development of depression and GAD, and vice-versa. According to Hill’s (1965) widely cited criteria, a causal relationship
can be inferred (but not confirmed) when: previous studies have consistently reported significant effects (even across cultures), large effect-sizes and a dose-response linear relationship; there are clear directions of inference (e.g., insomnia causes depression); the relationship is biologically plausible and corresponds with the known facts of the disorders; experimental evidence is available; and a judgment be made in similar circumstances.

Indeed, previous findings, along with the results from the current thesis, largely satisfy Hill’s (1965) criteria. Studies across many cultures have consistently reported a wide range of dose-linear associations, with varying effect-sizes, and have not seriously conflicted with the known facts about insomnia, depression or anxiety (Gregory & O’Connor, 2002; Gregory, et al., 2009; Jansson-Fröjmark & Lindblom, 2008; Kaneita, et al., 2009; J. M. Kim, et al., 2009). Such studies have often control for potential covariates, and hence further strengthen the notion of a cause-effect relationship. There has also been experimental evidence based on treatment studies (Alfano, et al., 2007; Manber, et al., 2008), and various biologically plausible explanations that have been discussed in chapters 3, 4 and 5. Furthermore, the current thesis, in accordance with previous research, supports the notion that insomnia is bidirectionally related to depression and GAD. Considering the evidence, it seems plausible to infer a bidirectional and at least partial cause-effect relationship between insomnia and depression, and insomnia and GAD.

6.3. The effects of chronotype on the relationship between insomnia, depression and subtypes of anxiety

Section 6.3. discusses the effects of chronotype on the relationship between insomnia, depression and subtypes of anxiety. Specifically, the prediction and confounding effects of chronotype will be considered, along with the relationship between chronotype and
insomnia, depression and anxiety across a 6-month period, and the mechanisms that underlie these relationships.

6.3.1. *The prediction and confounding effects of chronotype*

Studies 2 and 3 found that an evening chronotype independently predicts insomnia at 6-month follow-up, but not depression or subtypes of anxiety. Furthermore, chronotype was not found to account for the relationships between insomnia and depression, or insomnia and subtypes of anxiety, as each relationship remained significant when chronotype was the only controlled variable. Together, these results suggest that chronotype effects the relationships between insomnia, depression and GAD by initiating a pathway for and hence contributing to the development of insomnia [which may then contribute to the development of depression or GAD (see section 6.4.1. for further details about potential pathways between chronotype, insomnia, depression and subtypes of anxiety)], rather than accounting for these relationships. Such results support the notion of the reviewer for study 2, who suggested a lack of empirical evidence for assessing the mediation effect of chronotype on the relationship between insomnia, depression and subtypes of anxiety.

In study 3, it was noted that eveningness is a risk-factor for the development of delayed sleep phase syndrome in adolescents. Eveningness is also a risk-factor for the development of sleep onset insomnia (Weitzman et al., 1981), which is likely reflected in the findings discussed above. Those with an evening chronotype may retire at a time that is earlier than, and does not align with their circadian preference, and hence experience problems with initiating sleep. This process can lead to maladaptive sleeping strategies, such as spending an excessive amount of time in bed and remaining awake while in bed (Perlis, et al., 1997; Spielman, et al., 1987), and presents an opportunity for physiological, cognitive
and somatic arousal. Such arousal can become conditioned to the sleep environment, and hence can develop into chronic, psychophysiological insomnia (Bonnet & Arand, 2010; Perlis, et al., 1997; Riemann, et al., 2010). Therefore, an evening chronotype is likely to be a risk-factor for the development of chronic psychophysiological insomnia.

6.3.2. Chronotype, insomnia, depression, and subtypes of anxiety across a 6 month period

The results from studies 2 and 3 found that eveningness was no longer associated with PD once insomnia was controlled, suggesting that the relationships between eveningness and PD is dependent on insomnia from baseline until at least a 6-month period. However, the relationships between eveningness and other subtypes of anxiety before controlling for potential confounders were inconsistent across studies 2 and 3. Eveningness may predict PD above and beyond insomnia, and chronotype may be correlated to other subtypes of anxiety given a longer period of time between assessments, but research has yet to be done in this area. Future studies could replicate the current methodology using longer follow-up time periods (one or two years).

Interestingly, study 2 found a relationship between depression and eveningness after insomnia and anxiety overall were controlled, whereas study 3 failed to report a relationship between chronotype at baseline and depression at follow-up once insomnia at baseline was controlled. These results suggest an inconsistent nature of the relationship between eveningness and depression across a 6-month period, in that eveningness is related to depression above and beyond insomnia and anxiety at a given point in time, but not to depression six months later above and beyond insomnia at baseline. A theoretical explanation is difficult to propose, as previous studies have not assessed the longitudinal associations between chronotype and depression during adolescence. Furthermore, the
disparity between study 2 and 3 is surprising given that, firstly, the daily pressures of life are suggested to accumulate during adolescence and hence promote later bedtimes, poorer sleep and more mental health problems (Carskadon, et al., 2004; Kaneita, et al., 2009), and secondly, various factors typical of those with an evening preference are also symptoms of depression and insomnia, such as persistent sleep deprivation, sleep displacement, difficulty adjusting to social constraints and a changing lifestyle (Giannotti, et al., 2002). The difference in results cannot be attributed to the differences in statistical analyses, as bootstrapped regression analyses at baseline yielded identical results as generalised estimating equations. Additional research is needed to further explore the effects of baseline insomnia on the longitudinal relationship between depression and chronotype. Biological markers of chronotype, objective measures of sleep and clinically assessed mental health variables could be used.

6.3.3. Mechanisms

The finding that baseline eveningness predicted follow-up insomnia may be explained by the notion that people with sleep-onset insomnia exhibit a phase delay pattern in body temperature rhythm (Morris, et al., 1990), which, paired with retirement before sleepy, could lead to prolonged wakefulness in bed and hence present an opportunity for hyperarousal and rumination as per psychophysiological insomnia. The indirect association between chronotype and the mental health variables contradicts the notion that personality factors, particularly low self-control, may explain the association between an eveningness chronotype, depression and anxiety (Saxvig, et al., 2012). Instead, a shift in preference for later bed and rise times during adolescence (Russo, et al., 2007) coupled with an enforced early rise time for school may result in sleep deprivation or insomnia symptoms (particularly sleep initiation problems), which could lead to depression or GAD. Sleep deprivation and
insomnia could also result in poorer stress management and coping skills (Killgore et al., 2008) that would otherwise act as preventative barriers for stress and mental health problems during adolescence (Dumont & Provost, 1999). Furthermore, the daily life pressures mentioned above may lead to later bedtimes, which may result in sleep deprivation during adolescence, and in turn more mental health problems (Carskadon, et al., 2004; Kaneita, et al., 2009).

These results also add to Gaspar-Barba et al.’s (2009) notion that the association between depression, anxiety disorders and eveningness may be related to corticotropin-releasing factor (Arborelius, et al., 1999). This hormone could be a biological factor that contributes to the relationship between eveningness and insomnia rather than eveningness and mental health, considering it is hypothesised to be related to the aetiology of insomnia (Roth, Roehrs, & Pies, 2007). The common association with corticotropin-releasing factors may also at least partially explain why the relationship between eveningness and depression, and eveningness and subtypes of anxiety is dependent on insomnia. Conversely, circadian abnormalities such as mutations to molecular clock genes have been reported to accelerate or delay circadian cycles (Bunney & Bunney, 2000), which may predispose an adolescent to sleep initiation problems or delayed sleep phase syndrome, and in turn contribute to the development of depression.

6.4. Pathways between insomnia, depression, subtypes of anxiety and chronotype

The results from this thesis suggest that insomnia is likely be developmentally related to depression and GAD, but not to other subtypes of anxiety during adolescence. Furthermore, eveningness is likely to be an independent risk-factor for the development of
insomnia, but not depression or subtypes of anxiety within a 6-month period. Such findings have theoretical implications on particular developmental pathways between insomnia, depression, subtypes of anxiety and chronotype. The following section discusses these pathways in further detail.

Studies 2 and 3 reported independent bidirectional relationships between insomnia and depression, and insomnia and GAD above and beyond chronotype, anxiety overall or depression, and age. Such evidence suggests but cannot infer direct (causal) bidirectional relationships alone, as treatment or induced sleep deprivation studies are needed to infer causality. Indeed, studies have shown that chronic partial sleep deprivation induced in caregivers of children with chronic illnesses mediates the severity of depressive symptoms in the caregivers (Meltzer & Mindell, 2006). Furthermore, an enforced six days of sleep restriction resulted in sleep EGG abnormalities and endocrine disturbances akin to those in depression (Spiegel, Leproult, & Van Cauter, 1999). Together, this evidence suggests that the developmental relationship between insomnia and depression is bidirectional and at least partially direct. Therefore, a pathway may follow from insomnia to depression or GAD, and vice-versa (Figures 7 and 8).

Figure 7. Pathways between insomnia and depression.

Figure 8. Pathways between insomnia and GAD.
Study 3 also reported partial indirect effects when insomnia predicted depression and GAD, and when GAD predicted insomnia. In particular, the magnitude of the predictive effect of insomnia on depression and GAD decreased once anxiety (as an overall construct) and depression, respectively, were statistically controlled. Similarly, the magnitude of the predictive effect of GAD on insomnia decreased once depression was controlled. These findings suggest that the relationship between insomnia and GAD may be at least partially attributable to depression, and that the predictive effect of insomnia on depression may be at least partially attributable to anxiety. Therefore, a complex interaction between insomnia, depression and GAD seems to occur during adolescence, where depression may partially account for the bidirectional relationship between insomnia and GAD, and anxiety may partially account for the predictive effect of insomnia on depression (Figures 9, and 10).

*Figure 9. Indirect pathways between insomnia and GAD.*

*Figure 10. Indirect pathways between insomnia and depression.*
The relationships between insomnia and OCD, PD, SAD and SP were found to be completely accounted for by depression. These findings suggest that the development of OCD, PD, SAD or SP may involve insomnia, and vice-versa, despite the fact that insomnia did not predict OCD, PD, SAD or SP once depression was controlled, and vice-versa.

Consequently, insomnia resulting in depression may in turn result in OCD, PD, SAD or SP; and OCD, PD, SAD or SP that leads to depression may in turn lead to insomnia (Figure 11). Those with sleep initiation problems may lie in bed awake in the dark, which might intensify depressive or anxious feelings about life, and in turn lead to anxiety problems or depression (Staner, 2010). Similarly, depressive symptoms such as feelings of worthlessness may result in heightened anxiety about life, which in turn result in problems with sleep initiation.

Alternatively, Staner (2010) suggested that insomnia may reduce an individual’s capacity to deal with personal and social problems, thereby increasing the likelihood of stressful life events or poor responses to such events that could result in depression or anxiety.

![Diagram](image)

*Figure 11. Pathways between insomnia and OCD, PD, SAD and SP.*

The results also suggest that eveningness is an independent risk-factor for the development of insomnia (Figure 12). However, eveningness was found to predict depression and GAD before but not after insomnia was statistically accounted for, suggesting that eveningness may to lead to insomnia, which then may lead to depression and GAD (Figure 13). Moreover, eveningness that leads to insomnia, which leads to depression may in
turn lead to OCD, PD, SAD and SP (Figure 14), as eveningness predicted OCD, PD, SAD and SP before but not after insomnia and depression were controlled. These findings suggest that pathways leading to insomnia, depression and each anxiety subtype may involve an evening preference in some capacity.

Figure 12. Pathways between eveningness and insomnia.

Figure 13. Pathways between eveningness, insomnia, and depression or GAD.

Figure 14. Pathways between eveningness and OCD, PD, SAD or SP.
6.5. Clinical implications

The results from the current thesis suggest that prevention and treatment efforts for insomnia should consider depression and GAD during adolescence, and vice-versa. Public health interventions and treatment plans that also focus on circadian preferences during adolescence may prevent and alleviate insomnia, and hence consequent depression and GAD. Finally, prevention and treatment plans for OCD, PD, SAD and SP should also focus on depression during adolescence, given that depression was associated with these anxiety subtypes beyond other covariates. Previous research suggesting that the treatment of sleep problems can alleviate or prevent depression and anxiety was considered in the discussion section of study 3. The following section discusses in further detail some prevention and treatment options for insomnia, depression and anxiety during adolescence.

6.5.1. Prevention

As argued in study 3, adolescents develop a stronger preference for evenings with age because of various circadian rhythm and environmental changes, but often rise earlier than desired due to an enforced school schedule (Crowley, et al., 2007). Consequently, adolescents may experience symptoms of sleeplessness and sleep deprivation, which may then contribute to mental health issues during adolescence (Liu & Zhou, 2002). Preventative approaches for insomnia, depression and subtypes of anxiety, then, may benefit from considering sleep deprivation, and therefore delaying school start time. A recent study found significant improvements in measures of satisfaction with sleep, motivation, alertness and class attendance, and reductions in fatigue, depressed mood, and daytime sleepiness following a 30 minute delay in school start time (J. A. Owens, Belon, & Moss, 2010).
Therefore, later school starts seem to improve sleep, emotional well-being, and other elements of adolescent life such as neurocognitive performance.

Recent studies have also suggested that a delay in school start time may result in improved academic performance (Carrell, Maghakian, & West, 2011), which is expected given the improvement in measures of motivation, alertness and class attendance described above (J. A. Owens, et al., 2010), and the association between insomnia, sleep deprivation, neurocognitive impairment and academic achievement (Curcio, et al., 2006). Furthermore, Danner and Phillips (2008) reported an increase in total sleep time, a decrease in recovery sleep on weekends, and a reduction in average motor vehicle collisions by 16.5% two years after baseline, following an one hour shift in school start times. In contrast, the average rate of motor vehicle collisions for those who started school at normal time increased by 7.8% over the two-year period (Danner & Phillips, 2008). Therefore, a delay in school start time may result not only in improved sleep, mental health and neurocognitive performance, but also everyday functioning, safety of adolescent (and other) drivers, and less sleep deprivation relative to adolescents who start school at normal time. Policy managers and public health strategists should consider postponing school start time in Australia to prevent the development of insomnia, depression and anxiety disorders, which in turn may improve academic performance, neurocognitive performance, and overall quality of life.

Alternatively, early regulation of circadian rhythms by, for example, increasing environmental bright light exposure in mornings and regulating weekend catch-up opportunities may prevent the onset of clinically significant problems.

As noted in study 3, education is important to preventative efforts for insomnia, depression and anxiety subtypes. In particular, psychological and emotional literacy can be taught to students and teachers. Educational sessions or programs can inform students
about the importance of sleep and mental health, aim to promote emotional well-being, and teach coping mechanisms that may be effective in enhancing mental health (and thereby preventing or treating sleep or psychological problems). Such sessions or courses could also aim to up-skill teachers in identifying the symptoms of insomnia, depression, and anxiety disorders, along with the potential mechanisms behind disruptive and difficult behaviour (e.g., school refusal, drug and alcohol use). Indeed, a systematic review of 17 studies reported that a universal approach to mental health promotion in schools was effective when implemented continuously for more than a year, and aimed to promote emotional well-being rather than prevent mental illness (Wells, Barlow, & Stewart-Brown, 2003).

6.5.2. Treatment

Treatment efforts for insomnia, depression and anxiety can be effective when targeting adolescents. Psychological treatment, in particular, a multifaceted cognitive behavioural therapeutic approach, emerged as the treatment of choice for insomnia during adolescence (Edinger & Means, 2005). Cognitive behavioural therapy (CBT) results in subjective and objective improvements in sleep that are stable over time and effective in clinical and primary care settings (Edinger & Means, 2005). Schlarb, Liddle, and Hautzinger (2011) found a reduction in problems with sleep initiation, sleep efficacy, sleep duration, lethargy, rumination, and mental health following a short-term multifaceted group cognitive behavioural therapy for adolescents and parents. Such evidence provides support for, and therefore highlights the importance of using interventions that focus on the psychological aspects of insomnia.

Recent studies have also provided support for the use of CBT and other psychological approaches to treat adolescent depression and anxiety (A. James, Soler, & Weatherall, 2005; Reinecke, Ryan, & DuBois, 1998). In their meta-analysis of six depression treatment studies
using CBT, Reinecke, et al. (1998) found a large effect of 1.02 (Cohen’s d) from baseline (before treatment) to follow-up (after treatment). Another systematic review suggested that CBT is an effective method of treatment for childhood and adolescent anxiety disorders in comparison to those on a waiting list who did not receive treatment, and those who received attention only (i.e., diary or support, but not cognitive behavioural therapy) (A. James, et al., 2005). Furthermore, a meta-analysis by Weisz, McCarty, and Valeri (2006) found that psychological therapies such as cognitive behavioural therapy are effective, although not as much as suggested by A. James, et al. (2005) when used to treat adolescent mental health disorders. In any case, a CBT program may help to increase the adolescents’ knowledge about sleep and mental health topics, such as sleep hygiene and helpful coping strategies, and in turn assist in cognitive restructuring, behavioural change (Schlarb, et al., 2011), and hence symptom change.

Pharmacotherapeutic treatment for insomnia, depression and anxiety during adolescence, on the other hand, may be useful in some settings but not others. A meta-analysis suggested that tricyclic antidepressants are no more effective than a placebo when treating depression in children and adolescents (Hazell, O’Connell, Heathcote, Robertson, & Henry, 1995). Moreover, in a review about the use of melatonin in paediatric insomnia, Armour and Paton (2004) found that melatonin reduced sleep latency, but was not shown to consistently improve other types of sleep disturbance. Furthermore, short-term concerns with regard to melatonin use in paediatric populations included the exacerbation of epilepsy and asthma (Armour & Paton, 2004). Other commonly used medication for mental health disorders have yielded dangerous side-effects. For example, selective serotonin reuptake inhibitors are widely used to treat adolescent depression (Safer, 1997; Weisz & Jensen, 1999), but adverse effects such as suicidal ideation and attempts have been reported.
(Vitiello & Swedo, 2004; Whittington et al., 2004). Also, despite the fact that antidepressants such as fluoxetine have been reported to produce significantly greater improvements in adolescent depression than placebo or cognitive behavioural therapy (Treatment for Adolescents with Depression Study Team, 2004), Weisz, et al. (2006) notes that the U.S. Food and Drug Administration had issued a warning on all antidepressants in 2004 to emphasise the possible risk of suicidality. Therefore, the use of medication as a form of treatment for depression and anxiety needs to be considered carefully during adolescence. Indeed, data from both published and unpublished studies indicate that the risks of pharmacotherapeutic treatment in children and young people out-way the benefits (Whittington, et al., 2004).

Recent studies have suggested that a combination of medication and CBT may be a superior approach to the use of either forms of treatment alone for adolescent mental health disorders. Firstly, studies that have assessed the combination effect of medication and CBT on mental health report fewer or no cases of suicidal ideation or attempts (March, 2004; Treatment for Adolescents with Depression Study Team, 2004; Walkup et al., 2008). Also, less suicidal ideation in adolescents treated with fluoxetine and CBT have been reported than in those treated solely with fluoxetine (Treatment for Adolescents with Depression Study Team, 2004), suggesting that a combination treatment program may yield less aversive effects and suicidality than medication alone. Finally, recent paediatric studies have also reported greater improvement in mental health following the combination of CBT and medication relative to CBT or medication alone (Treatment for Adolescents with Depression Study Team, 2004; Walkup, et al., 2008). Together, these studies suggest that a multifaceted treatment approach that considers biological and psychosocial aspects of
depression and anxiety disorders are safer, more efficacious, and therefore should be the preferred method of intervention when treating adolescents (Whittington, et al., 2004).

Studies have also suggested that bright light therapy (BLT), a treatment method for adolescent delayed sleep phase syndrome (of which eveningness is an essential symptom), may be useful for treating adolescent insomnia and depression when used in conjunction with CBT and other therapies (Bootzin & Stevens, 2005; Gradisar et al., 2011). Bootzin and Stevens (2005) note that BLT is used to alter the sleep/wake circadian rhythm, particularly in those who are phase delayed, cannot initiate sleep until the early morning, and struggle with morning awakenings. A shift from a delayed sleep phase to a neutral sleep preference may reduce sleeplessness, depression and anxiety symptoms. Indeed, Gradisar, Dohnt, et al. (2011) found that, when compared to a waitlist, CBT plus BLT leads to significantly reduced sleep onset latency, time of sleep onset, wake after sleep onset, sleeplessness and fatigue; earlier sleep onset and rise times; increased total sleep times on school nights; and less depressive symptoms. Furthermore, Bootzin and Stevens (2005) reported that adolescents who completed at least four sessions of a six-session group treatment for sleep disturbances that included stimulus control instructions, BLT, sleep hygiene education, cognitive therapy and mindfulness-based stress reduction showed improved sleep onset latency, number of awakenings, total sleep time, and self-rated quality of sleep; and reduced sleepiness, worry, mental health distress, and substance abuse problems at 12-month follow-up. Therefore, not only is a multifaceted program that considers biological and psychosocial factors the preferred method of treating adolescent insomnia, anxiety and depression, but also delayed sleep phase syndrome and other psychiatric disorders.
6.6. Limitations and future research

The limitations discussed in studies 1, 2 and 3 include the use of self-report measures; insomnia assessed as an overall variable rather than as different symptoms; the lack of control over potential confounding variables such as other sleep disorders, other psychiatric disorders, and genetic/neurobiological vulnerabilities. The future research that was suggested includes bidirectionality studies that assess different insomnia symptoms; and replication of study 3 with objective measures and/or clinical assessments for insomnia, depression and subtypes of anxiety, the assessment of other sleep and psychiatric disorders, and the consideration of genetic and neurobiological vulnerabilities. The current section discusses the limitations and future research that is directly relevant to the thesis topic, but beyond the scope of studies 1, 2 and 3. The topics to be discussed include bidirectionality across insomnia symptoms and sleep deprivation; stressful life events; physical exercise; and sleep, chronotype and technology. Insomnia symptoms and physical exercise were included in the current section, because the discussion provided in study 1 was deemed insufficient considering different anxiety subtypes had been assessed.

6.6.1. Insomnia subtypes

The current study assessed insomnia as an overall variable rather than specific symptoms. Ohayon (2005) found people who reported non-restorative sleep were 3.64 and 4.02 times more likely to suffer from anxiety and mood disorders respectively than those who reported other insomnia symptoms (troubles initiating and maintaining sleep). Similarly, Hartz et al.’s (2007) investigation of risk factors for insomnia in a rural population found that restless sleep (considered similar to non-restorative sleep) (Hartz, et al., 2007, p. 941) yielded the highest association with low energy levels and depression, whereas anxiety
symptoms were more often associated with difficulty maintaining sleep. Together, these results suggest that different aspects of insomnia have different risk-factors and therefore possibly different aetiologies. Each insomnia subtype (e.g., problems with sleep initiation, sleep maintenance, early morning awakenings, and non-restorative sleep) would then require different preventative and treatment strategies. Given the findings of study 3, depression and certain anxiety subtypes may be risk-factors and aetiologically related to different types of insomnia.

The current study did not assess bidirectionality across insomnia subtypes, as the authors could not locate an inventory that assessed different subtypes of insomnia and that was validated in adolescent populations. Nevertheless, future studies could assess insomnia subtypes via subjective measures such as sleep diary, objective measures (e.g., polysomnography, actigraphy) or clinical interviews. Longitudinal methodology could be used to investigate bidirectionality, and treatment studies could be used to investigate aetiology. Large samples would be needed in both cases, which would likely be obtained through the general population.

6.6.2. Sleep deprivation

Previous research has reported an association between sleep deprivation, depression and anxiety during adolescence (Fredriksen, Rhodes, Reddy, & Way, 2004; Talbot, McGlinchey, Kaplan, Dahl, & Harvey, 2010). Fredriksen, et al. (2004) found that increased sleep deprivation over time independently predicted increased depressive symptoms and reduced self-esteem over time. Furthermore, Talbot, et al. (2010) reported that younger adolescents considered their main worry as more threatening when sleep deprived compared to when well rested. The same study also reported a greater increase in anxiety during a catastrophic event in younger and middle adolescents when sleep deprived relative
to when well rested (Talbot, et al., 2010). Considering the research, sleep deprivation may be a risk-factor for the development of depression and anxiety during adolescence.

Future research could assess the bidirectionality of the relationship between sleep deprivation, depression and anxiety subtypes. Sleep deprivation could be assessed by objective measures (e.g., polysomnography, actigraphy), while depression and anxiety could be assessed by clinical interviews. Longitudinal methodology and treatment studies could be used to investigate directionality and aetiology.

6.6.3. Insomnia, depression, anxiety and stressful life events

The current study did not assess stressful life events. Bernert, Merrill, Braithwaite, Van Orden, and Joiner Jr (2007) found that family life stress predicted insomnia at three week follow-up in older adolescents and young adults after controlling for depression. Furthermore, Braet, et al. (2013) found that stress induced by different factors strongly predicts depressive symptoms in younger, middle, and older adolescence. Moreover, Moksnes, Espnes, and Haugan (2014) reported that stress related to academic performance significantly predicted symptoms of depression and anxiety, whereas stress related to peer pressure significantly predicted depression. Finally, stressful life events are risk-factors for clinically significant symptoms and a diagnosis of post-traumatic stress disorder (PTSD) in adolescents (Trickey, Siddaway, Meiser-Stedman, Serpell, & Field, 2012), which has been associated with sleep disturbances (Garrison, Weinrich, Hardin, Weinrich, & Wang, 1993), depression (Luo, et al., 2012) and anxiety (Giannopoulou et al., 2006). Stressful life events and PTSD, then, may be a confounding factor for and hence affect the bidirectionality of the relationship between insomnia, depression and anxiety in adolescents.
Future research could assess whether stressful life events and PTSD are separate risk-factors for the development of insomnia, depression and anxiety; mediate the relationships between these variables; or moderate the relationship between these variables. A replication of the current study that includes measures of stressful life events may be the simplest method, but studies using objective measures and clinical assessment of insomnia, depression and anxiety would be the preferred option. In the case of self-report measures, inventories based on the DSM-5 could be developed and used.

**6.6.4. Insomnia, depression, anxiety and physical activity**

Physical activity has also been associated with insomnia, depression, and anxiety. Brand, et al. (2010) found that adolescent athletes report better sleep and less depressive and anxiety symptoms. Furthermore, there is emerging evidence that physical activity can be protective against developing depression and reduce anxiety symptoms that are common in depression (Martinsen, 2008). This evidence suggests that physical activity may be a risk-factor for the development of depression and symptoms of anxiety, but it is currently unknown whether physical activity is a separate risk-factor for the development of insomnia. Furthermore, physical activity may mediate or moderate the relationships between insomnia and depression or insomnia and anxiety. The current study included physical activity variables, but did not include such variables in the analyses due to extremely skewed data.

Future research could assess the effects of a treatment program based on physical activity to prevent or improve rates of insomnia, depression and anxiety. For example, a group of adolescents with diagnosed insomnia, depression and/or an anxiety disorder could be subjected to 45 minutes (the approximate length of period for a class in South Australian schools) of moderately intensive exercise over a determined time period (e.g., everyday for one week), and compared to adolescents who have a physically inactive class or a placebo
intervention. Indeed, group exercise has been found to improve depressive symptoms compared to usual activity, with improved hormonal responses to stress and physical fitness in young females (Nabkasorn et al., 2006). Perhaps more interestingly, a study could assessed the preventative and treatment effects of physical activity and bright light therapy on insomnia, depression and anxiety. For example, a physical education class could be moved to the first morning lesson under bright lights (outdoors or indoor gymnasium), and compared to bright light therapy alone, morning physical education classes under dimmer light, and no change to school class schedule. Such a study would be inexpensive, effective, and possible for most schools.

6.6.5. Technology, sleep, and chronotype

Previous research has reported associations between sleep disturbances and night time technology use (Calamaro, et al., 2009; King, Delfabbro, Zwaans, & Kaptsis, 2013). Calamaro, et al. (2009) found that high school students who slept between 8 – 10 hours per night had a 1.5 to two-fold decrease in night time technology use than those with 6 – 8 hours and 3 – 5 hours, while those who fell asleep during school were much more likely to use technology at night than those who remained awake (OR 69.9). Furthermore, a South Australian adolescent study reported associations between technology use and sleep duration on weekdays and weekends, bedtime delays, and sleep interruptions (King, et al., 2013). The association between sleep disturbances and night time technology use may at least partially result from a disruption to the circadian rhythm cycle caused by bright light emitted by the device. Perhaps depending on the timing of duration of exposure (Heath et al., 2014), bright light suppresses melatonin production (Lewy, Wehr, Goodwin, Newsome, & Markey, 1980), inducing wakefulness and inhibiting sleep (Cajochen, Kräuchi, & Wirz-Justice, 2003). Bright lights at night from electronic devices, then, may delay melatonin secretion,
and consequently result in later bedtimes, and induce sleep onset insomnia and delayed sleep phases during adolescence. These findings, paired with the notion that technology use at night increases cognitive, emotional, and physiological arousal at bedtime, and in turn sleep onset latency while reducing total sleep time (King, et al., 2013), suggests that nighttime technology use may be a risk-factor of and hence potentially contribute to the aetiology of sleep deprivation and insomnia.

Future research could investigate the impact of technology on chronotype and the development of insomnia during adolescence. A controlled experimental design that assesses the effects of induced night time technology use on sleep and the circadian rhythm would be ideal, particularly where technology use is controlled and recorded, and sleep and the circadian rhythm are assessed in a sleep laboratory via objective means. Such a study could be run overnight or across several nights. Alternatively, a longitudinal study that assessed night time technology use via questionnaires, and sleep and circadian rhythm variables via objective measures or self-report measures would also advance current research. Variables that could be assessed include melatonin levels, core body temperature, wakefulness at night, bedtime, duration of sleep onset, time of sleep onset, wake-time, rise-time, time between wake and rise-time, difficulty falling asleep and rising, sleep efficiency, sleep quality, and number of awakenings. A significant relationship between technology use and insomnia from either study design would suggest that the former may be related to the aetiology of the latter. Lower melatonin levels; progressively later bedtimes, time of sleep onset, wake-times, and rise-time; and shorter time between wake and rise-time during the week due to light from induced technology use would suggest a progressively later circadian preference. Preventative and treatment efforts for insomnia or delayed sleep phase syndrome during adolescence may then consider night time technology use, which, given
the results of this thesis, could impact the development or maintenance of depression and GAD.

6.7. Conclusions

Best available evidence suggests a bidirectional longitudinal relationship between insomnia and depression, and insomnia and anxiety. After controlling for covariates and assessing different anxiety subtypes, insomnia seems to be bidirectionally related to depression and GAD, but not longitudinally related to OCD, PD, SAD or SP. Furthermore, eveningness at baseline seems to predict insomnia 6 months later after controlling for covariates, but not depression, GAD, OCD, PD, SAD or SP. Prevention and treatment efforts for insomnia may also consider depression, GAD and an eveningness preference, whereas prevention and treatment efforts for depression and GAD may consider insomnia. Finally, given the strong effect of depression on anxiety subtypes, prevention and treatment plans for OCD, PD, SAD and SP should concurrently focus on depression.
### 7. Appendix – bootstrapped regression analyses when controlling for outcome variables at baseline

<table>
<thead>
<tr>
<th>Model</th>
<th>Predictor</th>
<th>β (Bootstrap)</th>
<th>CI Lower</th>
<th>CI Upper</th>
<th>R(^2) adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Depression</td>
<td>0.178</td>
<td>0.018</td>
<td>0.334</td>
<td>0.538</td>
</tr>
<tr>
<td></td>
<td>Chronotype</td>
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<td>-0.146</td>
<td>0.031</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anxiety</td>
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<td>-0.024</td>
<td>0.071</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>0.254</td>
<td>-0.092</td>
<td>0.615</td>
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</tr>
<tr>
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<td>Gender</td>
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<td>-1.165</td>
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<tr>
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<td>Insomnia</td>
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<td>0.374</td>
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</tr>
<tr>
<td>2</td>
<td>GAD</td>
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<td>-0.096</td>
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<td>0.538</td>
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<td></td>
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<td>0.627</td>
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<tr>
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<td>0.540</td>
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<tr>
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<tr>
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<td>Gender</td>
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<td>0.085</td>
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<td>Age</td>
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<td>0.103</td>
<td>0.388</td>
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<td>-0.140</td>
<td>0.581</td>
<td></td>
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<td>0.390</td>
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<tr>
<td>6</td>
<td>SP</td>
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<td>-0.011</td>
<td>0.204</td>
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<td>Anxiety</td>
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<td>0.035</td>
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<td></td>
<td>Gender</td>
<td>-0.332</td>
<td>-1.276</td>
<td>0.619</td>
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</table>

Note. Bootstrapped regression analyses for when depression and subtypes of anxiety at baseline were used to predict insomnia at follow-up after controlling for insomnia at baseline.  5000 bootstrapped were computed. β= regression co-efficient, CI= Bca 95% Confidence Interval, GAD= Generalised anxiety disorder, OCD= Obsessive compulsive disorder, PD= Panic disorder SAD= Separation anxiety disorder, SP= Social phobia.
Table 18

Regression analyses with insomnia as the predictor variable

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Predictor</th>
<th>β (Bootstrap)</th>
<th>Lower</th>
<th>Upper</th>
<th>adjusted R²</th>
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</thead>
<tbody>
<tr>
<td>Depression</td>
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<td>Anxiety</td>
<td>0.049</td>
<td>0.000</td>
<td>0.099</td>
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<tr>
<td></td>
<td>Age</td>
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<td>0.764</td>
<td></td>
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<tr>
<td></td>
<td>Gender</td>
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<td>-0.804</td>
<td>1.181</td>
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<td>Depression</td>
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<td>GAD</td>
<td>Insomnia</td>
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</tr>
<tr>
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<td>1.140</td>
<td></td>
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<tr>
<td></td>
<td>GAD</td>
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<td>0.759</td>
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Note. Bootstrapped regression analyses for when insomnia at baseline was used to predict depression and subtypes of anxiety at follow-up after controlling predicted variable at baseline. 5000 bootstrapped were computed. GAD= Generalised anxiety disorder, OCD= Obsessive compulsive disorder, PD= Panic Disorder, SAD= Separation anxiety disorder, SP= Social phobia, CI= Bca 95% Confidence Interval


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Spence, S. H., Najman, J. M., Bor, W., O’Callaghan, M. J., & Williams, G. M. (2002). Maternal anxiety and depression, poverty and marital relationship factors during early


