Excessive Daytime Sleepiness in Children and Adolescents across the Weight Spectrum

by

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A thesis submitted in conformity with the requirements for the degree of Master of Science
Institute of Medical Science
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Abstract

A relationship between overweight and excessive daytime sleepiness (EDS) has been suggested in the adult population, and to a limited extent in the pediatric population. Daytime sleepiness can interfere with various components of daytime function. In light of the increase in the rates of pediatric overweight and obesity, the aim of this study was to investigate the relationship between weight and EDS in a pediatric population.

Using a retrospective approach, data collected in a pediatric sleep clinic was analyzed. Objective measures of EDS were correlated with age, gender, body mass index percentile, and overnight sleep test recording variables.

In males and in all children under the age of 13 years old, EDS was more common in those weighing above the normal range, EDS was present particularly during mid-morning hours. Additionally, weight above the normal range correlated with evidence of EDS after adjusting for measures of sleep pathologies.
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List of Abbreviations

AHI - Apnea Hypopnea Index

AI - Arousal Index

BMI - Body Mass Index

BMI% - Body Mass Index Percentile

CSHQ - Children Sleep Habit Questionnaire

CASQ - Cleveland Adolescents Sleep Questionnaire

CSA - Central Sleep Apnea

DLMO - Dim light melatonin onset

DSPS - Delayed Sleep Phase Syndrome

ECG - Electrocardiogram

EDS - Excessive Daytime Sleepiness

EEG - Electroencephalography

EMG - Electromyography

EOG - Electrooculography

ESS - Epworth Sleepiness test

GI - Gastrointestinal

HPA - Hypothalamic-Pituitary-Adrenal

MSL – Mean Sleep Latency

$\text{MSL}_{\text{MSLT}}$ - Mean Sleep Latency on the MSLT
MSLnap - Mean Sleep Latency in a nap

MSLT- Multiple Sleep Latency Test

NREM- Non Rapid Eye Movement

OB- Obese

OSA- Obstructive Sleep Apnea

OW- Overweight

OWr - Overweight range

PDSS-Pediatric daytime Sleepiness Test

PLMD-Periodic Leg Movement Disorder

PSG- Polysomnography

PSQS-Pediatric Sleep Quality Scale

PSQ-SS- Pediatric Sleep Questionnaire- Sleepiness Scale

REM- Rapid Eye Movement

RLS- Restless Leg Syndrome

SCN- Suprachiasmatic nucleus

SDB- Sleep Disordered Breathing

SEM- Slow Eye Movement

SMR- Sexual Maturity Rating

SOL- Sleep Onset Latency

SSHS- School Sleep Habits Survey
SQS- Sleep Quality Scale

SWS- Slow Wave Sleep

TST-Total Sleep Time
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Appendix B- List of medical conditions that rendered exclusion from the study during data collection.

Appendix C- Questionnaires and scales to assess EDS.
1 INTRODUCTION AND BACKGROUND

1.1 Statement of the problem

In recent years obesity has been identified as a rising pandemic in modern society, affecting adults and children alike (1). In Canada, the prevalence of obesity is estimated to have tripled in children over the last 25 years (2).

Daytime sleepiness has been recognized as a frequent complaint among adult obese individuals (3). Excessive daytime sleepiness (EDS) in obese adults is traditionally perceived as a consequence of the high prevalence of obstructive sleep apnea (OSA). OSA occurs when the sleeping individual experiences repeated episodes of total (apnea) or partial (hypopnea) upper airway obstruction which results in the temporary reduction of blood oxygen levels and usually ends with a brief arousal from sleep (4). Since the mid-nineties our group and other researchers have suggested that obesity may be related to daytime sleepiness even without the presence of OSA (3;5-9).

The concept that obesity per se may be related to EDS has also been explored in the pediatric literature (10-13), but the evidence in children and adolescents is limited by methodological issues.

Impaired sleep has been noticed to have a negative effect on memory, learning and academic performance, as well as on mental wellness (14-20). In children in particular, difficulties with academic achievement and mental integrity may have a devastating effect on academic future and psychosocial development. Moreover, sleepiness can also contribute to life-threatening situations such as motor vehicle accidents, particularly in adolescents (21).

Despite the rise in pediatric obesity, there is a paucity of evidence about its relationship to EDS. In light of the impact of sleepiness on daytime performance, there is a need for further investigation on the interplay between weight and daytime sleepiness in children and adolescents. The purpose of this study was to investigate the relationship between weight and daytime sleepiness in children and adolescents.
1.2 Sleep and Sleepiness

1.2.1 Sleep

**Definition:**

Using a simple behavioral approach, sleep can be defined as a behavioral state of temporary disengagement from, and unresponsiveness to, the environment (22-24).

The modern study of sleep was made possible with the demonstration of spontaneous electrical brain activity and the invention of the electroencephalograph (EEG) by Hans Berger in Germany in the second decade of the 20th century. This invention made it possible to measure and quantify sleep without disturbing the sleeper (25). Sleep measurement today uses EEG with other measurements such as tracing of muscle tone and eye movements to establish a state of sleep and to follow the various changes in brain activity throughout the sleep process. A detailed description of the process of sleep measurement called polysomnography (PSG) are described below.

**Normal Sleep:**

In order to understand the unique features of pediatric sleep, including the developmental aspects, an understanding of normal adult sleep is needed. Sleep is viewed as involving two basic components: non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. These alternate periodically throughout the sleep session (22). These two components differ by the type of cortical activity viewed on the EEG, muscle tone, eye movements and psychological activity. In NREM sleep, cortical activity, as recorded on the EEG, is synchronized while muscle tone is minimal. In REM sleep, the EEG shows desynchronized cortical activity, the body is physiologically paralyzed and dreaming usually occurs (22).

NREM sleep is further divided into stages. Sleep staging was standardized in 1968 with the acceptance of the Rechtschaffen and Kales manual of sleep scoring (26). NREM sleep was divided into four stages simply named stages 1-4. In 2007, the American Academy of Sleep Medicine published new scoring recommendations in which stages 3 and 4 were merged into one stage and NREM sleep stages were renamed N 1-3 (27). Since this recommendation was not
accepted as a mandatory standard of practice outside the United States and in Canada, the
traditional 4 stages of NREM sleep will be used throughout this thesis.

**Normal sleep stages:** The various graphs recorded on a PSG study are observed in 30 minute
sections called epochs. These are scored individually as a specific sleep stage according to the
criteria outlined below(23;26;28).

− **Awake**

In active wakefulness, the EEG usually shows desynchronized high frequency low amplitude
waves probably due to differences in the processing time of the various activities conducted
when a person is awake (23). During ‘relaxed wakefulness’ the EEG shows rhythmic alpha
activity most prominent at the posterior head region (above the occipital region of the cortex)
when eyes are closed and low voltage mixed frequencies when eyes are open. Eye movement
changes with slow eye movement (SEM) appearing with drowsiness. Muscle tone is relatively
high with voluntary movements occurring.

− **NREM sleep**

*Stage 1-* This is usually the transitional stage between waking and sleep, where awareness of the
external environment gradually disappears. It tends to be of short duration. This stage is
generally characterized by slowing of the EEG waves, with low voltage, mixed frequency and
occasional vertex sharp waves and theta waves. In children, bursts of synchronized high voltage
theta waves may emerge. SEM is visible and usually precedes the change in EEG. Muscle tone
may slightly decrease.

*Stage 2-* The EEG shows relatively low voltage mixed frequency activity interrupted by wave
forms called sleep spindles and K-complexes. SEM gradually disappears and muscle tone is
similar to stage 1.

*Stage 3-* ≥ In each of the epochs there is 20% and ≤ 50% high amplitude slow frequency waves
(delta waves). Eye and muscle tone are not changed.

*Stage 4-* More than 50 % delta activity is evident in each epoch. Eye and muscle tone are not
changed.
Stages 3 and 4 are commonly considered together and termed as ‘slow wave sleep’ (SWS) or deep sleep. Sleep intensity is evaluated, in part, as the amount and quality of the delta waves. In children, the amplitude of these delta waves is generally greater.

- **REM sleep**

EEG shows relatively low voltage mixed frequency waves with theta and alpha activity, and stage specific saw tooth waves. This stage is also characterized by phasic rapid eye movements (REM) and by a general suppression of muscle tone.

The above listed scoring criteria and sleep stages are demonstrated in figures 1.1.a to 1.1.f. These figures were all taken with permission from the records of a healthy eight year old child without sleep complaints who attended the Youthdale Child and Adolescent Sleep Centre. This child was a volunteer for another project with the aim to collect normative data on pediatric PSG.

The first six lines (labeled F3, F4, C3, C4, O1, and O2) in each figure are the EEG channels. The next lines labeled LOC and ROC are recording of eye movement via electro-oculography, and the line labeled CHIN1 reflects the chin muscle tone via electromyography. The remaining lines as well as a complete description of the PSG recording technique are available in section 1.2.3).
Figure 1.1.a: PSG recording of awake child. Alpha waves (rectangle) are visible especially above the occipital region, EEG channels O1 and O2. The eyes are open, blinking occasionally (ellipses).

Figure 1.1.b: PSG recording of sleep stage 1. General slowing of the EEG waves is present in all the EEG channels. Slow eye movements are visible (colorless rectangle). An arousal was also marked by the PSG scorer (colored rectangle).
**Figure 1.1.c: PSG recording of sleep stage 2.** Mixed frequencies in the EEG. Sleep spindles (rectangle) and K-complex (circle) are present.

**Figure 1.1.d: PSG recording of sleep stage 3.** High amplitude delta waves are present, but do occupy more than 50% of the epoch.
Figure 1.1.e: PSG recording of sleep stage 4. High amplitude delta waves are present in more than 50% of the epoch.

Figure 1.1.f: PSG recording of REM sleep. Mixed frequency on the EEG with stage specific saw tooth waves (rectangle). Phasic eye movements are present (ellipse) and muscle tone is reduced (throughout the CHIN channel).
Developmental aspects of sleep in children and adolescents:

**Figure 1.2: Age-related trends for sleep stages.** Age (years) related trends for stage 1 sleep, stage 2 sleep, slow wave sleep (SWS), rapid eye movement (REM) sleep, wake after sleep onset (WASO) and sleep latency (in minutes). (Image taken from Ohayon et al., 2004)

The total amount and composition of sleep changes throughout the life span (22;29)(Figure 1.2). The main differences in sleep during childhood are seen in total sleep time (TST), SWS, REM latency and Stage 2. These changes are both quantitative and qualitative (22;29;30). While TST and SWS show a steep decline during the adolescent years (29), several studies have also demonstrated the superior quality of SWS in young children (under 10 years old) by demonstrating the difficulty in disturbing a child’s sleep while in SWS (22).

**Newborns (0-2 months)**

Newborn babies sleep 16-20 hours per day and this is divided into 1-4 hour periods. Sleep and wake are initially governed by hunger and satiation in the newborn, regardless of light/dark changes and other external cues. Through the first months of life, consolidation of a night sleep
period is usually achieved, driven by the growing awareness to external cues both biological (light/dark) and social (31). In a newborn baby, the previously described EEG patterns of sleep stages cannot be identified. Only three distinct stages can be recognized in a newborn baby: active sleep, quiet sleep and indeterminate sleep. The terms ‘active sleep’ and ‘quiet sleep’ were created in the early years of sleep research and continue to be relevant. The terms ‘active sleep’ and ‘quiet sleep’ describe a ‘REM like’ sleep and a ‘NREM like’ sleep, respectively (32). Active sleep comprises about 50% of the sleep period. It resembles REM sleep with visible rapid eye movements, irregular heart rate, respiration and frequent small movements of limbs and face muscles (32). Babies at this age usually enter the sleep period through this stage. Quiet sleep resembles NREM sleep with regular respiration and heart rate, minimal body movement and no eye movement (32). Indeterminate sleep has some features of both (33;34). Most sleep problems at this age are caused by a mismatch between parents’ expectations in regards to their child’s sleep or their difficulties interpreting their baby’s behavior (33).

Infants (2-12 months)

Sleep time gradually declines to a minimum of about 13 hours per day at 6 months and then further declines to about 12 hours per day at 12 months (33). It should be noted that great individual variation in sleep can be found in this age group (34). Longer night sleep periods and shorter daytime naps are apparent by the age of 3 months. About 70% of infants sleep with no intermittent wake period at night by the age of 9 months and have about 2 naps during the day (33). Distinctive NREM and REM sleep become apparent during the first 6 months of life with 50 minute cycles (from the start of one NREM to the start of the next one) (32;33). Most sleep problems at this age revolve around sleep onset and night awakenings.

Toddlers (1-3 years)

TST at this age is about 12 hours per day. By the age of 1.5 years most toddlers only require one nap a day. Most sleep problems at this stage have to do with sleep onset difficulties and bedtime resistance (33).

Preschoolers (3-5 years old)

Sleep time for most children at this age is about 11-12 hours per 24 hours. From infancy through early childhood, naps are needed; approximately 25% of children at age 5 still require a nap (35).
This will be further discussed in the segment addressing daytime sleepiness in children. Sleep cycles reach the typical adult duration of 90-110 minutes. The percentage of SWS and REM is high (34). Sleep problems at this age are still mainly of the sleep onset and bedtime resistant type, but problems such as sleepwalking and night terrors may appear. OSA is also common, mainly due to the high prevalence of tonsil and adenoid enlargement at this age (33).

**School age (6-12 years)**

TST needed at this age is 10-11 hours per day. Children at this age are usually very alert, making any sign of daytime sleepiness highly suggestive of the presence of sleep problems. There are a wide range of sleep problems at this age including insufficient sleep, anxiety-related difficulties and OSA (33).

**Adolescents (13-18 years)**

TST should be about 9-9.25 hours per day at this age. However, several studies, including one from our group, have pointed out that this desired amount of sleep is seldom achieved by adolescents (30;33;36). Sleep architecture (sleep stage distribution) resembles adult sleep architecture with a gradual reduction in the amount of SWS and REM sleep coupled with an increase in stage 2 sleep (29;33). A physiological delay in sleep time onset (delayed sleep phase) of about 2 hours is common at this age group, with a preference of later bedtimes and wakeup times. The exact mechanism behind this delay is not yet clear. Increased sensitivity to light, slower development of the drive to sleep (sleep pressure) and possible effects of gonadal hormones on sleep regulation have been suggested and explored in humans and animal studies (37). Together with the social demands of school and extracurricular activities, insufficient sleep and EDS is common among adolescents (29;33). This will be further discussed in section 2.1.2. The spectrum of sleep disorders at this age is wide and includes many sleep pathologies that are found in adults.
Sleep- wake regulation

The sleep-wake cycle is controlled by the balance between arousal and sleep-promoting agents such as hormones and neuroreceptors mainly in the brainstem and hypothalamus (38). The most widely accepted model for the regulation of the sleep-wake cycle in mammals comprises two main processes (39-41):

1) A homeostatic system (Process S) located mainly within the preoptic area of the brain regulates the quantity and intensity of sleep (39). This system generates ‘sleep pressure’ – a need to sleep which increases progressively with time from the end of the previous sleep period (41).

2) A circadian system (Process C) regulates the timing of sleep during the day-night cycle. The circadian rhythm of the sleep/wake cycle is controlled by a circadian pacemaker located in the anterior hypothalamus in the suprachiasmatic nucleus (SCN). This is mediated through a hormone named melatonin. Melatonin secretion is entrained by light (42). Melatonin is suppressed to an almost non-existent level by light and rises in the evening when light intensity declines (41). The circadian system has a pacemaker which has a natural duration slightly longer than 24 hours but is entrained by environmental cues (also called zeitgebers) to fit the 24-hour day (30). The circadian pacemaker influences not only the sleep/wake cycle but other behaviors as well such as feeding and sexual behavior (41).

It has been suggested that these two processes (S and C) act both as allies and opponents. The increased sleep pressure generated by the homeostatic system combined with the circadian drive to sleep with darkness in the evening time works to initiate sleep. Later through the night, while the sleep pressure declines, the continued circadian signal works to maintain the sleep period. Sleep ends when both the sleep pressure and circadian sleep drive are decreased (40;41).
Figure 1.3: The two process model  This is a graphical representation of sleep regulation according to the two-process model. S represents the homeostatic sleep drive, rising during waking and declining during sleep. C represents the circadian rhythm cycle and is measured by body temperature. The optimal time for sleep occurs when S is at its peak and C is in its low. This coincides with the typical nighttime sleep period. Wake up typically occurs where C and S intersect. (Taken with permission from Borbely AA. Sleep homeostasis and models of sleep regulation. In: Kryger MH, Roth T, Dement WC, (eds.), Principles and Practice of Sleep Medicine (2nd ed). Philadelphia: WB Saunders Co., 1994: 316.)

There is an intricate net of interactions between these two systems and other subsystems that together govern the process of sleep and wakefulness. It is beyond the scope and purpose of this manuscript to describe this interplay in full. However, the relevance of neurotransmitters orexin A and orexin B to sleep regulation and feeding behavior will be described.

Orexin A and orexin B also referred to hypocretin 1 and hypocretin 2 are neuropeptides first reported in 1998 by two separate research groups (hence the two names used) (43;44). While De Lecea’s group could not report on the peptides function, Sakurai and colleagues reported that these peptides increase appetite when given to rats. A link between these peptides and sleep in canines and mice were reported a year later (45;46). Both groups reported that narcolepsy- a sleep disorder characterized by excessive sleepiness- was present when orexin deficiency was induced in these animals. Orexin neurons have been demonstrated to be active in wakefulness and inactive during sleep (47). Other studies showed that lower numbers of orexin neurons and a mutation in the orexin related genes were linked with narcolepsy in humans as well (48;49). Orexin has also been linked with weight control. These peptides are found in the hypothalamus (where both sleep and hunger control centers are located), and are regulated by glucose and hunger-satiation related hormones such as ghrelin and leptin. High levels of the orexins promote
wakefulness and appetite(50). Some case reports have suggested a link between orexin and sleep disorders characterized by excessive sleepiness, as well as with weight control difficulties. These include Prader-Willi syndrome and Klein-Levine syndrome (51) (See section 1.4.3. for more details).

**Figure 1.4. The regulation and functions of hypocretin.** Hypocretin (Hcrt also referred to as orexin) neurons are present in the hypothalamus. Leptin and glucose inhibit Hcrt secretion while ghrelin increases Hcrt secretion. Increased Hcrt promotes wakefulness, increases appetite, is involved in reward/pleasure-seeking behaviours, and stimulates sympathetic activity. (Taken with permission from Ganjavi and Shapiro 2007 (51)).
1.2.2 Sleepiness and Excessive Daytime Sleepiness

Definition of sleepiness

There is no clear consensus as to the definition of sleepiness. Sleepiness can be thought of as the tendency to actually fall asleep or sleep propensity, but it is also described using facets of cognitive ability, mood, motivation and physiological changes (52). While a state of sleepiness will generally be accepted as normal at nighttime, feeling sleepy during the daytime may be perceived as abnormal. What defines daytime sleepiness as excessive is debatable (52). Similarly, alertness is not easily defined. Definitions can vary between the simple ability not to fall asleep to a more complex concept using indices of cognition and mood (52). It appears that choosing just one definition may be a simplistic approach. While the propensity to fall asleep or stay awake may be objectively measured, other definitions of sleepiness and alertness may be viewed as subjective impressions of these states, and the two aspects do not necessarily correlate (52). Furthermore, sleep and alertness should not necessarily be considered mirror images of each other. Moller et al. examined four groups of subjects with different sleep pathology. While sleepiness scores differed between these groups, alertness evaluated by two separate scales did not vary significantly between the groups (53).

Excessive daytime sleepiness (EDS)

Excessive daytime sleepiness (EDS) is a clinical term used to describe a condition in which individuals fall asleep during the daytime when they would usually be expected to be awake (52;54;55). Our group (52) has reported a wide range of estimated prevalence of EDS (0.3-35.8), depending on the method of assessment and the type of population studied. The situation is similar in children and adolescents with estimates of EDS ranging from 17% to 68%. The highest rates were reported in adolescents (36;55;56).

While EDS may be caused by poor sleep habits or bedtime restriction, EDS may also be a result of an underlying medical condition or sleep pathology. The consequences of EDS may range from social embarrassment (falling asleep on the bus or in class) to lower scholarly achievements, to impaired daytime function that may even be life threatening (falling asleep while driving a car). EDS is highly treatable in most cases, once the underlying condition has been identified (57).
The presence and level of EDS can be evaluated by subjective or objective measures (52). Subjective measures include asking patients about EDS as part of the medical sleep history and using various questionnaires designed to assess EDS (58-61). The most widely used validated objective measure of EDS in sleep medicine is a sleep laboratory test called the Multiple Sleep Latency Test (MSLT) (54). This and other methods to assess daytime sleepiness will be described below.

**EDS in children**

In children, as in adults, the exact prevalence of EDS is not clear due to differences in definition and measuring methods. Some estimates show that 17-21% of school-aged children experience EDS and that up to 68% of adolescents complain of EDS (55).

**Table 1.1. EDS in children according to age**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants, toddlers and school preschoolers (0-5 years old)</td>
<td>Daytime sleepiness may be a perfectly normal condition in children of preschool age and under. Most toddlers and some pre-school children need a day-time nap (35).</td>
</tr>
<tr>
<td>School aged children (6-12 years old)</td>
<td>It is very rare for school-aged children to have a daytime nap. Reports of daytime sleep in pre-pubertal children are considered a cause for concern in regards to the integrity of their night sleep (31;55).</td>
</tr>
<tr>
<td>Adolescents (12-18 years old)</td>
<td>Daytime sleepiness is more common in adolescents (30;36;62-64).</td>
</tr>
</tbody>
</table>
Causes of excessive daytime sleepiness in children

A child may be considered sleepy when either longer night sleeps or longer and more frequent daytime naps are present compared to other children of the same age, or compared to the child’s previous sleep patterns. A sleepy behavior at a time when peers are not sleepy may also be present (55).

Daytime sleepiness is a symptom that can be attributed to many different causes. In a recent review, Kothare and Kaleyias (2008) offer a convenient approach to categorization of these causes. The first two categories are somewhat intuitive, with sleepiness as a product of either insufficient sleep quantity or quality. The third category reflects conditions in which the need for sleep is increased (55). (Table 1.2)

To date, obesity as an independent cause for sleepiness is not mentioned in any review concerning childhood sleepiness. A few studies examining obesity per se as a cause for pediatric EDS have been published and will be reviewed in section 1.4.
Table 1.2: Causes for EDS in children and adolescents (adapted from Kothare and Kalevis).

<table>
<thead>
<tr>
<th>Decreased quantity of sleep</th>
<th>Decreased quality of sleep</th>
<th>Increased need for sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-induced or socially determined sleep restriction</td>
<td>Idiopathic sleep fragmentation</td>
<td>Inherited or acquired neurological and medical conditions</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Sleep disordered breathing (SDB) e.g. OSA.</td>
<td>Drug related (medical or illicit)</td>
</tr>
<tr>
<td>Circadian rhythm disorders</td>
<td>Movement disorders</td>
<td>Depression related</td>
</tr>
<tr>
<td>Parasomnias</td>
<td></td>
<td>Narcolepsy</td>
</tr>
<tr>
<td>Medical conditions (e.g. nocturnal asthma attacks)</td>
<td></td>
<td>Klein–Levin syndrome</td>
</tr>
<tr>
<td>Environmental (noise, temperature)</td>
<td></td>
<td>Idiopathic hypersomnia</td>
</tr>
</tbody>
</table>

Decreased sleep quantity

It is widely agreed that the most common cause of EDS in children and adolescents at any age is lack of sufficient total sleep time due to inadequate sleep hygiene and self restriction of sleep time. The reasons for this include homework, extra-curricular activities, social demands, use of technology (e.g., television, video games, and internet), and the use or consumption drugs (e.g., caffeine, alcohol). This type of sleep loss increases through the adolescent years when school and work loads rise while parental control over sleep behavior decreases (35;65-67). Li et al studied parents’ report of 19,299 elementary school children and showed a positive correlation between the presence of media devices in the bedroom and a reduction in sleep duration (65). Gibson and colleagues reported findings from two surveys with a total of 3235 Canadian adolescents
(secondary school) from diverse socioeconomic backgrounds, in which EDS as well as other sleep-related topics were assessed with a self-reported questionnaire. The study used anonymous self-reported measures and suffered from low participation rate in some schools. However, its results were consistent with those of others, showing high prevalence of sleep deprivation in this age group to be associated with EDS and reduced performance in school as well as in extracurricular activities (36). A larger survey of younger adolescents conducted in Japan (9,261 middle school children) showed similar results (64). An interesting study from Brazil reported finding in a unique sample of adolescents (age 11-16 years). Although living in the same rural area and attending the same school, close to a half of this study subjects lived without electricity. The researchers showed decreased sleep times in subjects living with electricity vs. those living without it (68).

Insomnia in toddlers and preschoolers is mainly of a behavioral nature with children resisting the appropriate bedtime. Adult type insomnia driven by social and psychological stressors and anxiety is more likely to emerge during the adolescent years. Given this, insomnia is most often a symptom of an underlying condition that requires further exploration. These underlying conditions include untreated or under treated sleep disorders, medical conditions including psychiatric conditions, medication use, and alcohol and drug abuse (33;35).

Another mechanism with particular relevance in pediatric EDS is a circadian sleep problem called Delayed Sleep Phase Syndrome (DSPS). DSPS is a disorder characterized by the continuous inability to fall asleep at a conventional bedtime with a tendency to fall asleep toward the early morning hours (69). This disorder has been noted to be more common in adolescents. During the adolescent years, along with the process of puberty, there is a physiological delay in the secretion of melatonin in some children and a general preference for later bedtime and wake up times (70). In some cases, this physiological shift in sleep phase causes a significant interference in daily function giving a clinical picture consistent with DSPS(41). DSPS may have debilitating implications, since personal and social schedules are skewed, which may lead to social and psychological problems (69;71). Once the diagnosis of DSPS has been established it can be successfully treated with either light therapy or with the use of exogenous melatonin (69;72). Being exposed to artificial electrical light has been shown to contribute in further promoting the natural sleep phase delay in adolescents (68). The phase delay that is seen in teenagers is sometime volitional and sometimes biological. It is self evident that for some
teenagers it would be a combination of the two. It is highly likely that “volitional” population will not present at a sleep clinic as this is a form of choice, where as within the biological group there will be many who find this undesirable and so will seek a remedy.

**Decreased sleep quality**

Sleep fragmentation is currently defined by the appearance of a brief arousal on the EEG recording (73). These repeated short interruptions in the sleep continuum have been linked to daytime sleepiness (74-76). Sleep fragmentation can occur without any apparent reason, but also accompanies many of the disorders in this category.

Sleep Disordered Breathing (SDB) is a term that refers to a group of conditions in which breathing is disturbed within the sleep period and ranges from simple snoring to actual pauses in breathing called sleep apnea (67). OSA is a situation in which the sleeping individual experiences repeated episodes of total (apnea) or partial (hypopnea) upper airway obstruction which result in temporary reduction of blood oxygen levels and usually ends with a brief arousal from sleep (4). In central sleep apnea (CSA), respiratory effort is reduced or absent intermittently due to central nervous system or cardiac system dysfunction. As with OSA, brief arousal usually occurs at the end of the respiratory compromised spell (4). All of these conditions have been linked with EDS in children at any age (77;78) although, unlike adults, children with these disorders may also appear to be hyperactive (35;79).

The main movement disorders linked with EDS is restless legs syndrome (RLS). This is a sensory motor disorder in which individuals experience a strong uncomfortable, almost irresistible urge to move their legs, which is made worse by rest. This is also typically more severe in the evening and nighttime. In many cases this is associated with a leg movement disorder during sleep called Periodic Limb Movement Disorder (PLMD) (4). RLS has been shown to be more common in adult patients with type 2 diabetes mellitus (80;81). The prevalence of RLS and PLMD is understudied in the paediatric population. A recent study reported a 2% prevalence of RLS in school-aged children and adolescents (20).

Parasomnias are arousal disorders that are more common in preschoolers and school-aged children than in adults and include a variety of unusual activities during sleep such as screaming, walking and talking (4). EEG arousals are apparent during transitions from SWS to REM sleep
and daytime sleepiness may occur (35).

Medical conditions such as asthma, cystic fibrosis, rheumatic diseases, burns and infection (viral, bacterial and fungal) and others may cause disturbances to night sleep due to pain or respiratory or neurological compromise (33).

**Increased sleep need**

This group consists of an assortment of inherited or acquired, relatively rare conditions that have a well known association with sleepiness or have sleepiness as a hallmark characteristic. Examples include narcolepsy and Klein-Levine syndrome (see section 1.4.3).

Some medications have been noted to interrupt sleep (mainly with insomnia) or to promote alertness or daytime sleepiness. In some cases both insomnia and EDS are listed in the side effect profile of a specific medication. Psychostimulant medication for the treatment of attention and hyperactivity deficit spectrum disorders, various antidepressants and anxiolytic medications, anticonvulsants and antipsychotic medications are among the pharmaceutical treatments employed in the pediatric population that have been noted to interact with sleep and sleepiness (82). While sleepiness related complaints have been recorded as adverse effects of these drugs in clinic trials, their effects on EDS were generally not studied with objective measures of daytime sleepiness (with the exception of a group of studies in treatment with psycho stimulants-Modafinil and Armodafinil in patients with narcolepsy (83-85)).

As in adults, psychiatric disorders in the pediatric population, mainly anxiety and depression, have been reported to interact with sleep. Insomnia, nightmares, early morning awakenings and lethargy are common in children and adolescents affected by these conditions and may all contribute to EDS (86).
Table 1.3: Primary causes of EDS by age group.

<table>
<thead>
<tr>
<th>Infants (2-12 months)</th>
<th>Toddlers (1-3 years)</th>
<th>Preschool (3-5 years)</th>
<th>School age (6-12 years)</th>
<th>Adolescents (12-18 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia – behavioral</td>
<td>Sleep restriction</td>
<td>Sleep restriction</td>
<td>Sleep restriction</td>
<td>Sleep restriction</td>
</tr>
<tr>
<td>Insomnia – behavioral</td>
<td>Insomnia- behavioral or other</td>
<td>Insomnia- behavioral or other</td>
<td>Insomnia- psychological or other</td>
<td></td>
</tr>
<tr>
<td>SDB</td>
<td>SDB</td>
<td>SDB</td>
<td>SDB</td>
<td>SDB</td>
</tr>
<tr>
<td>Parasonnias</td>
<td>Parasonnias</td>
<td></td>
<td>RLS</td>
<td>RLS</td>
</tr>
</tbody>
</table>

1.2.3 Consequences of EDS in Children and Adolescents

Daytime consequences of sleep disorders have been studied extensively across the age range. Despite the different etiologies that lead to EDS, sleepiness seems to be an incapacitating condition in adults. Sleepiness has been shown to have an impact on family and social interaction, work and cognition (including memory, concentration and decision making) (87). Chronic EDS has been linked with an undesirable effect on mood, decreased work performance and indications of reduced quality of life (88-90). Safety is also compromised when daytime sleepiness occurs with higher rates of traffic or motor vehicle and workplace accidents (91;92).

Research in children and adolescents has produced similar findings. Children who report being poor sleepers were shown to have more behavioral difficulties, daytime hyperactivity, and more depression and anxiety symptoms (93-95). This association was demonstrated in studies using various subjective and objective measures of sleep and behavioral issues; some showing behavioral issues to be reversible after sleep problems are treated (14-19).

Smedje et al. studied a large group (n=635) of 6-8 years old children using subjective measures (parent completed questionnaires) to assess for both sleep and behavioural issues. Findings from this study indicate an association between behavioural difficulties and sleep problems such as restless sleep, bed wetting, sleep walking and nightmares (18). In a small case control study,
designed to assess the effect of adenotonsillectomy on behaviour and psychological function, vigilance and continuous performance tests were shown to improved after surgery and parents reported a reduction in aggressive behaviour, inattention and hyperactivity (15).

Chervin and colleagues reported PSG findings from 113 children and adolescents (2-18 years) who were assessed for behavioural difficulties with parent-completed questionnaires, showing an association between behavioural issues with both SDB and PLMD (17). In another study by the same group, indicators of conduct problems and aggressive behaviour were two to three times more prevalent in children at high risk for SDB and PLMD (96). PLMD and SDB were also shown to be highly prevalent in a sample of sleep clinic patients with attention deficit and hyperactivity disorders (19).

In a large survey including children and their parents, RLS has been reported (by parents and children alike) to negatively affect mood. Children and adolescents with RLS were more commonly diagnosed with attention-deficit disorder, depression and anxiety (20).

Using actigraphy (a technique used to record rest and activity levels over days or weeks - see section 1.2.3.) along with questionnaire assessment of behavioural problems, researchers from Finland showed shorter sleep duration to be associated with behavioural problems in primary school aged children (16). Another study using similar methods (actigraphy and questionnaires assessments) and population (healthy elementary school-age children) failed to show a connection between sleep duration and behavioural problems. However, they reported a lower intelligence quotients in individuals who had shorter sleep time (97).

School problems are repeatedly reported in children with sleep-related breathing disorders and may be due to any of the above behavioral and cognitive issues. Lower scholastic achievement was shown to be more common in children with sleep-related breathing disorders, and vice versa. Sleep related breathing disorders were found to be more common among children in the lower range of academic performance (98-101). Recently, Beebe et al (102) studies a group of overweight children and adolescents, age 10-16 years old with SDB. These researchers were able to demonstrate an association between SDB, lower grades and behavioral issues at school. They were able to show (though not definitively) that behavior, specifically attention difficulties, were the mediator between SDB and lower school performance.
As children reach late adolescence and obtain a license to drive, increased motor vehicle accidents associated with sleep disorders occur, as is the case in adults (21).

1.2.4 Measuring Sleep

As with most medical evaluations, proper assessment of sleep in adults and children alike requires an initial interview to obtain medical and sleep histories. These should take into account social, environmental and psychological factors (35). The information obtained is then used to determine the need and nature of further testing.

Assessment of nocturnal sleep: Polysomnography (PSG)

History and development

As noted earlier, the modern study of sleep came into being following the invention of the EEG which was used to give one of the earliest descriptions of sleep stages in 1936 (28). The addition of eye movement monitoring made the identification of REM sleep possible by Kleitman’s group in Chicago in 1953. Throughout the years, additional monitoring elements were added and about half a century passed until the term polysomnography (PSG) was given. Early technology involved heavy, cumbersome, paper-based equipment. Today PSG uses computer-based, digital recordings. This has improved the recording and analyzing abilities and has gradually contributed to better understanding of sleep (103).

Current method

The current PSG allows for the simultaneous monitoring of several body system activities using electrodes placed on the patients body and enables the interpreter to correlate events happening in one body system to those of another one (104).

- The standard PSG consists of monitoring:
  - electrical brain activity, using electroencephalography (EEG)
  - muscle tone using electromyography (EMG)
  - eye movement using electr-oculography (EOG)
- heart rate using at least one lead electrocardiography (ECG)

- respiratory effort using chest wall and abdomen movement with piezoelectric belts to evaluate respiratory effort (other types of electrodes may be used for this purpose as well)

- airflow: several types of transducers are used for this. These are mainly thermister/thermocouples (devices that sense temperature as a surrogate of airflow) and a pressure transducer (PFlo—a device that detects the fluctuations in pressure caused by inspiration and expiration).

- blood oxygen saturation, using a pulse-oximeter (a non-invasive indirect method relying on changes in light absorption)

- audio and video monitoring

- time

The data collected during the PSG is then analyzed using criteria established by Rechtschaffen and Kales 1968 (26) combined with arousal scoring rules set by the American Sleep Disorders Association position paper from 1992 (105). The recording is divided into 30 second periods, called epoch, that are viewed and manually scored by a trained individual. Sleep is staged into wake and 5 sleep stages. These are stages 1-4 (also called non-REM or NREM sleep) and REM (Rapid Eye Movement) sleep. The differentiation between the stages is made based on the type of brain waves seen on the EEG, eye movements and the chin muscle tone. The total sleep time (TST), sleep onset latency (SOL) (the time it took the patient to fall asleep), REM onset latency (the time from the beginning of the sleep period to the beginning of the first REM period) any intervening wakefulness, and percentage of time spent in each stage is calculated. Respiratory analysis, along with any movements or behavioral abnormalities completes the sleep analysis.
Figure 1.5: International 10-20 System used to record EEG. This method was first described by Jasper in 1958 (106), and was designed to create a reproducible method to place EEG electrodes. The letters used are: “F”, frontal lobe; “T”, temporal lobe; “C”, central lobe; “P”, parietal lobe; “O”, occipital lobe; “A”, ear. Even electrode numbers (2, 4, 6, and 8) refer to the right hemisphere and odd electrode numbers (1, 3, 5, and 7) refer to the left hemisphere. “Z” refers to an electrode placed on the midline. The smaller the number, the closer the position to the midline. “Fp” stands for Front polar. (The Figure was taken with permission from Avidan and Zee, 2006).
Figure 1.6: An example of one epoch on a polysomnography recording. The first six lines (F3, F4, C3, C4, O1 and O2) represent the EEG recording. The next two lines - LOC and ROC - represent the EOG recording. EMG of the submental muscles is next (CHIN1-CHIN2) followed by the ECG recording. The next two lines - LAT and RAT are the EMG for the anterior tibialis muscles of the legs. The next portion of the epoch screen is dominated by the big wavy graphs of the breathing channels - airflow, Pflow & respiratory effort. Next are snoring and body position. The last two graphs represent oxygen saturation heart rate measurement. (Taken with permission from a recording of an eight years old child done at the Youthedale Child and Adolescents Sleep Centre).

Special considerations when conducting PSG in children

There are numerous challenges in conducting reliable sleep studies in the young pediatric population (especially in babies, toddlers and pre-school children), including difficulties with fitting many electrodes on the small body of a frequently impatient child. There are compliance issues especially in toddlers. Familiarizing the child with the sleep test process beforehand is important in creating a more child-friendly sleep laboratory (talking with the child, showing the sleep laboratory and equipment to be used). Pediatric PSG scoring requires a very experienced scorer familiar with the special features existing in PSG at different ages throughout childhood (32;103). (A review of the discrete features in every age is beyond the scope of this thesis).
Assessment of daytime sleepiness

The objective and subjective assessment tools used to assess daytime sleepiness are listed below. The results of these tests do not necessarily concur. It has been suggested that they may be considered complimentary to each other as each group measures EDS in light of a different definition (52) (as previously discussed in section 1.2.2).

Objective measure of daytime sleepiness

The Multiple Sleep Latency Test (MSLT).

This is the most widely used objective measure to assess daytime sleepiness. The MSLT is conducted after a PSG overnight study and consists of four 20 minute naps separated by 2-hour intervals starting at 1.5 to 3 hours after the participant has awakened from his overnight sleep study. Between the sessions, the participant is required to stay awake and is monitored by a technician for compliance with this instruction. During the nap sessions, the participant lies down in bed and is instructed to try to go to sleep while EEG, EOG, ECG and EMG are recorded. Sleep latency is defined as the time from lights off to the first epoch scored as any stage of sleep or at 20 minutes if no sleep occurs. If a patient falls asleep within the 20 minute nap, he/she is allowed to sleep for 15 minutes. If after 4 naps there is REM onset in only one session, then a 5th session should be performed. If there are two naps with REM onset within the first 4 naps, then there is no need for the fifth nap. A mean sleep latency (MSL) is calculated. In adults, it is generally accepted that an MSL of less than 11 minutes is considered suggestive of mild sleepiness, between 8-5 minutes moderate sleepiness and a mean sleep latency of less than 5 minutes suggests severe sleepiness1 (54;107;108).

Despite its wide popularity as an objective measure of EDS, the MSLT is also subject to criticism. The most basic argument revolves around what exactly does the MSLT measures. Is

1 A clear classification of what is mild, moderate and severe objective sleepiness is described in the 1st edition of the International Classification of Sleep Disorders (ICSD), but is absent from the current (2nd) edition. That classification describes the level of sleepiness in relation to the level of physical activity and attention needed during the activity in which a daytime sleep episode occur, the frequency in which sleep episode occur and the impact of these episodes on the person’s occupational and social function.
measuring a subject’s ability to fall asleep- or sleep propensity- is enough to encompass the entire scope of sleepiness? Does the ability to fall asleep under isolated and “ideal” conditions that usually do not occur in day-to-day life represent sleepiness? Johns argues that looking at sleep propensity alone in a specific situation is a too narrow approach to EDS, and suggests that the questionnaire developed and validated by him- the Epworth Sleepiness Scale- has a wider and better view of daytime sleepiness(109). The MSLT results may be influenced by sleep restriction or longer than usual sleep duration in the days prior to the test (regretfully objective monitoring of sleep schedule with actigraphy prior to the MSLT is relatively rare in clinical practice) (52).

These rules defining the severity of daytime sleepiness per the MSLT are generally agreed upon for adults, but some dispute still exists. Johns argues that EDS on the MSLT should be noted only when MSL is lower then 3.2 minutes (110). If this criterion is correct then the MSLT’s ability to discriminate between levels of sleepiness is highly questionable. Others suggest an even higher cut-off point, an MSL of 13 and below considered indicative of mild EDS (111). Indeed clinical practice indicates that the wider definition may be a more valid one (Colin Shapiro-personal communication, 2010).

However, in the pediatric population the criteria for categorization of EDS on the MSLT are even less clear. In children and adolescents there is insufficient research to establish such normative MSLT criteria. One reason may be the differences in MSLT protocols used in term of nap length (20 or 30 minutes). That may give a different impression as to what is normal. For example, a few studies in pre-pubertal children using nap lengths of more than 20 minutes showed mean MSL values ranging from 21 to 28 minutes (10;112;113) while research using shorter nap times showed a mean MSL of approximately 18 minutes (114). This shorter mean MSL may be the result of a ‘ceiling effect’ created by a nap opportunity that was too short. In addition, it has been shown that MSL varies in children at different stages of puberty with children in earlier stages of puberty having longer MSL than adolescents at the end of puberty (115). Our clinic has initiated a study of MSLT norms in the pediatric population. Since commencing this study we have become aware that Gozal’s group in Chicago have a large database of MSLTs in normal children (i.e. without sleep disorders) and we eagerly await the publication of pediatric norms.
In light of the comment cited above, it is logical to assume that one should not use the same MSL value to define subjective EDS for all children regardless of pubertal stage and age. This point is demonstrated well by Kotagal and Goulding in their review of the literature about sleepiness measurements in children (116). Their example shows how a decrease in MSL by the same percentage would give a different MSL value for a child in the first stages of puberty compared to a child who has completed the pubertal process. It renders the former not excessively sleepy and the latter as excessively sleepy by the standardized adult criteria (116).

Another confounding factor in the utility of the MSLT in children is age. Given that 5-year-old children may still need a daytime nap, makes interpretation of MSLT results at this age very problematic (108).

Due to this uncertainty and based on clinical impression and personal communications with specialists in the field of pediatric sleep analysis, our laboratory defines MSLT results as ‘abnormal’ if the MSL is under 16 minutes for children 13 years and older or under 19 minutes for children under 13 years of age (based on the longer normative MSL in pre- or early pubertal children)(116;117).

Subjective measures of daytime sleepiness

There are a few validated scales and questionnaires designed to detect the level of daytime sleepiness in adults (52). The most popular and widely used is the Epworth Sleepiness Scale (ESS), although its correlation with the MSLT has been questioned (ranging from no correlation found at all to a week negative correlation of r=-0.37) (52;58;110;118). In children and adolescents even fewer questionnaires have been carefully investigated (60;61;119;120). Table 1.4 summarizes the various scales and questionnaires used in paediatric sleep assessment.
Table 1.4: Assessment of subjective daytime sleepiness in children and adolescents *

<table>
<thead>
<tr>
<th></th>
<th>Epworth sleepiness scale (ESS) (121)</th>
<th>Paediatric daytime sleepiness scale (PDSS) (61)</th>
<th>Children Sleep Habit Questionnaire (CSHQ) (60)</th>
<th>Paediatric Sleep Questionnaire-Sleepiness Scale (PSQ-SS) (59)</th>
<th>School Sleep Habits Survey (SSHS) (122)</th>
<th>Cleveland Adolescents Sleepiness Questionnaire (CASQ) (120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation</td>
<td>+ in adults</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Target age (years)</td>
<td>adults</td>
<td>11-15</td>
<td>4-12</td>
<td>2-18</td>
<td>13-19</td>
<td>11-17</td>
</tr>
<tr>
<td>Completed by:</td>
<td>Adult, or child in modified un-validated versions</td>
<td>Child</td>
<td>Parent</td>
<td>Parent</td>
<td>Child</td>
<td>Child</td>
</tr>
</tbody>
</table>

*These questionnaires are shown in appendix C, for the purpose of providing a more comprehensive review of this aspect.

The ESS has only been validated for use in adults and contains questions that may be inappropriate for young children (e.g. driving a car). Scales completed by parents may have reliability issues, especially in adolescents. All self-completed questionnaires have a somewhat limited target age range. An interesting attempt to create a pictorial sleepiness scale has been reported by a group in South Africa which may be of potential use in children since it does not require literacy skills, but more research is needed (123).

At the Youthdale Child and Adolescents Sleep Centre, the Pediatric Daytime Sleepiness Scale (PDSS) for children 15 years old and under (61) and the Epworth Sleepiness Scale (ESS) for older adolescents (110) are used to aid in the evaluation of daytime sleepiness. In our view, there are currently no superior tools available for assessment of subjective pediatric daytime sleepiness. In both of these questionnaires, a higher score implies more daytime sleepiness.
Miscellaneous methods to assess daytime sleepiness

There are several additional methods that have been experimented with to assess daytime sleepiness in adults. These methods are not widely used due to the complexity of execution or due to lack of validity. To date, none of these have been used for the purpose of evaluating EDS in children or adolescents.

− Pupillometry- This method is based on the finding that a larger variability in pupil diameter is present with sleepiness. The patient is seated in a dark room and asked to keep a fixed gaze on a red target. Pupil diameter is then measured by infrared light. This method was found to poorly correlate with the MSLT and to lack discrimination between levels of sleepiness (124).

− Evoked Potential- This method measures the changes in EEG evoked potentials, usually in response to auditory stimulus. It is not widely used mainly due to large inter-subject variability (125).

− Alpha Attenuation Test- EEG alpha waves decrease when the eyes are closed and increase with eyes open. The patient is seated in a lighted room and asked to alternate between open and closed eyes, remaining a whole minute in each state. This is repeated 8 times. By measuring the differences in EEG alpha power between these two states in a controlled manner an alpha attenuation coefficient is calculated. A good correlation with the MSLT has been found. However, due to the small samples studied there is a need for a greater number of larger studies in order to validate this methods (126). This test is shorter in time to complete and may have particular utility in children but this remains to be evaluated.

− Cognitive and psychometric testing- This is an indirect approach to evaluate EDS and therefore less reliable. It is based on the observation that cognitive and psychomotor performance deteriorate when EDS is present. However, a wide variability in patients performance on these test has been observed, making this a poor measure for EDS (127).
Evaluation of sleep circadian rhythm disorders

Dim Light Melatonin Onset

The presence of circadian rhythm disorder can be assessed through measurements of melatonin secretion (42;128) which is accurate but is also both labour intensive and costly. In order to measure the natural rhythm of melatonin secretion without the suppressive impact of artificial light, individuals are kept in a dim lit environment from about 2 hours prior to the common melatonin secretion onset time. Melatonin is measured hourly throughout the night by the collection of saliva samples which have been found to reliably represent circulating melatonin levels (42). While this technique, called the dim light melatonin onset (DLMO) test is highly reliable, it is very labour intensive and somewhat uncomfortable for the tested subject (subjects are awake, can listen to music, but are not allowed to have light so they cannot read, watch television or play video games).

An indirect measure of the sleep-wake cycle can be achieved using actigraphy. An actigraph is a small device resembling a wrist watch that is usually worn on the wrist. The device senses movement and so activity/non-activity periods are recorded. Besides estimating the sleep-wake cycle of an individual, it can also be used to evaluate daytime sleepiness, usually as an adjuvant to PSG and MSLT. A sleep diary will be completed in conjunction with the actigraph to help determine lights-off and lights-on times on the actigraphy recording (129).

Conducting two PSG- one on the preferred “delayed schedule” and another on an enforced conventional schedule- can provide supporting evidence for DSPS. If the findings show normal sleep analysis on the preferred schedule while on the enforced schedule sleep onset latency is dramatically increased, then the diagnosis of DSPS is supported (4;41).
1.3 Childhood Obesity

Obesity is defined as a state of excess body fat (130). The presence of excess fat impairs the functioning of many important organs and can lead to adverse health problems effecting almost every body system (131).

1.3.1 Measurements

There are several methods used to evaluate overweight and obesity in general:

- Calculating the Body Mass Index (BMI) using measured weight and height.

- Skin-fold thickness as a measure of body fatness. This technique is relatively fast and inexpensive; however, measurements have been noted to vary widely between measurers.

- Hydro-densitometry- underwater weighing. This method relies on the lower density of fat tissue compared to bone and muscle tissue, which is responsible to different weight reading in and out of water.

- Air-displaced phthysmography- relying on a similar principle as the above noted method, but with measurement of the amount of air displaced after a person is seated in a closed container for 20 seconds.

- Imaging techniques such as Computed Tomography or Magnetic Resonance Imaging or Dual Energy X-ray Absorptiometry (DEXA) to evaluate total body or regional fat.

- Bio-electrical impedance. This method measures fat free body mass and a calculation of fat mass can be extrapolated.

- Total body potassium- A rarely available technique of measuring total body potassium levels based on the amount of naturally occurring radioactive potassium detected using a whole body counter. This again is a measurement of lean body mass by which fat body mass can be calculated (132).
The BMI is calculated by dividing weight in kilograms by the squared height in meters (kg/m²). It is an easy and cost-effective method and is used in clinical practice. The other listed methods are generally more difficult to perform (both from the measured and the measurer perspective) and may require training and experience, and involve expensive equipment (133-135). The BMI is limited by not being specific to fat tissue. High weight can be a result of high muscle tissue percentage, in which case the BMI will be increased in spite of actual low body fat percentage. Nonetheless, the use of BMI was noted as being reliable because it correlates with other measures of excess fat tissue and weight related complications, as well as being simple to use (133).

Defining a uniform measure for overweight and obesity in children is complicated due to wide changes in body morphology influenced by age and gender. There are several internationally agreed cut-off points to define overweight and obesity in children (136). Due to age and gender differences in weight and height in children and adolescents, the BMI percentile (BMI%) is a better indicator of overweight and obesity. Children who are at or above the 85th percentile and are below the 95th percentile are considered overweight. Those at or above the 95th percentile are considered obese (134;137). Charts plotting BMI% for age (figure 1.7) and gender based on USA data are available from the Center for Disease Control (138). This can be used for Canadian youth as the general prevalence of overweight and obesity is similar between Canada and the USA (2).
Figure 1.7.a: CDC BMI for age percentile growth charts for boys
Figure 1.7b: CDC BMI for age percentile growth charts for girls
1.3.2 Prevalence of childhood obesity

The prevalence of childhood obesity has been rising substantially over the last three decades around the world (131;136;139). This rise has been documented in industrialized countries as well as in urban centers of developing countries. North and South America are leading this trend with as many as 46% of school-aged children estimated to be overweight and obese as of 2010 (139).

In Canada, over the past 25 years the rate of overweight in children and adolescents (2-17 years old) has increased from 12% to 18% and the rate of obesity has almost tripled from 3% to 8% in. This means that over a quarter of Canadian children and adolescents are currently overweight or obese. This increase is generated mainly by children over the age of 12 years old. The rates of overweight and obesity vary between ethnic groups with Aboriginal youth having the highest rates and South and East Asian youth showing the lowest rates (2;140).

1.3.3 Consequences of childhood obesity

There are many serious physiological and psychological conditions associated with pediatric obesity (Figure 1.8). These complication may be evident in children as young as 5 years old (2). While some conditions promoted by childhood obesity are specific to the pediatric population (e.g. slipped capital femoral epiphysis) others used to be considered as diseases of adulthood. Examples of the latter are conditions such as the metabolic syndrome (co-existence of glucose regulation abnormalities, hypertension and dislipidemia) and type 2 diabetes mellitus that have in recent years been reported to appear in obese children (131;137;141-143). Low vitamin D and iron deficiency anemia are more common among obese children and pubertal changes including bone maturation are accelerated in this population(137).

Childhood obesity increases the risk of developing cardiovascular disease in the adult years and a relationship between childhood obesity and mortality during adulthood has also been noted (131;136;137). Obese children also tend to remain obese as adults (144). Some complications of obesity (e.g. exercise induced asthma) may create a vicious cycle perpetuating obesity(131).
Figure 1.8: Complications of childhood obesity (Reproduced with permission from Ebbeling et al. 2002).
1.3.4 The biological pathways controlling energy balance

Weight is determined by the balance between energy intake and energy expenditure (145). High energy intake and/or low energy expenditure will result in increased weight. The regulation of hunger and satiety is governed by a complex interaction of several hormonal and neurological pathways. Hormones secreted from the gastrointestinal (GI) tract as well as from fat tissue, in response to food intake, influence short and long-term feeding behavior and body weight set point. The hypothalamus is recognized as the control centre for appetite and is the recipient of all the different signaling pathways (135). The main hormones involved in this signaling pathway are leptin, insulin and ghrelin.

A major breakthrough in understanding the biological pathway controlling this balance was the discovery of leptin by Freidman’s molecular genetics lab in 1994 (146). This group identified a gene in mice that when mutated resulted in obese mice. This gene was appropriately named by the group the obese(ob) gene. The protein, or hormone, encoded by this gene was later named leptin. Leptin is secreted in proportion to body fat. It signals satiety to the hypothalamus resulting in decreased hunger and elevated thermogenesis (135). In obese individuals, leptin levels are generally high due to high body fat content. However, research suggests that a resistance to its action is present in these individuals with several mechanisms suggested for this dysfunction.

Another hormone related to adipose tissue and fasting versus fed state is insulin. Insulin is secreted after food intake and promotes glucose storage into body tissues. It has been shown to affect the hypothalamus, working together with leptin in reducing hunger (135). Insulin levels are usually high in obese individuals with high rates of insulin resistance in its end organs (136). Thus, satiety effects of insulin are reduced in obese individuals. There are several peptides that are secreted in the GI tract in relation to feeding, most of which signal the end of feeding as satiation is reached (135).

Short-term up regulation of appetite is governed by ghrelin, a hormone secreted from the stomach and duodenum (135;136).

All of these hormones- insulin, leptin and ghrelin—have been shown to be affected by sleep (and vice versa). Insulin resistance and glucose intolerance have been shown to be prevalent in
patients with OSA, while having OSA has been named as a risk factor for developing insulin resistance (147). Treating OSA has been demonstrated to improve the insulin and glucose pathway (148). The hormonal regulation of appetite by leptin and ghrelin have been showed to be altered with sleep deprivation (149).

**Suggested factors contributing to obesity**

Causes for increased weight can be divided into genetic and environmental. There are very few single gene mutations that cause obesity. Research suggests that genetic predisposition is influenced by a complex interaction between many obesity related genes (131). However, the rise of obesity rates in genetically stable populations (e.g. Japan, China) and rapidly increased rates of obesity over a span of only decades suggest a strong role for the environmental contribution to obesity. For this reason, and given the nature of the research presented here, the following sections will focus on the contribution of environmental factors to weight gain.

Over the last 50 years, the way we eat has changed dramatically. Consumption of ready made, refined and processed food and drinks, which are high in sugar and caloric content, has become very common both within and outside the home. On the other hand, consumption of fruit and vegetables is low (2;131). Modern eating habits, such as eating out or eating while watching television, has been noted to promote higher caloric intake during meals (131).

The availability of motorized transportation, electricity and screen-related modes of entertainment (television, computer) promote a sedentary way of life among youth. Research compared these youth with youth in communities in which a traditional un-motorized way of life is practiced (i.e., Amish, Mennonites). The results showed significantly lower levels of activity and physical strength and higher body fat levels (as measured by BMI and skin fold measurements) amongst children living a contemporary lifestyle compared to those living a more traditional lifestyle (150).

Sleep, in terms of quality as well as quantity, has been also linked to obesity (151). This connection will be further discussed in the following section.
1.4 Excessive Daytime Sleepiness and Obesity

In recent years, research has focused on the connection between sleep and weight and, more specifically, between EDS and obesity in adults (6-9;152;153). Our group has shown that within an obese group, those with greater obesity had more daytime sleepiness independent of any specific sleep disturbances (153).

1.4.1 Suggested pathways for the relationship between sleep disorders and weight gain

A few pathways connecting sleep disorders with weight gain have been suggested by current research.

- Up-regulation of appetite

Clinical experiments using sleep restriction in healthy young volunteers showed dysregulation of neuroendocrine control of appetite and a negative alteration in glucose tolerance with restricted sleep (154). Van Cauter and colleagues reviewed evidence from a number of cross-sectional studies done in various European, Asian and North American countries showing that the rate of obesity in each country was inversely proportional to the average duration of sleep in that country (155). Another study showed changes in the levels of appetite-inhibiting or -stimulating hormones, such as leptin and ghrelin, with sleep deprivation (149). Hypocretin (also known as Orexin), a neurotransmitter found in the hypothalamus, has been shown to have moderate appetite stimulating properties. There is some evidence of changes in its expression in patients with narcolepsy, Klein-Levin syndrome and Prader-Willi syndrome, all of which have been associated with appetite control issues and/or obesity at times when symptoms of disturbed sleep exists (51).

- Decreased energy expenditure

A reduction in the levels of physical activity and energy is often reported by subjects with sleep problems and/or EDS. This may suggest a direct impact of sleep impairment on activity-related energy expenditure (156;157). In rats, sleep loss is accompanied by increased food intake along with weight loss whereas in humans weight seems to be gained under the same conditions (158;159). There is evidence in rodents showing that energy expenditure is also influenced by
leptin and ghrelin, with the former increasing energy expenditure and the latter decreasing energy expenditure. However, this has not been observed in human subjects (149).

1.4.2 The relationship between obesity and sleep and EDS- the role of inflammation

Obesity is a known risk factor for OSA in adults and EDS is a recognized feature of OSA. However, while EDS is useful in identifying individuals who may have OSA in the general population, only about 20% of adult OSA patients complain of sleepiness (5). Bixler and colleagues have shown that while EDS is associated with measures of OSA, it’s association with BMI, diabetes and age is stronger (6). Obesity as well as diabetes have been identified as pro-inflammatory states (160). Interleukin-6 (IL-6) and tumor-necrosis-factor α (TNFα) are two pro-inflammatory cytokines secreted by fat cells that have been shown to be positively correlated with the degree of obesity. They were also shown to be associated with sleep disturbances (12;161). The work of Vgontzas, Bixler and Chrousos (5), among others, suggests that in obese adults the interaction between these pro-inflammatory cytokines and the hypothalamic-pituitary-adrenal (HPA) axis influences sleep. These authors suggest that while IL-6 and TNFα are elevated in overweight and obese individuals only when there is a concurrent hypoactivity of the HPA axis, there is more deep sleep at night but also more EDS (5).
1.4.3 Sleep and obesity in pediatric research

Several cross-sectional survey studies of children across the age spectrum have indicated a possible connection between shorter sleep duration and obesity (162). A recent, prospective study conducted in Canada showed that having shorter sleep duration regularly throughout the toddler and preschool years increases the risk for obesity at the age of 6 years (163).

There are a few, rare medical syndromes that are well known to feature EDS as well as weight and appetite issues. These three unique medical conditions offer a window into a possible connection between sleep, EDS, and obesity by showing some common symptoms and biological findings:

- **Kleine-Levin syndrome:** This syndrome is characterized by transient episodes of EDS. Excessive eating and increased sexual activity are among additional symptoms defining this disease, for which the cause is unknown (51). There has been one case report of low orexin levels during an episode in a patient with both Kleine-Levin syndrome and Prader-Willi syndrome (164).

- **Prader-Willi syndrome:** This is a genetic syndrome. Some of the main features are low muscle tone, developmental delay, increased appetite and childhood obesity. Indeed, many individuals with Prader-Willi syndrome have CSA and/or OSA, but EDS seems to persist regardless of successful treatment of these SDBs (165). Some patients also show cataplexy—a symptom of sudden muscle weakness, typically described by patients with narcolepsy (165). Our laboratory has shown (166) that there are variable reason for this link. Considering obesity and OSA alone as a cause of EDS in this population is simplistic. Other sleep changes such as sleep fragmentation exist in this population, and when treated improve EDS.

- **Narcolepsy:** This is a sleep disorder in which EDS is the main symptom. Other symptoms include cataplexy, hypnogogic hallucinations, sleep paralysis and fragmented nocturnal sleep. Obesity has been noted to be common in patients with narcolepsy. Low orexin levels have been demonstrated in the cerebrospinal fluid of patients with narcolepsy suggesting an impairment of in a signaling pathway responsible for both sleep and feeding regulation (167). A case-control study from the Netherlands showed higher
levels of food disorder symptomatology in patients with narcolepsy, specifically with food craving and binge eating (168).

1.4.4 EDS and obesity in children and adolescents

Little is currently known about sleep and EDS in overweight children and adolescents. To date, there are a few studies addressing this issue. Some used subjective measures of sleepiness, such as questionnaires, while other studies used an objective measures, such as the MSLT. Each study has specific methodological limitation.

Table 1.5: A summary of all the currently published studies examining the relationship of EDS and obesity in children and adolescents

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of subjects</strong></td>
<td>22 OB subjects</td>
<td>92 OW/OB subjects-54 OSA, 14 snoring, 24 control</td>
<td>100 OB subjects-50 subject with SDB, 50 control</td>
<td>150 subjects-76 NW controls, 42 OW/OB controls, 32 OW/OB subjects with OSA.</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>2-20</td>
<td>6-9</td>
<td>6-9</td>
<td>5-17</td>
</tr>
<tr>
<td><strong>Measure of EDS</strong></td>
<td>MSLT</td>
<td>MSLT, Subjective measures used but not reported.</td>
<td>MSLT</td>
<td>Subjective measure (Parental reports – PSQ).</td>
</tr>
<tr>
<td><strong>Population source</strong></td>
<td>Primary care clinic</td>
<td>Sleep clinic</td>
<td>Sleep clinic</td>
<td>Sleep clinic</td>
</tr>
<tr>
<td><strong>Conclusion</strong></td>
<td>Correlation between EDS and obesity</td>
<td>Correlation between EDS and obesity, EDS and OSA, each independently.</td>
<td>In any severity of OSA obese children exhibit more daytime sleepiness</td>
<td>Obesity and not the severity of sleep disorder is associated with sleepiness</td>
</tr>
<tr>
<td><strong>Limitations</strong></td>
<td>No control group, small sample size coupled with wide age range.</td>
<td>Focus on SDB, much smaller sample size for the snoring and the control group.</td>
<td>Focus on SDB.</td>
<td>No objective sleepiness measurement.</td>
</tr>
</tbody>
</table>

Marcus and colleagues (13) reported MSLT findings in a group of 22 obese children and adolescents, ages 2-20 years. The participants were recruited while attending an urban primary care facility located within a hospital for routine health care and did not necessarily have
previous sleep complaints. Patients that had past upper airway surgery were excluded. Sleep assessment for all participants included overnight PSG and an MSLT. Their findings showed a correlation between daytime sleepiness (measured with the MSLT) and obesity. This study was limited by the lack of a control group. Additionally, the sample size was small while the age range was wide. Considering the developmental aspects of sleep, the use of a mall population with a wide age range diminishes the quality of the analysis.

In a later study (10) objective EDS evaluated by MSLT was assessed in a subset of pre-pubertal children (age 6-9 years old) who were previously diagnosed with OSA or primary snoring due to adenotonsillar enlargement. They were compared to a control group with no previous sleep-related diagnosis recruited from the community. The number of participants varied between the groups (54-OSA, 14-primary snoring, 24-controls). PSG and MSLT were performed for all the study subjects. Daytime sleepiness on the MSLT was again independently associated with both obesity and OSA.

Recently, another study by Gozal et al. reported measurement of daytime sleepiness in obese versus non-obese, habitual-snoring, prepubertal children (ages 6-9) with adenotonsillar hypertrophy. This study showed that at any severity of OSA, obese children exhibit more daytime sleepiness as measured by MSLT than their non-obese counterparts (11).

Table 1.5 outlines the limitations associated with these pediatric studies. As noted above, all of these studies have limitations: a small sample size, restricted ethnic and socioeconomic background (Marcus et al.), restricted age group (Gozal et al.), and a focus on SDB and OSA. Despite these limitations, they all suggest a link between EDS and obesity.

A very recent study in Greece examined the relationship between EDS and excessive weight in 150 children aged 5-17 years recruited from a sleep clinic. While sleep was assessed objectively using PSG, EDS was assessed subjectively by the parents of the study subjects. Their findings again supported the idea that obesity, and not the severity of the sleep disorder, is associated with sleepiness (12). This study also showed elevated pro-inflammatory cytokines in obese children with SDB. However, the gold-standard test, the MSLT, was not performed.
The paucity of data and limitation of both methodologies (subjective vs. objective) and age range (ever more limited data in teens) merits further investigation into the relationship between EDS and weight in the pediatric population.

As previously noted, EDS can have a great impact on various aspects of everyday life: social, psychological and academic (30). Therefore expanding the body of evidence about EDS in children, and adolescents in particular, is of great importance.

With the rise in pediatric obesity and the interaction between sleep and weight, an understanding of how EDS correlates with weight is significant. Most of the limited research in the literature discussed to date has examined OSA and EDS. There is a need to broaden the spectrum of sleep parameters analyzed in regards to the above correlation. Finally, it is hoped that this effort will add to our understanding in assessing sleepiness in the pediatric setting.
2 METHODS AND MATERIALS

2.1 Research Aim and Hypothesis

2.1.1 Aim

The primary aim of this study was to examine the relationship between EDS and BMI percentile in children and adolescents.

2.1.2 Study question

Does EDS correlate better with BMI percentile rather than with measures of sleep pathology in children and adolescents?

2.1.3 Hypothesis

Children and adolescents who are overweight or obese will exhibit more EDS compared to normal-weight, aged matched individuals, independent of measures of sleep pathology.
2.2 Methods

2.2.1 Study design
This was a retrospective chart review using an existing data set of paediatric patients between 6 and 18 years old, who had undergone an overnight polysomnography at the Youthdale Child and Adolescent Sleep Centre in Toronto, followed by an MSLT. The study procedures were reviewed and approved by the independent Institutional Review Board Services at Aurora, ON, Canada.

2.2.2 Data collection
Consecutive charts of patients who had previously completed an MSLT assessment at the Youthdale Child and Adolescent Sleep Centre between October 2006 and May 2010 were reviewed. All medical and sleep history records were reviewed to screen for the relevant inclusion and exclusion criteria.

Inclusion criteria:

- Children and adolescents between 6-18 years old at the time the sleep tests were conducted. The minimum age was dictated by the minimal age for which an MSLT may be considered to be reliable (108).

- Complete records of BMI and MSLT results.

Exclusion criteria:

These criteria were set to exclude patients with specific conditions or pharmaceutical treatments that are known to cause daytime sleepiness:

- Congenital or acquired neuromuscular abnormalities, brain injury, anatomical malformations (see appendix B).

- Specific sleep disorders with daytime sleepiness as a main diagnostic criteria- narcolepsy, delayed sleep phase syndrome.
Chronic medication use that may influence or interfere with sleep (see appendix A).
Although this group was not included in the study population, this group was examined in a subsequent and separate analysis. (see section 3.6).

The initial reason for PSG’s in this population is very broad. Elsewhere in this thesis we report that 18% of the population studied have obstructive sleep apnea. By most standards this would represent a relatively low percentage and emphasizes the diversity of conditions treated in this clinic. Patients are referred with any significant sleep disruption. The co-morbidities would include rare genetic disorders, foetal alcohol syndrome, a wide array of psychiatric problems including PTSD and depression, idiopathic hypersomnolence, attention related problems and parasomnias. I believe that for the purposes of the present study this is an advantage in as much as issues of obesity are not simply yoked to OSA. Furthermore, the threshold for performing an MSLT is intentionally low. This is based on both clinical experience where the need to intervene in what might appear to be relatively mild disorders is upgraded in the face of objective daytime sleepiness. A secondary reason is our academic interest in understanding the drivers of daytime sleepiness. The clinical utility is by far and away the major factor.

All of the data was recorded anonymously using a coding system. This included age, gender, height and weight as recorded on the day of the sleep study. Medications used at the time of the sleep studies were recorded as well, so as to be considered for the inclusion and exclusion criteria. PSG and MSLT parameters were also recorded.

The BMI percentile (BMI %) was calculated for each participant. This was done by plotting the subjects BMI on the gender appropriate BMI for age percentiles charts (See figure 1.7). Values at or above the 85th percentile and below the 95th percentile for age and gender were considered overweight (OW), while values at or higher than the 95th percentile for gender and age were considered obese (OB) (134;137). These OW and OB were later merged into one group—referred to as the overweight range group (OWr). All other values were considered normal weight (NW). BMI% was also used as a continuous variable in some of the analysis.
2.2.3 Outcome measures

Primary outcome

- **Mean Sleep Latency on the MSLT (MSL<sub>MSLT</sub>).** This is defined in minutes, ranging from 0 to 20 minutes. As noted earlier, low MSL<sub>MSLT</sub> values are indicative of sleepiness, but specific validated criteria are lacking in the pediatric population.

Secondary measures

These were measures of sleep pathology. From the various measures of sleep pathology indicated in a PSG, two were chosen as the focus of this analysis: the **Apnea Hypopnea Index (AHI)** and the **Arousal Index (AI).** The reasons for choosing these parameters are described below.

- **Apnea Hypopnea Index (AHI)**

This is a PSG parameter used in the diagnosis of sleep apnea. Since sleep apnea is the most common reason for the referral of pediatric patients to sleep clinics, and since it has been linked with overweight and daytime sleepiness (each separately) in adults and children (33;169;170), it was chosen as a secondary measure to be analyzed in this study.

The AHI is the total number of apneas and hypopneas divided by the total sleep time in hours (giving the average number of apnea and hypopnea events per hour of sleep). According to the American Academy of Sleep Medicine “criteria for respiratory events during sleep for infants and children can be used for children <18, but an individual sleep specialist can choose to score children ≥ 13 years using adult criteria” (27). At the Youthdale Child and Adolescents Sleep Centre a cutoff of 13 years is employed. For children under 13 years an AHI >1 is considered pathological, while children 13 years and older are generally judged by adult standards, meaning AHI >5 is considered pathological.
**Figuer 2.1** - A graphic representation of apnea (obstructive-right) and hypopnea (left).

- **Arousal Index (AI)**

This is the average number of arousals per hour of sleep. It is an indicator of sleep fragmentation. Sleep fragmentation due to various mechanisms have been linked to daytime sleepiness. There are no standard criteria defining pathological AI, but it is generally accepted that an AI ≥10 is considered abnormal in adults (73;74). In the absence of normative data and with many children having a more ‘solid’ sleep than adults, some report an AI>5 (i.e. an arousal every 12 minutes) as abnormal for children. In the clinical experience in our sleep clinic, a treatment intervention that reduced AI from 8 to 4 has lead to both subjective and MSLT reduction in sleepiness, along with parental reports of improved school performance (Shapiro Colin- personal communication, 2011).

- **Group Mean Sleep Latency for a nap (MSLnap).**

The MSL_{MSLT} does not reflect the diurnal pattern of EDS. Therefore, for the group of subjects with an abnormal MSL_{MSLT}, the group mean MSL for each nap was calculated (MSLnap). MSLnap was then compared for the various weight, gender and age groups.

### 2.3 Sample Size and Statistical Power Considerations

A sample size calculation was performed to estimate the sample size necessary to detect a clinically significant difference in mean MSL_{MSLT} between obese and non-obese children and adolescents. A formula (shown below) to estimate the sample size needed to detect the difference in the mean of a continuous variable between two groups was used.

**Sample size calculation formula:** \( n = 1 + 2C(s/d)^2 \).
C is a constant, dependent on values chosen for significance level (α) and power (1-β). S is the standard deviation and d is the clinically significant difference (or effect size). For the purpose of the analysis done in this study, the significant level was chosen to be 0.05 and the power 0.8, making \( C = 7.85 \). 

Recognizing that there is no well established standardized criteria for MSLT in the pediatric population, it was challenging to determine the standard deviation and the size of the clinically significant difference in MSLT needed for the calculation. Upon reviewing the literature, there were a few principles we used to help us determine a standard deviation that would be acceptable in our patient population. Age has been shown to have a significant impact on MSLT (54). MSLT has been shown to vary between pre-adolescent and adolescent children in relation to puberty (10;112;114;117). While the actual value of MSLT in normal sleepers differs between the age groups, the standard deviation (SD) reported in most cases ranges between 2.8 to 3.5 (10;112;114;117). Therefore, an estimated standard deviation of 3 minutes was used for the sample size and power calculation. As for the clinically significant difference in MSLT between the weight groups, one standard deviation was used as this was supported by the accepted adult criteria for daytime sleepiness on the MSLT. As previously noted, an MSLT of less than 11 minutes in adults is indicative of excessive sleepiness, an MSLT of less than 8 minutes but no less than 5 is considered suggestive of moderate sleepiness, and an MSLT of less than 5 minutes suggests severe sleepiness (54;107;108). The difference between each level of sleepiness is 3 minutes. Hence, for the purpose of this study, a difference of 3 minutes on the MSLT between obese and non-obese children and adolescents was considered clinically significant.

After applying the above noted values to the formula, the total number of subjects needed in each weight group (obese and non-obese) in order to detect a clinically significant difference in MSLT was 17, giving a total sample size of 34.
2.4 Statistical Analysis

Descriptive measures (means, standard deviations, medians, ranges, and proportions) were used to summarize demographic information at presentation. Kolmogorov-Smirnov tests were used to assess whether the distribution of a variable was normal. As a result, non-parametric statistical analysis was used (with the exception of a multiple regression analysis).\(^2\)

Differences in MSL\(_{(MSLT)}\) between weight groups were compared using the Mann–Whitney U test. Frequency analysis using the chi square test was performed to investigate the difference in the prevalence of abnormal MSL\(_{(MSLT)}\) between the weight groups. Both of these analyses were then repeated to investigate the affects of potential confounding factors such as age and gender. In order to investigate diurnal patterns in EDS the Mann–Whitney U test was used again to compare MSLnap between weight groups.

Spearman’s rank-order correlation procedure was used to examine the relationship between the variables. Multiple regression analysis was used to build models predicting the presence of EDS in the study population. This analysis was done while acknowledging that a normal distribution of the residuals was not present for parts of the analysed population, even after log transformation. This violates one of the assumptions of multiple regression analysis. Nevertheless, such an analysis was considered important to obtain a better understanding of the associations between the variables. The results of the regression analysis should be considered with caution.

Subsequent to the above described analysis, a similar analysis was done for the group of subjects who were excluded due to being treated with medications that promote sleep disorders and daytime sleepiness. The differences in MSL\(_{(MSLT)}\) and in MSLnap between weight groups was again compared using the Mann–Whitney U test. The chi square test was performed to investigate the difference in the prevalence of abnormal MSL\(_{(MSLT)}\) between the weight groups.

\(^2\) The Kolomogorov-Smirnov test was chosen over the Shapiro-Wilk test since it is more appropriate for the sample size. The main disadvantage of the Kolomogorov-Smirnov test is in being less sensitive to detect deviation from normality. Since a deviation from normal distribution was detected in the study population this issue does not apply here.
The Spearman’s rank-order correlation procedure was repeated to examine the relationship between the variables in this group as well.

The level of all statistical significance was set at P value <0.05. All statistical analysis was conducted using SPSS v19.

### 2.5 Ethical Considerations

This was a retrospective chart review using an existing data set, so there were no anticipated risks for the subjects of this research. The data for this study was collected from patients’ consultation notes and sleep study results. All data was recorded using a coding system in which each chart received a code name. No personal information that could be used to identify the patients was collected. All information collected was kept confidential. In order to ensure that data from the patient’s charts was entered accurately into the database a random sample of about 15% of the files was reviewed again. The study procedures were reviewed and approved by the independent Institutional Review Board Services at Aurora, ON, Canada.
3 RESULTS

3.1 Study Population

From a total of 1350 charts present at the Youthdale Child and Adolescents Sleep Center at the time of reviewing, 466 patients within the age range had an MSLT performed. A total of 188 patients’ charts were included in the study. Table 3.1 shows the exclusion process during the data collection for this study.

**Table 3.1- Exclusion process details.**

<table>
<thead>
<tr>
<th>Reason for exclusion</th>
<th>Number of chart excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missing data</td>
<td>15</td>
</tr>
<tr>
<td>Exclusionary medical conditions and specific sleep disorders</td>
<td>195</td>
</tr>
<tr>
<td>(see methods section for a complete description of excluded conditions)</td>
<td></td>
</tr>
<tr>
<td>Prohibited medications</td>
<td>68</td>
</tr>
<tr>
<td>Final population – 188</td>
<td></td>
</tr>
</tbody>
</table>

The population’s demographics and characteristics are described in table 3.2. There were 116 (62%) males and 72 (38%) females. Mean age was 11.8 (±3.6 SD). Almost half of the study population (47%) was overweight or obese (15% and 32% respectively). While 54% of our population had abnormal MSLT results, only 18% had abnormal AHI indicating the presence of sleep apnea, and 40% had abnormal AI implying fragmented sleep.
Table 3. 2- Characteristics for the total population (n=188)*.

<table>
<thead>
<tr>
<th></th>
<th>Groups</th>
<th>N (%)</th>
<th>Mean (STD)</th>
<th>Median (min,max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Males</td>
<td>116(62)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Females</td>
<td>72(38)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Age (years)</td>
<td>Total</td>
<td>-</td>
<td>11.8(3.6)</td>
<td>12.0(6.18)</td>
</tr>
<tr>
<td>Weight (BMI%)</td>
<td>Normal weight</td>
<td>100(53)</td>
<td>47.3(26.7)</td>
<td>47(1.85)</td>
</tr>
<tr>
<td></td>
<td>Overweight</td>
<td>28(15)</td>
<td>89.5(3.4)</td>
<td>89(85, 94.1)</td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>60(32)</td>
<td>98.3(1.3)</td>
<td>98.8(95.3, 99.9)</td>
</tr>
<tr>
<td>Total</td>
<td>-</td>
<td>69.9(31.2)</td>
<td>82.5(1,99)</td>
<td></td>
</tr>
<tr>
<td>MSL/MSLT (Minutes)</td>
<td>Abnormal(C:&lt;19 A:&lt;16)</td>
<td>102(54)</td>
<td>13.5(4.1)</td>
<td>14.0(2.5, 18.7)</td>
</tr>
<tr>
<td></td>
<td>Normal (C: ≥19 A: ≥16)</td>
<td>86(46)</td>
<td>19.2(1.3)</td>
<td>20.0(16, 20)</td>
</tr>
<tr>
<td>Total</td>
<td>-</td>
<td>16.1(4.2)</td>
<td>17.5(2.5,20)</td>
<td></td>
</tr>
<tr>
<td>AHI</td>
<td>Abnormal(C:&gt;1 A:&gt;5)</td>
<td>33(18)</td>
<td>11.3(19.1)</td>
<td>3.9(1.1, 95.3)</td>
</tr>
<tr>
<td></td>
<td>Normal (C: ≤ 1 A: ≤5)</td>
<td>155(82)</td>
<td>0.4(0.5)</td>
<td>0.2 (0, 2.8)</td>
</tr>
<tr>
<td>Total</td>
<td>-</td>
<td>2.3(8.9)</td>
<td>0.4(0, 95.3)</td>
<td></td>
</tr>
<tr>
<td>AI</td>
<td>Abnormal (&gt;10)</td>
<td>76(40)</td>
<td>16.6(7.1)</td>
<td>14.3(10.1, 48)</td>
</tr>
<tr>
<td></td>
<td>Normal (≤10)</td>
<td>112(60)</td>
<td>7.3(1.9)</td>
<td>7.4(0, 10)</td>
</tr>
<tr>
<td>Total</td>
<td>-</td>
<td>11.0(6.6)</td>
<td>9.4(0, 48)</td>
<td></td>
</tr>
</tbody>
</table>

*C=children, age <13, A= adolescents, age ≥ 13 and over.

Kolmogorov-Smirnov tests were conducted in order to assess whether the variables' distributions were normal. All the variables' distributions (BMI%, MSL/MSLT, AHI and AI) significantly deviated from normality (all p’s<.001). Next, a log-transformation was conducted, and normality was examined again. This time, all variable distributions deviated from normality (p’s<.001), except for AI (p=.19). Given the non-normal distributions of the variables, all further analysis was conducted using non-parametric statistical methods. Specifically, comparisons between groups were conducted using the Mann-Whitney test, unless stated differently.
3.2 Differences in $\text{MSL}_{M\text{SLT}}$ by Weight Group

For the frequency analysis the overweight (OW) and obese (OB) groups were merged into one group referred to as the overweight range group (OWr). This group was then compared against the normal weight group (NW).

Mean $\text{MSL}_{M\text{SLT}}$ was lower in the OWr group compared to the NW group ($15.5 \pm 4.4$ vs. $16.6 \pm 4.0$ respectively) however, this was not statistically significant relative to the standard alpha level of .05 (Mann-Whitney test, $Z=1.89$, $p=0.058$). Nevertheless, with a $p$ value under .1, this difference was approaching significance.

Figure 3.1 shows differences in the distribution of normal versus abnormal $\text{MSL}_{M\text{SLT}}$ values between the two weight groups for the total study population. Again, although the rate of abnormal $\text{MSL}_{M\text{SLT}}$ was higher in the OWr group, the difference was not significant relative to the standard alpha level of .05. However, here as well the $p$ value was under .1, and so this difference was approaching significance ($\chi^2(2)=3.37, P=.067$).

**Figure 3.1 – The frequency of normal vs. abnormal $\text{MSL}_{M\text{SLT}}$ in each weight group for the total study population (n=188).** Normal $\text{MSL}_{M\text{SLT}}$ (C: $\geq 19$ A: $\geq 16$), Abnormal $\text{MSL}_{M\text{SLT}}$(C:<19min A:<16min). NW=Normal Weight group, n=100(53%), OWr= Overweight and obese group, n=88(47%). Frequency of abnormal $\text{MSL}_{M\text{SLT}}$, 48% NW vs. 61% OWr, $\chi^2(2)=3.3$, $p=.067$. 
Next potential confounders—gender and age—were considered. Both were found to have an effect, as will be described in the following section.

3.2.1 Differences in MSL_{MSLT} by weight group and gender

While weight distribution was the same for the entire population and within each gender group (see tables 3.2 and 3.3), the majority of the male group (70%) was under the age of 13 years (vs. 51% in the female group). The rate of abnormal AHI values was also higher in the male group (20% vs. only 7% in females). However, the female group had higher rates of abnormal MSL_{MSLT} values (63% vs. 49% in males). AI values had a similar distribution between the genders (M; 40% vs. F; 42% abnormal AI values).

**Table 3.3- Mean MSL_{MSLT} by gender group.**

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=116(62%)</td>
<td>n=72(38%),</td>
</tr>
<tr>
<td>Mean</td>
<td>MSL_{MSLT}=16.4 ± 4.3.</td>
<td>MSL_{MSLT}=15.6 ± 4.1</td>
</tr>
<tr>
<td>Median</td>
<td>18.2</td>
<td>16.5</td>
</tr>
<tr>
<td><strong>NW</strong></td>
<td>N=62 (53%)</td>
<td>N=38 (53%)</td>
</tr>
<tr>
<td>Mean</td>
<td>MSL_{MSLT}=17.3 ±3.7</td>
<td>MSL_{MSLT}=15.6 ±4.4</td>
</tr>
<tr>
<td>Z</td>
<td>2.08, p=.04</td>
<td>Z=.31, p=.76</td>
</tr>
<tr>
<td><strong>OWr</strong></td>
<td>N=54 (47%)</td>
<td>N=34 (47%)</td>
</tr>
<tr>
<td>Mean</td>
<td>MSL_{MSLT}=15.4 ± 4.7</td>
<td>MSL_{MSLT}=15.6 ±3.8</td>
</tr>
</tbody>
</table>

*Mean MSL_{MSLT} in min±STD. Median in min.*

Mean MSL_{MSLT} was similar for males and females (16.4 ± 4.3 and 15.6 ± 4.1 respectively). When divided by weight group, MSL_{MSLT} for males was 17.3 ±3.7 in NW patients vs. 15.4 ±4.7 in patients in the OWr group. This difference was found to be statistically significant (Z=2.08, p=.04). The frequency analysis for the male group also showed a significant difference (Chi-squared=4.14, p=.042) in the frequency of abnormal MSL_{MSLT} between the weight groups (Figure 3.2).
For female patients mean MSL\textsubscript{MSLT} was similar for the two weight groups (15.6 ±4.4 NW and 15.6 ±3.8 OWr, Z=.31, p=.76) and no significant difference in frequency was found (χ\textsuperscript{2}(2)=.13, p=.71) (Figure 3.3).

![Bar chart showing normal vs. abnormal MSL\textsubscript{MSLT} in each weight group for male subjects.](image)

**Figure 3.2** The frequency of normal vs. abnormal MSL\textsubscript{MSLT} in each weight group for male subjects (n=116). Normal MSL\textsubscript{MSLT} (C: ≥19 A: ≥16), Abnormal MSL\textsubscript{MSLT}(C:<19min A:<16min).

NW=Normal Weight group, n=62(53%), OWr= Overweight and obese group, n=54(47%). Frequency of abnormal MSL\textsubscript{MSLT}, 40% NW vs. 59% OWr, χ\textsuperscript{2}(2)=4.14, p=.042.
Figure 3.3- The frequency of normal vs. abnormal MSL\textsubscript{MSLT} in each weight group for female subjects (n=72). Normal MSL\textsubscript{MSLT} (C: \(\geq 19\) A: \(\geq 16\)), Abnormal MSL\textsubscript{MSLT}(C:<19min \text{A:<16min}). NW=Normal Weight group, n=38(53%), OWr= Overweight and obese group, n=34(47%). Frequency of abnormal MSL\textsubscript{MSLT} , 60% NW vs. 65% OWr, \(\chi^2(2)=.13, p=.71\).

3.2.2 Differences in MSL\textsubscript{MSLT} by weight group and age

Since sleep pattern changes according to age (29;33), the studied population was divided according to the age cut-off point used to determine abnormal MSLT results. The younger age group of children (under 13 years) is referred to as the C (children) group and the older group of adolescents (>13 and <18 years old) is referred to as the A (adolescents) group.

The rates of male gender (69%), overweight and obesity (49%), and abnormal AHI values (22%) were higher in group C then in group A (49%, 43%, and 10% respectively). However, group A had higher rates of abnormal MSL\textsubscript{MSLT} values (58% vs. 52% in group C) and AI values (51% vs. 34% in group C).
Table 3.4- Mean $M_{MSL}$ by age group.

<table>
<thead>
<tr>
<th></th>
<th>C group</th>
<th>A group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=119 (63%)</td>
<td>n=69 (37%),</td>
<td></td>
</tr>
<tr>
<td>Mean $M_{MSL}$</td>
<td>17.5 ±3.2</td>
<td>13.6 ±4.7</td>
</tr>
<tr>
<td>Median</td>
<td>18.7</td>
<td>14.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>NW</th>
<th>OWr</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=61 (51%)</td>
<td>N=58 (49%)</td>
<td>N=39 (57%)</td>
</tr>
<tr>
<td>Mean $M_{MSL}$</td>
<td>18.4 ±2.2</td>
<td>16.5 ±3.7</td>
</tr>
<tr>
<td>Z</td>
<td>2.71, p=.007</td>
<td>.30, p=.77</td>
</tr>
</tbody>
</table>

*Mean $M_{MSL}$ in min ±STD. Median in min.

Mean $M_{MSL}$ for group C was 17.5 ±3.2 vs. 13.6 ±4.7 for group A. When divided by weight, group mean $M_{MSL}$ for group C was 18.4 ±2.2 in NW patients vs. 16.5 ±3.7 in patients in the OWr group, a statistically significant difference ($Z=2.71$, $p=.007$). In the A group, mean $M_{MSL}$ was similar for the two weight groups, 13.7 ±4.6 and 13.4 ±4.8 respectively ($Z=.30$, $p=.77$).

Frequency analysis for each weight group was performed (Figure 3.4 and 3.5). The frequency of abnormal $M_{MSL}$ differed significantly between the weight groups only among the younger age group ($\chi^2 (2)=4.5$, $P=.034$).
Figure 3.4- The frequency of normal vs. abnormal MSL\textsubscript{MSLT} in each weight group for subjects age <13, C group (n=119). Normal MSL\textsubscript{MSLT} (C: ≥19 A: ≥16), Abnormal MSL\textsubscript{MSLT}(C:<19min A:<16min). NW=Normal Weight group, n=61(51%), OWr= Overweight and obese group, n=58(49%). Frequency of abnormal MSL\textsubscript{MSLT} , 43% NW vs. 62% OWr, $\chi^2(2)=4.5$, $p=.034$. 
Figure 3.5- The frequency of normal vs. abnormal MSL_MSLT in each weight group for subjects age ≥13, A group (n=69). Normal MSL_MSLT (C: ≥19 A: ≥16), Abnormal MSL_MSLT (C: <19min A: <16min). NW=Normal Weight group, n=39 (57%), OWr= Overweight and obese group, n=30 (43%). Frequency of abnormal MSL_MSLT, 56% NW vs. 62% OWr, $\chi^2(2) = .09$, p=.77.
3.3 Differences in MSL for each nap between weight, gender and age groups

As previously noted there were 102 subjects who had an abnormal MSL_{MSLT}. The MSL_{MSLT} does not reflect the diurnal pattern of EDS. Therefore, for the group of subjects with an abnormal MSL_{MSLT} the MSL for each nap was calculated (MSL_{nap}). MSL_{nap} was then compared for the various weight, gender and age groups (Figure 3.6).

![Figure 3.6: MSL_{nap} by subjects weight, gender and age group.](image)

NW=Normal Weight, OWr=OW range, M=males, F=females, C=group C, A=group A.

There was a significant difference in MSL_{nap} between weight groups in males on the second nap (z=2.30, p=.02) and in the C age group on the second and fourth nap (Z=2.74, p=.006 and Z=2.11, p=.035 respectively).
3.4 Correlations

The correlations between the examined variables for the entire study population are summarized in table 3.5. BMI% showed a statistically significant negative correlation with MSL<sub>MSLT</sub> (figure 3.7) and a positive correlation with AHI. MSL<sub>MSLT</sub> also negatively correlated with AI. A significant positive correlation was also shown between AHI and AI.

Table 3.5- Correlations between BMI%, MSL<sub>MSLT</sub>, AHI, and AI for the entire group.

<table>
<thead>
<tr>
<th></th>
<th>BMI%</th>
<th>MSL&lt;sub&gt;MSLT&lt;/sub&gt;</th>
<th>AHI</th>
<th>AI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI%</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSL&lt;sub&gt;MSLT&lt;/sub&gt;</td>
<td>-.18*</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI</td>
<td>.21**</td>
<td>-.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AI</td>
<td>.06</td>
<td>-.23**</td>
<td>.33***</td>
<td>-</td>
</tr>
</tbody>
</table>

* p<.05, ** p<.01, *** p<.001

Figure 3.7- The Correlation between BMI%, MSL<sub>MSLT</sub>, for the entire group.
3.4.1 Correlations between BMI%, MSL\textsubscript{MSLT}, AHI and AI by gender

Table 3.6 summaries the correlations between all the examined variables by gender.

**Table 3.6- Correlations between BMI%, MSL\textsubscript{MSLT}, AHI and AI by gender.**

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMI%</td>
<td>MSL\textsubscript{MSLT}</td>
<td>AHI</td>
<td>AI</td>
</tr>
<tr>
<td>BMI%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSL\textsubscript{MSLT}</td>
<td>-.25**</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI</td>
<td>.21*</td>
<td>-.05</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>AI</td>
<td>.06</td>
<td>-.22*</td>
<td>.35***</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMI%</td>
<td>MSL\textsubscript{MSLT}</td>
<td>AHI</td>
<td>AI</td>
</tr>
<tr>
<td>BMI%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSL\textsubscript{MSLT}</td>
<td>-.06</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI</td>
<td>.23</td>
<td>-.05</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>AI</td>
<td>.07</td>
<td>-.23</td>
<td>33**</td>
<td>-</td>
</tr>
</tbody>
</table>

* p<.05, ** p<.01, *** p<.001

The correlations in the male group showed similarity to the correlations observed for the entire study population. Among the male subjects, BMI% showed a statistically significant negative correlation with MSL\textsubscript{MSLT} as well as a positive correlation with AHI. MSL\textsubscript{MSLT} also negatively correlated with AI. AHI and AI showed a positive correlation as well. However, the only statistically significant correlation in the female group was a positive correlation between AHI and AI, similar to one showed in the male group.

The following figure illustrates the correlation between BMI% and MSL\textsubscript{MSLT} for males and females.
Figure 3.8- Correlation between BMI% and MSL_{MSLT} for males and females.
3.4.2 Correlations between BMI%, MSL, AHI and AI by age

In the younger age group (group C), BMI% showed a statistically significant negative correlation only with MSL_{MSLT} (figure 3.9). MSL_{MSLT} also negatively correlated with AI. There was no correlation between BMI% and AHI in group C. However, in group A BMI% correlated only with AHI, while no correlation was observed between MSL_{MSLT} and any of the variables examined. AHI and AI again showed similar positive correlations for both age groups. Figure 3.8 illustrates the correlations observed for each age group. The correlations between the variables by age are specified in table 3.7.

**Table 3.7 - Correlations between BMI%, MSL\textsubscript{MSLT}, AHI and AI by age group.**

<table>
<thead>
<tr>
<th>Group C (age&lt;13)</th>
<th>BMI%</th>
<th>MSL\textsubscript{MSLT}</th>
<th>AHI</th>
<th>AI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI%</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSL\textsubscript{MSLT}</td>
<td>-.25**</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI</td>
<td>.11</td>
<td>-.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AI</td>
<td>.03</td>
<td>-.19*</td>
<td>.35***</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group A (Age ≥13)</th>
<th>BMI%</th>
<th>MSL\textsubscript{MSLT}</th>
<th>AHI</th>
<th>AI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI%</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSL\textsubscript{MSLT}</td>
<td>-.08</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI</td>
<td>.32**</td>
<td>.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AI</td>
<td>.16</td>
<td>-.02</td>
<td>.34**</td>
<td></td>
</tr>
</tbody>
</table>

* p<.05, ** p<.01, *** p<.001
Figure 3.9- Correlation between BMI% and MSL\textsubscript{MSLT} by age group.
3.5 Multivariate Regression Analysis- predictors of EDS

Multiple regression analysis was used to build models predicting the presence of EDS in the study population. These results should be considered with caution in light of the non-normal distribution of the residuals for parts of the studied population.

A multiple regression model for the entire population was created including MSL as a dependent variable, and age, gender, AHI, AI and BMI % as independent variables. The Kolmogorov-Smirnov test for normality of the residuals was approaching significance, Z=1.26, p=.08 (indicating that the residuals distribution was close to depart from normality). The model was significant, \( F(5,182)=18.13, p<.001 \), adjusted \( R^2 = .314 \).

<table>
<thead>
<tr>
<th>Predictor variable</th>
<th>Beta</th>
<th>t</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-.496</td>
<td>-7.74</td>
<td>&lt;.001**</td>
</tr>
<tr>
<td>Gender</td>
<td>-.012</td>
<td>-.19</td>
<td>.85</td>
</tr>
<tr>
<td>AHI</td>
<td>-.281</td>
<td>-3.63</td>
<td>&lt;.001**</td>
</tr>
<tr>
<td>AI</td>
<td>.049</td>
<td>.63</td>
<td>.53</td>
</tr>
<tr>
<td>BMI%</td>
<td>-.108</td>
<td>-1.77</td>
<td>.079</td>
</tr>
</tbody>
</table>

* p<.05, **p<.001

Age and AHI were shown to be significant predictors of EDS in the study population. However, BMI% was a non-significant predictor relative to the standard alpha level of .05. Nevertheless, with a p value under 0.1, BMI% was approaching significance as a predictor of EDS in this study population.

Since age was shown to be significant predictor a multiple regression analysis was also used for the two age groups, C and A (table 3.9).
### Table 3.9- Multiple regression model predicting EDS for each age group.

<table>
<thead>
<tr>
<th></th>
<th>Predictor variable</th>
<th>Beta</th>
<th>t</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group C</strong> (Age &lt;13)</td>
<td>Gender</td>
<td>-.002</td>
<td>-.03</td>
<td>.63</td>
</tr>
<tr>
<td></td>
<td>AHI</td>
<td>-.364</td>
<td>-3.63</td>
<td>.002*</td>
</tr>
<tr>
<td></td>
<td>AI</td>
<td>-.042</td>
<td>-.40</td>
<td>.18</td>
</tr>
<tr>
<td></td>
<td>BMI%</td>
<td>-.248</td>
<td>-3.18</td>
<td>.001*</td>
</tr>
<tr>
<td><strong>Group A</strong> (Age ≥13)</td>
<td>Gender</td>
<td>-.025</td>
<td>-.20</td>
<td>.78</td>
</tr>
<tr>
<td></td>
<td>AHI</td>
<td>-.250</td>
<td>-1.58</td>
<td>.12</td>
</tr>
<tr>
<td></td>
<td>AI</td>
<td>.120</td>
<td>.80</td>
<td>.46</td>
</tr>
<tr>
<td></td>
<td>BMI%</td>
<td>.023</td>
<td>.18</td>
<td>.93</td>
</tr>
</tbody>
</table>

* p<.05, **p<.001

This model was significant only in the C age, F(4,114)=10.4, p<.001, adjusted $R^2 = .242$. BMI% was shown to be a significant predictor of EDS in the C age group (p=.002).

It should be noted that in this regression model the Kolmogorov-Smirnov test for normality of the residuals was significant for group C, Z=1.64, p=.009, indicating a non-normal distribution of the residuals in this group. For group A the residuals showed a normal distribution, Z=.82, p=.51. Log-transformation of the variables did not normalize the distribution of the residuals for group C (Z=1.74, p=.005).
3.6 Subsequent Analysis of Data from Subjects Treated with Medications that Influence Sleep and Sleepiness

As noted in Section 3.1, there were 68 subjects who were excluded as they were being treated with various medications that are known to either interrupt nocturnal sleep (mainly with insomnia) or to promote daytime somnolence. Many of these had both insomnia and somnolence listed in their side effects profile (82). Therefore, this group was examined separately in regards to the study question. Table 3.5 shows the characteristics of each weight group within the medicated subjects group.

Table 3.10- Characteristics of the medicated subjects group*.

<table>
<thead>
<tr>
<th></th>
<th>NW n=32 (47%)</th>
<th>OWr n=36 (53%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>19(60%)</td>
<td>22(60%)</td>
</tr>
<tr>
<td>F</td>
<td>13(40%)</td>
<td>14(40%)</td>
</tr>
<tr>
<td><strong>Age (Years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (STD)</td>
<td>12.8(±3.2)</td>
<td>13.3(±3.0)</td>
</tr>
<tr>
<td>C age group</td>
<td>14(44%)</td>
<td>18(56%)</td>
</tr>
<tr>
<td>A age group</td>
<td>20(56%)</td>
<td>16(44%)</td>
</tr>
<tr>
<td><strong>MSL_MSLT (Minutes)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (STD)</td>
<td>16.4(±4.9)</td>
<td>12.9(±5.8)</td>
</tr>
<tr>
<td>Abnormal(C:&lt;19 A:&lt;16)</td>
<td>13(41%)</td>
<td>29(81%)</td>
</tr>
<tr>
<td>Normal (C:≥19 A:≥16)</td>
<td>19(59%)</td>
<td>7(19%)</td>
</tr>
<tr>
<td><strong>AHI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (STD)</td>
<td>7.6(±1.5)</td>
<td>1.4(±2.5)</td>
</tr>
<tr>
<td>Abnormal(C:&gt;1 A:&gt;5)</td>
<td>3(9%)</td>
<td>7(19%)</td>
</tr>
<tr>
<td>Normal (C:≤1 A:≤5)</td>
<td>29(91%)</td>
<td>29(81%)</td>
</tr>
<tr>
<td><strong>AI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (STD)</td>
<td>10.1(±6.5)</td>
<td>9.8(±7.0)</td>
</tr>
<tr>
<td>Abnormal (&gt;10)</td>
<td>12(37%)</td>
<td>14(39%)</td>
</tr>
<tr>
<td>Normal (≤10)</td>
<td>20(63%)</td>
<td>22(61%)</td>
</tr>
</tbody>
</table>

* Variables other then means are given in N(%). C=children, age <13, A=adolescents, age ≥ 13 and over.
Gender distribution was essentially similar between the weight groups. The OWr group had a somewhat higher portion of children less than 13 years of age. The rate of abnormal AHI was again slightly higher in the OWr group, but the rate of abnormal AI values was similar.

Figure 3.9 shows the distribution of the type of medication used by subjects in each weight group. Note that since many subjects received more than one medication, the distributions do not add up to 100%.

![Figure 3.9](image)

**Figure 3.10 - Distribution of the type of medication used between the weight groups.**

About half of the children in each weight group -15(47%) of the NW group and 19(53%) of the OWr group- were treated with more than one medication group. Given that the chi-square test assumes that each observation belongs to only one category, an omnibus 2 (groups) * 5 (medication category) chi-square test could not be used to examine the differences in frequency of medication use in each weight group. Instead, separate chi-square tests were performed to examine the differences in distribution of weight in each medication group versus the distribution of weight in the entire medicated patients group. In all three major medication groups (comprising 79% of the medications used)- psychostimulants, antipsychotic and antidepressants- weight distribution did not differ significantly from that of the entire medicated population ($\chi^2(1) = .08$, p=.78; $\chi^2(1) = .004$, p=.95; and $\chi^2(1) = .08$, p=.78 respectively). In the other 3 medication groups (comprising 21% of the medications used) the number of subjects in
each category was too small to enable conducting a valid statistical analysis. Hence, since only a portion, albeit the major portion, of this group has been proved to be comparable the following analysis should be taken with a grain of salt.

### 3.6.1 Differences in MSL\textsubscript{MSLT} by Weight Group

In the medicated subjects group the mean MSL\textsubscript{MSLT} was lower in the OWr group than in the NW subjects, 12.9(5.8) vs. 16.4(4.9) respectively. This difference was found to be significant ($Z=3.06$, $p=.002$). The frequency analysis also showed a statistically significant difference in the frequency of abnormal vs. normal MSL\textsubscript{MSLT} values between weight groups in the medicated subjects’ sample $p=.001$.

![Figure 3.11](image)

**Figure 3.11- The frequency of normal vs. abnormal MSL\textsubscript{MSLT} in each weight group for the medicated subjects (n=68).** Normal MSL\textsubscript{MSLT} (C: ≥19 A: ≥16), Abnormal MSL\textsubscript{MSLT}(C:<19 min A:<16min). NW=Normal Weight group, n=32(47%), OWr= Overweight and obese group, n=36(53%). Frequency of abnormal MSL\textsubscript{MSLT} , 41% NW vs. 81% OWr, $\chi^2(2)=11.44, \ p=.001$. 

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3.6.2 Differences in MSL for each nap between weight groups

In order to examine the diurnal pattern of EDS in the medicated subjects group MSLnap was calculated for the 42 subjects in this group who had an abnormal MSL_{MSLT}. MSLnap was then compared for between the weight groups (Figure 3.12). Although the OWr group had a lower MSLnap on the first nap, there were no significant differences in MSL nap between the weight groups (all p’s >.59).

![Figure 3.12: MSLnap by subjects weight, gender and age group.](image)

Figure 3.12: MSLnap by subjects weight, gender and age group.

NW=Normal Weight, OWr=Overweight range.
3.6.3 Correlations between BMI%, AHI, AI and in MSL_{MSLT}

In the medicated group the only statistically significant correlation found between the examined variables was a medium negative correlation between BMI% and MSL_{MSLT} ($r_s = -.42$, p<.001). See figure 3.10.

![Figure 3.13](image-url)  
*Figure 3.13- The correlation between BMI% and MSL_{MSLT} in the medicated group.*
4 DISCUSSION

The main objective of this research was to investigate the relationship between EDS and weight in children and adolescents. For this purpose, the pre-existing data from medical records of patients in a pediatric sleep clinic was analyzed. The results of this study suggests that in a pediatric population referred for a clinical investigation of sleep and daytime sleepiness, EDS (as measured by the MSLT) is more common among individuals who are above the normal weight range, in children age 6-13 years old and in males (each separately). This association is independent of measures of sleep apnea and sleep fragmentation. EDS in these populations is present mainly during the morning hours.

These findings are in concordance with previously published studies (10;11;13). However, while most of these studies focused on pediatric OSA and its association with weight and EDS, the study reported here is unique by having a population with a relative minority diagnosed with OSA. This further strengthens the impression that weight may contribute to a state of EDS in children independent of OSA, as suggested by the literature concerning adults (3;6-9;153).

4.1 Study Population

There were more males than females in this study population (116; 62% males vs. 72; 38% females). Most of the subjects (82; 71%) were under the age of 13 years. The male predominance in the younger age group was an interesting incidental finding. Are young boys referred for sleep evaluation more than young girls, or are they more prone to be evaluated for EDS? And if so, is it the result of gender differences in sleep morbidity prevalence at this age or should it be attributed to a referral bias generated by another mechanism?

EDS has been linked with behavioural problems and hyperactivity in pre-pubertal children (94;95), both of which are more common among boys. Is it the case that more young males were in the study population due to sleep being a part of an investigation into behavioral problems, or vice versa?

Gender differences have been pointed out in adults, in regards to prevalence as well as presentation and consequences of sleep pathology (172). In adults, these are commonly attributed to the female hormonal cycle, pregnancy and child rearing responsibilities. With the exception of the female hormonal cycle, these causes are not applicable to most of this study’s population.
One of the most common reasons for pediatric sleep clinic referral is suspected OSA due to enlarged tonsils, a condition that has been reported to be more prevalent in boys (173). Given that the data presented in this thesis originated from clinically referred individuals, this may pose a possible explanation for the gender distribution in this study sample.

Close to a half of the study population (47%) was overweight or obese (15% and 32% respectively). This is much higher than the current, estimated prevalence of excess weight in children in Canada (25.8% of 6–11 year-olds and 29.2% of 12–17 year-olds)(140). Keeping in mind that all of the data analyzed here originated from files of clinical patients who were suspected of EDS (and therefore assigned to complete an MSLT assessment), this may suggest that overweight and obese individuals complain of, or are suspected of EDS more than individuals within the normal weight range. Indeed the populations referred for sleep investigation generally tend to have a large proportion of overweight individuals mainly due to suspected OSA. However, it is important to note that, in the study's sample, only a minority (18%) eventually had an AHI indicative of sleep apnea, while at the same time more than half of the charts reviewed had indications of abnormal daytime sleepiness (54% of the total population had abnormal MSLT results).

4.2 EDS and Weight

For the total population there was no statistically significant difference in the level and in the frequency of EDS as measured by the MSLT between the different weight groups. Nevertheless, a correlation between EDS and BMI% was observed for the study’s population. Also, BMI% was marginally significant as a predictor of EDS in the study’s population. However, when age and gender were accounted for, the relationship between weight and EDS emerged.

4.2.1 The role of gender and age

As noted before, there were more males in the study sample (116 males vs. 72 females). However, weight was distributed in a similar manner between the gender groups (53% NW and 47% OWr in both gender groups). Nevertheless, the rate of EDS was significantly different between the weight groups only in the male group (p=.042), with higher rates of EDS observed in males who weigh above the normal range.
Similarly, there were more children under the age of 13 years in the study sample (119 vs. 69 in the older age group). The younger age group (group C) had a slightly higher rate of individuals above the normal weight range (49% vs. 43% in the older age group-A). The rate of EDS was significantly different between the weight groups only in the younger age group (p=.034), with higher rates of EDS observed in overweight and obese children younger than 13 years.

It may be suggested that the higher rate of abnormal MSL\textsubscript{MSLT} in the younger age group may be due to the less stringent criteria of MSL\textsubscript{MSLT} considered abnormal for the younger age group (19 minutes vs. only 16 minutes for age group A). In order to examine this possibility a frequency analysis using the same MSL\textsubscript{MSLT} cut off, set at 16 minutes, for both age groups was performed. The results were similar to the original analysis, i.e. showing statistically significant higher frequency of abnormal MSL\textsubscript{MSLT} being observed in the C age group ($\chi^2 (2) = 9.71, p=.002$ age group C, $\chi^2 (2) = .28, p=.387$ Age group A]. It should be noted that the original conceptualization of a differential between the two groups can be supported by the observation that sleep architecture features are different in different ages in children and adolescents.

The correlation analysis revealed a correlation between weight and EDS only in the above noted groups – the male group and in the C age group. Indeed, gender did not emerge as a significant predictor of EDS when regression analysis was employed. However, given that the distribution of the residuals was approaching statistically significant departure from normality; this finding should be considered carefully.

There is little and conflicting data in the published literature as to gender differences in regards to EDS in adults as well as in pediatric populations. In adults Goel et al. reported men to exhibit more EDS than women while Hara et al reported the opposite (174;175). Joo et al. reported adolescent girls to have more daytime sleepiness while Lee and colleagues reported the opposite (176;177). A study conducted in Libya (Benghazi) surveyed 277 grade five children and their teachers and showed no differences in sleep problems reporting between genders (178). The differences in population characteristics, age groups and methods of EDS evaluation used vary greatly among the studies, making it difficult to establish a general rule or trend. It appears that when a difference in EDS was noted between genders in adults and adolescents, female gender tended to be associated with EDS. There is no data published to date in regards to gender differences in EDS in younger children.
Given the developmental aspects of sleep and age, it is not surprising that age was found to make a difference in regards to the study's variables. EDS has been recognized in adolescents. A physiological sleep-phase-delay in adolescents as well as social and behavioral habits leading to sleep restriction in this age group has been suggested as a cause. Indeed in the study presented here, mean MSL\textsubscript{MSLT} was 4 minutes lower in group A compared to group C. However, the study presented in this thesis suggests that a new variable, namely weight, be considered in pre- or early adolescent children when EDS is suspected.

One possible explanation for the more clear association between eight and sleepiness in younger children than in the older group may be that in the older children there are other and stronger determinants of sleepiness. These would include self imposed sleep deprivation, non clinical phase delay and greater medication use.

As noted above, the male group and the C age group showed some congruence in their composition. In this study the sample size prevented further sub-analysis of the interaction between gender and age in the various weight groups. However, the regression analysis suggested that gender may not be a valid predictor of EDS. It therefore seems possible to conclude that young age is the major contributor to the correlation between EDS and weight. Still, given that one of the regression procedure assumptions was compromised, further research will be needed to differentiate between the effects each of these variables poses. The few previous studies examining the connection between weight and EDS did not report a gender difference in this relation.

In this thesis a cut-off point at 13 years of age was employed for the MSL\textsubscript{MSLT}, regardless of gender. Given that puberty has been noted to have a role in levels of EDS, and that females start puberty at an earlier age then males (usually around 10 vs. 12 years of age, respectively) (179), this cut-off point may be misleading. A sexual maturity rating (SMR) scale may be the most accurate approach on which to base the MSL\textsubscript{MSLT} cut-off; however, good quality SMR may not always be available in a sleep clinic. Although self assessment of SMR has been shown to be fairly reliable, it’s validity in overweight and obese individuals has been questioned (180). It may be that the age and gender cutoff should be employed, with an age of 11 and above used for females. This of course should be further examined in a carefully designed study.
An attempt to explore the above noted possibility was done during the data analysis for this thesis. However, in this study population only 17 females were 11≤ age<13 years old, and only for 7 of them the judgment in regards to the MSL\textsubscript{MSLT} was changed with the newly suggested cutoff point. The frequency analysis remained similar to that reported using the general cutoff for MSL\textsubscript{MSLT} at 13 years of age [$\chi^2(2)=3.08$, p=.08 for the entire population, $\chi^2(2)=4.14$, p=.042 by gender, $\chi^2(2)=4.38$, p=.036 by age].

**4.2.2 The role of sleep pathology: sleep apnea and sleep fragmentation**

Measures of sleep apnea and sleep fragmentation were added into the analysis to further account for possible confounders for the relationship between weight and EDS.

A correlation analysis was then performed, with male gender and age under 13 years (each separately) again showing to be significant. A significant correlation between BMI\% - MSL\textsubscript{MSLT} was shown only in males and in the younger age group ($r_s=-.25$, p=.007; $r_s=-.25$, p=.006 respectively). It is important to note that the correlation between weight and EDS in both the male and the C groups was isolated from other correlations between the studies variables. In other words, the connection between excess weight and EDS was not shown to be mediated through polysomnography variables- AHI or AI.

On the other hand, in the regression analysis, AHI was a significant predictor for EDS for the total study group and the C age group. However, given the compromise in the regression’s assumption, especially in the C age group, this finding should be considered with some reservations.

High arousal index, also known as sleep fragmentation, has been previously linked with daytime sleepiness (74-76). This finding was repeated in the correlation analysis reported in this thesis. However, AI was not shown to be a valid predictor of EDS in the regression analysis.

As noted before, apnea episodes tend to end in an arousal, which is commonly termed respiratory arousal (4). The AI reported here does not differentiate between respiratory and other types of arousals. It is therefore not surprising that a correlation has been found between AHI and AI. However, in the correlation analysis, no relationship was found between sleep apnea and EDS, despite the link between AHI and AI in all groups, and between weight and AHI in the older patients.
The independent correlation between weight and EDS reported here for part of the study’s population is supported in the literature. Bixler and colleagues reported an association between weight and EDS that was stronger than an association between AHI and EDS in adults (6). In the pediatric literature, Gozal and Kheirandish-Gozal (11) have demonstrated that heavier children with OSA showed more EDS regardless of the level of severity of OSA.

4.2.3 Changes in EDS levels throughout the day

An examination of mean sleep latency per group in each nap revealed information in regard to changes in daytime sleepiness levels throughout the day. Figure 3.6 shows that the level of sleepiness as measured by the MSLT decreases as the day progresses in all groups.

Both NW males and NW C age groups showed two peaks of decreased daytime sleepiness at 10:30 and 2:30. However, at 10:30am in the OWr male group the opposite was found, with an increase in sleepiness at this time of day. In the younger age group such an increase in daytime sleepiness was not present, however, the decreased in sleepiness present in the NW C group was significantly absent in the OWr group of this age range.

Thus, the study reported in this thesis not only demonstrates that some groups of children and adolescents who are overweight and obese are sleepier than their NW peers, it also shows that this sleepiness is present mainly during the morning hours. This is of great importance when considering that the morning hours are school hours. This may put children and adolescents who are overweight and obese at a disadvantage in regard to school performance compared to their thinner peers.

Interestingly, an association between increased weight and lower intelligence quotients has been reported in a large group of children of the exact same age as the C group (6-12 years) (181). Increased sleepiness may present a possible explanation for such an association.

4.2.4 EDS and weight in children and adolescents treated with medications that are known to influence sleep and sleepiness.

This data group was analyzed separately since the medications used represent a confounding factor.
When divided by weight groups, for the medicated subjects gender distribution was identical between the weight groups. The size of the groups was close as well as the age distribution (C age group vs. A). However, it should be noted that the OWr group had a larger portion of children younger than 13.

The mix of medications used in this group was relatively similar between the weight groups, although there was a slightly higher amount of medication used in the OWr group (figure 3.9).

The OWr group of medicated subjects showed significantly higher EDS levels. Also EDS and correlated solely with weight. No correlation was noted between AHI and EDS despite slightly higher rates of abnormal AHI in the OWr medicated group. No unique diurnal pattern of EDS was noted in regards to weight in this group.

This part of the analysis is influenced by the slight imbalances of age and rate of medication use between the weight groups. Also, the doses of the medications used were not taken into account. The weight differences in EDS noted in this group should be considered with caution in light of this limitation.

Despite these cautions, this is the first study to date examining MSLT results and their association with weight in children treated with medications. (With the exception of a group of studies in the treatment with psycho stimulants- Modafinil and Armodafinil in patients with narcolepsy (83385)). This therefore represents the first analysis of the impact of predominantly psychoactive drugs on EDS in relation to weight using an objective measure of sleepiness. In light of this and of the results of the analysis in this group further research in this topic seems justified.

The following is a summery of key learning points from the findings:

- This study adds to the limited body of evidence about the relationship between excessive weight and EDS in children and adolescents.

- Excessive weight is associated with higher levels of EDS in a sleep clinic population of children and adolescents.
- The level of EDS in this population is worse during the morning hours and improves in the afternoon.

- This relationship seems to be independent of the presence of OSA and sleep fragmentation.

- Age and gender may have an impact on EDS in OW and OB in children and adolescents, with males and age under 13 years significant factors for EDS.

- The same relationship between weight and EDS seems to exist in children who are being treated with psychoactive drugs.

4.3 Limitations

There are several limitations to this study. First and foremost, this study was done using data from a population referred to a sleep clinic and as such does not represent the general population of children and adolescents. However, this can be viewed positively as this is the population sleep specialists deal with. The findings of this study support the notion that sleep specialists should employ higher levels of suspicion for the presence of EDS when presented with overweight and obese children. While it may be thought that using a clinic based population would tend to magnify the outcome, which is probably correct one can take the attitude that the point at which this becomes critical is in the assessment of children presenting at a sleep clinic. In this setting the issue of discerning likely diagnosis and the utility of a sleep assessment is crucial. In this situation an awareness of factors that might influence sleepiness and when a test to measure sleepiness is being contemplated (with cost implications as well) and awareness of factors that make unappreciated (from the patients perspective) sleepiness more likely is helpful in making clinical decisions. It would be a separate exercise to evaluate contributors to sleepiness in the general population.

Another limitation was the retrospective nature of this investigation. The superior accuracy and reliability of conducting two, consecutive overnight PSG sleep studies in order to overcome the first night effect (the effect of sleeping in a new environment and having PSG equipment attached) has been established in the literature (182-184). This is of particular relevance when
sleep architecture parameters are examined, with more awakenings (hence higher AI values) and lower sleep efficiency reported. Unfortunately, mainly due to financial considerations, a single night PSG is the common practice in many sleep clinics, hence the quality of data analyzed for this study is typical for that used by sleep specialists in regular clinical practice.

Next, although patients of our sleep clinic are generally instructed to maintain reasonable sleep schedules prior to attending their overnight sleep study, patients' compliance with this instruction is not objectively monitored, as actigraphy prior to a sleep study is not routinely used. Subjective reports of compliant behavior, such as sleep diaries, in this age group should be considered with suspicion. Consequently, the possibility exists that a substantial number of the charts reviewed for this study contained PSG and MSLT data that was distorted by sleep restriction. In the A age group in total, more patients (58% vs. 52% in group C) had an abnormal MSLT result. High rates of EDS have been previously reported in regards to high school aged children(36;185). The most common reason identified for EDS in this age group is sleep deprivation due to self inflicted sleep restriction (extracurricular activities, after-school work, and mostly electronic media related activities)(36). Interestingly in the research presented here, for this age group no correlation was found between EDS and any of the variables examined. While this may be attributed to the small sample size of this group, it may also be a result of the higher sleep deprivation rates in this group. This probably represents the quality of data presented to sleep specialists in everyday practice as well. While we should strive to conduct research using the most precise methodology and data, such approaches sometimes makes it difficult to infer conclusions that can be applied to the more complex medical backgrounds presented by some patients.

Another limitation of this research given by the retrospective approach is our inability to compare the MSLT results with subjective measures of EDS, as no questionnaires designed to evaluate EDS were routinely used by our clinic at the time the data was collected. Since subjective reports and objective reports have been shown to vary (109), this may have been an important addition that our data can not provide. This has since been changed and a detailed 28 page questionnaire booklet is now routinely completed for each patient examined at the clinic. The above comments should be amplified to emphasize that subjective and objective measures of sleepiness do not invariably run pari-pasu. The implication of this is that whatever the subjective results would have shown, one would be left with the need to discuss the findings. One would
not be able to make the conclusion that a subjective assessment would necessarily be equitable to the objective measures.

Moreover, there was no data in regards to the stage of physical maturation, such as SMR, to extract from the patients file (also now completed routinely with the questionnaire booklet). Given that some sleep parameters differ between pre- and post pubertal children this may have lowered the quality of our analysis. Nonetheless, a major age related differences around a cut-off age of 13 was found, which may be related to the state of puberty. However, one must realize that due to the modest sample size of the older age group (A) any conclusions in regards to this group may be less accurate.

Lastly, our analysis can only show correlation and can not imply any causality. More longitudinal-focused research is required to determine causality.

### 4.4 Strengths

One of the strengths of this study is in presenting a large number of subjects across a range of ages from childhood to adolescence. Also, it reports the use of MSLT in the largest cohort of children and adolescents to date, almost double the samples previously reported on (11). Hence, when considering the paucity of data in regards to pediatric MSLT, this study is an important addition. In addition, contrary to previously reported studies, the population was not comprised of SDB patients only, giving wider view of the connection between weight and EDS.

Mean MSL\textsubscript{MSLT} was 4 minutes lower in the A age group versus group C (see table 3.4). If the age groups created in the analysis is considered as roughly corresponding to pre- and early-adolescent (group C) versus mid and late-adolescent (group A), then the result of this research further supports the evidence that EDS increases with the processes of adolescence (115;116).

In the groups in which obesity was shown to be associated with EDS there is a “dose –response relationship” between BMI\% and EDS (as shown by the negative correlation found). This strengthens the conclusion.
To date, this is the only study published that has looked at diurnal patterns of EDS in relation to weight in a pediatric population.

The OWr group compared to a NW control group in this study was not comprised of purely obese individuals. About a third of the OWr group was only overweight, thus diluting the strength of the weight difference between the compared groups. However, a statistically significant difference in EDS was demonstrated. This further strengthens the conclusion of the study.

### 4.5 Conclusions

In children and adolescents referred to a sleep clinic and evaluated for daytime sleepiness, weight above the normal range is associated with higher rates of EDS, in children under 13 years and in males (each separately). This association is independent of measures of sleep apnea and sleep fragmentation. The EDS in these populations is present mainly during the morning hours. Findings from this study are in agreement with the latest scientific literature. Moreover, the wide age range examined here, and the larger sample size used add to the available literature, making this an important addition to current knowledge as well as a starting point for further investigation.

As overweight and obesity become more common in children and adolescents over time, understanding the various implications of excessive weight is of great importance. EDS is related to daytime performance (94;95). Academic achievements and mental health integrity are influenced by the level of daytime sleepiness(20;93;100). Awareness of the characteristics of the population at risk for EDS is important, so that these individuals can be examined and treated when indicated. Childhood is a stage of life when academia, social interaction, and character development are intensely pursued. It is desirable to be able to identify obstacles on this route. Indeed, excessive weight has many well known implications in regards to general health. This research adds another factor to be considered both by health professionals and by the general public in an increasingly ‘heavier’ society.
4.6 Future directions

Further studies to confirm these findings and improve on methodology include:

- a prospective study design through childhood and adolescence.

- subjective measures of sleepiness (using questionnaires) to compare with objective measures.

- SMR performed by a physician’s examination.

- evaluation of sleep using actigraph prior to performing the PSG and MSLT.

- an examination of the patient’s complaints at the time of presentation versus the outcome of the sleep laboratory investigation may reveal important clues as to the how and why sleepiness is presented in children and adolescents.

- recruitment of a more balanced population in terms of age, gender and weight groups in order to differentiate between the effect of age and gender on the relationship between weight and sleepiness.

- recruitment of subjects from the general population. Comparing the rate and reasons for EDS in children in the general population compared to those who have been referred to a sleep clinic may also be merited.

- Performance of two overnight PSG recording in order to account for first night effect.

- Measurement of biochemical measures associated with sleep pathology including inflammatory cytokines.

Further research directions inspired by this thesis include:

- One of the goals of any health related research should be to implement change in health care management. Including an interventional component with follow up may help to achieve this goal. If good evidence is found for a relationship between weight and EDS in children and adolescents, what can be done? Would treating the sleep pathology alone (in cases where one is found) reduce the level of EDS? Would it affect the subjects’ weight?
Would a weight-related intervention change the level of EDS? Would it change anything in regards to the subject’s sleep?

- With the rise in the percentage of those who are overweight or obese children and youth there has been noted a rise in excess weight co-morbidities in this population. This includes type 2 diabetes (143). Type 2 diabetes has severe implications on the general health of inflicted patients. Obesity and type 2 diabetes have been linked with sleep disturbances in adults, with evidence showing that sleep disturbances promote the development of type 2 diabetes in adults (186). Type 2 diabetes has also been shown to improve when sleep disturbances are treated (163). Is there a similar connection in children and adolescents? All of the research done thus far to examine the relationship between sleep and diabetes in children and adolescents examined type 1 diabetes (187-189). If sleep disturbances promote the development of type 2 diabetes in adults, how early does this process start? Are children with type 2 diabetes sleepier than their weight- and gender-matched peers? If such a connection also exists in children, is it reversible? Would the examination of sleep in diabetic young patients be recommended as part of the disease management? In a society in which sleep is constantly compromised by the temptation of electrical entertainment, this connection should be further investigated. (These questions were the topic of the study originally intended to be perused for this master’s thesis. Difficulties with subjects’ recruitment dictated a change in the study’s topic).

- Both obesity and diabetes have been regarded in recent literature as inflammatory states. The interaction between inflammatory cytokines and the HPA axis has been suggested as a mechanism. Further exploring this connection in obese individuals with and without diabetes is needed.

- On a different topic, as previously noted there is a controversy in sleep research about the interpretation of the MSLT. While there are arguments in regards to the proper length of the naps and the cut-off points used to determine excessive sleepiness, some have suggested that not only the sleep latency should be looked at, but that the number of naps in which sleep occurred and the time of day should be considered as well. The data used for this study can be utilized to inspect this concept further.
− Exploring the possibility of age and gender cut-off criteria for the MSLM

− Another possibility that may be worth exploring is that a scale integrating various PSG variables (e.g. sleep onset latency, percentage of SWS or REM sleep) may be constructed to predict daytime sleepiness levels. This of course will require systematic construction and validation.
References


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(85) Garnock-Jones KP, Dhillon S, Scott LJ. Armodafinil. CNS Drugs 2009 Sep 1;23(9):793-803.


(102) Beebe DW, Ris MD, Kramer ME, Long E, Amin R. The association between sleep disordered breathing, academic grades, and cognitive and behavioral functioning among overweight subjects during middle to late childhood. Sleep 2010 Nov;33(11):1447-56.


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Appendices

Appendix A-List of medications that rendered exclusion from the study during data collection

**Psychostimulants:**
Adderall, Methylphenidate.

**Psychoactive drugs:**
*Hypnotics* – Clonazepam, Lorazepam, Temazepam, Zopiclone.

**Antipsychotics:**
Risperidone, Olanzapine, Quetiapine.

**Antidepressants:**
Buprion, Trazodone
*Serotonin norepinephrine reuptake inhibitors* - Venlafaxine
*Selective serotonin reuptake inhibitors* - Citalopram, Escitalopram, Fluoxetine, Fluvoxamine, Sertraline hydrochloride.
*Tricyclics* - Imipramine.

**Anticonvulsants:**
Carbamazapine, Lamotrigine, Oxcarbazepine, Primidone, Topiramide.

**Miscellaneous:**
Atomoxetine
Buspirone.
Clonidine
Codeine
Montelukast
Appendix B-List of medical conditions that rendered exclusion from the study during data collection

**Congenital syndromes:**

Asperger syndrome, Autism, Prader-Willi syndrom.

**Neurological compromise:**

Brain injury, Cerebral palsy, Developmental delay, Fetal alcohol syndrome, Seizure disorders, Tourette syndrome.

**Sleep disorder defined by daytime sleepiness.**

DSPS, Narcolepsy.

**Miscellaneous conditions:**

Anemia, Fibromyalgia, Lupus erythematosus.
Appendix C- Questionnaires and scales to assess EDS

Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in the **PAST WEEK**. Even if you have not done some of these things recently, try to work out how they would have affected you. Use the following scale to choose the most appropriate for each situation:

0= would **never** dose  
1= **slight** chance of dozing  
2= **moderate** chance of dozing  
3= **high** chance of dozing

**Please check (   ) one response for each question.**

<table>
<thead>
<tr>
<th></th>
<th>Sitting and reading</th>
<th>Never-0</th>
<th>Slight-1</th>
<th>Moderate-2</th>
<th>High-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Watching TV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Sitting, inactive in a public place (e.g. a theatre or a meeting)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>As a passenger in a car for an hour without a break</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Lying down to rest in the afternoon when circumstances permit</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Sitting and talking to someone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Sitting quietly after a lunch without alcohol</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>8</td>
<td>In car, while stopped for a few minutes in the traffic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The scores for the eight questions are added together to obtain a single number. A number in the 0–9 range is considered to be normal while a number in the 10–24 range indicates that expert medical advice should be sought.*
Pediatric Daytime Sleepiness Scale

Please answer the following questions as honestly as you can by circling one answer.

1. How often so you fall asleep or get drowsy during class periods?
   Always  Frequently  Sometimes  Seldom  Never

2. How often do you get sleepy or drowsy while doing your homework?
   Always  Frequently  Sometimes  Seldom  Never

3.* Are you usually alert most of the day?
   Always  Frequently  Sometimes  Seldom  Never

4. How often are you ever tired and grumpy during the day?
   Always  Frequently  Sometimes  Seldom  Never

5. How often do you have trouble getting out of bed in the morning?
   Always  Frequently  Sometimes  Seldom  Never

6. How often do you fall back to sleep after being awakened in the morning?
   Always  Frequently  Sometimes  Seldom  Never

7. How often do you need someone to awaken you in the morning?
   Always  Frequently  Sometimes  Seldom  Never

8. How often do you think that you need more sleep?
   Very Often  Often  Sometimes  Seldom  Never

* Reverse score this item

Scoring:
4 = Very often, Always
3 = Often, Frequently
2 = Sometimes
1 = Seldom
0 = Never

Abnormal Values: 6th and 7th Grade > 26, 8th Grade >30
Children’s Sleep Habit Questionnaire

(ABBREVIATED)

The following statements are about your child’s sleep habits and possible difficulties with sleep. Think about the past week in your life when you answer the questions. If last week was unusual for a specific reason, choose the most recent typical week. Unless noted, check Always if something occurs every night, Usually if it occurs 5 or 6 times a week, Sometimes if it occurs 2 to 4 times a week, Rarely if it occurs once a week, and Never if it occurs less than once a week.

BEDTIME

Write in your child’s usual bedtime: Weeknights _____:____ am/pm, Weekends _____:____ am/pm

7 5-6 2-4 1 0

Always Usually Sometimes Rarely Never

1. Child goes to bed at the same time at night.
2. Child falls asleep within 20 minutes after going to bed.
4. Child falls asleep in parent’s or sibling’s bed.
5. Child falls asleep with rocking or rhythmic movements.
6. Child needs special object to fall asleep (doll, special blanket, stuffed animal, etc.
7. Child needs parent in the room to fall asleep.
8. Child resists going to bed at bedtime.
9. Child is afraid of sleeping in the dark.
SLEEP BEHAVIOR

Write in your child’s usual amount of sleep each day (combining nighttime sleep and naps): _____ hours and _____ minutes

<table>
<thead>
<tr>
<th>Always</th>
<th>Usually</th>
<th>Sometimes</th>
<th>Rarely</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>5-6</td>
<td>2-4</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

10. Child sleeps about the same amount each day.
11. Child is restless and moves a lot during sleep.
12. Child moves to someone else’s bed during the night (parent, sibling, etc.).
13. Child grinds teeth during sleep (your dentist may have told you this).
15. Child awakens during the night and is sweating, screaming, and inconsolable.
16. Child naps during the day.
   Write in the number of minutes the nap usually lasts: ____ minutes

WAKING DURING THE NIGHT

<table>
<thead>
<tr>
<th>Always</th>
<th>Usually</th>
<th>Sometimes</th>
<th>Rarely</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>5-6</td>
<td>2-4</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

17. Child wakes up once during the night.
18. Child wakes up more than once during the night.

MORNING WAKE UP

Write in the time child usually wakes up in the morning: Weekdays _____:____ am/pm, Weekends _____:____ am/pm

<table>
<thead>
<tr>
<th>Always</th>
<th>Usually</th>
<th>Sometimes</th>
<th>Rarely</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>5-6</td>
<td>2-4</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

19. Child wakes up by him/herself.
20. Child wakes up very early in the morning (or, earlier than necessary or desired)
21. Child seems tired during the daytime.
22. Child falls asleep while involved in activities.
**Paediatric Sleep Questionnaire-Sleepiness Scale (PSQ-SS)**

The Pediatric Sleep Questionnaire is 10 pages long; however, the Sleepiness Scale component of it is made from questions B1, B2, B4 and B6 (circeled). The following is section B of the PSQ from which the Sleepiness Scale is derived.

<table>
<thead>
<tr>
<th>Question</th>
<th>Y</th>
<th>N</th>
<th>DK</th>
</tr>
</thead>
<tbody>
<tr>
<td>... wake up feeling unrefreshed in the morning?</td>
<td></td>
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<tr>
<td>... have a problem with sleepiness during the day?</td>
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<tr>
<td>... complain that he or she feels sleepy during the day?</td>
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<tr>
<td>Has a teacher or other supervisor commented that your child appears</td>
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<tr>
<td>sleepy during the day?</td>
<td></td>
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<tr>
<td>Does your child usually take a nap during the day?</td>
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<tr>
<td>Is it hard to wake your child up in the morning?</td>
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<tr>
<td>Does your child wake up with headaches in the morning?</td>
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<tr>
<td>Does your child get a headache at least once a month, on average?</td>
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<tr>
<td>Did your child stop growing at a normal rate at any time since birth? If</td>
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<tr>
<td>so, please describe what happened:</td>
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<tr>
<td>Does your child still have tonsils? If not, when and why were they</td>
<td></td>
<td></td>
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<tr>
<td>removed?: HAS YOUR CHILD EVER ...</td>
<td></td>
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<tr>
<td>... had a condition causing difficulty with breathing? If so, please</td>
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<tr>
<td>describe:</td>
<td></td>
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</tr>
<tr>
<td>... had surgery? If so, did any difficulties with breathing occur before,</td>
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<tr>
<td>during, or after surgery?</td>
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<tr>
<td>... become suddenly weak in the legs, or anywhere else, after laughing or</td>
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<tr>
<td>being surprised by something?</td>
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<td></td>
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<tr>
<td>... felt unable to move for a short period, in bed, though awake and able</td>
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<tr>
<td>to look around?</td>
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<td></td>
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</tr>
<tr>
<td>Has your child felt an irresistible urge to take a nap at times, forcing</td>
<td></td>
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<tr>
<td>him or her to stop what he or she is doing in order to sleep?</td>
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<td></td>
<td></td>
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<tr>
<td>Has your child ever sensed that he or she was dreaming (seeing images or</td>
<td></td>
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<td></td>
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<tr>
<td>hearing sounds) while still awake?</td>
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<tr>
<td>Does your child drink caffeinated beverages on a typical day (cola, tea,</td>
<td></td>
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<tr>
<td>coffee)? If so, how many cups or cans per day?</td>
<td></td>
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<td></td>
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<tr>
<td>Does your child use any recreational drugs? If so, which ones and how</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>often?:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does your child use cigarettes, smokeless tobacco, snuff, or other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tobacco products? If so, which ones and how often?:</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
School Sleep Habits Survey-sleepiness subscale

The Scholl Sleep Habits Survey is 8 pages long and has 63 questions. Below is questioning 43 from which the sleepiness subscale is derived. The points key is: No=1, Struggled to stay awake=2, Fallen asleep=3, Both struggled to stay awake and fallen asleep=4, making the score range for the scale between 10 (not sleepy) and 40 (sleepy).

Questions 43 to 46 are about things that have happened in the last two weeks.

43. During the last two weeks, have you struggled to stay awake (fought sleep) or fallen asleep in the following situations? (Mark one answer for every item.)

- Both struggled to stay awake and fallen asleep
- Fallen asleep
- Struggled to stay awake
- No

- in a face-to-face conversation with another person? ..........................................................
- traveling in a bus, train, plane or car? ..............
- attending a performance (movie, concert, play)? ..........................................................
- watching television or listening to the radio or stereo? ..........................................................
- reading, studying or doing homework? ............
- during a test? ..........................................................
- in a class at school? ..............................
- while doing work on a computer or typewriter? ..........................................................
- playing video games? ..............................
- driving a car? ..............................

Do you drive?  
- Yes
- No
Cleveland Adolescents Sleepiness Questionnaire

Today’s Date: (fill in) __ __ / __ __ / __ __

What is your age? (fill in years) ______

What is your sex? (check one) 1. Female 2. Male

We would like to know about when you might feel sleepy during a usual week. For each statement, mark the circle under the response that best fits with how often it applies to you. It’s important to answer them yourself – don’t have people help you. There are no right or wrong answers. For example, if we asked “I sleep with a pillow,” and the response that best fit how often you sleep with a pillow was “often,” you would mark the item as follows:

<table>
<thead>
<tr>
<th>EXAMPLE</th>
<th>Never (0 times per month)</th>
<th>Rarely (less than 3 times per month)</th>
<th>Sometimes (1-2 times per week)</th>
<th>Often (3-4 times per week)</th>
<th>Almost every day (5 or more times per week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I sleep with a pillow</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

Sleepiness Questions

<table>
<thead>
<tr>
<th>1. I fall asleep during my morning classes</th>
<th>Never (0 times per month)</th>
<th>Rarely (less than 3 times per month)</th>
<th>Sometimes (1-2 times per week)</th>
<th>Often (3-4 times per week)</th>
<th>Almost every day (5 or more times per week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. I go through the whole school day without feeling tired</th>
<th>Never (0 times per month)</th>
<th>Rarely (less than 3 times per month)</th>
<th>Sometimes (1-2 times per week)</th>
<th>Often (3-4 times per week)</th>
<th>Almost every day (5 or more times per week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. I fall asleep during the last class of the day</th>
<th>Never (0 times per month)</th>
<th>Rarely (less than 3 times per month)</th>
<th>Sometimes (1-2 times per week)</th>
<th>Often (3-4 times per week)</th>
<th>Almost every day (5 or more times per week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. I feel drowsy if I ride in a car for longer than five minutes</th>
<th>Never (0 times per month)</th>
<th>Rarely (less than 3 times per month)</th>
<th>Sometimes (1-2 times per week)</th>
<th>Often (3-4 times per week)</th>
<th>Almost every day (5 or more times per week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. I feel wide-awake the whole day</th>
<th>Never (0 times per month)</th>
<th>Rarely (less than 3 times per month)</th>
<th>Sometimes (1-2 times per week)</th>
<th>Often (3-4 times per week)</th>
<th>Almost every day (5 or more times per week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. I fall asleep at school in my afternoon classes</th>
<th>Never (0 times per month)</th>
<th>Rarely (less than 3 times per month)</th>
<th>Sometimes (1-2 times per week)</th>
<th>Often (3-4 times per week)</th>
<th>Almost every day (5 or more times per week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Never (0 times per month)</td>
<td>Rarely (less than 3 times per month)</td>
<td>Sometimes (1-2 times per week)</td>
<td>Often (3-4 times per week)</td>
</tr>
<tr>
<td>---</td>
<td>------------------------------------------</td>
<td>---------------------------</td>
<td>--------------------------------------</td>
<td>-------------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>7</td>
<td>I feel alert during my classes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>I feel sleepy in the evening after school</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>9</td>
<td>I feel sleepy when I ride in a bus to a school event like a field trip or sports game</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>In the morning when I am in school, I fall asleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>When I am in class, I feel wide-awake</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>I feel sleepy when I do my homework in the evening after school</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>I feel wide-awake the last class of the day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>I fall asleep when I ride in a bus, car, or train</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>During the school day, there are times when I realize that I have just fallen asleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>I fall asleep when I do schoolwork at home in the evening</td>
<td></td>
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</tbody>
</table>
Cleveland Adolescent Sleepiness Questionnaire
Score Sheet

Name: ___________________________ Date: __ __/ __ __/ ____

Once you complete the questionnaire, use the scoring keys below to determine your score for each statement. Then add the numbers together to get your total sleepiness score.

**Sleepiness Statements**

<table>
<thead>
<tr>
<th>Statement #</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td></td>
</tr>
<tr>
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</tbody>
</table>

**Scoring Key:**

Sleepiness Statements

1 = Never  
2 = Rarely  
3 = Sometimes  
4 = Often  
5 = Almost every day

**Alertness Statements**

<table>
<thead>
<tr>
<th>Statement #</th>
<th>Your Score</th>
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<tbody>
<tr>
<td>2.</td>
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<td>5.</td>
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<td>7.</td>
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<tr>
<td>11.</td>
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<tr>
<td>13.</td>
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</tr>
</tbody>
</table>

**Scoring Key:**

Alertness Statements

5 = Never  
4 = Rarely  
3 = Sometimes  
2 = Often  
1 = Almost every day

**Total Score:**

How sleepy are you? A higher score means that you are sleepy during the day and need to get more sleep on school nights. A higher score also could be a sign that you may have a sleep disorder called obstructive sleep apnea (OSA).

You should discuss your score with your parents and your doctor.

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Appendix D- PSG Variables in NW vs OWr groups for the entire population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>NW, n=100</th>
<th>OWr, n=88</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOL</td>
<td>32.7 ±31.5</td>
<td>28.6 ±28.2</td>
<td>NS</td>
</tr>
<tr>
<td>TST</td>
<td>459.9 ±72.5</td>
<td>451.2 ±58.6</td>
<td>NS</td>
</tr>
<tr>
<td>SE</td>
<td>89.6 ±7.5</td>
<td>88.9 ±8.4</td>
<td>NS</td>
</tr>
<tr>
<td>REML</td>
<td>133.6 ±61.9</td>
<td>126.6 ±67.9</td>
<td>NS</td>
</tr>
<tr>
<td>S1%</td>
<td>5.1 ±2.5</td>
<td>5.2 ±4.9</td>
<td>NS</td>
</tr>
<tr>
<td>S2%</td>
<td>43.4 ±8.5</td>
<td>42.0 ±7.9</td>
<td>NS</td>
</tr>
<tr>
<td>S3%</td>
<td>4.8 ±2.6</td>
<td>4.8 ±2.8</td>
<td>NS</td>
</tr>
<tr>
<td>S4%</td>
<td>19.9 ±6.4</td>
<td>19.3 ±5.6</td>
<td>NS</td>
</tr>
<tr>
<td>REM%</td>
<td>19.8 ±5.1</td>
<td>19.9 ±5.5</td>
<td>NS</td>
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<tr>
<td>AHI</td>
<td>1.1 ±2.3</td>
<td>4.8 ±13.9</td>
<td>=.029</td>
</tr>
<tr>
<td>AI</td>
<td>10.0 ±5.3</td>
<td>11.2 ±6.0</td>
<td>NS</td>
</tr>
<tr>
<td>PLMI</td>
<td>5.8 ±10.9</td>
<td>2.8 ±3.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are given as the mean ± SD. SOL= sleep onset latency, TST=total sleep time, SE=sleep efficiency, REML=rapid eye movement latency, S1%-S4%= percentage of sleep stage 1-4, REM%=percentage of rapid eye movement sleep stage, AHI=apnea hypopnea index, AI=arousal index, PLMI=periodic limb movement index.