Sleep and cardiometabolic risk: a cluster analysis of actigraphy-derived sleep profiles in adults and children

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Abstract:

Study objectives: Sleep plays an important role in cardiometabolic health. While the importance of considering sleep as a multidimensional construct is widely appreciated, studies have largely focused on individual sleep characteristics. The association between actigraphy-derived sleep profiles and cardiometabolic health in healthy adults and children has not been examined.

Methods: This study used actigraphy-measured sleep data collected between February 2015 and March 2016 in the Child Health CheckPoint study. Participants wore actigraphy monitors (GENEActiv Original, Cambs, UK) on their non-dominant wrist for seven days and sleep characteristics (period, efficiency, timing and variability) were derived from raw actigraphy data. Actigraphy-derived sleep profiles of 1,043 Australian children aged 11-12 years and 1337 adults were determined using K-means cluster analysis. The association between cluster membership and biomarkers of cardiometabolic health (blood pressure, body mass index, apolipoproteins, glycoprotein acetyls, composite metabolic syndrome severity score) were assessed using Generalised Estimating Equations, adjusting for geographic clustering, with sex, socioeconomic status, maturity stage (age for adults, pubertal status for children) and season of data collection as covariates.

Results: Four actigraphy-derived sleep profiles were identified in both children and adults: *Short sleepers, Late to bed, Long sleepers,* and *Overall good sleepers.* The *Overall good sleeper* pattern (characterised by adequate sleep period time, high efficiency, early bedtime and low day-to-day variability) was associated with better cardiometabolic health in the majority of comparisons (80%).

Conclusion: Actigraphy-derived sleep profiles are associated with cardiometabolic health in adults and children. The *Overall good sleeper* pattern is associated with more favourable cardiometabolic health.

Key words: Sleep, children, profiles, cardiometabolic health

The Statement of Significance

While the importance of understanding the multidimensional nature of sleep is widely recognised, few studies have examined sleep as a multidimensional construct. This is the first study to determine the association between actigraphy-derived sleep profiles and cardiometabolic health in a community sample of adults and children. Four actigraphy-derived sleep profiles were examined *Short sleepers, Late to bed*, *Long sleepers,* and *Overall good sleepers.* The *Overall good sleeper* pattern is associated with more favourable cardiometabolic health (blood pressure, body mass index, apolipoproteins, glycoprotein acetyls, composite metabolic syndrome severity score). Four characteristics of sleep examined (sleep period, midsleep, sleep efficiency, day-to-day variability) appear to play an important role in cardiometabolic health. Future efforts to improve population sleep need to consider all characteristics of sleep, rather than isolated variables.

Introduction:

Cardiometabolic diseases are the leading cause of morbidity, mortality, and disability.[1, 2] Several public health initiatives have been proposed and initiated to improve the detection, prevention and treatment of cardiometabolic risk factors, including obesity, hypertension, elevated blood glucose and cholesterol levels, and elevated inflammatory markers.[1] While lifestyle behaviours, such as physical activity and diet, have long been recognised as important modifiable risk factors of cardiometabolic disease, sleep has recently been suggested as an equally important, modifiable risk factor.[3, 4]

Sleep is thought to play an important role in regulating complex physiological processes that are critical for maintaining metabolic homeostasis.[5] Short sleep duration, poor sleep quality, delayed sleep timing and variable sleep patterns are thought to adversely affect diet, activity levels and processes occurring in the hypothalamic–pituitary–adrenal axis (HPA), resulting in increased oxidative stress, systemic inflammation, endothelial dysfunction and sympathetic systemic activation.[6-8] These changes manifest as raised inflammatory markers, hypertension, dyslipidemia and obesity, which are all known to increase cardiovascular risk. Given that cardiometabolic risk factors track into adulthood,[9-11] it is important to understand how sleep may be associated with these risk factors both in adults and children.

A number of methods have been used to assess cardiometabolic risk in adults and children.[12-16] Several studies use a "metabolic syndrome score", a composite score of multiple biomarkers reflective of cardiometabolic risk. While there is currently no universal definition, Eisenmann[16] provides recommendations on a continuous score, which can be used for both adults and children. It

has been shown to track from childhood to young adulthood[17-20] and predict the development of type 2 diabetes and cardiovascular disease (CVD) morbidities in adulthood.[21, 22] Other cardiometabolic risk factors such as obesity, blood pressure, certain inflammatory markers (e.g. glycoprotein acetyls [GlycA]) and dyslipidemia (i.e. apolipoprotein B/A1 ratio [Apo B/A1]) are also of interest. This is particularly because these biomarkers are independent predictors of cardiometabolic diseases[23, 24] and track into adulthood.[20]

While body mass index (BMI) and blood pressure, measured in terms of systolic and diastolic blood pressure, are well-known measures of cardiovascular risk, GlycA and ApoB/A1 are relatively new and novel biomarkers, with few studies investigating links with sleep.[25-27] High sensitivity C-reactive protein (hsCRP), which is commonly examined in sleep studies, is a marker of acute and (in adults) chronic inflammation. A recently described composite nuclear magnetic resonance (NMR) marker, GlycA, is suggested to better reflect chronic inflammation and in adults is predictive of cardiometabolic risk, however, there are few data from children and adolescents.[28, 29 30] Recent studies also suggest GlycA is a strong predictor of future cardiovascular events,[24, 31] incident type 2 diabetes mellitus,[32] and overall mortality,[24] beyond traditional measures of inflammation, such as hsCRP.[33] Apolipoproteins are structural and functional proteins of lipoprotein particles (e.g. LDL, HDL, vLDL) that have an important role in lipid metabolism.[34] ApoB/A1 reflects the ratio of apolipoprotein A (the largest structural component of HDL and responsible for reverse cholesterol transport) and apolipoprotein B (the largest structural component of LDL and responsible for circulating cholesterol transport), and has been suggested to more accurately reflect cholesterol balance and potential athrogenic and anti-athrogenic particles.[34] ApoB/A1 ratio has been reported an important predictor of cardiovascular risk, superior to conventional lipid profiles and tracks from childhood to adulthood.[35]

To date, few studies have examined the association between sleep and cardiometabolic risk, with most studies adopting a variable-based approach, and almost all focusing on sleep duration.[25] While traditional variable-based approaches may provide insight into how isolated sleep characteristics are associated with cardiometabolic risk factors, analyses do not reflect the multidimensional nature of sleep. Given that sleep is a multidimensional construct, it is essential to adopt a "whole person approach" that considers all characteristics of sleep within the individual, particularly when considering population health.[36]

In line with efforts to better understand sleep as a multidimensional construct and as a determinant of cardiometabolic health, the current study aimed to determine the association between actigraphy-derived sleep profiles and cardiometabolic health of Australian children aged 11-12 years and their parents. In this study, we examined cardiometabolic health in terms of BMI and blood pressure, a continuous cardiometabolic risk score, and biomarkers of inflammation (GlycA) and dyslipidaemia (ApoB/A1).

Methods:

Data examined in this study were collected between February 2015 and March 2016 as part of the Child Health CheckPoint (CheckPoint) study, a one-off, comprehensive physical health and biomarker cross-sectional study nested between waves 6 and 7 of the Longitudinal Study of Australian Children (LSAC) at child age 11-12 years. The LSAC commenced in 2004 with the recruitment of two cohorts (B and K – the latter not relevant to this paper), which have since been

followed biennially [37]. Further details of the CheckPoint study design and recruitment are outlined elsewhere.[38, 39]

Ethics and Consent: The CheckPoint study protocol was approved by The Royal Children's Hospital Melbourne Human Research Ethics Committee (33225D) and the Australian Institute of Family Studies Ethics Committee (14-26). The attending parent/caregiver provided written informed consent for themselves and their child to participate in the study.

Measures:

Sleep

Objectively-measured sleep characteristics were collected using tri-axial, wrist-worn GENEActiv accelerometers (Activinsights, Cambs, UK). This device has been used in previous studies to examine sleep of adults [40] and children.[41, 42] The GENEActiv has been shown to be valid for measuring sleep duration and efficiency when compared to the Actiwatch [43] and polysomnography [40] in adults, but not in children. GENEActiv-measured sleep duration correlate well with both sleep diary and self-reported sleep durations in children.[44] Participants were included for analysis if they had at least four nights of sleep data recorded, had an average sleep time >200 min and at least one non-school night (Fri-Sat) of sleep data. Sleep characteristics were derived from raw accelerometer data and processed using *Cobra* custom software developed by co-author FF (available on request to FF). Details of data processing have been reported elsewhere.[45] The van Hees [40] sleep algorithm was used to detect sleep and wake between self-reported bedtime and get up time, and collapsed into 1-min epochs. Each minute was classified as sleep or wake if it contained a majority of sleep or wake 5-s epochs, respectively. Minutes containing equal numbers of sleep and wake 5-s epochs were classified as sleep. Sleep onset was defined as the start of the first three consecutive minutes scored

as sleep. Sleep offset was defined as the end of the last five consecutive minutes scored as sleep. Sleep data for the first night were excluded, as recordings started at 2300. Further details of sleep data processing has been reported elsewhere.[45-47]

Four actigraphy-derived sleep variables were used to develop sleep clusters. These included sleep period (the difference between sleep onset and offset), sleep timing (the midpoint between sleep onset and offset), day-to-day sleep variability (the coefficient of variation of sleep period) and sleep efficiency (the percent of minutes scored as sleep between onset and offset). These variables are poorly correlated ($r<0.3$ for children and $r<0.2$ for adults) and were selected to represent sleep duration, timing, variability and quality (respectively). Mooi and colleagues[48] report that if highly correlated variables ($r>0.9$) are used in cluster analysis, specific aspects of these variables will be overrepresented. K-means cluster analysis was then used to identify sleep clusters. This process, summarized in the methods section and reported in detail elsewhere,[47] identified four sleep clusters that were labelled *Late to bed*, *Long sleeper*, *Short sleepers*, and *Overall good sleepers* for both adults and children within the CheckPoint study.

Cardiometabolic health

We examined whether sleep cluster membership was associated with cardiometabolic health, considered in terms of cardiometabolic markers, anthropometric measures and a composite metabolic syndrome score.

Cardiometabolic markers

Semi-fasted venous blood samples were taken from consenting adults and children in the CheckPoint study. In some cases, participants declined to provide venous samples but provided capillary blood samples instead. Appropriately trained researchers or phlebotomists collected venous blood samples

within assessment centres. Samples were then processed within 2 h on-site and stored at −80°C prior to shipping in dry ice as a single batch to the Melbourne Children's Bioresource Center (Murdoch Children's Research Institute) for processing. Further detail of blood collection, storage, and processing has been reported elsewhere.[49] Biomarkers examined in this study included concentrations of triglycerides, total cholesterol, HDL, LDL, ApoB/A1 and GlycA. Further detail as to how these measures were derived have been reported elsewhere.[29]

Anthropometric measures

Waist circumference was measured by trained research assistants with a steel anthropometric measuring tape (Lufkin Executive Diameter W606PM, Maryland) and assessed as the narrowest point between the 10th rib and iliac crest, or midpoint between if no visible narrowing. Two measures were taken, or a third (if the first two values differed by ≥1 cm), and the average was calculated. Height was assessed using a portable rigid stadiometer (Invicta IP0955, Leicester, UK). Two measures were taken, or a third (if the first two values differed by ≥0.5 cm), and the average was calculated. Weight was recorded via the InBody 230 Bioelectrical Impedance Analyser scales.[50] BMI (kg/m^2) was determined and BMI z-score calculated for children using the Centers for Disease Control CDC reference dataset[49]. Waist circumference measures have been shown to have good intra-rater and inter-rater reliability >0.88.[51-53] Similarly, the intra-rater and inter-rater reliability of BMI measures have been shown to be greater than 0.90.[54]

Blood pressure

Blood pressure was measured by a trained research assistant. Blood pressure cuff size was selected based on arm circumference. Readings were taken using the SphygmoCor[55] automated blood pressure monitoring device after participants were seated for a minimum of three minutes of quiet

rest. Automated blood pressure recordings in children, following similar protocols adopted in this study have been shown to have good intra-rater reliability (r=0.83-0.86).[56]

Three blood pressure measures were considered: systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP). Mean arterial pressure was determined using the following calculation: MAP = [SBP+(2*DBP)]/3 and was used to calculate a metabolic syndrome score.

Metabolic syndrome severity score

The metabolic syndrome is a cluster of cardiovascular risk factors that identify individuals who are more likely to develop future CVD and Type 2 diabetes.[21, 57] While there is no standard method of assessing metabolic syndrome, methods that use binary cut-offs have been criticised, with growing research in favor of z-score calculations.[58]

In the current study, a metabolic syndrome severity score (MetSS) was calculated to reflect metabolic syndrome severity. In line with Eisenmann's recommendations,[16] we used the sum of the z-scores of MAP, triglycerides, glucose, waist circumference, and HDL. Since HDL is inversely related to metabolic risk, it was subtracted. A higher score indicates a less favorable cardiometabolic profile. While an age- and sex- adjusted metabolic syndrome severity score has been recommended,[16] we used an unadjusted score as our analysis adjusted for sex, children's puberty stage, and adult's age.

Covariates

Analyses were adjusted for socioeconomic position (SEP), sex, parental age, children's puberty stage and season of data collection. SEP was operationalised using a composite measure consisting of self-reported parental income, education and occupation, which was derived from the LSAC dataset.[59, 60]

Using this scale, higher scores represent higher socio-economic position. Puberty was assessed using the Puberty Development Scale, a validated questionnaire that requires participants to answer five questions, using a four-point scale, with higher overall score representing advanced pubertal development.[61, 62] Season of data collection included all four seasons of the year: Summer (December-February), Autumn (March-May), Winter (June-August), Spring (September-November), as defined in Australia. These covariates were selected as they have been associated with cluster membership and cardiovascular outcomes.[47] The primary sampling unit of the original (LSAC) cohort was postal code, therefore we included an indication of which participants belonged to the same postal code.

Statistical Analysis:

All actigraphy variables were computed for each day. Measures of sleep duration, timing and quality, were averaged using a 5:2 weighting for a weeknight (Sunday–Thursday) and weekend (Friday–Saturday).

Details on how sleep clusters were developed have been reported elsewhere.[47] Briefly, cluster analysis was performed for both adults and children separately using SPSS, Software version 25 and guided by methods outlined by Mooi and Sarstedt [48]. Sleep variability data were normalised using log transformation and all sleep values standardised (using z-score) prior to analysis. The agglomerative hierarchical clusters method (using Ward's method and squared Euclidean distance) was used to help determine the number of clusters. K-means cluster analysis was then used to determine specific sleep clusters. Given that cluster analysis is primarily exploratory in nature and practical considerations have been suggested to be of utmost importance when deciding on the number of clusters,[48] we selected the optimal number of clusters by visualizing the hierarchical

cluster dendrogram (Supplement 1), considering the coefficient change in the hierarchical agglomerative schedule (Supplement 2), and the interpretability of K-means cluster solutions. Stability of clusters was assessed following the common approach outlined by Mooi and colleagues[48] whereby we repeated the cluster analysis on a random split of the original sample and compared the cluster centroids of the two solutions. One-way ANOVA did not find a significant difference in cluster centroids (p-value 0.7 for children and 0.2 for adults), suggesting a high degree of stability in the overall solution.

Cardiometabolic markers were examined for normality through visual inspection of histogram plots and assessment of kurtosis. Skewed variables were assessed by visual inspection, assessment of kurtosis (>3) and skewness (>1) values and were normalised using log transformation (glycA for adults; glycA and ApoB/A1 for children). All outcome variables were standardised prior to analysis.

The association between sleep cluster membership and cardiometabolic risk was assessed using Generalised Estimating Equation (GEE) in which standardised cardiometabolic risk measures were considered as dependent variables and cluster membership as predictor. Robust standard errors were used to account for the clustered sampling design of the study by adjusting for geographic clustering of observations by postal code. All outcome measures were normally distributed and modelled using a linear model, adjusted for sex, SEP, maturity stage (age for adults, puberty score for children) and season of data collection. P-values have been reported. Since many comparisons were undertaken, Holm Sequential Bonferroni correction was performed to address the risk of capitalisation on chance.

Results:

As presented in Figure 1, of the 1874 parent-child CheckPoint participants, 1043 children and 1337 adults had complete sleep data available for cluster analysis. Table 1 presents a comparison of participants included and excluded for analysis. As shown, children included for analysis were younger, had less advanced pubertal status, were of higher SEP and lower BMI z-score compared to those excluded. Similar differences were observed for adults, except, those included for analysis were older than those excluded. There were no sex differences.

Table 2 presents sample characteristics. Most participants were born in Australia and spoke English at home. Few were of Indigenous background. Sleep characteristics of the four actigraphy-derived sleep profiles examined are reported in Table 3. As presented, each cluster was named according to key sleep characteristics. Cluster names are provided as mnemonic labels only. Further details of sleep clusters and correlates have been reported elsewhere.[47]

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Adjusted GEE results for adults and children are presented in Table 4. As shown, cluster membership was significantly associated with MetSS, BMI and ApoB/A1 in adults and MetSS in children. Compared to *Overall good sleepers*, adults with a *Late to bed* sleep profile had a higher MetSS and BMI, while children with a *Short Sleep* profile had significantly higher MetSS, BMI and ApoB/A1. Adjusted marginal means are presented in Table 5

Figure 2 illustrates cluster membership and adjusted, standardised effect sizes for each cardiometabolic outcome measure. As shown, the *Overall good sleeper* pattern is associated with better cardiometabolic health in both adults and children. As illustrated, effect sizes are generally larger for adults, compared to children.

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Discussion:

This is the first study to determine the association between actigraphy-derived sleep profiles and cardiometabolic risk in a community sample of adults and children. We examined cardiometabolic risk in terms of a continuous metabolic syndrome severity score, as well as traditional and novel biomarkers that have been shown to track into adulthood and predict the development of type 2 diabetes and CVD morbidities in adulthood.[20-24] We found that *Overall good sleepers* had better cardiometabolic health across a variety of individual and summary cardiometabolic indicators in both adults and children. The differences were most pronounced for MetSS in both adults and children, and for BMI and ApoB/A1 levels in adults.

In our study, we found that MetSS (and to a lesser extent other cardiometabolic risk factors) was worse in the short sleep group in children and the late sleep group in adults. Short sleep and delayed sleep timing have been associated with poorer cardiometabolic health.[25, 36, 63-65] Short sleep is thought to increase allostatic load, increase appetite for unhealthy foods and cause fatigue, which limits physical activity.[66, 67] In contrast, delayed sleep timing is thought to provide fewer opportunities for physical

activity, greater opportunities for sedentary behaviours and may also be a marker of a generally chaotic lifestyle.[63, 68] This may explain why the *Late to bed* adults (perhaps busy parents of children) in our sample are particularly prone to less favourable cardiometabolic health. These findings have important implications when considering sleep interventions to help improve cardiometabolic health- while it is important to consider all sleep characteristics, short sleep duration in children and delayed sleep timing in adults may be of particularly importance.

Previous studies and interpretation of results

Studies examining the association between sleep and cardiometabolic risk in non-clinical samples have typically adopted a variable-based approach and examined the role of isolated, or at the most two or three, often subjectively-measured sleep characteristics.[36] Nevertheless, previous studies that have examined the role of sleep duration, quality, timing and variability tend to support findings in the current study. That is, sleep is a multidimensional construct and all characteristics of sleep are likely to play an important role in cardiometabolic health.

Short sleep duration is thought to adversely affect cardiometabolic health via a number of mechanisms. One theory suggests that short sleep increases allostatic load and disrupts processes occurring in the hypothalamic–pituitary–adrenal axis and the autonomic sympathetico-adrenal system. This results in increased cortisol and catecholamine release, oxidative stress, systemic inflammation, endothelial dysfunction, sympathetic systemic activation and subsequent hypertension, dyslipidemia and obesity.[6, 7] Another theory suggests that short sleep simply results in more time awake, particularly at night, and therefore greater time exposed to psychological stressors and unhealthy behaviours such as snacking on high-calorie foods, excess caffeine consumption and

sedentary screen-time activities.[69] Supporting these hypotheses, systematic reviews suggest short sleep is associated with increased risk of metabolic syndrome[70] in adults and adiposity[25, 71] and hypertension[65, 72] in both adults and children. While some studies report an association between short sleep duration and unfavourable blood lipid profiles and raised inflammatory markers, systematic reviews are yet to support this association.[25, 65]

Sleep quality, such as sleep duration, is thought to play an important role in mediating inflammatory processes and regulating catecholamine and growth hormone levels.[11, 73] Poor sleep quality has been associated with obesity,[74] hypertension[11, 75] and metabolic syndrome.[76] However, sleep quality has been defined in a variety of ways including validated questionnaires, subjective rating scales and objective measures of sleep efficiency. Consistent with our measure of sleep efficiency, Feliciano and colleagues,[64] in a study of 829 adolescents aged 13 years, reported higher sleep efficiency was associated with a more favorable cardiometabolic profile, measured in terms of a metabolic risk score, systolic blood pressure and HDL cholesterol levels.

Sleep timing and variability are also thought to play an important role in cardiometabolic health. Observational studies consistently suggest that findings that shift workers are at an increased risk of cardiometabolic disease and deranged cardiometabolic markers are attributable to variable sleep schedules and circadian misalignment (i.e. sleep timing).[77] Poor sleep timing has also been shown detrimental to children's health. For example, Olds and colleagues,[68] in a study of 2200 Australian children and adolescents, reported later bedtimes and rise time were associated with higher BMI, independent of sleep duration. The authors hypothesised that delayed sleep timing provided fewer opportunities for physical activity and greater opportunities for sedentary behaviours and increased calorie consumption (i.e. staying up late at night watching television and eating snacks). Indeed,

Golley and colleagues,[63] in a study of the same 2200 Australian children and adolescents, reported delayed bedtimes were associated with a higher intake of energy-dense, nutrient-poor foods.

To date, there are no studies, that we are aware of, that have applied cluster analysis to determine the association between sleep profiles and cardiometabolic health in adults and children. Although some studies attempt to decipher how different sleep characteristics are associated with different health outcomes, they generally only examine the effects of two or three different sleep characteristics, which are often measured subjectively.[36] Of the few available studies[25, 64] that have examined multiple characteristics of sleep, findings are consistent with the current study, that multiple characteristics of sleep may be important for health.

Strengths and limitations

To our knowledge this is the first population-based study to examine the association between actigraphy-derived sleep profiles and cardiometabolic health of adults and children, using objective, free-living sleep measures of duration, timing, quality and variability. Strengths include the objective examination of sleep via actigraphy and assessment of a wide range of standard and novel biomarkers in a large number of adults and children, as well as accounting for children's pubertal stage, seasonal influences and sampling clustering. However, there are several methodological issues that also need to be considered. Firstly, although the GENEActiv monitor has been shown valid for measuring sleep when compared to polysomnography in adults,[40] there are as yet no studies that have validated the monitor against polysomnography in children. Secondly, the narrow age range for children (11-12 years) precludes generalisation to other childhood ages and SEP. Thirdly, this study is cross-sectional and hence we are unable to infer causality. Fourth, we examined sleep clusters based on four sleep characteristics (duration, timing, variability and quality), each operationalised by a single variable (sleep period, midsleep, coefficient of variation and sleep efficiency). While this is a standard approach, it must be noted that there are a number of potentially different sleep

characteristics and variables that may be assessed (e.g. number of night-time awakenings). Further, although clusters were developed using a heuristic approach, guided by a recent review which suggested sleep duration, quality, timing, and variability are important sleep characteristics for the of health children,[25] a model-based approach could have also been used.[36] This study only examines adults and children in the CheckPoint study who had complete sleep data available and who agreed to have blood samples take, blood pressure assessed and/or body mass index calculated. It is also important to note that participants included in the current study were Australian children aged 11-12 year and adults (mean age 43 years), who were of higher SES and lower BMI compared to those excluded from the analysis. Results are therefore no longer representative of Australian children (aged 11-12 years) and their parents and cannot used to make generalisations to other childhood and adult age groups as well as other cultures and SES groups. Lastly, we acknowledge that testing more than one hypothesis increases the chances of significant findings. While there are tests to correct for multiplicity, they were not appropriate for the current study as outcomes were correlated.

Meaning and implications for clinicians and policy makers and areas in need of future research:

The findings of this study suggest that *patterns* of sleep (sleep period, quality, timing and variability) play an important role in cardiometabolic health. An *Overall good sleep* pattern is desirable for favourable cardiometabolic health. For example, compared to *Overall good sleepers*, adults in the *Late to bed* group was associated with a 0.29 SD increase in BMI (approximately 1.7 kg/m^2), while children in the *Short sleep* group was associated with a 0.18 SD increase in BMI (approximately 0.6 kg/m^2). Our study moves beyond the traditional approach of examining individual self-report sleep characteristics and provides a more holistic view of population sleep. Further research is however needed to determine the relative importance of each sleep characteristics and to determine how sleep as a component of the 24-h day affects cardiometabolic health.

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Figures

Figure 1: Flow diagram of participants included for analysis

Figure 2: Visual representation of standardised β coefficients for GEE analysis, adjusted for sex, age (for parents), pubertal stage (for children), socioeconomic position, season of data collection.

Table 1: Comparison of CheckPoint children and adults included and excluded for analyses

		Included	Excluded	P-value
Children				
	Age (years)			
	n	1043	831	
	Mean (SD)	12.0 (0.4)	12.1 (0.4)	0.000
	Sex			
	n	1043	831	
	% (males)	50%	53%	0.244
	Pubertal stage			
	n	963	757	
	Mean (SD)	2.1(0.6)	2.2(0.620)	0.040
	SEP			
	n	1038	829	
	Mean (SD)	0.23 (1.02)	0.11 (0.96)	0.009
	BMI z-score			
	n	1043	828	
	Mean (SD)	0.39 (1.14)	0.60 (1.15)	0.000
Adults				
	Age (years)			
	n	1337	537	
	Mean (SD)	44.0 (5.1)	43.2 (5.6)	0.003
	Sex			
	n	1337	537	
	% (males)	13%	12%	0.205
	SEP			
	n	1331	533	
	Mean (SD)	0.21 (0.99)	0.09 (0.98)	0.015
	BMI (kg/m^2)			
	n	1330	527	
	Mean (SD)	27.4 (5.9)	28.9 (6.5)	0.000

SEP=Socioeconomic position; BMI=body mass index

Table 2: Sample characteristics

	Children	Parents
Characteristics Values are %, unless indicated		
Demographic		
Age in years, mean (SD)	12.0 (0.4)	44.0 (5.1)
Sex (% males)	50	13
SEP, mean (SD)	0.23 (1.02)	0.21 (0.99)
Not born in Australia	0.8	19.7
Speak a language other than English at home	7.6	9.3
Parent is of Indigenous background	0.8	0.8
Season of data collection (%)		
Summer	24.1	25.0
Autumn	20.9	19.7
Winter	27.2	27.3
Spring	27.8	28.0
Remoteness of area of residence		
Highly accessible	54.6	42.6
Accessible	27.0	21.1
Moderate	15.0	11.7
Remote	1.7	1.3
Very remote	0.7	0.5
Not determined	0.7	0.5

SEP=Socioeconomic position; BMI=body mass index. Remoteness of area of residence was derived using the Accessibility/Remoteness Index of Australia (ARIA) remoteness area code[49]

Table 3: Sleep characteristics of clusters

	All		**Cluster 1** *Short sleepers*		**Cluster 2** *Late to bed*		**Cluster 3** *Long sleepers*		**Cluster 4** *Overall good sleepers*	
Children										
n	1043		284 (27%)		182 (17%)		254 (24%)		323 (31%)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Efficiency (%)	86.0	4.7	88.9	3.3	85.0	4.2	81.4	4.1	87.6	3.2
Time in bed (min)	544	43	505	33	541	38	577	37	552	29
Midsleep (24-hr:min)	2:35	48	2:30	34	3:46	38	2:15	33	2:16	36
Variability (%)	10.4	5.3	12.6	4.5	13.8	5.6	11.2	4.8	5.8	1.8
Bedtime (24-hr:min)	21:59	52	22:18	41	22:54	46	21:26	35	21:40	38
Rise time (24-hr:min)	7:24	50	7:37	36	8:33	44	7:17	39	7:10	37
Adults										
n	1337		347 (26%)		269 (20%)		297 (22%)		424 (32%)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Efficiency (%)	85.8	6.8	87.7	4.8	86.6	5.3	78.1	6.7	89.1	4.6
Time in bed (min)	497	54	464	42	473	47	544	47	508	42
Midsleep (24-hr:min)	2:51	52	2:12	45	3:46	38	2:58	46	2:45	36
Variability (%)	9.6	5.9	11.2	5.1	15.0	6.4	9.4	5.0	5.0	2.2
Bedtime (24-hr:min)	22:41	60	22:24	58	23:41	61	22:25	49	22:33	44
Rise time (24-hr:min)	7:02	58	6:09	44	7:43	45	7:31	55	6:59	39

Table 4: Adjusted GEE analysis to determine the association between cluster membership and standardised cardiometabolic health in children and adults

Children

	MetSS (P-value: 0.003)		BMI (P-value: 0.135)		SBP (P-value: 0.766)		DBP (P-value: 0.526)		ApoB/A1 (P-value: 0.065)		GlycA (P-value: 0.414)	
Cluster	β(95% CI)	P-value	β(95% CI)	P-value	β(95% CI)	P-value	β(95% CI)	P-value	β(95% CI)	P-value	β(95% CI)	P-value
Short sleepers	0.32(0.12,0.51)	**0.001**	0.18(0.01,0.34)	0.035	0.07(-0.08,0.22)	0.360	0.05(-0.13,0.22)	0.606	0.26(0.06,0.46)	0.011	0.15(-0.06,0.36)	0.163
Late to bed	-0.05(-0.29,0.20)	0.715	0.01(-0.18,0.20)	0.937	-0.01(-0.20,0.18)	0.923	-0.01(-0.22,0.20)	0.915	0.07(-0.17,0.30)	0.569	0.12(-0.12,0.35)	0.331
Long sleepers	0.09(-0.11,0.28)	0.388	0.11(-0.04,0.26)	0.161	0.01(-0.16,0.17)	0.953	-0.09(-0.26,0.08)	0.314	0.09(-0.11,0.29)	0.366	0.14(-0.05,0.34)	0.149

Adults

	MetSS (P-value: 0.009)		BMI (P-value: 0.001)		SBP (P-value: 0.062)		DBP (P-value: 0.629)		ApoB/A1 (P-value: 0.038)		GlycA (P-value: 0.055)	
Cluster	β(95% CI)	P-value	β(95% CI)	P-value	β(95% CI)	P-value	β(95% CI)	P-value	β(95% CI)	P-value	β(95% CI)	P-value
Short sleepers	0.02(-0.13,0.17)	0.814	0.12(-0.01,0.26)	0.072	0.10(-0.03,0.24)	0.133	0.07(-0.06,0.20)	0.284	-0.10(-0.25,0.05)	0.189	-0.08(-0.24,0.08)	0.346
Late to bed	0.28(0.10,0.47)	**0.003**	0.29(0.15,0.44)	**<0.001**	0.13(-0.04,0.29)	0.131	0.05(-0.11,0.21)	0.554	0.13(-0.02,0.29)	0.099	0.08(-0.07,0.23)	0.274
Long sleepers	0.12(-0.04,0.28)	0.130	0.13(0.00,0.26)	0.051	-0.06(-0.21,0.08)	0.384	-0.02(-0.17,0.12)	0.749	0.09(-0.07,0.24)	0.262	0.15(-0.02,0.32)	0.091

Reference group: *Overall good sleepers*; Overall significance indicated P-value beside headings.
95% CI= 95% confidence interval; MetSS= Metabolic syndrome severity score; BMI= body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; ApoB/A1: Apolipoprotein B/A1; GlycA: glycoprotein acetyls
Bolded text: P-values that remained significant following Holm Sequential Bonferroni adjustment have been bolded.

Table 5: Adjusted estimated marginal means for each cardiometabolic health outcome measure, according to sleep cluster

Children

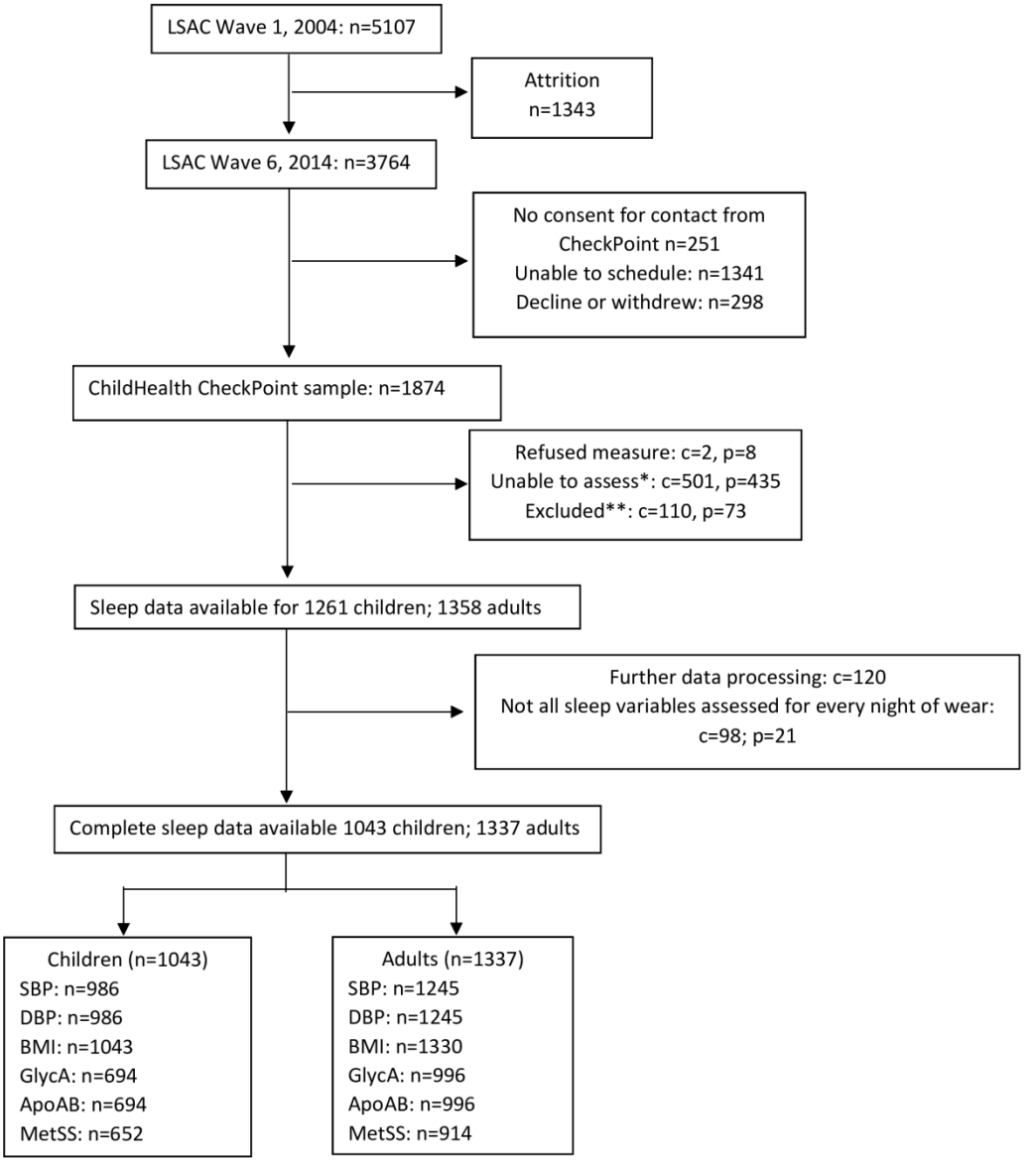
	MetSS	BMI (kg/m^2)	SBP (mmHg)	DBP (mmHg)	ApoB/A1 (g/L)	GlycA (mmol/L)
Sleep cluster	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Short sleep	0.71(0.28,1.15)	19.2(18.8,19.6)	108.3(107.3,109.2)	62.7(62.0,63.5)	0.48(0.46,0.49)	0.99(0.96,1.01)
Late to bed	-0.32(-0.85,0.21)	18.9(18.4,19.4)	107.6(106.5,108.8)	62.4(61.5,63.4)	0.46(0.44,0.48)	0.98(0.96,1.00)
Long sleep	0.06(-0.35,0.46)	18.9(18.5,19.3)	107.8(106.8,108.7)	62.0(61.2,62.7)	0.46(0.45,0.48)	0.98(0.97,1.00)
Good sleep	-0.19(-0.57,0.19)	18.6(18.3,18.9)	107.7(106.3,108.6)	62.5(61.8,63.2)	0.45(0.44,0.47)	0.97(0.95,0.98)

Adults

	MetSS	BMI (kg/m^2)	SBP (mmHg)	DBP (mmHg)	ApoB/A1 (g/L)	GlycA (mmol/L)
Sleep cluster	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Short sleep	1.02(0.60,1.44)	27.9(27.3,28.6)	122.7(121.5,124.0)	74.7(73.8,75.7)	0.55(0.53,0.57)	1.05(1.02,1.07)
Late to bed	1.89(1.35,2.43)	28.9(28.2,29.7)	123.1(121.3,124.8)	74.5(73.4,75.7)	0.59(0.56,0.61)	1.07(1.05,1.10)
Long sleep	1.36(0.89,1.83)	28.0(27.3,28.6)	120.6(119.1,122.2)	73.9(72.8,75.0)	0.58(0.56,0.60)	1.09(1.06,1.12)
Good sleep	0.96(0.56,1.36)	27.2(26.5,27.8)	121.5(120.0,122.9)	74.1(73.2,75.0)	0.57(0.55,0.59)	1.06(1.04,1.09)

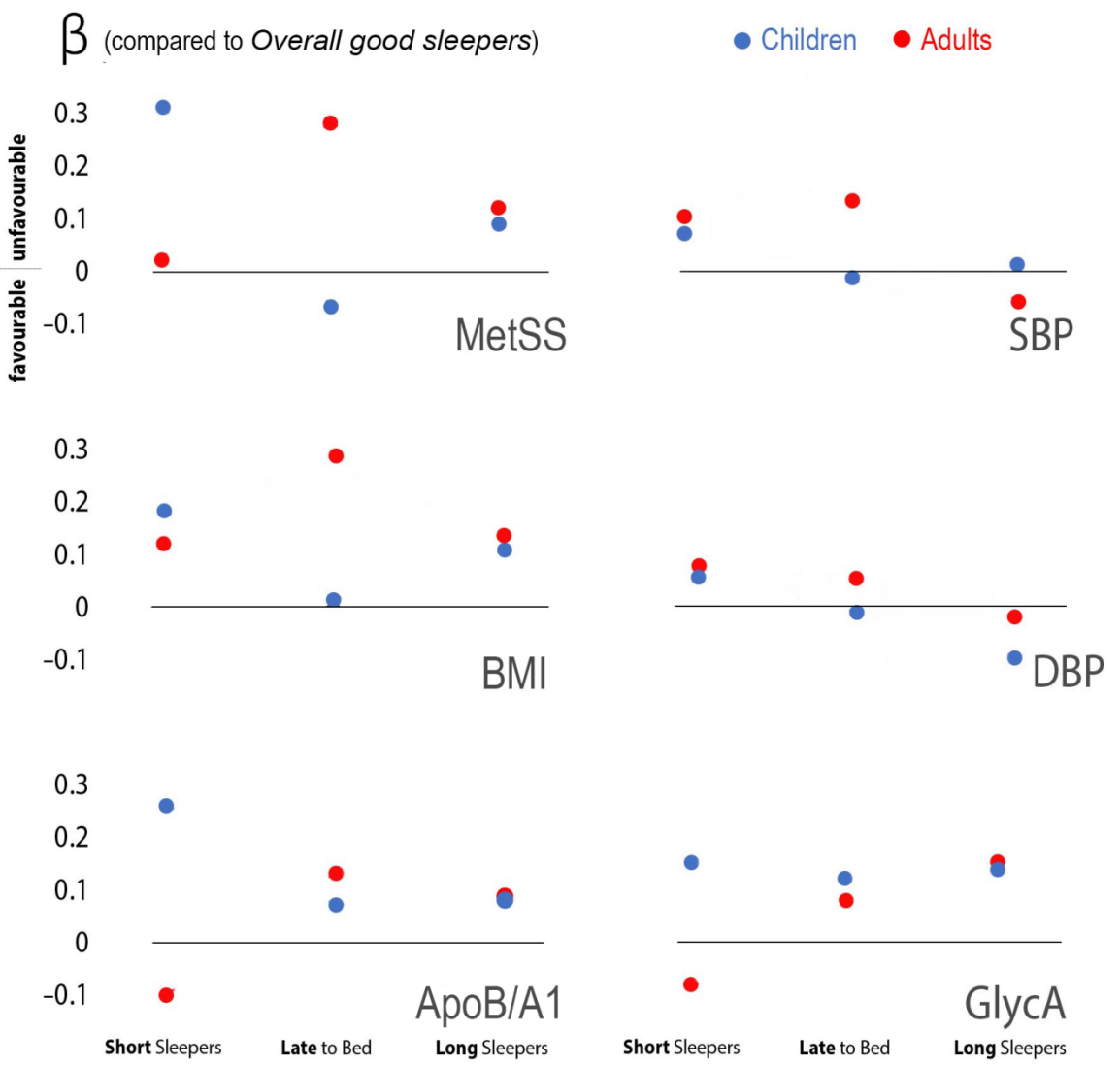
95% CI= 95% confidence interval; MetSS= Metabolic syndrome severity score; BMI= body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; ApoB/A1: Apolipoprotein B/A1; GlycA: glycoprotein acetyls

Figure 1



*Inability to assess due to equipment failure, poor-quality data or time constraints. **Participants excluded if valid days available did not meet the minimum criteria of at least 4 days of any type, ≥200min sleep and ≤1000min sedentary time. MetSS = Metabolic syndrome severity score; BMI=body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; APO AB: apolipoprotien AB; GlycA: glycoprotein acetyls

Figure 2



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