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Sleep patterns are associated with cardiometabolic risk factors in nine-year-old Swedish children

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Abstract

Aim: Sleep duration and bedtime may play a role in children's cardiometabolic health, but research is lacking. This study examined associations between sleep patterns and cardiometabolic risk factors in Swedish nine-year-olds.

Methods: This cross-sectional study used data from three studies, where identical outcome measures were conducted in 411 nine-year-olds, 51% boys, between 2016 and 2020. Sleep was assessed with wrist-worn accelerometers and sleep journals. Children were grouped based on meeting the sleep guidelines of 9–11 h and going to bed early or late based on the median bedtime. Analysis of covariance was used to examine associations between sleep patterns and cardiometabolic risk factors.

Results: Meeting sleep guidelines and going to bed early were associated with lower metabolic syndrome score (−0.15 vs. 0.42, $p = 0.029$), insulin resistance (0.30 vs. 0.60, $p = 0.025$) and insulin levels (6.80 vs. 8.87 mIU/L, $p = 0.034$), compared with their peers who did not meet the guidelines and went to bed later. When adjusting for total sleep time, analyses still showed associations with the metabolic syndrome score (−0.19 vs. 0.50, $p = 0.011$).

Conclusion: The findings indicate that good sleep patterns could help mediate positive overall cardiometabolic health in children.

KEYWORDS
bedtime, cardiometabolic health, school-aged children, sleep duration, sleep patterns

1 | INTRODUCTION

Sleep is essential for children's optimal development and growth, with insufficient sleep duration being associated with negative implications on socioemotional, cognitive and behavioural functions, both in short and long term.[1] Insufficient sleep duration has also been linked to health implications, such as an increased risk of obesity in children and adolescents.[2] Correspondingly, insufficient sleep duration may have a negative impact on cardiometabolic health already in childhood.[3] To illustrate, Sun et al.[3] conducted a systematic review including systematic reviews, meta-analyses and individual studies on sleep duration and cardiovascular risk in children and adolescents. The meta-review included 37 systematic reviews and meta-analyses and found strong evidence regarding associations between short

sleep duration and individual risk factors, such as high blood pressure and increased adiposity measures. Findings also showed some evidence for an association with insulin resistance.[3] Furthermore, 4 of 15 studies in their systematic review reported an inverse association between sleep duration and cardiometabolic risk score.[3] Correspondingly, a review by Quist et al.[4] including 75 studies suggested that insufficient sleep duration was associated with cardiometabolic risk, with the strongest evidence for abdominal adiposity, high blood pressure and decreased insulin sensitivity in children and adolescents.[4] However, many studies have used self-reported measures of sleep and not considered the combination of sleep duration and other aspects of sleep, such as bedtime. The time that children wake up is mostly determined by school schedule and family routines, and bedtime is more likely to be modifiable. Interestingly, Lucas-de la Cruz et al.[5] recently reported an independent association between bedtime and a cardiometabolic risk profile in Spanish children aged 8–11 years.[5] Their study found that children who went to bed later than 23:15 had poorer levels of an insulin resistance marker and a cardiometabolic risk index than children who went to bed earlier, taking sleep duration into account.[5]

To conclude, scientific evidence on the role of sleep duration on cardiometabolic risk factors in children is emerging, but current knowledge is limited in other sleep parameters, such as bedtime. In addition, studies to date have primarily focused on populations with overweight, obesity or diabetes, but cardiometabolic risk factors may also be prevalent among lean subjects.[6] Furthermore, research is emerging that cardiometabolic risk factors in childhood may track into adulthood.[7] Thus, the aim of this study was to examine the associations of sleep patterns, including sleep duration and bedtime, with cardiometabolic risk factors in healthy nine-year-old Swedish children.

2 | METHODS

2.1 | Study design and participants

Data from the Studies of Prospective Health Determinants in Infancy and Childhood (SPINACH), which pools data from the nine-year follow-ups of three studies in Region Östergötland, Sweden, were used. These studies included one randomised controlled trial, conducted when the children were four years of age,[8] and two birth cohorts.[9,10] Inclusion criteria were full-term gestation of at least 37 weeks, healthy singleton infant for the birth cohorts[9,10] and a healthy four-year-old child for the randomised controlled trial.[8] Uniform measures for all outcomes were collected at the nine-year follow-up for all three studies which occurred between 2016 and 2020.

A total of 632 children initially participated in the three studies, 411 agreed to take part in the nine-year follow-up, of which 211 (51.3%) were boys. At the nine-year follow-up, participating parents and children were asked to provide a fasting blood sample in order to assess cardiometabolic risk factors. Among the 411 participants,

> **Key Notes**
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> - This is one of the first studies investigating how sleep duration combined with bedtime impact children's cardiometabolic health.
> - Children that met sleep guidelines and went to bed early had a better metabolic syndrome score than children that did not meet guidelines and went to bed later, even when adjusting for total sleep time.
> - Findings indicate that good sleep patterns can contribute to positive cardiometabolic health in children.

175 provided blood samples and were representative of the 236 children who did not, with regard to several aspects. Their mean age was 9.6 versus 9.5 years, body mass index (BMI) was 17.0 versus 16.9 kg/m^2, sex distribution was 55.1% versus 46.6% boys and maternal level of education was 80.5% versus 75.0% who had a university degree, respectively.[11] All caregivers provided written informed consent and the Research and Ethics Committees in Linköping and Stockholm approved this study (Dnr: 2016/300–31; 2018/2220–32, respectively).

2.2 | Measures

2.2.1 | Sleep and physical activity

The accelerometer ActiGraph GT3X+ (ActiGraph, Pensacola, Florida, USA) was used to assess sleep and physical activity. The participants wore the accelerometer around their non-dominant wrist for seven consecutive 24-hour periods and were instructed to wear it at all times except for water-based activities. The participants were also instructed to fill in a sleep journal and record the time they went to bed each night and when they got up each morning. The accelerometers were set to sample at 90 Hz. Children providing at least one valid day were included in this study. A day was considered valid if the accelerometer was worn for at least two-thirds of the 24-hour period, namely 16 h, and if the accelerometer was worn for at least two-thirds of the participant's waking hours. Non-wear time was detected using raw acceleration of the three axes in 15-minute blocks.[12] A block was classified as non-wear time either if the range or standard deviation of the value for two of the three axes was <50 milli-gravity or <13 milli-gravity throughout the surrounding 60-minute movement window, respectively. Invalid epochs were imputed as averages during the same time interval from the other recorded days. Out of the 411 participants, 402 provided valid accelerometer data and 398 provided sleep journals, flowchart presented in Figure S1.

Sleep duration was assessed automatically with the open-source R-package GGIR algorithm, guided by the sleep journals.[13] Wrist-worn accelerometer data was used to measure sleep, by estimating arm angle relative to a horizontal plane. From visualisation of the angle of the arm, sleep was described as a period with low frequency of changes

in the arm angle.[13] Two different variables of sleep duration were used in this study, the total sleep time and the total time spent in bed, which were both derived from the accelerometer data. For physical activity, over five-second epochs, the Euclidean Norm of the raw acceleration Minus one G with negative values rounded to zero were calculated. The amount of time spent in moderate-to-vigorous and vigorous physical activity were classified based on the following thresholds: ≥200 milli-gravity and ≥700 milli-gravity, respectively.[14,15] The software GGIR version 2.3–0 (Accelting, Almere, The Netherlands) in R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria) was used to process the accelerometer data.

2.3 | Anthropometry

Trained staff conducted all anthropometric measures when the children were wearing light clothing and no shoes. Weight was measured to the nearest gram with an electronic scale attached to the BodPod (BodPod, COSMED, Concord, California, USA). Height was measured to the nearest 0.5 cm with a stadiometer (Tillquist, Spånga, Sweden) attached to the wall. Body mass index was calculated as body weight in kilograms divided by height in meters, squared, and BMI cut-offs by Cole and Lobstein[16] were used to classify children into weight status categories.

2.4 | Cardiometabolic risk factors

Fasting venous blood samples were analysed for glucose, insulin, total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, as well as triglycerides. The analyses have been described in detail previously[17] and the blood samples were analysed at the Department of Clinical Chemistry, Linköping University (ISO/IEC 17025). The homeostatic model assessment for insulin resistance (HOMA-IR) was calculated as insulin (mIU/L) multiplied by fasting glucose (mmol/L) divided by 22.5. Systolic and diastolic blood pressures were assessed using an electronic sphygmomanometer (WelchAllyn, ProBP 3400 series, New York, USA). The children's blood pressure was measured when they were sitting upright after at least 5 min of rest. Two readings were conducted and if the readings differed by more than 10 millimetres of mercury (mmHg), a third reading was done. The mean blood pressure was used in the analyses.

A continuous cardiovascular risk score for metabolic syndrome was assessed. The metabolic syndrome score was calculated as the sum of the sex-specific z-scores for triglycerides, inverted HDL cholesterol, glucose, the average of systolic and diastolic blood pressure and waist circumference. The z-score for both the metabolic syndrome score and HOMA-IR were computed and used in the analyses. Metabolic syndrome was defined as girls and boys meeting at least three criteria. These criteria were reduced levels of HDL (<1.25 mmol/L and <1.13 mmol/L, respectively), elevated triglycerides (>1.60 mmol/L and >1.44 mmol/L, respectively), elevated blood glucose (>5.6 mmol/L), high systolic (>121 mmHg) or

diastolic (>80 mmHg and >76 mmHg, respectively) blood pressure,[18] or high waist circumference (>72.6 cm and >74.3 cm, respectively).[19] Meeting one or two of these criteria was categorised as being metabolically unhealthy.[18–20]

2.5 | Energy intake

Energy intake was assessed using the digital food frequency questionnaire School Meal-Q which is a version of the Meal-Q for adults[21] adapted for school-aged children. Parents were asked to fill in this questionnaire based on their child's dietary habits over the past one month, and energy intake in kilojoules per day for each child was calculated by linkage to the food database provided by the Swedish Food Agency.

2.6 | Statistical analyses

Means and standard deviations or frequencies were used to report the descriptive characteristics of the participants. Due to a skewed distribution, HOMA-IR values were transformed in the analyses using the natural logarithm. Independent t-tests were used to investigate sex differences. Pearson correlations were applied to investigate relationships between continuous sleep variables including total time in bed and total sleep time and cardiometabolic risk factors.

Participants were divided into four groups based on their sleep patterns. Sleep patterns were categorised as meeting or not meeting the sleep guidelines,[22] combined with going to bed earlier or later than the median bedtime of the study population, which was 21:39. Among those that did not meet the sleep guidelines, 90 children had a late bedtime, and 28 children had an early bedtime. The two groups that did meet the guidelines included 109 children with a late bedtime and 171 children with an early bedtime. Meeting or not meeting the sleep guidelines is equivalent to sleeping 9–11 h or less than 9 h per night, respectively.[22] No child slept more than 11 h per 24 h. Analysis of covariance was used to investigate associations between the sleep patterns as explanatory variables, fixed factor and cardiometabolic risk factors as outcomes. The child's continuous age, sex categorised as boy or girl, as well as maternal education categorised as university degree or no university degree, were included as covariates in the first model. However, sleep duration and bedtime can influence each other, making sleep duration an important confounder to consider in this analysis. Thus, a second model was included, where total sleep time was added as a covariate. Post hoc pairwise comparisons with Bonferroni correction were applied to investigate mean differences between the four sleep pattern groups. The chi-square test was conducted to examine differences between meeting or not meeting the sleep guidelines and having and early or late bedtime. We also conducted sensitivity analyses, where adjustment for accelerometer-derived time in minutes per day spent on vigorous physical activity or moderate-to-vigorous physical activity, as well as energy intake in kilojoules per day assessed through a food frequency questionnaire,

were included. Finally, possible interactions by sex in the aforementioned models were also investigated. All statistical analyses were conducted in SPSS Statistics Version 28 (IBM, Armonk, New York, USA) using a 5% level of significance.

3 | RESULTS

Descriptive characteristics of all participants, and stratified by sex, are presented in Table 1. Table S1 presents characteristics

TABLE 1 Descriptive characteristics of the participants, stratified by sex. Significance level 0.05.

	n	All	n	Girls	n	Boys	p Value[a]
General characteristics, mean (SD)							
Age, years	411	9.5 (0.1)	200	9.5 (0.1)	211	9.5 (0.1)	0.882
Height, cm	411	139.4 (6.1)	200	138.7 (5.9)	211	140.2 (6.2)	**0.013**
Weight, kg	411	33.2 (6.8)	200	32.7 (6.8)	211	33.6 (6.7)	0.165
BMI category							
Underweight	45	10.8%	26	13.0%	19	9.0%	
Normal weight	313	75.5%	148	74.0%	165	78.2%	
Overweight	45	10.8%	22	11.0%	23	10.9%	
Obesity	8	1.9%	4	2.0%	4	1.9%	
Sleep characteristics, mean (SD)							
Total time in bed, minutes	398	554 (34)	197	560 (32)	201	549 (35)	**<0.001**
Total sleep time, minutes	398	463 (49)	197	470 (41)	201	456 (56)	**0.005**
Cardiometabolic risk factors, mean (SD)							
Waist circumference, cm	411	64.4 (7.3)	200	64.4 (7.7)	211	64.4 (6.9)	0.953
Systolic BP, mmHg	409	110.7 (9.3)	198	111.5 (9.8)	211	110.0 (8.9)	0.106
Diastolic BP, mmHg	409	68.5 (5.8)	198	69.0 (5.7)	211	68.0 (5.8)	0.083
Glucose, mmol/L[b]	173	5.1 (0.4)	92	5.0 (0.4)	81	5.1 (0.4)	0.225
Insulin, mIU/L[c]	169	7.4 (3.8)	89	8.1 (4.0)	80	6.7 (3.5)	**0.016**
ln HOMA-IR[d]	166	0.4 (0.5)	87	0.5 (0.5)	79	0.3 (0.6)	**0.014**
Total cholesterol, mmol/L[b]	175	4.2 (0.7)	94	4.3 (0.6)	81	4.1 (0.7)	**0.047**
LDL cholesterol, mmol/L[b]	175	2.2 (0.6)	94	2.3 (0.6)	81	2.1 (0.6)	**0.022**
HDL cholesterol, mmol/L[b]	175	1.7 (0.4)	94	1.7 (0.4)	81	1.7 (0.3)	0.455
Triglycerides, mmol/L[b]	175	0.6 (0.2)	94	0.7 (0.2)	81	0.6 (0.2)	0.109
Metabolic syndrome score, z-score	173	0.0 (1.0)	92	0.0 (1.0)	81	0.0 (1.0)	0.998
Metabolic health, number of children (%)							
Having metabolic syndrome[e]		10		4		6	
Being metabolically unhealthy[e]	411	106 (26%)	200	54 (27%)	211	52 (25%)	
Glucose > 5.6 mmol/L	173	13 (7.5%)	92	6 (6.5%)	81	7 (8.6%)	
Elevated triglycerides	175	2 (1.1%)	94	1 (1.1%)	81	1 (1.2%)	
Low HDL cholesterol	175	15 (8.6%)	94	12 (12.8%)	81	3 (3.7%)	
Systolic BP >121 mmHg	409	45 (11.0%)	198	26 (13.1%)	211	19 (9.0%)	
High diastolic BP	409	0 (0.0%)	198	3 (1.5%)	211	20 (9.5%)	
High waist circumference	411	45 (10.9%)	200	25 (12.5%)	211	20 (9.5%)	

Note: Bold p values indicate statistical significance, level 0.05.

Abbreviations: BMI, body mass index; BP, blood pressure; HDL, high density lipoprotein; HOMA-IR; homeostatic model assessment for insulin resistance; LDL, low density lipoprotein; mmHg, millimetres of mercury; n, number of children; SD, standard deviation.

[a]Difference between girls and boys measured with an independent *t*-test.

[b]Measured in plasma.

[c]Measured in serum.

[d]Values are transformed with the natural logarithm, due to skewed distribution.

[e]Metabolic syndrome was defined as meeting at least three, while metabolically unhealthy was defined as meeting one or two, of the following: fasting glucose >5.6 mmol/L, elevated triglycerides (>1.60 mmol/L for girls and >1.44 mmol/L for boys), reduced HDL cholesterol (<1.25 mmol/L for girls and <1.13 mmol/L for boys), systolic BP >121 mmHg, high diastolic BP (>80 mmHg for girls and >76 mmHg for boys), high waist circumference (>72.6 cm for girls and >74.3 cm for boys).

stratified by sleep patterns. No statistically significant differences were found for general characteristics between boys and girls, except boys being slightly taller than girls (140 vs. 139 cm, $p = 0.013$). Approximately two-thirds of the children were classified as normal weight. Furthermore, girls spent more time in bed per 24 h than boys (560 vs. 549 min, $p < 0.001$) and slept more per 24 h (470 vs. 456 min, $p = 0.005$). In terms of cardiometabolic risk factors, there were no statistically significant differences between boys and girls for waist circumference, systolic or diastolic blood pressure, blood glucose, HDL cholesterol, triglyceride levels or metabolic syndrome score. However, boys had lower insulin levels ($p = 0.016$), HOMA-IR ($p = 0.014$), total cholesterol ($p = 0.047$), and LDL cholesterol ($p = 0.022$), compared to girls. A total of 85 children were categorised as being metabolically unhealthy, and four were categorised as having metabolic syndrome. Of the 402 participants with accelerometer data, 172 provided blood samples and were representative of the 230 that did not in terms of mean bedtime (21:41 vs. 21:43) and mean total sleep time (468 ± 39 min vs. 460 ± 56 min). No correlations were found between cardiometabolic risk factors and total sleep time, nor total time in bed, as presented in Table S2. The chi-squared test showed a significant difference regarding the categorical variables of meeting or not meeting sleep duration guidelines and having an early or late bedtime ($p < 0.001$). The group that did meet the guidelines were more prone to go to bed early, and the group that did not meet the guidelines were more prone to go to bed late.

Table 2 presents the differences in sleep indicators between the children classified in each one of the four pre-defined sleep patterns. There were statistically significant differences between groups regarding total sleep time ($p < 0.001$) and total time in bed ($p < 0.001$). More specifically, children that did not meet the sleep guidelines and went to bed later, defined as later than the median bedtime which was 21:39, accumulated less total sleep time and total time in bed. For total time in bed, differences were found between all groups.

Table 3 presents the cardiometabolic risk factors stratified by sleep patterns. There were statistically significant differences between groups with regard to metabolic syndrome score, HOMA-IR and insulin. Post hoc pairwise comparisons with Bonferroni correction revealed that the group who did not meet the sleep guidelines and went to bed earlier than the median had a lower metabolic syndrome score (-0.15 vs. 0.42, $p = 0.029$), HOMA-IR (0.30 vs. 0.60, $p = 0.025$) and insulin levels (6.80 vs. 8.87 mIU/L, $p = 0.034$) than the group that did not meet the guidelines and went to bed later than the median (Figure 1). There were no statistically significant differences for the remaining cardiometabolic risk factors. When including total sleep time as an additional covariant in the analysis of covariance model, the association to insulin disappeared. Nevertheless, the association to HOMA-IR was still evident, although weaker ($p = 0.041$), and the association to metabolic syndrome score became stronger ($p = 0.014$). However, post hoc analysis for the pairwise comparison across groups revealed that when models were additionally adjusted for total sleep time, the statistical significance remained only for the metabolic syndrome score (-0.19 vs. 0.50, $p = 0.011$, Figure 1). Sensitivity analyses including time in minutes per day spent in vigorous physical activity, moderate-to-vigorous physical activity or energy intake in kilojoules per day as a covariate did not change the results. With regard to interactions by sex, a significant interaction was found for insulin ($p = 0.031$) and for the rest of the cardiometabolic variables the p-values were ≥ 0.130.

4 | DISCUSSION

To our knowledge, this was the first study investigating the impact of sleep duration combined with bedtime on children's cardiometabolic health. In the present study, children that did meet the sleep guidelines and went to bed earlier than 21:39 had a better metabolic syndrome score, HOMA-IR and insulin level, compared to children that did not meet the sleep guidelines and went to bed later than 21:39. Part of these differences seemed to be explained by the sleep duration, yet bedtime was still relevant for metabolic syndrome score after considering sleep duration in the analysis, indicating that bedtime influences overall cardiometabolic health.

TABLE 2 Sleep indicators of the participants, stratified by sleep patterns.

| | Did not meet sleep guidelines[a] | | | | Did meet sleep guidelines[a] | | | | |
| | Bedtime later than median[b] | | Bedtime earlier than median[b] | | Bedtime later than median[b] | | Bedtime earlier than median[b] | | |
	n	Mean (SEM)	n	Mean (SEM)	n	Mean (SEM)	n	Mean (SEM)	p Value[c]
Total time in bed, minutes	90	513 (2.4)[d,e,f]	28	527 (4.3)[d,g,h]	109	566 (2.2)[e,g,i]	171	574 (1.7)[f,h,i]	**<0.001**
Total sleep time, minutes	90	434 (4.9)[j,k]	28	450 (8.8)[l]	109	469 (4.5)[j]	171	477 (3.6)[k,l]	**<0.001**

Note: Common letters ([d-l]) in superscript indicate that post-hoc analysis revealed a statistically significant *p* value (<0.05) between groups.

Abbreviations: *n*, number of children; SEM, standard error of the mean.

[a]In accordance with the Canadian 24-Hour Movement Guidelines for Children and Youth.[22]

[b]Median bedtime of participants is 21:39.

[c]Analysis of covariance model adjusted for age, sex and mother's education.

TABLE 3 Cardiometabolic risk factors of the participants, stratified by sleep patterns.

| | | Did not meet sleep guidelines[a] | | | | Did meet sleep guidelines[a] | | | | |
| | | Bedtime later than median[b] | | Bedtime earlier than median[b] | | Bedtime later than median[b] | | Bedtime earlier than median[b] | | |
		n	Mean (SEM)	n	Mean (SEM)	n	Mean (SEM)	n	Mean (SEM)	p Value[c]
Waist circumference (cm)	Model 1	90	65.4 (0.8)	28	65.4 (1.4)	109	64.1 (0.7)	171	63.7 (0.5)	0.252
	Model 2	90	65.3 (0.8)	28	65.3 (1.4)	109	64.2 (0.7)	171	63.8 (0.6)	0.422
Metabolic syndrome score	Model 1	36	0.42 (0.16)	16	−0.19 (0.24)	42	−0.03 (0.15)	76	−0.15 (0.11)	**0.029**
	Model 2	36	0.50 (0.17)	16	−0.14 (0.25)	42	−0.05 (0.15)	76	−0.19 (0.11)	**0.014**
HOMA-IR[d]	Model 1	33	0.60 (0.09)	16	0.24 (0.13)	41	0.44 (0.08)	73	0.30 (0.06)	**0.025**
	Model 2	33	0.60 (0.10)	16	0.24 (0.13)	41	0.44 (0.08)	73	0.30 (0.06)	**0.041**
Systolic BP (mmHg)	Model 1	90	112.63 (0.97)	28	108.78 (1.74)	109	109.29 (0.89)	170	110.66 (0.71)	0.055
	Model 2	90	112.42 (1.02)	28	108.69 (1.74)	109	109.32 (0.89)	170	110.76 (0.72)	0.087
Diastolic BP (mmHg)	Model 1	90	69.47 (0.61)	28	67.59 (1.09)	109	67.98 (0.55)	170	68.48 (0.44)	0.246
	Model 2	90	69.34 (0.64)	28	67.53 (1.09)	109	68.00 (0.56)	170	68.55 (0.45)	0.334
Glucose (mmol/L)	Model 1	36	5.18 (0.46)	16	4.94 (0.35)	42	5.09 (0.37)	76	5.04 (0.29)	0.116
	Model 2	36	5.20 (0.07)	16	4.94 (0.09)	42	5.09 (0.06)	76	5.03 (0.04)	0.078
Insulin (mIU/L)	Model 1	34	8.87 (0.61)	16	6.66 (0.89)	42	7.73 (0.55)	74	6.80 (0.41)	**0.034**
	Model 2	34	8.73 (0.66)	16	6.58 (0.91)	42	7.75 (0.56)	74	6.87 (0.43)	0.085
Total cholesterol (mmol/L)	Model 1	37	4.07 (0.11)	16	4.30 (0.16)	43	4.37 (0.10)	76	4.20 (0.07)	0.208
	Model 2	37	4.09 (0.11)	16	4.31 (0.17)	43	4.37 (0.10)	76	4.19 (0.08)	0.261
LDL cholesterol (mmol/L)	Model 1	37	2.16 (0.10)	16	2.39 (0.15)	43	2.31 (0.09)	76	2.18 (0.07)	0.423
	Model 2	37	2.17 (0.11)	16	2.40 (0.16)	43	2.31 (0.09)	76	2.18 (0.07)	0.425
HDL cholesterol (mmol/L)	Model 1	37	1.60 (0.06)	16	1.65 (0.09)	43	1.75 (0.05)	76	1.73 (0.04)	0.162
	Model 2	37	1.60 (0.06)	16	1.65 (0.09)	43	1.75 (0.05)	76	1.73 (0.04)	0.269
Triglycerides (mmol/L)	Model 1	37	0.65 (0.04)	16	0.56 (0.06)	43	0.68 (0.04)	76	0.60 (0.03)	0.178
	Model 2	37	0.67 (0.04)	16	0.57 (0.06)	43	0.68 (0.04)	76	0.59 (0.03)	0.670

Note: Bold p values indicate statistical significance, level 0.05.

Abbreviations: BP, blood pressure; HDL, high density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LDL, low density lipoprotein cholesterol; mmHg, millimetres of mercury; *n*, number of children; SEM, standard error of the mean; WC, waist circumference.

[a]In accordance with the Canadian 24-Hour Movement Guidelines for Children and Youth.[22]

[b]Median bedtime of participants is 21:39.

[c]Analysis of covariance, model 1 adjusted for age, sex, and mother's education, and model 2 adjusted for age, sex, mother's education and total sleep time.

[d]Values are transformed with the natural logarithm, due to skewed distribution.

The metabolic syndrome score was significantly better in the children with the best sleep pattern compared to the children who did not meet the guidelines and went to bed later. Similar findings were presented in a cross-sectional study by Matricciani et al.,[23] that examined sleep profiles and cardiometabolic health in 1043 children aged 11–12 years. Children that had an average time in bed of 8 h 25 min, which was considered a short sleep duration, had a higher metabolic syndrome severity score and dyslipidemia marker levels, compared to overall good sleepers. The children that were categorised as overall good sleepers were defined as having adequate sleep duration, high efficiency, early bedtime and low day-to-day variability.[23] Likewise, in a study by Lucas-de la Cruz et al.[5] that used ActiGraphs together with sleep journals, children aged 8–11 years who spent more than 9 h 15 min in bed had a better cardiometabolic risk index compared to children that spent less time in bed. Furthermore, they found that not only sleep duration but also having a later bedtime, in this case defined as later than 23:15, was associated with a poorer cardiometabolic profile.[5] In the present study, going to bed later than the median bedtime, which was 21:39, was associated with higher cardiometabolic risk in those who did not meet the guidelines, compared to the group with the best sleep pattern. This finding indicates that the combination of sleep duration and bedtime is of importance for nine-year-olds' cardiometabolic health. In the cross-sectional study by Matricciani et al.[23] in slightly older children, aged 11–12 years, no significant differences were observed for cardiometabolic health when having a mean bedtime of 22:54, which was considered a late bedtime, compared to earlier bedtimes. Nonetheless, the group with a late bedtime still had
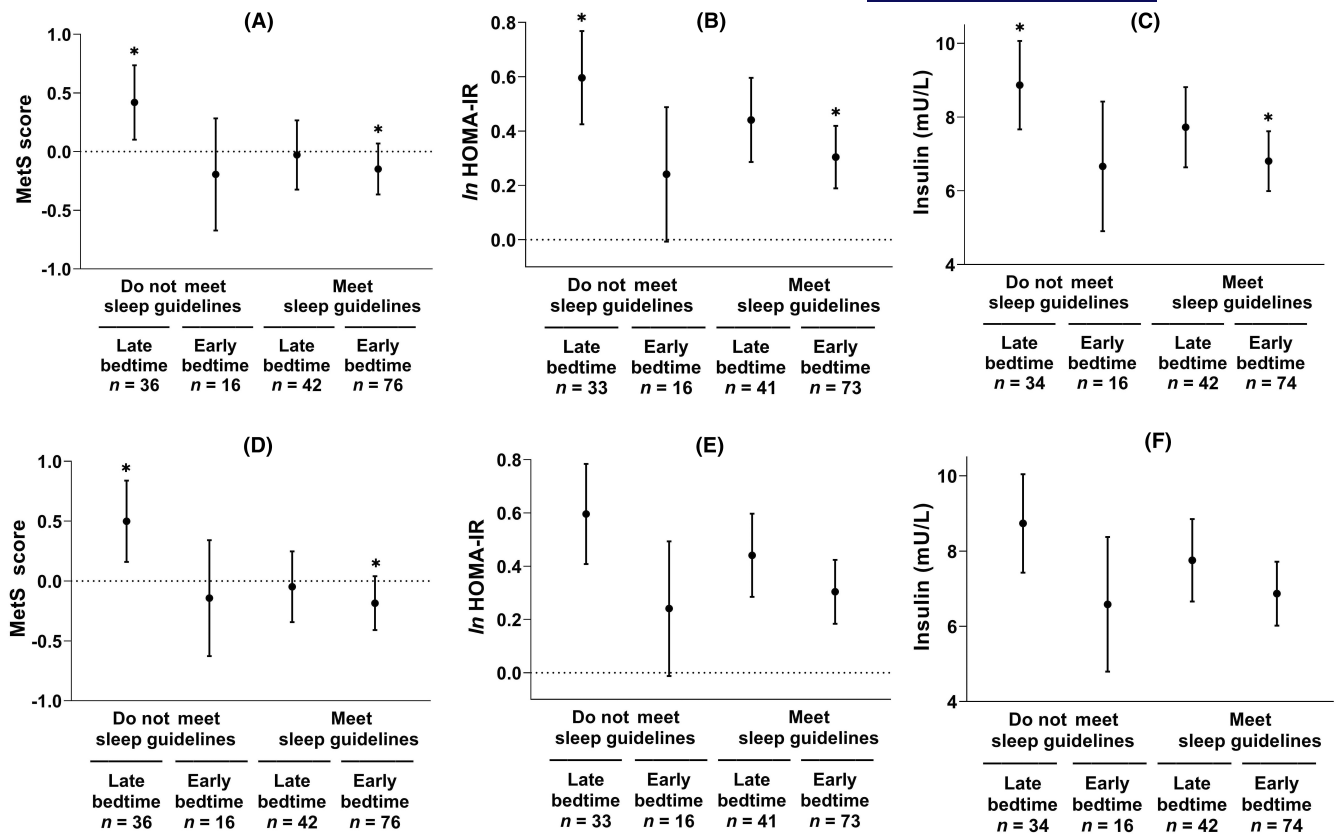
FIGURE 1 Post-hoc analysis for the pairwise comparisons on metabolic syndrome score, *In* HOMA-IR, and insulin (mIU/L) across the sleep subgroups. The models were adjusted for age, sex, and mother's education in (A–C), while total sleep time also was included in (D–F). Measures are sgrouped after meeting or not meeting sleep guidelines[22] in combination with having a late or early bedtime, with 21:39 as cut-off. Asterisks above bars indicate a statistically significant difference between those groups, significance level 0.05. HOMA-IR, homeostatic model assessment for insulin resistance.

a sleep duration above 9 h, and the combination of having a late bedtime and a sleep duration below 9 h was not investigated. Finally, it is possible that children aged 11–12 years may be less sensitive to late bedtimes and short sleep duration than younger children.

With regard to HOMA-IR, children that did not meet the guidelines and went to bed later had higher values than children with the best sleep pattern in the crude analyses that were not adjusted for sleep duration. Chen et al.[24] investigated associations between accelerometer-assessed sleep and cardiometabolic risk factors in children aged 9–18 years. They studied sleep duration and bedtime separately and found that having a shorter sleep duration on weekdays or going to bed later than their peers was associated with higher HOMA-IR.[24] This agrees with our finding that sleep patterns influence HOMA-IR values, although this finding did not remain after adjustment for sleep duration.

The possible underlying mechanisms for the associations observed in this study should also be discussed. First, eating patterns may play a role. Indeed, having a late bedtime routine has been associated with a different eating behaviour than having an early routine.[25,26] For instance, in 236 children aged 6–10 years, having a late bedtime, calculated with the median as a cut-point, was associated with poorer eating habits during weekdays, such as irregular breakfast consumption and increased snacking, compared to normal

sleepers.[25] Interestingly, sleep duration was not associated with neither breakfast consumption nor snacking habits.[25] Also, going to bed late may result in eating a late dinner, which in adults is suggested to delay the postprandial period and influence blood glucose and lipid levels.[26] However, this has not yet been investigated in children. Additionally, sleep as well as the circadian rhythm influence the levels of various hormones.[27] A delayed bedtime may cause a disrupted circadian rhythm and hormone secretion, which has been suggested to increase cardiometabolic risk.[27,28]

This study found that sleep duration and bedtime were associated with cardiometabolic risk in healthy nine-year-old Swedish children. Specifically, children who did not meet the sleep guidelines and went to bed late had a higher risk of impaired metabolic health compared to children who did meet the sleep guidelines and went to bed early. Our findings have important implications for researchers as well as parents, caregivers, educators and professionals working with children's health and health care. Clearly, future studies on sleep and cardiometabolic health in young children should take both sleep duration and bedtime into consideration. Furthermore, our findings suggest that it is important that caregivers establish consistent bedtimes aligning with current sleep guidelines for children, to minimise cardiometabolic risk. However, before such recommendations could be given to parents, more studies are needed in order to

identify the appropriate time points for going to bed. In the present study, a statistically significant sex interaction for insulin was observed. This result must be interpreted cautiously as it is the only interaction that was observed. The limited sample size in the present study does not allow us to stratify by sex, thus future studies are needed to investigate potential interactions by sex in the association of sleep with cardiometabolic outcomes in children. In addition, future studies including randomised controlled studies with larger sample sizes should investigate the interaction between sleep duration and sleep timing in more detail. Finally, our results will also serve as an important part of the scientific evidence base when developing future national and international guidelines on children's sleep behaviours as well as 24-hour movement behaviours. For instance, in 2019, the World Health Organisation published such 24-hour movement guidelines for younger children, 0–5 years.[29]

There are several strengths and limitations of this study that should be considered. First, sleep was objectively assessed with accelerometry, limiting errors that can arise when using self-report only. This study was further strengthened by the fact that children were measured within a narrow time frame, with a standard deviation of 0.1 years at 9.5 years of age. However, for some measures, the sample size of the group that did not meet the sleep guidelines but had an earlier bedtime was smaller than the other groups, which may have concealed possible true differences. A limitation of the current study is that the sample size of the children providing blood samples was low; however, it is important to note that the children that provided blood samples were representative of the whole SPINACH population. Moreover, in Swedish nine-year-olds measured in 2018 and 2019, 23% of girls and 22% of boys had overweight and about 9% of girls and 11% of boys had obesity.[30] In the current population, the prevalence of overweight and obesity was lower, 11% and 2%, respectively, which may limit the generalisability of the results. Nevertheless, associations between sleep and cardiometabolic risk factors in the current study were still evident, which highlights the importance of sleep on cardiometabolic health even in normal weight populations. In addition, the participating mothers had slightly higher education than the general Swedish population; however, all analyses were adjusted for maternal education. This study focused on the association between sleep and cardiometabolic risk factors, but other lifestyle behaviours, such as diet, may influence the participants' cardiometabolic health.[31] However, our adjustments for energy intake did not change the results. Finally, it should be noted that the observational design does not allow for causation inference on the observed associations and there is also a need for more research in this field, in particular with longitudinal study design.

5 | CONCLUSION

In this study, nine-year-olds meeting the sleep guidelines and going to bed early had better metabolic syndrome score, HOMA-IR and insulin level, compared to not meeting the guidelines and having a late bedtime. When adjusting for sleep time, the association to metabolic syndrome remained, suggesting that not only sleep duration but also bedtime has an overall impact on children's cardiometabolic health. This study underscores the importance of sleep duration and bedtime for children's cardiometabolic health and highlights the need for continued research in this area as well as the promotion of healthy sleep habits in children.

AUTHOR CONTRIBUTIONS

Ellinor Nilsson: Investigation; formal analysis; writing – original draft. **Christine Delisle Nyström:** Methodology; investigation; data curation; formal analysis; writing – review and editing. **Jairo H. Migueles:** Methodology; investigation; data curation; formal analysis; funding acquisition. **Hanna Baurén:** Data curation; writing – original draft. **Nuria Marin-Jimenez:** Data curation; formal analysis; writing – review and editing. **Maria Henström:** Investigation; writing – review and editing. **Lucía V. Torres López:** Data curation; formal analysis; writing – review and editing. **Marie Löf:** Conceptualization; methodology; investigation; supervision; funding acquisition; data curation; formal analysis; resources; writing – review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

ETHICS STATEMENT

All caregivers provided written informed consent and the Research and Ethics Committees in Linköping and Stockholm approved this study (Dnr: 2016/300–31; 2018/2220–32, respectively).

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SUPPORTING INFORMATION

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