Early life determinants of physical activity and sedentary time: Current knowledge and future research

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ABSTRACT

Previous findings of the association between low birth weight and subsequent health outcomes have led to the “developmental origins of health and disease hypothesis”. Furthermore, modifiable and partly modifiable early life factors may also influence behaviors such as physical activity and sedentary behavior. The aim of the present review was to summarize the existing knowledge on early life determinants (birth weight, rapid infant weight gain, motor development and infant temperament) of childhood physical activity and sedentary time, and suggest opportunities for future research based on the Mother and Child Cohort Study (MoBa). Inconsistent results have been observed when relating birth weight to later physical activity, likely explained by differences in methodology when assessing physical activity between studies. There is limited data on whether rapid weight gain in early life predicts later physical activity and few studies have examined the association between birth weight and infant weight gain with subsequent sedentary time. Motor development may be a predictor for childhood physical activity, however methodological limitations preclude firm conclusions. The association between motor development and sedentary time has rarely been examined. Conflicting results have been reported for the association between infant temperament and subsequent disease outcomes, suggesting that a life-course approach is necessary to more completely understand the development of some NCD (1,2). This has led to the “developmental origins of health and disease (DOHAD) hypothesis” (3,4), suggesting that many NCD at least partly have their origin in utero or during early life (4-6). The impetus to this hypothesis are findings suggesting an association between low birth weight, used as a marker of fetal growth restriction, and increased risk of cardiovascular diseases (2,7-9), hypertension (1,10) and type 2 diabetes (11,12). Additional research has linked both low and high birth weight to subsequent obesity (13), and rapid infant weight gain to hypertension (10), cardiovascular disease (14,15), clustering of metabolic risk factors in children (15,16) and obesity (17-20).

Factors early in life may also influence lifestyle behaviors, such as physical activity and sedentary time (21). This association is less well-explored. The main aim for many of the existing birth-cohorts, e.g. the Norwegian Mother and Child Cohort study (MoBa-study), is to study the development and determinants of diseases in the human population (22,23). However, birth-cohorts are also ideally suited to explore early life determinants of behaviors such as physical activity and sedentary time. Since these lifestyle behaviors are associated with beneficial health outcomes already in apparently healthy young people (24-28), increased knowledge about their potential early life determinants may provide valuable knowledge to aid future intervention programs and public health prevention strategies.

Recent data from relatively large cross-sectional studies suggest that total physical activity (24,29,30), and time spent in moderate-to-vigorous physical activity (MVPA) (26) are inversely associated with clustering of cardio-metabolic risk factors (i.e. blood pressure, insulin levels, glucose, fasting triglycerides, inverted high-density lipoprotein (HDL) cholesterol). Some of these studies have also shown that this association is independent of adiposity and other potential confounding factors (26,29). Furthermore, physical activity, and especially MVPA and vigorous physical activity (VPA), is inversely associated with adiposity (24,27,31,32) and waist circumference (26,31). However, most of the existing knowledge is based on cross-sectional observational studies and there is paucity of prospective data limiting the possibility to address temporal associations and indicating stronger inference...
for causality compared with cross-sectional studies. Whether time spent sedentary and sedentary behaviors are associated with health indicators is less consistent. Cross-sectional studies have suggested an association between objectively measured sedentary time and adiposity (27,31-33) and cardio-metabolic risk factors (26) in children. However, these associations were attenuated after further adjustment for physical activity, time spent in MVPA or VPA (26,27,31). In contrast, TV-viewing (a proxy for sedentary behavior) has been associated with risk factors for type 2 diabetes (29,34), although some have suggested the relationship may be mediated by adiposity (29). Taken together, it appears that specific sedentary behaviours, such as watching TV, is more closely related to health indicators than total amount of sedentary time (27,35). It has also been suggested that the association between time watching TV and adiposity is mediated by other behaviors, such as snacking while watching TV (27). Thus, some national authorities have proposed that screen time in youth should be limited to less than two hours per day (36,37).

According to the Norwegian Guidelines for Nutrition and Physical Activity children and youth are recommended to participate in at least 60 minutes of MVPA per day. Furthermore, children and youth are recommended to reduce sedentary time (38). In a nationally representative population from Norway in which physical activity was measured objectively, the prevalence of sufficiently active children and youth were 95.7% and 87% in 6 year olds, 86.2% and 69.8% in 9 year olds, and 58.1% and 43.2% in 15 year olds, boys and girls respectively (39). Longitudinal analysis showed that activity level declined from 9 to 15 years (39). Due to various definitions of MVPA when assessed objectively, the prevalence of sufficiently active children and youth (6 to 15 years) varies from 99.6% to 0.4% in comparable studies (40-46). Using a similar definition as adopted in the Norwegian youth, Owen et al. (46) suggested that 76% and 53% of 9-10 year old boys and girls, from a multi-ethnic district in England, met the recommended levels of physical activity. Whereas Pate et al. (43) suggested that no more than 11.8% of 12 year old girls from the US were active according to the recommendations for public health. It appears that boys are more physical active than girls (39,40,42,44-47), and that activity level declines with age (39-42, 47), also confirmed in longitudinal analysis (39,41). Children and youth from Norway, England and European countries spent between 376 and 576 minutes sedentary per day, when measured by accelerometry (39,44-46). In the Norwegian sample this corresponds to approximately 50% of the day (when the monitor is worn) in 6 year olds, whereas sedentary time exceeded 70% of the day in 15 year olds. Furthermore, girls appears to spend more time sedentary than boys in all age-groups (39).

Given the associations between physical activity and health outcomes in young people, and since children spend a substantial amount of time every day sedentary, it is important to identify factors (correlates and determinants) that potentially influence these lifestyle behaviors. A correlate refers to a factor associated with physical activity and sedentary time, however, the causality of the association is unclear (48). On the other hand, a factor that is associated with change in physical activity or sedentary time, from longitudinal observational research or randomized controlled trials, is defined as a determinant (48,49).

Several possible correlates and determinants of physical activity have been identified, including individual and biological (being boy, white ethnic origin), psychosocial (self-efficacy, perceived competence, perceived behavioral control), behavioral (previous physical activity) and environmental factors (walkability, little amount of traffic, proximity to homes and shops, residential density) (50,51). Less research has been conducted to identify possible determinants of sedentary time and behavior, and the evidence is inconclusive (52). Age, ethnicity and maturity have been related to sedentary time (53), whereas lower socioeconomic status, family and parental TV-viewing, lack of parental rules, number of TV and computers in household, TV in bedroom and unlimited screen time has been associated with sedentary behavior (53,54), although these associations may be less pronounced in younger children (≤7 years) (54). A positive association between parental TV habits and young girl’s daily TV time has also been observed in longitudinal analysis, which may suggest parental TV habits being a determinant of their daughter’s behavior (55).

Most of the research of correlates and determinants of physical activity and sedentary time have focused on behavioral and environmental factors, and there is a paucity of data on early life and biological determinants of these lifestyle behaviors. Therefore, the aim of the present narrative review is to summarize the existing knowledge on early life determinants (birth weight, rapid infant weight gain, motor development and infant temperament) of childhood physical activity and sedentary time, and suggest opportunities for future research.

**Methods**

In the present review we aimed to summarize the available knowledge on four potential early life determinants of later physical activity and sedentary time/behavior; birth weight, infant weight gain, motor development and infant temperament. A literature-search was performed in PubMed and PsycINFO. The following terms was included in the search: “birth weight”; “infant weight gain”, “motor development”, “infant temperament”, “early life determinants” in a combination with [AND] “physical activity”, “sedentary behavior”, “sedentary time” or “TV-viewing”. In addition, we examined the reference lists of all relevant articles to search for additional papers that met
the inclusion criteria.

We included English-written papers that specifically examined the defined early life factors’ associations with physical activity and sedentary time/behavior in a healthy population of children/adolescence up to the age of 18 years. One article (56) which examined the associations between birth weight and later physical activity in an older age group (14 to 74 years) was included because results presented in the younger age-group included adolescents (14 to 34 years).

In total, the literature-search resulted in eight papers (21,56-62) examining birth weight and physical activity and four studies (58,60-62) examining birth weight and sedentary time. Three studies (59,62,63) examined motor development in relation to physical activity, and one study (62) reported results on the association between motor development and sedentary time. Infant temperament’s was examined in relation to physical activity in one study (62), and sedentary time/sedentary behavior (TV-viewing) in two (62,64). All included papers were longitudinal observational studies. Two articles (56,61) used a retrospectively reported birth weight whereas all other papers included data on birth weight obtained at birth, either measured (21,57,58,60,62) or maternally reported shortly after birth (59,62). Motor development was parentally reported at the age 6 months (59) or 12 months (62,63). In the study by Thompson et al. (64) infant temperament was maternally reported at regular intervals from 3-18 months old, whereas in the study by Wijtzes et al. (62), infant temperament was parentally reported at the age 6 months. See Table 1 for summary of study designs and results.

**RESULTS AND DISCUSSION**

**Birth weight**

Animal experiments imply that under-nutrition in fetal life, followed by postnatal weight gain, is associated with reduced motor activity (65,66) and increased sedentary behavior (67). Some human data tend to support these observations. Individuals born pre-term with a very low birth weight (<1500g) (68,69), and extremely low birth weight (≤800g) (70), reported less participation in leisure time physical activity in adolescence and adulthood, compared to those born at term. However, this association may be mediated by lower cardio-respiratory fitness and/or lower muscle mass in those born prematurely. A meta-analysis of 13 cohorts (Table 1) suggested a reversed U-shaped association between birth weight and self-reported leisure time physical activity, however this association was no longer significant when stratified by gender and age-group (56). A particular strength of this meta-analysis is the large sample size including men and women varying in age and activity levels. However meta-analyzing results from different cohorts in which physical activity have been self-reported with different instruments is problematic and may introduce bias. One additional study suggested a weak but statistically significant positive association between birth weight and self-reported physical activity in 10-12 year olds from Pelotas in Southern-Brazil (21). In contrast, none of the studies in which physical activity was assessed by an objective method observed any association between birth weight and later physical activity (Table 1) (57-62). One of the studies (62) may have been limited in power since the low birth weight group (< 2500g), which was compared to the reference group (normal birth weight), only included nine participants. In addition, although physical activity and sedentary time were measured objectively, the accelerometer was only worn for two days, one weekday and one weekend day. Much stronger inference of a non-significant association between birth weight and physical activity comes from the Avon Longitudinal Study of Parents and Children (ALSPAC) which included 5058 children in which physical activity was objectively measured at age 11-12 years (59). The meta-analysis by Ridgway et al. (61) included four studies, three cohorts from Europe and one from Southern Brazil (Table 1). The combined meta-analysis confirmed previous observations and suggested no association between birth weight and later physical activity, but when cohorts were analyzed separately, the results from one of the cohorts (from Southern Brazil) suggested an association between higher birth weight and lower levels of physical activity and increased sedentary time, although attenuated after adjustment for gestational age. Taken together, it may be that the association between birth weight and subsequent physical activity is limited to those born with very low birth weight (68-70). Few studies have examined the associations between birth weight and sedentary time, and no association was observed (58,60-62). However, the studies by Pearce et al. (60) and Wijtzes et al. (62) may be limited by their definition of objectively measured sedentary time due to a remarkably high threshold. It is likely these studies misclassified a substantial amount of sedentary time as light intensity activity (71,72).

**Infant weight gain**

Low birth weight is usually associated with a rapid infant weight gain, as those who are born small or thin often compensate with a rapid postnatal weight gain (19). It has been suggested that postnatal and early childhood rapid weight gain, rather than birth weight and size at birth per se, is more strongly associated with subsequent health outcomes, particularly obesity (19,73). And it could be hypothesized that rapid infant weight gain promote subsequent adiposity (17-19), and contribute to lower levels of physical activity and increased sedentary time in youth. This is because adiposity appears to predict lower levels of physical activity (74,75). Hallal et al. examined infant weight gain with subsequent self-reported physical activity in 10-12 year olds (21), and objectively assessed physical activity and sedentary time in 13 year olds (58), from the Pelotas cohort study (Table 1). None of the defined
Table 1. Longitudinal observational studies examining the association between early life factors and physical activity and sedentary time/behavior in children/adolescents.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study population</th>
<th>Follow-up period</th>
<th>Exposure (assessment)</th>
<th>Outcome (assessment)</th>
<th>Summary of results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andersen et al. (56)</td>
<td>Nordic countries, 13 cohorts (n=43 482) 24 890 men, 18 592 women</td>
<td>Birth up to 74 years, Younger group, 14-34 years</td>
<td>Birth weight, maternally reported or measured (retrospective and prospective)</td>
<td>LTPA: self-reported (active/inactive)</td>
<td>Low birth weight and high birth weight was not associated with lower probabilities of being active when stratified by age-group and gender. (adjusted for gestational age, education, body mass index, smoking status)</td>
</tr>
<tr>
<td>Campbell et al. (57)</td>
<td>Kingston, Jamaica, The Vulnerable Windows Cohort Study (n=102)</td>
<td>Birth to 13 years</td>
<td>Birth weight, measured</td>
<td>PA: objectively assessed with Actigraph monitor</td>
<td>No association</td>
</tr>
<tr>
<td>Hallal et al. (58)</td>
<td>Southern Brazil, Pelotas-cohort (n=4453)</td>
<td>Birth to 10-12 years</td>
<td>Birth weight, measured, from birth-3months, 3 months, 6 months, 1 year and 4 years</td>
<td>PA and SED: objectively assessed with Actigraph accelerometer</td>
<td>A small positive association between birth weight and physical activity (p=0.05), crude analysis. No association between weight gain and physical activity or inactive lifestyle.</td>
</tr>
<tr>
<td>Hallal et al. (59)</td>
<td>Southern Brazil, Pelotas-cohort (n=457)</td>
<td>Birth to 13 years</td>
<td>Birth weight, measured, from birth-3months, 3 months, 6 months, 1 year and 4 years</td>
<td>PA and SED: objectively assessed with Actigraph accelerometer</td>
<td>No association</td>
</tr>
<tr>
<td>Mattocks et al. (59)</td>
<td>Avon, United Kingdom, ALSPAC (n=482)</td>
<td>Birth to 11-12 years</td>
<td>Birth weight, reported Ponderal index (kg/m²)</td>
<td>PA: objectively assessed with Actigraph accelerometer</td>
<td>No association</td>
</tr>
<tr>
<td>Pearce et al. (60)</td>
<td>Gateshead, England, GMS (n=482)</td>
<td>Birth to 8-10 years</td>
<td>Birth weight, measured</td>
<td>PA and SED: objectively assessed with Actigraph accelerometer</td>
<td>No association</td>
</tr>
<tr>
<td>Ridgway et al. (61)</td>
<td>4 studies: EYHS: European countries (n=1240) Roots: UK (n=811) Speedy: Pelotas: Southern Brazil (n=1647) Pelotas: Birthing Birth to 12-14 years</td>
<td>Birth weight, retrospectively maternally reported in EYHS, Roots and Speedy. Measured at birth in Pelotas.</td>
<td>PA and SED: objectively assessed with Actigraph (EYHS, Speedy, Pelotas and Actigraph (Roots)</td>
<td>No association in the combined analysis</td>
<td>No association</td>
</tr>
<tr>
<td>Wijtzes et al. (62)</td>
<td>Rotterdam, Netherlands, The Generation R (n=347)</td>
<td>Birth to 2 years</td>
<td>Birth weight, from delivery reports or maternally reported 2 months post-partum</td>
<td>PA and SED: objectively assessed with uniaxial Actigraph accelerometer.</td>
<td>No association</td>
</tr>
<tr>
<td>Mattocks et al. (59)</td>
<td>Avon, United Kingdom, ALSPAC (n=482)</td>
<td>Birth to 11-12 years</td>
<td>6 months: maternally reported motor coordination, combined score</td>
<td>PA: objectively assessed with Actigraph accelerometer (average cpm)</td>
<td>Motor coordination at 6 months associated with PA at 11-12 years. β (95%CI): 0.7(0.25,11.29), p=0.041 (adjusted for sex, age, parental social class, mothers education).</td>
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<tr>
<td>Ridgway et al. (63)</td>
<td>South Korea: Unaided PE grade, participation in number of different sports and frequency of sports participation per week</td>
<td>Birth to 12 years</td>
<td>Age at walking supported (months) associated with frequency of sports participation</td>
<td>Age at standing unaided (months) associated with PE grade -0.06(-0.09,-0.04) (adjusted for sex, gestational age, birth season, fathers’ social class, birth weight and BMI).</td>
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<tr>
<td>Wijtzes et al. (62)</td>
<td>Rotterdam, Netherlands, The Generation R (n=347)</td>
<td>Birth to 2 years</td>
<td>12 months: maternally reported gross motor development,Minnesota Infant Development Inventory.</td>
<td>PA and SED: objectively assessed with uniaxial Actigraph accelerometer.</td>
<td>Crude analysis: Association β (95%CI) between delayed motor development and sedentary time 1.20(2.2,3.3), and inverse association with MVPA and total PA, -0.71(1.2,-0.1) and -46.2(-83.3,-9.2) respectively. No association after adjustment for sex, age, number of siblings and season</td>
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weight-gain periods were associated with physical activity (21,58) or sedentary time (58). However, it is possible that early life factors influence lifestyle behaviors differently in developing and developed countries, although this has rarely been explored.

**Motor development**

During the first year of life movement capabilities changes dramatically and the infant achieve several developmental motor milestones, e.g. sitting alone, crawling, standing unaided and eventually walking (76). Stooden et al. (77) hypothesized that physical activity in early childhood is driven by their development of motor skills. Suggesting that early motor development is associated with physical activity, which further influences motor skills, and a positive spiral occurs. Infant motor development has been associated with physical performance at age 31 years (78), and standing balance, chair raising (79) and handgrip strength (80) at age 53 years. Ridgway et al. (63) examined the association between age at reaching certain developmental milestones and self-reported sport participation at age 14 (Table 1). Age at walking supported was associated with higher sport participation (PE grade, frequency of sport participation, participation in number of different sports), and earlier age at standing unaided was associated with higher physical education (PE) grades. However, these results did only consider self-reported sport participation and PE grades and it is likely children may be active without participating in sports. Further, it is unclear whether PE grades are a good proxy for habitual physical activity. Mattocks et al. (59) found an association between motor coordination at six months and overall physical activity in 11-12 year olds, after adjustment for age, sex, parental social class and maternal education. A major strength of this study was the inclusion of objectively measured physical activity in a large sample of well characterized children. Although the observed associations in these two studies were statistically significant, the magnitudes of associations were relatively small (59,63) (Table 1). Wijtzes et al. (62) examined the association between birth weight, infant temperament and motor development with subsequent objectively assessed physical activity and sedentary time in 2 year olds. The univariate analysis showed a positive association between delayed motor development and sedentary time, and an inverse association between delayed motor development and physical activity. However, the associations were attenuated after adjustment for sex, age, number of siblings and season, and it is a possibility that the sample size were too small to detect any meaningful associations in multivariate analysis. Taken together, there is a tendency that motor development influence subsequent physical activity, however some studies are limited by methodology, e.g. physical activity measurement (63) and relatively small sample size (62). Additional high quality studies are therefore needed to provide sufficient evidence whether early motor development act as a determinant of childhood physical activity and sedentary time.

**Infant temperament**

Temperament refers to biologically based individual differences in behavioral style (affect, activity and attention), i.e. the characteristics of an individual’s emotional nature (81). Infant temperament may be associated with infant weight gain (82-85), and temperament in early childhood appears to be associated with overweight and obesity later in life (86). Cross-sectional (87) and longitudinal data (88) from the MoBa-study, suggest that 18 months old infants who were perceived as sad, anxious, deficient and aggressive were more likely to be given sweet foods and sweet drinks in infancy, at 3 years and 7 years. It has been suggested that the TV (64) and additional feeding (82, 85) are used to soothe and entertain the child, and that the TV is used as a “babysitter” (64). Wijtzes et al. (62)
were born thin or small (>). Exercising regularly and with moderate intensity had a
Erikson et al. participating in at least 25 min of leisure time VPA per
and metabolic syndrome was attenuated in men parti-
ag
between ponderal index at birth (kg/m
2) appears associated with later health outcomes
DETERMINANTS AND HEA
ASSOCIATIONS BETWEEN
status and other parental factors.
may be mediated or confounded by socio-
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life factors with obesity and cardio-
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future studies are needed to explore the role of
physical activity and MVPA on these associations.

DOES PHYSICAL ACTIVITY MODIFY THE
ASSOCIATIONS BETWEEN EARLY LIFE
DETERMINANTS AND HEALTH OUTCOMES?
Since birth weight and rapid weight gain in infancy
appears associated with later health outcomes (7,15-
20), the question arises whether physical activity act as
a modifier on the association between birth weight,
accelerated weight gain in infancy and childhood clus-
tering of cardio-metabolic risk factors and adiposity.
Laaksonen et al. (89) examined whether self-reported
physical activity alleviate or attenuate the association
between ponderal index at birth (kg/m²), low birth
weight and risk for metabolic syndrome in middle-
aged men. The association between low birth weight
and metabolic syndrome was attenuated in men parti-
cipating in at least 25 min of leisure time VPA per
week. Similarly results was observed in a study by
Erikson et al. (90) in elderly (aged 65 to 75 years).
Exercising regularly and with moderate intensity had a
protective effect on glucose intolerance in those who
were born thin or small (>3000g). Physical activity
was assessed by self-reports in both studies (89,90).
Two studies have examined the modifying effect of
objectively assessed physical activity on the association
between birth weight and health outcomes in youths,
with contrary results (91,92). Ortega et al. (91) sugges-
ted that being classified as active (physical activity
level above median) attenuated the association between
low birth weight and markers of insulin resistance in
adolescence. On the other hand, Ridgway et al. (92)
found no modifying effect of total physical activity
and MVPA on the association between birth weight
and fat mass index (FMI = fat mass [kg/height [m²]])
and waist circumference in 9 to 15 year olds. Further-
more, adjustment for physical activity and MVPA
made little changes to the association between low
birth weight and insulin resistance. None of the iden-
tified studies have adjusted for gestational age (89-92),
which may be an important confounding factor (61).
Due to conflicting results in the two studies examining
the modifying effect of physical activity on the associ-
ation between birth weight and health outcomes in
youth, future studies are needed to explore the role of
physical activity and MVPA on these associations.

FUTURE DIRECTIONS
Physical activity and sedentary time are complex beha-
viors determined by several factors throughout life
(50), and it is possible that also partly modifiable
factors acting during the first years of life influence
physical activity level and sedentary behaviors in
youth. Well characterized birth cohorts are ideally
suited to further explore this hypothesis and whether
physical activity modify the associations between early
life factors with obesity and cardio-metabolic risk fac-
tors in youth. The MoBa cohort study is perfectly placed
to provide a valuable addition to existing research.
The MoBa study is a prospective population-based
pregnancy cohort run by the Norwegian Institute for
Public Health (NIPH) (23). The objective of MoBa is
to study the causes of disease among mothers and
children. All women in Norway who gave birth at
maternity units with more than 100 births annually
were invited, and 38.5% consented to participate. The
participants were recruited during gestational week 18,
and mother and child are followed-up regularly with
postal questionnaires (23). In total, the cohort includes
108 000 pregnancies from the inclusion period between
1999 and 2008. Data on weight and length are avail-
able at birth and with regular intervals up to the age of
7 years. The mothers were asked to copy data from the
children’s personal health chart when reporting
length/height and weight in the questionnaires. Infant
temperament was habitually reported at age 6 months
and motor development; e.g. age at walking and stand-
ing unaided, were habitually reported at 18 months
by standardized questionnaires. The children’s leisure
time physical activity and sedentary behavior were
maternally reported at age 7 years. The mothers were
asked about their child’s leisure time physical activity as frequency and hours per week, and hours per day using TV, DVD, electronic games or computer. At present almost 36 000 mothers have answered the 7-year follow-up questionnaire. In addition to the self-reported questionnaire data, a sub-cohort including randomly selected children born between July 2002 and December 2003 is currently underway. The sub-cohort (approximately 500 participants) will provide data on objectively measured physical activity and sedentary time (by accelerometer, Actigraph GT3X+) and anthropometry (height, weight, waist circumference and body composition). The objectively measured physical activity and sedentary time from the sub-cohort can be used to replicate the findings from the questionnaires, and will therefore contribute to strengthening the inference from the results obtained by self-report. By using this data from the MoBa we can further examine the research questions on the associations between early growth, motor development and infant temperament with physical activity and sedentary time/behaviors in 7 and 10-12 year old children.

**CONCLUSION**

There is insufficient evidence to conclude whether any of the included early life factors predicts childhood physical activity and sedentary time. Few studies including a wide variety of possible early life determinants are available, and some are limited by their methodology. Therefore, additional research on possible determinants of physical activity and sedentary time using data from well characterized birth-cohorts are needed to inform evidence based public health interventions.

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