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Physical activity of children in the "Childhood Obesity Project" trial

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1. Abbreviations

BMI	Body mass index
CHOP	Childhood Obesity Project
FMI	Fat mass index
PA	Physical activity
SB	Sedentary behavior
MVPA	Moderate-to-vigorous physical activity
KA	Körperliche Aktivität
ST	Sitzende Tätigkeit

2. Publications

This thesis consists of the following publications:

Publication I:

Physical Activity and Sedentary Behavior From 6 to 11 Years.
Schwarzfischer, P., Gruszfeld, D., Stolarczyk, A., Ferre, N., Escribano, J., Rousseaux, D., Moretti, M., Mariani, B., Verduci, E., Koletzko, B., Grote, V. *Pediatrics,* 2019, 143(1): e20180994.

Publication II:

Longitudinal analysis of physical activity, sedentary behaviour and anthropometric measures from ages 6 to 11 years.
Schwarzfischer, P., Gruszfeld, D., Socha, P., Luque, V., Closa-Monasterolo, R., Rousseaux, D., Moretti, M., Mariani, B., Verduci, E., Koletzko, B., Grote, V. *The International Journal of Behavioral Nutrition and Physical Activity,* 2018; 15(1): 126.

3. Introduction

In the last decades, there was a steady progress in information technologies and entertainment electronics, which substantially influence our daily life. These inventions especially affect our daily movement behavior, which consists of physical activity (PA) and sedentary behavior (SB) during waking hours. In adulthood, office work is dominated by SB and a limited amount of PA. An extended duration of education (school, university) shapes the time spent in PA and SB in childhood and adolescence. Long sitting hours have become the norm. Additionally, leisure time and commuting are spent predominantly in sitting positions. This led to a substantial increase of physical inactivity, which plays a major role in the worldwide epidemic of non-communicable diseases [1]. Lee et al. estimated on basis of an extensive literature review that physical inactivity is responsible for 6-10% of major worldwide non-communicable diseases [2]. As a result of this contribution to global disease, physical inactivity is responsible for a substantial economic burden [3]. Despite this alarming evidence, large proportions of the world's population remain inactive [4]. To fight this epidemic, it is a major public health interest to promote PA and to reduce SB [5]. Since PA showed strong tracking into adulthood [6] promotion of PA in childhood and adolescence is especially important.

PA and SB in childhood are characterized by changes with age. During preschool age, motor development is ongoing and everyday life offers many possibilities for movement. During this period, parents have a great impact on their child's PA and SB [7]. In primary school age, children start to sit on a regular basis during school hours and with the start of adolescence SB during school hours further increases. With increasing age, peer groups start to play the major role in PA engagement during leisure time [8].

Due to this transient period of different influencing factors, it is important to understand the development of PA and SB in each age period to ensure an effective intervention planning. So far, school-based interventions are thought to be the most effective way, as the biggest decline of PA is happening during this time when children spent most of their time in school [9]. In the last years the focus shifted towards younger age groups, targeting both parents and their children. This is a promising approach for increasing preschoolers' PA [10]. In order to improve intervention quality and to identify the best age period to tackle the problem of extensive physical inactivity, continuous measurements and quantification of PA and SB is needed.

Measurement methods of physical activity and sedentary behavior

Measurement of PA started in the late 1960s and early 70s. First methods relied on unstandardized recall questionnaires in epidemiologic studies [11]. The comparison of activity levels in different populations was difficult and recommending an appropriate amount of PA per day was not possible. First standardized questionnaires – the international PA questionnaire and later the global PA questionnaire – were developed in the late 1990s [12, 13]. These standardized methods helped greatly in the development of today's PA guidelines. Those recommend a daily amount of 30 min per day in PA for adults and 60 min in moderate-to-vigorous PA (MVPA) for children from 5 to 17 years of age [14, 15].

When looking at these guidelines, the problem of quantifying intensity levels of PA becomes apparent. PA is commonly classified into three intensity levels: light PA, moderate and vigorous PA. The latter two are often combined into moderate-to-vigorous PA. However, cut-offs for these intensity levels are not standardized and thus remain rather ambiguous. A common classification is done by the use of metabolic equivalents of task. One metabolic equivalent of task is defined as metabolic energy expenditure during one minute of sitting activity. Different activities are classified based on this reference level and summed in different compendiums [16, 17]. It is being discussed if this definition for metabolic equivalents of tasks holds true for children [18]. Their metabolism can differ substantially from adults, resulting in different cut-offs for intensity levels of PA. An adaption of cut-offs for children was developed, but is not applied throughout studies [19, 20].

In order to measure PA by questionnaire, the above mentioned biological definitions of intensity levels have to be transferred into subjective categories. Therefore, intensity levels are generally described by subjective "symptoms" and feelings, which are transferred into semantic expressions (e.g.: "moderate-intensity activity: causes small increases in breathing or heart rate" [21]) or scales (e.g.: the Borg scale [22]). A limitation of this approach is the dependence on the subject's experience or attitude towards PA [23]. Additionally, when answering a questionnaire about their activity levels, people tend to answer more positively, which results in an overestimation of PA levels [24]. Despite these caveats of PA questionnaires, they remain a valid tool for assessing context-specific activities, like time spent in front of a screen.

From the 1980s onwards device-based measures with the help of accelerometer technology were progressively developed and adapted in order to objectively asses PA and SB levels [25]. These devices measure with the assumption, that PA equals a certain acceleration of the body. This acceleration is recorded and cut-offs for intensity levels are developed in validation studies based on different activities [25]. This method eliminates the recall bias and social desirability of answers in PA questionnaires. Furthermore, this method enables continuous monitoring over several days, giving measurements of volume of total daily PA and SB. Even though device-based measurements produce more consistent results than questionnaires, they have also some limitations [26]. The acceleration specific cut-offs – reflecting the biological defined intensity levels of PA – are not standardized across studies [19]. This limits the comparability across study populations and overall objectivity, as the choice of cut-off to define intensity levels is up to each researcher [18]. Additionally, with common accelerometers it is difficult to take into account weight bearing activities, posture of the user and movement of different body parts [27]. In order to improve quality of measurement, devices were developed, which combine accelerometers with additional sensors. These include e.g. posture measuring, heart rate, body temperature and heat flux [28]. With the additional data from these sensors the assessment of energy expenditure can be improved by applying activity-specific algorithms. However, cut-off determination for intensity levels often remains a problem.

In summary, there are three different kinds of measurement: device based accelerometry, multi-sensor devices and questionnaires. They can be used for different study outcomes (MVPA, light PA, screen time, overall daily SB) and research questions.

Outline of this doctoral thesis

In this work, I investigate PA and SB in children from 6 to 11 years and their association to anthropometric measures. Previous studies have shown that PA and SB play a key role in the prevention of overweight and obesity in children [29-31]. I use longitudinal data to investigate the development of PA and SB and its associated factors. This time dependent analysis gives useful insight for intervention planning, as to identify the best time point to intervene. Further, I investigate associations of PA and SB with anthropometrics with the hypothesis that the amount of activity or inactivity influences the energy expenditure and subsequently the body weight of children. Additionally, I will look at possible bi-directional effects of PA and SB with anthropometrics. There is no clear consensus in the literature whether PA and SB influence anthropometrics or if a specific body size predispose specific activity levels.

Data is drawn from the “Childhood Obesity Project” trial (CHOP), a European multicenter double blind randomized control trial. Healthy term infants were recruited at birth and randomized either into higher or lower protein content formula [32-34]. An additional observational breastfed group was recruited. Possible effects of the intervention are tested and all analyses were accounted for intervention type. The three publications, research questions, and statistical approaches will be outlined in more detail in the following.

Publication I + II – Development of PA and SB in primary school age and its association with anthropometric measures

High levels of childhood overweight and obesity are an important public health problem worldwide. The latest fact sheet from the World Health Organization’s Childhood Obesity Surveillance Initiative shows that prevalence of overweight and obesity amongst preschool children can reach up to 43% in certain European countries [35]. Childhood obesity is related to many co-morbidities and adverse health outcomes in later life [36, 37]. Obesity and overweight is caused by an energy imbalance between calories consumed and calories expended [38, 39]. One way to change this imbalance is altering the energy expenditure by being physical active [40]. Subsequently it is hypothesized that an inactive lifestyle can lead to an increase in weight, whereas high levels of PA could reduce body size. Various studies have shown an association of PA and SB with anthropometric measures [29, 31, 41]. However, it is not clear whether PA and SB influence anthropometric markers like BMI and FMI or if higher weight or body fat percentage lead to lower levels of PA [42]. Understanding these bi-directional effects is necessary for an adequate public health planning. Additionally, research in activity levels of children and its change over time could bring insight, when to intervene by increasing PA levels and reducing SB in order to prevent childhood obesity. For example, a study by Basterfield et al. found an earlier onset of PA decrease and SB increase than most invention studies assume. Therefore, research questions for the two papers of my thesis were: 1) How does total PA, MVPA, LPA and SB change from 6 to 11 years and which factors are associated with this age development? 2) Are there associations between total PA, light PA, MVPA, SB and the development of body mass index (BMI) and fat mass index (FMI) from 6 to 11 years of age? 3) Do bi-directional effects between body size and PA and SB occur?[43, 44]

In the CHOP trial, physical activity was measured at the ages 6, 8 and 11 years with the Sensewear Armband 2, a reliable device-based tool for the assessment of PA and SB in children [45-47]. The longitudinal setup of the study and the long-term follow-up to the age of 11 years provided an optimal basis for an examination of PA and SB during the course of school age.

The key findings are that total PA showed a steady decline and SB a steady increase between the ages of 6 to 11 years. The development in intensity levels of PA showed sex differences: Boys showed higher levels of MVPA and girls higher levels of LPA. Total PA and SB showed no sex differences. Higher time in SB was associated with an increased BMI during preschool age, regardless of time spent physical active. However, associations with anthropometric measures and PA and SB were bi-directional: PA and SB were associated with a different body size and body size was associated with different levels of PA and SB.

With regard to the research questions I can conclude: 1, There is a clear decline of PA and increase of SB from preschool age onwards. This implicates that activity levels of children should be tackled by interventions as early as possible, when levels of activity are still high. 2, The consistent associations of SB with higher BMI indicate that a reduction of sitting activities might play an important role in the prevention of obesity. 3, In the light of the present bi-directional associations and the fact that results are from an observational study, the role PA and SB play in the development and prevention of childhood obesity is not clear yet and more research is needed.

Introduction summary

The overreaching aim of this doctoral thesis is to contribute to our understanding of the development of PA and SB in childhood and explore its associations with anthropometrics measures. To accomplish this, different analysis with different measurement methods have been performed. A time-dependent analysis of objectively measured PA and SB was performed to explore growth curves and influencing factors in primary school age. These results can be useful for practitioners to get a sense of normal development of PA and SB in childhood. Additionally, associations of overall daily PA and SB with anthropometric measures are looked at. This analysis follows the hypotheses, that the amount of activity or inactivity influences the energy expenditure and subsequently the body weight of children. The insights gained from this analysis add to the body of knowledge about which role PA and SB play in the development and prevention of childhood obesity.

4. Summary

Objectives:

Daily movement behavior during childhood has a great influence on children's present and later health status. Higher levels of physical activity (PA) and less time spent in sedentary behavior (SB) during early life are positively associated with activity levels in adulthood. An adequate amount of PA and a reduction of inactivity could contribute to the prevention of childhood overweight and obesity. In this thesis, I investigated PA and SB in children from 6 to 11 years of age to gain a better understanding of the extent of change in PA and SB and its association with anthropometric measures.

Subjects/Methods:

The data used in this thesis were drawn from the European Childhood Obesity Project trial (CHOP), which was conducted in five European countries. The *SenseWear* Armband 2 was used to measure PA and SB at the ages of 6, 8 and 11 years. The children's weight, fat mass and height were assessed at each time point and anthropometric measures body mass index (BMI) and fat mass index (FMI) were calculated.

Results:

Total PA and moderate-to-vigorous PA (MVPA) showed a significant quadratic decline with age (PA: -75.3 min/day, $p < 0.001$; MVPA: -30.7 min/day, $p < 0.001$). The amount of SB increased significantly in the same timeframe (+107min, $p = 0.001$). Boys showed a steeper decline in light PA ($p = 0.003$) and MVPA ($p < 0.001$) than girls. Higher levels of total PA and MVPA (predictor) were consistently associated with lower BMI and FMI (outcome) and higher SB with higher BMI and FMI. When looking at the age dependent effects, negative associations of MVPA ($p = 0.007$) and positive associations of SB ($p < 0.001$) with BMI increased with each year of age. In a reversed model, a higher BMI or FMI (predictors) showed a negative association with MVPA and a positive association with SB (outcomes), but no age interactions were found.

Conclusions:

In this thesis, I showed that PA decreased and SB increased as early as six years. Sex differences in intensity levels of PA were prominent. Throughout childhood, daily SB was consistently associated with a higher BMI, regardless of time spent physical active. These results emphasize the need to tackle SB by activity interventions as early as possible. An integrated approach of reducing SB by replacing it with PA seems appropriate. Based on our results, the choice of intensity of PA in interventions should not be based on effects on anthropometric measures, but rather the sex of the target group.

5. Zusammenfassung

Ziele:

Das tägliche Bewegungsverhalten in der Kindheit hat einen großen Einfluss auf die momentane und zukünftige Gesundheit von Kindern. Ein höheres Niveau an körperlicher Aktivität (KA) und weniger Zeit in sitzenden Tätigkeiten (ST) während den ersten Lebensjahren ist positiv mit dem Bewegungsverhalten im Erwachsenenalter assoziiert. Zudem kann ein adäquater Umfang an KA und eine Reduktion von Inaktivität zur Prävention von kindlichem Übergewicht und Adipositas beitragen. In dieser Arbeit untersuche ich sowohl KA als auch ST bei Kindern vom 6. Bis zum 11 Lebensjahr, um ein besseres Verständnis für die Veränderung des Bewegungsverhaltens während der Kindheit zu erhalten. Ein weiteres Ziel ist es, mögliche Assoziationen mit anthropometrischen Messgrößen zu untersuchen.

Methoden:

Die Daten für diese Arbeit stammen aus der europäischen Childhood Obesity Project Studie (CHOP), die in fünf europäischen Ländern durchgeführt wurde. Der Umfang an KA und ST wurde mit sechs, acht und elf Jahren mit Hilfe des Sensewear Armbands 2 gemessen. Gewicht, Fettmasse und Größe der Kinder wurden den jeweiligen Messzeitpunkt erhoben und die anthropometrische Messgrößen body mass index (BMI) und fat mass index (FMI) berechnet.

Ergebnisse:

Die gesamt-KA und moderate bis intensive KA zeigte einen quadratisch abfallenden Verlauf mit steigendem Alter (KA: -75.3 min/Tag, $p < 0.001$; moderate bis intensive KA: -30.7 min/Tag, $p < 0.001$). Der Umfang an ST stieg im selben Zeitraum signifikant an (+107min, $p = 0.001$). Jungen zeigten einen steileren Abfall an leichter KA ($p = 0.003$) und moderate bis intensive KA ($p < 0.001$). Ein höheres Niveau an gesamt-KA und moderate bis intensive KA (als unabhängige Variablen im Model) waren durchgehend mit einem niedrigeren BMI und FMI assoziiert, wohingegen mehr ST mit einem höheren BMI und FMI assoziiert war. Bei der Betrachtung von alters-abhängigen Effekte, war zu sehen, dass sich die negativen Assoziationen von KA ($p = 0.007$) mit BMI und die positiven Assoziationen von ST ($p < 0.001$) mit BMI mit jedem zusätzlichen Lebensjahr vergrößerten.

Schlussfolgerungen:

In dieser Arbeit konnte ich zeigen, dass bereits ab dem 6. Lebensjahr die KA abnimmt und ST zunimmt. Geschlechterunterschiede im Intensitätsniveau der KA waren sichtbar. Im Verlauf der Kindheit war ST durchgehend mit einem höheren BMI assoziiert, unabhängig von der KA im selben Zeitraum. Diese Ergebnisse unterstreichen die Notwendigkeit übermäßige Sitzzeiten so früh wie möglich mit Interventionen zu bekämpfen. Ein integrativer Ansatz, bei dem ST durch KA ersetzt wird, erscheint dabei am sinnvollsten. Das Intensitätsniveau der KA sollte sich dabei nicht an den Effekten auf anthropometrische Messgrößen orientieren, sondern an dem Geschlecht der Zielgruppe.

6. Publication I

Physical Activity and Sedentary Behavior From 6 to 11 Years

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abstract

OBJECTIVES: Physical activity (PA) is presumed to decline during childhood and adolescence, but only few long-term studies about PA development during this period of life exist. We assessed PA and sedentary behavior (SB) over a 5-year period to gain a better understanding of the extent of change in activity and potential influencing factors.

METHODS: PA and SB of 600 children from the Childhood Obesity Project were objectively measured with the SenseWear Armband 2 at the ages of 6, 8, and 11 years, resulting in 1254 observations. Longitudinal changes of total PA, moderate-to-vigorous physical activity (MVPA), light physical activity (LPA), and SB were modeled with mixed-effects models.

RESULTS: Total PA revealed a significant quadratic decline with age ($P < .001$), resulting in a change of total PA by −75.3 minutes per day from 6 to 11 years. LPA linearly declined ($P < .001$) by 44.6 minutes per day, MVPA quadratically declined ($P < .001$) by an overall 30.7 minutes, whereas SB increased significantly (+107 minutes; $P = .001$). Boys showed a steeper decline in LPA ($P = .003$) and MVPA ($P < .001$) than did girls. Higher fat mass index and BMI *z* scores were associated with lower levels of total PA and MVPA and higher levels of SB (all $P < .001$).

CONCLUSIONS: We showed that PA decreased, and SB increased in earlier years than previously thought. MVPA remained relatively stable until 8 years, but revealed a drop-off at 11 years, identifying this period as a crucial time for intervention.

FREE

WHAT'S KNOWN ON THIS SUBJECT: Physical activity and sedentary behavior are thought to decline with the start of adolescence. Decline can be influenced by biological or environmental factors. Low levels of activity during childhood can be the cause of the increasing inactivity in adults.

WHAT THIS STUDY ADDS: In our study, the decline of physical activity and increase of sedentary behavior started well before adolescence. The only major influencing factors were sex, country, and body size. Interventions to prevent inactivity might need to focus more on younger children.

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Mr Schwarzfischer analyzed the data and drafted and finalized the manuscript; Dr Gruszfeld, Ms Stolarczyk, Dr Ferre, Dr Escribano, Ms Rousseaux, Ms Moretti, Ms Mariani, and Dr Verduci conducted the study, entered data at study sites, and critically reviewed the manuscript; Dr Koletzko designed the research and critically reviewed the manuscript; Dr Grote designed the research, participated in the data analysis, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

This trial has been registered at www.clinicaltrials.gov (identifier NCT00338689).

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An increase of sedentary behavior (SB) and lack of physical activity (PA) is connected to a number of noncommunicable diseases worldwide.[1,2] Because of the continuance of PA and SB from childhood into adulthood,[3] the transition period from childhood to adolescence is the focus of many PA interventions.[4,5]

A natural and biologically determined decline of total PA throughout the life span seems likely.[6] This decline is also represented in recommendations from the World Health Organization (WHO): preschool-aged children should accumulate a minimum of 180 minutes per day of total PA, children and adolescents (4–17 years old) at least 60 minutes per day, and adults only a minimum of 30 minutes per day in moderate-to-vigorous physical activity (MVPA).[7] For a long time, the prevailing opinion about the development of total PA and SB in youth was that the steepest decline of total PA happens between 12 and 18 years.[8,9] Authors of recent studies, however, suggest that an early decline of total PA already starts at 6 years of age.[10,11] Most of these longitudinal studies are focused on total PA and MVPA, excluding light physical activity (LPA) and SB.[12–15] The analysis of SB has become more important because of the massive increase in sitting activities in children over the last decades.[16] The development of accelerometers has made it possible to measure SB and LPA as separate behaviors and has changed the understanding of LPA and its influence on health.[17] MVPA is thought to have a higher impact on health, but far longer periods of time are spent on LPA. Yet reliable data of LPA levels and development in children are scarce.

To get deeper insight into the origins of activity and inactivity, prospective studies are needed in which authors differentiate between intensity levels and identify influencing factors.[18] Most studies used to look at influencing factors of PA and SB are cross-sectional, precluding statements about causal relationships.[19] Evidence from longitudinal studies will give better insight into potential causal relationships and will thus improve the target selection of interventions. The aim of this study, therefore, is to analyze the change of total PA, MVPA, LPA, and SB from 6 to 11 years and to identify factors that influence this development with age.

METHODS

Study Subjects and Design

The underlying sample of children is part of the Childhood Obesity Project (NCT00338689). The design and results of this European double-blind, randomized controlled trial are reported elsewhere.[20] Briefly, 1678 infants, who were born between October 2002 and July 2004, entered the trial during their first 8 weeks of life. Children were randomly assigned to 2 formula-fed groups, with either a lower or higher protein content for the first year of life. Additionally, an observational group of children who were exclusively breastfed was included. The aim was to test whether early protein intake predicts infant growth and later risk of childhood obesity.

Data for this analysis were collected during the 6- (time point 1; T1), 8- (time point 2; T2), and 11- (time point 3; T3) year follow-up examinations. Data collection was performed in the following 5 European countries: Germany, Italy, Belgium, Poland, and Spain. The sample for the following analysis combines intervention and control groups into a single longitudinal cohort, treating possible intervention effects as a covariate. The trial was approved by the ethics committee in each study center, and informed consent was obtained from parents and children. All research was performed in accordance with the Declaration of Helsinki.

Activity Assessment (Outcome Variable)

PA was measured with the SenseWear Armband 2 (BodyMedia, Inc, Pittsburgh, PA). The device is worn over the right triceps muscle and incorporates 5 sensors: 2-axis accelerometer, galvanic skin response, skin temperature, near–body temperature sensor, and heat flux.[21] Following the study protocol, children were told to wear the armband on 3 consecutive days for at least 20 hours per day. The data processing was done with the Professional InnerView Software 6.1 (BodyMedia, Inc), already described elsewhere.[22] Briefly, total PA was categorized into the following 2 groups on the basis of recommendations by Trost et al[23]: LPA (1.5–3.9 metabolic equivalents of task) and MVPA (≥4 metabolic equivalents of task). Time spent in activity <1.5 metabolic equivalents of task (minus the time lying down and sleeping) was considered to be SB. Studies have revealed that the SenseWear Armband is a valid tool to measure energy expenditure (EE) and PA in children and adolescents.[24,25]

Time-Varying Covariates

Weight and height were measured during each follow-up visit at the study sites. Standard operating procedures relied on the WHO's Multicentre Growth Reference Study.[26] BMI (weight [kilograms] divided by height [meters squared]) was transformed into BMI *z* score (zBMI), adjusted for sex and age according to the WHO growth standards.[26] Body fat mass and fat mass index (FMI) (total body fat mass [kilograms] divided by height [meters squared]) were calculated from bioelectrical impedance assessed in duplicate with the octopolar Tanita BC-418 (Tanita Corporation, Tokyo, Japan). This has been validated for use in children.[27]

Time Invariant Covariates

In addition to sex and study country, data from parents were collected during the initial study visit. The educational status of parents was assessed with the help of the International Standard Classification of Education 1997 levels and defined as low (level 0–3), middle (level 3–4), and high (level 5–6); it included the highest education level of both parents.[28] Housing type was asked and defined as either house (free standing or semidetached) or flat (flat, maisonette, or apartment). Additionally, the prepregnancy BMI of mothers was calculated from self-reported prepregnancy weight and on-site measurements of height after study recruitment. Family status (single mother or living with partner) and smoking during pregnancy were assessed at the initial study visit. At 11 years, puberty status was assessed with the "Pubertal Development Scale" and categorized as "pre-pubertal" and "pubertal."[29]

Data Analyses

Data are reported as mean and SD for continuous variables and as number (*n*) and percentage (%) for factors. Differences in accelerometer measurement participation rate were calculated with χ^2 tests and Student's *t* tests. Observations are defined as 1 accelerometer measurement of each child at 1 of the 3 time points. Observations at any of the 3 time points with just 1 day of recording were excluded. Observations with 2 days of recording revealed no differences to observations with 3 or more days and were therefore kept for analyses.

For each outcome variable, total PA, MVPA, LPA, and SB, mixed models with an individual random intercept and random slope for age were used. Age was centered to the lowest age of any participant (5.89 years) and was included in all models with a quadratic term to analyze the development of outcomes over time. Covariates were entered separately, and all models were optimized by maximum likelihood estimation and likelihood ratio tests for the best model fit.

Because residuals of MVPA models were not normally distributed, MVPA was log transformed for mixed-model analysis and later back transformed for interpretability. For the LPA model, the quadratic age term was removed, because it worsened the model fit. Each model 1 was calculated as the minimal adjusted model, with factor covariates sex (2 levels) and study country (5 levels) added as fixed effects. Country and sex were tested as random factors but revealed no improvement to model fit. Sex and age interactions were added to the LPA and MVPA model, because they revealed significant results and improved the overall fit. In model 2, additional adjustments for season of measurement and time invariant covariates (as described above) were tested. Variables were added separately to the model and were only kept when improving the overall model fit. In model 3, time-varying covariates in the form of *z*BMI (model 3.1) or FMI (model 3.2) were added and tested for interaction with age. For visualization of effects, estimates of model 1 for SB, total PA, LPA, and MVPA in minutes per day from 6 to 12 years (grouped by sex) were plotted. Models were calculated in *R* using the "lme4" package. Significance was assumed at an error probability <.05.

RESULTS

Descriptive Information

Figure 1 reveals the participation flow during the study. Overall, 725 children between 6 and 11 years of age participated; 600 children had valid accelerometer data and were included in the analysis with a total of 1254 observations. The average participation rate for accelerometer measurements (over all time points) was highest in Poland (78.2%) and Belgium (71.8%) and lowest in Italy (64.5%) and Spain (63.8%). There were no differences in anthropometric data between children who participated in accelerometer measurement and those who did not. At T1, accelerometer measurement participation rate of children of parents with low education was significantly (P = .04) lower (50.0%) when compared with children of parents with middle (72.9%) or higher education (71.8%), but no significant differences were seen at T2 and T3.

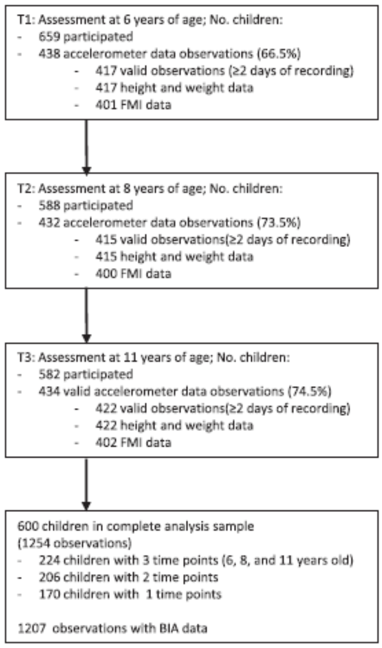

FIGURE 1
Flowchart of participating children and available data. BIA, bioelectric impedance analysis.

Times in different activity levels and anthropometric data by time point are presented in Table 1. The total sample had more observations from girls (n = 680; 54.2%) than boys (n = 574; 45.8%), and girls had a significantly (P < .001) higher

TABLE 1 Characteristics and Activity Levels of Participants

	6 y, *n* = 417	8 y, *n* = 415	11 y, *n* = 422
Age, y, mean (SD)	6.1 (0.1)	8.1 (0.1)	11.2 (0.2)
Boy, *n* (%)	184 (44.1)	199 (48.0)	191 (45.3)
Anthropometry, mean (SD)			
BMI	15.9 (2.0)	16.8 (2.6)	18.7 (3.3)
zBMI	0.3 (1.2)	0.4 (1.2)	0.4 (1.2)
FMI	3.4 (1.1)	3.9 (1.6)	4.5 (2.0)
FFMI	12.6 (1.1)	13.0 (1.2)	14.3 (1.6)
Activity levels in min per d, mean (SD)			
Sedentary	299.0 (79.6)	332.0 (79.9)	406.0 (96.7)
Total PA	532.9 (82.3)	519.8 (80.4)	457.6 (100.6)
LPA	418.3 (69.7)	397.8 (71.8)	373.7 (81.1)
MVPA	114.6 (59.5)	122.1 (72.3)	83.9 (53.6)
Adhere to PAGs, *n* (%)	340 (81.5)	329 (79.3)	264 (62.6)

zBMI was calculated by WHO reference population; PAGs by WHO: children (4–17 y) should spend 60 min per d in MVPA. FFMI, fat-free mass index (fat mass [kilograms] divided by height [meters squared]).

FMI than boys at all 3 time points. In both girls and boys, mean SB increased by 107 minutes per day from T1 to T3, whereas total PA and LPA decreased (PA: −75 minutes per day; LPA: −48 minutes per day). MVPA development differed by sex, in which boys' MVPA between T1 (mean = 126.0 minutes per day; SD = 59.7 minutes per day) and T2 (mean = 147.0 minutes per day; SD = 75.7 minutes per day) increased and sharply decreased to T3 (mean = 103.8 minutes per day; SD = 53.5 minutes per day). Girls remained steady between T1 (mean = 105.6 minutes per day; SD = 57.8) and T2 (mean = 99.1 minutes per day; SD = 60.6 minutes per day) followed by a steep drop-off by T3 (mean = 67.5 minutes per day; SD = 47.9 minutes per day). Adherence rates to current physical activity guidelines (PAGs) of 60 minutes per day of MVPA were high at T1 (83%) and T2 (81%) and plummeted by almost 20% at T3.

Longitudinal Changes of PA and SB and Influencing Factors

With Table 2, we display results of longitudinal data analysis using model 1. In summary, a significant decline in all PA variables was seen. Total PA and MVPA declined quadratically, whereas LPA declined linearly (all $P < .001$). SB significantly increased ($P < .001$) over the same period. Age-dependent sex effects were visible in LPA and MVPA with opposite directions: boys spent less time in LPA ($P = .003$) and more time in MVPA ($P < .001$) than girls with an increasing difference from 6 to 11 years of age. The complete models with random effects are shown in Supplemental Table 4. All models revealed a negative random intercept-slope covariance and correlation, meaning children with higher intercepts tend to have lower slopes.

When looking at further influencing factors in model 2, adding the season of measurement revealed a significant improvement of LPA and MVPA models but resulted in no major differences in β-estimates or significance (not shown). The addition of time-invariant covariates (educational status, housing, prepregnancy BMI, maternal age, family status and smoking during pregnancy, pubertal status at 11 years, and intervention type) had no influence on any of the 4 models.

Adding a time-varying variable zBMI in model 3.1 (Table 3) revealed an association with SB, total PA, and MVPA (all $P < .001$). The interaction between zBMI and age was only significant in MVPA ($P = .014$). When the time-varying variable FMI (model 3.2) was added instead of zBMI, similar results were obtained with slightly larger effect sizes. Additionally, there was a negative association between LPA and FMI ($P = .012$). However, age and FMI interactions were not significant in all of the models.

Figure 2 reveals the plotted estimates of SB, total PA, LPA, and MVPA in minutes per day from 6 to 12 years, grouped by sex (model 1). When looking at MVPA and comparing it to current PAGs, girls fall on average below the 60 minutes per day of MVPA at the age of 10.7 years and boys at 13.0 years.

DISCUSSION

Principal Findings

We observed a decline in time spent in total PA as well as in low- and high-intensity levels, from 6 to 11 years of age, even after adjustment for various covariates. Total PA and LPA gradually declined, whereas MVPA remained constant between 6 and 8 years but steeply dropped off by 11 years of age. This effect was also visible in the number of children fulfilling current PAGs of 60 minutes per day in MVPA, which revealed a steep decline between 8 and 11 years (T1: 83.1%; T2: 81.4%; T3: 63.9%). Major influencing factors were sex and study country, as well as zBMI and FMI.

TABLE 2 Four Separate Mixed-Effects Models With Random Intercept and Slope Examining the Change of PA and SB Between Age 6 and 11 Years (Model 1)

	SB			Total PA			LPA			MVPA		
	β	95% CI	*P*	β	95% CI	*P*	β	95% CI	*P*	β	95% CI	*P*
Fixed effects												
Intercept	274.8	258.8 to 290.9	<.001	520.4	503.9 to 537.0	<.001	428.8	415.2 to 442.3	<.001	82.3	73.0 to 92.8	<.001
Sex (boys)	9.2	−2.2 to 20.6	.115	−1.0	−12.8 to 10.8	.867	−21.7	−34.1 to −9.4	<.001	21.3	10.5 to 32.2	<.001
Country												
Spain	11.7	−6.6 to 30.0	.210	23.6	4.7 to 42.5	.015	6.9	−8.1 to 21.9	.370	10.5	−0.8 to 23.4	.073
Germany	−.8	−21.5 to 19.8	.936	27.9	6.6 to 49.3	.010	6.4	−10.7 to 23.4	.464	14.3	0.8 to 29.9	.034
Italy	39.9	20.9 to 58.9	<.001	5.1	−14.6 to 24.7	.615	−6.0	−21.7 to 9.7	.455	−3.2	−12.9 to 8.7	.610
Poland	39.1	19.3 to 58.9	<.001	4.4	−16.0 to 24.8	.672	−9.7	−26.0 to 6.6	.244	7.8	−4.8 to 21.3	.235
Age (centered)	10.8	4.4 to 17.2	.001	−.6	−7.5 to 6.3	.860	−6.4	−8.7 to −4.0	<.001	3.4	−1.6 to 8.7	.161
Age × age (centered)	1.8	0.7 to 2.9	.001	−2.6	−3.8 to −1.4	<.001	—	—	—	−2.4	−3.2 to −1.6	<.001
Sex × age (centered)	—	—	—	—	—	—	−5.3	−8.8 to −1.8	.003	5.1	2.5 to 7.8	<.001

All values are min per d; reference for "country" variable is Belgium; age was centered to the lowest age of any participant (5.89 y). CI, confidence interval; —, not applicable.

Implications and Comparison With Other Studies

Our study, used to cover the critical transition phase between childhood and adolescence, suggests that a decline of total PA beginning as early as 6 years of age is possible. This is a novel finding, because authors of most current literature suggest that total PA increases between the ages of 3 and 8 years[30] with a steep decline during adolescence (12–18 years).[8,9,31] As a result, most longitudinal studies are focused on PA and SB development in adolescence.[32] Only few longitudinal studies start at an earlier age but are supportive of our observation of an earlier decline in total PA than previously thought.[10,11] The overt explanation for this earlier decline could be the increased sitting times due to school. However, time-specific analysis of PA has revealed that in addition to the increased SB during school hours, there was also a distinct decline on weekends, out-of-school days, and during lunchtime.[12,33] This emphasizes that a precise measurement and detailed analysis of intensity levels already at an early age can give deeper insights into PA development, which are needed for adequate public health planning. In our results, it is further suggested that future intervention programs should already start at earlier ages than school age, to convey the importance of PA when levels of activity are still high.

In our study, SB and LPA were the main components of children's activity during hours awake. LPA decreased from 6 to 11 years of age accompanied by a steady increase of time spent in SB. Other studies have revealed that the trend of increased inactivity is likely to be continued during adolescence[33–35] and is followed into adulthood.[3,36] In light of this observation, it may be more feasible for interventions to replace SB with LPA, to prevent the negative

TABLE 3 Effects of zBMI and FMI on PA From 4 Separate Adjusted Mixed-Effects Models (Model 3.1 and Model 3.2)

	SB			Total PA			LPA			MVPA		
	β	95% CI	P	β	95% CI	P	β	95% CI	P	β	95% CI	P
zBMI	11.5	7.0 to 16.0	<.001	−8.0	−12.7 to −3.3	<.001	−1.8	−5.6 to 2.0	.360	−6.0	−8.1 to −3.0	<.001
FMI	12.1	8.6 to 15.5	<.001	−10.6	−14.2 to −7.0	<.001	−3.8	−6.7 to −0.8	.012	−9.1	−12.0 to −7.1	<.001

All values are min per d; reference for "country" variable is Belgium; age was centered to the lowest age of any participant (5.89 y). All models were adjusted for sex and country and for season in LPA and MVPA; zBMI was calculated by WHO reference population. CI, confidence interval.

effects of too much inactivity on health, as suggested by Healy et al.[37]

Sex differences were not visible in total PA and SB but in intensity levels of total PA (LPA and MVPA). Girls seem to be more active in light-intensity activities and boys more in high-intensity activities. Similar effects were also seen in a study by Nader et al,[13] yet it remains unclear whether this has an effect on health outcomes in girls later in life. Differences in total PA and SB between sexes are present in many studies, mostly with girls being less active than boys.[12,13,32] An explanation might be the earlier onset of puberty and sexual maturation in girls[38]; however, sex differences were already present at the 6-year-old mark in our study (well before puberty). This information can be useful when planning activity programs, tailoring suggested activities' intensity and duration.

Higher zBMI and FMI values resulted in a significantly lower volume of total PA and a higher volume of SB at baseline but revealed no effect on the development over time. PA is thought to be a major influencing factor in the prevention and management of overweight and obesity in youth. In the literature, there is no certainty about the direction and magnitude of influence. The inverse causality hypothesis assumes that overweight and obesity are not the result but the cause of reduced activity,[39–41] which might explain our findings. In light of these results, an indirect effect of the original nutritional intervention cannot be ruled out, as Weber et al[42] have shown that intake of a higher-protein formula during the first year of life resulted in a higher risk of obesity at 6 years.

Strengths and Limitations

One strength of our study is the longitudinal design. The study can be used to give an insight into the activity development during the critical period between childhood and adolescence. The results are generalizable for Europe because they were based on a birth cohort conducted in 5 countries. However, the population might not be fully representative because children were mainly from metropolitan areas and some were taking part in the intervention during the first year of life. Additionally, results are limited because of the relatively small sample size, the fact that not all children participated in every measurement, and the lack of more measurement points during adolescence. This makes stratification for certain subgroups difficult and challenging and limits the certainty about the continuous PA decrease during puberty.

Furthermore, a lack of common standard cutoffs for intensity levels, either for total PA[17] or SB,[43] results in different databases. This limits the possibility of comparing accelerometer-based studies. We chose cutoffs for LPA and MVPA on the basis of the fact that other studies consistently reveal an EE of 4 metabolic equivalents of task in children and adolescence from brisk walking (a common moderate activity).[23,44] Additionally, the use of different epoch lengths should be treated with caution when comparing PA and SB studies.[45] For our study, the epoch length was chosen on the basis of the storage and energy restrictions of the device used and was similar to many accelerometer-based studies.[46–48] Another limitation of most accelerometers is the inability to measure water-based activities, like swimming, because most devices cannot be worn in water. The SenseWear Armband tries to take this into account by calculating off-body estimates of EE during nonwear time, but this can never fully represent true measurements.

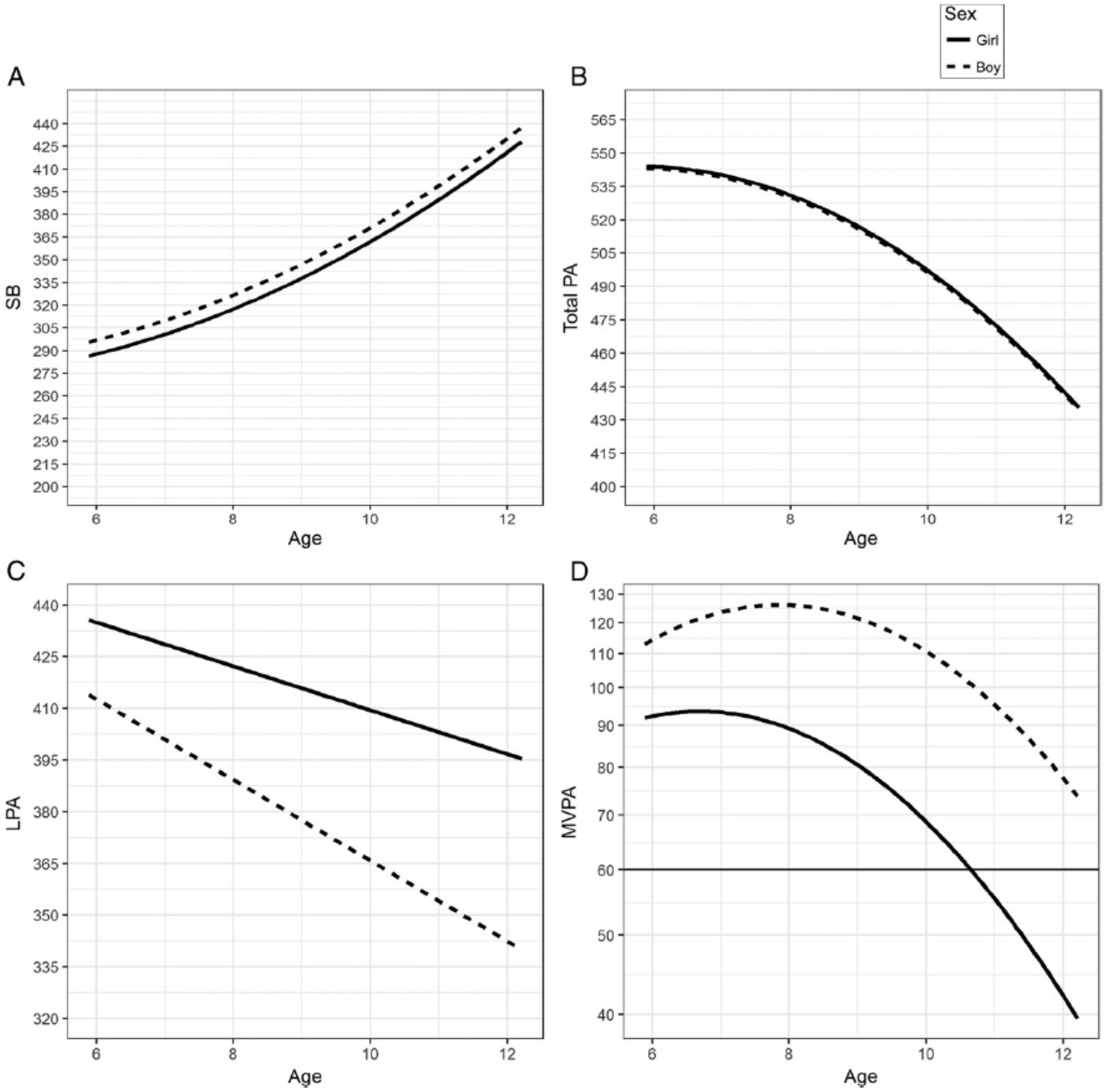

FIGURE 2

Plotted predicted values of mixed-effects models examining the change of PA and SB between age 6 and 11 years (model 1). Factor sex and sex and age interactions were only significant in LPA ($P = .003$) and MVPA models ($P < .001$); the MVPA model was calculated and plotted on log-scale because of the skewness of data; the horizontal line represents 60 minutes per day in MVPA recommended in guidelines. A, SB. B, Total PA. C, LPA. D, MVPA.

CONCLUSIONS

In this study, total PA activity decreased, and SB increased between the ages of 6 and 11 years. When looking at intensity levels of total PA, MVPA revealed a steep decline after 8 years, indicating a possible need for intervention. Sex effects on activity development were seen, which need to be taken in account when planning interventions and future studies.

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ABBREVIATIONS

EE: energy expenditure
FMI: fat mass index
LPA: light physical activity
MVPA: moderate-to-vigorous physical activity
PA: physical activity
PAG: physical activity guideline
SB: sedentary behavior
T1: time point 1
T2: time point 2
T3: time point 3
WHO: World Health Organization
*z*BMI: BMI *z* score

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RESEARCH Open Access

Longitudinal analysis of physical activity, sedentary behaviour and anthropometric measures from ages 6 to 11 years

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Abstract

Background/Objectives: The aim of this study was to examine the effect of physical activity (PA) and sedentary behaviour (SB) on body mass index (BMI) and fat mass index (FMI) in children over the course of five years and identify potential bi-directional associations.

Subjects/Methods: Data were drawn from the EU Childhood Obesity Project (CHOP). PA and SB were measured with the *SenseWear* Armband 2 at the ages of 6 (T1), 8 (T2) and 11 (T3) years. Height and weight were measured and BMI was calculated at each time point, resulting in 1254 complete observations from 600 children. Bio impedance analysis was used to measure body fat mass and eventually calculate FMI. To examine the longitudinal association between PA/SB and BMI/FMI as well as to account for repeated measure on these children, mixed model analysis was employed.

Results: Higher levels of total PA and moderate-to-vigorous PA (MVPA) were associated with lower BMI and FMI and higher SB with higher BMI and FMI over the five year period. When looking at the age dependent effects, negative associations of MVPA ($\beta_{MVPA \times age}$: – 0.05, 95% confidence interval (CI): – 0.09 – -0.01, $p = 0.007$) and positive associations of SB ($\beta_{SB \times age}$: 0.04, 95% CI: 0.02–0.06, $p < 0.001$) increased with each year of age. In a model combining these two effects, only SB x age interaction remained significant ($\beta_{SB \times age}$: 0.04, 95% CI: 0.03–0.06, $p = 0.01$). No significant interaction between MVPA and SB could be discerned. Light Physical activity showed no significant associations with BMI or FMI. When reversing outcome and predictor; higher BMI or FMI showed a negative association with MVPA and a positive association with SB, but no age dependency.

Conclusions: More time per day in SB was associated with a higher BMI over the course of five years, whereas higher MVPA had an inverse effect. In a combined model, only effects of higher SB remained significant, emphasizing the importance of SB in obesity prevention. Present bidirectional associations, where lower body size was associated with higher PA and lower SB, indicated the need for an integrated approach of activity and weight control for obesity prevention.

Trial registration: ClinicalTrials.gov Identifier: NCT00338689. Registered: June 19, 2006 (retrospectively registered).

Keywords: Obesity, Accelerometer, *SenseWear* armband, Light physical activity, MVPA, CHOP

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Introduction

The increase of childhood obesity is a major public health problem in Europe and other affluent countries [1–3]. Changes in childhood movement behaviour might play an important role in childhood obesity risk. High levels of physical activity (PA) are thought to be protective against excess body weight [4]. A recent systematic review showed that sedentary behaviour (SB) is related to many adverse health indicators, including unfavourable body composition [5]. Many of the studies included in the systematic review used subjective methods for measuring SB. Subjective methods can be a good estimate for context-specific SB like screen time, however, device-based methods can provide a more reliable and valid assessment of overall SB [6].

Overall the associations of PA and SB with obesity are inconsistent [7–10] and there is a lack of high quality studies examining the combined effect of device-based measurements of SB and PA on anthropometric measures. It remains unclear if positive health effects of moderate-to-vigorous PA (MVPA) outweigh negative health effects of high SB. Additionally, the direction of the effects need further clarification, as reversed causality could not be ruled out [11]. Evidence for reverse causality was found in a longitudinal observational analysis of 785 children, with a follow-up of 200 days and device-based measurement of PA [12]. In that study, a higher fat mass index (FMI) at baseline was associated with lower PA and more SB, whereas baseline movement behaviour did not predict any subsequent change of FMI. The results of other prospective observational studies employing device-based PA measurement found a bi-directional association [13] or no association in either direction [14]. Therefore, there is a need for more analyses of bi-directional associations.

This study is a secondary analysis of data from the EU Childhood Obesity Project (CHOP) a multicentre, randomized intervention trial taking place in five European countries. The current study may help to better understand the interplay of PA and SB in development of excess weight, by employing device-based measurement of PA and SB in a long-term cohort study. The primary aim is to examine associations between PA, light PA (LPA), MVPA, SB and the development of body mass index (BMI) and fat mass index (FMI) from 6 to 11 years of age. The secondary aim is to test for potential bi-directional effects of associations.

Methods

Study subjects and design

The CHOP study was initially started in 2002 and recruited 1678 infants in Europe during the first 8 weeks of life. This randomized control trial (clinical trial registry: NCT00338689) investigated the influence of higher and lower protein content infant formula during the first year of life on length and weight gain during infancy and childhood. Besides those two intervention groups the study also included an observational group of breastfed children. Its design and outcomes are reported elsewhere [15, 16]. Data for this analysis were collected during the 6- (T1), 8- (T2) and 11-year (T3) follow-up examinations. Sample collection was coordinated by 5 study teams in 8 municipalities in Germany (Nuremberg, Munich), Italy (Milano), Belgium (Brussels, Liege), Poland (Warsaw) and Spain (Reus, Tarragona). The trial was approved by ethics committees in each study centre and informed consent was obtained by parents. All research was performed in accordance with the Declaration of Helsinki.

Activity assessment

At each of the three study visits, parents and children participated in accelerometer measurements. SB and PA levels were measured using the *SenseWear* Armband 2 (Body Media Inc., Pittsburgh, PA, USA). This device is worn over the right triceps muscle and incorporates five sensors: two-axis accelerometer (for movement patterns and step-count), galvanic skin response, skin temperature, near body temperature sensor and heat flux [17]. Recording epoch length were 1 min intervals. Children wore the armband day and night on 3 consecutive days, including one weekday and one weekend day. Valid days were defined as at least 20 h·day^{-1} of recording. This time frame was proposed by Trost et al. [18] for accelerometer based studies. Observations are defined as one accelerometer measurement of each child at one of the three time points. Observations with only one day of recording were excluded. Two-day observations showed no differences to 3-day observations and were included in the analysis. Additionally, only observations with at least one weekday and one weekend day were included.

Data from armbands were processed with the Professional *InnerView* Software 6.1 (Body Media Inc., Pittsburgh, PA) already described elsewhere [19]. Intensity levels of PA were classified by Metabolic Equivalents of Task (METs): LPA 1.5–3.9 METs and MVPA ≥4 METs [20], were total PA included both LPA and MVPA minutes (i.e. > 1.5 METs). Awake minutes below 1.5 METs were seen as SB, in accordance to the cut-off set by the Sedentary Behavior Research Network [21, 22]. This definition additional includes the posture component of SB, i.e. sitting and reclined positions. The *SenseWear* Armband 2 cannot differ between standing and sitting and no direct observations or questionnaire data about activities were available. However, the armband was validated against a posture measuring device in children (11–13 year old) and were found to be accurate in measuring resting activities [23]. Other validation studies in children showed that the *SenseWear InnerView* algorithms (version 6.1) used in our study produce valid estimates of energy expenditure for assessing PA and SB in children [24, 25].

Anthropometry

During each follow up visit weight and height measurements were taken. The same scale (SECA 702, seca gmbh & co. kg., Hamburg, Germany) for weight and the same stadiometer (SECA 242, seca gmbh & co. kg., Hamburg, Germany) for height were used in each site. Standard operating procedures relied on the World Health Organisation's Growth Reference Study [26]. BMI (weight [kg]/height [m]^2) was calculated. Body fat mass was calculated from bioelectrical impedance assessed in duplicate with the octopolar *Tanita BC-418* (Tanita Corporation, Tokyo, Japan). FMI was calculated (total body fat mass [kg]/height [m]^2). Measurement with the *Tanita BC-418* was validated for use in 7 year old children from our sample [27]. It was seen that the device can give precise measurements to estimate children's body composition in an epidemiological setting, but should be treated with caution at an individual level.

Covariates

Gender, intervention group (higher and lower protein infant formula) or breasted group, wear time of device per day and study country data were available for all children. Additional known risk factors for childhood obesity with potential effect on PA and SB were available. This includes birth weight of the child, which was measured by study nurses right after birth or retrieved from medical records. Caloric intake (kcal) was assessed at each time point. While 3-day food protocols were used at T1 and T2, a food frequency questionnaire was used at T3. To facilitate the analysis of this data, tertiles were formed, which represent low, mid and high caloric intake at each time point. At 11 years puberty status was assessed with the 'Pubertal Development Scale' and categorised as 'pre-pubertal' and 'pubertal' [28].

Data analyses

Data are reported as mean with standard deviation (SD) for continuous variables and as number (n) and percentage (%) for categorical variables. Mixed models with a random individual intercept and random slope over age were used with either BMI or FMI at T1, T2 and T3 as time variant outcomes. Primarily, the effects of SB, total PA, MVPA and LPA on respective outcomes were modelled separately. We scaled all activities to 60 min/day to ensure meaningful effect sizes and make results of each model comparable. Gender, intervention group and study country were included in all models and additional covariates (birthweight and caloric intake) were added separately and kept for all following models upon improving overall model fit. In a second step, age interactions for each significant main predictors (PA x age, MVPA x age, LPA x age and SB x age) were added, to test for potential age dependent effects. As a last step, MVPA and SB (and their respective interaction with age) were jointly included in one model to test mutual adjusted main effects (Model 1) and age dependent associations (Model 2). To avoid collinearity, we looked at correlations between total PA, SB and MVPA at each time point. Additionally, interaction between SB and MVPA was tested (Model 3). Age was centred to the lowest age of participants, 5.89 years. To test if associations in a mutual adjusted model are moderated by either SB or MVPA, models were replicated only in children with high MVPA or high SB. High MVPA and SB was defined by the highest tertile of the average time in MVPA and SB over the 5 year period (all 3 measurement points). To examine possible bi-directional effects, mixed effects model outcomes (FMI and BMI) and main predictors (SB and MVPA) were reversed and adjusted for age, age^2 (as both SB and MVPA showed a quadratic development with age), gender and country. Interaction of FMI and BMI with age (BMI x age and FMI x age) and other covariates were tested in both models. In FMI and MVPA models, outcomes were log transformed for analysis, due to skewness of residuals. For interpretation, log transformed values were later back transformed. All models were optimized by maximum likelihood estimation and likelihood-ratio tests were used to test for the best model fit.

To assess the influence of missing data, we ran two sensitivity analyses, one with the sample restricted to those with 3 days of accelerometer recording per observation and one with the sample of children with two or more time points. Models were calculated in R using the 'lme4' package. Significance was assumed at an error probability < 0.05.

Results

Due to loss to follow-up, the number of children attending follow up visits decreased from 661 children at T1 to 589 children at T2 and 583 children at T3. Participation rate of accelerometer measurement increased from 63.1% at T1 (417 of 661 children) to 70.5% at T2 (415 of 589 children) and 72.4% at T3 (422 of 583 children). In total, 600 children with complete data on BMI and accelerometer data were included in the analysis, resulting in 1254 observations (Table 1); 430 children had at least two measurements. FMI was missing in 47 observations, resulting in 1207 valid observations of 586 children. There were no differences in anthropometric data between children, who participated in accelerometer measurement ($n = 600$) and those who did not ($n = 126$).

Table 1 Characteristics and activity levels of participants for each time point

		6 years	8 years	11 years
n		417	415	422
Male	n (%)	184 (44.1%)	199 (48.0%)	191 (45.3%)
Age, years	mean (SD)	6.1 (0.1)	8.1 (0.1)	11.2 (0.2)
Anthropometry				
BMI	mean (SD)	15.9 (2.0)	16.8 (2.6)	18.7 (3.3)
FMI	mean (SD)	3.4 (1.1)	3.9 (1.6)	4.5 (2.0)
Activity levels in minutes per day				
Sedentary	mean (SD)	299.0 (79.6)	332.0 (79.9)	406.0 (96.7)
PA	mean (SD)	532.9 (82.3)	519.8 (80.4)	457.6 (100.6)
Light PA	mean (SD)	418.3 (69.7)	397.8 (71.8)	373.7 (81.1)
MVPA	mean (SD)	114.6 (59.5)	122.1 (72.3)	83.9 (53.6)

Abbreviations: BMI Body mass index, *FMI* Fat mass index, *SB* Sedentary behaviour, *PA* Physical activity, *MVPA* Moderate-to-vigorous physical activity

Table 2 shows the effects of SB, total PA, MVPA and LPA in a mixed model analysis with either BMI or FMI as outcome. In summary, more time spent per day in SB was associated with a 0.13 kg/m^2 higher BMI ($p < 0.001$) and 0.05 kg/m^2 higher FMI ($p < 0.001$), whereas PA levels showed inverse associations. Each additional hour in total PA was associated with a − 0.11 kg/m^2 reduced BMI ($p < 0.001$) and a − 0.03 kg/m^2 reduced FMI ($p = 0.001$). Similar results were seen for MVPA with BMI and FMI with slightly lager effect sizes. Time in LPA showed no significant results. Adding caloric intake and puberty status showed no improvement of model fit. Birthweight improved model fit of BMI models and thus was included in all BMI outcome models.

Table 3 shows the age dependent associations between time in PA levels, SB and anthropometric measures. An additional 60 min/day of MVPA were associated with an 0.05 kg/m^2 lower BMI per year ($p = 0.006$) and 60 min more SB per day were associated with a 0.04 kg/m^2 higher BMI per year ($p < 0.001$). Interaction between

Table 2 Mixed model estimates of the association between SB and PA levels and anthropometric measures

	BMI			FMI		
	β	95% CI		β	95% CI	
SB	0.13	0.07–0.19	***	0.05	0.03–0.06	***
Total PA	−0.11	− 0.17 – − 0.05	***	− 0.03	− 0.06 – − 0.01	**
MVPA	− 0.14	−0.21 – − 0.08	***	− 0.05	−0.08 – − 0.03	***
LPA	0.00	−0.07 – 0.06		0.00	0.03 – −0.03	

Abbreviations: SB Sedentary behaviour per 60 min/day, *Total PA* Total physical activity per 60 min/day, *MVPA* Moderate-to-vigorous PA per 60 min/day, *LPA* Light PA in 60 min/day, *BMI* Body mass index (kg/m^2), *FMI* Fat mass index(kg/m^2), *CI* Confidence interval

Data were analysed with the use of 8 separate mixed models, adjusted for covariates intervention group, gender, wear time and country

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

total PA and age was not significant ($p = 0.080$). Association of total PA, MVPA and FMI did not significantly differ with age.

Total PA and SB were highly correlated at all time points ($r > 0.75$) and were not included in a combined model. As correlation between MVPA and SB was low to medium at each time point (T1: $r = -0.45$, $p < 0.001$; T2: $r = -0.45$, $p < 0.001$; T3: $r = -0.55$, $p < 0.001$) we included both in a combined model. Table 4 shows the results of this joint analysis. Model 1 shows the main effects. Both MVPA and SB remained significant with similar effects sizes in opposite directions (β_{MVPA}: -0.10, 95% CI: -0.17 – -0.02, $p = 0.014$; β_{SB}: 0.09, 95% CI: 0.03–0.16, $p = 0.013$). When including age interactions in model 2, only SB x age remained significant (β_{SB}: 0.01, 95% CI: -0.08 – 0.10, $p = 0.824$; $\beta_{SB\ x\ age}$: 0.03, 95% CI: 0.01–0.05, $p = 0.012$). Testing for an interaction between SB and MVPA showed a negative association with BMI, but was not significant ($\beta_{SB\ x\ MVPA}$: -0.02, 95% CI: -0.06 – 0.02, $p = 0.275$; Table 4, Model 3). Analysis of effects of SB and SB age interaction in a sample of children with high MVPA can be found in Additional file 1: Table S1. In summary moderating effects of MVPA can be ruled out, even though significance for the SB x age interactions were lost ($\beta_{SB\ x\ age\ (high\ MVPA)}$: 0.03, 95% CI: -0.00 – 0.06, $p = 0.074$). This was probably caused by loss of power ($n = 200$) due to splitting the sample in tertiles.

When reversing outcome and predictor, higher FMI and BMI were associated with higher levels of SB (β_{BMI}: 6.26, 95% CI: 4.27–8.25, $p < 0.001$; β_{FMI}: 12.05, 95% CI: 8.64–15.47, $p < 0.001$), but no significant age interactions (BMI x age, FMI x age) were found. Similar results were seen for MVPA outcome models (β_{BMI}: -7.61, 95% CI: -8.07 – -3.04, $p < 0.001$; β_{FMI}: -9.09, 95% CI: -11.95 – -7.14, $p < 0.001$), with no significant age interactions.

Sensitivity analysis on the per-protocol subsample with 3 days of recording (1090 observations, 566 children) was performed with all models. Significance did not change in all BMI and FMI models and only slight changes in estimates were seen. Further analyses were repeated with children who participated at least 2 time points (1084 observations, 430 children) and similar results were achieved with only slight changes of estimates and associations remaining significant.

Discussion

Main study findings and implications

In this study, more time spent in SB was consistently associated with higher BMI. In a mutually-adjusted model, effects sizes of SB and MVPA were of equal magnitude but in opposite directions. When testing age interactions, only associations between SB and BMI remained significant. Further analysis showed that the positive association between SB and BMI increased with age,

Table 3 Age dependent associations of time spent in sedentary behaviour, total and moderate-to-vigorous physical activity and anthropometric measures

	SB model			PA model			MVPA model		
Outcome: Body mass index									
	β	95% CI		β	95% CI		β	95% CI	
Age	0.26	0.13–0.39	***	0.66	0.48–0.84	***	0.60	0.53–0.67	***
SB	0.04	−0.04 – 0.11							
SB x Age	0.04	0.02–0.06	***						
Total PA				−0.06	−0.14 – 0.01				
Total PA x Age				−0.02	−0.04 – 0.00				
MVPA							−0.04	−0.14 – 0.05	
MVPA x Age							−0.05	−0.09 – −0.01	**
Outcome: Fat mass index									
Age	0.10	0.03–0.23	***	0.08	0.02–0.21	**	0.11	0.06–0.21	***
SB	0.05	0.02–0.09	**						
SB x Age	0.00	0.00–0.00							
Total PA				−0.05	−0.05 – 0.00	**			
Total PA x Age				0.00	0.00–0.00				
MVPA							−0.03	− 0.05 – 0.00	
MVPA x Age							0.00	−0.03 – 0.00	

Abbreviations: SB sedentary behaviour per 60 min/day, *Total PA* total physical activity per 60 min/day, *MVPA* moderate to vigorous PA per 60 min/day, *CI* confidence interval *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$
Data were analysed with the use of 3 separate mixed models, adjusted for covariates gender, intervention group, wear time and study country; Age was centred to the lowest age of any participant (5.89 years).

whereas BMI showed a stable association with SB over time, regardless of age. Overall, our results suggest that SB may play an important role in childhood overweight and obesity development.

The study confirms emerging evidence of a negative association between SB in childhood (device-based measurements) with BMI, even when concurrent levels of MVPA are considered. A study by Mitchell et al. [29] also used device-based measurement methods in 789 children between 9 and 15 years of age. Over the observed age period, SB was associated with an increasing BMI in children on the 50th, 75th and 90th BMI percentiles, when applying quantile regression. Another recent study by Mann et al. [30] employed bivariate linear spline models to test the independent effect of SB on adiposity markers in children 7 to 15 years of age, after adjustment for MVPA. Increasing SB was associated with an annual increased BMI (0.07 kg/m^2, 95% CI: 0.06–0.09) and annual increased FMI (0.14 kg/m^2, 95% CI: 0.10–0.18). However, the reported associations between SB and obesity indices are not uniform. Another international cross-sectional study in a sample of 6539 children examined the relationship between MVPA, SB and obesity. It found that only MVPA, but not SB, was

Table 4 Combined main effects (Model 1) and age dependent effects (Model 2) and interaction (Model 3) of time spent in sedentary behaviour and moderate-to-vigorous physical activity on body mass index

	Model 1			Model 2			Model 3		
	β	95% CI		β	95% CI		β	95% CI	
Age	0.49	0.45–0.54	***	0.33	0.13–0.52	**	0.49	0.45–0.54	***
SB	0.09	0.03–0.16	**	0.01	−0.08 – 0.10		0.12	0.03–0.21	*
MVPA	−0.10	−0.17 – −0.02	*	−0.06	− 0.17 – 0.05		0.01	− 0.20 – 0.22	
SB x Age				0.03	0.01–0.06	*			
MVPA x Age				−0.02	−0.06 – 0.03				
SB x MVPA							−0.02	−0.06 – 0.02	

Abbreviations: SB sedentary behaviour per 60 min/day, *MVPA* moderate to vigorous PA per 60 min/day, *CI* confidence interval
Data were analysed with the use of 3 separate mixed models, adjusted for covariates gender, intervention group, wear time and study country; age was centred to the lowest age of any participant (5.89 years)
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

significantly associated with BMI in a mutually adjusted model [31]. Thus, the interplay of higher SB, low PA and obesity needs further clarification. Long-term cohort studies in childhood (with multiple measurement points) would help to better understand the impact of levels and changes of PA and SB on later obesity risk.

In the present study, cross-sectional associations between movement behaviour and BMI as well as FMI were found, but no age interactions between movement behaviour and FMI were found. Basterfield et al. [32] reported that proxies for body weight (like BMI) are inferior to direct measures of body composition, when looking at adiposity outcomes. However, body fat mass from impedance measurements give fairly good body composition measures but lack precision [33], which might explain the lack of significant longitudinal effects of PA on FMI in our study. Additionally, effects sizes of associations with BMI in our study and other studies were rather small [12, 30, 34]. This brings to question, whether PA promotion is an adequate or effective tool for obesity prevention. Intervention studies are needed to clarify whether a substantial increase in habitual PA and a reduction of SB can result in a meaningful change of obesity markers in children.

In our study, results of an inverse analysis showed that higher BMI or FMI are associated with lower levels of MVPA and higher levels of SB, supporting the hypothesis of a bi-directional association. We also showed an age-dependent association between higher SB and higher BMI; higher BMI showed a stable association with higher SB over time. These results are similar to findings of a study from Marques et al. [9] where in a sample of 10- to 11-year old children a bi-directional association was only seen on cross-sectional, but not prospective analysis. These ambiguous results, taken together with inconsistent results from other studies [12–14], do not yet allow a firm conclusion about the direction of effects. Our study indicates that a consistently increased SB results in a higher BMI at later ages, whereas a consistently high BMI seems not to increase SB levels.

Our results stress the importance of reducing excess time in SB for the prevention of childhood obesity. Nevertheless, the practical application of our findings is difficult. In order to reduce SB, time spent in SB needs to be replaced by a form of PA, either LPA or MVPA. LPA comprises the majority of PA, about 80% of total PA measured in our cohort. Due to its light intensity, LPA is an "easy" substitute to SB. Effects of LPA on anthropometric measures range from showing a negative association with fat mass [35, 36], to no relationship, a finding reported in our study as well as other studies [37]. Thus, increasing LPA as a preventative measure for obesity is still unclear. Furthermore, interventions trying to increase children's PA and MVPA lack convincing results [38] and show variable success rates for childhood obesity prevention [39, 40]. Additionally, when looking at effect sizes from our results and others [30, 37], even with substantial increases in MVPA, only small reductions of BMI could be achieved.

Strengths and limitations

A strength of our study includes the longitudinal multicentre design of children born after the year 2000. Other strengths include device-based measurement of activity at each time point with high quality measurements of outcomes using standardised methods, with adjustment for various potential confounders.

In terms of generalizability of the findings, study participants were from Western European countries and mainly from metropolitan areas, making the results of this study generalizable to children with similar demographics. This was a secondary analysis of a randomized intervention trial whose a-priori hypothesis was the effect of varying protein content in infant formula on obesity risk. The intervention (high and low protein infant formula) showed an effect on BMI until 6 years of age [16], which might have influence the results. However, in this secondary analysis of childhood movement behaviour, the high and low protein intervention did not directly affect SB or PA levels. Adjustment for the intervention groups improved the overall fit of our statistical models. No confounding effects or interactions of early life intervention groups were observed.

PA and SB were measured at each of the three time points, which allowed for change in activity levels to be accounted for, over the observed time period, and allowed for modelling potential effects on anthropometric outcomes. Final models included age interactions for PA as well as SB, an aspect which other published studies are lacking [14, 34]. Accounting for possible age effects is of unique importance, since the period between childhood and adolescence is characterized by various changes in PA and SB [41]. The generation of children born after the year 2000 generally have a different lifestyle, compared to older generations, which is largely influenced by digitization of extracurricular activities. For example, universal access to telecommunication via mobile phones, use of smart phones, video games, time spent watching television or other 'screen time' activities, which influences PA and SB is significantly higher compared to older generations.

The results of our study are based on a European birth cohort and employed high quality measurement methods, which makes results generalizable to European children. However, some methodological factors, together with the relatively small sample size due to attrition, limit the external validity of our study to some extent.

Although device-based measurement of PA and SB can be a more reliable and more valid type of assessment of overall daily SB compared to self-report [6], it is difficult to compare results of accelerometer-based studies to other studies due to various differences. These differences include: cut-off values for intensities, epoch's lengths, number of days measured and the various devices used for PA and SB measurement. The *SenseWear* armband provides many advantages over other instruments, since it is a combination of a conventional accelerometer but with additional body sensors. Nevertheless, it is rarely used in PA-related science. This makes our study difficult to directly compare to other studies which did not sure the *SenseWear* armband.

Another limitation of our measurement is the relatively short measurement period (3 days). Additionally, there was a lack of a wear-time protocol, which might have biased the activity measurement results. However, the identification of wear-time and non-wear-time was not an issue, as the *SenseWear* armband automatically detects when the device is taken off, due to its detection of body heat. Due to the detection of body heat, the advantage of measuring SB with the *SenseWear* device is that the number for minutes in SB is more reliably measures than with other devices. Most other accelerometer-based studies approximate non-wear-time by consecutive zeros in device outputs (non-wear criteria ranging from 20 min of consecutive zeros to 60 min with and without allowance of interruptions). Problems arose when identifying time spent sleeping. With an average of 7 h of sleep per day, daily sleeping time classified by the *Sensewear*, was relatively short. After adding lying time to time spent sleeping, a more realistic daily average was calculated, at about 9.2 h per day. Potential lying time or time spent in reclined positions during the day (which is normally defined as SB [22]) was excluded, resulting in a slight underestimation of SB. Additionally, validation studies in children found inaccurate measures of energy expenditure in children when using armbands, which subsequently lead to a misclassification of activities [42–44]. While the algorithm of the armband and its software has improved over the years, the latest versions were not available for our data [45].

Conclusion

In summary, children that spent a longer time in SB had a higher BMI, even when adjusting for time spent in MVPA. This observation supports inactivity as an independent risk factor for childhood obesity. On the other hand, a shorter time spent in MVPA predicted a reduced BMI over a 5-year period. Effect sizes were rather small, however, and were no longer significant after adjustment for SB. In future interventions for obesity prevention, the focus shouldn't solely be on increasing high intensity PA, but should also emphasise reducing time spent in SB. Although LPA showed no associations with BMI, promotion of LPA to reduce SB might be a more realistic target than promotion of MVPA alone. Lack of results regarding adiposity measures, like FMI, demonstrates the need for more studies examining the combined effects of SB and PA on obesity and adiposity.

Additional file

Additional file 1: Table S1. Age dependent associations of time spent in sedentary behaviour and anthropometric measures in a subsample of children of the highest tertile of MVPA over the three measurement points ($n = 200$). (DOCX 13 kb)

Abbreviations

CHOP: Childhood obesity project; CI: Confidence interval; FMI: Fat mass index; LPA: Light physical activity; MET: Metabolic equivalents of task; min: Minutes; MVPA: Moderate to vigorous physical activity; PA: Physical activity; SB: Sedentary behaviour

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Availability of data and materials

The CHOP cohorts' data are available only to the collaborating scientists from the respective CHOP participating centres. The data may be available upon request for some of the participating centres but not for all due to relevant data protection laws.

Authors' contributions

PS: analysis of the data, drafted and finalized the manuscript; MW: participated in the data analysis and critical reading of manuscript; DG, PS, VL, RC-M, DR, MM, BM, EV: conduct of study, data entry at study sites and critical reading of manuscript; BK: designed the research and critical reading of manuscript; VG: designed the research, participated in the data analysis and critically reviewed the manuscript. All authors have read and approved the final version of this manuscript.

Ethics approval and consent to participate

Belgium: Comitè d'Ethique Medicale de Centre Hospitalier Chretien Liege; No. OM87. Germany: Bayerische Landesärztekammer Ethik-Kommission, No. 02070. Italy: Azienda Ospedaliera San Paolo Comitato Etico, No 14/2002. Poland: Instytut Pomnik-Centrum Zdrowia Dziecka Komitet Etyczny, No 243/KE/2001. Spain: Comité ético de investigación clínica del Hospital Universitario de Tarragona Joan XXIII, Comité ético de investigación clínica del Hospital Universitario Sant Joan de Reus. Written informed consent has been obtained from all participants included in the analysed study and the study is being conducted in accordance with the declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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