 doi:10.20944/preprints202103.0476.v1

Title

Lifestyle factors and metabolically unhealthy obesity in youth. Findings from the OSPEL study

Short title

Lifestyle and metabolically unhealthy obesity in youth

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ABSTRACT
Metabolically unhealthy obesity (MUO) was associated with increased cardiometabolic risk. However, it is not fully understood which lifestyle factors are associated with MUO in youth. We aimed to investigate the relationship between MUO and lifestyle patterns in youth.
7-17 years old youth with overweight (N=48; 60.4% girls) and obesity (N=71; 56.3% girls) were recruited in the Pediatric Clinic, Luxembourg (cross-sectional study). Eating and sedentary habits, moderate to vigorous physical activity (MVPA) and vigorous physical activity (VPA) were assessed. 72.3% of the participants had MUO. Multivariable logistic regressions showed that MUO is most likely to be associated with moderate to low weekly levels of MVPA [OR: 2.09 (95% CI: 1.07 – 4.09; p = 0.030)] and moderate to high weekly soda and lemonade drinks consumption [OR: 2.92 (95% CI: 1.32 – 6.48; p = 0.008)]. After adjustment for age, gender and Tanner stages, MUO was most likely to be associated with moderate to high soda and lemonade drinks consumption [OR: 2.72 (95% CI: 1.21– 6.12; p = 0.016)] and with Tanner stages [OR: 2.06 (95% CI: 1.08– 3.94; p = 0.029)]. We support the promotion of MVPA and the moderation in the sugar-sweetened beverages consumption to manage cardiometabolic health in youth with obesity.

Keywords: Overweight. Obesity paradox. Physical activity. Nutrition. Sugar-sweetened beverages

INTRODUCTION

Metabolically healthy obesity (MHO) is recognized as a subtype of obesity with a high body mass index (BMI), but absence of cardiometabolic abnormalities. Conversely, metabolically unhealthy obesity (MUO emerged as a new concept associating obesity to a high cardiometabolic risk, including at least one confirmed disturbance: hyperglycemia, dyslipidemia, hypertension, inflammation and insulin-resistance [1,2].

In adults, MUO was linked to an increased risk of type 2 diabetes and cardiovascular diseases, a decreased physical functional capacity and muscle strength and/or a highest likelihood to develop depression [3-5]. MUO was associated in adults with low levels of cardio-respiratory fitness (CRF), physical activity (PA) during leisure time, active commuting and transportation, as well as with a sedentary lifestyle [2,6-15]. A significant impact of a poor nutritional status was highlighted in the development of MUO in adults, in association with high consumption of sugar-sweetened beverages and low consumption of fruits and vegetables, olive oil, lean meat, beans and grain [16-20].

MUO might be influenced from early life stages. This covers from metabolic programming in utero, eating and sedentary habits during infancy, childhood and adolescence that defines lifestyle patterns potentially impacting adulthood health status [21]. Most of the studies focusing on MUO were conducted in adults. However, the importance to identify the lifestyle risk and protective factors associated with MUO development at early stages of life emphasizes the importance of studying pediatric populations [22].

The few available studies investigating the relationship between lifestyle and MUO in childhood are rather scarce and controverted. Some studies highlighted the harmful impact of sedentary habits and poor nutrition on cardiometabolic health and the benefits of a MVPA [19,23-28]. Roberge et al. showed that MHO profiles might be preserved in 8-10 years old children, at least for 2 years, by an increase of the regular consumption of vegetables and fruits, each additional daily portion being associated with MUO decrease by 39% [29]. Other pediatric studies concluded that screen time and MVPA were not significantly associated with MUO and MHO and that CRF did not significantly differ between both profiles. PA was not consistently associated with MHO in some studies [12,27,30,31]. A better understanding of the role played by lifestyle factors on metabolic health in youth with obesity is needed. Thus, the objective of the present study was to investigate the relationship between MUO and lifestyle factors in children and adolescents.

 doi:10.20944/preprints202103.0476.v1

PARTICIPANTS AND METHODS

Recruitment: The present work included the data of 119 youth aged between 7 and 17 years that took part to the OSPEL (Overweight and obeSity in PEdiatric population in Luxembourg) cross-sectional study [32-36]. OSPEL study was conducted between 2005 and 2007 in volunteer youth, with overweight or obesity [37], attending the Diabetes and Endocrinology Care department (Pediatric Clinic, Luxembourg) for medical weight loss consultation [32-36]. Participants were free of diseases associated with body composition alterations. All participants and their legally authorized representative signed the informed consent, before taking part to the study. The National Medical Ethics Committee (CNER) and the National Committee for Data Protection (CNPD) approved the present research work.

Clinical and biological assessment: During their visit at the Paediatric Clinic, the participants benefited from a medical anamnesis. BMI, waist circumference (WC), Tanner stages, fasting blood glucose, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, systolic (SBP) and diastolic blood pressure (DBP) were assessed [32-36].

Metabolically healthy and unhealthy obesity including overweight: The "MUO group" included participants having overweight or obesity and at least one of the five components of the metabolic syndrome as defined by the International Diabetes Federation (IDF) [38]: 1. Abdominal obesity (WC ≥ 90th percentile). 2. Fasting hyperglycemia (≥100 mg/dL) or previously diagnosed type 2 diabetes. 3. High triglycerides (≥110 mg/dL). 4. Low HDL cholesterol (< 40 mg/dL). 5. High blood pressure (systolic ≥130 / diastolic ≥ 85 mm Hg) or previously diagnosed hypertension (HTA) [38]. Adults IDF criteria were applied for ≥ 16 years old youth: 1. Abdominal obesity (WC ≥ 94 cm in men, ≥ 80 cm in women). 2. Fasting hyperglycemia (≥ 100 mg/dL) or previously diagnosed type 2 diabetes. 3. High triglycerides (≥150 mg/dL) or specific treatment for raised triglycerides. 4. Low HDL cholesterol concentrations (< 40 mg/dL in men, < 50 mg/dL in women) or specific treatment for reduced HDL cholesterol. 5. High blood pressure (systolic ≥130 / diastolic ≥ 85 mm Hg) or treatment of previously diagnosed HTA [39]. The "MHO group" included participants having no cardiometabolic abnormality.

Lifestyle pattern: We used the last version of the Health Behaviour in School aged Children (HBSC) survey conducted at this time in Luxembourg [40,41] (Annex 1).

Eating habits: Participants were asked: "How many times per week do you eat and/or drink fruits, vegetables, sweets and chocolate, sodas and lemonades, chips, fries, hamburger and hot dogs, brown bread and cereals, milk, dairy products, coffee and coffee with milk, meat and fish and/or energy drinks?" 1. Low consumption (never, less than one time per week, one time per week); 2. Moderate consumption (2 to 4 days per week); 3. High consumption (5 to 6 days per week, 1 time per day, several times per week).

Sedentary behavior was investigated as following:

- "How many hours per day do you use a computer to play, chat, send emails, for web surfing in your free time in the school days and weekend?" 1. Low use of computer (0, one half or 1 hour per day); 2. Moderate use (2 or 3 hours per day); 3. High use (4, 5, 6 or 7 hours per day).
- "How many hours per day do you watch television (TV) and videos in your free time in the school days and weekend?" 1. Low TV watching (0, one half or 1 hour per day); 2. Moderate TV watching (2 or 3 hours per day); 3. High TV watching (4, 5, 6 or 7 hours per day).
- "How many hours per day do you spend on homework in your free time in the school days and weekend?" 1. Low free time spent on homework (0, one half or 1 hour per day); 2. Moderate free time spent on homework (2 or 3 hours per day); 3. High free time spent on homework (4, 5, 6 or 7 hours per day).

Physical activity was investigated as following:

- Moderate to Vigorous Physical Activity (MVPA)**:** "activities increasing heart rate and getting participants out of breath for some time, outside school hours" [41]. 1. Low MVPA (never, less than

 doi:10.20944/preprints202103.0476.v1

one time per month, one time per week or one time per month); 2. Moderate MVPA (2 to 3 times per week); 3. High MVPA (4 to 6 times per week or every day).

- *Vigorous Physical Activity (VPA)*: "number of days per week where children are physically active until getting out of breath or sweating for at least 60 minutes" [41]. 1. Low VPA (less than 3 days per week); 2. Moderate VPA (3 to 4 days per week); 3. High VPA (5 to 7 days per week).

Statistical analyses: The distribution of the variables was checked with the Kolmogorov–Smirnov test. Continuous variables were expressed as median ± interquartile range (IQR), minimal and maximal values. Categorical variables were expressed as frequencies (%). The non-parametric Mann-Whitney *U* test was used to compare the differences in continuous variables between boys and girls and between the MHO and MUO groups. The Chi-square ($\chi 2$) test was used to compare the categorical variables. Multivariable logistic regressions were used to investigate the relationship between MUO as dependent variable and lifestyle factors as independent variables, adjusted for age, gender and Tanner stages. Odds Ratio (OR) and Wald coefficients were estimated. The predictive variables were retained based on their significant contribution in the model (p-value<0.05 for significant Wald coefficients). The statistical significance was set at p value ≤ 0.05 and the level of confidence was 95%. All analyses were performed using the statistical software SPSS for Windows (version 22.0, IBM, Chicago, IL, USA).

RESULTS

The general characteristics of the participants are detailed in Tables 1-3. 40.3% of the participants had overweight (N=48), 59.7% had obesity (N=71). The stage 4 was the smallest Tanner stages group (7.6%). 63.0% of the participants (N=75) had abdominal obesity, 15.1% (N=18) had hypertension, 9.2% (N=11) had high triglycerides levels, 21.0% (N=25) had low levels of HDL-cholesterol and 1.7% (N=2) had fasting hyperglycemia. 27.7% (N=33) of the participants had MHO and 72.3% (N=86) had MUO. Tables 2-3 describe the central tendency of the clinical and biochemical markers.

Table 1: Participants characteristics

Characteristics		**Number**	**Percentage %**
Gender	Boys	50	42.0
	Girls	69	58.0
Weight status	Overweight	48	40.3
	Obesity	71	59.7
Abdominal obesity	Yes	75	63.0
	No	44	37.0
Tanner stages	1	44	37.0
	2	29	24.4
	3	13	10.9
	4	9	7.6
	5	24	20.2
Hypertension	Yes	18	15.1
	No	101	84.9
High triglycerides level	Yes	11	9.2
	No	108	91.8
Low HDL-Cholesterol level	Yes	25	21.0
	No	94	79.0
High fasting blood glucose level	Yes	2	1.7
	No	117	98.3
Metabolically healthy obesity including overweight		33	27.7
Metabolically unhealthy obesity including overweight		86	72.3

	Median	Interquartile Range	Minimum	Maximum
Age (years)	12.0	3.3	7.3	16.9
Body mass index (kg/m^2)	27.3	6.8	19.8	40.4
Body mass index Z-score	2.45	0.84	1.36	3.65
Waist circumference (cm)	83.0	14.0	63.0	108.0
Systolic blood pressure (mmHg)	120.0	10.0	90.0	150.0
Diastolic blood pressure (mmHg)	70.0	10.0	50.0	95.0
Fasting glucose (mg/dL)	85.6	7.9	70.4	126.5
HDL cholesterol (mg/dL)	53.0	12.6	27.0	103.0
Triglycerides (mg/dL)	82.0	57.0	28.0	468.0

	Number (%)		χ2 value	p value
	Boys (N=50)	Girls (N=69)		
Overweight	19 (38.0%)	29 (42.0%)	0.196	0.658
Obesity	31 (62.0%)	40 (58.0%)		
MHO	**19 (38.0%)**	**14 (20.3%)**	**4.537**	**0.033***
MUO	**31 (62.0%)**	**55 (79.7%)**		
	Median ± IQR		z value	p value
	Boys	Girls		
Age (years)	11.7 ± 3.0	12.6 ± 3.5	1.693	0.090
BMI (kg/m^2)	27.6 ± 6.7	27.2 ± 7.2	0.428	0.669
BMI Z-score	**2.81 ± 0.64**	**2.37 ± 0.83**	**3.368**	**0.001***
Waist circumference (cm)	84.5 ± 16.0	82.0 ± 43.0	1.422	0.155
Systolic blood pressure (mmHg)	120.0 ± 21.0	120.0 ± 10.0	0.535	0.593
Diastolic blood pressure (mmHg)	70.0 ± 10.0	70.0 ± 10.0	0.395	0.693
Fasting glucose (mg/dL)	85.6 ± 8.8	85.5 ± 7.7	0.030	0.976
HDL cholesterol (mg/dL)	51.5 ± 14.5	54.0 ± 12.0	0.105	0.916
Triglycerides (mg/dL)	82.0 ± 65.0	82.0 ± 54.0	1.045	0.296

The participant characteristics according to the gender are detailed in Table 2. Girls had a significantly higher percentage of MUO compared to boys (79.7% vs. 62.0%, p = 0.033). Significant differences amongst boys and girls were observed for the BMI Z-score (2.81 ± 0.64 versus 2.37 ± 0.83; p = 0.001).

Table 2: Participant characteristics according to the gender

Abbreviations: **MHO:** Metabolically healthy obesity including overweight. **MUO:** Metabolically unhealthy obesity including overweight. **BMI**, body mass index.
Chi-square (χ2) was used to compare the categorical variables. Central tendency was expressed by Median ± IQR (Interquartile Range). A non-parametric Mann-Whitney U test was used to compare the differences between boys and girls. *Significant differences for P Values < 0.05 (2-tailed).

The "MUO group" included 31 boys and 55 girls (12.7 ± 3.9 years old). The "MHO group" consisted of 19 boys and 14 girls (11.6 ± 2.7 years old) (Table 3).
The participants with MUO were significantly older than the participants with MHO (12.7 ± 3.9 years versus 11.6 ± 2.7 years; p = 0.009). BMI Z-score (MUO: 2.78 ± 0.71; MHO: 2.04 ± 0.72; p < 0.001), WC (MUO: 86.0 ± 14.0 cm; MHO: 75.0 ± 10.0 cm, p < 0.001), systolic blood pressure (MUO: 120.0 ± 15.0 mmHg; MHO: 110.0 ± 20.0 mmHg; p < 0.001) and triglycerides (MUO: 87.0 ± 57.0 mg/dL; MHO: 61.0 ± 43.0 mg/dL; p < 0.001) were significantly higher in participants with MUO, compared

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to MHO. HDL-cholesterol (MUO: 51.0 ± 14.0 mg/dL; MHO: 55.0 ± 10.0 mg/dL; p = 0.006) was significantly lower in the MUO group (Table 3). According to the IOTF definition [37], 56.3% of the participants constituting the "MUO group" had obesity and 16.8% had overweight, compared to the "MHO group" (overweight: 23.5%, obesity: 3.4%) (p-value < 10^{-4}). Abdominal obesity mainly characterized participants presenting a MUO (63.0%, p-value < 10^{-4}).

Table 3: Characteristics of the participants having a metabolically healthy respectively unhealthy obesity profile

Characteristics	MHO (n=33)	MUO (n=86)	z value	p value
Age (years)	**11.6 ± 2.7**	**12.7 ± 3.9**	**z = 2.606**	**0.009***
BMI (kg/m²)	**23.5 ± 3.9**	**29.3 ± 5.4**	**z = 6.271**	**<0.001***
BMI Z-score	**2.04 ± 0.72**	**2.78 ± 0.71**	**z = 5.266**	**<0.001***
Waist circumference (cm)	**75.0 ± 10.0**	**86.0 ± 14.0**	**z = 6.050**	**<0.001***
Systolic blood pressure (mmHg)	**110.0 ± 20.0**	**120.0 ± 15.0**	**z = 3.911**	**<0.001***
Diastolic blood pressure (mmHg)	70.0 ± 10.0	70.0 ± 10.0	z = 1.700	0.089
Fasting glucose (mg/dL)	83.9 ± 5.9	85.7 ± 9.4	z = 1.425	0.154
HDL cholesterol (mg/dL)	**55.0 ± 10.0**	**51.0 ± 14.0**	**z = 2.771**	**0.006***
Triglycerides (mg/dL)	**61.0 ± 43.0**	**87.0 ± 57.0**	**z = 3.912**	**<0.001***

Abbreviations: **MHO:** Metabolically healthy obesity including overweight. **MUO:** Metabolically unhealthy obesity including overweight. **BMI**, body mass index.
Central tendency was expressed by Median ± IQR (Interquartile Range).
A non-parametric Mann-Whitney U test was used to compare the differences between MHO and MUO. *Significant differences for P Values < 0.05 (2-tailed).

Table 4 displays a **description of the eating habits in the study population**. The majority of the participants had a high consumption (5 to 6 days per week, 1 time per day or several times per week) of fruits (51.3%), vegetables (49.6%), whole breads and cereals (46.2%), milk (64.7%), dairy products (52.1%) and meat and fish (60.5%). As well, the majority of the participants indicated that they had a low consumption (never, less than one time per week, one time per week) of sweet and chocolate (55.5%), soda drinks and lemonade (61.4%), potato chips (98.4%), French fries (95.8%), hot dogs and burgers (95.8%), coffee and milk coffee (89.1%) and energy drinks (94.1%) (Table 4).

Table 4: Description of the eating habits in the study population

Eating habits		Number	Percentage %
Weekly consumption of fruits	Low	20	16.8
	Moderate	38	31.9
	High	61	51.3
Weekly consumption of vegetables	Low	26	21.8
	Moderate	34	28.6
	High	59	49.6
Weekly consumption of sweet and chocolate	Low	66	55.5
	Moderate	28	23.5
	High	25	21.0
Weekly consumption of soda drinks and lemonade	Low	73	61.4
	Moderate	26	21.8
	High	20	16.8
Weekly consumption of potato chips	Low	117	98.4

	Moderate	1	0.8
	High	1	0.8
Weekly consumption of French fries	Low	107	89.9
	Moderate	11	9.3
	High	1	0.8
Weekly consumption of hot dogs and burgers	Low	114	95.8
	Moderate	5	4.2
	High	--	--
Weekly consumption of whole breads and cereals	Low	41	34.5
	Moderate	23	19.3
	High	55	46.2
Weekly consumption of milk	Low	29	24.4
	Moderate	13	10.9
	High	77	64.7
Weekly consumption of dairy products	Low	26	21.8
	Moderate	31	26.1
	High	62	52.1
Weekly consumption of coffee and coffee with milk	Low	106	89.1
	Moderate	7	5.9
	High	6	5.0
Weekly consumption of meat and fish	Low	15	12.6
	Moderate	32	26.9
	High	72	60.5
Weekly consumption of energy drinks	Low	112	94.1
	Moderate	5	4.2
	High	2	1.7

Central tendency was expressed by Median ± IQR (Interquartile Range).

Table 5 displays the **description of the eating habits according to the MHO and MUO profiles.** A significantly higher level of high and moderate consumption of sweets and chocolates was observed amongst the participants with MUO (47.6%), compared to the participants with MHO (36.4%) ($p=0.043$). Similar findings were observed for soda drinks and lemonade intake ($p=0.005$) (Table 5).

Table 5: Description of the eating habits according to the metabolically healthy and unhealthy obesity

Food item	Consumption	MHO (n=33)	MUO (n=86)	$\chi 2$ value	p value
Fruits	Low	3 (9.1%)	17 (19.8%)	2.001	0.368
	Moderate	11 (33.3%)	27 (31.4%)		
	High	19 (57.6%)	42 (48.8%)		
Vegetables	Low	8 (24.2%)	18 (20.9%)	0.158	0.924
	Moderate	9 (27.3%)	25 (29.1%)		
	High	16 (48.5%)	43 (50.0%)		
Sweet and chocolate	**Low**	**21 (63.6%)**	**45 (52.3%)**	**6.297**	**0.043***
	Moderate	**10 (30.3%)**	**18 (20.9%)**		
	High	**2 (6.1%)**	**23 (26.7%)**		
Soda drinks and lemonade	**Low**	**28 (84.8%)**	**45 (52.3%)**	**10.651**	**0.005***
	Moderate	**3 (9.1%)**	**23 (26.7%)**		
	High	**2 (6.1%)**	**18 (20.9%)**		
Potato chips	Low	33 (100%)	84 (97.6%)	0.781	0.677
	Moderate	--	1 (1.2%)		
	High	--	1 (1.2%)		
French fries	Low	32 (97.0%)	75 (87.2%)		

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	Moderate	1 (3.0%)	10 (11.6%)	2.544	0.280
	High	--	1 (1.2%)		
Hot dogs and burgers	Low	33 (100%)	81 (94.2%)	2.003	0.157
	Moderate	--	5 (5.8%)		
	High	--	--		
Whole breads and cereals	Low	8 (24.2%)	33 (38.4%)	2.924	0.232
	Moderate	9 (27.3%)	14 (16.3%)		
	High	16 (48.5%)	39 (45.3%)		
Milk	Low	7 (21.2%)	22 (25.6%)	1.630	0.443
	Moderate	2 (6.1%)	11 (12.8%)		
	High	24 (72.7%)	53 (61.6%)		
Dairy products	Low	3 (9.1%)	23 (26.7%)	4.594	0.101
	Moderate	11 (33.3%)	20 (23.3%)		
	High	19 (57.6%)	43 (50.0%)		
Coffee and coffee with milk	Low	28 (84.8%)	78 (90.6%)	0.985	0.611
	Moderate	3 (9.1%)	4 (4.7%)		
	High	2 (6.1%)	4 (4.7%)		
Meat and fish	Low	2 (6.1%)	13 (15.1%)	1.823	0.402
	Moderate	10 (30.3%)	22 (25.6%)		
	High	21 (63.6%)	51 (59.3%)		
Energy drinks	Low	32 (97.0%)	80 (93.0%)	0.956	0.620
	Moderate	1 (3.0%)	4 (4.7%)		
	High	--	2 (2.3%)		

Abbreviations: **MHO:** Metabolically healthy obesity including overweight. **MUO:** Metabolically unhealthy obesity including overweight.
Chi-square ($\chi 2$) was used to compare the categorical variables. Central tendency was expressed by Median ± IQR (Interquartile Range). A non-parametric Mann-Whitney U test was used to compare the differences between MHO and MUO. *Significant differences for P Values < 0.05 (2-tailed).

Table 6 summarizes the **physical activity and sedentary habits in the study population.** The majority of the participants indicated that they had MVPA during their free time outside school hours (51.3%), while the largest group of participants indicated rather low levels of VPA during an ordinary week (38.6%). The majority of the participants indicated that they had low computer use (≤1 hour/day) during the weekdays (73.9%) and weekends (55.5%). There were 48.7% having low TV watching during the weekdays (≤1 hour/day), while 42.9% had moderate TV watching (2-3 hours/day) during the weekends. The majority of the participants indicated that they spend less than 1 hour per day to complete their homework during the weekdays (54.6%) and weekends (63.9%).

Table 6: Description of the physical activity and sedentary habits in the study population

Physical activity and sedentary habits		**Number**	**Percentage %**
MVPA during the free time	Low	34	28.6
	Moderate	61	51.3
	High	24	20.2
VPA during an ordinary week	Low	46	38.6
	Moderate	42	35.3
	High	31	26.1
Computer use, weekdays	Low	88	73.9
	Moderate	25	21.0
	High	6	5.1

Computer use, weekend	Low	66	55.5
	Moderate	32	26.9
	High	21	17.6
Television watching, weekdays	Low	58	48.7
	Moderate	49	41.2
	High	12	10.1
Television watching, weekend	Low	28	23.5
	Moderate	51	42.9
	High	40	33.6
Homework, weekdays	Low	65	54.6
	Moderate	47	39.5
	High	7	5.9
Homework, weekend	Low	76	63.9
	Moderate	36	30.2
	High	7	5.9

Abbreviations: **MVPA:** moderate to vigorous physical activity. **VPA:** vigorous physical activity.
Central tendency was expressed by Median ± IQR (Interquartile Range).

The **physical activity and sedentary habits are described according to the MHO and MUO** profiles in Table 7. A higher percentage of low MVPA during the free time, outside school hours, was observed amongst the participants having MUO (34.9%), compared to the participants with MHO (12.1%). A higher percentage of high MVPA during the free time, outside school hours, was observed in the youth with MHO (27.3%) compared to the youth with MUO (17.4%) (p = 0.044). The participants with MUO had higher levels of TV watching during the weekdays (14.0%) compared to the participants with MHO (0.0%) (p = 0.035) (Table 7).

Table 7: Description of the physical activity and sedentary habits according to the metabolically healthy and unhealthy obesity profiles

Physical activity and sedentary habits		MHO (n=33)	MUO (n=86)	χ2 value	p value
MVPA during the free time	**Low**	**4 (12.1%)**	**30 (34.9%)**	**x^2 = 6.246**	**0.044***
	Moderate	**20 (60.6%)**	**41 (47.7%)**		
	High	**9 (27.3%)**	**15 (17.4%)**		
VPA during an ordinary week	Low	10 (30.3%)	36 (41.9%)	x^2 = 2.217	0.330
	Moderate	15 (45.5%)	27 (31.4%)		
	High	8 (24.2%)	23 (26.7%)		
Computer use, weekdays	Low	28 (84.8%)	60 (69.8%)	x^2 = 2.817	0.245
	Moderate	4 (12.1%)	21 (24.4%)		
	High	1 (3.0%)	5 (5.8%)		
Computer use, weekend	Low	20 (60.6%)	46 (53.5%)	x^2 = 2.310	0.315
	Moderate	10 (30.3%)	22 (25.6%)		
	High	3 (9.1%)	18 (20.9%)		
Television watching, weekdays	**Low**	**15 (45.5%)**	**43 (50.0%)**	**x^2 = 6.688**	**0.035***
	Moderate	**18 (54.5%)**	**31 (36.0%)**		
	High	**--**	**12 (14.0%)**		
Television watching, weekend	Low	7 (21.2%)	21 (24.4%)	x^2 = 0.591	0.744
	Moderate	16 (48.5%)	35 (40.7%)		
	High	10 (30.3%)	30 (34.9%)		
Homework, weekdays	Low	18 (54.5%)	47 (54.7%)	x^2 = 3.097	0.213
	Moderate	15 (45.5%)	32 (37.2%)		

	High	--	7 (8.1%)		
Homework, weekend	Low	22 (66.7%)	54 (62.8%)	$x^2 = 0.688$	0.709
	Moderate	10 (30.3%)	26 (30.2%)		
	High	1 (3.0%)	6 (7.0%)		

Abbreviations: **MHO:** Metabolically healthy obesity including overweight. **MUO:** Metabolically unhealthy obesity including overweight. **MVPA:** moderate to vigorous physical activity. **VPA:** vigorous physical activity.

Chi-square ($\chi 2$) was used to compare the categorical variables. Central tendency was expressed by Median ± IQR (Interquartile Range). A non-parametric Mann-Whitney U test was used to compare the differences between MHO and MUO. *Significant differences for P Values < 0.05 (2-tailed).

The multivariable logistic regressions investigating the relationship between MUO and lifestyle factors showed that MUO is most likely to be associated with moderate to low weekly levels of MVPA [OR: 2.09 (95% CI: 1.07 – 4.09; $p = 0.030$)] and moderate to high weekly soda and lemonade drinks consumption [OR: 2.92 (95% CI: 1.32 – 6.48; $p = 0.008$)] (Table 8).

Table 8: Logistic multivariable regressions investigating the relationship between metabolically unhealthy obesity and lifestyle factors

Variable	Wald	OR	95% CI		p value
			Lower	Upper	
Moderate to low MVPA	**4.686**	**2.093**	**1.072**	**4.086**	**0.030***
Moderate to high television watching, in weekdays	0.022	0.948	0.468	1.919	0.882
Moderate to high weekly sweet and chocolate consumption	0.109	1.114	0.587	2.115	0.742
Moderate to high weekly soda and lemonade drinks	**6.950**	**2.921**	**1.317**	**6.482**	**0.008***
Constant					**0.029***

Abbreviations: 95% CI: 95% confidence interval. **OR**: Odds Ratio

After adjustment for age, gender and Tanner stages, MUO was most likely to be associated with an increased consumption of soda and lemonade drinks [OR: 2.72 (95% CI: 1.21– 6.17; p = 0.016)] and with the Tanner stages [OR: 2.06 (95% CI: 1.08– 3.94; p = 0.029)] (Table 9).

Table 9: Logistic multivariable regressions investigating the relationship between metabolically unhealthy obesity and lifestyle factors, adjusted for age, gender and Tanner stages

Variable	Wald	OR	95% CI		p value
			Lower	Upper	
Gender	0.018	1.073	0.383	3.008	0.894
Age	0.290	0.915	0.661	1.266	0.590
Tanner stages	**4.779**	**2.060**	**1.078**	**3.938**	**0.029***
Low to moderate MVPA	2.414	1.791	0.859	3.736	0.120
Moderate to high television watching, in weekdays	0.076	0.896	0.410	1.959	0.783
Moderate to high weekly sweet and chocolate consumption	0.019	1.053	0.507	2.186	0.890
Moderate to high weekly soda and lemonade drinks	**5.816**	**2.716**	**1.206**	**6.116**	**0.016***
Constant					0.270

Abbreviations: 95% CI: 95% confidence interval. **OR**: Odds Ratio

DISCUSSION

This work showed that a weekly MVPA decreases the likelihood of developing MUO in children and adolescents. A high intake of sodas and lemonades increases the likelihood to develop MUO. This is in agreement with other studies performed in similar age groups, identifying PA as the most dominant modifiable lifestyle factor in controlling metabolic abnormalities [42]. Thus, PA appears as a potential important factor to discriminate MUO from MHO. In particular, high cardio-respiratory fitness (CRF) might help controlling metabolic abnormalities in children [43]. Even though the relationship between aerobic fitness (i.e. CRF) and PA is more complex, the assumption that a certain level of PA intensity might induce higher CRF in children and adolescents was substantiated by certain data [44,45]. As a matter of fact, CRF might be a mediator in the association between VPA and obesity-related metabolic disturbances in youth. Prince *et al.*[23] observed that MVPA was the strongest independent predictor of MHO and cardiometabolic risk factors in children aged 8 to 17 y (21). Cadenas-Sanchez *et al.* [27] observed a pattern of significantly higher MVPA amongst European adolescents with MHO, compared to MUO [27].

To the best of our knowledge, the relationship between soft drinks consumption and MUO has not been investigated in the literature yet. Nevertheless, some authors highlighted the negative impact of soft drinks consumption, sodas and sweetened juice on type 2 diabetes and obesity development, possibly due to high fructose corn syrup ingestion, although no distinction was done between MUO and MHO [46,47].

In contrast with our findings, Camhi *et al.,* based on exploratory analyses from the NHANES 2003-2005, found that neither MVPA nor VPA were able to differentiate MHO from MUO in adolescents [12]. Differences in the criteria used to define PA might explain this lack of discrimination. Camhi et *al.* chose >10 min/day over the past 30 days of "any vigorous activities causing heavy sweating or large increases in breathing or heart rate" as a cut point to define VPA. They chose >10 min/day over the past 30 days of "moderate activities causing light sweating or slight to moderate increase in breathing or heart rate" as a cut point defining MVPA [12,48]. In our study, MVPA was defined through the activities increasing heart rate and getting people out of breath only for some time [41]. VPA was defined through at least 2 hours per week where children are physically active during the free time, outside school hours, until getting out of breath or sweating [41]. Prince et *al.* considered an average cut-off of 10 min/day for MVPA and VPA [23], while Cadenas-Sanchez et *al.* did not use any threshold, assessing PA all over the day [27]. High levels of PA are well known to positively impact cardiometabolic health amongst youth (38). These benefits include improvements on components of the metabolic syndrome as well as a higher insulin sensitivity [42]. The WHO and the European Commission recommend at least 60 min/d of MVPA to children and adolescents [49,50]. However, there is still a need to clearly define when children and adolescents are sufficiently active physically. Reported cut-offs in the literature varied from 1000 to 4000 counts/min [51].

Regarding sedentary behavior, our results are similar to Camhi *et al.* [12], who observed that screen time including computer use, television and video watching, did not differ in 12-18 y adolescents having MHO and MUO. Cadenas-Sanchez *et al.* [27] observed a significantly higher sedentary time in adolescents with MUO, compared to MHO. However, they used accelerometers instead of questionnaires to quantify sedentary behavior. Thus, we acknowledge this limitation in our study, that it is actually restrictive to use questionnaires in order to assess sedentary behavior and PA, rather than more objective tools such pedometers or accelerometers [51]. We also acknowledge that our study on eating patterns did not consider standardized methods such as 24 hours dietary recalls to have a more accurate estimation of dietary habits. Most of the evidence on dietary patterns showed that low fat intake were significantly associated with a higher presence of MHO [19,23-26]. Overall, the evidence on dietary assessment showed that diets rich in natural food, e.g. fruits and vegetables, are more predominant in MHO, unlike diets highly based on ultra-processed products, e.g. junk food [19,23-26]. However, recent evidence highlighted that energy expenditure, through high levels of PA

 doi:10.20944/preprints202103.0476.v1

and low sedentary behavior, rather than dietary intake, appears to be more helpful in preserving cardiometabolic health in youth [52].

Future studies should also strengthen the definition of MUO by incorporating gold standard measurement of body composition, particularly ectopic fat, using methods such as magnetic resonance imaging, computerized tomography and/or accurate anthropometric substitutes of visceral adiposity [22,35,51,53-55]. We also acknowledge that inference of causality was limited due to the cross-sectional study design.

In conclusion, our findings support the promotion of a weekly MVPA and a moderate consumption of sugar-sweetened beverages as lifestyle approaches to manage cardiometabolic health in youth having obesity. A priority should be given to the management of MUO in youth.

Author contributions: MSE (PhD) performed the statistical analyses and interpretation and co-drafted the initial manuscript. AB (PhD) co-drafted the initial manuscript. CDB (MD, PhD) was involved in the study planning and conduction, and provided a critical review of the manuscript. TB (PhD) provided a critical review of the manuscript. BG (PhD) supervised the aspects related to physical activity (findings interpretation, discussion) and provided a critical review of the manuscript. HS (PhD) planned and conducted the present work, and drafted the initial manuscript. All authors critically reviewed and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Funding: Luxembourg Institute of Health.

Acknowledgement: We acknowledge all the children and adolescents who accepted to take part to the OSPEL (Overweight and obeSity in PEdiatric population in Luxembourg) study, as well as their parents and legally authorized representative.

Conflict of interest disclosures: MSE, CDB, TB, BCG and HS have no conflicts of interest to declare. AB has worked as independent consultant for DSM Nutritional products, for the Société des Produits Nestlé SA and for Global Healthcare Focus LLC.

Abbreviations

MUO: Metabolically Unhealthy Obesity.
OSPEL: Overweight and obeSity in PEdiatric population in Luxembourg.
MVPA: Moderate to Vigorous Physical Activity.
VPA: Vigorous Physical Activity.
BMI: Body Mass Index.
CRF: Cardio-Respiratory Fitness.
PA: Physical Activity.
WC: Waist Circumference.
HDL cholesterol: High-density lipoprotein cholesterol.
LDL cholesterol: Low-density lipoprotein cholesterol.
SBP: systolic blood pressure.
DBP: diastolic blood pressure.
IDF: International Diabetes Federation.
HTA: hypertension.
HBSC: Health Behaviour in School aged Children.
TV: television.
IQR: interquartile range.
χ2: Chi-square.
OR: Odds Ratio.

REFERENCES

1. Bervoets, L.; Massa, G. Classification and clinical characterization of metabolically "healthy" obese children and adolescents. *J Pediatr Endocrinol Metab* **2016**, *29*, 553-560, doi:10.1515/jpem-2015-0395.
2. Bluher, S.; Schwarz, P. Metabolically healthy obesity from childhood to adulthood - Does weight status alone matter? *Metabolism* **2014**, *63*, 1084-1092, doi:10.1016/j.metabol.2014.06.009.
3. Bouchard, D.R.; Langlois, M.F.; Brochu, M.; Dionne, I.J.; Baillargeon, J.P. Metabolically healthy obese women and functional capacity. *Metab Syndr Relat Disord* **2011**, *9*, 225-229, doi:10.1089/met.2010.0101.
4. Hamer, M.; Batty, G.D.; Kivimaki, M. Risk of future depression in people who are obese but metabolically healthy: the English longitudinal study of ageing. *Molecular psychiatry* **2012**, *17*, 940-945, doi:10.1038/mp.2012.30.
5. Hamer, M.; Stamatakis, E. Metabolically healthy obesity and risk of all-cause and cardiovascular disease mortality. *The Journal of clinical endocrinology and metabolism* **2012**, *97*, 2482-2488, doi:10.1210/jc.2011-3475.
6. Bell, J.A.; Hamer, M.; van Hees, V.T.; Singh-Manoux, A.; Kivimaki, M.; Sabia, S. Healthy obesity and objective physical activity. *The American journal of clinical nutrition* **2015**, 10.3945/ajcn.115.110924, doi:10.3945/ajcn.115.110924.
7. Ortega, F.B.; Lee, D.C.; Katzmarzyk, P.T.; Ruiz, J.R.; Sui, X.; Church, T.S.; Blair, S.N. The intriguing metabolically healthy but obese phenotype: cardiovascular prognosis and role of fitness. *Eur Heart J* **2013**, *34*, 389-397, doi:10.1093/eurheartj/ehs174.
8. Bell, J.A.; Kivimaki, M.; Batty, G.D.; Hamer, M. Metabolically healthy obesity: what is the role of sedentary behaviour? *Preventive medicine* **2014**, *62*, 35-37, doi:10.1016/j.ypmed.2014.01.028.
9. Katzmarzyk, P.T.; Church, T.S.; Janssen, I.; Ross, R.; Blair, S.N. Metabolic syndrome, obesity, and mortality: impact of cardiorespiratory fitness. *Diabetes Care* **2005**, *28*, 391-397.
10. Larsson, C.A.; Kroll, L.; Bennet, L.; Gullberg, B.; Rastam, L.; Lindblad, U. Leisure time and occupational physical activity in relation to obesity and insulin resistance: a population-based study from the Skaraborg Project in Sweden. *Metabolism: clinical and experimental* **2012**, *61*, 590-598, doi:10.1016/j.metabol.2011.09.010.
11. Brandon, L.J.; Owen, J. Inflammation and Healthy Lifestyle Choices Influence Cardiometabolic Risks in African American Women. *South Med J* **2017**, *110*, 278-282, doi:10.14423/SMJ.0000000000000640.
12. Camhi, S.M.; Waring, M.E.; Sisson, S.B.; Hayman, L.L.; Must, A. Physical activity and screen time in metabolically healthy obese phenotypes in adolescents and adults. *Journal of obesity* **2013**, *2013*, 984613, doi:10.1155/2013/984613.
13. Kalantar-Zadeh, K.; Ahmadi, S.F. Carrying a heavier weight is healthy: Obesity-reinforced fitness hypothesis in metabolically healthy obesity. *Obesity (Silver Spring)* **2016**, *24*, 281-282, doi:10.1002/oby.21399.
14. Korhonen, P.E.; Korsoff, P.; Vahlberg, T.; Kaaja, R. Lifestyle of metabolically healthy obese individuals. *Prim Care Diabetes* **2015**, *9*, 179-183, doi:10.1016/j.pcd.2014.09.006.
15. Samouda, H.; Ruiz-Castell, M.; Karimi, M.; Bocquet, V.; Kuemmerle, A.; Chioti, A.; Dadoun, F.; Stranges, S. Metabolically healthy and unhealthy weight statuses, health issues and related costs: Findings from the 2013-2015 European Health Examination Survey in Luxembourg. *Diabetes Metab* **2019**, *45*, 140-151, doi:10.1016/j.diabet.2017.11.007.

16. Green, A.K.; Jacques, P.F.; Rogers, G.; Fox, C.S.; Meigs, J.B.; McKeown, N.M. Sugar-sweetened beverages and prevalence of the metabolically abnormal phenotype in the Framingham Heart Study. *Obesity (Silver Spring)* **2014**, *22*, E157-163, doi:10.1002/oby.20724.

17. Gutierrez-Repiso, C.; Soriguer, F.; Rojo-Martinez, G.; Garcia-Fuentes, E.; Valdes, S.; Goday, A.; Calle-Pascual, A.; Lopez-Alba, A.; Castell, C.; Menendez, E., et al. Variable patterns of obesity and cardiometabolic phenotypes and their association with lifestyle factors in the Di@bet.es study. *Nutr Metab Cardiovasc Dis* **2014**, *24*, 947-955, doi:10.1016/j.numecd.2014.04.019.

18. Mathew, H.; Farr, O.M.; Mantzoros, C.S. Metabolic health and weight: Understanding metabolically unhealthy normal weight or metabolically healthy obese patients. *Metabolism* **2016**, *65*, 73-80, doi:10.1016/j.metabol.2015.10.019.

19. Camhi, S.M.; Whitney Evans, E.; Hayman, L.L.; Lichtenstein, A.H.; Must, A. Healthy eating index and metabolically healthy obesity in U.S. adolescents and adults. *Prev Med* **2015**, *77*, 23-27, doi:10.1016/j.ypmed.2015.04.023.

20. Phillips, C.M.; Dillon, C.; Harrington, J.M.; McCarthy, V.J.; Kearney, P.M.; Fitzgerald, A.P.; Perry, I.J. Defining metabolically healthy obesity: role of dietary and lifestyle factors. *PLoS One* **2013**, *8*, e76188, doi:10.1371/journal.pone.0076188.

21. Li, S.; Chen, W.; Srinivasan, S.R.; Xu, J.; Berenson, G.S. Relation of childhood obesity/cardiometabolic phenotypes to adult cardiometabolic profile: the Bogalusa Heart Study. *Am J Epidemiol* **2012**, *176 Suppl 7*, S142-149, doi:10.1093/aje/kws236.

22. Vukovic, R.; Dos Santos, T.J.; Ybarra, M.; Atar, M. Children With Metabolically Healthy Obesity: A Review. *Front Endocrinol (Lausanne)* **2019**, *10*, 865, doi:10.3389/fendo.2019.00865.

23. Prince, R.L.; Kuk, J.L.; Ambler, K.A.; Dhaliwal, J.; Ball, G.D. Predictors of metabolically healthy obesity in children. *Diabetes Care* **2014**, *37*, 1462-1468, doi:10.2337/dc13-1697.

24. Zamrazilova, H.; Weiss, R.; Hainer, V.; Aldhoon-Hainerova, I. Cardiometabolic Health in Obese Adolescents Is Related to Length of Obesity Exposure: A Pilot Study. *J Clin Endocrinol Metab* **2016**, *101*, 3088-3095, doi:10.1210/jc.2016-1706.

25. Elmaogullari, S.; Demirel, F.; Hatipoglu, N. Risk factors that affect metabolic health status in obese children. *J Pediatr Endocrinol Metab* **2017**, *30*, 49-55, doi:10.1515/jpem-2016-0128.

26. Li, L.; Yin, J.; Cheng, H.; Wang, Y.; Gao, S.; Li, M.; Grant, S.F.; Li, C.; Mi, J.; Li, M. Identification of Genetic and Environmental Factors Predicting Metabolically Healthy Obesity in Children: Data From the BCAMS Study. *J Clin Endocrinol Metab* **2016**, *101*, 1816-1825, doi:10.1210/jc.2015-3760.

27. Cadenas-Sanchez, C.; Ruiz, J.R.; Labayen, I.; Huybrechts, I.; Manios, Y.; Gonzalez-Gross, M.; Breidenassel, C.; Kafatos, A.; De Henauw, S.; Vanhelst, J., et al. Prevalence of Metabolically Healthy but Overweight/Obese Phenotype and Its Association With Sedentary Time, Physical Activity, and Fitness. *J Adolesc Health* **2017**, *61*, 107-114, doi:10.1016/j.jadohealth.2017.01.018.

28. Kuzik, N.; Carson, V.; Andersen, L.B.; Sardinha, L.B.; Grontved, A.; Hansen, B.H.; Ekelund, U.; International Children's Accelerometry Database, C. Physical Activity and Sedentary Time Associations with Metabolic Health Across Weight Statuses in Children and Adolescents. *Obesity (Silver Spring)* **2017**, *25*, 1762-1769, doi:10.1002/oby.21952.

29. Roberge, J.B.; Van Hulst, A.; Barnett, T.A.; Drapeau, V.; Benedetti, A.; Tremblay, A.; Henderson, M. Lifestyle Habits, Dietary Factors, and the Metabolically Unhealthy Obese Phenotype in Youth. *The Journal of pediatrics* **2019**, *204*, 46-52 e41, doi:10.1016/j.jpeds.2018.08.063.

30. Heinzle, S.; Ball, G.D.; Kuk, J.L. Variations in the prevalence and predictors of prevalent metabolically healthy obesity in adolescents. *Pediatric obesity* **2016**, *11*, 425-433, doi:10.1111/ijpo.12083.

31. Senechal, M.; Wicklow, B.; Wittmeier, K.; Hay, J.; MacIntosh, A.C.; Eskicioglu, P.; Venugopal, N.; McGavock, J.M. Cardiorespiratory fitness and adiposity in metabolically healthy overweight and obese youth. *Pediatrics* **2013**, *132*, e85-92, doi:10.1542/peds.2013-0296.

32. Samouda, H.; de Beaufort, C.; Stranges, S.; Guinhouya, B.C.; Gilson, G.; Hirsch, M.; Jacobs, J.; Leite, S.; Vaillant, M.; Dadoun, F. Adding anthropometric measures of regional adiposity to BMI improves prediction of cardiometabolic, inflammatory and adipokines profiles in youths: a cross-sectional study. *BMC Pediatr* **2015**, *15*, 168, doi:10.1186/s12887-015-0486-5.

33. Samouda, H.; De Beaufort, C.; Stranges, S.; Hirsch, M.; Van Nieuwenhuyse, J.P.; Dooms, G.; Gilson, G.; Keunen, O.; Leite, S.; Vaillant, M., et al. Cardiometabolic risk: leg fat is protective during childhood. *Pediatr Diabetes* **2016**, *17*, 300-308, doi:10.1111/pedi.12292.

34. Pit-Ten Cate, I.M.; Samouda, H.; Schierloh, U.; Jacobs, J.; Vervier, J.F.; Stranges, S.; Lair, M.L.; Beaufort, C. Can health indicators and psychosocial characteristics predict attrition in youths with overweight and obesity seeking ambulatory treatment? Data from a retrospective longitudinal study in a paediatric clinic in Luxembourg. *BMJ Open* **2017**, *7*, e014811, doi:10.1136/bmjopen-2016-014811.

35. Samouda, H.; De Beaufort, C.; Stranges, S.; Van Nieuwenhuyse, J.P.; Dooms, G.; Keunen, O.; Leite, S.; Vaillant, M.; Lair, M.L.; Dadoun, F. Subtraction of subcutaneous fat to improve the prediction of visceral adiposity: exploring a new anthropometric track in overweight and obese youth. *Pediatr Diabetes* **2017**, *18*, 399-404, doi:10.1111/pedi.12415.

36. Samouda, H.; De Beaufort, C.; Gilson, G.; Schritz, A.; Vaillant, M.; Ghaddhab, C.; Ruiz-Castell, M.; Huiart, L.; Dohet, F.; Weber, B., et al. Relationship of oxidative stress to visceral adiposity in youth and role played by vitamin D. *Pediatric diabetes* **2020**, *21*, 758-765, doi:10.1111/pedi.13055.

37. Cole, T.J.; Bellizzi, M.C.; Flegal, K.M.; Dietz, W.H. Establishing a standard definition for child overweight and obesity worldwide: international survey. *Bmj* **2000**, *320*, 1240-1243, doi:10.1136/bmj.320.7244.1240.

38. Zimmet, P.; Alberti, G.; Kaufman, F.; Tajima, N.; Silink, M.; Arslanian, S.; Wong, G.; Bennett, P.; Shaw, J.; Caprio, S., et al. The metabolic syndrome in children and adolescents. *Lancet* **2007**, *369*, 2059-2061, doi:10.1016/S0140-6736(07)60958-1.

39. Alberti, K.G.; Zimmet, P.; Shaw, J.; Group, I.D.F.E.T.F.C. The metabolic syndrome--a new worldwide definition. *Lancet* **2005**, *366*, 1059-1062, doi:10.1016/S0140-6736(05)67402-8.

40. Roberts, C.; Currie, C.; Samdal, O.; Currie, D.; Smith, R.; Maes, L. Measuring the health and health behaviours of adolescents through cross-national survey research: recent developments in the Health Behaviour in School-aged Children (HBSC) study. *J Public Health* **2007**, *15*, 179–186, doi:DOI 10.1007/s10389-007-0100-x.

41. Currie, C.; Gabhainn, S.N.; Godeau, E.; Roberts, C.; Smith, R.; Currie, D.; Picket, W.; Richter, M.; Morgan, A.; Barnekow, V. *INEQUALITIES IN YOUNG PEOPLE'S HEALTH. HEALTH BEHAVIOUR IN SCHOOL-AGED CHILDREN. INTERNATIONAL REPORT FROM THE 2005/2006 SURVEY.*; HBSC INTERNATIONAL COORDINATING CENTRE. Child and Adolescent Health Research Unit (CAHRU). The Moray House School of Education. University of Edinburgh: Edinburgh, SCOTLAND., 2008; pp 1-183.

42. Guinhouya, B.C.; Samouda, H.; Zitouni, D.; Vilhelm, C.; Hubert, H. Evidence of the influence of physical activity on the metabolic syndrome and/or on insulin resistance in pediatric populations: a systematic review. *Int J Pediatr Obes* **2011**, *6*, 361-388, doi:10.3109/17477166.2011.605896.

43. McMurray, R.G.; Bangdiwala, S.I.; Harrell, J.S.; Amorim, L.D. Adolescents with metabolic syndrome have a history of low aerobic fitness and physical activity levels. *Dyn Med* **2008**, *7*, 5, doi:10.1186/1476-5918-7-5.

44. Martinez-Gomez, D.; Ruiz, J.R.; Ortega, F.B.; Casajus, J.A.; Veiga, O.L.; Widhalm, K.; Manios, Y.; Beghin, L.; Gonzalez-Gross, M.; Kafatos, A., et al. Recommended levels and intensities of physical activity to avoid low-cardiorespiratory fitness in European adolescents: The HELENA study. *American journal of human biology : the official journal of the Human Biology Council* **2010**, *22*, 750-756, doi:10.1002/ajhb.21076.

45. Ruiz, J.R.; Rizzo, N.S.; Hurtig-Wennlof, A.; Ortega, F.B.; Warnberg, J.; Sjostrom, M. Relations of total physical activity and intensity to fitness and fatness in children: the European Youth Heart Study. *The American journal of clinical nutrition* **2006**, *84*, 299-303, doi:10.1093/ajcn/84.1.299.

46. Tahmassebi, J.F.; BaniHani, A. Impact of soft drinks to health and economy: a critical review. *Eur Arch Paediatr Dent* **2019**, 10.1007/s40368-019-00458-0, doi:10.1007/s40368-019-00458-0.

47. Patterson, M.E.; Yee, J.K.; Wahjudi, P.; Mao, C.S.; Lee, W.P. Acute metabolic responses to high fructose corn syrup ingestion in adolescents with overweight/obesity and diabetes. *J Nutr Intermed Metab* **2018**, *14*, 1-7, doi:10.1016/j.jnim.2018.08.004.

48. USDHHS. Physical Activity Guidelines for Americans. Availabe online: http://www.health.gov/paguidelines/ (accessed on

49. EU European Union (EU) Working Group "Sport & Health". *EU Physical Activity Guidelines. Recommended Policy Actions in Support of Health-Enhancing Physical Activity.*; Brussels: EU commission, 2008.

50. WHO. *Global recommendations on physical activity for health*; Geneva: World Health Organization (WHO). 2010.

51. Guinhouya, B.C.; Samouda, H.; de Beaufort, C. Level of physical activity among children and adolescents in Europe: a review of physical activity assessed objectively by accelerometry. *Public Health* **2013**, *127*, 301-311, doi:10.1016/j.puhe.2013.01.020.

52. Fletcher, E.; Leech, R.; McNaughton, S.A.; Dunstan, D.W.; Lacy, K.E.; Salmon, J. Is the relationship between sedentary behaviour and cardiometabolic health in adolescents independent of dietary intake? A systematic review. *Obes Rev* **2015**, *16*, 795-805, doi:10.1111/obr.12302.

53. Taksali, S.E.; Caprio, S.; Dziura, J.; Dufour, S.; Cali, A.M.; Goodman, T.R.; Papademetris, X.; Burgert, T.S.; Pierpont, B.M.; Savoye, M., et al. High visceral and low abdominal subcutaneous fat stores in the obese adolescent: a determinant of an adverse metabolic phenotype. *Diabetes* **2008**, *57*, 367-371, doi:10.2337/db07-0932.

54. Brown, J.C.; Harhay, M.O.; Harhay, M.N. Anthropometrically predicted visceral adipose tissue and blood-based biomarkers: a cross-sectional analysis. *Eur J Nutr* **2016**, 10.1007/s00394-016-1308-8, doi:10.1007/s00394-016-1308-8.

55. Brown, J.C.; Harhay, M.O.; Harhay, M.N. Anthropometrically-predicted visceral adipose tissue and mortality among men and women in the third national health and nutrition examination survey (NHANES III). *Am J Hum Biol* **2017**, *29*, doi:10.1002/ajhb.22898.