CHILDHOOD OBESITY AND ITS IMPACT ON BLOOD PRESSURE

PhD THESIS

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I. **Andrea Emese Jakab**, Miklós Illyés, Attila Cziráki, Erzsébet Valéria Hidvégi, Csaba Bereczki. Prevalence of Overweight and Obesity in Hungarian Children and Adolescents. *Annals of Nutrition and Metabolism.* 2018; 72:259-264. (**IF: 2,424**)

II. **Andrea Emese Jakab**, Erzsébet Valéria Hidvégi, Miklós Illyés, Attila Cziráki, Tibor Kalmár, Zoltán Maróti, Csaba Bereczki. Prevalence of Hypertension in Overweight and Obese Hungarian Children and Adolescents. *Orvosi Hetilap.* 2020; 161:151-160. (**IF: 0,564**)

III. **Andrea Emese Jakab**, Miklós Illyés, Attila Cziráki, Csaba Bereczki, Erzsébet Valéria Hidvégi. Prevalence of Overweight and Obesity in a Population Aged between 3-18 Years in Szolnok. *Gyermekgyógyászat.* 2018; 68:107-112.

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I. Erzsébet Valéria Hidvégi, **Andrea Emese Jakab**, Miklós Illyés, Attila Cziráki. Childhood obesity: Does it Have any Effect on Young Arteries? ARTERY18, 18-20 October 2018, Guimarães, Portugal. *Artery Research.* 2018; 24:75.

II. **Andrea Emese Jakab,** Erzsébet Valéria Hidvégi, Miklós Illyés, Attila Cziráki, Csaba Bereczki. Non-Invasive Assessment of Arterial Function in Overweight and Obese Children and Adolescents. 51st Annual Meeting of the Association for European Paediatric and Congenital Cardiology. 29 March - 01 April 2017, Lyon, France. *Cardiology in The Young.* 2017; 27:Suppl.2 p.12.

III. Erzsébet Valéria Hidvégi, **Andrea Emese Jakab**, Miklós Illyés, Attila Cziráki, Csaba Bereczki. Non-invasive Assessment of Arterial Function Parameters in Overweight and Obese Children and Adolescents. Annual Meeting of the Hungarian Society of Cardiology. 05-07 May 2016, Balatonfüred, Hungary. *Cardiologia Hungarica* 2016; 46:53-54.

IV. **Andrea Emese Jakab,** Erzsébet Valéria Hidvégi, Miklós Illyés, Attila Cziráki, Csaba Bereczki. Prevalence of Overweight and Obesity in a Population Aged between 3-18 Years in Szolnok. Annual Meeting of the Hungarian Society of Peadiatrics. 22-24 September 2016, Szeged, Hungary. *Gyermekgyógyászat.* 2016; 67:298.

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III. Andreas Petropoulos, Peter Fritsch, Doris Ehringer-Schetitska, Vesna Herceg-Cavrak, **Andrea Emese Jakab,** Erzsébet Valéria Hidvégi, Renate Oberhoffer. Adapting Pulse Oximetry Measurements for Early Detection of Critical Congenital Heart Disease in Early Neonatal Period. 50th Annual Meeting of the Association for European Paediatric and Congenital Cardiology (AEPC). 1-4 June 2016, Rome, Italy. *Cardiology in the Young.* 2016; 26:Suppl.2 p.12.

Abbreviations

ABPM: ambulatory blood pressure monitor

BMI: body mass index

BP: blood pressure

CI: confidence interval

DBP: diastolic blood pressure

DI: diurnal index

E BP: elevated blood pressure

ECG: electrocardiography

GP: general practitioner

H BP: high blood pressure

HR: heart rate

HTN: hypertension

IOTF: International Obesity Task Force

N BP: normal blood pressure

N: normal weighted

O: obese

OR: odds ratio

OW: overweight

SBP: systolic blood pressure

SD: standard deviation

SP: school physician

TEE: total energy expenditure

WHO: World Health Organisation

Introduction

Childhood Obesity

According to the World Health Organisation (WHO), overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health. A crude population measure of obesity is the body mass index (BMI), a person's weight (in kilograms) divided by the square of his or her height (in metres). An adult person with a BMI of 25 to 29.99 is generally considered overweight, with a BMI equal to or more than 30 is considered obese. Obese class I means that BMI is between 30.00−34.99, in obese class II the BMI is between 35.00−39.99 and finally, obese class III are patients with BMI equal to or above 40.00. For children under 5 years of age: overweight is weight-for-height greater than 2 standard deviations (SD) above WHO Child Growth Standards median; and obesity is weight-for-height greater than 3 SD above the WHO Child Growth Standards median. Overweight and obesity are defined as follows for children aged between 5–19 years: overweight is BMI-for-age greater than 1 SD above the WHO Growth Reference median; and obesity is greater than 2 SD above the WHO Growth Reference median [1]. World Obesity / Policy & Prevention (formerly International Obesity Task Force or IOTF) has adapted adult BMI cut-off values (16, 17, 18.5, 25, 30 and 35 kg/m^2) to child centiles [2], which is easy to derive and they can be expressed as BMI centiles. It is more useful in paediatric population, because WHO standards (due to its construction method) are relatively low in young patients and high in older subjects [2].

Prevalence of Overweight and Obesity in the World

The increasing number of overweight and obese children and adolescents has become a serious and alarming phenomenon worldwide. Between 1980 and 2013, the prevalence of overweight and obesity increased from 10% to 12.7% in the population aged 2−19. This rate is even worse in the industrialised countries: during the period analysed, the prevalence increased from 16.9% to 23.8% in boys, and from 16.2% to 22% in girls [3]. Between 1975 and 2016, the mean BMI raised in boys, as well in girls worldwide. The pace of the increment is shocking, in cc. 40 years the prevalence increased from 10 million to more than 70 million in boys in the Central and Eastern Europe region, and from 10 million to 50 million in girls in the same region [4]. The epidemic of overweight and obesity has intensified the speed of research, in order to identify the possible reasons and the harmful consequences of this conditions not only in childhood, but in adults as well.

Etiology of Childhood Obesity

Obesity is subdivided in two subgroups: exogenous and endogenous [5]. Endogenous may be caused by different endocrine malfunctions, genetic or syndromic causes; whereas exogenous could be resulted from the imbalance between energy intake and expenditure, or from medications (e.g., glucocorticoids, tricyclic antidepressants), or even from impaired metabolic programming [5]. Considering the fact, that the target population of this research were children with exogenous obesity, the following part of the thesis will give a summary about this subgroup.

Although researchers have took efforts to explore the genetic factors and molecular background of the individual susceptibility to obesity, these findings cannot explain the obesity epidemic entirely. Genes of the human body have not changed substantially during the past decades [6]. Promotions of the obesogenic behaviour is responsible for obesity nowadays. Gaining weight in this increasing obesogenic environment is very easy for children, while it requires sustained efforts remaining fit and healthy [6]. Contributing environmental factors for increased BMI could be divided into three subgroups. Firstly, individual behaviours such as unhealthy dietary habits including the consumption of energy dense food, large portion sizes and excessive snacking [7], reduced sleep time resulting from increased screen time (television, mobile phone or tablets) [8], lack of regular physical activity or sedentary lifestyle [9]. Secondly, to micro-environmental factors belong family (parenting styles and different patterns of diet and physical activity, smoking and alcohol consumption influence the child's choices) [10,11] school (lack of healthy lifestyle education, sport facilities, unhealthy lunches) [12,13] and neighbourhood (playgrounds, closeness of healthy food groceries) [14–16]. Thirdly, macro-environmental factors are food industry - which have an impact on the risk of obesity with the production, marketing and advertising of high fat and sugar containing foods - and government, which should provide a healthy environment for children and should follow a strict, restrictive policy aiming the reduction of the availability of unhealthy snacks [7,17]. Considering the highlights of the literature, we may conclude to the possible solution: we must "cure" environment first, to combat the alarming increase of obesity [6].

Consequences of Childhood Obesity

Medical researchers have long recognized that being overweight or obese carries many serious health risks for adults [18]. The question rises, whether children face the same range of risks as adults or they form an exceptional group. Several conditions, thought to be only applicable in adulthood are now being represented in youth, moreover, they are becoming more frequent than

before. Children are more vulnerable to obesity-related diseases, because their bodies are in a growing and developing phase. Overweight and/or obesity are not merely an aesthetical issue for the individuals, but consequences of this condition having an adverse, either immediate or long-term effect on their health. These obese children are more prone to have early atherosclerosis [19], hypertension [20] or diabetes mellitus [21] as adults. Moreover, this condition may also result in insulin resistance [22], metabolic syndrome [23], dyslipidaemia [24], it may contribute to obstructive sleep apnoea [25]; furthermore, non-alcoholic fatty liver disease [26], gastroesophageal reflux [27], tibia vara (Blount disease) [28] may also be developed, or even psychic condition may be affected (depression) [29].

Obesity Related Cardiovascular Morbidity

The cardiovascular system consists of a dynamic series of conduits, which are vulnerable to many illnesses that may result in myocardial infarction – in the case of heart arteries – or in stroke – in the case of cerebral arteries. These processes make the heart also assailable to thickening of the heart muscles resulting in diminished function [30].

Hypertension

Overweight and obesity are main contributing factors to develop hypertension not only in adulthood but in childhood, as well [31]. There are factors simultaneously attenuating and stimulating the development of high blood pressure in overweight adolescents. Stimulating factors may be older age, low birth weight or pubertal status, while attenuating factors are high cardiorespiratory fitness or Central European ethnicity [32]. Recent study has found that the odds for hypertension are 1.5 times higher in children with overweight, while in obese patients these odds are 1.8 – 3.5 – 5.7 times higher for primary hypertension compared to their normal weight pupils [33]. Consequently, the higher is the frequency of children with overweight or obesity, the higher is the portion of children suffering from hypertension [34].

Left Ventricle Hypertrophy

Uncontrolled high blood pressure - resulting in an increased load - forces the heart to provide increased effort to pump blood via the aorta into the rest of the human body. This process may lead to thickening of the main pumping chamber, to left ventricle hypertrophy. Similarly to hypertension, left ventricle hypertrophy also shows a strong correlation with increased BMI in childhood [35]. Researchers have found, that the reason for this could be that the development of the heart follows the development of the body composition [36]. This suggests that in a body

with excessive amount of fat tissue, the left heart chamber should thicken itself ultimately. Subsequently this hypertrophy could moderately increase the risk for CV morbidity [37].

Atherosclerosis

Hardening of the arteries is a progressive condition, called atherosclerosis, which starts with a fatty streak on the inner layer of the vessel (endothelium), and it continues with a fibrous plaque, finally it may be followed by a rupture and thrombosis of the plaque leading to a blockage in the blood flow. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study [38] and the Bogalusa study [39] helped to clarify the prevalence of atherosclerosis in adolescents and in young adults and the connection between obesity and atherosclerosis. In the PDAY study autopsy was used to identify lesions on the surfaces of the aorta and left coronary artery in subjects who died of accidents, murders or suicides, hypothesized that they were "healthy" subjects, not suffering from any disease at the time of the death. This working group described, that atherosclerosis begins already in youth, and the prevalence of fatty streaks and clinically significant lesions raises suddenly in the 15- to 34-year age span. Surprisingly, the prevalence of fatty streaks was 100% in white and black subjects in each age group. In the age group 15−19 years a total of 13.1% white men and 6.8% of white women suffered from fibrous plaque in the abdominal aorta, and 3.3% of white men and 1.5% of white women suffered from fibrous plaque in the thoracic aorta [38]. Bogalusa study identified with the help of antemortem analysis the possible link between elevated BMI and early atherosclerosis [39]. These results demonstrate the presence of atherosclerosis even in children at very young age and the harmfulness of increased BMI on the cardiovascular system. Health professionals should bear in mind that atherosclerosis starts decades earlier before having clinical manifestation, already in childhood, moreover overweight and obesity are significantly related to the atherosclerotic lesions.

Considering the detailed facts above, it is strongly suggested to perform proper measurements regularly, in order to monitor the possible effects of several prevention projects and trends in the investigated population regarding body weight, furthermore overweight and obesity associated hypertension. This thesis was designed to assess these changes in Hungarian children and adolescents.

Aims

Goals of this thesis are the followings:

1. To determine the prevalence of overweight and obesity in a healthy population aged 3−18 in Szolnok city and the surrounding area.

       A. To discover if there is any difference in age and sex distribution regarding the prevalence of overweight and obesity.

       B. To observe if there have been any changes in the prevalence and in the trends of overweight and obesity from the data measured previously in Hungary.

2. To assess the prevalence of overweight and obesity associated hypertension in children aged 3−18 in Szolnok city and the surrounding area.

       A. To observe if there is any difference in age and sex distribution in this population.

       B. To establish if there is any relationship between BMI categories and frequency of hypertension.

       C. To compare our data with international findings on overweight and obesity associated hypertension.

Materials and Methods

Subjects

In order to assess the prevalence of overweight (OW), obese (O) and normal weighted (N) children in the first analysis 6.824 subjects (3.673 boys) aged 3–18 years were recruited from elementary, primary and high schools in Szolnok town (Hungary) between 2012 and 2016. For the second study 8.624 subjects (4.719 boys) aged 3–18 years were enrolled between 2005 and 2018 to estimate the prevalence of hypertension in subjects with elevated BMI. All the subjects were Caucasian without any chronic diseases, and they were not on any regular medications. Informed consent for the measurements was asked for from the parents of the subjects. The protocol was reviewed and approved by the local Institutional Ethics Committee of the University of Pécs, Pécs, Hungary.

Methods

Height and weight measurements were performed in accordance with the Hungarian professional rules [40], using a Kern MGB 150K 100 type personal scale and a MSF 200 type mechanical height rod (Kern & SOHN GmbH, Germany). The subjects were categorised by their body mass index (BMI) into normal weight, overweight and obese groups regarding their age and sex, as well [2].

Blood pressure was taken with an occlusive-oscillometric device (Arteriograpgh, Tensiomed Ltd., Hungary), which has been validated both invasively and non-invasively [41,42]. In patients, where the systolic (SBP) and/or diastolic blood pressure (DBP) were found to be equal or over 90th percentile according to age, height and sex blood pressure (BP) measurement was repeated two times with 10 minutes pause in between. If these results were found to be elevated (95th>BP≥90th) or hypertension was suspected (BP≥95th) [43–46], it was suggested to perform regular check-ups by the school physicians or by the general practitioner. If blood pressure was still found to be over the normal percentile, the subject was referred to a paediatric cardiologist for a detailed examination. Firstly, to exclude secondary hypertension abdominal ultrasound was performed (especially focusing on the kidneys and the adrenal glands), followed by a blood test (including bloodwork, fasting glucose, ions, renal- and liver functions, lipids, thyroid stimulating hormone). The examination composed of 12-leads ECG, echocardiography (also to rule out coarctation aortae and to assess left ventricular hypertrophy), and finally 24-hours ambulatory blood pressure monitoring (ABPM) (CardioTens 01, CardioTens 02, Meditech Ltd, Budapest, Hungary). For the ABPM four different sizes of cuff were used according to the arm

circumference of the non-dominant arm [43,46]. Relevant guidelines were applied to analyse the ABPM results [47,48]. The diagnosis of hypertension was set up if the average SBP and/or DBP was equal or above the 95th percentile according to age, sex and height and secondary hypertension was excluded. "Elevated BP" subgroup ($90^{th} \leq BP < 95^{th}$) was created for the appropriate result-comparison with the relevant literature.

Statistics

Data are reported as mean and SD for continuous data. For data comparison, Student's *t*-test was carried out after checking that the assumption of normality was met. Significance levels were set at the 5% level using the student t-test. To ensure data comparison between sexes, chi-squared test was carried out. Fisher's exact test was applied to compare the prevalence with the previous Hungarian data. Statistical analysis was performed with the SPSS 23.0 statistical package (SPSS Inc., Chicago, Illinois, USA).

Results

Prevalence of Overweight and Obesity

Table 1 contains the results of the prevalence of overweight and obesity. The prevalence of overweight was 13.4% (n=915), and 6.6% of obesity, which is 20% (n=1.363) of the studied population aged 3−18, in total.

Table 1 Prevalence of overweight and obesity

	boys		girls		total	
	n	%	n	%	n	%
normal BMI	2881	78.4	2580	81.9	5461	**80.0**
overweight	518	14.1	397	12.6	915	**13.4**
obese	274	7.5	174	5.5	448	**6.6**
overweight + obese	792	21.6	571	18.1	1363	**20.0**

BMI; body mass index

Table 1 demonstrates that the rate of overweight and obesity is higher in case of boys, than in girls, since the total prevalence of overweight and obesity was 21.6% (n=792) in boys and 18.1% (n=571) in girls. This difference was proven by statistical analysis (chi-square test, p<0.005). In order to ensure more informative data the age and weight distribution of the participants is indicated in percentage in Figure 1 and 2.
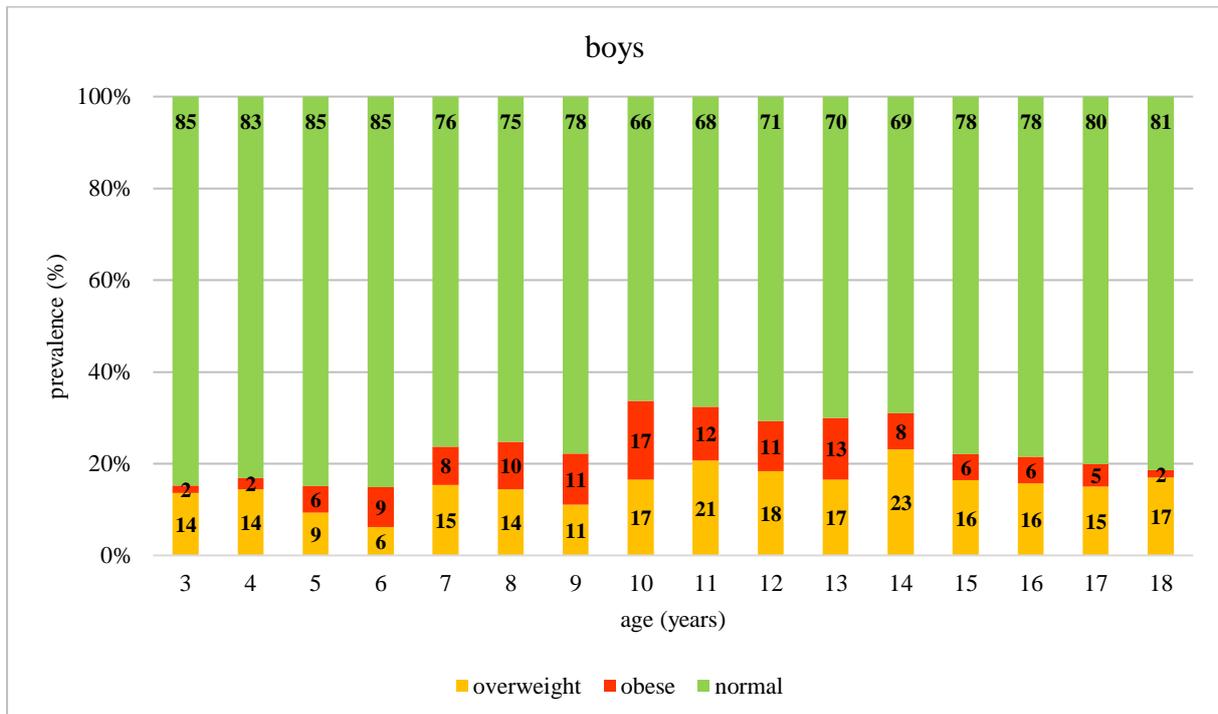
Figure 1 Age-related distribution of BMI categories
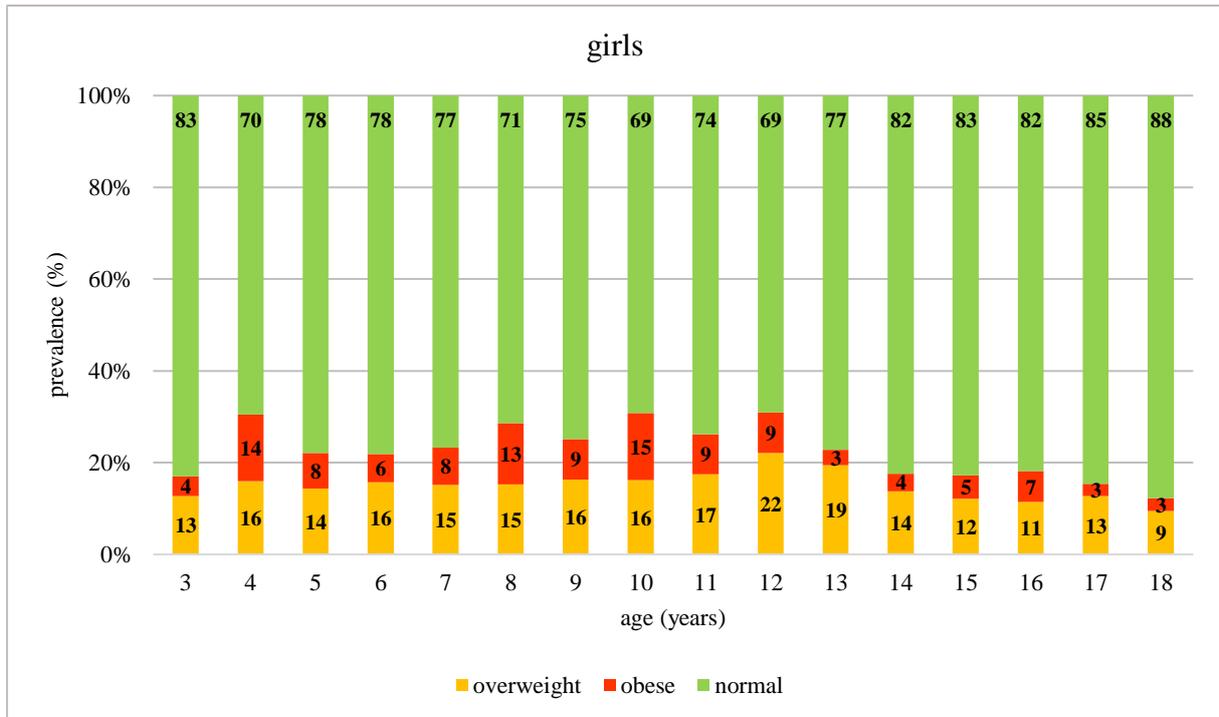
Figure 2 Age-related distribution of BMI categories

The total prevalence of overweight and obesity increases between the ages of 3 to 10 in both sexes, however, this increase is not even. The peaks are observed at the age of 10 in both genders. From 3 to 9 years total frequency of OW and O is higher in girls, until it turns from the age of 10. From 10 to 18 this condition is more common in boys. Although these differences are visible on the chart, statistically it is only different at the age of 4 and 14. After puberty, there is a moderate decreasing trend both in boys and girls; however, the decrease is more significant in girls (Figure 3).
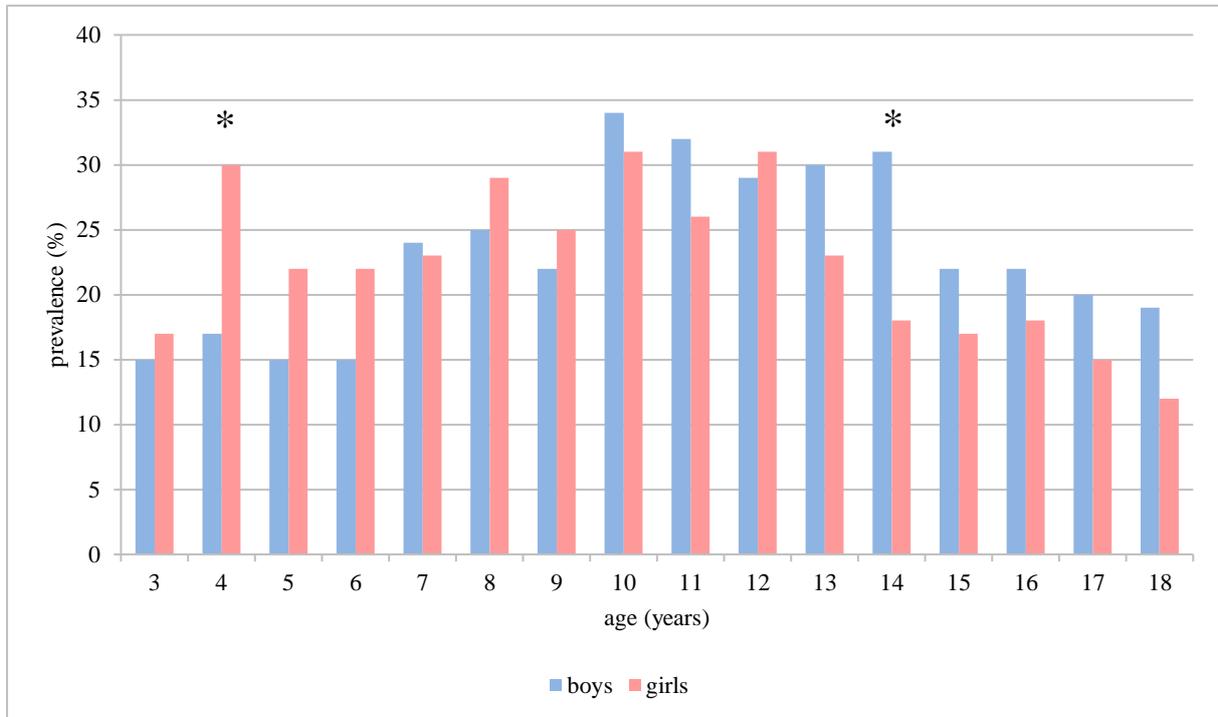
Figure 3 Prevalence of overweight and obesity in different age groups.
*; significant difference (p<0.05)

Prevalence of Overweight and Obesity Associated Hypertension

Characteristics of the N, OW and O subjects are performed in Supplementary Table 1 for boys (1/A), and girls (1/B), including the statistical findings and p-values of each examined parameter. On average, bodyweight, height, BMI, SBP and DBP were shown to have a simultaneous increase with age, however, heart rate (HR) decreases with years in boys and girls, as well. In Supplementary Table 1 there is a clear trend of elevated weight, BMI and SBP in OW and O children (in both sexes) compared to N patients, while height and HR did not show any statistical differences.

Supplementary Table 2 summarizes the enrolling method of subjects into this study for normal weighted (2A), for overweight (2B) and for obese (2C) boys and girls. The 3th, 4th and 5th columns of this table show the absolute number of subjects with normal (N), elevated (E) and high (H) BP measured on the first meeting. It can be seen that in children with normal weight 3044 boys and 2775 girls had normal, 209 boys and 185 girls elevated, while 305 boys and 169 girls high blood pressure, respectively. After this, in 1.594 (18.5%) cases regular BP control was suggested, due to suspicion of hypertension (patients with elevated and high BP). Further BP measurements were performed by general practitioners (GP) and/or school physicians (SP). Based on the results of the repeated BP measurements they decided whether the patients should visit a specialist in order to perform a detailed examination targeting hypertension. The 6th

column contains the number of patients, who were referred to paediatric cardiologist (693 patients, 43.5%). The 7th, 8th and 9th columns present the number of patients with normal (N), elevated (E) and high (H) BP based on the detailed examination and ABPM performed by specialist. Finally, from the admitted subjects (n=693), elevated BP was found in 177 cases (25.5%), while hypertension was diagnosed in 353 cases (50.9%). Our findings suggest that "white coat effect" was around 23.6% in this population, considering the fact, that from the admitted patients after the detailed examination 25.5% had elevated BP and 50.9% of the patients hypertension.

Figure 4 summarizes total numbers of the patients enrolled to this study according to their sex, age and weight categories (all patients). As this figure shows, most of the majority of the enrolled patients were between the age of 12 and 17 in both sexes. Moreover, on the chart it can be seen the proportions of HTN patients (HTN based on ABPM) among the total population in each age group. The figure shows that the frequency of HTN was higher in every weight category in boys compared to girls.

A

normal weighted boys

normal weighted girls
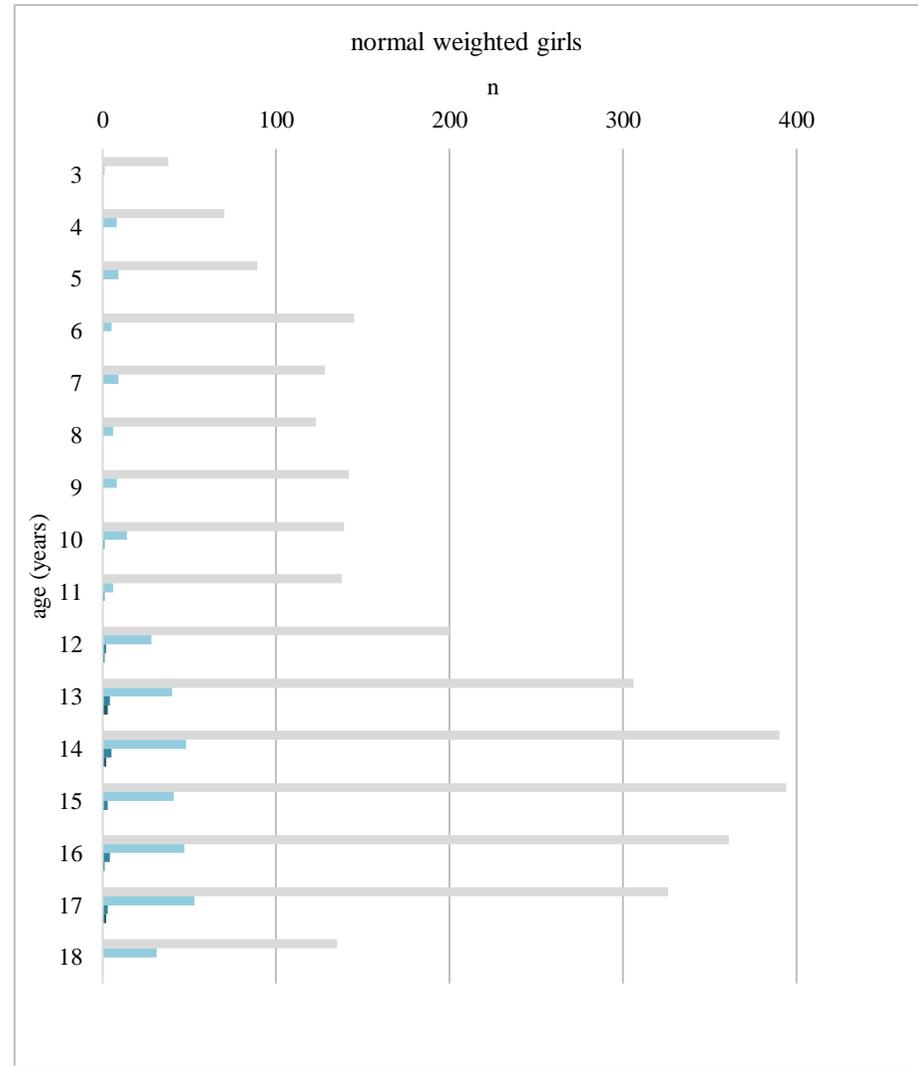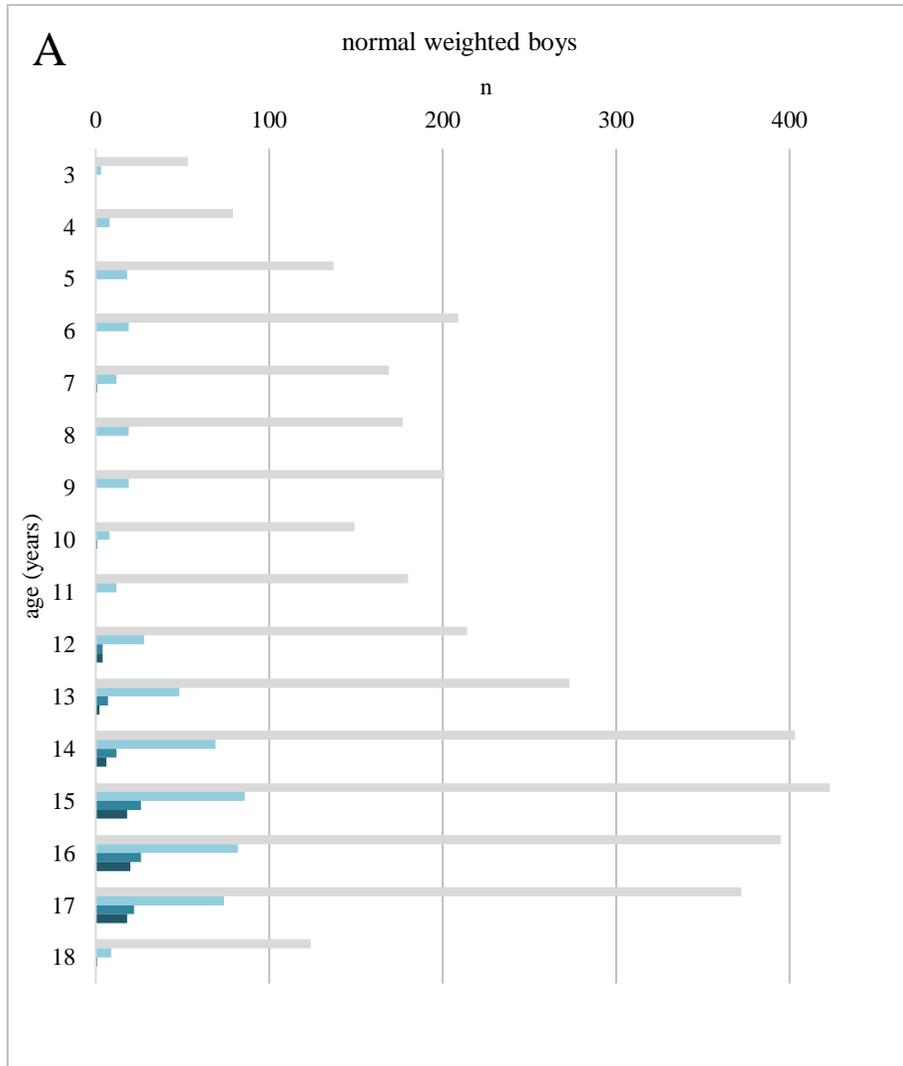
all patients   elevated / high BP at first measurement   proposed examination   elevated / high BP based on ABPM
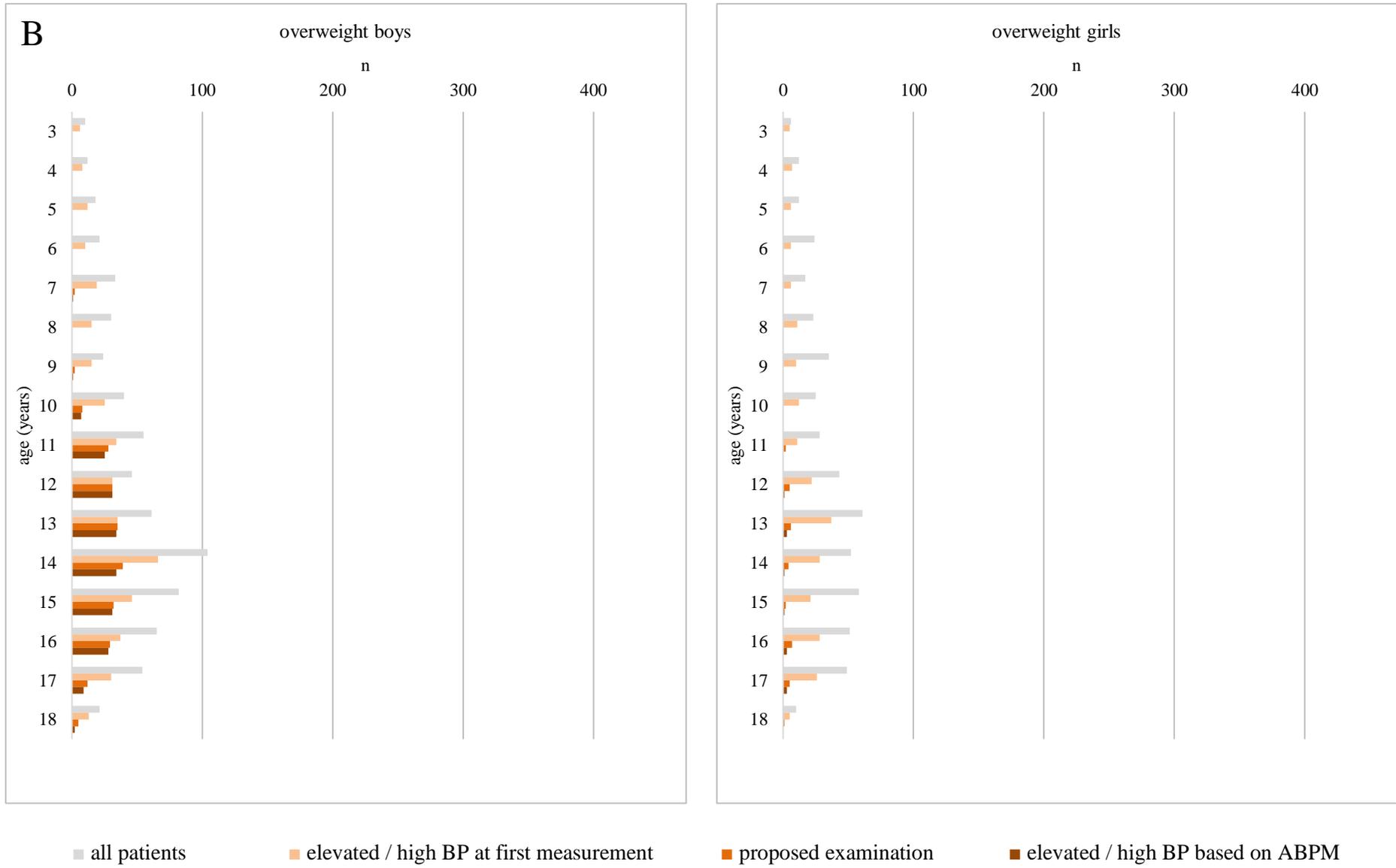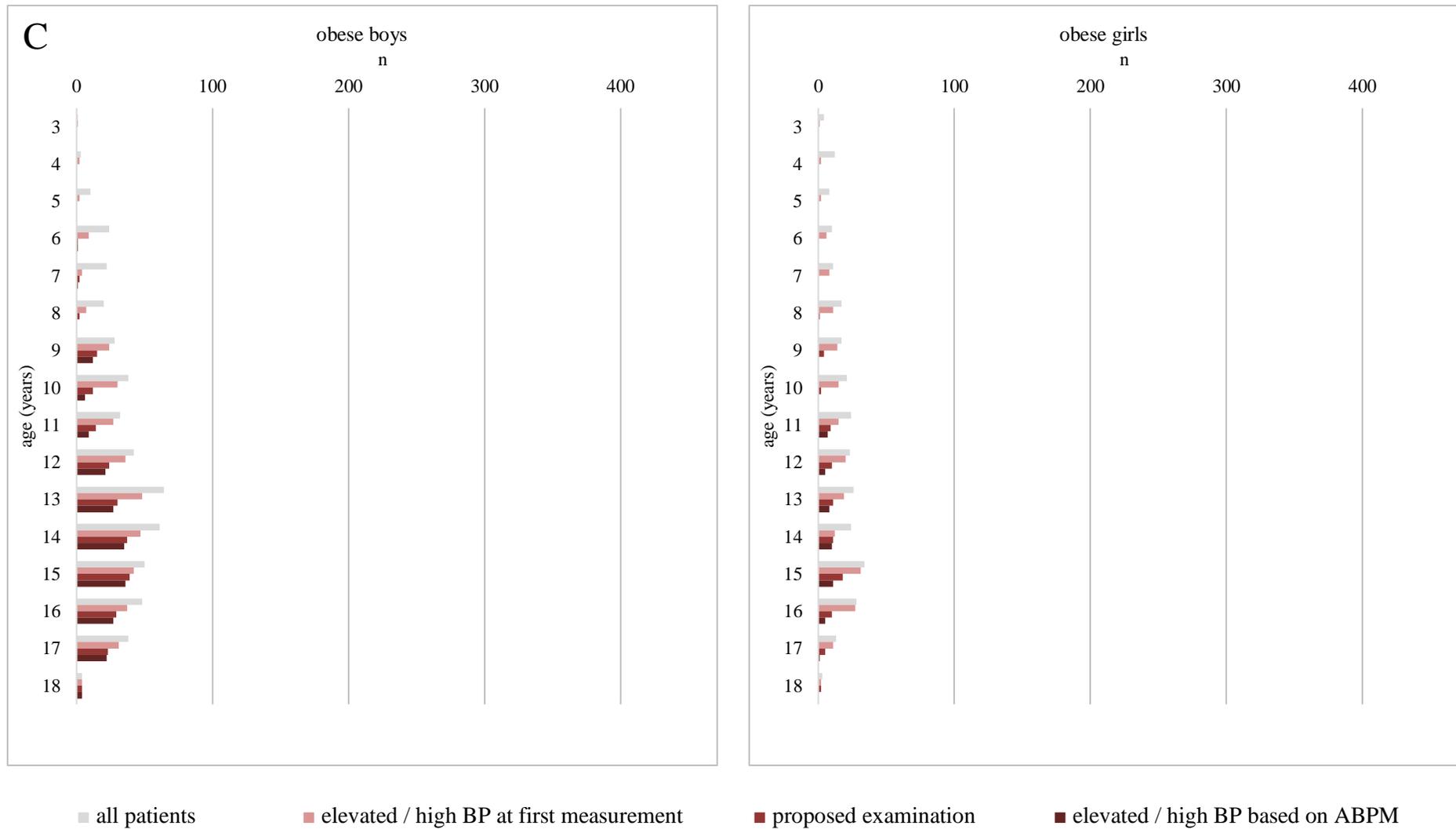
Figure 4 Distribution of elevated / high blood pressure at first measurement, proposed examination and elevated /or high blood pressure based on ABPM in different age groups in both sexes among normal weighted (A), overweight (B) and obese subjects (C)

Figure 5 represents the numbers of subjects with normal, elevated BP and hypertension in OW and O subgroups in boys (5/A) and girls (5/B). From 725 OW boys 86 and from 520 O boys 156 proved to have hypertension. From 506 OW girls 12, from 275 O 117 subjects were diagnosed with hypertension. Elevated BP was observed in 117 cases among OW boys, and 35 among O boys. Interestingly, in girls no elevated BP was found after the examination.
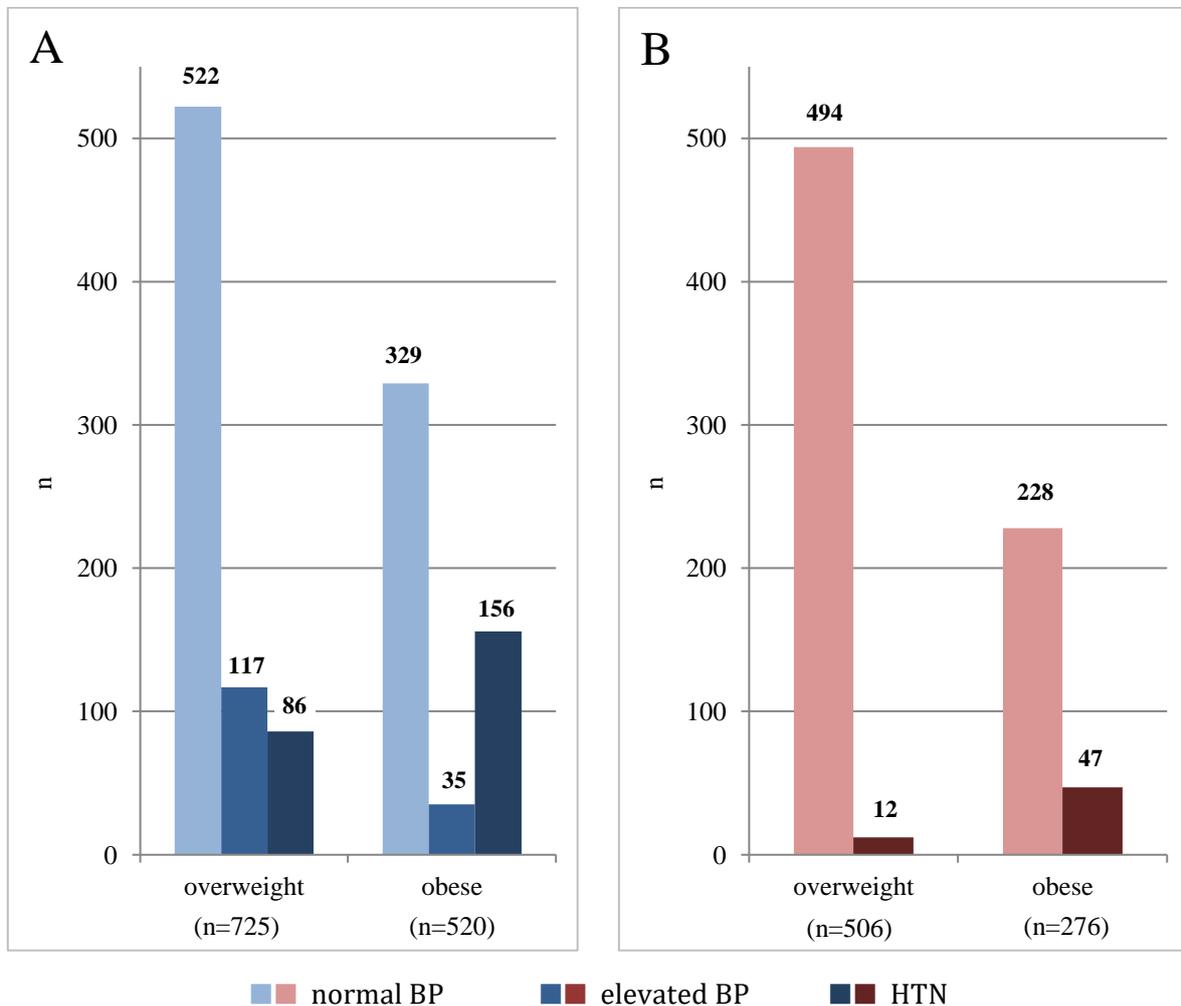
Figure 5 Distribution of normal BP, elevated BP and hypertension in OW and O subgroups in boys (A) and girls (B)

BP; blood pressure, OW; overweight, O; obese, n; number of patients

Figure 6 provides the summary of the distribution of normal BP, elevated BP and hypertension percentages in different weight categories. From this graph we can see that in boys hypertension was identified in 1.3% - 12.7% - 32.2% of the subjects in N, OW and O groups respectively (6/A). In girls hypertension was diagnosed in 0.2% - 2.4% - 17.1% of the individuals, in N, OW and O groups respectively (6/B). Both in OW and O boys the prevalence of HTN was significantly higher compared to girls (p<0.0001). In both genders, the frequency of HTN was 8.3% in OW patients, and 26.7% in O patients (6/C). The rate of elevated BP was

0.6% - 17.3% and 7.2% in N, OW and O boys respectively. In N girls this rate was 0.1%, surprisingly there was no patient with elevated BP in OW or O girls. Considering the whole investigated population, elevated BP was identified in 0.4% of N, 9.8% of OW and 4.6% in O patients.
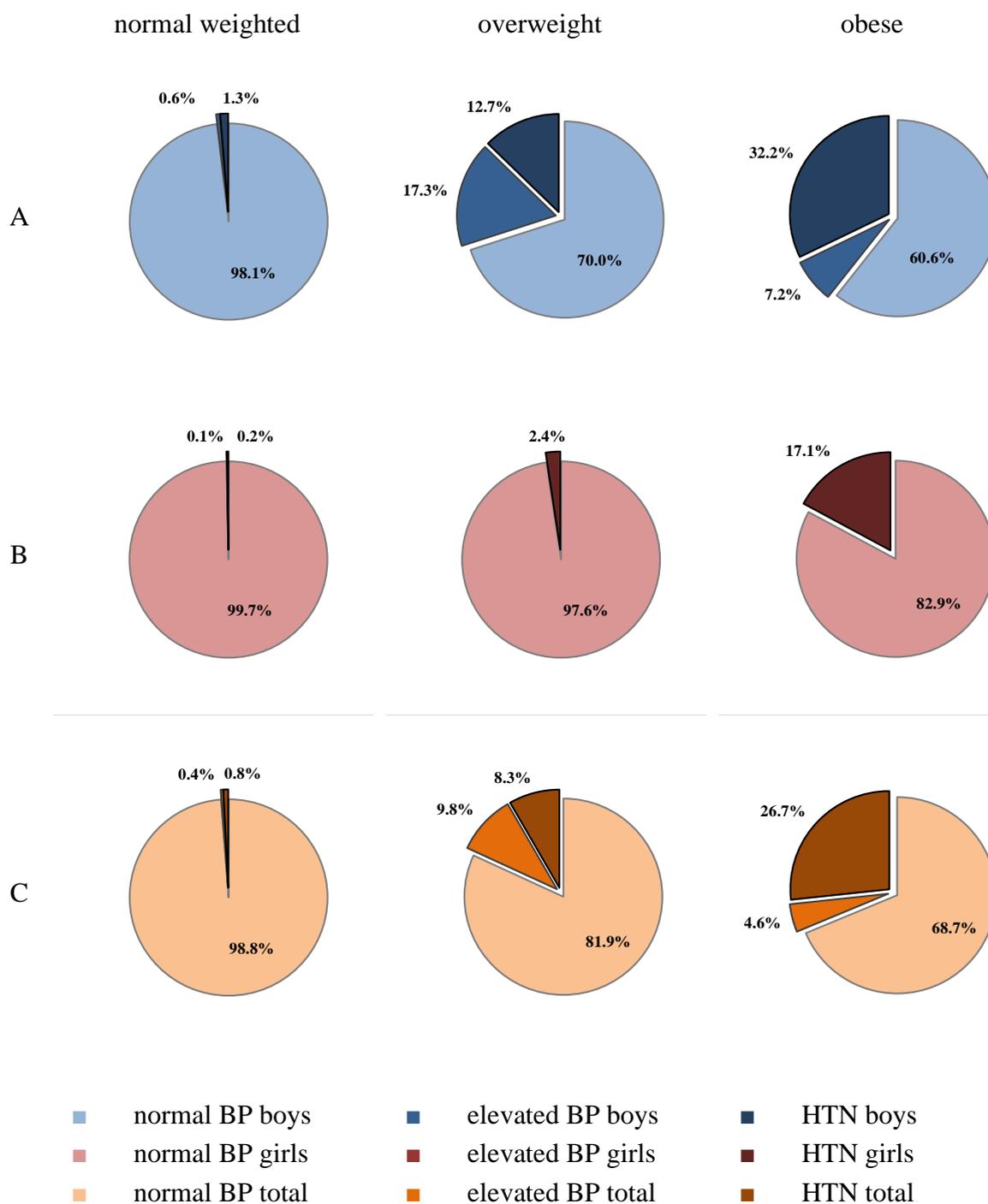
Figure 6 Prevalence of normal BP, elevated BP and HTN in N, OW and O boys (**A**), girls (**B**) and in the total population (**C**);

BP; blood pressure, HTN; hypertension, N; normal weight, OW; overweight, O; obese

Figure 7 presents and overview of HTN frequency in the examined population.
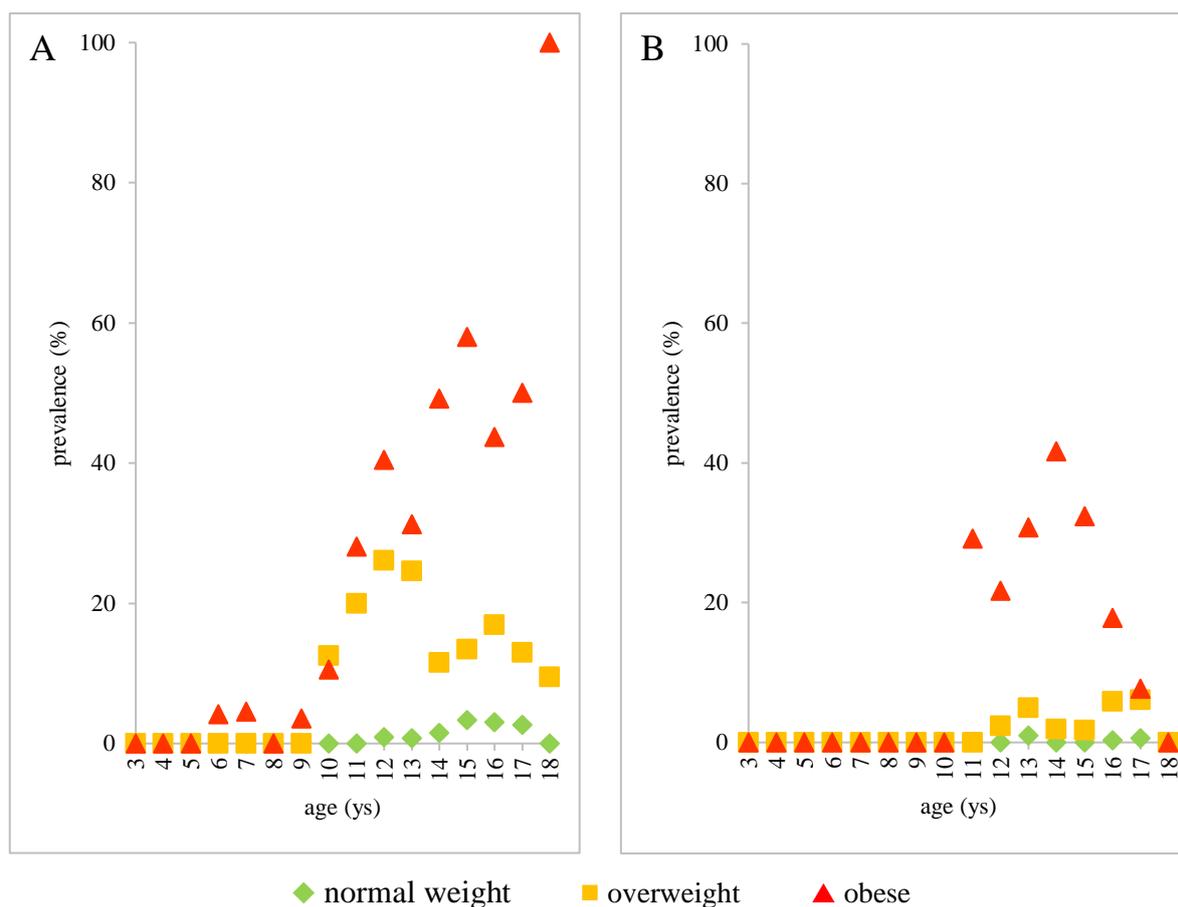
Figure 7 Distribution of HTN in normal, overweight and obese children based on their age

(A: boys, B: girls)

As can be seen, in N boys the prevalence of HTN was the highest between the ages of 15 and 17, and between the ages of 13 and 14 in N girls. In OW boys the peak was between the ages of 11 and 13 years, and in OW girls aged 16 to 17. In O groups, HTN was most common in 14-18-year-old and in 13-15-year-old girls.

Results from the statistical analysis of the HTN prevalence between boys and girls in different ages are presented in Table 2.

Table 2 Comparison of high blood pressure prevalence values between sex, age and weight categories (Student's t-test)

age (years)	boys			girls			boys vs girls		
	overweight vs normal weight	obese vs normal weight	overweight vs obese	overweight vs normal weight	obese vs normal weight	overweight vs obese	normal weight	overweight	obese
3	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-	-
6	-	p < 0.0001	p < 0.0001	-	-	-	-	-	p < 0.0001
7	-	p < 0.0001	p < 0.0001	-	-	-	-	-	p < 0.0001
8	-	-	-	-	-	-	-	-	-
9	-	p < 0.0001	p < 0.0001	-	-	-	-	-	p < 0.0001
10	p < 0.0001	p < 0.0001	p < 0.0001	-	-	-	-	p < 0.0001	p < 0.0001
11	p < 0.0001	p < 0.0001	p < 0.0001	-	p < 0.0001	p < 0.0001	-	p < 0.0001	NS
12	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001
13	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	NS
14	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001
15	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001
16	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001
17	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001
18	p < 0.0001	-	p < 0.0001	-	-	-	-	p < 0.0001	-

Data from table shows us, that the frequency of HTN was statistically higher (p<0.0001) in OW and O patients compared to N patients in both genders. Furthermore, this prevalence is even higher in O patients compared to OW age groups. Due to the lack of HTN individuals in some age groups, statistical analysis was not applied in these categories (marked as "–" in Table 2).

Underlaying causes of HTN in the examined patients were heterogeneous: in one case cardiological (17-year-old girl, coarctation of aortae); in one case endocrinological (14-year-old girl, hyperthyroidism). In 34 cases clinical admission was suggested based on abnormal ultrasound findings of the kidneys (cysts, dilatation of upper collecting system). Finally, from these patients in 26 cases no nephrogenic cause was observed in the background of the HTN and in 8 cases no feedback was received about the final diagnose.

Discussion

Prevalence of Overweight and Obesity

The prevalence of overweight and obesity is constantly increasing in children, adolescents, and adults, in developed and developing countries, as well [4]. This condition – beside several other profound consequences – raises the risk of cardiovascular mortality, thus on the one part substantially shortens life expectancy for persons, and on the other part, imposes a burden on health care and social welfare systems. Between 1975 and 2016 the global mean BMI raised from 16.8 kg/m^2 to 18.5 kg/m^2 in boys, and from 17.2 kg/m^2 to 18.6 kg/m^2 in girls. The Hungarian mean BMI increased from 18.8 kg/m^2 to 20.0 kg/m^2 in boys, and from 18.2 kg/m^2 to 19.9 kg/m^2 in girls [4]. In the ranking of 200 countries -where 1st place means the most overweight or obese country-, regarding mean BMI in boys, Hungary moved to the 65th place (2016) from the 23rd (1975), and from 79th (1975) to 70th (2016) place in girls. In the same ranking, but regarding overweight, Hungarian boys are at the 50th place (from the 46th place) and girls stepped down to the 99th place from 78th place. In the case of obesity, Hungarian boys are on the 51st place (from 54th) and girls became 85th from 64th. Nauru, Cook Islands and Paulu are in the top three in the rank of overweight and obesity, meanwhile Vietnam, Cambodia, India, Burkina Faso and Nepal are represented in the last 5 positions on these lists [4]. In 2016, the mean BMI in the World was 18.5 kg/m^2 in girls and 18.6 kg/m^2 in boys, compared to 19.9 kg/m^2 and 20.0 kg/m^2 in Hungarian girls and boys, respectively.

Studies have suggested that there is a strong correlation between elevated BMI and geographical location, local habits and traditions, socio-economic culture, considering eating habits as well as physical activity patterns [49,50]. Changes in environmental factors, lifestyle, eating habits and in physical activity may affect the prevalence of overweight and obesity in a negative or positive way, as well. Such changes and the geo-economical differences justify the repeat of large population studies, in order to follow-up potential changes in the frequency of overweight and obesity. For this purpose, several studies have been carried out in Europe involving more than 10 European countries, including Hungary.

Between 2002 and 2006 in the "HELENA" study [51] adolescents (aged 12.5 - 17.5 years), between 2006 and 2012 in the "IDEFICS" [52] study children (aged 2 - 9 years), and between 2010 and 2013 in the "ENERGY" study [53] children aged 10-12 years were assessed. These three projects cover a remarkable period of time (>11 years). *Antal and her co-workers* have conducted their study in the first semester of the academic year 2005/2006 [57]. Our research

lasted for 3 years, and the 3−18-year-old population was basically assessed simultaneously. Due to such circumstances, our findings may give a more accurate picture of the condition of a well-balanced, young generation with significant number (n=6.824) of participants. Figure 8 represents our findings compared with the data previously measured in IDEFICS and in the study of Antal and her co-workers in Hungary [52,54].
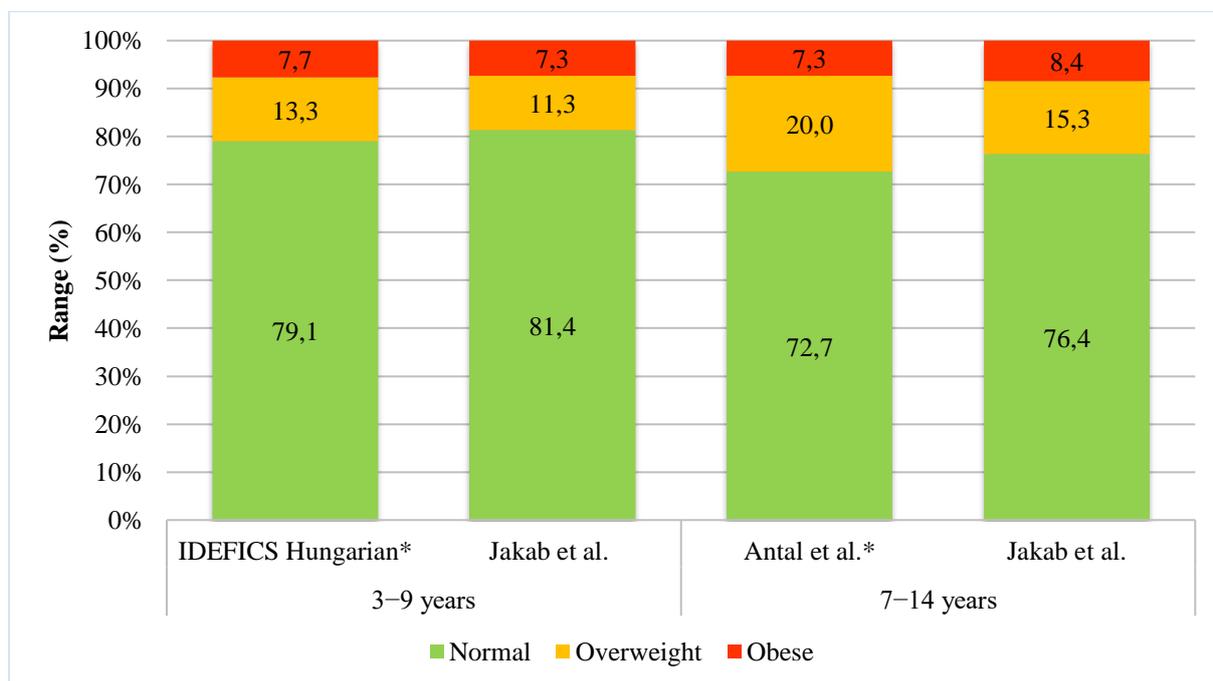
Figure 8 Comparison of normal weight, overweight and obesity prevalence between European data [52], latest Hungarian data [54] and results from this study

To ensure the comparability of the data, our data have been determined in accordance with the age groups applied in the previous studies (3−9 years, 7−14 years). Since prevalence is available only in percentages in the HELENA and ENERGY studies and absolute numbers regarding Hungary are not published therein, the proper statistical analysis in these cases could not be applied. Statistically, compared to the previous Hungarian data, there has been no changes in any of the sexes, in any respect (Fisher's exact test, overweight p=0.055 and obesity p=0.66) in the youngest age group (3−9 years). However, a slight decrease is observed in the prevalence, since the p-value of the overweight is relatively close to the level of significance. In contrast, a significant decrease is presented in the older age group (7−14 years), in both sexes, with respect to overweight: the total prevalence has decreased from 20% to 15.3% (p<0.005), while in this age group the prevalence of normal BMI increased from 72.7% to 76.4% (p<0.001), and no difference is presented in the case of obesity (p=0.2). Prevalence of OW/O in the studied population is detailed in Table 1.

In our study, the prevalence of overweight and obesity was significantly higher in boys than in girls. Our findings essentially correspond to the global prevalence published by Ng and her co-workers [3]. BMI differences between the sexes have long been recognized [55]. Such differences may arise from biological, sociological and cultural differences, or perhaps from the combined effect of these [56,57]. There is a close correlation between the total energy expenditure (TEE) and body weight [58]. Goran and his co-workers found in their longitudinal study, that between the age of 5 to 10 years TEE is continuously increasing in case of boys, however in case of girls, this marker rises from 1,400 kcal (at age 5) to 1,800 kcal (at age 6) and falls to 1,600 kcal (at age 9). This significant decrease is due to the fact that the girls' physical activity decreases by 50% between the age 6 to 9 years [59]. Studies have found that adolescent girls are more likely to give attention to healthy nutrition, whilst boys are more apt to consume more fast food. These differences may stem from the Western societies' perception of the ideal body figure and from the fact that certain foods are gendered. For example, power and virility is symbolized by meat, therefore men eat more meat than women, while fat and carbohydrate rich foods are more often consumed by women in accordance with their menstrual cycle [60].

The above described reasons may explain the age-related increase in prevalence of overweight and obesity, namely that it increases between the age of 3 and 10 in both sexes, and afterwards shows a gradual decrease in both sexes; however, such decrease is more significant in case of girls.

One of the most important observation of this study is that compared to the previous Hungarian data, mild decrease occurred in the youngest age group (3−9 years) in both sexes, in respect of overweight. Furthermore, the prevalence of overweight significantly decreased, while the prevalence of normal BMI significantly increased in the older age group (7−14 years).

The interesting fact that the total prevalence of overweight and obesity has not significantly changed in the age group 3−9 year compared to the previous Hungarian data, may be explained by several factors. The lower supply of protein from human milk (9 and 10 g/d at ages 3 and 6 month) as compared with formula (14 and 18 g/d, respectively) [61] might attenuate both early weight gain and later obesity [62]. One of the best predictors of later obesity risk is weight gain during the first year of life [63–65]. Recent studies have pointed out that increased protein intake (+6−8 g daily) during the first year of life could lead to 2.43 times higher risk for obesity at the age of 6 [66]. Moreover, the daily rhythm of nutrition of this age group is not well-balanced, some meals are often omitted, which may also increase the risk of obesity [67]. Since parents have the greatest influence on nutrition at this age, they may have a key role at

eliminating these anomalies. Consequently, education of parents in the field of nutrition is crucial, since they are the ones who are mostly responsible for the daily eating routine of their children.

Recognising these factors, several acts have been adopted in Hungary aimed to prevent obesity in childhood (daily physical education, regulation of the products offered at the school buffet, maximized trans-fatty acids in products).

When examining the prevalence of these conditions in other European countries we have found that in Switzerland the total prevalence of overweight and obesity shows a significant decline, due to the school-based promotion of physical activity and healthy nutrition. In France and Sweden data demonstrate that the raising trend has stopped, similarly to the United Kingdom, where it has reached its peak in 2005 (26.4%) and no notable change was observed until 2008 [68].

Detailed interview questionnaire (physical activity patterns and nutritional habits) that is required to assess the progress examined, and measurement of hip and waist circumference, and upper arm skinfold thickness are planned in the future. These can give us more informative results, which could help in understanding the changes in the prevalence of increased BMI.

Prevalence of Overweight and Obesity Associated Hypertension

Juvenile hypertension affects males in majority, the prevalence is 5.5% in Caucasian males between the ages of 18 and 29 years, and 0.8% in females [69]. *Roberts* highlights the fact that this differentiation starts at the ages of 12 to 17 [70], caused by genetical and biological triggers and lasts until menopause [71]. A possible explanation for this finding might be that boys - compared to girls - reaches greater body height and weight during puberty, and this anabolic demand could only be balanced via increased cardiac output by the cardiovascular system. This might lead to disproportion between the peripheral vascular volume and increased cardiac output resulting in increased or elevated BP. Furthermore, OW and O are more common in boys and increased amount of adipose tissue raises BP via numerous pathophysiological pathways, these facts will lead to the higher prevalence of HTN in boys compared to girls. Researchers from the Pediatric Department from the University of Pécs published Hungarian data on O associated HTN in children [72,73]. *Csábi* and her co-workers established the prevalence of metabolic cardiovascular syndrome in O adolescents. In their analysis of 103 O boys, HTN was confirmed in 39.8%, whereas in 77 O girls, HTN was observed in 41.6% based on 24-hours-ABPM results [72]. In an investigation into circadian rhythm of BP, *Török* and her co-workers took 24-hours-ABPM measurements in 73 children and based on their diurnal index (DI)

divided the subjects into "dipper" (DI is 10%<) and "non-dipper" (DI is >10%) groups. They found that HTN was more common in the non-dipper group (83.9%) compared to the dipper group (45.2%) [73]. *Csábi and Török* reported higher prevalence of O associated HTN, than described in our study. This might stem from the difference of the included subjects: both studies [72,73] enrolled patients from the obesity outpatient clinic, in contrast with our normal population. Much of the available literature on OW and O associated HTN deals with the question of the frequency in children and adolescents. Analysing the current literature we collected the most relevant articles, based on the following including criteria: timing of the study (between 2005 and 2018), number of cases (minimum as much cases as in our research), published odds ratio (OR), to understand how OW and O rise the risk for HTN in this population. Outlines of the finally included articles are shown in Table 3.

Table 3 Comparison of our results with those of two earlier-published large-population studies

	normal BP (<90th percentile) n / %	elevated BP (≥90th - <95th percentile) n / %	high BP (≥95th percentile) n / %	odds ratio (95% CI)	nationality
Lu *et al*; 2013 [74]					
overweight (n = 10.252)	8 890 / 86.1	No data	1 362 / 13.9	1.67	Chinese
obese (n = 7.397)	5 797 / 78.4	No data	1 600 / 21.6	2.17	
Lo *et al;* 2014 [33]					
overweight (n = 11.016)	9 454 / 65.6	3 402 / 23.6	1 562 / 10.8	1.5 (0.9 – 2.3)	American
obese (n = 4.582)	3 348 / 51.6	1 906 / 29.4	1 234 / 19.0	1.8 (1.1 – 3.0) 3.5 (2.1 – 5.8) 5.7 (3.6 – 8.9)	
Jakab *et al*; 2019					
overweight (n = 1.231)	1 016 / 81.9	117 / 9.8	98 / 8.3	1.1 (0.8 – 1.3)	Hungarian
obese (n = 795)	557 / 68.7	35 / 4.6	203 / 26.7	3.6 (3.0 – 4.3)	

Lu et al. in 2009 completed a prospective, cross-sectional study in China (Shanghai) involving a total of 78.114 children (7−14 years) [74]. BP was measured only once with mercury sphygmo-manometer. There is no available data on patients with elevated BP. Prevalence of HTN was 13.9% in OW patients (OR: 1.67) and 21.6% in O patients (OR: 2.17).

Between 2007 and 2010 Lo et al. analysed data of 117.618 children and adolescents (6−17 years) in a retrospective, cross-sectional study. In this research, BP was measured once with an oscillometric device, repeating the measurement if needed (elevated SBP and/or DBP) [33]. Obese children were further classified into 3 different subgroups on BMI expressed as a percentage above the 95th BMI percentile according to age and sex. In this study, the frequency of elevated BP was 23.6% among OW patients, and 29.4% among O patients. Furthermore, prevalence of HTN was 10.8% in OW subjects, whereas it was 19% in O patients (OR: 1.8-3.5-5.7).

In our study this rate was 8.3% in OW and 26.7% in O patients. Our findings show a great accordance with the above mentioned results, however, minor discrepancies may origin from the following methodical difference: on one hand, in the Chinese study local reference values were used to categorize subjects based on their BP [75], on the other hand, in the American study the reference values published in 2004 and revised in 2012 were applied [43]. In the study conducted by us European cut-off values were adopted to create subgroups based on BP [47,48].

Surprisingly, after the detailed examination we did not found any patient with elevated BP in OW or O girls. The underlying causes for this could be the fact, that HTN is a more common morbidity in boys compared to girls [69,70]. Secondly, total number of OW and O girls was markedly lower than in boys. Lastly, prevalence of HTN was even lower in OW and O girls. These factors may lead to the observed result, which is considered to an accidental finding. Hereby we highlight the fact that in N girls in 3 cases elevated BP was diagnosed.

OW, O and associated HTN is a major public health problem, since the rising frequency of OW and O consequently increases the incidence of HTN in these patients. Nowadays, it is suggested to closely follow-up patients with OW, O in order to monitor possible comorbidities, and supporting them in a body weight reducing lifestyle, finally, if needed treating them appropriately. However, the final goal should be proper primary prevention targeting these abnormal conditions.

Summary

A summary of the main findings and of the principal issues which have arisen in this thesis are the followings:

1. We have found the prevalence of overweight is 13.4% and 6.6% of obesity in Szolnok, in Hungary.

2. Overweight and obesity are more common in boys, than in girls (p<0.005).

3. Compared to the previous Hungarian data, we have identified a mild decrease in the youngest age group (3−9 years) in both sexes, in respect of overweight (2006−2012 vs 2012−2016). We have established, that the prevalence of overweight significantly decreased, while the prevalence of normal BMI significantly increased in the older age group (7−14 years) (2005−2006 vs 2012−2016).

4. Prevalence of overweight and obesity associated hypertension was 8.3%, and 26.7% respectively.

5. Increased BMI associated hypertension was more common in boys. In overweight boys the peak was between the ages of 11 and 13 years, and in OW girls between 16 to 17. In O groups, HTN was most common in boys aged 14 to 18, while 13 to 15 in girls.

6. Overweight raises the risk for hypertension (odds ratio: 1.1) not as much, as obesity, where the odds ratio is 3.6.

7. Regarding the prevalence of overweight and obesity associated hypertension, our findings show a great accordance with the great, international, relevant and contemporary population studies.

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Supplementary Table 1A/a Characteristics of normal weight, overweight and obese boys

age (ys)		normal weight							overweight							obese					
	n	weight (kg)	height (cm)	BMI (kg/m^2)	SBP (mmHg)	DBPbrach (mmHg)	HR (1/min)	n	weight (kg)	height (cm)	BMI (kg/m^2)	SBPbrach (mmHg)	DBPbrach (mmHg)	HR (1/min)	n	weight (kg)	height (cm)	BMI (kg/m^2)	SBPbrach (mmHg)	DBPbrach (mmHg)	HR (1/min)
3	53	15.9±2.3	104.3±6.4	14.6±1.7	93.6±7.5	58.9±5.9	96.9±15	10	19.1±2.5	102.5±6.4	18.1±0.5	107.4±8.9	60.9±4.7	100.8±13.2	1	21.0±n.a.	104.0±n.a.	19.4±n.a.	111.0±n.a.	65.0±n.a.	110.0±n.a.
4	79	17.7±2.6	109.3±7.1	14.8±1.5	94.9±9.3	57.5±7.2	92.5±12.8	12	23.1±4.9	111.7±11.5	18.3±0.5	111.0±9.0	64.5±7.1	89.8±10.9	3	26.3±2.5	115.0±5.0	19.9±0.2	117.7±15.2	56.7±3.5	84.7±11.5
5	137	20.1±2.7	116.2±6.2	14.9±1.5	97.9±8.8	59.5±6.5	91.1±13.1	18	25.5±3.1	117.9±5.9	18.3±0.7	113.8±8.4	67.1±7.3	89.2±13.7	10	32.9±5.2	121.2±7.0	22.3±2.3	126.0±15.1	64.8±7.5	93.5±16.0
6	209	22.1±2.9	122±5.8	14.8±1.4	98.5±9.6	59.5±7	86.4±12.4	21	29.2±3.8	125.4±7.9	18.5±0.6	113.0±12.0	62.9±7.1	83.1±10.9	24	37.0±7.7	126.5±5.3	23.0±3.3	120.0±12.6	65.3±7.7	85.7±14.3
7	169	24.7±3.4	127.3±6.2	15.2±1.4	100.1±9.3	60.1±6.7	82.3±13.1	33	33.2±3.6	131.7±6.4	19.1±0.8	116.4±8.6	67.3±5.6	84.8±13.4	22	44.8±8.9	135.0±5.8	24.4±3.7	126.0±12.3	68.7±8.1	84.0±13.0
8	177	28.3±4.2	133.7±6.8	15.8±1.5	100.8±10.3	60.2±6.4	79.3±12.8	30	37.5±4.3	136.9±6.8	20.0±1.0	116.0±9.3	67.4±5.7	80.8±10.4	20	49.0±6.7	139.3±8.0	25.2±2.6	121.8±9.9	69.3±5.3	80.1±10.8
9	201	31.2±5.0	138.6±7.3	16.2±1.7	102.5±9.7	61.7±7.0	79.1±13.7	24	41.5±4.0	141.0±6.3	20.9±1.0	119.8±8.7	67.2±6.4	77.0±9.6	28	56.2±10.4	146.1±6.2	26.2±3.6	127.5±15.0	72.0±7.7	86.8±14.6
10	149	35.3±5.4	144.2±6.7	16.9±1.7	102.3±9.9	61.6±5.8	75.1±11.5	40	49.5±4.9	149.2±6.3	22.2±1.1	122.4±10.1	70.3±6.0	80.6±13.8	38	64.1±11.0	150.9±7.0	28.0±3.7	128.0±13.3	69.2±9.2	79.0±14.7
11	180	37.5±6.6	148.2±8.0	17.0±1.9	103.1±10.2	61.6±6.2	73.9±12.3	55	53.4±7.2	152.3±8.5	22.9±1.4	122.1±10.6	68.9±6.4	75.0±11.3	32	71.8±10.8	158.3±7.8	28.5±2.6	133.0±14.2	73.9±9.9	79.8±14.8
12	214	43.1±8.3	155.6±9.1	17.7±2.0	108.1±11.4	63.3±7.2	77.1±13.7	46	60.2±7.7	160.5±8.5	23.3±1.4	122.5±8.6	68.1±7.0	75.0±12.7	42	84.3±12.6	164.4±7.5	31.1±3.6	134.8±11.2	72.9±7.8	82.3±13.2
13	273	49.7±8.7	163.4±9.1	18.5±2.0	111.7±11.6	63.6±6.7	76.4±13.6	61	68.9±8.2	167.6±8.4	24.5±1.5	125.8±10.6	67.7±7.1	73.2±10.4	64	88.2±13.0	169.0±7.6	30.8±3.2	137.5±14.7	72.4±10.2	79.8±13.9
14	403	56.4±9.2	171.2±9.3	19.1±1.9	115.7±12.3	65.6±7.8	73.2±13.4	104	75.8±9.2	173.3±9.1	25.1±1.3	131.3±11.7	70.1±7.7	73.6±14.1	61	98.4±17.1	173.9±8.4	32.4±4.1	143.4±16.5	78.9±10.1	81.8±14.7
15	423	60.6±8.9	175.2±7.7	19.7±2.1	118.3±13.9	67.2±8.2	70.9±13.5	82	79.2±8.5	175.8±7.3	25.6±1.5	132.1±12.2	70.9±7.5	69.9±11.8	50	102.2±13.0	174.8±6.7	33.5±4.2	148.4±11.9	79.7±7.9	77.1±14.5
16	395	63.7±9.5	177±7.3	20.3±2.3	122.3±13.8	68.8±8.1	72.1±14.7	65	82.4±8.1	178.1±7.5	25.9±1.2	134.1±12.2	73.4±8.4	70.4±12.7	48	105.3±13.5	177.4±7.2	33.4±3.4	146.1±13.2	80.5±9.1	76.8±11.8
17	372	66.1±9.2	178.4±7.2	20.7±2.2	123.6±15.1	68.8±8.2	70.2±13.2	54	86.0±9.4	179.5±8.1	26.6±1.4	137.9±12.0	73.5±8.4	71.7±11.4	38	107.6±12.4	179.3±7.5	33.4±3.4	148.3±13.1	81.5±8.7	76.5±14.4
18	124	68.2±8.1	179.5±6.8	21.1±2.0	122.8±12.5	65.3±7.4	71±13.6	21	85.1±10.6	178.3±8.5	26.7±1.4	143.2±13.3	74.6±8.4	77.0±16.5	4	100.0±13.7	175.3±6.6	32.4±2.3	143.3±17.5	80.8±4.5	73.8±3.8

Data are presented as mean ± SD. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; NS, non-significant difference; n.a., not applicable

Supplementary Table 1A/b Comparison of normal weight, overweight and obese boys' characteristics (Student's t-test)

age (ys)	overweight vs normal weight						obese vs normal weight						overweight vs obese					
	weight	height	BMI	SBP	DBP	HR	weight	height	BMI	SBP	DBP	HR	weight	height	BMI	SBP	DBP	HR
3	$p < 0.0003$	NS	$p < 0.0001$	$p < 0.0001$	NS	NS	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
4	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.003$	NS	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0002$	NS	NS	NS	NS	$p < 0.0001$	NS	NS	NS
5	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.02$	$p < 0.0001$	$p < 0.0001$	$p < 0.02$	NS	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.02$	NS	NS
6	$p < 0.0001$	$p < 0.02$	$p < 0.0001$	$p < 0.0001$	$p < 0.04$	NS	$p < 0.0001$	$p < 0.0005$	$p < 0.0001$	$p < 0.0001$	$p < 0.002$	NS	$p < 0.0002$	NS	$p < 0.0001$	NS	NS	NS
7	$p < 0.0001$	$p < 0.0003$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.002$	NS	NS
8	$p < 0.0001$	$p < 0.02$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0008$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.05$	NS	NS
9	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0003$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.007$	$p < 0.0001$	$p < 0.005$	$p < 0.0001$	$p < 0.04$	$p < 0.02$	$p < 0.008$
10	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.02$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.05$	NS	NS
11	$p < 0.0001$	$p < 0.002$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.02$	$p < 0.0001$	$p < 0.002$	$p < 0.0001$	$p < 0.0002$	$p < 0.006$	NS
12	$p < 0.0001$	$p < 0.001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.03$	$p < 0.0001$	$p < 0.03$	$p < 0.0001$	$p < 0.0001$	$p < 0.003$	$p < 0.02$
13	$p < 0.0001$	$p < 0.002$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.004$	$p < 0.004$
14	$p < 0.0001$	$p < 0.04$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.04$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.0005$
15	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0003$	NS	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.003$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.003$
16	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.04$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.009$
17	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	$p < 0.007$	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0002$	$p < 0.0001$	NS
18	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$	NS	$p < 0.0001$	NS	$p < 0.0001$	$p < 0.002$	$p < 0.0001$	NS	$p < 0.03$	NS	$p < 0.0001$	NS	NS	NS

Data are presented as mean ± SD. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; NS, non-significant difference; n.a., not applicable

Supplementary Table 1B/a Characteristics of normal weight, overweight and obese girls

age (ys)	normal weight							overweight							obese						
	n	weight (kg)	height (cm)	BMI (kg/m²)	SBP (mmHg)	DBP (mmHg)	HR (1/min)	n	weight (kg)	height (cm)	BMI (kg/m²)	SBP (mmHg)	DBP (mmHg)	HR (1/min)	n	weight (kg)	height (cm)	BMI (kg/m²)	SBP (mmHg)	DBP (mmHg)	HR (1/min)
3	38	15.8 ± 2.4	102.7 ± 6.1	14.9 ± 1.2	94.1 ± 7.1	57.1 ± 8.1	98.7 ± 14.0	6	18.7 ± 3.2	100.5 ± 7.9	18.4 ± 0.6	112.3 ± 6.7	62.3 ± 3.7	104.7 ± 8.8	4	22.8 ± 2.9	104.0 ± 5.5	21.0 ± 1.0	122.3 ± 6.1	70.8 ± 3.1	92.3 ± 9.4
4	70	17.2 ± 2.5	108.8 ± 6.5	14.5 ± 1.7	97.0 ± 9.5	57.7 ± 6.4	93.5 ± 11.2	12	21.1 ± 3.5	108.1 ± 8.4	17.9 ± 0.4	110.9 ± 9.0	62.5 ± 6.2	97.7 ± 17.0	12	29.8 ± 4.0	113.5 ± 6.4	23.1 ± 2.5	119.9 ± 6.6	62.3 ± 5.8	97.8 ± 10.4
5	89	18.7 ± 2.9	114.4 ± 6.9	14.3 ± 1.5	97.6 ± 10.8	58.8 ± 7.6	93.9 ± 12.0	12	27.1 ± 3.1	122.3 ± 6.6	18.1 ± 0.7	119.3 ± 14.8	67.6 ± 9.6	91.8 ± 15.5	8	30.4 ± 5.7	118.6 ± 8.0	21.4 ± 1.9	117.4 ± 12.0	65.0 ± 6.3	88.8 ± 11.1
6	145	21.5 ± 3.2	121.5 ± 6.6	14.5 ± 1.5	99.0 ± 10.3	59.4 ± 6.9	88.7 ± 14.2	24	28.6 ± 4.4	124.0 ± 8.6	18.5 ± 0.8	112.8 ± 10.5	64.8 ± 7.7	85.0 ± 10.9	10	32.8 ± 5.2	120.3 ± 4.9	22.5 ± 2.1	117.4 ± 14.5	66.4 ± 9.6	90.6 ± 7.4
7	128	23.8 ± 4.2	126.8 ± 7.0	14.7 ± 1.8	100.2 ± 10.5	60.5 ± 6.9	86.6 ± 12.8	17	32.4 ± 2.8	131.2 ± 4.6	18.8 ± 0.8	115.4 ± 8.4	64.1 ± 5.6	85.4 ± 9.0	11	40.6 ± 6.7	131.5 ± 4.2	23.4 ± 2.5	125.6 ± 17.0	70.1 ± 8.2	88.3 ± 16.4
8	123	27.2 ± 4.6	132.9 ± 6.5	15.3 ± 1.7	101.8 ± 10.3	60.9 ± 6.2	84.5 ± 12.4	23	36.0 ± 5.0	134.2 ± 6.7	19.9 ± 1.2	118.0 ± 10.0	68.0 ± 7.0	81.7 ± 13.7	17	48.5 ± 4.4	141.4 ± 3.9	24.2 ± 1.6	124.5 ± 10.7	70.1 ± 6.2	86.3 ± 9.1
9	142	29.8 ± 5.2	137.6 ± 7.5	15.7 ± 1.8	102.8 ± 10.3	61.3 ± 6.4	83.0 ± 12.4	35	41.2 ± 5.5	139.7 ± 7.8	21.0 ± 1.0	118.5 ± 11.9	66.8 ± 7.1	83.4 ± 15.3	17	55.3 ± 7.3	146.0 ± 7.8	25.9 ± 2.0	125.9 ± 14.0	68.6 ± 9.5	82.0 ± 12.2
10	139	34.0 ± 5.9	143.7 ± 7.3	16.4 ± 1.9	105.6 ± 10.9	62.3 ± 6.5	83.5 ± 13.8	25	47.5 ± 4.8	147.7 ± 6.7	21.7 ± 0.9	121.5 ± 12.6	69.4 ± 8.3	87.4 ± 15.7	21	69.5 ± 10.5	154.3 ± 8.6	29.1 ± 3.1	139.2 ± 14.9	73.3 ± 6.4	94.4 ± 13.6
11	138	38.4 ± 7.2	149.2 ± 9.3	17.1 ± 2.0	105.2 ± 10.1	63.1 ± 7.0	80.4 ± 13.3	28	56.5 ± 7.7	155.8 ± 8.7	23.2 ± 1.4	124.0 ± 11.0	66.3 ± 8.7	83.0 ± 15.0	24	72.5 ± 10.3	157.3 ± 8.1	29.2 ± 2.3	128.6 ± 13.3	70.8 ± 9.9	85.5 ± 13.1
12	200	43.4 ± 7.3	155.7 ± 7.5	17.8 ± 2.0	109.7 ± 12.2	64.4 ± 7.5	82.1 ± 14.5	43	63.2 ± 7.0	160.7 ± 7.1	24.4 ± 1.7	127.0 ± 12.3	70.4 ± 7.7	82.5 ± 12.1	23	79.5 ± 10.8	161.0 ± 6.7	30.8 ± 4.8	134.7 ± 16.0	74.9 ± 10	83.7 ± 14.6
13	306	49.4 ± 6.9	161.6 ± 6.9	18.9 ± 2.0	111.5 ± 12.6	64.8 ± 7.4	79.3 ± 14.1	61	65.4 ± 7.5	161.9 ± 9.1	24.9 ± 1.5	129.2 ± 12.6	71.5 ± 7.9	81.0 ± 14.3	26	87.8 ± 13.8	162.9 ± 8.5	33.0 ± 4.2	140.4 ± 13.6	76.7 ± 9.9	84.1 ± 13.5
14	390	52.3 ± 7.4	164.3 ± 6.6	19.3 ± 2.1	111.5 ± 11.9	65.3 ± 7.1	76.6 ± 14.1	52	69.1 ± 7.5	163.2 ± 7.2	25.9 ± 1.5	128.1 ± 12.0	71.6 ± 7.5	78.7 ± 13.8	24	87.4 ± 12.2	163.8 ± 5.6	32.5 ± 3.5	141.6 ± 15.2	79.3 ± 9.2	86.4 ± 12.5
15	394	53.9 ± 7.5	164.8 ± 6.7	19.8 ± 2.2	110.8 ± 11.8	66.2 ± 7.3	76.1 ± 13.8	58	70.3 ± 6.3	164.3 ± 6.5	26.0 ± 1.3	125.1 ± 10.6	72.0 ± 6.5	76.8 ± 12.7	34	96.8 ± 13.5	168.5 ± 7.1	34.1 ± 4.6	142.8 ± 15.4	79.4 ± 7.4	83.7 ± 13.4
16	361	54.8 ± 7.1	165.4 ± 6.6	20 ± 2.2	112.7 ± 11.3	68.0 ± 7.3	76.6 ± 13.3	51	72.2 ± 7.5	165.4 ± 7.2	26.3 ± 1.3	130.2 ± 12.9	74.0 ± 8.2	78.2 ± 13.4	28	92.4 ± 10.9	165.6 ± 5.6	33.7 ± 3.4	137.6 ± 11.2	78.5 ± 5.2	79.6 ± 11.7
17	326	55.6 ± 7.2	165.9 ± 6.2	20.2 ± 2.1	113.5 ± 12.1	67.2 ± 7.5	76.8 ± 12.6	49	75.5 ± 8.6	166.6 ± 7.7	27.1 ± 1.5	131.0 ± 14.1	73.6 ± 8.8	73.5 ± 11.5	13	95.6 ± 12.9	161.1 ± 5.9	36.8 ± 4.0	143.9 ± 14.5	76.2 ± 9.2	76.8 ± 9.2
18	135	56.6 ± 6.4	166.0 ± 6.7	20.6 ± 2.0	116.6 ± 13.6	67.8 ± 7.1	79.5 ± 13.0	10	76.6 ± 7.0	166.3 ± 7.6	27.7 ± 1.6	125.9 ± 10.8	71.5 ± 3.7	86.5 ± 8.5	3	102.0 ± 9.8	169.0 ± 7.1	35.7 ± 3.6	133.7 ± 15.0	62.0 ± 9.5	77.7 ± 1.2

Data are presented as mean ± SD. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; NS, non-significant difference; n.a., not applicable

Supplementary Table 1B/b Comparison of normal weight, overweight and obese girls' characteristics (Student's t-test)

age (ys)	overweight vs normal weight						obese vs normal weight						overweight vs obese					
	weight	height	BMI	SBP	DBP	HR	weight	height	BMI	SBP	DBP	HR	weight	height	BMI	SBP	DBP	HR
3	p < 0.02	NS	p < 0.0001	p < 0.0001	NS	NS	NS	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.002	NS	NS	p < 0.0007	p < 0.0001	p < 0.05	p < 0.006	NS
4	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.02	NS	p < 0.0001	p < 0.003	p < 0.0001	p < 0.0001	p < 0.03	NS	p < 0.0001	NS	p < 0.0001	p < 0.02	NS	NS
5	p < 0.0001	p < 0.0004	p < 0.0001	p < 0.0001	p < 0.0005	NS	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.03	NS	NS	NS	p < 0.0001	NS	NS	NS
6	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0005	NS	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.04	NS	p < 0.03	NS	p < 0.0001	NS	NS	NS
7	p < 0.0001	p < 0.02	p < 0.0001	p < 0.0001	p < 0.05	NS	p < 0.0001	p < 0.03	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0002	NS	p < 0.0001	p < 0.05	p < 0.03	NS
8	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	p < 0.0003	p < 0.0001	NS	NS	NS
9	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	p < 0.009	p < 0.0001	p < 0.05	NS	NS
10	p < 0.0001	p < 0.02	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0009	p < 0.0001	p < 0.005	p < 0.0001	p < 0.0001	NS	NS
11	p < 0.0001	p < 0.0006	p < 0.0001	p < 0.0001	p < 0.04	NS	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	NS	p < 0.0001	NS	NS	NS
12	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	p < 0.002	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	NS	p < 0.0001	p < 0.04	p < 0.05	NS
13	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	NS	p < 0.0001	p < 0.0004	p < 0.02	NS
14	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.001	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0003	p < 0.03
15	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	p < 0.003	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.003	p < 0.0001	p < 0.005	p < 0.0001	p < 0.0001	p < 0.0001	p < 0.02
16	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	NS	p < 0.0001	p < 0.02	p < 0.01	NS
17	p < 0.0001	NS	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	p < 0.006	p < 0.0001	p < 0.0001	p < 0.0001	NS	p < 0.0001	p < 0.02	p < 0.0001	p < 0.005	NS	NS
18	p < 0.0001	NS	p < 0.0001	p < 0.04	NS	NS	p < 0.0001	NS	p < 0.0001	p < 0.04	NS	p < 0.005	p < 0.0001	NS	p < 0.0001	NS	p < 0.02	p < 0.0002

Data are presented as mean ± SD. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; NS, non-significant difference; n.a., not applicable

Supplementary Table 2A Distribution of blood pressure by sex, age

		normal weight boys							normal weight girls							
		based on first BP measurement			further examination proposed by GP / SP	based on ABPM				based on first BP measurement			further examination proposed by GP / SP	based on ABPM		
		N	E	H		N	E	H		N	E	H		N	E	H
age (ys)	n	< 90	90-95	95 ≤		< 90	90-95	95 ≤	n	< 90	90-95	95 ≤		< 90	90-95	95 ≤
3	53	50	1	2	0	0	0	0	38	37	0	1	0	0	0	0
4	79	71	6	2	0	0	0	0	70	62	5	3	0	0	0	0
5	137	119	8	10	0	0	0	0	89	80	8	1	0	0	0	0
6	209	190	8	11	0	0	0	0	145	140	2	3	0	0	0	0
7	169	157	9	3	1	1	0	0	128	119	7	2	0	0	0	0
8	177	158	8	11	0	0	0	0	123	117	3	3	0	0	0	0
9	201	182	8	11	0	0	0	0	142	134	4	4	0	0	0	0
10	149	141	6	2	1	1	0	0	139	130	9	5	1	1	0	0
11	180	168	8	4	0	0	0	0	138	132	3	3	1	1	0	0
12	214	186	16	12	4	0	2	2	200	172	15	13	2	1	1	0
13	273	225	18	30	7	5	0	2	306	266	10	30	4	1	0	3
14	403	334	22	47	12	6	0	6	390	342	24	24	5	3	2	0
15	423	337	28	58	26	8	4	14	394	353	27	14	3	3	0	0
16	395	313	35	47	26	6	8	12	361	314	25	22	4	3	0	1
17	372	298	26	48	22	4	8	10	326	273	27	26	3	1	0	2
18	124	115	2	7	1	1	0	0	135	104	16	15	0	0	0	0
Total	3558	3044	209	305	100	32	22	46	3124	2775	185	169	23	14	3	6
		85.6%	5.9%	8.6%	2.8% * 19.5% **	0.9%	0.6%	1.3%		88.8%	5.9%	5.4%	0.7% * 6.5% **	0.4%	0.1%	0.2%

BP, blood pressure; GP/SP, general practitioner and/or school physician; ABPM, 24-hs blood pressure monitoring; N, normal blood pressure; E, elevated blood pressure; H, high blood pressure; * further examination recommended by GP / school physician compared to the total group size; ** further examination recommended by GP / school physician compared to the proposal of our researchers

Supplementary Table 2B Distribution of blood pressure by sex, age

		overweight boys							overweight girls							
		based on first BP measurement			further examination proposed by GP / SP	based on ABPM				based on first BP measurement			further examination proposed by GP / SP	based on ABPM		
		N	E	H		N	E	H		N	E	H		N	E	H
age (ys)	n	< 90	90-95	95 ≤		< 90	90-95	95 ≤	n	< 90	90-95	95 ≤		< 90	90-95	95 ≤
3	10	4	0	6	0	0	0	0	6	1	0	5	0	0	0	0
4	12	4	2	6	0	0	0	0	12	5	6	1	0	0	0	0
5	18	6	1	11	0	0	0	0	12	6	3	3	0	0	0	0
6	21	11	3	7	0	0	0	0	24	18	3	3	0	0	0	0
7	33	14	4	15	2	1	1	0	17	11	2	4	0	0	0	0
8	30	15	3	12	0	0	0	0	23	12	7	4	0	0	0	0
9	24	9	1	14	2	1	1	0	35	25	2	8	0	0	0	0
10	40	15	7	18	8	1	2	5	25	13	2	10	0	0	0	0
11	55	21	12	22	28	3	14	11	28	17	6	5	2	2	0	0
12	46	15	14	17	31	0	19	12	43	21	11	11	5	4	0	1
13	61	26	10	25	35	1	19	15	61	24	20	17	6	3	0	3
14	104	38	13	53	39	5	22	12	52	24	14	14	4	3	0	1
15	82	36	19	27	32	1	20	11	58	37	11	10	2	1	0	1
16	65	28	17	20	29	1	17	11	51	23	18	10	7	4	0	3
17	54	24	9	21	12	3	2	7	49	23	14	12	5	2	0	3
18	21	8	5	8	5	3	0	2	10	5	3	2	1	1	0	0
Total	676	274	120	282	223	20	117	86	506	265	122	119	32	20	0	12
		40.5%	17.8%	41.7%	32.9% * 55.5% **	2.9%	17.3%	12.7%		52.4%	24.1%	23.5%	6.3% * 13.2% **	3.9%	0.0%	2.4%

BP, blood pressure; GP/SP, general practitioner and/or school physician; ABPM, 24-hs blood pressure monitoring; N, normal blood pressure; E, elevated blood pressure; H, high blood pressure; * further examination recommended by GP / school physician compared to the total group size; ** further examination recommended by GP / school physician compared to the proposal of our researchers

Supplementary Table 2C Distribution of blood pressure by sex, age

		obese boys								obese girls						
		based on first BP measurement			further examination proposed by GP / SP	based on ABPM				based on first BP measurement			further examination proposed by GP / SP	based on ABPM		
		N	E	H		N	E	H		N	E	H		N	E	H
age (ys)	n	<90	90-95	95 ≤		<90	90-95	95 ≤	n	<90	90-95	95 ≤		<90	90-95	95 ≤
3	1	0	0	1	0	0	0	0	4	3	1	0	0	0	0	0
4	3	1	0	2	0	0	0	0	12	10	1	1	0	0	0	0
5	10	8	1	1	0	0	0	0	8	6	2	0	0	0	0	0
6	24	15	3	6	1	0	0	1	10	4	2	4	0	0	0	0
7	22	18	2	2	2	1	0	1	11	3	1	7	0	0	0	0
8	20	13	2	5	2	2	0	0	17	5	2	9	1	1	0	0
9	28	4	3	21	5	3	1	1	17	3	4	10	4	4	0	0
10	38	8	6	24	12	6	2	4	21	6	2	13	2	2	0	0
11	32	5	4	23	14	5	0	9	24	9	2	13	9	2	0	7
12	42	6	6	30	24	3	4	17	23	5	3	17	10	5	0	5
13	64	16	6	42	30	3	7	20	26	7	5	14	11	3	0	8
14	61	14	7	40	37	2	5	30	24	6	1	11	11	1	0	10
15	50	8	2	40	39	3	7	29	34	5	2	29	18	7	0	11
16	48	11	6	31	29	2	6	21	28	3	4	23	10	5	0	5
17	38	7	2	29	23	1	3	19	13	3	0	11	5	4	0	1
18	4	0	2	2	4	0	0	4	3	1	0	2	2	2	0	0
Total	485	134	52	299	222	31	**35**	156	275	79	32	164	83	36	**0**	47
		27.6%	10.7%	61.7%	45.8% * 63.2% **	6.4%	**7.2%**	**32.2%**		28.7%	12.7%	59.6%	30.2% * 42.3% **	13.1%	**0.0%**	**17.1%**

BP, blood pressure; GP/SP, general practitioner and/or school physician; ABPM, 24-hs blood pressure monitoring; N, normal blood pressure; E, elevated blood pressure; H, high blood pressure; * further examination recommended by GP / school physician compared to the total group size; ** further examination recommended by GP / school physician compared to the proposal of our researchers

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