CHARACTERISATION AND PRACTICAL IMPORTANCE OF EXERCISE-INDUCED CARDIOVASCULAR RESPONSES

IN a 6 - TO 18-YEAR-OLD POPULATION

Ph.D. Thesis

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List of publications related to the subject of this thesis

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Reference values for resting and post exercise hemodynamic

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List of abbreviations

ABPM – Ambulatory Blood Pressure Monitor

AMI – Acut Myocardial Infarction

BP – Blood Pressure

BP0’ – Pre-Exercise Blood Pressure

BP 1’ – Post-Exercise Blood Pressure measured at first minute after exercise

BP5’ – Post-Exercise Blood Pressure measured 5 minutes after exercise

BP10’ – Post-Exercise Blood Pressure measure 10 minutes after exercise

CV – Cardiovascular

CVD – Cardiovascular Disease

CRF – Cardiorespiratory Fitness

CI – Chronotopic Incompetence

DALY - disability-adjusted life years

Δ - Delta, show a change of any quantity

*Δ*SBP 0’- 1’ – Difference between pre-exercise and post-exercise Blood Pressure

*Δ*SBP 1’-10’ – Difference between post-exercise and recovery Blood Pressure 10 minutes after exercise

*Δ*HR 0’-1’ - Difference between pre-exercise and post-exercise Heart Rate

*Δ*HR 1’-10’ - Difference between post-exercise and recovery Heart Rate 10 minutes after exercise

DTT – Distance Time Trial

DRT – Distance Running Test

GXT - graded exercise testing

GP - General Practitioner

HR - Heart Rate

HR0’ – Pre-Exercise Heart Rate

HR1’ - Post-Exercise Heart Rate measured at first minute after exercise

HR5’ - Post-Exercise Heart Rate measured 5 minutes after exercise

HR10’- Post-Exercise Heart Rate measured10minutes after exercise

HRR - Heart Rate Recovery

HT - Hypertension

IT - Information Technology

MAS - Maximal Aerobic Speed

MHT - Masked Hypertension

SBP – Systolic Blood Pressure

DBP – Diastolic Blood Pressure

PE – Physical Education

VO2 - oxygen uptake

VO2max - maximal oxygen uptake

WCHT -White Coat Hypertension

1. Introduction

Cardiovascular diseases (CVDs) taking an estimated 17.9 million lives each year, are the number 1 cause of death globally [1], and also in Hungary [2].

In the last century, humanity has defeated the most devastating epidemics that have plagued the adult population by vaccinating children. There is a growing body of evidence that the key to the public health challenge of our century, to control the "epidemic" of non-communicative diseases, may be worth looking for in childhood. To achieve this a new approach needs to evolve. We are looking for one possible basis for this by researching the regularities and individual differences of the exercise-induced cardiovascular (CV) response in an entire pediatric population. We do this in the hope that early recognition of abnormalities will help identify an individual's risk and thus bring them closer to individualized prevention of the development of subsequent cardiovascular diseases (CVD).

„Many seminal longitudinal cohort studies have clearly shown that the antecedents to adult disease have their origins in childhood" [3]. In an effort to slow the current trajectory, professional societies have called for more rigorous, evidence-based guideline development to aid primary care providers and subspecialists in improving recognition, diagnosis, evaluation, and treatment of pediatric hypertension (HT) [3].

Everyone has seen a student lagging behind others at a physical education (PE) class, but nobody could say whether it was laziness, or there were other reasons behind their weak cardiopulmonary fitness. In our work we integrate novel results of hypertension research and knowledge about applicability, diagnostic and predictive value of juvenile exercise stress test.

First, we determined the characteristic change of heart rate and blood pressure of the population after the distance-running test, which can be considered as a maximal aerobic stress for children. Next, in a pilot project, we explored the possibility of recognizing the risk population and those hypertonic students based on deviation of blood pressure, whose condition remained undetected by regular screenings.

Recognizing the effect of obesity on blood pressure, age and sex specific cut-off points have been modified recently in international child hypertension guidelines by excluding overweight and obese children from the base population. In the light of that, we deemed it necessary to determine standard age and sex specific values for normal weight population.

Our precise description of a low budget and easily used method and publishing of age and sex specific standard values is the first publication of hemodynamic effects of field exercise test on a large healthy population. This provides the means for international comparison of under-stress hemodynamic parameters of both under the 12 years old and the above 12 years old population.

With establishment of age and sex specific exercise induced hemodynamic changes of a healthy school-aged population, we took a step towards classification of abnormal and healthy values in every case, even without correctly answering the original question: is it caused by laziness or by other reasons? But it is also true, that more children could be classified with CVD risk and conseqently allowed to prevent their disease.

Determining a standard interval opens up possibilities for identification of risk groups, thereby for early, targeted and efficient prevention and intervention. This might decrease the frequency of one of the most significant endemic groups, of cardiovascular diseases.

1.1. Prevalence and consequences of hypertension and cardiovascular disease

Despite advances in diagnosis and treatment over the past 30 years, the disability-adjusted life years (DALY) attributable to hypertension have increased worldwide by 40% since 1990 [4–7].

In 2015, the global prevalence of hypertension was 1.13 billion and over 150 million in Central and Eastern Europe [5]. The increased blood pressure worldwide, is responsible for 7.6 million early deaths and 92 million disabled years [5], out of which 80% is manifested in developing and moderately developed countries. The populations of Central and Eastern European countries harbour permanently high blood pressure [8]. In Hungary during the last 10 years the occurrence of high blood pressure patients multiplied by 1.5 times, while the number of patients with ischemic heart disease increased by 60-70 % [9].

When structured population screening programmes have been undertaken, an alarming number of people (30%) were unaware that they had hypertension [10]. This high rate of undetected hypertension occurred irrespective of the income status of the countries studied across the world [11]. Around 5% of children suffer from high blood pressure and it correlates with the increased rate of obesity [12]. Lifestyle is playing a major role in the progression or regression of the disease [12,13].

The prevention of CVD and stroke, besides the proper lifestyle, is based on the early detection of high blood pressure. In order to achieve a successful therapeutic intervention, the early diagnosis and continuous monitoring is indispensable.

All of these combined supports the necessity of a complex cardiovascular disease prevention program and press for the development of new research methods both in primary and secondary prevention.

1.2. **Impact of elevated blood pressure at childhood**

Hypertension in children and adolescents is becoming a major concern, not only because of its rising prevalence but because almost half of the adults with hypertension had elevated blood pressure values during their childhood [14–17]. As already established by multiple research groups, elevated blood pressure in childhood correlates with carotid intima-media thickness, atherosclerosis, left ventricular hypertrophy, and kidney failure in adulthood [14,18].

The higher percentile for blood pressure values in childhood frequently persisted during development until adulthood [18]. This phenomenon is called the tracking effect. The different effects of CVD risk factors are combined together during the lifetime; therefore, the childhood effects play a major role in the later development of CVD [11,14,19,20], and the lack of primary prevention in childhood cannot be substituted. Consequently, early diagnosis and control of hypertension in childhood are likely to have an important effect on long-term outcomes of hypertension-related cardiovascular complications [21].

1.3. The causes of underdiagnosis of childhood and adolescent hypertension

1.3.1. Missed screening and diagnosis measures

Despite the significant CVD risks and outcomes, pediatric hypertension frequently remains unidentified [22]. One of the reasons of this, is that despite the international recommendations during the children's medical visits, blood pressure (BP) determination is only occasionally taking place.

1.3.2. Specific types of hypertension

The progression of essential hypertension (HT) starts with increased cardiac output, i.e. prehypertension, rather than with the increase of vasculature resistance, early hypertension develops, followed by sustained HT. The individual phases follow each other after 10-20 years and in default of appropriate treatment complicated HT i.e. target organ damage, AMI, stroke could develop as soon as 40 years of age [21]. During the analysis of White Coat Hypertension (WCHT) it was found that in 60% of cases it doesn't require any treatment, though in childhood it is possible that WCHT could be a type of preHT, which could be accompanied by increased left ventricular muscle mass and could turn into persistent HT [23,24]. Pre-Hypertension (preHT), is systolic and/or diastolic blood pressure between 90-94 percentil. It is an independent CVD risk factor and could be significantly influenced by lifestyle changes [25]. Masked Hypertension (MHT he opposite of WCHT) in spite of normal medical data, it denotes real hypertonic disease which leads to persistent HT and target organ damage [26–28]. The correct diagnosis of MHT is a challenge for the paediatricians, because there are no predictive screening facilities or tests by which the affected children could be identified [29,30].

1.3.3. Percentile -bound threshold values.

The classification of BP in an adult population is carried out according to unified cut-off points. Contrary to this, the classification of childhood and adolescent BP is taking place according to age-, gender-, height- dependent percentiles, i.e. according to a great number of different threshold values.

1.3.4. Specific needs to measure children's BP

In order to accurately measure childhood bloodpressure at home, devices are needed that are specially validated for children and have a suitable cuff size. These are difficult to obtain because a significant proportion of devices in circulation have not been validated for the pediatric population. This is true for oscillometric devices, but even more so for auscultation devices.

1.3.5. Out-of-office blood pressure

Though in most cases the screening for high blood pressure is taking place by in-office measurements, the underdiagnosis of hypertension in children and adolescents is the consequence of using only resting (casual) BP values to define high BP and especially in younger age groups, various influences limit the reliability of the in-office BP measurements

[23,31,32]. Home- and school blood pressure measuring is not recommended for diagnosis of childhood HT in US guidelines [33] but is recommended in the new European guideline [12]. Further knowledge and research are needed on the method and evaluation of off-site measurements [3,34].

Out-of-office BP might be a more reliable parameter than casual BP, it has a strong association with cardiovascular disease outcomes [30] moreover exercise BP and cardiopulmonary fitness has robust, inverse, and independent association with cardiovascular and overall mortality risk [35–37]. Beside the in-office classical measurements, in the recent published protocols the gold standard of BP is the determination of Ambulatory Blood Pressure Monitor (ABPM), because it is a better predictor for brain vasculature abnormalities than the regular methods and it can be used for the precise distinction between WCHT and MHT. The ABPM is reproducible and useful for the diagnosis of childhood hypertension. Other BP measures such as exercise BP, and central BP, may be considered and are valuable tools for research [11].

1.4. Impact of anthropometry, obesity on HT and CVD

The obesity epidemic in children and adolescents makes it plausible that prevalence rates of HT are increasing over time [38] HT was found in 1.4% of normal weight, 7.1% of overweight and 25% of obese adolescents [39]. The relative risk of HT for overweight patients is 3.26 (CI: 2.5–4.2) [40] and based on a multiple regression model – apart from gender — BMI is the strongest determining factor of adolescent BP [41].

1.5. Impact of cardiorespiratory fitness (CRF) to HT and CVD;

Cardiovascular fitness represents the efficiency of the heart, lungs and vascular system in delivering oxygen to the working muscles so that prolonged physical work can be maintained.

Evidence supports that aerobic fitness and other cardiovascular risk factors track from childhood and adolescent to adulthood [17]. Over the past three decades, CRF has emerged as a strong, independent predictor of all-cause and disease-specific mortality. The evidence supporting the prognostic use of CRF is so powerful that the American Heart Association recently advocated for the routine assessment of CRF as a clinical vital sign. There is ample evidence that changes in CRF over time, either increases or decreases, are associated with reciprocal changes in risk of mortality [37,42].

While these observations highlight the potential clinical utility of exercise BP measurements for diagnostic and prognostic purposes, they have yet to be widely adopted into clinical practice given the limitations such as the lack of standardized methodology and limited empirical evidence across a wide range of populations. Our knowledge of the CRF and its relevance, especially in relation to the whole children and adolescents population, is incomplete knowledge of the CRF [37,43].

1.6. Screening CRF

In the development of prehypertension (high-normal BP) and hypertension, cardiorespiratory fitness exhibits preventive, prognostic, and therapeutic properties [42]. Currently, only a small number of screening methods enable simple determination of cardiorespiratory fitness, particularly in children. Most of these methods (treadmill or cycle ergometry) need a special environment and conditions [44–46]. While sophisticated laboratory equipment and appropriate testing protocols are required for the most valid assessment of aerobic and anaerobic fitness, properly conducted field tests offer a simple, cheap, feasible, practical, reasonably valid, and reliable alternative [36,45].

1.7. Out of office running test

When the evaluation of individual's maximal oxygen uptake (VO2max) attained during a laboratory test is not feasible, the 1.5 mile and 12 min [47] or 2000 meter [48] walk/run tests represent useful alternatives to estimate cardiorespiratory fitness [47]. Meanwhile performing longer walk/run tests could be an unnecessary extra time and effort, shorter tests showed poorer results of criterion- related validity [47], in the age group older than 12 years.

Out of office running tests can be expressed as **average running speed (m/s**), since mass-specific oxygen uptake (VO2) and VO2max linearly related to speed and maximal speed, average running speed should better reflect VO2, that is the oxygen cost of the performance, in addition more normally distributed [45].

1.7.1. Distance running test (DRT)

A summary of 22 studies, average running speed of 1600-2200 m is the most valid estimator of peak VO2 [36,45]. According to recent results the 2000 meter or 1.5 mile running tests give the best correlation with the laboratory measurements in the age groups over 12 years old [48]. In the young generation the predictive value of these tests coincides with the result of the shuttle running test [47].

DRT is a good alternative of ergometer exercise measuring hemodynamic variables during exercise in childhood. The accuracy of the determination of CRF outside the laboratory is necessarily lower than in the laboratory settings. CRF and consequently the hemodynamic parameters significantly correlate with the maximal aerobic speed (MAS) during ergometer test. Since MAS could have been predicted from average speed during DRT, DRT gives us a simple, standardized option to test CRF by measuring hemodynamic parameters, (pulse and blood pressure) during the test.

1.8. Exercise heart rate (HR); diagnostic, predictive value

Exercise heart rate, heart rate recovery (HRR), and chronotopic incompetence (CI) are independent risk factors of CVD and all cause mortality. HRR is mainly thought to be due to parasympathetic reactivation and has been shown to be a remarkable complement to a medical and/or physical assessment of an individual [49–51]. CI is common in patients with cardiovascular disease, is an independent predictor of major adverse cardiovascular events and overall mortality [52].

Postexercise heart rate recovery, though a readily obtainable parameter and a powerful independent predictor of unexpected cardiovascular mortality in healthy adults and in those with cardiovascular diseases, is often overlooked as an indicator of cardiovascular fitness [51,53,54]

1.9. Exercise BP; diagnostic, predictive value, limitations.

The predictive power for cardiovascular disease of an exaggerated BP response during exercise was suggested as superior to resting BP not only in adult but in childhood and adolescent populations as well [37,44].

Significant increases in the systolic blood pressure (SBP) and diastolic blood pressure (DBP) during effort, low or falling levels of SBP during effort, low amplitude of the ΔSBP and slow recovery of the SBP are considered abnormal responses of the BP and have a significant prognostic value of future hypertension and/or cardiovascular events and indicate the need for additional examinations [55].

There is some evidence that an excessive rise in BP during exercise predicts the development of hypertension, independently from BP at rest [56,57].

Moreover, the pupils with MHT could have been diagnosed only with out of office BP determination. Currently there is strong evidence that fitness constitutes an important predictor of morbidity and mortality [16,37,42]. Therefore, it is considered one of the most powerful markers of health, compared to other traditional indicators such as weight status, blood pressure or cholesterol level [58].

Exaggerated BP response to exercise is a clinical indicator for home or ambulatory blood pressure monitoring. Currently there is no consensus on normal BP response during exercise [59] because of various limitations, including a lack of standardization of methodology and definitions [59].

Other BP measures and indices (pulse pressure, BP variability, exercise BP, and central BP) may be considered but are not often used for routine clinical practice at present. They may provide useful additional information in some circumstances and are valuable tools for research.

The BP response during physical exercise has been suggested for that diagnostic assessment of BP in children. To establish the clinical usefulness of BP response to exercise testing in children and adolescents with HT, a larger body of data is needed [60].

2. Objectives

In spite of the fact that hypertension is a major cause of worldwide mortality and morbidity and increasing evidence prove that it initiates in childhood, it is not properly diagnosed in this population.

In order to establish the clinical usefulness of BP response to exercise testing in children and adolescents with HT, a larger body of data is needed [12]. In order to achieve this, we aimed to:

1. Establish the characteristics of exercise induced changes of blood pressure and heart rate in the general population of students between 6-18 years, with an easily reproducible, widely used exercise test.
2. Investigate the applicability of the exercise induced haemodynamic changes as a screening test for early detection of special hypertension types. Establish a school and exercise-based, CVD screening method.
3. Define reference values of haemodynamic changes of healthy, normal-weight, 6 - to 18-year-old population, during a field exercise test. Present a dataset for anthropometric and hemodynamic parameters measured both before and after the exercise, and after five- and ten-minute recovery times.

3. Methods

3.1. Participant characteristics

This investigation was conducted as a prospective, multicenter study in 3 Hungarian cities (Hódmezővásárhely, Mártély and Mindszent), in South-East Hungary between 2007 and 2018. In order to exclude the possibility of error in the selection of the examined subpopulation, we aimed to accomplish a comprehensive survey of the students of Hódmezővásárhely, which is the most populated of the three cities. Population: 43,700 (2018) mainly Caucasian type, (self-declaration basis, CSO census: in the region, 1.9% Roma population, other races do not occur in larger numbers) [61]. Inward and outward migration was negligible in the period under review. Till 2011, 26,963 measurement sequences, 10,692 students were tested and used as reference for the whole population pilot project.

At 2018 we had 102,642 data acquisition points from 14,267 individuals (7,239 boys, and 7,028 girls), out of which 65,345 acquisition points of 10,894 individuals were selected to establish the reference values for the population with normal weight.

The involvement in the anthropological measurements in the school is compulsory for everyone. Participation in physical education is also mandatory (except for those, who are exempt from exercise) for all students. The additional BP parameter measurements before and after the running-test were optional, but no one opted out, all participants gave consent.

Ethical License: This research was conducted with the permission of the Research Ethics Committee of the University of Szeged.

3.2 Measurement Protocol/Data Collection

The survey was performed at the beginning and at the end of the school year, except for those who were banned from physical exercise and data was recorded in an information technology (IT) system. The measurements were obtained during regular Physical Education (PE) classes between 8 am and 2 pm.

Biometric Data: Anthropometric data including weight, height measured by trained data collectors. In the school-health offices, with a certified, calibrated, non-stretchable, wall-mounted Stadiometer Height Measuring equipment was used for measuring pupil’s heights.

The perpendicular headpiece brought down to touch the crown of the head with enough pressure to compress the hair.

Certified, calibrated, electronic scales with a taring capability were used to measure the weight of the participants, wearing lightweight underwear, standing in the middle of the scale platform. The weight to the nearest 0.1 kg was noted and was rounded to the whole kg. Every year an external company calibrated all the devices.

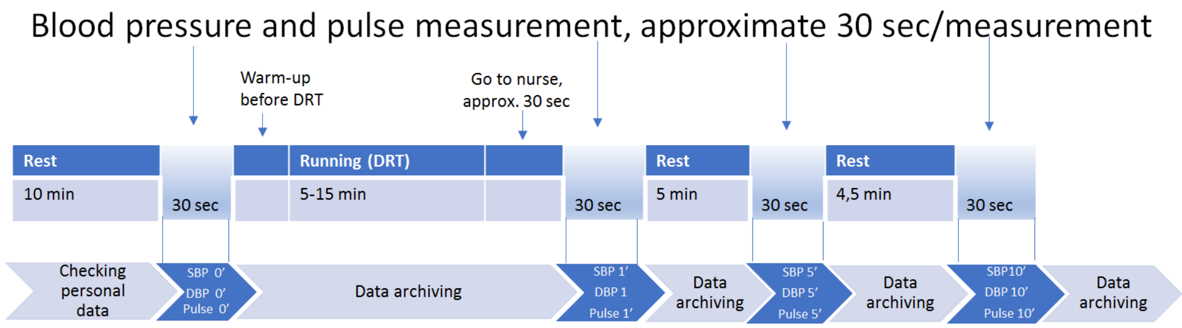

Figure 1 Measurement/Fit-test Protocol. The duration of the whole experiment was approximately 40-45 minutes. Four pulse (P), systolic (SBP) and diastolic blood pressure (DBP) measurement were collected per subject during a single Fit-test.

In the hours before the measurements, the students were not exposed to significant physical exertion. The students from the nearby schools came to the survey on foot and from remote schools by school buses. The anthropological measurements carried out before the running test and carried out by school doctors/nurses in the office indoors with calibrated instruments. Blood pressure and pulse values were measured with a validated, automatic OMRON blood pressure monitor, in accordance with the daily practice of school screening and the Hungarian Hypertension Society (MHT) protocol [62]. On arrival they sat on chairs and benches for about 5-10 minutes (Figure 1). The whole class was surveyed at the same time, with an average of 20-30 students. A nurse group (of 10 to15 nurses) performed blood pressure and heart rate measurements on the tables alongside the track. The student's blood pressure and heart rate were measured on a chair with a back rest, with a comfortably placed arm, at heart level (SBP 0’, DBP 0’, Pulse 0’) (Figure 1).

The running test was concluded as follows: the whole class (except children banned from exercise) was tested outdoors. After the initial measurement, before the survey, the PE teacher performed warm-up exercises with the students. During the test, under the supervision of physical educators, everyone had to run 1000 meters/0.62 miles (1-4 classes age between 6-10) or 2000 meters/1.24 miles (5-13 classes age between 10-18) as fast as possible on the same 400 meter (0.24 miles) long, flat, oval outdoor runway. The PE teacher measured the running time with a manual stopwatch and recorded the result of the run. After completing the distance, the student immediately went to one of the nurses who measured her/his blood pressure (SBP 1', DBP 1', Pulse 1') and informed her/him of the time of his next measurement, which was taking place at 5 and 10-minutes after exercise (SBP 5', DBP 5', Pulse 5' and SBP 10', DBP 10', Pulse 10'), and the data immediately recorded (Figure 1.) All BP measurement carried out once in each point in time.

Students were excluded from Physical Education: with severe cardiopulmonary, pulmonary or musculoskeletal disorders; acute fever, acute exacerbation of asthma, very high BP values and/or other complaints. Students with high blood pressure but no complaints and those who were controlled by medication for bronchial asthma, hypertension, diabetes mellitus, cystic fibrosis, and mild scoliosis participated.

On average 77.27% of the participants completed the running test.

3.3. Technical Validation

Measuring Blood Pressure

During the 12 years three different, ESH validated devices were used for measuring blood pressure (Omron3, Omron2, and URight TD3128). OMRON M3 blood pressure(BP) monitors are equivalent with the OMRON M6 BP device, which is validated to children, obese and elderly [63–67] and URight TD3128 Blood Pressure Monitor is also (ESH validation equal to TD3124, CE and FDA validated [68].

The appropriate cuff size to the size of the child's upper arm was used. If a cuff was too small, the next largest cuff was used even if it appears too larger than recommended [69].

3.4. Screening methods

Obesity status (BMI percentiles), heart rates, and blood pressure data at rest were all referenced to appropriate national statistics [70,71]. Exercise and recovery percentiles representative of the population, normal values by gender and by age, were calculated based on our 55,000 series of measurements. All students were referenced individually to these percentiles. The observed significant differences in the hemodynamic parameters of pupils with the same gender, age, and BMI percentiles, may be caused by differences between individuals with cardiovascular regulation in connection to the individual HT or CVD risk.

The pupils were classified with elevated BP in cases of more than two BP values above 95pc. The hypertension status was evaluated according to national and international diagnostic protocols [62,72–74].

3.5. Motivational questionnaire

In the course of autumn 2012, all of the students participating in DRT were asked to complete an anonymous, self-completed, non-validated questionnaire (Appendix, 1.). Overall 3,728 students, including 2,258 primary school students (1,108 boys, 1,150 girls) and 1,480 secondary school students (714 boys and 766 girls) completed the questionnaire. Simple, closed ended, and alternative questions were asked about the students' attitudes. It was asked what they think about regular and strenuous exercise, about their health and fitness control, and about interest in the result of being in physical shape or in early diagnosis.

3.6. De-identification

To make our experience internationally comparable and to analyze its generalizability, we have created a high-quality, normal population dataset, in line with the latest international guidelines.

In the process of creating the dataset, all identifiable personal information has been removed. Each individual thus has only an ID which links the measurements at different corresponding dates in the database.

3.7. Data cleaning

To ensure high-quality dataset we performed a data integrity screening for the measured parameters. Since the actual height of an individual could vary (~1-2cm) even in a course of a day (as physical activity alters spinal length) and the measured height also depends on how much the subject draws oneself up at the measurement time, we would expect a natural variation of height data even when the height of the individual is the same. Furthermore, the measured height was rounded to the nearest integer, so it could also cause 1 cm difference in height without having significant difference measured by the stadiometer.

First, we identified all individuals with more than 2 cm difference between consecutive height measurements and presumed that either of the higher or the lower value is potentially invalid. Then we performed logarithmic regression for all combinations with potentially invalid values. According to the adjusted R-square of the different models we excluded the most unfitting values from the height data of such individuals. Altogether 1,249 height values of 1,182 individuals were excluded from the 102,642 records.

We tested for obviously invalid haemodynamic parameters not compatible with life (pulse (P), systolic (SBP) and diastolic blood pressure (DBP)) in our dataset. Pulse: accepted between 40-200 beat/min (rejected:6 records), SBP: accepted between 70-220 mmHg (rejected:75 records) and DBP: accepted between 30-120 mmHg (rejected:46 records).

Running speed: accepted between 0.5-6.0 m/sec (rejected: 212 records)

3.8. Generation of normal population hemodynamic dataset

Since obesity and being overweight influence cardiac parameters, we included only the normal-weight subpopulation to generate a representative exercise-induced cardiac parameter dataset [33]. The WHO criteria (-2 to +1 SD z-scores) were used to identify the normal weight population (denoted as green points in Figure 9.). The running speed was calculated using the running time and distance values of the dataset.

From this normal subpopulation dataset, we also excluded the outlier measurements of the hemodynamic (before/after exercise pulse, SBP and DBP) and running speed based on the 1.5 IQR method [75].

A high-quality normal population dataset was distributed to make it internationally comparable to analyze the generalizability of our experience.

The datasets are distributed in the normal standard file formats (text, xlsx) and can be read and processed by a variety of commonly used statistical packages, including SPSS, Matlab, Python, and R.

4. Results

4.1 Haemodinamic effect of DRT in the general school age population

Characteristics of heart rate and blood pressure induced immediately after DRT and in the restitutional period were investigated.

10 692 students were measured from 2007 to 2011 and their 26 963 measurement sequences were included for the characterisation of haemodinamic parameters in resting state and after DRT. The hemodynamic parameters of the whole population at rest and their changes due to DRT were determined.

The distribution of changes in heart rates and blood pressure that are the consequence of the effect of DRT are represented respectively in Figure 2. and 4., in 1 minute and after 10 minutes of recovery. In the course of a running test the distribution of changes in the observed heart rate (HR, beats/minute) and blood pressure (BP, mmHg) are represented by the horizontal axis. The pulse and the systolic blood pressure changes are defined as differences before and after running measure at the 1st minute after running and after 10 minutes resting. The vertical axis represents the number of children whose heart rate (Figure 2) and blood pressure (Figure 4.) increased as indicated by the horizontal axis.

4.1.1. Exercise heart rate

There is a significant difference observed between HR changes in individual children due to exercise, but overall, they show a normal distribution. 90% of students had a heart rate increase between 11/min and 79/min. The average was 44.9/min (SD 21.8/min, n: 26,920). The background of excessively high or low pulse increase, or the decrease of it, can be a measurement error or, less likely, too low or too excessive exertion, occasionally for health reasons. To answer this question, we plan to compare and further evaluate the before-, and after exercise measured, performance-dependent heart rate values of each student. A future analysis is considered to be important, to direct affected individuals to the necessary examinations in case an undiagnosed disease is suspected.

Due to the effect of DRT, the degree of change in the resultant pulse and blood pressure measurements compared to those of the starting point.

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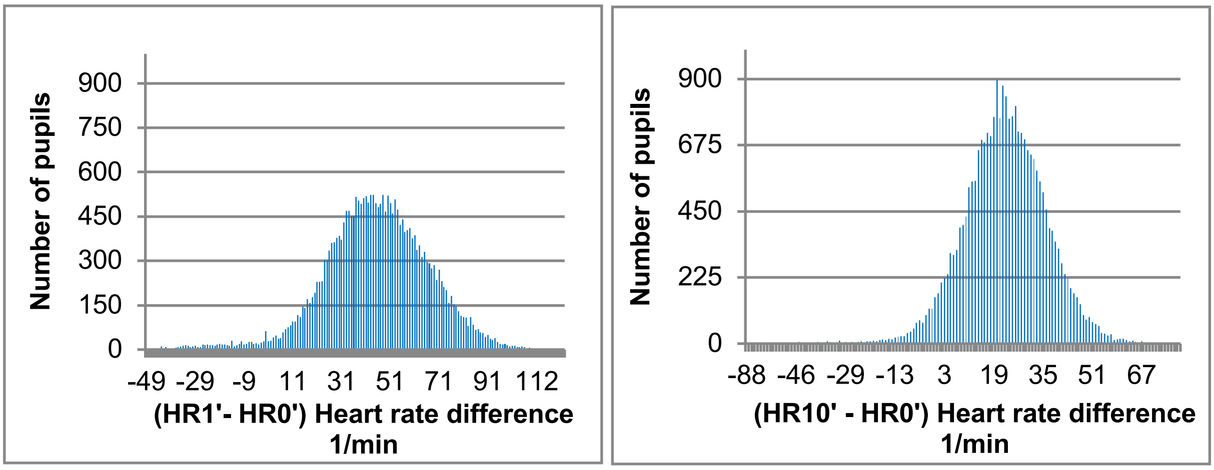


Figure 2 HR change by DRT and at recovery time, n=26,920; p<0,001; data was measured from 2007 to 2011, in connection to DRT

A) Distribution change of HR 1 minute after running difference of exercise heart rate and pre-exercise heart rate (HR1' – HR0')

B) Distribution of change of HR 10 minutes after running: Difference of 10 minute and pre-exercise heart rate (HR10' – HR0')

4.1.2. Recommended target HR

Recommended target HR helps in evaluating wether the physical exertion was appropriate for a given student or a group. The attained HR in the course of exercise is linked to individual categories according to age and level of physical condition.

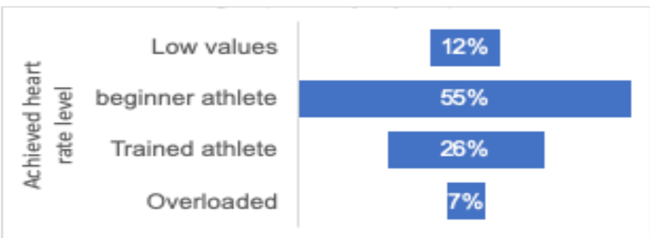


Figure 3 Advanced HR level by age, n=26,963, data was measured from 2007 to 2011, in connection to DRT. Fitness lavel based on national data [76]

The Figure 3. based on national data [76], exercise HR achieved in the course of a running trial are referenced to desired working pulse rates by age category.

We found that while close to 90% of the children reached the working pulse rate recommended for those who did not practice sports (55% of max pulse), 25% of them reached the target zone of athletes (75-80% of max pulse) after DRT. 7% of them even exceeded it, for them this exercise meant a significant overload. Further analysis can give a point of reference to differentiate whether this overload rose from weak fitness, poor health, or excessive motivation.

4.1.3. Recovery heart rate (HRR)

After 10 minutes of recovery the recommended HR is 10% more than pre-run HR [76]. 16,5% of the examined population of pupils belongs to this group. 4,5% of them produced lower HR than that. For them the trial was less burdening than their daily routine. HR of 83,5% however stayed higher than required.

Pupils' HR, rised by DRT, remained high after 10 minutes rest, in numerosus cases, in 83,5% ($p< 0{,}001$; average: 22,4/min; SD: 13,5; n:26938). We can interpret that for the majority (83,5%) of pupils this trial meant a bigger load than their actual fitness levels were able to safely tolerate.

This measure should be further analyzed, because at a few percent of children really high pulse rates were found, which may arise from their unconditioned state, but it also might refer to a acute or chronic or later sickness. This group with the highest probability could develop a hidden respiratory illness, e.g. bronchoconstriction, asthma bronchial or CVD.

4.1.4. Exercise Blood Pressure

Effect of exercise was examined on BP of the children. First measurement, which also meant a screening happened right before running. When an abnormally high BP was found, the pupil was not allowed to take part in load test and was directed to the General Practitioner (GP). While we had reference values for the pulse changes under load, there were not published age -connected normal values of BP response to PE class exercise.

A B

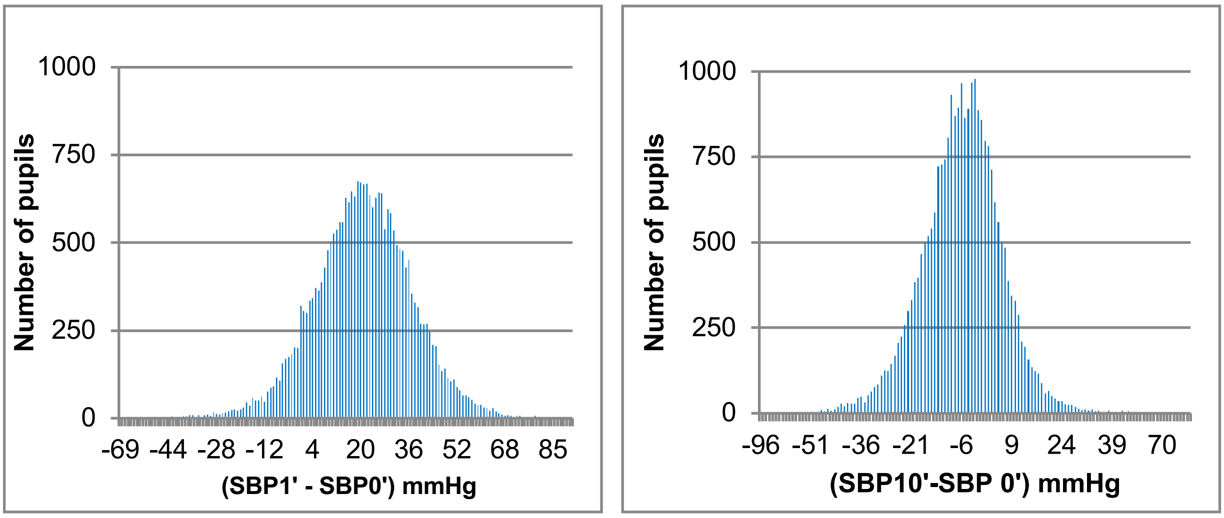


Figure 4 SBP change by DRT and at recovery time, n=26,599; p<0,001; data was measured from 2007 to 2011, in connection to DRT

„A" Distribution changes of SBP: difference of 1 minute after running test and pre-exercise systolic blood pressure (SBP 1'- SBP 0')

„B" Distribution changes of SBP: difference of 10 minutes after running an pre-exercise blood pressure (SBP10' – SBP0')

After DRT most of the children produced a higher BP than before, similarly to the change of pulse rate. (Fig.4.A). Average SBP rise: 20,8 mmHg (SD: 16), p<0,001, n=26599.

DBP rise at the same measurements: 1,86 mmHg (SD:12,14) mmHg.

SBP rise at 65% of the pupils was between 10-40 mmHg immediately after DRT. We also experienced exaggerated BP rise, which could be an early sign of HT, which predicts future hypertension [77–81].

4.1.5. Recovery Blood Pressure

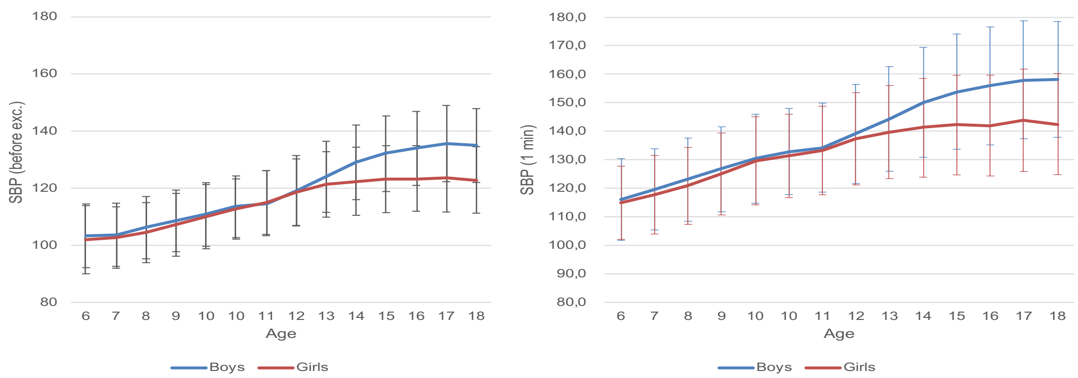
Average difference of SBP values measured before and 10 minutes after running: -5,8 mmHg (SD: 12,2 mmHg) median -5,0 mmHg; p <0,001 (FIG. 6/B). Meeting with expectations, there was a decrease of BP comparing to the values measured before the load in 61% of cases, in 17% the values are essentially the same as the initials (difference less than 2 mmHg), and only at 22% of the cases showed higher BP values than at the beginning. In case of a missing rebound effect, so the physical exercise does not cause BP decline derived from peripherial resistence, it may cause by dysfunctional blood pressure control.

4.1.6. Comparison of resting and exercise blood pressure values by age and gender,

In the study population, the mean blood pressure of boys and girls is approximately the same between the ages of 6 and 12 years, with a difference of 1-2 mmHg in favor of boys. However, from the age of 13, the trend lines are separated. 13-year-old boys have SBP higher than girls with 3mmHg. The difference grows steeply and steadily until it reaches 12 mmHg by the age of 17y.

Exercise SBP also moves together in both sexes up to 12 years of age, with a difference of 1-2 mmHg in favor of boys. At 13 years of age, boys have 4 mmHg of high blood pressure, and the difference continues to increase until the age of 16, when they reach 14 mmHg. Boy-girl differences and the slope of trend lines are similar for resting and loaded SBP values (Figure

A, B,



	Age	6	7	8	9	10	10	11	12	13	14	15	16	17	18
		N	N	N	N	N	N	N	N	N	N	N	N	N	N
Boys	1 min	111	1484	2223	2285	1766	335	1681	1977	2015	2210	2337	2292	1993	1273
Girls	1 min	153	1667	2350	2290	1812	442	1947	2260	2350	2348	2319	2477	2131	1412

Figure 5 Comparison of resting and exercise blood pressure values by age and gender, age related mean (±1 SD) systolic blood pressure (SBP) at rest (A) and exercise BP values (B) during a distance running (DRT) exercise test, Fit-Test project, 2018

4.2. New, sensitive, reliable, simple screening method: “Fit-test”

With the methodology described previously, CRF measured during the field exercise test was evaluated together with body ratios/BMI status, resting- exercise- and recovery HR and BP values.

4.2.1. E-health

Development and deployment of E-health solutions reduced administration time, improved data capture accuracy, solved challenges with the immediate, non-human data transfer and statistical analysis of data, facilitating their understanding and use of access rights of stakeholders and eligible persons.

4.2.1.1. Fit-test.hu, website

Students and their parents, numerically, with info graphics and textual explanations, were able to view their fitness and health results on a web interface. Where appropriate, they also received lifestyle advice or suggestions for medical consultation. GP, school physician and specialists could see th data through the same IT system with percentile values and graphs to assist with accurate diagnosis. Regular and system-wide, multidisciplinary screening, with equal access, may call attention to screening for blood pressure, abnormal leanness and overweight, deterioration of general fitness, or respiratory, hematopoietic, hormonal, cardiac or renal diseases.

The storing, statistical and decision support software developed for recording and analyzing survey data, along with its associated web interface, facilitated accurate data capture, enabled analysis and evaluation of an extremely large number of measurement results, and information was made available to those involved, health providers, and those interested, by authorization levels,

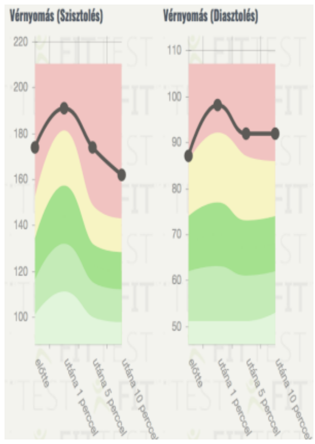
4.2.2. Fit-test, as a screening pilot project

We measured the hemodynamic effect of DRT on students, and every pupil’s individual data was classified to normal values of population by gender and by age.

In our work, we applied BP elevation - induced by physical exercise and physiological load of our school survey - to screen the risk of HT and found that exercise-related screening was also suitable for examination of MHT, preHT, and HT students, proven by the specific cases below (Figures 6-8).

Blood pressure percentiles in the range above normal were highlighted in the tables below and in the graph. Background coloring shows normal and abnormal values by age and gender: yellow for prehypertonic (90-94pc), red for hypertensive (95-100pc) in the chart and graph. The graph next to the table, taken from the **fit-test** IT system, depicts the individual's load-bearing hemodynamic response to normal age values. The coloring of the normal and abnormal values helped parents and students to understand the results.

Age (year)	BMI pc	Running speed pc	0' SBP pc	1' SBP pc	5' SBP pc	10' SBP pc	0' DBP pc	1' DBP pc	5' DBP pc	10' DBP pc
10,7	50	72	100	99	96	92	100	98	98	99
11,2	59	83	100	100	100	99	98	98	91	97
11,7	44	75	99	95	99	99	99	96	91	96
12,2	49	84	100	98	100	100	98	92	98	99
12,7	34	75	100	100	100	100	98	99	99	98
13,2	44	79	100	99	100	100	100	97	92	97
13,7	40	82	90	88	90	88	86	96	92	89
14,2	54	74	99	92	92	95	98	98	97	89
Colour code		90	: 90-94 percentilis			95	: 95-100 percentilis			



Graph from fit-test.hu

Figure 6 Percentiles and graph of pupil with sustained systolo-diastolic hypertension, without antihypertensive therapy;

Figure 6. Shows untreated, persistent hypertension values of a normal weight (BMI 34-59pc), and well-trained boys (CPF 72-84pc) between the ages of 10 and 14 years. The graph shows that the values measured at age 12.7 are in the very high range (160-190 mmHg, which is 100 percentile), but follow the normal trend for all measurements.

age (year)	BMI pc	Running speed pc	0' SRR pc	1' SRR pc	5' SRR pc	10' SRR pc	0' DRR pc	1' DRR pc	5' DRR pc	10' DRR pc
8,2	74	78	98	96	84	46	99	92	17	58
8,7	80	80	94	89	80	87	91	89	85	68
9,2	85	53	60	97	74	64	99	93	92	60
9,7	85	41	98	97	98	76	99	98	97	94
10,2	79	25	50	29	64	80	92	89	65	84
10,7	89	37	96	54	91	93	91	68	87	95
11,2	89	34	87	24	100	99	95	98	100	100
11,7	84	32	90	42	100	98	95	89	98	85
12,2	85	9	100	90	99	90	86	77	98	77
12,7	85		94	kivizsgálás miatt			78			
13,2	72		69	nem fut			68			
13,7	75		81	72	85	34	91	87	76	46
14,2	68		60	39	69	78	71	66	72	85
14,7	63		45	12	62	55	38	58	59	52
15,2	59		11	5	15	40	9	14	38	30
15,7	62		53	16	35	40	28	51	27	10
16,2	66		65	26	79	79	62	57	71	37
16,7	70									
17,2	62		81	34	95	71	73	73	98	98
	Colur code		90	: 90-94 percentil			95	: 95-100 percentil		

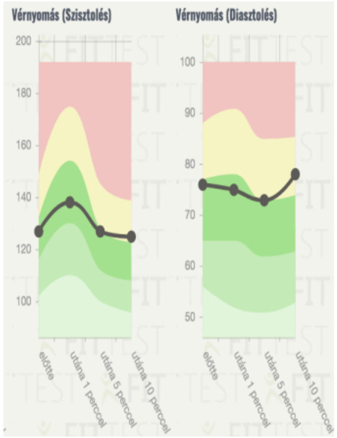


Figure 6 Sustained systolo-dyastolic hypertension, with antihypertensive therapy (Graph from fit-test.hu)

In the case shown on Figure 7, pupil had sustained systolo-dyastolic hypertension from his 8 to 12 years. Antihypertensive therapy was initiated from13 years, and during the next screening period he had target values and showed normal values at rest and at exercise from 13 to 17 years of age.

Masked hypertension, without antihypertensive terapy										
Age (year)	BMI pc	Running speed pc	0' SBP pc	1' SBP pc	5' SBP pc	10' SBP pc	0' DBP pc	1' DBP pc	5' DBP pc	10' DBP pc
8,5	69	9	64	94	81	39	24	87	85	24
9,0	81									
9,5	77	23	55	39	87	74	67	27	32	38
10,0	81	9	49	91	26	62	91	95	42	84
10,5	82		86	81	95	100	87	62	89	93
11,0	87		81	99	100	100	90	77	94	98
Colour code		90	: 90-94 percent		95	: 95-100 percentilis				

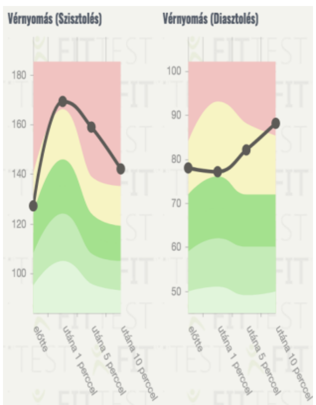


Figure 7 Masked hypertension, with normal resting blood pressure (Graph from fit-test.hu)

In Figure 8, all of the resting SBP values are within the normal range, but some of the measurements have high exercise values over several years. Previously, a normotensive student at age 10.5-11 showed normal resting and increased exercise and recovery values. In the case of MHT, the diagnoses can be delayed, because actual screening protocolls (only with office BP measuring) are not able to recognize this HT type.

Although BP values are variable and show individual pattern, high values are seen in several measurement series for HT (Figure 6-8.), with changes reflecting lack of therapy (Figure 6.) or efficacy (Figure 7.). Although BP values are variable and shows individual pattern, the high values are seen in several measurement series of HT pupils (Figure 6-8.), with changes reflecting of therapy (Figure 7.) or without efficient therapy (Figure 6.).

4.2.3. Specificity, sensitivity

The first year of screening supplemented with IT, 58% of students screened for higher BP during an exercise test, had confirmed HT disease (compared to 1-3% in the general population). Blood pressure values of screened but untested students varied over the years, with increases or decreases in BP associated with both fitness and BMI (like non-drug therapy). Specificity of screening test: 0.998, Sensitivity: 0.83, Positive predictive value for hypertension: 0.58. In addition, among false positive cases there are students with prehypertension, requiring additional care and monitoring.

4.3. Compliance:

Table 1. shows numbers of persons with elevated BP identified with exercise screening method and willingness to participate in a further medical examination

Year	2012	2016
Number of participants	4980	5800
Number of identified height BP cases	45 (0,9%)	53 (0,9%)
Present at check up from the identified	26 (57%)	41(77,4%)
Were not present at check up from the identified	19 (42,2%)	12(22,6%)

Table 1. Compliance at 2012 and 2016

At first year of special screening only 57% of pupils presented at medical check up from the identified and four years later it was 77%. The method of medical check up also was very different. It can be stated that due to the lack of consensus therapies and of connection between the individual care sites, screening is often not followed up adequately, and therapeutic habits are not uniform, meaning that the guidelines are not always followed. One in three (18, 32%) of filtered pupils were recommended ABPM and lab testing, in six cases 6 (10%) home measurements were suggested and 9 pupils (15%) were checked-up only with an office BP measurement. Among the screened patients were 5 chronic patients, of them two with cardiac disease and one with endocrine disease regularly go to check their condition, but the 2 known hypertensive students have not been in care for years. 1 person gets herbal "treatment" against HT which is completely contrary to HT evidences. Our findings support the international experience that well-defined patient follow-up is required between individual screening sites, clinicians, and primary care [82,83].

Year	2012	2016
Number of participants	4980	5800
Number of identified height BP cases	45 (0,9%)	53 (0,9%)
Obese among them	8 (18%)	13 (24%)
Overweight among them	13 (29%)	13 (24%)
Proportion of obese plus overweight patients	21 (47%)	26 (49%)

Table 2. Obesity and elevated BP 2012 and 2016, Hódmezővásárhely

At 2016, BMI ≥ 97 pc: 325 students of these, 15 (4.6%) had high blood pressure (2 known hypertensive and 13 newly screened students). The same is 0.9% of the total population. So obese students are five times more affected (Table 2) in this population according to our study.

4.4. Health Awareness

According to an anonymous questionnaire survey - as shown in Table 3 - 90 -96% of students (in both primary and secondary schools) consider daily physical activity and early detection of illness to be important. This is a good basis for this generation to have regular exercise later in life and to undergo regular screening tests. Question 5. was used to verify the accuracy of the answers to our questions. It was known that mostly adolescent girls, but many in other groups, do not like DRT.

Question	Answere	Elementary school pupils (n)		Secondary school pupils (n)	
		BOYS	**GIRLS**	**BOYS**	**GIRLS**
1. Do you consider daily exercise important?	Yes	1046	1076	652	680
	No	62	74	62	86
2. Are you satisfied with your fitness?	Yes	809	855	444	284
	No	299	295	270	482
3. Do you like measuring your performance?	Yes	804	735	413	301
	No	304	415	301	465
4. Interested in measuring results?	Yes	816	995	543	544
	No	292	155	171	222
5. Do you like running 2000m?	Yes	611	431	210	99
	No	497	719	504	667
6. Do you find it good to measure your blood pressure?	Yes	911	1097	642	708
	No	197	53	72	58
7. Are you interested in the result of it?	Yes	942	1020	519	647
	No	166	130	195	119
8. Do you find it important to find out if you have a disease?	Yes	1050	1116	667	745
	No	58	34	47	21

Table 3. Health awareness questionnaire, 2012

4.5. Data Records

In the complete datasets at 2018, we provide repeated measurements on the same individuals of various anthropometric and hemodynamic parameters (102 642 records) of a large (14 267 participants) school-aged (6-18 years of age) cohort. It is prospective over 8 years (3.44 (SD 2.92), and 7.19 (SD 5.21) datapoints of participants). The anthropometric dataset can be used to analyze age and sex-dependent BMI changes leading to either obesity or normal body weight to identify risk-groups and proper time of intervention.

4.5.1. Anthropometric dataset of 6-18-year-old children

The *fit_database_anthropometric_all.xlsx* is deposited in the anthropometric_all[84] folder. Each data record contains the individual ID (that links different time series measurement dates of the same individual), measurement date, age (in years), age bin (age category in years), gender, height (cm), weight (kg) values, the calculated BMI, WHO z-score and WHO z-score categories of 102,642 data acquisition points from 14,267 individuals (7,239 boys, and 7,028 girls). We also provided this dataset as ***fit_database_anthropometric_all.tsv***[84]**.**

The descriptive statistic (N, mean, SD) of this dataset for the different age and gender categories can be viewed in the XLSX table: ***descriptive_anthropometric_all.xlsx***[84].

The calculated gender- and age-specific height, body weight and BMI percentiles (1, 3, 5, 10, 25, 50, 75, 90, 95, 97, 99) and the corresponding number of individuals in this dataset can be found at the XLSX table: ***percentiles_anthropometric_all.xlsx***[84].

4.6. BMI and WHO z-score calculation

The BMI was calculated by the formula of $BMI = \frac{weight}{height^2}$ The WHO z-scores were calculated by the methodology described in [85], using the WHO age and sex normalized LMS reference tables [86]. The z-score weight categories were determined according to the rules set by WHO (z-score < -3 - severely thin, -3 <= z-score < -2 - thin, -2 <= z-score < 1 - normal, 1 <= z-score < 2 - overweight, 2 <= z-score - obese). We also calculated the standard deviation (in range of -3 to +3) of experimental BMI values in our dataset for all age and sex categories. To compare the Hungarian population with the WHO data we visualized our data by colouring the individuals according to their WHO z-score weight categories and plotting the -3 to +3 standard devia

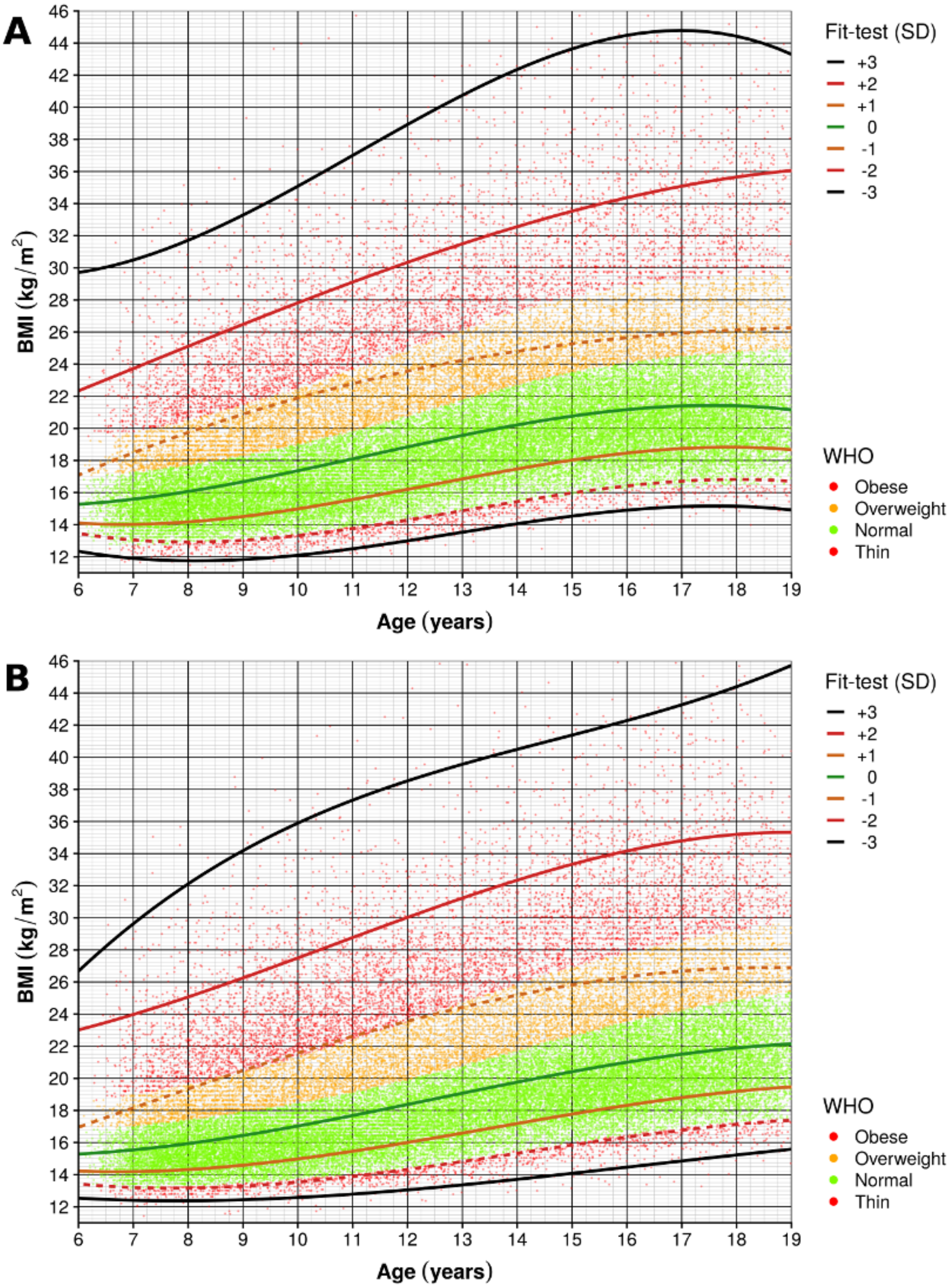


Figure 9 Body Mass Index (BMI) for Age

Figure 9. Body Mass Index (BMI) for Age plot for girls (A) and boys (B). The lines represent SD (+3 to -3) values for BMI calculated for the whole tested population, and each individual is represented by a dot colour-coded based on the WHO criteria. Using the WHO criteria (-2 to +1 SD) we identified the normal-weight subpopulation (denoted as green points). WHO and Fit-Test z-score categories of 102,642 data acquisition points from 14,267 individuals (7,239 boys, and 7,028 girls, 2007-2018

4.7. Cardiovascular parameters before and after the DRT in the normal-weight children's population

In order to determine the cardiovascular parameters in a student cohort with normal weight 10,894 students were selected (65,345 acquisition points)

As the running distance was selected by the class of the participant (1000 meter for class 1-4 and 2000 meter for class 5-8) and not by their age, we had some measurements of age > 10 individuals with 1000 m running distance and age < 10 years with 2000 m running distance. However, since the number of data points was greatly smaller than that of the other categories, we also excluded these measurement points from this dataset.

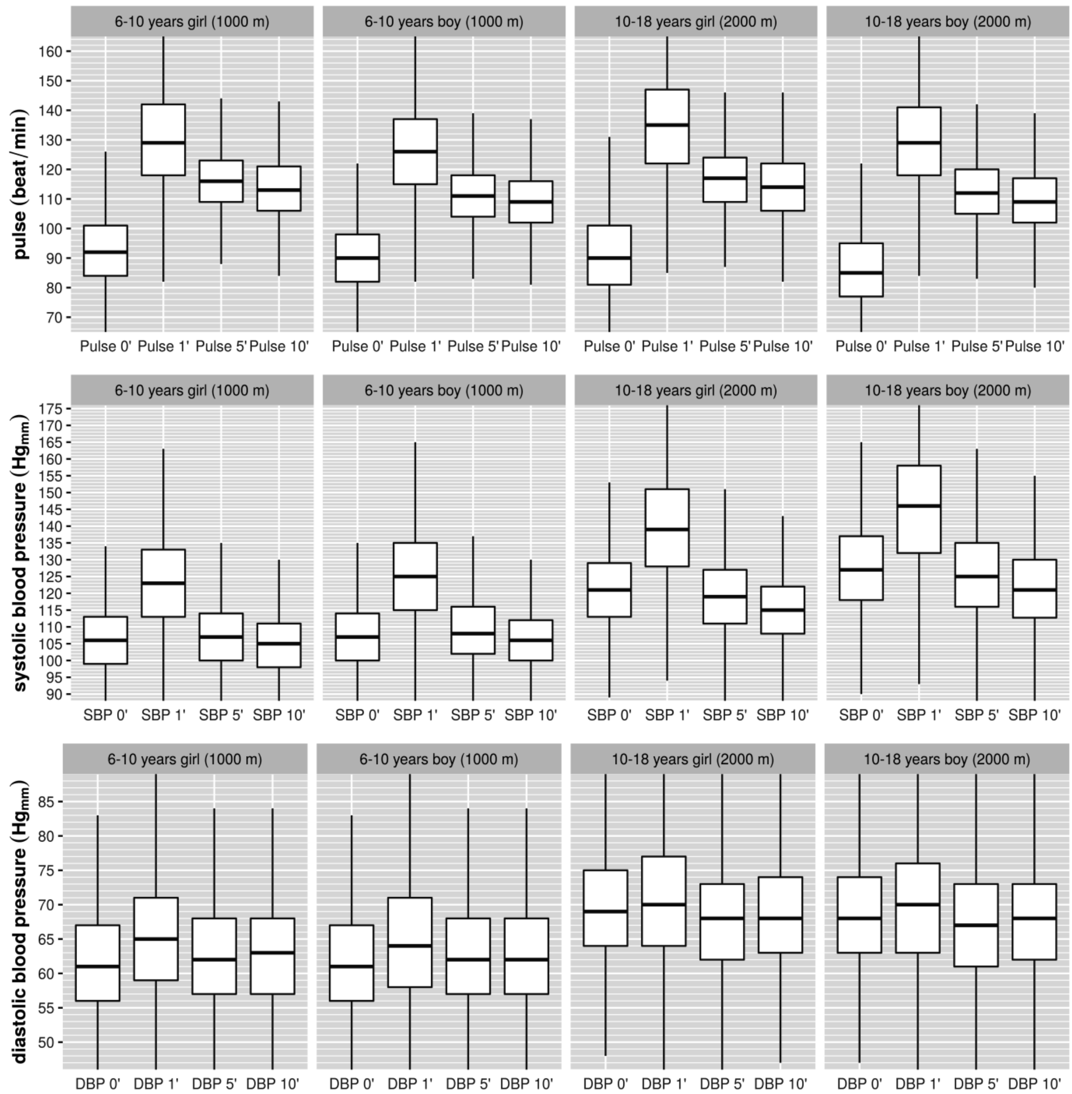


Figure 10 Pre and post Fit-Test hemodynamic data of the normal-weight subpopulation. Pulse, systolic (SBP) and diastolic blood pressure (DBP) data organised based on the age groups/running distance (6-10 and 10-18 years) and on the gender. Cardiovascular

parameters in a student cohort with normal weight 10,894 students were selected (65,345 acquisition points), 2007-2018

Fit-test allowed us to monitor the changes in the cardiovascular parameters before and after the DRT in normal-weight (age and gender separated) reference children and young adolescent (6-18 years of age) population (Figure 10) The normal weight cardiac parameter dataset can be used as a standardized reference chart, to develop complex strategies utilizing exercise-induced parameters to screen for cardiovascular abnormalities.

4.8. Exercise induced cardiac parameter dataset

Each data record contains the individual **ID** (that links different time series measurement points of the same individual), **measurement date**, **age** (in years), **age bin** (age category in years), **gender**, **running distance**, **running speed** and the **0'**, **1'**, **5'** and **10' pulse, systolic blood pressure** (SBP), **diastolic blood pressure** (DBP) values collected from normal weight individuals according to the Fit-test protocol (Figure 1.) This dataset consists of 65345 data points of 10894 individuals (5408 boys and 5486 girls) and is deposited in the **excercise_normal** folder as ***fit_database_exercise_normal.xlsx***[84] (and as ***tsv*** file as well).
The descriptive statistic (N, mean, SD) of this dataset for the different age and gender categories can be viewed in the XLSX table: ***descriptive_ excercise_normal.xlsx***[84].
The calculated gender- and age-specific running speed and cardiac (pulse, systolic and diastolic blood pressures at 0', 1', 5' and 10' measurement points) for the normal weight Fit-test population can be found at the ***percentiles_runningspeed_exercise_normal.xlsx*** *and the* ***percentiles_cardiac_exercise_normal.xlsx*** tables [84].
The number of excluded outliers for each exercise-induced measurement (pulse, SBP, DBP and running speed are included in the **outlier_counts_exercise_normal.xlsx** [84]**.**
The dataset has been fully uploaded to the network, and users can download them through the Figshare repository (10.6084/m9.figshare.9948296) with the the title DataRecords. The dataset comprises 2 data folders with 8 XLSX and 2 tsv files.

Fit-test allowed us to monitor the changes in the cardiovascular parameters before and after the DRT in normal-weight (age and gender separated) reference children and the young adolescent (6-18 years of age) population (Figure 10.). The normal weight cardiac parameter dataset can be used as a standardized reference chart, to develop complex strategies utilizing exercise-induced parameters to screen for cardiovascular abnormalities. The datasets are distributed in the normal standard file formats (text, xlsx) and can be read and processed by a variety of commonly used statistical packages, including SPSS, Matlab, Python, and R.

5. Discussion

5.1. New approach to one of the biggest public health issues,

During our work, we investigated one of the most important, therefore the most thoroughly studied public health challenge: the possibility of decreasing morbidity and mortality of CV diseases. Our objective is to explore a rather scarcely studied field in one of Europe’s most affected regions.

By studying haemodynamic changes of children and adolescents caused by physical exercise, we aim to determine standard intervals by age and sex in order to classify healthy and pathologic results. We also explored the possibility of the screening of diseases and our future goals include charting the effects of individual reactions to exercise on later health. Evidence of causes and possible outcomes of significant differences of test results between students is yet to be discovered, even though it might be a key factor to early prevention of CVD to delay or prevent its occurrence.

At first, we determined and published, the age and sex related standard haemodynamic values of schoolage population for 2000m DRT (upper 12y) and 1000 m (under 12 y) tests. These field tests show the best correlation with laboratory exercise stress tests from distance-time trial tests and can be considered to induce maximal aerobic load. This way the result is relevant as a fitness and health screening method and it is possible to compare different students or groups of pupils.

As a new approach, we recorded running speed as a new health related parameter, which correlates with cardiopulmonary fitness, an evidently independent CVD risk factor.

Our exercise hemodynamic dataset for normal-weight population was determined with the methodology of international pediatric HT guidelines [12,33] and according to WHO Child Growth Standards [87,88] rendering our results applicable for international use.

5.2. The need for early detection of CVD risk and HT

Elevated blood pressure is the principal risk factor for cardiovascular diseases worldwide, affecting one billion individuals globally [7,89].

It is the cause of 54% of strokes and 47% cases of ischaemic heart disease, and is responsible for 7·6 million premature deaths per year (ie, 13·5% of all deaths worldwide) and 92 million disability-adjusted life-years [90]. During the past four decades, the highest worldwide blood pressure levels have shifted from high-income countries to low-income countries, while blood pressure has been persistently high in central and eastern Europe [7]. Raised blood pressure is an important risk factor for cardiovascular diseases, by many longitudinal surveys.

In the place of our survey, a Hungaryan middle sized city, Hódmezővásárhely, surpasses the national and European average in mortality caused by circulatory diseases, HT, and mortality caused by strokes [91]. All of this not only indicates the need for a complex cardiovascular (CVD) prevention program, but also prompts finding a new approach for early identification of risk population.

5.3. Pros and cons of screening hypertension in children

The early recognition of BP abnormalities is crucial if there are to be early interventions that may reduce cardiovascular morbidity and mortality later in life.

Despite this the pros and cons of screening HT in children have been widely debated, recently [92,93].

The routine measurement of BP in children and adolescents is recommend by guidelines [12,33]. However, these recommendations are not deeply grounded, and controversy has been raised about benefits and costs of routine screening [94]. Moreover current evidence is insufficient to assess the balance of benefits and harms of screening for primary hypertension in asymptomatic children and adolescents to prevent subsequent CV disease in childhood or adulthood' [94]. The consensus of the present guidelines is that BP should be measured in children starting from the age of 3 years. Before 3 years it needs to be measured only under special conditions.

Because the BP screening in children demands minimal cost and time inputs, does not include invasive tests, and it may also lead to further actions improving health outcomes [95]. For this reason, the most prominent specialists have considered that lack of evidence does not necessarily justify in action [12].

5.3.1. Tracking effect also confirms the importance of early screening

The so-called "tracking effect" [30,34,96] justifies the use of sensitive childhood screening [94]. Childhood BP is associated with BP in later life, and early intervention is important [17]. We are assuming that the dynamics of exercise-induced changes in blood pressure are also related to individual blood pressure regulation and vascular adaptability, so the analysis of those might be useful for developing a population-wide screening.

5.4. The need to integrate the value of physical activity into the healthcare paradigm

Compared to in-office readings, out-of-office blood pressures are a greater predictor of renal and cardiac morbidity and mortality [97].

Exercise tests are motivated by the fact that abnormal cardiovascular response during physical exertion is an early indicator of CVD [42]. Measuring and evaluating these provides a wealth of information about CVD and also about later sport performance. In addition to diagnostics, there is increasing attention to the prognostic significance of workload testing [55,98] for both workload and restitution BP changes. Further strategies and research are critical to better integrate the value of physical activity into the healthcare paradigm. The reduction in mortality risk increase in exercise capacity in studies has ranged between 10% and 25% [43]. This is evident in both young and elderly subjects, men and women, and individuals with and without cardiovascular disease [99–102]. In the interim, healthcare professionals can invest the extra moment to discuss physical activity with their patients [103].

5.5. Evidences

The main evidences upon which we primed our study are the following:

- Pathological background of CVD (atherosclerosis) occurs as early as 4-8 years of age and its malignancy correlates with significance and duration of risk factors [14,104,105] (HT, obesity, high level blood cholesterin).
- Blood pressure and heart rate are regulated by numerous humoral and neurovegetative subsystems; its change (e.g. after physical stress) depends on several effects in this control system. Long term abnormal function shows strong correlation with the occurrence of CV diseases. Amongst healthy young people, long term consequences of short-time abnormal function are yet unknown. Keeping up standard value for exercise parameters requires normal function from all subsystems of the body, meaning that any abnormality will show deviancy in these parameters. This means, that we see an aggregated picture of genetic and acquired effects and function of the sympathetic, parasympathetic, cardiovascular, renin-angiotensin, respiratory and hematopoietic

system. Based on these it is reasonable to claim that sizable changes in idle, exercise and recovery BP and HR values reflect the momentary condition of the subject, and lets us conclude, that behind consequently deviant values there is the suggestion of the presence of abnormal function [106–109].

5.6. Health consequences of exercise testing

Exercise "stress tests" in sport medicine and in cardiology provided useful data with CRF and predictive value for hypertension and CVD.

5.6.1. Heart rate (HR), heart rate recovery (HRR)

Changes in heart rate during exercise and recovery from exercise are mediated by the balance between sympathetic and vagal activity. The analysis of post-exercise cardiac autonomic recovery is a practical clinical tool for the assessment of cardiovascular health [110], so assessment and follow-up changes of this in population level is an effective way for sensitive screening of cardiovascular health. Chronotropic incompetence (CI) produces exercise intolerance that impairs quality of life, and is an independent predictor of major adverse cardiovascular events and overall mortality [52]. A reduced heart rate recovery – an indicator of autonomic dysfunction – has been found in a broad range of cardiovascular diseases and has been associated with increased risks of both cardiac and all-cause mortality [110]. The heart-rate profile during exercise and recovery is a predictor of sudden death. A very rapid HR recovery immediately after exercise was associated with lower risk of CHD and CVD events [111]. The post-exercise HRR provides information that is complementary to the traditional cardiovascular fitness indices and should be added to the list of indicators of cardiovascular fitness [49,109,112].

5.6.2. Blood pressure (BP), blood pressure recovery (BPR)

Longitudinal studies have shown that SBP or the calculated heartrate and SBP product during exercise are positively associated with future resting BP, even independent of resting SBP and other cardiovascular risk factors [81,113]. An exaggerated BP response to treadmill exercise has been observed in children with white-coat HT [114]. Likewise, an exaggerated SBP during in-office exercise tests has also been reported in children at risk for early damage in vascular structure and functioning [78,114] the exaggerated BP responses to exercise, characteristic of hypertensive patients, may be present in normotensive adolescents with an increased risk of developing the disorder, and may reflect pathophysiological changes that precede sustained BP elevation [115]. The determination of exercise blood pressure (BP) has been established in the evaluation of hypertension and cardio- vascular prognosis in adults [56,77,79,81,108,113,116–119],

Previously it had not been accounted for in a large population in children and adolescents. BP measurement during exercise testing provides valuable information on a potentially inadequate hemodynamic response to acute exercise [49,74,120] The health effect of stress impactis known in some special cases (i. e. exaggragated BP) [80,114,115,121,122] but the cause and effect of many phenomena requires further research.

This work may eventually lead to the discovery of physiological phenomena that have only been recognized by autopsy of those of a young age but are found to indicate the onset of later CVD disease, even at a very young age. This could pave the way for individual, targeted primary prevention.

5.7. We confirmed the evidence for post exercise SBP lowering at school age population

The haemodinamyc effect of exercise at childhood and adolescent ages needs further survey, since although meta-analyses and randomized controlled trials consistently show lower BP after exercise training in adults during the recovery period [33,123–130].

Our research, confirmed this fact, showing lower BP 10 minute after exercise in both the preadolescent and adolescent populations of both sexes, based on a large database. Moreover, we found, that this phenomenon also exists and is experienced even if exercise was overwhelming or overlading for schoolchildren as indicated by recovery HR rate.

The average daily stress even in school age, in long term, may contribute to the development of hypertension in predisposed individuals. This effect can be interrupted by intense physical exertion, even if the amount is not ideal for the individual. This phenomenon may justify and explain the known fact that regular physical activity results in a significant reduction in the development of the most common public diseases, including hypertension.

Its real significance lies in the potential, that physical exercise could provide definite data as a predictive factor for the cardiovascular fitness, of the individual and measurable predictive indicators of the efficiency, expected consequences and long-term effects of different exercise programs.

5.8. Comparing the exercise BP of Kiel EX.PRESS graded cycle test test and „Fit-test" DRT

Mean running speed in a well-adjusted DRT test serves as a good predictor for maximal aerobic speed during a graded test and O_2 consumption. Diagnostic and predictive significance of a laboratory stress tests is well-known, for example either systolic (SBP) or diastolic BP (DBP) during graded exercise testing (GXT) are associated with more than 30% increased risk of cardiovascular events and mortality in normotensive individuals [131].

The grade by which exercise results of DRT converge with results of laboratory graded ergometer tests is important for evaluation and applicability of hemodynamic parameters measured in our work. Due to lack of comparative literature we compared effects of our proposed "Fit-Test" on blood pressure with age and sex related systolic blood pressure values of the "Kiel EX.PRESS Study" [44,132]' published for children of 12-17 years of age.

Compared to results of exercise blood pressure values published by Hacke and Weiser in 2006 (based on the Kiel EX.PRESS Study, cycle ergometer, 12-17 years old), not only trend lines, but also dynamics of the age and sex related increase and after-exercise mean values show similar tendency between 12-16 years of age. However, our measurements did not reinforce their measurement of equilibration between sexes of 17 years of age. Blood pressure of 17 years old males is higher than of females the same age, both by international data (ESH, USA) and our study data (for idle and for exercise blood pressure). For children younger than 12 years we do not have comparable data.

Both of the studies agree in the following statements:

· The mean blood pressure of boys and girls is approximately the same at12 years, both before and after exercise

· Seemed a year-by-year increase in difference of resting and peak blood pressure of males after 13 years of age, compared to SBP of females of the same age, in favor of males.

· Boy-girl differences and the slope of trend lines are similar for resting and loaded SBP values.

· Exercise mean SBP values of males of 14 years of age is approximately 150 mmHg.

· Boys reach peak exercise SBP of approximately 160 mmHg at the age of 16 years.

· Trend lines of exercise values follow idle values for both sexes over age.

Comparing our exercise SBP mean values to published values of exercise SBP values of the graded exercise test, characteristic effect of DRT on the cardiovascular system shows similarity with physiological processes measures in stress laboratory examinations [44].

Similarity in the age and sex related trends and measure of mean values reinforce the suggestion that causes behind abnormal results might carry significance similar to already known phenomena (e.g. exercise capacity, chronotropic response to exercise, HR recovery, blood pressure response to exercise) [133], making them a possibly lucrative subject of future research. This also reinforces the possibility of abnormal exercise CV reactions discovered with our simple screening to have diagnostic or long-term prognostic significance [133].

Despite exercise values being in the same interval, idle SBP measurements of the Kiel EX.PRESS study show significantly lower mean values than ours. This might be caused by the well-known fact, that circumstances of measurement, population difference and differing methodology can strongly affect idle SBP measurement [134]. Exercise SBP values, difference between sexes and exercise trend lines show a remarkable match.

5.9. The need to decrease the underscreened and underdiagnosed hight BP before adulthood

Adolescents with elevated BP progressed to HT at a rate of 7% per year, and elevated BMI predicted sustained BP elevations [33]. In addition, young patients with HT are likely to experience accelerated vascular aging. Both autopsy and imaging studies [135] have demonstrated BP-related CV damage in youth. These intermediate markers of CVD (eg, increased LV mass [136], carotoid-intima and media thickness [137], arterial stiffness [138] are known to predict CV events in adults, making it crucial to diagnose and treat HT early.

Higher blood pressure values in childhood may predispose to adult HT, even a single high value at the age of 5-7 years, 3.8-4.5 times more often developed HT after 30 years [16]. Thus, repeatedly higher BP values at school, on which our test is based on, indicate CVD risk, even if it is normal during in-office inspections. Lifestyle also plays an important role in the development of long-term HT [139]. Early onset without proper treatment can lead to serious complications at a young age.

Nonetheless, childhood HT is underdiagnosed, problematic in recognition, partly due to blood pressure variability, percentile boundaries, more complex classification of special forms of HT (MHT, WCHT), and partly due to rare occasional BP measurement during routine visits [83]. According to a 2008 US study, only 35% of patients underwent BP screening [127,140]. Even if high values are measured, the HT-specific examination in 75% of hypertensive and 90% of preHT children [22] is not taking place.

Accurate national data are unknown, but we found a similar trend in our research.

5.10. Develop a cheap, reliable, reproducible, exercise-based pilot screening test, named "Fit-test"

Numerous studies have shown that it is possible to detect vascular lesions early and thereby predict disease before symptoms and manifestations occur, for example by examining the elasticity of blood vessels or the rate of blood flow [135] and possibly detecting changes in the daily rhythm and dynamics of blood pressure [29].

Diseases in the group of non-communicative endemic diseases develop over decades, so the population-level effectiveness of prevention programs can only be quantified over decades and are influenced by many factors. Considering these, the identification and research of predictive and short-term measurable physiological effects are of special importance for future health.

5.10.1. Low budget DRT predict the result of laboratory exercise tests

Laboratory tests require specific settings, and specially trained professionals, which are not widely available [50]. Many field tests were investigated, and criterion validated, and it is true, not a direct measure only an estimate of CRF, that about 2000m DRT tests represent the best useful alternatives for estimating cardiorespiratory fitness. [47]. We aimed to adapt this knowledge to a cheap, reliable, reproducible exercise test. For this purpose, a pilot screening test, was developed named "Fit-test". Analysis of haemodynamic changes in a large population for screening is suitable only if the test is easy to perform, reproducible, and has reference values. A condition for reproducibility is that a standardized exercise test is used. According to recent results the 2000 meter running test gives the best correlation with the laboratory measurements in the age groups over 12y [47]. Below 12 years, data are lacking, so our survey is the first to assess correlation between preadolescent and adolescent group's exercise haemodinamic parameters [47].

In the young generation the predictive value of 2000m DRT tests coincide with the result of the **shuttle running test** [47,48]. The reference values, that is, the normal and cut-off values for gender and age, were determined in our current work.

5.10.2. Pilot screening test

As a pilot project (fit-test) was screening for hypertensive cases according to gender and age-based resting and exercise BP percentile. Screened and detected sustained HT cases, their BP percentiles's without treatment, and the change of BP results after antihypertensive treatment had shown. We also have demonstrated that a specific type of hypertension, such as MHT, also can be screened with this method, but the currently valid guidelines actually used protocols are not suitable.

The Hungarian population has one of the largest CVD risk ratios in Europe. In this high-risk environment, we aimed to decrease the CVD risk of the upcoming adult generation. A novel screening method has been established with a new approach for early detection of risk factors and HT at school children. In this approach we have combined the prior knowledge related to exercise tests from the boundary between pediatrics and sports medicine with screening tests of the known and influenceable risk factors. This method is easily feasible and is based on existing resources of the medical care system of schools and existing physical education tests. This enables the screening of large population of school age students with a low requirement for time, professionals and resources.

The primary focus of known and influenceable risk factors were supplemented with parameters that were proven independent like exercise and recovery HR and BP. Associated DRT results were also registered. With this approach, we were able to identify risk cases and diseases that were hidden during regular medical examination room tests. Adaptability of children born with organ dysfunction is very good. Since these children do not know the feeling of living with healthy function, they will not raise a complaint of illness even if it was a symptom of serious disease.

This new method was also able to identify a higher ratio of hypertension students than the resting measurements. This method is sensitive and has significantly improved the early diagnosis of students with hidden and asymptomatic HT.

This IT-supported workload screening system enabled the identification of previously unrecognized hypertensive students, improved the proportion of cooperative families (57% vs. 79%), shortened the time between the onset and detection of high BP (6 in 2016). -8 years after BP elevation (diagnosed as opposed to the previous 24%), filtering of MHT and compliance with hypertensive students for effective therapy were also possible. The program reduced the proportion of screenings without consequences.

Measuring individual results carries information about fitness and health of a population. Analysis of population-level changes, however, can provide the key to understand the positive impact on public health, and predict the health impact of each exercise program.

It was used by PE taechers, general and school medicine practitioners, and by involved school childrens'parents on-line, and the measurement data for further survey.

5.10.3. Need for well-defined and tracked patient pathways

Our model demonstrates the need for well-defined and tracked patient pathways from screening through definitive care to follow-up, in which school health and analytical information can play a more effective role. A wide-ranging extension of the system of well-regulated pathways connecting primary and specialized care is warranted.

As example was presented a normal weight (BMI 34-59pc), and well-trained boys (CPF 72-84pc) who has sustained hipertension between the ages of 10 and 14 years. He is a good example that "look-alike", ie, trained, non-obese students can easily "slip through" screening tests, his hypertension was not treated although increased pressure in their vessel walls trigger atherosclerosis and vascular remodeling just like their unhealthy-looking counterparts.

Regular and systemic, multidisciplinary screening, with equal access, may point out abnormal leanness and overweight, deterioration of general fitness, or respiratory, hematopoietic, hormonal, cardiac, or renal disease beyond screening for blood pressure. School screening and physical education classes can reveal a wealth of information that can help the clinician or primary care provider make the right diagnosis and implement the right therapy and help the student with a more equal chance of becoming a healthy adult.

5.10.4. Meeting the requirements of WHO towards screening tests

Serious public health challenges of communicative diseases in adults in the previous centuries were solved by vaccination in childhood. It is imaginable to solve the challenges nowadays of non-communicative diseases by prevention starting in childhood as well. A suitable screening method for early detection of risk group is one possible tool for this. Our recommended and tested method meets all the 10 principles of screening methods set by the WHO [141] : It target an important health problem which has accepted treatment for diagnosed patients, available facilities for diagnosis and treatment.With this method can recognise latent phase, test is suitable for diagnosis, method acceptable to the population, and both diagnosis and treatment are cost effective. The continuation screening CVD risk is assured. So, our method meets all these criteria. By building on the existing school and medical systems it is cost-effective, also enables continuation in screening twice a year. Continuation of screening also allows the follow-up on previously diagnosed cases as well as identifying newly developed cases or newly joint members of the screened population.

A suitable childhood HT screening method is a great possibility to prevent subsequent CVD with complications. Our 'Fit-Test' method meets the WHO recommendations and our research shows that combining the existing screening methods with exercise BP and HR measurements is an easy-to-use and low-budget method with health benefits. Reproducibility and feasibility anywhere are also assured by the described protocol and our measured and published percentile values.

5.11. New normative pediatric blood pressure (BP) tables

5.11.1. New guidelines' office blood pressure (BP) tables based on normal-weight children

New normative BP tables based on normal-weight children are included with these guidelines. The decision to create these new tables was based on evidence of the strong association of both overweight and obesity with elevated BP and HT. Including patients with overweight and obesity in normative BP tables was thought to create bias.

These tables are based on the same population data excluding participants with overweight and obesity, and the same methods used in the Fourth Report [33,73].

5.11.2. Haemodynamic dataset of normal weight children population

Many well controlled trials are underway worldwide to develop opportunities for primary and early secondary prevention. Along with hereditary predisposition, blood pressure increase is significantly influenced by changes in body ratios and obesity [14,38,142,143], which is also a risk factor for the development of the metabolic syndrome [144].

During the course of our research, the methodology for determining cut-off values for childhood and adolescent hypertension was modified [11,12,33]. Due to the well-known blood pressure-raising effect of obesity, international hypertension protocols excluded blood pressure data of overweight or obese children and adolescents [33] and only used data of the normal weight population to calculate reference percentiles. Therefore, according to the new recommendation for normative tables of office-BP [33], a dataset was created containing the exercise hemodynamic parameters of the normal weight-group of our population, using the WHO BMI and BMI percentile classifications, which is a niche. According to our knowledge, our dataset is the first at this area.

By fulfilling the goal of the present study, we proposed SBP reference values during aerobic submaximal field-exercise in 6- to 18-year-old children and adolescents, its data table can serve as a basis for clinical evaluation.

6. Summary

In our research we have established a public screening protocol for school aged children to facilitate early diagnosis of multiple hypertension types and CVD risk. In this thesis I have introduced the implementation and caracteristics of the screening program, as well as demonstrated the applicability of our dataset as detailed below.

6.1. Haemodynamic effect of excercise has both individual and population-level relevance

Measurement of individual outcomes carries information about fitness and health specifics of that individual. The analysis of population-level changes can provide the key to understanding positive public health impact of regular exercise and predicting the public health impact of different exercise programs. Differences between the recovery trends of HR and BP after exercise were observed

6.1.1. Recovery HR trends after excercise

At the end of the 10 min. recovery time most of schoolchildren's heart rate remained at a high level, higher by more than 10 percent than their HR before the exercise test. Since this is higher than the expected recovery, we have concluded that most of the students were loaded more than recommended based on their fitness level.

6.1.2. Differences exist between recovery HR and recovery BP trends after exercise

In contrast to the recovery HR trends, the recovery blood pressure decreased to starting level or below. This phenomenon was described before for adults, however we also demonstrated to multiple youth groups. According to our analysis, this phenomenon is the same in multiple subgroups, i.e. school aged boys and girls, as well as total population, normal weight population, even when exercise load was higher than fitness level.

6.2. Pilot screening test, called "Fit-test"

We suggest a **field test (called "Fit-test"),** a 1000 meter DRT for 1-4 classes (age between 6-10 years) and a 2000 meter DRT (for 5-13 classes, age between 10-18 years) which is one of the best predictor of cardiorespiratory fitness (CRF) according to latest studies [56,57], as an alternative to laboratory stress tests for screening CRF and calculating the age and gender-specific percentiles associated with it. Such test, in addition to establishing the reference values also provides an opportunity to gain new insight into the relationship between later manifestations of illness and juvenile burden response.

6.2.1. Exercise-related screening is suitable for screening for different HT types

In our work, we applied BP elevation induced by physical exertion and psychological exertion provoked by school rating, in addition to resting BP, to screen for the risk of HT. We have found that exercise-related screening is also suitable for screening for MHT, preHT, and sustained HT students, and for monitoring the effects of treatment (Figures 5-7).

6.2.2. Fit-test easily fits into the recent school and school health system.

Our low-budget, whole-population screening test fits seamlessly into the recent school and school health screening system. It provides the opportunity of risk mitigation for HT, MHT, high-blood pressure, caused by low physical and cardiorespiratory fitness, overweight, obesity and reduce poor compliance-caused CVD risk.

Our research also confirms that fitness status assessed by exercise testing should play a more integral part in the cardiovascular risk paradigm [43]. Based on these results, we suggest its widespread implementation.

6.3. First large dataset of haemodynamic changes of normal-weight pupils during a DRT, field exercise test

This **database** is the first large dataset of haemodynamic changes of normal-weight pupils during a field exercise test. Here, we present a dataset for anthropometric and hemodynamic parameters measured both during relaxation and after exercise containing 1,173,342 data segments from 65,345 acquisition points of 10,894 normal weight subjects, covering an age range of 6 to18 years collected in a course of 12 years.

6.3.1. The population-specific dynamics and experienced individual dissimilarities

We determined **the population-specific dynamics** of pre- and post exercise and at recovery pulse and blood pressure changes and found significant dissimilarities. This indicate individual differences in blood pressure control and may show the risk of individual hypertension or other health related factor. This phenomenon may be the basis for early detection of subsequent CVD risk and for sensitive early screening.

6.3.2. Importancce of the combined evaluation of physical and CV fitness

Our database also provides an opportunity to evaluate both the physical and cardiovascular fitness of the affected age group, even internationally for a population level comparision, as well as to assess the CV fitness and endurance of selected students.

6.3.3. Established the possibility to subsequent monitoring

The unique database and the subsequent monitoring of the health status of the affected generation could help to understand the causes and significance of the individual pattern of juvenile exercise induced haemodynamic variations.

This dataset is useful for physical education teachers, coaches, physicians and exercise physiologists to evaluate actual cardiovascular fitness and haemodynamic responses to exercise in children or adolescents and follow its change. It is also a useful tool to detect children with low cardiopulmonar or cardiovascular fittness, known as low exercise tolerance or abnormal haemodynamic responses to exercise.

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Appendix

1, Motivation quiestionere:

Nemed: **Osztályod:**		
Kérdések:	**IGEN**	**NEM**
1. Fontosnak tartod-e a mindennapos testmozgást?		
2. Elégedett vagy-e az edzettségeddel?		
3. Szereted-e, ha mérik a teljesítményedet?		
4. Érdekel-e a mérések eredménye?		
5. Szereted-e a 2000 m-es futást?		
6. Jónak tartod-e, hogy megmérik közben a vérnyomásodat?		
7. Érdekel-e ennek az eredménye?		
8. Fontosnak tartod-e, hogy kiderüljön, ha valami betegséged van?		

n

2, List of abstracts related to the subject of the thesis –

I. EUSUHM London, 17th Congress of European Union for School and University Health and Medicine. Breaking down the Barriers, London 27-29 june 2013, „Pupils' cardiovascular response to load” population-based study, Session: E.2.

II. Magyar Gyermekorvosok Társasága 2014 évi Jubileumi Nagygyűlése a Magyar Gyermeksebész Társaság Jubileumi Kongresszusa Gyermekgyógyászati Továbbképző Tanfolyam, Populációs prevenció: szûrõvizsgálat és az egészségtudatosság fejlesztése P 027 (Gyermekgyógyászat 2014; 65. évfolyam, 3. szám)

III. International Academy for Cardiovascular Sciences (IACS) 2014 European Section Meeting, 8-11. October. 2014. Balatongyörök: Fit-test – a novel screening method. Anthropometric, cardiovascular and sport measurement of the school-age population P.15

IV. Magyar Gyermekorvosok Társaságának 2016. évi Nagygyűlése, Szeged2016. szeptember 22-24. A mozgás hatása a kövérségre, a kövérség hatása a mozgásra a vérkeringés „szemével” (Gyermekgyógyászat 2016; 67. évfolyam, 5. szám)

V. MGYT Magyar Gyermekorvosok Társasága 2017.évi Naggyűlése, 2017: Sport alkalmassági vizsgálat a házi gyermekorvosi, háziorvosi praxisokban

KÉNYSZER VAGY LEHETŐSÉG? (Gyermekgyógyászat 2017; 68. évfolyam, 5. szám)

3, Publications related to the subject of this thesis