This doctoral thesis provided normative data on maximal cycle ergometer test parameters in a population sample of children. The updated values are needed, because cardiorespiratory fitness (CRF) has declined in children. It is also important to identify factors associated with CRF, because higher CRF has many beneficial effects on health and well-being. The thesis showed that unsupervised physical activity, lean body mass, and static balance are associated with CRF in girls and boys.
Cardiorespiratory fitness, its determinants and cardiorespiratory responses in maximal exercise test among children
NIINA LINTU

Cardiorespiratory fitness, its determinants
and cardiorespiratory responses in maximal
exercise test among children

To be presented by permission of the Faculty of Health Sciences, University of Eastern Finland for
public examination in Medistudia auditorium MS301, Kuopio, on Friday, January 20th 2017,
at 12 noon

Publications of the University of Eastern Finland
Dissertations in Health Sciences
Number 395

School of Medicine, Institute of Biomedicine/Physiology, Faculty of Health Sciences
University of Eastern Finland
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ABSTRACT

Higher cardiorespiratory fitness has beneficial effects on health and well-being both in children and adults. However, cardiorespiratory fitness among children has declined in the last decades. It may also track from childhood to adulthood. Therefore, there is urgent need for updating data of cardiorespiratory fitness and related hemodynamic and respiratory parameters among children and for identifying factors which are associated with higher cardiorespiratory fitness.

The aim of this thesis was to provide normative data about cardiorespiratory fitness and related parameters assessed by maximal cycle ergometer test as well as to study sex differences in these parameters among population-based sample of children aged 6–11 years and to investigate sex-specific determinants of cardiorespiratory fitness among children aged 6–9 years. The analyses are derived from the baseline and 2-year follow-up data of the Physical Activity and Nutrition in Children (PANIC) study.

Peak workload per kg of weight was as means (2 SDs) 2.7 (0.9) W/kg in girls and 3.1 (1.0) W/kg in boys aged 6–9 years (difference between sexes, p<0.001) and 3.1 (0.9) W/kg in girls and 3.4 (1.3) W/kg in boys aged 9–11 years (difference between sexes, p=0.003). Peak oxygen uptake per kg of weight was 47.6 (13.0) ml/kg/min in girls and 51.9 (15.5) ml/kg/min in boys aged 9–11 years (difference between sexes, p<0.001). A plateau or decline in systolic blood pressure close to the end of the exercise test was found in about a third of children aged 6–9 years and was considered a normal response. Heart rate (HR) decreased during 2 min recovery as means (2 SDs) 53 (18) beats/min in girls and 59 (22) beats/min in boys aged 6–8 years (difference between sexes, p<0.001) and 56 (22) beats/min in girls and 64 (20) beats/min in boys aged 9–11 years (p<0.001). Peak oxygen pulse was as means (2 SDs) 7.9 (2.3) ml/beat in girls and 9.1 (2.6) ml/beat in boys aged 9–11 years (difference between sexes, p<0.001). The lowest value of ventilation per carbon dioxide output during the test was as means (2 SDs) 29 (5) in girls and 28 (4) in boys with no sex difference. Peak HR, unsupervised physical activity, lean body mass and static balance were the strongest determinants of cardiorespiratory fitness, accounting for 25.7% of its variation, among girls aged 6–9 years. In boys of the same age, unsupervised physical activity, resting HR, hand grip strength, static balance, participation in organized football training and unsupervised trampoline jumping were the strongest determinants of cardiorespiratory fitness, accounting for 29.7% of its variation.

The results enable the evaluation of cardiorespiratory fitness and function during and after maximal exercise test and the identification of children with a low exercise tolerance and abnormal hemodynamic or respiratory function among children aged 6–11 years. This normative data can be used in clinical work and utilized in research community. The results suggest that higher amount of unsupervised physical activity, larger muscle mass and better balance are associated with a higher cardiorespiratory fitness in girls and boys aged 6–9 years.
Lintu, Niina
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National Library of Medicine Classification: QT 256, WF 110, WG 106, WG 108, WG 141.5.F9
Medical Subject Headings: Physical Fitness; Cardiorespiratory Fitness; Oxygen Consumption; Hemodynamics; Heart Rate; Blood Pressure; Exercise Test; Sex Factors; Child
TIIVISTELMÄ
Hyvä kestävyyskunto vaikuttaa positiivisesti terveyteen ja hyvinvointiin lapsuudesta lähtien.

Lasten kestävyyskunto on kuitenkin tutkimusten mukaan heikentynyt viime vuosikymmeninä. Huono kestävyyskunto lapsena voi johtaa huonoon kestävyyskuntoon myös aikuisena. Näistä syistä johtuen on tärkeää päivittää kestävyyskunnon viitearvot ja tutkia tekijöitä, jotka ovat yhteydessä hyvään kestävyyskuntoon jo lapsuudessa.


Painoon suhteutettu maksimaalinen työteho oli keskiarvoina (2 SD) 2,7 (0,9) W/kg 6–9-vuotiailla tytöillä ja 3.1 (1.0) W/kg samanikäisillä pojilla (sukupuolten välinen ero, p<0,001) ja 3,1 (0,9) W/kg 9–11-vuotiailla tytöillä ja 3,4 (1,3) W/kg pojilla (sukupuolten välinen ero, p=0,003). Maksimaalinen painoon suhteutettu hapenottokyky oli keskimäärin 47,6 (13,0) ml/kg/min 9–11-vuotiailla tytöillä ja 51,9 (15,5) ml/kg/min samanikäisillä pojilla (sukupuolten välinen ero, p<0,001). 6–9-vuotiaista lapsista noin kolmanneksella havaittiin kuormituskokeen lopputunnassa systolisen verenpaineen tasanne tai lasku, minkä todettiin olevan normaali löydös. Sydämen sykintätaajuus laski 6–9-vuotiailla tytöillä kuormituksen jälkeisen 2 minuutin aikana keskimäärin 53 (18) lyöntiä/min ja pojilla 59 (22) lyöntiä/min (sukupuolten välinen ero, p<0,001) ja 9–11-vuotiailla tytöillä keskimäärin 56 (22) lyöntiä/min ja pojilla 64 (20) lyöntiä/min (sukupuolten välinen ero, p<0,001). Maksimaalinen happipulssi oli 9–11-vuotiailla tytöillä 7,9 (2,3) ml/lyönti ja pojilla 9,1 (2,6) ml/lyönti (sukupuolten välinen ero, p<0,001). Ventilaation ja hiilidioksidin tuoton suhteen matalin arvo oli keskimäärin 29 (5) tytöillä ja 28 (4) pojilla 9–11-vuoden iässä, eikä se eronnut sukupuolten välillä. Maksimaalinen sykintätaajuus, omatoiminen liikunta, lihasmassa sekä staattinen tasapaino selittivät 25,7 % 6–9-vuotiaiden tyttöjen kestävyyskunnon vaihtelusta. Pojilla omatoiminen liikunta, sydämen sykintätaajuus levossa, käden puristusvoima, ohjatuissa jalkapaloharjoituksissa käyminen, staattinen tasapaino ja omatoiminen trampoliinilla hyppiminen selittivät 29,7 % kestävyyskunnon vaihtelusta.

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Viitearvojen avulla voidaan arvioida lasten hengitys- ja verenkiertoelimitsoinnin toimintakykyä kuormituksessa ja siitä voidaan päätellä, mitä tulee sujuvasti ja mitä on mahdollista tehdä. Viitearvojen avulla voidaan arvioida lasten kestävyyskuntoa ja selittää se keskeyttäviä tekijöitä, joilla on vaikutusta kestävyyskunnoon. Viitearvojen avulla voidaan päätellä, että terveyden puhtaus, lihaskunnan tai lihaskunnan arvot ovat olleet normaali ja että lasten kestävyyskunto on hyvä. Viitearvojen avulla voidaan päätellä, mitkä ovat lasten kestävyyskuntoon vaikuttaneet tekijökertoelmistö ja se, miten lasten kestävyyskunto voi vaikuttaa heidän terveyteen ja hyvinvointiin.
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This work was carried out at the Institute of Biomedicine, University of Eastern Finland, Kuopio Campus.

First of all, I want to thank the children who participated in this study, performed maximal cycle ergometer exercise tests and made this thesis possible.

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Kuopio, November 2016

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<th>Abbreviation</th>
<th>Description</th>
<th>Unit</th>
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<tbody>
<tr>
<td>BIA</td>
<td>bioimpedance analysis</td>
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<tr>
<td>BMI</td>
<td>body mass index</td>
<td></td>
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<td>BMI-SDS</td>
<td>body mass index-standard deviation score</td>
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<tr>
<td>BP</td>
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<td></td>
</tr>
<tr>
<td>BSA</td>
<td>body surface area</td>
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<tr>
<td>CO</td>
<td>cardiac output</td>
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<td>DXA</td>
<td>dual-energy X-ray absorptiometry</td>
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<td>min</td>
<td>minute</td>
<td></td>
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<tr>
<td>ml</td>
<td>milliliter</td>
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</tr>
<tr>
<td>O₂ pulse</td>
<td>oxygen pulse</td>
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<td>PANIC</td>
<td>Physical Activity and Nutrition in Children study</td>
<td></td>
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<tr>
<td>RER</td>
<td>respiratory exchange ratio</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>standard deviation</td>
<td></td>
</tr>
<tr>
<td>SV</td>
<td>stroke volume</td>
<td></td>
</tr>
<tr>
<td>VCO₂</td>
<td>carbon dioxide output</td>
<td></td>
</tr>
<tr>
<td>VE</td>
<td>ventilation</td>
<td></td>
</tr>
<tr>
<td>VE/VCO₂</td>
<td>ratio of ventilation and carbon dioxide output</td>
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1 Introduction

“Exercise is a journey, not a destination. It must be continued for the rest of your life. We do not stop exercising because we grow old - we grow old because we stop exercising.”
Kenneth Cooper

Cardiorespiratory fitness is made up of cardiovascular, respiratory and hematological components of oxygen delivery and the oxidative mechanisms of working muscles (1). Higher cardiorespiratory fitness has been associated with lower levels of conventional cardiometabolic risk factors (2), less stiff arteries and better arterial dilation capacity (3) in children and a lower incidence of overweight among adolescents (4). Lower body mass index at preschool has been related to higher cardiorespiratory fitness among adolescents (5). Furthermore, the increase of aortic intima-media thickness between ages 11 and 17 years has been found to be smaller in adolescents who had higher cardiorespiratory fitness at age 17 than adolescents with lower cardiorespiratory fitness (6). Higher cardiorespiratory fitness in childhood may also protect against raised blood pressure in early adulthood (7). Among adults, higher levels of cardiorespiratory fitness have been associated with a lower incidence of a number of chronic diseases, such as cardiovascular disease, type 2 diabetes and lung and colorectal cancers, as well as lower premature mortality (8-10).

Higher levels of cardiorespiratory fitness have beneficial effects on health and well-being both in children and adults. Instead, poorer cardiorespiratory fitness in childhood may have far-reaching consequences in whole life span. Cardiorespiratory fitness may track from childhood to adolescence (11,12) and to adulthood (13) and unfit child tends to be unfit also in adult. This may for instance increase morbidity to different chronic diseases in adulthood and affect ability to work, which can increase the use of health-care services and related costs in society. Lower levels of cardiorespiratory fitness among children could cause enormous societal problems in the future. Therefore, it is very important to find out factors which are associated with higher cardiorespiratory fitness already in childhood and pay attention to them in early life.

In many countries cardiorespiratory and neuromuscular fitness have declined during the last decades and it may be due to increased sedentary behavior and decreased habitual physical activity (14-16). This universal trend highlights the need for updating data of cardiorespiratory fitness and related parameters among children.

This thesis provides new and valuable information about present state of cardiorespiratory fitness and related parameters among Finnish children. Also sex differences in cardiorespiratory fitness and related parameters are important themes for this research. Furthermore, determinants of cardiorespiratory fitness are main interests. According to the previous findings, the results of this thesis are needed.
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Kenneth Cooper

Cardiorespiratory fitness is made up of cardiovascular, respiratory and hematological components of oxygen delivery and the oxidative mechanisms of working muscles (1). Higher cardiorespiratory fitness has been associated with lower levels of conventional cardiometabolic risk factors (2), less stiff arteries and better arterial dilation capacity (3) in children and a lower incidence of overweight among adolescents (4). Lower body mass index at preschool has been related to higher cardiorespiratory fitness among adolescents (5). Furthermore, the increase of aortic intima-media thickness between ages 11 and 17 years has been found to be smaller in adolescents who had higher cardiorespiratory fitness at age 17 than adolescents with lower cardiorespiratory fitness (6). Higher cardiorespiratory fitness in childhood may also protect against raised blood pressure in early adulthood (7). Among adults, higher levels of cardiorespiratory fitness have been associated with a lower incidence of a number of chronic diseases, such as cardiovascular disease, type 2 diabetes and lung and colorectal cancers, as well as lower premature mortality (8-10).

Higher levels of cardiorespiratory fitness have beneficial effects on health and well-being both in children and adults. Instead, poorer cardiorespiratory fitness in childhood may have far-reaching consequences in whole life span. Cardiorespiratory fitness may track from childhood to adolescence (11,12) and to adulthood (13) and unfit child tends to be unfit also in adult. This may for instance increase morbidity to different chronic diseases in adulthood and affect ability to work, which can increase the use of health-care services and related costs in society. Lower levels of cardiorespiratory fitness among children could cause enormous societal problems in the future. Therefore, it is very important to find out factors which are associated with higher cardiorespiratory fitness already in childhood and pay attention to them in early life.

In many countries cardiorespiratory and neuromuscular fitness have declined during the last decades and it may be due to increased sedentary behavior and decreased habitual physical activity (14-16). This universal trend highlights the need for updating data of cardiorespiratory fitness and related parameters among children.

This thesis provides new and valuable information about present state of cardiorespiratory fitness and related parameters among Finnish children. Also sex differences in cardiorespiratory fitness and related parameters are important themes for this research. Furthermore, determinants of cardiorespiratory fitness are main interests. According to the previous findings, the results of this thesis are needed.
2 Literature review

2.1 CARDIORESPIRATORY RESPONSES IN MAXIMAL EXERCISE TEST IN CHILDREN

2.1.1 Cardiac output, stroke volume and heart rate
Cardiac output (CO) is a product of stroke volume (SV) and heart rate (HR) (17). CO increases almost linearly during progressive exercise because it is closely related to the metabolic demands of working muscles (17-19). SV also rises continuously with increasing work rate during progressive exercise in the majority of children (18). However, SV has been found to decrease as work rate increases above the anaerobic threshold despite rising CO in a minority of children (18).

CO at a given oxygen uptake (VO₂) during maximal exercise test is significantly lower in children than in adults (20). Among children, CO is usually higher in treadmill tests than in cycle ergometer tests (17). Children have also lower SV than adults because of their smaller body size (17). Moreover, girls have been found to have lower CO and SV than boys due to a smaller body size, lean body mass and heart (17,19,21). However, not all studies have confirmed this difference in SV during exercise between sexes among prepubertal children (21).

The cardiovascular system responds immediately to exercise by increasing HR due to a decrease in vagal tone (17). Children have a smaller heart than adults and compensate for this difference by a higher increase in HR at different work rates and by a higher maximal HR than adults (17). Maximal HR during progressively increasing exercise among children is dependent on motivation and co-operation as well as the protocol and ergometer used (17). Also better mechanical efficiency may lead to increased maximal intensity of exercise and higher maximal HR (17). Maximal HR is approximately 200 beats/min during a running test on a treadmill and 190-195 beats/min during a cycle ergometer test among children (19). In general, sex or cardiorespiratory fitness have no influence on maximal HR among children (19). However, boys appear to have a lower resting HR than girls (22).

Maximal HR at the end of progressive maximal exercise test is often used as an indicator of maximal effort. Maximal HR >85-90% of age-predicted maximal HR is commonly thought to indicate maximal exhaustion (23). However, there are several equations for maximal HR prediction. The equation of 208 - (0.7 x age) has been shown to be valid and appropriate in the prediction of maximal HR among children and adolescents, whereas the commonly used equation of 220-age appears to overestimate maximal HR among children (24).

HR decreases quickly after maximal exercise test in children mainly due to re-activation of the parasympathetic activity (25). Parasympathetic re-activation was found to be larger in exercise tests using small muscle mass, such as arm cranking, compared to exercise tests using large muscle mass, e.g. cycling, among healthy boys aged 13 years (26). The HR decrease within one minute after a maximal cycle ergometer exercise test was observed to be greater in boys than in girls aged 7-12 years (27) but similar among girls and boys aged 10 years (28). The HR decline during the first minute after exercise test attenuates with increasing age among children (22,29).

Impedance cardiography is a simple noninvasive method to measure CO during a cycle ergometer exercise test among healthy children and adolescents (18). Furthermore, CO has been measured indirectly using the CO₂-rebreathing equilibration method in cycle ergometer and treadmill tests among healthy children (20). SV has been measured by
Cardiac output (CO) is a product of stroke volume (SV) and heart rate (HR) (17). CO is dependent on motivation and cooperation as well as the protocol and ergometer used (17). Maximal HR during progressively increasing exercise among children (19). However, boys appear to have a lower resting HR than girls (22). Girls have been found to have lower CO and SV than boys due to a smaller body size (17). Moreover, girls have been found to decrease as work rate increases above the anaerobic threshold despite rising metabolic demands of working muscles (17-19). SV also rises continuously with increasing work rate during progressive exercise in the majority of children (18). However, SV has been measured by impedance cardiography during a cycle ergometer exercise test among healthy children and adolescents (18). Furthermore, CO has been found to decrease as work rate increases above the anaerobic threshold despite rising metabolic demands of working muscles (17-19). SV also rises continuously with increasing work rate during progressive exercise in the majority of children (18). However, SV has been measured by impedance cardiography during a cycle ergometer exercise test among healthy children and adolescents (18). Furthermore, CO has been found to decrease as work rate increases above the anaerobic threshold despite rising metabolic demands of working muscles (17-19).

2.1.2 Blood pressure

Higher blood pressure (BP) is associated with higher CO and peripheral vascular resistance (32). Systolic BP normally rises during exercise test because of an increase in CO in response to exercise (32,34). A lack of increase in systolic BP may indicate cardiac dysfunction (32), but a drop in systolic BP of even more than 10 mmHg during exercise among children often occurs without symptoms or cardiac abnormalities (35). Systolic BP increases much less in children than in adults, and maximal systolic BP seldom exceeds 200 mmHg in children (17). The reason for this is better arterial compliance and a larger decrease in total peripheral vascular resistance during exercise in children than adults (17,36). The magnitude of the systolic BP rise during exercise increases with age and body size (17). Among children aged 8-10 years, there were no sex differences in systolic BP responses to maximal exercise test (37). In another study among children 7-12 years of age, maximal systolic BP rose with increasing body surface area (BSA) from 122 to 139 mmHg in boys and from 126 to 142 mmHg in girls, and there was no difference in systolic BP increase between sexes within a BSA group. Diastolic BP usually remains unchanged or may even slightly fall during exercise because of vasodilation (19,32). However, in some studies a rise in diastolic BP with increasing exercise intensity has been observed (27,34). Maximal diastolic BP was found to increase during exercise from 77 to 83 mmHg in boys and from 77 to 80 mmHg in girls (27).

Systolic BP usually declines rapidly after a maximal exercise test, reaching resting levels within 6 minutes (17). After exercise systolic BP can drop precipitously because of venous pooling and a delayed increase in systemic vascular resistance to match the reduction in CO (38).

BP is an important variable to monitor during exercise test. It can be measured indirectly using cuff, an aneroid device and a stethoscope to detect Korotkoff sounds (17,32). Among children, it may be difficult to hear Korotkoff sounds to detect diastolic BP, especially near exhaustion (17). Therefore, also automated and electronic devices can be used (17,32). The appropriate cuff size according to the arm size of the child is important to get reliable BP measurements (17,32). BP is usually measured at rest before the exercise test, several times during the progressive exercise phase until exhaustion and during the recovery period (32).

Ambulatory and resting BP have been found to have a positive association with age and height among children and adolescents (39,40). At a given sex and age, BP percentiles varied by height (39). Systolic and diastolic BP were similar until 13 years of age but the rise in BP during puberty was more pronounced among boys than girls, resulting in larger BP difference between sexes since age 13 years (39).

2.1.3 Respiratory function

To obtain reliable respiratory data during exercise tests it is important to collect respiratory gases and analyse oxygen and carbon dioxide from expired air (32). In pediatric exercise testing, it is essential to use pediatric masks or mouthpieces to avoid air leak and ensure measurement reliability (32). The breath-by-breath method is nowadays the most popular way to conduct respiratory gas analysis, because it provides valuable exercise test
parameters that can be directly measured or indirectly calculated using the measured variables (32). The exercise test parameters include ventilation (VE), respiratory rate, tidal volume, VO₂ and carbon dioxide output (VCO₂) (32). The ventilatory equivalent for oxygen and carbon dioxide (VE/VCO₂) and respiratory exchange ratio (RER) can be derived from these parameters (32). Also oxygen pulse (O₂ pulse) is a valuable calculated parameter which has both respiratory and hemodynamic components.

**Oxygen uptake**
VO₂ increases quickly when dynamic exercise begins (17). Maximal oxygen uptake (VO₂max) is the highest amount of oxygen that an individual can consume during dynamic exercise (23). Adults have been reported to reach often a plateau in VO₂ near the end of progressive dynamic exercise, after which the value does not increase despite continuing exercise (17). However, only a minority of children reach a plateau during maximal progressive dynamic exercise and therefore, the highest VO₂ observed during the test is often defined as peak VO₂ (23). VO₂ is strongly related to fat-free mass (17). Among children, VO₂ increases about 10-fold during exercise, whereas adults can obtain 10-15-fold increase (17).

**Ventilation**
Peak VE has been reported to be dependent on the maximal level of aerobic metabolism achieved, the carbon dioxide by-product of anaerobic metabolism, the level of ventilatory drive caused by arterial acidosis and the test protocol used (41). Peak VE increases with age during childhood through an increase in the size of lungs and change in pulmonary mechanisms (41). Also lean body mass and body height are important determinants of peak VE (41). Peak VE at the end of progressive maximal exercise test is usually smaller than maximal voluntary ventilation (41). Moreover, children have a higher VE per body weight (VE/kg) than adults (41). There is some evidence that peak VE does not increase linearly with body size in childhood, and therefore allometric scaling is reasonable (41). Peak VE during treadmill test was on average 58 l/min in boys and 50 l/min in girls aged 11 years, and this sex difference was statistically significant (42). In another study among children aged 10 years, peak VE during treadmill test was 78 l/min in boys and 71 l/min in girls with no statistically significant sex difference (43).

**Respiratory exchange ratio**
RER, the ratio between VCO₂ and VO₂ (17), increases during progressive exercise. The maximal RER achieved in a maximal exercise test can be used as an indicator of intense effort (23). Anaerobic metabolism is not yet developed in children and glycolytic activity is lower in children than in adults (44), which can decrease RER values achieved during exercise test (45). RER values vary a lot among individuals. Although a RER≥1 has been used as an indicator of maximal effort among children, young children can achieve maximal effort with a RER<1 (23). Furthermore, RER is often higher in cycle ergometer tests than in treadmill tests and is also dependent on the protocol used (23). In a study among children aged 6-7 years, maximal RER in treadmill test was 1.05 in boys and 1.10 in girls (46). In another study among children 8-11 years of age, maximal RER in cycle ergometer exercise test was 1.02 in both sexes (47).

**Oxygen pulse**
O₂ pulse is an indicator of the amount of oxygen consumed by one heartbeat (VO₂/HR) (32) and it can be used as a non-invasive indirect estimate of SV (48). O₂ pulse can be used to study whether SV rises normally with increasing workload (32). As it is difficult to measure CO accurately by non-invasive methods during exercise, O₂ pulse is often used to assess ventricular function during exercise test (49). An abnormally blunted increase of O₂ pulse is observed if SV does not rise normally during exercise, for instance among patients with ventricular dysfunction (49). O₂ pulse is also influenced by blood hemoglobin and arterial
oxygen saturation (50). The mean maximal O2 pulse in treadmill exercise test was 8 ml/beats among children aged 10 years and 13.4 ml/beats among adults (51). In another study among children aged 8-13 years, maximal O2 pulse during a cycle ergometer test varied between 6 and 11 ml/beats in boys and between 5 and 11 ml/beats in girls depending on their BSA (27).

VE/VCO2
The lowest value of VE/VCO2 during exercise test is a feasible noninvasive method to estimate ventilatory efficiency (52). This measure is useful, for example, in the diagnostics of congenital heart diseases and cystic fibrosis (53,54). The VE/VCO2 slope has also been used to estimate ventilatory efficiency in some studies among healthy children (29,55), but the lowest VE/VCO2 during maximal exercise test is preferred (52). Data on ventilatory efficiency during exercise among children are limited (56). VE/VCO2 decreases progressively to its nadir in the beginning of the progressive maximal exercise test and then rises gradually until the end of the test (56). High VE/VCO2 may reflect the diminished capacity of pulmonary perfusion and cardiac output and may therefore be a sign of cardiac dysfunction (56). VE/VCO2 during a cycle ergometer exercise test was found to be higher among girls than boys at the age of 8 years, but this sex difference was only moderately statistically significant (57). Furthermore, VE/VCO2 in treadmill exercise test has been observed to decrease with age in both girls and boys aged 6-17 years (58).

2.2 CARDIORESPIRATORY FITNESS IN CHILDREN

2.2.1 Definition of cardiorespiratory fitness
Cardiorespiratory fitness is made up of respiratory, cardiovascular and hematological components of oxygen delivery and the oxidative mechanisms of working muscles (1). It refers to the ability to perform exercise using large muscle groups with moderate to high intensity for long periods (59). However, also psychological factors such as motivation may have an effect on cardiorespiratory fitness achieved in maximal exercise test (60). According to the central governol model of exercise regulation, central nervous system regulates exercise performance (61,62). Fatigue during the exercise is a complex phenomenon and its effects on cardiorespiratory fitness depend on many factors (63).

VO2max is recognized as the golden standard measure of cardiorespiratory fitness (23), but maximal workload achieved during maximal exercise test is also a good measure of cardiorespiratory fitness, because it has been shown to have a strong positive correlation with VO2max in population studies among children (64). When comparing the levels of cardiorespiratory fitness among growing and maturing children with different body sizes, it is reasonable to use appropriate scaling methods for assessing cardiorespiratory fitness (65). A simple ratio scaling is not necessarily feasible when comparing the levels of cardiorespiratory fitness among individuals, but for instance allometric scaling could be used (65). VO2max and maximal workload divided by lean body mass are not confounded by adiposity, and are therefore more valid measures of true cardiorespiratory fitness than VO2max and maximal workload scaled by body weight (66,67). Interestingly, allometric scaling of peak VO2 by lean body mass of both legs provided a better measure of cardiorespiratory fitness than allometric scaling by total lean body mass in children aged 10 years (68). Boys have higher VO2max than girls during growth independent of body size, but the development of VO2max during childhood is also influenced by factors other than sex or body size (69). These factors might include for instance differences in intensity of habitual physical activity between girls and boys and varying rates of development of muscle aerobic enzyme capacity or myocardial contractility (69).
2.2.2 Assessments of cardiorespiratory fitness in children

Cardiorespiratory fitness can be assessed in field conditions, but exercise physiology laboratories offer sophisticated equipment and appropriate testing protocols for the most valid assessments of cardiorespiratory fitness (32). On the other hand, properly conducted field tests are not only simpler and more practical, but they can also be reliable way to assess cardiorespiratory fitness among children (59). In order to achieve true maximal cardiorespiratory performance during exercise testing, it is important to give strong verbal encouragement to a child in both laboratory and field conditions (23).

Assessment of cardiorespiratory fitness at an exercise physiology laboratory

The pediatric exercise physiology laboratory must have ergometers that are appropriate for the size and age of children and an environment that is ideal for vigorous exercise, including standardized climate and sufficient space (32). In addition to a progressive exercise phase, exercise test protocol typically includes preceding baseline and warm-up phases and a following recovery phase (32). The ideal duration of exercise test is 10±2 minutes until exhaustion (32). Cardiorespiratory fitness can be assessed with or without respiratory gas analysis. When assessing cardiorespiratory fitness without respiratory gas analysis, VO2max can be estimated by the highest achieved workload or treadmill rate (70). However, there may be a marked difference between measured and estimated VO2max for instance because of the formulas used for estimation and interindividual variation in the relationship between measured and estimated VO2max (70). Masks or mouthpieces used for respiratory gas analysis may disturb exercise testing among children. However, recent evidence suggests that a pediatric mask does not impair maximal performance among children (71).

Cardiorespiratory fitness tests can be conducted using maximal or submaximal protocols. Maximal testing provides an accurate measure of cardiorespiratory fitness, but submaximal testing may also be valuable in many situations (70). Submaximal exercise test protocols can, for instance, be used in assessments of patients with chronic diseases who may be unaccustomed to vigorous exercise and results of submaximal tests can easily be applied in everyday activities (70). In submaximal exercise testing, submaximal work rates and corresponding HRs are measured, and maximal cardiorespiratory performance is extrapolated from these parameters (70).

Cycle ergometers and treadmills, the most common ergometers in pediatric exercise physiology laboratories (23), are feasible equipment for measuring maximal cardiorespiratory performance in children. However, treadmill testing has been found to result in about 10% higher VO2max than cycle ergometer testing in children aged 7-9 years (72). It is also noteworthy that untrained individuals may terminate cycle ergometer exercise test because of quadriceps muscle fatigue before achieving their true maximal performance (70). The exercise test protocol used can also affect cardiorespiratory performance among children (17). For instance in progressive cycle ergometer exercise test with incremental stages, the effort which is required to push the pedals during the later stages may be too high in relation to muscle strength among children with less muscle mass (23).

Cycle ergometers are cheaper and less noisy and require less space than treadmills (32). It is very important to adjust the cycle ergometer, including crank lengths and saddle height, carefully and individually for each child before the exercise test (73). Furthermore, there are several possible exercise test protocols, including multi-stage incremental and progressive incremental cycle ergometer protocols (32). James and McMaster cycle ergometer protocols are commonly used multistage incremental protocols (17), whereas continuously incremental ramp protocols are typical progressive incremental cycle ergometer protocols (32).
Assessment of cardiorespiratory fitness at field circumstances

There are at least 3 types of commonly used field tests for measuring cardiorespiratory fitness among children and adolescents (59). These field tests include the distance run test, such as 1500 m run; the timed run test, such as the 12-min run; and the endurance shuttle run test, for instance the 20-m endurance shuttle run test. The 20-m endurance shuttle run test has been used in many studies among children and adolescents from different age groups (74-76). In this test, cardiorespiratory fitness is measured as the number of completed 20 m laps with progressively increasing running speed (59). Peak VO₂ can be calculated using previously published equations for 20-m endurance shuttle run test, but these equations may not be suitable to estimate cardiorespiratory fitness at individual level of healthy children aged 8-10 years (77). Furthermore, step tests can also be used to estimate cardiorespiratory fitness in children (78).

2.2.3 Normal values of cardiorespiratory fitness in children

Cardiorespiratory fitness has declined over time, and there is an increased polarization between the fittest and the unfittest children (79). The decline of cardiorespiratory fitness during the last decades may be due to the insufficient amount of vigorous physical activity (14). Table 1 shows the means (standard deviations) of cardiorespiratory fitness among healthy children aged 6-13 years from different European countries assessed in laboratory circumstances by maximal cycle ergometer or treadmill tests. There are only few studies which have reported on cardiorespiratory fitness especially in younger children. Instead, among children with particular diseases, such as congenital heart disease (80) or cystic fibrosis (81,82), cardiorespiratory fitness has been measured more often to assess the ability to perform daily activities.
### Table 1. Cardiorespiratory fitness among healthy children aged 6-13 years from European countries

<table>
<thead>
<tr>
<th>Reference</th>
<th>Country</th>
<th>Age of children</th>
<th>Number of children</th>
<th>Cycle ergometer/treadmill</th>
<th>Respiratory gas analysis (Yes/No)</th>
<th>Cardiorespiratory fitness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Boys</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2)</td>
<td>Portugal, Denmark, Estonia</td>
<td>9.7 (0.4)</td>
<td>716</td>
<td>Cycle ergometer</td>
<td>No</td>
<td>3.0 (0.6) W/kg</td>
</tr>
<tr>
<td>(83)</td>
<td>Denmark</td>
<td>6.8 (0.4)</td>
<td>229</td>
<td>Treadmill</td>
<td>Yes</td>
<td>48.9 (6.1) ml/kg/min</td>
</tr>
<tr>
<td>(47), (64)</td>
<td>Sweden</td>
<td>9.9 (0.6)</td>
<td>137</td>
<td>Cycle ergometer</td>
<td>Yes</td>
<td>41.4 (7.2) ml/kg/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.3 (0.6) W/kg</td>
</tr>
<tr>
<td>(46)</td>
<td>Denmark</td>
<td>6.8 (0.4)</td>
<td>309</td>
<td>Treadmill</td>
<td>Yes</td>
<td>48.5 (6.0) ml/kg/min</td>
</tr>
<tr>
<td>(84)</td>
<td>Estonia, Sweden</td>
<td>9.6 (0.4)</td>
<td>295</td>
<td>Cycle ergometer</td>
<td>No</td>
<td>3.2 (0.5) W/kg</td>
</tr>
<tr>
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<td>Denmark</td>
<td>9.8 (0.4)</td>
<td>175</td>
<td>Cycle ergometer</td>
<td>No</td>
<td>3.2 (0.6) W/kg</td>
</tr>
<tr>
<td>(29)</td>
<td>The Netherlands</td>
<td>12.5 (2.9)</td>
<td>93</td>
<td>Cycle ergometer</td>
<td>Yes</td>
<td>47.0 (7.0) ml/kg/min</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.4 (0.6) W/kg</td>
</tr>
<tr>
<td><strong>Girls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2)</td>
<td>Portugal, Denmark, Estonia</td>
<td>9.6 (0.4)</td>
<td>729</td>
<td>Cycle ergometer</td>
<td>No</td>
<td>2.6 (0.6) W/kg</td>
</tr>
<tr>
<td>(83)</td>
<td>Denmark</td>
<td>6.7 (0.3)</td>
<td>207</td>
<td>Treadmill</td>
<td>Yes</td>
<td>44.9 (5.5) ml/kg/min</td>
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<td>9.7 (0.6)</td>
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<td>35.8 (6.4) ml/kg/min</td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>2.9 (0.5) W/kg</td>
</tr>
<tr>
<td>(46)</td>
<td>Denmark</td>
<td>6.7 (0.4)</td>
<td>283</td>
<td>Treadmill</td>
<td>Yes</td>
<td>44.8 (5.6) ml/kg/min</td>
</tr>
<tr>
<td>(84)</td>
<td>Estonia, Sweden</td>
<td>9.5 (0.4)</td>
<td>295</td>
<td>Cycle ergometer</td>
<td>No</td>
<td>2.7 (0.5) W/kg</td>
</tr>
<tr>
<td>(37)</td>
<td>Denmark</td>
<td>9.7 (0.4)</td>
<td>192</td>
<td>Cycle ergometer</td>
<td>No</td>
<td>2.9 (0.5) W/kg</td>
</tr>
<tr>
<td>(29)</td>
<td>The Netherlands</td>
<td>12.5 (2.9)</td>
<td>82</td>
<td>Cycle ergometer</td>
<td>Yes</td>
<td>42.0 (6.0) ml/kg/min</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.1 (0.5) W/kg</td>
</tr>
</tbody>
</table>

Values are means (standard deviations)
Normative population-based data on cardiorespiratory fitness are important not only from clinical but also from public health and health political perspective because of the relevance of cardiorespiratory fitness for health, well-being and functional capacity (85).

### 2.2.4 Determinants of cardiorespiratory fitness in children

Higher cardiorespiratory fitness among men than women is due to larger muscle mass, maximal stroke volume, blood volume and blood hemoglobin concentration among men (38). In a study among children 5-6 years of age, there was no difference in cardiorespiratory fitness between boys and girls (86). However, boys have been reported to have higher cardiorespiratory fitness than girls at the age of 6-18 years irrespective of scaling method used (29,47,83). The reasons for the sex difference in cardiorespiratory fitness in these age groups is that there is a larger increase in muscle mass, maximal stroke volume and blood hemoglobin concentration during puberty in boys than in girls (1). Peak VO$_2$ was observed to increase almost linearly from childhood to adolescence and early adulthood among boys, whereas in girls, peak VO$_2$ increased until the age of 14 years but not after this age (1). Besides chronological age, also maturation has been found to improve cardiorespiratory fitness among children (87).

Higher lean body mass, lower adiposity and higher maximal HR have been found to be strong determinants for higher cardiorespiratory fitness among children (47,83,88). Also higher left ventricular inner diastolic diameter has been associated with higher cardiorespiratory fitness, albeit only modestly (47). Moreover, higher body mass index (BMI) at the age of 2-7 years has predicted lower cardiorespiratory fitness at the age of 17 years (5). Longitudinal analysis have revealed that lower BMI, higher amount of moderate-to-vigorous physical activity, better psychosocial well-being and more frequent breakfast consumption were associated with higher cardiorespiratory fitness among children aged 6-11 years (89).

Higher levels of total and moderate-to-vigorous physical activity (90) and lower levels of screen-based sedentary behavior (91) have been associated with higher cardiorespiratory fitness in children. Instead in another study, sedentary behavior had no association with cardiorespiratory fitness (92). Furthermore, a higher amount of moderate and vigorous physical activity (≥3 metabolic equivalents) was related to higher cardiorespiratory fitness and a higher amount of light physical activity (1.5-2.9 metabolic equivalents) was associated with lower cardiorespiratory fitness among children aged 12 years (92).

Skipping breakfast has been associated with lower cardiorespiratory fitness in male youth (93). There is also some evidence that longer breastfeeding duration could be associated with higher cardiorespiratory fitness among children and adolescents (94). Furthermore, higher socioeconomic status of family has been related to higher cardiorespiratory fitness among adolescents (95).

In a longitudinal study among twins, children with the lowest and highest birth weight had the lowest cardiorespiratory fitness in adolescence. However, the association disappeared after adjustment for parental BMI (96). Furthermore, low birth weight and accelerated infant growth have been related to poorer cardiorespiratory fitness among children aged 8-9 years (97).

Genetic factors have a strong influence on cardiorespiratory fitness, explaining about 50% of the variation in VO$_2$max among adults (98). The twin-sibling study and meta-analysis have showed that heredity determines more than half of the variation in VO$_2$max among adolescents (99). Genetic factors have been found to have a stronger effect on endurance performance expressed as total work output than VO$_2$max among individuals aged 16-34 years (100). Genetic factors have also been observed to have a considerable effect on cardiorespiratory fitness among prepubertal children (101). A number of gene variants have been associated with physical performance and health-related fitness, but most of the data is based on small sample sizes and cannot provide definite evidence on these associations (102). There are some gene alleles which are more common in unfit population
controls and patients with type 2 diabetes than in athletes with high cardiorespiratory fitness (103). Because poor cardiorespiratory fitness is associated with higher risk of type 2 diabetes among adults, the cardiorespiratory fitness might be a mediator between certain genotype and type 2 diabetes (103). Moreover, there are certain gene alleles which have impact on the effectiveness of aerobic exercise training to improve cardiorespiratory fitness among adults (104). In a twin study, physically active co-twins achieved significantly higher cardiorespiratory fitness in maximal exercise tests than physically inactive co-twins in adults (105). It is also possible that genetic component of physical activity is shared with genetic component of some chronic diseases and this pleiotropy may affect observed health related results and interpretations and may cause bias (106).

### 2.2.5 Cardiorespiratory fitness and health in children

Higher cardiorespiratory fitness has been related to lower levels of conventional cardiometabolic risk factors (2), less stiff arteries and better arterial dilation capacity (3) in children and lower incidence of overweight in adolescents (4). Furthermore, the increase in aortic intima-media thickness between ages 11 and 17 years was smaller in adolescents who had higher cardiorespiratory fitness at age 17 than adolescents with lower cardiorespiratory fitness, indicating improved vascular health in fit adolescents (6). Higher cardiorespiratory fitness estimated by a submaximal cycle ergometer exercise test has also been associated with lower diastolic BP independent of adiposity among children aged 9 years (107). Decline in cardiorespiratory fitness has been related independently to unfavorable changes in cardiovascular risk factors in a 3-year follow-up study among children aged 6-9 years (108). Higher cardiorespiratory fitness has also been observed to modify the expression of certain genes in childhood and adolescence, which can contribute to the prevention of metabolic and cardiovascular diseases in later life (109,110). Peak VO₂ below 42 ml/kg/min in boys aged 8-17 years and below 35 ml/kg/min in girls at the same age has associated with higher cardiorespiratory disease risk (111).

Higher levels of cardiorespiratory fitness have been associated with better neurocognitive function, such as working memory and response speed, during cognitive tasks among children (112) and better skills to manage distraction (113). Furthermore, higher cardiorespiratory fitness has been related to better reading and arithmetic skills among children and adolescents (114). Cardiorespiratory fitness has also been reported to have a positive correlation with life satisfaction during childhood and adolescence (115).

Cardiorespiratory fitness may track from childhood to adolescence (11,12) and even to adulthood (13). Cardiorespiratory fitness in childhood has been found to have an inverse association with obesity and BP in early adulthood (7). Higher levels of cardiorespiratory fitness can also reduce the risk of developing metabolic syndrome in adulthood, even among individuals who had abdominal obesity as a child (116). Higher cardiorespiratory fitness and lower BMI in late adolescence has been associated with a lower risk of hypertension in adulthood (117). Higher cardiorespiratory fitness has been related to a lower incidence of metabolic syndrome (118), type 2 diabetes (119), cardiovascular disease (9,120-122), lung and colorectal cancer (8), depressive symptoms (123) and premature mortality (9,124) among adults. These beneficial health effects highlight the importance of good cardiorespiratory fitness for health across the life span. The significance of cardiorespiratory fitness for functional ability and cardiovascular health has been highlighted by the American Heart Association, which has stated a need for setting up a national cardiorespiratory fitness registry (85).
2.3 SUMMARY OF LITERATURE

Higher cardiorespiratory fitness is an important indicator for health and well-being during the whole life span. Cardiorespiratory fitness may track from childhood to adolescence and to adulthood. Therefore, knowledge on the normal range of cardiorespiratory fitness, respiratory function and responses of HR and systolic BP to exercise is needed already in childhood. From individual, public health and societal points, it is important to identify children with poorer cardiorespiratory fitness and encourage them to improve their fitness already in early life. However, few population studies have provided normative data concerning maximal exercise test parameters in population-based samples of children from different age groups. It is also noteworthy that cardiorespiratory fitness has declined among children during past years in many countries. Therefore, there is urgent need for updating data of cardiorespiratory fitness and related parameters among children. Furthermore, it is important to find out lifestyle and other factors which are associated with higher cardiorespiratory fitness already in childhood and pay attention to them. However, there are few recent studies on the determinants of cardiorespiratory fitness in population-based samples of girls and boys. Little is also known about differences in the determinants of cardiorespiratory fitness between sexes. This thesis aim to provide recent data about cardiorespiratory fitness and related parameters among children to be used in clinical work and utilized in research community as well as in public health and societal purposes.
3 Aims

The overall aim of this thesis was to provide and describe normative data concerning maximal exercise test parameters among population-based sample of children to be used in clinical work and to be utilized in research community. Furthermore, this thesis aimed to investigate sex-specific determinants of cardiorespiratory fitness among children.

The specific aims of this doctoral thesis were to
1. Describe the levels of cardiorespiratory fitness and changes in HR and systolic BP during and after maximal cycle ergometer exercise test in a population sample of girls and boys 6-9 years of age, to provide reference values for these exercise test parameters in both sexes as well as to study sex differences in these parameters (Study I)
2. Describe the levels of cardiorespiratory fitness, respiratory function and hemodynamic responses during and after maximal cycle ergometer exercise test in a population sample of girls and boys 9-11 years of age, to provide reference values for these parameters and to investigate sex differences in these parameters (Study II)
3. Investigate determinants of cardiorespiratory fitness among population sample of girls and boys aged 6-9 years (Study III)
4 Methods

4.1 STUDY DESIGN AND STUDY POPULATION

The Physical Activity and Nutrition in Children (PANIC) study is a long-term, ongoing controlled physical activity and dietary intervention study (ClinicalTrials.gov NCT01803776) in a population sample of children who have been followed retrospectively since the fetal period and who will be followed prospectively until adulthood. We invited 736 children 6–9 years of age who started the 1st grade at the public schools from the city of Kuopio, Finland, in the baseline study in 2007-2009. We sent invitation letters to the principal custodians of children by mail and asked parents to contact the study personnel to participate. If they did not contact us, we asked their willingness to participate by telephone. Altogether 512 (70%) of the children participated. The participants did not differ in age, sex distribution or body mass index-standard deviation score (BMI–SDS) from all children who started the 1st grade in the city of Kuopio in 2007-2009 based on register data from the standard school health examinations done by school nurses and performed to all Finnish children before the 1st grade started (data not shown). We allocated the children at baseline by location and size of the schools in the physical activity and dietary intervention group or the control group. We invited the children in the 2-year follow-up study in 2009-2011 as the children were in the 3rd grade, and 440 (86%) of the children participated. The analyses of this doctoral thesis are based on cross-sectional data at baseline (Studies I and III) and cross-sectional data at 2-year follow-up (Study II) of the PANIC study.

The participants in Study I included 425 children (204 girls, 221 boys) aged 6.6–9.0 years with complete baseline data on cardiorespiratory fitness and hemodynamic changes during and after maximal exercise tests. The participants in Study II included 140 children (69 girls, 71 boys) 8.8–11.3 years of age from the control group with complete 2-year follow-up data on cardiorespiratory fitness, respiratory function and hemodynamic changes during and after maximal exercise tests. The data of control group were used to avoid confounding effect of 2-year physical activity and dietary intervention on normative data of cardiorespiratory fitness and related parameters. The participants in Study III included 339 children (162 girls, 177 boys) 6.8–9.0 years of age with complete baseline data on determinants of cardiorespiratory fitness. In Study III children who had entered puberty were excluded. The children who were included in the analysis in Studies I, II and III did not differ in age or BMI-SDS from those children who were excluded from the analysis (data not shown). Children in Studies I, II and III had no diseases or conditions that could affect cardiorespiratory fitness or hemodynamic and respiratory function.

We received the approval on the PANIC study protocol from Research Ethics Committee of Hospital District of Northern Savo in 2006. The children and their parents have been informed verbally and in writing about the study and have been asked for their informed consent to participate in the study.

4.2 ASSESSMENTS

4.2.1 Exercise test protocol
Maximal exercise tests were carried out with an electromagnetic cycle ergometer using a pediatric saddle module (Ergoselect 200 K, Ergoline, Bitz, Germany; Figure 1). The children were informed about the course of the exercise stress test before the test. The length of the crank arms was 150 mm, and saddle height was set to a knee angle of 160° when the leg on
the pedal was extended (73,86). The protocol included a 3-minute warm-up period with a workload of 5 Watts (W); a 1-minute steady-state period with a workload of 20 W and exercise period with increase in workload of 1 W per 6 seconds until voluntary exhaustion. The children were asked to keep the cadency stable within 70-80 rounds per minute with a minimum of 65 rounds per minute. Children were verbally encouraged to exercise until voluntary exhaustion. The exercise test was considered maximal, if the reason for terminating the test indicated maximal effort and maximal cardiorespiratory capacity.

4.2.2 Cardiorespiratory responses in maximal exercise test
HR was measured by 12-lead electrocardiography (Cardiosoft GE Healthcare Medical Systems, V 6.5) continuously from the beginning of the supine rest of 5 minutes before the exercise test to the end of the recovery period (Figure 1). Peak HR was defined as the highest HR during the test. The HR increase during the test was calculated as the difference between peak HR and HR measured before the test at rest in supine position and was expressed as absolute and percentual increase. The HR decrease after the test was defined as the difference between peak HR and HR measured 0.5, 1, 2, 3 or 4 minutes after the test and was expressed as absolute and percentual decrease.

Systolic BP (mmHg) was measured from a right arm with an aneroid sphygmomanometer (Heine Gamma G7, Herrsching, Germany) (Figure 1) by the Korotkoff method before the exercise test at the end of supine rest of 5 minutes and again when the children were sitting on a cycle ergometer. As systolic BP was reported the pressure, when the first Korotkoff sound was heard at the first time. During the exercise test systolic BP was measured at the end of the 3-minute warm-up period and at 2-minute intervals until exhaustion. Systolic BP was not measured near the end of the test, if the measurement was assumed to disturb the child’s pedaling rhythm and maximal performance. During the 4-minute cooling-down period systolic BP was measured immediately (within 0.5 minute) and 2 and 4 minutes after the peak workload. The systolic BP increase during the exercise test was defined as the difference between peak systolic BP and systolic BP measured before the test at rest in supine position and was expressed as absolute and percentual increase. The systolic BP decrease after the test was defined as the difference between peak systolic BP and systolic BP measured 0.5, 2 or 4 minutes after the test and was expressed as absolute and percentual decrease. In Study I, it was possible to measure systolic BP within 2 minutes before the peak workload for 56% of the girls and 40% of the boys aged 6-9 years and in Study II, the corresponding percentages were 33% and 14%, respectively in children aged 9-11 years. In study II, we used systolic BP measured within 2 min before peak workload to assess peak systolic BP to achieve as a close estimate of true peak systolic BP as possible. In Study I, systolic BP response close to the end of the exercise test was categorized arbitrarily according to difference between systolic BP measured closest to the end of the exercise test and systolic BP measured 2 minutes earlier as follows: 1) elevation (>2 mmHg), 2) plateau (±2 mmHg) or decline (>2 mmHg). We did not utilize measures of diastolic BP in analysis of this thesis.

Respiratory gases were collected using pediatric masks (Hans–Rudolph, Shawnee, Kansas, USA) during the test. The respiratory gas analyzer (Jaeger Oxycon Pro, Hoechberg, Germany) was calibrated according to the manufacturer’s instructions. Respiratory gases were measured directly by the breath–by–breath method from the 2.5-minute anticipatory period sitting on the ergometer to the post–exercise rest and were averaged over consecutive 15-second periods. The peak values of VO₂, RER and VE were defined as the highest 15-second average value recorded during the last minute of the test. O₂ pulse was calculated as peak VO₂/peak HR (ml/beat). The lowest 15-second average value of VE/VCO₂ during the maximal exercise test was also calculated.
4.2.3 Physical activity and sedentary behavior
Physical activity (min/day) during a usual week and sedentary behavior (min/day) during usual 5 weekdays and 2 weekend days were assessed by the PANIC Physical Activity Questionnaire administered by the parents together with their children at home (125). The questionnaire has been validated in a subsample of children using the Actiheart device, a combined HR and movement sensor (CamNtech Ltd, Papworth, UK) (125). Total physical activity (min/day) assessed by the questionnaire had a modest positive correlation with total physical activity (min/day) measured by the Actiheart monitor ($r=0.37$, $p=0.03$) (125). The types of physical activity included supervised physical activity (organized sports and supervised exercise organized by societies), unsupervised physical activity, physically active school transportation and physical activity during recess. The parents were also asked whether their children had engaged in any of the 12 most common forms of unsupervised and organized physical activity among children in this population based sample. These forms of physical activity included unsupervised and organized football, organized floorball, organized dancing, organized gymnastics, unsupervised playing outdoors, unsupervised bicycling, unsupervised swimming, unsupervised skiing, unsupervised skating, unsupervised walking and unsupervised trampoline jumping. The types of sedentary behavior included watching TV and videos, using a computer and playing video games, using a mobile phone and playing mobile games, which were expressed as screen-based sedentary behavior and listening to music, playing a musical instrument, reading, writing, drawing, doing arts and crafts, playing board games and resting, which were expressed as other sedentary activities.

4.2.4 Dietary factors
The number of meals and snacks per day and the intake of nutrients were assessed by food records of 3-4 consecutive days, including at least one weekend day, and were checked by a clinical nutritionist (126). We analyzed the food records and calculated the intake of nutrients using the Micro Nutrica dietary analysis software, Version 2.5 (the Social Insurance Institution of Finland), which utilizes Finnish and international data on the nutrient content of foods (127).

4.2.5 Body composition
Body fat percentage and lean body mass in kilograms were assessed with the bladder emptied and the child lying in light clothing without metal objects (128) by a dual-energy X-ray absorptiometry (DXA) device (Lunar Prodigy Advance, GE Medical Systems, Madison, WI, USA) in Study III and by bioimpedance analysis (BIA) (InBody 720, Biospace,
Seoul, Korea) using 8-point tactile electrode method in Studies I and II after overnight fasting with the bladder emptied and the child standing in light underwear. Body weight was measured twice by the calibrated BIA device to an accuracy of 0.1 kg after overnight fasting with the bladder emptied and the child standing in light underwear. The mean of these 2 values of body weight was used in the analyses. Body height was assessed 3 times in the Frankfurt plane without shoes by a wall-mounted stadiometer to accuracy of 0.1 cm. The mean of the nearest 2 values was used for the analyses. Waist circumference was measured after expiration at mid-distance between the bottom of the rib cage and the top of the iliac crest with an unstretchable measuring tape. Hip circumference was measured at the level of the great trochanters. The waist-to-hip ratio was calculated by dividing the waist circumference by hip circumference.

4.2.6 Resting blood pressure
Resting BP was measured manually by trained study nurses by a calibrated aneroid sphygmomanometer (Heine Gamma G7, Herrsching, Germany) 3 times in the sitting position from right arm at 2-minute intervals after a rest of 5 minutes. The method of Korotkoff sounds were used. The means of all 3 values were used as the systolic and diastolic BP.

4.2.7 Biochemical factors
Venous blood samples were taken after a 12-hour fast. Biochemical analyses were performed using Cobas 6000 analyzers (Hitachi High Technology Co, Tokyo, Japan). Blood hemoglobin concentrations were determined using the HemoCue B-Hemoglobin Analyser (HemoCue AB, Angelholm, Sweden). A hexokinase method was used to analyze plasma glucose (Roche Diagnostics Co, Mannheim, Germany) (129). Serum insulin was analyzed using an electrochemiluminescence immunoassay with the sandwich principle (Roche Diagnostics Co) (129). Homogeneous enzymatic colorimetric assays were used to analyze high-density and low-density lipoprotein cholesterol (Roche Diagnostics Co) (129). Plasma high-sensitivity C-reactive protein was measured using enhanced immunoturbidimetric assay with CRP (Latex) High Sensitive Assay reagent (Roche Diagnostics Co) (129). The limit of detection was 0.15–0.20 mg/L (129). A kinetic method according to International Federation of Clinical Chemistry was used to analyze alanine aminotransferase (Roche Diagnostics Co) and gamma-glutamyltransferase (Roche Diagnostics Co). Serum dehydroepiandrosterone sulfate was analyzed using an ELISA kit (Alpha Diagnostic International) (130). The intra-assay coefficient of variation of dehydroepiandrosterone sulfate assay was 7.5% to 11.5%, and the interassay coefficient of variation was 7.0% to 11.0% (130). The detection limit of the assay was 0.52 µg/dL (0.014 µmol/L) (130).

4.2.8 Neuromuscular function
Hand grip strength was measured by a vigorimeter (Martin, Tuttingen, Germany) (131). The children were asked to keep the elbow close to the body and the arm flexed at 90° and to press a rubber bulb maximally 3 times with the right and left hand. The mean of the best result of both hands was used in the analyses. Static balance was assessed the children standing barefoot on one leg with eyes closed for 30 seconds (131). The test score was the number of floor touches with a free foot or eye openings during 30 s, higher number of floor touches and eye openings indicating poorer static balance. Lower back and hamstring muscle flexibility was measured by the sit-and-reach test (131). The children were asked to sit down with the heels at the zero line and the heels 25 cm apart. The measuring stick was placed to -38 cm from the zero line. The children were asked to reach slowly forward as far as possible, keeping the hands parallel and to repeat the same task 3 times. The test score was the longest distance in centimeters reached with the fingertips from the starting line of -38 cm.
4.2.9 Other assessments
The parents were asked to report in a questionnaire their annual household income (≤ 30,000 €, 30,001–60,000 € and ≥ 60,001 €) and their highest completed or ongoing educational degrees (vocational school or less, polytechnic, university). The degree of the more educated parent was used in the analyses. Birth weight data were acquired from the records of Kuopio University Hospital or birth weight was reported by the parents. Prevalent asthma was assessed using a questionnaire administered by the parents. Pubertal stage of the children was assessed by Tanner criteria and defined as breast development at Tanner stage ≥2 for girls and testicular volume ≥4mL assessed using an orchidometer for boys (132,133).

4.3 STATISTICAL ANALYSES
The statistical analyses of this thesis were performed with IBM SPSS Statistics, Versions 19-21 (IBM Corp., Armonk, NY, USA) (Studies I, II and III), and R software, Version 3.2 (Study III). The normality of the distributions of the variables was tested with the Kolmogorov-Smirnov test and visually from histograms. We have presented values as means (2 standard deviations, 2 SDs) in Studies I and II and as means (1 SDs) in Study III for normally distributed variables and medians (interquartile ranges, IQRs) for variables with skewed distributions in all studies. We calculated predicted peak HR using a formula 208-(0.7*age) (24). All associations were considered statistically significant if the P-value was <0.05.

Study I
Variables of interest were presented in 5 categories according to their distributions (very low [<2.5%], low [2.5-15.9%], medium [16-83.9%], high [84-97.5%], very high [>97.5%]) in the girls and the boys, as reported by Hakola et al. who assessed cardiorespiratory fitness among older adults (134). Aerobic work capacity was described in 5 categories also in a study by Åstrand (135). Reference limits are the values of population-based sample of children under 2.5% and over 97.5% and this means that 95% of values belongs to reference range (136). We used the independent samples t-test for normally distributed variables and the Mann-Whitney U-test for variables with skewed distributions to study the differences between the boys and the girls. The correlation between lean body mass measured by BIA and DXA was assessed with Pearson’s coefficients for correlation. Lean body mass measured by BIA and DXA were strongly correlated in the girls (r=0.92, p<0.001) and the boys (r=0.92, p<0.001). Due to the strong correlation, we used lean body mass measured by BIA in the analyses, because BIA is a more feasible, more cost-effective and easier method than DXA in clinical practice wherein these reference values can be used. We studied differences in peak workload and peak HR between 3 different types of systolic BP response close to the end of the exercise test with general linear models.

Study II
Variables of interest were presented in 5 categories according to their distributions (very low [<2.5%], low [2.5-15.9%], medium [16-83.9%], high [84-97.5%], very high [>97.5%]) in the girls and the boys, as reported by Hakola et al. who assessed cardiorespiratory fitness among older adults (134). Aerobic work capacity was described in 5 categories also in a study by Åstrand (135). Reference limits are the values of population-based sample of children under 2.5% and over 97.5% and this means that 95% of values belongs to reference range (136). We used the independent samples t-test for normally distributed variables and the Mann-Whitney U-test for variables with skewed distributions to study the differences between the boys and the girls. The Mann-Whitney U-test was also used for investigating differences between prepubertal and pubertal girls and boys. Because peak VE does not increase linearly with increasing body size, simple scaling by body size is not appropriate (41). We therefore divided VE by body height $^{1.44}$ in the girls and by body height $^{1.35}$ in the
boys. The exponents for height were calculated according to description by Bergh et al. (137). For further systolic BP analyses, data of girls and boys whose systolic BP could be measured within 2 minutes of peak workload were combined and divided into 3 height groups (125.0-134.9 cm, 135.0-144.9 cm, 145.0-154.9 cm), as done by Soergel et al. (138). Medians (IQRs) of systolic BP measured closest to the end of exercise test were calculated in these groups.

**Study III**

Data were analyzed separately for boys and girls to find possible differences in the determinants of cardiorespiratory fitness between sexes. The univariate associations of cardiorespiratory fitness with its possible determinants were estimated with Pearson’s correlation coefficients for continuous variables and with point biserial correlation coefficients for dichotomous variables. Firstly, we used the automated bootstrap feature selection with a maximum of 4 variables in each subset and 100,000 permutations to screen the strongest determinants of cardiorespiratory fitness among 66 variables (139). Secondly, we forced the strongest determinants of cardiorespiratory fitness one by one into linear regression models to identify determinants that significantly improved model fit measured by multivariate coefficient of determination (R squared). Determinants that improved model fit and had also significant univariate correlations with cardiorespiratory fitness were used in final multivariate analyses to identify the strongest determinants of cardiorespiratory fitness.

**Unpublished data (not published in Studies I, II and III)**

Figures 3, 4 and 5 presents previously unpublished data about the relation between age and cardiorespiratory fitness expressed as peak workload and peak VO2 scaled by height, weight and lean body mass. The lines in the figures indicate mean values (linear regression fit of age on cardiorespiratory fitness) and their 95% confidence intervals.
5 Results

5.1 BASIC CHARACTERISTICS

The percentage of the peak HR of predicted peak HR was as medians (IQRs) 97% (93-100) in the girls and 97% (94-100) in the boys (p=0.25 for difference between sexes) in Study I, 101% (97-103) in the girls and 101% (96-102) in the boys (p=0.80) in Study II and 96% (93-100) in the girls and 97% (95-100) in the boys (p=0.21) in Study III. Table 2 shows other basic characteristics of the children in Studies I, II and III.

Children aged 6-9 years (Study I)
The boys were taller (p=0.001) and had more lean body mass (p<0.001) but a lower fat percentage (p<0.001) than the girls. The mean (2 SDs) duration of the maximal exercise test was 9.1 (2.5) minutes in the girls and 10.3 (2.8) minutes in the boys (p<0.001 for difference between sexes). Altogether 9 (4.4%) of girls and 2 (0.9%) of boys were pubertal.

Children aged 9-11 years (Study II)
The boys were slightly heavier (p=0.05) and had more lean body mass (p=0.001) than the girls. The mean (2 SDs) duration of the maximal exercise test with a 3-minute warm-up period was 12.3 (3.1) min in the girls and 13.9 (3.4) min in the boys (p<0.001 for difference between sexes). Altogether 28 (40.6%) of girls and 6 (8.5%) of boys were pubertal.

Children aged 6-9 years (Study III)
The boys were taller (p<0.001), heavier (p=0.001) and had higher lean body mass (p<0.001) and lower fat percentage (p<0.001) than the girls. The mean (2 SD) of cardiorespiratory fitness was 44.1 (12.7) W/m^{1.93} in the girls and 43.6 (12.1) W/m^{2.51} in the boys (p=0.53 for difference between sexes). Peak HR was at least 85% of the predicted peak HR (>171 beats/min) in all 339 children and at least 90% of the predicted peak HR (>182 beats/min) in 320 children. All children were prepubertal.
### Table 2. Basic characteristics of the children in Studies I, II and III

<table>
<thead>
<tr>
<th></th>
<th>Study I</th>
<th></th>
<th>Study II</th>
<th></th>
<th>Study III</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Girls (n=204)</td>
<td>Boys (n=221)</td>
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<td>Boys (n=71)</td>
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<td>9.9</td>
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<tr>
<td>(0.8)</td>
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<td>(9.5-10.1)</td>
<td>(0.4)</td>
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<td>129.9</td>
<td>140.2</td>
<td>141.8</td>
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</tr>
<tr>
<td>(11.5)</td>
<td>(10.4)</td>
<td>(15.5)</td>
<td>(11.2)</td>
<td>(5.5)</td>
<td>(4.9)</td>
<td></td>
</tr>
<tr>
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<td>32.6</td>
<td>35.6</td>
<td>25.0</td>
<td>26.9</td>
</tr>
<tr>
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<td>(27.9-38.1)</td>
<td>(30.1-39.5)</td>
<td>(22.8-28.3)</td>
<td>(24.0-29.8)</td>
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<tr>
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<td>(25.3-29.2)</td>
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<td>(11.3-21.5)</td>
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</tbody>
</table>

Values are means (SDs) for normally distributed variables and medians (IQRs) for variables with skewed distributions.
5.2 CARDIORESPIRATORY RESPONSES IN MAXIMAL EXERCISE TEST IN GIRLS AND BOYS

Cardiorespiratory responses in maximal test among girls and boys aged 6-9 and 9-11 years are presented in Table 3.

Children aged 6-9 years (Study I)

HR at rest before the exercise test was 73 (67-79) beats/min in the girls and 70 (65-78) beats/min in the boys and it was significantly lower in the boys than in the girls (Table 3). Peak HR was as means (2 SDs) 196 (19) beats/min in the girls and 197 (17) beats/min in the boys and there were no sex difference (Table 3). The HR increase during the test was 122 (24) beats/min in the girls and 125 (24) beats/min in the boys and it was larger among the boys than the girls (Table 3). HR increased on average by 170% in the girls and by 180% in the boys. HR decreased at 1-minute recovery by 20% in the girls and by 23% in the boys and at 2-minute recovery by 27% in the girls and by 30% in the boys. The boys had a larger HR decrease at 0.5-, 1-, 2-, 3 and 4-minute recovery than the girls (Table 3).

Systolic BP increased during the exercise test on average by 25% in the girls and by 22% in the boys. There were no sex differences in systolic BP at different phases of the exercise test (Table 3). Systolic BP decreased at 0.5-minute recovery by 5% in the girls and by 4% in the boys, at 2-minute recovery by 6% in both sexes, and at 4-minute recovery by 11% in the girls and by 10% in the boys. There were no sex differences in systolic BP decrease at 0.5-minute, 2-minute or 4-minute recovery (Table 3).

We found a plateau in systolic BP close to the end of the exercise test in 27% of the girls and in 21% of the boys and a decline in 11% of the girls and in 10% of the boys (Figure 2). Decline in systolic BP during the exercise test was more than 10 mmHg in 4 (2.1%) girls and in 5 (2.3%) boys. Peak workload and peak HR were similar among children with plateau or decline in systolic BP and among children with elevation in systolic BP (data not shown). If only children whose systolic BP was possible to measure within 2 minutes before the peak workload were taken into account, there was no difference in peak workload or peak HR between children with plateau or decline in systolic BP and children with elevation in systolic BP, either (data not shown).
Children aged 9-11 years (Study II)

HR at rest before the exercise test was as means (2 SDs) 67 (13) beats/min in the girls and 65 (15) beats/min in the boys and was slightly higher in the girls than in the boys (Table 3). HR increase during exercise test was similar in the girls (203%) and the boys (214%). HR decreased during 1-min recovery on average by 18% in the girls and by 22% in the boys and during 2-min recovery by 28% in the girls and by 32% in the boys. The difference in HR decrease between sexes remained similar until the end of the recovery period (Table 3).

Systolic BP increased during the maximal exercise test on average by 36% in the girls and by 35% in the boys. Systolic BP decreased during 0.5-min recovery on average by 14% in the girls and by 17% in the boys, during 2-min recovery by 11% in the girls and by 9% in the boys and during 4-min recovery by 17% in both sexes. Children whose height was 125.0 - 134.9 cm (n=9), 135.0 - 144.9 cm (n=19) and 145.0 - 154.9 cm (n=5) had the medians (IQRs) of peak systolic BP of 140 (128 - 146) mmHg, 148 (130 - 160) mmHg and 160 (147 - 168) mmHg, respectively (p=0.05). There were no sex differences in systolic BP changes during and after maximal exercise test (Table 3).

Peak VE as absolute values was as means (2 SDs) 63 (18) l/min in the girls and 69 (20) l/min in the boys and it was significantly higher in the boys than in the girls, but peak VE relative to height with allometric scaling did not differ between sexes (Table 3). Peak RER was as means (2 SDs) 1.09 (0.10) in the girls and 1.06 (0.09) in the boys and it was significantly lower in the boys than in the girls (Table 3). Peak oxygen pulse was as means (2 SDs) 7.9 (2.3) ml/beat in the girls and 9.1 (2.6) ml/beat in the boys. The lowest value of VE/VCO2 during the test was as means (2 SDs) 29 (5) in the girls and 28 (4) in the boys with no sex difference. Peak O2 pulse as absolute values and relative to weight and lean body mass was higher in the boys than in the girls (Table 3).

Pubertal girls (n=28) achieved a higher absolute peak workload (p<0.001), anticipatory HR (p=0.02), peak HR (p=0.001), HR increase (p=0.001), absolute peak VO2 (p<0.001), peak VE (p<0.001) and absolute peak O2 pulse (p<0.001) and a lower peak workload relative to weight (p<0.001), peak VO2 relative to weight (p<0.001), peak O2 pulse relative to weight (p<0.001) and peak O2 pulse relative to lean body mass (p=0.04) than prepubertal girls (n=41). Pubertal girls (n=5) had a higher peak systolic BP (p=0.007) and systolic BP change during 0.5-min recovery (p=0.007), 2-min recovery (p=0.02) and 4-min recovery (p=0.009) than prepubertal girls. Pubertal boys (n=6) achieved a higher absolute peak workload (p=0.02) and VE (p=0.004) than prepubertal boys (n=59).
Pubertal girls (n=28) achieved a higher absolute peak workload (p<0.001), anticipatory HR (p=0.02), peak HR (p=0.001), HR increase (p=0.001), absolute peak VO₂ (p<0.001), peak VE (p<0.001) and absolute peak O₂ pulse (p<0.001) and a lower peak workload relative to weight (p<0.001), peak VO₂ relative to weight (p<0.001), peak O₂ pulse relative to weight (p<0.001) and peak O₂ pulse relative to lean body mass (p=0.04) than prepubertal girls (n=41). Pubertal girls (n=5) had a higher peak systolic BP (p=0.007) and systolic BP change during 0.5-min recovery (p=0.007), 2-min recovery (p=0.02) and 4-min recovery (p=0.009) than prepubertal girls. Pubertal boys (n=6) achieved a higher absolute peak workload (p=0.02) and VE (p=0.004) than prepubertal boys (n=59).
Table 3. Heart rate, systolic blood pressure and respiratory function in maximal exercise test among girls and boys

<table>
<thead>
<tr>
<th></th>
<th>Girls aged 6-9 years (Study I)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Boys aged 9-11 years (Study II)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=204)</td>
<td>(n=221)</td>
<td></td>
<td></td>
<td></td>
<td>(n=69)</td>
<td>(n=71)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting HR (beats/min)¹</td>
<td>73 (67-79)</td>
<td>70 (65-78)</td>
<td>0.01</td>
<td></td>
<td></td>
<td>67 (13)</td>
<td>65 (15)</td>
<td>0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticipatory HR (beats/min)²</td>
<td>93 (23)</td>
<td>90 (23)</td>
<td>0.007</td>
<td></td>
<td></td>
<td>91 (23)</td>
<td>87 (22)</td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak HR (beats/min)</td>
<td>196 (19)</td>
<td>197 (17)</td>
<td>0.32</td>
<td></td>
<td></td>
<td>203 (195-206)</td>
<td>203 (193-206)</td>
<td>0.63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR increase (beats/min)³</td>
<td>122 (24)</td>
<td>125 (24)</td>
<td>0.02</td>
<td></td>
<td></td>
<td>137 (129-141)</td>
<td>138 (130-142)</td>
<td>0.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR decrease during 0.5 min recovery (beats/min)</td>
<td>21 (16-24)</td>
<td>22 (16-29)</td>
<td>0.02</td>
<td></td>
<td></td>
<td>19 (14-22)</td>
<td>21 (17-29)</td>
<td>0.007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR decrease during 1 min recovery (beats/min)</td>
<td>39 (18)</td>
<td>44 (22)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td>37 (28-42)</td>
<td>44 (37-50)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR decrease during 2 min recovery (beats/min)</td>
<td>53 (18)</td>
<td>59 (22)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td>56 (22)</td>
<td>64 (20)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
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<tr>
<td>HR decrease during 3 min recovery (beats/min)</td>
<td>60 (20)</td>
<td>64 (22)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td>64 (23)</td>
<td>72 (22)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR decrease during 4 min recovery (beats/min)</td>
<td>61 (56-69)</td>
<td>67 (60-74)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td>67 (22)</td>
<td>76 (19)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting systolic BP (mmHg)¹</td>
<td>103 (18)</td>
<td>104 (17)</td>
<td>0.12</td>
<td></td>
<td></td>
<td>104 (100-110)</td>
<td>104 (98-110)</td>
<td>0.52</td>
<td></td>
<td></td>
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<tr>
<td>Anticipatory systolic BP (mmHg)²</td>
<td>105 (19)</td>
<td>106 (19)</td>
<td>0.45</td>
<td></td>
<td></td>
<td>110 (101-116)</td>
<td>110 (102-114)</td>
<td>0.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak measured systolic BP (mmHg)³</td>
<td>128 (27)</td>
<td>127 (31)</td>
<td>0.46</td>
<td></td>
<td></td>
<td>146 (130-160)</td>
<td>151(133-170)</td>
<td>0.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP increase (mmHg)³</td>
<td>25 (25)</td>
<td>23 (27)</td>
<td>0.08</td>
<td></td>
<td></td>
<td>34 (26-52)</td>
<td>38 (22-55)</td>
<td>0.95</td>
<td></td>
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</tr>
<tr>
<td>Systolic BP decrease during 0.5 min recovery (mmHg)⁴</td>
<td>7 (30)</td>
<td>6 (32)</td>
<td>0.88</td>
<td></td>
<td></td>
<td>20 (6-38)</td>
<td>29 (10-40)</td>
<td>0.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP decrease during 2 min recovery (mmHg)⁴</td>
<td>8 (24)</td>
<td>8 (28)</td>
<td>0.90</td>
<td></td>
<td></td>
<td>14 (0-28)</td>
<td>17 (7-20)</td>
<td>0.83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP decrease during 4 min recovery (mmHg)⁴</td>
<td>15 (24)</td>
<td>14 (26)</td>
<td>0.53</td>
<td></td>
<td></td>
<td>22 (20-34)</td>
<td>30 (20-33)</td>
<td>0.66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak VE (l/min)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>63 (18)</td>
<td>69 (20)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak VE/height¹,⁴ for girls, 1.55 for boys (l/m/min)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>38.5 (9.2)</td>
<td>40.1 (10.5)</td>
<td>0.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak RER</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>1.09 (0.10)</td>
<td>1.06 (0.09)</td>
<td>&lt;0.001</td>
<td></td>
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</tr>
<tr>
<td>The lowest VE/VCO₂ during the exercise test</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>29 (5)</td>
<td>28 (4)</td>
<td>0.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak O₂ pulse (ml/beat)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>7.9 (2.3)</td>
<td>9.1 (2.6)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak O₂ pulse/kg of weight (ml/kg/beat)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>0.24 (0.06)</td>
<td>0.26 (0.07)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak O₂ pulse/kg of lean body mass (ml/kg/beat)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>0.31 (0.05)</td>
<td>0.34 (0.06)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are means (2 SDs) for normally distributed variables and medians (IQRs) for variables with skewed distributions. Sex differences were analyzed with the independent samples t-test for normally distributed variables and with the Mann-Whitney U-test for variables with skewed distributions. HR=heart rate, ml=millilitter, min=minute, kg=kilogram, systolic BP=systolic blood pressure, VE=ventilation, RER=respiratory exchange ratio, VE/VCO₂=ratio of ventilation and carbon dioxide output, O₂ pulse=oxygen pulse. ¹Value measured at rest in supine position before the exercise test. ²Value measured on the cycle ergometer before the test. ³Calculated as peak value - value measured at rest in supine position before the exercise test. ⁴The numbers of girls and boys are 23 and 10, respectively, among children aged 9-11 years because of difficulties to measure systolic BP near the end of the maximal test. In these children, systolic BP could be measured within 2 min before peak workload.
Table 3.

Table 3 presents distributions of HR among girls and boys aged 6-9 years (Study I) and 9-11 years (Study II). Altogether 95% of the girls had peak HR between values 177 beats/min and 211 beats/min at the age of 6-9 years and between values 181 beats/min and 214 beats/min at the age of 9-11 years. The corresponding reference ranges were 177-209 beats/min and 181-214 beats/min in the boys, respectively. The 95% ranges of HR decrease during 2 min recovery was 36-74 beats/min in the girls aged 6-9 years and 37-76 beats/min in the girls aged 9-11 years. The corresponding ranges were 38-79 beats/min in the boys aged 6-9 years and 43-80 beats/min in the boys aged 9-11 years.

Table 5 shows distributions of respiratory parameters among girls and boys aged 9-11 years (Study II). Altogether 95% of the girls and 95% of the boys had peak RER values between 0.98 and 1.17 and between 0.95 and 1.12, respectively. The 95% reference range of the lowest value of VE/VCO2 during the maximal exercise test was 25.0-33.8 in the girls and 24.0-32.9 in the boys. The 95% range of peak O2 pulse divided by kg of lean body mass was 0.270-0.373 ml/kg/beat in the girls and 0.276-0.381 ml/kg/beat in the boys.
Table 4. Distributions of heart rate (beats/min) among girls and boys

<table>
<thead>
<tr>
<th></th>
<th>Very low (&lt;2.5%)</th>
<th>Low (2.5-15.9%)</th>
<th>Medium (16.0-83.9%)</th>
<th>High (84.0-97.5%)</th>
<th>Very High (&gt;97.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls 6-9 years (n=204)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak HR</td>
<td>&lt;177</td>
<td>177-183</td>
<td>184-204</td>
<td>205-211</td>
<td>&gt;211</td>
</tr>
<tr>
<td>HR increase during the test</td>
<td>&lt;96</td>
<td>96-110</td>
<td>111-134</td>
<td>135-144</td>
<td>&gt;144</td>
</tr>
<tr>
<td>HR decrease during 1 min recovery</td>
<td>&lt;21</td>
<td>21-29</td>
<td>30-47</td>
<td>48-56</td>
<td>&gt;56</td>
</tr>
<tr>
<td>HR decrease during 2 min recovery</td>
<td>&lt;36</td>
<td>36-44</td>
<td>45-61</td>
<td>62-74</td>
<td>&gt;74</td>
</tr>
<tr>
<td>Girls 9-11 years (n=69)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Peak HR</td>
<td>&lt;181</td>
<td>181-190</td>
<td>191-206</td>
<td>207-214</td>
<td>&gt;214</td>
</tr>
<tr>
<td>HR increase during the test</td>
<td>&lt;110</td>
<td>110-124</td>
<td>125-142</td>
<td>143-149</td>
<td>&gt;149</td>
</tr>
<tr>
<td>HR decrease during 1 min recovery</td>
<td>&lt;20</td>
<td>20-25</td>
<td>26-42</td>
<td>43-57</td>
<td>&gt;57</td>
</tr>
<tr>
<td>HR decrease during 2 min recovery</td>
<td>&lt;37</td>
<td>37-44</td>
<td>45-65</td>
<td>66-76</td>
<td>&gt;76</td>
</tr>
<tr>
<td>Boys 6-9 years (n=221)</td>
<td></td>
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</tr>
<tr>
<td>Peak HR</td>
<td>&lt;177</td>
<td>177-186</td>
<td>187-204</td>
<td>205-209</td>
<td>&gt;209</td>
</tr>
<tr>
<td>HR increase during the test</td>
<td>&lt;100</td>
<td>100-111</td>
<td>112-135</td>
<td>136-146</td>
<td>&gt;146</td>
</tr>
<tr>
<td>HR decrease during 1 min recovery</td>
<td>&lt;23</td>
<td>23-33</td>
<td>34-54</td>
<td>55-67</td>
<td>&gt;67</td>
</tr>
<tr>
<td>HR decrease during 2 min recovery</td>
<td>&lt;38</td>
<td>38-47</td>
<td>48-69</td>
<td>70-79</td>
<td>&gt;79</td>
</tr>
<tr>
<td>Boys 9-11 years (n=71)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak HR</td>
<td>&lt;181</td>
<td>181-189</td>
<td>190-207</td>
<td>208-214</td>
<td>&gt;214</td>
</tr>
<tr>
<td>HR increase during the test</td>
<td>&lt;113</td>
<td>113-122</td>
<td>123-143</td>
<td>144-154</td>
<td>&gt;154</td>
</tr>
<tr>
<td>HR decrease during 1 min recovery</td>
<td>&lt;27</td>
<td>27-33</td>
<td>34-51</td>
<td>52-54</td>
<td>&gt;54</td>
</tr>
<tr>
<td>HR decrease during 2 min recovery</td>
<td>&lt;43</td>
<td>43-54</td>
<td>55-75</td>
<td>76-80</td>
<td>&gt;80</td>
</tr>
</tbody>
</table>

HR=heart rate; min=minute. The reference range is values between 2.5% and 97.5%.
Table 4. Distributions of heart rate (beats/min) among girls and boys

<table>
<thead>
<tr>
<th></th>
<th>Very low (&lt;2.5%)</th>
<th>Low (2.5-15.9%)</th>
<th>Medium (16.0-83.9%)</th>
<th>High (84.0-97.5%)</th>
<th>Very High (&gt;97.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-11 years (n=204)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak HR</td>
<td>&lt;177</td>
<td>177-183</td>
<td>184-204</td>
<td>205-211</td>
<td>&gt;211</td>
</tr>
<tr>
<td>HR increase during the test</td>
<td>&lt;96</td>
<td>96-110</td>
<td>111-134</td>
<td>135-144</td>
<td>&gt;144</td>
</tr>
<tr>
<td>HR decrease during 1 min recovery</td>
<td>&lt;21</td>
<td>21-29</td>
<td>30-47</td>
<td>48-56</td>
<td>&gt;56</td>
</tr>
<tr>
<td>HR decrease during 2 min recovery</td>
<td>&lt;36</td>
<td>36-44</td>
<td>45-61</td>
<td>62-74</td>
<td>&gt;74</td>
</tr>
<tr>
<td>Boys</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>9-11 years (n=69)</td>
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<td></td>
</tr>
<tr>
<td>Peak HR</td>
<td>&lt;181</td>
<td>181-190</td>
<td>191-206</td>
<td>207-214</td>
<td>&gt;214</td>
</tr>
<tr>
<td>HR increase during the test</td>
<td>&lt;110</td>
<td>110-124</td>
<td>125-142</td>
<td>143-149</td>
<td>&gt;149</td>
</tr>
<tr>
<td>HR decrease during 1 min recovery</td>
<td>&lt;20</td>
<td>20-25</td>
<td>26-42</td>
<td>43-57</td>
<td>&gt;57</td>
</tr>
<tr>
<td>HR decrease during 2 min recovery</td>
<td>&lt;36</td>
<td>36-44</td>
<td>45-65</td>
<td>66-76</td>
<td>&gt;76</td>
</tr>
</tbody>
</table>

HR=heart rate; min=minute. The reference range is values between 2.5% and 97.5%.

Table 5. Distributions of peak respiratory exchange ratio, the lowest value of ratio of ventilation and carbon dioxide output during the maximal exercise test and peak O2 pulse among girls and boys

<table>
<thead>
<tr>
<th></th>
<th>Very low (&lt;2.5%)</th>
<th>Low (2.5-15.9%)</th>
<th>Medium (16.0-83.9%)</th>
<th>High (84.0-97.5%)</th>
<th>Very High (&gt;97.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-11 years (n=69)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Peak RER</td>
<td>&lt;0.98</td>
<td>0.98-1.03</td>
<td>1.04-1.12</td>
<td>1.13-1.17</td>
<td>&gt;1.17</td>
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<tr>
<td>The lowest VE/VCO2 during the test</td>
<td>&lt;25.0</td>
<td>25.0-27.1</td>
<td>27.2-30.9</td>
<td>31.0-33.8</td>
<td>&gt;33.8</td>
</tr>
<tr>
<td>Peak O2 pulse/kg of lean body mass (ml/kg/beat)</td>
<td>&lt;0.270</td>
<td>0.270-0.284</td>
<td>0.285-0.339</td>
<td>0.340-0.373</td>
<td>&gt;0.373</td>
</tr>
<tr>
<td>Boys</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-11 years (n=71)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak RER</td>
<td>&lt;0.95</td>
<td>0.95-1.00</td>
<td>1.01-1.10</td>
<td>1.11-1.12</td>
<td>&gt;1.12</td>
</tr>
<tr>
<td>The lowest VE/VCO2 during the test</td>
<td>&lt;24.0</td>
<td>24.0-26.6</td>
<td>26.7-30.1</td>
<td>30.2-32.9</td>
<td>&gt;32.9</td>
</tr>
<tr>
<td>Peak O2 pulse/kg of lean body mass (ml/kg/beat)</td>
<td>&lt;0.276</td>
<td>0.276-0.312</td>
<td>0.313-0.365</td>
<td>0.366-0.381</td>
<td>&gt;0.381</td>
</tr>
</tbody>
</table>

kg=kilogram, ml=milliliter, RER=respiratory exchange ratio, VE/VCO2=ratio of ventilation and carbon dioxide output, O2 pulse=oxygen pulse. The reference range is values between 2.5% and 97.5%.
5.3 CARDIORESPIRATORY FITNESS IN GIRLS AND BOYS

Cardiorespiratory fitness among girls and boys aged 6-9 years (Study I and III) and aged 9-11 years (Study II) are presented in Table 6. Values are means (2 SDs). Cardiorespiratory fitness expressed as peak workload per kg of weight was 2.7 (0.9) W/kg in the girls aged 6-9 years and 3.1 (0.9) W/kg in the girls aged 9-11 years and as peak workload per kg of lean body mass 3.5 (0.9) W/kg in the girls aged 6-9 years and 4.1 (0.8) W/kg in the girls aged 9-11 years. Cardiorespiratory fitness expressed as peak VO₂ divided by kg of weight was 47.6 (13.0) ml/kg/min and as peak VO₂ divided by kg of lean body mass 63.0 (11.5) ml/kg/min in the girls aged 9-11 years. Peak workload per kg of weight was 3.1 (1.0) W/kg among boys aged 6-9 years and 3.4 (1.3) W/kg among boys aged 9-11 years. Corresponding values for peak workload per kg of lean body mass was 3.8 (1.0) W/kg and 4.4 (1.0) W/kg, respectively. Peak VO₂ scaled by kg of body weight was 51.9 (15.5) ml/kg/min and peak VO₂ divided by kg of lean body mass was 67.3 (12.6) ml/kg/min in the boys aged 9-11 years. The boys had a higher absolute peak workload and peak workload per body weight and lean body mass than the girls at the age 6-9 years. There was no sex difference among children aged 6-9 years in cardiorespiratory fitness divided by allometrically scaled height. Among children aged 9-11 years, the boys had a higher peak workload and peak VO₂ as absolute values and relative to weight and lean body mass than the girls.
Cardiorespiratory fitness among girls and boys aged 6-9 years (Study I and III) and aged 9-11 years (Study II) are presented in Table 6. Values are means (± SDs). Cardiorespiratory fitness expressed as peak workload per kg of weight was 2.7 (0.9) W/kg in the girls aged 6-9 years and 3.1 (0.9) W/kg in the girls aged 9-11 years and as peak workload per kg of lean body mass 3.5 (0.9) W/kg in the girls aged 6-9 years and 4.1 (0.8) W/kg in the girls aged 9-11 years. Cardiorespiratory fitness expressed as peak VO₂ divided by kg of weight was 47.6 (13.0) ml/kg/min and as peak VO₂ divided by kg of lean body mass 63.0 (11.5) ml/kg/min in the girls aged 9-11 years. Peak workload per kg of weight was 3.1 (1.0) W/kg among boys aged 6-9 years and 3.4 (1.3) W/kg among boys aged 9-11 years. Corresponding values for peak workload per kg of lean body mass was 3.8 (1.0) W/kg and 4.4 (1.0) W/kg, respectively. Peak VO₂ scaled by kg of body weight was 51.9 (15.5) ml/kg/min and peak VO₂ divided by kg of lean body mass was 67.3 (12.6) ml/kg/min in the boys aged 9-11 years. The boys had a higher absolute peak workload and peak workload per body weight and lean body mass than the girls at the age 6-9 years. There was no sex difference among children aged 6-9 years in cardiorespiratory fitness divided by allometrically scaled height. Among children aged 9-11 years, the boys had a higher peak workload and peak VO₂ as absolute values and relative to weight and lean body mass than the girls.

Table 6. Cardiorespiratory fitness in girls and boys

<table>
<thead>
<tr>
<th>Manpower</th>
<th>Children aged 6-9 years (Study I and Study III)</th>
<th>Children aged 9-11 years (Study II)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Girls (n=204)</td>
<td>Boys (n=221)</td>
</tr>
<tr>
<td>Peak absolute workload (W)</td>
<td>71 (25)</td>
<td>83 (28)</td>
</tr>
<tr>
<td>Peak workload/kg of weight (W/kg)</td>
<td>2.7 (0.9)</td>
<td>3.1 (1.0)</td>
</tr>
<tr>
<td>Peak workload/kg of lean body mass (W/kg)</td>
<td>3.5 (0.9)</td>
<td>3.8 (1.0)</td>
</tr>
<tr>
<td>Peak workload/m of height (W/m^{1.93 for girls, 2.51 for boys})</td>
<td>44.1 (12.7)</td>
<td>43.6 (12.1)</td>
</tr>
<tr>
<td>Peak absolute VO₂ (l/min)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Peak VO₂/kg of weight (ml/kg/min)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Peak VO₂/kg of lean body mass (ml/kg/min)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Values are means (± SDs). Sex differences were analyzed with independent samples t-test. kg=kilograms, l=liter, m=meter, ml=milliliter, min=minute, VO₂=oxygen uptake, W=watt. 1Study III, numbers of girls and boys are 162 and 177, respectively.
Table 7 shows distributions of peak workload divided by body weight and lean body mass among girls and boys aged 6-9 years (Study I) and 9-11 years (Study II) and peak VO2 divided by body weight and lean body mass among boys and girls aged 9-11 years (Study II). Altogether 95% of the girls had peak workload per kg of weight between values 1.85 W/kg and 3.49 W/kg at the age of 6-9 years and between values 2.12 W/kg and 3.83 W/kg at the age of 9-11 years. The corresponding reference ranges were 1.90-4.05 W/kg and 2.18-4.57 W/kg in the boys, respectively. The 95% ranges of peak workload scaled by kg of lean body mass was 2.54-4.38 W/kg in the girls aged 6-9 years and 3.49-4.79 W/kg in the girls aged 9-11 years. The corresponding ranges were 2.76-4.74 W/kg among boys aged 6-9 years and 3.28-5.38 W/kg among boys aged 9-11 years. The 95% ranges of peak VO2 per kg of weight was 34.2-60.1 ml/kg/min in the girls and 39.1-66.7 ml/kg/min in the boys aged 9-11 years. The corresponding ranges of peak VO2 per kg of lean body mass was 53.9-74.0 ml/kg/min in the girls and 55.6-78.7 ml/kg/min in the boys aged 9-11 years.

<table>
<thead>
<tr>
<th>Table 7. Distributions of cardiorespiratory fitness expressed as peak workload and peak oxygen uptake among girls and boys</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Girls</strong></td>
</tr>
<tr>
<td><strong>6-9 years</strong></td>
</tr>
<tr>
<td><strong>Peak workload/kg of weight (W/kg)</strong></td>
</tr>
<tr>
<td>&lt;1.85</td>
</tr>
<tr>
<td>1.85-2.24</td>
</tr>
<tr>
<td>2.25-3.14</td>
</tr>
<tr>
<td>3.15-3.49</td>
</tr>
<tr>
<td>&gt;3.49</td>
</tr>
<tr>
<td><strong>Peak workload/kg of lean body mass (W/kg)</strong></td>
</tr>
<tr>
<td>&lt;2.54</td>
</tr>
<tr>
<td>2.54-2.98</td>
</tr>
<tr>
<td>2.99-3.90</td>
</tr>
<tr>
<td>3.91-4.38</td>
</tr>
<tr>
<td><strong>Peak VO2/kg of weight (ml/kg/min)</strong></td>
</tr>
<tr>
<td>&lt;34.2</td>
</tr>
<tr>
<td>34.2-40.6</td>
</tr>
<tr>
<td>40.7-53.9</td>
</tr>
<tr>
<td>54.0-60.1</td>
</tr>
<tr>
<td><strong>Peak VO2/kg of lean body mass (ml/kg/min)</strong></td>
</tr>
<tr>
<td>&lt;53.9</td>
</tr>
<tr>
<td>53.9-57.0</td>
</tr>
<tr>
<td>57.1-68.6</td>
</tr>
<tr>
<td>68.7-74.0</td>
</tr>
<tr>
<td>&gt;74.0</td>
</tr>
</tbody>
</table>

W=watt, kg=kilogram, VO2=oxygen uptake, ml=milliliter. The reference range is values between 2.5% and 97.5%.
Table 7. Distributions of cardiorespiratory fitness expressed as peak workload and peak oxygen uptake among girls and boys

<table>
<thead>
<tr>
<th></th>
<th>Very low (&lt;2.5%)</th>
<th>Low (2.5-15.9%)</th>
<th>Medium (16.0-83.9%)</th>
<th>High (84.0-97.5%)</th>
<th>Very High (&gt;97.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Girls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-9 years (n=204)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak workload/kg of weight (W/kg)</td>
<td>&lt;1.85</td>
<td>1.85-2.24</td>
<td>2.25-3.14</td>
<td>3.15-3.49</td>
<td>&gt;3.49</td>
</tr>
<tr>
<td>Peak workload/kg of lean body mass (W/kg)</td>
<td>&lt;2.54</td>
<td>2.54-2.98</td>
<td>2.99-3.90</td>
<td>3.91-4.38</td>
<td>&gt;4.38</td>
</tr>
<tr>
<td>9-11 years (n=69)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak workload/kg of weight (W/kg)</td>
<td>&lt;2.12</td>
<td>2.12-2.68</td>
<td>2.69-3.59</td>
<td>3.60-3.83</td>
<td>&gt;3.83</td>
</tr>
<tr>
<td>Peak workload/kg of lean body mass (W/kg)</td>
<td>&lt;3.49</td>
<td>3.49-3.62</td>
<td>3.63-4.53</td>
<td>4.54-4.79</td>
<td>&gt;4.79</td>
</tr>
<tr>
<td>Peak VO₂/kg of weight (ml/kg/min)</td>
<td>&lt;34.2</td>
<td>34.2-40.6</td>
<td>40.7-53.9</td>
<td>54.0-60.1</td>
<td>&gt;60.1</td>
</tr>
<tr>
<td>Peak VO₂/kg of lean body mass (ml/kg/min)</td>
<td>&lt;53.9</td>
<td>53.9-57.0</td>
<td>57.1-68.6</td>
<td>68.7-74.0</td>
<td>&gt;74.0</td>
</tr>
<tr>
<td><strong>Boys</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-9 years (n=221)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak workload/kg of weight (W/kg)</td>
<td>&lt;1.90</td>
<td>1.90-2.53</td>
<td>2.54-3.54</td>
<td>3.55-4.05</td>
<td>&gt;4.05</td>
</tr>
<tr>
<td>Peak workload/kg of lean body mass (W/kg)</td>
<td>&lt;2.76</td>
<td>2.76-3.41</td>
<td>3.42-4.30</td>
<td>4.31-4.74</td>
<td>&gt;4.74</td>
</tr>
<tr>
<td>9-11 years (n=71)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak workload/kg of weight (W/kg)</td>
<td>&lt;2.18</td>
<td>2.18-2.75</td>
<td>2.76-3.98</td>
<td>3.99-4.57</td>
<td>&gt;4.57</td>
</tr>
<tr>
<td>Peak workload/kg of lean body mass (W/kg)</td>
<td>&lt;3.28</td>
<td>3.28-3.87</td>
<td>3.88-4.85</td>
<td>4.86-5.38</td>
<td>&gt;5.38</td>
</tr>
<tr>
<td>Peak VO₂/kg of weight (ml/kg/min)</td>
<td>&lt;39.1</td>
<td>39.1-43.9</td>
<td>44.0-59.3</td>
<td>59.4-66.7</td>
<td>&gt;66.7</td>
</tr>
<tr>
<td>Peak VO₂/kg of lean body mass (ml/kg/min)</td>
<td>&lt;55.6</td>
<td>55.6-60.8</td>
<td>60.9-73.0</td>
<td>73.1-78.7</td>
<td>&gt;78.7</td>
</tr>
</tbody>
</table>

W=watt, kg=kilogram, VO₂=oxygen uptake, ml=milliliter. The reference range is values between 2.5% and 97.5%.
Cardiorespiratory fitness expressed as peak workload divided by height with allometric scaling, body weight and lean body mass increased by age in the girls and the boys, but decreased when expressed as peak VO$_2$ per body weight and lean body mass in both sexes (Figure 3, 4 and 5) (previously unpublished data). The decrease was the highest among girls when peak VO$_2$ was divided by body weight (Figure 4).

**Figure 3.** The relation between age and cardiorespiratory fitness expressed as peak workload per body height with allometric scaling among A) 162 girls and B) 177 boys aged 6.8-9.0 years. The lines indicate mean values (linear regression fit of age on peak workload divided by body height with allometric scaling) and their 95% confidence intervals.
Cardiorespiratory fitness expressed as peak workload divided by height with allometric scaling, body weight and lean body mass increased by age in the girls and the boys, but decreased when expressed as peak VO2 per body weight and lean body mass in both sexes (Figure 3, 4 and 5) (previously unpublished data). The decrease was the highest among girls when peak VO2 was divided by body weight (Figure 4).

Figure 3. The relation between age and cardiorespiratory fitness expressed as peak workload per body height with allometric scaling among A) 162 girls and B) 177 boys aged 6.8 - 9.0 years. The lines indicate mean values (linear regression fit of age on peak workload divided by body height with allometric scaling) and their 95% confidence intervals.

Figure 4. The relation between age and cardiorespiratory fitness expressed as peak workload divided by A) body weight and B) lean body mass among 204 girls aged 6.8 - 8.6 years and 69 girls aged 8.8 - 10.8 years and between age and cardiorespiratory fitness expressed as peak oxygen uptake (VO2) divided by C) body weight and D) lean body mass among 69 girls aged 8.8 - 10.8 years. The lines indicate mean values (linear regression fit of age on peak workload and peak VO2 divided by body weight and lean body mass) and their 95% confidence intervals.
5.4 Determinants of cardiorespiratory fitness in girls and boys

The univariate determinants of cardiorespiratory fitness in the girls and the boys aged 6-9 years are presented in Table 8 (Study III). Cardiorespiratory fitness was not related to diastolic blood pressure at rest, weight, waist circumference, waist to hip circumference, serum dehydroepiandrosterone sulfate, insulin, glucose, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, alanine aminotransferase and gamma-glutamyltransferase, uric acid, plasma high-sensitivity C-reactive protein, physical activity during recess, the most popular unsupervised and organized forms of leisure-time physical activity except for unsupervised cycling, organized football and unsupervised trampoline jumping, screen-based sedentary behavior, other sedentary activities, nutrient intake except for energy intake of polyunsaturated fat, the number of meals and snacks per day, asthma, birth weight, the level of education in the family and the annual household income of family among girls or boys (data not shown).

In the girls, peak HR accounted for 9.0%, unsupervised physical activity for 8.2%, lean body mass for 5.1% and static balance for 2.0% of variation in cardiorespiratory fitness. These variables together accounted for 25.7% of variation in cardiorespiratory fitness.
Figure 5. The relation between age and cardiorespiratory fitness expressed as peak workload divided by A) body weight and B) lean body mass among 221 boys aged 6.6-9.0 years and 71 boys aged 8.8-11.3 years and between age and cardiorespiratory fitness expressed as peak oxygen uptake $\left( V\text{O}_2 \right)$ divided by C) body weight and D) lean body mass among 71 boys aged 8.8-11.3 years. The lines indicate mean values (linear regression fit of age on peak workload and peak $V\text{O}_2$ divided by body weight and lean body mass) and their 95% confidence intervals.

5.4 DETERMINANTS OF CARDIORESPIRATORY FITNESS IN GIRLS AND BOYS

The univariate determinants of cardiorespiratory fitness in the girls and the boys aged 6-9 years are presented in Table 8 (Study III). Cardiorespiratory fitness was not related to diastolic blood pressure at rest, weight, waist circumference, waist to hip circumference, serum dehydroepiandrosterone sulfate, insulin, glucose, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, alanine aminotransferase and gamma-glutamyltransferase, uric acid, plasma high-sensitivity C-reactive protein, physical activity during recess, the most popular unsupervised and organized forms of leisure-time physical activity except for unsupervised cycling, organized football and unsupervised trampoline jumping, screen-based sedentary behavior, other sedentary activities, nutrient intake except for energy intake of polyunsaturated fat, the number of meals and snacks per day, asthma, birth weight, the level of education in the family and the annual household income of family among girls or boys (data not shown).

In the girls, peak HR accounted for 9.0%, unsupervised physical activity for 8.2%, lean body mass for 5.1% and static balance for 2.0% of variation in cardiorespiratory fitness. These variables together accounted for 25.7% of variation in cardiorespiratory fitness (Figure 6). In boys, unsupervised physical activity accounted for 6.2%, resting HR for 5.4%, hand grip strength for 4.0%, static balance for 2.1%, participation in organized football trainings for 2.1% and unsupervised trampoline jumping for 1.4% of variation in cardiorespiratory fitness. They accounted altogether for 29.7% of variation in cardiorespiratory fitness (Figure 6). When only children who reached at least 90% of the predicted peak HR were included in the analyses, peak HR, unsupervised physical activity and lean body mass remained statistically significant determinants of cardiorespiratory fitness, whereas static balance was no longer statistically significantly associated with cardiorespiratory fitness in girls (data not shown). Among boys, the independent determinants remained unchanged.
### Table 8. The determinants of cardiorespiratory fitness among girls and boys

<table>
<thead>
<tr>
<th></th>
<th>Girls (n=162)</th>
<th>Boys (n=177)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD), median (IQR) or proportion</td>
<td>Correlation coefficient</td>
</tr>
<tr>
<td>Age (years)</td>
<td>7.6 (0.4)</td>
<td>0.10</td>
</tr>
<tr>
<td>Resting heart rate (beats/min)</td>
<td>71 (9)</td>
<td>-0.14</td>
</tr>
<tr>
<td>Maximal heart rate (beats/min)</td>
<td>196 (9)</td>
<td><strong>0.32</strong></td>
</tr>
<tr>
<td>Systolic blood pressure at rest (mmHg)</td>
<td>99 (7)</td>
<td><strong>0.19</strong></td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>19.4 (2.0)</td>
<td><strong>0.24</strong></td>
</tr>
<tr>
<td>Body fat percentage (%)</td>
<td>20.1 (16.7-25.9)</td>
<td>-0.04</td>
</tr>
<tr>
<td>Hemoglobin (g/l)</td>
<td>124 (8)</td>
<td><strong>0.16</strong></td>
</tr>
<tr>
<td>Hand grip strength (kPa)</td>
<td>45.8 (8.4)</td>
<td><strong>0.26</strong></td>
</tr>
<tr>
<td>Number of errors in static balance test</td>
<td>3 (1-4)</td>
<td><strong>-0.24</strong></td>
</tr>
<tr>
<td>Lower back and hamstring muscle flexibility (cm)</td>
<td>1 (-4-4)</td>
<td>0.15</td>
</tr>
<tr>
<td>Unsupervised physical activity (min/day)</td>
<td>38.6 (21.4-64.3)</td>
<td><strong>0.28</strong></td>
</tr>
<tr>
<td>Unsupervised trampoline jumping (%)</td>
<td>37.7</td>
<td>0.04</td>
</tr>
<tr>
<td>Unsupervised cycling (%)</td>
<td>84</td>
<td>0.14</td>
</tr>
<tr>
<td>Supervised physical activity (min/week)</td>
<td>60 (0-120)</td>
<td>0.11</td>
</tr>
<tr>
<td>Organized football (%)</td>
<td>9.3</td>
<td>0.004</td>
</tr>
<tr>
<td>Physically active school transportation (min/week)</td>
<td>100 (50-200)</td>
<td>-0.02</td>
</tr>
<tr>
<td>Polyunsaturated fat, (E%)</td>
<td>4.7 (4.0-5.6)</td>
<td><strong>0.21</strong></td>
</tr>
</tbody>
</table>

Values are means (SDs) for normally distributed variables and medians (IQRs) for variables with skewed distributions. Correlation coefficients of cardiorespiratory fitness with possible determinants were estimated with Pearson correlation coefficients for continuous variables or with point biserial correlation coefficients for dichotomous variables.
Table 8.
The determinants of cardiorespiratory fitness among girls and boys

<table>
<thead>
<tr>
<th></th>
<th>Girls (n=162)</th>
<th>Boys (n=177)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD), Correlation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>P</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>7.6 (0.4)</td>
<td>7.7 (0.4)</td>
</tr>
<tr>
<td><strong>Resting heart rate</strong></td>
<td>71 (9)</td>
<td>68 (63-0.33)</td>
</tr>
<tr>
<td>Maximal heart rate</td>
<td>196 (9)</td>
<td>197 (8)</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>19.4 (2.0)</td>
<td>21.8 (2.1)</td>
</tr>
<tr>
<td>Hemoglobin (g/l)</td>
<td>124 (8)</td>
<td>125 (7)</td>
</tr>
<tr>
<td>Hand grip strength (kPa)</td>
<td>45.8 (8.4)</td>
<td>49.5 (7.9)</td>
</tr>
<tr>
<td>Number of errors in static balance test</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Lower back and hamstring muscle flexibility (cm)</td>
<td>1 ( -4)</td>
<td>-</td>
</tr>
<tr>
<td>Unsupervised physical activity (min/day)</td>
<td>38.6 (21.4)</td>
<td>51.4 (34.3)</td>
</tr>
<tr>
<td>Unsupervised trampoline jumping (%</td>
<td>37.7</td>
<td>37.3</td>
</tr>
<tr>
<td>Unsupervised cycling (%</td>
<td>84</td>
<td>85.3</td>
</tr>
<tr>
<td>Supervised physical activity (min/week)</td>
<td>60 (0-120)</td>
<td>90 (60-180)</td>
</tr>
<tr>
<td>Organized football (%)</td>
<td>28.2</td>
<td>28.2</td>
</tr>
<tr>
<td>Physically active school percentage (%)</td>
<td>100 (50-200)</td>
<td>100 (28-194)</td>
</tr>
<tr>
<td>Polyunsaturated fat, (E%)</td>
<td>4.7 (4.0-5.6)</td>
<td>4.8 (4.0-5.8)</td>
</tr>
</tbody>
</table>

Values are means (SDs) for normally distributed variables and medians (IQRs) for variables with skewed distributions. Correlation coefficients of cardiorespiratory fitness with possible determinants were estimated with Pearson correlation coefficients for continuous variables or with point biserial correlation coefficients for dichotomous variables.

Figure 6. The strongest determinants of cardiorespiratory fitness among girls and boys

5.5 SUMMARY OF FINDINGS

Study I provided normative data and reference values for measures of cardiorespiratory fitness and responses of HR and systolic BP in a maximal exercise test on a cycle ergometer in a population sample of children aged 6-9 years. Means (2 SDs) of peak workload per kg of weight were 2.7 (0.9) W/kg in the girls and 3.1 (1.0) W/kg in the boys. The corresponding values of peak workload scaled by kg of lean body mass was 3.5 (0.9) W/kg in the girls and 3.8 (1.0) W/kg in the boys. The girls had lower cardiorespiratory fitness, indicated by peak workload per body weight (p<0.001) and lean body mass (p<0.001) than the boys. A plateau or decline in systolic BP close to the end of the test was found in about a third of children. HR decreased during 2 min recovery as means (2 SDs) 53 (18) beats/min in the girls and 59 (22) beats/min in the boys (difference between sexes, p<0.001).

Study II provided normative data and reference values for measures of cardiorespiratory fitness, respiratory function, such as O₂ pulse and the lowest value of VE/VCO₂ during the exercise test, and hemodynamic responses in a maximal exercise test on a cycle ergometer in a population sample of children aged 9-11 years. Means (2 SDs) of peak workload per kg of weight was 3.1 (0.9) W/kg in the girls and 3.4 (1.3) W/kg in the boys (difference between sexes, p=0.003). The corresponding values of peak workload scaled by kg of lean body mass was 4.1 (0.8) W/kg in the girls and 4.4 (1.0) W/kg in the boys (p=0.001). Peak VO₂ per kg of weight was 47.6 (13.0) ml/kg/min in the girls and 51.9 (15.5) ml/kg/min in the boys (p<0.001) and peak VO₂ per kg of lean body mass was 63.0 (11.5) ml/kg/min in the girls and 67.3 (12.6) ml/kg/min in the boys (p<0.001). HR decreased during 2 min recovery as means (2 SDs) 56 (22) beats/min in the girls and 64 (20) beats/min in the boys and it was slower in the girls than in the boys (p<0.001). There were no sex differences in systolic BP and its changes during and after maximal exercise test. Peak oxygen pulse was as means (2 SDs) 7.9 (2.3) ml/beat in the girls and 9.1 (2.6) ml/beat in the boys aged 9-11 years (difference between sexes, p<0.001). The lowest value of ventilation per carbon dioxide output during the test was as means (2 SDs) 29 (5) in the girls and 28 (4) in the boys with no sex difference.
Study III provided determinants of cardiorespiratory fitness for girls and boys. Peak HR, unsupervised physical activity, lean body mass and static balance were the strongest determinants of cardiorespiratory fitness among girls, accounting for 25.7% of its variation. In boys, unsupervised physical activity, resting HR, hand grip strength, static balance, participation in organized football training and unsupervised trampoline jumping were the strongest determinants of cardiorespiratory fitness, accounting for 29.7% of its variation.
6 Discussion

6.1 METHODOLOGICAL ASPECTS

6.1.1 Study design and study population
We invited 736 children 6–9 years of age who were registered for the first grade in the 16 primary schools, selected out of all 24 public primary schools of Kuopio, in 2007–2009, and who spoke Finnish and had no physical disabilities to participate in physical activity intervention. Altogether 512 children, who represented 70% of those invited, participated in the baseline examinations. The 512 participants of the baseline examinations were rather homogenous in age, ethnicity and place of residence. According to the school health examination data collected from every Finnish child before he or she starts the first grade, the study participants did not differ in age, sex distribution or BMI-SDS from all children who started the first grade in the primary schools of Kuopio during years 2007–2009. No data on cardiorespiratory fitness, physical activity or socioeconomic status were available from children who did not participate in the PANIC study. The non-participants were not asked why they did not participate. Therefore, the possibility of selection bias has to be taken into account. It is possible that the participating families were more motivated and prepared to make their lifestyle habits healthier (140) or already had healthier lifestyle habits and were more interested in them than non-participating families. It is possible that children who participated in this study had higher cardiorespiratory fitness than those who did not participated which can slightly overestimate the true levels of cardiorespiratory fitness.

We excluded 6 children from the intervention study at baseline because of physical disabilities that could hamper participation in the intervention or lack of time or motivation to attend (141). The remaining 506 children included 245 girls and 261 boys, and such a balanced sex distribution is important because of health-related behavior differences between sexes (142). We divided the 506 children in the intervention group (306 children, 60%) and the control group (200 children, 40%) stratifying them by location (urban vs. rural) and size (large vs. small) of the schools to minimize differences in baseline characteristics between the groups. Children from 9 schools were allocated to the intervention group and children from 7 schools were allocated to the control group. Of the 506 children who participated in the baseline study, 440 (87%) attended in the 2-year follow-up study indicating a good compliance among the participants. Of these 440 children 216 were girls and 224 were boys.

The participants of Study I included 204 girls and 221 boys 6-9 years of age at the first grade at school who had been examined at baseline of the lifestyle intervention study, and those of Study III included 162 girls and 177 boys 6-9 years of age examined at baseline. The participants of Study II included 69 girls and 71 boys 9-11 years of age at the third grade at the school who had been in the control group of the lifestyle intervention study for 2 years and who had been examined at 2-year follow-up. Thus, the sex distribution was balanced in all these 3 studies. These cross-sectional analyses in a representative population sample of children provided normative data and reference values for cardiorespiratory fitness, respiratory function and hemodynamic changes during and after maximal exercise test (Studies I and II) as well as valuable information on the determinants of cardiorespiratory fitness (Study III) in girls and boys separately. Because of the cross-sectional study design, however, it is not possible to draw conclusions on the causality of the determinants of cardiorespiratory fitness among children (Study I). However, the cross-sectional design is justified because of a descriptive nature of the Studies in this thesis (143).
In Study I, 97% of the children aged 6-9 years were prepubertal. In Study III, the few children aged 6-9 years who had entered puberty were excluded, because puberty could have confounded the analyzes on the determinants of cardiorespiratory fitness. In Study II, 24% of the children (41% of girls, 8% of boys) aged 9-11 years were pubertal. According to other studies, girls enter puberty on average at the age of 9.9 years and boys at the age of 11.7 years (144,145).

6.1.2 Assessments of cardiorespiratory responses in maximal exercise test

Heart rate
HR was measured continuously from the supine rest before exercise test until the end of the recovery period after exercise test using 12-lead ECG to get accurate information of HR responses during and after maximal exercise test. We calculated predicted peak HR using a formula 208-(0.7*age) that has been shown to be valid in children (24). The medians of the peak HR as a percentage of predicted peak HR indicates true exhaustion in both girls and boys. There were no sex differences in peak HR values, either. However, it is possible that some individuals who had small muscle mass did not achieve their true peak HR at cycle ergometer exercise test, because of the weakness of the quadriceps muscles (23). Furthermore, motivation, co-operation and mechanical efficiency may also affect the peak HR achieved (17).

Blood pressure
BP was assessed by aneroid sphygmomanometer from the supine rest before exercise test until the end of the recovery period after exercise test. The size of the arm was measured to choose an appropriate cuff size. Cycle ergometer tests permits better conditions for accurate BP and ECG measurements because the upper body is more stable on a cycle ergometer than on a treadmill (49). BP determination during exercise may be difficult because of noise and movements of the child (32). Noise during the test could complicate the hearing of first Korotkoff sound which is reported as systolic pressure and therefore noise can cause underestimation of true systolic BP values. However, there is less noise in cycle ergometer tests than in treadmill tests (17). Furthermore, our study nurses were trained and experienced to measure BP also during exercise tests. The assessments were done using one calibrated blood pressure meter. We have also compared blood pressures measured by our study nurses as quality control. In some children, Korotkoff sounds can be audible until 0 mmHg which makes accurate diastolic BP measurements impossible (17). In our study, diastolic BP was measured down to 40 mmHg because below that it was not possible to obtain reliable values. Diastolic BP was, however, below 40 mmHg in the majority of children. Therefore, we did not utilize measures of diastolic BP in statistical analysis. In Study I, it was not possible to measure systolic BP 2 minutes before the peak workload for all children, so the measured values slightly underestimate true peak systolic BP. In Study II, difficulties to measure systolic BP near the end of the maximal test limited the number of children with peak systolic BP values. Peak systolic BP was reported using values that could be measured within 2 min before peak workload. In Study II, we also presented peak systolic BP in 3 height groups, because the increase in systolic BP during exercise is affected by age and size (21). Sphygmomanometers were calibrated once a year.

Respiratory function
Children aged 9-11 years performed maximal exercise test with respiratory gas analysis (Study II). We used the breath-by-breath system, which is the most popular method to measure respiratory gases nowadays. We also used face masks, which are reported to be more comfortable among children than mouthpieces and nose clips because they permit breathing through both the mouth and nose (32). We used masks appropriate for small children and additionally, sealant gel was used to get face mask properly fit and to avoid
air leaks among some children. We have reported previously that respiratory gas analysis during the maximal exercise test did not impair maximal performance among children (71). In the analysis, we divided VE by body height\textsuperscript{1.44} in the girls and by body height\textsuperscript{1.54} in the boys because peak VE does not increase linearly with increasing body size and because simple non-allometric scaling by body size is not appropriate (41). The exponents for height were calculated according to a previous report (137). The measurement system was calibrated before each exercise test according to recommendations (48).

6.1.3 Assessment of cardiorespiratory fitness

We assessed cardiorespiratory fitness by maximal cycle ergometer exercise test using an electromagnetic cycle ergometer, which allows accurate measurement of mechanical power output and enables very low workrates for warm-up (32). Both the cycle ergometer and treadmill offer a reliable way to assess cardiorespiratory fitness, although the treadmill is the most commonly used apparatus worldwide (17,32). However, cycle ergometers have plenty of advantages compared to treadmill testing. It is safer than the treadmill and some physiological measurements, such as VO\textsubscript{2} assessment, are also easier to perform during cycle ergometer tests (32). On the other hand, small children may have difficulties to maintain steady pedaling rate during the whole test period (32). However, in Finland children are familiar with riding a bicycle at very young age and in our maximal cycle ergometer tests there were only minor technical problems among some individuals. Furthermore, we adjusted the ergometer individually for each child and used a pediatric saddle module to obtain reliable results (32).

We used ramp-on mode in which the workload increased linearly by 1 Watt per 6 seconds until exhaustion. This protocol allows the cardiovascular system and skeletal muscles in the legs to adapt to increasing workload during maximal exercise test. Therefore, the protocol with linear increase of workload also minimize the termination of the test before true cardiorespiratory fitness has achieved due to muscle weakness. The exercise test was considered maximal if the reason for terminating the test indicated maximal effort and maximal cardiorespiratory performance. In most children, the duration of exercise test was between 8 and 12 minutes, which is the recommendation in order to avoid premature muscle fatigue and lack of attention and motivation (49). The ergometer was calibrated every 2 years according to the manufacturer’s instructions.

We have used both peak workload (Study I, Study II and Study III) and peak VO\textsubscript{2} (Study II) as measures of cardiorespiratory fitness and presented them not only as absolute values, but also relative to weight and lean body mass (Study I and Study II) and to allometrically scaled height (Study III) to eliminate the effect of body size. In Study III, we decided to express cardiorespiratory fitness as peak workload divided by allometrically scaled height instead of dividing it by lean body mass or traditionally by body weight because we were interested in whether body weight and lean body mass are determinants of cardiorespiratory fitness. The expression of cardiorespiratory fitness per body weight or lean body mass might have induced multicollinearity problems in statistical analysis (146). Peak workload per height (147) and allometrically scaled height (148) has been used as index of cardiorespiratory fitness also previously.

Peak workload and peak VO\textsubscript{2} relative to lean body mass are not confounded by body adiposity and are therefore more valid measures of true cardiorespiratory fitness than these measures divided by body weight in children and adults (66,67). Also allometric scaling of lean body mass is recommended (149). Cardiopulmonary exercise test parameters normalized by lean body mass have greater prognostic value for patients with heart failure, especially in obese individuals, than parameter that are divided by total body weight (150). Besides lean body mass, also height could be used when scaling peak workload and VO\textsubscript{2} to obtain data of true cardiorespiratory fitness among children (67).
We have presented values of cardiorespiratory fitness separately for girls and boys because of the sex differences observed in many parameters. In contrast, many studies having investigated cardiorespiratory fitness and cardiovascular responses to exercise among children have not reported data separately for girls and boys, although boys have for instance lower HR than girls at a given exercise intensity (21). Furthermore, we found sex differences in basic characteristics, such as body weight and amount of lean body mass, especially among children aged 6-9 years, which can affect cardiorespiratory fitness and cardiorespiratory responses to exercise. However, another study reported no sex differences in body composition, such as muscle mass and fat mass, among children aged 6-12 years (151).

We did not measure respiratory gases among children aged 6-9 years, although directly measured peak VO\textsubscript{2} is considered to be the best single marker of cardiorespiratory fitness and exercise capacity (50). However, peak workload has been shown to have a strong association with peak VO\textsubscript{2} in population studies among children (64). Furthermore, maximal exercise test without respiratory gas analysis provides a methodologically simpler and easier way to assess cardiorespiratory fitness among small children. We wanted to maximize the number of children with reliable data from the exercise tests and performed, therefore, the tests without respiratory gas analysis among children aged 6-9 years. We did not assess blood lactate during exercise among children aged 6-9 or 9-11 years, either. However, we assessed many other important parameters from pre-rest to post-rest during the maximal cycle ergometer exercise test.

6.1.4 Other assessments

**Physical activity and sedentary behavior**

Different accelerometers or combined HR and movement sensors are used for objective measurement of physical activity (152,153). In the PANIC study children wore an objective combined HR and movement sensor, Actiheart, for at least 4 consecutive days. However, in Study III, the PANIC Physical Activity Questionnaire administered by the parents together with their child was used to assess physical activity, sedentary behavior and their components to study their relationship with cardiorespiratory fitness among children. Questionnaires and other self-reports are feasible ways to assess the components of physical activity and sedentary behavior which can not be done by using objective sensors (154). Our aim was to investigate whether some special forms of physical activity or sedentary behavior have associations with cardiorespiratory fitness among children. We have also validated the questionnaire in a subsample of 38 children who were examined at baseline of the PANIC study using Actiheart monitor. Physical activity questionnaires often overestimate the intensity and duration of physical activity (154) but objective measures have their limitations as well. For instance, there are several cut-off points for moderate-to-vigorous physical activity in different studies which complicates the comparison of results (155,156). Furthermore, it is possible that an individual is physically more active than normally in a fixed, quite short period when he or she is wearing the monitor. There could also be variation in physical activity between different days among individuals and this can cause under- or overestimation of real amount of physical activity when assessing physical activity with objective monitor during a short period. An objective monitor may also be uncomfortable to use.

**Body composition**

In Study III, fat percentage and lean body mass were measured by the DXA method, which is a valid and accurate measure for body composition and feasible also among children (157-159). Furthermore, the radiation dose of DXA is very low (159). In studies I and II which provided normative data and reference values for measures of cardiorespiratory fitness to be used for instance in clinical work, we used lean body mass measured by BIA,
because BIA is a more feasible and more cost-effective method in clinical practice than DXA when assessing cardiorespiratory fitness scaled by lean body mass. Furthermore, it agreed well with lean body mass measured by DXA in girls and boys (128).

Neuromuscular fitness
Our trained personnel performed modified Eurofit tests in schools or in a sports hall to measure neuromuscular performance which are well-known, widely used and easy to carry out field tests (160,161). A physician performed assessments of hand grip strength, static balance and sit and reach tests. Clear instructions about how to do all these tests were given to the children. There are some issues that have to be taken into account in analyzing data of neuromuscular fitness tests. Besides flexibility, the sit and reach test is influenced also by body dimensions. Static balance may also be influenced by concentration of a child. However, the room for the test was quiet and there were no other persons than the child, a parent and a physician.

Other assessments
Biochemical measurements, such as blood hemoglobin, plasma glucose, serum insulin, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol, plasma high-sensitivity C-reactive protein, alanine aminotransferase, gamma-glutamyltransferase and serum dehydroepiandrosterone sulfate were performed by experienced laboratory personnel after the child had fasted for 12 hours and they were studied as possible determinants of cardiorespiratory fitness. The number of meals and snacks per day and the intake of nutrients were assessed using food records reported by the parents with their child, which may have caused misreporting. However, food records are considered to be the most valid method to assess diet at population level (162). Birth weight of the child was acquired from the records of Kuopio University Hospital, whereas in case of missing data, self-reported values given by the parents were used. Socioeconomic status included annual household income and parental education level and they were reported by the parents. These self-reported data may be remembered wrongly or misunderstood and therefore reported incorrectly.

6.2 RESULTS COMPARED WITH PREVIOUS FINDINGS

6.2.1 Cardiorespiratory responses in maximal exercise test in girls and boys
Children aged 6-9 years (Study I)
In our study, the peak HR was close to the predicted peak HR in the girls and the boys. The peak HR in both sexes was also almost the same as reported in another study using a cycle ergometer test among children 7-9 years of age (20). Among children and adolescents 8-18 years of age, HR recovery after maximal exercise test has been fastest in the youngest children (29). HR recovery within 3 minutes after a maximal cycle ergometer exercise test was 85 beats/minutes in boys and 79 beats/minutes in girls aged 6-7 years with a significant sex difference (163). We also observed that boys have faster HR recovery after maximal exercise test than girls, but our results indicate slower recovery during first 3 minutes after maximal exhaustion compared to the result of Pels et al. (163).

In our study systolic BP increased during the maximal exercise test on average by 25 mmHg in the girls and by 23 mmHg in the boys and the mean highest value close to the end of the exercise test was below 130 mmHg in both sexes. To the best of our knowledge, there are very few other studies among apparently healthy children aged 6-9 years from population-based sample in which systolic BP would have been reported during progressive maximal exercise test. In a recent review only one study was identified in
which BP was measured among healthy children who have undergone ergospirometry (164). In that study, the mean peak systolic BP was 122 mmHg among boys aged 7.5 years (27). In a study among participants aged 5-33 years, children shorter than 1.20 m with BSA smaller than 1 m² had peak systolic BP of 119 mmHg (34). These findings together with our findings indicate that small and young children have low peak systolic BP during maximal exercise. In our study among children most of the decrease in systolic BP after peak workload was observed during the first 0.5 minutes indicating fast recovery.

We arbitrarily categorized children according to systolic BP responses close to the end of the exercise test in those with elevation, plateau or decline in systolic BP. We surprisingly found a plateau in systolic BP in 20-25% of children, and even a decline of more than 2 mmHg in systolic BP in about 10% of the children. Children with such a response in systolic BP did not differ in peak workload or peak HR from those with elevation in systolic BP and had no symptoms or ECG findings that would have resulted in premature termination of the exercise test. This finding suggests that the plateau and decline in systolic BP is not due to poor cardiovascular fitness or submaximal effort in these children. Moreover, the systolic BP decline was more than 10 mmHg in 2% of the girls and boys and none of them had symptoms during the exercise test or had cardiac disease. A previous study also showed that a drop in systolic BP of more than 10 mmHg during exercise in children often occur without symptoms and cardiac abnormalities (35). Therefore, it is likely that the plateau or decline in systolic BP observed in our population-based study is a physiological phenomenon due to decreased peripheral resistance in response to exercise rather than being a sign of cardiac disease that decreased SV and thereby systolic BP. It is also possible that pedaling rate fluctuated near exhaustion, inducing plateau or decline in systolic BP. However, it is important to verify in other studies that the plateau and decline in systolic BP are normal responses to exercise in children.

Children aged 9-11 years (Study II)

In a study among children 8-13 years of age, peak HR was 196 beats/min in girls and varied between 191 and 194 beats/min in boys depending on BSA during cycle ergometer test (27). Girls and boys in our study reached the predicted peak HR, and the peak HR was higher than that in the study by Washington et al. (27). We found that HR decreased during recovery more in the boys than in the girls. The same phenomenon was observed after cycle ergometer test in a study among children aged 9 years (165). In that study, HR decreased during the first minute of recovery by 39 beats/min in girls and by 45 beats/min in boys. These HR decreases were similar to those in our study. In another study among healthy children aged 12 years decrease in HR within one minute after a maximal treadmill exercise test was 35-38 beats per minute (166), which is a slightly slower recovery than in our study.

Peak systolic BP varied between 122-139 mmHg in boys and between 126-142 mmHg in girls depending on BSA in the study among children 8-13 years of age (27). In our study peak systolic BP was higher, especially in the boys, than observed in the study by Washington et al. (27). In another study, the mean systolic BP was 159 mmHg among prepubertal boys aged 11.5 years at the end of maximal cycle ergometer exercise test, which is slightly higher than among boys aged 9-11 years in our study. The magnitude of increase in systolic BP during exercise increases with age and body size (17), and therefore our results are in line with these previous findings (167). Concordant with other studies among children (39,40), peak systolic BP was higher in taller children than in shorter children in our study. In our study among children aged 9-11 years, systolic BP decreased rapidly immediately after peak workload in the girls and the boys. Also in another study the greatest fall in systolic BP occurred during the early recovery in prepubertal boys aged 11.5 years (167).

The lowest VE/VCO₂ was similar among girls and boys in our study. No sex differences in the VE/VCO₂ slope have been observed in previous studies, either (29,55). The
ventilatory response to exercise expressed as VE/VCO₂ slope may decrease progressively from age 10 because of changes in the central control of ventilation (168).

The absolute peak O₂ pulse in our study population was similar to that in another study among children 10 years of age whose mean peak O₂ pulse was 8 ml/beat in a treadmill test (51). In a study among children 8-13 years of age peak O₂ pulse varied between 6 and 11 ml/beat in boys and between 5 and 11 ml/beat in girls during a cycle ergometer test depending on children’s BSA, indicating no sex difference (27). However, boys in our study had significantly higher O₂ pulse than girls as an absolute value and when scaled to body weight and lean body mass.

In our study peak RER was slightly higher than the RER values observed in a study among children aged 8-11 years in which RER was 1.02 in both sexes during a maximal cycle ergometer test (47). We observed that girls had higher RER than boys which has been found also in other studies among children from different age groups (72,83).

Absolute peak VE was higher in the boys than in the girls in our study. A previous study reported no significant sex difference in minute VE among children 10 years of age (43), whereas another study showed that minute VE was higher in boys than in girls 11 years of age (42). On the other hand, we found no sex difference in VE with allometric scaling, whereas in another study, the sex difference of VE with allometric scaling was statistically significant among prepubertal children aged 11 years at treadmill test (169). There is variation in peak VE between studies among children who are almost at the same age because in one study absolute peak VE was 58 l/min in boys and 50 l/min in girls during a treadmill test (42), whereas in another study corresponding values were 78 l/min in boys and 71 l/min in girls during a treadmill test (43). In a cycle ergometer exercise test, peak minute VE was 54 l/min among children aged 10 years (168). The treadmill tests has been found to result in significantly higher peak VE values in children aged 7-9 years than cycle ergometer tests (72). However, the peak VE measured in our study was between values observed in previous 2 studies using a treadmill.

6.2.2 Cardiorespiratory fitness in girls and boys
Children aged 6-9 years (Study I)
In a previous study among children aged 8 years, peak workload per body weight was 2.7 W/kg in girls and 2.9 W/kg in boys (29). In our study cardiorespiratory fitness was similar among girls but slightly higher among boys compared to the values in the earlier study. In another previous study among children 6-7 years of age, boys had a higher peak VO₂, expressed in l/min, ml/kg of body weight and ml/kg of lean body mass, in an exercise test using a treadmill than girls (46). On the other hand, one study reported no sex differences in cardiorespiratory fitness or peak HR measured on a treadmill or cycle ergometer among healthy children 5-6 years of age (86). In our study among children aged 6-9 years, the boys had a higher absolute peak workload and peak workload per body weight and lean body mass than the girls, although peak HR was similar.

One reason for the higher cardiorespiratory fitness in boys could be that they are physically more active than girls. Boys 6-7 years of age had higher levels of cardiorespiratory fitness and physical activity than girls of the same age (46). Another explanation for the sex difference in cardiorespiratory fitness in the present study is that the girls had more fat mass and less lean body mass than the boys. The difference in peak VO₂ between boys and girls have been observed to decrease when it was expressed relative to lean body mass instead of relative to body weight (46). However, in our study the sex difference in peak workload was almost the same when it was divided by lean body mass or body weight. There are very few studies which have reported on normative data of cardiorespiratory fitness among healthy children at this age group.
Higher peak VO₂ among boys than girls 8-18 years of age (29). Mean values for peak VO₂ per body weight peaks at the age 9 years among females and at the age of 12-13 years among males and it is then on average 44 ml/kg/min in girls and 50 ml/kg/min in boys. Furthermore, cardiorespiratory fitness levels expressed as peak VO₂ below 42 ml/kg/min in boys and below 35 ml/kg/min in girls aged 8-19 years have been associated with higher cardiovascular risk (111). The levels of cardiorespiratory fitness among girls and boys in our study were significantly higher than those values.

According to previously published studies, cardiorespiratory fitness of children has declined during the last years (14,16). Positively, cardiorespiratory fitness was higher both in girls and boys among our study population compared to cardiorespiratory fitness among children from past decades in a study by Shvartz and Reibold (170). There were also no secular changes in cardiorespiratory fitness among Finnish adolescents from 2003 to 2010 (171). Interestingly, Finnish children and adolescents also belonged to the best performing group, when investigating worldwide variation in cardiorespiratory fitness assessed by 20-m endurance shuttle run tests between years 1981 and 2003 among children and adolescents aged 6-19 years (172).

Concordant with the results of the study by Dencker et al. (64), the boys had a higher peak workload and peak VO₂ than the girls in our study. Also in another study peak workload and peak VO₂ relative to body weight in cycle ergometer exercise tests were higher among boys than girls 8-18 years of age (29). Mean values for peak VO₂ have been found to be higher among boys than girls in childhood and adolescence (1). Cardiac function and body size and composition account for the differences in peak VO₂ between prepubertal boys and girls (173). Boys aged 8-11 years were observed to have 8-18% higher peak VO₂ values than girls of same age, depending on the measures used for scaling (47). However, only 3-5% of the variation in peak VO₂ could be explained by sex independently of differences between sexes in body composition, heart size or physical activity (47). Moreover, maturation has been found to increase absolute peak VO₂ among children (87). In our study, pubertal boys had a higher absolute peak VO₂ than prepubertal girls whereas there was no such difference between prepubertal and pubertal girls. One explanation for this difference could be that more girls had entered puberty than boys that increased the statistical power and the likelihood to observe the difference between pubertal and prepubertal girls. However, the larger number of pubertal girls is probably not the only reason for the observed difference because the difference in mean absolute peak VO₂ was higher between prepubertal girls and pubertal girls than between prepubertal boys and pubertal boys.
6.2.3 Determinants of cardiorespiratory fitness in girls and boys

In Study III, peak HR, unsupervised physical activity, lean body mass and static balance were the strongest determinants of cardiorespiratory fitness among girls aged 6-9 years, accounting for 26% of its variation. In boys at the same age, unsupervised physical activity, resting HR, hand grip strength, static balance, participation in organized football training and unsupervised trampoline jumping were the strongest determinants of cardiorespiratory fitness, accounting for 30% of its variation. Unsupervised physical activity with varying intensity levels was one of the strongest determinants of cardiorespiratory fitness among both sexes.

Total physical activity has been directly related to cardiorespiratory fitness assessed by a 20-meter shuttle run test among children aged 4-6 years (174) and by a maximal cycle ergometer exercise test among children aged 9-10 years (90). However, physical activity was found to have a direct relationship to peak VO₂ using a treadmill exercise test only in boys aged 6-8 years (175). Moreover, baseline vigorous physical activity was associated with a 9-month change in cardiorespiratory fitness assessed by 20-meter shuttle run test among children aged 4-6 years (174). Our findings show that there is a direct association between unsupervised physical activity and cardiorespiratory fitness among girls and boys aged 6-9 years. It was a positive finding that higher levels of unsupervised physical activity was associated with higher cardiorespiratory fitness both in girls and boys, suggesting that supervised physical activity such as organized sports and supervised physical activity organized by societies was not a necessity to achieve higher cardiorespiratory fitness among children in this population-based sample. Unsupervised physical activity often means that children are spontaneously physically active with variable intensities. They for instance walk, run and jump longer periods at a time with varying intensity levels which may improve cardiorespiratory fitness. Instead in many forms of organized sports, there may be passive periods when children listen to instructions or wait their turn to perform. Therefore, these forms of physical activity may not necessarily improve cardiorespiratory fitness, but they may improve for instance balance performance and stretching.

Larger lean body mass had a strong association with higher cardiorespiratory fitness scaled by body size among girls, but not among boys in our study. Also in another study among children aged 8-11 years lean body mass was an important contributing factor for absolute peak VO₂ measured with cycle ergometer exercise test (47). On the other hand, hand grip strength, which has been related to total muscle mass in children and adolescents (176), was directly associated with cardiorespiratory fitness among boys, but not girls in our study. Taken together, these findings indicate that larger muscle mass or strength, measured by lean body mass or hand grip strength, are important for performance during maximal cycle ergometer exercise test in girls and boys.

Static balance was one of the strongest determinants of cardiorespiratory fitness among both sexes. Balance is linked to motor development, and it improves during growth (177). Improved motor skills and balance have also been associated with habitual physical activity among children (178). Moreover, poorer motor ability and balance impair neuromuscular performance needed in bicycling. However, this may not be a problem among Finnish children, who learn to cycle early in childhood. It is a very popular form of physical activity among children in Finland. Bicycling is an easy way to go around and it is also safe in Finland. Also in this population based sample of children, it belonged to the 12 most common forms of physical activity. When only children whose peak HR at the end of the maximal exercise test was at least 90% of the predicted peak HR were included in the analyses, static balance was no longer a statistically significant determinant of cardiorespiratory fitness. This finding suggests that children with poorer balance did not achieve their real maximal performance in the cycle ergometer exercise test.

Peak HR was the strongest determinant of cardiorespiratory fitness among girls. With stricter HR criterion for maximal performance peak HR still remained as the strongest
determinant of cardiorespiratory fitness among girls. In line with our results, peak HR was an important determinant of absolute peak VO₂ in studies among children aged 6-7 years (83) and 8-11 years (47).

Resting HR was an important determinant of cardiorespiratory fitness among boys. Lower resting HR has been associated with higher levels of physical activity in children and adolescents (179,180). Moreover, higher amounts of physical activity have been related to higher cardiorespiratory fitness among children aged 9-10 years (90). Among boys, also organized football and unsupervised trampoline jumping were associated with higher cardiorespiratory fitness. Both of these activities have a quite high energy cost among children and adolescents (181,182), and especially vigorous physical activity has been directly related to cardiorespiratory fitness among children and adolescents (90,183). Furthermore, both of these forms of physical activity are very popular among Finnish children.

We found that our models explained about 30% of the variation in cardiorespiratory fitness among girls and boys. Heredity is known to be a very important determinant of cardiorespiratory fitness, because genetic factors explain about 50% or even more of the variation in cardiorespiratory fitness among adolescents and adults (98,99). Peak VO₂ and endurance performance are trainable phenotypes in both sexes, but there are, however, considerable individual differences in response to exercise training because of genetic background (184). Some individuals are even almost nonresponders to aerobic training, whereas some individuals with certain gene alleles have a significantly higher peak VO₂ response to training than individuals who do not have those gene alleles (184). Genetic factors may make it easier to some individuals to achieve higher levels of physical activity and cardiorespiratory fitness and live longer with no diseases (185,186). Also individual exercise behavior has been found to be affected by genetic variation (187). We did not study associations of heredity with cardiorespiratory fitness among children in our study, because the size of our study population was not large enough to study the role of genetic factors as determinants of cardiorespiratory fitness among children in this study. However, our genetic data of cardiorespiratory fitness can be combined with data of other studies and utilize in investigating genetic factors of cardiorespiratory fitness.

Unsupervised physical activity was one of the strongest determinants of cardiorespiratory fitness among girls and boys in our study. Therefore, it is important that parents, teachers and other adults involving in life of children encourage them to physical activity and promote physical activity of children in every possible ways, play physically active outdoor games with them and act as role models. Also the society has a remarkable role in supporting physically active lifestyle for instance by building play parks and taking care of swimming beaches, skating rinks and recreational centres. It is important that every child finds her or his own form of physical activity and adopts physically active lifestyle. Diversity of physical activity is also important. The new Finnish Recommendations for physical activity in early childhood (2016) recommends at least 3 hours physical activity per day for children under 8 years (188). The Finnish recommendations for school aged children (7-18 years of age) recommends physical activity at least 1-2 hours per day dependent on the age group (189).
7 Conclusions

Results of Study I show that peak workload per body weight was as means (2 SDs) 2.7 (0.9) W/kg in girls and 3.1 (1.0) W/kg in boys aged 6-9 years. The corresponding values of peak workload per lean body mass was 3.5 (0.9) W/kg in girls and 3.8 (1.0) W/kg in boys. The level of cardiorespiratory fitness in our population-based sample of girls is similar and slightly higher in boys compared to level of cardiorespiratory fitness among children at the same age in a previous study (29). There were sex differences in many parameters of cardiorespiratory fitness and hemodynamic changes during and after maximal exercise test. The results are useful for physicians and exercise physiologists to evaluate cardiorespiratory fitness and systolic BP and HR responses to exercise in children aged 6-9 years and to detect children with a low exercise tolerance or abnormal hemodynamic responses to exercise.

Results of Study II indicate that peak workload per body weight was as means (2 SDs) 3.1 (0.9) W/kg in girls and 3.4 (1.3) W/kg in boys aged 9-11 years. The corresponding values of peak workload per lean body mass was 4.1 (0.8) W/kg in girls and 4.4 (1.0) W/kg in boys. In girls, peak \( \text{VO}_2 \) divided by body weight was as means (2 SDs) 47.6 (13.0) ml/kg/min and divided by lean body mass 63.0 (11.5) ml/kg/min. The corresponding values in boys were 51.9 (15.5) ml/kg/min and 67.3 (12.6) ml/kg/min. The level of cardiorespiratory fitness among our population-based sample of girls and boys aged 9-11 years is higher than level of cardiorespiratory fitness among children at the same age reported in previous studies (2,64,170). Peak oxygen pulse was as means (2 SDs) 7.9 (2.3) ml/beat in girls and 9.1 (2.6) ml/beat in boys aged 9-11 years and it was higher in boys than in girls (p<0.001). The lowest value of VE/VCO\(_2\) during the test was as means (2 SDs) 29 (5) in girls and 28 (4) in boys with no sex difference. There were sex differences in many parameters of cardiorespiratory fitness and related respiratory and hemodynamic parameters. This study adds the current knowledge on reference values for cardiorespiratory fitness, respiratory function and hemodynamic responses to exercise, and especially for the ventilatory efficiency expressed as the lowest value of VE/VCO\(_2\) during maximal exercise test, peak \( \text{O}_2 \) pulse and systolic BP responses to maximal exercise test, among children aged 9-11 years.

Findings of Study III show that higher amount of unsupervised physical activity has association with higher cardiorespiratory fitness in girls and boys aged 6-9 years. Furthermore, larger muscle mass and better balance are related to higher cardiorespiratory fitness in children. This has to be taken into account when assessing cardiorespiratory fitness using a maximal cycle ergometer exercise test. Long-term follow-up and intervention studies are needed to investigate the possible causal relationships of various factors with cardiorespiratory fitness among children.

7.1 IMPLICATIONS AND FUTURE PERSPECTIVES

Although the findings of previous studies emphasize knowledge on the normal range of and reference values for cardiorespiratory fitness, respiratory function and HR and systolic BP responses to exercise already in childhood, there are few population studies on normative data concerning maximal exercise test parameters in apparently healthy children from different age groups. It is also important to take into account the decrease in habitual physical activity among children and adolescents during recent years (190,191) which may decrease cardiorespiratory fitness. Therefore, normative values reported earlier may not be
appropriate to contemporary children, and there is need for up-to-date normal values (192). For instance, the well-known and widely used norms for aerobic fitness reported by Schwartz and Reibold may be not suitable to general population of today (170). Moreover, in addition to the maximal values obtained with cardiopulmonary testing, also slopes calculated from the data obtained throughout the test could be analyzed and reported more often when assessing cardiorespiratory fitness and hemodynamic changes during and after maximal exercise testing, because these slopes might be useful in clinical work and future research (193). Therefore, it is important to calculate these slopes and analyze them in further studies.

Besides knowing normal range of cardiorespiratory fitness among children, also information about changes in hemodynamics during and after a maximal exercise test and knowing the normal variation already in childhood are of potential importance for the prevention of hypertension as well as metabolic and cardiovascular diseases later in life. A larger increase in systolic BP during a maximal exercise test has been associated with metabolic risk factors in children (37). Furthermore, higher waist circumference, indicating elevated metabolic risk, is associated with a slower decrease in HR after a maximal exercise test in healthy children (194). In contrast, a faster HR decrease during the first minute after maximal exercise test among children has been related to lower BMI and higher aerobic fitness (22). Faster HR recovery after submaximal treadmill test has been related to better metabolic profile among adolescents and adults (195). In adults, a slow HR recovery during the first minute after maximal exercise test has been observed to be an important predictor of premature deaths (196,197). Previous study among adults has also suggested that exaggerated systolic BP during exercise test and slow decline in systolic BP after maximal exercise test may predict hypertension and cardiovascular disease later in life (120). The long-term PANIC study from fetal period to adulthood among population-based sample of children make it possible to investigate these cross-sectional and longitudinal associations and determinants for them in the future.

Furthermore, there are only a few recent studies on sex-specific determinants of cardiorespiratory fitness in large population-based samples, although poor cardiorespiratory fitness has been associated with many risk factors for health as well as for diseases and even premature mortality in childhood and adulthood. A child with poor cardiorespiratory fitness often has low cardiorespiratory fitness also as adult. Therefore, it is important to find out determinants of cardiorespiratory fitness already in childhood and focus on modifiable factors to ensure an appropriately high cardiorespiratory fitness throughout the lifespan. It is important, for instance, encourage children to physical activity. According to the findings of this thesis, it is not necessary to exercise in sport clubs to get higher cardiorespiratory fitness. Instead, higher levels of unsupervised physical activity had association with higher cardiorespiratory fitness both in girls and boys according to the Study III. Outdoor games, such as playing tag are excellent ways to improve physical fitness and they can be played together with whole family. Trampoline jumping is also very popular form of physical activity among children nowadays. Many children enjoy jumping on trampoline and practice different somersaults. They do not even think that they are exercising although they are dripping with sweat. Jumping on a trampoline was also associated with higher cardiorespiratory fitness among boys in Study III of this thesis.

In the future, more longitudinal studies in population-based samples of children and adolescents are needed to investigate the impact of cardiorespiratory fitness and hemodynamic and respiratory responses during exercise on health and chronic diseases. Furthermore, long-term physical activity intervention studies are warranted to investigate the effects of long-term changes in physical activity on cardiorespiratory fitness and hemodynamic and respiratory responses to exercise. Long-term intervention studies are also needed to investigate the causes of changes in cardiorespiratory fitness since childhood.
and to examine the reasons for success or failure in improving cardiorespiratory fitness and in maintaining improved cardiorespiratory fitness since childhood. When improving physical fitness among children via physical activity interventions it may be essential to focus also on the parents’ attitudes towards physical activity and motivate families to exercise together (198). Furthermore, it is also important to study the optimal level of cardiorespiratory fitness that is associated with lower cardiometabolic risk since childhood. It would also be interesting to examine whether cardiorespiratory fitness or neuromuscular fitness has a stronger association with health. It has been found, for instance, that better results in sit-up and flexed arm hang tests in adolescence have predicted higher health-related fitness in adulthood (199). In addition, from the health promotion point of view, it is important to identify children and adolescents with poor cardiorespiratory fitness and encourage them to be physically active. Although heredity has a strong influence on cardiorespiratory fitness, also lifestyle related habits play a role. Finally, as cardiorespiratory fitness is recognized as an important indicator of functional capacity and cardiovascular health (85), it would be interesting to investigate the associations of cardiorespiratory fitness with the use of healthcare services and associated expenses among children, adolescents and adults. Our unique long-term physical activity and dietary intervention study among population sample of children enables these cross-sectional and longitudinal analysis of different factors and outcomes.
References


61. Noakes TD. Fatigue is a brain-derived emotion that regulates the exercise behavior to ensure the protection of whole body homeostasis. Front Physiol 2012 Apr 11;3:82.


This doctoral thesis provided normative data on maximal cycle ergometer test parameters in a population sample of children. The updated values are needed, because cardiorespiratory fitness (CRF) has declined in children. It is also important to identify factors associated with CRF, because higher CRF has many beneficial effects on health and well-being. The thesis showed that unsupervised physical activity, lean body mass, and static balance are associated with CRF in girls and boys.