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## Muscle strength and physical education: epidemiological studies of factors in adolescence and their association with later morbidity

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# **Muscle Strength and Physical Education**

**Epidemiological studies of factors in adolescence  
and their association with later morbidity**

Simon Timpka



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Lund 2013



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## Abstract

Although Physical Education (PE) is a part of the school curriculum in many countries, the association between the performance in PE and later morbidity is largely unknown. An important marker of health, cardiorespiratory fitness is inversely associated with future cardiovascular disease (CVD) and mortality. It has been suggested that muscle strength is associated in a similar way. However, whether low muscle strength in youth is a risk factor for CVD independently of cardiorespiratory fitness is not known. In a cohort of men and women, I investigated the association between PE performance in adolescence and morbidity in middle age (paper I and II). In cohorts of adolescent men, I investigated isometric muscle strength as a risk factor for later musculoskeletal pain (paper III), CVD, and mortality (paper IV).

In women, low PE performance was associated with having a musculoskeletal diagnosis as well as with increased sick leave and increased number of physician visits. Men with low muscle strength did not have an increased risk for musculoskeletal pain but an increased risk of ischemic CVD as well as middle age CVD mortality. Notably, the associations were independent of cardiorespiratory fitness. In summary, I conclude the following 1) Adolescent girls with low PE performance could be important to target with early interventions to reduce future musculoskeletal illness and health impairment. 2) General isometric muscle strength in youth is not a risk factor for adult musculoskeletal pain in men. 3) The role of muscle strength in the development of CVD warrants further attention.

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## List of Papers

The thesis is based on the following papers, referred to in the text by roman numerals:

- I. Timpka S, Petersson IF, Englund M. The grade in physical education in adolescence as predictor for musculoskeletal pain diagnoses three decades later. *Pain*. 2010 Sep;150(3):414-9.
- II. Timpka S, Petersson IF, Rylance R, Kedza L, Englund M. Performance in physical education and health impairment 30 years later--a community based cohort study. *PLOS One*. 2012;7(4):e35718.
- III. Timpka S, Petersson IF, Zhou C, Englund M. Muscle strength in adolescent men and future musculoskeletal pain: a cohort study with 17 years of follow-up. *BMJ Open* 2013;3(5).
- IV. Timpka S, Petersson IF, Zhou C, Englund M. Muscle strength in young men and later risk of ischemic cardiovascular disease and mortality: a prospective cohort study (*Submitted*)

Paper I is reprinted with permission from Elsevier.

## Thesis at a Glance (Popularized Q&A)

### Paper I

**Q:** *Is PE performance associated with later conditions in the musculoskeletal system?*

**&**

**A:** Yes, in women. A low PE performance was associated with having a musculoskeletal condition in middle age, especially unspecific soft tissue pain.

I followed 2,225 students (48.4% women) for 30 years. I identified individuals with a diagnosis of interest using a health care register and adjusted the results for occupation and education.

### Paper II

**Q:** *Is PE performance associated with adult health impairment?*

**&**

**A:** Yes, in women. A low PE performance was associated with more days with sick leave compensation and visits to physicians in primary care.

I followed 2,225 students (48.4% women) for 30 years. I used health care contacts and data on sick leave compensation to identify individuals with health impairment and adjusted the results for occupation and education.

PE = Physical education

**Paper III**

**Q:** *Is low muscle strength in young men a risk factor for later pain in muscles, tissues, or joints?*  
&

**A:** No. Contrarily, men with low muscle strength had decreased risk of pain.

I followed 5,489 Swedish men, typically aged 18 when performing muscle strength test at conscription, for (mean) 17 years. For data on adult pain, I used answers from a population survey. I adjusted the results for factors such as physical activity and smoking.

**Paper IV**

**Q:** *Is muscle strength in young men associated with later heart and vascular disease?*  
&

**A:** Yes, probably independently of general fitness.

I studied 38,588 Swedish men, typically aged 18, whom had tested their muscle strength during conscription. For follow-up in middle age, I used data on hospitalizations and cause of death and adjusted the results for common risk factors including smoking and general fitness.



## Description of Contributions

### Paper I

Study design: Simon Timpka  
Ingemar Petersson  
Martin Englund  
Data collection: Simon Timpka  
Data analysis: Simon Timpka  
Martin Englund  
Writing: Simon Timpka  
Martin Englund  
Ingemar Petersson

### Paper III

Study design: Simon Timpka  
Martin Englund  
Ingemar Petersson  
Caddie Zhou  
Data collection: Simon Timpka  
Data analysis: Caddie Zhou  
Simon Timpka  
Writing: Simon Timpka  
Martin Englund  
Ingemar Petersson  
Caddie Zhou

### Paper II

Study design: Simon Timpka  
Martin Englund  
Ingemar Petersson  
Data collection: Simon Timpka  
Data analysis: Rebecca Rylance  
Ljuba Kedza  
Writing: Simon Timpka  
Martin Englund  
Ingemar Petersson  
Rebecca Rylance  
Ljuba Kedza

### Paper IV

Study design: Simon Timpka  
Martin Englund  
Ingemar Petersson  
Data collection: Simon Timpka  
Data analysis: Caddie Zhou  
Simon Timpka  
Writing: Simon Timpka  
Martin Englund  
Ingemar Petersson  
Caddie Zhou

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## Abbreviations

<b>BMI</b>	Body mass index
<b>CI</b>	Confidence interval
<b>CVD</b>	Cardiovascular disease
<b>HEPA</b>	Health enhancing physical activity
<b>HR</b>	Hazard ratio
<b>ICD</b>	International Classification of Disease
<b>IQ</b>	Intelligence quotient
<b>IRR</b>	Incidence rate ratio
<b>ISCO</b>	International Classification of Occupations
<b>MET</b>	Metabolic equivalent
<b>MHR</b>	Maximal heart rate
<b>MSDs</b>	Musculoskeletal disorders
<b>SHR</b>	Skåne Health Care Register
<b>OA</b>	Osteoarthritis
<b>OR</b>	Odds ratio
<b>PE</b>	Physical Education (in school)
<b>RR</b>	Relative risk
<b>SD</b>	Standard deviation
<b>WHO</b>	World Health Organization

# Introduction

## Rationale of the thesis

In the four studies constituting this thesis, I primarily investigate factors in adolescence and their association with later morbidity. In adolescence, I focus on the performance in Physical Education (PE) and muscle strength. In the adult follow-up, the outcomes in focus are musculoskeletal disorders and cardiovascular disease (CVD), both being prevalent causes of disability and death.<sup>1</sup> Throughout my investigations (papers I-IV), I have used retrospective study designs to follow large cohorts over decades. However, all outcome data has been prospectively collected in different comprehensive registers. In the following sections, I will introduce the context and concepts of this thesis. However, I will first briefly outline the rationale of my research; why investigate the association of PE performance and muscle strength in youth with later morbidity?

One of the main goals of PE is to provide a basis for a future healthy lifestyle.<sup>2</sup> However, although physical activity is known to be beneficial for health<sup>3</sup> and physical fitness is a predictor of later mortality in adults,<sup>4</sup> little is known about how the actual PE performance in school is associated with later disease and health impairment.<sup>5</sup> Thus, my main focus in paper I and II has not been the physical capacity or physical activity of the students but rather the PE performance as such. However, physical capacity, or more precisely muscle strength, is in focus for papers III and IV.

Musculoskeletal and cardiorespiratory fitness are two main aspects of physical capacity (also called physical fitness),<sup>6</sup> the ability to perform physical tasks (Figure 1). Whereas cardiorespiratory fitness is a well established predictor of CVD morbidity,<sup>7</sup> low muscle fitness measured as muscle strength, is associated with early mortality and low health in older populations.<sup>8,9</sup> However, compared to cardiorespiratory fitness, musculoskeletal fitness has been much less investigated in terms of being a determinant

of future health in children.<sup>10</sup> Arguably, this may be attributed to the cardiorespiratory fitness being a proxy of the state of the cardiovascular system and simultaneously the presence, or proneness of, CVD. However, the long term benefits of high muscle fitness has received increased interest over the last decade, both due to the muscles as a metabolic hub<sup>11</sup> and as a complementary aspect of physical capacity with lasting implications on mortality risk.<sup>12</sup> In papers III and IV, it has been my intention to further elucidate these previous investigations by studying the long term associations of isometric muscle strength in adolescent men.

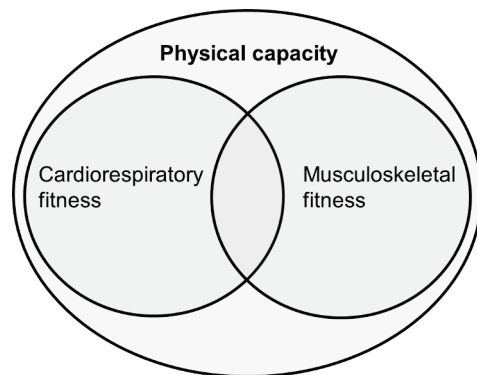


Figure 1. A simplified model of physical capacity.

## The childhood experience - a foundation of adult health?

During the past decades, it has become evident that the health of the mother and the immediate environment during pregnancy have implications for the disease risk of the fetus as an adult.<sup>13,14</sup> When investigating childhood circumstances, it is evident that both the economic strength of the parents and the child's own health have lasting effects on later health in adulthood.<sup>15</sup> Other examples with effects, or at least associations, over decades include IQ early in life<sup>16,17</sup> and

body mass index (BMI),<sup>18</sup> both being predictors of later mortality. Although BMI during childhood has implications for the adult health, the recurring reports of prevalent child obesity<sup>19-21</sup> and physical inactivity<sup>22,23</sup> have put focus on the more immediate positive effects of physical activity on the health of children.<sup>24-26</sup> However, when investigating the effects of physical capacity in youth, most studies focus on risk factors of disease, such as cholesterol levels or adiposity, rather than the morbidity as such.<sup>10</sup> This can probably be attributed to the long follow-up time required to study actual disease.

Whereas adolescence is defined as the period spanning from 10 to 19 years by WHO,<sup>27</sup> middle age can be broadly defined as the part of adulthood prior to old age. It is generally regarded to start around 40 years of age and end at 65 years of age. During this period in life, both sexes are subjected to changes in physiology that affect the future health. In women, the menopause induces hormonal changes that have direct impact on the spectrum of diseases, early onset in associated with increased morbidity and mortality risk.<sup>28</sup> In men, the decrease of sex hormones during middle age is more gradual but may still play a role in the development of obesity and CVD.<sup>29,30</sup> As levels of estrogens and androgens start to decline, middle age is also the period in life when the prevalence of conditions mostly associated with older age groups starts to increase. To name a few examples, both sarcopenia<sup>31,32</sup> and osteoporosis<sup>33</sup> increase in prevalence before the age of 65 years whereas neuromuscular control is decreasing by middle age when compared to younger adults.<sup>34</sup>

Around the world, infections and birth related complications are the most common causes of death in young children.<sup>35</sup> Thus, the challenges of primary prevention directed towards children can differ greatly depending on the setting. In some less developed countries, providing access to food support, clean drinking water, and vaccinations might be vital for the children to survive their first years. However, in many industrialized countries it is not the shortage of food and physical rest that causes adverse health outcomes, that the quite opposite situation exists is well known. Obesity is potentially not only a serious threat to the health and well-being of the

child as an adult, but also has adverse short term effects.<sup>36</sup> However, to improve the health of a population it is particularly important to target subgroups with increased risk of disease, e.g. musculoskeletal disease, as these individuals have most to gain.<sup>37</sup> In theory, early intervention as primary prevention is also important as causal chains, i.e. the chain of events eventually resulting in the outcome, can be broken early or the onset of disease substantially delayed. In summary, a successful intervention should start early, include individuals with relatively high risk, and be suitable for the predefined goals. In the 1960's, a national system with future health as one of the main focuses was introduced in Sweden; the modern form of PE in compulsory school.

### **Physical Education in schools - objective and history**

Currently, PE is a mandatory part of the compulsory education in many countries including Sweden, whereas in other parts of the western hemisphere, such as North America, enrollment decline with age and is associated with ethnicity and socioeconomic group.<sup>2,38</sup> Interventions of increased or modified PE in the school setting have been reported to reduce adiposity<sup>39</sup> and increase future physical activity in women.<sup>40</sup> However, there is very limited evidence of actual long-term effects of PE on health impairment by middle age, probably due to the long follow-up required.<sup>5</sup> In terms of enhancing future physical activity, PE is generally considered to mediate a carry-over effect by engaging students in sports and physical activity throughout childhood and adolescence.<sup>2,41</sup> Engström<sup>42</sup> has extended this view and uses the term "habitus" - originally suggested by the French sociologist Pierre Bourdieu when describing cultural capital - in a framework for the carry-over effects of physical activity. In summary, by creating habits of activity and a self-imagery of being active during childhood, adequate levels of physical activity would then be more likely to continue into adulthood.

In Sweden, PE took its modern form in the beginning of the 1960s.<sup>43</sup> Historically, physical activity has been a part of the curriculum since

the implementation of primary school in 1842.<sup>44</sup> However, throughout the 19th century, focus was on exercises according to a system developed by Per Henrik Ling. Ling developed a system of movements that were supposed to foster the youth while also preparing the boys for military service. Although the militaristic elements of physical activity in school decreased during the first half of the 20th century, many of the fostering aspects remained. Implemented simultaneously as a unified educational system, the reform of PE in the 1960s stated that all students should participate in scheduled physical activity with focus on present and future physical activity and health.<sup>45</sup> In the curriculum used during the 1970s, the allocated time of PE in the curriculum was three lessons of 40 minutes per week for students aged 13-16 years. Although uncommon in Sweden today, girls and boys were recommended to be taught separately at the time.<sup>43</sup> Preadolescent students of both sexes were in general considered to benefit from the same types of physical activity. However, by puberty it was recommended that the teacher adapted the lessons to better accommodate an assumed sex-specific need of activity. Teenage girls were recommended esthetic features and gymnastics, whereas the education for boys were more focused on ball sports and strength. However, a main goal of PE was to ensure that each student would have the opportunity to try various forms of physical activity; it was only the main focus that should differ. Each student should have had the opportunity to try each recommended activity every second semester. These activities included, but were not strictly limited to the following: gymnastics, dancing, ball sports, athletics, orienteering, skating, skiing, and swimming. Later on, in the early 1980s, a new curriculum underlined the importance of health and recommended boys and girls to be taught together.<sup>43</sup>

In the first part of this thesis (paper I and II) I use PE grades given during the 1970s. At the time, a relative grade scale based on a theoretical normal distribution was used. Thus, the students were measured by their relative abilities (i.e. theoretically to the whole body of students in the same grade on a national level) and not by their absolute abilities. A similar rationale has since

been applied to the European Credit Transfer and Accumulation System (ECTS) of the European Union.<sup>46</sup> The percentage of students given each grade was ideally 7-24-38-24-7 (grade 1-5), but the proportions were allowed to differ locally depending on the characteristics of the students in each class.

### **Musculoskeletal disorders, cardiovascular disease, and muscle strength**

Musculoskeletal disorders (MSDs) are common in the general population, with about 20% experiencing the most prevalent complaint, musculoskeletal pain. However, it has been reported that up to 40% of the working-age population experience chronic pain.<sup>47-48</sup> Moreover, MSDs also contribute to a substantial burden of disease from middle age and onwards<sup>1</sup> while musculoskeletal pain also is associated with low health status.<sup>49</sup> Although pain emanating from the musculoskeletal system might be attributed to a wide range of diseases with diverse causal chains, many MSDs have common risk factors such as heavy occupational work load,<sup>50-51</sup> a high BMI,<sup>52-54</sup> and a low socio-economy.<sup>55-57</sup> Although smoking in some studies have been identified as a risk factor for certain MSDs,<sup>58-59</sup> its main effect on musculoskeletal pain might be as an effect modifier of the pain sensation.<sup>60</sup> As physical work load is a risk factor for many MSDs,<sup>61</sup> a model in which muscle strength in the loaded parts of the body are protective for future disorders is appealing. Furthermore, physical exercise with focus on muscle strength is an important secondary and tertiary prevention of MSDs.<sup>62-63</sup> Moreover, the promotion and effect of Health-enhancing physical activity (HEPA),<sup>64</sup> i.e. recommended levels of physical activity, is currently being investigated in patients with rheumatoid arthritis.<sup>65</sup> A handful of studies have hitherto longitudinally investigated the strength of isolated muscle groups in adulthood as a determinant of later MSDs.<sup>66-69</sup> However, in adult subjects, there is for the time being conflicting evidence of the value of muscle strength as a protective factor of musculoskeletal pain, such as neck/shoulder pain and low back pain.<sup>66</sup>

To design proper strategies of primary prevention, the association between the outcome and potential causal factors in youth is of high relevance. However, when focusing on the association between muscle strength in youth and later musculoskeletal disorders, relatively little is known.<sup>10</sup> Two studies have investigated the result of single muscle strength tests as determinants of musculoskeletal complaints decades later.<sup>70 71</sup> The first, using number of sit-ups during 30 seconds as a strength measure, found no association with later low back pain or tension neck in men. In women, the high strength group had a decreased odds ratio (OR) of tension neck.<sup>70</sup> The second study found a decreased OR for MSDs in men who either had a strong performance in isotonic bench press or in an isometric two hand lift test.<sup>71</sup> Neither of the two studies includes a measure of overall muscular capacity. In summary, although there is some evidence of an association between low muscle strength in youth and later risk of MSDs, the association between general muscle strength in adolescence and later musculoskeletal pain has not been studied.

A common concern in the field of musculoskeletal pain research is how complaints are divergently defined, reported, and categorized.<sup>72</sup> Therefore, the reported prevalence may vary from study to study depending on the method used. As stated above, the most common self-reported disorders of the musculoskeletal system are low back pain and pain in the neck and shoulders, with prevalence around 20% in the general population, corresponding numbers in the age group 45-64 years being somewhat higher.<sup>48 73</sup> Furthermore, osteoarthritis (OA), affecting mainly hands, hips and knees, is common in the elderly, especially in women.<sup>74</sup> In the middle age however, the overall prevalence of self reported OA is between 5-7% for hip, hand and knee OA.<sup>75</sup>

As described in the introductory section, physical capacity can be regarded as having two main components; cardiorespiratory fitness and muscles strength. When measuring cardiorespiratory, or cardio-pulmonary, fitness in the laboratory setting the gold standard is peak oxygen uptake.<sup>76</sup> However, there is also a plethora of field testing tests with strengths and weaknesses.

Describing the different forms of cardiorespiratory testing is out of scope for this introduction. In short, the more muscle strength involved in the testing procedure, the less accurate proxy of cardiorespiratory fitness is acquired.<sup>76</sup> Low cardiorespiratory fitness is an established risk factor for CVD morbidity,<sup>7</sup> and cardiorespiratory fitness can be regarded as a central node when predicting CVD. However, there is increasing evidence that muscle strength also is inversely associated with all-cause mortality in adults, independently of cardiorespiratory fitness.<sup>12 77</sup> It has also been suggested that low muscle strength in adolescent men increases the risk for future CVD, CVD mortality, and all-cause mortality.<sup>78</sup><sup>79</sup> Though the studies do not include data on neither cardiorespiratory fitness nor smoking, they include >1 million men and follow the mean participant from adolescence until his early 40s. Moreover, muscle fitness may predict future morbidity, including CVD, throughout adulthood.<sup>11 80 81</sup>

Apart from being associated with cardiorespiratory fitness, the effects of muscle strength on future CVD risk might be mediated by, or effect modified, by other factors such as physical activity, muscle mass, or genetics.<sup>11 80 82-84</sup> However, there are studies that suggest a direct linkage between muscle strength and cardiovascular risk factors, such as arterial stiffness and long term weight gain.<sup>85 86</sup>

### **Cohort studies using Swedish registers: the personal identification number is the key**

In contrast with many other countries, every individual living officially in Sweden for longer periods gets a personal identification number assigned.<sup>87</sup> The number is unique and frequently used in contact with authorities, banks, and the healthcare system. For research purposes, the number can be used to link register entries after approval from an ethical review board. In this thesis, data from a number of different registers is used, all linked via the personal identification number. Below, I give a brief overview of the registers I have used for my investigations. For a few variables of particular interest for this thesis, such as measurement of muscle strength in the

Swedish conscription register, I make a more in-depth description.

### *Healthcare, cause of death and sick leave*

The National Board of Health and Welfare (Socialstyrelsen) has been authorized to collect and manage a number of Swedish registers on a national level. Examples include the Cause of Death Register, in which the diagnoses from the death certificate are registered, and the National in-patient register. With few exceptions, a single payer health care system is implemented in Sweden. Although private health care providers exist, particularly in primary care, a great majority of patients pay a heavily subsidized fee for each health care visit, independently of provider. Some regional health care registers have more extensive data than what is available on a national level. For this thesis, I have used health care data on both the national (paper IV) and on the regional level (papers I and II). For the studies using regional data, I have used the comprehensive Skåne Health Care Register (SHR), covering both in-patient and out-patient care, including primary care, in Sweden's southernmost region. Although the register contains data on all visits to a publicly funded health care provider, the register only contained diagnoses on visits made to the public providers at the time of study.

For paper II, I have used data on sick leave compensation. This type of data is held by The Swedish National Insurance Agency (Försäkringskassan) in a national register of sick leave compensation. In Sweden, the employer pays the first two weeks of an employee's sick leave, excluding the first day of absenteeism for which no compensation is given. Hence, sick leave of short duration for employees ( $\leq 14$  days), is not included in the data. However, students, self-employed, and unemployed are generally qualified from day two. A certificate from a physician is mandatory for future compensation from day eight.

### *The Swedish conscription register*

In paper III and IV, I have used data from the Swedish conscription register. The register is well characterized and has been used for research purposes previously, the referenced stud-

ies only being a minor selection.<sup>88-90</sup> Until 2010, conscription was mandatory by law for all Swedish men, a basis for the continuous collection of data performed over decades. During the period relevant for this thesis (1969-1994), only men with serious health complaints were excused from conscription. In 1969, a centralized system to test tens of thousands of men each year was implemented, having been developed during the decade prior.<sup>91</sup> During a two-day session, specially trained employees at six regional conscription offices administrated the tests that also included separate evaluations by a medical doctor and a psychologist. The conscripts' weight was measured in underwear to the kilogram whereas height was measured without shoes to the centimeter. Blood pressure was measured manually with a sphygmomanometer.

During conscription, the physical capacity of the men was evaluated with tests of muscle strength and work capacity. The testing of isometric muscle strength was mainly based on the investigations by Tornvall,<sup>92</sup> who tested a range of muscle groups to identify those with high correlation with general, i.e. the total body, muscle strength. During conscription, three tests of muscle strength were performed; hand grip, elbow flexion, and knee extension. At the start of test period in 1969, the tests of muscle strength were performed as previously described<sup>93</sup> (Nordesjö, Lars-Olof, Personal communication, December 19, 2012) and remained unchanged in general until 1994. In summary, hand grip was measured with a 90° flexion at the elbow with the humerus in parallel to the torso. Knee extension was measured in a sitting position with 90° knee flexion and arms crossed over chest. The pelvis was fixed to the seat and a strap fastened above the lateral malleolus. Also, elbow flexion was measured in a sitting position with 90° flexion at the elbow and the humerus in parallel to the torso. A strap was fastened at the level of the radial styloid process.

In 1969, most conscripts performed a maximal work test ( $W_{max6}$ ) on a cycle ergometer.<sup>92-94</sup> The test has been reported to be well correlated with  $V_{O2max}$  in young male students ( $r=0.9$ ).<sup>95-96</sup> Each subject started on the same load (230 W) and worked until exhaustion or the prescribed pedaling rate (60 rotations/minute) could not be

upheld. For a minority still working at 12 minutes, further increments of 30 W were made every 6 minutes. Due to change of testing method to a more frequent stepwise increase of load in 1984, comparison of work capacity past and prior this year is associated with difficulty. For a minority of conscripts, for which a maximal test was assessed as inappropriate due to disease or disability, a sub-maximal test was used.

### *The registers of Statistics Sweden*

Statistics Sweden (Statistiska centralbyrån) is a Swedish government agency with ancestry. With predecessor "Tabellkommissionen" established in 1756,<sup>97</sup> its current function is to produce and provide information on demography, economy, and attitudes of the Swedish population. Introduced in the 1970s, the Swedish Living Conditions Surveys are performed by Statistics Sweden to measure habits, attitudes, and health of a

general population sample of Swedes and have previously been used for research purposes.<sup>98-100</sup> In paper III, I use questions on musculoskeletal pain and habits from this survey. During the time period relevant for this thesis (1980 to 2005), the surveys were generally performed as interviews in person by trained interviewers, with a minority of the interviews being performed by phone.

Statistics Sweden also holds registry data on family relations in a multi-generation register, making connections between relatives possible. Such possibilities include connections of registry entries on migration, marital status, and population surveys of relatives. Other registers administered by Statistics Sweden include the Occupational Register (Yrkesregistret), which holds data on attained level of education and also present occupation according to the International Classification of Occupations (ISCO).



## Aims

### **General aim**

To study the long term associations of general muscle strength and PE performance with adult morbidity.

### **Specific aims**

To investigate the association between PE performance in adolescence and musculoskeletal disorders in adulthood.

To investigate the association between PE performance in adolescence and health impairment in adulthood.

To investigate general muscle strength in adolescent men as a risk factor for later musculoskeletal pain.

To investigate general muscle strength in adolescent men as a risk factor for later ischemic CVD and mortality.

## Methods and Results

### Ethical considerations

All studies included in this thesis were approved by the Ethical Review Board of Lund University (2008/514, 2011/500).

### Is adolescent PE performance associated with musculoskeletal disorders in middle age? (I)

#### Subjects

I included all students (typically aged 16 years) whom completed nine years of compulsory education from 1974 to 1976 in the municipality of Lund (total population in 1975: 76,284) in southern Sweden. Students were born from 1957 to 1962 with 97.5% born between 1958 and 1960. In total, I identified 2,335 students from the hand-written municipal archive of whom 2,225 (95.3%) had a PE grade and a valid 10-digit personal identification number (Figure 2). 48.4% were women (Table 1).

#### Methods

Using the five item PE grade scale, I categorized subjects into three groups; low (grades 1 and 2), average (3), and high (4 and 5) PE performance. I ensured via the National Population Register that subjects were still alive and resident in the county in the period from 2003 to 2007, and used the SHR to identify health care contacts. All in- and outpatient clinic visits from 2003 to 2007 with a musculoskeletal condition as a main diagnosis were identified. The diagnoses were registered as a code according to the Swedish version of the World Health Organization's (WHO) International Classification of Disease (ICD) version 10.

I also retrieved data from Statistics Sweden, including income 2006, the highest level of education achieved, and occupation according to the Swedish three digit version of ISCO version 1988. The level of education was divided into four groups (9 years of compulsory school or less, 10-12 years, 13-15 years, >15 years).

PIN = Personal identification number  
PE = Physical Education

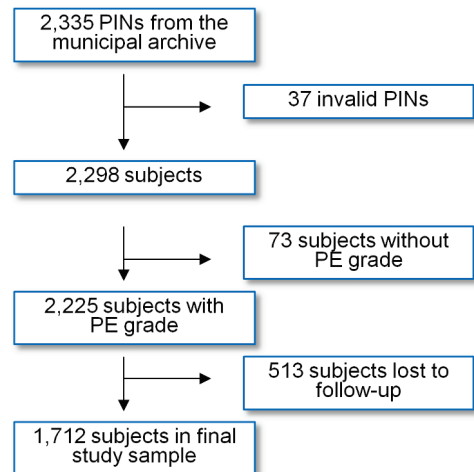


Figure 2. Flowchart detailing the identification of the study sample and loss to follow-up.

Occupation was also divided into four groups with a blue collar/white collar approach based on the major groups of the ISCO classification.

The outcomes were to have been diagnosed with any of the diagnoses of my focus during 2003 to 2007, when the study subjects were typically aged 42 to 49 years. I studied “Diseases of the musculoskeletal system and connective tissue” (ICD-10 chapter XIII, code M) and focused on three types of disorders; soft tissue pain, back pain, and knee OA. Thus, I investigated three chapter subgroups; “Arthropathies” (M00-M25), “Dorsopathies” (M40-M54) and “Soft tissue disorders” (M60-M79). Each chapter subgroup contains a second level of subgroups of which I investigated three additional groups; “Arthrosis” (M15-M19), “Other dorsopathies” (M50-M54) and “Other soft tissue disorders” (M70-M79). Moreover, on a specific diagnostic level I investigated the knee OA (M17), back pain (M54) and chronic pain (Other tissue disorders, M79) subgroups. In “Other soft tissue disorders” however, “Other

**Table 1. Descriptive statistics of the study sample and the loss to follow-up (paper I and II)**

	Women		Men	
	Study sample	Loss to follow-up	Study Sample	Loss to follow-up
Number of subjects	835	241 (22.4 %)	877	272 (23.7 %)
Age at end of follow up (SD)	48.0 (0.9)	48.0 (0.9)	48.0 (0.9)	48.0 (0.9)
PE grade (%)				
Low	186 (22.3)	39 (16.2)	252 (28.7)	60 (22.1)
Average	333 (39.9)	85 (35.3)	321 (36.6)	107 (39.3)
High	316 (37.8)	117 (48.5)	304 (34.7)	105 (38.6)
Education (%)				
9 years or less	90 (10.8)	6 (2.5)	151 (17.2)	10 (3.7)
10-12 years	337 (40.4)	41 (17.0)	406 (46.3)	53 (19.5)
13-15 years	299 (35.8)	73 (30.3)	208 (23.7)	57 (21.0)
16+ years	109 (13.1)	60 (24.9)	112 (12.8)	75 (27.6)
Not registered (i.e. at least 9 years)	-	61 (25.3)	-	77 (28.3)
Occupation (%)				
Upper white collar	35 (4.2)	10 (4.1)	91 (10.4)	33 (12.1)
Lower white collar	376 (45.0)	118 (49.0)	345 (39.3)	109 (40.1)
Clerks	285 (34.1)	28 (11.6)	96 (10.9)	13 (4.8)
Blue collar	78 (9.3)	7 (2.9)	255 (29.1)	18 (6.6)
Not registered	61 (7.3)	78 (32.4)	90 (10.3)	99 (36.4)

PE = Physical Education

Enthesopathies” (M77) was also investigated due to a high prevalence. Starting with a crude analysis of relative risks (RR), I also estimated odds ratios (OR) adjusted for level of education and occupation using logistic regression. All statistical analyses were made in SPSS for Windows version 15.0 (IBM Corporation).

### Results

In the crude analysis I found an increased relative risk (RR) in women with a low PE grade to develop musculoskeletal disorders RR=1.4 (95% CI=1.1-1.8), but not for men (0.90, 0.69-1.2). Furthermore, women with a low PE grade had higher RR of several outcomes including “Dorsopathies” (1.7, 1.1-2.7), “Back pain” (1.7, 1.0-2.9), and “Other soft tissue disorders, not classified elsewhere” (2.3, 1.4-3.6). Men with a high grade in PE had a reduced risk of “Other soft tissue disorders” (0.62, 0.43-0.89), and in particular “Other entesopathies” (0.33, 0.13-0.82).

In the multivariate model, the association between a low PE grade and having a musculo-

skeletal diagnosis in women remained, including the subgroups “Dorsopathies”, “Soft tissue disorders”, “Other soft tissue disorders”, and “Other soft tissue disorders, not elsewhere classified” (Table 2). In men, a high PE grade was associated with a reduced likelihood of “Soft tissue disorders”, “Other soft tissue disorders, not elsewhere classified”, and “Other enthesopathies”.

By PE grade group in women, the proportion of visits with a confirmed diagnosis in public primary care ranged from 0.83 (average grade) to 0.85 (high grade). In men, the same proportions ranged from 0.83 (high grade) to 0.86 (average grade). Of the total number of visits made to a physician in primary care, 64.3% of the visits made by women with a low PE grade were assigned a diagnosis in the SHR while 58.4% of the visits made by women with an average grade were assigned a diagnosis ( $p=0.005$  for difference). 52.7% of visits made by men with an average PE grade had a diagnosis registered while the corresponding numbers for men with a high PE grade were 54.4%

**Table 2. Adjusted ORs for musculoskeletal diagnoses in middle age by PE performance in adolescence**

Diagnosis (ICD-10)	Women		Men	
	Low grade	High grade	Low grade	High grade
	OR <sup>a, b</sup> (95% CI)	OR <sup>a, b</sup> (95% CI)	OR <sup>a, b</sup> (95% CI)	OR <sup>a, b</sup> (95% CI)
Musculoskeletal disorders	<b>1.5</b> (1.0-2.2)	1.1 (0.80-1.6)	0.74 (0.50-1.1)	0.85 (0.59-1.2)
Arthropathies	1.1 (0.63-1.9)	0.79 (0.48-1.3)	0.74 (0.38-1.4)	1.6 (0.90-2.7)
Arthrosis	2.4 (0.90-6.4)	0.36 (0.09-1.4)	0.60 (0.15-2.5)	1.9 (0.69-5.5)
Gonarthrosis	2.2 (0.62-7.8)	0.37 (0.07-2.0)	0.60 (0.11-3.4)	1.7 (0.48-6.3)
Dorsopathies	<b>1.8</b> (1.0-3.2)	0.88 (0.50-1.5)	0.92 (0.51-1.7)	0.84 (0.46-1.5)
Other dorsopathies	1.7 (0.96-3.0)	0.83 (0.46-1.5)	0.80 (0.43-1.5)	0.83 (0.45- 1.5)
Back pain	1.7 (0.97-3.1)	0.73 (0.39-1.4)	0.82 (0.43-1.6)	0.73 (0.38- 1.4)
Soft tissue disorders	1.7 (1.0-2.6)	1.2 (0.81-1.9)	0.63 (0.39-1.0)	<b>0.54</b> (0.33-0.86)
Other soft tissue disorders	1.6 (0.99-2.6)	1.3 (0.85-2.0)	0.63 (0.39-1.0)	<b>0.56</b> (0.35-0.92)
Other enthesopathies	1.5 (0.71-3.0)	1.2 (0.62-2.4)	0.91 (0.44-1.9)	<b>0.29</b> (0.11-0.78)
Other soft tissue disorders	<b>1.9</b> (1.0-3.3)	1.3 (0.72-2.2)	0.77 (0.38-1.5)	0.90 (0.47-1.7)

95% CI = 95% confidence interval, OR = Odds ratio, PE = Physical education, ICD-10 = International Classification of Disease version 10  
 Results in bold if p<0.05  
<sup>a</sup> All ORs compared to an average grade  
<sup>b</sup> Adjusted for education and occupation

(p=0.41 for difference). Of all visits made to a physician, 35.7% were to a private health care provider. However, 31.4% of those who had visited a private primary care physician during the study period had also received a musculoskeletal diagnosis by a public health care provider.

## Is adolescent PE performance associated with health impairment in middle age? (II)

### Subjects

2,225 students as described in paper I (Figure 2, Table 1).

### Method

I categorized the PE performance into three groups as described for paper I. I ensured via the National Population Register that the subjects were still alive and residing in the county of Skåne from 2003 to 2007. Using the SHR, I then identified all hospitalizations and visits to physicians in primary health care for the time period. I also collected the number of days with sick leave

compensation from 2004 to 2007 from the National Social Insurance Agency. Furthermore, I also retrieved data on attained education and occupation from Statistics Sweden.

All statistical analyses were made in STATA v. 11.0 (Statacorp inc.). For physician visits in primary care and number of days with sick leave, I used a negative binomial regression model to calculate unadjusted and adjusted sex specific incidence rate ratios (IRR). For inpatient care I used a dichotomous outcome (having been hospitalized/not hospitalized) in log binomial regression models to estimate relative risks (RRs). PE performance was categorized as in paper I with an average grade serving as reference. As also described for paper I, education and occupation were categorized into four groups, respectively, and included in all multivariate models.

As a first sensitivity analysis, I investigated the confounding effect of general academic performance in adolescence on the adjusted model. In the two subjects Mathematics and English, each student took either the general or the special course. I grouped academic performance into three categories; low (those who

**Table 3. Risk estimates for proxies of health impairment by performance in Physical Education**

Outcome	Women		Men	
	Low grade IRR <sup>a, b</sup> (95% CI)	High grade IRR <sup>a, b</sup> (95% CI)	Low grade IRR <sup>a, b</sup> (95% CI)	High grade IRR <sup>a, b</sup> (95% CI)
Visits to GPs <sup>c</sup>	<b>1.30</b> (1.06-1.60)	1.06 (0.89-1.26)	1.14 (0.93-1.40)	0.90 (0.75-1.09)
Sick leave	<b>1.44</b> (1.05-1.95)	0.86 (0.64-1.15)	1.06 (0.73-1.53)	1.06 (0.73-1.52)
Hospitalization	RR <sup>a, b</sup> (95% CI) 1.26 (0.88-1.80)	RR <sup>a, b</sup> (95% CI) 0.79 (0.55-1.12)	RR <sup>a, b</sup> (95% CI) 0.70 (0.44-1.10)	RR <sup>a, b</sup> (95% CI) 1.11 (0.76-1.61)

95% CI = 95% confidence interval, GP = General Practitioner, IRR = Incidence rate ratio, RR = Relative risk  
 Results in bold if p<0.05  
<sup>a</sup> Compared to an average grade  
<sup>b</sup> Adjusted for education and occupation  
<sup>c</sup> Visits to physicians in primary care

either had not taken any special course or received a grade lower than 2 when doing so), average (those who had received a grade of at least 2 in one of the special courses), and high (those who had received a grade of at least 2 in both courses).

As a second sensitivity analysis, investigating whether employment status introduced bias on the risk estimate of sick leave, I excluded individuals with no formal employment in 2006 from the main model.

### Results

Women with a low grade in PE had more physician visits in primary care as well as more days with sick leave when I adjusted for education and occupation (Table 3). A similar, although not significant, risk increase was also observed for in-patient care. However, no correspondent pattern was observed in men. High grade in PE in men and women was neither associated with increased nor decreased risk for health impairment. In the crude analysis, most risks were similar to the adjusted models (data not shown). However, men with low grade had increased IRR for sick leave compensation (1.34, 0.95-1.90) which was attenuated in the adjusted model. Compared to the study sample, subjects lost to follow-up tended to have a higher grade in PE and a higher level of education (Table 1). The sensitivity analysis of academic performance resulted only in minor risk adjustments towards one. The largest difference was observed for number of days with sick leave in women with

low PE performance (sensitivity IRR 1.37, 1.00-1.87 vs. adjusted IRR 1.44, 1.05-1.95).

The sensitivity analysis for risk of sick leave (excluding 195 individuals) showed very little effect of employment status, leaving IRRs, for all groups but women with a low PE grade, unaffected or adjusted towards 1 (data not shown). The difference was also small also in women with a low PE grade. However, the association was strengthened somewhat (IRR 1.51, 1.09-2.09) compared to the main model.

### Is adolescent muscle strength associated with later risk of musculoskeletal pain in men? (III)

#### Subjects

The study cohort included 5,489 men (Figure 3, Table 4). I used two main criteria to identify the study cohort. First, the men should have performed mandatory conscription testing in Sweden between 1970 and 1994, with the exception of the years 1978 and 1985. Secondly, they should have been included in the Swedish Living Conditions Surveys any year between 1980 and 2005 when questions regarding musculoskeletal problems, smoking status, and physical activity were simultaneously included. Furthermore, I excluded all men who were surveyed prior to the baseline testing or were younger than 17 years or older than 19 years at baseline. I also excluded men with an existing musculoskeletal diagnosis and those who had missing data on variables included in the primary model (muscle

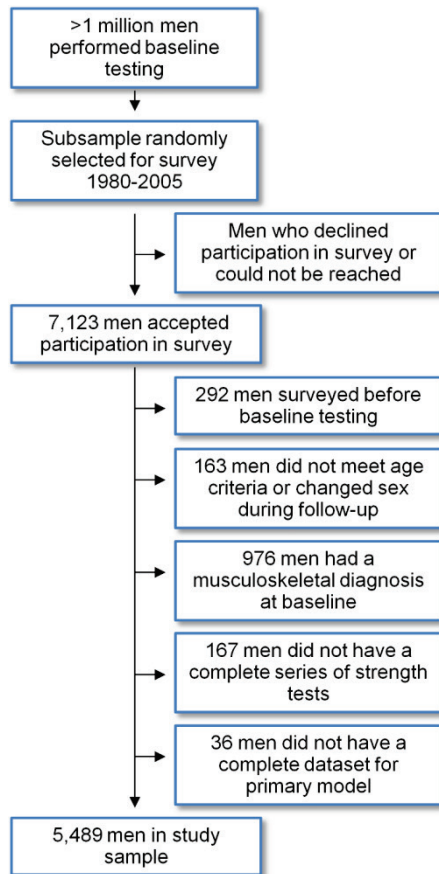


Figure 3. The identification of the study sample and the loss to follow-up.

strength, smoking, BMI, physical activity, level of education). Probably due to rare errors of data entry, there are unlikely extreme values in the conscription data. Therefore, I excluded all subjects with registered extreme values on height (<150, >210 cm), weight (<40, >150 kg), or an extreme calculated value for BMI (<15, >60 kg/m<sup>2</sup>).

### Methods

Isometric muscle strength was tested using three different types of tests: elbow flexion, hand grip, and knee extension. For an in-depth description of the procedures, please see the introduction. As a proxy for general muscle strength, I standardized and combined the three tests of muscle strength as follows. First, to avoid bias due to

Table 4. Description of study sample (paper III)

Mean age at baseline (SD)	18.2 (0.5)
BMI (%)	
<18.5	477 (8.7)
18.5-24.9	4,498 (81.9)
25-29.9	448 (8.2)
>30	66 (1.2)
Muscle Strength (%)	
Low	1,371 (25.0)
Average	2,747 (50.0)
High	1,371 (25.0)
Pain in back/hips (%)	
Yes	1,645 (30.0)
of which severe	321 (5.8)
No	3,842 (70.0)
Missing	2 (0.0)
Pain in neck/shoulders (%)	
Yes	1,562 (28.5)
of which severe	246 (4.5)
No	3,925 (71.5)
Missing	2 (0.0)
Pain in arms/legs (%)	
Yes	1,243 (22.6)
of which severe	196 (3.6)
No	4,243 (77.3)
Missing	3 (0.0)
Smoking status (%)	
Yes	827 (15.1)
No	4,662 (84.9)
Level of education (%)	
Compulsory	589 (10.7)
Secondary	2,889 (52.6)
Higher	2,011 (36.6)
Physical Activity (%)	
Practically non	583 (10.6)
Now and then	1,613 (29.4)
Regularly	2,077 (37.8)
Regularly strenuous	1,216 (22.2)

BMI = Body mass index

cohort effects, I categorized the cohort into five subgroups based on period of conscription (1970-1973, 1974-1977, 1979-1984, 1986-1990, 1990-1994) and within each subgroup calculated the relative muscle strength. I then standardized the three tests of muscle strength [standardized value = (value–mean) /standard deviation] within each subgroup and used the mean of the three

**Table 5. Adjusted risk estimates for self-reported musculoskeletal pain in adulthood by muscle strength in adolescent men**

Outcomes	Low muscle strength	High muscle strength
	RR <sup>a</sup> (95% CI)	RR <sup>a</sup> (95% CI)
Musculoskeletal pain	<b>0.93</b> (0.87-0.99)	0.99 (0.93-1.05)
Severe musculoskeletal pain	0.96 (0.79-1.18)	1.07 (0.89-1.29)
Pain in back/hips	0.93 (0.84-1.03)	1.03 (0.94-1.13)
Pain in neck/shoulders	0.93 (0.83-1.03)	1.00 (0.90-1.10)
Pain in arms/legs	0.97 (0.86-1.10)	1.06 (0.94-1.19)

RR= Relative risk, 95% CI= 95% Confidence interval  
 Results in bold if p<0.05  
 Men with average muscle strength serve as reference  
<sup>a</sup> adjusted for smoking status, physical activity, education, body mass index

test scores as a proxy for general muscle strength. I then categorized the cohort into three groups of muscle strength using percentiles; the 25th to 75th percentile defined the average category.

At follow-up, I used data collected during a total of 10 years (1980, 1988, 1989, 1997-1999, 2002-2005) of the Swedish Living Conditions Surveys, a random population based survey conducted by Statistics Sweden. The men were asked three questions regarding any current musculoskeletal pain: 1) Do you have pain in neck or shoulders? 2) Do you have back-pain, hip-pain or sciatica? 3) Do you have ache or pain in hands, elbows, legs or knees? For each type of complaint one of three answers was possible: 1) Yes, severe 2) Yes, mild and 3) No. I defined the primary outcome as having reported either severe or mild musculoskeletal pain, whereas my secondary outcomes were having reported severe or location specific pain. From the surveys, I also included data on self-reported current smoking status (yes/no), physical activity (practically none, now and then, regularly, regularly strenuous), and level of education (compulsory school or less, secondary education, higher education). Drop-outs from the survey, i.e. those who have declined participation, cannot be individually identified. However, on a group level, 11.3-31.0% of the relevant men declined participation in the years of study.

All statistical analyses were made in SAS 9.3 (SAS Institute inc., Cary, NC, USA). I used log binomial regression to estimate relative risks (RR) and control potential confounders. In the

multivariate model (main model), I included muscle strength, BMI, smoking status, physical activity and level of education. As a first sensitivity test, I tested whether cardiorespiratory aspects of physical capacity confounded the results, using physical work capacity measured as  $W_{max}^{92,94}$  as a proxy. Acceptable data quality on work capacity was available in the subsample of men performing the baseline testing in 1976 to 1982. Of all men in the cohort conscripted during the time period, 1,154 men (74.6%) completed a physical work capacity test on a bicycle ergometer deemed acceptable (i.e. heart rate >174 at the end of testing). I added the work capacity in relation to body weight as a continuous variable to a model also adjusted for BMI. Furthermore, I also performed three additional sensitivity analyses on the multivariate model with musculoskeletal pain as the dependent variable. In the first, I added test center to the model. For the second, to test whether my categorization of muscle strength influenced the results, I treated the standardized muscle strength as a continuous variable. For the third test, I treated the standardized muscle strength as a categorical variable based on quintiles in the multivariable model.

### Result

The mean time to follow-up was 17 years. Men with low muscle strength did not have an increased risk, but rather a statistically significant decreased risk, for the primary outcome "Musculoskeletal pain" (Table 5). To summarize the observations of the secondary outcomes, I did

not observe any statistically significant risk estimates for neither men with a low nor high muscle strength. Compared to a crude model only adjusted for BMI, the multivariate model produced similar results (data not shown).

In the sensitivity analyses, work capacity had a significant effect in the subsample analysis ( $p=0.04$ ) whereas it had only minor effect on the risk estimates for musculoskeletal pain, being 0.94 (0.82-1.08) and 1.02 (0.90-1.16) for low and high strength, respectively. The pattern of association in the secondary outcomes were in general somewhat strengthened when I adjusted for work capacity (data not shown). Using muscle strength as a continuous variable (hence assuming a linear relationship) did weaken the association with later musculoskeletal pain ( $p=0.23$ ). When I instead used quintiles to categorize muscle strength, I observed no increased risk for the group with lowest strength compared to average strength (RR=0.93, 95% confidence interval 0.85-1.01).

### Is adolescent muscle strength associated with risk of cardiovascular disease and mortality in middle age? (IV)

#### Subjects

I identified 38,588 Swedish men, typically aged 18 years, whom in 1969 or 1970 performed conscription testing. I used the same definitions for rare extreme values on height, weight and BMI as described in paper III. Moreover, I also excluded men who were younger than 17 years or older than 19 years during conscription (Figure 4, Table 6). To control censoring during follow-up, I used data on emigration and immigration.

#### Methods

As described for paper III, general muscle strength was approximated by standardizing and combining test results of isometric elbow flexion strength, hand grip, and knee extension. Unlike study III however, the strength of each conscript was compared to the whole cohort, irrespectively of year of conscription. For all men living in Sweden January 1, 1991, I collected data from the Swedish inpatient register<sup>101</sup> on hospitalizations with an ischemic CVD diagnosis until

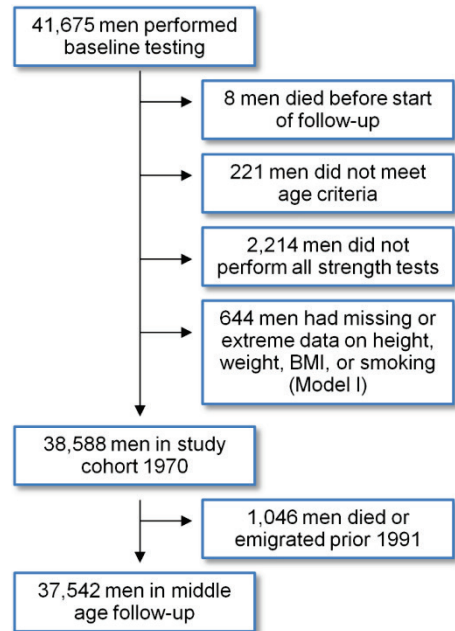


Figure 4. The identification of the study sample.

December 31, 2010. I defined ischemic CVD as coronary heart disease or stroke morbidity (including hemorrhagic stroke but excluding transient ischemic attack). I used diagnoses based on the ICD version 9 (342, 344, 410-414, 430-438) and version 10 (I20-I25, I60-I66).

Starting June 1, 1970, I followed-up on all deaths until August 2, 2012. However, the cause of death registered according to the ICD (versions 8, 9, or 10) was only available until December 31, 2011. Thus, the analyses of all-cause and specific mortality differ somewhat in time to follow-up. For the period 1970 to 2011, I separately identified deaths due to CVD (ICD-8, ICD-9: 390-459 ICD-10: I00-I99). For the period January 1, 1991 to December 31, 2011 (21 calendar years) I also identified deaths due to cancer (ICD-9: 140-239 ICD-10: C00-D48) and suicide (ICD-9: E950-E959, E980-E989 ICD-10: X60-X84, Y10-Y34). All other causes of death were defined as "other causes".

All statistical analyses were made in SAS 9.3 (SAS Institute inc., Cary, NC, USA). I used Cox proportional hazards models to calculate hazard ratios (HR) and control potential confounders. In model I, I adjusted for BMI and



**Table 6. Descriptive statistics of total study sample and the categories of muscle strength (paper IV)**

Characteristics	Cohort (%)	Categories of muscle strength		
		Low (%)	Average (%)	High (%)
Number of men	38,588	9,647	19,294	9,647
Age at start of follow-up	19.0	19.0	19.0	19.0
Mean height in meters $\pm$ SD	178.0 $\pm$ 6.3	176.4 $\pm$ 6.5	178.0 $\pm$ 6.2	179.5 $\pm$ 6.1
Mean mass in kilograms $\pm$ SD	66.5 $\pm$ 9.3	60.9 $\pm$ 7.8	66.3 $\pm$ 8.0	72.4 $\pm$ 9.4
Body mass index				
<18.5	5,323 (13.8)	3,169 (32.8)	1,971 (10.2)	183 (1.9)
18.5-24.9	30,697 (79.6)	6,246 (64.7)	16,340 (84.7)	8,111 (84.1)
$\geq$ 25.0-29.9	2,242 (5.8)	204 (2.1)	880 (4.6)	1,158 (12.0)
$\geq$ 30.0	326 (0.8)	28 (0.3)	103 (0.5)	195 (2.0)
Smoking				
Non-smoker	15,754 (40.8)	4,125 (42.8)	7,664 (39.7)	3,965 (41.1)
1-10 daily cigarettes	12,646 (32.8)	3,128 (32.4)	6,438 (33.4)	3,080 (31.9)
10+ daily cigarettes	10,188 (26.4)	2,394 (24.8)	5,192 (26.9)	2,602 (27.0)
Alcohol as gram/week				
0	2,331 (6.2)	738 (7.9)	1,058 (5.6)	535 (5.7)
1-100	22,923 (60.9)	5,643 (60.0)	11,473 (61.0)	5,807 (61.6)
101-250	9,529 (25.3)	2,354 (25.0)	4,800 (25.5)	2,375 (25.2)
251+	2,837 (7.5)	666 (7.1)	1,468 (7.8)	703 (7.5)
Cardiorespiratory fitness				
Low	15,509 (50.1)	3,403 (47.4)	7,910 (50.4)	4,196 (52.0)
High	15,432 (49.9)	3,771 (52.6)	7,784 (49.6)	3,877 (48.0)
Education				
Compulsory	12,534 (35.5)	2,887 (32.8)	6,057 (34.3)	3,590 (40.6)
Secondary	14,188 (40.2)	3,432 (38.9)	7,270 (41.1)	3,486 (39.4)
Higher	8,610 (24.4)	2,496 (28.3)	4,351 (24.6)	1,763 (19.9)
Parental socioeconomic position				
Blue collar	19,469 (50.5)	4,674 (48.5)	9,729 (50.4)	5,066 (52.5)
Lower white collar	10,986 (28.5)	2,696 (28.0)	5,492 (28.5)	2,798 (29.0)
Upper white collar	6,214 (16.1)	1,822 (18.9)	3,110 (16.1)	1,282 (13.3)
Other	1,912 (5.0)	453 (4.7)	959 (5.0)	500 (5.2)

SD = Standard deviation

smoking. In model II, I further adjusted for alcohol. In model III and IV, I further adjusted for cardiorespiratory fitness and socioeconomic position respectively. For the middle age analyses, I included all men alive and living in Sweden on January 1, 1991 in model I (37,542 men). In Model II, 36,604 men (97.5%) had a full dataset. For model III and IV, the corresponding numbers were 29,425 (78.4%) and 27,766 men (74.0%). For the mortality analysis starting in 1970, 30,186 men (78.2%) had full dataset in model IV.

Smoking at baseline was categorized into three groups (non-smokers, 1-10 cigarettes per day, and >10 cigarettes per day). Self reported total intake of alcohol was measured in grams per week by a questionnaire as previously reported<sup>102</sup> and categorized in four groups (0, 1-100, 101-250, >250).

As a proxy for cardiorespiratory fitness, I used physical work capacity in relation to body weight categorized as low or high. Men who were not limited by disease performed a maximal test ( $W_{max6}$ ) on a cycle ergometer<sup>92-94</sup> as described in the introduction of this thesis. I

**Table 7. Adult cardiovascular morbidity and mortality risk in men with high adolescent muscle strength**

Outcome	Model I <sup>a</sup>	Model II <sup>b</sup>	Model III <sup>c</sup>	Model IV <sup>d</sup>
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Middle age morbidity				
Ischemic CVD <sup>f</sup>	0.91 (0.81-1.01)	0.91 (0.82-1.02)	0.89 (0.78-1.00)	<b>0.87</b> (0.77-0.99)
Middle age mortality				
All-cause	1.03 (0.94-1.14)	1.02 (0.93-1.13)	1.05 (0.94-1.17)	0.98 (0.87-1.10)
CVD	1.11 (0.92-1.34)	1.07 (0.88-1.30)	1.06 (0.85-1.32)	0.98 (0.78-1.24)
Cancer	0.96 (0.80-1.14)	0.95 (0.80-1.14)	1.02 (0.83-1.24)	0.98 (0.80-1.21)
Suicide	<b>1.38</b> (1.02-1.87)	<b>1.37</b> (1.01-1.86)	1.40 (0.99-1.98)	1.24 (0.86-1.80)
Other causes	0.98 (0.82-1.17)	0.99 (0.83-1.18)	1.01 (0.82-1.23)	0.94 (0.76-1.17)
Total Mortality				
All-cause	1.03 (0.95-1.12)	1.02 (0.94-1.12)	1.05 (0.95-1.15)	1.04 (0.95-1.15) <sup>e</sup>
CVD	1.08 (0.90-1.30)	1.05 (0.87-1.26)	1.04 (0.84-1.28)	1.03 (0.84-1.28) <sup>e</sup>

HR = Hazard ratio, 95% CI = 95% Confidence interval, CVD = Cardiovascular disease

Results in bold if  $p < 0.05$

Men with average muscle strength serve as reference

<sup>a</sup> Adjusted for body mass index, smoking

<sup>b</sup> Adjusted for body mass index, smoking, alcohol

<sup>c</sup> Adjusted for body mass index, smoking, alcohol, cardiorespiratory fitness

<sup>d</sup> Adjusted for body mass index, smoking, alcohol, cardiorespiratory fitness, attained education

<sup>e</sup> Model includes parental socioeconomic position instead of own education as follow-up starts in adolescence

<sup>f</sup> Coronary heart disease or stroke diagnosis from in-patient care

**Table 8. Adult cardiovascular morbidity and mortality risk in men with low adolescent muscle strength**

Outcome	Model I <sup>a</sup>	Model II <sup>b</sup>	Model III <sup>c</sup>	Model IV <sup>d</sup>
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Middle age morbidity				
Ischemic CVD <sup>f</sup>	0.98 (0.87-1.10)	0.98 (0.87-1.10)	0.98 (0.86-1.12)	0.99 (0.86-1.13)
Middle age mortality				
All-cause	<b>1.17</b> (1.06-1.29)	<b>1.18</b> (1.07-1.30)	<b>1.14</b> (1.02-1.28)	<b>1.18</b> (1.04-1.33)
CVD	<b>1.23</b> (1.01-1.51)	<b>1.25</b> (1.02-1.53)	1.21 (0.96-1.53)	<b>1.31</b> (1.02-1.67)
Cancer	0.94 (0.78-1.14)	0.96 (0.80-1.16)	1.00 (0.81-1.24)	1.03 (0.82-1.28)
Suicide	<b>1.72</b> (1.28-2.31)	<b>1.70</b> (1.27-2.29)	1.41 (0.98-2.03)	<b>1.49</b> (1.02-2.19)
Other causes	<b>1.21</b> (1.02-1.43)	<b>1.22</b> (1.02-1.45)	1.15 (0.93-1.42)	1.13 (0.91-1.41)
Total Mortality				
All-cause	<b>1.16</b> (1.07-1.27)	<b>1.17</b> (1.07-1.27)	<b>1.13</b> (1.02-1.25)	<b>1.14</b> (1.03-1.26) <sup>e</sup>
CVD	<b>1.28</b> (1.06-1.55)	<b>1.30</b> (1.07-1.58)	1.20 (0.96-1.51)	1.21 (0.96-1.51) <sup>e</sup>

HR = Hazard ratio, 95% CI = 95% Confidence interval, CVD = Cardiovascular disease

Results in bold if  $p < 0.05$

Men with average muscle strength serve as reference

<sup>a</sup> Adjusted for body mass index, smoking

<sup>b</sup> Adjusted for body mass index, smoking, alcohol

<sup>c</sup> Adjusted for body mass index, smoking, alcohol, cardiorespiratory fitness

<sup>d</sup> Adjusted for body mass index, smoking, alcohol, cardiorespiratory fitness, attained education

<sup>e</sup> Model includes parental socioeconomic position instead of own education as follow-up starts in adolescence

<sup>f</sup> Coronary heart disease or stroke diagnosis from in-patient care

excluded subjects whom did not reach 90% of age-predicted maximal heart rate (MHR) at the end of testing, i.e.  $<175$  beats/minute ( $MHR = 208 - 0.7 * 18.5$ ).<sup>103</sup> The test result was registered as a stanine score with known limits. To allow estimation of cardiorespiratory fitness in relation to body weight, I estimated the exact result using the mean of the upper and lower limit. An exception was all subjects with the highest score, whom I categorized as having high fitness, independently of weight. Otherwise, those with the highest score but with, relatively to the cohort, a heavy weight would be systematically categorized as having low cardiorespiratory fitness.

I collected data on adult and childhood socioeconomic position from Statistics Sweden. As a proxy for the conditions during childhood, I used information on the occupation and education of parents as registered in 1960. For categorization into four groups, I used a white-/blue collar approach. For adult socioeconomic position, I used attained level of education in 1990. As sensitivity analyses, I investigated if another measure of socioeconomic position, year of birth, marital status, conscription office, or blood pressure had any influence HR estimates. In two separate analyses, I also excluded subjects with cardiovascular (ICD 8: 390-459) or psychiatric (ICD 8: 290-319) disease at baseline.

## Results

During 709,702 person years of follow-up in middle age, 1,966 men (2.8 per 1,000 person years) were hospitalized with ischemic CVD. Men with high strength had a statistically significant decreased HR for ischemic CVD when I

adjusted for BMI, smoking, alcohol, work capacity, and education (Table 7).

During 1,569,422 person years of total follow-up, 3,390 men (2.2 per 1,000 person years) died. Of the deaths with a confirmed diagnosis, 687 of 3,223 deaths (21.3%) were due to CVD. 77.0% of all deaths occurred during middle age (1991-2012) when 2,610 men died. Of 2,443 deaths with a diagnosis in middle age, 629 deaths (25.7%) were due to CVD, 750 (30.7%) due to cancer, 266 (10.9%) due to suicide, and 798 (32.7%) due to other causes. Men with low muscle strength had a statistically significant increased risk of total all-cause mortality adjusted for BMI, smoking, alcohol, cardiorespiratory fitness, and parental socioeconomic position (Table 8). Low muscle strength was also associated with all-cause mortality during middle age. This risk increase was mostly mediated by increased HRs for CVD and suicide mortality. No similar associations were found in men with high muscle strength (Table 7).

Year of birth and conscription office did not alter the pattern of HR estimates. In general, being unmarried was associated with the outcome, although I observed no major changes in the HR estimates of muscle strength. High diastolic blood pressure was typically associated with having a cardiovascular outcome but had only minor effects on risk estimates (data not shown). Adjusting for socioeconomic position instead of education did not have any effect on the overall pattern of association. When I in two separate analyses excluded men with psychiatric ( $n=4,324$ ) and cardiovascular ( $n=1,271$ ) disease at baseline, I observed only minor changes of HRs and the overall pattern remained (data not shown).

## Discussion

### **A model to explain how low PE performance in women is associated with later musculoskeletal pain and health impairment (I, II)**

In papers I and II, I found the PE performance in adolescent women to be associated with later musculoskeletal pain and health impairment. Other studies have reported weak association between PE grade and adult physical activity,<sup>41 104</sup> indicating that my findings cannot solely be explained by PE performance being a proxy for physical activity. Therefore, I hypothesize that the results may be explained by a "bio-psycho-social-model",<sup>105 106</sup> common in the area of low back pain research (Figure 5). Another example of such a model is the one<sup>107</sup> that is the foundation of WHO's International Classification of Functioning, Disability and Health.<sup>108</sup> Though diseases can differ in etiology and clinical presentation, many diagnoses, as well as sick leave,<sup>109</sup> share common risk factors such as smoking,<sup>58 110 111</sup> obesity,<sup>112-114</sup> and inadequate levels of physical activity.<sup>3</sup> Findings from the Trois-Rivières study, an intervention of daily PE the first six years of education, suggested that daily PE was associated with a reduced risk of adult smoking in men.<sup>40</sup> Several studies have reported clustering of risk factors such as smoking and diet in both adolescence and adulthood.<sup>115 116</sup> In young women, smoking is associated with a decline in physical activity and a high consumption of alcohol while inversely associated with a high fiber diet.<sup>117 118</sup> Furthermore, the model is supported by two studies with baseline data from a similar time period.<sup>42 119</sup> Using grades based on the same curriculum as the grades in the present study, the first study reports a reduced risk of smoking in adulthood in girls with a high grade in PE.<sup>119</sup> Moreover, a high grade was associated with increased cardiorespiratory fitness in both boys and girls, whereas only boys with a high grade had increased levels of physical activity. These results are somewhat supported by a study reporting the

PE grade in adolescence to be a predictor of later physical activity for boys but not for girls.<sup>41</sup> The second study identified the PE grade as the best predictor of exercise in the middle age in a set of variables collected in adolescence.<sup>42</sup> In summary, results from previous studies suggest that the associations observed could hypothetically be explained by a grade group difference in the clustering of risk factors as part of a bio-psycho-social-model. In terms of prevention, this would favor a multifaceted approach.

In contrast to their female counterparts, men with a low grade in PE did not appear to have increased risk for future health impairment or musculoskeletal morbidity. Sex and/or gender may influence explanatory factors at both baseline and follow-up. In students with a low PE grade, it is possible that the reported gender differences in structural and behavioral determinants of health,<sup>120</sup> as well as health care utilization,<sup>121</sup> might mediate part of the gender difference in risk of future morbidity. However, it has also been reported that girls have benefited from PE interventions in form of better fitness,<sup>122</sup> increased adult levels of physical activity,<sup>40</sup> and decreased sedentary behavior<sup>123</sup> when boys have not. This could potentially be explained by the reports of boys being more physically active in general<sup>124</sup> and less anxious of PE.<sup>125</sup> With the habitual physical activity level of boys being higher than that of girls, an absolute increase in physical activity might affect boys' health less than girls'. Furthermore, the PE curriculum was at the time of the subjects' education somewhat depending on sex. Thus, the PE grade as such might reflect different abilities in girls as compared to boys, e.g. dancing being more important for grading in girls. However, the specific gender aspects of PE and later causal musculoskeletal consequences thereof warrant separate studies.

Dotted lines: Interactions of variables adjusted for in the study

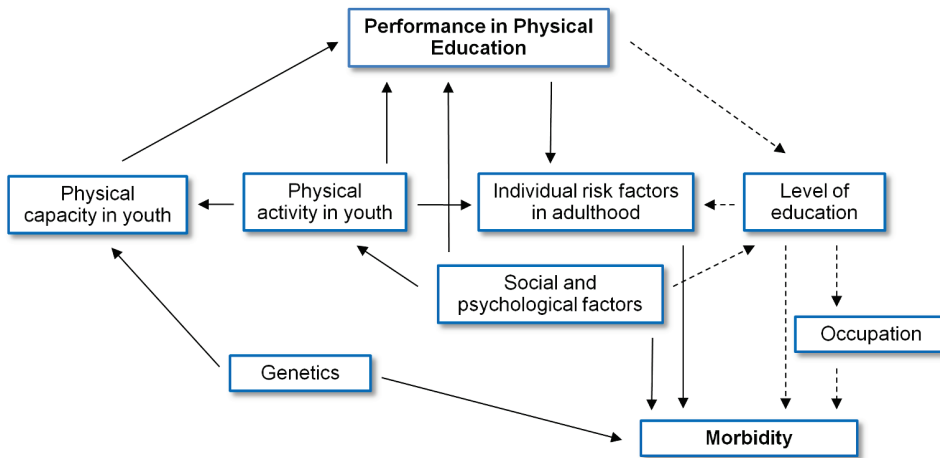


Figure 5. A hypothetical outline of the association between the performance in Physical Education and middle age morbidity.

### Proxies for health impairment (II)

In 1946, WHO defined health as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity".<sup>126</sup> However, there is still an ongoing debate about which aspects of well-being that should be included in the definition of health.<sup>127</sup> Although fascinating in many ways, I will not expand on the subject of health theory in this text. However, as the relevant framework of health impairment was not included in the published version of paper II, I will briefly outline it here.

In the mentioned study, I use a framework in which health impairment is defined as the fraction of an individual's theoretical maximum health that currently is not experienced. It is important to note that of all the causes that might lead to health impairment, disease, i.e. the objective measurement of pathology, and illness, the subjective experience of ill health, are two main factors. I have not surveyed the participants about their perceived health (illness), instead I have used variables from registers as proxies for impaired health, i.e. health impairment. The associations of similar variables have previously been investigated<sup>128</sup> and I use them as a foundation for my model (Figure 6). I regard the proxies of having received sick leave compensation,

hospitalizations, and primary care visits to be associated but complimentary proxies of health impairment. However, there is one major disadvantage; if the variables would be included in a working definition of health impairment; individuals who experience high thresholds to both health care and sick leave compensation (or being unemployed) would appear less health impaired compared to those who had access to adequate care. However, as the study sample resides in a region with publicly financed health care and sick leave systems, any thresholds to the system must be regarded as comparably low.

### Low muscle strength in adolescence is not a risk factor for later musculoskeletal pain in men (III)

In contrast to my hypothesis, men with low muscle strength in adolescence appeared to have a decreased risk of later musculoskeletal pain. It has previously been suggested that there is a U-shaped association between physical activity and later back pain.<sup>129 130</sup> As former occupational exposure and certain sport participation are established risk factors for future MSDs,<sup>61 131</sup> it lends some evidence for a more general model including musculoskeletal pain in general, in which certain forms of physical activity is negative for the musculoskeletal health. Primarily,

Dotted lines: The conceptual definition of *health impairment*

### Health impairment

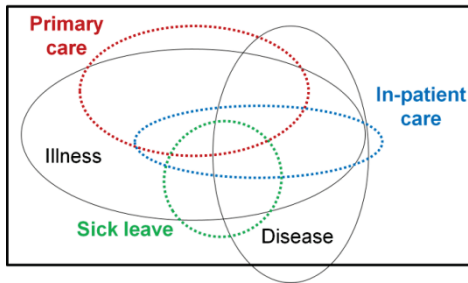


Figure 6. Hypothetical relation of primary care, in-patient care and sick leave with illness and disease (adapted from Wikman, 2005<sup>128</sup>).

my observations do not support low muscle strength in youth as a protecting factor for later musculoskeletal pain. Instead, I suggest that my results can be explained by muscle strength in youth being one selection criterion for future high risk activities with a negative influence on the musculoskeletal health, e.g. higher risk of joint injury due to sports participation or manual repetitive work load. This would also include more immediate exposure such as more physically demanding military service.<sup>132</sup> Although I have controlled for level of education, which might serve as a proxy for occupational exposure, there is potential for residual confounding as I did not have access to more specific data. In other words, individuals with low general muscle strength might to a certain degree be deselected for high risk activities compared to men with an average or high strength. On the other hand, I cannot exclude the possibility that muscle strength is an intermediate (or associated with one) on a biological causal chain leading to musculoskeletal pain. For example, the strength of an individual is associated with the muscle fiber type distribution, which have a large genetic component.<sup>133</sup> Type I fibers are more common in endurance athletes<sup>134</sup> whereas high type II percentage have been reported to be associated with isometric muscle strength<sup>135</sup> as well as low back pain.<sup>136</sup> Thus, the decreased risk observed in men with low strength could hypothetically be mediated by muscle fiber phenotype. Partly in contrast with a previous study,<sup>71</sup> I did not observe a negative effect of low muscle strength on the risk future of musculoskeletal problems in

men. Although I in the present study only included measurements of isometric strength, the previous study observed associations with both an isometric strength measure (static two hand lift) and an isotonic strength measure (bench press). In a study on the same cohort,<sup>137</sup> it is reported that the result in bench press, but not two hand lift, was associated with both future cardiovascular fitness and future physical activity, potentially explaining part of the difference. As another study reported flexibility as a sit and reach test,<sup>70</sup> but not strength measured as sit-ups, to be negatively associated with future risk of back pain, it is possible that other aspects of muscular and musculoskeletal function is of greater importance to the future risk of MSDs than isometric muscle strength.

The association between muscle strength and later musculoskeletal pain diminished when I used muscle strength as a continuous variable. This was not surprising, as the observed association was non linear in the main model. When I included cardiorespiratory fitness in the model, most risk estimates decreased in absolute values, furthering strengthening the observations in the main model. By using the relative muscle strength during testing periods of five years, I partially address the potential systematic change in testing procedure over the years. Although the methods of measurements have not changed at large, minor adjustments cannot be excluded.

### Muscle strength in adolescent men is inversely associated with cardiovascular disease in middle age (IV)

My observations suggest an inverse association between muscle strength in young men and later risk of CVD. However, the pathway of potential causality still remains as a central question. Does high muscle strength add CVD protection apart from cardiorespiratory fitness or does it merely decrease the risk of accumulating other CVD risk factors during adulthood? Notably, there are previous studies supporting a biological link between muscle strength and later CVD, such as obesity protection<sup>12</sup> through increased resting energy expenditure<sup>138</sup> and lower arterial stiffness in young men with high muscle strength.<sup>85</sup> Early developmental aspects might also play a role as

birth size is associated with both low adult muscle strength<sup>139</sup> as well as ischemic heart disease.<sup>140</sup> Whereas we observed a decreased risk of ischemic CVD in men with high muscle strength, the group had no decreased risk of CVD mortality. In contrast, having low muscle strength was associated with increased risk of CVD mortality but not for ischemic CVD. Potentially, this could be explained by muscle strength having different thresholds of protective effect depending on the severity of the outcome measurement.

As also previously reported,<sup>79</sup> low muscle strength in youth was associated with increased risk of later suicide in this study. Although I also observed an increased risk of suicide in men with high strength, this risk estimate was not statistically significant when I adjusted for attained education in adulthood. Moreover, it is plausible that subjects with CVD at baseline in general also performs less well on physical capacity test, possibly introducing bias. However, when I excluded subjects with CVD or psychiatric disease at baseline, the risk estimates were only marginally adjusted. Also intelligence, measured as IQ, is associated with later mortality in men.<sup>16</sup> Although IQ at baseline was measured in the present cohort, the Ethical Review Board did not permit me to use this variable. When I adjusted for conscription office, a few offices appeared statistically significant without altering the risk estimates. As the offices tested men from different geographical backgrounds, this was no surprise to me.

It should be possible to generalize the study results if the limitations are duly considered. For example, the study includes men from all education strata, addressing a limitation of an earlier study in the area.<sup>12</sup> As the population in Sweden at baseline was ethnically homogenous and predominantly white, generalization to other ethnicities should be made with some caution. However, muscle strength has been shown to be an important predictor of mortality also in other ethnicities, such as men of Japanese ancestry.<sup>141</sup>

### **Methodological considerations**

A major argument for using registry based data for research is that it allows the combination of

retrospective study design and prospective data collection. When investigating outcomes over decades this is a cost effective and time saving approach. However, there are some possible limitations that should be considered when using registry data for research. First, as the researcher often is not the primary data collector, it is important that the quality and validity of the data is investigated. Secondly, when using data primary collected for other purposes, such as military conscription or payment to health care providers, it is important to consider how the circumstances of collection and reporting might influence the available data.

### *Investigating PE performance and later morbidity (I, II)*

The use of a comprehensive health care register and data on sick leave compensation in combination with municipality archives allows decades of follow-up. However, the studies also have important limitations. First and most importantly, I did not have access to information on students' smoking, anthropometry, and physical activity which all associated with future health. In fact, these covariates may act as either confounders or intermediate variables on a causal chain (from physical fitness/activity/sporting ability in school to health as an adult). Even so, I was interested in the predictive capabilities of the grade received in PE as such. Moreover, it is known that OR estimates by log regression differ from RR when the outcome is common. Thus, this should be considered when interpreting the results reported in paper I. Other limitations of the studies can be attributable to incomplete registers. First, the SHR does not contain a diagnosis as used in paper I for every visit, as all visits to private health care providers are registered without a diagnosis. However, as the Swedish health care system is publicly financed, having a private primary health care provider is more a matter of choice than of income. Furthermore, there is a fairly high grade of exchange between private and public health care, meaning that many individuals with a chronic condition occur at least at one time point with their ICD diagnosis in the register. Thus, the large portion of private health care users also having received a musculoskele-

tal diagnosis by a public health care provider is a sign of overlap in the type of health care provider used. Second, the drop-outs differed in achieved education and in median income, inducing potential bias in the study. A potential explanation is relocation outside the region due to university studies, which also predisposes for a higher income. However, as drop-outs also had somewhat higher PE performance and higher education is associated with better health, this would arguably at most dilute my results. Third, by defining outcome as having a diagnosis set by a physician the detection threshold could potentially limit the possibility of generalization to musculoskeletal illness in general. Fourth, the municipality under study includes a university town with inhabitants whom might differ from the general population. However, simultaneously with the start of the study, adjacent rural municipalities were incorporated in the study municipality, thus possibly decreasing this effect. Nevertheless, the regional approach of the study calls for larger studies. Fifth and finally, I have not controlled for pre-existing disease at baseline. However, I have only included subjects with a valid grade in PE, thus excluding those students who were excused from PE because of medical reasons.

### *Investigating muscle strength and musculoskeletal pain (III)*

Using a historical cohort design with prospective registration of the exposure and the outcome, the study includes a large sample and thus allows better control for known confounders compared to previous studies. All covariates (muscle strength, BMI, smoking, education, physical activity) included in the multivariate model for musculoskeletal pain also had a significant association with the outcome. Furthermore, by investigating the effects of physical work capacity in a sensitivity analysis, I aimed to isolate the direct effect of muscle strength from other aspects of physical capacity. However, the study also has important limitations. First and foremost, the possible bias connected with the use of conscription data warrants attention. Although it provides a rich dataset from a structured environment, the subjects' motivation for military service may have biased the performance during

the testing procedure. However, assuming there is no association between motivation at conscription testing and later risk of musculoskeletal pain (or the loss to follow-up) any bias would at most dilute my observations. Nevertheless, stronger recruits are more likely to be assigned to positions with heavy load duty. Secondly, the conscription was mandatory for men only. As the pattern of physical activity and occupational exposure differ between men and women, any generalization of the results to women must be made with great caution. Third, the physical activity measurement consisted of a single question and did neither allow calculation of metabolic equivalent of task (MET) nor included occupational exposure. Also musculoskeletal pain is measured by questions that combine more than one site, decreasing the precision. However, the categories are fairly well demarcated anatomically save for the question regarding pain in arms/legs. Fourth, the covariates collected with musculoskeletal pain at follow-up (smoking, physical activity, level of education) are cross-sectional and might thus be mediators of reverse causation. However, the adjusted estimates are much in line with the crude estimates.

### *Investigating muscle strength, cardiovascular morbidity, and mortality (IV)*

The study has several strengths; it includes a large general population sample, includes prospectively ascertained exposure information and baseline data on known confounders, has long follow-up of four decades, and small loss to follow-up using comprehensive registers. However, there are also limitations that should be considered when interpreting the results. Just as for study III, a limitation of study IV is that it does not include women. Secondly, the motivation for military service may have biased my observations. However, as few men were fully discharged, most hypothetical underachievers would still have to enlist, possibly raising motivation for testing. Thirdly, the measure of work capacity as a proxy for cardiorespiratory fitness is a potential concern as I cannot exclude the possibility of residual confounding. However, work capacity had a statistically significant effect on the HR estimate of total cardiovascular



mortality (low vs. high 1.34, 1.11-1.61). Finally, when using a Cox proportional hazards model to study other outcomes than all-cause mortality, competing risks (i.e. death) might bias the results. However, no major difference in shape was noted when I compared subgroup curves of cumulative incidence, using mortality from other causes as a censor, to curves adjusted for competing risks.<sup>142</sup>

### Future perspectives

As I demonstrated in paper I and II, it is important to consider gender aspects when planning and presenting future studies on PE, especially enabling stratified analysis on gender in future randomized clinical trials. Furthermore, to better identify and understand any cause-effect relationship of PE performance and future morbidity, studies with data on individual risk factors such as smoking and physical activity are needed.

Although I found no increased risk of future musculoskeletal problems in men with low muscle strength in adolescence (paper III), future studies need to better quantify the effects of occupational exposure and leisure time physical activity. Since the physical activity pattern and physical fitness profiles differ between men and women, further investigations should also include women.

In the light of my observations in paper IV, I consider muscle fiber type distribution (type I or type II) to be of an area of interest for future research. Muscle fiber type distribution has a major congenital component,<sup>133</sup> is affected by physical activity,<sup>143</sup> and is associated with isometric muscle strength<sup>135</sup> as well as obesity and type 2 diabetes.<sup>144 145</sup> With promising techniques that measure muscle fiber type non-invasively,<sup>146</sup> large cohort studies on how muscle phenotype is associated with CVD risk is possible. As I use work capacity in relation to body weight as a proxy for cardiorespiratory fitness, future studies should address this limitation to minimize the potential of residual confounding. It is also important to better understand how different kinds of fitness interventions alter the cardiovascular risk for individuals with different levels of baseline fitness. Currently, the WHO recommends adults to perform muscle strengthening activities on at least two separate days per week.<sup>147</sup> However, those with the lowest physical capacity might also benefit the most. Muscle strengthening activities might potentially be a better alternative for people who are not motivated to, or due to medical reasons cannot, participate in more focused cardiorespiratory exercise. To add to the understanding of the role of muscle strength in the prevention of CVD, future investigators should also study the observed association in older age groups.

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## Conclusions

### **Paper I and II**

Adolescent girls with low PE performance could be an important group to target with early interventions to reduce future musculoskeletal illness and health impairment.

### **Paper III**

Men with low isometric muscle strength in late adolescence do not have increased risk of musculoskeletal pain in adulthood.

### **Paper IV**

Isometric muscle strength in adolescent men is inversely associated with later risk of ischemic cardiovascular disease in middle age, independently of important confounders.

## Popular Summary in Swedish

Avhandlingen består av fyra delstudier och är tematiskt uppdelad i två delar. I den första delen undersöker jag vilken betydelse betyget i Gymnastik (nuvarande Idrott & Hälsa) har för framtida sjukdom med fokus på rörelseorganen. I den andra delen undersöker jag vilken betydelse isometrisk muskelstyrka (d.v.s. kraft alstrad utan nämnvärd förkortning av muskeln) har för framtida utveckling av smärta i rörelseorganen och hjärt/kärlsjukdom hos män. Gemensamt för alla fyra delarbeten är att jag använder svenska register för att följa upp större grupper av människor vad gäller sjukdom och levnadsförhållanden under decennier.

I många skolor runt om i världen ingår ett gymnastikliknande ämne på schemat i vilket eleverna ska få möjlighet till fysisk aktivitet under skoltid. Ett huvudfokus för ämnet är ofta elevens hälsa, både nuvarande och framtida. Det är dock oklart vilken betydelse denna typ av aktivitet i skolan har på sjukligheten senare i livet.

För att undersöka detta närmare använde jag mig i *den första delstudien* av data baserad på elever som gick ut grundskolan i Lunds kommun 1974-1976. Jag undersökte vilken betydelse betyget i gymnastik har för framtida utveckling av sjukdomar i rörelseorganen genom att sammanlänka betyg i Gymnastik, uppgifter angående utbildningslängd, och yrke med ett regionalt sjukvårdsregister. Bland kvinnor med lågt betyg i Gymnastik var det vanligare med sjukdomar i rörelseorganen, särskilt smärta i mjukdelarna.

I *den andra delstudien* använde jag mig av samma grupp ungdomar som i den första delstudien. Med hjälp av register över sjukskrivning och sjukvård undersökte jag vilken betydelse betyget i Gymnastik har för framtida sjukskrivning, läkarbesök i primärvård samt inläggning på sjukhus. Kvinnor med lågt betyg hade fler dagar med sjukskrivning och fler

besök. Gruppen hade även fler inläggningar på sjukhus, men denna ökning var inte statistiskt säkerställd.

I de två första delstudierna var inte elevernas fysiska förmåga huvudfokus. Två viktiga aspekter av fysisk förmåga är dock hjärt/lungfunktion och muskelstyrka. Att nedsatt hjärt/lungfunktion är en riskfaktor för framtida sjukdom, framför allt i hjärta och blodkärl, är numera vedertaget. Det är dock fortfarande ganska okänt hur stor roll muskelfunktionen har för framtida sjukdom, särskilt när den studeras oberoende av hjärta/lungfunktion.

I *den tredje delstudien* använde jag mig av data från mönstring och en undersökning utförd av Statistiska centralbyrån. Då urvalet till undersökningen är nästan helt slumpmässigt kunde jag använda mig av svar angående smärta i rörelseorganen i kombination med muskeltester från mönstringen. I motsats till vår hypotes, visade det sig att män med låg styrka hade minskad risk för smärta. Jag spekulerar att detta skulle kunna förklaras av att dessa män mer sällan utsätts för belastande aktiviteter p.g.a. tidiga livsval.

I *den fjärde delstudien* studerade jag en grupp män som mönstrade 1969/70. Via nationella register över sjukhusvård och orsak till död kunde jag sedan följa männen fram till 2010-2012. Män med låg muskelstyrka visade sig ha ökad risk för förtida död, även då den orsakades av hjärta/kärlsjukdom. Män med hög styrka hade minskad risk för sjukdom orsakad av syrebrist i vävnad såsom hjärtinfarkt och stroke.

Avhandlingsarbetet medför följande tre huvudsakliga slutsatser: (1) Flickor i tonåren kan vara en viktig grupp att tidigt rikta preventiva insatser mot (2) Låg muskelstyrka är inte en riskfaktor för muskuloskeletal smärta hos män (3) Hög muskelstyrka i ungdomen kan indikera en lägre risk för hjärtinfarkt och stroke i medelåldern för män.

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