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# Knee osteoarthritis in relation to physical workload and lifestyle factors

– epidemiological studies

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To my family

*Ne quid nimis*  
Terentius  
185–159 B.C.

## List of original papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals (I-VI).

- I. Vingård E, Sandmark H, Alfredsson L. Musculoskeletal disorders in former athletes. A cohort study in 114 track and field champions. *Acta Orthop Scand* 1995;66:289-91
- II. Sandmark H, Hogstedt C, Lewold S, Vingård E. Osteoarthritis of the knee in men and women in association with overweight, smoking and hormone therapy. *Ann Rheum Dis* 1999;58:151-55
- III. Sandmark H, Hogstedt C, Vingård E. Primary osteoarthritis of the knee in men and women - the effect of lifelong physical load from work. *Scand J Work Environ & Health*. (In press)
- IV. Sandmark H, Vingård E. Sports and risk for severe osteoarthritis of the knee. *Scand J Med&Science in Sports*. (In press)
- V. Sandmark H. Musculoskeletal dysfunctions in physical education teachers. Submitted.
- VI. Sandmark H, Wiktorin C, Hogstedt C, Klenell-Hatschek E-K, Vingård E. Physical workload in physical education teachers. *Appl Ergon*. (In press)

## List of abbreviations

BMI	Body Mass Index
CI	Confidence Interval
OA	Osteoarthritis
OR	Odds Ratio
PE teachers	Physical Education Teacher
PR	Prevalence Ratio
RPE	Rate of Perceived Exertion
RR	Relative Risk

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# 1. Introduction

Osteoarthritis (OA) is a degenerative joint disease and is recognized as a major public health disorder, which causes pain and functional disability in those who are affected, as well as loss of working capacity in the population (Kraemer 1983, Rothfuss et al. 1997). It is the most common articular disease and the joints most frequently affected are the metacarpophalangeal joints, the knees and the hips (Croft 1996, Dieppe 1991, van Saase et al. 1989).

In the search for the risk factors related to this disease it is important to bear in mind that OA is a multidimensional dysfunction, and that external as well as internal conditions determine its course. The interaction of systemic predisposition and local, often biomechanical, stress factors has to be taken into consideration (Dieppe 1991).

Knee OA mainly affects age groups over 45, and causes morbidity, which will increase with larger proportions of elderly people in the population (Kelsey 1984, van Saase et al. 1989). Besides increasing age as a major risk factor, it has been demonstrated that overweight is associated with knee OA (Anderson and Felson 1988, Cooper et al. 1994, Davies et al. 1990a, Hart and Spector 1993), and that occupational activities among men with estimated increased biomechanical load on the knees are hazardous (Anderson and Felson 1988, Felson 1990).

The focus in this thesis has been on studying both men and women regarding the association between physical load, lifestyle factors and sports and symptomatic knee OA. Few earlier investigations on knee OA have focused on a detailed description of the physical workload in occupational groups or in populations, and women have not been studied much either.

The focus has also been to investigate the occupational group of physical education (PE) teachers, which has not been studied to any great extent regarding the health consequences of their workload. Besides their occupational exposure, this group often has leisure time sports exposure in addition.



## **2. Aims of the thesis**

The overall aim of this thesis was to examine the association between physical load, physically demanding activities, and lifestyle factors, and the development of knee OA among men and women.

The specific aims were:

- To study the relationship between musculoskeletal disorders, especially OA of the knee and hip, and exposure to track-and-field sports on an elite level.
- To examine the association between exposure to physical load at work and in leisure time, sports, overweight, smoking, and hormone therapy, and knee OA leading to knee replacement.
- To estimate the exposure to physical load and the occurrence of musculoskeletal disorders, especially OA of the knee and hip, in physical education teachers.

# 3. The knee joint

## 3.1 Anatomy and biomechanics

The knee is a two-joint structure consisting of the tibiofemoral joint and the patellofemoral joint. It is situated between the two longest lever arms of the body and is subjected to high forces during motion and loading. Both joint structures are exposed to substantial forces. The tibia plateaus along with the cartilage, the menisci, and the ligaments are all weight-bearing structures, and the main forces derive from the body weight, the muscles and other soft tissues, and from external load. In the tibiofemoral joint the surface motion is mainly in the sagittal plane, and in the patellofemoral mostly in the frontal plane, and also in the transverse plane.

The articular cartilage is an organized tissue consisting of type II collagen fibrils, which are solid matrix, and proteoglycans, which are produced by chondrocytes. Together with water, these are the structural components, which determine the biomechanical behaviour of the cartilage. One of the functions of the articular cartilage in a diarthrodial joint, such as the knee joint is to increase the area of load distribution and thus to decrease the stress of contacting joint surfaces. The function is to provide a smooth and wear-resistant bearing surface. During joint articulation the forces within the joint and the joint surface vary from almost zero to several times the body weight. The joint load and its variation causes repetitive articular cartilage stress. During rotation and sliding, regions of the articular surface move in and out of the loaded contact area, and thus they are repeatedly stressed. Under normal conditions the articular cartilage provides enough lubrication to the joint (Nordin and Frankel 1989).

## 3.2 The osteoarthrotic process

OA is the result of progressive breakdown of the joint surface, which begins with failure of the articular surface. Loosening of the collagen network, entailing abnormal expansion of the proteoglycans and tissue swelling, seems to be the most important initiating factor. Further alterations in cartilage function are followed by a decrease of cartilage stiffness and an increase in cartilage permeability. The smooth surface of cartilage is breached, the collagen fibres break and the surface becomes rough. The normal ability to carry load is altered and lubrication insufficiency appears. Friction against the rough surface generates particles of cartilage, which are shed into the joint and absorbed by the synovium. There they cause an inflammatory response, which the patient feels as stiffness or aching in the joint after exercise and movements. The irritation of the synovium is probably due to release of intracellular enzymes, which produce hyperaemia and a reaction in the synovial layers. Hyaline cartilage does not regenerate, but limited cartilage repair might occur in lesions penetrating the cortical bone. The subchondral bone is also involved in the arthrotic process, and abnormal activity increases the bone density, resulting in the appearance of new bone forms, osteophytes. The osteophytes can restrict joint movement. The articular surface is eroded and the subchondral bone is exposed. Raw bone against raw bone is painful and friction is increased. Parts of the joint can be overloaded and microfractures often occur. The healing of these fractures increases the rigidity of the bone and it becomes denser, more sclerotic and less resilient. Cysts appear in the cancellous bone. The symptoms involve three principal features: pain, loss

of movement and altered function, which entail difficulties in the activities of daily living (Dandy 1993, Nordin and Frankel 1989).

### **3.3 Definition of knee OA**

Case definition is basic in any epidemiological study. The reason for a clear definition of OA in population studies is to determine presence or absence of disease. However, there is no accepted general definition or consensus of knee OA, and the classification of the disease is therefore a problem. There are investigations, which have shown a low agreement between radiological and clinical features of knee OA, even when the disease is in an advanced stage (Brandt et al. 1991, Spector and Hart 1992, Petersson 1997).

Definitions of OA can be concluded principally in three different ways: by clinical features, pathological findings or radiological gradings. It is also possible to make up with serological and synovial markers of disease (Spector et al. 1993).

The focus in many earlier population studies (Anderson and Felson 1988, Felson et al. 1991, Shouten et al. 1992) of knee OA has been based on structural changes, assessed by radiographic investigations of the tibiofemoral compartment (Ahlbäck 1968, Kellgren et al. 1963). The grading in these studies has been on the existence of osteophytes and joint space narrowing. In the NHANES study the definition of knee OA was based on radiographic changes of minimal joint space narrowing and definite osteophytes (Anderson and Felson 1988). In the Framingham study Felson and co-workers (1997) suggested that knee OA should be defined as the existence of either osteophytes, or moderate or severe joint space narrowing. Spector et al. (1993) suggested that definite osteophytes should define the presence or absence of knee OA for epidemiological studies in populations samples, and a scoring system for both the tibiofemoral and patellofemoral joints was developed. It was suggested that the assessment of joint space narrowing could be used for evaluating the severity of OA rather than presence or absence of the disease (Spector et al. 1993).

The American Rheumatism Association (ARA) has developed clinical criteria for knee OA, which combine clinical examination with radiographs (Altman et al. 1986). Knee pain for most days of the previous month, and osteophytes should be present. There are also options of more than 50 years of age, morning stiffness, and crepitus. These criteria have been further developed by adding the status of the synovial fluid, and by slightly changing the scoring (Altman 1995).

In conclusion there is no clear consensus on the definition of what is considered knee OA in the scientific literature, and different criteria for disease can be used.

## 4. Literature review

### 4.1 Epidemiology

The occurrence of knee OA increases with age, and is a common chronic disorder in the elderly general population (Bergström et al 1986, Felson et al 1987). The prevalence is higher in men than in women up to the age of 45, and thereafter it is more common in women (Anderson and Felson 1988, Felson et al. 1987).

In a study of Spector and co-workers (1991) radiological knee OA with symptoms was found in 2.9% of women in the general population between 45 and 65 years of age. In a recent investigation it was demonstrated that 1% of men and women in the population, aged 35-54 years had radiographic knee OA combined with chronic pain (Peterson 1997).

The results from all relevant investigations of solely radiological knee OA according to the Kellgren and Lawrence grading 2-4 (1957), show that the prevalence rates vary between age groups, and also between studies (Table 1). The studies, which are displayed in Table 1, have been transformed to allow comparisons between age groups. However, the differences in prevalence of knee OA are considerable in the same age groups. The variation could appear due to populations studied, differences in study design, and epidemiological techniques. Certainly the exposure among the different populations could also vary substantially depending on what kind of exposures there are in the population area studied.

The radiographs have been analysed differently; in some of the studies only one knee has been included, and in others an average of severity of both knees has been used. In the NHANES 1 survey (Anderson and Felson 1988) the radiographs were taken under non-weight-bearing conditions, while in other investigations the weight-bearing technique was the most commonly practised.

In spite of these differences, it could be concluded that the prevalence of radiological knee OA is considerably higher in the age groups over 55.

**Table 1.** Age-specific prevalence rates (%) of radiological knee OA in different population groups. (After *State of the art - Knäartros*, Socialstyrelsen, Stockholm, Sweden 1999.)

Study	Sex	Age					
		23-34	35-44	45-54	55-64	65-74	>75
USA (N=6913) (NHANES 1979)	M	0.0	1.7	2.3	1.1	8.3	
	W	0.1	1.5	3.6	7.3	18.0	
Gothenburg, Sweden (N=81) (Bergström et al. 1986)	M					33.3	
	W					45.0	
Sofia, Bulgaria (N=4318) (Tzonchev et al. 1968)	M	3.1	3.6	7.0	10.0	9.6	
	W	1.6	4.7	9.6	11.3	9.6	
North England (N=1448) (Williams et al. 1994)	M		7.0	12.1	28.7	42.3	
	W		6.0	17.4	48.6	56.3	
Zoetemeer, Holland (N=2957) (Valkenburg 1980)	M			9.3	16.8	20.9	22.2
	W			13.9	18.5	35.2	44.1
Framingham, USA (N=1420) (Felson et al. 1987)	M					30.8	30.5
	W					30.8	41.8
Malmö, Sweden (N=1179) (Hernborg and Nilsson 1973)	M			3.0	4.5	4.5	4.5
	W		7.0	4.0	11.0	26.5	36.0

## 4.2 Occupation

Data from studies on the effect of occupation and occupational physical load on the development of knee OA have been reported over the years in studies of different designs. Some of these earlier investigations have presented the prevalence of symptoms and radiographic knee OA in different occupational groups (Kellgren and Lawrence 1952, Lindberg and Montgomery 1987, von Nauvald 1986, Partridge and Duthie 1968, Wickström et al. 1983). Male dockers, concrete workers, pipe fitters and shipyard workers showed an increased risk of knee OA in these studies.

In a longitudinal register-based study on occupational titles, it was found that men working as farmers, construction workers and mail men, and women working as cleaners have an increased relative risk of being hospitalized because of knee OA (Vingård et al. 1991a).

In two large population studies from the USA the occupational physical load exposure was also indirectly assessed from job titles, which served as exposure measures, and not by monitoring or questioning the subjects (Anderson and Felson 1988, Felson et al. 1991).

In the Framingham study (Felson et al. 1991), which is a population-based prospective cohort study, physically demanding jobs, including lifting and knee bending, were found to be risk factors for radiographic knee OA, both in men and women, although the number of professionally active women was low. In the cross-sectional NHANES I survey (Anderson and Felson 1988) an increased risk of radiographic knee OA was found for those who had had occupational exposure considered to involve extensive knee bending. In the same study it was

found that exposure to high physical demands in jobs increased the risk for women, and also for men, although the association for men was weaker.

By assessing the physical workload exposure from current job titles, as in these above-mentioned studies, subjects who had changed jobs due to reasons related to the disease cannot be considered. This could have caused an underestimation of the effect of high physical workload.

In a Finnish study it was found that kneeling work investigated among floor layers might cause later knee degeneration (Kivimäki et al. 1992).

In a study of Cooper and co-workers (1994), where radiographic knee OA with symptoms was studied among 327 men and women, knee bending, kneeling, squatting, and climbing stairs were found to be risk factors, but not lifting as an independent factor. The most evident risk factor was exposure to prolonged or repetitive squatting/knee bending. The exposure was assessed individually by interviewing the subjects.

In a case-control study of 46 men and women who had undergone total knee arthroplasty due to knee OA, the results show that heavy work, obesity, and earlier knee injury were risk factors (Kohatsu and Schurman 1990). In these last two studies the data were not analysed separately for men and women.

### **4.3 Sports**

Results from different studies on the effect of regular exercise on the development of knee and hip OA have been somewhat conflicting. In some studies it has been demonstrated that running or jogging, on a non-elite level, would not be a risk factor for knee OA (Klunder et al. 1980, Lane et al. 1986, Sohn and Micheli 1985). In a study of Spector et al. (1996) an increased risk for both hip and knee OA among former middle-aged female ex-elite athletes was found, and it was concluded that long-term sports activities such as jogging, squash, hockey, badminton and aerobics are correlated to these disorders. In two Swedish studies it was shown that high exposure to all kind of sports increased the risk of hip OA in men and women, and that track-and-field and racket sports were the most hazardous in this respect for men (Vingård et al. 1993, 1998). In a Swiss study of hip OA a positive association with running was found (Marti et al. 1989). No such correlation could be found in a study on former Finnish elite runners (Puranen et al. 1975).

Former soccer players, both with and without former injuries, have been found to have an increased risk of both hip and knee OA (Klunder et al. 1980, Lindberg et al. 1993, Roos et al. 1994). It has also been established that the risk is more pronounced for elite players (Kujala et al. 1995, Roos et al. 1994), which would indicate an exposure-response relationship.

Two studies on daily, moderate physical activity have not demonstrated any association with knee OA (Hannan et al. 1993, Kohatsu and Schurman 1990). Kohatsu and Schurman (1990) studied knee OA leading to prosthetic surgery, and Hannan et al. (1993) studied radiographic changes.

**Table 2.** Studies on knee OA and exposure from occupation and occupational physical load.

Study	Study design	Population and gender studied	Reference group	Outcome	Exposure	Confounders adjusted for	Results given in OR unless otherwise indicated
Kellgren and Lawrence 1952	Cohort	Miners age: 40-50 n=84	Office workers n=42 Manual workers n=45	Knee OA (x-ray) Knee OA signs (clin exam)	Job title	None	1.9 (prevalence ratio)
Lawrence 1955	Cohort	Miners Dockers age:41-50 n=362	Light manual workers Sedentary workers age:41-50 n=87	Knee OA (x-ray)	Job title kneeling heavy lifting	None	2.8 2.9 (prevalence ratio) p<0.05
Partridge and Duthie 1968	Cohort	Dockers age:25-64 n=206	Civil servants n=138	Severe knee OA (clin exam)	High physical strain	None	1.6 (prevalence ratio)
Wickström et al 1983	Cohort	Concrete reinforcement workers age:20-64 n=252	Painters age:24-64 n=231	Knee OA (x-ray) Knee OA signs (clin exam)	Lifting loads>20kg	Age	All knee OA 1.1 (prevalence ratio) Severe knee OA 1.0 (prevalence ratio)
Von Nauvald 1986	Cohort	Pipe fitters age:35-63 n=101	No knee-bending work n=74	Knee OA (x-ray) Knee OA signs (clin exam, interview)	Kneeling and squatting		All knee OA 1.4 (prevalence ratio) Severe knee OA 4.0 (prevalence ratio)

**Table 2 continued.**

<b>Study</b>	<b>Study design</b>	<b>Population and gender studied</b>	<b>Reference group</b>	<b>Outcome</b>	<b>Exposure</b>	<b>Confounders adjusted for</b>	<b>Results given in OR unless otherwise indicated</b>
Lindberg and Montgomery 1987	Cohort	Shipyard workers age:65-83 n=332	Office workers and teachers age: 65-85 n=352 General population age: 65-83 n=438	Knee OA (x-ray) Knee OA signs (clin exam)	Heavy work in shipyard <30 years	None	Severe knee OA 2.5-2.8 (1.1-7.7) (prevalence ratio) p<0.05
Anderson and Felson 1988	Cross-sectional	General population, random sample age:35-74 n=5193		Knee OA (x-ray)	Job title Knee bending Strength demands	Age Race	2.45 (CI 1.21-4.97) /men/ 3.49 CI 1.22-10.52) /women/
Kohatsu and Schurman 1990	Case-referent	Cases with severe knee OA treated age:<55 n=46 /28 women, 18men/	Matched referents age:<55 n=46	Severe knee OA (x-ray, knee replacement)	Light, moderate, heavy or very heavy occupational work		2.3-3.4 (CI 0.9-11.4)
Vingård et al 1990	Case-referent	Disability pension diagnosis age:45-69 n=1307 /men/	General population, age-matched men n=298	Disability pension due to knee OA	Occupational groups, estimated physical load on the lower extremities	Age	Medium exposed:4.5 (CI 2.6-7.6) High exposed: 14.3 (CI 8.1-25.4)



**Table 2 continued.**

<b>Study</b>	<b>Study design</b>	<b>Population and gender studied</b>	<b>Reference group</b>	<b>Outcome</b>	<b>Exposure</b>	<b>Confounders adjusted for</b>	<b>Results given in OR unless otherwise indicated</b>
Vingård et al 1991	Cohort	General population with blue collar jobs age:36-78 n=250.217 /men and women/	Within the cohort, those with jobs with low physical demands on knee joints	Hospital care due to knee OA	Job title	Age Urbanisation	Male fire-fighters, farmers, construction workers 1.36-2.93 (CI 1.13-5.46) Female cleaners 2.18 (CI 1.26-3.00)
Bagge et al 1991	Cohort	General population /men and women/ age:75 and 79 n=340		Knee OA (x-ray)	Physically heavy occupation	BMI	No association between occupational physical load and knee OA
Felson et al 1991	Longitudinal cohort	General population /men and women/	No knee bending, light strength demands	Knee OA (x-ray)	Occupational knee bending and lifting		2.2 (1.4-3.6) /men/ 0.4 (0.1-1.4) /women/
Schouten et al 1992	Longitudinal cohort	General population grade 2 of knee OA age:46-68 n=105 /men and women/	General population	Knee OA (x-ray)	Self-reported occupational physical load	Age Gender BMI	No increased risk of knee OA
Cooper et al 1994	Case-referent	General population, age:55-90 n=30 men, 79 women	Age and sex matched from general population, without knee pain and X-ray changes n=218	Knee OA (x-ray) Knee OA signs (clin exam)	Lifetime occupational physical load: squatting, kneeling, climbing stairs,	Obesity Heberden's nodes	Squatting 6.9 (1.8-26.4) Kneeling 3.4 (1.3-9.1) Climbing stairs 2.7 (1.2-6.1)

**Table 3.** Studies on hip and knee OA and exposure from sports.

Study	Study design	Population and gender studied	Reference group	Outcome	Exposure	Confounders adjusted for	Results given in OR unless otherwise indicated
Puranen et al 1975	Cohort	Former runners /men/ age:31-81 n=74	Patients /male/ age: n=115	Hip OA (x-ray)	Running during 8-50 years (range) Soccer	None	4% hip OA in runners 8.7% in referents
Klunder et al 1980	Cohort	Former soccer players /men/ age: 40-79 n=62	Age-matched community referents n=57	Hip OA (x-ray) Hip OA signs (clin exam) Knee OA (x-ray) Knee OA signs (clin exam)	Soccer	None	49% hip OA in foot-ball players, 26% in referents No increased risk of knee OA
Lane et al 1986	Case-referent	Female and male long-distance runners age:50-72 n=41	Age-matched community referents	Knee OA (x-ray) Knee OA signs (clin exam)	Running	The women were matched according to variables afflicting bone density	No association with clinical knee OA
Marti et al 1989	Cohort	Long-distance runners /men/ mean age:42 n=27	Untrained men mean age:35 n=23	Hip OA (x-ray) Hip OA signs (clin exam)	Running	Age	Joint space narrowing in runners increased (p=0.032)
Lindberg et al 1993	Cohort	Former male soccer players /men/ age: mean 55 n=286	Age-matched general population /men/ n=286	Hip OA (x-ray)	Soccer until 25 years of age	Age	2.1 p=0.04 Elite versus referents: 3.7

**Table 3 continued.**

Study	Study design	Population and gender studied	Reference group	Outcome	Exposure	Confounders adjusted for	Results given in OR unless otherwise indicated
Vingård et al 1993	Case-referent	Men with severe hip OA age:50-70 n=233	General population, age matched men n=302	Severe hip OA (prosthetic surgery)	All sports	Age BMI Occupational physical load Smoking	2.6 (1.5-4.5) /medium exposure/ 4.5 (2.7-7.6) /high exposure/
Kujala et al 1994	Cohort	Former elite male athletes n=2448	Community referents n=1403	Hip, knee, ankle OA (hospital care)	Elite sports participation	Age Occupation BMI	Hip, knee ankle taken together: Endurance sports 1.7 (1.0-3.0) Mixed sports 1.9 (1.2-2.9) Power sports 2.2 (1.4-3.3)
Roos et al 1994	Cohort	Former soccer players age:40-88 n=286	Age-matched men n=572	Knee OA (x-ray)	Soccer	None	All 4.4 (2.0-9.9) Elite 3.7 (1.5-9.3) Non-elite 2.7 (1.0-6.8)

**Table 3 continued.**

<b>Study</b>	<b>Study design</b>	<b>Population and gender studied</b>	<b>Reference group</b>	<b>Outcome</b>	<b>Exposure</b>	<b>Confounders adjusted for</b>	<b>Results given in OR unless otherwise indicated</b>
Kujala et al 1995	Cohort	Former male elite athletes age:45-68 years 31 soccer players 28 runners 29 weight lifters	Age-matched shooters n=29	Knee OA (x-ray) Knee OA signs (clin exam)	Soccer Running Weight-lifting All on an elite level	Age Occupation BMI	Soccer 12.3 (1.3-111.0) Weight lifting 12.9 (1.5-113.0)
Spector et al 1996	Cohort	Former female elite athletes age:40-65 n=81	Female age-matched general population n=977	Knee OA (x-ray) Hip OA (-ray)	Running Tennis	Age Height Weight	Knee OA 1.2 (0.7-1.9) (narrowing) 3.6 (1.9-6.7) (osteophytes) Hip OA 1.6 (0.7-3.5) (narrowing) 2.5 (1.0-6.3) (osteophytes)
Vingård et al 1998	Case-referent	Women with severe hip OA age:50-70 n=230	General population, age matched women n=273	Severe hip OA (rosthetic surgery)	All sports	Age BMI Occupational physical load Smoking Hormone therapy	1.5 (0.9-2.5) /medium exposure/ 2.3 (1.5-3.7) /high exposure/

#### 4.4 Lifestyle factors

Different studies on the impact of constitutional and lifestyle factors for the development of knee OA have produced partially inconsistent results (Anderson and Felson 1988, Cooper et al 1994, Davis et al. 1990a, Felson et al. 1989, Hannan et al. 1990, Hart and Spector 1993, Samanta et al. 1993, Rosner et al.1986, Spector et al. 1988).

Overweight is the most consistent risk factor identified, and the effect seems to be strongest in women (Anderson and Felson 1988, Cooper et al. 1994, Davis 1990a, Felson 1996, Jensen and Rofail 1999, Kohatsu and Schurman1990, Manninen et al 1996, Spector et al. 1994). It has been suggested that the stress and amount of force on the weight-bearing joints of the lower extremities are increased in overweight subjects. This additional physical load might cause cartilage breakdown leading to osteoarthritis (Felson 1996). It has also been proposed that overweight persons have a higher bone density, which could be a risk factor for knee OA (Felson 1996). The gender difference indicates that other factors associated with an increased body mass index (BMI) but solely mechanical could affect the development of knee OA. Studies have shown that obesity is associated with OA in non-weight-bearing joints such as the small joints of the hand, which might indicate metabolic effects of overweight involved in the arthrotic process (Davies 1988, Davies et al 1990a). A positive relationship was found between knee OA in women and having had hypertension, raised serum cholesterol, and raised blood glucose, but independent of obesity (Hart et al. 1995). However, Davies and co-workers (1988) and Hochberg et al. in the Baltimore Longitudinal Study of Aging (1995) did not find any association between metabolic factors such as serum cholesterol, blood pressure or diabetes and the development of knee OA.

There are a few clinical, laboratory and epidemiological studies suggesting that there is a relationship between sex hormones and the development of OA (Felson 1990, Rosner et al. 1986, Spector et al. 1988).

However, some epidemiological investigations have concluded that oestrogen use is not associated with knee OA (Hannan et al. 1990, Samanta et al.1993). Other investigations on postmenopausal oestrogen substitution and the development of knee OA have shown inconsistent results (Nevitt and Felson 1996). There are four studies indicating a possible inverse relation between oestrogen intake and knee OA, but in all four studies the confidence interval included unity (Hannan et al. 1990, Samanta 1993, Wolfe et al. 1994, Zhang et al. 1995). Spector and co-workers (1997) have published results from the Chingford Study where it was found that current use of oestrogen has a protective effect on knee OA. In a study of Oliveria and Felson (1996) a tendency of a possible inverse relation was found for past use, but new or current use in women over the age of 55 was not associated with knee OA.

Smoking has in certain studies shown to decrease the risk of knee OA (Anderson and Felson 1988, Samanta et al. 1993), and in others no association has been found (Hart and Spector 1993). In the Framingham study, smoking showed an exposure-response relationship, and heavier smokers were more protected than light smokers (Felson et al. 1989). In the NHANES survey the results also demonstrated a protective effect in men and women, and also in this study heavier smokers were more protected than light smokers (Anderson and Felson 1988). In the Chingford study a protective effect of smoking for radiological OA in the hand and knee could not be seen, but for subjects with generalised OA a possible preventive association was found (Hart and Spector 1993).

## 5. Subjects and methods

This thesis is based on material from four studies: a cohort study on musculoskeletal disorders in former athletes, a case-referent study on severe knee OA, a cohort study of physical education teachers, and a field study on physical workload. All studies were approved by the local ethics committee at Karolinska Hospital, Stockholm, Sweden.

### 5.1 Study populations, case definition and study designs

In paper I the effect of track-and-field activities on an elite level among men was considered, with regard to knee and hip OA, and other musculoskeletal dysfunction. A cohort of 114 Swedish men between 50 and 80 years of age, who at least once in their lifetime had been winners of an international or national championship in track-and-field sports were identified through a register kept by the Swedish Athletic Association. These men were compared with 355 randomly selected, age-matched male subjects from the population register. A postal questionnaire was answered by 109 (96%) of the former athletes and 309 (85%) of the referents. Persons were classified as having OA if they specified an exact diagnosis set by a physician. For other musculoskeletal disorders strict diagnostic criteria do not exist and more descriptive explanations had to be accepted.

In paper II, III and IV the relationship between physical load factors, lifestyle factors and sports and the development of knee OA leading to knee replacement was studied in a population-based case-referent study. The study base comprised all men and women, born between 1921 and 1938, and living in 14 counties in Sweden. The cases had undergone prosthetic knee replacement during the period 1991-93 because of clinically significant primary knee OA, and were of ages 55-70 at the time of the surgery. They were identified through the Swedish Knee Arthroplasty Register, which is a national register system of knee arthroplasties performed at orthopaedic units in Swedish hospitals (Knutsson et al. 1994). The referents were men and women randomly selected from the study base, through the central population register in Sweden.

Cases and referents were excluded if they reported earlier trauma or surgery to the knee or the surrounding tissues, rheumatoid arthritis or systemic disease involving the joints such as poliomyelitis or rachitis, or if they had any musculoskeletal malformation. Among the referents, those who reported OA of the knee or had experienced severe pain or dysfunction from the knees were excluded. In all, 369 male cases and 380 female cases were invited to the study. The participation rate was 88% and 79%, respectively. The numbers among the referents were 330 males and 370 females contacted; 80% and 77% of those, respectively, participated in the whole study.

Paper V comprised all Swedish men and women, born between 1925 and 1945, who had graduated from physical education teacher training college in Sweden (GCI) between the years 1957-65. They formed a cohort of 290 men and 281 women. Twelve of the subjects in the cohort had died, and 48 could not be reached. Among the men 214 (76%) participated in the study, and among the women 202 (73%). Fifty-one women and 45 men did not want to participate in the study.

Age-matched referents, 255 men and 257 women, were randomly selected from the Swedish population register. At the time of this investigation all subjects were between 51 and 71 years of age. The participation rate for the male referents was 193 (77%), and for the women 194 (76%). Fifty-three (21%) of the male referents and 54 (21%) of the females did not want to participate. The classification of knee OA was accepted if the subjects reported that it was settled by a physician, but for other musculoskeletal disorders, reported pain and dysfunctions were accepted.

In paper VI, which is a field study, twenty female and ten male teachers in physical education volunteered to participate. In this study the physical workload exposure was monitored on each one of the teachers during one full workday. The subjects were all living in the Stockholm area, and working in different schools. The aim when selecting the teachers was to invite those who were of different ages, both men and women, who were working at different levels in the school system. Fourteen teachers worked in the upper secondary school where the students' age range is 17 to 19 years, and the rest in the nine-year compulsory school system where the students are from 7 to 16 years of age. Ninety per cent of the teachers were working full-time and the rest part-time. On average they had been working as teachers of physical education for 15 years (range 1-32 years).

## **5.2 Exposure assessment and classification**

### *5.2.1 Physical load exposure assessments*

Physical exposure or biomechanical load may be expressed as an unlimited number of force vectors, one for each point of the body. Each one varies in magnitude and direction, and there is a time dimension in these variations. This is the conceptual definition of biomechanical load, and a complete description of the exposure could only be produced through continuous time registrations, including the magnitude and direction of all force vectors. Operationally the physical load exposure is usually assessed by estimations of exposure amplitude, repetitiveness and duration (Winkel and Mathiasen 1994).

In paper I the exposure to elite track-and-field activities on an elite level was considered for all the members of the cohort once they belonged to the register "Stora grabbar", that is those who had at some time won an international or national championship.

In paper II, III and IV the self-reported physical load exposure between 15 and 50 years of age during occupational work and housework was the basis for the exposure assessment. For the variables kneeling, whole body vibrations, standing and sitting posture, the reporting was hours per day spent in these exposures. Stairs taken every day, squattings and knee bendings, and jumps were all reported in number per day. Lifting burdens in occupational work was estimated by the subjects with regard to frequency and weight, and then summed up in kilos for the same period as the rest of the variables. Lifting in housework and during leisure time was estimated only by the summed up frequency per day. The lifelong exposure (15 to 50 years of age) was then summed up for all the different self-reported variables.

In paper V the PE teachers who had been working at least ten years in their profession were included in the analysis. Those who had been working less than ten years were excluded, as their occupational exposure as a PE teacher was considered too low.

In paper VI the physical load exposure on the lower extremities and the back, as well as the general physical strain during work, were assessed through continuous registrations of postures, movements, and heart rates over an entire working day. The measurement devices

were either applied directly to the body, or indirectly used, in systematic and computerized observations.

Walking distance was registered with a pedometer (Selin and Winkel 1994). Duration and frequency of jumps, knee-bends, and lifting were registered using a hand-held computer with a software program for entering frequency and duration of these exposure parameters (Fransson-Hall et al. 1995). Trunk flexion was measured using an inclinometer, which registers the sagittal angle between the trunk and the reference trunk position (Ericsson 1994). General physiological strain was assessed through registrations of the circulatory stress, using a heart rate recorder (Léger and Thivierge 1988). A 15-graded scale (RPE), graded 6-20, was used for ratings of the perceived exertion and was thus a physiological stress indicator for the day (Borg 1990).

### *5.2.2 Occupational titles and non-occupational work*

All the occupational titles, which were reported in paper III, were classified according to the Standard Occupational Classification (1995). Subjects who had worked in certain occupations considered to involve the highest physical load on the knees, according to a score, which has been elaborated and used in previous studies, were identified (Vingård et al. 1992). Ten years of exposure to occupations with high physical load was the criterion for being exposed, and those subjects who had never had any of these physically demanding jobs were considered unexposed.

Number of years in physically demanding tasks (paper III), outside occupational work during adult life was also asked for. These were mostly tasks such as taking care of an elderly or handicapped person at home.

### *5.2.3 Sports*

In papers I and IV the sports exposure and exposure to recreational physical activity in general, was investigated from the age of 15 to 50 years of age. For each sports activity the subjects were asked if they had ever participated on a regular basis, and, if the answer was positive for how many years, how many months per year, and how many hours per week. Totals of hours in each sport, and also to all sports combined, were then calculated.

For the ex-athletes in study I it was primarily the exposure to track-and-field on an elite level that was investigated, but also to what extent they had been exposed to other sports activities.

In paper V the reporting started for the period 15-24 years and thereafter in periods of 10 years until the age of 54. All sports activities reported were indexed, and those subjects who reported they were active in sports 4 times per week or more during one of those periods got 20 points, and for activity 1 to 3 times per week they received 10 points. Thus the maximum number of points per period was 20, and for a whole lifelong sports exposure (4 periods), 80 points.

### *5.2.4 Cigarette smoking*

Lifelong cigarette smoking habits in paper II, III, IV, and V were calculated as pack years. One pack year is the equivalent of 20 cigarettes/day during 1 year. The subjects were divided into three groups: never smokers, light smokers, and smokers. Light smokers were those with 1-14 pack years, and smokers were those with 15 or more pack years.



### *5.2.5 Body mass index*

BMI was used as an indicator of overweight, and was calculated as weight (kg) divided by height squared ( $m^2$ ). In paper I a BMI of 30 or more was used as the limit of overweight, and in paper II, III, IV, and V the referents' BMI were the basis for the classification of BMI into three groups. The values in the highest quartile were considered as high, and those in the lower quartile as low BMI. The 50% in between were the medium BMI values.

### *5.3 Statistical methods*

In paper I and V, the cross-sectional cohort studies, the ex-athletes and the PE teachers, respectively, were compared with referents, and prevalence ratios of each investigated disorder or other variable were calculated according to the Mantel-Haenszel method (Mantel and Haenszel 1959).

In the case-referent study (paper II, III and IV) the odds ratios were interpreted as estimates of the relative risks, since the design was a population-based case-referent study (Miettinen 1975). The effect on the odds ratios from potential confounding factors was considered by stratified analysis and calculating the odds ratios according to the Mantel-Haenszel method (paper II and IV) (Mantel and Haenszel 1959), or by using logistic regression (paper III). In a multivariate regression model, which included the physical load variables, it was possible to assess how the variables were related to each other in the association to the outcome (Hosmer and Lemeshow 1989).

All calculated odds or prevalence ratios in papers I, II, III, IV and V were analysed with 95% confidence interval.

The results of frequency and duration of the recorded parameters in paper VI were expressed as median value and range, except for the heart rate values, which were presented as mean value, standard deviation and range, while the values were normally distributed. The agreement between the recordings and the individual's own assessments was analysed using non-parametric rank order correlation (Spearman's rho).

## 6. Results

### 6.1 Musculoskeletal disorders in former athletes

*Objective:* To investigate whether former male Swedish track-and-field athletes on the elite level suffer more or less from musculoskeletal disorders, especially osteoarthritis of the hip and knee, than the general population.

Of the former athletes 80 per cent rated their health as good compared to 61 percent of the referents. Only three per cent of the athletes considered that they had a poor health status. Fitness training of different kinds from walking more than 30 minutes 2-3 times a week to vigorous exercises, was more common among the athletes, and their BMI was lower compared to the referents'. They had fewer neck and shoulder disorders, and more hip OA. They probably also had more knee OA, although unity was included in the confidence interval. The ex-athletes had had light workload during their occupational work compared to the referent group (Table 4).

**Table 4.** Assessments of good health, fitness training, musculoskeletal disorders and physical workload. Prevalence ratios (PR) with 95 % confidence intervals (CI), comparing the athletes with the referents.

	PR	95% CI
Good health	1.3	1.2-1.5
Fitness training regularly	1.4	1.2-1.6
Low back disorders	0.8	0.6-1.3
Neck/shoulder disorders	0.6	0.3-1.0
Feet disorders	1.7	0.9-3.1
Other disorders	0.8	0.5-1.1
Heavy workload main part of occupational life	0.4	0.3-0.6
BMI>30 at the age of 25	1.9	0.3-11
BMI>30 now	0.2	0.1-0.8
Hip OA	3.6	1.4-9.3
Knee OA	2.8	0.7-11

### 6.2 Osteoarthritis of the knee in men and women in association with overweight, smoking and hormone therapy

*Objective:* To examine the relationship between OA of the knee leading to prosthetic surgery among men and women, and overweight, smoking, and hormone therapy.

Overweight was associated with knee OA at the ages of 30, 40 and 50, before the onset of symptoms. At the age of 40, women with high BMI (24 or more) had an odds ratio of 9.2 (95% CI 5.3-16.0) for developing knee OA, and men with high BMI (25 or more) had an odds ratio of 3.9 (95% CI 2.3-6.4). At the age of 50, the odds ratio for women was 7.8 (95% CI 4.6-13.39), and for men 5.9 (95% CI 3.1-11.1).

Smokers were less likely to develop severe knee OA compared to non-smokers, and the odds ratios were 0.6 (95% CI 0.4-1.0) for men, and 0.4 (95% CI 0.2-0.8) for women, respectively. There was a dose-response association, as smokers were more protected than light smokers.

Thirty-three per cent of the female cases and 22% of the referents had oestrogen substitution after the age of 50, and the mean value of the duration of this therapy was 9 years among both cases and referents. The odds ratio for severe knee OA was 1.8 (95% CI 1.2-2.6) for those who had had this substitution.

### **6.3 Primary osteoarthritis of the knee in men and women - the effect of lifelong physical load from work**

*Objective:* To investigate the effect of lifelong physical load from occupational work, housework and leisure time activities on the development of primary knee OA leading to prosthetic surgery, and to find out which jobs might be hazardous in this respect.

Those who had had occupational titles considered to involve heavy physical load on the knees for at least 10 years had an odds ratio of 2.5 (95% CI 1.7-3.6) for men, and 2.5 (95% CI 1.6-3.9) for women to develop knee OA, compared with those who never had any of these titles. Male forestry and construction workers and both female and male farmers ran the highest risk.

The male subjects had considerably higher exposure, especially to lifting at work, and a higher exposure to jumps and vibrations compared with the females. The strongest physical load variables associated with knee OA among the men were lifting at work (OR 3.0, 95% CI 1.6-5.5), squatting/knee bending (OR 2.9, 95% CI 1.7-4.9), kneeling (OR 2.1, 95% CI 1.4-3.3) and jumping (OR 2.7, 95% CI 1.7-4.1). Lifting at work seems to be a substantial risk factor, because even a medium exposure demonstrated a significant positive association.

Exposure to physically demanding tasks at home, such as nursing and taking care of an elderly or handicapped person, was significantly associated with knee OA in women (OR 2.2, 95% CI 1.3-3.6), and was the strongest risk factor for women among the physical load variables investigated. Among women, high exposure to lifts at work (OR 1.7, 95% CI 1.0-2.9) and a standing posture (OR 1.6, 95% CI 1.0-2.8) were positively associated, while kneeling, climbing stairs and lifting at home showed increased point estimates, but wide confidence intervals.

### **6.4 Sports and risk for severe osteoarthritis of the knee**

*Objective:* The objective of the present study was to investigate the relationship between sports activities and primary knee OA leading to prosthetic surgery in men and women.

Lifelong self-reported sports exposure was considerably higher among the men, compared to both female cases and referents. Soccer had been the most usual sports activity among both male cases and referents. Jogging was twice as common among the male referents compared to the male cases. The most common sports activity among the female cases had been cross-country skiing, and in the female referent group, it was gymnastics.

The association between knee OA and sports was strongest among the highly exposed men under 65 years of age (OR 2.9, 95% CI 1.3-6.5), and the highest risk estimates were for those

who reported exposure to cross-country skiing (age<65: OR 2.5, 95% CI 1.3-5.1), and soccer (OR 2.0, 95% CI 1.4-2.8). Exposure to ice hockey/bandy and track-and-field also increased the relative risk among the men compared to those who were never exposed. We found no association between sports and severe knee OA among women, because both cases and referents had very little sports exposure. Moderate daily general physical activity among men and women was not correlated with knee OA.

Men with high exposure to both sports activities and physical workload (n=20) had an increased relative risk of 3.2 (95% CI 1.2-9.1), compared to those with low exposure to both variables. For women with high exposure to both variables (n=16) the relative risk was 1.8 (95% CI 0.8-4.0). The occupational titles among those cases with high exposure to sports represented a considerable variation, but with a few exceptions, they were all titles referring to blue-collar work.

### 6.5 Multivariate analysis models in paper II, III, and IV

In the multivariate analysis of all variables included in the case-referent study (paper II, III, and IV) it was found that high BMI was the most prominent risk factor for both men and women. The highest risk estimate was for women. Jumping, squatting/knee bending, kneeling and lifting were other strong risk factors for men, while physically demanding tasks at home, entailed increased relative risk for women. Smoking showed a negative association among both men and women (Table 5 and 6).

**Table 5.** Multivariate logistic regression analysis of the relationship between knee OA, and the different physical load and lifestyle variables *in men*. Comparisons are between highly exposed and low/non-exposed men. The odds ratios (OR) and 95% confidence intervals (CI) are demonstrated. The model is demonstrated in three different ways, due to co-variation between the variables kneeling and squatting/knee bending.

	OR	(CI) <sup>a</sup>	OR	(CI) <sup>b</sup>	OR	(CI) <sup>c</sup>
Standing	1.3	(0.7-2.3)	1.1	(0.6-2.1)	1.1	(0.6-2.1)
Climbing stairs	1.0	(0.5-1.6)	0.8	(0.5-1.5)	0.9	(0.5-1.6)
Lifts at work	1.9	(0.9-3.8)	1.6	(0.8-3.1)	1.6	(0.8-3.3)
Jumps	2.0	(1.2-3.3)	2.0	(1.2-3.2)	2.0	(1.2-3.2)
Kneeling	1.6	(1.0-2.6)				
Squatting/knee bending			2.0	(1.1-3.6)		
Kneeling/squatting/knee bending					1.8	(1.2-2.8)
Sports	1.4	(0.9-2.3)	1.4	(0.9-2.3)	1.4	(0.9-2.3)
BMI	2.4	(1.0-5.6)	2.4	(1.0-5.6)	2.4	(1.0-5.6)
Smoking	0.7	(0.4-1.0)	0.6	(0.4-1.0)	0.6	(0.4-1.0)

a. Hosmer and Lemeshow test p=0.45

b. Hosmer and Lemeshow test p=0.60

c. Hosmer and Lemeshow test p=0.47

**Table 6.** Multivariate logistic regression analysis of the relationship between knee OA, and the different physical load and lifestyle variables *in women*. Comparisons are between highly exposed and low/non-exposed women. The odds ratios (OR) and 95% confidence intervals (CI) are demonstrated. The model is demonstrated in three different ways due to co-variation between the variables kneeling and squatting/knee bending.

	OR	(CI) <sup>a</sup>	OR	(CI) <sup>b</sup>	OR	(CI) <sup>c</sup>
Standing	1.2	(0.6-2.2)	1.2	(0.7-2.3)	1.2	(0.7-2.3)
Climbing stairs	1.2	(0.6-2.2)	1.3	(0.7-2.3)	1.3	(0.7-2.3)
Lifts at work	1.3	(0.7-2.3)	1.4	(0.8-2.6)	1.4	(0.8-2.5)
Jumps	1.3	(0.8-2.4)	1.5	(0.8-2.6)	1.4	(0.8-2.5)
Physically demanding tasks at home	1.7	(1.0-2.9)	1.8	(1.0-3.1)	1.8	(1.0-3.1)
Kneeling	1.2	(0.7-2.0)				
Squatting/knee bending			0.6	(0.3-1.2)		
Kneeling/squatting/knee bending					0.8	(0.5-1.2)
BMI	4.5	(1.9-10.5)	4.6	(1.9-10.8)	4.6	(2.0-10.8)
Smoking	0.4	(0.2-0.8)	0.4	(0.2-0.8)	0.4	(0.2-0.8)

a Hosmer and Lemeshow test p=0.47

b Hosmer and Lemeshow test p=0.21

c Hosmer and Lemeshow test p=0.72

## 6.6 Musculoskeletal dysfunctions in physical education teachers

*Objective:* The aim of this study was to investigate the extent of OA of the knee and hip, musculoskeletal dysfunction, general health status and lifestyle factors among PE teachers.

The PE teachers had a higher prevalence ratio of knee OA (men: 2.8, 95% CI 1.6-4.8; women: 3.2, 95% CI 1.8-5.5), and knee injury compared with the referents. The female PE teachers also had more hip OA (PR 2.7, 95% CI 1.0-7.1). The PE teachers had more absence from work, and were obliged to change jobs more often because of knee disorders. At the age of 25 the male PE teachers' BMI was higher compared to the male referents, but at an older age both the female and male PE teachers had considerably lower BMI than the referents. The PE teachers smoked less, and had fewer serious diseases compared with the referents.

## 6.7 Physical workload in physical education teachers

*Objective:* To measure and quantify exposure to physical load of teachers in physical education during an entire working day, and to establish the reproducibility of self-reported physical workload, and evaluate the agreement between self-reported and objectively registered physical load in the same group.

The most common activity was warming up exercises, and the second most common was different kinds of indoor ball games. The activities that placed the highest demands on the circulatory system were warming up activities, aerobics, dance, floor hockey, and circuit training, and there were heart rate peaks of 150 beats or more per minute in 22 (3 men, 19 women) subjects. The teachers walked or ran up to 10 kilometers during the day. The results show that biomechanical load on the lower extremities, as well as cardiovascular strain among PE teachers, is considerable compared to other occupational groups and that occasional high loads of short duration appear.

The best correlations between registered and self-reported exposure the same day and after three weeks were found in lifting more than 20 kilos, sitting, and jumping. It was concluded that questionnaires can be used when assessing physical load in this occupational group on a dichotomised level or with pooled classes regarding walking distance, jumping, light and deep knee bending and lifting light loads. For questions on exposure to heavy lifting and sitting these subjects could be asked on a more detailed level.

## 7. General discussion

Previous studies have documented that there are a number of risk factors involved in the complex association between different exposures and knee OA. There are usually several causes for the development of a disease, and the strength of a factor's effect could be measured by the change in disease frequency produced by introducing the factor into a population. The impact of a risk factor for disease occurrence depends not only on the presence of other risk factors, but also on their extension and interaction in the population (Rothman and Greenland 1998).

The focus in this thesis has been to study the association between physical load, sports, lifestyle factors and knee OA. The main findings show evidence that a high BMI is an important risk factor for symptomatic knee OA. Physical workload factors, such as lifting, jumping, kneeling and squatting, taking care of elderly or handicapped persons at home, and sports are also associated with knee OA. Certain occupations, especially farming, construction work and teaching in physical education, entail risk factors for knee OA. The effect of smoking showed a negative relation to knee OA.

The following sections will discuss methodological issues and the results in relation to earlier investigations.

### 7.1 Study design

In non-experimental research the investigator cannot control the circumstances of exposure, and therefore the selection of subjects is essential in obtaining valid evidence of the hypothesis under study (Rothman and Greenland 1998). In occupational epidemiology investigations, the distinctions between study designs are primarily attributable to variations in the availability of data and the feasibility of study conduct (Checkoway 1989). In this thesis both the cohort and the case-referent design were used.

#### 7.1.1 Cohorts

Choosing a cohort design provides a study of possible health effects from one single exposure. There are often two cohorts in this design. One of them is usually described as the exposed cohort, which consists of individuals who have experienced a putative causal event or condition. The other cohort is thought to be the unexposed or referent cohort. Cohort studies provide the feature of studying the entire available study population (Rothman and Greenland 1998).

The studies presented in paper I and V were both of a cohort design with information on exposure collected retrospectively.

The choice of the cohort design was possible due to the existence of registers of sufficient quality that could be used to find the exposed cohorts. The exposed cohorts of ex-elite champions and PE teachers were of limited size, and not possible to extend. This sometimes caused very small subgroups when analysing the material.

### 7.1.2 Case-referent

Case-referent design was used for the investigation presented in paper II, III, and IV because the aim was to study several different potential risk factors. Case-referent studies can be viewed as efficient versions of cohort studies, where the referents are a sample of the source population (Rothman and Greenland 1998). Due to the fact that everyone in Sweden has free hospital care and is referred to a certain hospital in the geographical area where they live, this case-referent investigation can be considered population-based. Together with the inclusion of both men and women in the study, this should increase the generalizability of the results.

## 7.2 Prevalence and classification of osteoarthritis

Prevalence may be defined as the proportion of a population that has disease at a specific point in time (Rothman and Greenland 1998). Knee OA (paper I, II, III, IV and V) and hip OA (paper I and V) are both non-fatal yet persistent conditions. The occurrence of OA has no clear moment of onset. Measuring the prevalence is possible without biasing the investigation by not measuring the incidence and duration, as individuals with symptoms and the diagnosis of OA generally do not recover. Further it is not possible to get OA on a specific site more than once. In this thesis the prevalence of symptomatic knee and hip OA diagnosed by a physician and knee OA subjected to knee prosthetic surgery, was studied.

The focus of interest in this thesis has been on clinically significant knee OA, with a strong interest in the individuals' activities in their daily life and their occupational situation. This kind of dysfunction entails more suffering and greater costs than non-symptomatic knee OA. Thus individuals with possible, not yet clinical knee OA among the referents were not misclassified.

Subjects with earlier trauma or injury to the knee and the surrounding tissues were not included in paper I, II, III and IV, as the aim of these studies was to identify risk factors of OA without major previous trauma or injury to the knee joint. It is well known that injuries and soft tissue lesions can cause a later development of knee OA. However, for those subjects in paper V who reported they had a diagnosis of knee OA from a physician, those with and without previous trauma were included. Stratification was not possible due to small numbers in the subgroups.

## 7.3 Physical load

The tibiofemoral joint is often highly loaded, and the joint reaction force during level walking is increased between two to four times the body weight, and six times during stair climbing (Andriacchi et al. 1980, Dahlkvist et al. 1982, Morrison 1970). However, the exact mechanisms of the pathogenesis of knee OA and the association to physical load factors have not been clarified. Results from earlier studies, in concordance with the results from this thesis, suggest that repetitive knee use, impact loading and heavy lifting in occupational work are all associated with knee OA (Anderson and Felson 1988, Cooper et al. 1994b, Felson 1990). These exposures might act directly on the knee joint, and when the physical loads exceed a critical level, it is possible that they could cause cartilage loss.

Physical or biomechanical load can be investigated differently depending on the aim of the investigation, which parts of the body are studied; the size of the study population, and whether the measurement concerns present or past loading.



It is generally not possible, except in advanced laboratory settings, to apply an instrument directly to body segments or tissues in order to measure the exact internal mechanical loading in static and dynamic courses. This would of course be the ideal way of estimating biomechanical load. To approximate the proportions and the variability of physical load, registrations of external physical load, expressed in frequency, duration and amplitude can be performed by using devices suitable for field studies in working life or in sports activities.

In the field study of PE teachers (paper VI) the physical load was monitored during one working day in each subject. It was demonstrated that the biomechanical as well as the cardiovascular workload in these teachers were considerable compared to other occupational groups and that occasional high loads of short duration appeared. However, such registrations can only be performed if the sample size is limited, as it is time-consuming and expensive, and for measurement of present conditions.

Questionnaires are usually used to collect exposure information in epidemiological studies. When concluding exposure assessments retrospectively, validity and reliability have to be considered. Retrospective assessment involves a certain degree of non-differential misclassification due to recall difficulties, giving a dilution of the true risk for the highly exposed, and an over- or underestimation of the risk for the medium exposed. Due to the unavoidable difficulty in remembering exposure, it has been suggested that when using detailed scales in questionnaires they should be pooled into fewer and wider classes in the analysis, in order to obtain greater precision (Wiktorin 1995). Thus in the analyses of the case-referent study (paper II, III, IV) three classes of exposure were used, which would, at least partially, diminish the problems of potential nondifferential misclassification.

If cases and referents recall their exposures differently, a differential misclassification can occur. This will result in an over- or underestimation of the true risk. To validate the reported physical workload (paper III), the individual cases and referents who had had similar jobs, considered as low exposure jobs, were compared regarding their assessments of the physical load. There was no difference, which indicates that differential misclassification was a minor problem and did not interfere too much with the validity of the exposure assessments in this study.

Also in the field study (paper VI) the validity and the reliability were investigated with regard to self-reported physical exposure by using a questionnaire. It was concluded that, if the classification is not too fine, questionnaires can be used when assessing physical load exposure, in this occupational group of PE teachers. In the analyses the classes should be pooled or dichotomised.

In paper I, in which the exposed cohort had been elite athletes, a questionnaire was used to obtain information on general health status and occupational history. Also in paper V a questionnaire was used in a similar way, and the physical load in PE teachers in general was known through the measurements demonstrated in paper VI. The job as a PE teacher has not changed much over the years regarding physical workload exposure, which is probably the basic problem. It was shown that the occupational physical load exposure on the lower extremity among the PE teachers was considerable, as were the circulatory demands. High exposure to lifting was also found in the occupational activity, especially when supporting the students in apparatus gymnastics, which produced the heaviest lifts.

In paper II, III and IV information was obtained on occupational titles and work history for up to 10 periods between 15 and 50 years of age. The job title has often been used to approximate the exposure to physical workload in epidemiological studies (Anderson and

Felson 1990, Felson et al. 1991, Kellgren and Lawrence 1952, Partridge and Duthie 1968). However, the physical workload can vary although the same job title has been reported. Nevertheless, it provides a hint of where to make further investigations and which job titles include high risks.

In many studies using job titles as a proxy for occupational load, it has been difficult to classify women. This is due to their low exposure to occupational work and therefore a lack of proper classification by job title. This has probably entailed an underestimation of the physical load exposure in women. It was found in this thesis (paper III) that women have had less occupational physical load exposure during their life, but have had more physical load exposure from housework and home nursing. The amount of housework was assessed to get a full picture of the total load, both from occupational and non-occupational work. By doing this we could identify physically demanding activities, such as taking care of an elderly or handicapped person at home, as strongly associated with knee OA in women. This exposure is somewhat more complex than several other physical load variables in the study. It certainly involves lifting, carrying, squatting/knee bending and kneeling altogether.

## **7.4 Sports**

In paper IV and V it was demonstrated that exposure to sports activities from the age of 15 and onwards was very limited among women in the population. For severe knee OA leading to prosthetic surgery among women it was not possible to show an association, as the cases and referents had about the same low sports exposure (paper IV). Whether sports exposure is a risk factor for women could therefore not be concluded in this study. The male cases (paper IV) had been more active in sports compared to the referents, and the increased relative risk was most pronounced in those men younger than 65 years of age. This could depend on differences in sports habits between the different age groups, or that sports exposure contributes to an earlier onset of knee OA, which would then explain the different odds ratios.

In paper V the sports exposure and the occupational exposure as a PE teacher are both approximations of exposure to biomechanical load on the lower extremities.

The drawback of analysing all sports exposure taken together is that the physical load on the lower extremities from different sports varies, and thus this is a rather rough exposure estimate.

Occupational physical load can be compared with loads from sports, but it was not possible to distinguish the impact from either exposure on knee or hip OA in the investigation of the PE teachers (paper V). It was demonstrated that the PE teachers differed substantially from the general population regarding leisure time sports exposure. The number of study persons did not allow calculations of stratum-specific estimates. The PE teachers' high sports exposure and their occupational exposure were highly correlated. It could be concluded that these two exposures probably have a joint effect, causing an effect modification on the development of knee disorders.

## **7.5 Overweight**

The male ex-athletes (paper I) and male PE teachers (paper V) had a higher BMI at the age of 25 compared to the male referents at the same age. However, at an older age the situation was the reverse. This demonstrates the difficulties in concluding what a high BMI stands for. It is

most likely that the ex-athletes and PE teachers' high BMI was due to well-trained muscles as a result of their sports activities and training. The referents' high BMI at an older age is more likely to depend on overweight due to various reasons, but probably mostly to a lack of physical activity.

In paper II a positive association between overweight and severe knee osteoarthritis was demonstrated, which was stronger in women. Cases who had symptoms of knee OA before the age of 50 were excluded from the study, which means that their overweight was not caused by a more sedentary level of activity because of knee pain due to the OA.

The attributable proportion is that proportion of the disease occurrence that would be eliminated if the exposed group were to have its incidence reduced to the level of the unexposed group (Rothman and Greenland 1998). The attributable proportion from a medium and high BMI on severe knee OA (paper II) is demonstrated in Table 7. It can be concluded that almost a third of all cases among the women, and a fifth of the male cases, is due to a high BMI.

**Table 7.** Attributable proportion (AP) for cases with medium and high BMI respectively, and for all cases at the age of 40. (BMI at the age of 40:men low –22, medium 23-24, high 25-, women low –21, medium 22-23, high 24-.)

	Women	Men
AP for cases with medium BMI	15%	20%
number of exposed cases	64	27
AP for cases with high BMI	50%	33%
number of exposed cases	82	38
AP for all cases	32%	21%
number of cases	288	313

The results from paper II that a high BMI is a risk factor for knee OA, with higher risk estimates for women agree with previous investigations (Anderson and Felson 1988, Felson 1996, Manninen et al. 1996).

It has been shown that individuals with a high body weight tend to underestimate, and light individuals to overestimate, self-reported weight (Stewart 1982). This could lead to less pronounced differences in the reported weight compared to the real weight, and risk ratios closer to unity.

## 7.6 Cigarette smoking

In paper II the results show that smokers had a lower relative risk of severe knee OA compared to non-smokers. This is in agreement with some earlier studies (Davies et al. 1990a, Felson et al. 1989, Hart and Spector 1993). As in NHANES 1 and in the Framingham study (Anderson and Felson 1988, Felson et al. 1989), the association showed a dose-response relationship, and smokers were more protected than light smokers.

The mechanism of a protective effect of smoking as regards to knee OA might be that of a biochemical effect of nicotine. Smoking has shown to be protective against developing ulcerative colitis, and it has been suggested that nicotine causes this effect (Bustamente et al

1998, Mokbel et al.1998, Sandborn 1999). Further investigations on the effect of smoking on OA are needed. Smoking could of course not be recommended for the prevention of knee OA, as other, harmful effects are overwhelming, but the aetiology of the potential association would be worth studying in the search for mechanisms of OA.

## 7.7 Selection

A selection bias arises from the procedures used to choose subjects and from factors that influence study participation. The selection biases cause that those who were chosen as study participants differ in their relation between exposure and disease, compared to all those who are theoretically eligible for the study (Rothman and Greenland 1998).

The register used in paper I of the cohort of male ex-athletes was not completely updated, since wrong addresses and also dead persons were still included. It is possible that more men may belong to the ex-athlete group than are covered by the register. However, it is not probable that inclusion in the register is related to subsequent health status.

The participation rate in the case-referent study covered by paper II, III, and IV was high, especially among the male cases. There were subjects who participated only in the telephone interview, but did not want to continue with the questionnaires. However, the information regarding occupational history obtained by the interview showed that there was no difference regarding job titles between those who filled in the questionnaires and those who did not, and there is no evidence that a selection because of the distribution of risk factors occurred.

Subjects with earlier trauma or injury to the knee and the surrounding tissues were excluded from the study group (paper II, III, and IV). This was carefully checked, and about 15% of the referents reported this condition, which was a somewhat higher rate than expected. As this was performed at the end of the investigation, it resulted in a lower number of referents than expected.

In Sweden, all citizens have free hospital care, which includes surgery, such as knee replacement. No selection should have occurred due to not being able to afford prosthetic surgery.

In paper V the original register from the National Archives of the PE teacher students was used, and the cohort was traced through the present population register. Twenty-four of the former students could not be found in the population register. The most likely explanation is that they had emigrated without registering their emigration, or that they had recently died. They could of course differ regarding exposure compared to the remaining study population. However, there were too few of them to influence the exposure to an extent that the results would be affected.

A common selection bias occurring in occupational epidemiology is the initial selection of relatively healthy persons into certain occupations and the fact that they are more likely to remain employed (Checkoway et al. 1989). In paper V this bias has probably occurred. The PE teachers were most likely a selected group of individuals who, at least at the time of choosing their training and profession, were fit and healthy enough to manage a physically demanding profession, and with a lower morbidity compared with the general population. The ex-athletes were also a selected group of individuals who once were healthy enough to compete at elite level in track-and-field activities. This "healthy worker effect" (McMichael et al. 1975, Östlin 1988) could bias the results in studies of occupational and other risks. Those subjects who are employed in certain occupations constitute a group with lower risk of

developing many diseases compared with the population as a whole, simply because the employed group must be healthy enough to work. The unemployed part of the population therefore has a higher risk of becoming ill. Thus, in a study that compares the morbidity experience of a certain occupational group with that of the total population, the healthy worker effect could lead to an underestimation of the relative morbidity in the exposed group. If there is a contribution from the healthy worker effect in paper I and V, which is most likely, the case, the rate ratios of disease would be underestimated.

## **7.8 Confounding**

Confounding is a systematic error which implies that the exposed and unexposed groups differ with regard to some other factor or factors, except for the determinant under study, that affect the risk of development of the disease (Rothman and Greenland 1998). In studies of work-related musculoskeletal disorders, such as OA, age is considered to be a confounder, and was therefore adjusted for in all investigations in this thesis. In paper IV it was found that the risk ratios differed between the older and younger age groups. However, the assumption is that this should not be considered as confounding, but rather a demonstration of the effect of sports. There are several causes for the development of knee OA; and sports might contribute, and cause an earlier onset and development of the process. This could explain why the age groups differed, and why the younger subjects showed a higher relative risk.

Other factors associated with an increased risk of knee OA, such as BMI/overweight, cigarette smoking, hormone therapy, sports and physical load variables were adjusted for in the analyses of the studies included in this thesis. It has been demonstrated that all these variables are independent risk or health factors for knee OA. When one variable was analysed, it was adjusted for confounding from the others. None of the potential confounders were found to bias the results.

In paper V, the study of the cohort of PE teachers, it was found that sports exposure during leisure time was highly correlated to this occupational group. This is due to PE teachers being an extreme group, with a complex exposure, which differs from the general population. Being a PE teacher does not only mean an occupational title, which involves a physically demanding exposure at work, but also a high sports exposure during leisure, practically no exposure to smoking, and not being overweight. It could be concluded from the results in paper V, that physical load exposure from work and from sports probably have a joint effect, causing an effect modification in this occupational group; and that it was not possible, in this study design, to study the effect of workload and sports separately.

## 8. Conclusions

The investigations included in this thesis show evidence that different risk factors contribute to the development of clinical knee OA in men and women. The most prominent risk factor, which indicated an exposure-response association was overweight, followed by physical load factors such as lifting, squatting, kneeling, jumping and taking care of elderly or handicapped persons at home, and sports.

Regarding weight it was concluded that those who were active in sports, PE teachers and possibly also ex-elite athletes, at the age of 25 had a higher BMI than the general population. At an older age the situation was the reverse. This demonstrates that BMI could not always be considered an indicator of overweight in the common sense. A high BMI in the young athletes is not the same as in the aging population.

Sports exposure in women in the population was very limited. The female cases and referents included in the case-referent study and the referents in the cohort study of PE teachers had about the same low exposure. The gender difference in the population is interesting to note, especially since the strongest risk estimates for overweight were found in women.

Men and women seemed to obtain a high physical workload in different ways. The men had more exposure to the single physical load variables asked for, and especially lifting, kneeling, jumping and squatting raised the relative risk for men. The women had increased risk estimates for standing posture, lifts at work, kneeling and climbing stairs, but the confidence intervals included unity. The women's exposure to physically demanding tasks at home, such as nursing elderly relatives or handicapped children, was their most important risk factor. This is a more complex exposure variable and it certainly involves all those single exposure variables asked for.

Those men and women who had had jobs classified as physically heavy for ten years or more had an increased relative risk of severe knee OA. This relative risk could be underestimated due to a selection of workers described as the healthy worker effect.

The monitoring of physical load exposure of PE teachers in paper VI is certainly the ideal way of estimating exposure in occupational groups. However, it is time-consuming and expensive and does not usually allow investigations of vast numbers of subjects or retrospective exposure assessments. The most used instruments in epidemiological studies are interviews and questionnaires, which often raise the question of validity and reliability. In the case-referent study the reports from those cases and referents who had job titles considered to involve low physical exposure were compared. The reported physical load exposure was very similar, and indicated that there was no differential misclassification.

Smoking was shown to be protective against knee OA, which is somewhat conflicting, as the health effects in general are hazardous. Smoking should not be recommended, but the possible mechanisms ought to be further investigated.

The most important preventive measure regarding knee OA according to the results in this thesis, is to prevent individuals from becoming overweight, and to encourage those who are to decrease their weight. Measures to reduce physical load exposure in occupational life and in unpaid work at home are also suggested in order to reduce the extent of knee OA. Leisure

time physical activities are beneficial for the health, but sports exposure, which is too extensive, could be hazardous as regards OA of the knee.

## 9. Summary

Hélène Sandmark: *Knee osteoarthritis in relation to physical workload and lifestyle factors - epidemiological studies*. *Arbete och Hälsa* 1999:12

This thesis investigates the relationship between physical workload, sports, and lifestyle factors and the development of knee osteoarthritis (OA) in ex-elite athletes, in men and women in the population, and in physical education (PE) teachers. It is based on four investigations: two cohort studies, one population-based case-referent study, and one field study.

In a cohort study of 114 male ex-elite athletes in track-and-field, and 355 referents from the population, the aim was to investigate if musculoskeletal dysfunctions, especially OA in knees and hips were more common. The results show that hip OA was more common among the ex-elite athletes (PR 3.6, 95% CI 1.4-9.3), and probably also knee OA (PR 2.8, 95% CI 0.7-11). The ex-elite athletes estimated their present general health to be better, they were more active in fitness activities, and were less overweight than the referents.

A case-referent study of 625 men and women who had had knee prosthesis surgery and referents from the population aimed to investigate risk factors for severe knee OA. The strongest risk factor was overweight (OR men 3.9, 95% CI 2.3-6.4, women 9.2, 95% CI 5.3-16.0). Forestry and construction workers, and female and male farmers had an increased relative risk of severe knee OA compared with the referents. Lifts, jumps, kneeling, squatting, and vibrations significantly increased the odds ratios two or three-fold for men. Those women who had taken care of elderly relatives or handicapped children at home had an increased relative risk of severe knee OA (OR 2.2, 95% CI 1.3-3.6). Sports activities increased the relative risk for men, but sports exposure in women, both cases and referents, was very limited, and no increased risk could therefore be found. Moderate, daily physical activities, such as cycling and walking did not increase the relative risk among men and women.

In a cohort study of 571 female and male PE teachers and referents from the population, the aim was to investigate if PE teachers develop more OA in the knees and hips, and other musculoskeletal disorders. The results show that men and women who had been working as PE teachers 10 years or more had a higher prevalence of knee OA compared with the population controls (PR men 2.8, 95% CI 1.6-4.8, women 3.2, 95% CI 1.8-5.5). They also had to change jobs more often due to knee dysfunction. There was an increased prevalence of hip OA for the female PE teachers. The PE teachers reported a better health status, and fewer serious diseases than the population referents. They were also less overweight, had a considerably higher lifelong sports exposure, and smoked less.

In a field study, physical load exposure was monitored during entire workdays in thirty female and male PE teachers. The measurements were performed with equipment attached to the body, or systematic registrations. The results indicate that PE teachers have a considerable physical workload on the lower extremities in their everyday work and a high cardiovascular load in comparison with several other occupational groups.

In conclusion the studies demonstrate that overweight is the most important risk factor for symptomatic knee OA among men and women, and high physical load in work, home nursing, and high sports exposure are contributing factors.



Keywords: elite athletes, health status, hip osteoarthritis, home nursing, overweight, musculoskeletal disorders, physical education teacher, physical load measurements, smoking, sports.

# Sammanfattning (Summary in Swedish)

Hélène Sandmark: *Knee osteoarthritis in relation to physical workload and lifestyle factors - epidemiological studies*. *Arbete och Hälsa* 1999:12

Syftet med avhandlingen var att studera fysisk belastning, sport och livsstilsfaktorer i relation till uppkomst av artros i knät i en grupp före detta elitidrottsmän, hos kvinnor och män i befolkningen samt hos idrottslärare. Den baseras på fyra projekt och består av två kohortstudier, en fall-referentstudie i befolkningen och en fältstudie.

Den första delstudien är en kohortstudie av 114 manliga f.d elitidrottsmän inom fri-idrott och 355 referenter från befolkningen. Syftet var att undersöka om muskuloskeletala besvär, särskilt artros i knä och höft var vanligare hos de f.d elitidrottsmännen. Resultatet visar att höftartros var vanligare hos de f.d elitidrottsmännen (PR 3.6, 95% CI 1.4-9.3) och förmodligen även knäartros (PR 2.8, 95% CI 0.7-11). De f.d elitidrottsmännen skattade sin nuvarande hälsa som bättre, motionerade mer och var mindre överviktiga än referenterna.

En fall-referentstudie av 625 knäprotesopererade kvinnor och män och referenter från befolkningen hade till syfte att undersöka riskfaktorer för svår knäartros. Den starkaste riskfaktorn var övervikt (OR män 3.9, 95% CI 2.3-6.4, kvinnor 9.2, 95% CI 5.3-16.0). Skogs- och byggnadsarbetare, samt kvinnliga och manliga lantbrukare hade en ökad relativ risk jämfört med referenterna. Lyft, hopp, knästående, huksittande och vibrationer ökade signifikant den relativa risken till mellan två och tre gånger för män. De kvinnor som hade vårdat äldre anhörig eller handikappade barn i hemmet hade en förhöjd relativ risk för svår knäartros (OR 2.2, 95% CI 1.3-3.6). Sportutövning förhöjde den relativa risken för för män, men eftersom såväl fall som referenter bland kvinnorna hade en låg exponering för sport kunde inga överrisker identifieras. Måttlig daglig fysisk aktivitet som cykling och promenader innebar inte någon ökad risk för knäartros för kvinnor och män.

I en kohortstudie av 571 kvinnliga och manliga idrottslärare och referenter från befolkningen var frågeställningen om idrottslärare i högre utsträckning drabbas av symptomgivande artros i knä och höft, samt andra muskuloskeletala besvär. Resultatet visar att kvinnor och män som varit idrottslärare i minst 10 år hade mer knäartros jämfört med befolkningskontrollerna (PR män 2.8, 95% CI 1.6-4.8, kvinnor 3.2, 95% CI 1.8-5.5). De hade även varit tvungna att i större utsträckning byta arbete på grund av knäbesvär jämfört med referenterna. Kvinnliga idrottslärare hade en ökad risk för höftartros, men ingen sådan riskökning kunde konstateras för männen. Idrottslärarna rapporterade bättre hälsa och led i mindre utsträckning av allvarliga sjukdomar jämfört med referenterna. Idrottslärarna hade sportat betydligt mer och rökt betydligt mindre och var inte lika överviktiga som referenterna.

I en fältstudie mättes fysisk belastning under hela arbetsdagar hos 30 kvinnliga och manliga idrottslärare. Mätningarna gjordes dels med personburen utrustning, dels genom systematisk registrering. Resultaten visar att idrottslärare har en betydande fysisk belastning på de nedre extremiteterna i sitt dagliga arbete och en centralcirkulatorisk belastning som ligger högt i förhållande till åtskilliga andra yrkesgrupper.

Sammanfattningsvis visar studierna att övervikt är den största riskfaktorn för symptomgivande knäartros hos både män och kvinnor, och att hög fysisk arbetsbelastning,

inklusive att att vårda sjuk anhörig i hemmet samt hög exponering för sport är andra viktiga riskfaktorer.

Nyckelord: elitidrottsmän, hälsotillstånd, höftartros, idrottslärare, muskuloskeletala besvär, mätning av fysisk belastning, rökning, sport, vård i hemmet, övervikt

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