



RAHMAN SHIRI

Erectile Dysfunction

Prevalence, Incidence and Risk Factors



ACADEMIC DISSERTATION

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the Faculty of Medicine of the University of Tampere,
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Public Health, Medisiinarinkatu 3, Tampere,
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ACADEMIC DISSERTATION

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List of original publications

This dissertation is based on the following original publications, referred to in the text by Roman numerals.

- I. Shiri R, Koskimäki J, Hakama M, Häkkinen J, Tammela TLJ, Huhtala H, Auvinen A (2003): Prevalence and severity of erectile dysfunction in 50 to 75-year-old Finnish men. *J Urol* 170:2342–4.
- II. Shiri R, Koskimäki J, Hakama M, Häkkinen J, Tammela TLJ, Huhtala H, Auvinen A (2003): Effect of chronic diseases on the incidence of erectile dysfunction. *Urology* 62:1097–102.
- III. Shiri R, Koskimäki J, Häkkinen J, Tammela TLJ, Huhtala H, Hakama M, Auvinen A (2004): Effects of age, comorbidity and lifestyle factors on erectile function, Tampere Aging Male Urological Study (TAMUS). *Eur Urol* 45:628–33.
- IV. Shiri R, Koskimäki J, Hakama M, Häkkinen J, Huhtala H, Tammela TLJ, Auvinen A (2004): Effect of lifestyle factors on the incidence of erectile dysfunction. *Int J Impot Res*, in press.

Abbreviations

ANOVA	ANalysis Of VAriance
BMI	body mass index
BPH	benign prostate hyperplasia
CHD	coronary heart disease
CI	confidence interval
DEC	depression, ED and cardiovascular disease
ED	erectile dysfunction
FSH	follicle-stimulating hormone
HDL-C	high-density lipoprotein-cholesterol
IIEF	International Index of Erectile Function
LH	luteinizing hormone
LUTS	lower urinary tract symptoms
MMAS	Massachusetts Male Aging Study
NIH	National Institutes of Health
OR	odds ratio
RR	rate ratio
TAMUS	Tampere Male Aging Urological Study
TURP	transurethral resection of prostate

Abstract

Objectives: To determine prevalence, incidence and major risk factors.

Materials and methods: This study forms part of the Tampere Aging Male Urological Study (TAMUS). In this population-based follow-up study, the target population comprised all 3152 men born in 1924, 1934 or 1944 residing in Tampere or 11 surrounding municipalities in 1994. Information was collected by means of a mailed self-administered questionnaire. The questionnaire was mailed to all 3152 men during the first quarter of 1994. A total of 2198 completed questionnaires (70%) was returned. Similar questionnaires were sent five years later in May 1999 to 2864 men. Between 1994 and 1999, 262 men had died, six had emigrated and 38 no longer had a permanent address on the Population Register. Altogether, 2133 (75%) returned the questionnaires. Overall 1683 (53.5%) men responded to both baseline and follow-up inquiries. Of these, 241 were excluded because of missing data on erection function and 1442 (46%) were included in the follow-up sample. Erectile dysfunction was assessed by the two questions of the International Index of Sexual Function questionnaire. Multivariate linear regression, multivariate logistic regression and multivariate Poisson regression models were used.

Results: The overall prevalence of ED was 76.5% (95% CI 72–81%). It increased steeply with age and was markedly higher after the age of 60 years (67% for men aged 50 years and 88.5% for men aged 75). The combined prevalence of moderate and complete ED increased from 12% for men aged 50 years to 58% for those aged 75. The prevalence of complete ED increased more rapidly than the combined prevalence of moderate and complete ED.

The annual incidence of moderate or severe ED was 39 cases per 1,000 man-years, increasing sharply with age from 22 cases per 1,000 man-years for ages 50–55 to 84 cases per 1,000 man-years for those ages 70–75 years. The incidence of combined moderate and complete ED increased by 80% (95% CI 40–120%) by each one-decade increment in age.

Applying the study prevalence and incidence estimates to the population of men aged 50–79 in Finland resulted in an estimated 207,000 prevalent moderate/ complete ED cases and 21,500 new cases of ED annually.

Education, urban-rural residence and marital status did not have a substantial effect on any degree of ED. Diabetes was the strongest factor contributing to the development of ED, while heart disease, hypertension, and cerebrovascular disease

were weak predictors of ED. Smoking was a weak risk factor of ED, while amount of alcohol and coffee consumed did not have a clear effect on erectile function. Current smoking doubled the risk of complete ED in men without comorbidity.

Conclusions: The present findings indicate that erectile dysfunction is a commonly occurring disorder at ages 50–75 years. The prevalence of moderate ED increased linearly and slowly, whereas that of complete ED increased exponentially and rapidly with age. Prevalence is the largest burden in men over 65 years old, whereas incidence is the largest burden in those below 65 years of age. The results of this study show that sociodemographic status, except age, and lifestyle factors seem to be of limited importance in the etiology of erectile dysfunction, while biological factors such as age, diabetes, hypertension, heart disease and cerebrovascular disease are important predictors of ED.

1 Introduction

Erectile dysfunction (ED) has been defined as the persistent or recurrent inability to attain and/or maintain an erection sufficient for satisfactory sexual function (National Institutes of Health (NIH) Consensus Conference 1993). Earlier ED was included in the general term impotence, with non-specific meaning, which also referred to other disorders of male sexual function, such as orgasmic and ejaculatory dysfunction (NIH Consensus Conference 1993). Erectile dysfunction has recently been the focus of public and scientific attention due to the development of novel effective oral therapies, sildenafil, tadalafil and vardenafil (Boolell et al. 1996, Hellstrom et al. 2003, Porst et al. 2003). It is an important public health concern (Laumann et al. 1999), and affects millions of men worldwide (Weissman et al. 1977, Parazzini et al. 2000). Desire, orgasmic and ejaculatory capacity may be intact even in the presence of ED or may be to some extent deficient and contribute to the sense of inadequate sexual function (NIH Consensus Conference 1993). Most men experience this inability at some point in their lives, usually by age 40. Some men experience chronic, severe erectile dysfunction, while others achieve only mild erections.

Although ED does not affect life expectancy and it is not a life-threatening disorder, it should not be regarded as benign. Sex is important to elderly men and it is important to preserve erection, orgasm and sexual desire (Helgason et al. 1996). In a society in which sexuality is widely promoted, ED impacts on feelings of self-worth and self-confidence and may impair the quality of life of affected men and their partners. ED is strongly associated with unsatisfying personal experiences and relationships, highlights the association of ED with emotional and physical satisfaction with sexual partners and with feelings of general happiness (Laumann et al. 1999).

ED can have a strong negative effect on interpersonal relationships, well-being, quality of life and sexual life dissatisfaction (Krane et al. 1989, Jonler et al. 1995, Kaiser 1996, Macfarlane et al. 1996, Ansong et al. 1998, Ventegodt 1998, Laumann et al. 1999, Abolfotouh and al-Helali 2001, MacDonagh et al. 2002, Meuleman et al. 2001, Seyam et al. 2003) and is associated with depression, anger, anxiety, loss of self-esteem and increased drug and alcohol abuse (Fugl-Meyer et al. 1997, Levine and Kloner 2000). Improved erectile function is accompanied by improved quality of life (MacDonagh et al. 2002) and decrease in general psychiatric symptoms (Carrol and Bagley 1990, Althof et al. 1991). The majority of men with ED express dissatisfaction with their relations with their partner (Panser et al. 1995, Read et al. 1997, Giuliano et al. 2002) and men with ED are preoccupied with this condition mainly at the time of sexual relations and some of them think about it during the course of the day. Partners

are more likely to be dissatisfied with their sex life if the other partner has a sexual problem (Dunn et al. 2000). The benefits of treating sexual problems have wide implications for both partners in a relationship.

Epidemiological studies on ED are needed for identifying risk factors and subsequently for developing appropriate service delivery and resource allocation models as well as for developing prevention strategies when modifiable risk factors are established. In addition, changing cultural attitudes and demographic shifts in the population have highlighted the pervasiveness of sexual concerns in all ethnic and age groups. Valid risk factor identification is essential for the prevention of ED (NIH Consensus Conference 1993). Cross sectional studies have shown that various chronic disorders including depression, diabetes, and cardiovascular and neurological diseases are associated with elevated prevalence of ED (Feldman et al. 1994a, Parazzini et al. 2000, Nicolosi et al. 2003b). Among lifestyle habits, smoking, obesity and high serum cholesterol level increase, while physical exercise reduces the prevalence of ED. Very few population-based follow-up studies are available concerning incidence and risk factors.

2 Aims of the study

The overall objective of the present study was to determine the occurrence and major risk factors of ED. The specific objectives were as follows:

To estimate the rate of decline in sexual function with age (I, II, III, IV)

To determine the prevalence of ED (I)

To estimate the incidence of ED (II)

To determine the relationship between sociodemographic factors and ED (III, IV)

To identify the influence of chronic diseases on ED (II, III)

To assess the effects of smoking, alcohol and coffee consumptions on ED (III, IV)

3 Review of the literature

3.1 Pathophysiology of erectile dysfunction

Erection is a complex neurovascular function mediated by nitric oxide. Nitric oxide has been identified as the principal neurotransmitter mediating penile erection (Kim et al. 1991, Rajfer et al. 1992). Neural regulation of the penile vasculature is not limited to the cavernous arteries but extends to the trabecular smooth muscle and endothelium of the intracorporeal sinusoids (Burnett et al. 1992). The endothelium is a highly active metabolic and endocrine organ involved in the control of the systemic vasculature. Activity in the cholinergic nerves of the penis with the release of acetylcholine as well as nitric oxide is the neurogenic signal for cavernous smooth muscle relaxation. Nitric oxide under the control of acetylcholine is also produced by the corporeal endothelium (Saenz de Tejada 1992). The endothelium is most likely innervated directly by cholinergic fibers. Within the penis, endothelial cells produce nitric oxide with the enzyme nitric oxide synthase (Lamas et al. 1992). Nitric oxide produced by the endothelium may not be the primary mediator of smooth muscle relaxation during erection, but endothelial nitric oxide synthase is an important determinant of cardiovascular homeostasis. It has a critical role in cell survival, blood vessel remodeling, atherosclerosis prevention and the inhibition of programmed cell death or apoptosis. The pathogenesis of ED indicates that a number of chronic diseases are interrelated with the disorder.

The etiology of ED may be organic or psychological. Often the cause is multifactorial and ED can be a manifestation of several diseases (Krane et al. 1989). Psychological, neurological, vascular (venous or arterial), endocrinological, traumatic or iatrogenic (drug and surgery) factors act in concert to increase the risk of ED (Shabsigh et al. 1988, Kirby 1994, Benet and Melman 1995, Schiavi and Rehman 1995, Bortolotti et al. 1997). The male erectile response is a vascular event initiated by neuronal action and maintained by a complex interplay between vascular and neurological events (NIH Consensus Conference 1993). Normal erectile function requires the co-ordination of psychological, hormonal, neurological, vascular, and cavernosal factors. Alteration in any one of these factors is sufficient to cause erectile dysfunction. Knowledge about the pathophysiology of erection has increased considerably during the past decade and ED is currently believed to be of organic etiology in most men (Feldman et al. 1994a) as most of the medical disorders associated with ED affect the arterial system. While most patients with ED are thought to have an organic component, the psychological aspect also plays a part, with self-confidence, anxiety, partner communication and conflict often being important contributing factors (NIH Consensus Conference 1993).

3.2 Prevalence of erectile dysfunction

The prevalence of erectile dysfunction has been difficult to estimate due to the fact that it is not life threatening, patients often do not seek treatment and the terminology for the condition has been confusing. It is estimated that in 1995 there were over 152 million men worldwide who had ED, and in 2025 the number of men with ED will be approximately 322 million, an increase of nearly 170 million men (Ayta et al. 1999). The greatest increases will be in the developing world, i.e. Africa, Asia and South America. The likely worldwide increase in the prevalence of ED (associated with rapidly aging populations) combined with newly available and highly publicized medical treatments will raise challenging policy issues in nearly all countries.

Establishing the prevalence of ED is important for understanding the need for services, which depends on the functional expectations of men as they age. The overall prevalence of ED has been reported as 13–80% (Feldman et al. 1994a, Chew et al. 2000, Dunn et al. 1998, Pinnock et al. 1999, Braun et al. 2000, Kongkanand 2000, Green et al. 2001, Marumo et al. 2001, Morales et al. 2001, Sanchez Merino et al. 2001, Moreira et al. 2002). Higher overall prevalences have been reported in Japan and Pakistan, and lower prevalences in France, Great Britain, Germany and Spain (Table 1). Approximately 5% to 20% of men have moderate to severe ED. Different definitions of ED, age distributions and risk factor profiles, as well as methodological differences, may explain much of the variance in reported prevalences (Kubin et al. 2003).

3.3 Incidence of erectile dysfunction

Prevalence estimates and cross-sectional studies correlates of erectile dysfunction have recently been reported in several studies. Yet, studies on the incidence of ED are necessary to identify etiological factors and to assess and plan preventive strategies. Few studies have been conducted on the incidence of ED (Table 2). The first incidence estimate was reported in a study conducted at Cooper Clinic, Dallas, Texas on 3,250 men aged 26–83 years (Wei et al. 1994). The overall incidence was 12 cases per 1,000 person-years. The rate increased with age, from 5.5 cases per 1,000 man-years for ages 45–54 to 52 for those aged 65 and older. A recent study on white males in the United States reported an incidence of 26 cases per 1,000 man-years (95% confidence interval 22.5 to 29.9) (Johannes et al. 2000), and an estimate of 66 was reported in a Brazilian study (Moreira et al. 2003) for men aged 40–69.

Table 1. Prevalence of erectile dysfunction by country

Country	Sample size	Age range	Prevalence		Reference
			Overall	Moderate or severe	
Pakistan	585	25–70	81.0	NR	Shaer et al. 2003
Japan	600	40–70	79.0	34.0	Nicolosi et al. 2003b
Finland	1941	50–70	74.0	26.0	Koskimäki et al. 2000
Turkey	1982	40+	69.0	36.0	Akkus et al. 2002
Italy	600	40–70	66.5	17.0	Nicolosi et al. 2003b
Egypt	805	20–70	NR	23.5	Seyam et al. 2003
	600	30–70	63.5	NR	Shaer et al. 2003
Malaysia	600	40–70	63.0	22.0	Nicolosi et al. 2003b
Belgium	799	40–70	61.5	35.0	Mak et al. 2002
Nigeria	984	35–70	57.5	NR	Shaer et al. 2003
Morocco	655	25+	54.0	16.0	Berrada et al. 2003
USA	2000	53–90	NR	33.0	Bacon et al. 2003
	1290	40–70	52.0	35.0	Feldman et al. 1994a
	1408	50–76	46.5	NR	Ansong et al. 2000
Singapore	729	30+	51.0	28.0	Tan et al. 2003
Argentina	2715	34–97	42.0	NR	Nicolazco et al. 2003
Brazil	600	40–70	41.0	15.0	Nicolosi et al. 2003b
	602		39.5	14.5	Moreira et al. 2002
	342	40–70	46.0	12.0	Moreira et al. 2002
	1286	18+	46.0	15.0	Moreira et al. 2001
Australia	1240	18–91	39.5	27.5	Chew et al. 2000
France	Review	18–70	39.0	NR	Virag and Beck-Ardilly 1997
	5099	18/70	25.0	NR	Costa et al. 2003
	1004	40+	32.0	NR	Giuliano et al. 2002
Thailand	1250	40–70	37.5	18.5	Kongkanand 2000
India	1,000	20–30 ±	24.0	NR	Verma et al. 1998
UK	789	50+	21.5	NR	Dunn et al. 1998
	<100	–	17.0	NR	Read et al. 1997
	2002	55–70	NR	13.0 *	Green et al. 2001
Iran	2444	20–70	19.0	15.5	Safarinejad 2003
Spain	2476	25–70	19.0	7.0	Martin-Morales et al. 2001
	830	19–90	64.0	NR	Sanchez Merino et al. 2001
Germany	4489	30–80	19.0	NR	Braun et al. 2000
Denmark	1230	18–88	NR	5.5	Ventegodt. 1998
	439	51	NR	4.0	Solstad and Hertoft 1993
Norway	1182	40+	NR	33.0	Vaaler et al. 2001

NR= Not reported

* Complete ED

± Majority

+ Median

Table 2. Reported incidences of ED by country and age per 1,000 person-years

Country	Sample size	Follow up time (years)	Age range	Age group			Overall
				40–49	50–59	60–69	
USA	3250	1.8	26–83	–	–	–	12
	847	8.8	40–69	12	30	46	26
Brazil	428	2.0	40–69	33	54	190	66

3.4 Risk factors of erectile dysfunction

3.4.1 Sociodemographic status

3.4.1.1 Age

A man's sexual activity generally declines in a slow, continuous process from adolescence through old age (Murray and Meacham 1993). The number of ejaculations per week rapidly accelerates during adolescence, peaks in the mid-teens, and gradually drops to zero by the eight or ninth decades of life (Kinsey et al. 1948), and the number of orgasms also declines steadily, beginning at about the age of 35 years (Martin 1977). The capacity for repeated orgasms in a short period of time declines most rapidly (Kinsey et al. 1948). However, aging itself is not necessarily associated with altered sex steroid levels in men (Murray and Meacham 1993).

Degenerative changes in the testes of older men increase with advancing age (Harman 1978). Advancing age is associated with a decline in the ejaculate volume, the concentration of spermatozoa, total sperm production and a decrease in the number of sperm per ejaculate as well as an increase in nonviable and abnormal spermatozoa (Hafez 1976, Johnson et al. 1984a). Pituitary gonadotropins, the luteinizing hormone (LH) and follicle-stimulating hormone (FSH) increase with age (Harman 1978, Johnson et al. 1984b). The rise in levels of FSH is usually greater than the increase in LH values. Failure of seminiferous tubular function is generally more prominent than loss of testosterone secretion as men age.

Age has the strongest association with ED and appears to be a major risk indicator in that it is associated with an increased likelihood of etiological risk factors, although physiological alteration related to hormonal agents may be involved. Erection problems are an age-dependent disorder, possibly resulting from physiological changes associated with the aging process. Erectile dysfunction is often assumed to be a natural concomitant of aging to be tolerated along with other conditions associated with aging (NIH Consensus Conference 1993). However, this assumption may not be entirely correct as ED may occur as a consequence of specific illnesses or of medical treatment for certain diseases. When the individual and his partner perceive changes in sexual function as a natural consequence of the aging process, they may modify their sexual behavior to accommodate the condition and maintain sexual satisfaction. Yet many men do not perceive ED as a normal part of aging and seek to identify means by which they may return to their previous level and range of sexual activity.

The prevalence and severity of ED increase while the satisfaction with sexual life decreases with age (Feldman et al. 1994a, Macfarlane et al. 1996, Koskimäki et al.

2000, Morales et al. 2001, Nicolosi et al. 2003b). Earlier studies have reported an increase in the prevalence of ED by 5% to 17% with each one-year increment in age in men older than 18 years (Moreira et al. 2001, Akkus et al. 2002, Nicolosi et al. 2003b, Shaeer et al. 2003). The prevalence of ED increases most markedly after 60 years of age (Pinnock et al. 1999, Marumo et al. 2001, Moreira et al. 2002). The age of 60 has been suggested as the turning point after which desire exceeds potency and sexual frequency diminishes (Pinnock et al. 1999). Older men are more worried about sexual function and express most dissatisfaction with sexual performance (Panser et al. 1995). The age-related increase in dissatisfaction could be accounted for by the age-related increase in ED, decreased libido and the interaction between them. Men with ED, who have normal or high libido, seem to be especially dissatisfied (Panser et al. 1995).

Age-related decline in male sex hormones, particularly testosterone, is referred to as andropause. Like menopause, andropause is associated with physical and emotional symptoms such as lack of concentration, nervousness, impaired memory, depressive mood, insomnia, lack of energy and general sense of well-being, periodic sweating, bone and joint complaints, fatigue, decrease in lean body mass, skin alterations, decrease in body hair and increase in visceral fat and obesity. It is also associated with decreased libido and erectile dysfunction (Tan and Pu 2004, T'Sjoen et al. 2003).

3.4.1.2 Marital status

Inconsistent results have been found regarding the effect of marital status on ED, with some studies reporting an effect (Laumann et al. 1999, Safarinejad 2003, Shaeer et al. 2003) that has not been confirmed in others (Ansong et al. 2000, Parazzini et al. 2000, Morales et al. 2001, Moreira et al. 2001, Akkus et al. 2002). Men who are separated, divorced or widowed have a higher prevalence of ED than those who are married or living with a partner (Feldman et al. 1994a, Laumann et al. 1999, Akkus et al. 2002). Some studies have reported that men who have never married have a lower prevalence of ED than married men (Klein et al. 1996, Seyam et al. 2003), whilst higher prevalence has been reported in others (Laumann et al. 1999, Nicolosi et al. 2003b). ED is also associated with younger age at marriage and longer duration of marriage (Seyam et al. 2003).

3.4.1.3 Education and income

An association between socio-economic status and ED has not been well established. Education is commonly used as an indicator of socio-economic status in population

surveys. Men with lower socio-economic status (income, education and occupation) tend to have lower sexual function (Pinnock et al. 1999). Education and household income have been shown to be inversely related to ED in some studies (Laumann et al. 1999, Johannes et al. 2000, Berrada et al. 2003, Moreira et al. 2003, Safarinejad 2003, Seyam et al. 2003). The effect of socio-economic status on ED is partly mediated by lifestyle factors and medical conditions (Aytac et al. 2000). Higher socio-economic status has been linked to better health and better-educated men have lifestyles that are physically and emotionally less stressful (Laumann et al. 1999). Low level of education is also a marker of the high prevalence of non-diagnosed diseases and low income is related to higher levels of stress.

3.4.1.4 Other sociodemographic factors

Erectile dysfunction has not been strongly associated with geographic location (Jonler et al. 1995, Ansong et al. 2000, Akkus et al. 2002, Seyam et al. 2003). The differences among geographic regions may reflect interregional cultural and socio-economic differences (Akkus et al. 2002). The difference in rural areas might be related to the significant effect on ED of marrying at a younger age, fathering more children, having a lower level of education and lower economic level (Seyam et al. 2003). These factors are counterbalanced to some extent by younger age and more physical exercise in rural areas. Black men are at higher risk of ED than whites (Laumann et al. 1999, Moreira et al. 2001, Moreira et al. 2003). Religion is not related to ED (Moreira et al. 2001). However, homo/bisexual orientation is associated with ED (Moreira et al. 2001), which may reflect differences in the perception of and attitude toward ED among homo/bisexual men. ED is also associated with being unemployed (Akkus et al. 2002, Seyam et al. 2003, Shaeer et al. 2003).

3.4.2 Chronic diseases

3.4.2.1 Diabetes

Diabetes is the main systemic disease causing ED. Erectile dysfunction has been shown to be at least three times more prevalent in diabetic individuals than in the general population, with estimates ranging from 20% to 86% (Kayigil et al. 1996, Klein et al. 1996, Fedele et al. 1998, 2000, Cummings and Alexander 1999, Parazzini et al. 2000, Alexopoulou et al. 2001, Siu et al. 2001, El-Sakka and Tayeb 2003, Nicolosi et al. 2003b). Onset of ED is reported to occur at an earlier age in individuals with diabetes

than in the general population, frequently occurring within 10 years of the diagnosis, whether of the insulin-dependent or non-insulin-dependent type (Whitehead and Klyde 1990).

The incidence of ED in diabetics has been estimated at 68 cases per 1,000 person-years for men aged 19–79 years (Fedele et al. 2001). It has been reported as 15 cases per 1,000 person-years for ages 19–29, 66 for ages 50–59 and 149 for ages 70–79. Erectile dysfunction increases with the duration of diabetes, deteriorating metabolic control and diabetes-related complications such as retinal, arterial, heart, neurological disease, abnormal albuminuria and decreased androgen (Klein et al. 1996, Fedele et al. 1998, 2000, 2001, Parazzini et al. 2000, Romeo et al. 2000, Alexopoulou et al. 2001, Bacon et al. 2002, Siu et al. 2001, El-Sakka 2003, Nicolosi et al. 2003b). The incidence is higher in type 2 than type 1, in diabetic men with hypertension, use of antihypertensive medications, increasing body mass index (BMI), ischemic heart disease and renal disease (Klein et al. 1996, Fedele et al. 2001). Diabetic foot, a marker of defective blood support, also in parts of the body other than feet, is associated with the higher incidence of ED (Klein et al. 1996, Fedele et al. 2001).

It is not known which of the many aspects of diabetes is the direct cause of ED, but vascular disease is the most frequently cited (Jevtich et al. 1982, Sullivan et al. 2001, Nicolosi et al. 2003b). Vascular disease causes arteriogenic ED mainly via interference with the arterial inflow to the cavernous body (Kayigil et al. 1996). In addition, autonomic neuropathy, gonadal dysfunction and vascular endothelium or neurogenic impairment of penile smooth muscle relaxation have been implicated (Saenz de Tejada et al. 1989, Cummings and Alexander 1999). Furthermore, medication for diabetes may aggravate the condition (Parazzini et al. 2000).

3.4.2.2 Hypertension

Previous studies have shown that hypertension is a risk factor for ED (Lochmann and Gallmetzer 1996, Braun et al. 2000, Naya et al. 2003, Shaeer et al. 2003). ED is more common and more severe in hypertensive men than in the general population (Burchardt et al. 2000). Furthermore, antihypertensive drugs used for treatment of hypertension may often cause or exacerbate ED as a side effect (Weiss 1991, Sanchez Merino et al. 2001, Moreira et al. 2003, Nicolosi et al. 2003b). Since adequate arterial blood supply is essential for erection, any disorder that impairs blood flow may be implicated in the etiology of ED (NIH Consensus Conference 1993), and long-term hypertension results in damage to the vascular system (Burchardt et al. 2000). It is unclear how much risk is related to hemodynamic impact on vascular smooth muscle and how much is caused by

side effects of antihypertensive medication. Increased severity of ED in hypertensive men may be due to a higher rate of vascular disease and long-term vascular damage.

3.4.2.3 Cardiac disease

Heart disease is a predictor of ED (Marumo et al. 1999, Berrada et al. 2003, Naya et al. 2003, Nicolosi et al. 2003b, Tan et al. 2003). Erectile dysfunction is associated with duration of heart disease with an increase of 5% per year of disease duration (Nicolosi et al. 2003b). Men with a history of myocardial infarction (Wabrek and Burchell 1980, Green et al. 2001) or coronary bypass surgery (Gundle et al. 1980) are at higher risk of ED. Some studies have found no (Moreira et al. 2001, Akkus et al. 2002) or only non-significant association between heart disease and ED (Moreira et al. 2003, Shaeer et al. 2003). Erectile dysfunction is an early correlate of coronary disease, arising from common atherogenic risk factors (Feldman et al. 2000). The onset of ED in older men can be interpreted as a forerunner of subclinical coronary disease (Morley et al. 1988, Lochmann and Gallmetzer 1996, Feldman et al. 2000, Levine and Kloner 2000). Erectile dysfunction is a sensitive indicator of wider arterial insufficiency, and ED may call attention to coronary risk and contribute to the prevention of morbidity and mortality from coronary heart disease. Diagnosis of ED increases among men with ischemic heart disease and vice versa after the introduction of sildenafil (Kaye and Jick 2003).

Cardiovascular diseases cause ED mainly by reducing the arterial function of the cavernous body. Erectile dysfunction and coronary heart disease share some behaviorally modifiable determinants, such as smoking, fatty diet, adverse serum lipid levels, hypertension, physical inactivity and obesity (Feldman et al. 2000, Jackson 2000). The same vascular/endothelial injuries that occur in the coronary arteries are likely to affect the cavernosal arteries, the primary arteries supplying penile erectile tissue. Progressive occlusive disease is manifest sooner in the microvasculature than in larger vessels.

3.4.2.4 Depression and other psychogenic factors

Underlying relationship problems are a common cause of ED. The ratio of organic to psychogenic male sexual dysfunction has been reported to be directly proportional to age (Aydin et al. 2001), with 70% of men under 35 years of age having psychogenic ED and 85% of men over 50 years of age having organic ED. Psychogenic influences are the most likely causes of intermittent erectile failure in young men. Anxiety about "performance" may result in inhibitory sympathetic nervous system activity, and

anticipatory anxiety can make the condition self-perpetuating (Kirby 1994). Index of dominant personality is inversely correlated with ED (Feldman et al. 1994a, Araujo et al. 2000). This may be related to improved tolerance of long-term stress by dominant individuals. ED is more likely to appear in men with a submissive personality (Araujo et al. 2000). Submissive individuals are unable to cope with stress, resulting in neuro-cardiovascular changes that could play a role in their subsequent development of ED. A psychogenic component is often present in older men, secondary to an organic cause (Krane et al. 1989).

Depression is related to a higher prevalence or incidence of ED (Araujo et al. 1998, Shabsigh et al. 1998, Araujo et al. 2000, Johannes et al. 2000, Vaaler et al. 2001, Mak et al. 2002, Berrada et al. 2003, Moreira et al. 2003, Okulate et al. 2003, Shaeer et al. 2003). Emotional problems are likely to contribute to the experience of ED (Laumann et al. 1999). Anger and depression were associated with prevalence of ED in the Massachusetts Male Aging Study (MMAS) baseline sample, but not with incidence of ED at follow-up (Araujo et al. 2000). Erectile dysfunction is associated with duration of depression (Nicolosi et al. 2003b). Younger men who reported difficulties with erections were more likely to be worried about these problems than older men (Macfarlane et al. 1996). Chronic anxiety, abnormal personality traits and problems with expression of emotions, particularly anger, cause excessive sympathetic outflow or elevated blood catecholamine levels, which may produce vasoconstriction and increase penile smooth muscle tone, opposing the events necessary for erection (Krane et al. 1989, Langeluddecke et al. 1990). On the other hand, men with ED may be anxious, depressed and lacking self-esteem and self-confidence.

The causal relationship between depression and ED is most probably bi-directional (Shabsigh et al. 1998, Seidman and Roose 2000). Erectile dysfunction follows depression and depression is also a consequence of ED. Men with ED have a higher rate of depression compared with those free from ED (Shabsigh et al. 1998). Effective treatment of ED results in the remission of comorbid depressive illness (Seidman et al. 2001) and the decrease in general psychiatric symptoms (Carrol and Bagley 1990, Althof et al. 1991). The relationship between treated ED and depression supports the construct of reactive depression (Roose et al. 2001). In some cases, ED causes or contributes to the development of depression, in other cases ED could be a symptom of depression (Seidman et al. 1999). ED may be associated with depression, loss of self-esteem, poor self-image, increased anxiety or tension with one's sexual partner, and fear and anxiety associated with contracting sexually transmitted diseases, including AIDS (NIH Consensus Conference 1993).

Depression is associated with a variety of neurophysiological disturbances. It can impair the functioning of the autonomic nervous system, and as a result, the para-

sympathetic nervous system may be unable to facilitate the relaxation of the penile smooth muscle tissue necessary for erection (Araujo et al. 1998). Another explanation is related to the behavior of depressed people. They may be critical of themselves or have a tendency to introspection. These behaviors may lead to performance anxiety, which may inhibit the man's ability to reach an erection.

Psychopathology or emotional factors play a significant role in the etiology of ED and they are difficult to identify in a non-direct assessment (Lee et al. 2000). Even in the presence of significant vascular risk factors, psychological abnormalities may be the primary etiology. Furthermore, fluctuations in erectile functioning may be attributable to psychological influences (Beutel 1999).

3.4.2.5 Prostatectomy and lower urinary tract symptoms

Prostate problems and lower urinary tract symptoms are related to sexual life dissatisfaction and ED (Laumann et al. 1999, Braun et al. 2000, Akkus et al. 2002, Nicolosi et al. 2003a,b). Radical prostatectomy increases the prevalence of ED (Rodriguez et al. 1997, Mulcahy 2000, Berrada et al. 2003, Meuleman and Mulders 2003, Shaeer et al. 2003). ED is more common in patients with benign prostatic hyperplasia (BPH) (Baniel et al. 2000, Akkus et al. 2002, Moreira et al. 2003, Shaeer et al. 2003), and after transurethral resection of prostate (TURP) (Tscholl et al. 1995, Bieri et al. 1997, Perera and Hill 1998). It has been shown that ED develops after prostate surgery or radiotherapy for prostate cancer, especially at older ages (Pinnock et al. 1999, Siegel et al. 2001), while in another study the frequency of sexual desire and sexual intercourse did not differ between those had undergone prostate surgery and the men who had not (Macfarlane et al. 1996). In a further study, subjects even reported a significant improvement in their sexual life after TURP (Doll et al. 1993a).

Capsular perforations adjacent to the neurovascular bundles may be a cause of ED after TURP, and small size adenomas carry a higher risk (Tscholl et al. 1995, Bieri et al. 1997). However, a randomized trial of patients with BPH found no difference in the risk of ED at three-year follow-up between those having undergone TURP and those assigned to watchful waiting (Diokno et al. 1990).

Erectile dysfunction is highly prevalent in men with lower urinary tract symptoms, and strongly related to lower urinary tract symptom severity (Macfarlane et al. 1996, Vallancien et al. 2003). The symptoms with the greatest effect are hesitancy, forcing, diminution of stream and dribbling. Patients with symptomatic prostatism are more likely to consider their sexual life more affected compared with those without such symptoms but with acute or chronic urinary retention (Doll et al. 1993b). Urinary symptoms probably do not have a direct effect on sexual satisfaction, but instead

adversely affect a sense of perceived general well-being and self-esteem, factors that may in turn have an effect on sexual life.

3.4.2.6 Hyperlipidemia

High blood triglyceride and cholesterol levels increased the prevalence and incidence of ED in some studies (Wei et al. 1994, Marumo et al. 1999, Pinnock et al. 1999, Morales et al. 2001, Sanchez Merino et al. 2001, Safarinejad 2003), while other studies did not find any relationship (Feldman et al. 1994a, 2000, Marumo et al. 2001, Moreira et al. 2001). In one study high-density lipoprotein cholesterol (HDL-C) was inversely correlated with ED (Feldman et al. 1994a).

A high level of total cholesterol or low level of HDL-C may result in arteriosclerosis and induce ED by arterial insufficiency. They could also cause degeneration of cavernous smooth muscle and inability to expand the cavernosal trabeculae against the tunica albuginea and compress the subtunical venules, thereby inducing ED by excessive blood outflow (Wespes et al. 1992). Hypercholesterolemia may cause impairment of endothelium-dependent relaxation. Oxidized low-density lipoprotein is the major causative cholesterol of the impaired relaxation response (Kim 2000).

It has been shown that lipid-lowering medications such as fibrates and statins, in addition to hyperlipidemia itself, increase the prevalence of ED (Bruckert et al. 1996). Diet or physical activity programs for preventing cardiovascular disease by lowering total cholesterol or increasing HDL-C may also lower the incidence of ED (Wei et al. 1994). Whether correcting a dyslipidemic profile results in a reduced risk of developing ED has not been established and it is not also known if such an intervention improves ED (Schachter 2000).

3.4.2.7 Medications

Several medications increase the prevalence of ED (Feldman et al. 1994a, Wei et al. 1994, Read et al. 1997, Green et al. 2001, Morales et al. 2001). Around 25% of erectile failures seen in clinic patients are thought to be caused by medication (O'Keefe and Hunt 1995). Erectile dysfunction may affect 10–20% of patients taking thiazide diuretics, and to a lesser extent, patients using beta-blocking drugs (Buffum 1986, Mikhailidis et al. 2000). Erectile dysfunction commonly complicates antidepressant treatment with both monoamine oxidase inhibitors and tricyclic antidepressants (O'Keefe and Hunt 1995, Read et al. 1997, Safarinejad 2003, Shaeer et al. 2003). Benzodiazepines and selective serotonin reuptake inhibitors have been reported to cause

erectile failure, as well as decreased libido and ejaculatory problems (Balon et al. 1993, O'Keefe and Hunt 1995, Derby et al. 2001). Cimetidine and ulcer medications (Read et al. 1997, Fedele et al. 2000, Berrada et al. 2003, Shaeer et al. 2003), digoxin and metoclopramide cause erectile dysfunction, as do anabolic steroids, either through a direct effect on the penile tissues or through suppression of normal androgen production (Guay 1995). Hypoglycemia resulting from insulin or oral hypoglycemic agents can cause ED or orgasmic dysfunction (Whitehead and Klyde 1990, Feldman et al. 1994a, Green et al. 2001, Berrada et al. 2003, Shaeer et al. 2003).

Other medicines reported occasionally to be associated with ED include nitrate, warfarin, digoxin (Green et al. 2001), antihypercholesterolemics (Green et al. 2001, Berrada et al. 2003), antihypertensive drugs (Feldman et al. 1994a, Barksdale and Gardner 1999, Fedele et al. 2000, Mikhailidis et al. 2000, Seyam et al. 2003), cardiac drugs (Feldman et al. 1994a, Fedele et al. 2000, Berrada et al. 2003, Seyam et al. 2003, Shaeer et al. 2003), diuretics (Klein et al. 1996, Fedele et al. 2000, Mikhailidis et al. 2000, Derby et al. 2001, Green et al. 2001), psychotropic and sleeping drugs (Fedele et al. 2000, Morales et al. 2001, Berrada et al. 2003, Safarinejad 2003), calcium channel antagonists (Vallancien et al. 2003) and vasodilators (Feldman et al. 1994a, Green et al. 2001). The use of angiotensin-converting enzyme inhibitors is inversely associated with ED among patients with end-stage renal disease (Rosas et al. 2001).

Several common drugs may increase the prevalence of ED. It is not known whether these medicines are causative or whether the underlying medical condition is the real cause of ED. The effects of dosage and duration of use on ED are also not obvious. The association between medications and ED is necessarily confounded by the underlying medical conditions. A drug-related effect on ED is difficult to distinguish from the effect of the disease and from concomitant exposure to other drugs.

3.4.2.8 Other chronic diseases

Erectile dysfunction is more common among men with arthritis (Blake et al. 1988, Feldman et al. 1994a, Morales et al. 2001, Seyam et al. 2003), which may be related to co-morbidity and medication. Cerebral infarction is also associated with erectile dysfunction (Agarwal and Jain 1989, Parazzini et al. 2000, Marumo et al. 2001), while peptic ulcer increases the prevalence of ED in some studies (Feldman et al. 1994a, Seyam et al. 2003, Shaeer et al. 2003), but not in others (Marumo et al. 2001, Moreira et al. 2001, Akkus et al. 2002, Moreira et al. 2002, Berrada et al. 2003, Nicolosi et al. 2003b). Renal failure (Breza et al. 1993, Carson and Patel 1999, Palmer 1999, Malavaud et al. 2000, Rosas et al. 2001, Seyam et al. 2003), pulmonary disease (Morales et al. 2001), treated schizophrenia (Aizenberg et al. 1995), chronic hepatitis

(Marumo et al. 2001, Seyam et al. 2003), allergy (Feldman et al. 1994a, Morales et al. 2001), Behcet's syndrome (Erdogru et al. 1999) and obstructive sleep apnea syndrome (Margel et al. 2004, Fanfulla et al. 2000) have also been associated with ED.

3.4.3 *Lifestyle (modifiable) factors*

Modifiable risk factors for erectile dysfunction include cigarette smoking, alcohol consumption, obesity and sedentary life style.

3.4.3.1 *Smoking*

The use of tobacco is a major public health problem worldwide and studies on its role on ED have yielded conflicting results. Several studies suggest that smoking increases the prevalence of ED (Shabsigh et al. 1991, Mannino et al. 1994, Klein et al. 1996, Pinnock et al. 1999, Feldman et al. 2000, Fedele et al. 2000, Morales et al. 2000, Kongkanand 2000, Bacon et al. 2003, Safarinejad 2003, Seyam et al. 2003), and both current and former smokers are at higher risk of ED (Mannino et al. 1994, Bortolotti et al. 1997, Parazzini et al. 2000, Mirone et al. 2002), while other studies showed negative results (Feldman et al. 1994a, Jeremy and Mikhailidis 1998, Vaaler et al. 2001, Akkus et al. 2002, Moreira et al. 2003). In some studies only heavy smoking (30–40 cigarettes or more per day) was significantly associated with ED (Moreira et al. 2002, Nicolosi et al. 2003a,b), or smoking was related to the higher prevalence of complete ED in current smokers without comorbidity such as cardiovascular disease, hypertension, diabetes or neuropathy (Feldman et al. 1994a, Mirone et al. 2002). Passive exposure to cigarette smoke, if present both at home and at work, also increases the risk of ED (Feldman et al. 2000).

The dose response effect of smoking on ED is also controversial. Some previous studies have found that the risk of ED is proportionate to the number of years spent smoking (Mirone et al. 2002, Nicolosi et al. 2003a), while others failed to detect such a relationship (Feldman et al. 1994a, Mannino et al. 1994). Number of years smoked (pack years) and cigarettes smoked daily (packs per day) were not significant predictors of ED in current smokers.

The possible effect of smoking may be mediated by systemic changes including hypercoagulability, enhanced platelet aggregation, an imbalance between thromboxane and prostacyclin concentrations and direct toxic effects on the vascular endothelium (Bornman and du Plessis 1986). Smoking decreases pelvic and penile vascular flow (McMahon and Touma 1999) and clinical and basic science studies provide strong

indirect evidence that smoking may affect penile erection by impairing endothelium-dependent smooth muscle relaxation (Levine and Gerber 1990, McVary et al. 2001). The long-term effect of smoking on ED may be related to atherosclerotic lesions in the internal, pudendal and common penile arteries of impotent men (Virag et al. 1985, Condra et al. 1986, Rosen et al. 1991, Shabsigh et al. 1991). Smoking may act in a synergistic or additive manner with other risk factors, such as hypertension, heart disease and diabetes (Mannino et al. 1994, Parazzini et al. 2000).

3.4.3.2 Alcohol consumption

The association between alcohol consumption and ED is controversial and dose response relationship may be nonlinear (Bortolotti et al. 1997, Parazzini et al. 2000). Cross-sectional studies have yielded partly contradictory results (Feldman et al. 1994a, Green et al. 2001, Morales et al. 2001, Giuliano et al. 2002). In several studies alcohol consumption did not increase the prevalence of ED (Shiavi 1990, Klein et al. 1996, Fedele et al. 2000, Feldman et al. 2000, Parazzini et al. 2000, Vaaler et al. 2001, Berrada et al. 2003, Okulate et al. 2003). Other studies have found that alcohol intake increases the prevalence of ED (Gambert 1997, Kongkanand 2000, Lue 2000, Abolfotouh and al-Helali 2001, Morales et al. 2001, Bacon et al. 2003). A reduction in heavy drinking does not decrease the risk of ED (Derby et al. 2000). Men who consume > 40 units / week have double the rate of ED compared with moderate or non-drinkers (Green et al. 2001). The effect of excessive alcohol consumption on the prevalence of minimal ED has been small (Feldman et al. 1994a), and a lower prevalence of ED has been reported among moderate drinkers (one to two drinks per day) than non-drinkers (Akkus et al. 2002, Nicolosi et al. 2003b, Shaeer et al. 2003). Only a single population-based follow-up study has evaluated the effect of alcohol consumption on the incidence of erectile dysfunction and it failed to show a clear effect (Feldman et al. 2000).

3.4.3.3 Obesity

Obesity has been shown to increase the prevalence of ED in some studies (Pinnock et al. 1999, Derby et al. 2000, Araujo et al. 2000, Moreira et al. 2002, Bacon et al. 2003, Vallancien et al. 2003), but no such relationship has been found in others (Feldman et al. 1994a). In a prospective study, overweight exerted a strong independent effect on ED (Feldman et al. 2000). A study conducted in the U.S. suggested that obesity is not a significant risk factor of ED in patients without any vascular risk factors (Keil et al. 1992). Body mass index predicts sexual frequency but not arousal problems (Khaw and

Barrett-Connor 1992), while central adiposity is inversely related to androgen levels. Obese patients also have an increased prevalence of vascular risk factors (Chung et al. 1999). Obesity is associated with adverse lipid profiles, hypertension and diabetes (Van Itallie 1985), and may be independently associated with atherosclerotic heart disease (Hubert et al. 1983). Obesity in itself may not be a direct risk factor, but can induce vasculogenic impotence through increasing risk of chronic diseases including diabetes, hypertension, heart disease and hyperlipidemia.

3.4.3.4 Sedentary lifestyle

Physical activity is inversely associated with the prevalence and incidence of ED (White et al. 1990, Derby et al. 2000, Johannes et al. 2000, Bacon et al. 2003, Nicolosi et al. 2003b). Erectile dysfunction is more common among men who are sedentary and infrequent among those who remain active or initiate physical activity. Physical activity may reduce the risk of ED even if initiated in midlife. Sedentary men may be able to reduce their risk of ED by adopting regular physical activity at a level of at least 200 kcal/day, which corresponds to walking briskly for two miles (Pate et al. 1995). Physical activity has been associated with a reduced risk of cardiovascular disease by inhibiting atherosclerosis, improving the lipid profile, enhancing vascular blood delivery and having favorable effects on thrombosis (Gordon and Scott 1991). Thus it is plausible that exercise has similar effects on blood flow in the penile vasculature (White et al. 1990).

3.4.3.5 Coffee consumption

Coffee drinking has been shown to reduce the prevalence of ED in two studies (Diokno et al. 1990, Akkus et al. 2002), while others have indicated it may increase the prevalence of ED (Kongkanand 2000, Shaeer et al. 2003). Other studies failed to show any relationship between coffee consumption and ED (Berrada et al. 2003, Nicolosi et al. 2003b). The previous findings on the direct effect of coffee drinking on ED are highly inconsistent.

3.4.4 Other predictors

Perceived health is an important determinant of ED (Ansong et al. 2000). Fat intake is associated with ED (Araujo et al. 2000, Feldman et al. 2000). Pelvic injury and surgery (Bortolotti et al. 1997, Braun et al. 2000, Parazzini et al. 2000, Safarinejad 2003, Shenfeld et al. 2003), urethral injury (Mark et al. 1995), disc herniation (Marumo et al. 2001), drug abuse (La Pera et al. 2003) and open abdominal aortic aneurysm repair (Xenos et al. 2003) have been associated with ED (Table 3). An inverse association has been found between serum dehydroepiandrosterone and ED (Feldman et al. 1994a).

Table 3. Risk factors of erectile dysfunction

Aging
<i>Chronic diseases</i>
Diabetes
Hypertension
Cardiac disease
Renal failure
Depression
Stroke
LUTS
Behcet's disease
Hyperlipidemia
Disc herniation
Obstructive sleep apnea syndrome
Arthritis
<i>Injury</i>
Spinal
Pelvic
Urethral
<i>Surgery</i>
Prostatectomy
Open abdominal aortic aneurysm repair
<i>Lifestyle factors</i>
Sedentary lifestyle
Obesity
Smoking
<i>Medications</i>

3.4.5 *Causal pathways*

It is largely unknown which of the associated risk factors, e.g. concomitant diseases or their treatments are the real causes of erectile dysfunction. Neither is it well understood which of the associations in fact exist, e.g. whether depression causes ED or whether ED causes depression. Diabetic men with hypertension and smokers with diabetes or hypertension are at higher risk of ED (Klein et al. 1996, Parazzini et al. 2000, Safarinejad 2003). Cigarette smoking greatly amplifies the effect of treated heart disease, treated hypertension, untreated arthritis and drug effects in those taking cardiac, antihypertensive and vasodilators (Feldman et al. 1994a). Current smokers with substance abuse have a high prevalence of ED (Mannino et al. 1994). Smokers with a history of pelvic surgery or radiation had 10 times higher prevalence of ED than smokers without such history (Mirone et al. 2002).

Depression, cardiovascular disease and ED share many risk factors and may be best modeled in a 3-way reinforcing relation (Goldstein 2000). Men with ED also frequently have cardiovascular disease and depression. Patients with both ischemic heart disease and depression are more likely to have ED than those with only one of these diseases (Roose and Seidman 2000). The prevalence of depression, ED, and coronary heart disease (CHD) increases with age, and the symptoms related to these three illnesses are closely interlinked. The term "DEC syndrome" has been introduced to refer to this triad of comorbid conditions (Tan and Pu 2003). Studies have shown that depression may predispose an individual to an increased risk of developing CHD. Likewise, patients with ED are more likely to be clinically depressed than those who are free of it, and patients with clinical depression often have ED. Furthermore, patients presenting with ED are often hypertensive or have a higher prevalence of cardiovascular disease.

Some risk factors of ED have a synergistic effect and potentiate each other's effect.

4 Materials and Methods

4.1 Population

Tampere is the third largest city in Finland with more than 175,000 inhabitants at the end of 1993 and almost 200,000 in 2002 (Statistics Finland 2002). Male residents of Tampere represented the urban source population for this study. Hämeenkyrö, Kuhma-lahti, Kuru, Kylmäkoski, Luopioinen, Pälkäne, Ruovesi, Sahalahti, Urjala, Viljakkala and Vilppula are small or medium-sized rural municipalities. Men living in these rural and semi-rural municipalities formed the rural source population in this study.

During the first quarter of 1994, all men in the city of Tampere and in the above-mentioned 11 rural municipalities born in 1924, 1934 or 1944 were identified from the Population Register Center (Koskimäki et al. 2000). Thus, the men in the target population were 50, 60 or 70 years old at the end of 1994. The size of the target population was 3,152. This cohort comprised 11% of the male population of the city of Tampere and 10% of the male population of the 11 rural municipalities aged 50 years and over. The study cohort represented the ages at which erectile dysfunction is common and increasing rapidly.

The questionnaire was mailed to all 3,152 men in the target population during the first quarter of 1994 (Figure 1). Nine men had died before receiving the questionnaire, leaving 3,143 eligible subjects. An identical questionnaire was sent three months later to the 1,433 men who did not respond to the first. A total of 2,198 completed questionnaires (70%) were returned. Of these, 257 were excluded from the study; 244 due to missing data regarding erectile function and 13 as the respondents were institutionalized or unable to respond independently. Hence, 1,941 men (62%) were included in the study at baseline.

Similar questionnaires were sent five years later in May 1999 to 2,864 men within the same target population, with a reminder to the 1,162 who did not respond to the first within three months. Between 1994 and 1999, 262 were confirmed deceased, six had emigrated and 38 no longer had a permanent address on the Population Register. Overall, 2,133 men (75%) responded to inquiry. Of these, 287 were excluded due to missing data on erection function and finally 1,846 (64%) composed the material for the 1999 survey.

Overall 1,683 (53% of the baseline population or 59% of those who were alive and eligible at follow-up) men responded to both the baseline and follow-up inquiries. Of these, 241 were excluded because of missing data on erection function and 1,442 (46% of baseline population or 50% of eligible survivors at follow-up) were included in

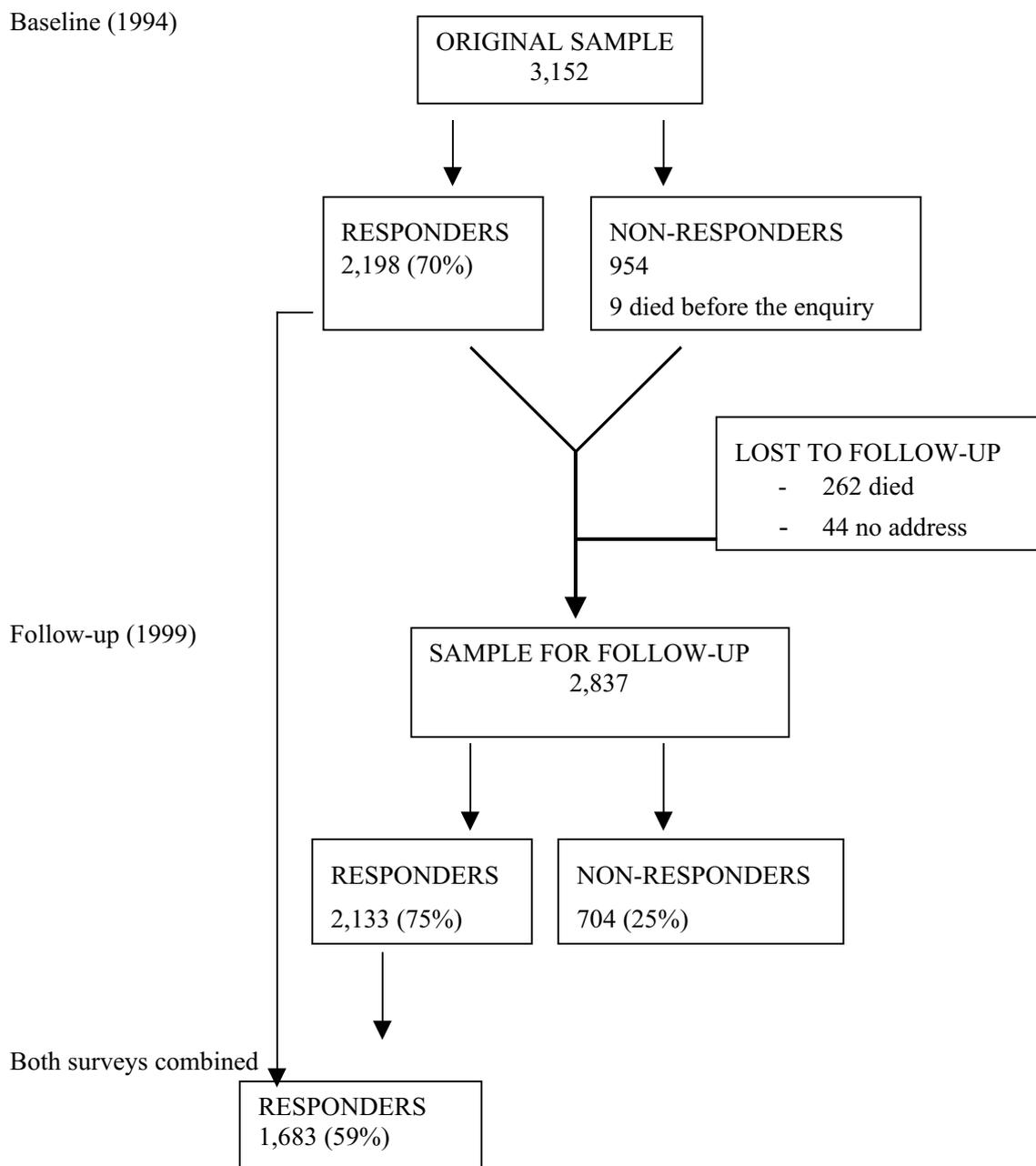


Figure 1. Flow chart of response rates to baseline, follow-up and to both inquiries.

the follow-up sample. A total of 499 men were lost to follow-up or without data on erectile function in 1999. Those men excluded from study at the beginning did not substantially differ from the study group in regard to age. Of those included in the baseline sample 72% were followed-up for five years.

4.2 Study instrument

Information was collected by means of a mailed self-administered questionnaire comprising items on sociodemographic status, lifestyle factors, medical conditions and medications, diet, physical activity, lower urinary tract symptoms, erectile capacity, and concern about erection problems. Each subject was informed in writing of the purpose of the study and our intention to keep the information confidential and anonymous.

Erectile dysfunction was defined according to the National Institutes of Health Consensus Panel on ED as the inability to achieve or maintain an erection sufficient for satisfactory sexual function (NIH Consensus Conference 1993). Subjects were asked two questions on their erectile capacity: “Have you had problems getting an erection before intercourse begins?” and “Have you had problems maintaining an erection once intercourse has begun?” For both questions four response options were: never, sometimes, quite often and always. The subjects were asked to choose the category that best described them as able to achieve or maintain an erection good enough for sexual intercourse.

It was decided not to elicit information from the regular partner in the assessment of ED, as this information may not be valid. The men may be more able or willing to achieve erection in masturbation or with someone other than their partner and the partner may be ignorant of such activities.

The two questions were combined to classify severity of erectile dysfunction. No difficulty in achieving and maintaining erection was defined as normal erectile function. Some difficulties in achieving and/or maintaining an erection was classified as minimal ED and fairly frequent difficulties as moderate ED. Complete ED was defined when intercourse did not succeed at all.

Subjects were considered smokers if they had smoked more than one cigarette/day for at least one year; ex-smokers if they had smoked more than one cigarette/day for at least one year, but had stopped more than one year before participating in the study, and non-smokers if they had never smoked or smoked less than one year. Intensity of smoking was not recorded.

Weekly consumption of alcohol was recorded in grams of absolute alcohol. The estimate was based on an approximation of a unit of alcohol (a bottle of beer, a glass of

wine and other drinks) as containing 11.5 g of absolute alcohol. Similarly, a bottle of wine was estimated to contain 6.3 glasses and a bottle of spirits 12.5 drinks. Coffee intake was recorded as cups per day.

4.3 Statistical analyses

The kappa statistic was used as a measure of agreement between achieving and maintaining an erection. It takes into account the agreement occurring solely on the basis of chance. The kappa coefficient is defined as the difference between observed and expected agreement, expressed as the actual agreement relative to complete concordance (Landis and Koch 1977). It ranges between -1 and 1 , the value zero indicating only chance agreement and one perfect agreement. Kappa values 0.4 – 0.6 represent moderate, 0.6 – 0.8 substantial and 0.81 – 1.00 almost perfect agreements. Here the interpretation is that value one indicates that one question is sufficient as two questions being compared provide identical information. Value zero indicates maximum usefulness of the other question as they measure independent components of ED.

Prevalence of ED was estimated as the ratio of men with erectile dysfunction to all men with data on erectile function. The age-specific prevalence of ED and 95% confidence intervals (CI) for these prevalences were estimated. A multivariate logistic regression model was used to assess the association of sociodemographic, medical and lifestyle factors with erectile dysfunction. Men with ED were defined as cases and men without ED as controls.

The incidence of ED was calculated by dividing the number of new cases occurring between the baseline and follow-up surveys by the number of person-years at risk. Person-years for estimating incidence and rate ratios of complete ED or combined moderate and complete ED were calculated by multiplying the number of men free from ED at end of follow-up by 5 years (the length of the follow-up period) and the number of those who developed ED during the follow-up by 2.5 years (half the duration). In the calculation of the incidence of minimal and moderate ED, a transition pattern was assumed that also took into account more severe forms of ED, on the assumption that the milder forms are a necessary intermediate stage in the development of more severe forms. Hence, person-years for minimal and moderate ED were calculated as:

Minimal: $5 \times N$ (no ED) + $5/2 \times N$ (minimal ED) + $5/3 \times N$ (moderate ED) + $5/4 \times N$ (complete ED)

Moderate: $5 \times N$ (no or minimal ED) + $5/2 \times N$ (moderate ED) + $5/3 \times N$ (complete ED)

Incidence was expressed as the number of cases per 1,000 person-years. The rate ratios were defined as the incidence of ED in the groups with the determinant at baseline divided by the incidence of ED in the groups without such a characteristic. The 95% confidence intervals for the rates and ratios were estimated on the assumption that the number of new cases follows a Poisson distribution. A multivariate Poisson regression model was used to evaluate whether selected sociodemographic, medical and lifestyle factors at baseline predicted incidence of ED at follow-up.

The age-specific incidence of ED by severity was also estimated by a simple method without the assumption of transition patterns, with incidence calculated on the basis of new cases of minimal/moderate cases only. The incidence was calculated by dividing the numbers of new cases at follow-up by the number of men free from ED at baseline.

The numbers of cases of moderate or severe ED in the general population of 2002 in Finland were projected. Age-specific prevalence was used to determine the proportion of men with and without ED. The number of men free from moderate or complete ED in the population obtained from the 2002 census data (Central Statistical Office of Finland) was multiplied by the age-specific incidence rates to estimate the expected number of new ED cases. The sums of age-specific expected cases were estimates of the total number of current ED cases and the annual number of expected new cases in 50 to 79-year-old men in Finland.

The study protocol was approved by the Tampere University Hospital and Tampere City ethical review committees.

5 Results

5.1 Response rate

The rate of participation was 70% in the 1994 and 75% in the 1999 inquiry before the exclusion of those men without information on erectile function. After exclusion the corresponding figures were 62% and 64% respectively. Of those included in the baseline sample 72% responded at follow-up, after five years. The youngest age group had a slightly lower participation than the other age groups in both surveys before exclusion. The oldest age group had a lower response to both surveys after exclusion of those with missing values on erectile function.

A comparison of respondents with non-participants at baseline showed no substantial age difference. The mean age was 57.1 among non-participants and those who were excluded from the study due to missing information on erectile function and it was 58.6 among those who were included in the study at baseline. Men who participated in the follow-up survey (Table 4) differed in some respects from those for whom no information on erectile function was available in 1999. The 499 men without follow-up information were older (on average 4 years older than the follow-up sample and 3 years older than the baseline population), less educated (13% beyond high school vs. 23%), smaller proportion married or living as married (72% vs. 83%), and were more likely to live in rural or semi-rural areas (26% vs. 23%). They reported heart disease (25% vs. 15%), cerebrovascular disease (9% vs. 5%) and diabetes (10% vs. 6%) at baseline more frequently than the participants.

5.2 Agreement between measures of erectile dysfunction

When ED was dichotomized into two categories, the kappa indices for agreement between achieving and maintaining erection were 0.86 and 0.82 for the baseline and follow-up surveys respectively. Considering ED severity in four categories, minimal ED had the lowest and complete ED the highest agreement between the two surveys. Minimal ED was often measured as minimal in only one question, either achieving or maintaining erection, but not in the other. Complete ED was correlated similarly for both achieving and maintaining erection.

Table 4. Distribution of sociodemographic, medical and lifestyle characteristics at initial survey among respondents to baseline, follow-up inquiries and those without data at follow-up.

Background characteristics	Baseline population		Follow-up population		Population without data at follow-up	
	N	%	N	%	N	%
Sociodemographic factors						
<i>Age (years)</i>						
50	768	39.6	629	19.2	139	27.9
60	673	34.7	537	37.2	137	27.4
70	500	25.7	277	43.6	223	44.7
<i>Education</i>						
Basic compulsory	966	49.8	684	47.4	282	56.5
Intermediate or high school	568	29.2	419	29.1	149	29.9
College or university	396	20.4	333	23.1	63	12.6
<i>Marital status</i>						
Married or living with partner	1561	80.5	1203	83.4	358	71.7
Single, widower or divorced	379	19.4	238	16.5	141	28.3
<i>Place of residence</i>						
Urban	1465	75.5	1098	76.1	367	73.5
Rural or semi-rural	467	24.1	337	23.4	130	26.1
Medical history						
Hypertension	560	28.9	417	28.9	143	28.7
Heart disease	347	17.9	223	15.5	124	24.8
Arthritis	510	26.3	371	25.7	139	27.9
Pulmonary disease	198	10.2	138	9.6	60	12.0
Diabetes	143	7.4	92	6.4	51	10.2
Cerebrovascular disease	124	6.4	78	5.4	46	9.2
Lifestyle factors						
<i>Smoking</i>						
Never smoked	635	32.7	502	34.8	133	26.7
Past smokers	853	43.9	644	44.7	209	41.9
Current smokers	445	22.9	292	20.2	153	30.7
<i>Alcohol intake (g / week)</i>						
None	637	32.8	452	31.3	185	37.1
1–150	858	44.2	661	45.8	197	39.5
≥151	405	20.9	303	21.0	102	20.4
<i>Coffee (cups / day)</i>						
0–1	258	13.3	186	12.9	72	14.4
2–4	920	47.4	692	48.0	228	45.7
≥ 5	753	38.8	561	38.9	192	38.5
Total	1941	100	1442	100	499	100

The frequencies do not always sum up to the total number due to missing information

5.3 Prevalence of erectile dysfunction

The overall prevalence of ED was 76.5% (95% CI 72–81%). It increased with age (Table 5) and was markedly higher after the age of 60 years (67% for men aged 50 years and 88.5% for aged 75). The combined prevalence of moderate and complete ED increased from 12% for men aged 50 years to 58% for those aged 75. The proportion of men with normal erectile function and minimal ED gradually decreased, while the prevalence of moderate and especially complete ED increased with age. The prevalence of moderate ED increased linearly and slowly, whereas that of complete ED increased exponentially and rapidly with age. The prevalence of complete ED increased more rapidly than the combined prevalence of moderate and complete ED.

Age was strongly associated with both prevalence and severity of ED. The excess odds ratio per each one-year increment in age was 0.06 (95% CI 0.05–0.07) for the overall prevalence and 0.10 (95% CI 0.09–0.11) for the combined prevalence of moderate and complete ED.

Table 5: Prevalence and severity of erectile dysfunction by age.

Age (baseline/follow up)	Severity of erectile dysfunction								
	None		Minimal		Moderate		Complete		Total
	n	%	n	%	n	%	n	%	N
50/55	511	31.2	886	54.1	190	11.6	51	3.1	1638
60/65	261	19.8	666	50.5	225	17.1	166	12.6	1318
70/75	118	14.2	271	32.6	161	19.4	281	33.8	831
Overall	890	23.5	1823	48.1	576	15.2	498	13.2	3787

5.4 Effect of background characteristics on the prevalence

The prevalence of moderate or complete ED increased markedly with age (Table 6), especially after the age of 60 years. Risk of ED was 10-fold in men aged 75 years compared with those aged 50. The combined prevalence of moderate and complete ED increased significantly with diabetes (OR=3.2), hypertension (OR=1.5), heart disease (OR=1.4), arthritis (OR=1.2) and smoking (OR=1.4). The prevalence of ED increased non-significantly in men with pulmonary or cerebrovascular diseases.

Table 6. Odds ratios for ED by age, chronic diseases and smoking in the 3,787 men

Background characteristics	Age-adjusted		Full model *	
	Odds ratio	95% CI	Odds ratio	95% CI
Age (years)				
50	1	Reference	1	Reference
55	1.5	1.1–2.0	1.4	1.1–1.9
60	2.3	1.7–3.0	1.9	1.4–2.5
65	4.0	3.0–5.2	3.4	2.5–4.5
70	7.3	5.5–9.6	5.5	4.1–7.4
75	10.0	7.4–13.6	8.2	5.9–11.3
Diabetes	3.8	2.9–5.0	3.2	2.5–4.2
Hypertension	1.7	1.4–2.0	1.5	1.3–1.8
Heart disease	1.7	1.4–2.0	1.4	1.2–1.7
Arthritis	1.2	1.1–1.5	1.2	1.0–1.4
Pulmonary disease	1.2	0.9–1.5	1.2	0.9–1.5
Cerebrovascular disease	1.6	1.2–2.3	1.3	0.9–1.8
Smoking	1.5	1.3–1.8	1.4	1.2–1.7

* Adjustment for each other

5.5 Incidence of erectile dysfunction

The crude incidence of minimal ED estimated with the simple method was 77 (95% CI 65–90) cases per 1,000 person-years in men who were free from any ED at baseline (Table 7). It increased from 70 per 1,000 person-years for men aged 50–55 years to 88 per 1,000 person-years for those aged 70–75.

The overall incidence of moderate ED was 24 (95% CI 20–29) cases per 1,000 person-years in men with no or minimal ED at baseline. It increased with each decade of age from 19 per 1,000 person-years for men aged 50–55 year to 24 per 1,000 person-years for men aged 70–75.

The mean incidence of complete ED was 17 (95% CI 14–21) in men with no, minimal or moderate ED at baseline, ranging from 5 per 1,000 person-years in men aged 50–55 to 46 per 1,000 person-years for those aged 70–75.

The incidence of all forms of ED increased markedly with age (Table 7–10). Incidence of moderate or complete ED was 39 (95% CI 34–45) in men with no or minimal ED at baseline.

Table 7. Age-specific incidence of erectile dysfunction by severity and with the simple method

Age group	Minimal		Moderate		Complete	
	Incidence	95% CI	Incidence	95% CI	Incidence	95% CI
50–55	70	54–86	19	14–24	5	2–7
60–65	85	63–108	29	22–36	22	16–27
70–75	88	50–125	31	19–44	46	33–59
Overall	77	65–90	24	20–29	17	14–21

Table 8. Incidence of severity of erectile dysfunction by sociodemographic status, 1994–1999

Background characteristics	Minimal			Moderate			Complete		
	Incident cases	Incidence /1,000	95% CI	Incident cases	Incidence /1,000	95% CI	Incident cases	Incidence /1,000	95% CI
<i>Education</i>									
Basic compulsory	90	142	116–175	57	38	29–49	34	18	13–26
Intermediate or high school	51	111	84–146	99	45	37–55	57	20	15–26
College or university	37	126	91–174	47	38	28–50	24	16	10–23
<i>Marital status</i>									
Married or living as married	148	130	110–152	175	43	37–49	99	19	15–23
Single, widower or divorced	30	117	82–168	27	31	21–46	16	15	9–25
<i>Place of residence</i>									
Urban	131	120	101–143	155	40	35–47	85	18	14–22
Rural or semi-rural	45	154	115–206	48	43	32–57	29	20	14–29

Table 9: Rate ratios for minimal, moderate and complete ED by sociodemographic status

Background characteristics	Minimal			Moderate			Complete		
	Age adjusted	Full model *		Age adjusted	Full model*		Age adjusted	Full model*	
	Rate ratio	Rate ratio	95% CI	Rate ratio	Rate ratio	95% CI	Rate ratio	Rate ratio	95% CI
Age, one decade increments	1.5	1.5	1.2–1.8	2.0	2.0	1.7–2.5	3.0	2.8	2.2–3.7
<i>Education</i>									
Basic compulsory	1.2	1.1	0.8–1.6	1.0	0.9	0.7–1.5	0.8	0.7	0.5–1.1
Intermediate or high school	1.0	R	R	1.0	R	R	1.0	R	R
College or university	1.2	1.1	0.7–1.7	1.0	1.0	0.7–1.3	0.8	0.8	0.4–1.3
<i>Marital status</i>									
Married or living as married	1.0	R	R	1.0	R	R	1.0	R	R
Single, widower or divorced	0.9	0.9	0.6–1.3	1.1	1.0	0.7–1.5	0.9	1.0	0.6–1.6
<i>Place of residence</i>									
Urban	1.0	R	R	1.0	R	R	1.0	R	R
Rural or semi-rural	1.1	1.0	0.9–1.2	0.9	0.9	0.7–1.2	1.0	1.0	0.8–1.3

* Adjustment for sociodemographic, medical and lifestyle factors
R=Reference category

5.6 Risk factors for erectile dysfunction

5.6.1 Sociodemographic status

The incidence rates of ED increased with each decade of age and were higher after the age of 60 years. The incidence of minimal ED increased by 50% (95% CI 20–80%), moderate ED by 100% (95% CI 70–150%) and complete ED by 180% (95% CI 120–270%) with each one-decade increment in age. The incidence of combined moderate and complete ED increased by 80% (95% CI 40–120%) with one-decade increment in age (Table 11). The findings indicate that healthy aging was an independent risk factor for ED. Education, urban-rural residence and marital status did not have a substantial effect on any degree of ED. Highly and lower educated men had non-significantly lower incidence of complete ED compared with moderately educated men.

5.6.2 Chronic diseases

The incidence of moderate or complete ED was higher in men with diabetes, hypertension, heart disease and cerebrovascular disease (Table 10 and 11). After adjustment for other factors the incidence significantly increased only in men with diabetes (OR=2.4, 95% CI 1.5–3.7) and hypertension (OR=1.5, 95% CI 1.1–2.0).

Table 10. Incidence of moderate or complete ED by age and medical conditions

Background characteristics	Incident cases	Incidence/1,000	95% CI
Overall	203	39	34–45
<i>Age (years)</i>			
50–55	59	22	17–29
60–65	91	49	40–60
70–75	53	84	64–110
<i>Medical history</i>			
<i>Hypertension</i>			
None	134	35	29–41
Yes	69	54	42–68
<i>Heart disease</i>			
None	161	35	30–41
Yes	42	69	51–94
<i>Diabetes</i>			
None	181	37	32–42
Yes	22	119	78–181
<i>Arthritis</i>			
None	133	33	28–39
Yes	70	63	50–79
<i>Pulmonary disease</i>			
None	178	38	33–44
Yes	25	57	38–84
<i>Cerebrovascular disease</i>			
None	182	37	32–43
Yes	21	97	63–148

Table 11. Rate ratios for moderate or complete ED by age and medical conditions

Background characteristics	Age-adjusted		Full model *	
	Rate ratio	95% CI	Rate ratio	95% CI
Age, one decade increments	1.9	1.6–2.3	1.8	1.4–2.2
<i>Medical conditions</i>				
Diabetes	2.7	1.7–4.2	2.4	1.5–3.7
Heart disease	1.5	1.0–2.1	1.4	0.9–2.0
Hypertension	1.5	1.1–2.0	1.5	1.1–2.0
Arthritis	1.4	1.1–2.0	1.3	0.9–1.8
Pulmonary disease	1.2	0.8–1.8	1.1	0.7–1.7
Cerebrovascular disease	2.1	1.4–3.4	1.6	0.9–2.6

* Adjustment for sociodemographic, medical and lifestyle factors

5.6.3 Lifestyle factors

There was a small, non-significant excess risk of ED in former smokers (Table 12 and 13) with an increasing trend by severity of the symptom (rate ratio, RR=1.2 for minimal, 1.3 for moderate and 1.5 for complete ED). However, none of the results were statistically significant. Current smoking had a small, non-significant effect only on moderate ED (RR=1.3).

The incidence of complete ED doubled in current smokers, within a sub-group of healthy men who were free from cerebrovascular disease, heart disease and diabetes or related medications and had not undergone prostatectomy or had spinal cord or urinary tract injury at both surveys. The rate ratio after controlling for effects of socio-demographic and lifestyle factors was 1.3 for minimal ED among 280 men free from ED, 1.3 for moderate ED in the 717 with no or minimal ED and 1.8 for complete ED among 806 with no, minimal or moderate ED at baseline. The corresponding figures for former smokers were 1.5, 1.0 and 1.3. None of the rate ratios was statistically significant.

Consumption of alcohol did not have a significant effect on the incidence of ED. The rate ratios among moderate drinkers were consistently less than one in all groups of ED severity. Minimal ED was somewhat more common in heavy drinkers than in non-drinkers (RR=1.4). Coffee drinking was inversely, but non-significantly related to ED, rate ratios ranged between 0.7 and 1.1, depending on the amount of consumption and severity of ED.

Table 12. Incidence of minimal, moderate and complete ED by lifestyle factors, 1994–1999

Background characteristics	Minimal			Moderate			Complete		
	Incident cases	Incidence /1,000	95% CI	Incident cases	Incidence /1,000	95% CI	Incident cases	Incidence /1,000	95% CI
<i>Smoking</i>									
Never-smoked	63	113	88–144	64	34	27–43	34	15	11–21
Past smokers	82	146	118–182	98	48	39–58	69	26	20–32
Current smokers	32	117	82–165	41	40	29–54	12	9	5–16
<i>Alcohol intake (g / week)</i>									
None	65	135	106–172	67	45	35–57	44	23	17–31
1–150	68	108	85–137	88	38	31–47	41	14	10–19
≥151	43	156	116–210	44	41	31–55	28	21	14–30
<i>Coffee (cups / day)</i>									
0–1	31	156	110–222	29	45	31–64	19	24	15–37
2–4	86	128	103–158	94	39	32–48	64	21	17–27
≥ 5	60	115	89–148	79	41	33–51	31	12	9–18

Table 13. Rate ratios for minimal, moderate and complete ED by lifestyle factors

Background characteristics	Minimal			Moderate			Complete		
	Age adjusted	Full model*		Age adjusted	Full model*		Age adjusted	Full model*	
	RR	RR	95% CI	RR	RR	95% CI	RR	RR	95% CI
<i>Smoking</i>									
Past smokers	1.2	1.2	0.8–1.7	1.2	1.3	0.9–1.7	1.4	1.5	0.9–2.2
Current smokers	1.0	1.1	0.7–1.7	1.3	1.3	0.9–2.0	0.8	0.8	0.4–1.7
<i>Alcohol intake</i>									
1–150 (g / week)	0.9	0.9	0.6–1.3	1.0	0.9	0.7–1.3	0.7	0.7	0.5–1.1
≥151 (g / week)	1.4	1.4	0.9–2.1	1.1	1.1	0.7–1.6	1.3	1.1	0.7–1.9
<i>Coffee consumption</i>									
2–4 (cups / day)	0.8	0.9	0.6–1.3	0.9	0.9	0.6–1.4	0.9	0.9	0.5–1.5
≥ 5 (cups / day)	0.8	0.8	0.5–1.3	1.1	1.1	0.7–1.7	0.6	0.7	0.4–1.2

* Adjustment for sociodemographic, medical and lifestyle factors

5.7 Projection of occurrence to Finnish population

Applying the study prevalence and incidence estimates to the population of men aged 50 to 79 in Finland resulted in an estimated 207,000 prevalent moderate/complete ED cases and 21,500 new cases of ED annually (Table 14). Prevalence is the greatest burden in men over 65, whereas incidence is the greatest burden below 65 years of age.

Table 14: Estimation of the prevalence and incidence of moderate or severe ED to the general population of 2002 in Finland

Age groups (year)	Population size	Prevalence of ED	Population with ED	Population without ED	Incidence /1,000	Annual new cases
50–54	208,985	12.1	25,290	183,700	22	4,040
55–59	181,388	17.0	30,840	150,550	22	3,310
60–64	129,277	24.1	31,160	98,120	49	4,810
65–69	105,749	35.5	37,540	68,210	49	3,340
70–74	91,018	50.0	45,510	45,510	84	3,820
75–79	63,520	58.0	36,840	26,680	84	2,240
Total	779,937		207,180	572,770		21,560

6 Discussion

Sexual dysfunction is an important public health concern (Carrier et al. 1994). It is recognized increasingly that maintaining quality of life is an important aspect of human well-being in its own right and has a profound implication for an individual's health status. Sexual function is an important component of quality of life for men. The last few decades have seen a marked increase in the mean life expectancy in Europe. This has made elderly people and their quality of life a matter of ever-increasing medical concern. As the population over 60 years increases, people expect to maintain quality of life. The expectations for sexual activity have increased in older people in response to increased sexual awareness and improved health and well-being. ED is contributing to dissatisfaction with sex life in a considerable proportion of men.

Over the last three decades there has been a significant increase in the understanding of the physiological mechanisms responsible for erectile dysfunction. Erectile dysfunction has become a topic of considerable media and societal interest. Paralleling the increase in knowledge has been an explosion in therapeutic options (Valiquette 2003). Nevertheless, our understanding of the etiology of ED has not improved at the same rate. This study was conducted to estimate the magnitude of the problem in the Finnish population and to identify the major risk factors for erectile dysfunction.

6.1 Participation

The response rate of 70% at baseline and 75% to follow-up survey in this study was relatively high. The proportion of men responding to both inquiries was 53%. Considering those who were alive and eligible at the second round inquiry, the response rate to both inquiries was 59%. Response to both surveys was similar to that achieved in comparable epidemiological studies.

The response rate has varied considerably between different studies (16–92%). Various approaches have been used in data collection, including self-administered questionnaire, telephone interview, and in-person and physician-conducted interview. Self-administered questionnaire has been shown to yield more reliable information on sensitive issues such as sexuality compared with face-to-face interviews (Catania et al. 1986). The response rates achieved in telephone interviews have been as low as 20% (Giuliano et al. 2002, Nicolosi et al. 2003b). The prevalence estimate may have been affected by selection bias.

The response rate also depends on the target population. It has been 22–52% in studies conducted in the United States (Feldman et al. 1994a, Ansong et al. 2000, Burchardt et al. 2000), 20–80% in Europe (Dunn et al. 2000, Mirone et al. 2002, Braun et al. 2000, Meuleman et al. 2001, Helgason et al. 1996, Green et al. 2001, Macfarlane et al. 1996, Morales et al. 2001, Nicolosi et al. 2003b, Giuliano et al. 2002, Blanker et al. 2001) and 16–92% in other countries (Moreira et al. 2003, Nicolosi et al. 2003b, Akkus et al. 2002, Mak et al. 2002, Pinnock et al. 1999, Moreira et al. 2002).

In the few population-based follow-up studies, the proportion of responders who were included at baseline and followed-up during a follow-up period was 68% in the Massachusetts Male Aging Study in the United States (Johannes et al. 2000), 83% in Brazil (Moreira et al. 2003) and 72% in the present study.

6.2 Methodology

Erectile dysfunction is a subjective term. It is therefore best described by the individual's personal assessment of his unique situation (Wabrek and Burchell 1980, Feldman et al. 1994b). Perfect erectile function is defined as no difficulty in achieving and maintaining an erection. There is variation in the definition of normal erectile function. Some difficulty in achieving or maintaining an erection has frequently been regarded as normal. In the present study, some difficulty either in achieving or maintaining an erection was defined as mild ED.

There is still no gold standard method for the assessment of ED in a population-based study (Kleinman et al. 2000). At least 30 hospital- or population-based studies on the prevalence of ED have been published in the past ten years. In most studies, a single self-assessment question (Feldman et al. 1994a, Pinnock et al. 1999, Meuleman et al. 2001, Moreira et al. 2001, Akkus et al. 2002, Moreira et al. 2002, Nicolosi et al. 2003b, Shaer et al. 2003) has been used for the assessment of erectile function, but also the International Index of Erectile Function (IIEF) questionnaire (Marumo et al. 2001, Giuliano et al. 2002, Mak et al. 2002, El-Sakka and Tayeb 2003, Kloner et al. 2003, Naya et al. 2003, Tan et al. 2003), the Brief Male Sexual Function Inventory, the International Continence Society male sex questionnaire (Frankel et al. 1998, Blanker et al. 2001), two questions of the IIEF (Dunn et al. 1998, Safarinejad 2003) and others such as the Cologne Erectile Dysfunction Questionnaire (Braun et al. 2000) have been used.

We used two questions from the IIEF for the assessment of erectile function. When ED was dichotomized into no/minimal versus moderate/complete, the agreement between the two questions was very high. Even with four categories of ED, the two

questions had a substantial agreement. Minimal ED had the lowest agreement and two questions were needed for assessing minimal ED in view of the substantial disagreement between the two questions.

Minimal ED is quite common and may represent a combination of intermittent problems and mild persistent ED. The overall prevalence of ED was 12% based on the single global question and 19% based on the IIEF instrument in a study conducted in Spain among 25–70 year-old men (Morales et al. 2001). The corresponding figures were 25% and 32% in a survey in France among men aged 40 years or over (Giuliano et al. 2002). The prevalence of minimal ED in the Spanish study was 5.2% based on the single self-assessment question and 16.2% based on the IIEF questionnaire, whereas the prevalence of severe ED was 6.9% based on the single global question and 2.7% according to the IIEF method.

The IIEF could be appropriate for detecting ED in its earliest stages, but not for severe forms. In contrast, the simple self-assessment question can be used for severe ED, but not for mild ED. A single global question may not be optimal for assessing minimal ED, and the IIEF is not a feasible method for population-based studies, due to its length and its weakness in estimating the prevalence of severe ED. So far, there appears to be no consensus on the optimal assessment of ED and various instruments have been used for evaluating its severity. The two-question method is similar to a single global question in assessing moderate and complete ED and comparable to the IIEF-5 in detecting minimal ED. For estimating the prevalence of minimal ED, at least two questions are needed due to poor concordance between achieving and maintaining erection. In addition, the use of a single question in some of the earlier studies may underestimate the prevalence of ED and explain the higher prevalence found in our study.

We estimated the incidence of minimal and moderate ED by assuming that more severe ED progresses through a milder form. Complete ED develops by progressing through mild and moderate ED. Mild and moderate ED are common problems. Erectile dysfunction has a progressive pattern, and the severe form is established by progressing through the mild and moderate forms, with some exceptions. Mild ED may be reversible and moderate ED may improve at least into mild ED by modifying risk factors. It is also informative to know whether the risk factors of mild ED are different from those of severe ED and the size of increment in the incidence of severity of ED with advancing age.

The simple method including only minimal cases as minimal ED and moderate cases as moderate ED would be appropriate for short follow-up and for irreversible events. If all forms of ED were combined and classified as absence or presence of ED, the results obtained with the two methods would converge. Yet, five years may be too

long a period for estimating the incidence of mild and moderate ED using the simple approach. This approach underestimates the incidence of these forms, especially for older ages. The association between severity of ED and age would be substantially diluted with the simple method. Age was not a significant risk factor for mild ED, and had only a slight effect on moderate ED. A high proportion of mild and moderate forms progress to severe ED in long-term follow-up. Furthermore, some conditions, e.g., diabetes, which are strong predictors of ED, were no longer risk factors for mild form after the exclusion of those men with the moderate or complete ED who had progressed to severe forms through minimal form. The simple method estimates properly only the incidence of complete ED, but underestimates the incidence of minimal and moderate ED and probably also the effect of various risk factors.

Furthermore, our method of estimating the incidence rate was technically complex. We did not have information on exact transition times between baseline and follow-up surveys nor on how many transitions. As a rule, we assumed the transitions took place in the midpoint of the follow-up. This assumption may cause slight inaccuracy in incidence estimates. Nevertheless, we firmly believe that our approach has more advantages than limitations e.g. our method gives an unbiased estimate of the annual rate of mild and moderate ED. This model also assumes that transitions between stages are independent and occur at a constant rate. It provides a reasonable approximation even if the true transition increases exponentially with age.

6.3 Representativeness

It is difficult to collect valid information from a representative sample. Most studies on ED are unrepresentative of the source population because the study population comprises responders who are willing to talk about sexual matters. Additionally, findings derived from volunteers may overrepresent disinhibited or sexually aggressive individuals (Freeman 1961). In clinical-based studies, men seeking medical care may be different from the general population. These men are more likely to be younger or have medical conditions such as diabetes and hypertension or have fewer undiagnosed and untreated health problems because of access to care than the general population. The men in most of the studies comprised those visiting their physician complaining of dysfunction. The overall population of impotent men consists of those who seek medical attention for ED and those who do not. Men who receive care are probably younger, more likely to have complete rather than mild ED, and more likely to have medical insurance.

Most studies of male sexuality have been conducted among convenience samples recruited through employees of companies or clinical populations; only a few investigations have been population-based and used samples representative of the general population. These studies also differ in many aspects, such as age range, method of data collection and methodology of assessment of ED. In addition, with relatively few exceptions, most sample sizes have been small, especially for older ages, leading to imprecise estimates of the prevalence and limited statistical power to detect associations. The generalizability of clinic-derived results is questionable because patients tend to overrepresent individuals with disorders known to cause ED such as diabetes (Cogen and Steinman 1990), multiple diseases, or men with rare etiologies leading to ED.

The study populations in some earlier studies have consisted of men passing by popular public places, such as beaches, squares or parks and can hardly be considered as representative of the general population, which is illustrated e.g. by higher education than general population. Study populations including employees of companies (Marumo et al. 2001) or men attending a screening program for prostate cancer (Jonler et al. 1995) are probably not representative of the general population. People seeking medical attention in a free screening program may be more concerned about their own health and quality of life than are the general population. They are more educated and differ in income and health behavior. On the other hand, patients with co-morbidity and a low quality of life may have no interest in participating in a screening program because of other substantial health and social problems. They were already diagnosed and therefore, had no motivation to attend a procedure aimed at detecting asymptomatic diseases.

Socio-economic and health status differences for subjects living in different countries could account for the differences. Age is an important confounding factor to examine as it has a strong correlation with ED. The assessment of the age-specific prevalence of ED is unreliable when there are few subjects in each of age range, especially older ages.

The MMAS population was not representative of the United States population at large in terms of ethnicity. The men included in the study were randomly selected in 11 cities and towns in the area of Boston, Massachusetts and included a majority (96%) of white men. This may be representative for the specific area chosen but generalization to the rest of Massachusetts or US may not be appropriate.

In the present study, the prevalence of smoking and pulmonary disease in the study sample was similar to that among Finnish men of these ages in general. The prevalence of diabetes was slightly higher only for the older age groups in the study sample compared with the general population (Helakorpi et al. 1994). The response rate

remained equally high in the second survey. The age distribution of men who refused to participate was comparable to that of participants. There was thus no evidence of notable selection bias in this study in this respect.

6.4 Prevalence of erectile dysfunction

Our results indicate a high prevalence of ED in 50 to 75 year-old Finnish men. Projection of this prevalence to the general population of 2002 in Finland yields an estimate of 207,000 out of 761,600 men aged 50 to 79 years with moderate or complete ED. Thus the results suggest that ED is a common condition and a public health concern in Finland.

The prevalence of ED has varied between countries, but its age pattern and associations with background diseases have been similar. The prevalence in Finland is intermediate, between the highest prevalence reported in Japan (80%), and the lowest prevalence reported in France (32%), Great Britain (26%), Germany (19%) and Spain (19%). Several elements must be taken into account to ensure reliable and valid international comparisons. The studies compared must have used similar age groups, method of data collection and comparable instruments to assess ED. The sample should adequately represent the general population.

The overall prevalence of ED was 80% in Japan (Nicolosi et al. 2003b), 70% in Turkey (Akkus et al. 2002), 65% in Italy, 65% in Malaysia (Nicolosi et al. 2003b) and 52% in the United States (Feldman et al. 1994a) for men aged ≥ 40 years. The age-adjusted prevalence of moderate or complete ED was 34% in Japan, 22% in Malaysia, 17% in Italy and 15% in Brazil (Nicolosi et al. 2003b) for men aged 40–70 years.

The first extensive study in the general population was carried out by Kinsey and associates between 1938 and 1941 in the United States on a sample of 6,000 men (Kinsey et al. 1948). It showed that 10% of men aged 50 years and 75% of men aged 80 years were impotent. A more recent study in the United States showed that 50% of men aged 50 years, 60% of aged 60 and 68% of those aged 70 had ED (Feldman et al. 1994a).

In the previous studies complete ED has been found in 3–26% in ages 50–60 years (Macfarlane et al. 1996, Green et al. 2001, Marumo et al. 2001, Vaaler et al. 2001, Akkus et al. 2002, Seyam et al. 2003), 12–49% between 60 and 70 (Macfarlane et al. 1996, Green et al. 2001, Marumo et al. 2001, Vaaler et al. 2001, Akkus et al. 2002, Seyam et al. 2003) and in 37–54% of those above 70 years of age (Macfarlane et al. 1996, Vaaler et al. 2001, Akkus et al. 2002, Seyam et al. 2003).

A high prevalence of moderate or complete ED has been reported for younger ages in the United States and France (Figure 2), and it increases slowly with age. Lower prevalence for younger ages has been found in Morocco, Turkey and Brazil, but increasing sharply with age. The combined prevalence of moderate and complete ED has been low in younger ages in Japan, Finland and the Netherlands, while it increases markedly with age.

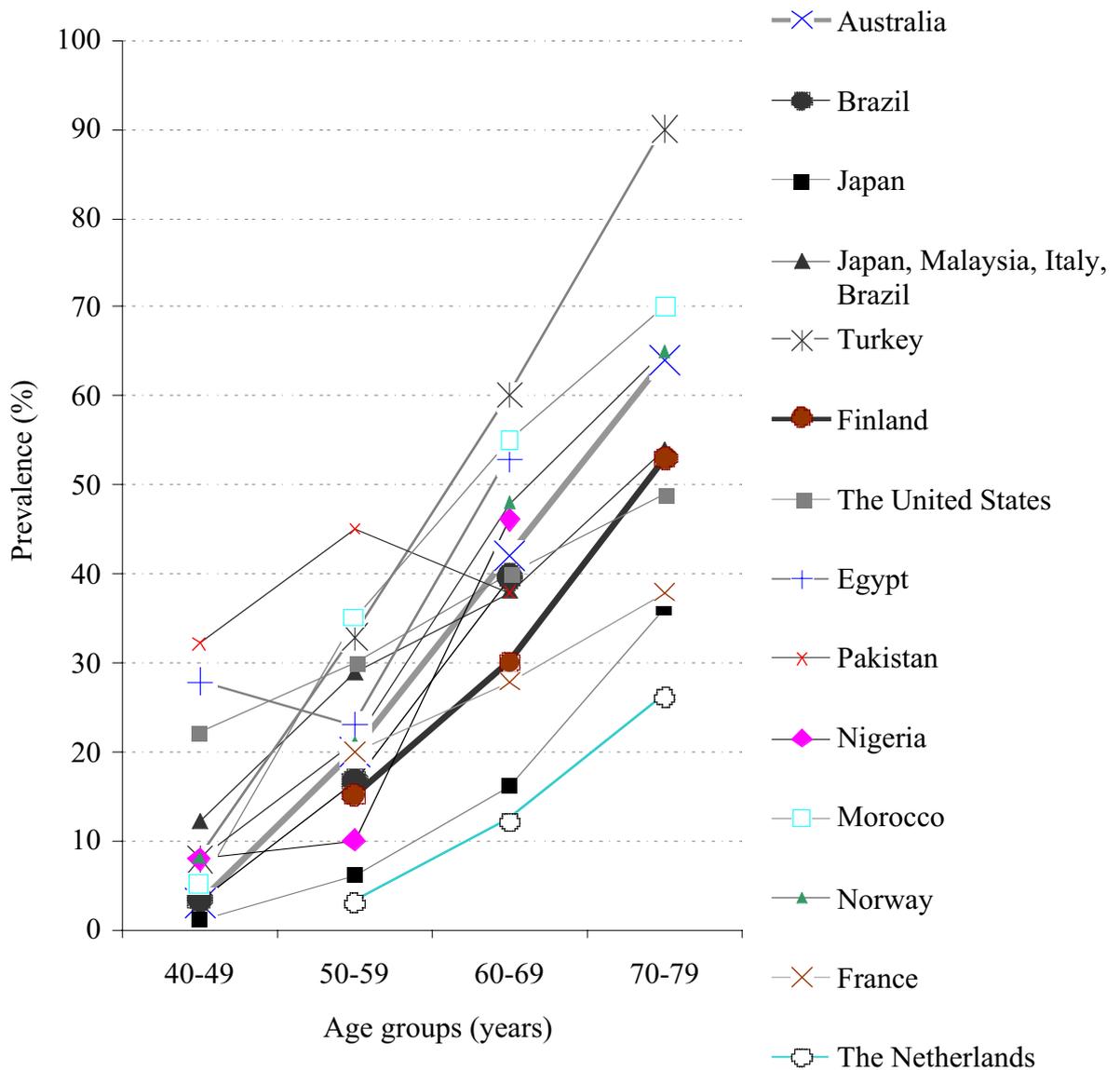


Figure 2: Prevalence of moderate or severe erectile dysfunction by age in different countries.

Most reported prevalences come from speciality clinics. It is possible that the higher frequencies result from overrepresentation of those with severe disease at such clinics.

The prevalence of complete ED in our study was higher than in similar age groups in the MMAS. Men with no regular sexual partner were excluded in the MMAS, and the MMAS population had less comorbidity. The lower prevalence of moderate or complete ED in Finland compared with the low-income countries and higher prevalence compared with the United States probably reflects difference in comorbidity, improvement in public awareness and openness in discussing and reporting ED.

6.5 Incidence of erectile dysfunction

Despite recent interest in ED, there is still little information regarding its incidence. Projection of the incidence estimates yielded by the present study to the general population of men 55 to 79 years old in Finland gives an expectation of approximately 21,500 new cases of moderate or severe ED annually.

The Massachusetts Male Aging Study (MMAS) (Johannes et al. 2000) and a Brazilian study (Moreira et al. 2003) are the only population-based follow-up studies published so far. The incidence of moderate or complete ED was 26 cases per 1,000 person-years in the MMAS, 39 in the present study and 66 in the Brazilian study. The mean age was 52.2 years in the MMAS study, 50.9 in the Brazilian study and 57.6 in the present study. The sample sizes were small for those aged 50–59 and 60–70 years in the Brazilian study, and incidence estimates were based on only 154 and 85 cases respectively in these age groups. Therefore, the precision was low.

The age-specific rates in the current study were similar to those of the MMAS. The incidence of ED in the MMAS was 30 cases per 1,000 person-years for ages 50 to 59 years and 46 for ages 60 to 65, while in the present study it was 22 cases per 1,000 person-years for 50 to 55 years of age and 49 for ages 60 to 65.

6.6 Risk indicators of erectile dysfunction

Accurate risk factor identification and characterization are essential for concerted efforts to prevent ED (NIH Consensus Conference 1993). Various chronic disorders are associated with elevated rates of ED including depression, diabetes, and cardiovascular and neurological diseases. Such disorders are more common in the elderly, which may partially explain the elevated prevalence of ED in men over 60 year of age. However, so

many men experience considerable distress from ED that the increasing awareness as well as the availability of non-invasive treatments may result in a greater proportion of patients seeking treatment, and eventually regaining satisfaction with their sex life.

Penile erection is a complex neurovascular phenomenon that may be affected by atherosclerotic vascular occlusive disease, cavernosal fibrosis, and neurological disease. Risk factors for ED overlap significantly with those for vascular disease and endothelial dysfunction.

6.6.1 Sociodemographic status

6.6.1.1 Age

In our study age was the only significant contributor to ED among sociodemographic characteristics. Consistent with a cross-national study (Nicolosi et al. 2003b) the prevalence of moderate or complete ED in the present study increased by 10% for each one-year increment in age. Age range has varied between studies, even in the most recent ones. Few studies included age ranges comparable to ours. In studies with similar age ranges, the sample size in the older group has been very small, for example the prevalence study in Turkey (Akkus et al. 2002). Only 131 men 70 years and over were included in the study, while there were 1,043 men in the 40–49 age group. This may explain the high prevalence of moderate and complete ED in Turkey compared with other countries (70% for ages 60–69 years and 90% for ages 70 and above).

Erectile dysfunction is experienced at least some of the time by most men who have reached 45 years of age. ED affects men of all ages and the prevalence increases greatly in the elderly (Seftel 2003). The prevalence of ED increases markedly due to secular trend and demographic transition. The extension of life expectancy is one of the most dramatic achievements of the 20th century. The elderly population, over 65 years, is the fastest growing age group. A large proportion of elderly men are afflicted by ED. The prevalence of ED is higher among older men, but they regard it as less of a problem than the younger age groups (Meuleman et al. 2001). Normal age-related changes in the structure and function of the penis may contribute to increased risk with age. The normal aging process and age-related accumulation of risk factors contribute to the increased prevalence of erectile dysfunction in the elderly. ED may diminish willingness to initiate sexual relationships because of fear of inadequate sexual performance or rejection. Men, especially older men, are particularly sensitive to the social support provided by intimate relationships; withdrawal from these relationships because of such fears may have a negative effect on their overall health (NIH Consensus Conference 1993).

The most common causes of ED in elderly men are organic (Carroll et al. 1992, Lim and Ng 1992), and multiple factors are related to ED. Vascular diseases account for a large proportion of organic ED. The pathophysiology of erectile dysfunction in the aging man mainly includes chronic ischemia, which triggers the deterioration of cavernosal smooth muscle and the development of corporeal fibrosis (Montorsi et al. 2003).

Although ED increases progressively with age, it is not an inevitable consequence of aging. Knowledge of the risk factors can guide prevention strategies. Specific antihypertensive, antidepressant and antipsychotic drugs can be chosen to reduce the risk of ED. Education and reassurance may be helpful in preventing the cascade into serious ED in individuals who experience minor ED due to medications, chronic illnesses or aging (NIH Consensus Conference 1993). With changing sexual mores and increasing attention to sexuality, one might expect an increasing number of elderly men to seek help for ED. It is very important for physicians and patients to be aware of the frequency of ED in the general population.

6.6.1.2 Education

In several previous studies educational level has correlated inversely with the development of ED. A low educational level is frequently associated with suboptimal nutrition, less access to preventive health measures, smoking and other risk factors. In the present study, the incidence of complete ED was only slightly and non-significantly lower among highly educated men compared with an intermediate category. The population in Finland is fairly homogenous in respect to socioeconomic status.

6.6.2 Chronic diseases

ED may be a symptom of underlying chronic illness. Erectile dysfunction is largely a vascular disease, consistent with findings of a higher prevalence or incidence of ED in men with diabetes, hypertension, heart disease and cerebrovascular disease. The common pathological process is at the level of the endothelium, and vascular risk factor control may be a key to preventing ED. Alteration in the flow of blood to and from the penis are thought to be the most frequent mechanism of ED. Arteriosclerosis related to diabetes, cardiovascular or cerebrovascular disease shares common determinants with vascular impairment of the erectile mechanism. Assessment of erectile function may indeed give clues to subclinical coronary, peripheral or cerebrovascular disease as well as to undiagnosed hypertension, diabetes or other diseases.

ED may be an early manifestation of systemic atherosclerosis and may precede the development of clinically significant vascular disease in other organs (Kawanishi et al. 2001, Bank et al. 2003). Endothelial dysfunction and atherosclerosis of the blood vessels that supply the penis are associated with the same cardiovascular risk factors that affect the coronary arteries, such as smoking, fatty diet, adverse serum lipid levels, hypertension, physical inactivity and obesity (Pinnock et al. 1999, Feldman et al. 2000, Kloner and Speakman 2002, Herschorn 2003, Solomon et al. 2003b). ED and coronary artery disease present in the same age group and the same vascular injuries that occur in the coronary arteries are likely to occur in the cavernosal arteries. ED may arise from progressive blockage of small vessels and reduced arterial compliance. Progressive occlusive disease manifests sooner in the microvasculature than in larger vessels, and ED is a sensitive indicator of wider arterial insufficiency (Kayigil et al. 1996, Feldman et al. 2000).

Men with ED are at increased risk for occult cardiovascular disease (Kawanishi et al. 2000, Solomon et al. 2003a), and incidence of complications from ischemic heart disease was found to be high in ED patients. It is now clear that the pathological processes in ED are common to those involved in vascular disease (O'Kane and Jackson 2001, Kloner et al. 2003). Although it is well established that cardiovascular risk factors are associated with erectile dysfunction, once it is present there is mixed information on whether treating the risk factors will treat the ED. An apparently healthy patient presenting with ED may have underlying vascular disease, and men may benefit both their cardiovascular health and their sexual function by improving their risk factors profile (Lowy 1999). Problems appear to be that lifestyle modification in midlife may simply be too late to reverse the process, and some antihypertensive and lipid lowering drugs may actually exacerbate ED.

Diabetes is an independent major risk factor for ED. Men with diabetes have ED at an earlier age and with higher prevalence and incidence. The development of ED in patients with diabetes is often caused by several interrelated mechanisms, including vascular disease, endothelial dysfunction, autonomic neuropathy, hormone imbalance, and certain medications (Saenz de Tejada et al. 1989, Feldman et al. 1994a, Ledda 2000b, Fedele et al. 2001). Despite the availability of many treatment options for ED, early intervention and prevention by such measures as improved glycemic control and general reduction of risk factors should be emphasized because many of the diabetes-related complications leading to ED are irreversible (Klein et al. 1996, Koppiker et al. 2003).

6.6.3 *Lifestyle factors*

6.6.3.1 *Smoking*

The evidence available on the association between smoking and ED is controversial (Bortolotti et al. 1997). A meta-analysis revealed that 40% of impotent men were current smokers compared with 28% of men in the general population (Tengs and Osgood 2001). A literature review concluded that smokers are 1.5 times more likely to suffer from erectile dysfunction than non-smokers (Dorey 2001). As warnings of cancer and heart disease have lost their ability to alarm, anti-tobacco advertisements now feature the risk of ED as a reason to avoid or cease tobacco use. The association between smoking and ED has mainly been based on prevalence studies that are not appropriate for clarifying the etiology of ED. The causal association of cigarette smoking with ED cannot be established based on randomized controlled trials because of ethical concerns with smoking. Owing to these unavoidable restrictions, it is difficult to demonstrate causality.

The Massachusetts Male Aging Study and the Brazilian study were the only population-based follow-up studies on ED published so far. The Brazilian study failed to show any association between smoking and incidence of ED. In the baseline sample of the MMAS, smoking was not independently associated with erectile dysfunction, but it exacerbated the effects of heart disease, high blood pressure and antihypertensive medication (Feldman et al. 1994a). Smoking was not associated with ED in the whole follow-up sample (Johannes et al. 2000). However, in the sub-group of men free from heart disease, diabetes or related medication at baseline or follow-up, and excluding those who had undergone radical prostatectomy or transurethral resection of prostate during the follow up, smoking at baseline doubled the incidence of moderate or complete ED at follow-up (Feldman et al. 2000). Former smokers did not have higher incidence of ED than non-smokers.

In the present study the incidence of minimal ED in current smokers was similar to that of non-smokers, whereas the rate among former smokers was higher than in current smokers. The incidence of complete ED was also elevated only in former smokers. Derby and associates (2000) reported no change in ED in smokers who stopped smoking in an 8-year period. Thus smoking cessation in middle-aged men does not decrease the risk of ED, with no significant difference in risk between men who quit and those who continue to smoke. McVary and associates (2001) reviewed the influence of smoking cessation on ED. They estimated that the excess risk in former smokers decreases substantially in the initial 2 to 3 years, thereafter the risk reduction slows down, so that up to 10 years is required for former smokers to achieve the risk levels of

individuals who have never smoked. In the present study only 13% of the study population who were free from any ED and 11% of those who were free from complete ED at baseline had stopped smoking in the last five years before entry into the study. The risk for minimal ED was small and statistically non-significant. Therefore, it may be due to random variation, while the risk was larger for complete ED and may be related to chronic diseases such as cardiovascular and cerebrovascular diseases caused by smoking.

Reversibility of risk by smoking cessation is another key component of any attempt to establish causality. The time frame for onset and reversal of ED after cessation of smoking is not known. It may be markedly different from those of other endothelial diseases, such as coronary heart disease. Ex-smokers had a higher rate of ED than non-smokers, probably because of a longer exposure resulting in damage to the vascular system and because the decision to stop smoking was often made after many years of tobacco use. It seems obvious that tobacco use precedes ED and that it is extremely unlikely that impotent men start to smoke after the onset of their condition, because most adults who currently smoke started to do so at the age of 18 or younger. The effect of former smoking on ED could be explained by comorbidity related to smoking. An inverse association between ever smoking and coronary artery diameter has been shown, with no difference in arterial diameter for current and ex-smokers. The effect of smoking is not clearly associated with time from stopping, suggesting a lasting effect of smoking on ED (Mirone et al. 2002).

The exact mechanism of the smoking effect on ED is not known. Smoking may be an independent risk factor, particularly for vascular ED, and may also contribute in a synergistic or additive manner to other risk factors of ED. Smoking appears to decrease pelvic and penile vascular flow, and the long-term effect of smoking on the pelvic arteries may be related to arteriosclerosis (McVary et al. 2001). The vascular supply to the penis is subject to the same degenerative diseases of blood vessels of the heart, kidneys, brain and major vascular systems (Shabsigh et al. 1991, Jeremy and Mikhailidis 1998). Smoking alters coagulability of blood and accelerates hypertension by promoting vasoconstriction and atherosclerosis. Associated hypertension increases the need for medications that induce or exacerbate existing ED (McVary et al. 2001).

Smoking is thought to impair endothelial nitric oxide synthase, which may have significant long-term effects on the corpus cavernosum (McVary et al. 2001). Numerous studies have proposed mechanisms of endothelial dysfunction in smokers, such as the decrease in the endothelial synthesis of nitric oxide by free radicals and aromatic compounds (Powell 1998). Smoking decreases dilatation of arterial endothelium (Lekakis et al. 1997) and impairs endothelium dependent relaxation of veins by a reduction in the activity of endothelial nitric oxide synthase (Higman et al. 1996). It also

impairs endothelium dependent vasodilatation, although this dysfunction appears to be rapidly reversible after smoking cessation (Moreno et al. 1998).

The effect of smoking is also evident in men without comorbidity. This suggests that smoking is associated with vascular damage, but when the damage is present, it does not cause any additional risk. Furthermore, an initial, undiagnosed smoke-induced cardiovascular condition can present with ED as the first sign (Kirby et al. 2001).

Since smoking is associated with an increased probability of ED, this information may motivate some patients to stop smoking because for some men, ED may be a more real and threatening prospect than the risks of cancer or heart disease. Quitting is the first-line therapy of ED and one of the most important measures for the prevention of atherosclerosis (Ledda 2002). The chief role of quitting smoking in sexual health is to prevent worsening of ED, but the best approach to preserve potency is early adoption of a healthy lifestyle that does not include smoking (Derby et al. 2000).

6.6.3.2 Alcohol consumption

The association between alcohol consumption and erectile function is also controversial (Bortolotti et al. 1997). The effect of alcohol consumption on erectile function has been studied mainly in cross-sectional studies. Some cross-sectional studies have yielded partly conflicting results (Feldman et al. 1994a, Parazzini et al. 2000, Green et al. 2001, Morales et al. 2001). The effect of excessive alcohol consumption on ED has been small (Feldman et al. 1994a), and a lower prevalence of ED has been reported among moderate drinkers (one to two drinks per day) than non-drinkers (Mannino et al. 1994, Akkus et al. 2003, Nicolosi et al. 2003b). Only a single population-based follow-up study has evaluated the effect of alcohol consumption on erectile function and failed to show a clear effect (Feldman et al. 2000).

The present study showed a statistically non-significant effect of alcohol consumption of more than two drinks per day only on minimal ED, but not on more severe dysfunction. Moderate alcohol consumption had a weak protective effect on the incidence of complete ED. Excessive alcohol consumption interferes with the metabolism of sex hormones. The possible effect of alcohol could be due to both psychological and biological mechanisms. The short-term psychological effects of alcohol include reduced inhibitions and possibly increased sexual desire. Moderate alcohol consumption may reduce the incidence of ED by reducing the incidence of coronary heart disease and risk of ischemic stroke (Shabsigh et al. 1991, Mukamal and Rimm 2001). Alcohol may exert its beneficial influence on cardiovascular and cerebrovascular vascular systems in several ways. The strongest and best-established effect is the rise in blood levels of high-density lipoprotein cholesterol (Kirby et al.

2001). A major long-term biological effect is likely to be attributable to an anti-atherogenic mechanism, including effects on lipids and coagulation (Hansagi et al. 1995, Parker et al. 1996, Zakhari and Gordis 1999). However, it would appear that the use of alcohol has only a minimal effect on ED.

6.7 Strengths of the study

We were able to follow-up 72% of the men responding to the baseline survey for a period of five years. The participants did not significantly differ from non-participants with respect to age. Because the questionnaire was self-administered, bias from interviewer and from different interview techniques was avoided.

Cross-sectional study design is not appropriate for investigating causal relationships. Cross sectional studies can only reveal the presence or absence of a relationship between the study variables and the prevalence of erectile dysfunction. It is not possible to know whether the erectile dysfunction followed the exposure in time or whether the exposure resulted from the erectile dysfunction, since information on both exposure and erectile dysfunction is collected at the same single point in time. This is a problem for exposures that change over time, such as smoking, alcohol intake and medications. There is difficulty in establishing the time sequence of events. Cohort studies do not have these problems. Exposures such as smoking, chronic diseases and alcohol consumption antedate the onset of erectile dysfunction. Therefore, the temporal relationship between these risk factors and erectile dysfunction is clear.

The main strengths of this study were its large sample and population-based longitudinal design. The population widely represents Finnish men aged 50 to 75. These features allowed us to estimate prevalence and incidence and to determine risk factors of ED in a valid and precise fashion.

6.8 Shortcomings of the study

Participation rate in the study was suboptimal, although relatively high and comparable with other studies. The men with no follow-up information were on average older, less educated, and had more frequently a history of chronic diseases than the participants. This group differed in some characteristics that put them at a higher risk for ED than the study sample. Therefore, the incidence results may underestimate the true incidence in the population. However, the incidence rate ratios are likely to be unbiased. Furthermore, design with incidence rate ratios is likely to provide less biased estimates

on the effects of risk factors than cross-sectional prevalence studies that are susceptible to bias.

Most of the epidemiological studies dealing with ED focus on the age groups between 40 and 70 years. Certainly many young men and also men older than 70 years suffer from ED, although only a few of them seek treatment. We did not cover younger age groups. Thus the overall prevalence in the current study cannot be compared with other studies because 40 year-old men were not included in the study.

There were many old men who did not have a partner. How might a man without a partner respond to these two questions? Those without a partner with difficulty in erection may consider themselves free from dysfunction.

A problem in achieving or maintaining an erection was defined with reference to one month before responding to the questionnaire in the follow-up survey, but the time period was not defined at the baseline survey. Men with intermittent or recurrent ED may be included in the study at the baseline, but not in the follow-up inquiry. Both the prevalence and incidence of ED may therefore be overestimated.

Furthermore, if the questionnaire had included a question of morning erection, we would also be able to classify "organic ED".

As we had to rely on self-report, it is possible that medical conditions that are frequently asymptomatic or underdiagnosed have been underreported by subjects not aware of their existence. Asymptomatic medical conditions are more likely to be diagnosed in men with contact to a physician. Therefore the asymptomatic diseases of men with treated ED are more likely to be diagnosed than those with untreated dysfunction. In this study, very few men received treatment for ED. This could likely result in non-differential misclassification and bias the results towards the null.

The number of cigarettes smoked daily (packs per day) was not collected at the baseline survey. Therefore dose response of smoking on ED cannot be assessed.

7 Summary

The present findings indicate that erectile dysfunction is a commonly occurring disorder at ages 50–75 years. The prevalence and incidence of ED increase with age, especially after the age of 60 years. The prevalence of moderate or severe ED was 28%, and increased from 12% for men aged 50 years to 58% for those aged 75. The annual incidence of moderate or severe ED was 39 cases per 1,000 man-years, increasing sharply with age from 22 cases per 1,000 man-years for ages 50–55 to 84 cases per 1,000 man-years for those ages 70–75 years.

The results of this study show that biological factors such as age, diabetes, hypertension, heart disease and cerebrovascular disease are important predictors of ED. Diabetes is the strongest factor contributing to the development of ED, while heart disease, hypertension, and cerebrovascular disease are weak predictors of ED. Smoking is a weak risk factor of ED, while amount of alcohol and coffee consumed do not have a clear effect on erectile function. Current smoking doubled the risk of complete ED in men without comorbidity. Sociodemographic status, except age, and lifestyle factors seem to be of limited importance in the etiology of erectile dysfunction, while vascular diseases, especially diabetes, are major predictors of ED.

Erectile dysfunction is a common problem and most frequently caused by atherosclerosis. Intervention could restore sexual function, the implication for the future burden of ED, prospects for prevention.

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