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Women's knowledge, attitudes, and management of the menopausal transition

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”Och klimakteriet, det finns delar av det här klimakteriet, det finns fysiska, det här med menstruationen, att dom uteblir, men det är också en psykologisk process”

Citat från en av de intervjuade kvinnorna

To Mats, Andreas, Daniel and Therese

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Summary in Swedish – svensk sammanfattning

Attityder, kunskaper och handhavande av klimakteriet och hormon behandling – ur kvinnans perspektiv.

Klimakteriet är en period i en kvinnas liv då produktionen av det kvinnliga könshormonet östradiol (det mest verksamma östrogenet som kvinnan själv bildar) successivt minskar. Den sista menstruationen, menopausen, inträffar vanligtvis vid 51-52 års ålder och fastställs först när 1 år förflutit utan ytterligare blödningar.

Klimakteriet brukar definieras som åren omkring menopausen. Majoriteten av alla kvinnor upplever någon gång under denna period symtom som värmevallningar och/eller svettningar. Andra symtom som kan förekomma och som orsakas av den minskade östrogenproduktionen är torra och sköra slemhinnor i underlivet. Även sömnstörningar, humörförändringar och minskad livskvalitet är vanligt förekommande hos kvinnor i klimakteriet. Symtom som värmevallningar och svettningar lindras med tiden och efter fem år har besvären vanligtvis avtagit hos 20-50 % av kvinnorna. Ungefär en femtedel av kvinnorna tycks däremot ha kvarstående besvär under en betydligt längre period.

Hormonbehandling (HT) har länge varit en väletablerad behandling i Sverige för att lindra klimakteriebesvär och består vanligen av både ett östrogen och ett syntetiskt framställt gulkroppshormon (gestagen). Under 1980- och 1990 talet ökade användningen av HT hos kvinnor kraftigt till stor del på grund av resultat från flera vetenskapliga observationsstudier som talade för positiva långtidseffekter av HT. Man såg t.ex. minskad risk för hjärtinfarkt, benskörhet och frakturer, liksom Alzheimers sjukdom hos kvinnor som använt HT under lång tid. Dessa resultat började ifrågasättas i slutet av 1990-talet då stora kliniska studier inte kunde påvisa sådana långtidseffekter. Dessa nya resultat fick stor genomslagskraft i massmedia och hos hälso- och sjukvårdspersonal och ledde till förändrade rekommendationer för användning av HT. Kvinnor rekommenderades att enbart använda HT vid besvärande vallningar och svettningar, under kortast möjliga tid och med lägsta möjliga dos. Dessutom rekommenderades kvinnor att göra utsättningsförsök med lämpliga intervall för att ta reda på om klimakteriebesvären avtagit eller försvunnit. Med denna bakgrund var det av intresse att undersöka vilka attityder och kunskaper kvinnor i klimakteriet har och hur det uppfattar och hanterar denna period i livet.

I *delarbete I* studerades med kvalitativ metod kvinnors uppfattningar av klimakteriet. Intervjuer genomfördes med 20 kvinnor som var mellan 44-59 år gamla och som sökte gynekolog för att diskutera klimakteriet och hormonbehandling. Intervjuerna spelades in varefter dessa transkriberades ordagrant och analyserades med fenomenografisk metod.

I *delarbete II*, som genomfördes åren 1999 och 2003, skickades en enkät ut till alla kvinnor i Linköpings kommun som var 53 respektive 54 år gamla (1999; n=1760, 2003; n=1733). Enkätstudierna undersökte kvinnors attityder till klimakteriet och HT samt om dessa attityder förändrats efter att nya forskningsrön om HT publicerats.

Delarbete III baserades på enkäten från år 2003 (n=1733) men med tillägg av ett antal frågor rörande kvinnors kunskaper om klimakteriet och HT. Syftet var att undersöka kvinnors kunskaper om klimakteriet, HT och äggstockarnas och livmoderns funktion samt om kunskaperna skiljde sig åt beroende på kvinnornas utbildningsnivå och hormonanvändning.

I *delarbete IV* inkluderades 87 kvinnor i en klinisk studie med syfte att jämföra två olika typer av utsättningsförfarande av HT avseende återfall i vallningar och svettningar, behov av att behöva återuppta HT samt påverkan på livskvalitet. Kvinnorna lottades till att avsluta sin HT abrupt eller till att trappa ner sin HT under fyra veckor innan den avslutades helt. De skatade sina vallningar och svettningar dagligen och fyllde i detta i en dagbok samt besvarade formulär rörande livskvalitet under studieperioden.

Intervjustudien visade att varje kvinna har en individuell uppfattning av klimakteriet. Uppfattningarna varierade påtagligt allt ifrån att kvinnan uppfattade klimakteriet som en rent biologisk process med fysiska symtom till att se klimakteriet som en naturlig process som påverkades av såväl hormonförändringar som åldrande.

Majoriteten av kvinnorna i enkätstudierna såg klimakteriet som en naturlig process som orsakas såväl av hormonella förändringar som åldrande. Attityderna till klimakteriet tycktes inte ha förändrats mellan 1999 och 2003. Dubbelt så många kvinnor ansåg 1999 jämfört med 2003 att HT skulle användas av alla kvinnor oavsett klimakteriebesvär. Det talar för att attityderna till HT har påverkats påtagligt av de nya forskningsrönen och behandlingsrekommendationerna som publicerades i början av 2000-talet.

Kvinnors kunskaper om klimakteriet och HT tycks inom vissa områden vara bristfälliga. Att klimakteriet orsakas av minskad östrogenproduktion samt att värmevallningar och svettningar är vanligt förekommande var välkänt. Däremot rådde bristande kunskaper om hur hormonbehandling påverkar fertiliteten och varför vanligen gestagen kombineras med östrogen i HT. Kvinnor med lägre utbildningsnivå tycktes i allmänhet vara osäkra i högre grad än kvinnor med en högre utbildningsnivå. Kvinnor som använde HT hade mer kunskaper om risker och fördelar med HT än de som inte använt HT.

Varken vallningarnas och svettningarnas antal eller svårighetsgrad skiljde sig åt mellan de två olika sätten att avsluta HT. Inom ett år hade närmare hälften av alla kvinnor valt att återuppta HT oavsett om de slutat abrupt eller trappat ner HT under fyra veckor. Vallningarnas svårighetsgrad och försämrade livskvalitet tycktes vara viktiga faktorer för om kvinnor valde att återuppta HT eller inte.

Sammanfattningsvis bör personal inom hälso- och sjukvården som möter kvinnor i klimakteriet vara medvetna om att varje kvinna har en individuell uppfattning och upplevelse av klimakteriet och HT. Kunskaper om klimakteriet och HT är ofta bristfälliga men hur detta påverkar den individuella kvinnan är oklart. Många kvinnor tycks få tillbaka besvärande symtom när HT avslutas oavsett om man trappar ner sin behandling eller avslutar abrupt. Många kvinnor väljer att återuppta HT. Större studier behövs för att undersöka hur HT ska avslutas på bästa sätt med minskad risk för kvinnan att återfå besvären eller få försämrade livskvalitet.

List of publications

This thesis is based on the following original articles, which are referred to in the text by their Roman numerals I - IV.

I. Lindh-Åstrand L, Hoffmann M, Hammar M, Kjellgren KI. Women's conception of the menopausal transition – a qualitative study. *J Clin Nurs* 2007;16(3):509-517.

II. Lindh-Åstrand L, Brynhildsen J, Hoffmann M, Liffner S, Hammar M. Attitudes towards the menopause and hormone therapy over the turn of the century. *Maturitas* 2007;56(1):12-20.

III. Lindh-Åstrand L, Brynhildsen J, Hoffmann M, Kjellgren KI, Hammar M. Knowledge of reproductive physiology and hormone therapy in 53- to 54-year-old Swedish women: a population-based study. *Menopause* 2007;14(6):1039-1046.

IV. Lindh-Åstrand L, Bixo M, Linden Hirschberg A, Sundström-Poromaa I, Hammar M. A randomized controlled study of taper-down or abrupt discontinuation of hormone therapy in women treated for vasomotor symptoms. Accepted for publication in *Menopause* (2009).

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Abbreviations

ANOVA	Analysis of variance
BMI	Body Mass Index
EPT	Estrogen plus Progestogen Therapy
ET	Estrogen Therapy
FMP	Final Menstrual Period
FSH	Follicle Stimulating Hormone
HERS	Heart Estrogen/Progestogen Replacement Study
HRQoL	Health Related Quality of Life
HT	Hormone Therapy
IQR	Inter Quartile Range
LH	Luteinizing Hormone
Md	Median
MWS	Million Women Study
QoL	Quality of Life
PGWB	Psychological General Wellbeing Index
RCT	Randomized Controlled Trial
STRAW	The Stages of the Reproductive Aging Workshop
SWAN	Study of Women's Health Across the Nation
WHI	Women's Health Initiative
WHO	World Health Organization

Introduction

Menopause, or the final menstrual period (FMP), and the menopausal transition are natural processes that occur in women's lives as a part of normal aging. In Sweden the median age of menopause is between 51 and 52 years¹ and commonly women live about one third of their lives after the menopause. Every year about 65 000 Swedish women will reach menopause² and the majority will experience hot flushes and/or night sweat at some period during the transition¹. For some women the climacteric symptoms are bothersome and a varying proportion of women seek medical advice due to symptoms related to the menopausal transition. It is a challenging task for health care providers to improve the counselling and management of the menopausal women.

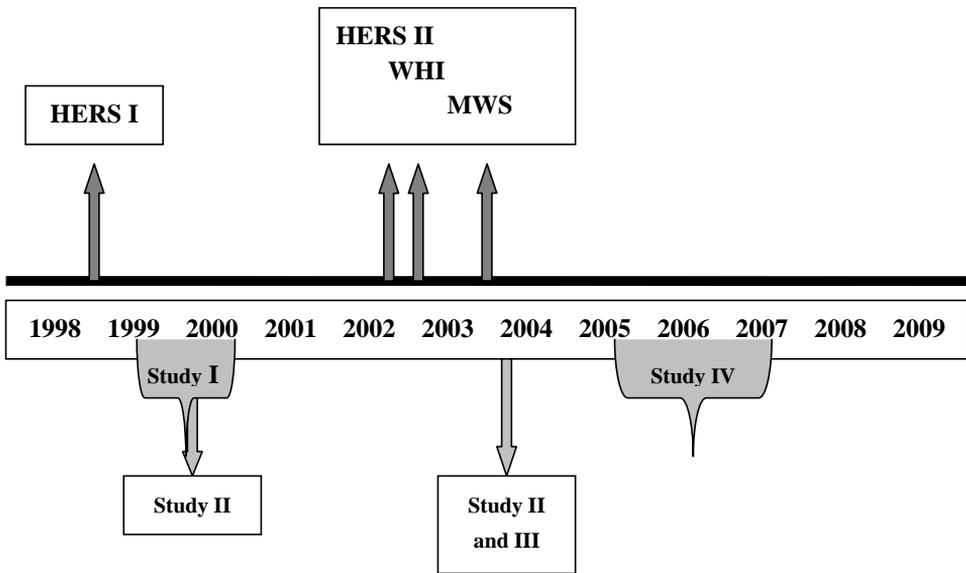
Hormone therapy (HT) has been considered as a safe and well-documented treatment for menopausal symptoms. Since the 1960s HT has been established as a treatment for menopausal women and used by Swedish women to varying extent. The HT use among 53 to 54 year old women increased from around 7 % in the 1980s¹ to more than 40 % in 1998³. The increase of HT use was probably caused by physicians' and women's confidence in results from several observational studies⁴⁻⁷ in the 1980s and 1990s reporting beneficial effects of long-term HT use. Results from several large randomized clinical trials (RCT)⁸⁻¹⁰ published after 1998 could not find evidence for these long-term benefits of HT, and these new results attracted great attention from media and seem to have had great impact. The new findings led to a dramatic change in the treatment guidelines¹¹ and in the use of HT among women^{3, 12, 13}.

Since 1998 I have been a member of a research team at the Department of Obstetrics and Gynecology at the Faculty of Health Sciences, in Linköping University. In my work as a research nurse I have had the privilege of meeting numerous women with different experiences of the menopausal transition. At the time I began my research there were few qualitative studies on women's conceptions of the menopausal transition, especially in Sweden, and also very few studies on women's knowledge about their reproductive function and HT. Furthermore, studies of the possible effects on attitudes caused by the new scientific findings had not yet been published. Beginning in 2003 national and international authorities and societies started to recommend limiting HT use to as short a time as possible. I also found it important to make studies which could contribute to evidence-based recommendations on how to abandon HT with the least risk of recurrence of symptoms. My experience in the area and a need to gain a deeper understanding of the impact of the results from the above mentioned trials on women's attitudes to the menopausal transition and HT have caused the following questions to arise:

- What do Swedish women really think about the menopausal transition?
- What attitudes do these women have about the menopausal transition and HT and are these attitudes affected by the scientific findings that began to appear in 1998 and by the resulting media coverage of the issue?
- What do women actually know about their own reproductive functions and the effects of HT?
- According to the new treatment guidelines the time for HT use should be limited and if HT is to be terminated, is there a difference if a woman stops the therapy abruptly or gradually?

– What impact does discontinuation of HT have on a woman’s quality of life?

Questions like these and many others made me curious about finding answers, and I decided to address them by becoming a Ph.D. student. I had at that time already been involved in a number of clinical studies and had together with my supervisor and co-supervisor participated in the design, data collection and analyses of the studies included in this thesis.



HERS = Publication of the Heart and Estrogen/progestin Replacement Study ^{8,9}

WHI = Publication of the Women’s Health Initiative ¹⁰

MWS = Publication of the Million Women Study⁹¹

Figure 1. Timeline for the studies included in this thesis and for the publications of results from HERS, WHI, and MWS study.

The menopausal transition

Definitions of menopausal phases

The terminology used for female reproductive aging and for the stages of the menopausal transition is not consistent and this lack of consistency has been repeatedly discussed for at least the past 30 years. Neither the World Health Organization definitions (WHO)^{14, 15} nor the International Menopause Society nomenclature from 1999¹⁶ were considered to be satisfactory for use in dealing with the menopause transition. In 2001¹⁷ the working group for “The Stages of the Reproductive Aging Workshop” (STRAW) suggested seven stages based on a variety of components such as time periods, menstrual cycle characteristics and reproductive hormone levels (Fig 2). This model was later modified by Harlow¹⁸ who suggested a shorter period of amenorrhea as defining the late menopausal transition. Serum follicle stimulating hormone (FSH) concentrations above 40 IU/l in late menopausal transition were also incorporated as an element of the staging system. The STRAW-model – with modifications – is not, however, applicable to women using HT, who have had a hysterectomy, are smokers, or who have a body mass index (BMI) below 18 or above 30 kg/m².

	Final Menstrual Period (FMP)							
Stages:	-5	-4	-3	-2	-1	0	+1	+2
Terminology:	Reproductive			Menopausal Transition		Postmenopause		
	Early	Peak	Late	Early	Late*	Early*	Late	
				Perimenopause				
Duration of Stage:	variable			variable		a 1 yr	b 4 yrs	until demise
Menstrual Cycles:	variable to regular	regular		variable cycle length (>7 days different from normal)	≥2 skipped cycles and an interval of amenorrhea (≥60 days)	Amen. ≥ 12 mos	none	
Endocrine:	normal FSH		↑ FSH	↑ FSH			↑ FSH	

*Stages most likely to be characterized by vasomotor symptoms ↑ = elevated

Figure 2. The menopausal stages as proposed by the STRAW¹⁷. Copyright by Elsevier and used with permission from the publisher.

The following definitions for menopausal phases were proposed by STRAW¹⁷;

The **menopause** is the anchor point that is defined after 12 months of amenorrhea following the final menstrual period, which reflects a pronounced decrease of ovarian steroid hormone secretion.

The **perimenopause** or the **menopausal transition** means “about or around the menopause”. Typical for this interval are increased concentrations of FSH and irregular bleeding patterns and intervals of amenorrhea. The perimenopause also includes the FMP.

The **postmenopause** is divided into an early and a late phase. The early postmenopause is defined as up to 5 years since FMP and may be further divided into a) the first 12 months after FMP and b) the next 4 years. The late phase has a definite beginning (5 years after FMP), but the duration is variable because it is lifelong.

The term **climacteric** is more general and denotes a phase in the normal aging process when a woman passes from the reproductive to the non-reproductive stage. It is recommended to be used synonymously with perimenopause¹⁷.

Menopause can be **natural or induced** and can be induced by means of surgery (hysterectomy, oophorectomy) or by e.g. chemotherapy. Other terms used are **premature menopause**, which refers to cases in which FMP is reached before 40 years of age whether natural or induced, and **early menopause**, which refers to cases in which FMP occurs at, or before, the age of 45 years.

In clinical trials several staging systems have been compared and changes in bleeding patterns seem to be an important marker that may be used to identify women in the early transition¹⁹. Changes in biomarkers such as FSH, inhibin A, inhibin B, and recently anti-Müllerian hormone may also be useful in predicting the onset and progression of the menopausal transition²⁰. Anti-Müllerian hormone levels can be measured in serum and they decrease with age to become undetectable in the post-menopausal period²¹.

Epidemiology of the menopause

The average age of FMP varies between different ethnical groups. In Europeans and North American Caucasians the average age is about 51 to 52 years²²⁻²⁴ whereas in African Americans²⁵, Hispanics and Mexican women²⁶ the average menopause age is a few years earlier than in Caucasian women. Dratva and co-workers²⁷ published data from a European cohort study showing that the mean age of menopause was 54 years and thus higher than previously reported but the results could have been affected by the high percentage of non-smokers in the cohort. Similar findings had previously been reported by Rödström and colleagues²⁸. Among factors other than genetic constitution that affect the age at menopause, smoking is associated with earlier menopause whereas parity, BMI, nutritional factors, age at menarche, hormonal contraceptives, and socioeconomic factors have all been discussed as factors but none has been proved to definitely affect age at menopause²⁹⁻³¹. A recent study³² showed that alcohol consumption significantly predicted the age of menopause with women who consume alcohol having menopause one year earlier, on average, than women who did not consume alcohol.

The endocrinology of the menopause

At birth the ovaries contain approximately 1-2 million primordial follicles, each consisting of a single oocyte surrounded by a single layer of granulosa cells. At puberty there are about 400 000 follicles remaining and each month a number of spontaneously developing follicles are further stimulated by FSH. Approximately two weeks after menstruation one of these follicles has developed into a dominant, mature follicle which, by means of negative feedback, makes the others go into atresia. This mature follicle produces the main part of the oestradiol and ovulates as a reaction to the midcycle Luteinizing Hormone (LH) surge after which the

follicle is transformed into a corpus luteum, now producing not only oestradiol but also progesterone. About one week after the ovulation the corpus luteum reaches its peak and thereafter starts to involute and hormone production decreases again, leading to a menstrual bleeding about two weeks after ovulation. As women age the ovarian follicle number falls due to continuous recruitment of primordial follicles of which some reach ovulation but the majority goes into atresia. The low activity of follicles after 40 to 50 years of age contribute to increased FSH and decreases in oestradiol and inhibin³³

During the last four years before menopause on the average the cycles are usually irregular. Some ovulatory cycles become shorter and others longer because some follicles are of lower quality and do not reach ovulation leading to irregular, anovulatory cycles³⁴. Finally oestradiol production is insufficient to stimulate the endometrium and the bleedings cease and menopause has been reached.

Women's fertility declines significantly in the perimenopause but as long as ovulation can occur some risk of pregnancy persists. In 40 year old women the monthly chance to conceive is about 8% and thereafter decreases continuously. Use of contraceptive methods is therefore recommended for two years after amenorrhea in women below 50 years of age and for one year in women above 50 years of age, i.e. when menopause may be confirmed³⁵.

Symptoms, signs and changes in women's health during the menopausal transition.

Many women pass through the menopausal transition without any health problems or symptoms. Many middle-aged women do, however, report a number of signs and symptoms during the menopausal transition^{22, 36} but only vasomotor symptoms (hot flushes and sweating) and vaginal dryness are associated with the decreased oestrogen production that arises in relation to menopause³⁶⁻³⁹. Vasomotor symptoms are often associated with sleep disturbances and decreased overall well-being^{36, 38, 40-43}. Other common signs and symptoms reported by women are mood changes, anxiety, decreased libido, headache, backache, and joint pain and stiffness^{36, 44} but proof of correlation with the hormonal changes is missing.

Vasomotor symptoms

The prevalence of vasomotor symptoms varies widely between populations around the world³⁸. In Western societies these symptoms are reported by 20 to 80 % of the women during the menopausal transition^{1, 22, 45} whereas the prevalence in South East Asia, for example, is substantially lower³⁸. Vasomotor symptoms usually decrease with time and four to five years after FMP hot flushes are reported by 20-50 % of women^{22, 46}. About 15-20 % of women still reported vasomotor symptoms more than ten years after FMP^{47, 48}. In a longitudinal study by Col and co-workers⁴⁶, vasomotor symptoms persisted substantially longer than had previously been reported, on average 5.5 years, and 23 % still reported such symptoms after 13 years of follow-up. Factors associated with hot flushes are smoking, rapid decrease in oestrogen levels, ethnicity, low level of physical activity, low socioeconomic status and educational level, and underweight, but except for smoking the findings for the importance of the other factors are contradictory⁴⁹.

Urogenital symptoms and sexual dysfunction

Atrophic vaginitis, dyspareunia and recurrent urinary tract infections are reported by women in the postmenopause. These symptoms are caused by the low oestrogen production, which affects the mucosa in the vagina and in the urinary tract and usually appear a few years after menopause. The prevalence of vaginal dryness increases with age and is about 20-30 % in women aged 60 years or more^{50, 51}.

Vaginal dryness could contribute to dyspareunia and decreased sexual enjoyment but other factors such as previous sexual function and partner-related issues seem to have a greater effect on the sexual function than the oestradiol level⁵².

Sleep disturbances

About 40-60 % of peri- and postmenopausal women reported sleep disturbances in observational studies⁵³. Hot flush frequency and severity are associated with disturbances in the sleeping pattern⁴¹ and the prevalence of sleep disturbances seems to increase through the transition⁵⁴. It remains unclear to what extent other factors such as hormone levels, physical and

psychological symptoms, concomitant medications and ageing contribute to the sleeping disturbances⁵⁵.

Mood changes

Between 10 - 50 % of women report mood changes in the menopausal transition⁴⁵. Results from several longitudinal and cross-sectional studies, however, could not establish with certainty whether these symptoms are caused by the hormonal changes during the transition or not⁵⁶. Other factors such as general health, prior depression, socioeconomic factors, and negative life events probably play an important role in development of mood changes in menopausal women^{57, 58}.

Cognition

Cognition comprises several mental abilities such as concentration, memory, learning, judgment, and language, all of which have a tendency to decline as we grow older. A relationship between the menopausal transition and cognitive disturbances has been suggested but the evidence is insufficient^{53, 59}.

Metabolic changes influenced by the menopause

Several metabolic changes have been related to decreasing oestrogen production; one such is changes in bone metabolism leading to increased bone loss⁶⁰. Also decreasing oestrogens increase both concentration and oxidation of Low Density Lipoprotein (LDL) and decrease concentrations of High Density Lipoproteins (HDL), all contributing to a higher risk of cardiovascular disease⁶¹.

Well-being and Quality of life in the menopausal transition

According to the World Health Organization⁶² the definition of quality of life (QoL) is “individuals’ perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns”.

The QoL is a multi-dimensional concept and incorporates all aspects of an individual’s life such as physical and psychological health, level of independence, social relationships, personal beliefs and relationship to salient features in the environment. The QoL is a subjective concept and takes into account positive as well as negative aspects of life.

Health-related quality of life (HRQoL) can be viewed as a dimension of QoL and refers to the effect of an individual’s physical, psychological, social and emotional functions on his or her overall QoL⁶³⁻⁶⁵. During the menopausal transition different signs and symptoms can be experienced by the women and HRQoL may be affected^{42, 43, 66}. Results from several cross-sectional and longitudinal cohort studies^{45, 67} have suggested that perimenopause is associated with a higher level of somatic symptoms leading to decreased well-being in women during this period of life. It was, however, unclear whether domains of HRQoL other than the physical domain were also affected. Results from the Study of Women’s Health Across the Nation

(SWAN)⁴² indicated that the HRQoL in perimenopausal women did not differ from the HRQoL in premenopausal women when adjusted for menopause-related symptoms (hot flushes, night sweats, vaginal dryness, urinary leakage) and this suggested that these symptoms contribute more to an impaired HRQoL than the menopause *per se*. Likewise Utian⁶⁸ concluded that vasomotor symptoms could have a negative impact on HRQoL and contribute to both physical and psychosocial impairment. On the other hand Smith-Di Julio and colleagues⁶⁹ found, in a longitudinal study, that self-control and satisfaction with social support predicted increased well-being, and negative life-events predicted the opposite whereas menopausal-related factors did not affect well-being significantly. This is in line with the findings of Mishra and co-worker⁷⁰ who suggested that the women's experience of the menopausal transition appeared to be complex and factors such as work- or family-related stress affected HRQoL more than the menopausal transition status. HT users, however, reported improvements in HRQoL after HT have been started. According to Dennerstein and co-workers⁷¹ factors contributing to well-being in general are self-rated health status, symptoms, stress, living with a partner, and attitudes towards aging and menopause.

Several population-based studies and RCTs have supported the hypothesis that an improvement in one or more aspects of HRQoL in symptomatic women treated with HT is probably due to a reduction in hot flush frequency and severity and meliorated sleep^{66, 72-75}. Results based on the Women Health Initiative (WHI) have failed, however, to show improvements in QoL during HT use⁷⁶ but some methodological issues have been discussed such as choice of instruments and patient material studied^{68, 77}. Although HT may positively affect QoL, especially in symptomatic women, no prospective study investigating the effect of different modes of discontinuation of HT on QoL has to my knowledge been published.

Counselling and management of climacteric symptoms

To counsel a woman in midlife about the menopausal transition and how to manage this period of life is a challenging task for professionals with responsibility for the care of the women⁷⁸. Several studies⁷⁹⁻⁸¹ performed after the results from the WHI study were published have reported that women either were without information about HT or were confused about the risks and benefits profile.

A decision process is an ongoing activity and several factors such as past experiences, attitudes and beliefs, external environment, personal preferences, and knowledge may influence the process⁸¹. Jones⁸² and Woods⁸³ describe the decision process as continuous and involving several steps. They identified on the one hand decision-making women who took control and decided themselves and on the other hand non-decision makers who relied on the physician's decision⁸². Hoffmann et al⁸⁴ found that the discussion of the pros and cons of using HT was aimed more at motivating the women to take HT than to empowering the women to take part in the decision-process. Moreover setting the agenda for the discussion was ordinarily dominated by the physician. Martin and Manson⁷⁸ suggested an algorithm that estimates cardiovascular, fracture and breast cancer risk that may be helpful for clinical decision-making in consultations with women in the menopausal transition. Results from RCTs^{85, 86} show that decision aids can help women to take an active role in the decision process, improve knowledge and also increase satisfaction and reduce decisional conflicts. Col⁸⁵ suggested that use of an

internet-based decision tool would be less time consuming for the professionals and could also be made easily accessible for the women. A well-educated nurse or midwife can act to enhance women's decision-making abilities through communication about the transition and HT⁸¹.

Use of hormone therapy

Hormone therapy, a term used for both oestrogen therapy (ET) and combined oestrogen-progestogen therapy (EPT), is considered to be a well tolerated "gold standard" therapy recommended to women around menopause for alleviation of moderate to severe vasomotor symptoms. Oral HT reduces hot flush frequency by about 75-80 % compared to placebo and also significantly reduces the severity of hot flushes⁸⁷.

The use of HT in Sweden increased rapidly during the last decades of the 20th century^{1, 3, 88}. This increase was probably influenced by the results from several observational studies that indicated benefits of long-term use of HT on risk of cardiovascular disease (CVD), osteoporosis and fracture risk, colon cancer and Alzheimer's disease as well as all cause mortality^{4-7, 89, 90}. In 1998 and 2002 results were published from two prospective, RCTs, WHI and the "Heart and Estrogen/progestin Replacement Study" (HERS) which were designed to investigate primary and secondary preventive effects of HT on a number of conditions including cardiovascular risks. Both studies were prematurely stopped by the safety monitoring boards due to a high rate of reported adverse events. Neither the WHI¹⁰ nor the HERS^{8, 9} could find evidence for primary or secondary preventive effects of HT on cardiovascular morbidity in the age groups studied. In addition, the Million Women Study⁹¹ confirmed and strengthened previous findings of an increased risk of breast cancer associated with long-term use of HT. The WHI study¹⁰ found an increased risk for venous thrombosis and stroke and decreased risk for hip fractures and colon cancer in the HT group. Thus these large RCTs questioned the conclusions from earlier observational studies on the risk/benefit profile of HT. After reanalyses of the results from the HERS and WHI studies the concept "*window of opportunity*" or the "*timing hypothesis*" was launched⁹². This concept suggests that the risk/benefit profile depends on when HT is initiated; if started within 4-6 years of menopause, HT does contribute to cardio- and neuro-protection^{92, 93}.

Guidelines from national¹¹ (shown in table 1) and international menopause societies^{59, 94} have been updated after publication of the WHI and HERS studies.

Table 1. National treatment recommendations for hormone therapy (HT) in the menopausal transition¹¹.

-
- HT is the most effective and safe therapy intended for women around menopause with moderate to severe menopause-related vasomotor symptoms
 - HT should be used with the lowest effective dose
 - HT should be used for the shortest possible duration
 - An individual risk/benefit profile should be performed before initiation of HT and on a regular basis during the treatment
-

The results from the WHI study had a rapid impact on professionals as well as the public^{79, 95-97} and the use of HT dramatically declined in the USA as well as in Europe^{12, 13, 80, 98-100}. In Sweden³ the percentage of current HT users declined nearly 40 % between 1999 and 2003. According to Vegter and colleagues¹³ the decline continued in Europe even thereafter, which also seems to be the case even in Sweden (Fig 3).

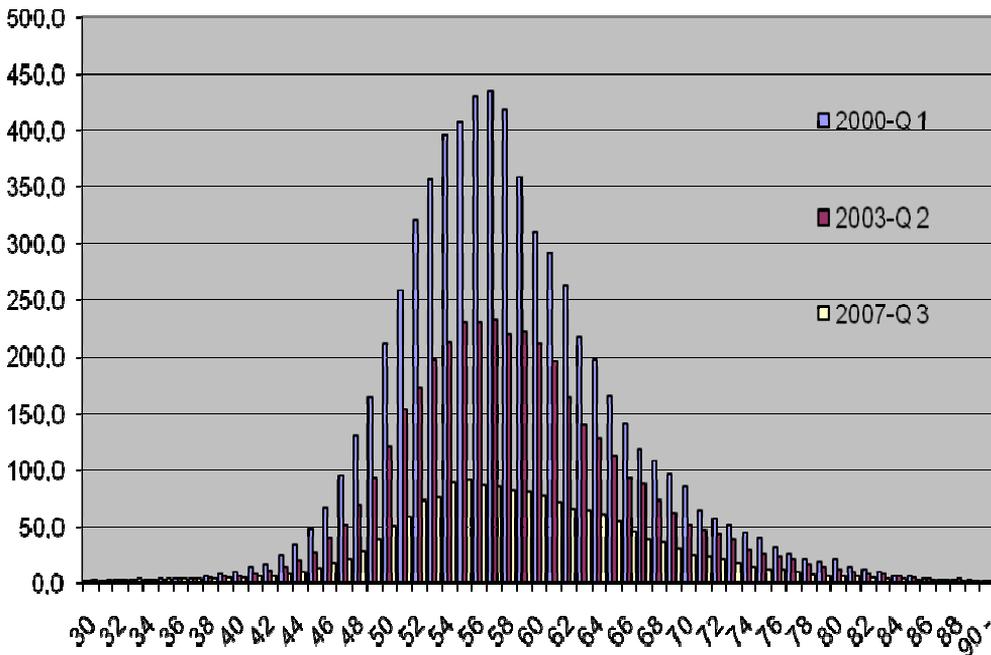


Figure 3. Total amount of hormone therapy (HT) sold at Swedish pharmacies to women in the first quarter of 2000 (blue), the third quarter of 2003 (red) and the third quarter of 2007 (yellow). Defined Daily Doses (DDD) per 1000 women and day in age groups 30-90 years.

Discontinuation of hormone therapy

Since national and international authorities and societies recommended the shortest possible HT use a need arose for the initiation of prospective controlled studies of different methods for discontinuing HT and for evaluating the risk for symptom recurrence.

Different ways to discontinue HT have been suggested. One method is to go “cold turkey”, a phrase referring to a method in which HT is abruptly discontinued. Tapering down is another method that can be done either by “dose tapering”, which entails decreasing the daily dose or by “day tapering”, which entails decreasing the number of days per week when HT is used¹⁰¹. The hypothesis that tapering would lead to lower risk of recurrence of hot flushes than abrupt discontinuation is based on the fact that a rapid decline in oestrogen level in

premenopausal women (e.g. premenopausal women who undergo bilateral oophorectomy) is associated with a higher incidence of moderate to severe vasomotor symptoms than the incidence in women in general who reach a natural menopause^{102, 103}. A tapering down method may possibly have an adaptive effect on the thermoregulatory system thereby affecting the risk of recurrence of vasomotor symptoms.

Results from two retrospective surveys^{104, 105} performed after the discontinuation of the WHI study have not shown any significant difference in recurrence of hot flushes between women who discontinued HT with the “cold turkey” method and the “tapering down” method. Grady and co-workers¹⁰⁴, however, reported that the proportion of women who resumed HT was lower, albeit not significantly, in the abrupt group (24 %) than in the tapering group (29%). About 43 % of women in both groups reported troublesome hot flushes and sweating after discontinuation. In observational studies^{105, 106} and RCTs^{107, 108} performed after the WHI study about 30-50 % of the women reported recurrence of vasomotor symptoms after discontinuation of HT. We found in a cross-sectional study¹⁰⁹ that 87 % of 53 to 54 year old women with vasomotor symptoms before initiation of HT reported recurrence of vasomotor symptoms after discontinuation of HT, which was a greater proportion than previously reported. The difference in recurrence rate probably arose because we only studied, in contrast with others, women who initiated HT due to vasomotor symptoms. Another factor may have been the age cohorts which differed from those in other studies. Factors associated with recurrence of vasomotor symptoms that are regarded as an indication for starting HT are hot flushes, troublesome withdrawal symptoms after discontinuation of HT, hysterectomy and long-term HT use^{104, 110, 111}.

Conceptions, attitudes, and knowledge related to the menopausal transition and hormone therapy

The menopausal transition is one of the most important transitions that women experience during lifetime¹¹². Expectations, experience, confirmation, regaining of balance and control, and freedom are suggested to affect how women experience the transition processes. Other transitions such as social changes related to both family and work are usually ongoing at the same time¹¹³. Women's conceptions and attitudes towards the menopausal transition can be influenced by biological, psychological, cultural, and social factors and the transition should not be seen as a process that is the same for all women. Attitude towards menopause vary between cultures^{114, 115} and individuals¹¹⁶. Women's knowledge of the menopause probably influences their management of the transition.

Three theoretical frameworks of the menopausal transition have been identified¹¹⁷. The *biological/medical model* looks at the climacteric as a deficiency condition which needs treatment.

The *psychosocial model* views the transition as a natural development phase in a woman's life and no treatment is needed. If the woman has troublesome vasomotor symptoms then she may be in conflict with expectations of psychosocial model, which may lead to decreased well-being.

The *holistic model* describes the menopausal transition as a multidimensional process which varies among women, and takes into account both biological and psychosocial factors. Adaption to this model can lead to increased wellbeing and empowerment if it is adapted to the individual woman's needs.

Conceptions

A "*concept*" is the way people see and understand something. The philosopher Immanuel Kant wrote in his Logic that a person must be able to compare, reflect and abstract to generate a concept¹¹⁸.

Marton¹¹⁹ argues that a conception is something that a person is not always aware of, has not always expressed or consciously thought of, as it has not previously been the subject of reflection. The conception constitutes the framework on which an argument is built. The more things are expressed or consciously reflected on, thought of, and brought to the surface, the more do we become aware of the phenomenon¹²⁰.

Attitudes

An "*attitude*" is according to Atkinson and Hilgard¹²¹

"a favourable or unfavourable evaluation of and reaction to objects, people, situations, or other aspects of the world".

It has been suggested by social psychologists that attitudes comprise factors such as cognition, affection, and behaviour^{122, 123}.

– The *cognitive component* concerns one's knowledge of something.

- The *affective part* includes feelings and evaluations that influence the strength of a standpoint for or against something.
- The *behavioural component* consists of how we act towards a situation or a person and the motivation to make changes.

Attitude formation and change

Attitudes are suggested to be formed by experiences throughout lifetime and are determined by beliefs about something and by the evaluations of such beliefs. Some attitudes are comprehensive and reflect an attitude to a phenomenon that plays a central or important role in a person's life whereas other attitudes are more unspecific. Usually the comprehensive attitudes are more stable over time and are held more strongly and are therefore harder to influence than the unspecific ones¹²³.

Strong and consistent attitudes can predict behaviour and if the aim is to change people's behaviour we first must know what these attitudes are and then employ methods designed to change these specific attitudes. Attitudes of which one is aware or that are based on one's own experience can predict behaviour to a higher degree than attitudes that do not meet these criteria¹²¹. Factors that could change or influence one's attitudes are the nature of the sender (e.g. the nurse or the doctor in a counselling situation) or the receiver (e.g. the patient), the message as such, and the social context where the message or communication takes place.

Trustworthiness, expertise, and interpersonal attraction are factors of importance for the impact of the sender on the receiver. Factors such as age, sex, knowledge, and self-esteem can play an important role in determining the sender's ability to influence the receiver¹²⁴. Message elements that present one or both sides of an argument contribute to the sender's ability to change an attitude. Emotions affect the cognitive process and emotional appeals are often used in advertising and health campaigns. Playing on emotions like fear or responses to threats is a technique that is often used to affect or change an attitude, probably most effectively when an individual cares strongly about the issue or has the ability to make a change¹²⁴.

Attitudes towards the menopausal transition

According to Kaufert¹²⁵ and Sinclair et al¹²⁶ women's attitudes and conceptions of the menopausal transition can vary from the view that the transition is simply a medical condition or that it is a natural event. In a qualitative study¹²⁷ the menopausal transition was described by women in terms of their expectations and experience, their understanding of the physical and emotional changes that occur, and their decisions about treatments and about entering a new phase of life.

Women's attitudes do not have to be stable and have been described as changing during the menopausal transition. Busch and co-workers¹¹⁶ stated in a longitudinal study that more than half of the women had neutral beliefs and about one third had negative beliefs about the menopausal transition before the menopause occurred. Five years later two-thirds had changed their attitudes in a positive direction. The authors thus confirmed previous results that the transition has a developmental potential for women¹²⁸.

Factors suggested to be related to women's attitudes towards the menopausal transition are menopausal status, menopause-related symptoms, and emotional health. Troublesome symptoms such as mood disturbances, bad memory, joint pain, and urogenital symptoms¹²⁹, and hot flushes and night sweats¹²⁸ as well as parity¹³⁰ are reported to be associated with negative attitudes towards the menopausal transition. Attitudes could become less negative if the woman is comfortable with talking about the menopause-related issues or has somebody who listens¹³¹.

Women's attitudes towards the menopausal transition are not always consistent with their doctor's beliefs about women's attitudes. Ejeby and co-workers¹³² found that the majority of the doctors but only one third of the women thought that women had a feeling of loss after the menopause had occurred. Half of the women instead perceived the menopausal transition as a relief whereas only 27 % of the doctors believed this to be so. Hvas and Gannik¹³³ concluded in a discourse analysis that even if the biomedical model used to discuss the menopausal transition was dominant as many as seven other different discourses were identified. The choice of appropriate model to be used when discussing the transition with a woman could affect the woman's position in the discussion and it thus seems essential for the care-giver to be open-minded and willing to listen before choosing an approach in the discussion.

Attitudes towards HT

Women have positive as well as negative attitudes towards HT and the attitudes are influenced by both positive factors such as symptom relief and negative factors such as side-effects and long-term risks¹³⁴. A Swedish cohort study¹³⁵ found that current users of HT had a higher proportion of positive attitudes to HT (76 %) than former (38 %) or never user (28 %). Personal, health-related, and psychosocial factors explained about 40 % of the relation between positive attitudes towards HT and current HT use. Stadberg and co-workers¹³⁶ reported that one fifth of the women who refrained from HT despite vasomotor symptoms stated that the reason why they refrained was that the menopausal transition was a natural process. Thunell and co-workers¹³⁷ found a more positive attitude to HT in 1998 than had been found in 1992 but the measure of attitudes that was used was merely based on a higher proportion of HT use and did not consist of answers to specific attitude questions. Counselling from health care providers about the menopausal transition and HT can also affect women's attitudes towards HT^{138, 139}.

Cultural differences

The conceptions and attitudes toward the menopausal transition vary across different cultures¹¹⁴. In "traditional" cultures the beliefs are often passed down through generations and linked to how middle-aged women are looked upon and what privileges they have. If fertility is valuable the attitudes towards menopause may be more negative¹⁴⁰. Positive feelings of relief and satisfaction after having had many children are common in some cultures¹⁴¹. In cultures where women have a low status where talking about or acknowledging sexuality is a taboo the menopause can provide freedom¹¹⁴.

In modern western cultures women have a greater opportunity to choose between education, being a housewife or being employed outside the home. These women are also more exposed to and influenced by media, often proclaiming the importance of youth and eternal health. Ageing and fear of diseases are often connected with negative attitudes and the menopause has often been viewed as a biomedical condition which can be treated with HT¹¹⁴. Others view the menopausal transition as a developmental phase of their life leading to a greater freedom and higher self-esteem^{114, 127}.

Immigrant women are often involved in a process taking them from a “traditional” to a modern culture, a process where they face challenges such as a new language, employment and economic issues¹¹⁴. These women have a tendency to view menopause as a negative life event probably because it can be so difficult to make several other complex transitions simultaneously¹⁴².

Knowledge

“*Knowledge*” is formed in interaction with the surroundings and the individuals themselves construct their understanding of the world through experience¹⁴³. Assimilation and accommodation of new information and experience are important factors in making fundamental change in our approach to the outside world possible and thus contributing to development of our knowledge¹⁴⁴.

Communication between people is an important factor affecting learning and in making it possible to bring new knowledge forward. Knowledge of a phenomenon varies depending on how the phenomenon is understood and interpreted by the individual. Individuals have different ideas about what it means to learn and possess knowledge. Exchange of knowledge is an important part of learning as well as in shaping the ability to convert theoretical and practical skills to new knowledge. Human knowledge is largely linguistic through communication and the communication processes are central. One-way communication with a sender who mediates knowledge and a recipient who stores knowledge is a traditional way of looking at knowledge transfer. Those who mainly try to memorize reach a lower, shallower, level of understanding, which is probably due to the fact that they do not always understand the meaning or context but focus on the text itself. A higher degree of learning is reached when the focus is on what the text is really about and what conclusions may be drawn from a text. Interest and motivation also appear to play a crucial role in how people learn and what level of understanding is achieved¹²⁰.

Knowledge of the menopausal transition and HT

When counselling menopausal women it is important that healthcare providers are able to give every woman prerequisites to understand the menopausal transition, the available treatments for troublesome symptoms, as well as the treatment-goals and possible effects. It is also important to assure that the woman receives understandable knowledge of an issue enough to incorporate and transform it into functional knowledge. According to Swedish authorities gynaecologists as well as midwives have responsibility for women’s reproductive health¹⁴⁵ and to provide knowledge of the menopausal transition and HT (gynaecologists). Still no na-

tional consensus for appropriate knowledge of the menopausal transition is available for women in midlife.

It is important when counselling menopausal women to know something about each individual woman's knowledge of for example 1) hormonal and age related changes in the transition, 2) risks and benefits of available treatment alternatives including no treatment and 3) the mechanisms behind different treatments. Such knowledge should be communicated in a manner that takes into account each woman's knowledge of HT and the menopausal transition and also her knowledge of her own reproductive functions. Lewin and co-workers¹³⁸ found that the proportion of correct answers about risks and benefits of HT declined in women between 1991 and 2000 and that a majority of the women were ambivalent whatever their age groups or educational level.

There are few studies on what women know about their own bodies, especially the reproductive organs and functions, and the effect of HT. In a cross-sectional study Berterö and Johansson¹⁴⁶ found that 40 % of the women using transdermal HT did not know why they should take progestagens together with oestrogen. About 60 % of the women stated that they had understood the information given by the health-care provider.

Aims

Overall aim

The overall aim of my research was to explore Swedish women's conceptions, knowledge, management, and attitudes regarding the menopausal transition and hormone therapy.

Specific aims

- With a qualitative method explore and describe the conceptions of the menopausal transition in women seeking medical advice due to climacteric symptoms.
- With a cross-sectional design assess attitudes to the menopausal transition and hormone therapy among women 53- and 54 years old in Linköping and if these attitudes changed after new scientific findings on the risks and benefits of hormone therapy began to appear.
- To assess if these attitudes differed between peri- and postmenopausal women and between users and non-users with hormone therapy.
- With a cross-sectional design investigate the knowledge of hormone therapy, reproductive physiology, and the menopausal transition in a population of Swedish women 53- and 54 years old.
- To determine if the knowledge differed between ever- and never users of hormone therapy or between women with different level of education.
- With a randomized controlled trial design compare effects of two different methods of discontinuing hormone therapy, i.e. tapering down or abruptly discontinuation, on recurrence of hot flushes, resumption of hormone therapy and on health related quality of life in women who displayed vasomotor symptoms before initiating hormone therapy. Possible predictors of resumption of hormone therapy will be investigated.

Material and methods

Settings

Table 2. Overview of designs, populations, and data collection methods used in the studies.

Study	Study I	Study II	Study III	Study IV
Design	Qualitative, phenomenography	Observational, cross-sectional	Observational, cross-sectional	Open, multi-centre RCT
Data-collection methods	Audio-taped, semi-structured interviews	Self-administered questionnaire	Self-administered questionnaire	- Self reported hot flush diary - Phone interview asking for resumption of HT - Quality of life questionnaire
Respondents or participants	Women aged 44-59 years with a scheduled consultation for a first time visit to discuss climacteric symptoms and/or HT	Two birth cohorts aged 53 and 54 years in the community of Linköping, Sweden in 1999 and 2003	Two birth cohorts aged 53 and 54 years in the community of Linköping, Sweden in 2003	Women at 12 out-patient clinics of gynaecology in Sweden suitable to inclusion and exclusion criteria
Number of women/ number included in analyses	26/20	Year 1999; 1760/1180 (67 %) Year 2003; 1733/1239 (72 %)	1733/1263 (73 %)	87/75
Data-collection period/ screening period	Year 1999 to 2000	Fourth quarter of 1999 Second quarter of 2003	Second quarter of 2003	March 2005 to December 2007

RCT = Randomized, controlled trial

HT= hormone therapy

Paper I-III

These three studies were performed in the community of Linköping, Sweden. Linköping is a university city with high technology industries and a mainly urban population (132 500 in 1999 and 136 231 in 2003)¹⁴⁷. In paper I three gynaecological out-patient clinics in Linköping participated with recruitment, one out-patient university based clinic and two community-based clinics. Paper II and III were population-based cross sectional studies.

Paper IV

The study was performed as a national collaboration between members of a working group within the Swedish Society of Obstetrics and Gynecology. Twelve out-patient clinics of gynaecology recruited eligible women. Four sites consisted of university clinics and eight sites were community-based clinics of gynaecology (Frösön, Helsingborg, Husqvarna, Kungsbacka, Motala, Linköping, Stockholm, Sundsvall, Umeå, Uppsala and Örebro).

Study subjects

Paper I

Twenty-six women, who had a first time scheduled visit to discuss climacteric discomfort and HT, were consecutively invited to participate in the study performed in 1999 to 2000. Four of the women could not participate due to scheduling problems, one woman declined participation and one interview could not be analyzed due to technical problems.

Inclusion criteria were first time consultations to discuss climacteric signs and symptoms, ability to speak and understand Swedish, and voluntarily given informed consent. The criteria for participation were deliberately wide in order to give both depth and breadth to the material. The sample size of 20 women was estimated to be sufficient and adequate for the purpose of the study. The corpus of data consisted of 243 pages of written text after transcription of the interviews.

The classification of menopause status used in this paper agrees mostly with the definitions according to STRAW¹⁷ but the women classified as perimenopausal were according to STRAW in the late phase (-1) and the premenopausal women in the early phase (-2). In the result and the discussion sections the term climacteric and the menopausal transition are used synonymously and refer to the period “about or around menopause” including the postmenopausal period.

Paper II-III

A questionnaire was sent to the total population of women, who were or were going to become 53 and 54 years old during the year, and who lived in the community of Linköping in 1999 (n=1760) and 2003 (n=1733). The local population authorities provided the names and addresses. The age groups were selected to assure a sufficient number of women in perimenopausal or menopausal state and with the menopausal transition and HT in focus. The women were classified as postmenopausal after six months of amenorrhea. Women with bleedings, no matter if regular or not, were classified as perimenopausal. Kaufert and colleagues stated,

however, that menstrual bleedings occur in less than 10 % of the women after six months of amenorrhea¹⁴⁸.

Paper IV

One hundred and nine women were consecutively invited to participate and screened for eligibility. Participants were recruited by their gynaecologist or by advertisement in the local press. The main inclusion criteria were current HT use due to hot flushes, with duration between 3 to 11 years, and with an oral continuous combined EPT regimen or tibolone at least during the preceding year. Inclusion and exclusion criteria are described in detail in paper IV.

Eighty-seven women aged 50-72 years (median 59, 25th -75th percentiles 55-61) were included and randomized between the two modes of discontinuation i.e. tapering down in four weeks or discontinuing abruptly. The major reason for not being included in the study was more than one hot flush per 24 hours on average during the screening period. Due to recruitment problems the study was prematurely discontinued before the originally planned number of 200 women were randomized. The low recruitment rate could probably be explained by the low prevalence of HT use at the time of study recruitment and the fact that many women recently had tried to discontinue their HT due to a recommendation from their doctors or on the basis of information in the media.

Methods

Phenomenography

Phenomenography is empirical and “describes things as they appear in the lived world around us”¹¹⁹. The method describes qualitatively different ways to experience, conceive, apprehend, and, understand a phenomenon; e.g. women’s conceptions of the menopausal transition (paper I). How individuals understand and relate to the phenomenon as such, are important¹¹⁹. In phenomenography it is suggested that the term “conception” or “ways of experience” be used because it stands for a broader meaning than “perception” which is described as a process more affected by sensory stimuli in the environment¹¹⁹. Marton argues that a conception is something subconscious which the person is not always aware of or has not reflected on¹¹⁹.

Interviews

Semi-structured interviews with open ended questions were used to explore the variations of conceptions of the menopausal transition in women around menopause¹²⁰ and to assure that the specific topics of the study were covered^{149, 150}. According to Patton¹⁵¹ a good qualitative interview question should be open-ended, neutral, sensitive, and clear. The purpose is to give the informants the opportunity to respond in their own words and to obtain access to the informants understanding of the phenomenon studied¹⁵⁰. The interview guide comprised a few entry questions, while probe questions were used during the interview according to the answers obtained. The entry questions used were “Can you describe what the climacteric transition means to you?”, “Which symptoms related to the transition did or do you experience during this period?” and “How do these symptoms affect you?” A probe question could for example be “Please can you explain what you mean about that?” It is recommended to avoid

questions that require answers such as “yes” or “no”. It is considered to be important to obtain an immediate interpretation in order to enable the interviewer to pose further questions to gain understanding. Three pilot interviews were performed with women in the menopausal transition to check the interview guide and the technical equipment. Before each interview the interviewer gave short information about the study and informed consent was obtained from each informant. It was also important to create confidence between the interviewer and the informant. The interviews took place in a room in private at the outpatient clinic directly after the consultations with the gynaecologist. The length of the interviews varied between 30 to 60 minutes each, which was considered to be required to elucidate the topics of interest but also depending on the interest and verbal capacity of the respondent. All interviews were performed by the first author (LLÅ), audio-taped and transcribed verbatim including every spoken word as well as capturing pauses¹⁵². The transcriptions were made by a professional transcriber.

Questionnaires and diaries (paper II- IV)

Questionnaires (paper II and III)

The two cross-sectional studies (paper II) were designed to investigate women’s attitudes to the menopausal transition and HT as well as benefits and risks with HT (the latter reported elsewhere³). The 12 statements about attitudes towards the menopausal transition were partly obtained from the Menopausal Attitude Questionnaire (MAQ) used in a study reported by Leiblum and Schwartzman¹⁵³ and in other studies measuring attitudes towards the menopausal transition and HT^{126, 138, 154}. Some additional statements were developed by the research team on the basis of the literature, results from the qualitative semi-structured interviews (reported in paper I) and clinical experience.

In the questionnaire used in 2003 (paper III) 15 questions concerning knowledge of the menopause, reproductive physiology, and HT were constructed by the research team and added to the questionnaire used in 1999. The questions were based on the clinical experience, questions that appeared after the qualitative study and on recently published data about risks and benefits of HT.

The self-administered questionnaires included questions about background characteristics, attitude statements with a Likert scale rated in five steps from “totally agree” to “totally disagree” and multiple choice questions concerning the knowledge of the menopausal transition and HT including the given alternative “I don’t know” (see appendix).

The questionnaires were mailed late in 1999 (before the results of the WHI-study were published) and in 2003 after the results of the WHI-study were published. A cover letter was enclosed with information about the aim of the study and emphasizing that participation was voluntary. The questionnaires were coded which enabled us to send a reminder to all women who had not replied four to six weeks after the first questionnaire was mailed.

Hot flush diary (paper IV)

The subjectively experienced frequency and severity of hot flushes were manually recorded by the women every day before bedtime and every morning after waking up throughout the study (see Study design, Paper IV). The frequency was based on total numbers of hot flushes per 24 h and the severity was based on a total sum rating score of all hot flushes experienced during the last 24 h and ranged from 0 (not bothersome at all) to 10 (extremely bothersome). The diaries included daily registration of adherence to HT intake in relation to randomization as well as resumption of HT up to six weeks after discontinuation of HT.

Health-related Quality of life (paper IV)

To measure HRQoL the instrument “Psychological General Well Being Index” (PGWB) tested for validity and reliability was used¹⁵⁵. PGWB is a general instrument containing 22 items referring to anxiety, depressed mood, well-being, self-control, general health and vitality. Each item is graded between 0-5 and the total score range adds up to between 0-110. The Swedish version has been validated and used in HT trials¹⁵⁶. PGWB is suggested to be an appropriate method to measure both positive as well as negative effects on well-being and to detect mood changes and has commonly been used in studies of the menopausal transition¹⁵⁷. The women filled in the form at inclusion and at the end of the 6th week after complete discontinuation of HT.

Intervention and randomization (paper IV)

All women who were eligible had an equal probability to be randomized either to tapering down, i.e. to take their ordinary EPT dose every other day during four weeks before complete discontinuation, or to discontinue their ordinary EPT abruptly. An independent statistician prepared a computer-generated separate randomization list for each centre and the randomization was carried out with blocks of four patients. The randomization process and block size were unknown to the investigators and nurses participating in the study. The study nurse at the central randomization unit allocated the next available number from the randomization list for the specific centre and gave instructions to the women about how to discontinue the EPT.

Trustworthiness, validity and reliability

In paper I all transcriptions were listened to and compared with original audio-tapes by two of the authors independently (LLÅ, KK). Some minor corrections were done and information that might have made it possible to identify informants or other persons in the material was deleted. To maintain objectivity repeated reflections were performed during the data collection and analyses.

Negotiated consensus was used to enhance the credibility¹⁵⁸. Two of the authors independently performed analysis steps called “grouping”, “articulating”, and “labelling” (table 3). The results were compared and the analysis was not considered complete until an agreement was reached and no overlapping occurred. Providing quotations from the interviews contributed to supporting the relationship between the empirical data and the categories used to describe the variety of conceptions. Peer debriefing was used by having a senior researcher perform an

audit. This researcher did not participate in the data collection or analyses but did evaluate the categories and subcategories and considered them to be relevant^{150, 159}.

The questionnaires used in paper II and III were tested for validity and reliability in several steps¹⁵⁰ and have been described in detail in paper II and III. Additional analyses for test-retest stability were performed (paper II) showing that a correlation between the 77 answers given twice was $r = 0.88$ (Spearman correlation test $p < 0.001$), Kappa 0.59 ($p < 0.001$).

The internal consistency for the PGWB index (paper IV) was measured with Cronbach's alpha coefficient which was 0.95 at baseline and 0.96 in the questionnaire answered after 6 weeks. These coefficients are in line with those found by Duphy¹⁵⁵ who reported high internal consistency (0.94).

The answered questionnaires were optically scanned and exported into SPSS for Windows for statistical analyses (paper II and III). Optical scanning was checked manually until total agreement existed between manual and optical reading in ten consecutive and complete questionnaires.

Missing data

External drop-outs

A number of questionnaires were excluded because the women did not answer consistently to the questions about the menopausal status or HT use (Fig 4). In the questionnaire used in 2003 the proportion of responding women with native language other than Swedish was 6 % whereas such women constituted 9 % of the same age groups in the region according to statistics from the Statistics Sweden.

In 2003 (paper III), the 76 women whose questionnaires were excluded due to inconsistent answers had a lower level of education and more often lived in rural areas than those women who had answered consistently. The difference in analyzable rate between paper II and III in the questionnaires from 2003 depends on the different ways of grouping the variables before analysis (Fig 4). In paper III the variables were analyzed according to HT use, and thus women who had answered inconsistently to questions about menopausal status could be included, in opposition to paper II.

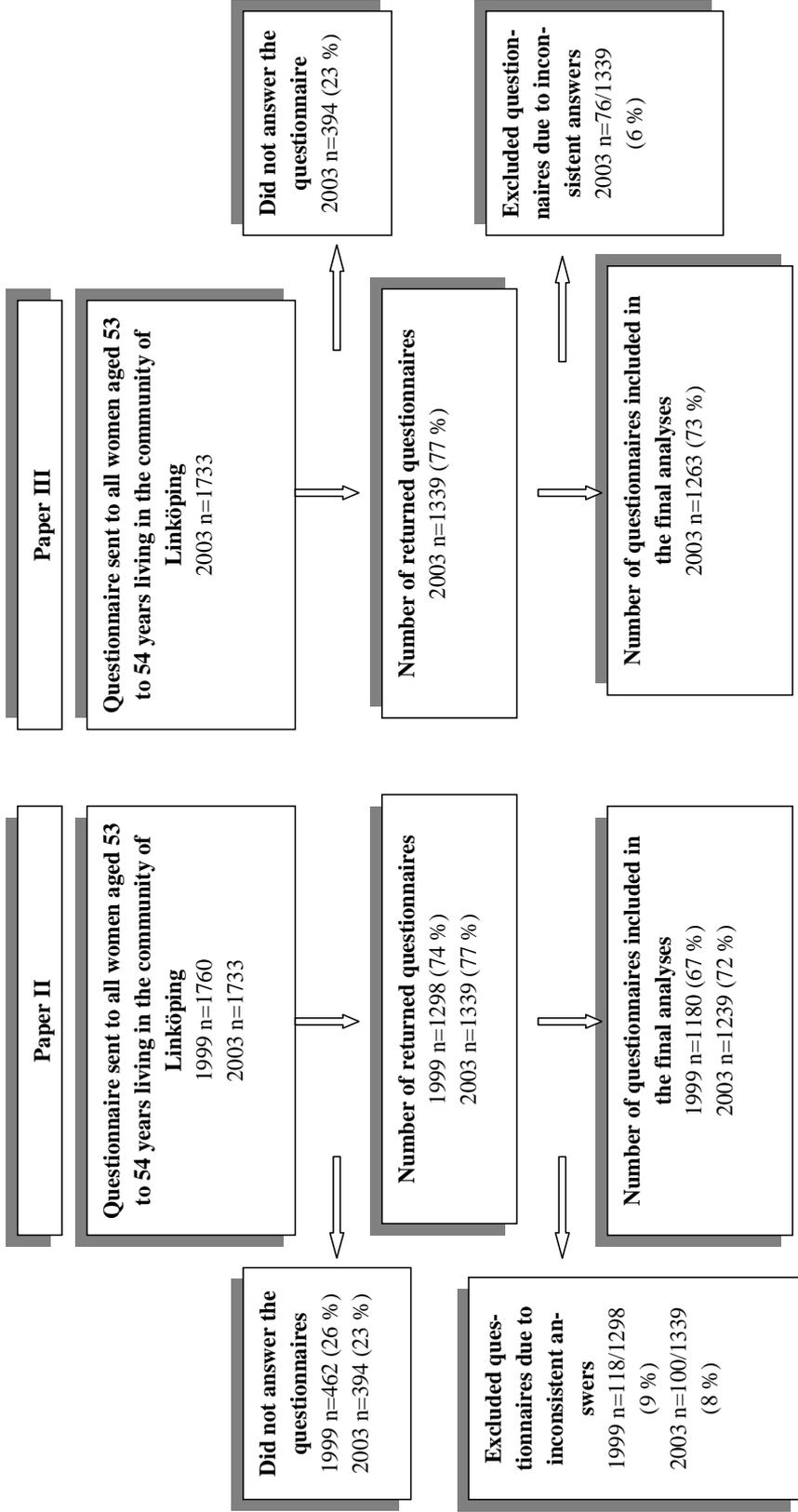
Internal drop-outs

Among the attitude questions (paper II) the rate of missing answers was 5-6 % and in the knowledge questions (paper III) missing answers varied between 0.5 % and 2.7 %. Before analysis of the knowledge questions one question about weight changes during the menopausal transition was omitted because of the high rate of missing data.

In paper IV about 5 % of the data on hot flush frequency and severity, which were planned to be collected over six weeks, were missing and replaced due to resumption of HT already before the end of the six week follow-up period. The mean value of hot flush frequency and severity from the last seven days for the specific woman before she resumed HT was carried forward to constitute the 6th week data. Data in diaries in which not every day was completed during the six weeks follow-up period (1.4 %) were replaced by using a similar method. Four

out of 162 PGWB questionnaires were missing (2.5 %) and were replaced by group mean at the visit concerned.

Figure 4. Flow chart of the questionnaire studies (paper II and III)



Data analyses

In paper I the analyses did not begin until all interviews were performed but the interviewer performed an immediate written reflection after each interview. The interviews were partly analyzed by using QSR NUD*IST VIVO® (version 1.3.146, Qualitative Solutions & Research Pty. Ltd.) and by manual handling. The analyse procedure, based on a phenomenographic procedure suggested by Dahlgren and Fallsberg¹⁶⁰, were performed by two of the researchers (LLÅ, KKN) independently and described in table 3.

Table 3. Description of the analysis procedure step-by step used in study I according to Dahlgren and Fallsberg¹⁶⁰.

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1. **Familiarization.** The researcher familiarizes her-/himself with the empirical material by reading the transcribed interviews and by listening to the tape-recordings several times to understand the meaning and to obtain a sense of the whole.
 2. **Condensation.** Identification of significant statements given by each informant. The material is reduced to retain central parts relevant for the research question.
 3. **Comparison.** The selected significant statements are compared in order to find sources of variations or agreement.
 4. **Grouping.** Statements showing similarities are put together into subcategories. Each quotation is provided with a code which makes it possible to track it in further analyses.
 5. **Articulating.** Preliminary categories are created. The essence of each group is identified and critically examined in order to find new dimensions.
 6. **Labelling.** Each category is assigned a name to emphasize the essence. Selection of quotations which illustrate the categories is performed.
 7. **Contrasting.** The final categories are compared with regard to similarities and differences to avoid overlapping.
-

Statistics

Table 4. Overview of the statistical methods used in this thesis.

Statistical methods	Study II	Study III	Study IV
Descriptive statistics			
Frequencies, and/or Md, IQR	x	x	x
Hypothesis-testing			
Pearson χ^2 –test or Fisher’s exact test	x	x	x
Mann-Whitney U-test	-	-	x
Comparison of several means			
Repeated measures, analysis of variance (ANOVA)	-	-	x
Kaplan Meyer survival curve	-	-	x
Regression analyse			
Logistic regression, forced entry method	-	x	x
Logistic regression, stepwise method	-	x	x
Internal consistency with Cronbach’s alpha	-	-	x
Power calculation	-	-	x
Significance level	P<0.05	P<0.05	P<0.05
Analyses performed by using SPSS for Windows release	10.1.0	14.0.0	14.0.0

The method used is marked with an x.

Md = median, IQR = interquartile range

The power calculation in paper IV was based on the clinical assumptions that the tapering down group would have a mean of two hot flushes/24 hours the 6th week after HT discontinuation while the abrupt group was expected to have a 20 % higher rate of hot flushes. The standard deviation (SD) for hot flushes was determined from previous studies, where diaries had been used for measurements of hot flushes.

In paper IV data were analyzed and presented according to “intention to treat”, i.e. including all women who fulfilled the inclusion criteria and had no exclusion criteria (except HT >11 years), who had initiated their change in EPT use according to randomization at least one day and who had any available measurements after randomization. Analyses were also checked according to the “per protocol” method for primary and secondary outcomes, including only women who had completely followed the protocol without major violations.

Ethics

The Declaration of Helsinki¹⁶¹ was followed and other applicable national legislation for clinical trials when applicable. All study protocols, including study design, questionnaires,

Quality of Life form, self-reported diaries and informed consent were approved by the local ethics committee at the Faculty of Health Sciences, University of Linköping (diary number 98-323, 99-247, 03-329, 156-04, T 12-05). Oral (paper I, IV) and written information (paper I-IV) was given to each woman before participation in the study. Informed consent was obtained before inclusion in the studies I (oral) and IV (oral and written) and all participants were informed orally and in writing that the participation was voluntary and that the consent always could be withdrawn without consequences for future care. All data were handled with confidentiality.

Results

Women's conceptions and attitudes towards the menopausal transition (Papers I and II).

The 20 women in the qualitative study (paper I) were between 44 and 59 years of age. Demographic characteristics are described in detail in paper I.

For the questionnaires in 1999 and 2003 the response rate was on average 70 % (67 % in 1999, 71.5% in 2003) after omitting the questionnaires with inconsistent answers. A slight difference between menopausal statuses was seen between the two cohorts with more perimenopausal women in 2003. Hysterectomised women were included in both analyses and were classified as postmenopausal. Demographic characteristics for women responding to the two questionnaires are summarized in table 5.

In study I and II women's conceptions of and attitudes towards the menopausal transition were analyzed with two different methods. The menopausal transition consisted of both physical and psychological changes irrespective of methods used to study the phenomenon. The majority of the women agreed that the menopausal transition is a natural event (92 % in the 2003 cohort, paper II), characterized by hormone deficiency (67 % in 2003, paper II) and about one third agreed that the transition is a sign of ageing (34 %, paper II) irrespective of menopausal status or HT use. In the qualitative study (paper I) it was a common belief that the transition was a result of hormonal changes but also changes related to ageing. For most of the women in the interview study (paper I) the cessation of menstruation was a strong marker of the menopausal transition. Both positive and negative feelings were expressed about the cessations of menstrual bleeding but also about the loss of fertility. In the questionnaire study (paper II) almost 10 % of the women disagreed totally or somewhat that it is a relief to no longer have a risk of becoming pregnant whereas 56 % agreed totally with that statement. The menopausal transition may be seen as a period of psychological alterations. Both beliefs of development and emotional instability were described by the women in the qualitative study (paper I). More than 50 % of the women in the quantitative study (paper II) totally or somewhat agreed that the transition was a period with increased freedom but about one third of the women were ambivalent about that statement. About 25 % of women were unsure if the psychological discomfort during the menopausal transition is caused more by changes in life than by hormonal changes *per se*.

In paper II the women defined as postmenopausal seemed to look upon the menopausal transition slightly more positively than the perimenopausal women with feelings of an increased freedom and relief at no having to think about contraception. However, the differences were small and the significance probably depended on the large sample size. More post- than perimenopausal women (about 30 % vs. 22 %) agreed that all women should use HT and this difference existed in both 1999 and 2003.

Table 5. Characteristics of the women answering the questionnaires in 1999 and in 2003.

Questionnaire	1999 (n=1180)	2003 (n=1239)	p ¹
Menopause status			
Pre- perimenopausal	245 (20.8)	301 (24.3)	<0.001
Postmenopausal	935 (79.2)	938 (75.7)	
Hormone therapy			
Current	478 (40.5)	313 (25.3)	<0.001
Previous	134 (11.4)	235 (19.0)	
Never	568 (48.1)	691 (55.6)	
Smoker			
	(n=1113)²	(n=1237)²	<0.001
Yes	294 (26.4)	249 (20.1)	
No	819 (73.6)	988 (79.9)	
Residency			
	(n=1170)²	(n=1236)²	0.001
Urban resident	1021 (87.3)	1019 (82.4)	
Rural resident	149 (12.7)	217 (17.6)	
Marital status			
	(n=1166)²	(n=1238)²	<0.001
Married/cohabiting	957 (82.1)	964 (77.9)	
Single	209 (17.9)	274 (22.1)	
Occupation			
	(n=1173)²	(n=1238)²	<0.001
Full or part time	1010 (86.1)	1001 (80.9)	
Housewife	16 (1.4)	15 (1.2)	
On sick leave/retired	103 (8.8)	180 (14.5)	
Student/unemployed	44 (3.8)	42 (3.4)	
Hysterectomy	115 (9.7)	122 (9.8)	NS
Oophorectomy	41 (3.5)	35 (2.8)	NS

Data are presented in numbers and (%).

¹ P-value according to χ^2 – test, two-sided

² The number of answers on this specific question

HT-users agreed to a greater extent than non-users towards the statements about HT and the statement that the transition is characterized by hormone deficiency. More than one third of HT-users in 2003 stated that all women should use HT versus only 11.3 % of the non-users. In 1999 the difference was similar but 59 % of the current users agreed totally or somewhat

compared to 22 % of the non-users, showing that the proportion positive to HT was substantially lower in 2003 (paper II). The same differences appeared when we compared women with moderate to severe vasomotor symptoms without HT with HT-users (data not presented in paper II).

In both cohorts about 10 % of the women had undergone a hysterectomy. An additional analysis of the questionnaire from 2003, not presented in paper II, showed that hysterectomised women seemed to be more prone to agree that women with vasomotor symptoms should use HT (48 % vs. 35 % in non-hysterectomised women, $p=0.003$) and HT should be used in all women regardless of symptoms (29 % vs. 17 %, $p=0.011$). The findings were similar in 1999 and 2003 with a higher proportion positive towards HT in 1999. Hysterectomised women also appeared to have used HT more often than non-hysterectomised women ($p<0.01$).

In addition to the results about attitudes towards the menopausal transition and HT (presented in paper II) we have analyzed the answers to attitude questions from 2003 in relation to different educational levels. In summary women with less education seem to think their partner regards women in the menopausal transition to be less attractive and women feel less feminine after menopause than women with a higher level of education. A greater proportion of women with a lower level of education also reported relief of not having to risk pregnancy and having to think about contraception.

Changes in women’s attitudes towards the menopausal transition and HT between 1999 and 2003 (paper II)

Women’s attitudes towards HT changed significantly between 1999 and 2003 and a lower proportion of women in 2003 agreed with the statements that all women should use HT irrespective of climacteric symptoms. In 2003 only 17.4 % thought that all women should use HT compared with 37 % in 1999 (Fig 5). The women in 1999 agreed to a greater extent that women with troublesome symptoms should use HT than did women from the 2003 cohort (44.3 % vs. 35.7 %). Women in the 2003 cohort agreed completely to a greater extent with the statements that menopause is natural, characterized by hormone deficiency or is a sign of ageing than did the women in 1999 ($p < 0.001$). Responses to the other statements regarding the menopausal transition did not differ between 1999 and 2003 (paper III).

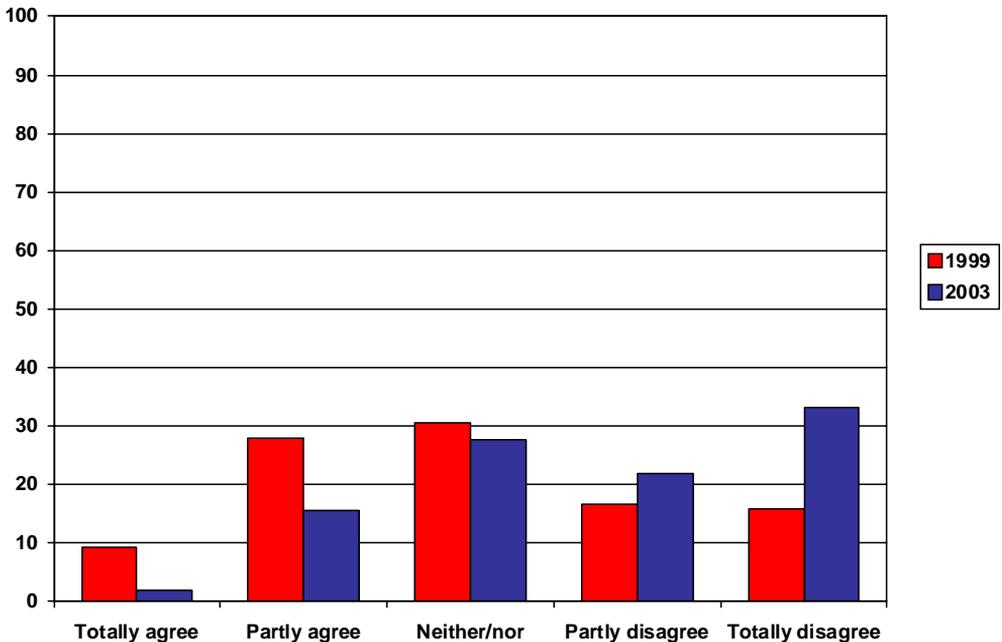


Figure 5. The distribution in percent of answers to the statement “Since the menopausal transition mean decreased oestrogen levels all women should use HT” in the questionnaire from 1999 (n = 1169/1180) and 2003 (n = 1218/1239).

Knowledge of the menopause and HT (Paper III)

Forty-four percent of the women were ever-users of HT and 56 % had never used HT. The educational levels were evenly distributed with about one third of the women represented in

every group (up to 9 years, 10-12 years, and > 12 years of education). More demographic characteristics are presented in paper III.

Women 53 and 54 years old had a rather limited knowledge of some parts of reproductive physiology, the menopausal transition and the effect and function of HT irrespective of HT use or educational level. This was especially evident concerning knowledge of two relevant aspects of HT. Many had little or no knowledge of the possible effect of HT on fertility. They also had even more difficulty in comprehending the function of progestagens in relation to management (Fig 6). Almost half of the women with the lowest educational level were unsure about the statement that a women who has regular bleedings due to HT is fertile (39.1 %) or if HT works as an oral contraception (48.5 %). Even one quarter of the women who were ever-users of HT were unsure about the latter statement. However, the majority of the women had an adequate knowledge of the cause of the menopause and related symptoms regardless of HT use or educational level. Knowledge of risks and benefits of HT was better among ever-users than never-users of HT but almost 25 % of the ever-users answered that the breast cancer risk was unchanged or were unsure what happens with this risk when using HT. Only 3-7 % of the women regardless of educational level or use of HT thought that all women should use HT. In general women with the lowest educational level had a propensity to be unsure to a greater extent than women with higher educational level.

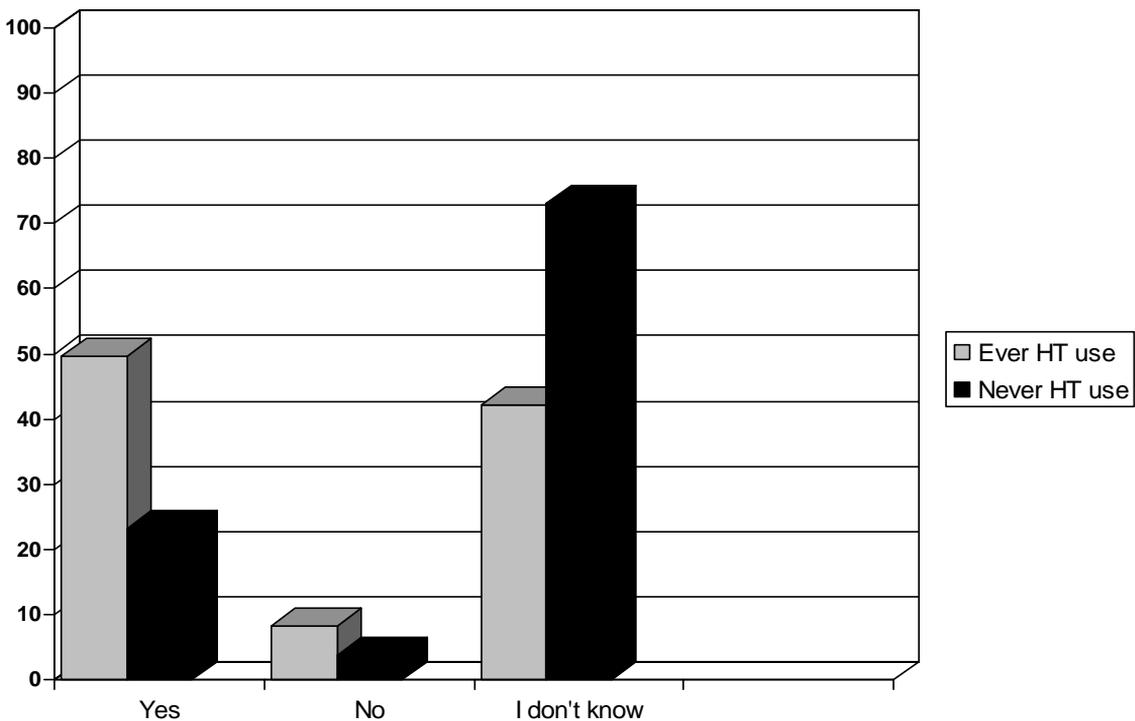


Figure 6. The distribution in percent of answers to the statement “Progestagens are used together with HT to counteract stimulating effects of oestrogens on the endometrium” in the questionnaire 2003 (n = 1237/1263).

In the univariate analyses never-users of HT were housewives to a slightly greater extent than ever-users. In the logistic model occupation predicted HT use ($p=0.031$) but the single variables did not however statistically predict HT use (not shown in paper III).

Discontinuation of HT (Paper IV)

This RCT failed to show significant differences in recurrence of hot flushes between the two different ways to discontinue HT. This may be a result of a small sample size resulting in low power caused by the premature discontinuation of the study. On the other hand the analyses of hot flush frequency, severity and deteriorating HRQoL in women who resumed HT showed that the severity and deterioration in HRQoL were important factors predicting HT resumption. Within one year of discontinuation almost 50 % of the women had returned to HT irrespective randomization group. No statistically significant differences between the two modes of discontinuing HT were found regarding reuptake of HT (Fig 7).

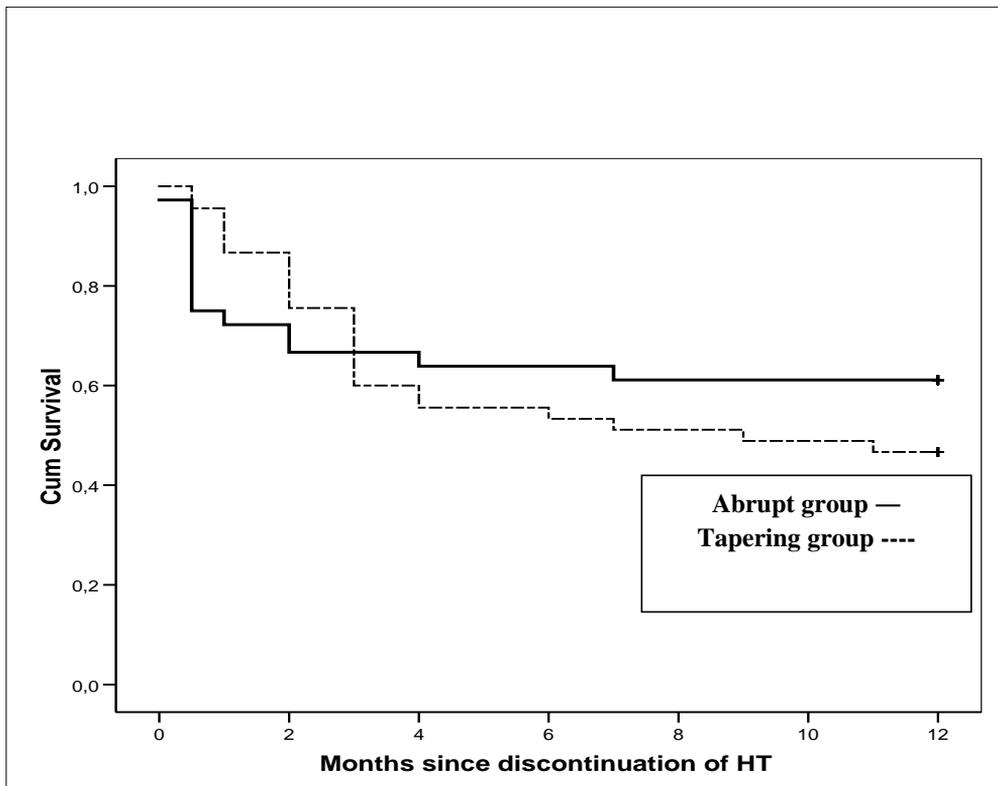


Figure 7. “Survival curve” for resumption of hormone therapy (HT) during the study period. The probability to not resume HT was slightly higher in the abrupt group ($n = 22/36, 61\%$) than in the tapering group ($n = 20/44, 45\%$) during the 12 months follow-up period but not statistically significant (Log-rank test, $p=0.43$), e.g. Cum Survival 0.8 denotes 20 % reuptake.

The demographic variables did not differ between women who resumed HT and those who did not (data not shown in paper IV).

There were no statistically significant differences between short- (≤ 5 years) and long-term users of HT (> 5 years) in the frequency of hot flashes at the 6th week after discontinuation or in resumption of therapy at six weeks, four or 12 months.

The repeated measures analysis of variance (ANOVA) indicated that flushes per day, per night and per 24 hours (Fig 8) increased significantly in both groups during the six weeks follow-up but the change over time did not differ between the groups ($p = 0.85$).

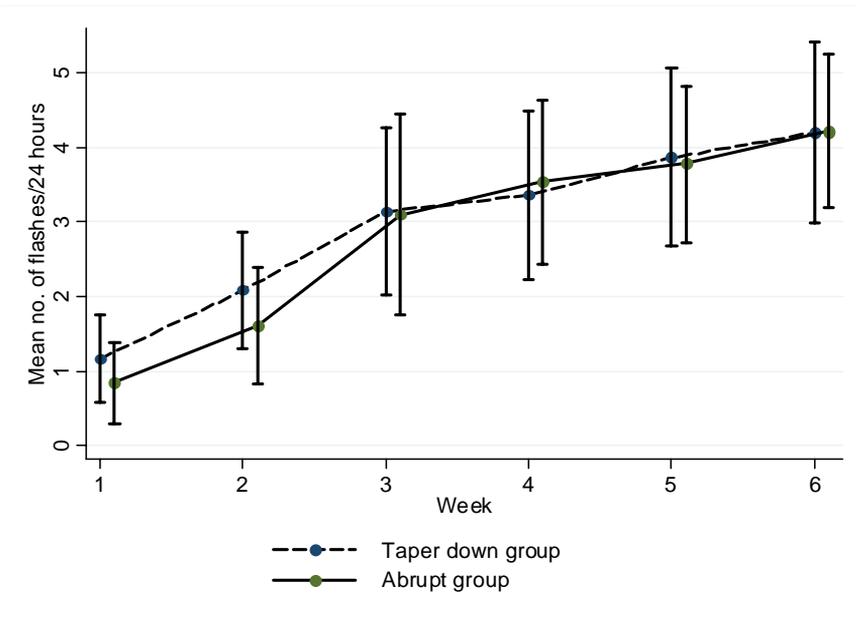


Figure 8. Mean (SD) number of hot flashes per 24 hours registered by the women in the two randomization groups (week 1-6).

General discussion

Main findings

Women's views of the menopausal transition seem to be individual and there is great variation between women. The transition is consisting of both physiological and psychological alterations and is viewed in both a positive and a negative way. After the major media reports in 2002 about the pros and cons with long-term use of HT, women's attitudes towards HT were modified and in 2003 only about half as many of the women as in 1999 agreed that all women should use HT.

Women's knowledge of some aspects of the menopausal transition and HT is limited. Many had difficulty comprehending the effects of HT use and the pros and cons of HT use in managing the transition. The effect of progestogens when added to oestrogens in HT and the nature of fertility during the menopausal transition did not seem to be understood among HT users. Women with a lower educational level tended to be unsure about many questions to a higher extent than women with a higher educational level.

Following the results from the WHI and HERS studies and the revision of the national guidelines regarding use of HT many women tried to abandon HT. In our small RCT we failed to find any differences in the recurrence of vasomotor symptoms or resumption of HT between women who used one or the other of the two modes of discontinuation. In most women the vasomotor symptoms recurred and about 50 % of the women restarted HT within one year of discontinuation. The severity of the flushes as well as the deterioration in well-being seemed to be important predicting factors which affected women's resumption of HT.

Paper I

This qualitative study took place before the intensive media reports on risks and benefits with HT^{9, 10} and only women who sought a health care provider to discuss troublesome climacteric symptoms and appropriate treatment were included. The fact that only symptomatic women participated in the study may have influenced the results because women with troublesome menopausal symptoms probably have thought about the transition to a greater extent and are more prone to seek information about the transition than women without troublesome symptoms. Furthermore physical and psychological symptoms have been shown to negatively affect the attitudes¹¹⁶. In the interview study women held both positive and negative conceptions of the menopausal transition despite the fact that almost all women reported menopausal symptoms.

Previous longitudinal studies^{116, 128} have shown that women's attitudes and conceptions towards the menopausal transition seemed to change during the transition with postmenopausal women having a more positive attitude compared with women in the perimenopausal stage. The present study included both peri- and postmenopausal women which could have contributed to the great variation of conceptions displayed. In a qualitative study Berterö found¹⁶² that premenopausal women's expectations about the menopausal transition were neutral or positive but that their apprehensions mostly referred to what they had heard from others, were more negative and were mostly linked to symptoms.

To establish validity and reliability, concepts commonly designed as “trustworthiness” in qualitative studies, Lincoln and Guba¹⁵⁹ suggested using different methods. It is important for the researcher to provide a trustworthy and complete description, i.e. a rich and thorough description of the setting, interviewer and context. Since the interviewer constitutes the scientific tool, it is important that the interviewer’s qualifications such as knowledge in the research area and skills and experience with interpersonal communication be presented fully^{151, 163}. It is also important to describe the selection of the participants, and to describe relevant background characteristics to make it possible for the reader to decide if the results could be transferred into other populations or into another context^{151, 159}. The fact that the results from paper I and II are in some ways congruent strengthens the results and increases the validity/trustworthiness of transferring the results to other populations of middle aged women. This could be considered a kind of triangulation, which is used in qualitative research to establish credibility¹⁵⁹. Methods or data sources could be triangulated but the conclusions must be interpreted with care when different research designs are used¹⁵⁰. Moreover negotiated consensus (described in detail in the method section) was used in the present study to establish credibility but it is possible that other categories might also have appeared. To follow a systematic procedure during the analysis as described by Dahlgren and Fallsberg¹⁶⁰ as well as to describe the range of variations in each category with appropriate quotations is essential to establishing credibility¹²⁰.

An issue is whether the results could have been biased by the fact that all interviews took place immediately after the consultation with the gynaecologist. It could be argued that the woman may have been influenced by the consultation *per se* and that her conceptions were coloured by the doctor’s own words. The interview could also have been performed before the consultation or even both before and after. Since the aim of the interview also was to explore how risk communication regarding HT had taken place in consultations with doctors^{84, 164} it was necessary to perform the interviews after the consultations. In qualitative studies the interviewer acts as the research tool and is responsible for avoiding superficial opinions and instead reaches a deeper level¹⁵⁹. During the interviews I had the possibility of going back to the informants to check whether my understanding was correct (member-check), to extend something the informants had said previously during the interview or had wanted to emphasize as recommended by Lincoln and Guba¹⁵⁹.

These results provide data on Swedish women’s conceptions about the menopausal transition and indicate that women’s conceptions are individual and reflect both physical and psychological views in positive as well as negative ways. Women’s views are in some ways in line with the holistic model suggested by Olazábal et al¹¹⁷ in which the menopausal transition was illustrated as a multidimensional process varying between women. The results confirm previous results from other contexts in the western world^{127, 162, 165-167} and even from recent qualitative studies performed in other cultural contexts^{168, 169}.

Paper II

The original questions used in paper II about attitudes (MAQ) were developed by Leiblum and Swartzman¹⁵³. Evaluation of the validity and reliability of the MAQ have to our knowledge not been published and we therefore performed a number of steps to control validity and

reproducibility (see Material and Methods). A method for increasing the internal validity was expressed in the different ways we asked about HT use and menopausal status in the questionnaires, an approach that enabled us to exclude those women who answered inconsistently. In the questionnaire sent in 2003 the women who were excluded due to inconsistent answers had a lower educational level than the women who were included. The percentage of immigrant women in the group that did not respond was higher than in the group who responded to the questionnaire (see Material and Methods). This fact should be considered when interpreting the results as concerns populations including women from other cultures. Cross-cultural studies have emphasized that women from different cultures define and experience menopause in different ways^{114, 165} and also seem to report having various menopausal symptoms to different degrees¹⁷⁰. Factors contributing to these differences are biological, psychosocial, environmental and cultural and were also discussed in the background section.

One important goal to be met when comparing two different populations (e.g. one from 1999, one from 2003) is to ensure that the demographic characteristics are as identical as possible. In this study, with two different populations, we found some slight difference in demographic variables such as menopausal status, smoking habits, occupation, and residency. Probably the main cause of these differences is that we asked for these data in slightly different ways in the two questionnaires, but the differences may also reflect the fact that smoking habits may have changed in Sweden as in other western countries. The cohort from 2003 seemed to have reached menopause somewhat later with a smaller proportion being postmenopausal, which is in accordance with recent data suggesting that menopausal age has been slowly increasing^{27, 28}. The proportion of non-smoker in the 2003 cohort was somewhat lower which probably could have affected the menopausal status²⁹. We do not consider, however, that these small but significant differences between the two populations jeopardize the conclusions.

It could be discussed if a prospective, longitudinal design would have been more suitable for meeting the aims of paper II. The main reason why we decided to include two different populations was, however, that we wanted to study if women's attitudes towards the menopausal transition and HT as well as actual use of HT had changed in relation to the research findings reported after the WHI and HERS studies. We therefore tried to select a sample of women who were "in the middle of" the menopausal transition with these issues therefore being highly topical for them. According to Avis and Busch^{116, 128} women seemed to redefine their attitudes towards the menopausal transition during the transition. Based on this observation a longitudinal design might have affected our results. Furthermore the experience of going through the menopausal transition can probably affect and influence the attitudes and lead to a process of psychological development¹¹⁶. The women defined as postmenopausal in our study seemed to look upon the menopausal transition slightly more positively than the perimenopausal women. However, the significant differences were small and probably depended on the large sample size. The classification of the women according to menopausal status could also have affected the results since the perimenopausal group consisted of both pre- and perimenopausal woman and the postmenopausal group of hysterectomised women and women with and without HT.

We found a number of small but significant changes in attitudes towards the menopausal transition between 1999 and 2003, which probably depend on the large sample size. However, women's attitudes towards HT have clearly changed from 1999 to 2003 possibly due to the enormous media reporting after publication of the WHI study as well as publications of changed guidelines for HT. Another possible factor which may have influenced the women's attitudes is the behaviour of the health professionals. Rolnick and co-workers¹⁷¹ reported that providers seemed to be highly responsive to the new guidelines, which is in line with the reported decrease of HT use in Sweden³ and other countries^{12, 13, 80, 98-100}. So both the women and their doctors seem to have been affected by scientific findings, media reports and the new guidelines.

A greater percentage of women in 2003 agreed that the menopausal transition is characterized by hormone deficiency than in 1999 but a significantly smaller percentage of the women in 2003 (17 %) compared to 1999 (37 %) agreed that all women should use HT, suggesting that attitudes towards HT could be more easily changed than could other attitudes. Comprehensive attitudes can be difficult to change^{123, 172} while attitudes towards HT probably were changed more easily due to both the extent of media coverage and the character and content of the message. Emotions and concern about the essentially negative effects of HT reported after the WHI could probably have affected the women's attitudes towards HT.

The women's perceptions about risks and benefits of HT changed significantly between 1999 and 2003; only 13 % in 1999 estimated the perceived risk of adverse drug reactions as rather but in 2003 25 % did so³. Interestingly, the level of HT use among female gynaecologists' was still high in 2003 (71 % current users of HT), albeit lower than 1996 (88 %)¹⁷³ and much higher than in the general female population during the same time³. However, even the gynaecologists' attitudes towards HT have changed with only 11 % in 2003 stating that all women without contraindications should be offered HT compared with 44 % in 1996¹⁷³. The physicians' attitudes may play an important role¹⁷⁴ but women's attitudes are probably also affected by many other factors such as knowledge of the issue, their own experiences of the menopausal transition and self-confidence with a treatment.

These results (paper I and II) emphasize the importance of being aware of and penetrating conceptions and attitudes when counselling women about the menopausal transition and HT. The health care provider should adapt the agenda to meet the individual woman's needs in contrast to what has been reported; the format of counselling today depends primarily on the individual physician's preconceived strategies, and not on any consideration of the woman's individual needs⁸⁴.

Paper III

To our knowledge, no existing instrument for measurement of knowledge about the menopausal transition was available when we started our study. Therefore a self-constructed questionnaire was developed and checked for validity and reliability in several steps (described in the Method section). The test-retest stability seemed to be quite good with 82 % of the answers being in total agreement between the two occasions. However, it could be discussed whether this method of assessing stability is suitable for questions about knowledge when the answer the second time could have been affected by recall or changed as a result of the first

administration^{150, 175}. Actually about 10 % of the women answered that they were unsure on the first occasion but took a position and answered yes/no the second time two weeks later.

To assess women's knowledge by asking the respondents to agree or disagree with statements in questionnaires may be a weak indicator of knowledge. Probably women on many occasions score high where they simply are asked to agree or disagree with each question that is posed, in spite of the fact that they may have considerable lack of knowledge of the nature of the condition. To answer open questions in one's own words is probably more demanding but elucidates the understanding in a more comprehensive way.

Women in our study seemed to have a limited and not functional knowledge of the role and importance of progestagens administered together with oestrogens in HT as well as what happens to the risk of conceiving during the menopausal transition and when using HT. This is in line with finding from another Swedish study performed by Berterö and colleague¹⁴⁶. The lack of adequate knowledge of the menopausal transition and HT is reported by Sahin and Kharbouch who found in a Turkish study¹⁷⁶ that about 80 % of the perimenopausal women did not know when to discontinue contraceptives. In a cross-sectional study it was reported that more than half of the women participating had not received any information about the menopausal transition and, if they said they had received information, they rated it as poor¹⁷⁷.

Factors such as education and HT use could probably covariate with women's knowledge of the menopausal transition and HT^{79, 178} with highly educated women and HT-users more likely to look for updated information yielding more correct knowledge of the effects of HT. In our study women with a university degree were more prone to give correct answers to the above mentioned questions but about 50 % of the women with this educational level were still unsure and about 50 % of the HT-users gave an incorrect answer or were unsure about the effect of progestagens. More than a third of the HT-users did not know the answers or gave an incorrect answer to the question about whether a postmenopausal woman who has a recurrence of menstrual bleeding due to sequential HT is fertile. Insecurity or lack of knowledge could possibly affect the women's sexual behaviour or lead to unnecessary use of contraception but unfortunately we did not ask about the use of contraceptive methods in our survey.

The previously reported differences in HT use between different educational levels^{179, 180}, with more highly educated women using HT, could probably influence the results. In our study, however, there was no significant difference in HT use between women with different educational levels and furthermore the previously reported difference in HT use between educational groups seems to have declined^{178, 179}. The proportion of immigrants among the women answering the questions was lower than in the local population and the women whose questionnaires were excluded were less well educated than the women who were included, which decreases the possibility of generalizing from the results.

The results from the HERS and the WHI studies showed fewer benefits and higher risks with HT than previously reported¹⁸¹. These unexpected results led to extensive media reports and a rapid, large scale decrease in HT use in Sweden as well as in other countries^{3, 12, 80, 98, 99} which seems to have persisted^{13, 182}. Many women were confused or had incorrect knowledge about the findings of the WHI study^{79, 80} despite the fact that many women had heard about the findings¹⁸³. In our study current or previous users of HT seemed to be more aware of risks and benefits of HT than never-users but still almost 25 % of the ever-users gave an incorrect

answer or were unsure about the effects of HT use on breast cancer risk. In line with reports from Strothmann and colleagues¹⁸³ the women seemed to be even more uncertain and confused about the effect of HT on cardiovascular and thromboembolic disease. This could probably be explained by the contradictory findings presented during the past decades and by the recently launched concept “window of opportunity”⁹³. In a Swedish population-based study (based on the same questionnaire and population as paper III) almost two thirds of the women reported that they had received new information about HT during the preceding year. The women reported that the main sources of new information about the results from the HERS and WHI studies were newspapers and magazines, television and radio, and, health care providers³ and similar findings have been reported by others^{97, 184}.

Unfortunately we did not ask the women if they believed that they had sufficient knowledge or not. Therefore the interpretation that women had limited knowledge is only based on our judgment. It is a challenge for health care providers to communicate with women and to give balanced and correct information about new scientific findings. Communication in health-care situations ought to include relevant information and important facts, and providers should also find out whether the information is understandable. A qualitative review⁸¹ suggested that women need information and knowledge of the menopausal transition and available treatments but that there is also a need for improvements in communication in the health care services provided for these women. Decision aids could be used as a tool for increasing women’s influence on treatment decisions and for improving their knowledge⁸⁶. Theroux suggested that nurses and midwives could play an important role in this process⁸¹.

Paper IV

The main methodological concern in our RCT was the lack of power in relation to the primary endpoint (hot flush frequency and severity). This disadvantage decreases the possibility of drawing conclusions from the data. An alternative power calculation for one secondary endpoint was based on the assumption that 33 % of women in the tapering-down group would resume HT and 66 % in the abruptly-terminating group. To obtain a power of 80 % we would need 35 women per group (a size we did reach) to detect a significant difference between groups ($p < 0.05$, two-sided test). Our main findings are in line with two prior RCTs^{107, 108} but those results could have been hampered by the small sample sizes and the short tapering-down period used¹⁰⁷. Population-based studies¹⁰⁴⁻¹⁰⁶ have also failed to show significant differences between gradual and abrupt discontinuation.

The open design used in our study could possibly have affected the results of the efficacy measurements because the participants were aware of the way in which they were to discontinue HT. The relevance of blinding is important especially when the outcome variable is a subjective one (hot flushes)¹⁸⁵. Although at the time of the study no evidence-based recommendations existed on how to discontinue HT, the women’s expectations may have influenced their propensity to resume HT and even to report vasomotor symptoms. A double-blinded design might have prevented this¹⁸⁵ but such a design was not feasible because of the number of different preparations of EPT used. The randomization procedure¹⁸⁶ and the concealing of the allocated “treatment”¹⁸⁷ by using a central randomization unit is a strength of our study, however, and minimized the risk of selection bias.

The use of subjective, self-reported diaries has been established as a valid approach and the registrations seems to have been reported in both an accurate and complete manner¹⁸⁸.

However, there is a risk for underestimation if subjectively registered hot flush frequency is used instead of objective, sternal skin conductance monitoring¹⁸⁹.

It could be argued that the difference in the number of weeks of measurement of the primary endpoint (hot flushes) may have affected the accuracy of women's registration of hot flushes. The precision may have been more exact in the beginning of the registration period and in the comparison of results in the 6th week after discontinuation it must be noted that the tapering-down group had 10 weeks of diary registration compared to six weeks registration in the abruptly-termination group. We did not, however, find any significant difference between the two groups in hot flush frequency or severity and we believe that this time effect is not important.

It could be questioned whether the women followed the study protocol when the control of their adherence to the study protocol was only based on the women's own diary reports of use of HT and on their answers to open questions in the telephone follow-ups. A study design using personal appointments would not have increased the validity regarding adherence to randomization group, whereas measurements of serum oestradiol concentrations would perhaps have strengthened the validity, at least for women originally using preparations including oestradiol.

In our study more than 45 % of the women irrespective of the discontinuation method resumed HT within one year, which is in line with previous reports¹⁰⁸. In contrast only about 5 % of the women participating in the WHI study who abruptly discontinued HT restarted after 8-12 months¹¹⁰. The high prevalence of reuptake in our study could partly be explained by the fact that all women had vasomotor symptoms as an indication for starting HT in contrast with the reason for HT use reported in other studies^{108, 110} or even that the women included may comprise a subgroup with a prolonged period of vasomotor symptoms. A history of hot flushes before HT use and the long duration of vasomotor symptoms are suggested to be important factors predicting resumption of HT and recurrence of vasomotor symptoms^{111, 190}.

An important question is whether HT use only postpones the appearance of vasomotor symptoms or, as previously reported, that a small proportion of women have a prolonged period with troublesome vasomotor symptoms^{46, 48}. In support of the former suggestion Okene and colleagues¹¹⁰ reported a 4.4 fold increase in the risk of experiencing recurrence of vasomotor symptoms in women with such symptoms at baseline after discontinuation of HT compared with previously symptomatic women assigned to and discontinuing placebo.

Guidelines from the Swedish Medical Product Agency¹¹ and international societies^{59, 94} now recommend HT use only in women with troublesome vasomotor symptoms for as short time as possible and at the lowest effective doses. The women included in the present study thus resemble those who at present are well suited for HT according to current guidelines. In a population-based study¹⁰⁹ 87 % of women who suffered from vasomotor symptoms before initiating HT reported recurrence of vasomotor symptoms after discontinuation of HT. About two thirds of the women, however, reported the symptoms to be less distressful than before HT was started. Additionally we could not find any evidence of lower symptom recurrence in

women who had used HT for more than 5 years than among those who had used HT for a shorter period but again this conclusion may have been affected by the small sample size. Thus the health care provider can probably expect a high proportion of women with symptom recurrence after discontinuation of HT and a discussion of possible outcomes should be included in the counselling, probably when the first discussion about possible initiation of treatment takes place.

Our results suggest that the severity of the flushes and the deterioration in well-being seem to affect the women's decision to resume HT more than hot flush frequency. Results from a population-based study¹⁹¹ confirmed the impact of both vasomotor symptoms and socio-demographic factors on HRQoL. Less frequent but severe hot flushes significantly interfere with work, social, and leisure activities as well as psychological wellbeing and sexual activity. Women with severe hot flushes were nearly three times more likely to experience a negative impact on work than women with mild to moderate hot flushes (OR: 2.82, 95% CI 2.00-3.98). HT has previously been reported to have a positive impact on HRQoL especially in women with troublesome vasomotor symptoms and sleep disturbances^{72, 75-77}.

In our study the mean PGWB baseline index in women treated with EPT was somewhat higher than the mean value in an unselected healthy population of Swedish women (mean 88 vs. 81)¹⁹² but somewhat lower than in postmenopausal women without vasomotor symptoms and HT (mean 90)¹⁹³. The women who have resumed HT within one year after discontinuation had a more pronounced decrease in PGWB index at the 6th week compared to the women who still abstained from HT but a somewhat higher PGWB index than Swedish postmenopausal women with vasomotor symptoms prior to HT (mean score 75 vs. 65)¹⁵⁶. It would have been interesting to measure if the PGWB index returned to the baseline score after resumption of HT but that was not included in our design.

The RCT designed to investigate how to best discontinue HT failed to show significant differences in recurrence of hot flashes and reuptake of HT between those who were assigned to abrupt discontinuation and those assigned to gradual discontinuation of HT. There is a need for larger RCTs with different kinds of tapering-down methods employed before the question about how to best discontinue HT can be answered satisfactorily.

Ethical considerations

The researcher must always be aware of and be prepared to take care of issues that may come to the surface when performing interviews. Therefore an inventory of possible supportive resources was compiled beforehand. The woman was informed whom to contact if there was a need for that afterwards. The interviewer was aware of the importance of acting in a balanced and skilful way in providing important and sensitive information, although in our study we did not expect to have to deal with such sensitive information. There is always a risk of giving women a feeling that her personal integrity is being questioned during an interview, but autonomy is protected by the woman's own choice to participate in the study or not to participate and to answer or not answer each question. The audio recordings and the transcriptions were treated as confidential data and were only accessible to the research team (paper I).

In the two cross-sectional surveys (paper II and III) a cover letter was enclosed with information about the study and the guaranteed confidentiality. The questions concerning risks and benefits with HT could cause anxiety in some women and therefore the names and telephone numbers of contact persons with experience in this area were given in the information letter. It was also emphasized that participation was voluntary.

In the RCT (paper IV) no serious adverse events were expected for the individual woman but all adverse events were registered during the study. All women had a contact person at the study coordinating centre who had experience in the area, and the gynaecologist and the study nurse at each centre could also be contacted if troublesome symptoms returned after discontinuation of HT. An benefit provided for the women who participated was support in making the decision that was provided by the study professionals who could aid in discussing risks and benefits of HT and whether and when it might be suitable to discontinue HT or not.

In summary we did not foresee nor did we experience any major ethical problems in any of the four studies.

Conclusions

We found that the majority of the middle aged women in our study viewed the menopausal transition as a natural process the nature of which is affected by both hormonal changes and by ageing. Each woman seems to experience a set of psychological and physical symptoms that are in some sense unique to her experience. Women were familiar with HT but answers to questions about HT demonstrate that attitudes towards HT held by women going through menopause have changed rather dramatically between 1999 and 2003. These changes reflect the influence on the women of media reports based on research that identified risks associated with HT some of which had not been identified before 1998. In contrast with this change in attitudes concerning HT, attitudes towards the menopausal transition itself remained relatively stable. We found that users of HT tend to have a more positive attitude towards HT use than do non-users and we also found that postmenopausal women tend to experience a feeling of freedom and a sense of a relief in not having to think about contraception that is not expressed by women who are still in the early stages of the transition.

Women in our study had a rather limited knowledge of the effects of HT, the pros and cons of HT, and even of reproductive physiology itself. Educational level and HT use may have an impact on the level of knowledge about these three subjects.

Neither tapering down HT during a four week period nor abrupt discontinuation of HT prevented the recurrence of hot flushes nor – albeit with low statistical power – did use of one approach in this RCT lead to a lesser tendency toward resumption of HT than use of the other approach. The severity of recurrent hot flushes and deterioration in wellbeing rather than the frequency of recurrent hot flushes seemed to be the two most important factors predicting the tendency to resume HT.

Implications for care and future research

Meet the individual woman's need

Healthcare professionals ought to adapt a holistic model and carefully take into consideration each individual woman's conceptions about and attitudes towards the menopausal transition and HT in order to be able to individualize the counselling situation to meet the needs of the individual women.

Empower the women for shared decision making and active management

Woman's active participation in decisions about HT is decisive for self management. It would be of interest to get a deeper understanding of women's functional knowledge of the menopausal transition to further identify important areas for improved self management. Such knowledge should make it possible to develop an "evidence-based" approach for shared decision making in clinical practice.

Further research about how to discontinue HT

Since many women who initiate HT due to hot flushes experience recurrence of vasomotor symptoms and impairment on HRQoL after discontinuation, they often resume HT even if they are aware of the associated risks. It is therefore of great importance to perform larger RCTs to investigate if our results can be confirmed or should be rejected.

Further research about alternative therapies to deal with the symptoms in the menopausal transition

It is of great interest to develop and investigate alternative therapies to use after discontinuation of HT in order to deal with recurrent symptoms rather than resuming HT.

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Appendix

Enkät kring övergångsåldern och östrogenbehandling.

Vi är mycket tacksamma om Du fyller i nedanstående frågor så noga du kan. Använd kulspetspenna och markera med ett tydligt kryss i rutan. Om Du ändrar Dig, fyll då i hela rutan med färg och sätt ett tydligt kryss i den ruta som är den rätta.

Frågeformuläret består av 3 delar. Först kommer några frågor om Dig och Din bakgrund. Sedan följer några kunskapsfrågor om övergångsåldern och slutligen kommer frågor om kunskaper om hormonbehandling mot övergångsbesvär.

Din bakgrund

1. Vilken skolutbildning har Du?

Ange den högsta helt genomförda utbildning?

- Grundskola, folkskola
- Gymnasieutbildning
- Universitets- eller högskoleutbildning

2. Vilket är Ditt modersmål?

- Svenska
- Annat nordiskt språk
- Annat språk

3. Röker Du varje dag?

- Ja
- Nej

4. Var bor Du?

- I tätort/stad
- På landsbygd

5. Vilket är Ditt civilstånd

- Gift/sambo
- Lever ensam utan partner
- Särbo

6. Är Du för närvarande?

- Förvärvsarbetande, hel- eller deltid
- Hemarbetande
- Sjukskriven/sjukpensionär
- Studerar/arbetsökande

7. Har Du opererat bort Din livmoder?

- Ja
- Nej
- Vet ej

8. Har Du opererat bort båda äggstockarna?

- Ja
- Nej
- Vet ej

9. Har Du mensblödningar?

- Ja, jag har regelbunden ”naturlig” mens (= blödning ungefär varje månad) eller blödningar p.g.a. östrogenbehandling
- Ja, jag har gles eller oregelbunden mens och senaste blödningen hade jag för mindre än 12 månader sedan.
- Nej, jag har inte haft någon blödning de senaste 12 månaderna och mensens slutade ”naturligt”.
- Nej, jag har inte haft någon blödning de senaste 12 månaderna eftersom jag opererat bort livmodern.
- Nej, jag har inte haft någon blödning de senaste 12 månaderna eftersom jag använder hormonspiral eller annat preventivmedel som tar bort mensens.

10. Använder Du eller har Du använt östrogen i samband med övergångsåldern?

*Med östrogen anses östrogenbehandling med tabletter, plåster eller gel men INTE lokalbehandling i slidan eller behandling med Ovesterintabletter. **OBS, ange endast ett alternativ!***

- Nej, jag har aldrig använt östrogen i samband med övergångsåldern.
- Ja, jag använder eller har använt östrogen **huvudsakligen** pga. vallningar och svettningar
- Ja, jag använder eller har använt östrogen **huvudsakligen** pga. nedstämdhet.
- Ja, jag använder eller har använt östrogen **huvudsakligen** pga. sömnproblem.
- Ja, jag använder eller har använt östrogen **huvudsakligen** för att förebygga benskörhet.
- Ja, jag använder eller har använt östrogen **huvudsakligen** pga. annan orsak.

11. Behandlas Du för närvarande med östrogen?

Med östrogen avses östrogenbehandling med tabletter, plåster eller gel men INTE lokalbehandling i slidan eller behandling med Ovesterintabletter.

Ja – gå vidare till fråga 18 men ange först namnet på Ditt Östrogenpreparat:

Nej

Om Du svarade NEJ på ovanstående fråga:

12. Har Du behandlats tidigare med östrogen?

Ja

Nej – gå vidare till fråga 18

Om Du svarade JA på ovanstående fråga:

13. När slutade Du med östrogen?

<12 månader sedan

12-24 månader sedan

>24 månader sedan

14. Under hur många år använde Du östrogen?

Under år.

15. Hade Du övergångsbesvär i form av svettningar/värmevallningar innan Du började med östrogen?

Ja

Nej – gå vidare till fråga 17

Om Du svarade JA på ovanstående fråga:

16. Återkom svettningar/värmevallningar när Du slutade med östrogen?

Ja, men mindre besvär än när jag började med östrogen.

Ja, lika mycket besvär som när jag började med östrogen

Ja, mer besvär än i när jag började med östrogen

Nej, besvären med svettningar/värmevallningar kom inte tillbaka.

17. Varför slutade Du med östrogenbehandling?

Ange ditt viktigaste skäl att sluta! Sätt kryss i EN ruta.

- Fick rådet av min läkare att sluta behandlingen
- Fick rådet av annan person än min läkare att sluta behandlingen
- Provade själv att sluta med östrogen och fick inte tillbaka besvär
- Blev orolig för risken att få biverkningar och slutade
- Fick biverkningar och slutade
- Fick inte tag i läkare att få nytt recept från och slutade därför med östrogen
- Annan orsak gjorde att jag slutade

OBS, denna fråga skall besvaras av alla!

18. Har Du haft biverkning som Du kopplat till att Du använt östrogen? OBS: Kryssa för de biverkningar du haft (Du kan kryssa i flera rutor)!

- Har aldrig använt östrogen.
- Inte haft biverkningar av östrogen.
- Önskade blödningar
- Bröstspänningar
- Viktökning
- Svullnadskänsla
- Påverkan på humöret
- Blodpropp
- Bröstcancer
- Kärlkramp eller hjärtinfarkt
- Annan biverkan, i så fall vad?

OBS, denna fråga skall besvaras av alla!

19. Har Du oroat dig för biverkningar som skulle kunna kopplas till östrogen? OBS: Kryssa för de biverkningar du oroat dig för även om du inte använder eller någonsin använt östrogen (OBS Du kan kryssa flera rutor)!

- Inte oroat mig för biverkningar av östrogen.
- Önskade blödningar
- Bröstspänningar
- Viktökning
- Svullnadskänsla
- Påverkan på humöret
- Blodpropp
- Bröstcancer
- Kärlkramp eller hjärtinfarkt
- Annan biverkan, i så fall vad?

20. Det finns också alternativ till traditionell hormonbehandling och lokalbehandling mot slemhinnebesvär. Ange nedan om Du har provat någon/några av dessa och om Du tyckte att de hade effekt på värmevallningar och svettningar.

	Aldrig provat	Provats men slutat	Använder idag	Effekt	Ej effekt
Naturläkemedel	<input type="checkbox"/>				
Vagitorier/kräm (Vagifem, Dienoestrol, Ovosterin, Estring)	<input type="checkbox"/>				
Ovosterintabletter	<input type="checkbox"/>				
Akupunktur	<input type="checkbox"/>				

Del 2- Kunskaper om övergångsåldern. Här ber vi Dig ange vad Du tycker eller tror.

21. Hur stor är sannolikheten för en kvinna i övergångsåldern att uppleva värmevallningar eller svettningar?

Sätt ett kryss i den ruta som bäst överensstämmer med din åsikt

Ingen drabbas	Mycket liten	Liten	Ganska liten	Måttlig	Ganska stor	Stor	Mycket stor	Alla drabbas
<input type="checkbox"/>								

22. Hur stor är sannolikheten för en kvinna i övergångsåldern att få blodpropp?

Sätt ett kryss i den ruta som bäst överensstämmer med din åsikt

Ingen drabbas	Mycket liten	Liten	Ganska liten	Måttlig	Ganska stor	Stor	Mycket stor	Alla drabbas
<input type="checkbox"/>								

23. Kvinnor i övergångsåldern upplever ofta värmevallningar och/eller svettningar

- Ja
- Nej
- Vet ej

24. Vad händer vanligen med kvinnors vikt i övergångsåldern?

- Vikten ökar
- Vikten minskar
- Vikten ändras inte
- Vet ej

25. Övergångsåldern beror på minskad östrogenproduktion.

- Ja
- Nej
- Vet ej

26. Östrogen – det viktigaste kvinnliga könshormonet, bildas framför allt i?

- Äggstockarna
- Livmodern
- Vet ej

27. Menstruationsblödningar slutar i övergångsåldern eftersom?

- Äggstockarna slutat att fungera
- Livmodern åldras
- Vet ej

Del 3 – Kunskaper om östrogenbehandling i övergångsåldern

28. Östrogen har både positiva effekter och biverkningar.

Hur ser Du på östrogenbehandling hos en kvinna i övergångsåldern?

Sätt ett kryss i den ruta som bäst överensstämmer med din åsikt

I huvudsak nackdelar				Varken bra eller dåligt				I huvudsak fördelar
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				

29. Vid östrogenbehandling i övergångsåldern – hur stor är NYTTAN för kvinnor i allmänhet?

Sätt ett kryss i den ruta som bäst överensstämmer med din åsikt

Obefintlig nytta	Mycket liten	Liten	Ganska liten	Måttlig	Ganska stor	Stor	Mycket stor nytta
<input type="checkbox"/>							

30. Vid östrogenbehandling i övergångsåldern – hur stor är RISKEN för besvär (biverkningar)?

Sätt ett kryss i den ruta som bäst överensstämmer med din åsikt

Obefintlig risk	Mycket liten	Liten	Ganska liten	Måttlig	Ganska stor	Stor	Mycket stor risk
<input type="checkbox"/>							

31. Hur bedömer Du att risken är för en kvinna i övergångsåldern, som använder östrogenbehandling, att drabbas av bröstcancer jämfört med en kvinna utan östrogenbehandling?

- Ökad risk
- Oförändrad risk
- Minskad risk
- Vet ej

32. Hur bedömer Du att risken är för en kvinna i övergångsåldern, som använder östrogenbehandling, att drabbas av blodpropp jämfört med en kvinna utan östrogenbehandling?

- Ökad risk
- Oförändrad risk
- Minskad risk
- Vet ej

33. Hur bedömer Du att risken är för en kvinna i övergångsåldern, som använder östrogenbehandling, att drabbas av hjärtinfarkt jämfört med en kvinna utan östrogenbehandling?

- Ökad risk
- Oförändrad risk
- Minskad risk
- Vet ej

34. Hur bedömer Du att risken är för en kvinna i övergångsåldern, som använder östrogenbehandling, att drabbas av benskörhet jämfört med en kvinna utan östrogenbehandling?

- Ökad risk
- Oförändrad risk
- Minskad risk
- Vet ej

35. Om en kvinnas mensblödningar har upphört MEN återkommer vid behandling med östrogen i övergångsåldern – kan hon då bli gravid?

- Ja
- Nej
- Vet ej

36. Östrogenbehandling i övergångsåldern fungerar som ett preventivmedel- dvs. en kvinna med östrogenbehandling behöver inte oroa sig för att bli gravid även om hon aldrig slutat menstruera då hon började med östrogenbehandling?

- Ja
- Nej
- Vet ej

37. Gulkroppshormoner används tillsammans med östrogenbehandling i övergångsåldern för att förstärka östrogenets effekt på värmevallningar och svettningar.

- Ja
- Nej
- Vet ej

48. Har rapportering i massmedia kring östrogenbehandlingen det senaste året påverkat Din syn på östrogenbehandling i övergångsåldern?

Sätt ett kryss i den ruta som bäst beskriver hur din uppfattning förändrats.

- Ja, till det sämre
- Nej, inte alls påverkat mig
- Ja, till det bättre
- Ej sett någon rapportering i massmedia

49. Har rapportering i massmedia kring östrogenbehandling i övergångsåldern det senaste året gjort att Du

- valt att börja med östrogenbehandling.
- övervägt att börja med östrogenbehandling.
- ej påverkat mitt beslut om östrogenbehandling
- övervägt att sluta med östrogenbehandling
- slutat med östrogenbehandling

- Ej sett någon rapportering i massmedia

Det finns många olika tankar och åsikter om övergångsåldern.

50. Hur ställer Du Dig till följande påståenden?

	instämmer helt	instämmer delvis	varken eller	tar delvis avstånd	tar helt avstånd
Övergångsåldern är ett naturligt tillstånd.....	<input type="checkbox"/>				
I övergångsåldern har man brist på hormoner.....	<input type="checkbox"/>				
Övergångsåldern är ett tecken på att man börjar bli gammal	<input type="checkbox"/>				
Kvinnor med besvärliga symtom i övergångsåldern bör använda hormonbehandling.....	<input type="checkbox"/>				
Övergångsåldern innebär mer frihet för kvinnan	<input type="checkbox"/>				
Eftersom övergångsåldern innebär sjunkande östrogennivåer bör alla kvinnor använda hormonbehandling.....	<input type="checkbox"/>				
Manliga partners till kvinnor i övergångsåldern ser dem som mindre tilldragande.....	<input type="checkbox"/>				
Det är skönt att inte längre kunna bli gravid	<input type="checkbox"/>				
En kvinna känner sig mindre kvinnlig efter att menssen upphört.....	<input type="checkbox"/>				
Det är skönt att inte längre behöva tänka på preventivmedel	<input type="checkbox"/>				
När man använder hormonbehandling kan man få tillbaka sina blödningar.....	<input type="checkbox"/>				
Psykologiska besvär i övergångsåldern beror mer på livsförändringar (t ex barn flyttar hemifrån) än på hormonförändringar.....	<input type="checkbox"/>				
	instämmer helt	instämmer delvis	varken eller	tar delvis avstånd	tar helt avstånd

Tack för Din medverkan!

Skicka in formuläret i det bifogade svarskuvertet till avdelningen för Obstetrik & Gynekologi, Hälsouniversitetet, Universitetssjukhuset, 581 85 Linköping.