

**THE CLIMACTERIC:
BLOOD, SWEAT AND TEARS?**

POPULATION BASED STUDIES OF
WELL-BEING, ATTITUDES AND
HORMONE REPLACEMENT THERAPY
AMONG 1947 WOMEN AGED 45-60 YEARS

Illustration on cover: 'Mensen onderweg'
T. Kreuger

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FPMJ Groeneveld, 1994

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BLOOD, SWEAT AND TEARS?**

Population based studies of
well-being, attitudes and
hormone replacement therapy
among 1947 women aged 45-60 years

Het climacterium:
Bloed, zweet en tranen?;

populatie onderzoek naar
welbevinden, attitude en hormoon substitutie
therapie onder 1947 vrouwen
in de leeftijd 45-60 jaar

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All generalizations are dangerous, even this one.

Alexandre Dumas

Aan:

Mijn ouders

Joke

Leonie, Yvette en Josephine

Abbreviations

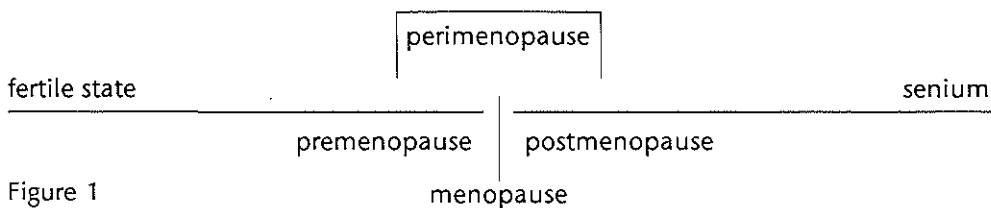
CI	Confidence interval
FSH	Follicle stimulating hormone
GP	General practitioner
HRT	Hormone replacement therapy
HST	Hormonale substitutietherapie
ISH	Inventory of Subjective health
LH	Luteinizing hormone
LMB	Last menstrual bleeding
SD	Standard deviation
SIP	Sickness impact profile

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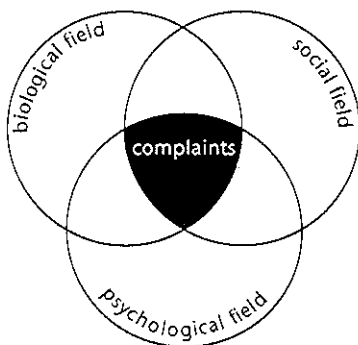
PREFACE

This thesis is about the climacteric years of women between the ages of 45 to 60 years. It is based on a cross-sectional population study and a longitudinal study in the same population. The climacteric is the period in which transition occurs from the fertile state into the infertile state. By hormonal change the menstrual cycles alter and finally cease. In figure 1 we see how this period is divided in a pre-, peri- and postmenopausal period, in which the menstruation is respectively regular, irregular and has ceased for more than 12 months.



When a woman presents symptoms and/or complaints in the climacteric period, it is not easy to distinguish whether these symptoms and/or complaints are caused by endocrine changes, chronological aging, social or psychological factors, or by interactions between these factors. This is illustrated in fig 2. Since the mere presence of symptoms does not reflect the experience of them, we have chosen for the concept of well-being. Well-being can be operationally defined as the sum score of a set of measurement scales, evaluating one's bodily state, one's feelings and aspects of daily life.

The power of well-being measures lies in the fact that different groups can be compared. We think there exists a relation between attitudes towards the climacteric and well-being in such a way that women with a more positive attitude towards menopause will experience the transition more positively. There are very few studies available which examined the use of hormone replacement therapy in relation to well-being, attitude towards menopause, menopausal status and personal variables.



The main objectives of this thesis are:

- I. To study the relationship between well-being and menopausal status.
- II. To establish the relationship between women's attitude towards menopause and well-being.
- III. To examine the aspects in which women differ who do or do not use hormone replacement therapy.

In *chapter 1* of this thesis a review of the literature is given starting from the question whether there exists a climacteric syndrome in terms of symptoms and complaints, exclusively and independently connected with the climacteric status. Another question we try to answer is if there is an association between serum hormone levels and a possible climacteric syndrome, analogous to for example diabetes mellitus, hypothyroidism and Addison's disease. Furthermore we ask ourselves the question, does estrogen replacement therapy bring about relief in symptoms and complaints of this feasible syndrome? The concept of well-being will be discussed in this chapter. Methodological issues get emphasis, because methodological imperfections may lead to wrong conclusions. Also the attitudes towards menopause will be discussed. Aside the medical view of a possible climacteric syndrome, it is interesting to know from the women themselves their attitudes and beliefs towards the menopause. Finally the use of hormone replacement treatment among women is discussed. *Chapter 2* describes the cross-sectional assessment of the relationship between menstrual age i.e. pre- peri- and postmenopausal women and well-being independent of differences in potential confounding variables in a population at large. *Chapter 3* reports the relationship between vasomotor symptoms, well-being and menopausal status. In *Chapter 4* is firstly described the attitude towards menopause of women aged between 45-60 years. Secondly the relationship between attitude towards menopause and well-being is assessed. Thirdly, the question about the relationship between medical attention and both well-being and attitude will be answered. *Chapter 5* concentrates on the opinion of women on the continuation or re-induction of artificial cycles with hormone replacement therapy. In *chapter 6* the cumulative incidence of HRT is described and the influences of women's well-being, attitude towards menopause, menopausal status and other variables on the initiation of HRT prescription in a population at large is studied during a 9 month follow-up period. *Chapter 7* deals with the duration of HRT and its determinants in a 2 1/4 year follow-up period. *Chapter 8* is a general discussion in which the implications of this thesis for the physician are given.

Each chapter can be read independently from the others; together they form a picture of the climacteric years seen from a scientific point of view and from the women themselves.

CHAPTER 1

GENERAL INTRODUCTION: A LITERATURE REVIEW

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1 IS THE CLIMACTERIC SYNDROME AN ENTITY ?

1.1 *Introduction*

During the premenopausal years the cyclical events gradually decrease until postmenopausal amenorrhea is established. The primary process takes place in the ovaries as a gradual decline and final cessation of the generative and endocrine functions, although a certain non-cyclical endocrine activity of the ovaries is maintained until advanced age.¹ Alexander found that the absence of ovarian steroids does not influence the hypothalamic secretion of gonadotropin releasing hormone (GnRH); the mean level of GnRH does not change with advancing age. The lack of response of postmenopausal ovaries to endogenous gonadotropin stimulation is a result of primary age-related changes in the ovaries, not in the hypothalamus.² As a result of the decrease in estrogens, the feed-back of ovarian estrogens on the hypothalamus diminishes, resulting in high FSH levels. A high serum FSH level is the only constant laboratory finding in the postmenopausal years. Apart from hormonal changes other effects of the aging do occur. No study so far has pointed out that in the climacteric years there is an acceleration of aging.³

1.2 *Symptomatology of the climacteric*

The climacteric years are associated with many symptoms. Consensus exists that severe (nocturnal) sweating and flushes (i.e. vasomotor symptoms) and menstrual disturbances are more frequent in the climacteric years than in other phases of life and therefore the symptoms are often qualified as typically climacteric. Dyspareunia caused by vaginal atrophia on the other hand, more frequently occurs in the postmenopause.^{4,5,6} These symptoms however are not pathognomonic of the climacteric. Hyperthyroidism, abuse of alcohol, carcinoid, nervousness, and drugs such as weight reducing drugs, vasodilatantia (nitrates) may mimic typical climacteric symptoms. Apart from these typical complaints, a variety of symptoms have been reported to be associated with the climacteric per se, i.e. to the change in steroid production of the ovaries. Incorrect attribution either by the doctor or the patient of symptoms in the climacteric to hormonal imbalance can cause unnecessary medicalization, a failure to recognize diagnoses and possible withholding of an appropriate treatment. In a very popular Dutch women's magazine 'Libelle', doctors recently wrote that in the years before and after the menopause, complaints like flushes, tachycardia, sleeping disturbances, painful joints, listlessness, depression, and numbness in the limbs often occur and can be treated by hormone therapy.⁷ Such unestablished remarks may be harmful, especially since women's magazines are proven to be the most important source of information on hormone replacement therapy.^{8,9} Furthermore there is 'The Gold-effect'. Professor T. Gold postulated that when hypothetical

ideas are formulated by authorities in a specific field, they become fixed views, which are very difficult to break through, especially when they are published in well-established medical magazines.¹⁰ Wilson with his book 'Feminine Forever' was harshly criticized for his disregard of the scientific procedure in his advocacy of HRT; yet there is no denying his impact. His clarion calls stirred millions of climacteric women.^{11,12} In the Netherlands the population of women aged between 45-60 years will increase to about 1,2 million women in the year 2000. Thus, incorrect attribution can augment to a notable extent.¹³ The true relationship between the climacteric and symptoms is a complex matter of determining the likelihood that alternative explanations such as chance, bias, or confounding could account for the findings.

Aside from biological changes there are many other phenomena occurring in this age period, which may be causally related to these symptoms or their intensity.¹⁴ In addition, inappropriate design strategies can distort the relationship between the climacteric and certain symptoms.

The most important issues, which influence the evaluating of the cause and the pattern of symptoms and complaints will be discussed below.

A. life events

Life events such as diseases and death of family members, loss of job, the maturation of children and their departure from home, often co-occur in the climacteric period. Psychological symptoms were found to be directly and linearly related to stress arising from miscellaneous sources. Somatic symptoms were elevated only if such stress was accompanied by stress arising from exits. The results suggest that both additive and multiplicative relationships between life events and distress exist.¹⁵ Cook found that 24% of the variance in psychological symptoms in the climacteric could be explained by independent life events, while the 27% of variance in somatic symptoms could be explained by the same variable. Furthermore, it is argued that social relationships may modify detrimental effects of life events in a positive way.¹⁶ Some studies found that women whose children left home were generally more satisfied than women whose children remained. It looks as though the empty nest period is not a stressful one.^{17,18}

B. Sociodemographic factors

Factors such as education, marital status, work outside the home are related to symptoms. Krause found that work outside home can reduce negative effects of several types of marital stress, but not stress arising from the childcare role.¹⁹ McKinlay and Hunter found single women less likely to be depressed, than married women, while those who were widowed or divorced were most likely to be depressed.^{20,21} Hunter found that unemployment was a predictor of somatic symptoms.²²

C. Personality

The premorbid personality and coping behaviour have been reported to determine the experience of symptoms. Veeninga found that women visiting a menopause clinic compared to controls, attending a general practitioner for routine screening i.e. cervical smear did not differ in the total number of life events and exits. The women visiting menopause clinic experienced these life events more seriously.²³ Holte found that women who reported that their mothers had perceived psychological complaints during menopause, expressed more vague somatic complaints themselves during menopause. Coping behaviour learnt from mother may play an important role.²⁴ This indicates that a higher susceptibility to stressful life events rather than the occurrence of specific life events plays an important role in the experience of symptoms which are often attributed to the menopause.

While not all studies, however, fully agree with the extent to which psychosocial variables influence the occurrence of symptoms. Yet, it is beyond dispute they do have an impact.

D. Cultural factors

Fourthly, cultural factors may determine the significance attached to concepts such as youth, menstruation, fertility, sexuality, menopause and aging. Muslim women for example regard menopause sometimes as a benefit since they are not allowed to perform religious rituals during their menstrual periods.²⁵ Margaret Lock found that there is no particular word for hot flush in Japanese. She suggested that this lack of perceived importance is due to the fact that menopause does not have any special social or ritual status in Japan. In the majority of Japanese women, menopause was seen more as an aging process than an important event.²⁶ Of course language problems, the way some cultures express emotional changes in different ways, as well as bias introduced by the investigators may influence cross-cultural comparisons.

E. Methodological strategies

Other difficulties in establishing the association between symptoms and hormonal changes during normal menopausal development are methodological problems in detecting the possible association. Every stage of an investigation is susceptible to systemic errors. These are potentially serious, since the bias they cause may lead to invalid conclusions. Many earlier studies about the climacteric have had several methodological shortcomings²⁷:

- a) The recruitment of women from visitors to menopausal clinics. This may lead to selection bias and reduces the generalizability of the results.^{28,29,30,31}

- b) Much attention has been paid in the questionnaire to the menopause (information bias: women could select from their experiences only those symptoms which they believe to be related to menopause).^{28,32}
- c) Retrospective studies which may lead to faulty recall bias.³⁰
- d) The menopausal status was inappropriately categorized, leading to either an underestimation or overestimation of the association.^{28,29}
- e) Confounding variables were not taken into account.^{28,29,30,31,32}

Confounding bias occurs whenever there are important differences between the groups being compared, which are also related to the variable of interest.³³ For example a lower level of education is associated with a lower level of well-being. The average postmenopausal woman (an older woman) is less well-educated than the average premenopausal woman (a younger woman). If there is no adjustment for difference in education, the fact that postmenopausal women experience a lower level of well-being than premenopausal women could be wrongly attributed to the climacteric.

F. Statistical analysis

The advancement of epidemiology corresponds with the fact that thinking about the causes of diseases from monocausal model, inherent to bacteriology, began slowly to make place for the multicausal model. One of the major essentials in family practice nowadays is to make an "integrated diagnosis" i.e. to record pathophysiological, social and personal factors of a particular patient at a definite moment. Till about 1975 only frequencies of symptoms were measured. Greene used factor analysis for the first time to get insight in the relationships between groups of symptoms and the climacteric.²⁹ Later on sophisticated statistical analysis together with advanced computer programmes came available. As a consequence, it is possible to investigate the joint influence of variables, the frequency of phenomena as a function of determinants, among large populations.

Thus till about 1977 a climacteric syndrome was described on the basis of numerical scores and not always an adequate methodology was applied. Blatt expressed the climacteric syndrome in 13 symptoms, Jaszmann only in 9, Neugarten no less than 41 and Greene summarized 21 symptoms. Most of the information supplied to the general population about the climacteric has been based purely on symptoms and clinical experience.^{28,29,32,34}

1.3 Well-being

By symptoms we mostly mean a sign we can objectively determine, for example coughing, sweating and vomiting. Complaints are the subjective experience of a patient, which are for the doctor hardly to objectify like headache and tiredness. On the other

hand not every objective 'diagnosed' symptom will be experienced in the same way by patients. Provided that there are symptoms caused by the hormonal changes in the climacteric, it is very difficult to measure the impact on women's health. Flushes can be bothersome, but to be free from periods may be a relief.

Holte found that the climacteric transition is also accompanied by relief; 40 to 51% reported less headaches and 46 to 48% had less breast tenderness after menopause.³⁵ These changes were mainly due to the relief from premenstrual and menstrual complaints. Although a significant increase was found in vasomotor symptoms, vaginal dryness, palpitations and social dysfunction, it was pointed out that 16 to 24% had fewer vasomotor complaints, 16 to 20% had less dryness of the vagina and 22 to 24% had less social dysfunction after menopause. Holte concluded that: the widely accepted perception of menopause as an event followed by uniformly negative change in health complaints is erroneous and that reality is far more complicated and involves large individual variation.

Describing symptoms is a narrow spectered view on patients and from sociological sciences the concept of well-being has entered medical practice. Well-being can be defined as a multifactorial construct. The relevant well-being dimensions include^{36,37,38}:

- a) subjective experience, self-assessed health, i.e. *illness*. The way people perceive their complaints may differ considerably from the way the complaint should be viewed objectively.
- b) functional aspects in daily life such as social duties and intellectual functioning, i.e. *the sickness*
- c) symptomatic aspects, the effects of diseases for instance the overwhelming ache with a heart attack, dyspnoea in case of asthmatic bronchitis i.e. *the disease*.

Numerous earlier studies used psychometrically undocumented measures, making comparisons between different populations and/or studies difficult. In the eighties many-sided descriptions of the impact of postmenopausal complaints extending beyond that of pure symptomatic relief were developed. These measurement instruments used standard questionnaires with well documented reliability and validity. However they often got different names such as well-being, quality of life and health status instruments, which are all synonyms, but are not interchangeable.³⁹ It should be noted that for the validity there is a lack of generally acceptable criteria, or a 'gold standard' for such constructs as well-being.⁴⁰

1.4 Recent cross-sectional and longitudinal studies

Studies of a representative sample of apparently healthy women experiencing normal aging are required to offset the biased portrait of the climacteric which was derived from studies in highly selective clinical populations. Studies of large unselected female populations using standardized methods of case detection and measurements of well-

being were carried out in several countries such as USA, Canada, Norway, England, Japan and the Netherlands. In table 1 and 2 characteristics are shown of the most important recent cross-sectional and longitudinal studies.

McKinlay included five measures of well-being, self-assessed health, measurement of chronic disease, daily activity, a sum score of common symptoms (such as persistent cough, diarrhoea, etc) and a list of symptoms of non-physical origin.⁴¹ In this study the utilization of formal and informal health was measured. The vast majority of peri- and postmenopausal women in this cross-sectional study did not report more symptoms or poorer health status and did not use more medical services than premenopausal women. The 'typical' menopausal woman is neither sick nor a high user of medical care. In a longitudinal study by the same author similar results were found, although insomnia was found to be associated with vasomotor symptoms.⁴² The symptom reporting however, appears to be transitory, with reported rates showing an increase in perimenopause and a compensatory decrease in the postmenopause. In the Manitoba cross-sectional as well as in the longitudinal study no significant increase in emotional symptoms in women throughout the different menopausal status was found.^{27,43} In order to avoid emphasis on menopausal symptoms Hunter studied women in the climacteric period naming the questionnaire used 'The Women's Health Questionnaire'.²¹ Thirty six symptoms were rated, a factor analysis was carried out resulting in the identification of the following groups of symptoms: somatic symptoms, depressed mood, cognitive difficulties, anxiety and fears, sexual functioning, vasomotor symptoms, sleep problems, menstrual symptoms. No significant change in sexual interest, sexual satisfaction, somatic symptoms or anxiety during menopause was found. However, the sum score on the symptom group 'sleep problems' and 'depressed mood' was higher in peri- and postmenopausal women compared to premenopausal women, but was of modest proportion. In the cross-sectional part in Hunter's study, menopausal status and socioeconomic status accounted for only 4% of the variation in the occurrence of depressed mood. In the longitudinal part of the study premenopausal depression was the strongest predictor of depressed mood during the menopause, accounting for 34% of the variance.⁴⁴ No association was found between vasomotor symptoms and concurrent mood. Holte concluded from a cross-sectional study that menopausal development played only a modest role, if any, in explaining variance of many measures of well-being such as vague somatic complaints, nervous complaints, mood and urogenital complaints.⁴⁵ In Holte's prospective study only a significant increase in social dysfunction after menopause was detected.³⁵ This may be caused by vasomotor symptoms as was shown by the regression analysis. A remarkably substantial number of women reported an improvement in well-being following menopause. Lock, using a 57 item symptom checklist, found that Japanese women who had stopped menstruating did not report any more emotional symptoms than women who were still menstruating.²⁶

Matthews investigated 541 initially premenopausal healthy women.⁴⁶ After three

years of follow-up, 69 women had ceased cycling for 12 months. A battery of sum score measures were used, evaluating for example anxiety, anger, self-consciousness, perceived stress, depression, job dissatisfaction and Neugarten's symptomlist. Comparison among groups at the baseline and follow-up examination showed an increase in hot flushes during menopause. Further, natural menopause led to few changes in psychological characteristics.

In a Danish eleven year prospective study it was not possible to demonstrate a significant correlation between menopausal status and sexual desire.⁴⁷ In this study the only significant predictor of decreased sexual desire at the age of 51 was the 40-year old women's anticipation of decreased sexuality as a consequence of menopause. This means for women that their negative anticipation towards their own sexuality in this period of life turned into a self-fulfilling prophecy.

Oldenhave in a cross-sectional study found no clear relationship between menopausal status and well-being.⁴⁸ Well-being was measured by a list of 21 atypical complaints, which correlated with a well-being measure, 'The General Health Questionnaire'. However, in the presence of vasomotor symptoms a more negative impact on well-being was apparent; a relationship between the severity of vasomotor symptoms and the severity of atypical complaints was established. This could support the 'domino-hypothesis' which regards certain psychological complaints as secondary manifestations of disabling vasomotor symptoms (hot flushes, sweating) and not causally related with the hormonal changes associated with menopause. It should be stressed, however, that in a cross-sectional study one can only study the association between vasomotor symptoms and atypical complaints, whereas a causal relation is difficult to discern in the absence of a longitudinal design. For example the relationship between night sweats and sleepingdisturbances may be explained in two ways. On one hand the night sweats can wake up the women in the night. On the other hand sleepingproblems, lying awake at night may magnify a woman's perception of night sweats. Moreover, potential confounding variables such as education and marital status were not taken into account in this study.

In the longitudinal study of Hunter there was a tendency for women who were depressed in the premenopause to develop vasomotor symptoms in the peri-and postmenopause. Ballinger found that women attending menopause clinics did suffer from significantly more life stress, symptoms and depression than a matched group of women who did not come to the clinic.⁴⁹ The clinic patients perceived the same events more distressing compared to the non-clinic patients. Moreover significantly more clinic patients had suffered from depression prior to the climacteric. There was no difference in the occurrence of hot flushes between these two groups (70-80%). However hospital patients reported hot flushes of significantly greater severity. In short, the relationship between flushes and other symptoms can be confounded by underlying factors such as depressed mood and life stress.

Table 1. Overview of recent crosssectional studies about the relationship between the climacteric and symptoms/well-being

Study	Recruitment (response rate)	Age of women approached	Variables included in the analysis apart from age and menopausal status	Measurement instruments	Analysis	Major outcomes
McKinlay ⁴¹ Massachusetts 1981/1982	N=8,050 (77%) Random sample	45-50	education number of friends way of cohabitation	health status: - self assessed - receiving treatment - daily activities - symptom list utilization of health	discriminant analysis	significant association between menopausal status and vasomotor symptoms, vaginal dryness and menstrual disturbances no association between menopausal status and symptom reporting, power health or increased use of medical services
Holte ^{24,45} Norway 1981	N=2,349 (80%) Random sample	45-55	medical condition education and work gender identification social network menopausal information/expectation mother's menopausal experience marriage, family, care	24-item symptom list	- factor analysis - analysis of variance - multiple regression	significant association between menopausal status and vasomotor symptoms, vaginal dryness and menstrual disturbances modest association between menopausal status and other symptoms
Hunter ²¹ England 1982-1984	N=1,090 (78%) Volunteers attending ovarian screening programme	45-65	marital status employment socio-economic status	Women's Health Questionnaire (36-item symptom list)	- factor analysis - analysis of variance - multiple regression	significant association between menopausal status and vasomotor symptoms and vaginal dryness significant association between menopausal status and sleep disturbances and depressed mood
Kaufert ⁴³ Manitoba	N=4,150 (67%) Random sample	40-59	education way of cohabitation	symptom list Bradburn index of well-being CES depression scale	- factor analysis	significant association between menopausal status and vasomotor symptoms and vaginal dryness no association between menopausal status and depression

Table 1. (continued)

Study	Recruitment (response rate)	Age of women approached	Variables included in the analysis apart from age and menopausal status	Measurement instruments	Analysis	Major outcomes
Lock ⁴⁶ Japan 1983/1984	N=1,738 (80%) Random sample	45-55	none	57-item symptom list	- factor analysis - one-way analysis of variance	significant association between menopausal status and vasomotor symptoms, prevalence of symptoms is low, night sweats do not load on the same factor as hot flushes
Oldenhav ^{e48} Netherlands 1987	N=10,598 (71%) Population	39-60	none	21-item symptom list	- analysis of variance - multiple regression	association with vasomotor symptoms and vaginal dryness and menopausal status no association between atypical complaints and menopausal status association between severity of vasomotor and the severity of atypical complaints

Table 2. Overview of recent longitudinal studies about the relationship between the climacteric and symptoms/well-being.

Study	Recruitment	Age of women approached	Follow up period	Variables included in the analysis apart from age and menopausal status	Measurement instruments	Analysis	Major outcomes
McKinlay ⁴² Massachusetts 1982	N=2,570 premenopausal continuation of cross-sectional study	45-55	5 year	smoking parity educational level body mass index	see cross-sectional study	- regression analysis	- significant increase of vasomotor symptoms and insomnia. - sleep disturbance associated with vasomotor symptoms
Holte ³⁵ Norway 1982	N=200 randomly selected premenopausal continuation of cross-sectional study	45-55	5 year	see cross-sectional study	24-item symptom list Personality test Psychosocial defence test Sex-role identification Self-esteem	- regression analysis - analysis of variance - summary measurements procedure	- significant increase in vasomotor symptoms, vaginal dryness, heart palpitations and social dysfunctioning following the menopause. - further analysis indicated that vasomotor symptoms caused the increase in social dysfunction
Kaufert ²⁷ Manitoba 1982	N=477 premenopausal continuation of cross-sectional study	40-59	3 year	marital status education level employment status	CES-D	- factor analysis	- only association between meno- pausal status and vasomotor symptoms
Hunter ⁴⁴ England 1983	N=200 premenopausal continuation of cross-sectional study	>47	3 year	marital status social class employment status	WHQ=36-item symptom list GHQ (General Health Question- naire); mood disturb- ance	- factor analysis - multiple regression	- vasomotor symptoms, sleepproblem and to a lesser extent depressed mood increase significantly during peri- and postmenopause. peri- and postmenopausal women do not more frequently visiting their doc- tors compared to premenopausal women. - no changes in sexual interest, sexual satisfaction, somatic symp- toms or anxiety.

Table 2. (continued)

Study	Recruitment	Age of women approached	Follow up period	Variables included in the analysis apart from age and menopausal status	Measurement instruments	Analysis	Major outcomes
Matthews ⁴⁶ Pennsylvania 1983	N=541 premenopausal sample of driving license list	42-50	5 year	marital status educational level current religion	Spielberger trait anxiety and anger SCI private Self- Consciousness SCI public Self-con- sciousness Cohen perceived stress Beck depression Inventory Paid Job dissatis- faction Number of symptoms	- analysis of variance - analysis of co- variance	- increase of hot flushes - natural menopause led to few changes in psychological charac- teristics, only a decline in introspectiveness.
Koster ⁴⁷ Denmark 1976	N=621	40	11 year	marital status social status	sexual items	- multiple logis- tic regression	- the 51-year-old women's experi- ence of frequency or change in sexual desire was not related to menopausal status.

1.5 Conclusions

Most large scale cross-sectional and longitudinal studies found that vasomotor symptoms and vaginal dryness are significantly related to menopausal status. The two vasomotor symptoms, hot flushes and night sweats, which are strongly associated with menopausal status in Western research literature, had a relative low incidence in Japanese women. In general these studies showed that the menopausal transition does not have an important impact on well-being, including sexuality. Some studies did report a relation between complaints (sleeping disturbances, social dysfunction) and the presence of vasomotor symptoms. Most complaints in the climacteric years were not associated with menopausal development, but could be explained by a mixture of other biological, psychological and social variables. Given the available recent evidence, apart from typical complaints, there are too few indications to speak of a well-defined climacteric syndrome.

2 THE ASSOCIATION BETWEEN HORMONE CHANGES AND SYMPTOM REPORTING

Many hormones, their metabolites and gonadotropins like FSH, LH, estrogen, epinefrine, norepinephrine, prolactin, 5-hydroxy-indole acetic acid (5-HIAA), androstendion have been studied in their relationship to vasomotor symptoms and other complaints. None of these have any value in predicting either the duration or the severity of symptoms and complaints. Although the drop in estrogen production at menopause is characteristic, levels of all hormones are similar in flushers and non-flushers.^{50,51}

3 EFFECTS OF ESTROGEN REPLACEMENT THERAPY DURING THE CLIMACTERIC

The question whether estrogen replacement therapy brings about relief in symptoms and complaints and does improve well-being, should be resolved by a randomized double blind placebo controlled trial, especially since vasomotor symptoms have been shown to be highly responsive to placebo. A randomized double blind placebo controlled trial has several methodological limitations.

- (i) In the seventies it became clear that the incidence of endometrium cancer is higher in postmenopausal women when estrogens are used.^{52,53} There is sufficient evidence that when progestogen is added to estrogen the risk of endometrium cancer decreases.^{54,55} Nowadays, a combination of estrogen with periodic progestogens is considered a safe hormonal therapy. Such a combination induces withdrawal bleedings in most women.⁵⁶ For women with irregular menses, such a hormonal schedule induces regular bleedings and for women who had stopped menstruating the periods start again. For these women it seems impossible to ensure a blind

comparison.

- (ii) Estrogens can alleviate vasomotor symptoms substantially, but often give tension in the mammae.^{57,58} This further reduces the possibility of blinding; the women may become aware of the effect of the hormone.
- (iii) By adding progestogens to estrogen treatment, the separate attribution of estrogens to the improvement of symptoms and complaints can not be measured.
- (iv) Another problem is the difficulty of defining and measuring the outcome measures which assess the efficacy of estrogen replacement therapy. In case of osteoporosis and heart disease the endpoints are quite pathophysiologically defined, however the problem then is the long follow-up period for 10-20 years. Vasomotor symptoms and vaginal dryness may be relatively easy to measure. However, to measure depression and the level of well-being it is necessary to use sensitive, valid and reliable psychometric tests.

It is disappointing to find, that quasi-experimental designs have dominated this research area. The most common study design applied is the single-group pre- versus posttest design. Wiklund used several measures of well-being and mood, which are psychometrically correct, such as the Psychological General Well-Being index (PGWB), the Sleep dysfunction Scale and the Women's Health Questionnaire.³⁸ From the 136 women in his 9-month follow-up study to assess the efficacy of HRT 110 completed the study. An open study design without a placebo control group is always questionable as Wiklund recognized himself, but he argued that the placebo effect disappears within a few months, so that if the follow up period is long enough this may compensate for the lack of a placebo controlled study. He simply passed the fact that without randomization, including a control group (irrespective of a placebo) there is no adjusting for the natural course of complaints. The severity of flushes varies enormously from time to time in the same woman. The author concludes cautiously that women using transdermal estrogen/progestogen therapy experienced relief from vasomotor symptoms and also enjoyed secondary beneficial effects on sleep disturbances and mood.

It appeared to be almost impossible to design a study to assess whether well-being is improved by estrogen therapy by means of a randomized double-blind placebo controlled study. Some investigators found a solution to the problem of blinding by performing studies among hysterectomized women. An additional profit is that only estrogen can be used, because there is no more intact uterus. However hysterectomized women are a selected group.

Dennerstein (N=49) performed a double blind cross-over study in hysterectomized bilateral oophorectomized women.⁵⁹ Ethnyloestradiol had a beneficial effect on mood as measured by the Hamilton depression rating scale scores and interview ratings of general well-being, fatigue, anxiety, irritability and insomnia.

Paterson (N=23) also studied hysterectomized women and found a significant reduction in hot flushes and night sweats. There was a slight improvement in insomnia

and an increase in energy.⁶⁰ No alteration in depression, anxiety, memory and even vaginal dryness was established.

Ditkoff (N=36) randomly assigned asymptomatic hysterectomized women to a double blind treatment regimen.⁶¹ He found a significant improvement in depression scores on the Beck Depression Inventory, although there was no dose-response effect.

Another way to maintain blinding is to use only estrogen therapy, which alone will mostly give no withdrawal bleedings. Only two studies are reported.

Campbell (N=64) found estrogen to be more effective than placebo in alleviating symptoms such as hot flushes, vaginal dryness, poor memory, anxiety.⁶² This effect was similar in women without flushes, indicating a direct positive effect of estrogen on mental status. Wiklund (N=223) blindly and randomly allocated to either estradiol or placebo.⁶⁴ The duration of the study was only 12 weeks and no progestogen was given. In this study several quality of life measurement scales were applied: Nottingham Health Profile, Psychological General Well-Being, Women's Health Questionnaire, McCoy sex scale and self-rated symptoms. Quality of life improved after both therapies, but was more pronounced for estradiol. However, it looks as though estradiol therapy is statistically significantly superior to placebo, no comment is given to the clinical relevance. Nevertheless, some studies pointed out that the beneficial effects of estrogens on mood and sexual functioning were reduced by progestogens.^{59,60,64}

Walling made an extensive review of studies in which the impact of hormonal replacement therapy on sexual behaviour and functioning in postmenopausal women was examined.⁶⁵ With estrogen, gynaecologic improvement i.e. reduction in atrophic vaginitis occurs. Specific effects of sexual behaviour (e.g., increase in coital frequency) are less often found, but there is a consistent trend of global improvements in sexual desire. It is difficult to know whether the sexual improvements are the result of the reduction of atrophic vaginitis or the direct effects on sexuality.

3.1 Conclusion

The best scientifically accepted design to establish the effect of estrogen therapy in relieving symptoms, complaints and improving well-being is a randomized double-blind placebo controlled trial. The major problem in the design is blinding, caused by the presence of withdrawal bleedings as a result of the combination of estrogens with progestogens. To maintain blinding, some studies were performed in hysterectomized women, of which the generalizability of the results are of course questionable. Other studies used estrogen only. Furthermore, different modifications in therapies have been used: different hormones, dosages and modes of administration.

In conclusion from the few randomized double blind control trials it was apparent that estrogen therapy (i) has a significantly and substantially effect in relieving vasomotor symptoms and vaginal dryness (ii) has a modest beneficial effect on mood, sleep

problems, sexual functioning and well-being; however, these may be reduced by adding progestogens (iii) has an outspoken placebo impact on these symptoms, complaints and well-being.

4 THE ATTITUDES OF WOMEN TOWARDS MENOPAUSE

4.1 *Introduction*

By attitudes towards menopause we mean the beliefs, feelings, and action tendencies of a group of women towards menopause. The opinion of the women themselves is of importance to the doctor in order to see the women's symptoms and complaints in the perspective of understanding. Attributions made about symptoms have important health consequences⁶⁶:

- a) When women tend to attribute symptoms to the menopause, which are not related to the menopause, this may lead to an unjustified emphasis on the climacteric origin of these complaints. As a consequence, another possible cause of the complaints may remain unrecognized leading to patient's or doctor's delay and to unsuitable treatment or unnecessary prescription of medicines.
- b) In contrast, women may refuse beneficial hormone replacement therapy to reduce hot flushes, vaginal dryness, menstrual disturbances and for the prevention of osteoporosis and cardiovascular diseases as a repercussion of their attitudes towards menopause.

In the Netherlands, the general practitioner is the first physician a 'climacteric' women will turn to for help. Van de Kar found that apart from the efficacy of the general practitioner's care and the perceived severity of complaints, the efficacy of self care, knowledge about the complaint and the need for information are important determinants in consulting the general practitioner.⁶⁷

Anderson found that 79 of the 100 women reported physical symptoms and 63 reported emotional symptoms as the primary reason for seeking medical attention at the Academic Menopause Clinic.⁶⁸ This selected group of women knew little about the menopause, but they had gained helpful new information about the menopause. To successfully break through the self-labelling processes, it is necessary to gain insight into attitudes of the women towards the menopause in populations at large. In the study of Frick-Bruder 60% of the women expressed the need for more information about the climacteric.⁶⁹ Surveys show a discrepancy between the doctor's perception of the attention and care he gives to his patients and the women's perception of the care he provides. Feeling of ignorance can increase both anxiety and symptoms.⁷⁰

Barlow found that 27% of the consultations related to menopause included advice and

discussion only, illustrating the role of doctors in informing and reassuring menopausal women.⁷¹ In general, anxiety reduction is also possible by giving clear information about the illness under discussion.⁷²

4.2 *Attitudes towards menopause in general*

Only a few studies assessed the women's attitude towards the climacteric concerning general statements.^{41,44,69,73,74,75} Neugarten found that the majority of women did not hold a negative attitude and that younger women had a more negative attitude than postmenopausal women.⁷³

Frick-Bruder studied 1127 women of which 908 had a positive attitude towards the menopause and 167 a negative attitude. The women older than 50 years had a more positive attitude compared to women under 50 years.⁶⁹

Leiblum administered a 10-item Menopause Attitude Questionnaire to a sample of 244 pre-, peri-, postmenopausal and hysterectomized women, recruited from a variety of settings.⁷⁴ The majority of women in this study, especially women with a lower educational level and older women, felt that the menopause should be viewed as a medical condition and treated as such. They did not subscribe to the notion however, that it was a particularly malevolent one. Although women in this study tend to agree that menopausal symptoms are brought about by changes in estrogen levels, they nevertheless prefer 'natural' treatments over estrogen replacement therapy for alleviation of menopausal complaints. This is probably caused by the general anxiety about the possible causal role of estrogen use in the development of endometrial- and breast cancer following publications in the seventies and late eighties respectively. From these studies it was apparent that women are united in their belief that their sexuality is undiminished subsequent to the menopause, this being even more strongly endorsed by postmenopausal women.

The studies mentioned above are based on small and usually non-representative samples of women. The study of Avis is an example of an excellent study on certain aspects of attitudes towards the menopause i.e. feelings about cessation of menses and statements about menopause (statements concerning HRT were not included).⁷⁵ The study was based on a large community sample (N=2,565). Further, a longitudinal analysis was performed taking into account some confounding variables including age, marital status, employment status, number of children. There was a classification of women into menopausal status according to the last menstrual bleeding excluding women who had undergone hysterectomy.²⁷ Another advantage of this study was the fact that the same statements concerning the menopause were used in two other studies, one in Japan and one in Canada, providing the opportunity to compare women's responses across cultures. Avis established that (i) The majority of women report relief or neutral feelings about the cessation of menses; (ii) The attitude of women who were

premenopausal at the beginning of the study changed towards more positive attitudes when they became post-menopausal; (iii) The variables that significantly discriminated between positive and negative feelings concerning the climacteric years were psychological symptoms, education, depression and physical symptoms. Negative attitudes towards menopause prior to experiencing menopause were related to higher symptom reporting during menopause. Also Holte found that nervous complaints are associated with negative expectations regarding 'the change'.²⁴ This supports the existence of a self-fulfilling prophecy as advocated by some authors. Avis, for example, stated that the so-called menopause syndrome may be more related to personal characteristics than to menopause per se.

4.3 *Attitudes towards HRT*

Apart from women's general attitudes towards menopause, it is interesting to know their desirability about starting hormone replacement. Women's own views on HRT have rarely been investigated.

The study of Ferguson and Sinclair estimated attitudes towards HRT in the USA and England respectively.^{76,77} Both studies used the same questions to measure attitude and showed:

- (i) Women taking HRT compared to women who have never taken HRT were far more likely to view menopause as a medical condition and were less likely to favour non-medical approaches.
- (ii) Women currently taking HRT are neutral to the statement 'sexual interest and comfort increase after menopause', while women who have never taken HRT are more often in agreement with this statement.
- (iii) Women on HRT more often agreed with the statement that one cannot control menopausal changes inside one's body.

Rothert and Robert found that women are mainly concerned about hot flushes and disruption of their daily life and this was for many women a more important consideration than morbidity and mortality of osteoporosis and cardiovascular diseases.^{9,78}

Hunskar pointed out that most women have already collected some information and have formed an opinion about the menopause before consulting their physician.⁸ Thus the role of the general practitioner consists of sensing the situation, discussing the subject, advising and if necessary correcting the views of the women. Hunskar further argued that women follow their doctor's recommendations, suggesting that simple communication could significantly alter the use of HRT. Many women were concerned about the risks of HRT, but their opinions on the actual risk profile did not correspond with present scientific knowledge of HRT. There was a strong association between a

negative attitude towards using hormones and belief in an increased risk of serious disease such as heart infarction, stroke, breast cancer and cancer in general.

4.4 Conclusions

Most women have a neutral to positive attitude towards menopause, evidently women who already experienced menopause are more positive than premenopausal women. Negative attitudes are clearly related to complaints. Women generally believe that sexuality is not influenced negatively by the menopause.

The women are divided regarding the issue of hormone replacement therapy. Only women who view menopause as a medical condition show a clear tendency to start the use of HRT.

An interesting but yet unresolved scientific question is how women acquire these different attitudes towards HRT.

5 HRT USE

5.1 Introduction

Figures about the prevalence and compliance with HRT will vary in time and differ in various countries. These figures give an impression of the doctor's agreement to prescribe HRT and to woman's willingness to start and comply with HRT.

5.2 Prevalence HRT

Relatively few women use hormone replacement therapy between the age of 40 to 70 years. Data about the prevalence of HRT use in some countries is shown in table 3. The prevalence in European countries is in Italy is 3%, UK 7%, France 13%, Germany 25% and in Denmark 16%. In South Australia the prevalence was 14% among women aged 40-65 years. In California current estrogen use was 32% among women aged 50-60 years. A clear discrepancy between the intention to prescribe HRT and the actual use

Table 3. Prevalence of estrogen replacement therapy

Country	Prevalence of estrogen use	Country	Prevalence of estrogen use
Italy	3%	Denmark	16%
United Kingdom	7%	South Australia	14%
France	13%	California	32%
Germany	25%		

of HRT has been reported in this study namely 75-95% of the gynaecologists would prescribe estrogen therapy to most of their patients.^{79,80,81,82,83}

5.3 *Physicians attitude towards HRT*

In the Netherlands Stouthamer studied the view of 195 GPs as to the climacteric.⁸⁴ Ninety-five percent of the GPs were of the opinion that women with climacteric complaints need some kind of medical help, 62% prescribed some kind of medication for climacteric complaints, 24% prescribed no treatment at all. Remarkably, 75% of all GPs were of the opinion that prescribing HRT for climacteric complaints is a form of medicalization. In case of preventive treatment 32% of the GPs said they would prescribe HRT for a period longer than 5 years.

In the UK Bryce studied the view of 1000 GPs, 310 returned completed questionnaires.⁸⁵ Less than 25% of the GPs were sympathetic to the idea of prophylactic HRT and only 7% routinely discussed this possibility with menopausal patients, while the majority felt that the duration of therapy should be limited to 2 years or less.

In Finland Hemminki studied the opinion of gynaecologists, internists, general practitioners and non-specialists on HRT prescription (n=500; response rate 74%).⁸⁶ Gynaecologist were far more favourable towards hormone therapy than were other physicians. One fourth of the physicians said HRT should be preventively given to all or to all those at risk from osteoporosis. Most agreed as to the benefits of HRT for the prevention of osteoporosis, but opinions as to other benefits and disadvantages varied. Furthermore, many physicians seemed to have difficulties in giving general opinions and preferred using individual judgement for each patient. In Norway, a questionnaire was mailed to a random sample of approximately 10% of the general practitioners in order to investigate attitudes to prescription of HRT. GPs indicated restrained attitude towards prescription of HRT.⁸⁷

5.4 *Determinants of HRT*

It was established in the USA that both gynaecologists and family physicians were influenced in their prescribing by cancer risk and by severity of vasomotor symptoms in their patients. The variation among physicians however was large.⁸⁸

A policy-capturing study of 283 perimenopausal women showed that the factor of frequent concern was relief from hot flushes.⁷⁸ Cauley found that the primary determinant of HRT was for women with surgical menopause.⁸⁹ Other determinants were higher levels of education, less obese women, more alcohol use and participation in sports and recreation compared to never users of HRT. Ringa found that surgical menopause and higher education were major determinants of HRT use.⁸⁰ Cigarette smoking was not associated with use of HRT, which is consistent with the American studies. In a study

among women in Massachusetts the only constant finding is that surgically menopausal women and women with symptoms are overrepresented among estrogen users.

5.5 *Compliance with HRT*

The compliance with HRT is deplorably poor. Utian cited data from a review of 200 American pharmacies in which 50% of those given new HRT prescription had stopped taking their medicine within one year; 49% of repeat prescriptions were never filled out, the average duration of HRT was nine months.⁹⁰ The occurrence of withdrawal bleeding, fear of cancer and side effects such as edema, bloating, premenstrual irritability, lower abdominal cramps, breast tenderness, all limit compliance with hormonal therapy.⁹¹ Apparently the decision for women to stay on HRT is complex, because even when there is no withdrawal bleeding as is the case with hysterectomized women compliance is also poor.⁹²

5.6 *Conclusions*

Hormone replacement therapy use rates especially in Europe are in general low and vary between countries from 3 to 13%. GPs in the various countries are cautious to prescribe HRT.

There is a wide gap between GPs own perceived prescribing practice and the actual prescribing practice. Less than 25% of the GPs in UK, Netherlands and Finland said hormones should be preventively given. Surgical menopause, educational level, former use of anticonceptiva, menopausal status and vasomotor complaints are determinants for HRT use. The compliance with HRT is low; most studies indicate that more than 50% of women take HRT no longer than one year.

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CHAPTER 2

THE CLIMACTERIC AND WELL-BEING

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INTRODUCTION

The climacteric years are associated with a variety of physiological and psychological symptoms that may influence the level of well-being of women.¹⁻⁸ However, because the climacteric is accompanied by other changes in life, it is important to assess the independent relationship between the climacteric and well-being.

Typical physiological symptoms related to the hormonal changes during the climacteric include hot flushes, night sweats and dyspareunia caused by vaginal atrophy. Many women report vasomotoric symptoms with the peak of complaints occurring in the first year after menopause.¹ However, these symptoms are not restricted to the climacteric period, but may also occur during other periods in life.

Many psychological symptoms have been reported to accompany this phase of life, e.g. nervousness, sleeping problems and irritability.^{9,10} The few published population-based studies suggest that the so-called 'climacteric symptoms' may be related more to personal characteristics than to menopause per se.^{11,3}

Further, several studies have shown that menopause is associated with a whole range of changes in sociodemographic variables, e.g. work outside the home and marital status.^{3,12} In addition, both the nature and frequency of symptoms are known to be influenced by cultural and/or racial factors.¹³ For example, hot flushes are less frequently reported among Japanese women than among western women.¹⁴

Although several studies have evaluated the occurrence of symptoms in the climacteric period, the interpretation of these results is hampered by a couple of reasons. First, most studies did not distinguish between symptoms believed to be related to the climacteric period and the feeling of general well-being. Nevertheless, this distinction is fundamental, as the presence of symptoms such as flushes may point at the climacteric, whereas the change in the level of the woman's well-being reflects the impact of the climacteric. Moreover the mere presence of symptoms is not indicative of a low level of well-being. Well-being can be defined as a multifactorial construct. The relevant well-being dimensions include: (a) subjective experiences i.e. self-assessed health (b) functioning aspects in daily life like social duties and intellectual functioning (c) symptomatic aspects i.e. the effects of disease.¹⁵ Second, only few studies adjusted their findings for variables which could distort the relationship between general well-being and menopausal status, i.e. confounding variables. When adjustments were made, they were mostly limited to age¹, social class and marital status.³

The objective of our study was to assess the relationship between menstrual age, i.e. pre-, peri- and postmenopausal and general well-being independent of differences in potential confounding variables. Apart from age, education and way of cohabitation we also adjusted for Body Mass Index (kg/m²), smoking behaviour, work outside the home, parity, difference in age with the partner and partner's employment.

The assessment of the independent influence of menopause on well-being rather than

on the well-known symptoms, may contribute to a better understanding of the climacteric.

METHODS

Recruitment

From the municipal authorities of Krimpen aan den IJssel, a commuter suburb of Rotterdam with approximately 28,000 inhabitants, names and addresses of all 2729 women aged between 45 and 60 years were obtained. In May 1990 they were sent a questionnaire and 1947 women responded (response 71.3%). A random sample (N=55) was taken of the non-respondents in order to evaluate the representativity of the respondent group. They were approached by telephone and 52 participated (response 95%).

The main principles of Dillman's Total Design Method were used to maximize response.¹⁶ In cases where the questionnaire was not returned within three weeks, a reminder was sent. To avoid emphasis on menopausal symptoms the questionnaire was named 'Health Questionnaire for Women' and questions about the menopause were placed in the second part.

The climacteric status of women was classified into six categories according to menstrual pattern characteristics and the number of months or years since the last menstrual bleeding (LMB) prior to the completion of the questionnaire (see Appendix II; question B.7.). Women having had a menstruation within twelve months prior to the survey (part a and part b of question B.7.) and a menstrual pattern which did not change (part c) formed one group: the premenopausal group. Women who had had a change in the menstrual cycles in the preceding year were categorized into two perimenopausal groups according to the number of months since the last LMB: three months or less (perimenopausal I) and four to twelve months (perimenopausal II). Women whose LMB had occurred over twelve months previous to the survey were categorized into three postmenopausal groups according to the number of years since the last LMB; 1-2½ years (postmenopausal I), 2½-4½ years (postmenopausal II) and 4½ or more years (postmenopausal III). As some women filled out the year of the LMB only and not the exact month, a classification was chosen which coincides with the calendar year. Women who had undergone hysterectomy and women who used estrogen therapy in the 6 months preceding answering the questionnaire, were excluded from the analyses (Figure 1).

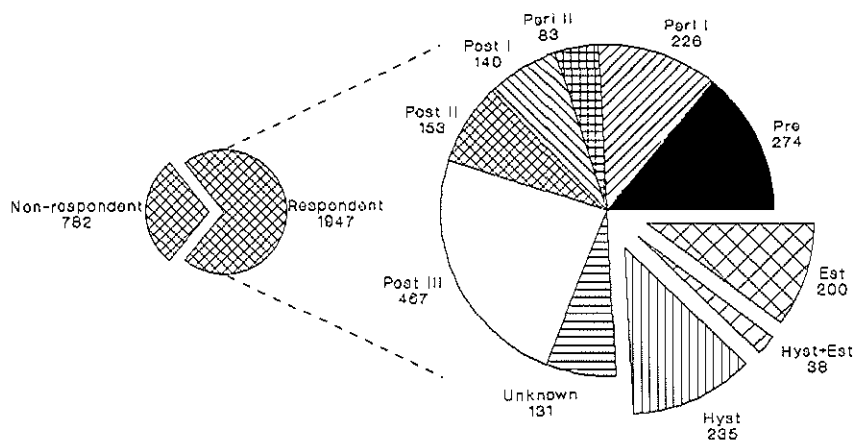


Figure 1. Selection of target population. Total register population $n = 2729$; response $N = 1947$ (71.3%). The segments placed apart are left out of consideration in the analyses.

Pre=Premenopausal; Peri=Perimenopausal; Post=Postmenopausal; Hyst=Hysterectomized; Est=Estrogen use. The study received approval from the Medical Ethical Committee of the Erasmus University Medical School and Academic Hospital Dijkzicht in Rotterdam.

Assessment of well-being

General well-being was measured by two validated inventories, namely the 'Inventory of Subjective Health' (ISH) and the 'Sickness Impact Profile' (SIP).

The ISH has proven to be a sensitive instrument to detect health problems. In recent years it has been used in several Dutch surveys to quantify subjective health status.^{17,18,19} In a large representative study in the Netherlands Cronbach's α equalled .87 and the ratio of the eigenvalues of the first and second principal component equalled $16.2/4.4 = 3.7$, both reflecting a strong unidimensional scale.²⁰ The ISH includes 49 items, concerning the experience in the past two weeks of complaints like pains in the chest, shaking hands, headache, sneezing and less appetite (see Appendix II; part A). On every item the respondent is asked whether she has experienced it during the last two weeks. All items must be answered with either 'yes' or 'no'. The sum score of all responses is computed, the maximum score being 49.

The SIP was developed in the United States as a behaviourally based measure of the impact of sickness.²¹ The Dutch validated version was used in this study.^{22,23} Both SIP overall scores and SIP category scores can discriminate between subsamples. To limit the time needed for filling out the questionnaire we chose three category scores which measure psycho-social impact on well-being: emotions, feelings and sensations (9 items), social interaction (18 items) and intellectual functioning (10 items). All items are rated a scaling factor. This scaling permits the calculation of three SIP percent category

scores. A percentage of 100 means maximal impairment on the corresponding category score.

The validated inventories formed the first part of the questionnaire. Furthermore, the women were asked to answer questions on social factors, smoking, body weight and length, menstrual pattern, medical consumption during the last two weeks, attitude towards menopause and knowledge of menopause-related problems.

Analysis

Variables that are related to both well-being and menopause can distort the relationship between well-being and menopause. Therefore, multivariate linear regression analysis which can adjust for these confounding variables, was used to compute the independent relationship between menopausal status and general well-being. Dummy variables for all nominal and ordinal variables were constructed to detect possible non linear effects.

Separate analyses were performed for the ISH and the three categories of the SIP. As a first step the relationship was computed adjusting for age only. As menopausal status inheres age, age was always adjusted for.

Further, variables that according to literature could be related to both well-being and menopausal status were selected. Body mass and smoking behaviour can influence menopausal status,²⁴⁻²⁶ and may be related to well-being as well. About the association between education, parity and work outside the home on one side and symptom reporting on the other, results are equivocal.^{27,28} Instead of marital status adjustment is made for the way of cohabitation as in the Netherlands a considerable number of people live together without being married. As the age-difference between the partners increases, women report more vague somatic complaints.¹² Finally, it is interesting to know whether the partner's employment status confounds the relationship between menopausal status and well-being. The measurement scales used for these variables are embodied in table 2.

Next, the relationship between these eight potential confounders and well-being was determined, while adjusting for age, by applying linear regression analysis. If a variable contributed on a $p < 0.10$ level to the explanation of one or more of the four measures of well-being it was selected as a potential confounder and included in the multivariate analyses.

Finally, to compute the independent relationship between menopause and the measures of well-being, again four separate linear regression analyses were carried out, with all selected confounders included in the regression equations.

RESULTS

The results of the comparison between respondents and non-respondents are shown in

table 1. No marked differences between respondents and non-respondents could be demonstrated.

After exclusion of all women with hysterectomy and/or estrogen therapy, 1343 women could be categorized according to menopausal status: 274 premenopausal women, 309 perimenopausal women (226 peri I + 83 peri II) and 760 postmenopausal (140 post I + 153 post II + 467 post III) women. Some characteristics of the participants are given in table 2. The median menopausal age (the age at which 50% of the women have stopped menstruating) was 50.5 years. In comparable studies in the Netherlands 51.2 years and 51.5 years were reported.^{1,29}

Table 1. Comparison of respondents (n=1947) and non-respondents (n=52)

	Respondent		Non-respondent		p-value
	n*		n		
Menopausal status	1343		38		.75
pre	274	20%	6	16%	
peri I + peri II	309	23%	10	26%	
post I + post II + post III	760	57%	22	58%	
Hysterectomy	1930		48		.75
yes	273	14%	6	13%	
no	1657	86%	42	88%	
Estrogen therapy	1946		48		.41
yes	238	12%	4	8%	
no	1708	88%	44	92%	
Mean age (years)	1893	52.4	49	53.2	.21
Level of education	1906		50		.23
lower	894	47%	20	40%	
middle	694	36%	24	48%	
higher	318	17%	6	12%	
Work outside the home	1791		49		.16
yes	630	35%	22	45%	
no	1161	65%	27	55%	
Visit to general practitioner last year	1879		50		.14
yes	1198	64%	37	74%	
no	681	36%	13	26%	

* The n differs as the number of women that give a valid answer differs per question.

Table 2. Some characteristics of the participating women (aged 45-60 years). Total number of women of which the menopausal status is known is 1343.

	n ^a	Total	Pre	Peri I	Peri II	Post I	Post II	Post III
Mean age (years)	1314	52.6	48.0	49.4	51.3	53.1	54.6	56.4
Mean Body Mass Index (kg/m ²)	1270	24.7	24.5	24.3	24.1	24.7	24.6	25.1
Severe sweating	1280	26%	16%	22%	43%	35%	33%	25%
Vaginal dryness	1274	21%	4%	14%	18%	30%	31%	30%
Smoking (cigarettes/day)	1303							
Never smoked		50%	46%	49%	52%	54%	56%	49%
Ever smoked		27%	35%	27%	31%	20%	22%	25%
≤ 5		5%	5%	7%	4%	5%	4%	6%
6-15		10%	7%	9%	5%	13%	10%	11%
> 16		8%	7%	9%	9%	5%	8%	9%
Education	1321							
Low		16%	9%	10%	13%	23%	22%	21%
Middle		66%	67%	68%	63%	62%	65%	66%
High		18%	24%	22%	23%	15%	14%	13%
Work outside the home	1241							
No work		65%	45%	52%	65%	71%	74%	78%
Working < 20 hrs		23%	33%	29%	21%	22%	21%	14%
Working ≥ 20 hrs		13%	22%	19%	15%	7%	6%	7%
Parity	1343							
None		7%	4%	6%	8%	9%	5%	9%
One		12%	11%	12%	13%	16%	12%	11%
Two		44%	51%	50%	40%	41%	43%	40%
Three		22%	20%	22%	29%	19%	24%	23%
Four and more		15%	14%	11%	10%	15%	16%	17%
Way of cohabitation	1340							
Living apart		7%	4%	4%	4%	9%	12%	8%
Living with husband/partner		39%	21%	24%	34%	41%	44%	55%
Living with children		6%	4%	6%	5%	6%	7%	5%
Living with partner & child		48%	70%	65%	58%	43%	37%	31%
Mean age of the partner (years)	1163	54.6	49.9	51.5	53.7	55.5	56.6	58.3
Employment partner	1157							
Working		75%	93%	90%	76%	81%	68%	56%
Retired		15%	2%	4%	9%	13%	22%	29%
Other		10%	5%	6%	15%	6%	10%	14%
Measures of well-being: mean (sd) ^b								
ISH	1020	9.6 (6.7)	8.7 (6.5)	9.7 (6.4)	10.6 (6.8)	9.8 (6.5)	10.1 (6.8)	9.8 (6.9)
SIP social interaction	1088	11.3 (11.9)	8.8 (9.9)	11.7 (12.5)	10.4 (10.1)	11.4 (10.0)	10.9 (12.6)	13.0 (13.1)
SIP emotions, feelings and sensations	1227	7.5 (13.7)	6.1 (11.7)	9.2 (15.4)	8.3 (14.9)	9.9 (15.9)	6.3 (14.0)	7.2 (12.8)
SIP intellectual functioning	1177	10.0 (17.4)	8.0 (16.3)	12.2 (19.4)	9.7 (15.8)	10.7 (18.5)	6.7 (14.4)	11.0 (17.7)

^a The n differs as the number of women that give a valid answer differs per question.

^b The standard deviation is placed in parentheses under the mean.

Table 3. The relationship between menopausal status and four measures of well-being, adjusted for differences in age. Regression weights of menopausal status.

Measure of well-being	Pre-menopausal		Peri-menopausal I				Peri-menopausal II				Post-menopausal I				Post-menopausal II				Post-menopausal III			
	n	B ^a	n	B	95% CI ^b	p	n	B	95% CI	p	n	B	95% CI	p	n	B	95% CI	p	n	B	95% CI	p
ISH	220	0	177	1.2	(-0.1, 2.5)	.08	58	2.2	(0.3, 4.2)	.03	108	1.8	(0.1, 3.4)	.04	111	2.0	(0.3, 3.8)	.02	328	1.9	(0.3, 3.5)	.02
SIP-social ^c	235	0	183	3.0	(0.7, 5.3)	.01	67	2.0	(-1.3, 5.3)	.24	109	3.3	(0.3, 6.2)	.03	121	2.7	(-0.3, 5.8)	.08	353	5.1	(2.3, 8.0)	.00
SIP-emotions ^c	253	0	200	3.5	(1.0, 6.1)	.01	73	3.2	(-0.4, 6.9)	.08	127	5.3	(2.1, 8.4)	.00	140	1.7	(-1.6, 5.0)	.31	409	3.3	(0.2, 6.4)	.04
SIP-intellectual ^c	242	0	195	4.2	(0.9, 7.5)	.01	74	1.9	(-2.7, 6.6)	.41	120	3.1	(-1.1, 7.3)	.15	136	-1.2	(-5.5, 3.1)	.58	390	3.5	(-0.5, 7.6)	.09

^a In all regression analyses the premenopausal group is taken as reference category. Therefore the regression weight (noted by B) of this group is fixed at 0.0. The other regression weights reflect the difference between the peri vs pre-menopausal group or the post vs pre-menopausal group.

^b 95% CI: 95% confidence interval of B.

^c SIP social: SIP social functioning; SIP emotions: SIP emotions and feelings; SIP intellectual: SIP intellectual functioning and alertness.

The relationship between menopausal status and the four different measures of well-being, adjusted for differences in age, is reported in table 3.

Early perimenopausal women (peri I) score statistically significantly higher -thus experience a lower level of well-being- on all measures but the ISH as compared to premenopausal women. Late perimenopausal women (peri II) report a lower level of well-being on the ISH only.

Early postmenopausal women (post I) have a statistically significantly reduced level of well-being on all measures but the SIP intellectual functioning again compared to premenopausal women. Intermediate postmenopausal women (post II) show a lower level of well-being on the ISH only. Late postmenopausal women (post III) have a diminished level of well-being on all scales except for the SIP intellectual functioning.

By applying linear regression analysis the influence of eight potential confounders on well-being was determined. The results are reported in table 4. Five potential confounders met the criteria as outlined in the method section and were included in the multivariate analyses: Body Mass Index, smoking behaviour, education, way of cohabitation and partner's employment.

Table 4. The influence of potential confounders on well-being: multiple regression coefficients.

Potential confounder	ISH		SIP social interaction		SIP emotions, feelings and sensations		SIP intellectual functioning	
	R ² -change ^a	F ^b	R ² -change	F	R ² -change	F	R ² -change	F
Body Mass Index	.02	18.1***	.01	5.8**	.00	0.2	.00	1.0
Smoking	.01	1.8	.01	2.6**	.00	2.4*	.01	2.8**
Education	.01	2.4**	.02	4.1***	.01	2.6**	.00	1.1
Work outside the home	.00	0.3	.00	0.1	.00	0.9	.00	0.5
Parity	.00	0.9	.01	1.7	.00	0.7	.00	0.1
Way of cohabitation	.01	2.4*	.00	1.7	.01	2.3*	.01	2.3*
Age difference between partners	.00	0.2	.00	0.7	.00	0.2	.00	0.1
Employment partner	.01	4.0**	.01	2.7*	.01	3.2**	.00	1.2

^a R²-change denotes the change of the multiple regression coefficient when the variable is removed from the regression equation; the regression equation always includes age.

^b Significance: * p < .10; ** p < .05; *** p < .01.

The results of the multivariate regression analyses are shown in table 5. In general, the differences in the level of well-being between the six menopausal status become less pronounced after adjustment for selected potential confounders, compared to the analysis where only differences in age are taken into account. However, the majority of results remain statistically significant ($p < 0.05$), except for the lower level of well-being of early postmenopausal women (post I) on the SIP social functioning. Three other statistically significant results seem to disappear as a consequence of a reduced number of women, whereas the regression weight B is about the same: the decreased level of well-being of late perimenopausal women (peri II), early postmenopausal women (post I) and of late postmenopausal women (post III) on the ISH.

Table 5. The relationship between menopausal status and four measures of well-being, adjusted for differences in age and selected confounders^a. Regression weights of menopausal status.

Measure of well-being	Pre-menopausal		Peri-menopausal I				Peri-menopausal II				Post-menopausal I				Post-menopausal II				Post-menopausal III			
	n	B ^b	n	B	95% CI ^c	p	n	B	95% CI	p	n	B	95% CI	p	n	B	95% CI	p	n	B	95% CI	p
ISH	205	0	166	0.9	(-0.4, 2.3)	.18	53	2.1	(0.0, 4.1)	.05	101	1.6	(-0.1, 3.4)	.07	102	2.1	(0.3, 3.9)	.02	301	1.7	(0.0, 3.4)	.05
SIP-social ^d	219	0	171	2.5	(0.1, 4.9)	.04	63	1.8	(-1.6, 5.4)	.30	103	2.3	(-0.8, 5.4)	.14	111	1.9	(-1.3, 5.1)	.25	316	4.4	(1.4, 7.4)	.00
SIP-emotions ^d	232	0	188	3.5	(0.8, 6.1)	.01	69	2.7	(-1.1, 6.5)	.16	117	4.9	(1.6, 8.3)	.00	126	2.1	(-1.4, 5.6)	.25	367	3.4	(0.1, 6.8)	.04
SIP-intellectual ^d	223	0	181	4.1	(0.7, 7.5)	.02	69	2.4	(-2.5, 7.2)	.34	111	2.3	(-2.1, 6.7)	.30	122	-2.1	(-6.6, 2.5)	.38	351	3.0	(-1.3, 7.3)	.17

^a Selected confounders: Body Mass index, smoking behaviour, education, way of cohabitation and partner's employment.

^b In all regression analyses the premenopausal group is taken as reference category. Therefore the regression weight (noted by B) of this group is fixed at 0.0. The other regression weights reflect the difference between the peri vs pre-menopausal group or the post vs pre-menopausal group.

^c 95% CI: 95% confidence interval of B.

^d SIP social: SIP social functioning; SIP emotions: SIP emotions and feelings; SIP intellectual: SIP intellectual functioning and alertness.

DISCUSSION

Our findings among women with natural menopause and without estrogen therapy suggest that in general, women in the climacteric report a lower level of well-being compared to women in the premenopausal period, even after adjusting for confounders. In the early peri-, early post- and late postmenopausal period a difference is mainly found on the SIP scales. In the intermediate postmenopausal period a difference is found on the ISH. The pattern is not constant over the six periods. Therefore future research should consider menopausal status as a nominal variable rather than an ordinal one. Although these differences are statistically significant, they are rather small. The question arises whether these small differences represent clinically significant differences.

It is difficult to compare the findings of this study with those of other studies because no uniform approach exists to study the influence of the climacteric on health. Some studies use a diversity of symptoms as outcome measures,³ others search for symptom-clusters,³⁰ or look for differences on already existing scales.^{1,27} In this study the measure of well-being best comparable to the measurements by other authors is the ISH as it consists of health complaints. In this respect our results are in accordance with other studies: for most women health is not much adversely affected by the climacteric. Further, most studies indicate that other factors, for example social class, may have more influence on well-being than menopause per se.³

In our view the results are based on a well controlled methodological design.³¹ As to the generalizability of the results, our study group encompassed a population at large and women were not selected according to the presence of medical complaints. No selection bias seems to be present, given the minor differences between respondents and non-respondents and the response rate (71.3%). This is a plus-point in contrast to other studies which were performed in highly selected populations, e.g. visitors of menopause clinics or women attending a routine ovarian screening clinic.

Efforts were made to avoid emphasis on the climacteric by naming the questionnaire 'Health Questionnaire for Women'. Questions on menstruation and menopause were included towards the end of the questionnaire. Thus the detection signal bias was minimized.

In order to classify menopausal status correctly, hysterectomized women and women using estrogens or having used estrogens in the past six months were excluded. As a consequence, it is not known whether our findings may be extrapolated to these women. Since the menstrual pattern can fluctuate over time it is possible, for instance, that women once classified as postmenopausal, start menstruating again. However, it seems plausible that the incidence of such phenomena is low.^{32,33}

Confounding is a serious danger in all types of epidemiological research. When there is a suspicion of confounding, the next three steps must be made: (a) identification of the confounders (b) evaluation of the presence of confounding (c) adjustment for confounders.³⁴

Therefore identification of potential confounders is a crucial step in this process. We identified confounders on the basis of literature on factors related to well-being, menopause or both. It is remarkable that in our study working outside the home, parity and age difference with the partner did not appear to confound the relationship between menopausal status and well-being, whereas Body Mass Index, smoking behaviour and the partner's employment did. In our view, future research on well-being in the climacteric should take these latter variables into account.

One might attribute the differences in well-being between the different menopausal status to the so-called 'consensus' complaints, i.e. flushes, severe sweating and vaginal dryness. The ISH is the only measure of well-being in this study that contains one of these consensus complaints, namely severe sweating. When severe sweating is included in the regression equation as a confounder the differences in well-being, as expressed by the regression weight B , decrease. As a consequence, the B 's of early perimenopausal women on the SIP social functioning and of late postmenopausal women on the SIP emotions, feelings and sensations are no longer statistically significant. The only statistically significant B of the ISH for intermediate postmenopausal women also disappears. However, despite this correction, the other differences remain. Furthermore, one should note that as the item 'severe sweating' is a component of the ISH, this correction may suppress the relationship between climacteric and well-being itself.

The ISH reflects one's tendency to express a lower level of well-being in vague somatic complaints. Hence, our findings indicate that the somatic aspects of well-being are not much influenced by the menopausal status per se. *Nota bene*: there may be *complaints* caused by the climacteric, but well-being is not much influenced by them.

The main differences are found on measurements of well-being that focus on the impact of menopause on daily life functioning. Social interaction is significantly worse in early peri and late postmenopausal women. The women in this study reported to be less interested in their family members and friends and acted less friendly towards them. Emotions, feelings and sensations are significantly lower in early peri-, early post- and late postmenopausal women. Women may feel more nervous, tense or depressive. Finally, the level of intellectual functioning is lower in early perimenopausal women only. On average women seem to be less able to concentrate and more forgetful during this period.

In conclusion, our results suggest that the independent influence of the climacteric on well-being is found in a small negative influence on behavioural functioning in the daily life of a woman.

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CHAPTER 3

VASOMOTOR SYMPTOMS AND WELL-BEING IN THE CLIMACTERIC YEARS

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Submitted

INTRODUCTION

Early studies of the climacteric reported a range of symptoms that occur more frequently among women whose menstrual cycles have changed. These include hot flushes, night sweats, lethargy, forgetfulness, tiredness, crying spells, irritability and headache.¹⁻⁴ Later studies differentiated between typical symptoms that are strongly related to the climacteric (i.e. vasomotor symptoms and vaginal dryness) and atypical symptoms that are weakly associated. These atypical symptoms appeared to be more related to co-occurring social, psychological and physically bothersome changes than to the climacteric *per se*.⁵⁻⁷ Since the study of mere symptoms may give a limited view of the experiences of women in the climacteric years, other studies have addressed the association between climacteric and measures of well-being. These studies pointed out that (emotional) well-being is not much adversely affected by the climacteric.⁸⁻¹¹

However, Oldenhave et al¹² recently concluded that the prevalence of vasomotor symptoms was highest in the late premenopause and early postmenopause (about 85%) and that this increase of vasomotor symptoms was related to an overall reduced level of well-being. In contrast, Matthews established that despite experiencing more vasomotor symptoms, women perceived lower levels of stress.¹³ Apparently, there are equivocal conceptions of the association between vasomotor symptoms and well-being.

The aim of our study was to examine more closely the relationship between vasomotor symptoms, well-being and climacteric status according to the last menstrual bleeding. As this association may depend on the perception of the climacteric status, another aim was to examine this relationship for climacteric status according to the women themselves.

METHODS

This study is part of a larger study aimed at assessing the relationships between the climacteric, well-being, women's attitude towards menopause, medical attention and the use of hormone replacement therapy. The methodology of this study has been reported in detail elsewhere.¹⁰ In short, from the municipal authorities of Krimpen aan den IJssel, a commuter suburb of Rotterdam with approximately 28000 inhabitants, names and addresses of all 2729 women aged 45 to 60 years were obtained. In May 1990 they were sent a questionnaire; 1947 women responded (response 71.3%). The comparison between respondents and a sample of 55 non-respondents did not reveal any statistically significant differences in age, menopausal status, hysterectomy, estrogen therapy, level of education, work outside the home or medical attention.

The study received approval from the Medical Ethical Committee of the Erasmus University and Academic Hospital Dijkzigt in Rotterdam.

Measurements

Well-being was measured by two validated inventories: the 'Inventory of Subjective Health' (ISH) and the 'Sickness Impact Profile' (SIP). The ISH has proven to be a sensitive instrument to detect health problems.¹⁴ The ISH includes 49 items, concerning the experience in the past two weeks of, for example, pains in the chest, shaking hands, headache, sneezing and lessening of appetite. With every item the respondent is asked whether she has experienced it during the last two weeks. All items must be answered with either 'yes' or 'no'. The sum score of all responses is computed, the maximum score being 49. The SIP was developed in the United States as a behaviourally based measure of the impact of sickness.¹⁵ In this study, the Dutch validated version was used. Both SIP overall scores and SIP category scores can discriminate between subsamples. To limit the time needed to fill out the questionnaire we have chosen three category scores which measure psycho-social impact on well-being: emotions, feelings and sensations (9 items), social interaction (18 items) and intellectual functioning (10 items). All items are rated a scaling factor. This scaling permits the calculation of three SIP percent category scores. A percentage of 100 means maximal impairment on the corresponding category score.

Women were categorized as having vasomotor symptoms when they reported severe sweating and/or hot flushes in the questionnaire. The presence of severe sweating was assessed by using both a closed question and an open question, whereas hot flushes were asked by using an open question only, to avoid emphasis on the climacteric.

The climacteric status of women was classified according to menstrual pattern characteristics and to the number of months or years since the last menstrual bleeding prior to the completion of the questionnaire. We defined six categories:¹⁰ women who had had a menstruation within twelve months and whose menstrual pattern did not change (premenopausal), women who had experienced a change in the menstrual cycles in the preceding year with a last menstrual bleeding occurring three months or less (perimenopausal I) or four to twelve months ago (perimenopausal II), women whose last menstrual bleeding occurred 1-2½ years ago (postmenopausal I), 2½-4½ years ago (postmenopausal II) and more than 4½ years ago (postmenopausal III). As some women filled out the year of the last menstrual bleeding only and not the exact month, a classification was chosen which coincided with the calendar year. Women who had undergone hysterectomy and women who had used estrogen therapy in the 6 months prior to answering the questionnaire, were excluded from the analyses as they can not be classified according to climacteric status.

The women were also asked to rate their climacteric phase themselves by choosing one of the following five categories: 'I have not reached the menopause', 'I have just reached the menopause', 'I am in the middle of the menopause', 'I have reached the end of the menopause', 'I reached the menopause long ago'.

Data analysis

Prevalences of vasomotor symptoms were computed for women in the different climacteric categories. Subsequently, a logistic regression analysis was performed with the dichotomized scores of well-being as the dependent variable and the presence of vasomotor symptoms as independent variable. Well-being scores were dichotomized around the median. In an earlier study we reported on the relationship between well-being and body mass index, smoking, education, the woman's employment status, parity, the way of cohabitation, age difference between the partners and the employment status of the partner.¹⁰ In this analysis age, education and body mass index were related on a $p < .01$ level to one or more of the four measures of well-being and were therefore entered in the logistic regression equation. Odds ratios with 95% confidence intervals were computed for the six menopausal status defined according to last menstrual bleeding as well as for the five categories of menopausal status according to the women themselves. In this study the odds ratios express the likelihood of women with vasomotor symptoms compared to women without these symptoms of having a score of well-being above the median. A relatively high score means a relatively low level of well-being.

RESULTS

In Table 1A, the prevalence of vasomotor symptoms is shown for the six climacteric status according to last menstrual bleeding. The prevalence varied from 25.0% in premenopause, to 69.1% in late perimenopause (peri II) and was 38.9% in late postmenopause.

The odds ratios of women with vasomotor symptoms as compared to women without these symptoms of experiencing a level of well-being below the median are shown in Table 1B.

Premenopausal women with vasomotor symptoms more often experienced a lower level on all four measures of well-being compared to women without these symptoms. Women with vasomotor symptoms had 4.8 (95% CI 2.3-9.7) times more often a lower level of well-being on the ISH. The corresponding odds ratio for the SIP emotions, feelings and sensations was 2.2 (95% CI 1.2-4.0) and for SIP intellectual functioning and alertness 2.7 (95% CI 1.4-5.0).

Early perimenopausal women (peri I) with vasomotor symptoms were somewhat more likely to experience a lower level of well-being than women without these symptoms: the odds ratios being slightly higher than 1.0, except for the ISH (odds ratio 2.1; 95% CI 1.4-4.0). In contrast, late perimenopausal women (peri II) with vasomotor symptoms *less* often report a relatively low level of well-being on all scales. However, none of these odds ratios were statistically significant.

Table 1A. Prevalence of vasomotor symptoms for menopausal status according to last menstrual bleeding.

	Menopausal status according to last menstrual bleeding					
	Pre	Peri I	Peri II	Post I	Post II	Post III
(N)	(274)	(226)	(83)	(140)	(153)	(466)
Prevalence	25.0%	41.0%	69.1%	61.3%	58.4%	38.9%

Table 1B. Odds ratio of women with vasomotor symptoms compared to women without these symptoms of being above the medium on four measures of well-being. A score above the medium means a relatively lower level of well-being. Figures are presented separately for menopausal status according to last menstrual bleeding^a.

Measure of well-being							
ISH	Odds Ratio	4.8	2.1	0.6	1.9	5.8	2.1
	95% CI	(2.3;9.7)	(1.1;4.0)	(0.2;2.3)	(0.8;4.8)	(2.4;14.0)	(1.3;3.4)
SIP social functioning	Odds Ratio	1.9	1.0	0.4	2.9	1.4	1.9
	95% CI	(1.0;3.5)	(0.5;1.8)	(0.1;1.2)	(1.2;7.1)	(0.6;3.0)	(1.2;3.1)
SIP emotions, feelings and sensations	Odds Ratio	2.2	1.5	0.5	0.8	2.0	1.4
	95% CI	(1.2;4.0)	(0.8;2.7)	(0.2;1.6)	(0.4;1.9)	(0.8;4.7)	(0.9;2.1)
SIP intellectual functioning and alertness	Odds Ratio	2.7	1.2	0.8	1.0	1.5	1.3
	95% CI	(1.4;5.0)	(0.6;2.1)	(0.3;2.5)	(0.4;2.3)	(0.7;3.5)	(0.8;2.0)

^a Odds ratios are adjusted for differences in age, education and body mass index.

For early postmenopausal women (post I) no association between vasomotor symptoms and the SIP intellectual functioning and alertness and the SIP emotions, feelings and sensations was found, whereas for the ISH and the SIP social functioning odds ratios of 1.9 (95% CI 0.8-4.8) and 2.9 (95% CI 1.2-7.1) respectively were found. Among middle postmenopausal women (post II) all women with vasomotor symptoms reported a relatively lower level of well-being. Finally, for late postmenopausal women (post III) with vasomotor symptoms all measures showed an odds ratio higher than 1.0. Statistically significant odds ratios were established on the ISH (odds ratio 2.1; 95% CI 1.3-3.4) and the SIP social functioning (odds ratio 1.9; 95% CI 1.2-3.1) only.

In Table 2 the relationship between vasomotor symptoms and the level of well-being is shown for the menopausal phases categorized according to the women themselves. The same pattern emerged. Here too, women with vasomotor symptoms who perceive themselves as not menopausal or menopausal long ago had significantly more often a relatively low level of well-being, whereas women with vasomotor symptoms who perceive themselves as in the middle of menopause had odds ratios that are notably lower.

Table 2A. Prevalence of vasomotor symptoms for menopausal status according to the women themselves.

Measure of well-being	Menopausal status according to the women themselves				
	Not reached menopause	Just reached menopause	Middle of menopause	End of menopause	Menopause long ago
(N)	(265)	(242)	(324)	(224)	(354)
Prevalence	17.2%	45.4%	68.3%	58.8%	27.7%

Table 2B. Odds ratio of women with vasomotor symptoms compared to women without these symptoms of being above the median on four measures of well-being. A score above the median means a relatively lower level of well-being. Figures are presented separately for menopausal status according to the women themselves^a.

		4.4	2.1	1.5	1.4	2.8
ISH	Odds Ratio	4.4	2.1	1.5	1.4	2.8
	95% CI	(2.0;9.6)	(1.1;3.9)	(0.8;2.8)	(0.7;2.8)	(1.5;5.2)
SIP social functioning	Odds Ratio	2.3	0.7	1.2	1.7	1.8
	95% CI	(1.1;4.9)	(0.4;1.4)	(0.7;2.1)	(0.8;3.3)	(1.0;3.2)
SIP emotions, feelings and sensations	Odds Ratio	2.6	1.0	0.8	1.0	1.8
	95% CI	(1.3;5.3)	(0.5;1.7)	(0.4;1.3)	(0.5;1.8)	(1.0;3.1)
SIP intellectual functioning and alertness	Odds Ratio	3.8	0.9	0.9	1.3	1.4
	95% CI	(1.8;7.8)	(0.5;1.7)	(0.5;1.5)	(0.7;2.5)	(0.8;2.4)

^a Odds ratios are adjusted for differences in age, education and body mass index.

DISCUSSION

Population based studies established no major difference in well-being between pre-, peri- and postmenopausal women.⁶⁻¹⁰ Studies in which a distinction was made between women with or without vasomotor symptoms showed a considerably lower level of well-being for women with these symptoms.^{12,16} In this cross-sectional study we also found a clear relationship between vasomotor symptoms and well-being which depended on climacteric status. Pre- and (middle and late) postmenopausal women with vasomotor symptoms more often experienced a relatively low level of well-being compared to women without these symptoms. However, in contrast to the above mentioned studies, when the prevalence of vasomotor symptoms is at its top, i.e. in late perimenopause, a difference in the level of well-being between women with and without vasomotor symptoms was absent.

An explanation for the fact that Oldenhave did not detect an absence of the relationship in perimenopausal women may be found in the differences between the measurement instruments applied to quantify health status. Furthermore, in the questionnaire Oldenhave first explained the meaning of vasomotor symptoms in order to quantify them, thereby drawing attention to the climacteric. In our study we tried to avoid any emphasis on the climacteric by calling the questionnaire 'Health Questionnaire for Women' and measuring vasomotor symptoms either in a list of several symptoms or using open questions.

In Daly's recently published study, it was concluded that the quality of life of women with menopausal symptoms may be severely compromised and that perceived improvements in quality of life in users of hormone replacement therapy seem to be substantial.¹⁶ In that study a sample of 31 women recruited from a specialist menopause clinic and 32 women consulting their general practitioner of which 9 women had menopausal problems. Apart from vasomotor symptoms, the participating women were asked to imagine menopausal symptoms such as tiredness, lack of concentration and confidence and less interest in sex. Subsequently they were asked how these experiences would influence their quality of life. The effect of hormone replacement therapy was measured by asking women actually using or having used this therapy to compare their quality of life before and after therapy.

The methodology of that study is hampered by several imperfections. Firstly, selection was present in the sample as mainly women were recruited who suffered from bothersome complaints which they labelled climacteric. Secondly, the validity of imagination of complaints is doubtful. Thirdly it is uncertain that, apart from the vasomotor ones, the 'menopausal complaints' are caused by the climacteric. Fourthly, any conclusion about the efficacy of hormone replacement therapy is inappropriate without a randomized, double blinded, and placebo controlled design.

The absence of modification by vasomotor symptoms in late perimenopausal women,

that we observed in this study, constitutes a puzzling phenomenon. Although the prevalence of vasomotor symptoms depends on the climacteric status, it is not obvious why in late perimenopausal women vasomotor symptoms were not related to well-being, whereas in pre- and postmenopausal women they were.

No study thus far has shown a clear relationship between serum hormone levels and vasomotor symptoms.¹⁷ Even if such a relationship exists it would still be difficult to explain the absence of a negative impact of vasomotor symptoms on well-being in perimenopausal women. Apart from a biological approach a social scientific explanation may be worthwhile. Social scientists stress the importance of the context in which a symptom is experienced.¹⁸⁻¹⁹ Aubuchon et al concludes that social expectancies influence the report of perimenstrual discomfort. Zola stated that there are two ways in which symptoms indicated in one part of a population may be ignored in another part. Firstly, when a symptom's prevalence is high, this condition may be perceived as the normal state. Secondly, it is the fit of certain symptoms with a society's major values (75% of the women in this study agreed with the statement 'physical changes in the climacteric are natural')²⁰, which accounts for the degree of attention they receive. This theory implies that vasomotor symptoms will be experienced as 'normal' in perimenopause, whereas the presence of vasomotor symptoms in pre- and postmenopausal women will be more difficult to understand. This line of reasoning is only valid when perimenopausal women according to last menstrual bleeding perceive themselves as such. In fact the results about the relationship between vasomotor symptoms and well-being for the climacteric status as perceived by the women themselves confirm this view.

An advantage of this study lies in its representativity. This study was performed in a non-selected population. The response rate was adequate and a sample of non-respondents did not differ from the respondents on a number of characteristics. No emphasis was placed on the climacteric. A limitation of this study is its cross-sectional design. To assess whether vasomotor symptoms induce a lower level of well-being or vice versa, longitudinal studies are necessary.

It is beyond question that hormone replacement therapy relieves vasomotor symptoms and thereby may improve a woman's well-being. Placebo's also proved to be beneficial, albeit to a lesser degree than hormone replacement, in the treatment of vasomotor symptoms.²¹ Presumably vasomotor symptoms can be influenced by other than pharmacological approaches. This is also supported by Whitehead's study,²² in which he claims that explanation and reassurance were sufficient helpful for 40% of women seeking help at menopausal clinics. The results of this study suggest that well-being may improve considerably when women would know more about the presence of vasomotor symptoms in pre- and postmenopause.

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CHAPTER 4

RELATIONSHIPS BETWEEN ATTITUDE TOWARDS MENOPAUSE, WELL-BEING AND MEDICAL ATTENTION AMONG WOMEN AGED 45-60 YEARS

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INTRODUCTION

Attitudes and well-being are both known to be related to medical attention.¹ However, little is known about this association for women in the climacteric years.

Doctors should be actively involved with their patients' beliefs and explanations about what determines their health and their interest in treatment. A patient-oriented approach may keep referrals to a specialist and prescribing of non-specific medicines to a minimum.² Moreover, lack of knowledge of a patient's attitudes may give rise to dissatisfaction of the patient with the consultation.³ A few studies report that the majority of women have a neutral or positive attitude towards menopause. In these studies women disagree with statements like "A woman feels less like a woman".⁴ Besides this, the attitude appears to be positively linked to the actual menopausal status of women: the opinion towards menopause tends to be more positive from pre- through peri- to postmenopausal women.⁵ Knowing the attitudes of women in the climacteric may also clarify the reported reluctance of women to the use of hormone replacement therapy (HRT), despite the fact that several studies have suggested that HRT may reduce the incidence of osteoporosis and ischaemic heart disease.⁶

The climacteric years are accompanied by an increased incidence of the so-called consensus complaints i.e. hot flushes, disturbances in menstrual pattern, dyspareunia. Nonetheless, the mere presence of these symptoms does not necessarily result in a low level of well-being. The relationship between climacteric and well-being has been reported elsewhere and showed that well-being is not much adversely affected by menopausal status per se.^{7,8} Yet, a considerable number of women consult their GP for problems believed to be climacteric.^{9,10}

Firstly, this study will explore the attitude towards menopause of women aged 45-60 years. Secondly, the relation between attitude towards menopause and well-being will be assessed. Thirdly, the question is answered on the relationship of medical attention with both well-being and attitudes.

By answering these questions we hope that women in the peri- and postmenopausal years who attend their doctors will find them better informed about the motives of their visit than perhaps before.

SUBJECTS AND METHODS

Recruitment

This study is part of a larger study concerning climacteric, well-being, women's attitudes towards and knowledge about menopause and HRT. Recruitment and measurement of well-being is reported in detail elsewhere.⁸ In short, from the municipal authorities of Krimpen aan den IJssel, a commuter suburb of Rotterdam with approximately 28.000

inhabitants, names and addresses of all 2729 women aged between 45 and 60 years were obtained. In May 1990 they were sent a questionnaire and 1947 women responded (response 71.3%). A random sample (N=55) was taken of the non-respondents in order to evaluate the representativity of the respondent group. They were approached by telephone and 52 participated (response 95%). The comparison between respondents and non-respondents revealed no statistically significant differences in age, menopausal status, hysterectomy, estrogen therapy, level of education, work outside the home or medical attention. The study received approval from the Medical Ethical Committee of the Erasmus University Medical School and Academic Hospital Dijkzigt in Rotterdam.

Measurements

Attitude towards menopause was measured using 28 items. Most items are taken from existing questionnaires to make comparisons possible. Twelve items are taken from a German study by Frick-Bruder.¹¹ Six items are taken from the Menopause Attitude Questionnaire (MAQ), constructed by Leiblum.⁴ Three items are derived from Ferguson.⁶ Finally, we constructed another seven items. The women were asked to rate their opinion on all the 28 statements, on a scale ranging from 1 (totally agree) to 5 (totally disagree).

To ascertain menopausal status women were classified into pre-, peri- and postmenopausal according to menstrual history. Premenopausal women were women having a regular menstruation pattern in the preceding twelve months. Women were considered perimenopausal when irregular cycles or amenorrhoe had developed in the twelve months prior to the questionnaire. Women were classified as postmenopausal in cases where the last menstrual bleeding occurred at least twelve months ago. Women who had undergone hysterectomy and women who used estrogen therapy within the six months preceding answering the questionnaire, were excluded from the analyses, because they could not be categorized according to menopausal status.

The women were also asked to rate their climacteric phase themselves. They were asked to choose one of the following five categories: 'I have not reached the menopause', 'I just have reached the menopause', 'I am in the middle of the menopause', 'I have reached the end of the menopause', 'I reached the menopause long ago'. If women agreed with the second, third or fourth category they were classified as 'women who perceive themselves as climacteric'.

Well-being can be defined as a multifactorial construct. The relevant well-being dimensions include: (a) subjective experiences i.e. self-assessed health (b) functioning aspects in daily life like social duties and intellectual functioning (c) symptomatic aspects i.e. the effects of disease.¹² Well-being was measured in this study by two validated inventories that measure (b) and (c) respectively: the 'Inventory of Subjective Health' (ISH) and the 'Sickness Impact Profile' (SIP).

The ISH has proven to be a sensitive instrument to detect health problems. In recent years it has been used in several Dutch surveys to quantify subjective health status.^{13,14} In a large representative study in the Netherlands Cronbach's α equalled .87 and the ratio of the eigenvalues of the first and second principal component equalled $16.2/4.4=3.7$, both reflecting a strong unidimensional scale.¹⁵ The ISH includes 49 items, concerning the experience in the past two weeks of complaints like pains in the chest, shaking hands, headache, sneezing and less appetite. On every item the respondent is asked whether she has experienced it during the last two weeks. All items must be answered with either 'yes' or 'no'. The sum score of all responses is computed, the maximum score being 49.

The SIP was developed in the United States as a behaviourally based measure of the impact of sickness.¹⁶ The Dutch validated version was used in this study.¹⁷ Both SIP overall scores and SIP category scores can discriminate between subsamples. To limit the time needed for filling out the questionnaire we chose three category scores which measure psycho-social impact on well-being: emotions, feelings and sensations (9 items), social interaction (18 items) and intellectual functioning (10 items). All items are rated a scaling factor. This scaling permits the calculation of three SIP percent category scores. A percentage of 100 means maximal impairment on the corresponding category score.

To measure medical attention, the women were asked to answer the following question with either 'Yes' or 'No': "At this moment I am being treated by my general practitioner and/or specialist".

Analysis

To give a view of the women's attitudes towards menopause, mean scores and standard deviations for the 28 separate items were computed. By means of factor analysis (using principal component analysis) these items were clustered. Three factors were extracted. All items loading 0.40 or more were considered potential items of a potential cluster. Subsequently for each cluster factor analysis and reliability analysis were executed. An item was definitely assigned to a definite cluster when (i) it loaded 0.40 or more on the first factor and/or (ii) the deletion of the item resulted in a decrease of Cronbach's α of the cluster. One item, "Psychological problems which women experience during the climacteric stand apart from coincidental life changes", did not meet either of the criteria and was excluded from further analyses.

The first cluster contains 11 items reflecting the attitude towards disadvantages of the menopause (Cronbach's $\alpha = 0.78$). The second cluster comprises 11 items reflecting the attitude towards advantages of the menopause ($\alpha = 0.65$). Finally, the third cluster encompasses 5 items reflecting attitudes towards (medical) treatment of the menopause ($\alpha = 0.59$). The mean total score per cluster was computed. Means were also computed for pre-, peri- and postmenopausal women separately. By means of analysis of variance

the differences between the menopausal categories were tested.

Pearson's correlations were computed between measures of well-being and attitude clusters for all women and for each menopausal status separately.

To determine the separate associations of menopausal status, well-being and attitude clusters with medical attention, logistic regression analyses were performed for each variable. As menopausal status inheres age, and as age can be related to attitude (e.g. "One starts to feel old in the climacteric"), age is always included in the regression equation. Dummy variables for menopausal status were constructed to detect possible non linear effects. Then logistic regression was performed entering all variables. As a result of the backward stepwise procedure only variables contributing on a $p < .10$ level are retained in the model. Finally, the extent to which the attitudes towards menopause are related to seeking of medical attention is probably dependent on the self-perceived climacteric status. Hence, an analysis restricted to women that perceive themselves as climacteric was performed.

RESULTS

After exclusion of all women with hysterectomy and/or estrogen therapy, 1343 women could be categorized according to menopausal status. The study population included 274 premenopausal women, 309 perimenopausal women and 760 postmenopausal women.

(i) The attitude of women in the climacteric years towards menopause

In Table 1, the women's attitude towards several aspects of the climacteric is shown. On the disadvantage cluster the women have a neutral attitude (mean total score 3.0). However, women disagree with the two items concerning the loss of (sexual) attractiveness (item 5 and 9). Women tend to agree with the items included in the advantage cluster (mean total score 2.3). In particular, women agree with statements that emphasize the view on the climacteric as a natural development (item 17 and 20). Furthermore, the impossibility of a pregnancy and the absence of the menstruation are considered as a relief (item 15 and 21). On the treatment cluster the women express moderate agreement (mean total score 2.7). The women agree most with the statement that women have to consult their GP with problems in the climacteric (item 23). Towards HRT more neutral attitudes are reported.

The relationship between the three attitude-clusters and the actual menopausal status of a woman according to the menstrual history is also shown in Table 1.

Table 1. Means and standard deviations of the items about the menopause and of the total scores of the three attitude-clusters. Figures for all women and for pre-, peri- and postmenopausal women separately^a.

	Mean ^b	S.D.	Pre	Peri	Post	P-value ^c
Disadvantage cluster (Items relating menopause with disadvantages)						
1. One starts to feel old in the climacteric	3.6	1.5	3.5	3.5	3.7	.582
2. In the climacteric women can stand less stress	2.3	1.2	2.3	2.3	2.4	.176
3. The climacteric coincides with bothersome complaints	2.5	1.3	2.5	2.4	2.5	.092
4. In the climacteric a woman often has more psychological problems	2.6	1.3	2.6	2.6	2.7	.690
5. Partners of postmenopausal women regard them as less sexual attractive	4.0	1.2	4.0	4.0	4.1	.382
6. For the woman the climacteric is an unpleasant period	2.3	1.3	2.3	2.1	2.4	.025
7. During the climacteric one feels less like undertaking something	3.1	1.4	3.0	3.0	3.2	.119
8. In the climacteric one often feels unwell	2.3	1.2	2.4	2.2	2.4	.053
9. A woman feels less attractive after the menopause	4.0	1.3	3.8	3.9	4.0	.543
10. After the menopause women have less sexual needs	3.0	1.3	3.4	3.2	2.8	.002
11. The cause of all problems in the climacteric is something that women can not control by themselves - something from outside	3.0	1.3	3.1	3.0	3.0	.732
Mean total	3.0	0.7	3.0	2.9	3.0	.258

^a N ranges from 1314 to 1397 as the number of women who give a valid answer differs per question.

^b Opinions range from 1 = strongly agree, via 3 = neutral to 5 = strongly disagree.

^c p-value based on analysis of variance, adjusted for age.

After adjustment for age the mean total score on the advantage cluster and the disadvantage cluster is comparable for the three menopausal categories. The mean total score on the treatment cluster is more negative from pre-, through peri-, to postmenopausal women (mean total score 2.5, 2.7 and 2.8 respectively; $p=0.001$).

Viewing the separate items of the disadvantage cluster, perimenopausal women agree more than pre- and postmenopausal women with the statement that the climacteric is an unpleasant period (item 6). Postmenopausal women agree more than pre- and perimenopausal women with the statement that after the menopause women have less sexual needs (item 10).

In the advantage cluster postmenopausal women agree more than pre- and perimenopausal women with the statement that the climacteric brings many positive

Table 1. (continued)

	Mean ^b	S.D.	Pre	Peri	Post	P-value ^c
Advantage cluster (Items relating menopause with advantages)						
12. The climacteric brings many positive aspects	2.8	1.3	3.0	3.1	2.6	.002
13. Problems in the climacteric disappear spontaneously	2.1	1.2	2.4	2.2	1.9	.203
14. Women expecting complaints in the menopause will get them	2.3	1.4	2.2	2.4	2.3	.148
15. It is pleasant that pregnancy is not possible after the menopause	1.7	1.2	1.9	1.8	1.6	.111
16. After the climacteric sex is more pleasant	3.1	1.2	3.2	3.0	3.2	.108
17. Women in the climacteric must have the insight that physical changes are natural	1.4	0.8	1.4	1.4	1.4	.105
18. One grows mature and more self-confident in the climacteric	2.4	1.3	2.6	2.5	2.3	.336
19. After the menopause the sexual relationship is better	3.3	1.1	3.3	3.2	3.3	.179
20. One should have a preference for natural approaches (i.e. attending to nutritional requirements, vitamin supplements, exercise programmes) for menopausal problems	1.5	0.9	1.5	1.3	1.6	.082
21. The absence of the menstruation after menopause is a relief	1.7	1.1	1.9	1.7	1.6	.005
22. After the climacteric one feels more free and more independent	2.7	1.3	3.0	2.8	2.6	.296
Mean total	2.3	0.5	2.4	2.3	2.2	.184
Treatment cluster (Items relating menopausal complaints with treatment)						
23. Women in the climacteric, with problems, should consult their GP	1.8	1.1	1.5	1.7	1.9	.002
24. Complaints in the climacteric must <i>not</i> be treated with drugs ^d	2.6	1.4	3.0	2.7	2.5	.001
25. Women with bothersome climacteric complaints must get HRT	3.0	1.3	2.8	2.9	3.1	.093
26. The benefits of HRT outweigh the risk	3.1	1.2	3.0	3.2	3.2	.105
27. Phenomena in the climacteric must be treated medically	2.5	1.3	2.4	2.5	2.6	.008
Mean total	2.7	0.8	2.5	2.7	2.8	.001

^d Computing the mean total score for the treatment cluster the category scores were reversed for this item^b Opinions range from 1 = strongly agree, via 3 = neutral to 5 = strongly disagree.^c p-value based on analysis of variance, adjusted for age.

aspects (item 12) and the statement that the absence of the menstruation after menopause is a relief (item 21).

Three items of the treatment cluster show the same pattern: postmenopausal women disagree more than pre- and perimenopausal women with statements that promote medical attention of climacteric complaints: "Women in the climacteric, with problems, should consult their GP" (item 23); "Complaints in the climacteric must *not* be treated with drugs" (item 24: association is reversed); "Phenomena in the climacteric must be treated medically" (item 27).

(ii) The association between attitude towards menopause and well-being

The correlations between the four measures of well-being and the three attitude clusters are reported in Table 2 ('total' columns). The disadvantage cluster is moderately correlated to well-being for all women (r varies from $-.31$ to $-.38$, all $p < .01$), whereas the advantage cluster is weakly correlated to well-being for all women (r varies from $.07$ to $.13$, all $p < .05$). The treatment cluster is not statistically significant correlated to any of the measures of well-being.

Table 2 also shows whether these reported correlations are different for women in the three menopausal status according to the menstrual history. The correlation between the disadvantage cluster and well-being is least strong for premenopausal women and strongest for postmenopausal women. This difference is most pronounced for the ISH and the SIP emotions, feelings and sensations. Only small differences are found for the SIP-social interaction and the SIP intellectual functioning. Such a different pattern over menopausal status is not present in the relationship between the advantage cluster and the treatment cluster on the one side and well-being on the other.

Table 2. Correlations between four measures of well-being and three attitude clusters towards menopause for the total group and the three menopausal status^a.

Measure of well-being	Disadvantage cluster				Advantage cluster				Treatment cluster			
	Total	Pre	Peri	Post	Total	Pre	Peri	Post	Total	Pre	Peri	Post
ISH	-.38**	-.25**	-.26**	-.46**	.08**	.02	.09	.08	.00	.04	-.13	.00
SIP social interaction	-.34**	-.29**	-.32**	-.38**	.08*	.09	.04	.13	-.03	.01	.00	.19**
SIP emotions, feelings and sensations	-.31**	-.17**	-.26**	-.37**	.13**	.01	.00	.19**	-.03	.16	-.03	.06
SIP intellectual functioning	-.31**	-.28**	-.31**	-.32**	.07*	.16	-.03	.06	.00	.04	-.02	-.03

^a Significance: * $p < .05$; ** $p < .01$ *(iii) The relationship of medical attention with both well-being and attitude towards menopause*

In Table 3, the association of well-being and attitude with medical attention, adjusted for differences in age, is shown. Both the menopausal status according to the menstrual history and the self-perceived menopausal status are not related with medical attention. Well-being as measured by the ISH and the three SIP-scales is strongly related to medical attention. For example, an increase of 5 points on the ISH corresponds to a 1.47 higher use of medical attention. Finally, of the three different attitude clusters the disadvantage cluster and the treatment cluster are moderately related to medical attention: an increase (thus: disagree more) of 1 point corresponds to a 25% (odds ratio 0.75) and a 18% (odds ratio 0.82) lower use of medical attention respectively.

The results of the multivariate logistic regression analysis are shown in Table 4. Of the three attitude clusters, only the treatment cluster, independent of age and well-being, is related to medical attention to a limited extent (odds ratio 0.78). When the analysis is restricted to women who perceive themselves as climacteric an increase of 1 point for the treatment cluster corresponds to a 37% lower use of medical attention (odds ratio 0.63).

Table 3. The influence of determinants on medical attention: odds ratio of determinants, adjusted for age^a.

Variable	Odds Ratio	95% CI ^b	P-value
<i>Measures of menopausal status</i>			
Menopausal status according to menstrual history ^c			
Perimenopausal	0.88	(0.61;1.28)	.509
Postmenopausal	0.92	(0.61;1.41)	.713
Self-perceived menopausal status ^c			
Perimenopausal	1.05	(0.74;1.50)	.786
Postmenopausal	1.13	(0.71;1.79)	.613
<i>Measures of well-being</i>			
ISH (per 5 points)	1.47	(1.33;1.62)	.000
SIP social functioning (per 5 points)	1.13	(1.07;1.19)	.000
SIP emotions, feelings and sensations (per 5 points)	1.12	(1.08;1.17)	.000
SIP intellectual functioning and alertness (per 5 points)	1.08	(1.04;1.11)	.000
<i>Attitude measurement</i>			
Disadvantages	0.75	(0.63;0.90)	.002
Advantages	1.08	(0.86;1.37)	.512
Treatment	0.82	(0.70;0.97)	.019

^a Results are based on logistic regression, where apart from the determinant, age is included.^b 95% confidence interval.^c Premenopausal is used as reference category.

Table 4. Multivariate logistic regression analysis of medical attention^a
(Multiple R = 0.31; variance accounted for = 9.6%)

Variable contained in the regression model	Odds Ratio	95% CI ^b	P-value
Age (per 5 years)	1.48	(1.20;1.82)	.000
ISH (per 5 points)	1.27	(1.07;1.50)	.005
SIP emotions, feelings and sensations (per 5 points)	1.09	(1.00;1.18)	.047
SIP intellectual functioning and alertness (per 5 points)	1.06	(1.00;1.13)	.065
Attitude towards treatment	0.78	(0.62;0.99)	.041

^a Backward stepwise procedure (variables that contribute on a $p < .10$ level are retained in the model).

^b 95% confidence interval.

DISCUSSION

In the attitude of women towards menopause three clusters may be discerned: a disadvantage cluster, an advantage cluster and a treatment cluster. In general women answer neutrally to, or slightly agree with respectively the items on the disadvantage cluster and the advantage cluster. Notwithstanding this overall pattern, the answers on the items about sexuality reflect a positive view: the women in this study believe that their attractiveness and their sexuality is not influenced by menopause. This attitude is somewhat more positive for postmenopausal women, whereas these women agree more than pre- and perimenopausal women with the statement that they have less sexual needs after the menopause. Apparently menopause is related to a decrease in sexual interest, but sexuality is equally appreciated. On the treatment cluster postmenopausal women disagree more than pre- and perimenopausal women with statements that favour HRT. These findings are in accordance with those of Leiblum et al.⁴

A possible explanation for the reported reluctance to the use of HRT may be found in the overall agreement with the statement that the absence of the menstruation after menopause is a relief. Another possibility is the strong agreement with statements that emphasize that the climacteric is a natural process. On the whole, the women report comparable means on the items taken from other studies in Germany and the USA.^{4,6,11}

In our study, well-being is significantly correlated to the disadvantage cluster. Avis and McKinley found a similar relationship between negative attitude towards menopause and a higher frequency of symptom reporting.⁵ A consequence of this relationship could be an iatrogenic effect, especially in the light of the small effect of menopause on well-being.^{7,18} It is surprising that the relationship between well-being and the disadvantage cluster is present even for women who have not yet experienced the climacteric. This relationship is strongest in postmenopausal women. This phenomenon could indicate that the attitude towards menopause is partly a consequence of experiences that are not associated with the menopause. This has also been demonstrated by Holte et al who reported that the mother's menopausal experiences affect those of the daughter.¹⁸

Another interesting result is the absence of a correlation between the (medical) treatment cluster and well-being. Evidently, women who experience a low level of well-being do not necessarily prefer to be treated. Similar results were found by Ferguson et al. In their study no relation between experiencing symptoms during menopause and use of HRT was reported.⁶

In our study no relationship was found between the menopausal status according to either menstrual history or self-perceived menopausal status, with medical attention. Thus, a woman seems not to experience the menopause as a medical condition that should be treated as such. As expected, all measures of well-being are clearly related to medical attention. Next to well-being, both the disadvantage cluster and the treatment cluster are related to medical attention. As the treatment cluster is not associated with

well-being, this attitude seems to have a function in explaining the need for medical attention independent of well-being. This is supported by the multivariate analysis with all variables present in which the treatment cluster, independent of well-being, is associated with medical attention. Its relationship, however, is rather weak. In the analysis restricted to women who perceive themselves as climacteric this effect is seen more clearly. This is an important finding. Apparently if women perceive themselves as climacteric and if they experience the same level of well-being, more positive ideas about treatment correspond to an increase in medical attention.

As to the generalization of the results, our study group encompasses a population at large and women were not selected according to the presence of medical complaints. The selection bias seems to be limited, given the minor differences between respondents and non-respondents and the response rate (71.3%).

Only static associations can be studied (which is a limitation inherent to the cross-sectional design), e.g. it remains undecided whether a low level of well-being leads to a more negative attitude towards menopause or vice versa among postmenopausal women. Causal relationships between attitude, well-being and medical attention can only be addressed in longitudinal studies.

In this study, we measured medical attention irrespective of the presence of menopausal complaints. As a consequence, medical attention that is not perceived by women as menopause-related will be included. Therefore, the reported relationships between well-being, attitude clusters and medical attention may be diluted, by the inclusion of, for example, prescriptions for chronic diseases. It is however difficult to distinguish complaints that are perceived by women as climacteric from those that are not.

In order to classify menopausal status correctly, hysterectomized women and women using estrogens or having used estrogens in the past six months were excluded. Hence, it is not known whether our findings may be extrapolated to these women. However, it may be assumed that women already using estrogens will, have a more positive view on medical treatment of menopausal complaints.

In conclusion, women in the climacteric period report a neutral to positive view towards menopause. Agreement with items that reflect disadvantages towards menopause is related to a low level of well-being, whereas agreement with items that reflect advantages towards menopause is weakly associated with a high level of well-being. The woman's opinion regarding the treatment of menopausal complaints is not related to well-being. Of the variables used in this study, well-being and age play the most important roles in explaining medical attention of women in the climacteric years. Apart from these variables, also the woman's ideas about treatment are related to medical attention.

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CHAPTER 5

WOMEN'S OPINION ON WITHDRAWAL BLEEDING WITH HORMONE REPLACEMENT THERAPY; A POPULATION-BASED STUDY

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INTRODUCTION

Hormone replacement therapy (HRT) is widely accepted as the appropriate treatment for the climacteric syndrome characterized by hot flushes and severe sweating.¹ Furthermore, HRT is used for the alleviation of atrophic symptoms of the urogenital tract.² In the past decade, much attention has been paid to the prevention of osteoporosis with oestrogen treatment³ and more recently, epidemiologic studies have reported a beneficial effect of estrogens in the prevention of ischaemic heart disease.⁴ Although the efficacy of HRT in reducing the incidence of ischaemic heart disease has not been assessed in randomised controlled trials, the overall benefits of HRT are now widely accepted.

For women with an intact uterus unopposed oestrogen therapy can not be advocated because of the increased risk of endometrial cancer and of the increased incidence of curettage and hysterectomy.⁵ There is consensus that oestrogen therapy has to be combined with periodic progestogens.⁶ Such a combination induces withdrawal bleedings in most women.⁷ It is generally felt that these withdrawal bleedings are a major disadvantage of HRT^{8,9}, but there is literature on the opinion of the women themselves.⁹⁻¹²

Several modifications¹³⁻¹⁵ of HRT have been proposed to diminish the problem of monthly withdrawal bleedings. In the Netherlands, general practitioners often prescribe continuous estrogens with the addition of progestogens during 10-12 days once every three months. Little is known, however, about the attitude of the women regarding this policy.

The aim of this study is to assess the opinion of women on the continuation or re-induction of artificial cycles with hormone replacement therapy after menopause.

METHODS

This study is part of a larger study to measure well-being in the climacteric. The framework of this study is described in detail elsewhere.¹⁶ In short, from the municipal authorities of Krimpen aan den IJssel, a commuter suburb of Rotterdam with approximately 28.000 inhabitants, names and addresses of all 2729 women aged between 45 and 60 years were obtained. In May 1990 they were sent a questionnaire and 1947 women responded (response 71.3%). A random sample (n=55) was taken of the non-respondents in order to evaluate the representativity of the respondent group. They were approached by telephone and 52 participated (response 95%). No differences between respondents and non-respondents could be demonstrated.

The climacteric status was classified according to menstrual pattern characteristics and the number of months or years since the last menstrual bleeding. Women having had a menstruation within twelve months prior to the survey and a menstrual pattern which

did not change were included in the premenopausal group. Women who had had a change in the menstrual cycles in the preceding year were categorized in the perimenopausal group. Women whose last menstrual bleeding had occurred more than twelve months previous to the survey were categorized as postmenopausal. Women who had undergone hysterectomy (n=273) were not included in the analysis. Of the remaining 1674 women, 200 women who used oestrogen therapy were considered as a separate group and 131 women could not be classified according to their climacteric status because of missing data. The analysis was performed using the answers of 274 premenopausal women, 307 perimenopausal women and 760 postmenopausal women.

Measurement of attitude towards withdrawal bleedings with HRT

At the end of the questionnaire we explained that estrogens could be helpful for climacteric complaints but that "When you still have your uterus, your menstrual cycle will continue or restart when using hormonal treatment". After that statement the following questions were asked:

- A: What is your opinion regarding hormonal treatment when your menstrual cycle will continue or restart when using this treatment?
- B: What is your opinion when this treatment leads to menstrual bleedings once every three months?

There were five possible answers: no objection, little objection, much objection, unwanted, no opinion.

Statistical methods

To detect statistical differences between the opinion on withdrawal bleedings of pre-, peri- and postmenopausal women the Chi-square test was used. As menopausal age is closely related to age, it is necessary to evaluate whether an observed difference between women in the three menopausal categories can be contributed to age. To assess this, a linear regression analysis was performed for each menopausal category with age as independent variable and the opinion of withdrawal bleedings as dependent variable. For purpose of these analyses the opinion categories were dichotomized. The categories 'no objection', 'little objection' and 'no opinion' were clustered, as were 'much objection' and 'unwanted'.

The study received approval from the Medical Ethical Committee of the Erasmus University Medical School and Academic Hospital Dijkzigt in Rotterdam.

RESULTS

The findings are summarised in the table. Only 17.2% of the women have no or little objection to monthly withdrawal after menopause with HRT. For trimonthly withdrawals this percentage is 22.4%. In addition, 28% of the women have no opinion on this subject. In general, premenopausal women have less objection than postmenopausal women against both monthly and trimonthly withdrawal bleedings. Approximately 60% of the postmenopausal women have problems with recurrence of withdrawal bleedings (60.8% and 58.4% in the case of monthly and trimonthly withdrawal bleedings, respectively), whereas approximately 30% of the premenopausal women have problems (30.2% and 34.8% respectively). The difference between pre-, peri- and postmenopausal women is highly significant ($p < 0.00001$ for monthly, and $p < 0.00001$ for trimonthly withdrawal bleedings). Of the current users of oestrogen therapy, 60.3% and 63.9% object to monthly and trimonthly withdrawal bleedings respectively.

The influence of age on the opinion on withdrawal bleedings is significant only in the perimenopausal group. An age difference of 5 years results in a 13% higher score (95% confidence interval: 3% to 23%) in the categories 'much objection' and 'unwanted' for monthly withdrawal bleedings. This figure is 10% (95% CI -4% to 24%) for premenopausal women and -2% (95% CI -8% to 4%) for postmenopausal women. For trimonthly withdrawal bleedings the figures are similar.

A similar opinion regarding the question about monthly and the question about trimonthly induced withdrawal bleedings was expressed by 84% of the women. Another 12% had a preference for trimonthly cycles, whereas 4% preferred monthly withdrawals.

Table - Opinion of women regarding continuation or re-inducing of withdrawal bleedings after menopause with HRT (in percentages)

Menopausal category n	Question A: monthly withdrawals				Question B: trimonthly withdrawals			
	All 1166	Pre 256	Peri 298	Post 612	All 1152	Pre 253	Peri 298	Post 601
No objection	6.3	14.8	7.0	2.3	9.5	21.7	11.4	3.5
Little objection	10.9	17.6	13.4	6.9	12.9	19.4	16.8	8.3
Much objection	12.4	12.1	14.4	11.6	10.2	9.1	9.4	11.1
Unwanted	41.7	28.1	37.9	49.2	40.1	25.7	37.9	47.3
No opinion	28.7	27.3	27.2	30.1	27.2	24.1	24.5	29.8

DISCUSSION

Hormone replacement therapy is gaining more acceptance in Europe. Currently, about 10% of women between 45 and 60 years are using HRT in the Netherlands. This proportion is comparable to reports from the United Kingdom,¹⁷ and substantially lower than reported in Denmark¹⁸ and the USA.¹⁹ Trimonthly addition of progestogen to estrogen treatment is popular among general practitioners in The Netherlands. However, it should be stated that scientific proof for the safety regarding the risk of endometrial cancer is lacking. The experience with this kind of HRT is only anecdotal and cannot be advocated before more is known about its potential cancer risk. Nevertheless it seems of interest to know, if this reduction in the frequency of menstrual periods is appreciated by women.

In our study among women aged 45-60, a considerable difference between the opinion of pre-, peri- and postmenopausal women exists. Whereas 32.4% of premenopausal women have no or little objection to continuation of monthly withdrawal bleedings, only 20.4% of the perimenopausal group and 9.2% of the postmenopausal group share that opinion. It should be underlined that this opinion was measured in women not currently taking oestrogens. Of women using oestrogens, 60.3% have no objection to monthly withdrawal bleedings.

Trimonthly withdrawals are somewhat more acceptable to all groups of women. Of the premenopausal women 41.4% have no or little objection to continuation of their menstruations in such a pattern. However, the score in the postmenopausal group, although higher than for monthly bleedings, is still low: only 11.8% are in favour of such a schedule and at least 58.5% have strong objections.

The opinion on monthly withdrawals with HRT of the total study group is in agreement with other authors.^{8-10,12} Draper et al⁸ in a postal survey in Cambridge reported that 18% of 84 women aged 50-52 perceived continuation of menstrual periods as a major disadvantage, 32% described it as a minor disadvantage and only 18% described it as neutral. In a study in a rural practice in Hampshire among 420 women aged 45-64, 40% of the women were deterred from using HRT by the thought of prolongation of periods after the menopause.⁹ Of the women 9% would consider a hysterectomy as an alternative. Hahn et al¹⁰ in a prospective follow-up study concluded that nearly all women discontinued therapy because of undesirable "physiologic" withdrawal bleedings. Ferguson et al.¹² assessed the factors that influenced the decision of women to use oestrogen replacement therapy. Withdrawal bleedings scored as the most negative factor both in postmenopausal women currently taking HRT, in postmenopausal women who never had taken HRT and in premenopausal women.

Our findings indicate that for some women, notably those in the premenopausal period, a HRT-schedule with trimonthly withdrawal bleedings contributes to their willingness to use oestrogens. For the majority of women (and especially for

postmenopausal women) monthly and trimonthly withdrawals are not acceptable. Research should continue on schedules of hormone replacement therapy without withdrawal bleedings.

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CHAPTER 6

DETERMINANTS OF FIRST PRESCRIPTION OF HORMONE REPLACEMENT THERAPY. A FOLLOW-UP STUDY AMONG 1689 WOMEN AGED 45-60 YEARS

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INTRODUCTION

Hormone replacement therapy has been available for about 40 years. The first placebo controlled efficacy study was reported in 1950.¹ Since then, many other studies have argued the benefits of HRT. They have provided evidence that HRT is profitable for women in the climacteric years with vasomotor complaints, vaginal dryness and disturbances in menstruation pattern (the so-called typical complaints). Further, HRT is probably useful in the prevention of postmenopausal bone loss²⁻⁴ and death from coronary heart disease⁵⁻⁷ Nevertheless, several authors report a low prevalence of HRT use.^{8,9}

Several factors that influence the decision to use HRT have been reported in the literature. The regular withdrawal bleeding as a result of the cyclic oestrogen/progestagen therapy is often experienced as unacceptable.^{10,11} Also, fear of cancer seems to be an important reason to refrain from HRT.¹² In contrast, women who are interested in health promotion and disease prevention measures are more willing to take estrogens.¹³ Furthermore, a higher rate of medical consultations, a belief in the efficacy of medical treatment (especially hormonal treatment), experience of hot flushes, women's overall experience of menopause, parity, education and smoking behaviour may influence the use of HRT.^{14,15}

Next to these factors which are related to the women, doctor-related factors may be equally important, e.g. the judgment of the physicians concerning HRT leads to considerable differences in prescribing behaviour and a clear inter-doctor variability has been documented.^{16,17}

The aim of this study was to estimate the cumulative incidence of first HRT prescription and the influence of the woman's well-being, attitude towards menopause, menopausal status and other variables on first HRT prescription in a population at large during a 9 month follow-up period. For women as well as their doctors the so-called typical complaints are probably the major indication for HRT.^{8,18,19} Therefore, the incidence and determinants of HRT were studied among women with and without these complaints.

METHODS

Recruitment

This study is part of a larger study aimed at assessing the relationships between climacteric, well-being, women's attitude towards menopause and medical attention. The methods applied to measure well-being and attitude towards menopause have been reported in detail elsewhere.^{20,21} In short, from the municipal authorities of Krimpen aan den IJssel, a commuter suburb of Rotterdam with approximately 28000 inhabitants, names and addresses of all 2729 women aged between 45-60 years were obtained. In

May 1990 they were sent a questionnaire; 1947 women responded (response 71.3%). A random sample (N=55) was taken of the non-respondents in order to evaluate the representativity of the respondent group. They were approached by telephone and 52 participated (response 95%). The comparison between respondents and non-respondents revealed no statistically significant differences in age, menopausal status, hysterectomy, estrogen therapy, level of education, work outside the home or medical attention.

To measure the cumulative incidence of first HRT prescriptions, assistance was given by the two pharmacies in Krimpen aan den IJssel. Both pharmacies are computerized. Of the women who returned the questionnaire, the 220 women (prevalence 11.5%) who had used estrogen therapy within six months preceding answering the questionnaire and the 7 women who used progestatives without estrogens were excluded. A further 31 women could not be traced in the pharmacies' database. The remaining 1689 women were registered at the pharmacies, included in the study and followed for a period of 9 months. The follow-up period lasted from July 1st 1990 till April 1st 1991.

The study received approval from the Medical Ethical Committee of the Erasmus University and Academic Hospital Dijkzigt in Rotterdam.

Measurements

General well-being was measured by two validated inventories: the 'Inventory of Subjective Health' (ISH) and the 'Sickness Impact Profile' (SIP). The ISH has proven to be a sensitive instrument to detect health problems.²²⁻²⁴ The ISH includes 49 items, concerning the experience in the past two weeks, for example of pains in the chest, trembling hands, headache, sneezing and loss of appetite. On every item the respondent is asked whether she has experienced this during the last two weeks. All items must be answered with either 'yes' or 'no'. The maximum score is 49. The SIP was developed in the United States as a behaviourally based measure of the impact of sickness.²⁵ In this study, the Dutch validated version has been used.²⁶ Both SIP overall scores and SIP category scores can discriminate between subsamples of respondents. We have chosen three category scores which measure psycho-social impact on well-being: emotions, feelings and sensations (9 items), social interaction (18 items) and intellectual functioning (10 items). All items are rated a scaling factor. This scaling permits the calculation of three SIP percent category scores. A percentage of 100 means maximal impairment on the corresponding category score.

Three attitude clusters towards menopause were distinguished: two clusters encompass items reflecting the idea that "menopause is advantageous" and "menopause is disadvantageous" and one cluster encompasses items reflecting the idea that "menopause should be treated (medically)".²¹ The women were asked to rate their opinion on all items on a scale ranging from 1 (totally agree) to 5 (totally disagree). Per cluster mean scores were computed.

To ascertain menopausal status according to last menstrual bleeding, women were classified into pre- peri- and postmenopausal according to menstrual history. Premenopausal women were women having a regular menstruation pattern in the preceding twelve months. Women were considered perimenopausal when irregular cycles or amenorrhoe had developed in the twelve months prior to the questionnaire. Women were classified as postmenopausal if last menstrual bleeding occurred at least twelve months ago. Women who had undergone hysterectomy were categorized as a separate group.

The women were also asked to rate their climacteric phase themselves by choosing one of the following five categories: 'I have not reached the menopause' (classified as premenopausal), 'I have just reached the menopause', 'I am in the middle of the menopause', 'I have reached the end of the menopause' (all three categories classified as perimenopausal), 'I reached the menopause long ago' (classified as postmenopausal). The methods used to measure the other potential determinants of the initial HRT such as body mass index, smoking behaviour, parity, age, general practice are shown in Table 1.

Women were categorized as having typical (climacteric) complaints when they reported one or more of the following symptoms on the questionnaire: hot flushes, severe sweating, vaginal dryness or menstruation disturbances. The presence of severe sweating and vaginal dryness were assessed by using both a closed and an open question, whereas the presence of hot flushes and menstruation disturbances were assessed using an open question only. The closed questions were incorporated in a symptom checklist, where the women could encircle either yes or no when they had regularly experienced a symptom during the last two weeks. In the open question the women could indicate any symptom they experienced the during the last four weeks.

Analysis

The cumulative incidence of first HRT prescriptions during 9 months was computed. Linear variables were dichotomized around the median. The association between possible determinants and first HRT prescriptions was studied by means of the χ^2 -test. Determinants that were associated with first HRT prescription on a $p < 0.10$ level were then included in a logistic regression analysis to ascertain the relative contributions. For all ordinal and nominal variables dummy variables were constructed to detect nonlinear effects. The backward stepwise procedure was used retaining only variables that contributed on a $p < 0.10$ level to the prediction of first HRT prescriptions.

As the relationships between the determinants and first HRT prescriptions may be modified by the presence of typical (climacteric) complaints, subgroup analyses were performed for the women without and women with typical complaints.

Table 1. Cumulative incidence within 9 months of first hormone replacement therapy among 1689 women aged 45-60 years (%).

	All women	P ^a	Without typical complaints	P	With typical complaints		All women	P	Without typical complaints	P	With typical complaints
Total (n)	6.2 (104)		4.4 (37)		8.0 (67)	<i>Other variables</i>					
<i>Measures of well-being^b</i>						Agegroup, years (1641)	.000	.004		.014	
ISH (1251)		.001		.002	.260	45-50	9.2	7.1		11.7	
below median	4.4		2.9		6.7	51-55	5.0	3.1		6.5	
above median	9.0		8.6		9.2	56-60	3.5	1.8		5.3	
SIP-social interaction (1335)		.316		.701	.700	Education (1651)		.089		.910	.055
below median	5.5		3.9		7.7	low	3.5	3.9		3.0	
above median	6.8		4.5		8.5	middle	7.0	4.6		9.3	
SIP-emotions, feelings and sensations (1509)		.005		.069	.082	high	6.0	5.0		7.2	
below median	5.1		3.9		6.5	Body mass index, kg/m ² (1585)		.681		.751	.452
above median	8.8		7.0		9.9	below median	5.9	4.8		7.0	
SIP-intellectual functioning (1454)		.518		.668	.974	above median	6.4	4.3		8.5	
below median	5.9		3.9		8.2	Smoking behaviour (1619)		.004		.092	.039
above median	6.7		4.5		8.2	never/ever	5.8	4.2		7.5	
<i>Attitude measurements</i>						1 to 15 per day	4.4	1.6		7.0	
Menopause is disadvantageous (1294)		.217		.308	.674	> 15 per day	12.6	8.5		15.8	
more positive	6.9		5.2		8.2	Contraceptive pill (1643)		.000		.037	.002
more negative	5.3		3.5		7.3	never used	3.2	2.6		4.0	
Menopause is advantageous (1299)		.168		.510	.221	formerly used	8.0	5.7		10.2	
more positive	5.1		3.6		6.5	Parity (1689)		.714		.267	.867
more negative	7.0		4.7		9.1	no children	5.0	1.8		7.8	
Menopause should be treated (1424)		.000		.182	.000	one child	7.5	5.4		9.2	
more positive	8.5		4.7		12.1	two children	6.2	3.6		8.7	
more negative	3.6		2.8		4.4	three children	6.8	7.0		6.6	
<i>Menopausal status</i>						≥ four children	4.7	3.2		6.7	
Menopausal status according to last menstrual bleeding (1332)		.401		.071	.877	Hysterectomy (1659)		.008		.109	.051
premenopausal	7.0		6.1		9.3	no	5.5	4.0		6.8	
perimenopausal	7.3		6.9		7.7	yes, unilateral oophorectomy	11.3	9.3		12.9	
postmenopausal	5.5		3.0		7.6	yes, bilateral oophorectomy	9.3	4.3		15.0	
Menopausal status according to the women themselves (1594)		.027		.128	.065	Medical attention last two weeks (1654)		.932		.850	.725
premenopausal	7.0		5.0		14.8	no	6.3	4.4		8.3	
perimenopausal	7.1		5.5		8.0	yes	6.4	4.7		7.7	
postmenopausal	3.3		2.1		5.2	General practice (1641)		.036		.088	.239
						A	3.3	1.1		5.4	
						B	3.5	2.1		4.8	
						C	8.1	6.1		9.8	
						D	6.5	4.0		9.7	
						E	6.7	7.1		6.3	

^a P-value based on the χ^2 -test. ^b ISH = Inventory of Subjective Health. SIP = Sickness Impact Profile.

RESULTS

The 9 month cumulative incidence of first HRT prescriptions was 6.2% (104 women). This equals a one year cumulative incidence of 8.2%. The incidence of first HRT prescriptions among women without typical complaints at baseline was 4.4%, whereas the incidence for women with typical complaints was 8.0%.

Determinants of first HRT prescriptions for all women

Table 1 shows the relationship between first HRT prescriptions and possible determinants. Only statistically significant associations are reported below. Two measures of well-being predicted first HRT prescriptions: women below the median of the ISH -i.e. the half of women that feels relatively well- had an incidence of 4.4% whereas the women above the median of the ISH had an incidence of 9.0%. For the SIP-emotions, feelings and sensations these figures were 5.1% and 8.8% respectively. From the attitude measurements, the cluster "menopause should be treated (medically)" was related to HRT prescription. Women who thought more positively had an incidence of 8.5%, whereas the other women had an incidence of 3.6%. Only the menopausal status according to the women themselves was associated with first HRT. Of the premenopausal women 7.0%, of the perimenopausal women 7.1% and of the postmenopausal women 3.3% started using HRT within the 9 months.

Furthermore, women who were younger, women who smoked more than 15 cigarettes per day, women who formerly used the contraceptive pill and women who were hysterectomized were more often prescribed HRT. Women who were enlisted in general practice C had the highest incidence of first HRT use (8.1%), while women in general practice A had the lowest 9 month prescription rate (3.3%).

The results of the multivariate logistic regression analysis are shown in Table 2. Within the 9 months of the study, women with typical complaints were prescribed HRT 1.7 times (95% CI 0.9;3.0) more often than women without these complaints. The likelihood of HRT prescription for women above the median of the ISH was 2.0 (95% CI 1.1;3.6) times higher than for women below the median. For the women who thought more positively about the attitude cluster "menopause should be treated" the odds ratio equalled 2.7 (95% CI 1.5;4.9) compared to the women who thought more negatively. Women who smoked more than 15 cigarettes a day had an odds ratio of 2.2 (95% CI 1.1;4.6) compared to women who have never or ever smoked. The former use of the contraceptive pill resulted in a 2.3 (95% CI 1.1;4.6) times higher prescription rate of HRT within the 9 months compared to women who never used the pill.

Determinants of first HRT for women with and without typical complaints

In the multivariate analyses (Table 2) all relationships between determinants and HRT prescription appeared to be modified by the presence of typical complaints.

For women without typical complaints the ISH and the former use of the contraceptive pill were determinants of initial HRT prescription. Women above the median of the ISH had a 5.5 (95% CI 1.9;15.5) higher rate of HRT than women below the median, while for former users of the contraceptive pill the odds ratio was 4.6 (95% CI 1.0;20.5).

For the women with typical complaints the attitude cluster "menopause should be treated" was related to HRT prescription. Women who thought more positively about treatment had an odds ratio of 3.8 (95% CI 1.8;8.0) compared to women who thought more negatively.

Table 2. Significant determinants from the multivariate logistic regression analysis of first hormone replacement therapy prescription among 1689 women aged 45-60 years

	All women		Women without typical complaints		Women with typical complaints	
Variance accounted for by the variables	3.8%		4.0%		2.8%	
Variable contained in the regression model	Odds Ratio	95% CI ^a	Odds Ratio	95% CI	Odds Ratio	95% CI
Typical complaints			---		---	
not present	1.0					
present	1.7	(0.9;3.0)				
ISH ^b					---	
below median	1.0		1.0			
above median	2.0	(1.1;3.6)	5.5	(1.9;15.5)		
Menopause should be treated			---			
more negative	1.0				1.0	
more positive	2.7	(1.5;4.9)			3.8	(1.8;8.0)
Smoking behaviour			---		---	
never/ever	1.0					
1-15 cigarettes	1.0	(0.4;2.2)				
> 15 cigarettes	2.2	(1.1;4.6)				
Contraceptive pill					---	
never used	1.0		1.0			
ever used	2.3	(1.1;4.6)	4.6	(1.0;20.5)		

^a 95% CI = 95% confidence interval. ^b ISH = Inventory of Subjective Health.

DISCUSSION

In this follow-up study of 1689 women aged 45-60 years in an open population, the 9 month cumulative incidence of first hormonal replacement therapy prescriptions was 6.2%. When the independent effects of several determinants were studied by means of a logistic regression analysis this incidence appeared to be higher for women (i) with typical complaints, (ii) with a lower level of well-being as measured by the ISH, (iii) with a more positive attitude towards "the menopause should be treated", (iv) smoking more than 15 cigarettes a day and (v) who formerly used the contraceptive pill.

In this 9 month study a cumulative incidence of 6.2% of first HRT was established, whereas the prevalence of HRT use at baseline was 11.5%. This implies that either the prevalence of HRT is rapidly increasing or that many women stop taking HRT. We were able to verify these options at the two pharmacies where the women were still registered. The pharmacies reported that one year and 9 months after the questionnaire 68 of the 103 (66%) women were no longer prescribed HRT (one woman moved). Therefore, the problem of a low prevalence of HRT as stated by several studies^{8,9,15} might be attributed to the problem of continuation rather than starting HRT.

Several determinants of HRT prescription that have been found in our study are in line with previous findings. An association between general well-being and HRT has not been reported as a determinant of HRT in other studies. However, these studies were cross-sectional and therefore the level of well-being may already have been influenced by HRT.^{14,15} The relationship between attitude towards treatment and HRT has been found before.²⁷ Apparently, the belief in the efficacy of medical treatment of the menopause is at least as important as the presence of typical complaints. The relationship between smoking behaviour and HRT was ascertained in one study²⁸, but absent in another study.¹⁵ Perhaps women who smoke may therefore experience typical complaints more intensely. In several earlier studies, the former use of the contraceptive pill was a determinant of HRT use.¹⁵ Probably, once a woman has decided to use hormones with a contraceptive purpose, she has less fear of cancer and other adverse effects.

In our study, hysterectomy was, in contrast to other studies^{15,29}, a determinant in the univariate analysis only. Once well-being, smoking behaviour and/or former use of the pill were taken into account by means of the logistic regression analysis, the prediction of HRT prescription did not depend on hysterectomy. The same was found for the SIP emotions, feelings and sensations, the menopausal status according to the woman, age and general practice.

The cumulative incidence for women with typical (climacteric) complaints was 8.0% versus 4.4% for women without typical complaints. Hence, for the majority of the women a therapeutic indication existed. For women without and with typical complaints it appears that the prediction of HRT use is determined by different factors, i.e. a lower

level of well-being and the former use of the contraceptive pill for women without these complaints and a positive attitude towards "menopause should be treated" for women with these complaints.

It is remarkable that a lower level of well-being as measured by the ISH determined HRT prescription (odds ratio equals 5.5) for women without typical complaints. As yet, no clear views exist about the beneficial effect of HRT on well-being in the absence of typical symptoms. From this we may tentatively conclude that a low level of well-being as measured by the ISH might be employed by the woman and/or her physician in the process leading to HRT prescription. In a study of Hunt a considerable influence of patient's demand on HRT prescription was apparent (21% of all prescriptions).¹⁹ This conclusion is also supported by the divergence in HRT prescription rates between the general practices, especially for women without typical complaints. Ferguson also observed differences between physicians in HRT prescription.²⁷ When typical complaints are present, the prescription of HRT mainly depends on the woman's attitude towards "menopause should be treated" and not on her experienced level of well-being.

To our knowledge this is the first study to assess the cumulative incidence of HRT and its determinants in an unselected population. By gathering the data from the pharmacists, neither the women's nor the doctor's attention was drawn to HRT prescription. A limitation of this study is the possibility of a change in typical complaints during the 9 month follow-up. Women were categorized as women with or without typical complaints according to the presence of these symptoms at the time of the questionnaire. Subsequent changes in the experience of these complaints, which were not measured, may have been of influence on the prescription of HRT. Most likely this resulted in an underestimation of the relationships reported in the separate analyses. Another limitation is the fact that we measured delivery of HRT prescriptions and not the actual use. Moreover, some women might have incidentally filled HRT prescriptions in other pharmacies than the two present in Krimpen aan den IJssel. As there is a considerable distance between this suburb and Rotterdam and only 31 out of 1947 women could not be traced at either pharmacy this will only have happened in few cases. Nevertheless a slight underestimation of the cumulative incidence of HRT may be present. Finally, although we evaluated most variables known to possibly influence the prescription of HRT, some other factors such as those related to the physician were not measured.

It may be concluded that the cumulative incidence of first HRT prescription is high, but that the majority of the women stop taking HRT within two years, which implies that most indications are rather therapeutic than preventive. When typical complaints are absent, women with a level of well-being above the median are prescribed HRT five times more frequently. The question arises whether for these women the indication is therapeutic, preventive or equivocal. For women with typical complaints the doctor's prescription is primarily related to the woman's attitude towards (medical) treatment of the menopause. The process of decision-making about starting and continuation of HRT

is complex, depending on a variety of determinants modified by the presence of the typical climacteric complaints. Insight in this process may contribute to a more rational prescription of HRT.

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CHAPTER 7

DURATION OF HRT USE IN GENERAL PRACTICE; A FOLLOW-UP STUDY.

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Submitted

INTRODUCTION

In the USA the prescription of estrogens in menopausal women was more than doubled in the period 1960 to 1974. This may partly be attributed to Wilson's advocacy of estrogen therapy in his widely read book 'Feminine for ever'.¹ In Sweden the consumption trebled between 1973 and 1977.² A drop in the use of estrogens appeared in the late seventies. This was probably due to the commotion about reports of a strong association between endometrial cancer and estrogen replacement therapy.^{3,4} Consensus exists that in addition to estrogens, women with an intact uterus should be given progestogens in order to prevent endometrial cancer.⁵ As a consequence of the acclaimed beneficial effects of hormone replacement therapy on osteoporosis and cardiovascular disease, a renewed interest in HRT has emerged.^{6,7} In recent years, however, conflicting data has become available about an increased risk of breast cancer associated with these drugs.⁸

Appropriate duration of HRT is about 6 to 12 months for short term beneficial effects (i.e. the alleviation of vasomotor symptoms) and at least 3 to 5 years to prevent osteoporosis and cardiovascular diseases.⁹⁻¹¹ Although only few studies have assessed the duration of use of HRT after its initiation, they indicate that estrogens are stopped earlier than the indication would require.¹² This has been attributed to the discomfort associated with the inherent withdrawal bleedings or side effects such as breast tenderness.¹³ Only few studies evaluated determinants of the duration of HRT use.

The aims of our study were (i) to assess the mean duration of use of HRT and (ii) to determine which variables predict the duration of HRT use.

METHODS

Recruitment

This study is part of a larger study aimed at assessing the relationships between climacteric, well-being, women's attitude towards menopause and medical attention. The methods applied to measure attitude towards menopause have been reported in detail elsewhere.¹⁴ In short, from the municipal authorities of Krimpen aan den IJssel, a commuter suburb of Rotterdam with approximately 28000 inhabitants, names and addresses of all 2729 women aged 45 to 60 years were obtained. These women were all enlisted in one of the five group practices of general practitioners in Krimpen aan den IJssel. In May 1990 they were sent a questionnaire; 1947 women responded (response 71.3%). A random sample (N=55) was taken of the non-respondents in order to evaluate the representativity of the respondent group. They were approached by telephone and 52 participated (response 95%). The comparison between respondents and non-respondents did not reveal any statistically significant differences in age, menopausal status, hysterectomy, estrogen therapy, level of education, work outside the home or

medical attention.

To measure the incidence of first HRT prescriptions (i.e. women who had not used estrogen therapy within six months preceding answering the questionnaire), assistance was given by the two pharmacies in Krimpen aan den IJssel. Both pharmacies are computerized. Of the women who returned the questionnaire, the 220 women (prevalence 11.5%) who had used estrogen therapy within six months and the 7 women who used progestogens without estrogens were excluded. A further 31 women could not be traced in the pharmacies' database. The remaining 1689 women who were registered at the pharmacies, were included in the study and followed for a period of 9 months. The recruitment period lasted from July 1st 1990 till April 1st 1991. In total, 103 women (incidence in 9 months 6.2%) were prescribed HRT. These 103 women were all followed from the initiation of HRT for 2¼ years.

The study received approval from the Medical Ethical Committee of the Erasmus University and Academic Hospital Dijkzigt in Rotterdam.

Measurements

The duration of HRT was assessed by using the data provided on the dispersions of HRT to the 103 women in the cohort. For each HRT dispersion the expected final date of use was computed. If the interval between the computed final date and the date of the next dispersion of HRT was less than 42 days, the use of HRT was considered to be continuous, irrespective of a possible change of application. Although 42 days is an arbitral interval, short-term beneficial effects may then be considered to have disappeared. When a next dispersion occurred before the computed final date of the previous dispersion the overlapping time was counted only once in the computation of the total period of HRT use. When a next dispersion occurred more than 42 days after the computed final date of the previous dispersion, the HRT use was considered as interrupted. Several variables that could influence the duration were measured. During the data analysis it became apparent that an important variable, i.e. the indication for HRT was not measured adequately by questionnaire, i.e. many women did not fill out the question about the indication. Therefore it was measured retrospectively by asking the general practitioners for their reason for prescription, with the assistance of the patient's record.

Three attitude clusters towards menopause were distinguished:¹⁴ two clusters encompass items reflecting the idea that "menopause is advantageous" and "menopause is disadvantageous" and one cluster encompasses items reflecting the idea that "menopause should be treated (medically)". The women were asked to rate their opinion on all items on a scale ranging from 1 (totally agree) to 5 (totally disagree). Per cluster mean scores were computed.

To ascertain menopausal status according to last menstrual bleeding, women were

classified into pre-, peri- and postmenopausal according to menstrual history. Premenopausal women were women having had a regular menstruation pattern in the preceding twelve months. Women were considered perimenopausal when irregular cycles or amenorrhoe had developed in the twelve months prior to the questionnaire. Women were classified as postmenopausal if the last menstrual bleeding occurred at least twelve months ago. Women who had undergone hysterectomy were categorized as a separate group.

The methods used to measure the other variables such as type of application, education, hysterectomy, use of contraceptive pill, smoking and group practice are shown in table 1 and table 2.

Analysis

For each category of a possible determinant of the duration of HRT the mean duration of continuous HRT use was computed. The attitude measurements were dichotomized around the median. By means of analysis of variance it was tested whether the submeans differed significantly from each other.

RESULTS

The mean duration of hormone replacement therapy use of the 103 women was 7 months (standard deviation 7.1; range from 0.5 to 27 months). In table 1 the duration of use for all women and for the women on different applications of HRT is shown. In figure 1 the proportion of users is depicted as a function of the period elapsed since the initial HRT prescription. Within 6 months more than 60 % of the women stopped using HRT. After two years 8% of the women were still using HRT. Tibolon showed the highest withdrawal rate within 6 months, being 93%, whereas these figures are 79%, 69% and 61% are for creams, transcutaneous and oral applications other than Tibolon respectively.

On average the oral application of HRT other than Tibolon is taken longer than the other applications. All indications for the prescription of HRT were primarily short term, i.e. to relieve vasomotor symptoms, dyspareunia caused by vaginal atrophy or menstruation disturbances.

Table 1. Mean duration in months of the continuous use of HRT according to type of application of HRT.

	< 6 months	6-12 months	12-18 months	18-24 months	> 24 months
All women (n = 103)	64%	21%	4%	3%	8%
Transcutaneous (n = 16)	69%	31%	0%	0%	0%
Oral (n = 49)	61%	20%	4%	2%	12%
Creams (n = 24)	79%	21%	0%	0%	0%
Tibolon (n = 14)	93%	7%	0%	0%	0%

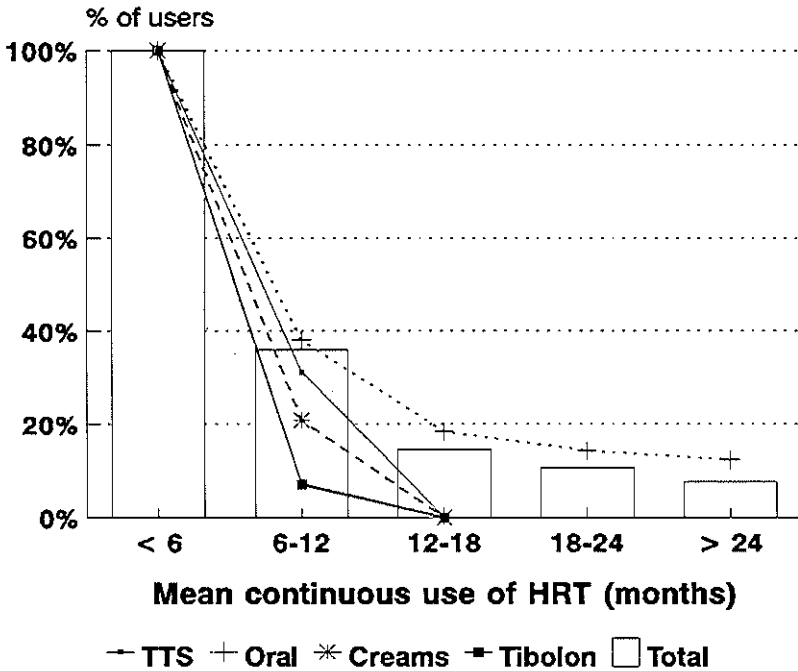


Figure 1. The mean duration in months of the continuous use of HRT according to the type of application (n = 103 women).

In table 2 the association between other variables and the mean duration of HRT use in months is shown. Three of these variables appear to be significantly related to the duration of HRT use. Women having a more positive attitude towards treatment stop using HRT 3.4 month later than women with a more negative attitude. Older women stayed on HRT less long than younger women. The mean duration of HRT use for women aged 45-50 years, 50-55 years and 55-60 years were 8.9, 6.0 and 4.4 months respectively. The mean duration of HRT appeared to vary according to the group practice from 4.4 months (group practice A) to 10.4 months (group practice D). Postmenopausal women as compared to pre and perimenopausal women tended to use HRT shorter.

Table 2. Mean duration in months of the continuous use of HRT for different possible determinants within a period of 2¼ year.

Determinant	Mean	Standard deviation	p-value
<i>Attitudes</i>			
Menopause is disadvantageous			0.14
Below median ^a	6.3	6.1	
Above median ^b	8.9	9.3	
Menopause is advantageous			0.76
Below median ^a	7.7	8.5	
Above median ^b	7.2	7.0	
Menopause should be treated			0.03
Below median ^a	8.7	8.4	
Above median ^b	5.3	5.9	
<i>Sociodemographic variables</i>			
Age group			0.03
45-50 years	8.9	8.6	
51-55 years	6.0	6.0	
56-60 years	4.4	3.4	
Education			0.78
low	6.6	7.4	
middle	6.7	7.0	
high	8.1	7.9	
<i>Gynaecological variables</i>			
Menopausal status according to last menstrual bleeding			0.10
premenopausal	9.1	8.6	
perimenopausal	8.4	7.9	
postmenopausal	5.0	4.9	
Hysterectomy			0.36
no	7.3	7.3	
yes	5.8	6.3	
Contraceptive pill			0.37
never used	5.6	5.8	
formerly used	7.2	7.3	
<i>Other variables</i>			
Smoking			0.61
never/ever	6.3	6.3	
1-15 per day	8.4	9.3	
> 15 per day	7.4	8.1	
Group practice			0.05
A	4.5	4.0	
B	9.3	8.3	
C	5.8	6.1	
D	10.4	10.0	
E	5.0	3.3	

^a Below median: the 50% of the women who agree most with the items.^b Above median: the 50% of the women who disagree most with the items.

DISCUSSION

In our follow-up study of 103 women who started using HRT in general practice more than 60% of the women stopped their HRT within 6 months and only 8% of the women remained on HRT for more than 2 years. The mean duration of use was 7 months. Determinants that predicted the duration of HRT use were type of application, age, attitude towards treatment of the menopause and the group practice.

Very few studies have assessed the duration of use of HRT. Wren found that 61% of 100 women was still on therapy after one year.¹⁵ Barlow found that after 2 years only 15% of the women were still on HRT.¹⁶ We found the same pattern, although the percentage of women who stopped HRT is higher in our study.

Many studies pointed out that one of the main reasons for stopping HRT are withdrawal bleedings.¹⁷ From this point of view one may expect hysterectomized women and women using preparations which do not result in withdrawal bleedings (i.e. tibolon), to use HRT for a longer period. We, however, could not confirm this in our study. Other studies also pointed out that the compliance with HRT of hysterectomized women was low.^{16,18} Thus, withdrawal bleedings inherent to most HRT do not appear to be a leading factor in the decision to stop HRT use. When the indications in this and other studies would be more often preventive, thereby implying a longer use of HRT, withdrawal bleeding could as yet negatively influence the duration of HRT.

Another main reason for early withdrawal from HRT was suggested by Draper. He found that 50% of the women judged the risks of HRT higher than the benefits.¹⁹ They were especially worried about the possibility of cancer.

In our study the role of the physician was of influence on the duration of HRT use. Ferguson also found that a major factor influencing HRT duration was the physician.²⁰ Doctors probably vary in their opinion about the necessity of HRT.^{21,22}

The attitude towards treatment of the menopause was a strong predictor of the duration of HRT use. In an earlier study we established that this attitude was also a predictor of the initiation of HRT.²³ Sinclair also reported that a positive attitude towards treatment was related to HRT use.²⁴

Why younger women comply more with HRT use than older women remains unresolved. Harris found that menopausal women who used estrogens were relatively young.²⁵ Possibly, younger women often still have menstruations when they start using HRT and are therefore less troubled by the withdrawal bleedings accompanying HRT use, compared to older women who have experienced a period without menstruations.²⁶ This idea is also supported by our finding that pre- and perimenopausal women had a longer duration of HRT use compared to postmenopausal women.

The majority of women in our study stopped using HRT within 6 months. This indicates that women take HRT for short term effects, notably to alleviate symptoms such as flushes. This was confirmed by the general practitioners. Roberts reported that eighty

percent of the women use HRT primarily to relieve menopausal symptoms, while only 6% use it as a prophylaxis against osteoporosis.²⁷

A disadvantage of our study is that we could not measure the reasons for stopping HRT. Another disadvantage lies in the fact that we measured the indication retrospectively, using information from both the patients' records and the general practitioners. An advantage of our study concerns the opportunity to observe aspects of HRT use without being influenced by defined prescriptions, strict inclusion criteria and closed monitoring of drug compliance inherent to randomized trials which may influence the duration of HRT and hamper generalizability. Another limitation is the restricted possibility of generalization: the results of this study only apply to Krimpen aan den IJssel in the Netherlands. Part of the relationship between group practice and the duration of use may be attributable to differences in age between the treated women in the practices. Adjustment for confounding variables however was not possible, as the total number of participants was 103, resulting in unstable estimates in multivariate analyses. Further research among larger populations is necessary to resolve these issues.

In conclusion the mean duration of HRT was 7 months; more than 60% stopped using HRT within 6 months, while only 8% of the women still use HRT after two years. We conclude that the mean duration is short, even if all indications are short term, i.e. for the alleviation of menopausal symptoms. Apparently, women are presently unwilling to take HRT for longer periods.

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CHAPTER 8

GENERAL DISCUSSION AND IMPLICATIONS

GENERAL DISCUSSION AND IMPLICATIONS FOR THE PHYSICIAN

The studies described in this thesis focus on the relationship between well-being, attitudes towards menopause, HRT use and menopausal status of women aged 45-60 years. The study was based on a literature review, a cross-sectional population based study and a longitudinal study. In this chapter the main conclusions from our study are put into perspective with literature, and their implications for the practising physician will be discussed.

Many studies have been performed to answer the question whether certain symptoms and complaints during the climacteric years could be classified in a well-defined entity, the so-called 'climacteric syndrome', caused by hormonal changes (*chapter 1*). During the last 10-15 years medical, psychological and sociological disciplines have carried out population based cross-sectional, as well as longitudinal studies among a large number of women in several countries, using an appropriate methodology and sophisticated statistics.¹⁻¹⁵ The majority of these studies concluded that symptoms of the so called climacteric syndrome were mainly excessive sweating, hot flushes, vaginal dryness and menstrual disturbances. These studies point out that psychosocial factors have more impact on the presentation of symptoms and complaints than does the menopause per se. Our own cross-sectional study, which applied well-being as an overall measure instead of the mere presence of symptoms, resulted in similar findings (*chapter 2*). We also established a strong relationship between menopausal status, vasomotor symptoms and dryness of the vagina; whereas the independent relationship between the climacteric and well-being as measured by the Inventory of Subjective Health (ISH) and the three subscales of the Sickness Impact Profile (SIP) is found a small negative association between behavioral functioning in the daily life of a woman and the menopausal status.

Only a few studies have explored the association between vasomotor symptoms and atypical complaints. They reported that sleep disturbances, social dysfunction and other atypical complaints were related to vasomotor symptoms. We found that no linear association between vasomotor symptoms and well-being exists (*chapter 3*). Furthermore, in pre- and postmenopause women with vasomotor symptoms had an impaired well-being compared to women without vasomotor symptoms. However, in the perimenopause, when the prevalence of vasomotor symptoms is at its highest level, there was no difference in well-being between women with or without vasomotor symptoms. In our opinion, the relationship between well-being and vasomotor symptoms is complex and not only depends on their severity and frequency but probably also on the circumstances under which they occur. From this, we pose that women who perceive a symptom in the climacteric as 'normal' (perimenopausal women) do not experience an impaired well-being, whereas pre- and postmenopausal women do. This hypothesis is supported by our findings: when women classify themselves as 'in the middle of the menopause', the difference in well-being between women with and

without vasomotor symptoms is smaller than when women are classified according to their last menstrual bleeding.

For the physician, some major conclusions can be drawn from this part of the thesis. Firstly, a woman with complaints in the climacteric years should not be stigmatized as a 'climacteric woman', in the sense of suffering from a disease or a syndrome entity. Aside from typical, but not pathognomonic symptoms (vasomotor symptoms, dry vagina and menstrual disturbances), there is not sufficient evidence to support the existence of a climacteric syndrome. Although a diagnosis is often defined as 'a provisional formula for action', it should not become a license to stop thinking about the nature of the patient's problem too soon.¹⁷ In addition, attribution of symptoms to a 'climacteric syndrome' by the doctor may hinder an integral approach, characteristic in family medicine i.e. to include somatical and psychosociological elements. In the appreciation of complaints, a preliminary attribution of symptoms to the climacteric may lead to serious doctor's and patient's delay. Therefore, it is better to speak of complaints and symptoms in the climacteric years instead of 'climacteric complaints'.

Secondly, as the level of well-being may depend on the perception of vasomotor symptoms as 'normal', this accentuates the need for the physician to explain to a woman the occurrence of these symptoms in pre- and postmenopausal women. Probably this explanation may give these women reassurance and this in turn may improve well-being.

To know the attitudes and beliefs of women towards menopause will help the physician to elicit and understand why and how a complaint is presented by a patient. From literature (*chapter 1*) and our own study (*chapter 3*) some attitudes and beliefs can be discerned. Brody stated, that physicians are prone to transmit to a patient the accepted scientific explanation for a symptom or condition and may pay little attention to the explanatory model that the patient may have devised. The extent to which the physician's and patient's understanding of a given symptom differs, influences the quality of the communication between doctor and patient.¹⁶

Most women have a neutral to positive attitude towards menopause. They especially agree that sexuality is not impaired in the climacteric years. An important conclusion of this thesis is that a more negative attitude towards menopause is related to a lower level of well-being. This relationship is strongest in premenopausal women, who (by definition) have not experienced the menopause. As impaired well-being can not be explained by menopausal status per se, this attitude may facilitate wrong attribution of complaints to the climacteric and may lead to either patient's delay or to extra medical attention. Indeed, in our study we confirmed that, next to age and impaired well-being, the women's idea about treatment towards menopause is related to medical attention in the climacteric years.

This part of the study illustrates that the physician should be aware of the existence of a subgroup of women who express a more negative attitude towards menopause, since

they will, in general, have a lower level of well-being compared to women with a less negative attitude towards menopause. The physician should provide more comprehensive health information to these women in order to avoid misattribution to the climacteric. Furthermore, the physician should realise that when he also misattributes the complaints this could result in iatrogenic effects. As the association between a negative attitude towards menopause and the level of well-being is most pronounced in premenopausal women, the risk of a self-fulfilling prophecy is present.

A limitation of our study lies in the cross-sectional design of parts of the study. Such an design often leads to the 'chicken-and-egg' problem, e.i. it remains undecided whether a low level of well-being leads to a more negative attitude, or vice versa. Another limitation is the restricted possibility of generalisation: the results of this study only apply to Krimpen aan den IJssel in the Netherlands. The advantages of our study were that we included a large population (N=2729) and adjusted for confounding variables. In contrast, most earlier studies were performed among women visiting clinics and data were not adjusted for potential confounding variables. Furthermore, several earlier studies used inadequate criteria to classify menopausal status.

Hormone replacement therapy (HRT) is accepted as the appropriate treatment for hot flushes and severe sweating, as well as for the alleviation of atrophic symptoms of the urogenital tract and the regulation of menstrual disturbances. As yet, no clear opinion exists about the beneficial effects of HRT in the absence of the above mentioned typical complaints. This can be ascribed to design difficulties, i.e especially blinding is a main problem (*chapter 1*). This is without dispute necessary to rule out the placebo effect.¹⁸ If any beneficial effects of estrogens on other symptoms and complaints in the climacteric years exist, they are probably of modest proportion.

More recently, epidemiological studies report the beneficial effects of estrogens in the prevention of demineralization of bones and ischaemic heart disease. Some disadvantages of HRT are (i) the withdrawal bleeding caused by the combination of estrogen therapy with progestogens for women with an intact uterus to prevent endometrial cancer (ii) other side effects like breast tenderness, edema (iii) worries about cancer, especially breast cancer among physicians and women.^{19,20,21}

Our study provides more insight into some aspects of HRT use e.g. women's opinion as to withdrawal bleedings, the determinants of initiating HRT and the determinants of the duration of HRT use. We found (*chapter 4*) a considerable difference in the opinions of pre-, peri- and postmenopausal women with respect to continuation or re-induction of withdrawal bleedings. Whereas 32.4% of the premenopausal women have no or little objection to continuation of monthly withdrawal bleedings, only 20.4 % of the perimenopausal women and 9.2% of the postmenopausal group share that opinion. Trimonthly withdrawal bleedings are somewhat more acceptable to all groups of women.

Seemingly, withdrawal bleedings may to some extent influence the decision of

women to take hormone replacement therapy. Initiating HRT before the cycles stop and regimens without withdrawal bleedings will possibly augment compliance with HRT. However, for the majority (and especially for the postmenopausal women) monthly or trimonthly withdrawals are not acceptable.

In a longitudinal part of our study (*chapter 6 and chapter 7*) we established the incidence of initiation and duration of HRT use and their determinants. Here, we discuss these two studies together. The 9 month cumulative incidence for women with typical complaints is 8.0% and for women without typical complaints 4.4%. This indicates that prescription is dominated by the typical complaints e.g. vasomotor symptoms, vaginal dryness and menstrual disturbances. Other determinants were well-being, attitude towards 'menopause should be treated' and former use of oral contraceptives.

Contrary to our expectations, hysterectomy appeared not to be a determinant for the initiation of HRT. Moreover, the duration of HRT use was not related to hysterectomy. Obviously, other factors in the decision to take HRT play a more important role than withdrawal bleedings. This is also supported by our findings that (i) trimonthly withdrawal bleedings hardly increase the women's willingness to take HRT and (ii) the duration of usage of preparations which give little or no withdrawal bleeding is not longer than that for other HRT products.

From literature it is known that fear of cancer is a major reason not to start HRT. Sixty percent of the respondents in a UK study expressed concern about side effects, including the risk of cancer, even though it is known that endometrial cancer can be prevented by progestogens and that any increase in breast cancer is controversial and probably offset by a reduction in cardiovascular mortality and fracture risk.^{19,22}

Another finding in this study is, that when typical complaints are absent, well-being as measured by the ISH plays an important role in starting HRT. The odds ratio for women with a relatively low level of well-being to starting HRT as compared to women who feel relatively well is 5.5 (95% CI 1.9;15.5). As we know from our data that the general practitioners do not prescribe HRT exclusively for preventive purposes and that well-being is only slightly influenced by the menopausal status, the giving of HRT to this group of women is debatable. In the presence of vasomotor symptoms only, the attitude towards 'menopause should be treated' is a determinant. The available research suggests that, in case of vasomotor symptoms a concrete indication is present, but the attitude of the woman plays the decisive role in the actual initiation of HRT. Our findings show a short mean duration of usage of HRT. More than 60% of the women ceased within 6 months and only 8% of these women still used HRT after 2 years. These data are in accordance with the fact that general practitioners seldom prescribe HRT for preventive measures only. In conclusion, the majority of the women start HRT for the alleviation of typical complaints. Some of the women may use HRT for other unspecified reasons, which can not be explained either by indication of typical complaints or by preventive measures. These women are probably prescribed HRT to test whether the complaints are

related to estrogen deficiency.

As yet, it appears that both women and physicians are not ready to use or prescribe HRT as a means of prevention for osteoporosis and cardiovascular disease. Future research should further explore the determinants of compliance with HRT. Furthermore, well-designed studies of the effects of HRT on well-being in the absence of typical complaints remain necessary.

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SUMMARY

SUMMARY

Chapter 1

In reviewing the literature we tried to answer the following questions (i) is there a climacteric syndrome in terms of symptoms and complaints, exclusively and independently connected with the climacteric status (ii) is there an association between serum hormone levels and a possible climacteric syndrome (iii) does estrogen replacement therapy bring about relief in symptoms and complaints of this feasible syndrome and improves well-being (iv) what are the attitudes and beliefs towards menopause among the women themselves (v) what is known about the usage of hormone replacement therapy among women.

Most studies found that vasomotor symptoms and vaginal dryness are significantly related to menopausal status. Hot flushes and night sweats are strongly associated with menopausal status in Western research literature. These symptoms have a relatively low prevalence among Japanese women. In general these studies showed that the menopausal transition does not have an important impact on well-being, including the experience of sexuality. Most complaints in the climacteric years were not associated with menopausal development, but could be explained by a mixture of other variables. Given the available recent evidence, apart from typical complaints, there are too few indications to speak of a well-defined climacteric syndrome. Some studies have reported a relationship between complaints (sleeping disturbances, social dysfunction) and the presence of vasomotor symptoms.

Although the drop in estrogen production at menopause is characteristic, levels of all hormones are similar in flushers and non-flushers.

The best scientifically accepted design to establish the effect of estrogen therapy in relieving symptoms, complaints and improving well-being is a randomized double-blind placebo controlled trial. The major problem in the design is blinding, caused by the presence of withdrawal bleedings as a result of the combination of estrogens with progestogens. To maintain blinding, some studies were performed in hysterectomized women, of which the generalizability of the results are questionable. Other studies used estrogen only. In conclusion, from the few randomized double blind control trials it is apparent that estrogen therapy (i) has a significant and substantial effect in relieving vasomotor symptoms and vaginal dryness (ii) has a modest beneficial effect on mood, sleep problems, sexual functioning and well-being; however, these may be reduced by adding progestogens (iii) has an outspoken placebo impact on these symptoms, complaints and well-being.

Most women have a neutral to positive attitude towards menopause. Obviously, women who have already experienced menopause are more positive than premenopausal women. Negative attitudes are clearly related to complaints. Women generally believe

that sexuality is not influenced negatively by the menopause. Only women who view menopause as a medical condition show a clear tendency to start the use of HRT.

Hormone replacement therapy use rates, especially in Europe, are in general low and vary between countries from 3 to 13%. Less than 25% of the GPs in the UK, the Netherlands and Finland stated hormones should be given preventively. Surgical menopause, educational level, former use of anticonceptiva, menopausal status and vasomotor complaints are determinants for HRT use. The compliance with HRT is low; most studies indicate that more than 50% of women take HRT for a year or less.

Chapter 2

The climacteric is accompanied by many changes in life, which may give rise to a variety of complaints. Thus, it may be difficult to discern to what extent the climacteric is related to well-being.

The association between menopausal status and well-being was determined in a population of 2729 women aged 45 to 60 years. A self-administered questionnaire was filled out and returned by 1947 women (response 71.3%). Well-being was measured by the Inventory of Subjective Health and the three subscales of the Sickness Impact Profile: (i) social functioning, (ii) emotions, feelings and sensations and (iii) intellectual functioning. The relationship between menopausal status and well-being was estimated using linear regression analysis, while adjusting for age and other potential confounding variables, including Body Mass Index, smoking behaviour, education, work outside the home, parity, way of cohabitation, difference in age with the partner and partner's employment.

The results show that early perimenopausal women report a lower level of well-being as compared to premenopausal women on all three SIP scales. Early postmenopausal women report a lower level of well-being on the SIP emotions, feelings and sensations. Intermediate postmenopausal women have a lower level of well-being on the ISH only. Finally, late postmenopausal women have a lower level of well-being on the SIP social functioning and SIP emotions feelings and sensations. We tentatively conclude that the influence of the climacteric on well-being independent of confounders is primarily found in behavioural functioning in the daily life of a woman.

Chapter 3

There are equivocal conceptions of the association between vasomotor symptoms and well-being. The aim of our study was to determine more closely the relationship between vasomotor symptoms, well-being and climacteric status according to the last menstrual bleeding and according to the women themselves.

This relationship was investigated in a population of 2729 women aged 45-60 years.

A self administered questionnaire was filled out and returned by 1947 (71.3%) women. Well-being was measured by the Inventory of Subjective Health (ISH) and three subscales of the Sickness Impact Profile (SIP). Women were categorized as having vasomotor symptoms when they reported severe sweating and/or hot flushes. A logistic regression analysis was performed using dichotomized well-being scores as dependent variable and the presence of vasomotor symptoms as independent variable, adjusting for selected confounders.

In this cross-sectional study we found that the relationship between vasomotor symptoms and well-being was dependent on the climacteric status. Pre- and (middle and late) postmenopausal women with vasomotor symptoms more often experienced a relatively lower level of well-being compared to women without these symptoms. However, in the perimenopause there was no difference in well-being between women with or without vasomotor symptoms, when the prevalence of vasomotor symptoms is at its highest level. In conclusion we suggest that, next to hormone replacement treatment, well-being may improve considerably when women are better informed about the presence and significance of vasomotor symptoms in pre- and postmenopause.

Chapter 4

This study aims to answer the following questions: (i) what is the attitude of women in the climacteric years towards menopause (ii) what is the association between attitude towards menopause and well-being (iii) to what extent is medical attention determined by both well-being and attitude towards menopause.

All 2729 women aged 45-60 years living in a suburb of Rotterdam were sent a questionnaire. Of these 1947 (71.3%) were returned. Attitude was measured on 5 point rating scales using 28 items that have been used in other studies. Well-being was measured by the Inventory of Subjective Health and the three subscales of the Sickness Impact Profile. Medical attention was measured by asking the women whether they were currently being treated by GP or specialist.

Results show that three clusters of attitudes towards menopause exist: two clusters encompass items reflecting attitudes towards disadvantages and advantages of the menopause, one cluster encompasses items reflecting attitudes towards (medical) treatment of the menopause. On the whole, women answer neutrally to items relating menopause with disadvantages and tend to agree with items relating menopause with advantages. The women slightly agree, premenopausal women more than others, with items that are in favour of treatment of menopausal complaints. Agreement with items on the disadvantage cluster is moderately associated with a low level of well-being, whereas agreement with items on the advantage cluster is slightly associated with a high level of well-being; the treatment cluster is not associated with well-being. Both relative low well-being and agreement with items on the treatment cluster are statistically

significantly associated with medical attention.

Chapter 5

The objective of the study was to assess the opinion of women about the use of hormone replacement therapy (HRT) in relation to continuation or re-induction of menstrual cycles after menopause.

The study was population-based cross-sectional using a postal questionnaire in Krimpen aan den IJssel, a commuter suburb of Rotterdam.

The participants were all 2729 women living in Krimpen aan den IJssel aged 45-60 years, of whom 1947 (71.3%) responded. The main outcome measure was an opinion on monthly or trimonthly withdrawal bleedings with HRT.

The results showed 16.9% of all women have no or little objection to use of HRT with monthly withdrawal bleedings. There is a marked difference between premenopausal women (32.4% have no or little objection) and postmenopausal women (only 9.2% have no or little objection). Trimonthly cycles during HRT tend to be perceived as more acceptable (41.4% of premenopausal women and 11.8% of postmenopausal women have no or little objection).

It is concluded that a reasonable proportion of premenopausal women accept continuation of the menstrual cycle with HRT. There is a preference for trimonthly cycles above monthly withdrawal bleedings. Most postmenopausal women object to having withdrawal bleedings with HRT, irrespective of a monthly or trimonthly cycle. Research should continue on schedules without withdrawal bleedings.

Chapter 6

The aim of the present study was to ascertain the cumulative incidence of first hormone replacement therapy (HRT) and the factors that predict its prescription.

In a general population 1689 women were followed for 9 months in order to trace first HRT prescriptions. Determinants (well-being, attitude towards menopause, menopausal status and another 9 variables) were measured by means of a questionnaire. Data analyses were performed for all women and for women with or without typical climacteric complaints.

The cumulative 9 month incidence of HRT was 6.2%. For women without typical complaints a lower level of well-being (odds ratio 5.5; 95% CI 1.9-15.5) and the former use of the contraceptive pill (odds ratio 4.6; 95% CI 1.0-20.5) were independently associated with HRT prescription. For women with typical complaints a positive attitude towards "menopause should be treated" (odds ratio 3.8; 95% CI 1.8-8.0) was a determinant of HRT prescription. The cumulative incidence of HRT prescription is high, but from additional data it is apparent that within a period of one year and nine months

the majority of women stop taking HRT. For women without typical complaints, physicians prescribe HRT five times more often to those with a lower level of well-being. For women with typical complaints the physician's prescription is primarily related to the woman's attitude towards (medical) treatment of the menopause.

Chapter 7

Little is known about the duration of the use of HRT. The aim of this study is (i) to assess the mean duration of use of HRT in general practice and (ii) to determine which variables predict the duration of HRT use.

A general population of 1689 women aged 45-60 years and enlisted in 5 group practices of general practitioners were followed for 9 months to trace first HRT prescriptions. The 103 women who were presented HRT were all followed for a period of 2¼ year. Duration of HRT was assessed by using the data provided on the dispensation of HRT. Possible determinants of duration of use such as attitude towards menopause, menopausal status and another 6 variables were measured by means of a questionnaire.

The 103 women were hardly ever prescribed HRT with a preventive purpose. More than 60% of the women stopped their HRT within 6 months and only 8% of the women remained for more than 2 years on HRT. The mean duration of use was 7 months. Determinants that significantly predicted the duration of HRT use were age, attitude towards treatment of the menopause and the group practice. We conclude that the mean duration is very low, even if all indications are short term, i.e. for the alleviation of menopausal symptoms. Apparently, women are presently unwilling to take HRT for longer periods.

Chapter 8

In the conclusive chapter the findings of the previous chapters are discussed, especially the implications for the physician are given.

SAMENVATTING

SAMENVATTING

Hoofdstuk 1

Middels literatuurstudie trachtten we een antwoord te vinden op de volgende vragen: (i) bestaat er een climacterieel syndroom in termen van symptomen en klachten, uitsluitend en onafhankelijk gerelateerd aan de menopauzale status (ii) bestaat er een associatie tussen serum hormoonspiegel en een climacterieel syndroom (iii) verbetert oestrogene substitutietherapie symptomen, klachten en welbevinden van een mogelijk climacterieel syndroom (iv) welke zijn de attitudes en verwachtingen van de vrouwen zelf ten aanzien van de overgang (v) wat is er bekend over het gebruik van hormonale substitutietherapie onder vrouwen.

De meeste studies stelden vast dat vasomotorische symptomen en vaginale droogte significante gerelateerd zijn aan de menopauzale status. Onderzoek in Westerse landen laat een duidelijk verband zien tussen de prevalentie van opvliegingen en nachtelijk zweten enerzijds en menopauzale status anderzijds. De prevalentie van deze symptomen is relatief laag onder Japanse vrouwen. In het algemeen blijkt uit studies dat de overgang een geringe invloed heeft op welbevinden en seksualiteitsbeleving. Sommige onderzoeken rapporteerden dat in het climacterium een relatie bestaat tussen vasomotorische klachten en atypische klachten (slaapstoornissen, minder sociaal functioneren). De meeste klachten in de overgangsjaren zijn niet geassocieerd met de overgang per se, maar worden verklaard door een diversiteit aan andere factoren. Uitgaande van recente gegevens kan gesteld worden dat, los van typische klachten, er weinig aanwijzingen zijn om te kunnen spreken van een goed gedefinieerd climacterieel syndroom.

Ofschoon een duidelijke vermindering in oestrogeenproductie karakteristiek is voor de menopauze, bestaat er geen verschil in hormoon spiegels tussen vrouwen met of zonder opvliegingen.

Een gerandomiseerde dubbel blind en placebo gecontroleerde studie is de geaccepteerde wetenschappelijke methode om vast te stellen dat behandeling met oestrogenen symptomen en klachten vermindert en het welbevinden verbetert.

Onttrekkingsbloedingen, een gevolg van de combinatie van oestrogenen met progestativa, vormen een groot probleem bij blinding van het onderzoek. Om blinding te kunnen bereiken werden sommige onderzoeken verricht onder vrouwen zonder baarmoeder, waarbij uiteraard de generaliseerbaarheid van de resultaten in het gedrang komt. Andere studies gebruikten alleen oestrogenen. Uit de weinige gerandomiseerde en dubbel blind uitgevoerde trials kunnen we concluderen dat therapie met oestrogenen: (i) een significant en substantieel effect heeft op het verlichten van vasomotorische symptomen en vaginale droogte (ii) een matige verbetering geeft van stemming, slaapstoornissen, seksueel functioneren en welbevinden; hoewel deze verbeteringen worden gereduceerd door het toevoegen van progestagenen (iii) een uitgesproken placebo effect heeft ten

aanzien van deze symptomen, klachten en welbevinden.

De meeste vrouwen hebben een neutrale tot positieve attitude ten opzichte van de overgang. Vrouwen die de overgang al hebben ervaren, zijn een meer positieve attitude toegedaan dan premenopauzale vrouwen. Het hebben van negatieve attitudes is duidelijk gerelateerd met klachten. Over het algemeen menen vrouwen dat de seksualiteit door de overgang niet negatief wordt beïnvloed. Slechts vrouwen die de overgang als een medische conditie beschouwen vertonen een duidelijke neiging om HST te gaan gebruiken.

Vooraf in Europa zijn de cijfers over gebruik van hormoon substitutietherapie (HST) over het algemeen laag en variëren van land tot land van 3 tot 13%. Minder dan 25% van de huisartsen in Engeland, Nederland en Finland zijn de mening toegedaan dat HST om preventieve redenen moet worden voorgeschreven. Chirurgische menopauze, opleidingsniveau, eerder gebruik van orale anticonceptiva, menopauzale status en vasomotorische klachten zijn determinanten van HST gebruik. De compliantie met HST is laag; de meeste studies laten zien dat meer dan 50% van de vrouwen HST niet langer dan een jaar gebruikt.

Hoofdstuk 2

De overgang wordt vergezeld door vele veranderingen in het leven, welke een verscheidenheid aan klachten kunnen oproepen. Het kan derhalve moeilijk zijn te bepalen in welke mate de overgang op zichzelf samenhangt met het welbevinden.

Het verband tussen de menopauzale status en welbevinden werd onderzocht in een populatie van 2729 vrouwen in de leeftijd van 45 tot 60 jaar. Een zelf ingevulde vragenlijst werd teruggestuurd door 1947 vrouwen (response 71,3%). Welbevinden werd gemeten met de VOEG (Vragenlijst Onderzoek Ervaren Gezondheid) en drie subschalen van de SIP (Sickness Impact Profile): (i) sociale interactie, (ii) emotioneel gedrag en (iii) alertheid en intellectueel functioneren. De relatie tussen menopauzale status en welbevinden werd bepaald middels lineaire regressie analyse, waarbij gecorrigeerd werd voor leeftijd en andere versturende variabelen zoals Quetelet index, roken, opleiding, werk buitenshuis, aantal kinderen, samenlevingsvormen, verschil in leeftijd met de partner en werkstatus van de partner.

De resultaten laten zien dat vroeg perimenopauzale vrouwen een lager niveau van welbevinden rapporteren vergeleken met premenopauzale vrouwen op de drie subschalen van de SIP. Vroeg-postmenopauzale vrouwen rapporteren een lager niveau van welbevinden op de SIP emotioneel gedrag. Vrouwen halverwege de postmenopauze hebben een lager niveau van welbevinden gemeten met de VOEG. Tenslotte hebben vrouwen die de overgang achter zich hebben een lager welbevinden op de SIP sociale interactie en de SIP emotioneel gedrag. Met enige terughoudendheid concluderen wij, dat de invloed van de overgang op het welbevinden, onafhankelijk van versturende

variabelen, voornamelijk aanwezig is in het dagelijks functioneren van de vrouw.

Hoofdstuk 3

Er bestaan tegenstrijdige opvattingen over het verband tussen vasomotorische klachten en welbevinden. Het doel van onze studie was de relatie vast te stellen tussen vasomotorische klachten, welbevinden en de climacteriële status bepaald naar de laatste menstruatie en bepaald naar de indeling van de vrouwen zelf.

Dit verband werd onderzocht in een populatie van 2729 vrouwen in de leeftijd van 45 tot 60 jaar. Een zelf ingevulde vragenlijst werd door 1947 (response 71,3%) vrouwen teruggestuurd. Welbevinden werd gemeten middels de VOEG (Vragenlijst Onderzoek Ervaren Gezondheid) en drie subschalen van de SIP (Sickness Impact Profile). Vrouwen werden ingedeeld in de groep met vasomotorische klachten wanneer zij ernstig zweten en/of opvliegers rapporteerden. Een logistische regressie met correctie voor geselecteerde versturende variabelen werd uitgevoerd; hierbij vormden de gedichotomiseerde scores op de 4 schalen van welbevinden de afhankelijke variabelen. De onafhankelijke variabele was het al dan niet aanwezig zijn van vasomotorische symptomen.

In deze dwarsdoorsnede studie vonden we dat het verband tussen vasomotorische symptomen en welbevinden afhankelijk was van de climacteriële status. Pre- en (midden en laat) postmenopauzale vrouwen met vasomotorische symptomen ervaren vaker een relatief lager niveau van welbevinden dan vrouwen zonder deze symptomen. Echter, in de perimenopauzale fase, wanneer de prevalentie van vasomotorische klachten het hoogst is, bestond er geen verschil in welbevinden tussen vrouwen met of zonder vasomotorische klachten. Het is aannemelijk dat vasomotorische symptomen door andere dan farmacologische middelen kunnen worden beïnvloed. Samenvattend stellen wij dat naast hormonale substitutietherapie het welbevinden aanzienlijk kan verbeteren wanneer vrouwen beter worden geïnformeerd over de aanwezigheid en de betekenis van vasomotorische symptomen in de pre- en postmenopauze.

Hoofdstuk 4

Deze studie wil de volgende vragen beantwoorden: (i) wat is de attitude ten aanzien van de overgang van vrouwen in de overgangsjaren (ii) wat is het verband tussen de attitude ten aanzien van de overgang en welbevinden (iii) in welke mate dragen welbevinden, als wel attitude bij aan de verklaring van doktersbezoek.

Alle 2729 vrouwen in de leeftijd van 45 tot 60 jaar, welke in een voorstad van Rotterdam wonen, kregen een vragenlijst per post toegezonden; van hen stuurden 1947 (71,3%) vrouwen deze vragenlijst terug. Attitude werd gemeten op een 5-punts schaal bestaande uit 28 vragen, welke ook in andere studies werden gebruikt. Welbevinden werd gemeten middels de VOEG (Vragenlijst Onderzoek Ervaren Gezondheid) en drie

subschalen van de Sickness Impact Profile. Doktersbezoek werd gemeten door de vrouwen te vragen of zij onlangs door de huisarts of medisch specialist behandeld werden.

De resultaten laten zien dat er drie groepen items bestaan: twee groepen omvatten items die ofwel een positieve ofwel een negatieve houding ten aanzien van de overgang weergeven, de derde groep omvat items welke een (medische) behandeling van de overgang voorstaan. Over het algemeen antwoorden vrouwen neutraal op items welke een negatieve voorstelling van de overgang geven en neigen zij het eens te zijn met de items welke een positief beeld van de overgang geven. Vrouwen zijn het matig eens met de items welke een voorkeur weerspiegelen voor behandeling van overgangsklachten, hetgeen sterker tot uitdrukking komt bij premenopauzale vrouwen. Instemming met items welke een negatief beeld van de overgang geven is geassocieerd met een laag niveau van welbevinden, terwijl instemming met items welke een positief beeld van de overgang schetsen in geringe mate geassocieerd is met een hoog niveau van welbevinden; de items welke een behandeling van overgangsklachten voorstaan zijn niet gerelateerd aan welbevinden. Zowel een laag welbevinden als instemming met items dat overgangsklachten behandeld moeten worden zijn statistisch significant geassocieerd met doktersbezoek.

Hoofdstuk 5

Het doel van de studie was de mening te bepalen van vrouwen over het gebruik van hormoon substitutietherapie (HST), waarbij het effect gezien werd van de voortzetting of het weer beginnen van de menstruele cyclus na de menopauze.

De studie was een dwarsdoorsnede van een populatie in Krimpen a/d IJssel, een voorstad van Rotterdam, waarbij gebruik werd gemaakt van een per post opgestuurde vragenlijst.

Alle 2729 vrouwen in de leeftijd tussen 45 en 60 jaar wonende in Krimpen a/d IJssel werden benaderd, hiervan deden er 1947 (71.3%) mee. De mening over een maandelijkse of een driemaandelijkse onttrekkingsbloeding als gevolg van HST werd gemeten.

De resultaten lieten zien dat 16,9% van alle vrouwen geen of weinig bezwaar hadden tegen gebruik van HST met maandelijkse onttrekkingsbloedingen. Een duidelijk verschil bestaat er tussen premenopauzale vrouwen (32,4% heeft geen of weinig bezwaar) en postmenopauzale vrouwen (slechts 9,2% heeft geen of weinig bezwaar).

Geconcludeerd kan worden dat een redelijk gedeelte van de premenopauzale vrouwen accepteert dat de menstruele cyclus doorgaat. Een lichte voorkeur van driemaandelijkse cycli boven maandelijkse onttrekkingsbloedingen is aanwezig. De meeste postmenopauzale vrouwen hebben bezwaar tegen onttrekkingsbloedingen ten gevolge van HST of dit nu maandelijks dan wel driemaandelijks is. Onderzoek naar behandelingsstrategieën zonder onttrekkingsbloedingen wordt aanbevolen.

Hoofdstuk 6

Het doel van deze studie was het vaststellen van de cumulatieve incidentie van het eerste gebruik van hormonale substitutietherapie (HST) en de factoren welke dit bepalen.

Om de eerste HST recepten te bepalen werden in een algemene populatie 1689 vrouwen gedurende 9 maanden gevolgd. Determinanten (welbevinden, attitude ten opzichte van de overgang, menopauzale status en 9 andere persoonsgebonden variabelen) werden gemeten middels een vragenlijst. Data analyse werd uitgevoerd voor alle vrouwen en afzonderlijk voor vrouwen met of zonder typische climacteriële klachten.

De cumulatieve 9-maands incidentie van HST was 6,2%. Voor vrouwen zonder typische klachten waren een laag niveau van welbevinden (odds ratio 5.5; 95% CI 1.9-15.5) en het gebruik van de anticonceptieve pil in het verleden (odds ratio 4.6; 95% CI 1.0-20.5) onafhankelijk geassocieerd met HST recepten. Voor vrouwen met typische klachten was een positieve attitude ten aanzien van "de overgang moet worden behandeld" (odds ratio 3.8; 95% CI 1.8-8.0) een determinant van HST voorschriften. De cumulatieve incidentie van HST voorschriften is hoog, maar uit aanvullende gegevens over een periode van 1 jaar en 9 maanden blijkt het merendeel van de vrouwen al gestopt te zijn met HST. Artsen schrijven vrouwen zonder typische klachten en met een laag niveau van welbevinden vijfmaal vaker HST voor. Daarnaast wordt voor vrouwen met typische klachten het voorschrijven van HST het sterkst bepaald door de attitude van de vrouw betreffende (medisch) behandelen van de overgang.

Hoofdstuk 7

Over de duur van het gebruik van HST is weinig bekend. Het doel van deze studie is: (i) de gemiddelde gebruiksduur van HST in de algemene praktijk vast te stellen en (ii) te bepalen welke variabelen de gebruiksduur van HST voorspellen.

Een algemene populatie van 1689 vrouwen in de leeftijd van 45 tot 60 jaar behorende tot vijf huisartsgroepspraktijken werd gedurende 9 maanden gevolgd om zodoende eerste HST recepten te traceren. De 103 vrouwen, welke een HST recept meekregen, werden allen 2¼ jaar gevolgd. De duur van het gebruik van HST werd gemeten aan de hand van hoeveelheid en dosering van de verstrekte middelen op het recept. Mogelijke determinanten van de duur van het gebruik, zoals attitude ten opzichte van de overgang, menopauzale status en een ander zestal variabelen, werden gemeten middels een vragenlijst.

De 103 vrouwen kregen zelden HST voorgeschreven voor preventieve doeleinden. Meer dan 60% van de vrouwen stopt hun gebruik van HST binnen 6 maanden, slechts 8% van de vrouwen gebruikt HST langer dan 2 jaar. De gemiddelde gebruiksduur bedroeg 7 maanden. Leeftijd, de attitude "de overgang dient behandeld te worden" en

de huisartsgroepspraktijk waren determinanten welke significant de gebruiksduur van HST voorspelden. Wij concluderen dat de gemiddelde gebruiksduur kort is, zelfs als alle indicaties voor de korte termijn zijn, dat wil zeggen voor de verlichting van menopauzale symptomen. Blijkbaar gebruiken vrouwen op dit moment HST niet voor een langere periode.

Hoofdstuk 8

In het slothoofdstuk worden de resultaten uit de vorige hoofdstukken bediscussieerd. Daarnaast wordt aandacht geschonken aan de betekenis van de resultaten voor de arts.

DANKWOORD

Velen ben ik dank verschuldigd bij de totstandkoming van dit proefschrift.

Allereerst dank ik alle 1947 vrouwen in Krimpen a/d IJssel, die de moeite hebben genomen een lange vragenlijst in te vullen.

Vervolgens richt ik mij tot mijn eerste promotor Prof. Dr. H.J. Dokter. Beste Heert, dank voor alle rust en deskundigheid in je begeleiding. Je gaf me de gelegenheid en gastvrijheid te werken op het Rotterdams Universitair Huisartsen Instituut en je wees de juiste medewerkers voor dit project aan.

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Dr. R. Barentsen, beste Ronald, jouw taak was veelzijdig. Samen met Prof. Dr. Drogendijk waren jullie de initiatoren van het project, je wist de financiering van dit project te regelen. Je gaf op een prettige manier kritiek en jij was bereid in de avonduren vanuit Deurne naar Rotterdam te komen, om de projectvergaderingen bij te wonen, hiervoor mijn dank.

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Mijn "maat" huisarts drs. D.S. Rooker, beste Dik jij hebt geregeld jouw agenda aan mij aangepast als ik weer eens naar het instituut moest of later thuiskwam, hiervoor dank ik je hartelijk.

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De gemeente Krimpen a/d IJssel, met name de heer Bijdevier, dank ik hartelijk voor het "aanleveren" van onze doelgroep.

Mevrouw de Haan-Meynell, dank ik voor haar correcties van de Engelse teksten.

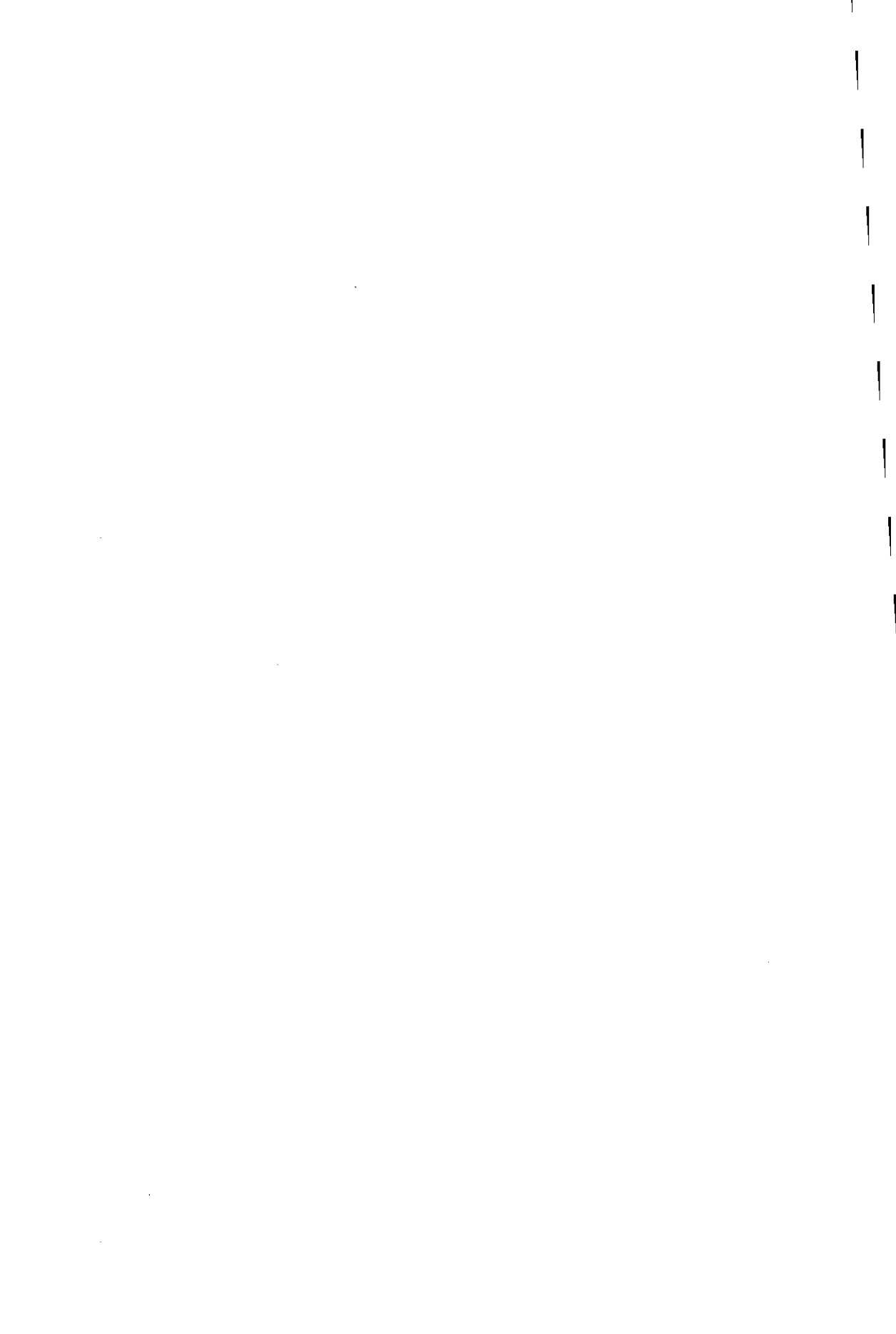
Bescheiden op de achtergrond, maar voor mij een onmiskenbare steun mijn vrouw Joke en mijn dochters Leonie, Yvette en Josephine. Jullie moesten vaak alleen op stap, of kwamen gezellig op mijn werkkamer "buurten" met koffie of gewoon "lukt het". Dank jullie wel.

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ABOUT THE AUTHOR

Frans PMJ Groeneveld was born on March 2nd, 1949 in Rotterdam, the Netherlands. He attended secondary school (HBS-B) at the Sint Franciscus College in Rotterdam and graduated in 1967. He entered the medical school of the Erasmus University Rotterdam in 1967 and received his medical degree in 1973. After his medical degree, he followed the newly started vocational training for general practitioners and was entered in the register of qualified General Practitioners of the Royal Dutch Medical Association in 1974. After this he joined the army and was active on the department of internal medicine of the military hospital in The Hague. From 1975 to mid 1976 he was part-time research associate of the department of general practice Rotterdam (Head: Prof Dr HJ Dokter). In January 1976 he started a general practice in Krimpen a/d IJssel, a commuter suburb of Rotterdam. In his general practice, he has received many medical students for educational programmes. He is married with Joke van Waas and has three daughters: Leonie, Yvette and Josephine.



APPENDIX I

LETTER TO ALL WOMEN AGED 45-60 YEARS LIVING IN KRIMPEN AAN DEN IJSSEL



ERASMUS UNIVERSITEIT ROTTERDAM
Afd. Huisartsgeneeskunde
Afd. Vrouwenziekten

Krimpen a/d IJssel, April 1990

Dear Madam,

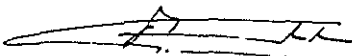
In Krimpen aan den IJssel, I want to examine women's health and their opinion as to health and medical care. This study will take place with the support of the Department of General Practice (Head Prof. Dr. H.J. Dokter) and the Department of Gynaecology and Obstetrics (Head: Prof. Dr. A.C. Drogendijk), both of the Erasmus University Rotterdam. The group of women, now being approached for this, are in the age group 45-60 years, as you are. Your cooperation is indispensable for the success of this study. Enclosed you will find a questionnaire.

I would appreciate it very much, if you would answer the questions. It takes about half an hour of your time. By means of the enclosed envelope, you can send back the questionnaire free post.

Later on it may perhaps be necessary to acquire additional data, therefore the questionnaire is sent to you by name. The questionnaire will be processed anonymously and only the undersigned knows the number and the name belonging to it.

If you would like a summary of the results of the study, please indicate this on the last page of the questionnaire.

Your sincerely,



F.P.M.J. Groeneveld, general practitioner
Meerkoetstraat 79
2922 GM Krimpen a/d IJssel

APPENDIX II

QUESTIONNAIRE

ERASMUS UNIVERSITY ROTTERDAM

Department of General Practice
Department of Obstetrics and Gynaecology**Women's Health Questionnaire**

A. If you regularly experienced the item concerned the PAST TWO WEEKS, please answer the question with circling 'Yes' or 'No' exclusively.

- | | |
|---|------------|
| 1. Feeling of tiredness..... | 1. YES/NO |
| 2. Listlessness..... | 2. YES/NO |
| 3. Sooner fatigued than normal..... | 3. YES/NO |
| 4. Not rested in the morning..... | 4. YES/NO |
| 5. Not tired after a strenuous day..... | 5. YES/NO |
| 6. Fit..... | 6. YES/NO |
| 7. Stomach upset..... | 7. YES/NO |
| 8. Stomach trouble..... | 8. YES/NO |
| 9. Pains in stomach region..... | 9. YES/NO |
| 10. Full and bloated feeling in the stomach.... | 10. YES/NO |
| 11. Belly upset..... | 11. YES/NO |
| 12. Bowel motion every day..... | 12. YES/NO |
| 13. Less appetite..... | 13. YES/NO |
| 14. Feeling hungry..... | 14. YES/NO |
| 15. Excessive thirst..... | 15. YES/NO |
| 16. Unpleasant sweet taste..... | 16. YES/NO |
| 17. Loss of hair..... | 17. YES/NO |
| 18. Too thin..... | 18. YES/NO |
| 19. Overweight..... | 19. YES/NO |
| 20. Acne/boils..... | 20. YES/NO |
| 21. Severe sweating..... | 21. YES/NO |
| 22. Nervous..... | 22. YES/NO |
| 23. Excited..... | 23. YES/NO |
| 24. Irritated..... | 24. YES/NO |
| 25. Tight in the chest..... | 25. YES/NO |
| 26. Short of breath..... | 26. YES/NO |
| 27. Pains in the chest..... | 27. YES/NO |
| 28. Heart palpitations..... | 28. YES/NO |
| 29. Watering eyes..... | 29. YES/NO |
| 30. Pains around the eyes..... | 30. YES/NO |
| 31. Headache..... | 31. YES/NO |
| 32. Dizzy..... | 32. YES/NO |
| 33. Roaring in the ears..... | 33. YES/NO |
| 34. Dry vagina..... | 34. YES/NO |
| 35. Itching..... | 35. YES/NO |
| 36. Accident prone..... | 36. YES/NO |
| 37. Bad effect of alcoholic beverages..... | 37. YES/NO |
| 38. Sleepy/sluggish..... | 38. YES/NO |
| 39. Sleeplessness..... | 39. YES/NO |
| 40. Fall asleep at once..... | 40. YES/NO |
| 41. Fall asleep at home from tiredness..... | 41. YES/NO |
| 42. Ache in bones and muscles..... | 42. YES/NO |
| 43. Backache..... | 43. YES/NO |
| 44. Numbed feelings in the limbs..... | 44. YES/NO |
| 45. Shaking hands..... | 45. YES/NO |
| 46. Weak aching feet..... | 46. YES/NO |
| 47. Cold fingers and toes..... | 47. YES/NO |
| 48. Coughing..... | 48. YES/NO |
| 49. Sneezing..... | 49. YES/NO |
| 50. Clearing the throat..... | 50. YES/NO |
| 51. Blocked nose..... | 51. YES/NO |
| 52. Feeling a lump in the throat..... | 52. YES/NO |

- B. 1. My height is.....m
2. My weight is.....kg
3. AT THIS MOMENT I am under the treatment of my general practitioner and/or specialist (circle the right answer).
1. NO
2. YES
- if yes, for what?.....
- Are you being prescribed medicines momentarily for this?
(circle).
1. NO
2. YES
4. IN THE PAST 12 MONTHS I have been under treatment from my general practitioner and/or specialist.
(circle).
1. NO
2. YES
- Was medicine prescribed for this?
- if yes, for what?.....
5. DURING THE PAST TWO WEEKS, I have used medicines (including Homeopathic and chemists remedies such as stomach tablets, pain-killers etc. I.e all the medicines, which you have taken the past two weeks, wether or not prescribed by a doctor.
(circle).
1. NO
2. YES
- if yes, which ones (write what is on the box)
-
6. This question concerns your smoking habits
(circle)
1. I HAVE NEVER SMOKED (OR ONLY ONE PER WEEK)
2. I HAVE SMOKED IN THE PAST
3. I DO SMOKE MOMENTARILY
- if you smoke
(circle) 1. 1-5 PER DAY
2. 6-15 PER DAY
3. MORE THAN 15 PER DAY

B. 7. This question encloses several parts and concerns YOUR MENSTRUATION.

- a) My last menstruation took place on
(date or only the year)
- b) During THE LAST 12 MONTHS I have had one or more menstruations
(circle your answer)
1. NO
 2. YES, (if circled, please answer c, d and e)
 - c) My menstruation cycles have CHANGED the last year as compared to the preceding year.
 1. NO
 2. YES
 - d) Last year I have had times a menstruation
 - e) If you have had menstruations during the past year, were these menstruations REGULAR
(please circle your answer)?
 1. NO
 2. YES

8. This question is about a possible HYSTERECTOMY you have undergone

- a) My uterus has been removed (circle)

1. NO
2. I DON'T KNOW
3. YES

if removed in which year 19

Have both your ovaries been removed?

1. NO
2. I DON'T KNOW
3. YES

9. This question encloses the use of ORAL ANTICONCEPTIVA ("THE PILL")

Have you used this?
(circle)

1. NO, NEVER USED
2. YES

if yes (circle one or more possibilities)

1. USED IN THE PAST SHORTER THAN 3 MONTHS
2. USED IN THE PAST LONGER THAN 3 MONTHS
STOPPED 19 (fill in the year).
3. I USE IT MOMENTARILY
SINCE 19 (fill in the year).

C. By the following questions, answer the statements you think are applicable to your PRESENT SITUATION and that are also connected to your health and well-being (Circle YES or NO)

- | | |
|---|------------|
| 1. I continually say how inferior and useless I feel
Eg. that I am an inconvenience to others | 1. YES/NO |
| 2. I began to cry or laugh without reason..... | 2. YES/NO |
| 3. I often complain of/groan with pain an discomfort | 3. YES/NO |
| 4. I have tried to end my life..... | 4. YES/NO |
| 5. I am nervous or restless..... | 5. YES/NO |
| 6. I continually rub or hold/grip parts of my body that hurt or feel unpleas-
ant/ache..... | 6. YES/NO |
| 7. I react irritably or impatiently with myself | 7. YES/NO |
| Eg. I say bad/evil/wicked things about myself, give myself the blame for things that
happen | |
| 8. I speak of the future without hope..... | 8. YES/NO |
| 9. I suddenly become fearful..... | 9. YES/NO |
| 10. I don't go out visiting/socially..... | 10. YES/NO |
| 11. I go out socially less often..... | 11. YES/NO |
| 12. I am less interested in other peoples' problems,
Eg. I don't listen when told about them or offer to help..... | 12. YES/NO |
| 13. I am often irritable with people around me | 13. YES/NO |
| Eg. I turn on them, answer sharply, criticize easily | |
| 14. I don't show my feelings easily | 14. YES/NO |
| 15. I take part less often in group activities..... | 15. YES/NO |
| 16. I don't stay as long when visiting friends..... | 16. YES/NO |
| 17. I avoid having visitors..... | 17. YES/NO |
| 18. I am less active sexually..... | 18. YES/NO |
| 19. I often show that I am concerned about what could happen to my
health..... | 19. YES/NO |
| 20. I talk less to the people around me..... | 20. YES/NO |
| 21. I am more demanding of others | 21. YES/NO |
| 22. Most of the time I remain alone..... | 22. YES/NO |
| 23. I am disagreeable to my nearest relations/family members/house-
maids..... | 23. YES/NO |
| 24. I regularly turn on my relatives/housemaids | 24. YES/NO |
| Eg I hit them, scream, throw things at them. | |
| 25. I isolate myself from the rest of my nearest relatives/family members/housemaids | 25. YES/NO |
| 26. I no longer have the normal concern or interest in my children or fam-
ily..... | 26. YES/NO |
| 27. I joke less than usual with nearest relatives/family members/housemaids | 27. YES/NO |
| 28. I'm confused and begin several things simultaneously | 28. YES/NO |
| 29. I have more small accidents eg. I drop things/stumble etc | 29. YES/NO |
| 30. I react slowly to what is said and done | 30. YES/NO |
| 31. I don't finish things that I start | 31. YES/NO |
| 32. I have difficulties thinking things through and solving problems | 32. YES/NO |
| 33. I sometimes act as though I'm confused, have no knowledge of place and time etc | 33. YES/NO |
| Eg I don't know where I am, who is with me, in which direction I am going, I don't
know which day it is | |
| 34. I'm forgetful, | 34. YES/NO |
| Eg Where I've left things, appointments I have made | |
| 35. I can't concentrate on things for long | 35. YES/NO |
| 36. I make more mistakes/errors than usual..... | 36. YES/NO |
| 37. I have difficulty doing things which I have to concentrate or think about | 37. YES/NO |

D. This Women Health Questionnaire has been sent to all women in Krimpen a/d IJssel between the ages of 45 and 60 years. As during this period most women experience the menopause, we would like to hear **THE WOMEN'S OWN OPINION**, irrespective of whether you have begun the menopause or not.

Give, by marking a figure, your opinion about the next statements.

- 1 = completely agree
- 2 = a little agree
- 3 = neutral
- 4 = do not agree a little
- 5 = completely do not agree

For example:

During the menopause the hair in the face augments.....agree (1) (3) (4) (5) not agree

By marking figure 2 you are a little agreed with the statement the hair grows in the face, but you are not quite convinced, as you would mark 1.

	AGREE	DISAGREE
1. The climacteric brings many positive aspects	(1) (2) (3) (4) (5)	
2. Problems in the climacteric disappear spontaneously	(1) (2) (3) (4) (5)	
3. Women expecting complaints in the menopause will get them	(1) (2) (3) (4) (5)	
4. It is pleasant that pregnancy is not possible after the menopause	(1) (2) (3) (4) (5)	
5. One starts to feel old in the climacteric	(1) (2) (3) (4) (5)	
6. Women in the climacteric, with problems, should consult their GP	(1) (2) (3) (4) (5)	
7. In the climacteric women can stand less stress	(1) (2) (3) (4) (5)	
8. The climacteric coincides with bothersome complaints	(1) (2) (3) (4) (5)	
9. Complaints in the climacteric must NOT be treated with drugs	(1) (2) (3) (4) (5)	
10. Women with bothersome climacteric complaints must get hormone therapy	(1) (2) (3) (4) (5)	
11. The benefits of hormone therapy outweigh the risk	(1) (2) (3) (4) (5)	
12. After the climacteric sex is more pleasant	(1) (2) (3) (4) (5)	
13. In the climacteric a women often has more psychological problems	(1) (2) (3) (4) (5)	
14. Women in the climacteric must have the insight that physical changes are natural	(1) (2) (3) (4) (5)	
15. One grows mature and more self-confident in the climacteric	(1) (2) (3) (4) (5)	
16. Partners of postmenopausal women regard them as less sexual attractive	(1) (2) (3) (4) (5)	
17. Phenomena in the climacteric must be treated medically	(1) (2) (3) (4) (5)	
18. For the women the climacteric is an unpleasant period	(1) (2) (3) (4) (5)	
19. During the climacteric one feels less like undertaking something	(1) (2) (3) (4) (5)	
20. After the menopause the sexual relationship is better	(1) (2) (3) (4) (5)	

	AGREE	DISAGREE
21. One should have a preference for natural approaches (i.e. attending to nutritional requirements, vitamin supplements, exercise programs) for menopausal problems	(1)	(2) (3) (4) (5)
22. In the climacteric one often feels unwell	(1)	(2) (3) (4) (5)
23. The absence of the menstruation after menopause is a relief	(1)	(2) (3) (4) (5)
24. A women feels less attractive after the menopause	(1)	(2) (3) (4) (5)
25. Psychological problems women experience during the climacteric stand apart from co-occurring changes in life i.e. children leaving home, the death of parents	(1)	(2) (3) (4) (5)
26. After menopause a women have less sexual needs	(1)	(2) (3) (4) (5)
27. The cause of all problems in the climacteric is something that women can not control by themselves-something from outside	(1)	(2) (3) (4) (5)
28. After menopause one feels more free and more independent	(1)	(2) (3) (4) (5)

E. The following questions concern complaints and treatment during and after the menopause

1. In which phase, your own opinion, would you place yourself AT THIS MOMENT?
(circle your answer)

- 1. I HAVE NOT REACHED THE MENOPAUSE
- 2. I HAVE JUST REACHED THE MENOPAUSE
- 3. I AM IN THE MIDDLE OF THE MENOPAUSE
- 4. I HAVE REACHED THE END OF THE MENOPAUSE
- 5. I REACHED THE MENOPAUSE LONG AGO

Please will you answer the following questions, even if you have not reached the menopause!

2. Which complaints or symptoms do you think that are present during menopause, are REALLY caused by the menopause?
(please write in capital letters)

.....

3. Which of the above mentioned complaints (question 2) have you YOURSELF experienced during the last four weeks.
Please will you state after the complaint, whether this has occurred regularly or only occasionally?

COMPLAINT	REGULAR	SOMETIMES
For example: coughing		X
.....
.....
.....
.....

4. When the periods stop, several changes arise in a woman's body, which could be caused by a deficiency of female hormones and of which symptoms only become clear after many years.

A. Which complaints and disease DO YOU KNOW that are linked to a deficiency of female (estrogens) hormones?
(again write in capital letters please)

.....

B. If you have filled out 4A, please will you indicate, if you would take hormones FOR THE PREVENTION of the diseases and complaints mentioned by yourself
(circle your answer).

- 1. UNDER NO CIRCUMSTANCES WOULD I WANT HORMONE TREATMENT FOR PREVENTION THE ABOVE MENTIONED DISEASES AND COMPLAINTS.
- 2. I WOULD ONLY DO THIS, WHEN AFTER CONSULTATION WITH MY GENERAL PRACTITIONER THERE IS AN AUGMENTED CHANCE OF THE DISEASES AND COMPLAINTS MENTIONED BY MYSELF
- 3. HORMONE TREATMENT FOR THE PREVENTION OF THE COMPLAINTS AND DISEASES, AS MENTIONED BY MYSELF, APPEALS TO ME VERY MUCH.

4. I DON'T HAVE A CLEAR OPINION ABOUT THIS.

F. Complaints during the climacteric years can sometimes be treated beneficially with estrogens. The following questions refer to this.

1. Do you want to take hormonal treatment for climacteric complaints?
(circle your answer).

- 1. UNDER NO CIRCUMSTANCES WOULD I WANT HORMONE TREATMENT FOR CLIMACTERIC COMPLAINTS.
- 2. I WOULD ONLY TAKE HORMONE TREATMENT IF SUFFERING GREATLY FROM CLIMACTERIC COMPLAINTS.
- 3. I SHOULD TAKE HORMONE TREATMENT ALSO IN THE CASE OF LESS SERIOUS CLIMACTERIC COMPLAINTS TOO.
- 4. I DON'T HAVE A CLEAR OPINION ABOUT THIS.

2. a) When you still have got your uterus, your periods will continue (or restart) after menopause as a consequence of hormone treatment.
What is your opinion of hormonal treatment when your menstrual cycle will continue or restart once a month when using this treatment.
(circle one answer)

- 1. I HAVE NO OBJECTION.
- 2. I HAVE LITTLE OBJECTION.
- 3. I HAVE MUCH OBJECTION.
- 4. I DON'T WANT THAT.
- 5. I HAVE NO OPINION ABOUT IT.

2. b) And when your menstrual bleedings would continue or restart once every three months (circle one answer)

- 1. I HAVE NO OBJECTION.
- 2. I HAVE LITTLE OBJECTION.
- 3. I HAVE MUCH OBJECTION.
- 4. I DON'T WANT THAT.
- 5. I HAVE NO OPINION ABOUT IT.

3. Please indicate how you experience (or experienced) your periods by circling one of the following numbers

- 1. I HAVE/HAD VERY MUCH DISCOMFORT DURING MY MENSTRUATIONS.
- 2. I HAVE/HAD MUCH DISCOMFORT DURING MY MENSTRUATION.
- 3. I HAVE/HAD SCARCELY ANY DISCOMFORT DURING MY MENSTRUATIONS.
- 4. I HAVE/HAD NO DISCOMFORT DURING MY MENSTRUATIONS.

4. DO YOU TAKE AT THIS MOMENT estrogens for the treatment of climacteric complaints?

- 1. NO
- 2. YES

If yes: WHICH ONES:

SINCE HOW MANY MONTHS:

5. Apart from treatment with hormones, there are other possibilities to lessen or prevent complaints caused by the transition.

We think hereby of discussion groups, homeopathic medicines and other non-hormonal medicines.

Could you indicate below which treatment(s) you prefer and why?

.....

.....

G. We start now with THE LAST PART of the questionnaire. This deals with some general data about yourself:

1. I was BORN: DAY MONTH YEAR
2. My MARITAL STATUS is:
(circle one answer)
 1. MARRIED
 2. SINGLE
 3. DIVORCED
 4. WIDOWED
3. Which EDUCATION(S) did you follow ?
(more answers are possible, circle)
 1. PRIMARY SCHOOL
 2. VOCATIONAL SCHOOL (LOWER SECONDARY)
 3. LOWER SECONDARY SCHOOL
 4. SECONDARY SCHOOL
 5. HIGHER SECONDARY EDUCATION
 6. VOCATIONAL SCHOOL (ADVANCED LEVEL)
 7. UNIVERSITY
4. I am a HOUSEWIFE.
(circle).
 1. YES
 2. NO
5. a) I have a PROFESSION
(circle).
 1. NO
 2. YES——> Which PROFESSION.....

b) do you work, apart from being a housewife, outside the home
(circle).

 1. NO
 2. YES——> if yes:
a) HOW MANY HRS/WK.....
b) which JOB:
.....
6. I live
(circle).
 1. ALONE——> GO TO QUESTION 10!
 2. WITH HUSBAND/PARTNER.
 3. WITH CHILD(REN).
 4. WITH HUSBAND/PARTNER AND CHILDREN.
7. The age of my husband/partner is years
8. The health of my husband/partner is:
(circle)
 1. GOOD.
 2. BAD.
 3. NEITHER GOOD NOR BAD.

G. 9. My husband/partner works
(circle)

1. YES
2. NO

- if no (circle)
1. RETIRED
 2. UNEMPLOYED
 3. WAO
 4. HOUSEMAN

10. I have CHILDREN (own, step-, or adopted children).
(circle)

1. NO
2. YES _____ > if yes:
 - a) HOW MANY.....
 - b) AGES.....
 -
 - c) HOW MANY STILL AT HOME.....

11. I have gained INFORMATION AND KNOWLEDGE about the climacteric years.
(circle one or more numbers).

1. FROM TALKS WITH FRIENDS, FAMILY MEMBERS, ACQUAINTANCES.
2. FROM THE GENERAL PRACTITIONER.
3. FROM MAGAZINES/NEWSPAPERS.
4. TV.
5. FROM OTHER SOURCES, WHICH ONES?
6. I HAVE NOT (YET) PAID ATTENTION TO THIS PERIOD OF LIFE

12. I am in need of extra information
(circle)

1. NO
2. YES

if yes, about which subject(s) would you like to gain information?
(circle one or more numbers).

1. THE CAUSE OF MENOPAUSE.
2. COMPLAINTS DURING THE MENOPAUSE.
3. (LATER) CONSEQUENCES AFTER MENOPAUSE.
4. REDUCING COMPLAINTS WITH HORMONAL TREATMENT.
5. OTHER MEANS OF REDUCING COMPLAINTS DURING MENOPAUSE.
6. PREVENTION OF LATER CONSEQUENCES OF HORMONE (OESTROGEN) DEFICIENCY I.E. OSTEOPOROSIS.
7. RISKS AND BENEFITS OF HORMONAL TREATMENT.

13. WHO IS YOUR GENERAL PRACTITIONER:

14. For a limited group of women we want to complete data from the questionnaire with questions about medical attention and use of medicines. Would you agree to us contacting your family physician and/or pharmacists concerning THIS SUBJECT.
(circle).

1. No, I object

2. Yes, no objection

_____ > Signature

.....

15. DO YOU WANT TO HAVE A SUMMARY OF THE RESULTS LATER ON?
(circle).

1. NO

2. YES

THANK YOU VERY MUCH FOR YOUR EFFORTS

Room for remarks:

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