The ACUFLASH study

Acupuncture treatment for postmenopausal hot flashes

Can traditional Chinese acupuncture in addition to self-care reduce hot flash frequency and intensity, compared with self-care alone?

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Preface

The ACUFLASH study was planned and the protocol written by Sameline Grimsgaard, Adrian White and Terje Alræk, starting in 2004. The Research Council of Norway decided to fund the study after a personal visit from Sameline Grimsgaard and Adrian White. A pilot study was run in the autumn 2005, and the full-scale study started in February 2006.

As a GP and acupuncturist since 1983, the time had come for me to face new challenges. I learnt about the vacant position as a PhD student at the National Research Center in Complementary and Alternative Medicine (NAFKAM) at the University of Tromsø in January 2006, and in March 2006 I joined the study team, as a replacement for the original PhD-student. At that time, the study was up and running. I have had a small part in the practical accomplishment of the study, and I have handled all the data, performed the statistical analyses and written the scientific papers.

I want to thank all my colleagues at NAFKAM for their friendliness and support, and all my collaborators in the ACUFLASH study for their excellent job during the study. Especially, I want to thank my supervisors, Sameline Grimsgaard and Terje Alræk, for their enthusiasm, knowledge, and affability, and for always being there for me.

Above all, I want to thank my dear wife Guri, for her acceptance and endurance of my peculiar notion; to quit my present job and travel 1700 kilometer north to do acupuncture research. A decision made during one week in January 2006, with her full support.

Abstract

Introduction. Hot flashes and night sweats are the most prevalent symptoms in menopause. Hormone therapy with oestrogen is considered the most effective treatment. However, recent research show that long term use of oestrogen increases the risk of serious adverse effects, and women and their health care providers are looking for alternatives. Acupuncture is one of the most frequently used complementary therapies in Norway, and is considered safe in the hands of competent practitioners. Previous data on acupuncture treatment for hot flashes were insufficient to draw any conclusions on the effect, but sufficient to justify further research. Acupuncture affects beta-endorphin activity in the central nervous system, and may thus also affect the calcitonin gene-related peptide (CGRP) excretion. CGRP is a potent vasodilator and stimulator of cholinergic sweat glands, and has been suggested as a mediator of hot flashes and sweating in postmenopausal women. The Women's Health Questionnaire (WHQ) is a health-related quality of life questionnaire, designed specifically to study possible changes that occur during menopause.

Aims. We wanted to estimate the effectiveness of acupuncture in practice. Thus, our objective was to assess the effectiveness of a policy of use of traditional Chinese medicine (TCM) acupuncture plus self-care on hot flash frequency in postmenopausal women, compared with a policy of use of self-care alone. The effects on hot flash intensity (0-10 scale) and sleep and on health-related quality of life as measured by the Women's Health Questionnaire (WHQ) were also assessed, as were the changes in urine excretion of CGRP. Secondary research questions were: "do TCM diagnoses predict the overall treatment response", and "are patients with different TCM diagnoses likely to experience a differential response in their symptoms"? The Norwegian version of the WHQ had not been validated, and the participants in the Acuflash study reported more vasomotor symptoms than participants in prior studies of the WHQ. Therefore, it was necessary to evaluate the psychometric properties of the instrument.

Materials and methods. The study was a multicenter, pragmatic, randomized, controlled trial with two parallel arms. Participants were postmenopausal women experiencing on average seven or more hot flashes per 24 hours during seven consecutive days. The acupuncture group received ten individualized TCM acupuncture treatment sessions after initial TCM diagnosis, the control group received advice on self-care only. Frequency and severity (0-10 scale) of hot

flashes and hours of sleep per night were registered in a diary. Urine excretion of calcitonin gene-related peptide (CGRP) was assessed at baseline and after 12 weeks. Primary endpoint was change in mean hot flash frequency from baseline to 12 weeks. Secondary endpoint was change in health related quality of life measured by the Women's Health Questionnaire (WHQ). Primary and secondary endpoints were also assessed at six and 12 months after study start. The acupuncturists recorded TCM diagnoses and acupuncture points for each treatment session. Treatment reactions and adverse events were also recorded. The evaluation of the WHQ was performed by examining the factor structure of the Norwegian version, assessing the internal consistency reliability and floor- and ceiling effects, and by exploring the construct validity of the instrument by comparing the WHQ to instruments measuring related constructs.

Results. Hot flash frequency decreased by 5.8 per 24 hours in the acupuncture group (n = 134) and 3.7 per 24 hours in the control group (n=133), a difference of 2.1, $p < 0.001$. Hot flash intensity decreased by 3.2 units in the acupuncture group and 1.8 units in the control group, a difference of 1.4, $p < 0.001$. The acupuncture group experienced statistically significant improvements in the vasomotor, sleep and somatic symptoms dimensions of the Women's Health Questionnaire, compared with the control group. Urine CGRP excretion remained unchanged from baseline to week 12. We did not find statistically significant differences between the study groups regarding primary and secondary endpoint at six and 12 months after study start. Fifty percent of the participants in the acupuncture group were diagnosed with Kidney Yin Xu as their primary TCM syndrome diagnosis. No statistically significant differences were demonstrated between the syndrome groups regarding the distribution of responders and non-responders, nor regarding the changes in health-related quality of life scores. A core of common acupuncture points (SP6, HT6, KI7, KI6, CV4, LU7, LI4, and LR3) were used in all the syndromes and in addition multiple idiosyncratic points. Core point selection and frequency of use did not differ between responders and non-responders. No serious adverse events were reported. Some deficiencies in the WHQ questionnaire were observed when applied to the present sample, including an unclear factor structure, low alpha values for some dimensions, and a strong floor effect in the vasomotor symptoms dimension.

Conclusions. Use of TCM acupuncture in addition to self care can contribute to a quicker reduction of hot flash frequency and increase in health related quality of life among

postmenopausal women, but probably has no long term effects. Other factors than the TCM syndrome diagnoses and the point selection may be of importance regarding the outcome of the treatment. When evaluating the psychometric properties of the WHQ, the total scale score appeared reliable. However, care should be taken when interpreting some of the subscales when the instrument is applied on women with a high frequency of hot flashes.

List of papers

This thesis is based on the following papers:

I. Borud EK, Alraek T, White A, Fonnebo V, Eggen AE, Hammar M, Astrand LL, Theodorsson E, Grimsgaard S: **The Acupuncture on Hot Flushes Among Menopausal Women (ACUFLASH) study, a randomized controlled trial**. *Menopause* 2009, **16**(3):484-493.

II. Borud EK, Alraek T, White A, Grimsgaard S: **The acupuncture treatment for postmenopausal hot flushes (Acuflash) study: traditional Chinese medicine diagnoses and acupuncture points used, and their relation to the treatment response.** *Acupunct Med* 2009,**27**;101-108

III. Borud EK, Martinussen M, Eggen AE, Grimsgaard S: **The Women's Health Questionnaire (WHQ): a psychometric evaluation of the 36-item Norwegian version.** *Scand J Psychol* 2009, **50:** 183-189.

IV. Borud EK, Alraek T, White A , Grimsgaard S: **The Acupuncture on Hot Flushes Among Menopausal Women (ACUFLASH) study: Observational follow up results at six and 12 months.** *Menopause* 2010 (in press).

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Study protocol:

V. Borud EK, Alraek T, White A, Fonnebo V, Grimsgaard S: **The effect of TCM acupuncture on hot flushes among menopausal women (ACUFLASH) study: a study protocol of an ongoing multi-centre randomised controlled clinical trial.** *BMC Complement Altern Med* 2007, **7:** 6.

The papers will be referred to by their Roman numerals in the text.

Figures and Tables

Introduction and background

Menopause – Hot flashes

When a woman is around 50 years old, the secretion of the ovarian hormones oestrogen and progesterone decreases, and eventually the menstrual bleedings stop. This period in life is called the menopause.[1] Vasomotor episodes with hot flashes and night sweating are the most prevalent complaints related to menopause. A hot flash is described as a feeling of intense heat in the face, neck and chest. It lasts on average four minutes, with a range from a few seconds up to 10 minutes or more. Around two thirds of all women experience hot flashes, and 10 – 20 percent of these find the flashes very distressing.[2] Other symptoms related to the menopause are disturbed sleep, anxiety and depression, somatic symptoms, reduced memory and concentration, urinary incontinence and sexual problems. However, the distinction between symptoms related specifically to the menopause and symptoms related to ageing in general, and other physical and psychosocial factors, may be difficult. Methodological differences between studies describing menopausal symptoms further complicate the picture.[1] Studies show that menopausal status is more consistently related to vasomotor symptoms than physical and psychological symptoms. Hence, the presence of a 'menopausal syndrome' including physical and psychological symptoms in addition to vasomotor symptoms, may be questioned.[3]

Women from different parts of the world report different symptoms related to the menopause. While vasomotor episodes may dominate in the West, women in the Far East report muscle aches and joint pain as their main symptoms.[4] Whether these differences are caused by biological or socio-cultural factors or both are not known.[1]

Reports on the duration of vasomotor symptoms vary considerably. Clinical guidelines report duration from half a year to two years for most women.[5 6] In 1990, Kronenberg reported that vasomotor symptoms resolve in 90% of all women within four to five years.[7]
A recent longitudinal study from Australia found that "the mean (SD) duration of bothersome menopausal symptoms for women who completed 13 years of follow-up and who never used HT was estimated to be 5.2 (3.8) years (median, 4 years). If women who used HT were included, the mean (SD) duration was 5.5 (4.0) years (median, 4 years)".[8] Hence, the reported duration of bothersome symptoms was longer than previously reported.

Hot flash mechanisms

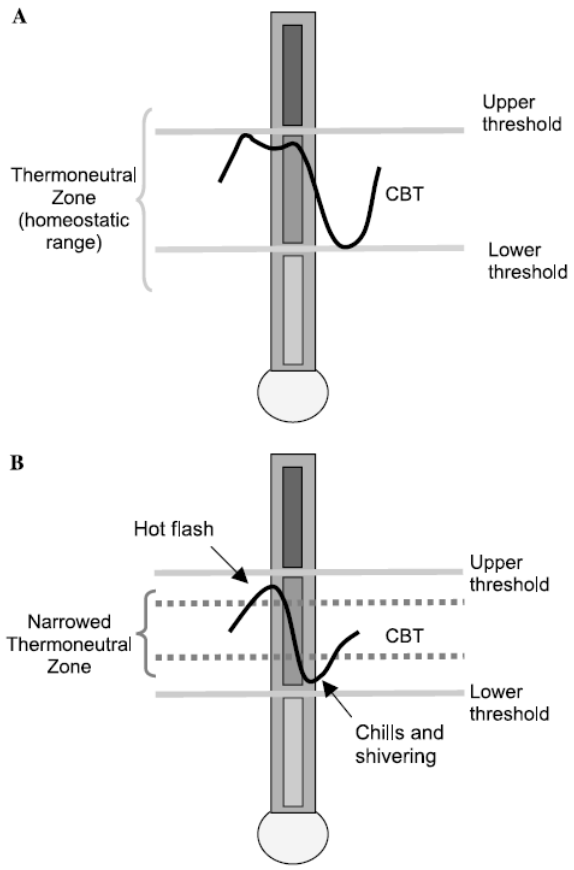
A stable core body temperature is important for optimal function and integrity of the body.[9] It has been hypothesized that the core body temperature is regulated within a thermoneutral zone, between an upper sweating threshold and a lower shivering threshold. Within this thermoneutral zone, sweating and shivering does not occur. These mechanisms maintain the core body temperature within the pre-set thresholds.[10]

Temperature regulation is considered a complex, highly regulated, and integrated network of neuroendocrine, autonomic, and somatomotor responses.[9] The three major components involved in thermoregulatory function include afferent thermosensitive pathways providing information about core body temperature; central processing areas in the CNS; and peripheral vasculature, which receives efferent signals controlling vasodilatation and vasoconstriction.[9]

The physiological mechanisms causing the vasomotor episodes are not known in detail, and different hypotheses have been studied. Facets of these theories may contribute, in part, to this thermoregulatory dysfunction.[8]

One major theory, originally proposed by Tataryn in 1980 [11] , and further studied by, among others, Freedman et al. [10 12-14], suggests that the physiological changes occurring during the menopausal transition include a narrowing of the thermoneutral zone. A normally insignificant increase in the core body temperature (CBT) will then trigger a heat loss response, i.e. a hot flash. This theory is illustrated in Figure 1.

Neurochemical changes are caused by the alterations in sex- hormones during the menopausal transition.[15] It has been suggested that the concentration of endorphins in the hypothalamus decreases with decreasing oestrogen concentrations. The reduced endorphin levels increase the release of serotonin and norepinephrine, and this may in turn cause a drop in the set point in the thermoregulatory centre in the hypothalamus and elicit inappropriate heat loss.[12 13 16] The heat loss is achieved by vasodilatation and sweating, and these reactions may be mediated by the potent vasodilator calcitonin gene-related peptide (CGRP).[17] Endogenous opioids modulate the release of CGRP at the spinal cord level [18], and postmenopausal women with vasomotor symptoms had increased urinary excretion of CGRP.[19]



CBT: CORE BODY TEMPERATURE

Figure 1 Temperature regulation

A: Normal temperature regulation B: Dysfunctional temperature regulation

From Deecher, 2007 [20]

A second theory postulates that "changes in reproductive hormone levels substantially alter thermoregulatory control of skin blood flow. This altered control might contribute to the occurrence of hot flashes".[21] Changes in vascular reactivity may interfere with the ability of blood vessels to respond rapidly and to the appropriate degree, resulting in an exaggerated response.[21] Skin blood control seems to be influenced by oestrogen and progesterone.[22]

Treatment of hot flashes

Hormone therapy with oestrogen is the most effective treatment for vasomotor dysfunction in most women, and will reduce hot flash frequency with about 75%-80%, compared with placebo.[23] In women with intact uterus, oestrogen is combined with progestogen to avoid the development of endometrial hyperplasia and endometrial cancer.

However, recent research has shown that long term treatment increases breast-cancer risks [24] [25], and oestrogen therapy initiated 10-15 years after menopause increases the risk of coronary heart disease and stroke.[26] The risks of adverse effects is related to duration of use [26] [27], dose, formulation and pre-existing morbidity.[28] The risk of venous thrombosis manifests shortly after commencing treatment, the risk of stroke after regular use in one to two years, and the breast cancer risk after five years of use of some hormone preparations. [26] [29-31] The osteoporosis - preventing effect will manifest after five to 10 years of continuous use.[32]

On this background the sales of systemic oestrogen preparations in Norway have been reduced by 48 % from 2002 to 2007 [33], and a comparable reduction in prescription rate has occurred in the USA.[34-36]

Concerns about the potential adverse effects of oestrogen have led to increased interest in non-hormonal therapies for menopausal symptoms. The use of 900mg/day of gabapentin (Neurontin®), approved for preventing epileptic seizures and neuropathic pain by the Norwegian Medicines Agency, has been shown to reduce hot flash frequency and severity with about two hot flashes per day.[37-39] Clonidine (Catapresan®) is an alpha-adrenergic agonist, in Norway approved for migraine prophylaxis and for treating menopausal hot flashes when oestrogen is contraindicated. In 50 % of the clinical trials of clonidine for hot flashes it reduced hot flash frequency and intensity significantly, and in the other half of the studies it did not. All trials combined suggested a reduction of about one hot flash per day.[40] Studies of the selective serotonin reuptake inhibitor (SSRI) paroxetine (Seroxat®, Paroxetin®) and the serotonin-norepinephrine reuptake inhibitor (SNRI) venlafaxine (Efexor®, Venlafaxin®) showed a reduction of about one hot flash per day.[40] Trials of other SSRIs and SNRIs have not shown any significant effect on hot flash frequency.[40]

Many women seek non-prescription alternatives to HT to relieve their climacteric complaints. Therapies based on phytoestrogens are among the most commonly used alternatives.[41] Phytoestrogens are non-steroidal compounds with a structure that resembles oestradiol, found in many plants. Among the most frequently used phytoestrogens are isoflavone extracts from red clover and soy. A 2007 Cochrane review concluded that there is no evidence for any effect of phytoestrogens in the alleviation of menopausal symptoms.[41] Other alternatives are herbal remedies such as black cohosh and vitamin E, but little evidence exists for any effectiveness of these therapies.[42 43]

Commonly recommended psycho-educational interventions include relaxation and stress reduction techniques, and cognitive-behavioural strategies. A systematic review found that these interventions seem to reduce hot flash frequency, but the methodological quality of the publishes studies is moderate to poor.[44] Other strategies include increased fruit and vegetable intake, reduced caffeine and alcohol intake, smoking cessation and increased physical exercise. The evidence for these is anecdotal, supported in some cases by epidemiological studies, but not by intervention trials.[5] Although increased physical activity is recommended,[5] a study found that higher levels of physical activity were significantly associated with increasing odds of moderate or severe hot flashes.[45]

Acupuncture

Traditional Chinese medicine (TCM) acupuncture.

Although traditional Chinese medicine (TCM) is one of the oldest healing systems in the world, it is a fully institutionalised part of Chinese health care. In 2006, the TCM sector provided care for over 200 million outpatients and some 7 million inpatients, accounting for 10%–20% of health care in China.[46] Acupuncture is one of the most frequently used complementary therapies in Norway. In two recent surveys, 28% reported lifetime use, and 10.8 % reported use within the previous year.[47 48] In the 2002 National Health Interview Survey in the US, 4.1% reported lifetime use and 1.1% reported use of acupuncture within the preceding year.[49]

TCM acupuncture is based on the traditional Chinese medical theories.[46 50] Most of the principles of TCM are derived from the philosophical basis that contributed to the development of Taoism, and Confucianism. The concept of Yin and Yang is central in Chinese philosophy. Yin and Yang can be described as two antagonistic, corresponding, mutually dependent, and transferable aspects of nature. Everything has both Yin and Yang aspects. These aspects continually interact, and are never in absolute stasis. Yin and Yang describe opposing qualities of a phenomenon; for example may the parasympathetic nerve system be Yin to the sympathetic nerve system's Yang in the autonomic nerve system.

The term Zhang-Fu is describing the inner organs in the body. The inner organs are divided into Yin organs (Heart, Kidney etc.) and Yang organs (Large Intestine, Gallbladder etc.). The Zhang-Fu organ systems do not represent organs as described in Western anatomy and physiology, but refers to whole systems of body and mind. The names of Zhang-Fu organ systems will be capitalized in this thesis.

Qi ('life-energy') is thought to circulate through the so-called channels or meridians, the so-called Jing-Luo system. The Jing-Luo consists of 12 main meridians and eight extra-meridians. The meridians are named after the Zhang-Fu, i.e. Liver-meridian, Lung-meridian

etc. Most of the acupuncture points are located on the meridians. Acupuncture-points are areas on the body surface believed to be the sites involved in most of the Qi convergence and transfer. Through the Jing - Luo the organs collaborate to preserve equilibrium, for instance between Yin and Yang. If the balance between Yin and Yang or flow of Qi or blood is disturbed, disease may occur. Imbalance and consequently disease may be caused by climatic factors, named external pathogenic factors, (wind, heat, cold, damp, etc.) or by internal pathogenic factors (unhappiness, happiness, way of life, etc.). When treating a disease, the objective is to re-establish equilibrium.

A TCM acupuncture consultation includes a thorough medical history and examination of the pulse and tongue, and may in the TCM tradition practiced by the acupuncturists in this study lead to a specific diagnostic 'pattern of disharmony' or syndrome diagnosis. Based on this diagnosis the treatment is individually tailored and may comprise lifestyle and self-help advice and needling in selected acupuncture points. An essential part of the TCM acupuncture session is the diagnostic process, which may result in a syndrome diagnosis. Four long-established examination methods (asking, listening and smelling, looking, and touching) are used to evaluate imbalance. All these examinations are considered of intrinsic value to TCM acupuncture, and as such indivisible from its clinical practice.

In addition to TCM acupuncture, variations of the original Chinese teaching have developed in other East-Asian countries, such as Japan, Korea and Vietnam.[51-53] 'Ishitsu-rei', the first medical law of Japan established in 701 explains the medical system of acupuncture in detail, showing that the national government authorized the administration of acupuncture. The Edo government decided to close the country in 1635, and Japan cut off exchange with foreign countries for over 200 years. The national isolation caused some development of acupuncture that is unique to Japan. Around the tenth century, Chinese medical books were introduced to Korea. Later, acupuncture in Korea has developed aspects of the therapy unique to Korea. It might be more appropriate to look upon acupuncture as a part of East-Asian or Oriental traditional medicine, rather than Chinese traditional medicine.[54]

Suggested pathogenesis and treatment of menopausal vasomotor symptoms according to TCM.

In TCM, some of the functions of the organ system Kidney are to control reproduction and growth, preserve bones and brain, manage the flow of urine and keep the will power strong. According to a widely used TCM textbook by Maciocia, a Kidney deficiency is always at the root of menopausal problems.[55] Zell et al. found that practitioners of TCM who diagnose postmenopausal women with vasomotor symptoms are likely to make a diagnosis that includes a deficiency of the Yin aspect of the Kidney; Kidney Yin Xu.[56] The theoretical foundation of the TCM acupuncture practiced in our study was mainly based on the above mentioned influential TCM textbook by Maciocia.[55] He describes menopausal symptoms as mainly due to Kidney deficiency, sub-divided into Kidney Yin deficiency, Kidney Yang deficiency or a combination of Kidney Yin and Kidney Yang deficiency. The aetiology of the Kidney deficiency may be emotional stress like worry, anxiety and fear; described as 'an extremely important cause of menopausal problems'.[55] The emotional stress is often combined with overwork, and together, overwork and emotional stress are the most important and frequent causes of Kidney Yin deficiency.[55] According to TCM theory, Kidney Yin is supposed to nourish Heart Yin; hence, a long-standing Kidney Yin deficiency may also cause a Heart Yin deficiency.

Scheid defines TCM as 'that interpretation of Chinese medical practice that is presented to us in contemporary Chinese medical textbooks, emerging in the late 1950s'.[57] Menopausal problems, as such, have not been described in ancient Chinese medical texts, but a TCM approach towards menopausal symptoms was 'constructed' by textbook authors in the 1960's for use in textbooks suitable for a western audience.[57 58] According to Scheid, the TCM understanding of menopausal symptoms, like TCM itself, is a direct consequence of Chinese medical modernisation, and only one of several possible interpretations of the classical medical texts. Practitioners in contemporary China have, in addition to the above-mentioned modern textbooks, other sources of information to draw on, such as direct access to the classical medical texts and personal transmission of knowledge from teachers.[57] These sources are not readily available in the West, and may suggest different syndrome patterns and point selection for the treatment of menopausal symptoms.[57] Table 1 lists symptoms and signs characteristic for TCM syndrome diagnoses often diagnosed in postmenopausal women with vasomotor symptoms.

To treat the imbalance, a TCM practitioner may use acupuncture or herbs or a combination. Herbs are considered more effective than acupuncture.[55] When using acupuncture, acupuncture points addressing the diagnosed imbalance will be selected. In addition, points treating the symptoms directly may be used. The acupuncture points are traditionally stimulated by inserting an acupuncture needle in the points, and 'De Qi', a characteristic dull and numb sensation, has to be achieved. The acupuncture points may further be stimulated with 'needle manipulation', either manually or by electricity. An alternative or additional method is heat stimulation with moxibustion. When using moxibustion, the herb mugwort is grinded to a fluff. This fluff is usually either burnt attached to the needle shaft, or processed into a 'moxa-cigar' that is used to heat the skin.

Table 1 TCM syndromes

Characteristic symptoms and signs in syndromes frequently diagnosed in women with postmenopausal vasomotor symptoms

Syndromes	Symptoms and signs
KI Yin Xu empty heat	Night sweating Hot flushes Restless Anxious Dry-, hair, skin, mouth Deep weak pulse Tongue red without coating
KI Yang Xu empty cold	Hot flushes but cold hands & feet Night sweating (early morning) Tiredness, low energy Depressed Deep pulse Tongue pale
KI Yin and KI Yang Xu	Hot flushes but cold hands & feet Night sweating Frequent pale urination Flushed around neck when talking Tongue pale or red
KI and LR Yin Xu with LR yang rising	Hot flushes Irritability Dizziness Blurred vision Tongue red without coating
KI and HT not harmonised	Hot flushes Palpitations Insomnia Mental restlessness Poor memory Tongue red without coating, redder tip

KI = Kidney, HT = Heart, LR = Liver, Xu = deficiency

From Maciocia, 1998 [55]

Biomedical acupuncture

Biomedical acupuncture is an "adaptation of Chinese acupuncture that seeks to explain the effects of the needling with theories from established medical physiology, anatomy and pathology".[59] 'Biomedical acupuncture' or 'Western medical acupuncture' is in widespread use in the Western world. The traditional concepts of Yin and Yang and Qi are not involved, and biomedical acupuncture is not considered an "alternative" treatment .[59] The physiological processes involved in acupuncture treatment are not fully known, but factors of importance may include changes in autonomic nerve functioning [60-62], hormones like cortisol [63-67] and oxytocin [68-72], neuropeptides such as ß-endorphin [68] and serotonin [73 74], cytokines [75-77], and alterations in collagen network communication.[78 79]

Acupuncture analgesia is among the most studied aspects of biomedical acupuncture. Acupuncture needling stimulates the nervous system by activating the Aß, Aδ and C afferent fibres, with the induced signals ascending mainly through the spinal ventro-lateral columns to the brain. Several brain nuclei constituting a complicated network are involved in the underlying process, including nucleus raphe magnus, nucleus accumbens, nucleus arcuatus, the periaqueductal grey, preoptic area, locus coeruleus, nucleus submedius, nucleus caudatus, septal area and amygdale.[80-82] These regions are also involved in emotional and reward processes.[83] It has been shown that activation of afferent nerve fibres with low frequency electrical stimulation on acupuncture needles (electroacupuncture) can cause an increase of neuropeptides in cerebrospinal fluid in human subjects.[84] Different neuropeptides are released by electroacupuncture at different frequencies. For example, electroacupuncture of 2 Hz increases the release of enkephalin, ß-endorphin and endomorphin, while that of 100 Hz selectively stimulates the release of dynorphin. Using the two frequencies simultaneously produces a release of all four opioid peptides, and this optimizes the treatment effect. Clinical studies of participants with different kinds of chronic pain, including low back pain and diabetic neuropathic pain, have verified these results.[85] Among evidence for the involvement of the ß-endorphin system is that the pain relieving effect can be blocked by the opioid antagonist naloxone. Acupuncture probably also affects serotonin and noradrenaline activity in the central nervous system,[68 85 86] and may thus influence the thermoregulatory center, making it more stable.[17] A change in the beta-endorphin concentration may also affect the CGRP excretion. A study showed that CGRP decreased in 24-hour urine after acupuncture therapy in women with hot flashes.[17]

Modern neuroimaging techniques such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have been used to gain new insight into the physiological responses in the brain and brainstem associated with acupuncture needling.[87-94] These studies have demonstrated a modulation or attenuation of the blood oxygenation level dependent (BOLD) signal in the limbic/paralimbic system, brainstem and neocortical regions.[90 94] However, the block-based needle stimulation paradigm generally used in these studies, with an initial insertion of the needle, and a repetitive "on/off" pattern, with manual or electrical stimulation of the needle representing "on", and no stimulation of the needle representing "off", is problematic. The choice of an appropriate baseline, to which the acupuncture-related activity in the brain can be compared, is fundamental.[95] In most of the present studies, it is assumed that the "off" periods, with no stimulation of the needle, represent baseline. However, the initial needling may induce persistent changes in neuronal activities which would extend across the inter-stimulus intervals (e.g., a block-based paradigm in an fMRI study).[95] Hence, the "off" periods may not represent "true" baseline, and the results from studies using this stimulation paradigm must be interpreted with care.

Direct needling in myofascial triggerpoints is another variant of 'Western medical acupuncture'. An analogy is found in the tender point (Ah-Shi point) needling in TCM. This treatment modality is mainly used for painful conditions in muscles and joints. Limited evidence exists for the effectiveness and efficacy of this treatment modality, as the existing studies have a limited sample size and are of poor quality.[96]

Studies of acupuncture for menopausal vasomotor symptoms

Primary studies

In 1995, Wyon et al. published a randomized trial with 24 participants, showing that hot flashes decreased significantly by more than 50% among women who received standardized electro-acupuncture.[17] A similar reduction of hot flashes was observed in the control group, receiving sham acupuncture with superficial needle insertion. Sham acupuncture or placebo acupuncture can be defined as "interventions mimicking 'true' acupuncture/'true' treatment, but deviating in at least one aspect considered important by acupuncture theory, such as skin penetration or correct point location". [97] A further study (N=30) compared standardized

electro-acupuncture with extremely superficially inserted needles at sham acupuncture points for climacteric symptoms.[98] The participants were given 14 treatments over 12 weeks, and the results showed a trend in favour of standardized electro-acupuncture.

A small RCT (N=18) found six treatment sessions of standardized TCM acupuncture over 9 weeks more effective than sham acupuncture, with a 76% reduction of hot flash severity.[99]

A study of 103 participants by Vincent et al. found that both standardized TCM acupuncture and sham acupuncture with needling in non-acupuncture points reduced daily hot flash score (product of hot flash frequency and hot flash intensity) with 40% and 38%, respectively, at the end of the treatment period (week six).[100] The participants received 10 treatments over five weeks. At week 12, the hot flash score reduction was 27% in the treatment group, and 45% in the control group.

A study of 29 participants by Nir et al. found that TCM acupuncture reduced hot flash severity, though not frequency, compared with sham acupuncture.[101] The participants received nine sessions over seven weeks. The participants in the active treatment arm were diagnosed and treated according to a standardized TCM diagnostic algorithm and a standardized treatment manual. The sham group received non-penetrating placebo needles at non-acupuncture points.

Avis et al. carried out a randomized study (N=56) with three arms (TCM acupuncture, sham acupuncture and usual care) that showed no significant difference in reduction of daily flash frequency between the three groups, but a significantly greater decrease in flashes in the two acupuncture groups compared with the usual care group.[102] The participants in the two acupuncture groups received a total of 16 treatments over eight weeks. The TCM acupuncture consisted of standardized core points, with the addition of points based on the acupuncturist's judgement of TCM diagnostic syndrome category. Sham acupuncture consisted of shallow needling in non-acupuncture points without eliciting De Qi.

Most of the cited studies had few participants. All of them used some sort of standardized acupuncture treatment in the active treatment group, although the studies by Nir et al. and Avis et al. used standardized algorithms and treatment manuals to take into account individual

TCM diagnoses. All the studies used sham acupuncture as control. Nir et al. used non-penetrating needles at non-acupuncture points, the other studies used needling/superficial needling at non-acupuncture points. It is interesting to note that virtually all the studies failed to demonstrate any differences in effect between 'true' acupuncture and 'sham' acupuncture.

According to TCM, all treatments should be applied individually. Individualized treatment can be defined as the practitioner performing individual TCM diagnostics and related point selection. None of the studies have fulfilled this criterion. The treatments given differ between the studies regarding point selection, number of treatments and interval between treatments, although all studies claim to investigate the same treatment, namely 'acupuncture'.

Systematic reviews

Recently, there have been two systematic reviews of acupuncture for hot flashes.[103 104] Lee et al. included six trials with 309 patients.[104] Four of these trials [17 100-102] have been commented on in the previous section. Choo & Whang adds five more trials from the Chinese literature.[103] Three of these additional trials use forms of therapy rarely offered in the West – embedding of catgut in the acupuncture point, and auricular acupressure. The other two RCTs found long courses of acupuncture (manual and electroacupuncture in which the needles are stimulated by low voltage electrical currents, respectively) significantly superior to hormone therapy.

Both reviews conclude that there is no evidence that acupuncture is an effective treatment for hot flushes in comparison with sham acupuncture, and both point to lack of rigour in the studies. One particular area of weakness is small sample sizes.

Unreliable evidence from primary studies does not become reliable simply by inclusion in a systematic review. Therefore, the results of these reviews should be regarded as indicative, not conclusive.

Health-related quality of life

Definitions

The term "quality of life" (QOL) refers to perceived physical and mental health over time.[105] Quality of life instruments are widely used in research, and the term "health-related quality of life" (HR-QOL) is frequently used in the medical field. HR-QOL represents those parts of QOL that are directly related to the person's health. It is claimed that this approach takes into account qualitative aspects, such as the effects of subjective symptoms on day to day functioning and well-being.[106] Hence, HR-QOL instruments can be used to better understand the effect of short- and long-term disorders and symptoms in single patients and in different populations.[105] A disease-related impairment and disability may influence a person's ability to meet her needs. Some authors have used a 'need-based' approach to HR-QOL, defining HR-QOL as the extent to which needs are fulfilled.[107]

Quality of Life measures

HR-QOL instruments are useful in medical research because a goal for therapy is to make patients feel better.[108] Effects of treatment may be assessed by measuring physiological parameters; however, these may change without the patient feeling any better. On the other hand, patients may feel better without any change in physiological parameters. Hence, it may be important to ask the patients directly. This may also give information about any potential trade-off between treatment effects and side-effects.

HR-QOL instruments are often divided into two subgroups: generic and specific. Generic HR-QOL instruments are designed to be applicable across a wide range of populations and interventions, while specific HR-QOL measures are designed to be relevant for particular interventions or in certain subpopulations.[109] Among frequently used generic instruments are the Short Form (SF) – 36 Health Survey [110], the Sickness Impact Profile [111] and the Euro QOL EQ-5D.[112] Several specific HR-QOL instruments that address the impact of menopausal symptoms on health-related quality of life have been developed. These include the Greene climacteric scale,[113] the Utian Quality of Life Scale,[114] the Menopause-specific Quality of Life Questionnaire,[115] and the Women's Health Questionnaire (WHQ).[116]

Psychometrics

Several issues need to be addressed before applying a HR-QOL measure in a clinical trial. The purpose for use of the instrument must be clarified, and the instrument must have measurement properties suitable for that purpose. The measurement properties of the HR-QOL instruments used in clinical trials affect their ability to detect meaningful treatment differences. These properties are a function of both the theoretical framework from which the HR-QOL are derived, and how well the scales perform in measuring those constructs. Reliable and valid measures of multi-symptom conditions generally come in the form of scales and subscales, developed on the basis of principles of test construction and scaling. In the field of psychology, the techniques developed to construct such measures are known as psychometrics.

Factor analysis

When analyzing the inter-relationship among a large number of variables, for instance symptoms or test items, a set of underlying concepts known as factors should be identified. To construct measures of psychological and behavioural characteristics, we often use a multivariate mathematical technique called factor analysis. The overall objective of factor analysis is data summarization and data reduction.[117] Factor analysis orders and gives structure to observed variables, and allows for the construction of instruments in the form of scales and subscales. A correlation coefficient called factor loading measures the relationship between a symptom or test item and a factor. This will permit the construction of an instrument which consists of several separate subscales. Based on the size of the factor loadings, symptoms or test items may cluster together in factors. As a result, a scale will yield a symptom or test profile for each subject. The identification of symptoms or test items which cluster together to form groups of factors serves to delineate facets of the symptom picture and to identify those symptoms or test items that are an essential part of a syndrome and those which are not. Scales for measuring a complex syndrome such as the menopausal transition are generally made up of a number of subscales; each measures a different facet of the syndrome.[107]

The Women's Health Questionnaire

The Women's Health Questionnaire (WHQ) is a self-administered questionnaire, with 36 items and nine domains, which measures aspects of the physical and mental health of women aged 40 to 65 years. It was developed in England, and designed specifically to study changes that may occur during menopause.[116 118] A revised 23 item version of the WHQ with improved psychometric properties has recently been developed.[119] The 36-item WHQ has demonstrated good internal consistency and test-retest reliability in several studies.[106 118 120 121] The questionnaire has been translated into 27 languages, and it has been validated in many countries, including Sweden, Italy and Brazil (Portuguese version).[106 120 121] The 36-item WHQ was translated into Norwegian by the Mapi Research Institute, but a psychometric validation of the Norwegian version had not been performed until the current study. Internationally the WHQ has been included as a quality of life measure in trials of hormonal preparations for postmenopausal women,[118] and it was therefore considered a natural choice as a secondary endpoint in the ACUFLASH study.

Aims

The main objective of this work was to estimate the effectiveness of TCM acupuncture treatment for postmenopausal vasomotor symptoms in practice.

Addressed questions were:

- What is the effectiveness of a policy of use of acupuncture plus self-care on hot flash frequency and intensity and hours of sleep per night in postmenopausal women, compared with a policy of use of self-care alone?

- What is the effectiveness of a policy of use of acupuncture plus self-care on health-related quality of life as measured by the Women's Health Questionnaire in postmenopausal women, compared with a policy of use of self-care alone?

- Is the urine excretion of calcitonin gene-related peptide (CGRP) affected by acupuncture treatment?

- Which TCM diagnostic syndromes and acupuncture points are used during the study, and what are their frequencies of use?

- Do TCM diagnoses predict the overall treatment response, and are patients with different diagnoses likely to experience a differential response in their symptoms?

- What is the relation between the acupuncture points used and the treatment response?

- Which treatment reactions and adverse events are reported during the study?

- Are the psychometric properties of the Norwegian translation of the Women's Health Questionnaire acceptable when applied on a population with a high frequency of hot flashes?

Materials and methods

The Acuflash study was a pragmatic, multi-center, randomized, controlled trial with two parallel arms. It was conducted in three centres in Norway; Oslo, Bergen and Tromsø, from February 2006 to May 2007.

Study participants

Postmenopausal women were recruited by newspaper advertisements and coverage of the study in newspapers and TV. Postmenopausal status was defined as at least one year since the last menstrual bleeding. Inclusion criterion was seven or more hot flashes per day. Potential participants received a diary by mail and recorded frequency and severity of hot flashes and duration of sleep at night for a period of 14 days. Altogether 535 women phoned the study coordinators and were assessed for eligibility. Of these, 428 women received the baseline diary, and 399 women completed and returned it. Women who returned the diary and fulfilled the inclusion criteria received an informed consent form and the baseline questionnaires by mail. The women completed the questionnaires at home, and brought them to the enrolment visit with the local study coordinator. The coordinator double-checked the eligibility criteria and obtained written informed consent. After enrolment, the local coordinator telephoned the central randomization unit at the University Hospital of North Norway (UNN) to obtain group allocation. The participants were stratified by center and thereafter block randomized (random block size of four, six or eight) to receive additional acupuncture or not receive additional acupuncture. Block randomization (organizing study participants into blocks and randomizing within each block) was used to ensure close balance of the numbers in each group at any time during the trial. Women randomized to receive acupuncture were referred to a local study acupuncturist, who was instructed to see her within a week. All participants attended the study coordinators again at the end of the study period of 12 weeks.

Intervention

All participants in both groups received an information leaflet (Appendix VI) with information about self-care strategies to relieve menopausal symptoms, and they were free to use any of these. The information included advice about sufficient sleep and rest, reduction of physical and psychological stress, regular exercise, healthy food and limited tobacco smoking and alcohol intake. The information leaflet was prepared by the project team, and was based on an authoritative book and best current advice.[5 122]

The participants in the acupuncture group were assigned to 10 acupuncture sessions over 12 weeks. The minimum number of sessions accepted as 'per protocol' was six. The acupuncturists were asked to use diagnostic methods according to the principles of TCM, and diagnose TCM syndromes associated with the menopausal symptoms. After the initial diagnosis, each participant should be treated with points selected according to the syndrome diagnosis. The acupuncturists were free to add individualised points to treat other symptoms related to the menopause (i.e. those included in the WHQ such as depression, anxiety, insomnia), but not unrelated symptoms (e.g. common cold). They could use moxibustion (warmed needles) if indicated. Herbal treatment was not allowed during the study. De Qi should be obtained, and needle manipulation could be used. Point location was not standardized in the study, but left to the acupuncturists to decide.

The participants in the control group did not see any acupuncturist, and were not prescribed any medical treatment for menopausal symptoms within the study. They were free to use any over-the-counter medication and self-provided non-pharmaceutical interventions, guided by the self-care information leaflet. They met with the study-coordinator at baseline and at week 12.

Measurements

Paper I and IV

Hot flash diary (Appendix II). The participants recorded the numbers of hot flashes in a daily diary. They scored the mean daily hot flash intensity on a visual analogue scale of zero to 10, where zero represents no bother at all and 10 represents the worst possible intensity of flashes. They also recorded hours of sleep per night. The diaries were administered for two weeks during the qualifying period, and for one week at week four, eight and 12 of the intervention period, and at six and 12 months after study start. Baseline values were calculated using data from the last seven days of the two-week qualifying period.

Baseline questionnaire (Appendix III) included socio-demographic data, medical history, previous experience with acupuncture and expectations of acupuncture effect for menopausal symptoms, previous use of other interventions to relieve climacteric complaints, current use of medication and dietary supplements, and level of physical activity, smoking status and alcohol consumption.

The Women's Health Questionnaire (Appendix IV). The range of subscales included in the WHQ enable an assessment of several dimensions of mental and physical health, including depression, anxiety, sleep problems, and somatic symptoms, along with subscales for menstrual problems and sexual difficulties.[118] The following domains are covered by the questionnaire: anxiety/fears (items 2, 4, 6, 9), attractiveness (items 21, 32), somatic symptoms (items 14-16, 18, 23, 30, 35), memory/concentration (items 20, 33, 36), vasomotor symptoms (items 19, 27), depressed mood (items 3, 5, 7, 8, 10, 12, 25), sleep problems (items 1, 11, 29), sexual behaviour (items 24, 31, 34) and menstrual symptoms (items 17, 22, 26, 28). The WHQ is scored on a four point Likert scale (1 = yes, definitely, 2 = yes, sometimes, 3 = no, not much, 4 = no, not at all). Items 7, 10 and 25 of the depressed mood category and items 21 and 32 of the attractiveness domain are reversed before scoring. The items are usually dichotomized before scoring, and within each domain an average score between 0 and 1 is calculated, where 0 is an indicator of "good health status" and 1 is an indicator of "poor health status". A clinically significant change within each domain of the WHQ is a difference of approximately 0.10 to 0.20. Norms are available for different age groups, nationalities and

menopausal status [118]. Assessment of health related quality of life was performed at baseline and week 12, and was repeated six and 12 months after study start.

Participant's questionnaires (Appendix IV, VII and VIII). At weeks four, eight and 12, all participants were asked about their use of health care providers, medication and dietary supplements during the last four weeks, and at months six and 12 during the last three and six months. At weeks four and eight they were asked whether they had changed their living habits (rest and sleep, physical activity, coffee drinking, alcohol intake, tobacco smoking) over the last four weeks. At week 12 and month six they were asked about changes in their living habits over the last three months, and at month 12 over the last six months. At week 12 and months six and 12 they were also asked a global question addressing any changes experienced regarding menopausal symptoms (intensity and frequency of hot flashes, quality of sleep, well-being) during the study period. At weeks eight and 12 the women in the acupuncture group were asked if they had experienced any of the following treatment reactions: temporary worsening of hot flashes, dizziness, tiredness, increased energy, more relaxed, hungrier.

Paper I

Urine CGRP and u-Creatinine were measured in morning and evening urine samples obtained from the participants in the Tromsø arm of the study. Samples were collected at baseline and before the visit at week 12. They were stored at -20 degrees C until analysis. Samples were then extracted and concentrated five times (coefficient of variation 4%) with the use of a reverse phase C18 cartridge (Sep Pak; Waters Corp, Milford, MA, USA) and analyzed in one batch for calcitonin gene-related peptide-like immuno-reactivity with the use of competitive radioimmunoassay. Calcitonin gene-related peptide (CGRP-LI) was analyzed using antiserum CGRPR8 raised in a rabbit against conjugated rat CGRP. HPLC-purified 125I-Histidyl rat CGRP was used as radioligand and human CGRP alpha as standard. The detection limit of the assay for human CGRP is 7 pmol/L and the crossreactivity of the assay to substance P, neurokinin A, neurokinin B, neuropeptide K, gastrin, neurotensin, bombesin, neuropeptide Y and calcitonin was less than 0.01%. Crossreactivity toward human CGRP alpha and beta was 93% and 24%, respectively and toward rat CGRP alpha and beta, 100% and 120%, respectively. Intra- and inter-assay coefficients of variation were 9% and 14%, respectively. The variation in the u-CGRP

excretion was evaluated by comparing the mean u-CGRP/u-Creatinine ratio values at baseline and at week 12 in the morning and evening urine samples separately and the morning and evening sample values added and divided by two.

Paper II

Acupuncturist's data collection form (Appendix IX). The data collection form prompted for each of nine specific TCM syndrome diagnoses, as listed in Table 2. The syndrome patterns are those listed by Maciocia,[55] with the addition of Liver Qi Stagnation and Stomach Heat at the suggestion of the study acupuncturists, see Table 1. Practitioners were also free to add any other diagnosis, and they were asked to record primary and secondary diagnoses at each session. At each session, practitioners were also asked to record acupuncture points used, and indicate laterality of needling, needle technique, whether De Qi was obtained, and reasons for eventual change of acupuncture points from the previous treatment session. They were asked to record the use of moxa and use of other interventions (massage, cupping, electro-acupuncture, herbs or other). Finally, they should record the prescription of home-based self-treatment such as specific physical exercises, tai chi, yoga, self-massage, relaxation exercises or other.

If the acupuncturist gave advice on facilitating and supporting lifestyle changes such as dietary advice (low dairy, avoid wine and spirits, low wheat, stop/reduce coffee, ensure food is warm and cooked) or non dietary advice (more exercise, stop/reduce smoking, more rest, protection from cold and damp, general support and empowerment or other), this had to be recorded.

The acupuncturists were asked to record treatment reactions. Treatment reactions were reactions which could be positive indicators of treatment effect, but could be experienced as adverse by acupuncture-naïve participants. Treatment reactions were communicated spontaneously by the patient during or after treatment, or at the next visit (recorded under the headings light-headedness, energised, tired, relaxed, hungry, drowsy, and other). Adverse events such as fainting, forgotten needle, fit (convulsions), broken needle, skin reactions, moxa burn, unacceptable bruising, pneumothorax, unacceptable bleeding, infection, unacceptable pain at a point from needling, unacceptable worsening of symptoms or other had to be recorded.

Paper III

The evaluation of the Norwegian version of the 36-item *Women's Health Questionnaire* (Appendix IV) was performed by examining the factor structure, and by exploring the construct validity of the instrument by comparing the WHQ to instruments measuring related constructs, such as a measure of psychosomatic complaints, *The Psychosomatic Complaints* (PSC), and a measure of positive health status (EQ-5D). We expected the WHQ total score and subscale scores to be negatively correlated with psychosomatic complaints and positively related to health status. The presence of floor or ceiling effects was evaluated by calculating the proportion of participants with the lowest or highest possible score. Floor or ceiling effects are considered to be present if more than 15% of the respondents achieved the lowest or highest possible score, respectively.[123]

EQ-5D (Appendix IV) is a standardised generic quality of life instrument that is used as a measure of health outcome. The first part of the EQ-5D descriptive system consists of five dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The second part of the EQ-5D is a 20 cm visual analogue scale (VAS), which has end-points labelled 'best imaginable health state' and 'worst imaginable health state' anchored at 100 and 0, respectively. The first part of the EQ-5D produces a health index based on a descriptive system, and the second part is a self-rated assessment of health status based on the VAS.[109]

The Psychosomatic Complaints (PSC) (Appendix V) is a checklist of 19 physical symptoms.[124] Subjects indicate how often they experience nineteen physical conditions (e.g., poor appetite, headaches, pain in the heart, sleep disturbances, backaches, restlessness during the past year) on a scale ranging from 1 = "never" to 4 = "often". The score is calculated as the mean score of the 19 items [124].

Statistical analysis

SPSS software, version 15.0 (SPSS Inc, Chicago, Ill., USA), was used for all statistical analyses. The primary analysis was intention to treat and the subgroup analyses were per protocol. Change was calculated as mean hot flash frequency at 12 weeks, 6 months and 12 months minus mean hot flash frequency during the last seven days of the qualifying period. Differences in change between groups were evaluated with two-sample t-tests and ANOVA,

and Chi-square tests were used for categorical variables. Two-sided $p < 0.05$ was considered statistically significant. When evaluating the psychometric properties of the WHQ, we used SPSS for factor analysis/principal components analysis (PCA), calculation of Cronbach's alpha and correlation analyses. The program Simple Interactive Statistical Analysis (SISA, Quantitative Skills, Consultancy for Research and Statistics, The Netherlands) was used for significance-testing (Hotelling's T^2 test) of differences between correlation coefficients.

Power and sample size calculations

We aimed to detect a 50 % reduction in hot flash rate in the acupuncture group and a 20 % difference between groups. The sample size was calculated using data from previous trials of HT, herbs and acupuncture. Assuming a baseline hot flash rate of 7.0, SD 3.5 for change in flash rate, and employing a two-sample t-test, 100 women in each group were needed to obtain 80% power with a two-sided α-value of 0.05. Assuming 30 % withdrawal and dropout rate, we estimated that 286 women were required.

Results

Paper I and IV

Study participants

Between February 2006 and March 2007, 535 women contacted the study coordinators, and 267 were included, 82 in Tromsø, 105 in Bergen and 80 in Oslo, see Figure 2. The study groups were well balanced with respect to background characteristics at baseline, see Table 2. Altogether 19 women (7%) dropped out; 16 in the control group and three in the acupuncture group. No participants withdrew due to adverse effects. Two women withdrew from the acupuncture group before week four and another one before week eight. Two participants withdrew immediately after being allocated to the control group. Another 14 withdrew from the control group before week four. A total of 131 participants in the acupuncture group and 117 in the control group were included in the final analyses of hot flash frequency at 12 weeks. At six months, 124 participants were analysed in the acupuncture group, and 112 in the control group, and at 12 months, 119 and 114 participants, respectively, were included in the analysis of hot flash frequency (Table 3). The dropouts were asked but were not willing to provide hot flash data after the termination of their study participation.

Missing data on hot flash frequency, intensity or sleep were found in a total of 16 hot flash diaries at week 12. The rate of missing information was 1.5%. At week 12, missing values for one day were substituted with the mean of the reported data in ten diaries, for two days in two diaries, for three days in two diaries and four days in two diaries. Analysis of the data excluding the hot flash diaries with missing data did not change any of the results. At six months, missing values for one day were substituted with the mean of the reported data in five diaries. At 12 months, missing values for one day were substituted with the mean of the reported data in one diary, and for two days in one diary.

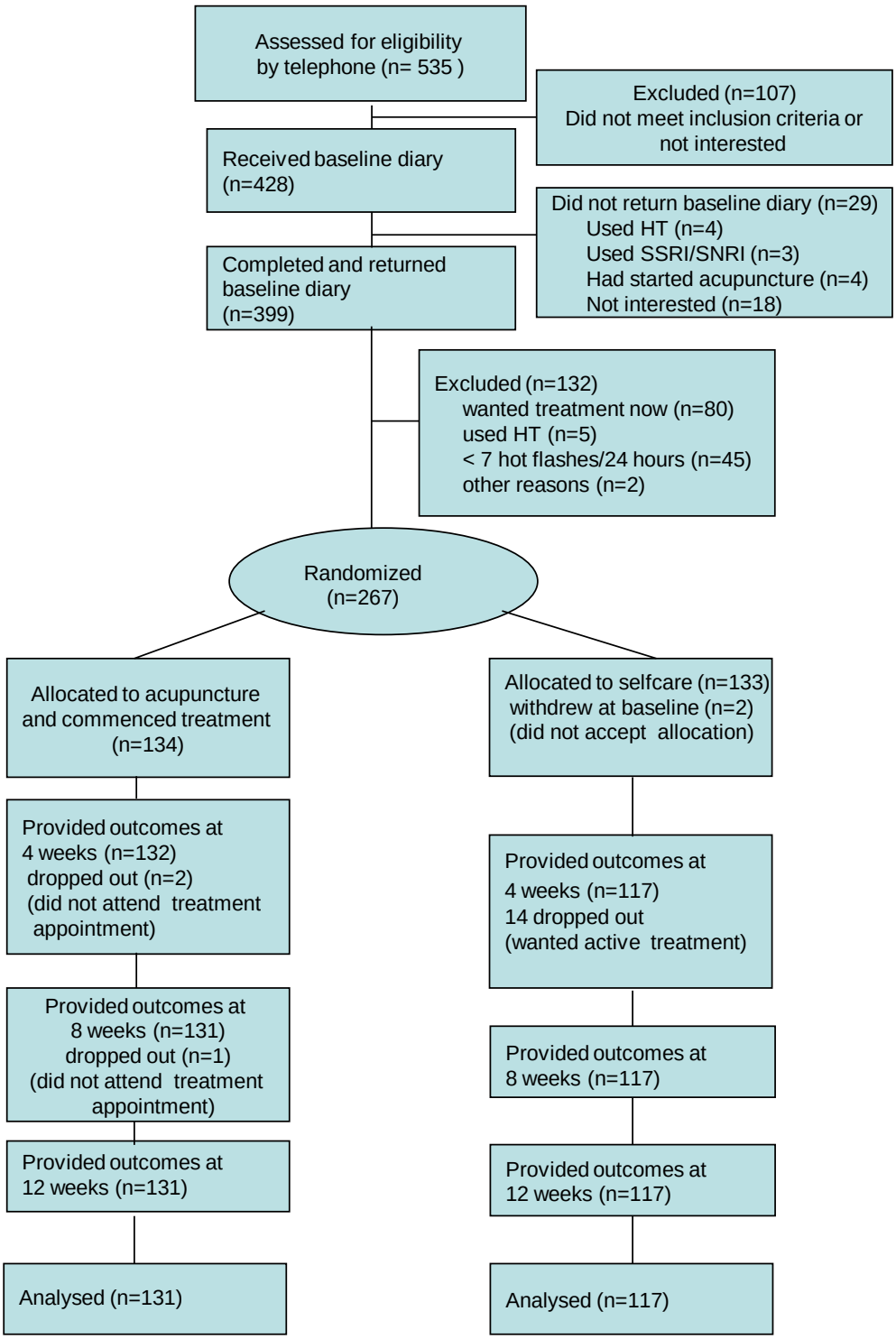


Figure 2 Trial flow diagram in the ACUFLASH study

HT, hormone therapy; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin norepinephrine reuptake inhibitor

Table 2 Baseline characteristics of the study participant in the ACUFLASH study

Characteristics	Acupuncture group (n = 134)	Self care group (n= 133)
Age at randomisation – year	53.5 ± 4.4	54.1 ± 3.7
Age at menopause – year	49.3 ± 4.0	48.6 ± 4.9
Baseline hot flash frequency/24 hours	12.0 (4.3)	13.1 (4.9)
Baseline hot flash intensity (0-10)	6.7 (2.0)	7.1 (1.7)
Self-reported weight – kg	71 ± 12	70 ± 12
Self-reported height – cm	167 ± 6	168 ± 6
Years of education		
≤ 10	60 (44.8)	64 (48.1)
11 – 13	12 (9.0)	13 (9.8)
14 – 17	31 (23.1)	18 (13.5)
> 17	31 (23.1)	36 (27.1)
Missing	0	2 (1.5)
Previous use of HT	71 (53.0)	61 (45.9)
Previous use of acupuncture	86 (64.2)	85 (63.9)
Expect acupuncture relieves hot flushes?		
Yes	80 (59.8)	68 (51.1)
No	0 (0)	0 (0)
Uncertain	53 (39.5)	61 (45.9)
Missing	1 (0.7)	4 (3.0)
Self reported health		
Very bad	2 (1.5)	3 (2.3)
Bad	31 (23.1)	37 (27.8)
Good	78 (58.2)	74 (55.6)
Excellent	22 (16.4)	16 (12.3)
Missing	1 (0.7)	3 (2.3)
Sleep problems		
Never	32 (23.9)	33 (24.9)
1-3 nights per month	22 (16.4)	19 (14.3)
Once a week	14 (10.4)	12 (9.0)
> Once a week	66 (49.3)	66 (49.6)
Missing	0	3 (2.3)
Baseline WHQ score		
Vasomotor symptoms domain	0.98 (0.09)	0.98 (0.10)
Sleep problems domain	0.57 (0.33)	0.61 (0.32)
Somatic symptoms domain	0.48 (0.26)	0.55 (0.24)

Data are either means (SD) or n (%)

Hot flash frequency and intensity

Mean frequency of hot flashes/24 hours among all participants was 12.6 (range 4.7 – 31.0) at baseline. At 12 weeks, the mean reduction in hot flash frequency/24 hours was 5.8 in the acupuncture group and 3.7 in the control group, a difference of 2.1 (95% CI 1.0 – 3.2), $p < 0.001$, see Table 3 and Figure 3. From baseline to six months the mean reduction in hot flash frequency/24 hours was 5.3 in the acupuncture group and 5.0 in the control group, a difference of 0.3 (95% CI -1.6 to 1.1). At 12 months the mean reduction in frequency was 6.0 in the acupuncture group and 5.8 in the control group, a difference of 0.2 (95% CI -1.7 to 1.3).

Mean hot flash intensity at baseline was 6.9 (range 2.1 – 10 on the 0 – 10 scale), among all participants. At 12 weeks, mean reduction in hot flash intensity was 3.2 units in the acupuncture group, and 1.8 units in the control group, a difference of 1.4 (95% CI 0.7 – 2.0), $p < 0.001$. At six months, mean reduction in hot flash intensity was 2.9 units in the acupuncture group, and 2.6 units in the control group, a difference of 0.3 (95% CI -1.0 to 0.4). At 12 months the mean reduction in intensity was 3.4 in both groups.

Baseline mean hours of sleep per night were 6.1, (range 2.9 to 8.3) among all participants. At 12 weeks, mean hours of sleep had increased by 0.42 hours in the acupuncture group and 0.14 hours in the control group, a difference of 0.28 (95% CI 0.05 – 0.50), $p = 0.015$. At six months, mean hours of sleep had increased by 0.37 hours in the acupuncture group and 0.14 hours in the control group, a difference of 0.23 hours (95% CI -0.01 to 0.48). At 12 months, mean hours of sleep had increased by 0.33 hours in the acupuncture group and 0.10 hours in the control group, a difference of 0.23 hours (95% CI -0.10 to 0.56).

There were no statistically significant differences between the study centers regarding changes in hot flash frequency and intensity and duration of sleep at 12 weeks, six months and 12 months.

Calcitonin gene-related peptide (CGRP)

There were no statistically significant changes in the u-CGRP/u-creatinine ratio in the morning and evening urine samples in the two groups from baseline to week 12 or between responders and non-responders at week 12 in a substudy. Median u-CGRP/u-creatinine ratios

at baseline in morning urine samples were 5.5 in the acupuncture group (n = 33) and 5.9 in the control group (n = 33), whereas the corresponding values at week 12 were 6.6 and 6.3, respectively. In evening urine samples, the median u-CGRP/ u-creatinine ratio at baseline in the acupuncture group (n = 33) was 5.9, and in the control group (n = 28), it was 6.8. At week 12, the corresponding values were 6.1 and 5.6. To evaluate the CGRP excretion among responders and nonresponders, the morning and evening u-CGRP/u-creatinine sample values were summated and divided by 2. No statistically significant differences were observed; the median value at 12 weeks was 8.0 among responders and 7.2 among nonresponders.

Table 3 Change in hot flash frequency and intensity in the ACUFLASH study

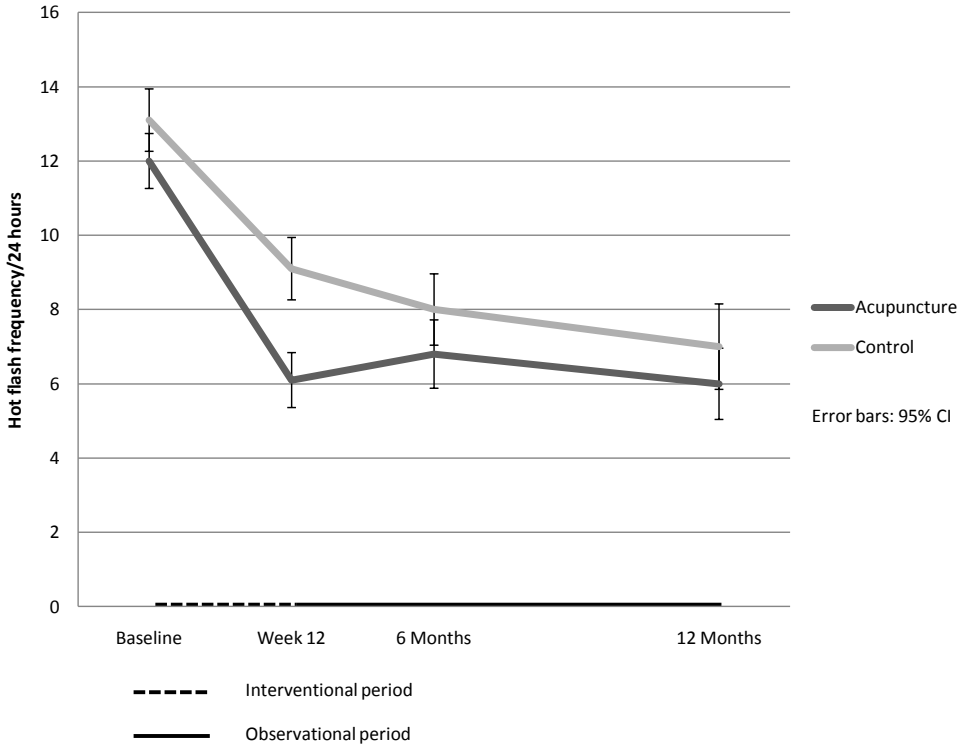
Change in hot flash frequency and intensity at week 12 in the study groups and at 6 and 12 months in the study groups and in selected sub-groups [a].

	Acupuncture group (n = 134)	**Control group (n = 133)**	**p** [b]
Hot flash frequency/24 hours			
Baseline	12.0 (4.3)	13.1 (4.9)	
Difference from baseline at:			
12 weeks (n=131/117)	- 5.8 (4.6)	- 3.7 (3.7)	< 0.001
6 months (n = 124/112)	- 5.3 (4.9)	- 5.0 (5.5)	0.736
Acupuncture use 3-6 Mo (n=32/10)	- 6.0 (4.8)	- 6.2 (9.7)	
No acupuncture use 3-6 Mo	- 5.0 (4.9)	- 4.9 (5.0)	
Higher expectation baseline (n = 75/58)	- 6.0 (4.9)*	- 5.3 (6.7)	
Lower expectation baseline	- 4.0 (4.6)*	- 4.7 (4.1)	
Dietary supplem/medic 3-6 Mo – yes (n = 95/89)	- 4.9 (5.1)	- 5.0 (5.8)	
Dietary supplem/medic 3-6 Mo - no	- 6.3 (4.3)	- 5.4 (4.4)	
Change living habits 3-6 Mo – yes (n = 34/35))	- 5.6 (4.3)	- 5.3 (4.8)	
Change living habits 3-6 Mo – no	- 5.1 (5.1)	- 4.9 (5.9)	
12 months (n = 119/114)	- 6.0 (5.2)	- 5.8 (6.3)	0.810
Acupuncture use 6 -12 Mo (n=29/16)	- 6.7 (4.4)	- 6.1 (6.9)	
No acupuncture use 6 -12 Mo	- 5.8 (5.5)	- 5.7 (6.2)	
Higher expectation baseline (n = 75/59)	- 7.0 (5.2)*	- 7.1 (7.6)*	
Lower expectation baseline	- 4.3 (4.9)*	- 4.3 (3.9)*	
Dietary suppl/medic. 6-12 Mo – yes (n = 95/87)	- 6.2 (5.3)	- 5.5 (6.5)	
Dietary suppl/medic. 6-12 Mo - no	- 5.9 (5.3)	- 7.0 (5.5)	
Change living habits 6 -12 Mo – yes (n = 27/32)	- 5.9 (4.9)	- 5.9 (5.5)	
Change living habits – no	- 6.1 (5.3)	- 5.8 (6.6)	
Hot flash intensity (0-10)			
Baseline	6.7 (2.0)	7.1 (1.7)	
Difference from baseline at:			
12 weeks (n = 111/107)	- 3.2 (2.5)	- 1.9 (2.2)	< 0.001

6 months (n = 107/101)	- 2.9 (2.6)	- 2.6 (2.7)	0.410
Acupuncture use 3-6 Mo (n=25/9)	*-3.3 (2.2)*	*-4.3 (3.5)*	
No acupuncture use 3-6 Mo	*-2.8 (2.7)*	*-2.5 (2.6)*	
Higher expectation baseline (n = 75/59)	*-3.3 (2.4)*	*-3.0 (2.9)*	
Lower expectation baseline	*-2.4 (2.9)*	*-2.2 (2.4)*	
Dietary supplem/medic 3-6 Mo – yes (n = 81/81)	*-2.8 (2.7)*	*-2.6 (2.8)*	
Dietary supplem/medic 3-6 Mo - no	*-3.5 (2.5)*	*-2.8 (2.2)*	
Change living habits 3-6 Mo – yes (n = 34/35))	*-3.0 (2.5)*	*-2.3 (2.6)*	
Change living habits 3-6 Mo – no	*-2.9 (2.7)*	*-2.7 (2.8)*	
12 months (n = 102/102)	- 3.4 (2.9)	- 3.4 (2.8)	0.924
Acupuncture use 6 -12 Mo (n=26/16)	*-3.7 (2.7)*	*-2.9 (2.2)*	
No acupuncture use 6 -12 Mo	*-3.3 (2.9)*	*-3.4 (2.9)*	
Higher expectation baseline (n = 61/53)	*-4.0 (2.8)**	*-4.2 (2.7)**	
Lower expectation basline	*-2.6 (2.7)**	*-2.3 (2.6)**	
Dietary suppl/medic. 6-12 Mo – yes (n = 79/79)	*-3.3 (2.8)*	*-3.2 (2.8)*	
Dietary suppl/medic. 6-12 Mo - no	*-3.7 (3.0)*	*-3.8 (2.7)*	
Change living habits 6 -12 Mo – yes (n = 22/29)	*-3.5 (2.2)*	*-3.0 (2.8)*	
Change living habits 6 -12 Mo– no	*-3.4 (3.0)*	*-3.5 (2.8)*	

[a] Data are means (SD) [b] Results from t-tests, acupuncture group versus control group
* Difference between sub-groups is statistically significant

Figure 3 Change in mean hot flash frequency in the ACUFLASH study



Health-related quality of life

When scoring the WHQ at baseline, the participants reported slightly better mental health and attractiveness and poorer somatic health, memory/concentration and sleep compared to a European reference population.[125] Mean vasomotor domain score was 0.98 (1.0 is worst possible), compared to 0.47 in the reference population.

At week 12 the acupuncture group experienced a mean reduction of 0.28 in the vasomotor symptoms domain score, 0.17 in the sleep domain score and 0.12 in the somatic symptoms domain score, compared to 0.04, 0.04 and 0.05 in the control group ($p < 0.001$, $p = 0.002$ and $p = 0.011$). Changes in WHQ domain scores from baseline to six and 12 months did not differ significantly between the groups. For further details, see Table 4.

Table 4 WHQ scores at baseline and mean change in scores in the Acuflash study [a]

WHQ dimensions	Acupuncture Mean (SD)	Control Mean (SD)	p [b]	Reference values [c] Mean (SD)
Depressed mood, baseline (n=265)	0.19 (0.21)	0.23 (0.22)		0.30 (0.26), n=4484
Mean change from baseline to 12 weeks (n=247)	-0.09 (0.18)	-0.04 (0.24)	0.083	
to 6 months (n=246)	-0.06 (0.19)	-0.04 (0.21)		
to 12 months (n=241)	-0.06 (0.18)	-0.05 (0.24)		
Somatic symptoms, baseline (n=265)	0.48 (0.26)	0.55 (0.24)		0.38 (0.28), n=4468
Mean change from baseline to12 weeks (n=247)	-0.12 (0.24)	-0.05 (0.21)	0.011	
to 6 months (n=246)	-0.08 (0.22)	-0.09 (0.26)		
to12 months (n=241)	-0.09 (0.23)	-0.10 (0.24)		
Memory/concentration, baseline (n=265)	0.49 (0.38)	0.54 (0.38)		0.37 (0.37), n=4461
Mean change from baseline to 12 weeks (n=247)	-0.09 (0.29)	-0.03 (0.30)	0.108	
to 6 months (n=246)	-0.03 (0.30)	-0.08 (0.34)		
to 12 months (n=241)	-0.10 (0.35)	-0.11(0.33)		
Vasomotor symptoms, baseline (n=263)	0.98 (0.09)	0.98 (0.10)		0.47 (0.45), n=4429
Mean change from baseline to 12 weeks (n=243)	-0.28 (0.39)	-0.04 (0.20)	<0.001	
to 6 months (n=244)	-0.23 (0.39)	-0.19 (0.37)		
to 12 months (n=239)	-0.29 (0.42)	-0.25 (0.40)		
Anxiety/fears, baseline (n=264)	0.22 (0.26)	0.29 (0.26)		0.30 (0.32), n=4502
Mean change from baseline to 12 weeks (n=246)	-0.09 (0.20)	-0.05 (0.27)	0.101	
to 6 months (n=245)	-0.05 (0.20)	-0.06 (0.26)		
to 12 months (n=240)	-0.07 (0.22)	-0.08 (0.27)		
Sleep problems, baseline (n=265)	0.57 (0.33)	0.61 (0.32)		0.46 (0.37), n=4549
Mean change from baseline to 12 weeks (n=247)	-0.17 (0.36)	-0.04 (0.27)	0.002	
to 6 months (n=246)	-0.11 (0.33)	-0.11 (0.34)		
to 12 months (n=241)	-0.13 (0.34)	-0.13 (0.32)		
Attractiveness, baseline (n=263)	0.35 (0.39)	0.31 (0.39)		0.58 (0.38), n=4193
Mean change from baseline to 12 weeks (n=240)	-0.14 (0.35)	-0.09 (0.34)	0.194	
to 6 months (n=246)	-0.07 (0.35)	-0.01 (0.38)		
to 12 months (n=239)	-0.10 (0.35)	-0.03 (0.37)		

[a] The values of the scores vary between 0 and 1, where 0 is an indicator of "good health status" and 1 is an indicator of "poor health status"
[b] Results from t-tests, acupuncture group versus control group
[c] Reference values are taken from the IQOD WHQ Database, postmenopausal wome

Sub-group analyses

Treatment for menopausal symptoms after the end of the interventional period

At six months, 35 participants in the acupuncture group and 20 participants in the control group had used alternative treatment for menopausal symptoms during the last three months (p=0.07), and at 12 months, 36 participants in the acupuncture group and 23 participants in the control group had used alternative treatment for menopausal symptoms during the last six months (p=0.14). Of these, a large proportion had used acupuncture treatment (see Table 3). Participants using acupuncture treatment in the period from 12 weeks to six months, and in the period from six months to 12 months, experienced a larger reduction in hot flash frequency and intensity than the participants not using acupuncture during this period, although the differences were not statistically significant (Table 3).

Seven participants had used hormone treatment (HT) for menopausal symptoms during the period from Week 12 to six months; three in the acupuncture group and four in the control group. Ten participants had used HT for menopausal symptoms during Months 6 to 12, five in the acupuncture group and five in the control group. Excluding HT users from the analyses did not change the results.

The number of participants that had used dietary supplements or changed their living habits during the observational period and the corresponding change in vasomotor symptoms are listed in Table 3.

Responders and expectation

Participants achieving 50% or more reduction in hot flash frequency were regarded as responders. At Week 12, 50% of the participants in the acupuncture group and 16% in the control group had experienced a ≥50% reduction in hot flash frequency. At six months, 48% of the participants in the acupuncture group and 34% in the control group were responders, a statistically significant difference (p=0.02). At 12 months, these percentages were 58% and 42%, respectively, (p=0.03).

In the acupuncture group, 16% of the participants who were responders at 12 weeks were non-responders at six months and 5% of the responders at six months were non-responders at 12 months. The corresponding percentages in the control group were 8% at both six and 12 months.

When asked at baseline if they believed acupuncture treatment would relieve their menopausal vasomotor symptoms, 80 participants in the acupuncture group answered "yes" and 53 answered "do not know," whereas nobody answered "no" and one was missing. At six months, 41 of the participants within the sub-group with higher expectancies were responders, compared with 19 in the lower-expectancy group ($p = 0.08$). At 12 months, 47 and 21 participants, respectively, were responders ($p=0.11$).

In the control group, 68 participants expected that acupuncture would relieve hot flashes, and 61 answered "do not know," four were missing. At six months, 18 participants within the higher-expectancy group and 19 within the lower-expectancy group were responders. At 12 months, 33 participants within the higher-expectancy group and 15 within the lower-expectancy group were responders, a statistically significant difference ($p < 0.01$).

In both study groups, the higher expectation sub-group experienced a larger reduction in hot flash frequency and intensity than the lower expectation sub-group at all points of time. In the acupuncture group, the differences between these sub-groups were statistically significant at six and 12 months regarding frequency and at 12 months regarding intensity (Table 3). In the control group, the differences between these sub-groups were statistically significant at 12 months regarding frequency and intensity.

Changes in climacteric complaints

At six months, 98 participants in the acupuncture group answered "yes" on the global question addressing if they had experienced any changes regarding their climacteric complaints, compared with 69 participants in the control group. This difference was

statistically significant (p = 0.005). At 12 months, the corresponding numbers were 95 and 83; the difference was not statistically significant.

Paper II

TCM syndrome diagnoses

At the first acupuncture treatment session, 127 participants received an initial primary TCM syndrome diagnosis and 106 participants received an initial secondary TCM syndrome diagnosis (Table 5). During the treatment sessions, the primary syndrome was revised once in 11 participants, and twice in one participant. The secondary syndrome was revised once in 14 participants, twice in three, three times in three, and four times in one participant. Fifty percent of the participants were diagnosed with Kidney Yin Xu as their primary syndrome.

Among the secondary syndromes, Liver Qi stagnation was the most prevalent diagnosis, with 19 percent of the participants. No statistically significant differences were demonstrated between the initial primary TCM syndrome groups or the revised primary TCM syndrome groups regarding the distribution of responders and non-responders, nor regarding the change in WHQ scores.

Table 5 Primary and secondary TCM syndromes on initial diagnosis in the ACUFLASH study

Syndromes	N as primary	%	N as secondary	%
KI Yin Xu empty heat	67	50	17	13
KI Yang Xu empty cold	22	16	10	7
KI Yin and KI Yang Xu	11	8	8	6
KI and LR Yin Xu with LR Yang rising	10	8	12	9
KI and HT not harmonised	14	10	18	13
Acc of phlegm and stagnation of Qi	1	1	12	9
LR Qi stagnation	0	0	25	19
Stomach heat	2	2	3	2
Stasis of blood	0	0	1	1
Missing	3	2	3	2
No syndrome	4	3	25	19
Sum	134	100	134	100

KI = Kidney, HT = Heart, LR = Liver, Xu = deficiency, Acc = accumulation

Treatment sessions and acupuncture points used

During the study, a total of 1285 treatment sessions were carried out on 131 participants. Of these, 123 received 10 treatment sessions, two received 9 sessions, three received eight sessions, one received seven sessions and two received three sessions. The mean number of treatments per participant was 9.8, and the median number of points stimulated per treatment session was 6.0 (SD 2.8, range 9). A total of 8599 acupuncture point stimulations were performed during the study, and a total of 104 different acupuncture points were used once or more. The eight most commonly used acupuncture points were SP6, HT6, KI7, KI6, CV4, LU7, LI4 and LR3, see Table 6.

Table 6 Acupuncture points used in responders and non-responders in the Acuflash study

Responders [a] (n = 67)				Non-responders [a] (n = 64)			
Acu-puncture points	**Number of Stimulations**	**Percent of total**	**Cumu-lative percent**	**Acu-puncture points**	**Number of Stimulations**	**Percent of total**	**Cumu-lative percent**
SP6	424	10.1	10.1	**SP6**	390	8.9	8.9
HT6	419	9.9	20.0	**KI6**	368	8.4	17.3
KI7	416	9.9	29.9	**KI7**	359	8.2	25.5
KI6	291	6.9	36.8	**HT6**	336	7.7	33.2
CV4	262	6.2	43.0	**CV4**	313	7.1	40.3
LU7	260	6.2	49.1	**LU7**	293	6.7	47.0
LI4	199	4.7	53.9	**LI4**	227	5.2	52.2
LR3	196	4.6	58.5	**LR3**	219	5.0	57.2
ST36	177	4.2	62.7	KI3	193	4.4	61.6
KI3	173	4.1	66.8	ST36	171	3.9	65.5
GV20	115	2.7	69.5	GB34	119	2.7	68.2
LI11	109	2.6	72.1	PC6	96	2.2	70.4
PC6	106	2.5	74.6	GV20	95	2.2	72.5
CV12	94	2.2	76.9	CV12	85	1.9	74.5
SP4	91	2.2	79.0	LI11	79	1.8	76.3
LR8	78	1.8	80.9	LR8	64	1.5	77.7
GB34	73	1.7	82.6	SP4	62	1.4	79.2
68 other points [b]	734	17.4	100.0	65 other points [c]	913	20.8	100.0
Total	4217				4382		

[a] Responder: ≥ 50% reduction in hot flash frequency, non-responder: < 50% reduction of hot flash frequency
[b] 32 points were stimulated 59 -10 times , 36 points were stimulated < 10 times
[c] 26 points were stimulated 59 -10 times, 39 points were stimulated < 10 times

SP = Spleen, HT = Heart, KI = Kidney, CV = "Conception Vessel", LU = Lung, LI = Large Intestine, LR = Liver, ST = Stomach, GV = "Governor Vessel", PC = Pericardium, SP = Spleen, GB = Gallbladder

Responders/non-responders

In the acupuncture group, 67 participants were responders, and 64 participants were non-responders. A total of 4217 point stimulations were performed among responders, and 4382 among non-responders. The ten most frequently used points were identical among responders and non-responders, and these ten points constituted two thirds of the total number of point stimulations throughout the study (Table 6). The distribution of responders/non-responders among primary syndromes is shown in Table 7, and the distribution of points used according to syndrome diagnosis is shown in Table 8. The eight most frequently used acupuncture points in total were among the thirteen most frequently used points in every syndrome group.

Table 7 Distribution of responders and non-responders among primary syndromes

Primary Syndromes*	N	Responder	Non-responder
KI Yin Xu empty heat	67	33	34
KI Yang Xu empty cold	22	14	8
KI Yin and KI yang Xu	11	5	6
KI and LR Yin Xu with LR yang rising	10	5	5
KI and HT not harmonised	14	6	8
Other syndromes	3	1	2
No primary syndrome	4	3	1
Total	131	67	64

KI = Kidney, HT = Heart, LR = Liver, Xu = deficiency

Table 8 Acupuncture points used according to syndrome diagnosis [a]

KI Yin Xu empty heat (n=69)		KI Yang Xu empty cold (n=22)		KI Yin and KI yang Xu (n=11)		KI and LR Yin Xu with LR yang rising (n=10)		KI and He not harmonised (n=14)	
Acu-points[a]	**No of stim.[b]**	**Acu-points**	**No of stim.**	**Acu-points**	**No of stim.**	**Acu-points**	**No of stim.**	**Acu-points**	**No of stim.**
SP6	6.3	**SP6**	7.1	**KI7**	6.5	**CV4**	6.0	**CV4**	7.8
KI7	5.7	**KI7**	6.5	**HT6**	5.4	LR8	5.0	**KI6**	7.6
HT6	5.5	**HT6**	6.4	**SP6**	5.2	**HT6**	4.7	**KI7**	7.1
KI6	5.1	**KI6**	5.0	**LR3**	3.5	**KI7**	4.0	**SP6**	7.1
CV4	4.3	**LU7**	4.6	**CV4**	3.4	**LR3**	3.9	**LU7**	6.9
LU7	4.1	**LI4**	2.6	KI3	3.3	**KI6**	3.8	**HT6**	6.6
KI3	3.7	**CV4**	2.4	**LU7**	3.3	LI11	3.8	CV15	4.1
LI4	3.6	ST36	2.3	**KI6**	3.0	SP4	3.8	**LR3**	3.8
ST36	3.3	PC6	2.1	CV12	1.8	**LI4**	3.5	**LI4**	3.7
LR3	3.3	**LR3**	2.0	GV20	1,7	GV20	3.4	GV20	2.3
GB34	1.9	SP4	1.8	**LI4**	1.6	PC6	3.1	KI3	1.9
LI11	1.5	KI3	1.7	ST36	1.6	**LU7**	3.0	SP4	1.9
CV12	1.3	CV12	1.5	KI10	1.5	**SP6**	2.9	HT7	1.9
66 other points	15.1	34 other points	13.3	32 other points	15.8	28 other points	24.5	32 other points	18.4

[a] The eight most frequently stimulated acupuncture points in total are shown in bold types.
[b] Mean number of stimulations per participant

SP = Spleen, HT = Heart, KI = Kidney, CV = "Conception Vessel", LU = Lung, LI = Large Intestine, LR = Liver, ST = Stomach, GV = "Governor Vessel", PC = Pericardium, SP = Spleen, GB = Gallbladder

Adverse events

No fainting, convulsions or bleeding were reported during the treatment sessions. One skin reaction and one unacceptable bruising were reported, as were five episodes of unacceptable needling pain. Two episodes with a forgotten needle were reported, but no broken needle, moxa burn, pneumothorax or infections.

Paper III

Factor analysis (principal component analysis – PCA)

The menstrual symptoms dimension of the WHQ was excluded from the study because all participants were postmenopausal. Items related to the sexual behaviour dimension were also excluded due to a preponderance of missing values. The initial factor analysis (principal component analysis - PCA) was performed on the remaining 29 items (Table 9). For this analysis, the scores in the different dimensions of the WHQ were calculated, after reversing the appropriate items, as mean scores based on the four-point Likert scale.

Eigenvalues for consecutive factors can be presented in a simple line plot. This so-called scree plot may be used to graphically decide the optimal number of factors. Based on the scree plot, five factors were identified. Four items from the original anxiety/fears dimension had the highest loadings on the first factor, in addition to items from the depressed mood dimension and the sleep dimension. Hence, factor one may represent an anxiety/depression dimension. The second factor included items that described feelings of attractiveness, well-being and liveliness; therefore, this factor may represent a 'well-being' dimension. The high loading items on factor three described a range of somatic symptoms; hence this factor represents a somatic symptoms dimension. The factor included all the items of the original somatic symptoms dimension, one item from the original anxiety/fears dimension and two items from the original sleep problems dimension. The highest loading items on factor four were the three items of the original memory/concentration dimension. In addition, items from the somatic symptoms and depressed mood dimension cross-loaded on this factor. Factor five included items that reflected symptoms related to menopausal complaints. Here we found the two items of the original vasomotor symptoms dimension and item one of the original sleep problems dimension. This dimension may thus represent a 'menopausal vasomotor symptoms/sleep problems' dimension.

Table 9 Descriptive statistics and principal component analysis results for the WHQ items (N = 266)

Item no[a]		*M* (*SD*)	Factor loadings[b]				
			1	2	3	4	5
2	I get very frightened or panic feelings for apparently no reason at all	3.54 (0.74)	0.70				
4	I feel anxious when I go out of the house on my own	3.82 (0.55)	0.67				
6	I get palpitations or a sensation of "butterflies" in my stomach or chest	2.96 (0.96)	0.54		0.36		
9	I feel tense or "wound up"	2.66 (0.96)	0.56	0.38			
21 (R)	I feel rather lively and excitable	2.95 (0.85)		0.77			
32 (R)	I feel physically attractive	2.74 (0.85)		0.69			
14	I have headache	2.62 (0.96)			0.62		
15	I feel more tired than usual	2.00 (0.92)		0.48	0.47	0.37	
16	I have dizzy spells	3.12 (0.93)			0.56		
18	I suffer from backache or pain in my limbs	2.04 (1.00)			0.67		
23	I feel sick or nauseous	3.32 (0.87)	0.33		0.49		
30	I often notice pins and needles in my hands and feet	2.75 (1.13)			0.63		
35	I need to pass urine more frequently than usual	2.32 (1.10)			0.39	0.39	
20	I am more clumsy than usual	2.90 (0.96)				0.70	
33	I have difficulty in concentrating	2.48 (0.92)				0.71	
36	My memory is poor	2.35 (0.86)				0.77	
1	I wake early and then sleep badly for the rest of the night	1.96 (0.94)			0.37		0.55
11	I am restless and can not keep still	2.84 (0.98)	0.52				
29	I have difficulty in getting off to sleep	2.33 (1.07)	0.39		0.46		
3	I feel miserable and sad	2.95 (0.91)	0.48	0.46		0.40	
5	I have lost interest in things	3.17 (0.93)	0.41	0.54			
7 (R)	I still enjoy the things I used to	3.71 (0.60)		0.58			
8	I feel life is not worth living	3.61 (0.82)	0.38				
10 (R)	I have good appetite	3.80 (0.48)					
12	I am more irritable than usual	2.63 (0.96)	0.42			0.36	
25 (R)	I have feelings of well-being	3.18 (0.82)		0.71			
19	I have hot flushes	1.03 (0.18)					0.34
27	I suffer from night sweats	1.23 (0.52)					0.83
13	I worry about growing old	2.92 (0.91)	0.36	0.34			
Variance explained (%)			12	12	10	9	5

Notes: Total variance explained (48%). Factor loadings <0.32 were omitted.
[a] (R) = items reversed before analysis.
[b] Original WHQ dimensions: 1: Anxiety/fears (items 2, 4, 6, 9), 2: Attractiveness (items 21, 32), 3: Somatic symptoms (items 14, 15, 16, 18, 23, 30, 35), 4: Memory concentration (20, 33, 36), 5: Vasomotor symptoms (19, 27). Depressed mood (items 3, 5, 7, 8, 10, 12, 25); Sleep problems (1, 11, 29). Item 13 is not considered belonging to any dimension.

Internal consistency

Internal consistency was evaluated by calculating Cronbach's alpha coefficient [126] for each dimension, see Table 10. Cronbach's alpha value is a function of the number of test items and the average correlation among the items. Values between 0.7 and 0.9 were found for the depressed mood, somatic symptoms and memory/concentration dimensions, while values between 0.5 and 0.7 were found for the anxiety/fears, sleep problems and attractiveness dimensions. Cronbach's alpha value for the vasomotor dimension was 0.12, and for the WHQ totals score it was 0.90.

Table 10 Cronbach's alpha and descriptive statistics for the WHQ dimensions and WHQ total score (N = 265)

WHQ dimensions	No of items	Alpha	*M* (*SD*)
Depressed mood	7	0.78	3.29 (0.53)
Somatic symptoms	7	0.72	2.64 (0.63)
Memory/concentration	3	0.76	2.57 (0.75)
Vasomotor symptoms	2	0.12	1.13 (0.28)
Anxiety/fears	4	0.69	3.25 (0.59)
Sleep problems	3	0.58	2.38 (0.74)
Attractiveness	2	0.60	2.85 (0.71)
WHQ total score	29	0.90	2.59 (0.42)

Correlation with other instruments

The WHQ total score and subscales correlated with the EQ-5D, EQ-5D VAS and PSC in the expected direction (Table 11). The correlations were all, except for the correlations between the vasomotor symptoms domain and the other instruments, significant and moderate to large in size, according to Cohen's criteria.[99] The correlation between PSC and the somatic symptoms domain was significantly larger (as indicated by Hotelling's T^2 test) than the correlations between PSC and all the other domains of the WHQ. Between PSC and the depressed mood domain the correlation was moderate, and significantly higher than between PSC and the attractiveness and vasomotor complaints domains. The correlation between PSC and the anxiety/fears domain was significantly larger than between PSC and the memory, vasomotor complaints and attractiveness domains. The correlations between EQ-5D/EQ-5D VAS and the somatic symptoms dimensions were significantly larger than the correlations between EQ-5D/EQ-5D VAS and all the other WHQ- dimensions.

Table 11 Correlations between the WHQ and the other measurement instruments in the study

WHQ (N = 265)	EQ5D (N = 263)	EQ-5D VAS (N = 265)	PSC (N = 181)
Depressed mood	0.39**	0.39**	–0.52**
Somatic symptoms	0.60**	0.53**	–0.72**
Memory/concentration	0.28**	0.35**	–0.41**
Vasomotor symptoms	0.03	0.01	–0.14
Anxiety/fears	0.36**	0.29**	–0.54**
Sleep problems	0.33**	0.29**	–0.59**
Attractiveness	0.29**	0.36**	–0.30**
WHQ total score	0.49**	0.49**	–0.70**

Note: ** $p < 0.01$ (two-tailed).

Floor and ceiling effects

A strong floor effect was present in the vasomotor complaints subscale, where 79% of the respondents scored one (yes, definitely) on the four-point Likert scale. A moderate ceiling effect was present in the anxiety/fears subscale, where 16% of the respondents scored four (no, not at all). The other subscales showed no floor or ceiling effects.

The 23-item version of the WHQ

To assess the new 23-item version of WHQ, another PCA with Varimax rotation was performed, including only the 23 items that remain in the new version. Six factors were identified, explaining 58 % of the variance. We clearly identified all dimensions in the 23-item version.

In our material, item 10 (appetite) had a low correlation (0.3) with the "Well-being" dimension. In the development of the original 23-item version, item 21 (I feel rather lively and excitable) in the 36-item version was removed because it may have both a positive and/or a negative connotation in different cultures and translations.[119] In the Norwegian translation, however, this question has a clear positive meaning. We removed item 10 and substituted item 21 and performed another PCA. The resulting model had six clearly identified dimensions that explained 60 % of the variance.

Discussion

Methodological issues

Study Design

The Acuflash study was a pragmatic/practical clinical trial, not explanatory. Explanatory trials measure efficacy, which is the benefits of a treatment under ideal conditions, often using carefully selected individuals in a research clinic. The goal of an explanatory study is to understand how and why an intervention works.[127] Pragmatic or practical clinical trials, like this study, measure the benefits of the treatment in everyday clinical practice – the effectiveness.[128] Characteristic elements of a pragmatic clinical study are that they select clinically relevant interventions to compare, they include a varied population of study participants, they recruit participants from different practice settings, and they collect data on a broad range of health outcomes.[127-129] It is important to describe the intervention in detail in both study types; however, this does not mean that exactly the same treatment is offered to each patient in a practical clinical trial. In a study of for example physiotherapy interventions or acupuncture interventions, the protocol may allow for individualization of the treatments; it is then the management protocol which is studied, not the individual treatments.[129]

In a practical clinical trial, a balance between the generalizability of the results (external validity) and the accuracy or reliability of the results (internal validity) has to be achieved.[130] Selection bias was dealt with by randomization in this study. Other sources of bias exist; the study was not blinded, hence both participants and acupuncturists were aware of which group they were allocated to, and which treatment was given. Explanatory trials use blinding to reduce bias, that is, to maximize internal validity. However, patient and therapist biases are not automatically viewed as unfavorable in a practical clinical trial, but accepted as part of patient's and therapist's reaction to treatment and included in the overall evaluation.[129] Hence, in this practical clinical trial, the treatment response is the total difference between the two groups, including both treatment and associated context-/expectation-/placebo-effects, 'as this will best reflect the likely clinical response in practice'.[129] Although the internal validity will be reduced in practical trials because of lack of blinding, they will more likely generalize better to a normal clinical setting, that is, have a higher external validity.[128]

Outcome measures usually differ between explanatory and practical studies.[128 129] In explanatory studies, intermediate outcomes, like change in joint movement, are often used. In a practical study, outcomes relevant to everyday life are chosen, as in our study, where hot flash frequency and intensity, sleep and health related quality of life were endpoints.

It is important to observe that the practical study design did not allow us to estimate what proportion of the clinical benefit was due to the effects of the needling itself, and what was due to other factors, such as natural fluctuation in symptoms, spontaneous improvement, regression to the mean, and placebo effects, including expectations and the patient-provider interaction.

We aimed to compare two 'real-life' treatment policies available to postmenopausal women with vasomotor symptoms, namely acupuncture plus self-care and self-care alone. To know whether the addition of acupuncture treatment to self-care contributes to a clinically relevant reduction of symptoms or not, is highly relevant for symptomatic women looking for alternatives to hormone therapy. It is also relevant for their health-care providers and for political decision-makers.

Participants

It is debated if it should be controlled for differences among participants in baseline covariates in RCT's. By principle, randomization controls for confounding at baseline, and covariate imbalance occurs by chance. The statistical analysis thus makes an average allowance for the covariate imbalance. If the analyses are adjusted for the baseline measure there is a risk of actually introducing bias in the reporting of results. An undue importance can thereby be assigned to the baseline measure and an over-adjustment can occur. In addition, the use of ANCOVA will only allow us to control for those covariate confounders that are actually measured. We therefore prefer to present the unadjusted analysis.

Study participants were self-selected through media coverage and advertisements, and had a positive attitude towards acupuncture. This self-selection bias may limit the generalizability of the findings. Almost two thirds of the participants in the study had used acupuncture previously, and 55% expected that acupuncture would relieve hot flashes. Hence, the study

participants had far more experience with acupuncture than the general population, and high expectations to the treatment. This may have affected the participants in the acupuncture group positively, and the participants in the control group, who probably hoped to receive acupuncture, negatively. Patient expectations can have a sizeable impact on clinical outcomes.[131] This may lead to an overestimation of the acupuncture treatment effect, and limit the generalizability of the findings. However, the positive expectation provided by the therapeutic context is understood to be an integral component of the neurological effects of acupuncture, and may even be essential for the central nervous system effects to occur.[92] Only 7% of the participants dropped out, and the low number of drop-outs can be considered one of the strengths of the study.

Practitioners of TCM acupuncture

The ten study acupuncturists were trained in TCM acupuncture; nine were graduates from the 'Akupunkturhøyskolen', a school located in Oslo, offering a bachelors degree in TCM acupuncture. Hence, the TCM acupuncture approach tested was TCM acupuncture as taught in Norway. They met the current membership criteria of the Norwegian Acupuncture Society (NAFO), (2500 hours of training), and had at least three years experience of practicing TCM acupuncture. They were suggested as study-acupuncturists by NAFO. Two acupuncturists were teachers at the 'Akupunkturhøyskolen'. There were four acupuncturists in Oslo, three in Bergen and three in Tromsø, all practicing in private clinics. Before study start, all the acupuncturists participated in a group meeting with the researchers to discuss the expected TCM diagnoses and the relevant acupuncture points.

Acupuncture treatment

TCM diagnosis, reliability and validity

The acupuncture treatment in this study was 'real life' TCM acupuncture. The acupuncturists were free to diagnose and select TCM acupuncture points for each patient. Before study start, all the acupuncturists participated in a group meeting with the researchers to discuss the expected TCM diagnoses and the relevant acupuncture points.

Fifty percent of the participants were diagnosed with Kidney Yin Xu. In his work "Traditional Chinese medicine--what are we investigating? The case of menopause", Scheid defines TCM as 'that interpretation of Chinese medical practice that is presented to us in contemporary Chinese medical textbooks, emerging in the late 1950's'.[57] In his opinion, the current interpretation of menopausal symptoms as mainly a result of Kidney deficiency is only one of several possible interpretations of the old Chinese texts, and the "correct " TCM diagnoses for menopausal vasomotor symptoms remain unclear.[57] The TCM acupuncture practiced in our study was mostly based on theories and principles from these Chinese textbooks written in the 1950's and 1960's, and a more recent interpretation by Maciocia, considering Kidney deficiency as the main cause of menopausal vasomotor symptoms.[55] Hence, the TCM acupuncture practiced might not be optimal, and the value of the syndrome differentiation and point selection based on these theories and principles might be questioned.

A TCM diagnostic syndrome differentiation, leading to an appropriate selection of traditional acupuncture points, are considered mandatory in the practice of TCM [46]. Although previous research has suggested that, among patients with recurrent cystitis, those with TCM diagnosis of Kidney fare better than those with other diagnoses,[132] the importance of TCM syndrome diagnostics and point selection has not been confirmed in clinical studies.[46] In addition, the validity and reliability of the TCM diagnostic process has been questioned, as has the inter-rater reliability.[133-135] A study showed that TCM diagnosis and treatment recommendations for specific patients with chronic low back pain vary widely across practitioners,[136] as did a study assessing the variability in the TCM diagnoses among patients with rheumatoid arthritis.[134] Hence, the reliability and validity of the diagnostic process in the present study may be low, resulting in 'wrong' diagnoses in some or many cases. In addition, as discussed earlier, the correct TCM syndrome patterns for menopausal vasomotor symptoms remain unclear. These facts may obviously affect the study results, which must be interpreted with this in mind.

Acupuncture point selection

A 'core' group of acupuncture points were used for all the TCM diagnostic syndromes, rendering a clinically and statistically significant effect.[137] The points were selected individually for each participant according to the TCM diagnosis, and represents 'best practice'. However, we do not know whether these acupuncture points were superior to treat

menopausal symptoms, nor if the acupuncture 'dose' was optimal. When comparing the point selection in this study with the points used in other studies evaluating acupuncture for menopausal symptoms,[98-102 138] the only point in common between all the studies was Sp6. The contribution of all the idiosyncratic acupuncture points used a few times during the Acuflash study remains unknown. The validity of TCM theories of point indications and locations has not been established,[139] and a systematic review of clinical acupuncture trials showed that sham acupuncture may be as efficacious as true acupuncture.[140] This is in accordance with the results of the studies of acupuncture for hot flashes previously cited.[17 98-102] Needle location is probably not as relevant as generally thought.

Acupuncture dose

White et al. have proposed the following definition of acupuncture dose: "The physical procedures applied in each session, using one or more needles, taking account of the patient's perception (sensory, affective and cognitive) and other responses (including motor). The dose may be affected by the state of the patient (e.g. nervous, immune and endocrine systems); different doses may be required for different conditions". The relationship between acupuncture dose and treatment response is probably not linear; due to properties of the nervous system, 'threshold' effects are possible.[141]

There is no common agreement on what is adequate acupuncture dose, but White et al. found that the core components of an adequate dose seems to be attention to the number of needles used, the needling technique, specific elicitation of a needling sensation (De Qi), the number of treatment sessions and the experience of the acupuncturist'.[141] In a systematic review of acupuncture for knee pain, adequate acupuncture was defined as 'consisting of at least six treatments, at least one per week, with at least four points needled for each painful knee for at least 20 minutes, and either needle sensation (De Qi) achieved in manual acupuncture, or electrical stimulation of sufficient intensity to produce more than minimal sensation.[142] The acupuncturists in the present study were well qualified and experienced. They were free to select the number of needles used and the needling technique. The mean number of treatments per participant was 9.8. The acupuncturists stimulated a median of 6 different acupuncture points per treatment, treated once a week and were asked to obtain needle sensation. On this background, the acupuncture stimulation or dose given seems adequate. However, classical

Chinese texts recommend treatments daily to every second day, use of several acupuncture points, and a combination of several acupuncture techniques, such as needling, moxibustion and massage, to obtain optimal effect. Sufficient time for stimulation of the acupuncture points is also considered important.[143 144] The treatment in the Acuflash study comprised of only one acupuncture technique, namely needling in traditional acupuncture points, and treatment once a week. Hence, these elements of the acupuncture dose were relatively small, and more intensive treatment might have changed the results.

Outcome measures, reliability and validity

Hot flash diary

The primary endpoint was frequency of hot flashes recorded in participant diaries. This is a subjective measure of vasomotor episodes, and as such vulnerable to variants of information bias. Participants may for instance exaggerate symptoms before treatment, and minimize them afterwards. Perceptual bias may occur; no real change may take place, but the participant may falsely perceive a change. The participant's real bother from vasomotor episodes may not change, but the criterion for labelling the degree of bother may be elevated, a so called response bias.[145] The information bias may falsely increase the reported effect of the acupuncture treatment.

Still, the use of hot flash diaries is considered a valid and reliable method of measuring vasomotor episodes, and it has been used in several studies of pharmacological treatment of menopausal complaints.[146] The use of self-report diaries for data collection is further established as a valid approach to obtain data on subjective phenomena such as patient-reported symptoms and perceptions.[146-149] However, in a comparison of subjective hot flash reports and continuous sternal skin conductance monitoring, the positive predictive value of the hot flash diary was low (34-52%), and the negative predictive value was high (94-97%). Hence, the use of hot flash diaries may seriously underestimate hot flash frequency.[150] A further study, assessing the validity of sternal skin conductance monitoring as a measure of hot flash distress and intensity, concluded that change in sternal skin conductance should not

be used as a proxy measure of subjective hot flash intensity or distress.[151] A possible reason for the discrepancy between the hot flash diary and the sternal monitoring may be that only bothersome hot flashes were registered in the hot flash diary. Not bothersome hot flashes registered by sternal skin conductance monitoring are hardly of any clinical importance. For future studies of hot flash interventions the use of a hot flash diary in addition to a daily rating of hot flash bother may still be the best option available. Others suggest a single daily rating of hot flash intensity in addition to a sternal monitoring device.[150]

Women's Health Questionnaire (WHQ)

The original 36 item version of the WHQ has nine domains. The sexual behavior and the menstrual symptoms domains were excluded from our analysis, which left 29 items, originally representing seven domains. The exploratory factor analysis was performed on these 29 items, and led to the identification of five factors, explaining a total of 48% of the variance. The original factor structure was only partially identified. The items of the original anxiety/fears, depressed mood and attractiveness dimensions regrouped on two factors, one representing anxiety/depression and the other positive feelings and well-being. Item one of the sleep dimension (waking early and then sleeping poorly for the rest of the night) loaded relatively high on the fifth factor, together with the items of the vasomotor symptoms dimension. Since the women participating in our study were highly selected, with a very high hot flash rate and related sleep problems, it seems likely that hot flashes, night sweating and sleep disturbances will load on the same factor for this group.

To assess the reliability of the questionnaire, Cronbach's alpha was calculated. Cronbach's alpha values between 0.7 and 0.8 are considered satisfactory.[126] Only three WHQ domains, in addition to the total score, showed alpha values in this interval: the depressed mood, somatic symptoms and memory/concentration dimensions. These results support the reliability of three of the seven dimensions of the questionnaire. Three other subscales showed alpha values above 0.5. These values were considered passable, whereas no internal consistency was demonstrated for the vasomotor symptoms dimension. The relatively low alpha values for several scales reflect the results of the factor analysis, where the original factor solution was only replicated to a limited extent. There were only three and two items, respectively, in the sleep problems and the attractiveness dimensions, and Cronbach's alpha value is a function of

the number of test items and the average correlation among the items. The low number of items partly explains the low alpha-value for these dimensions. The alpha value of the vasomotor symptoms dimension was only 0.12. This dimension consisted of only two items, and in our sample, these items show very little variance, which contributes to the low alpha value.

To assess the construct validity, the WHQ was correlated with an instrument measuring psychosomatic complaints (PSC), a self-rated assessment of general health status (EQ-5D VAS) and, finally, a measure producing a general health index (EQ-5D). Except for the vasomotor dimension, where no correlations were observed, the correlations between the WHQ separate dimensions/WHQ total score, and the scores of the other instruments were moderate to large. The results support the construct validity of the WHQ.

Our evaluation of the psychometric properties of the Norwegian translation of the 36-item version of the WHQ showed that it had some deficiencies when applied to a group of women with a high hot flash frequency. When applied to this kind of sample, it appears safe to use the total scale score, but care should be taken when interpreting some of the subscales.

When evaluating a model including the items in the new 23-item version only, we found that it had a better factor structure than the 36-item version. Based on our data, the Norwegian version of the 23-item questionnaire would profit from the removal of item 10 (appetite) and inclusion of item 21 (lively and excitable). This model had a better factor structure, and a higher percentage of the variance was explained than in the original 23-item version. However, we did not apply the 23-item version in the study; the data were extracted from the 36-item version used. Hence, the results might have been different if the 23-item version had been used, and these analyses were not included in the original paper (Paper III).

Discussion of the main results of the Acuflash study

The Acuflash study was a pragmatic study, testing acupuncture as a complete treatment package. We found that the overall reduction of hot flash frequency at the end of the interventional period was 48% among women who received acupuncture, compared with 28% reduction in the control group. The results suggest that a policy of use of 10 sessions of TCM acupuncture during 12 weeks plus self-care can reduce hot flash frequency by 50 % or more in half of the postmenopausal women experiencing frequent hot flashes. Strengths of the study are the randomized design, large sample size and high follow-up rate. The study showed consistent results across hot flash diary data and quality of life outcomes, and this supports the validity of the results.

As far as we know, this is the first study that observed the long-term effects of acupuncture treatment for menopausal vasomotor symptoms. Six and 12 months after study start, the statistically significant differences between the study groups that were seen at the end of the interventional period were no longer present. The participants in the control group experienced a continuous decrease in hot flash frequency from baseline to 12 months. The participants in the acupuncture group experienced a corresponding decrease during the 12-weeks interventional period, and subsequently, a steady state to 12 months. The number of responders was still significantly larger in the acupuncture group at six and 12 months. The WHQ scores in the control group had decreased to the level of the acupuncture group at six and 12 months; hence, no statistically significant differences between the study groups regarding health-related quality of life were present at these points of time.

Menopausal women experience more sleep-problems than non-menopausal women,[152 153] partly due to vasomotor symptoms.[154 155] At baseline, 48 % of our study participants reported sleep problems affecting work last year. Mean hours of sleep per night increased significantly in the acupuncture group compared with the control group during the interventional trial, and the sleep domain in the WHQ showed a statistically and clinically significant improvement. It has been observed that acupuncture treatment may improve sleep in patients with fibromyalgia,[156] but a Cochrane review concluded that recent evidence do not support the use of acupuncture for insomnia,[157] mainly due to a small number of studies and poor

methodological quality. Some of the improvement in sleep seen in our study may be due to the reduction of hot flashes during the night.

The secondary endpoint was health-related quality of life, measured by the WHQ. Participants in the acupuncture group experienced statistically and clinically significant improvements in the vasomotor, sleep and somatic symptoms dimensions of the WHQ from baseline to 12 weeks. These findings are supported by the results from a qualitative study among the participants in the acupuncture group in the ACUFLASH study.[158] The participants in this group were asked to give a written statement about any changes that had occurred during the interventional period, and many women reported a substantial reduction in frequency and intensity of hot flashes, increased sleep quality and other physical and mental changes such as better mood and more energy.[158] From week 12 to 12 months, the quality of life scores in the vasomotor, sleep and somatic symptoms dimensions did not change significantly in the acupuncture group, whereas the scores in the control group decreased to the level of the acupuncture group at six and 12 months.

Increased somatic symptoms are inconsistently associated with menopause.[1] Current evidence suggests that acupuncture is a useful treatment for musculoskeletal pain.[159] This finding supports our finding of a statistically and clinically significant improvement in the somatic symptoms dimension of the WHQ in the acupuncture group.

We observed that more participants in the control group than in the acupuncture group had changed their living habits (rest and sleep, physical activity, coffee drinking, alcohol intake, tobacco smoking) during the study, and twice as many participants in the control group as in the acupuncture group used dietary supplements for menopausal symptoms at week 12. The differences were statistically significant, and these confounding factors may lead to an underestimation of the acupuncture effect.

Acupuncture probably affects serotonin and beta-endorphin activity in the central nervous system,[68 86] and may thus influence the thermoregulatory center and make it more stable. A change in the beta-endorphin concentration may also affect the CGRP excretion.[17] We found no statistically significant changes in u-CGRP concentration in morning and evening urine samples from baseline to week 12 or between responders and non-responders in a sub-study. Urine CGRP concentration analyses should ideally have been performed in 24-hour urine

samples. This was not feasible in the present study, thus morning and evening samples were analyzed and we used the u-CGRP/u-Creatinine ratio to evaluate possible changes in CGRP excretion. The analysis may therefore suffer from poor precision, and must be interpreted with care.

The effect of the acupuncture treatment is comparable to effect of SSRIs/SNRIs on hot flashes.[40] Ten acupuncture treatment sessions cost NOK 3,000 to 3,500 (US $550-640), compared with NOK 500 to 1,000 (US $90-180) for 3 months of SSRI or SNRI use. The acupuncture treatment is more expensive, but the rate of adverse effects with acupuncture treatment is low[160] and may be lower than that seen with SSRI/SNRI treatment.

Post-hoc analyses

A sub-group of participants in both study groups used acupuncture treatment in the period from Week 12 to six and 12 months (Table 3). The subgroups using acupuncture treatment after Week 12 experienced a larger reduction in hot flash frequency and intensity and a larger increase in duration of sleep from Week 12 to six and twelve months. Although the observed differences were not statistically significant, the findings support practitioners observations that follow-up treatments may be desirable after the initial series of treatments for optimal long-term effects.

We found a larger, although not statistically significant, proportion of responders among the participants in the acupuncture group assuming that acupuncture treatment would relieve their vasomotor symptoms than among those that "did not know" at six and 12 months. In the control group, we found a significant majority of responders in the higher expectation subgroup at 12 months. Participants with higher expectations experienced a larger reduction in hot flash frequency and intensity than those with lower expectations. In a systematic review on expectancy of therapeutic gain, 15 of 16 studies reported that positive patient expectations were associated with better health outcomes.[161] Other studies of acupuncture have shown that patient expectations can have a large impact on clinical outcomes.[131 162 163] Our results support these findings. It is interesting to note that expectations of acupuncture effect also were of importance among participants in the self-care group. The differences between the sub-groups were not statistically significant; however, the study was not powered to detect sub-group differences. When interpreting these results, it is also important to have in mind that these

sub-group analyses were not planned a priori; hence, they are post-hoc analyses, susceptible to the problems of inflating the total number of statistical tests. Multiple testing procedures could have been used to compensate for this.

Acupuncture and the Placebo effect

In his paper "Deconstructing the Placebo Effect and Finding the Meaning Response", Daniel E. Moerman concludes: "Placebos are inert. You can't do anything about them. For human beings, meaning is everything that placebos are not, richly alive and powerful".[164]

In 1799, the author of the first known placebo-controlled study concluded: "An important lesson in physics is here to be learnt; the wonderful and powerful influence of the passions of the mind upon the state and disorder of the body".[165] Today, some of the neurobiological and psychological effects and mechanisms that constitute part of the placebo effect have been identified, and modern research design and technology allow further exploration of the complex mind-brain-body interaction.[166] Brody has defined the placebo effect as " a change in the patients health or bodily state that is attributable to the symbolic impact of medical treatment or the treatment setting ".[167] According to Benedetti, "placebo is an inert medical treatment, and the placebo effect is the response to it. An inert medical treatment is administered within a context, and it is the context that plays the crucial role" [168]. The identification of placebos as inert agents or procedures present us with a paradox, as an inert medical treatment has no inherent properties that allow it to cause an effect. Today, "focus has shifted from the inert content of the placebo agent to the concept of a simulation of an active therapy within a psychosocial context".[166]

The starting point of the neurobiology of the placebo effect is considered to be 1978, when it was shown that placebo analgesia could be blocked by naloxone, indicating an involvement of endogenous opioids.[169] The interaction between the therapist and the patient triggers physiological mechanisms, including the release of endogenous opioids and dopamine and the modulation of endogenous cholecystokininergic systems, but we do not yet know how it acts.[168] It is generally believed that cognitive factors such as expectancies are involved, and a

mechanism of classic conditioning may play a role without involving expectancies, meanings and symbols.[168]

The terms ‘placebo effects’, ‘incidental effects’, ‘non-specific effects’ and ‘context effects’ have been used more or less interchangeably, and Di Blasi advises the use of the term ‘context effect’ to emphasize that it is the context that influences the specific treatment.[170] The contextual factors contributing to the placebo effect may be verbal, visual, tactile, olfactory, auditory; in short “any clue that leads to the knowledge that a medical treatment is being performed”.[168] Another term used is the ‘meaning response’, defined as the “physiologic or psychological effects of meaning in the origins or treatment of illness”.[164]

In addition to the above mentioned ‘incidental effects’ (placebo, non-specific, context, meaning), a treatment session may contain ‘characteristic’ effects (specific effects).[171] Paterson and Dieppe define characteristic factors as “therapeutic actions or strategies that are theoretically derived, unique to a specific treatment, and believed to be causally responsible for the outcome”.[172]

Traditionally, needling has been considered the only characteristic factor of acupuncture, in the same way as the tablet or capsule with the drug in pharmacological treatment. This may be correct for certain acupuncture techniques, for example needling of the point PC6 for post-operative nausea and vomiting.[173] However, it may not be correct when acupuncture is practised as a complex intervention, “an intervention that contains several interacting components”.[174] MacPherson and Thomas found that advice on self-help during acupuncture treatment fulfils Paterson’s and Dieppe’s definition of an characteristic factor,[172] and therefore must be considered another characteristic factor of acupuncture, in addition to the needling of acupuncture points.[173]

The acupuncture treatment setting is probably able to elicit strong ‘meaning responses’. The acupuncturists use TCM terms as ‘deficiency’, ‘excess’ and ‘stagnation of Qi’ (life energy) when diagnosing, and often when explaining the aetiology of the illness to the patient, and when giving life-style advice.[173] These terms are unique for TCM; hence the context is

unique, and the process of explaining and giving advice may be considered a characteristic factor. It seems reasonable that explaining and giving advice are contributing considerably to the 'meaning response', in addition to other factors, like the 'oriental' setting, the smell of moxa etc. However, the principle of creating a strong meaning response, which in turn may result in physiological responses, is most likely a general principle, more or less valid for all medical treatment methods. In that way, it is not unique for TCM acupuncture, but the TCM acupuncture is probably a way of maximizing the meaning response. A significant part of the effect seen in our study is probably due to the context effect/meaning response.

In RCT's testing needling of the acupuncture point as the characteristic factor, the need for some form of control procedure that replicates acupuncture but is an inactive control is rather obvious, but so far has not been satisfied in practice. For control arms, many studies use "sham acupuncture"; acupuncture needles inserted at locations that are believed not to be acupuncture points. These needles are often inserted superficially, compared with intra-muscular insertion in the "true" acupuncture group. However, neither superficial- nor minimal-acupuncture, needling of 'non-acupuncture' points, nor 'stage-dagger' needles that do not penetrate the skin, can be considered physiologically inert placebo controls.[175] Sham acupuncture is obviously simply another form of acupuncture from the physiological perspective.[176] In addition, sham needles that do not penetrate the skin are technically difficult to use in practice. A great variety of sham interventions has been used in acupuncture trials, but these are hardly true 'placebo controls'.[177] Needling in acupuncture points usually elicit de Qi, by many considered essential for the effect of acupuncture.[178] Thus, to obtain single blinding we may have to recruit acupuncture naïve study participants. In the present study, 60 % of the participants had tried acupuncture previously, suggesting that acupuncture naïve individuals may be difficult to recruit. Blinding of the practitioners in addition to the participants, i.e. double blinding, seems very difficult. Hence; designing double blind, sham-controlled studies of acupuncture treatment appears challenging.

Further acupuncture research

The present study provides a good basis for further studies of the efficacy of acupuncture treatment for hot flashes. When planning further acupuncture studies, essential questions to be answered are: Which factors are the characteristic factors of acupuncture treatment, or

which are the ‘core’ elements obligatory for obtaining clinical effect of acupuncture treatment, and what are their relative contributions to the total treatment effect?

An acupuncture point selection according to a TCM diagnosis and needling in traditional acupuncture points is probably not necessary to obtain optimal results.[140] Superficial needling in non-acupuncture points renders similar results in several studies. A systematic review of all controlled, clinical trials of acupuncture published in English in 2006 and indexed in PubMed found that traditional acupuncture theories often lead to null outcomes and are unreliable for creating distinct exposures in clinical trials.[139] In our study, we found that factors other than the TCM syndrome diagnoses and point selection may be of importance regarding the outcome of the treatment, and that needle location is probably not as relevant as generally thought.

In real life, acupuncturists apply a diversity of acupuncture treatment styles, point selections, acupuncture point stimulation methods and acupuncture treatment ‘doses’, within different theoretical frameworks. Point stimulation methods include needles, moxa, electro-stimulation, laser and massage. Other elements of importance for the acupuncture ‘dose’ comprise needle gauge, depth of needle penetration, if de Qi was obtained or not, degree of needle manipulation, number of points stimulated in each treatment session, frequency, duration and number of treatment sessions. As previously described, needling of acupuncture points has been considered the only characteristic factor in the majority of acupuncture studies so far, and MacPherson and Thomas have proposed that within the TCM framework, advice on self-help may be a second characteristic factor.[173] The TCM diagnostic process may be another characteristic contextual factor within this framework. Finally, general contextual factors such as attention, time and care may be of importance. Figure 4 illustrates that the total effect of acupuncture treatment may be considered as the sum of contributions from general contextual components, specific contextual components and specific point stimulation components. The relative contribution of each component is so far unknown, and may probably vary considerably.

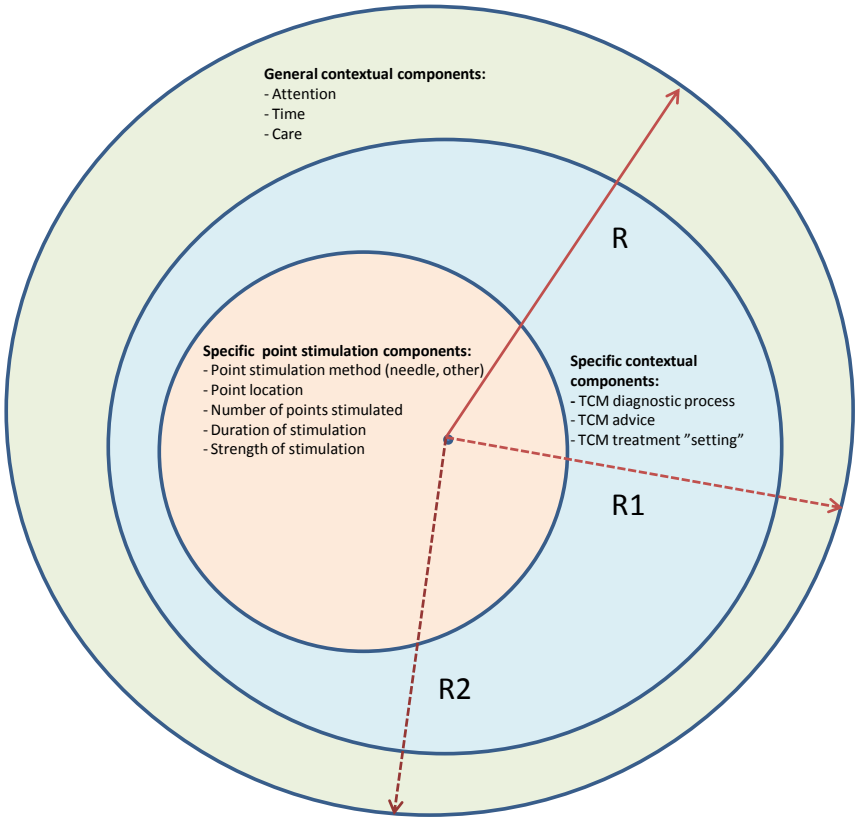


Figure 4 Components contributing to the acupuncture treatment effect

The radius R illustrates the total outcome of the acupuncture treatment. Moving R to different positions (R1, R2), illustrates that the relative contribution of each component may vary considerably in a situation where the total outcome is constant.

Development of research models that acknowledge the different components of the acupuncture treatment effect seems important for the continuous progress of the research within this field.

Conclusion

The thesis has focused on the potential effectiveness of TCM acupuncture treatment on postmenopausal vasomotor symptoms among highly bothered, postmenopausal women.

The results obtained in this work suggest that TCM acupuncture in addition to advice on self-care can lead to a quicker reduction of these symptoms than self-care alone.

More specifically the main conclusions from this thesis can be summarized as follows:

- The results suggest that a policy of use of TCM acupuncture plus self-care can lead to a quicker reduction of hot flash frequency and intensity and increase in hours of sleep per night than self-care alone, but probably has no long term effects.

- A policy of use of TCM acupuncture plus self-care can cause a quicker increase in health-related quality of life regarding vasomotor symptoms, sleep problems and somatic symptoms than self-care alone, but probably has no long term effects.

- Urine excretion of calcitonin gene-related peptide (CGRP) was not affected by acupuncture treatment.

- Kidney Yin Xu was diagnosed as primary TCM diagnostic syndrome in 50% of the participants in the acupuncture group.

- A ‘core’ group of ten TCM acupuncture points made up two thirds of all point stimulations among responders and non-responders.

- TCM diagnoses did not predict the overall treatment response, and patients with different diagnoses were not likely to experience a differential response in their symptoms.

- The acupuncture points used did not differ between responders and non-responders. Other factors than the TCM syndrome diagnoses and the point selection may be of importance regarding the outcome of the treatment.

- No serious adverse events were reported during the study.

- The WHQ total scale score appeared reliable, but care should be taken when interpreting some of the subscales.

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Paper I

Paper II

Paper III

Paper IV

Paper V

Appendix I

Consent form

NAFKAM
Nasjonalt forskningssenter innen komplementær og alternativ medisin

Klinisk Forskningssenter, Universitetssykehuset i Nord-Norge

Forespørsel om å delta i forskningsprosjekt

Hensikten med undersøkelsen/ studien
Målet med studien er å finne ut om behandling med akupunktur mot hetetokter i overgangsalderen reduserer antall hetetokter og øker helserelatert livskvalitet sammenlignet med det kvinner kan gjøre på egen hånd for å lindre plagene. Vi vil også undersøke mekanismer for en eventuell effekt av akupunkturbehandling. Videre ønsker vi å kartlegge hvordan kvinnenes symptomer utvikler seg etter at studien er avsluttet.

En del kvinner er plaget med hetetokter i forbindelse med overgangsalderen. Inntil for få år siden var hormonbehandling med østrogentilskudd mye brukt ved denne typen plager. Mange norske kvinner har sluttet å ta østrogentilskudd etter undersøkelser som viste at østrogenbehandling øker risikoen for hjertesykdom og brystkreft. Behandling med akupunktur kan være et alternativ, men foreløpig er dette for lite undersøkt til at vi kan anbefale norske kvinner å bruke akupunktur mot plager i overgangsalderen.

Hva kjennetegner behandlingen?
I Norge praktiseres hovedsaklig akupunktur basert på tradisjonell kinesisk medisin (TKM). Behandlingen innebærer at akupunktøren intervjuer deltakeren og stiller en diagnose ut i fra TKM. Deretter gis livsstilsråd og individtilpasset behandling ved at 6-12 akupunkturnåler plasseres i akupunkturpunkter på armer, ben, mage og evt. i hodet. Nålene fjernes etter ca. 20 minutter. Erfarne akupunktører anser at minimum 6 behandlinger er nødvendig for å fastslå eventuell effekt og 8-10 behandlinger er nødvendig for å gi en mer varig effekt på plagene. Alle behandlere i studien er erfarne TKM akupunktører og medlemmer av Norsk Akupunkturforening (NAFO).

Hvem kan delta?
Du kan delta i undersøkelsen hvis du er plaget med hetetokter, er i overgangsalderen og det er minst ett år siden siste menstruasjonsblødning. Du kan ikke bruke blodtynnende medisin, hormontabletter, hormonplaster eller andre medisiner som har effekt på forekomsten av hetetokter. Du kan ikke ha hjerteklaffefeil eller aktiv kreftsykdom. Dersom du ønsker å delta må du først registrere hvor mange hetetokter du har i løpet av to uker. Hensikten med registreringen er å finne ut om du har nok hetetokter til å delta i studien.

Hvordan foregår undersøkelsen?
Studien varer i 12 uker. Deltakere blir tilfeldig fordelt i to grupper. Den ene gruppen (akupunkturgruppen) får 10 akupunkturbehandlinger hos en TKM akupunktør (ca. 1 behandling ukentlig). Den andre gruppen (kontrollgruppen) får ingen behandling mens studien pågår, men kan gjøre nærmere angitte livsstilsendringer. Mens studien pågår vil alle deltakere registrere antall hetetokter ved studiestart og etter 4, 8 og 12 uker. Ved studiestart og etter 12 uker innkalles alle studiedeltakere til møte med studiesykepleier i hhv. Oslo, Bergen og Tromsø. I Tromsø finner møtet sted på Forskningsposten ved Universitetssykehuset i Nord Norge (UNN), hvor det gjøres tilleggsundersøkelser av hjerterytme, beintetthet, blod og urin. Urinprøven vil bli analysert i Sverige. Alle deltakere fyller ut et skjema til måling av livskvalitet ved studiestart og etter 12 uker. Deltakere som får akupunkturbehandling vil også registrere eventuelle bivirkninger av behandlingen. Akupunktørene i studiens behandlerteam registrerer TKM diagnose, punktvalg for nåler og eventuelle bivirkninger ved hver behandling. Studien betaler utgiftene til akupunktur-behandling. Etter at studien er avsluttet ønsker vi å følge opp deltakere med spørreskjema (6 og 12 mnd etter studiestart) og måling av beintetthet (12 mnd. etter studiestart).

Følgende forhold er viktig å kjenne til:
1. Deltakelse er frivillig. Det er ikke nødvendig å begrunne hvorfor man eventuelt ikke ønsker å delta.
2. Deltakere i studien kan når som helst og uten begrunnelse trekke seg fra studien og be om at deres personlige opplysninger slettes.

3. De ansvarlige for gjennomføringen av studien, og alle behandlere som deltar i studien er underlagt taushetsplikt.

4. Det er viktig at deltakerne kan gjennomføre 10 akupunkturbehandlinger innenfor et gitt tidsrom.

5. Akupunktur er ansett som trygg behandling når den utføres av kompetente og erfarne akupunktører. Deltakere kan få lett rødme, eller små hudblødninger omkring innstikkstedet for nålene. Noen blir søvnige etter akupunkturbehandling, men dette er forbigående.

6 Akupunktørene som er med i studien har ansvarsforsikring som dekker eventuelle uhell i forbindelse med behandlingen, der det kan påvises skyld. Dette er en mer begrenset forsikringsdekning enn den som følger av Pasientskadeloven, der det gis erstatning for svikt ved ytelsen av helsehjelp, selv om ingen kan lastes. Eventuelle uhell som måtte oppstå på vei til eller fra behandlingen dekkes ikke.

7. Risiko og ubehag ved å delta i studien av biologiske målinger på UNN vil være å utsette seg for blodprøvetaking. Hjerterytmemålingen foregår ved at deltakeren ligger på en benk mens hjerterytmen måles ved hjelp av en hjerterytmemonitor. Undersøkelse av beintetthet foregår mens deltaker ligger på en benk og medfører minimal røntgenbestråling. De nevnte undersøkelsene gir intet ubehag. Undersøkelse av urinen foregår ved at deltaker avgir prøve av morgenurin og kveldsurin og sender en urinprøve til forsøksledelsen. Eventuelle uhell i forbindelse med disse undersøkelsene dekkes av forsikring ved Norsk Pasientskadeerstatning (Pasientskadeloven).

8. Deltakelse i studien har ikke betydning for eventuell annen medisinsk behandling man mottar, men husk:
   - Deltakerne kan ikke bruke blodtynnende medisin, hormontilskudd eller andre reseptbelagte medikamenter som har innvirkning på hetetokter.
   - Deltakere kan bruke soyaprodukter.

9. Alle kvinnene som deltar i studien vil bli fulgt opp for registrering av hetetokter og helserelatert livskvalitet dersom de i studieperioden:
   - Oppsøker en behandler i eller utenfor det etablerte helsevesen for å få behandling mot plager i overgangsalderen, eller
   - Starter behandling med reseptbelagte medisiner som har innvirkning på hetetokter.
   Dette gjelder med mindre de ønsker å trekke seg fra studien i følge punkt 2.

10. Deltakerne har til enhver tid rett til innsyn i de opplysninger som er registrert om seg selv mens studien pågår. Erfaringene fra prosjektet sammenfattes og sendes til deltakerne etter at studien er avsluttet.

11. Data som samles inn i deltakerjournalene avidentifiseres før de registreres i en database. Det er kun de ansvarlige for gjennomføringen av studien som har innsyn i deltakerjournalene og databasen. Ved prosjektslutt i 2007 vil alle direkte og indirekte personopplysninger slettes slik at det ikke er mulig å føre opplysningene tilbake til enkeltpersoner i datamaterialet.

12. Studien er et samarbeidsprosjekt mellom NAFKAM og Klinisk Forskningssenter på Universitetssykehuset i Nord-Norge (UNN), og er finansiert av Norge-Kinasamarbeidet innen Tradisjonell Kinesisk Medisin ved NAFKAM. Prosjektleder er Sameline Grimsgaard (UNN).

13. Studien er vurdert av Regional komité for i medisinsk forskningsetikk i Nord-Norge og er tilrådd av Personvernombudet for forskning og meldt til Biobankregisteret.

14. Deltakere som fullfører det planlagte studieopplegget (i henhold til protokoll) i 12 uker honoreres med kroner 400 for å dekke tapt arbeidsfortjeneste ved deltakelse.

15. Dersom du har spørsmål underveis, kan du kontakte konsulent Sissel Andersen,
tel. 77 64 48 19 eller 97 63 48 15, e-post: Sissel.Andersen@ism.uit.no

16. Dersom du ønsker å delta i studien ber vi deg undertegne to eksemplarer av samtykket nedenfor. Det ene eksemplaret beholder du selv. Det andre eksemplaret bes sendt til forsøksledelsen i vedlagte returkonvolutt.

Samtykke

Jeg har lest informasjonen om undersøkelsen og samtykker i å delta.

Fødselsdato _____ Navn _____

Sted _____ Dato _____

Underskrift _____

Appendix II

Hot flash diary - baseline

Registrering nr. …… Deltaker nr. …… Deltaker initialer …… Dato for utsendelse ……

Skjema for registrering av hetetokter

Utfylling: Oppgi antall hetetokter i løpet av dagen og siste natt. Velg et tall fra 0 (*ikke i det hele tatt*) til 10 (*svært mye*) for å angi gjennomsnittlig hvor mye hetetoktene har plaget deg. Noter hvor mange timer du sov siste natt. Skriv ned svaret ditt hver kveld ca. kl. 22, eventuelt tidligere dersom du legger deg før kl. 22.

0 *Ikke i det hele tatt* **1 2 3 4 5 6 7 8 9 10** *Svært mye*

	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……	Dag/ Dato ……
Dag nr.	1	2	3	4	5	6	7	9	9	10	11	12	13	14
DAG Antall svette- eller hetetokter i løpet av dagen	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..	Antall/ tall ……..
NATT Antall svette- eller hetetokter i løpet av siste natt	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..
Tall for hvor mye svette- eller hetetoktene plaget meg siste døgn	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..
Antall timer med søvn siste natt	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..	……..

Registrering nr. …… Deltaker nr. …… Deltaker initialer …… Dato for utsendelse ……

Appendix III

Questionnaire - baseline

Deltaker: _____

Dato: _____

Randnr.: _____

ACUFLASH SPØRRESKJEMA

UTDANNING, ARBEID OG BOFORHOLD

Hvilken utdanning er den høyeste du har fullført?

- ☐ Mindre enn 7 år grunnskole
- ☐ Grunnskole 7-10 år, framhaldsskole, folkehøyskole
- ☐ Realskole, middelskole, yrkesskole, 1-2 årig vid. skole
- ☐ Artium, øk. gymnas, allmennfaglig retning i vid. skole
- ☐ Høgskole, universitet, mindre enn 4 år
- ☐ Høgskole, universitet, 4 år eller mer

Hvor mange hele års skolegang har du gjennomført?
(Ta med alle år du har gått på skole eller studert)

Antall år: ____

Er du i lønnet arbeid ☐ Ja ☐ Nei

Hvis ja, hvor høy er bruttoinntekten i husholdet pr. år?

- ☐ Under 150.000
- ☐ 151.000-300.000
- ☐ 301.000-450.000
- ☐ 451.000-600.000
- ☐ 601.000-750.000
- ☐ 751.000-1 million
- ☐ over 1 million

Bor du sammen med noen? ☐ Ja ☐ Nei

Hvis ja,

Ektefelle/samboer ☐ Ja ☐ Nei

Andre personer, 18 år og eldre ☐ Ja ☐ Nei Ant. ____

Personer under 18 år ☐ Ja ☐ Nei Ant. ____

MENSTRUASJON

Hvor gammel var du da du fikk menstruasjon første gang?

____ år

Hvor mange år tok det før menstruasjonen ble regelmessig?

Ett år eller mindre	Mer enn ett år	Aldri	Husker ikke
☐	☐	☐	☐

Da du hadde menstruasjon, hadde du noen av disse plagene?
(Sett ett kryss for hvert spørsmål)

Var du nedtrykt (deprimert) eller irritabel?

Nei	Ubetydelig	Merkbart	Plagsomt
☐	☐	☐	☐

Hadde du smertefulle bryst?

Nei	Ubetydelig	Merkbart	Plagsomt
☐	☐	☐	☐

Hadde du hovne hender/føtter, vektøkning eller følelse av å ese ut?

Nei	Ubetydelig	Merkbart	Plagsomt
☐	☐	☐	☐

Hvordan stoppet menstruasjonen?

- ☐ Av seg selv
- ☐ Operert vekk eggstokkene
- ☐ Operert vekk livmoren
- ☐ Usikker, har brukt hormontilskudd som gav regelmessige blødninger
- ☐ Annet

Alder da menstruasjonen opphørte ____ år

GRAVIDITET, FØDSLER OG PREVENSJON

Har du barn? ☐ Ja ☐ Nei

Egne barn ☐ Ja ☐ Nei Ant. ____

Adoptivbarn ☐ Ja ☐ Nei Ant. ____

Angi fødselsår for hvert barn du har født om (også dødfødte eller barn som døde senere). Dersom du ikke har født barn fortsett til neste spørsmål.

Barn 1 Fødselsår ____ Barn 4 Fødselsår ____

Barn 2 Fødselsår ____ Barn 5 Fødselsår ____

Barn 3 Fødselsår ____ Barn 6 Fødselsår ____

Har du hatt svangerskap som varte i mindre enn 6 mnd., dvs spontanabort eller selvbestemt abort?

☐ Ja ☐ Nei

Hvis ja, hvor mange aborter har du hatt i alt? Ant. ____

Har du noen gang brukt p-piller, minipiller inkludert?

☐ Ja ☐ Nei

Hvis ja, hvor lenge har du brukt p-piller i alt? ____ år

Hvor gammel var du første gang du brukte p-piller? ____ år

BRUK AV HORMONPREP. I OVERGANGSALDEREN

Har du noen gang brukt hormontabletter/-plaster?

☐ Ja ☐ Nei

Hvis JA, hvor lenge har du brukt hormontabletter/-plaster i alt?

_____ ant. år _____ ant. mnd

Hvor gammel var du første gang du brukte hormontabl./plaster?

_____ år

Hvorfor begynte du å bruke hormontabletter/-plaster?

☐ Lindre plager i overgangsalderen (hetetokter, underlivsplager mm.

☐ Forebygge beinskjørhet

☐ Forebygge hjerte-/karsykdommer

☐ Annet

Når sluttet du å bruke hormontabletter/-plaster?

_____ mnd _____ årstall

Bruker du østrogenpreparat i skjeden nå? (krem/stikkpiller/vaginaltabletter/vaginalinnlegg)

☐ Ja ☐ Nei

Hvis ja, hvor lenge har du brukt det? _____ år _____ mnd

Bruker du hormonspiral nå? ☐ Ja ☐ Nei

HELSE OG BRUK AV HELSETJENESTER, MEDISINER OG KOSTTILSKUDD

Hvor høy er du? _____ cm

Hvor mye veier du i dag? _____ kg

Hvordan er helsen din nå? (Sett bare ett kryss)

☐ Dårlig

☐ Ikke helt god

☐ God

☐ Svært god

Har du eller har du hatt?	Ja	Nei	Alder første gang
Høyt blodtrykk	☐	☐	_____
Stoffskiftesykdom	☐	☐	_____
Diabetes (sukkersyke) (ikke svangeskapsdiabetes)	☐	☐	_____

Hvor ofte er du plaget av søvnløshet?

☐ Aldri, eller noen få ganger i året

☐ 1-3 ganger i måneden

☐ Omtrent 1 gang i uken

☐ Mer enn en gang i uken

Har du siste året vært plaget av søvnløshet som har gått ut over arbeidsevnen?

☐ Ja ☐ Nei

Med tanke på egen helse eller sykdom siste år, hvor mange ganger har du vært: (Sett 0 hvis du **ikke** har hatt slik kontakt)

	Ant. ganger siste år
Innlagt i sykehus	_____
Hos psykolog eller lege (allemennlege/ legevakt/spesialist)	_____
Hos fysioterapeut eller kiropraktor	_____
Hos utøver av alternativ behandling (homeopat/ akupunktør/soneterapeut/naturmedisiner	_____

Har du noen gang fått akupunkturbehandling?

☐ Ja ☐ Nei

Hvis JA, angi sykdom/plage som du har brukt akupunkturbehandling for og effekt av behandlingen:

Sykdom/plage	Forverring	Ingen effekt	Litt effekt	God effekt
_____	☐	☐	☐	☐
_____	☐	☐	☐	☐
_____	☐	☐	☐	☐
_____	☐	☐	☐	☐

Tror du akupunkturbehandling kan ha effekt (generelt)?

☐ Ja

☐ Nei

☐ Vet ikke

☐ Andre kommentarer _____

Har du noen gang brukt alternativ behandling mot plager i forb. med overgangsalderen? (enten ved å oppsøke utøver eller som egenbehandling)

☐ Ja ☐ Nei

Hvis JA, hvilken type behandling har du fått

Angi behandlingsform	Egenbehandling	Hos utøver/behandler
_____	☐	☐
_____	☐	☐
_____	☐	☐
_____	☐	☐

Tror du at plagene du har i forbindelse med overgangsalderen kan lindres av akupunktur?

☐ Ja

☐ Nei

☐ Vet ikke

☐ Andre kommentarer _____

BRUK AV MEDISINER OG KOSTTILSKUDD

Har du i løpet av de siste 4 ukene brukt legemidler eller kosttilskudd (herunder reseptbelagte og reseptfrie legemidler, naturmidler, kosttilskudd)?

☐ Ja ☐ Nei

Hvilke preparater har du brukt og hvor ofte?

Angi preparat	Daglig	Hver uke men ikke daglig	Sjeldnere enn hver uke	Grunn til at du har brukt dem
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____

	Ja, daglig	Iblant	Nei
Bruker du tran, trankapsler, fiskeoljekapsler?	☐	☐	☐

FYSISK AKTIVITET I FRITID OG ARBEID

Fritid siste året.
Hva slags aktivitet har du utført i din fritid siste året? Dersom aktiviteten varierer mye, for eks. mellom sommer og vinter, så tenk deg et gjennomsnitt (sett ett kryss i den ruten som passer best)

☐ Leser, ser på TV eller annen stillesittende aktivitet

☐ Spaserer, sykler eller beveger deg på annen måte minst 4 timer i uka (her kan du også regne med gang eller sykling til arbeidssted, søndagsturer mm.)

☐ Driver du med mosjonsidrett, tyngre hagearbeid eller lignende? (merk at aktiviteten skal vare minst fire timer i uken)

☐ Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uken

Arbeidsaktivitet siste året.
Hva slags aktivitet har du vanligvis i arbeidet ditt?

☐ For det meste stillesittende arbeid (eks. kontorarbeid)

☐ Arbeid som krever at du går mye (du blir ikke svett og hjertet slår ikke fortere, eks. ekspeditør, lærer, frisør)

☐ Arbeid der du går mye og løfter mye (du svetter litt og hjertet slår raskere, eks. syke-/hjelpepleier, postbetjent)

☐ Tungt kroppsarbeid (du svetter en del og hjertet slår raskt, tunge løft, jordbruk, tungt omsorgsarbeid)

Har du vært yrkesaktiv de siste 12 mnd.? ☐ Ja ☐ Nei

Hvor stor stillingsprosent har du? _____ %

FYSISK AKTIVITET SISTE 3 MND

Angi i skjemaet nedenfor de fritidsaktiviteter du har deltatt i siste tre måneder. Oppgi hvor ofte og hvor lenge pr. gang du holdt på. Angi aktivitetsnivået (se nedenfor) på en skala fra 1 (lavt) til 4 (høyt)

A. Lese bøker/TV-titting

B. Gå til/spasere

C. Gå i skogen/på fjellet/jakte

D. Jogge/løpe

E. Sykle (også trimsykkel)

F. Svømme

G. Tennis/badminton/squash

H. Golf/bowling

I. Gymnastikk/aerobic/trim/turgåing/dans/ballett

J. Stryketrening/vekttrening

K. Husarbeid

L. Ski (langrenn), turgåing/konkurranse

M. Kjøre slalåm/telemark

N. Ake/sparke, gå på skøyter (også rulleskøyter)

O. Ro/padle/seile

P. Plukke bær/sopp/fiske

Q. Annet

Aktivitetsnivå for fritidsaktiviteter

1. = Overveiende stillesittende
2. = Lett trening. Du blir ikke svett og hjertet slår ikke fortere
3. = Middels hard trening. Du svetter litt og hjertet slår litt fortere
4. Hard trening. Du svetter mye og hjertet slår fort.

Aktivitet	Gj.snitt tid pr. g. (min)	Gj.snitt Ant. pr. mnd	Aktivitetsnivå			
			1	2	3	4
Eks. A	*35*	*12*	*x*			

TRANSPORT TIL OG FRA ARBEID

Spørsmålene gjelder transport mellom hjem og arbeidsplass siste 3 måneder

Hvordan kommer du deg vanligvis til/fra arbeid?

Ta et gjennomsnitt for en måned. (Angi antall ganger du bruker de forskjellige transportmidlene).

	Ant. ganger pr. mnd
Bil/buss/trikk/tog/båt	_____
Sykkel	_____
Til fots	_____

Hvor lang tid tar vanligvis transporten til/fra arbeid?
(Du kan fylle ut flere kategorier)

Bil/buss/trikk/tog/båt	_____ min.
Sykkel	_____ min.
Til fots	_____ min.

LEVEVANER

Er du vegetarianer? ☐ Ja ☐ Nei

Har du røykt/røyker du?

Ja, daglig	Ja, men ikke daglig	Ja, tidligere	Nei, har aldri røykt
☐	☐	☐	☐

Hvor mange kopper kaffe og te drikker du daglig?

Koffeinholdig kaffe	_____ kopper
Koffeinfri kaffe	_____ kopper
Te	_____ kopper

Er du totalavholdskvinne? ☐ Ja ☐ Nei

Hvis nei, hvor ofte og hvor mye drakk du i gj.snitt siste år?

	Aldri, sjelden	1 pr.mnd	2-3 pr. mnd	1 pr. uke	2-4 pr. uke	5-6. pr. uke	1+ pr. dag
Øl (1/2 l)	☐	☐	☐	☐	☐	☐	☐
Vin (glass)	☐	☐	☐	☐	☐	☐	☐
Brennevin (drinker)	☐	☐	☐	☐	☐	☐	☐

Mange takk for hjelpen!

Appendix IV

Questionnaires – interventional trial, including WHQ and EQ-5D

Deltaker: _____

Dato: _____

Randnr.: _____

ACUFLASH SPØRRESKJEMA

Registrering 1 (uke 4)

BRUK AV HELSETJENESTER, MEDISINER OG KOSTTILSKUDD

Er du tildelt akupunkturbehandling i studieperioden?

☐ Ja ☐ Nei

Med tanke på egen helse eller sykdom siste 4 uker, hvor mange ganger har du vært:
(Gjelder ikke akupunktur, dersom du er i akupunkturgruppen)

	Ant. ganger siste 4 uker
Innlagt i sykehus	____
Hos psykolog eller lege (allemennlege/ legevakt/spesialist)	____
Hos fysioterapeut eller kiropraktor	____
Hos utøver av alternativ behandling (homeopat/ akupunktør/soneterapeut/naturmedisiner)	____

Har du siste 4 uker brukt alternativ behandling mot plager i forbindelse med overgangsalderen? (Enten ved å oppsøke en utøver eller som egenbehandling).
(Gjelder ikke akupunktur, dersom du er i akupunkturgruppen)

☐ Ja ☐ Nei

Hvis Ja; hvilken type behandling har du brukt?

Angi behandlingsform	Egenbehandl.	Hos utøver/ behandler
_____	☐	☐
_____	☐	☐
_____	☐	☐
_____	☐	☐

Har du i løpet av de siste 4 ukene brukt legemidler eller kost tilskudd (herunder reseptbelagte og reseptfrie legemidler, naturmidler, kosttilskudd)?

☐ Ja ☐ Nei

Angi preparat	Daglig	Hver uke men ikke daglig	Sjeldnere enn hver uke	Grunn til at du har brukt dem
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____

Bruker du østrogenpreparat i skjeden nå (krem/stikkpiller/ vaginaltabletter/vaginalinnlegg)?

☐ Ja ☐ Nei

Hvis Ja; hvor lenge har du brukt det?

Ant. år ____ Ant. mnd. ____

Hvor ofte har du vært plaget av søvnløshet i de siste 4 uker?

1-3 ganger i måneden	Omtrent 1 gang i uken	Mer enn 1 gang i uken
☐	☐	☐

LEVEVANER

Har du endret dine levevaner for å lindre hetetoktene i de siste 4 uker?

☐ Ja ☐ Nei

Hvis Ja; angi hvilke endringer du har gjort (sett et kryss på det som passer)

	Økt	Redusert
Hvile og søvn	☐	☐
Bruk av avspenningsteknikk	☐	☐
Fysisk aktivitet	☐	☐
Inntak av koffeinholdig drikke	☐	☐
Inntak av alkohol	☐	☐
Røyking	☐	☐

Andre endringer, beskriv hvilke _____

Vennligst send utfylt skjema sammen med registrering av hetetokter og fysisk aktivitet til forsøksledelsen. Bruk vedlagte returkonvolutt.

Mange takk for hjelpen!

Registrering nr. 1 (uke 4): _____

Randnr.: _____

Deltaker intialer: _____

SKJEMA FOR REGISTRERING AV FYSISK AKTIVITET

	Dag/dato	Dag/dato	Dag/dato	Dag/dato	Dag/dato	Dag/dato	Dag/dato
	_____	_____	_____	_____	_____	_____	_____
TYPE AKTIVITET	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter
Transport til/fra arbeid:							
Bil/buss/trikk/tog/båt	_____	_____	_____	_____	_____	_____	_____
Sykkel	_____	_____	_____	_____	_____	_____	_____
Til fots	_____	_____	_____	_____	_____	_____	_____
	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*
Fritid:							
Lese bøker/TV-titting	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Gå/spasere	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Gå i skogen/fjellet/jakte	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Jogge/løpe	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Sykle (også trimsykkel)	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Svømme	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Tennis/badminton/ squash	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Golf/bowling	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Gymnastikk/aerobic/trim	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Styrke/vekttrening	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Husarbeid	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Ski, langrenn/turgåing	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Slalåm/telemark	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Ake/sparke/skøyter	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Ro/padle/seile	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Plukke bær/sopp/fiske	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Annet	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____

Intensitetsnivåer for fritidsaktiviteter:

1 = Overveiende stillestittende

2 = Lett aktivitet. Du blir ikke svett og hjertet slår ikke fortere.

3 = Middels hard aktivitet. Du svetter litt og hjertet slår litt fortere.

4 = Hard trening. Du svetter mye og hjertet slår fort.

*** Bruk av tabellen:**

Varighet av fritidsaktiviteten skriver du i minutter til venstre for hver dato og intensitet (1 – 4) til høyre i hver rute

Registrering nr. 1 (uke 4): _____

Randnr.: _____

Deltaker intialer: _____

SKJEMA FOR REGISTRERING AV HETETOKTER

Utfylling: Oppgi antall hetetokter i løpet av dagen og siste natt. Velg et tall fra 0 *(ikke i det hele tatt)* til 10 (*svært mye)* for å angi gjennomsnittlig hvor mye hetetoktene har plaget deg. Noter hvor mange timer du sov siste natt. Skriv ned svaret ditt hver kveld før du legger deg.

0	1	2	3	4	5	6	7	8	9	10
Ikke i det hele tatt										Svært mye

	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____
	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall
DAG Antall svette- eller hetetokter i løpet av dagen	_____	_____	_____	_____	_____	_____	_____
NATT Antall svette- eller hetetokter i løpet av siste natt	_____	_____	_____	_____	_____	_____	_____
Tall for hvor mye svette- eller hete-toktene plaget meg siste døgn	_____	_____	_____	_____	_____	_____	_____
Antall timer med søvn siste natt	_____	_____	_____	_____	_____	_____	_____

Deltaker: _____

Dato: _____

Randnr.: _____

ACUFLASH SPØRRESKJEMA

Registrering 2 (uke 8)

BRUK AV HELSETJENESTER, MEDISINER OG KOSTTILSKUDD

Er du tildelt akupunkturbehandling i studieperioden?

☐ Ja ☐ Nei

Med tanke på egen helse eller sykdom siste 4 uker, hvor mange ganger har du vært:
(Gjelder ikke akupunktur, dersom du er i akupunkturgruppen)

	Ant. ganger siste 4 uker
Innlagt i sykehus	____
Hos psykolog eller lege (allemennlege/ legevakt/spesialist)	____
Hos fysioterapeut eller kiropraktor	____
Hos utøver av alternativ behandling (homeopat/ akupunktør/soneterapeut/naturmedisiner)	____

Har du siste 4 uker brukt alternativ behandling mot plager i forbindelse med overgangsalderen? (Enten ved å oppsøke en utøver eller som egenbehandling).
(Gjelder ikke akupunktur, dersom du er i akupunkturgruppen)

☐ Ja ☐ Nei

Hvis Ja; hvilken type behandling har du brukt?

Angi behandlingsform	Egenbehandl.	Hos utøver/ behandler
_____	☐	☐
_____	☐	☐
_____	☐	☐
_____	☐	☐

Har du i løpet av de siste 4 ukene brukt legemidler eller kost tilskudd (herunder reseptbelagte og reseptfrie legemidler, naturmidler, kosttilskudd)?

☐ Ja ☐ Nei

Angi preparat	Daglig	Hver uke men ikke daglig	Sjeldnere enn hver uke	Grunn til at du har brukt dem
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____

Bruker du østrogenpreparat i skjeden nå (krem/stikkpiller/ vaginaltabletter/vaginalinnlegg)?

☐ Ja ☐ Nei

Hvis Ja; hvor lenge har du brukt det?

Ant. år ____ Ant. mnd. ____

Hvor ofte har du vært plaget av søvnløshet i de siste 4 uker?

1-3 ganger i måneden	Omtrent 1 gang i uken	Mer enn 1 gang i uken
☐	☐	☐

LEVEVANER

Har du endret dine levevaner for å lindre hetetoktene i de siste 4 uker?

☐ Ja ☐ Nei

Hvis Ja; angi hvilke endringer du har gjort (sett et kryss på det som passer)

	Økt	Redusert
Hvile og søvn	☐	☐
Bruk av avspenningsteknikk	☐	☐
Fysisk aktivitet	☐	☐
Inntak av koffeinholdig drikke	☐	☐
Inntak av alkohol	☐	☐
Røyking	☐	☐

Andre endringer, beskriv hvilke _____

Vennligst send utfylt skjema sammen med registrering av hetetokter og fysisk aktivitet til forsøksledelsen. Bruk vedlagte returkonvolutt.

Mange takk for hjelpen!

Registrering nr. 2 (uke 8): _____

Randnr.: _____

Deltaker intialer: _____

SKJEMA FOR REGISTRERING AV FYSISK AKTIVITET

	Dag/dato	Dag/dato	Dag/dato	Dag/dato	Dag/dato	Dag/dato	Dag/dato
	_____	_____	_____	_____	_____	_____	_____
TYPE AKTIVITET	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter
Transport til/fra arbeid:							
Bil/buss/trikk/tog/båt	_____	_____	_____	_____	_____	_____	_____
Sykkel	_____	_____	_____	_____	_____	_____	_____
Til fots	_____	_____	_____	_____	_____	_____	_____
	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*
Fritid:							
Lese bøker/TV-titting	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Gå/spasere	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Gå i skogen/fjellet/jakte	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Jogge/løpe	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Sykle (også trimsykkel)	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Svømme	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Tennis/badminton/ squash	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Golf/bowling	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Gymnastikk/aerobic/trim	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Styrke/vekttrening	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Husarbeid	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Ski, langrenn/turgåing	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Slalåm/telemark	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Ake/sparke/skøyter	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Ro/padle/seile	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Plukke bær/sopp/fiske	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Annet	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____

Intensitetsnivåer for fritidsaktiviteter:

1 = Overveiende stillestittende

2 = Lett aktivitet. Du blir ikke svett og hjertet slår ikke fortere.

3 = Middels hard aktivitet. Du svetter litt og hjertet slår litt fortere.

4 = Hard trening. Du svetter mye og hjertet slår fort.

*** Bruk av tabellen:**

Varighet av fritidsaktiviteten skriver du i minutter til venstre for hver dato og intensitet (1 – 4) til høyre i hver rute

Registrering nr. 2 (uke 8): _____

Randnr.: _____

Deltaker intialer: _____

SKJEMA FOR REGISTRERING AV HETETOKTER

Utfylling: Oppgi antall hetetokter i løpet av dagen og siste natt. Velg et tall fra 0 *(ikke i det hele tatt)* til 10 (*svært mye)* for å angi gjennomsnittlig hvor mye hetetoktene har plaget deg. Noter hvor mange timer du sov siste natt. Skriv ned svaret ditt hver kveld før du legger deg.

0	1	2	3	4	5	6	7	8	9	10
Ikke i det hele tatt										Svært mye

	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____
	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall
DAG Antall svette- eller hetetokter i løpet av dagen	_____	_____	_____	_____	_____	_____	_____
NATT Antall svette- eller hetetokter i løpet av siste natt	_____	_____	_____	_____	_____	_____	_____
Tall for hvor mye svette- eller hete-toktene plaget meg siste døgn	_____	_____	_____	_____	_____	_____	_____
Antall timer med søvn siste natt	_____	_____	_____	_____	_____	_____	_____

Registrering nr. 2 (uke 8): _____

Randnr.: _____

Deltaker nr: _____

REAKSJONER PÅ AKUPUNKTURBEHANDLING

Merk av på skjema de reaksjonene du har erfart etter akupunkturbehandling og hvordan du opplevde dem. Sett en sirkel rundt det alternativet som passer best for deg.

Reaksjon	**Har du opplevd dette?**	**Hvis Ja, hvor sterk var reaksjonen? (sett en sirkel)**			**Hvis Ja, hvor mye plaget reaksjonen deg? (sett en sirkel)**				**Hvis Ja, kunne du tenke deg å oppleve det igjen?**
A. Forbigående forverring av hetetokter	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
B. Svimmel, omtåket	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
C. Trett, søvning	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
D. Mer energi	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
E. Avslappet	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
F. Sulten	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
G. Andre reaksjoner, spesifiser	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei

Vennligst send utfylt skjema sammen med registrering av hetetokter og fysisk aktivitet til forsøksledelsen. Bruk vedlagte svarkonvolutt.

Mange takk for hjelpen!

Deltaker: _____

Dato: _____

Randnr.: _____

ACUFLASH SPØRRESKJEMA

Registrering 3 (uke 12)

BRUK AV HELSETJENESTER, MEDISINER OG KOSTTILSKUDD

Er du tildelt akupunkturbehandling i studieperioden?

☐ Ja ☐ Nei

Med tanke på egen helse eller sykdom siste 4 uker, hvor mange ganger har du vært:
(Gjelder ikke akupunktur, dersom du er i akupunkturgruppen)

	Ant. ganger siste 4 uker
Innlagt i sykehus	____
Hos psykolog eller lege (allemennlege/ legevakt/spesialist)	____
Hos fysioterapeut eller kiropraktor	____
Hos utøver av alternativ behandling (homeopat/ akupunktør/soneterapeut/naturmedisiner)	____

Har du siste 4 uker brukt alternativ behandling mot plager i forbindelse med overgangsalderen? (Enten ved å oppsøke en utøver eller som egenbehandling).
(Gjelder ikke akupunktur, dersom du er i akupunkturgruppen)

☐ Ja ☐ Nei

Hvis Ja; hvilken type behandling har du brukt?

Angi behandlingsform	Egenbehandl.	Hos utøver/ behandler
_____	☐	☐
_____	☐	☐
_____	☐	☐
_____	☐	☐

Har du i løpet av de siste 4 ukene brukt legemidler eller kost tilskudd (herunder reseptbelagte og reseptfrie legemidler, naturmidler, kosttilskudd)?

☐ Ja ☐ Nei

Hvilke preparater har du brukt og hvor ofte?

Angi preparat	Daglig	Hver uke men ikke daglig	Sjeldnere enn hver uke	Grunn til at du har brukt dem
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____

Bruker du østrogenpreparat i skjeden nå (krem/stikkpiller/ vaginaltabletter/vaginalinnlegg)?

☐ Ja ☐ Nei

Hvis Ja; hvor lenge har du brukt det?

Ant. år ____ Ant. mnd. ____

Hvor ofte har du vært plaget av søvnløshet i de siste 4 uker?

1-3 ganger i måneden	Omtrent 1 gang i uken	Mer enn 1 gang i uken
☐	☐	☐

LEVEVANER OG BEHANDLINGSERFARINGER

Har du endret dine levevaner for å lindre hetetoktene mens studien har pågått? (siste 3 mnd.)

☐ Ja ☐ Nei

Hvis Ja; angi hvilke endringer du har gjort siste 3 mnd (sett et kryss på det som passer)

Hvile og søvn	Økt	Redusert
Bruk av avspenningsteknikk	☐	☐
Fysisk aktivitet	☐	☐
Inntak av koffeinholdig kaffe	☐	☐
Inntak av alkohol	☐	☐
Røyking	☐	☐

Andre endringer, beskriv hvilke _____

Opplever du at plagene du har i forbindelse med overgangs-alderen har endret seg mens studien har pågått?

☐ Ja ☐ Nei

Hvis ja, spesifiser og sett kryss ved de plagene som har endret seg

	Betydelig økning	Litt økning	Litt reduksjon	Betydelig reduksjon
Antall hetetokter pr. døgn	☐	☐	☐	☐
Intensiteten av hetetokter	☐	☐	☐	☐
Søvnkvalitet	☐	☐	☐	☐
Generell velvære	☐	☐	☐	☐
Andre plager, spesifiser	☐	☐	☐	☐
_____	☐	☐	☐	☐

Besvares kun av deltakere i akupunkturgruppen:

Vil du anbefale akupunktur til andre ☐ Ja ☐ Nei

Kan du tenke deg å prøve akupunktur igjen ☐ Ja ☐ Nei

Registrering nr. 3 (uke 12): _____

Randnr.: _____

Deltaker intialer: _____

SKJEMA FOR REGISTRERING AV FYSISK AKTIVITET

	Dag/dato	Dag/dato	Dag/dato	Dag/dato	Dag/dato	Dag/dato	Dag/dato
	_____	_____	_____	_____	_____	_____	_____
TYPE AKTIVITET	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter	Varighet i minutter
Transport til/fra arbeid:							
Bil/buss/trikk/tog/båt	_____	_____	_____	_____	_____	_____	_____
Sykkel	_____	_____	_____	_____	_____	_____	_____
Til fots	_____	_____	_____	_____	_____	_____	_____
	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*	Varighet og intensitet*
Fritid:							
Lese bøker/TV-titting	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Gå/spasere	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Gå i skogen/fjellet/jakte	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Jogge/løpe	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Sykle (også trimsykkel)	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Svømme	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Tennis/badminton/ squash	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Golf/bowling	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Gymnastikk/aerobic/trim	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Styrke/vekttrening	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Husarbeid	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Ski, langrenn/turgåing	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Slalåm/telemark	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Ake/sparke/skøyter	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Ro/padle/seile	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Plukke bær/sopp/fiske	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____
Annet	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____	____ ____

Intensitetsnivåer for fritidsaktiviteter:

1 = Overveiende stillestittende

2 = Lett aktivitet. Du blir ikke svett og hjertet slår ikke fortere.

3 = Middels hard aktivitet. Du svetter litt og hjertet slår litt fortere.

4 = Hard trening. Du svetter mye og hjertet slår fort.

*** Bruk av tabellen:**

Varighet av fritidsaktiviteten skriver du i minutter til venstre for hver dato og intensitet (1 – 4) til høyre i hver rute

Registrering nr. 3 (uke 12): _____

Randnr.: _____

Deltaker intialer: _____

SKJEMA FOR REGISTRERING AV HETETOKTER

Utfylling: Oppgi antall hetetokter i løpet av dagen og siste natt. Velg et tall fra 0 *(ikke i det hele tatt)* til 10 (*svært mye)* for å angi gjennomsnittlig hvor mye hetetoktene har plaget deg. Noter hvor mange timer du sov siste natt. Skriv ned svaret ditt hver kveld før du legger deg.

0	1	2	3	4	5	6	7	8	9	10
Ikke i det hele tatt										Svært mye

	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____	Dag/dato _____
	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall	Antall/ tall
DAG Antall svette- eller hetetokter i løpet av dagen	_____	_____	_____	_____	_____	_____	_____
NATT Antall svette- eller hetetokter i løpet av siste natt	_____	_____	_____	_____	_____	_____	_____
Tall for hvor mye svette- eller hete-toktene plaget meg siste døgn	_____	_____	_____	_____	_____	_____	_____
Antall timer med søvn siste natt	_____	_____	_____	_____	_____	_____	_____

Registrering nr. 3 (uke 12): _____

Randnr.: _____

Deltaker nr: _____

REAKSJONER PÅ AKUPUNKTURBEHANDLING

Merk av på skjema de reaksjonene du har erfart etter akupunkturbehandling og hvordan du opplevde dem. Sett en sirkel rundt det alternativet som passer best for deg.

Reaksjon	**Har du opplevd dette?**	**Hvis Ja, hvor sterk var reaksjonen? (sett en sirkel)**			**Hvis Ja, hvor mye plaget reaksjonen deg? (sett en sirkel)**				**Hvis Ja, kunne du tenke deg å oppleve det igjen?**
A. Forbigående forverring av hetetokter	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
B. Svimmel, omtåket	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
C. Trett, søvning	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
D. Mer energi	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
E. Avslappet	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
F. Sulten	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei
G. Andre reaksjoner, spesifiser	Ja Nei	Mild	Moderat	Alvorlig	Ikke i det hele tatt	Litt	Mye	Svært mye	Ja Nei

Vennligst send utfylt skjema sammen med registrering av hetetokter og fysisk aktivitet til forsøksledelsen. Bruk vedlagte svarkonvolutt.

Mange takk for hjelpen!

Deltaker: _____

Dato: _____

Randnr.: _____

SPØRRESKJEMA OM HELSE FOR KVINNER

Vennligst oppgi hvorledes du har det nå, eller hvorledes du har hatt det DE SISTE DAGENE, ved å krysse av i den rette ruta som svar på hvert av de følgende utsagnene:

1. Jeg våkner tidlig og sover deretter dårlig resten av natta

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

2. Jeg får anfall av angst eller panikk tilsynelatende uten noen som helst grunn

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

3. Jeg føler meg elendig og trist

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

4. Jeg kjenner meg engstelig når jeg går hjemmefra alene

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

5. Jeg har mistet interessen for saker og ting

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

6. Jeg får hjertebank eller en følelse av "sommerfugler i magen"

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

7. Jeg gleder meg fremdeles over ting jeg har pleid å glede meg over

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

8. Jeg føler at livet ikke er verdt å leve

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

9. Jeg føler meg anspent eller har mye indre spenning

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

10. Jeg har god appetitt

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

11. Jeg er rastløs og kan ikke holde meg i ro

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

12. Jeg er mer irritabel enn vanlig

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

13. Jeg bekymrer meg for å bli gammel

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

14. Jeg har hodepine

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

15. Jeg kjenner meg mer sliten enn vanlig

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

16. Jeg får anfall av svimmelhet

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

17. Brystene mine kjennes ømme eller ubekvemme

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

18. Jeg plages av ryggsmerter eller smerter i armer eller ben

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

19. Jeg får hetetokter

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

20. Jeg er mer klønete enn vanlig

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

21. Jeg kjenner meg ganske livlig og energisk

Ja, helt klart ☐ | Ja, noen ganger ☐ | Nei, ikke så mye ☐ | Nei, ikke i det hele tatt ☐

22. Jeg får kramper eller føler ubehag i underlivet

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

23. Jeg føler meg kvalm

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

24. Jeg har mistet interessen for seksuell aktivitet

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

25. Jeg opplever tilfredshet og velvære

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

26. Jeg får sterke menstruasjonsblødninger
(vennligst hopp over hvis det ikke forekommer menstruasjoner)

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

27. Jeg plages av svettetokter om natta

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

28. Underlivet føles oppblåst

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

29. Jeg har vanskelig for å falle i søvn

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

30. Jeg merker ofte en prikkende følelse i hender og føtter

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

31. Jeg er tilfreds med mitt nåværende seksualliv
(vennligst hopp over hvis ikke seksuelt aktiv)

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

32. Jeg føler meg fysisk tiltrekkende

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

33. Jeg har problemer med å konsentrere meg

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

34. På grunn av tørr skjede har samleie blitt ubehagelig
(vennligst hopp over hvis ikke seksuelt aktiv)

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

35. Jeg må tisse oftere enn vanlig

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

36. Hukommelsen min er dårlig

Ja, helt klart	Ja, noen ganger	Nei, ikke så mye	Nei, ikke i det hele tatt
☐	☐	☐	☐

37. Er det svært vanskelig for deg å klare å leve med eller mestre ett eller flere av de symptomene som er nevnt ovenfor?

☐ Ja ☐ Nei

Hvis ja, hvilke(t): _____

GENERELL HELSERELATERT LIVSKVALITET

EQ-5D

Sett et kryss under hvert av punktene 1 til 5, som best beskriver din helsetilstand i dag

1. Gange

☐ Jeg har ingen problemer med å gå omkring

☐ Jeg har litt problemer med å gå omkring

☐ Jeg er sengeliggende

2. Personlig stell

☐ Jeg har ingen problemer med personlig stell

☐ Jeg har litt problemer med å vaske meg eller kle meg

☐ Jeg er ute av stand til å vaske meg eller kle meg

3. Vanlige gjøremål (f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)

☐ Jeg har ingen problemer med å utføre mine vanlige gjøremål

☐ Jeg har litt problemer med å utføre mine vanlige gjøremål

☐ Jeg er ute av stand til å utføre mine vanlige gjøremål

4. Smerte og ubehag

☐ Jeg har verken smerte eller ubehag

☐ Jeg har moderat smerte eller ubehag

☐ Jeg har sterk smerte eller ubehag

5. Angst og depresjon

☐ Jeg er verken engstelig eller deprimert

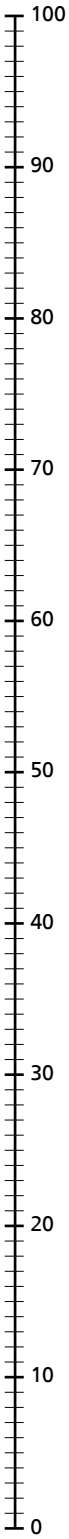
☐ Jeg er noe engstelig eller deprimert

☐ Jeg er svært engstelig eller deprimert

HELSETILSTAND

For at du skal kunne vise oss hvor god eller dårlig din helsetilstand er, har vi laget en skala (nesten som et termometer), hvor den beste helsetilstanden du kan tenke deg er markert med 100 og den dårligste med 0.

Vi ber om at du viser din helsetilstand ved å trekke ei linje fra boksen nedenfor til det punkt på skalaen som passer best for din helsetilstand.



NÅVÆRENDE HELSETILSTAND

Appendix V

Questionnaire – Psychosomatic complaints (PSC)

FYSISKE PLAGER

Her er en liste over noen vanlige fysiske plager. Vær vennlig å angi hvor ofte du har opplevd disse plagene i løpet av det siste året. Sett ring rundt det nummeret som samsvarer med din mening.

		Aldri	Sjelden	Noen ganger	Ofte
1.	Leggkramper	1	2	3	4
2.	Vondt i hjertet	1	2	3	4
3.	Stramninger i brystet	1	2	3	4
4.	Pusteproblemer eller kortpustet	1	2	3	4
5.	Hovne ankler	1	2	3	4
6.	Vondt i ryggen	1	2	3	4
7.	Magesmerter	1	2	3	4
8.	Hodepine	1	2	3	4
9.	Hoste eller forkjølelse	1	2	3	4
10.	Stivhet, opphovning eller verk i ledd eller muskler	1	2	3	4
11.	Problemer med å sovne	1	2	3	4
12.	Problemer med avbrutt søvn	1	2	3	4
13.	Vanskeligheter med å stå opp om morgenen	1	2	3	4
14.	Kraftig hjertebank	1	2	3	4
15.	Svette eller klamme hender	1	2	3	4
16.	Nervøs eller rastløs og anspent	1	2	3	4
17.	Dårlig appetitt	1	2	3	4
18.	Blir fort trett	1	2	3	4
19.	Fullstendig utmattet etter endt arbeidsdag	1	2	3	4

Appendix VI

Self-care information

Self-care

The climacteric
The period between 45 and 55 years is often called the climacteric. During this period the production of sex-hormones will be gradually reduced. When a woman is around 50, she will experience her last menstruation, also called the menopause. Many women will experience changes related to work, family and health in this period, and these changes will influence her quality of life.

Symptoms related to the climacteric
Many women will experience hot flashes and night sweating during the climacteric. Other symptoms can be variable mood, sleep problems, pain in joints, dry mucous membranes and urinary problems. We still don't know why these symptoms appear, but often they can be ameliorated by simple means.

Self-care
You have been allocated to the self-care group. During the study period (12 weeks) you are not allowed to consult a health care professional for symptoms related to the menopause.

What can you do yourself to relieve the symptoms?
Sufficient sleep and rest, reduction of physical and psychological stress, regular exercise, healthy food and limited tobacco smoking and alcohol intake are general recommendations to relieve symptoms related to the menopause. Listed below are things you can do yourself to relieve the complaints:

- *Relaxation- and breathing- techiques may reduce the hot flash frequency. You can learn these techniques from books or CDs.*
- *Increased physical activity may reduce both the frequency and the intensity of hot flashes and sweating, so regular physical activity is recommended.*
- *A healthy diet should preferably consist of fresh food. Increased intake of soy beans, whole grain, rye bread, fresh vegetables and fat fish is recommended.*
- *Soy beans and legumes contain natural plant estrogens. Various soy-products are used as alternative treatment of menopausal complaints. You can obtain these products in your local drugstore or pharmacy, and you may use them during the study.*
- *Dry mucous membranes in vagina can be relieved by estrogen vagitories or cream, or by a vaginal gel without hormones.*
- *Ingrid Bergman once said: 'Getting older is like climbing a mountain; you'll get a bit dyspnoeic, but the view is fantastic'. Focusing on positive things in life may contribute to less bother from menopausal symptoms.*

What can you do as a participant in ACUFLASH?
As a participant in the ACUFLASH study you may use the advice given and the remedies suggested in the paragraph above, not involving a health care professional. You may use soy-products, herbal medicine like Dong Quai and relaxation-techniques to relieve your menopausal symptoms.

If you consult a health care professional (medical doctor, physiotherapist, homeopath etc.) and receive treatment for menopausal complaints, your participation in the study will be terminated. We will still want you to continue filling in the study questionnaires.

If you use relaxtion techniques, soy products or other alternative treatments not involving a therapist, we kindly ask you to inform us by answering the relevant questions in the questionnaire.

Please observe that the product Femal® is not allowed, nor are creams containing progesterone or products containing St. John's Wort.

If you are in doubt about what is allowed, please contact:

Tromsø: Sissel Andersen, tlf. 77 64 48 19, e-post: Sissel.Andersen@ism.uit.no

Bergen: Merete Allertsen, tlf. 55 58 61 33, e-post: Merete.Allertsen@isf.uib.no

Oslo: Heidi Hveem Holtestaul, tlf. 97 64 79 11, e-post: hveeho@online.no

Please bring this information leaflet the next time you visit your family doctor or gynaecologist.

Appendix VII

Questionnaire – 6 Months

6 måneders kontroll

Dato: _____

Randnr.: _____

ACUFLASH SPØRRESKJEMA

BRUK AV HELSETJENESTER, MEDISINER OG KOSTTILSKUDD

Med tanke på egen helse eller sykdom siste 3 mnd, hvor mange ganger har du vært:

	Ant. ganger siste 3 mnd
Innlagt i sykehus	____
Hos psykolog eller lege (allemennlege/ legevakt/spesialist)	____
Hos fysioterapeut eller kiropraktor	____
Hos utøver av alternativ behandling (homeopat/ akupunktør/soneterapeut/naturmedisiner)	____

Har du siste 3 mnd brukt alternativ behandling mot plager i forbindelse med overgangsalderen? (Enten ved å oppsøke en utøver eller som egenbehandling).

☐ Ja ☐ Nei

Hvis Ja; hvilken type behandling har du brukt?

Angi behandlingsform	Egenbehandl.	Hos utøver/ behandler	Ant. behandl.
_____	☐	☐	☐
_____	☐	☐	☐
_____	☐	☐	☐
_____	☐	☐	☐

Har du i løpet av de siste 3 mnd brukt legemidler eller kosttilskudd (herunder reseptbelagte og reseptfrie legemidler, naturmidler, kosttilskudd)?

☐ Ja ☐ Nei

Hvilke preparater har du brukt og hvor ofte?

Angi preparat	Daglig	Hver uke men ikke daglig	Sjeldnere enn hver uke	Grunn til at du har brukt dem
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____

Bruker du østrogenpreparat i skjeden nå (krem/stikkpiller/ vaginaltabletter/vaginalinnlegg)?

☐ Ja ☐ Nei

Hvis Ja; hvor lenge har du brukt det?

Ant. år ____ Ant. mnd. ____

Hvor ofte har du vært plaget av søvnløshet i de siste 3 mnd?

Aldri	1-3 ganger i mnd.	Omtrent 1 gang i uken	Mer enn 1 gang i uken
☐	☐	☐	☐

Har du siste 3 mnd vært plaget av søvnløshet som har gått ut over arbeidsevnen?

☐ Ja ☐ Nei

LEVEVANER OG BEHANDLINGSERFARINGER

Er du vegetarianer? ☐ Ja ☐ Nei

Har du røykt/røyker du?

Ja, daglig	Ja, men ikke daglig	Ja, tidligere	Nei, har aldri røykt
☐	☐	☐	☐

Hvor mange kopper kaffe og te drikker du daglig?

Koffeinholdig kaffe	____ kopper
Koffeinfri kaffe	____ kopper
Te	____ kopper

Er du totalavholdskvinne? ☐ Ja ☐ Nei

Hvis nei, hvor ofte og hvor mye drakk du i gj.snitt siste år?

	Aldri, sjelden	1 pr.mnd	2-3 pr. mnd	1 pr. uke	2-4 pr. uke	5-6. pr. uke	1+ pr. dag
Øl (1/2 l)	☐	☐	☐	☐	☐	☐	☐
Vin (glass)	☐	☐	☐	☐	☐	☐	☐
Brennevin (drinker)	☐	☐	☐	☐	☐	☐	☐

Arbeidsaktivitet siste året.
Hva slags aktivitet har du vanligvis i arbeidet ditt?

☐ For det meste stillesittende arbeid (eks. kontorarbeid)

☐ Arbeid som krever at du går mye (du blir ikke svett og hjertet slår ikke fortere, eks. ekspeditør, lærer, frisør)

☐ Arbeid der du går mye og løfter mye (du svetter litt og hjertet slår raskere, eks. syke-/hjelpepleier, postbetjent)

☐ Tungt kroppsarbeid (du svetter en del og hjertet slår raskt, tunge løft, jordbruk, tungt omsorgsarbeid)

Har du vært yrkesaktiv de siste 6 mnd.? ☐ Ja ☐ Nei

Hvor stor stillingsprosent har du? ____ %

Har du endret dine levevaner for å lindre hetetoktene etter at studien var avsluttet (siste 3 mnd.)

☐ Ja ☐ Nei

Hvis Ja; angi hvilke endringer du har gjort siste 3 mnd (sett et kryss på det som passer)

Hvile og søvn	Økt	Redusert
Bruk av avspenningsteknikk	☐	☐
Fysisk aktivitet	☐	☐
Inntak av koffeinholdig kaffe	☐	☐
Inntak av alkohol	☐	☐
Røyking	☐	☐

Andre endringer, beskriv hvilke _____

Opplever du at plagene du har i forbindelse med overgangsalderen har endret seg etter at studien har pågått? (siste 3 mnd)

☐ Ja ☐ Nei

Hvis ja, sett kryss eller spesifiser hva som har forandret seg

	Betydelig økning	Litt økning	Litt reduksjon	Betydelig reduksjon
Antall hetetokter pr. døgn	☐	☐	☐	☐
Intensiteten av hetetokter	☐	☐	☐	☐
Søvnkvalitet	☐	☐	☐	☐
Generell velvære	☐	☐	☐	☐
Andre plager, spesifiser	☐	☐	☐	☐
_____	☐	☐	☐	☐

Besvares kun av deltakere i akupunkturgruppen:

Er du tildelt akupunkturbehandling i studieperioden?

☐ Ja ☐ Nei

Vil du anbefale akupunktur til andre ☐ Ja ☐ Nei

Kan du tenke deg å prøve akupunktur igjen ☐ Ja ☐ Nei

Hvis nei, hvorfor? _____

Bruk vedlagte returkonvolutt og returner skjemaet så rask som mulig.

Mange takk for hjelpen!

Appendix VIII

Questionnaire – 12 Months

12 måneders kontroll

Dato: _____

Randnr.: _____

ACUFLASH SPØRRESKJEMA

BRUK AV HELSETJENESTER, MEDISINER OG KOSTTILSKUDD

Med tanke på egen helse eller sykdom siste 6 mnd, hvor mange ganger har du vært:

	Ant. ganger siste 6 mnd
Innlagt i sykehus	____
Hos psykolog eller lege (allemennlege/ legevakt/spesialist)	____
Hos fysioterapeut eller kiropraktor	____
Hos utøver av alternativ behandling (homeopat/ akupunktør/soneterapeut/naturmedisiner)	____

Har du siste 6 mnd brukt alternativ behandling mot plager i forbindelse med overgangsalderen? (Enten ved å oppsøke en utøver eller som egenbehandling).

☐ Ja ☐ Nei

Hvis Ja; hvilken type behandling har du brukt?

Angi behandlingsform	Egenbehandl.	Hos utøver/ behandler	Antall behandl.
_____	☐	☐	☐
_____	☐	☐	☐
_____	☐	☐	☐
_____	☐	☐	☐

Har du i løpet av de siste 6 mnd brukt legemidler eller kosttilskudd (herunder reseptbelagte og reseptfrie legemidler, naturmidler, kosttilskudd)?

☐ Ja ☐ Nei

Hvilke preparater har du brukt og hvor ofte?

Angi preparat	Daglig	Hver uke men ikke daglig	Sjeldnere enn hver uke	Grunn til at du har brukt dem
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____
_____	☐	☐	☐	_____

Bruker du østrogenpreparat i skjeden nå (krem/stikkpiller/ vaginaltabletter/vaginalinnlegg)?

☐ Ja ☐ Nei

Hvis Ja; hvor lenge har du brukt det?

Ant. mnd. ____

Hvor ofte har du vært plaget av søvnløshet i de siste 6 mnd?

Aldri	1-3 ganger i mnd.	Omtrent 1 gang i uken	Mer enn 1 gang i uken
☐	☐	☐	☐

Har du siste 6 mnd vært plaget av søvnløshet som har gått ut over arbeidsevnen?

☐ Ja ☐ Nei

LEVEVANER OG BEHANDLINGSERFARINGER

Er du vegetarianer? ☐ Ja ☐ Nei

Har du røykt/røyker du?

Ja, daglig	Ja, men ikke daglig	Ja, tidligere	Nei, har aldri røykt
☐	☐	☐	☐

Hvor mange kopper kaffe og te drikker du daglig?

Koffeinholdig kaffe	____ kopper
Koffeinfri kaffe	____ kopper
Te	____ kopper

Er du totalavholdskvinne? ☐ Ja ☐ Nei

Hvis nei, hvor ofte og hvor mye drakk du i gj.snitt siste 6 mnd?

	Aldri, sjelden	1 pr.mnd	2-3 pr. mnd	1 pr. uke	2-4 pr. uke	5-6. pr. uke	1+ pr. dag
Øl (1/2 l)	☐	☐	☐	☐	☐	☐	☐
Vin (glass)	☐	☐	☐	☐	☐	☐	☐
Brennevin (drinker)	☐	☐	☐	☐	☐	☐	☐

Har du vært yrkesaktiv de siste 6 mnd.? ☐ Ja ☐ Nei

Hvor stor stillingsprosent har du? ____ %

Arbeidsaktivitet siste 6 mnd.
Hva slags aktivitet har du vanligvis i arbeidet ditt?

☐ For det meste stillesittende arbeid (eks. kontorarbeid)

☐ Arbeid som krever at du går mye (du blir ikke svett og hjertet slår ikke fortere, eks. ekspeditør, lærer, frisør)

☐ Arbeid der du går mye og løfter mye (du svetter litt og hjertet slår raskere, eks. syke-/hjelpepleier, postbetjent)

☐ Tungt kroppsarbeid (du svetter en del og hjertet slår raskt, tunge løft, jordbruk, tungt omsorgsarbeid)

SNU

Har du endret dine levevaner for å lindre siste 6 mnd. ?

☐ Ja ☐ Nei

Hvis Ja; angi hvilke endringer du har gjort siste 6 mnd (sett et kryss på det som passer)

	Økt	Redusert
Hvile og søvn	☐	☐
Bruk av avspenningsteknikk	☐	☐
Fysisk aktivitet	☐	☐
Inntak av koffeinholdig kaffe	☐	☐
Inntak av alkohol	☐	☐
Røyking	☐	☐

Andre endringer, beskriv hvilke _____

Opplever du at plagene du har i forbindelse med overgangs-alderen har endret seg siste 6 mnd ?

☐ Ja ☐ Nei

Hvis ja, sett kryss eller spesifiser hva som har forandret seg

	Betydelig økning	Litt økning	Litt reduksjon	Betydelig reduksjon
Antall hetetokter pr. døgn	☐	☐	☐	☐
Intensiteten av hetetokter	☐	☐	☐	☐
Søvnkvalitet	☐	☐	☐	☐
Generell velvære	☐	☐	☐	☐
Andre plager, spesifiser	☐	☐	☐	☐
_____	☐	☐	☐	☐

Besvares kun av deltakere i akupunkturgruppen:

Fikk du akupunkturbehandling i studieperioden?

☐ Ja ☐ Nei

Vil du anbefale akupunktur mot denne type plager til andre?

☐ Ja ☐ Nei

Kan du tenke deg å prøve akupunktur mot denne type plager igjen?

☐ Ja ☐ Nei

Hvis nei, hvorfor? _____

Bruk vedlagte returkonvolutt og returner skjemaet så rask som mulig.

Mange takk for hjelpen!

Appendix IX

Acupuncturist's data collection form

Date: _____

Therapist: _____

Rand no.: _____

Treatment no.: _____

SYNDROME FORM

Fill in primary (1°) and secondary (2°) syndromes at first treatment.

	❑	*Uforandret (krysses av ved etterfølgende behandling, hvis forandring krysses det av nedenfor)*	
1°	2°	**SYNDROMES**	**AETIOLOGY**
❑	❑	❑ **Kid Yin Xu empty heat** ❑ Night sweating ❑ Restless ❑ Anxious ❑ Dry-, hair, skin, mouth ❑ Deep weak ❑ Red tongue without coating ❑ Other (specify)	❑ Constitution ❑ Overwork (too many children) ❑ Emotional stress ❑ Other (specify)
❑	❑	❑ **Kid Yang Xu: empty cold** ❑ Hot flushes but cold hands & feet ❑ Night sweating (early morning) ❑ Tiredness, low energy ❑ Depressed ❑ Deep pulse ❑ Pale tongue ❑ Other (specify)	❑ Constitution ❑ Overwork (too many children) ❑ Emotional stress ❑ Other (specify)
❑	❑	❑ **Kid yin and Kid yang Xu** ❑ Frequent pale urination ❑ Flushed around neck when talking	❑ Constitution ❑ Overwork (too many children) ❑ Emotional stress ❑ Other (specify)
❑	❑	❑ **Kid–and Liv-Yin Xu with Liver yang rising** ❑ Irritability ❑ Blurred vision	❑ Constitution ❑ Overwork (too many children) ❑ Emotional stress ❑ Emotional stress ❑ Other (specify)
❑	❑	❑ **Kidneys and Heart not harmonised** ❑ Palpitations ❑ Insomnia ❑ Mental restlessness ❑ Poor memory ❑ Other (specify)	❑ Constitution ❑ Overwork (too many children) ❑ Emotional stress ❑ Other (specify)
❑	❑	❑ **Accumulation of phlegm and stagnation of Qi** ❑ Obesity ❑ Oppression of chest ❑ Fullness of epigastrium ❑ Belching, nausea, no appetite ❑ Tongue: red sides (slight), sticky coating ❑ Pulse: Wiry, slippery	

Date: _____

Therapist: _____

Rand no.: _____

Treatment no.: _____

1°	2°	SYNDROMES cont.	AETIOLOGY
❑	❑	❑ **Stasis of blood** ❑ Menopause preceded by a period when menses are very irregular ❑ High blood pressure ❑ Abdominal pain	(list aetiology)

❑	❑	❑ **Liver Qi Stagnation (list symptoms)**	

❑	❑	❑ **Stomach heat** ❑ Night sweating ❑ Restless ❑ Anxious ❑ Dry-, hair, skin, mouth ❑ Deep weak ❑ Red tongue without coating ❑ Other (specify)	❑ Constitution ❑ Overwork (too many children) ❑ Emotional stress ❑ Other (specify)

❑	❑	❑ **Kid Yang Xu: empty cold** ❑ Hot flushes but cold hands & feet ❑ Night sweating (early morning) ❑ Tiredness, low energy ❑ Depressed ❑ Deep pulse ❑ Pale tongue ❑ Other (specify)	❑ Constitution ❑ Overwork (too many children) ❑ Emotional stress ❑ Other (specify)

		❑ **Other patterns (list symptoms)**	

Date: _____

Therapist: _____

Rand no.: _____

Treatment no.: _____

TREATMENT FORM

(to be completed at every session)

ACUPUNCTURE INTERVENTIONS

Acupuncture interventions: List acupuncture points used and indicate unilateral or bilateral:

❑ Uforandret (hvis etterfølgende behandling er uforandret fra tidligere)

Include reasons for change of acu points from previous treatment.
Notes: attaining *deqi*, needle technique, etc.

Moxa interventions:

Moxa ❑ sparrow-pecking ❑ moxa box

Approximate location:

Other interventions:

❑ Massage
❑ Cupping
❑ Electro-acupuncture
❑ Chinese herbs ❑ To be taken internally ❑ For external use
❑ Other (specify)

Home-based self treatment prescribed:

❑ Specific physical exercises
❑ Tai chi
❑ Yoga
❑ Self massage
❑ Relaxation exercises
❑ Other (specify)

Facilitating and supporting lifestyle change:

❑ <u>Dietary advice</u>
❑ Low dairy ❑ Avoid wine & spirits
❑ Low wheat ❑ Stop coffee/reduce
❑ Ensure food is warm and cooked ❑ Other dietary advice (specify)
❑ <u>Non dietary change</u>
❑ Stop smoking/reduce ❑ Protect from cold and damp
❑ Take more exercise ❑ Other (specify)
❑ Take more rest

❑ General support and empowerment (describe):

Date: _____

Therapist: _____

Rand no.: _____

Treatment no.: _____

REACTIONS TO TREATMENT

Type 1: Reactions to normal treatment, which could be positive indicators (but could be experienced as adverse by newer patients), and are communicated spontaneously by the patient during or after treatment, or at the next visit:

- ❑ Light-headedness
- ❑ Energised
- ❑ Tired
- ❑ Relaxed
- ❑ Hungry
- ❑ Drowsy
- ❑ Other (specify)

Type 2: Reactions to normal treatment which result in an aggravation of symptoms followed by a significant improvement (better than before treatment) as a result of asking if the patient had any reactions to the previous treatment:

List symptoms that worsened:

When starting after treatment?

For how long did symptoms last?

Any other details:

Type 3: Adverse events:

- ❑ Fainting
- ❑ Fit (convulsions)
- ❑ Skin reactions
- ❑ Unacceptable bruising
- ❑ Unacceptable bleeding
- ❑ Unacceptable pain at a point from needling
- ❑ Unacceptable worsening of symptoms

Please write about the incident in some detail:

- ❑ Forgotten needle
- ❑ Broken needle
- ❑ Moxa burn
- ❑ Pneumothorax
- ❑ Infection
- ❑ Other (specify)

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