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## Position Statement

# Menopause and aging, quality of life and sexuality

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*The aim of this meeting was to suggest state-of-the-art guidelines for research and practice on these themes. This paper was prepared following the presentations and the discussion during the Workshop. Thereafter, the manuscript draft was circulated and was edited by the presenters and Chairmen of the sessions. The final version has been extensively discussed and finally approved, but does not necessarily express or replicate the exact opinion of each individual presenter.*

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## A HISTORICAL PERSPECTIVE

In 19th century society, education and sexual activity were not considered appropriate for respectable women. There was a belief that neurasthenia, menstrual madness and hysteria were due to too much reading and listening to music. Certainly, women were too weak from their monthly loss to be worthy of education. Nymphomania, masturbation and moral insanity

were generally believed by psychiatrists and gynecologists alike to be severe disorders which led to depression, coma, paralysis and death. There were many operations to treat these conditions, including ovariectomy for menstrual madness, pioneered by Robert Battey of Atlanta and Lawson Tait of Birmingham. Clitoridectomy for nymphomania, masturbation and various vague gynecological disorders was recommended by Isaac Baker Brown of London.

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These operations were fashionable for up to 30 years in Europe and North America before they were utterly discredited. But it is interesting that, although it became a public scandal, recognized by all authorities, there is no mention of these operations in contemporary writings. Indeed, in the late 19th century, novels (and operas) always had the certain outcome of extra-marital sex being suicide, murder or deportation. Examples of this are Tolstoy's *Anna Karenina*, Flaubert's *Emma Bovary*, and Dicken's *Lady Deadlock* or Emily in *David Copperfield*. There are virtually no exceptions to this judgmental outcome. The fate of operatic heroines of Wagner, Puccini or Verdi in the 19th century was the same.

Perhaps the first occasion in literature when those women who enjoyed sexual freedom outside of marriage escaped such a fate was in *Ann Veronica* by H. G. Wells in 1903 and in the opera *Der Rosenkavalier* by Richard Strauss in 1909. Subsequently, with the work of Marie Stopes, Kinsey and Masters and Johnson, sexual pleasure is recognized to be a fundamental need for most women, with therapy available for those with a hyposexual disorder.

## SEXUALITY, AGING AND QUALITY OF LIFE

Sexuality is an important determinant of health-related and overall quality of life in adulthood but its relevance becomes less predictable in the elderly, particularly older women.

After controlling for other health and relationship factors, there is an age-related decrease in sexual interest and activity in both sexes. Physical health problems associated with aging may impair sexual interest and responsiveness of both men and women. Age-related decline in androgens contributes to the decline in sexual interest and erectile response that in aging men is particularly affected by vascular and neurological disease. Mental health is important for maintenance of sexual interest, especially in women. In postmenopausal women, the quality of the relationship and the presence of sexual problems in the partner are probably as important as are hormonal change in the maintenance of sexual interest and response. Psychological factors, including depression, presence or absence of a partner, quality of the relationship and the partner's health or sexual problems are important elements in determining the sexuality of postmenopausal women. Sexual activity, libido and testosterone levels show some association, although this is not completely clear.

In older women, maintenance of sexual interest is largely dependent on the existence of a relationship, and older women are much less likely to be in a relationship than men of the same age.

Studies on aging couples demonstrate that sexuality problems are gender-specific: in females vaginal dryness and lack of a partner or the presence of health problems such as urinary incontinence, depression, dementia, arthritis, stroke and breast cancer are major determinants. In males, stronger determinants are erectile dysfunction and decreased sex desire.

## SCIENTIFIC ASSESSMENT OF QUALITY OF LIFE AND SEXUALITY

Several methods have been developed to measure health-related quality of life. Patient-assessed health outcome measures are categorized as specific (disease-, function- or population-specific, and dimension-specific), generic, utility (preference-based) or individualized. There is no single ideal method. Generic measures permit comparisons among health problems; specific measures are often more responsive and focus on the concerns of patients with that health problem. Each method highlights characteristics that have to be considered in relation to the populations studied. Specific and generic or utility measures often complement each other.

Among the most widely used generic measures of health-related quality of life are several profile measures, including the Short-Form 36, the Nottingham Health-Profile and the Sickness Impact Profile. Health concepts included in general health status and health-related measures are represented by the World Health Organization International Classification of Functioning, Disability and Health. Disease- and population-specific measures may relate to quality of life in the climacteric. The currently available and climacteric-specific scales such as the Greene Climacteric Scale, the Women's Health Questionnaire and the Menopause Rating Scale include between three and nine domains and apply Likert-type scaling and aggregate within domains. Professional consensus should determine the most suitable measure for a particular application in assessing quality of life in an aging population.

Sexual health is a complicated puzzle affected by biological, psychological and relational factors. Female sexual dysfunction is multicausal and multidimensional. It is mainly related to age, partner and reproductive stages and often leads to personal distress. The assessment methods of

sexual function need to include: sexual history and measurement tools (structured interviews, diary/event log measures, self-administered questionnaires). There are several questionnaires among which the most used is the Female Sexual Function Index. However, different aspects of sexuality need to be analyzed with specific questionnaires, and clinical primary endpoints of a successful therapy should be based on the number of successful and satisfactory sexual events.

## DETERMINANTS OF QUALITY OF LIFE AND SEXUALITY

### The aging brain and mind

Throughout life, the brain is constantly assaulted by internal toxins and external environmental/microbial agents, etc. These assaults may result in self-destructive inflammatory over-responses that unleash reactive oxygen species, cytokines, etc. Since they play key roles in the responses to these assaults, the brain's immune and vascular systems are closely regulated. Estrogen is a key agent of this regulation. The immune system works constantly to maintain homeostasis, constantly removing noxious materials and waste with the least possible inflammatory response. Estrogen, especially estradiol, acting on estrogen receptor (ER)- $\beta$ -expressing microglial cells, maintains this homeostasis by acting as an anti-inflammatory agent. By keeping the response to assaults local (phagocytosis, etc.) rather than general (inflammatory cytokines, reactive oxygen species, etc.), estrogen avoids collateral damage to neighboring neurons and fibers, and eventual dystrophy in the aging brain. In the absence of estrogen, less restricted immune responses can hasten clinical brain disorders, development/deposition of toxic materials, hyperphosphorylation of microtubule-associated proteins, etc. Lack of estrogen may also retard the reparative properties of brain vessel endothelium and failure of vascular clearance or occlusions. Thus, decline of estrogen with aging may result in cognitive/motor decline and Alzheimer/vascular dementia.

Hormones are also implicated in the regulation of the specific brain pathways for sexual arousal, desire, reward and inhibition. Excitatory pathways for desire include limbic, hypothalamic, and midbrain structures. Hypothalamic and mesolimbic dopamine systems are important for desire, as are certain neuropeptide systems such as the melanocortins. The meso-cortico-limbic

dopaminergic is also the neurotransmitter system most involved in the neural 'reward circuit'. Dopaminergic projections from the ventro tegmental area innervate the nucleus accumbens, in the limbic region, and the prefrontal cortex. Other important areas interconnected with this circuit are the amygdala, the thalamus and the hypothalamus. Reward has a fundamental role for survival and reproduction and it is a biological mechanism motivated by events commonly associated with pleasure. Sexual reward involves the activation of opioid systems. This activation is critical for the formation of conditioned place and partner preferences. This 'reward circuit' is particularly sensitive and vulnerable to the actions of drugs of abuse, and chronic stimulation by these drugs leads to the pathological status of the brain called 'addiction'. Vulnerability to addiction is also consistently influenced by environmental and genetic factors.

Menopause *per se*, independently of the effects of aging, can be associated with changes in sexual desire in a substantial proportion of women. Decreased sexual desire is linked to decreased sexual satisfaction among postmenopausal women. Hormonal changes at menopause can negatively impact women's sexual function, either directly by causing sexual pain (dyspareunia) or indirectly via a number of psychological mechanisms (e.g. decreased self-esteem, body image, weight gain and depression).

Obesity interacts in complex ways with sexuality and sexual quality of life. Although epidemiological data are mixed with regards to the efficacy of weight loss to reduce morbidity and mortality in elderly men or women, there are little data on the effect of weight loss on sexual quality of life, especially in the elderly and after menopause. Emotional bonding cues may play a particularly important role in triggering sexual desire among postmenopausal women.

The menopausal transition is associated with an increased risk for clinically significant depression in women, even in those without a history of premenopausal depression. Depression is a risk factor for several medical illnesses, such as cardiovascular risk, osteoporosis and Alzheimer's disease. Major depression is highly under-recognized, and undertreated, potentially altering the currently available quality-of-life measurements in the general population. Estrogen administration to women who develop depressive symptoms at the time of menopause results in amelioration of these symptoms, both in women with and without other climacteric symptoms, as hot flushes.

## Cardiovascular and musculoskeletal systems

In addition to the aging-related phenomena, the menopause-related estrogen depletion may result in a series of metabolic consequences (worsening lipid profile, altered body fat distribution and central obesity, altered glucose and insulin metabolism, increased blood pressure and disturbed coagulation and fibrinolysis) that can exacerbate or disclose cardiovascular risk. Metabolic and cardiovascular diseases affect quality of life through the development of debilitating conditions such as peripheral or autonomic neuropathy, nephropathy and ophthalmic diseases induced by severe diabetes, or important limitation of physical activity resulting from coronary heart disease.

Osteoporosis is one of the major health problems of modern society. Current estimates indicate that up to 40% of women aged 50 years or older will suffer an osteoporosis-related fracture within their lifetime. Osteoporosis-related fractures are an important cause of morbidity, disability and mortality. Both health-related quality of life and global quality of life are negatively affected by fractures. The impact of fractures on quality of life is dependent on the skeletal site and severity of fracture. Hip fractures are the most serious of osteoporosis-related fractures, resulting in excess mortality, in long-term morbidity and considerable use of resources for long-term care. However, spinal fracture has also been shown to be associated with increased mortality. As already well documented for the bone, gonadal steroids play a pivotal role in the regulation of collagen metabolism. Cartilage is sensitive to estrogens, and estrogens and other estrogen receptor-targeted compounds have chondroprotective effects. Intervertebral disks are composed of a rich content of collagen types, elastin, hydrophilic glycosaminoglycans and water, showing progressive changes throughout life. Intervertebral disk height decreases with age, but a sharp decrease in disk height is evident in the year after menopause.

## Gynecological cancers, urogenital system, skin and mucosa

Cancer has a powerful impact on health and on quality of life. In genital cancer survivors, radical surgery with or without chemo-radiotherapy to the pelvis often leads to organ dysfunction due to nerve or lymphatic damage. Strategies that reduce nerve damage and lymphatic edema and that aim at fertility preservation have been developed and

are important to improve quality of life. Breast cancer adjuvant therapies (tamoxifen, aromatase inhibitors, bilateral oophorectomy, gonadotropin releasing hormone analogues) may also have a profound impact on health and quality of life. Quality of life must be considered an issue in the management of cancer patients. A more extensive discussion of the patient's symptoms, within the setting of a physician-patient relationship, seems to be effective in reducing the burden of complaints. The urogenital system represents another important factor for the determination of quality of life and sexual activity. The lack of estrogens can lead to vaginal dryness, loss of vaginal compliance, dyspareunia and increased vulnerability to infections and trauma. Vaginal dryness in patients treated for gynecological cancers can be addressed with lubricants or, if needed, with ultra-low dosages of vaginal estrogens.

The female genital and lower urinary tract both derive embryologically from the urogenital sinus and are both sensitive to the actions of estrogen, with estrogen receptors present throughout the urinary tract, apart from the dome of the bladder. The pelvic floor musculature is also estrogen-sensitive.

Epidemiological studies implicate estrogen deficiency in the etiology of lower urinary tract symptoms. Seventy percent of women relate the onset of urinary stress incontinence to their menopause. Fifty percent of women attending a menopause clinic report stress urinary incontinence and 20% severe urge incontinence.

Estrogens affect continence by increasing urethral resistance, raising the sensory threshold of the bladder, increasing  $\alpha$ -adrenoreceptor sensitivity in urethral smooth muscle and promoting adrenoreceptor-mediated relaxation of the detrusor muscle. Estrogens increase urethral closure pressure and vascular dilatation in periurethral vessels.

Estrogen therapy (the type, dose and route of administration are not clearly defined) particularly improves the symptoms of urgency but has a less clear effect on stress urinary incontinence, although there seems to be subjective symptom improvement and increased maximal urethral closure pressure in patients. Therapy with combined estrogen-progestogens reduces the probability of improvement in symptoms.

Menopause increases aging of the skin and mucosae, with negative effects on quality of life and sexuality. Menopause is associated with atrophic changes of the skin and skin collagen changes. Hormone treatment preserves collagen

content in the skin. Estrogen therapy improves collagen synthesis throughout the body. Intervertebral discs show reduced height with age, which might impair the shock-absorbing function of the disks, possibly leading to vulnerability to compression fractures. Hormone therapy increases intervertebral disk height. Estrogen reduces wrinkling and improves the mechanical properties of the skin. Skin thickness and elasticity correlate with bone mineral density. Hair changes with menopause, with increased facial hair, decreased body hair, decreased pubic hair, diffused alopecia and sometimes androgenic alopecia.

## THERAPEUTICAL STRATEGIES TARGETING QUALITY OF LIFE AND SEXUALITY

### The aging brain and mind

Steroid hormones have several actions on the brain. Estrogen promotes neuronal growth and synaptic plasticity, reduces cell apoptosis and modulates mitochondrial activity and brain immune function. Androgen acts on the central nervous system by modulating cognitive function, mood, libido, sexual arousal and emotional satisfaction. Progesterone and neurosteroids increase neuronal survival, nerve regeneration and remyelination. While progesterone and 19-norprogesterone enhance estrogen-induced neuroprotection in experimental models, medroxyprogesterone acetate antagonizes this effect. One important metabolite of progesterone in the brain is allopregnanolone, but some progestins are not converted to active neurosteroids (such as levonorgestrel, desogestrel, gestodene, norgestimate). Allopregnanolone has concentration-dependent effects: hypnotic/sedative, anxiolytic, anesthetic, and anticonvulsant. After the menopause, there is a reduction in  $\beta$ -endorphin concentration, involved in alteration of mood, pain perception and therefore quality of life. Estrogen plus progesterone restores  $\beta$ -endorphin levels, improving some symptoms and quality of life, but not all progestins have similar effects. Age-related reduced production of growth hormone and sex steroids and the increased production of cortisol negatively affect the balance of neurotoxic and neuroprotective steroids in the brain. Estrogen and androgen replacement therapy are able to restore this unbalanced status, improving quality of life and sexual well-being.

During the perimenopausal period, women complain of an increase in anxiety and tension. Cortisol has been shown to increase during

transition into perimenopause (between 7 and 12 months after transition into late perimenopause). Women have greater increases in cortisol, following a laboratory stressor, as they age, compared to men, and this increase is up to three times higher in women. Cortisol levels in women predict higher memory deficits. After an acute laboratory stressor, women show greater memory deficits compared to men. Women with hot flushes have higher cortisol levels compared to women without hot flushes. Effects of estrogen on stress responsivity are variable, with some studies showing anxiolytic effects and others showing anxiogenic effects. Basic science studies suggest that ER- $\alpha$  agonists increase anxiety, while ER- $\beta$  agonists decrease anxiety. This has not been tested in humans.

In postmenopausal women with climacteric symptoms, lower than standard doses of hormone replacement therapy (HRT) have been shown to be adequate in significantly improving individual domains (attractiveness, menstrual symptoms, sleep problems, sexual behavior, anxiety/fears, vasomotor symptoms, memory/concentration, somatic symptoms and depressed mood) and generally overall measures of quality of life with both generic- and disease-specific tools. Standard doses of HRT may achieve a rapid response on flushing, sweating and sleep, but, initially, with uterine bleeding disturbances, as well as breast discomfort. Lower-dose preparations have been considered in order to achieve a better risk/benefit profile. Low-dose and ultra-low-dose HRT can reduce hot flushes in 2–3 weeks, with a significant improvement in quality-of-life domains at 10–12 weeks, along with a high incidence of amenorrhea from the initiation of treatment. The ultra-low-dose combinations may also have very little, or even neutral effects, on the breast. Additional paths to an enhanced risk/benefit profile with hormonal treatments derive from the pairing of an estrogen(s) with a selective estrogen receptor modulator (SERM), creating a tissue-selective estrogen complex. Indeed, the biological actions of estrogens and SERMs may be similar in some tissues and different in others. Different estrogens or SERMs acting through the same receptors (ER- $\alpha$  or ER- $\beta$ ) can induce different receptor conformations, resulting in different biologies and different actions in different target tissues. The combination of SERMs and estrogens will determine clinical results based on their blended tissue-selective activity profile. An ideal pairing of estrogen with a SERM at appropriate doses may achieve most of the goals of menopause treatment: improvement in menopausal symptoms, neutral breast effects, prevention of

endometrial stimulation, high amenorrhea rates and bone-sparing effects.

### Androgens in the aging individual

As men age, their testosterone levels gradually fall, leading eventually to hypogonadism. Late-onset hypogonadism is a clinical and biochemical syndrome associated with advancing age and characterized by typical symptoms such as loss of bone and muscle mass, decreased sex drive, lack of energy, depression and insulin resistance. Low testosterone levels are more common in patients with the metabolic syndrome, cardiovascular diseases, or diabetes type 2 than in the normal population, and epidemiological studies have shown associations between plasma levels of total testosterone and risk factors for the metabolic syndrome. Low testosterone levels are associated with anemia and increased mortality. Testosterone levels are also decreased in aging men with erectile dysfunction.

The goals of androgen therapy in men are: to restore metabolic parameters to the eugonadal state; to increase muscle mass, strength and function; to maintain bone mineral density and to reduce fracture risk; to improve neuropsychological function (cognition and mood); to improve psychosexual function; and to improve quality of life. Testosterone may be considered for the treatment of erectile dysfunction in men with low to low-normal testosterone who have failed prior treatment with PDE-5 inhibitor therapy.

The basic principle of testosterone treatment is to use natural testosterone and to achieve a physiological serum profile. For aging men, short-acting preparations (transdermal or oral) should be preferred over long-acting preparations (intramuscular or subdermal).

Testosterone administration is absolutely contraindicated in men suspected of, or having, carcinoma of the prostate or breast, significant polycythemia, untreated sleep apnea, severe heart failure, or severe symptoms of lower urinary tract obstruction. Digital rectal examination and determination of serum prostate-specific antigen are mandatory in men as baseline measurements of prostate health prior to therapy with testosterone, at 3-monthly intervals for the first 12 months and yearly thereafter.

In women, testosterone and free testosterone levels decline progressively with age, independently of the occurrence of the menopausal transition. Low testosterone levels and low sexual desire are not correlated, although clinical mea-

surement of circulating testosterone levels in women remains unreliable. No relationship between total/free testosterone, well-being and cognitive function has been established so far. Sexual function, well-being and cognitive function in women correlate with circulating levels of dehydroepiandrosterone sulfate, a major precursor for tissue steroid production and activity.

In postmenopausal women with hypoactive sexual desire disorder, testosterone administered by transdermal patch (300 µg/day) increases desire, the number of satisfactory sexual events and self-reported sexual function. Testosterone therapy at this dose is associated with a low risk of androgenic side-effects. No data indicate an increased risk of breast cancer or cardiovascular disease or of endometrial adverse effects to date.

Tibolone is a comprehensive treatment, treating climacteric symptoms and improving general quality of life, as well as improving sexual function in postmenopausal women. Tibolone improves sexual function and especially sexual desire, arousal and satisfaction more effectively than transdermal estradiol/progestin. Tibolone has indirect androgenic effects by decreasing sex hormone binding globulin levels and increasing free testosterone serum levels.

### Lifestyle, body weight and the aging cardiovascular system

The adipose tissue is an endocrine organ. Muscle mass decreases and central adipose tissue increases with age, even without major changes in body weight. Menopause is associated with redistribution towards central adiposity, reduced fat oxidation, decreased energy expenditure and a predisposition towards the metabolic syndrome. Obesity is associated with reduced quality of life and an increased mortality. Weight loss may increase quality of life, improving intermediate risk factors for cardiovascular disease and diabetes; however, there is no clinical evidence that weight loss can reduce mortality.

Quality of life is improved by cardiovascular disease prevention and treatment. Antihypertensive treatment reduces this risk, but the therapeutic choice has to consider gender differences and possible influences on sexual function and quality of life. It is recommended to always treat and control hypertension, a major risk factor of cardiovascular death, especially from stroke.

Estrogens have profound effects on the cardiovascular system through a complex array of genomic and non-genomic signaling mechanisms,

by which estrogens orchestrate cell and organ function. The lack of sex steroid hormones after the menopause has a strong impact on cardiovascular function. The menopausal transition brings functional alterations that make the arteries more susceptible to damage. For instance, estradiol deprivation, reducing arterial elasticity, favors increased age-related incidence of hypertension. Thus, at the time of the menopausal transition, the changing hormonal exposure leads to less functional arteries in the presence of increasing damaging insults, due to the appearance or worsening of a number of cardiovascular risk factors (e.g. central adiposity, increased body weight, increased blood pressure, and increased cholesterol levels). Therefore, the arteries of a postmenopausal woman are at the same time less protected and more injured. Indeed, aged women are much more exposed to the risk of cardiovascular events than men, and menopause adds to the aging process, increasing the risk of cardiovascular disease. The currently available evidence supports the concept that HRT started at the time or near to the menopausal transition can exert a cardioprotective effect. Patient selection, type, dose and route of administration may influence the effects of HRT on cardiovascular disease. Oral estrogens, through hepatic first pass, induce a hypercoagulable state and activate the renin-angiotensin-aldosterone system. Conversely, transdermal estradiol exerts positive effects on the endothelium, without affecting coagulation (no increase in thromboembolic events). HRT optimization, which could potentially result in long-term protection from cardiovascular disease, may be particularly achieved by administration of estradiol through a transdermal route. The activation of the renin-aldosterone system by estrogen may be relevant in susceptible individuals, leading to an increase in water and salt retention and possibly unpredictable blood pressure rise. Unlike other currently available progestogens, drospirenone has a pharmacologic profile that closely mimics that of endogenous progesterone, notably with respect to its potent aldosterone receptor antagonism. The antialdosterone activities of drospirenone and progesterone counteract the salt and water retention elicited by estrogen; therefore, they may contribute to maintaining a stable body weight and may exert favorable effects on blood pressure in postmenopausal women. In addition, micronized progesterone does not counteract the actions of estrogens on vascular cells and on lipid metabolism. To this extent, the antialdosterone properties of progesterone and drospirenone may provide additional

metabolic advantages and clinical benefits, particularly on the cardiovascular system.

## Bone and joints

Vertebral and non-vertebral fractures negatively impact on health-related measures of quality of life. This negative effect on quality of life increases with increasing age. Antiresorptive agents effectively reduce fracture risk. The reduction of fracture events prevents the loss of health-related quality of life associated with incident fractures. The World Health Organization is developing a model that will use bone density information and global clinical risk factors to estimate a 10-year absolute risk of fracture. This model will help us to identify the patients at risk of fracture who need to be treated. In the near future, the threshold for treatment will be based on 10-year absolute fracture risk rather than on diagnostic thresholds. Based on this, intervention thresholds may vary world-wide based on differences in pharmacoeconomic parameters.

HRT reduces the risk of fractures at the spine and the hip, even in populations at low risk for fractures, such as the population in the Women's Health Initiative (WHI) study. The reduction of fractures is present only if a sufficient supplementation with calcium is provided. HRT given for a short period (2–3 years) at the time of menopause may have a long-term (after 5–15 years) impact on fracture risk. Due to the individual balance between possible risks and benefits, an appropriate HRT should be given only after a complete individual clinical evaluation. Future research is needed to identify new formulations for HRT, to reduce or eliminate its potential risks. SERMs, such as raloxifene, are a good alternative to HRT in postmenopausal women at risk for osteoporosis. In these women, there would be the clear advantage of estrogen receptor-positive breast cancer prevention, although SERMs are not effective on vasomotor symptoms; this can make it difficult to use them in a population of symptomatic postmenopausal women. Established osteoporosis can benefit more from specific treatments with bisphosphonates (alendronate or risedronate) or, in more severe and selected cases, with agents promoting bone formation (parathyroid hormone (PTH) and strontium ranelate). Potential differences among bisphosphonates must be taken into account for the possible side-effects in long-term prevention and treatment.

Epidemiological studies show a possible association of estrogen and decreased risk of osteoarthritis; indeed, in the estrogen-alone arm

of WHI, there were lower rates of arthroplasty. Recent studies show beneficial effects of estrogen on cartilage turnover.

Bisphosphonates reduce fracture risk at all skeletal sites even when given intermittently. PTH (1-84), given once daily, leads to an increase in osteoblast number, increased bone formation and increased bone mass. A short treatment with PTH results in an increase in bone mass and enhances the effects of subsequent bisphosphonate administration. When teriparatide is added to HRT, it increases bone formation independently from hormone therapy. Strontium ranelate reduces the risk of vertebral fractures in women without prevalent vertebral fractures and reduces vertebral fracture risk in osteopenic women. Hip fracture risk is reduced by strontium ranelate only in elderly patients at very high risk.

## SUMMARY

Quality of life and sexuality are key factors to be considered in the management of the aging individual. The aging process sets new standards for quality of life and sexuality. The symptoms and diseases associated with aging also have a variable impact. Likewise, most therapeutic interventions in the aging individual are likely to impact on quality of life or sexual function. In

women, the climacteric process adds to the effects of aging. The ensuing hormonal decline has a profound impact on the functionality of the whole organism and causes symptoms that significantly affect quality of life and sexuality. These considerations raise the issue of the importance of enquiring about quality of life and sexuality as part of the routine work-up of the aging patient. The presence of immediate or imminent discomfort demands attention, objective documentation and appropriate intervention. The presence of relevant climacteric symptoms that disrupt quality of life or sexuality might be considered as a hallmark of a biological vulnerability of the individual, which might predict the likelihood of developing degenerative diseases. The administration of individualized hormonal therapies in these patients clearly improves quality of life and sexuality and should therefore be recommended whenever necessary, at the dose and for the time that are necessary to improve symptoms and to give back to the patient a satisfying quality of life and sexual function. The value of the different therapeutic interventions that have the potential to impact on the development or progression of chronic diseases, such as cancer, cardiovascular disease or osteoporosis, should be weighed both for efficacy and cost-effectiveness, but also for the potential to alter (or improve) quality of life and sexual function.

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