Review

Health issues for menopausal women: The top 11 conditions have common solutions

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A R T I C L E   I N F O

Article history:
Received 17 September 2014
Received in revised form 25 September 2014
Accepted 26 September 2014
Available online xxx

Keywords:
Noncommunicable diseases  
Menopause  
Risk Factors  
Interventions  
Nutrition  
Lifestyle

A B S T R A C T

Multiple health issues affect women throughout the life course differently from men, or do not affect men at all. Although attention to women’s health is important in all stages in life, health among middle-aged and elderly women has not received sufficient attention by scientists and policy-makers. Related to the menopausal transition and the experiences accumulated until that age, many diseases occur or further develop in middle-aged and elderly women. To improve women’s quality of life and guarantee a long-lasting and active role for middle-aged and elderly women in society, prevention of chronic diseases and disability is a key aspect.

In this manuscript we give an overview of the major health issues for peri- and post-menopausal women, we summarize risk factors and interventions to improve menopausal health. Based on the available scientific literature and the global burden of disease endeavor, we have selected and herein describe the following top 11 key health issues, selected in terms of burden exerted in women’s mortality, morbidity, disability and quality of life: cardiovascular disease, musculoskeletal disorders, cancer, cognitive decline and dementia, chronic obstructive pulmonary disease, diabetes mellitus, metabolic syndrome, depression, vasomotor symptoms, sleep disturbances and migraine.

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http://dx.doi.org/10.1016/j.maturitas.2014.09.013
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Please cite this article in press as: van Dijk GM, et al. Health issues for menopausal women: The top 11 conditions have common solutions. Maturitas (2014), http://dx.doi.org/10.1016/j.maturitas.2014.09.013
1. Introduction

Although specific attention to women’s health is important in all stages of life, health in middle-aged and elderly women (50+ years) is of particular interest in life course health research. Related to menopause and the experiences accumulated until that age, many diseases occur or develop in middle-aged and elderly women. On average, women live 6–8 years longer than men [1]. Considering the increase in the prevalence of various health issues with advancing age, women constitute a greater proportion of older people suffering disability. Based on the Global Burden of Diseases 2010 study, the difference between life expectancy and healthy life expectancy is 11.5 years for females [2]. To improve women’s quality of life and guarantee a long-lasting and active role for elderly women in the society, prevention of chronic diseases and disability is a key aspect.

In the present review, we aim to give an overview of the key health issues, risk factors and care approaches for women during and after menopause.

2. Major health issues for menopausal women

Middle-aged and elderly women may experience a variety of disorders leading to death or hampering their quality of life. According to the Global Burden of Diseases [3], the top causes of death in women in developed countries worldwide are cardiovascular diseases (CVDs; including ischemic heart disease and stroke), cancer, chronic obstructive pulmonary disease (COPD), and diabetes (Table 1). Disease prevalence differs between women aged 50–69 and women aged over 70. Notably, the top 5 causes of death for women aged 50–69 has not changed since 1990.

All these diseases cause disability at different levels. Table 2 displays disabling diseases presented by years of life lived with disability (YLD) and by disability adjusted life years (DALY). Musculoskeletal diseases, cancer, CVD, diabetes, COPD, Alzheimer’s diseases and depression are identified in the top list of disabling diseases in both age groups. The top 5 diseases presented by DALY for both age groups and for YLD for women aged 50–69 has not changed since 1990, only the order of the diseases has changed.

A wide variety of conditions have been studied in peri- and postmenopausal women. A systematic search in PubMed (July 2013) revealed that in line with the Global Burden of Diseases findings, the most frequently studied conditions were CVD (including coronary heart disease – CHD, hypertension and stroke), cancer and depression. Although not part of the top 10 causes of death or disability in the Global Burden of Disease study, vasomotor symptoms but also osteoporosis were often studied in peri- and postmenopausal women. Other frequently studied diseases found in PubMed were body weight change, type 2 diabetes mellitus (DM), metabolic syndrome (MetS), sleep disturbances and urogenital symptoms. Less frequently mentioned in the literature were cognitive decline and dementia and migraine. COPD and respiratory infections were not found to be extensively studied in (post)menopausal women.

Based on the available scientific literature and the Global Burden of Disease study, we selected the following top eleven major health issues in peri- and postmenopausal women to be discussed in this review (Fig. 1): CVD, musculoskeletal diseases, cancer, dementia, chronic respiratory disease, diabetes, MetS, depression, vasomotor symptoms or hot flashes, sleep disturbances and migraine.

Table 1
Top causes of death (presented in descending order) in developed countries globally for women aged 50–69 years and women aged over 70 years, according to the Global Burden of Disease Study in 2010.

<table>
<thead>
<tr>
<th>Causes of death</th>
<th>50–69 years</th>
<th>70+ years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic heart disease</td>
<td>Ischemic heart disease</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>Stroke</td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>Alzheimer’s disease</td>
<td></td>
</tr>
<tr>
<td>Lung cancer</td>
<td>Lower respiratory infections</td>
<td></td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>COPD</td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Other cardiological and circulatory diseases</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>Colorectal cancer</td>
<td></td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>Hypertensive heart disease</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>Lung cancer</td>
<td></td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>Breast cancer</td>
<td></td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>Chronic kidney disease</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1. “Meta woman”: top eleven major health issues in peri- and postmenopausal women.
Most – not all – of these conditions are closely related to menopause or to changes occurring during this period of life.

The Global Burden of Disease study indicates several risk factors for death and disability among women over 50 years including dietary risks, metabolic factors such as high blood pressure and total cholesterol, high and low body mass index (BMI), physical inactivity, smoking, household air pollution and alcohol [3]. Besides some general risk factors, each health issue in menopausal women has its specific risk factors.

3. Cardiovascular disease: number one cause of mortality and morbidity

CVD is the leading cause of mortality and morbidity among women in developed countries and is a major cause of disability. About 54% of all deaths and 39% of all disability among women over 70 are caused by CVD. Corresponding percentages are 31% and 18% for women aged 50–69 [3].

However, there is still a paucity of information about CVD in women. This is probably because the disease rarely occurs in women younger than 50 years, while CVD incidence and mortality begin to increase in men in their forties. Women presumably lose their apparent female advantage regarding CVD after menopause. The prevalence of CVD and risk factors such as hypertension and CHD, increases rapidly at the onset of menopause and continues to increase through the postmenopausal period [3–5]. The increased risk of CVD among menopausal women appears to be associated with loss of ovarian function, accompanied by loss of estrogen and alterations in progesterone secretion [4]; and with the substantial metabolic changes occurring during menopause that emerge with estrogen deficiency [6] (of which the accumulation of excess abdominal fat during menopause plays an important role) and also with deleterious changes in nutrition and lifestyle factors that accumulate during this period of time. Conventional CVD risk factors include smoking, poor diet, decrease in physical activity, alcohol, metabolic factors including high blood pressure, dyslipidemia (high cholesterol and low high-density lipoprotein – HDL – cholesterol), and sleep disturbances [4,7,8]. Hormone replacement therapy (HRT) – although might be beneficial in early postmenopause [9,10] – has been suggested as a potential risk factor for CVD in menopausal women. CVD may also result from genetic factors including single-gene mutations, gene–gene or gene–environment interactions (REF Cardiogram).

Guidelines for CVD management do not recommend HRT but focus on lifestyle and management of overweight and obesity. The recent ACC/AHA guidelines recommend heart healthy lifestyle behaviors; consuming a healthy diet, engaging in physical activity and achieving and maintaining a healthy weight [11,12]. The guidelines also address cardiovascular risk assessment and cholesterol treatment to reduce the risk; however they do not include advises regarding vitamin supplementation for which no convincing evidence has been found [13].

4. Musculoskeletal disorders: the burden increases with age

Musculoskeletal disorders are highly prevalent among older adults [3]. 9.5% of disability among women over 70% and 17% among women aged 50–69 is caused by musculoskeletal disorders. Peri- and postmenopausal women frequently suffer osteoporosis, sarcopenia and osteoarthritis.

Osteoporosis, characterized by a reduction of bone mineral density (BMD) and micro-architectural deterioration of bone tissue, resulting in high risk of fractures, is becoming increasingly prevalent with the aging of the world’s population [14]. BMD decreases with age showing a steeper decline at menopause [15]. Consequently, osteoporotic fracture rate is higher in older women than in older men [14]. Deleterious changes in lifestyle factors, loss of ovarian function and changes in the estrogen level are associated with a significant increase in the prevalence of osteoporosis [4]. Besides hormonal factors, risk factors such as cigarette smoking, low physical activity, low intake of calcium and vitamin D, inadequate sun exposure, and race are associated with osteoporotic fractures. Although HRT had a positive effect on fracture prevention (especially in combination with calcium and vitamin D supplementation) [16], adverse effects might outweigh possible benefits. Clinical management should, therefore, focus on other modifiable risk factors, such as adequate sun exposure and maintenance of adequate dietary calcium and vitamin D intake. Vitamin D and calcium supplementation seem to be beneficial in older postmenopausal women [17,18], though caution is warranted because of possible formation of renal stones [22]. Phyto-estrogens seem to have no effect on bone health [19].

Osteoarthritis is a common joint disorder in the elderly, characterized by the breakdown of the joint’s cartilage. It is a leading cause of disability [3,20] and is more common among post-menopausal women than men of the same age. Changes in sex hormones are assumed to play a role in the OA development [21]. Besides female gender, other identified risk factors are age, obesity, physical inactivity, race, history of injury, joint mal-alignment and diet [20]. Besides avoidance of injuries and stress to the joints, prevention strategies aim at reaching/maintaining ideal body weight by nutritional and lifestyle changes and above all maintenance of optimal levels of physical activity. There is no consensus on the effect of glucosamine supplementation to prevent osteoarthritis and current guidelines do not support glucosamine intake.
5. Cancer in middle-aged and elderly women

Cancer is one of the leading causes of death and disability worldwide [3,22]. Of all deaths, 41% among women aged 50–69% and 16% among women 70+ are attributed to cancer. Cancers of lung, breast, colorectal, ovaries, pancreas and cervix are the most prevalent types among middle-aged and elderly women. General behavioral and lifestyle risk factors for cancer include high BMI, low fruit and vegetable intake, lack of physical activity, smoking and alcohol [22]. Evidence regarding the influence of multivitamin supplementation on cancer has not been convincing [13]. Healthy diet, physical activity and reduction of smoking and alcohol are important preventive interventions.

Lung cancer accounts for 7% of deaths among women aged 50–69% and 2.2% in 70+ women. It accounts for 3.6% disability in women aged 50–69% and 1.9% in 70+ women. Lung cancer is primarily caused by tobacco smoking and therefore eliminating smoking is the important preventive measure.

Breast cancer accounts for 7.8% of deaths in women aged 50–69% and 1.9% in 70+ women. Statistically, one woman in eight will develop invasive breast cancer at some time in her life. The chance of death from breast cancer is one in thirty-six in the United States [23]. Established risk factors include HRT [24], obesity, family history, and age [25]. Diet seems to be associated with breast cancer risk, especially at post-menopause [19,26].

Colorectal cancer accounts for 4.5% of total deaths in women 50–69 years and for 2.6% in 70+ women. Risk factors include genetics, obesity, lifestyle (physical inactivity and smoking) and dietary factors (high intake of fat, red meat and alcohol) [27].

Ovarian cancer accounts for 3% of deaths in women aged 50–69% and 0.7% in women aged over 70. Several studies have shown that HRT increases the risk of ovarian cancer. This association is strongest for estrogen only replacement, especially when used for longer durations [28–30]. Contradictory results were found on the effects of estrogen–progestogen replacement, although evidence suggests that any HRT might increase the risk of ovarian cancer [28–30]. Furthermore, obesity is associated with enhanced ovarian cancer risk through a hormonal mechanism [31].

Cervical cancer is the second most common type of cancer for women worldwide. Half of the women diagnosed with the disease are 35–55 years of age. It accounts for 1.6% of deaths in women aged 50–69% and 0.4% in women 70+. Infection with some types of human papilloma virus is the greatest risk factor for cervical cancer, followed by smoking. To prevent infection with certain species of human papilloma virus (HPV) and decrease cervical cancer at a later age, in developed countries, HPV vaccines are recommended for women who are 9–25 years old and have not been exposed to HPV [32]. Furthermore, regular Pap smear screening for cervical cancer is advised for women and has proven to be successful in preventing cervical cancer [32,33].

6. Cognitive decline and dementia

Dementia refers to major cognitive impairment which affects an individual’s daily activities. Although conflicting, most studies support a higher prevalence and incidence of dementia in postmenopausal women [3,34,35]. Alzheimer’s is one of the leading causes of disability in elderly women; causing 5.7% of disability among 70+ women and 1.0% among women 50–69 years [3]. Sex differences in disease prevalence might be explained by the longer life expectancy and longer survival after initial diagnosis among women as well as declining levels of estrogen at menopause, which potentially affect neurological functions relevant to dementia and cognitive aging. Putative protective effects of HRT, due to its adverse effects [36], are at debate. Whether HRT has a positive effect on dementia risk in younger women, is still largely unclear. Sleep fragmentation and sleep deprivation as well as physical inactivity in older adults have also been associated with the incidence of Alzheimer’s disease and with the rate of cognitive decline [37]. Mediterranean-style diet and increased vegetable intake might have positive effect on cognitive decline and dementia [38,39].

7. Chronic respiratory disease

2.9% of deaths and 1.0% of disability among women aged 50–69 is caused by COPD. Corresponding percentages are 3.7% and 5.7% in women 70+ [3]. COPD is a progressive lung disease defined by persistently poor airflow as a result of breakdown of lung tissue (known as emphysema) and dysfunction of the small airways. COPD is primarily caused by (tobacco) smoke. Genetics, occupational exposure to smoke and pollution from indoor fires may also contribute to COPD. Smoking cessation may decrease the risk of death from COPD by 18% [40]. Diet, especially increased intake of vitamin C and E, appears to be an important modifiable factor in disease development [41].

8. Diabetes

Diabetes is one of the most common chronic diseases worldwide and due to deterioration of lifestyle and the aging population, its prevalence is increasing. Diabetes accounts for 2.4% of deaths and 3.4% of disability in women aged 50–69 and for 2.2% of deaths and 3.1% disability in women 70+ [3]. Postmenopausal women are at higher risk of type 2 DM compared to their premenopausal counterparts. This increased risk is influenced by the development of metabolic risk factors during menopause emerging from hormonal changes [6]. An important metabolic risk factor for DM is the change in body composition and abdominal fat. Estrogen levels before menopause might mask a genetic predisposition for metabolic risk factors associated with DM, such as insulin resistance with small, dense low-density lipoprotein (LDL) and elevated PAI-1 [6]. Diabetic women have a 2.5–times increased risk of CVD and a 2.2-times increased risk of mortality once CVD has developed compared with non-diabetic women at a similar age. Estrogen therapy might influence metabolic factors, such as body composition and consequently decreases the incidence of diabetes [42]. But, like in CVD, caution due to adverse effects of HRT is warranted. Prevention- and treatment guidelines for diabetes include weight loss, physical activity, pharmacological therapy, reduction of alcohol and smoking and dietary changes, rather than HRT.

9. Understanding metabolic health

Metabolic syndrome (MetS) is a combination of closely related factors that, together, increase risk of CVD and type 2 DM. Approximately 20–30% of the middle-aged population suffers from MetS and prevalence is increasing with obesity and sedentary lifestyle. Features of MetS include central obesity, insulin resistance, dyslipidemia with elevated triglycerides, reduced HDL and small, dense LDL particles, high blood pressure, hypercoagulate state and pro-inflammatory state [6]. Not all individuals with MetS show identical combination of factors [43]. Emerging from ovarian failure and, indirectly, from central fat redistribution with estrogen deficiency, risk of adverse changes in metabolic factors and MetS is higher in peri- and postmenopausal women [44]. Two combinations of factors confer significantly higher risks of CVD and mortality. Both have high blood pressure as a central cause. One, additionally, has central obesity and hyperglycemia, the other is characterized by additional dyslipidemia [43]. To reduce risk of CVD and type 2 DM, screening for risk factors is important. Prevention- and treatment
10. Depressive disorders

Depression is a highly debilitating and prevalent condition among middle-age and elderly women. Symptoms of depression are often present in individuals with dementia, often preceding cognitive decline [45]. Depression is more common in women. Depressive disorders, including anxiety, unipolar and bipolar depressive disorder, account for 2.3% of disability in women 70+ and 6.3% in women 50–69 years. Menopause, especially in women with a history of mood disorders [46] raises the risk of depression and anxiety. Symptoms are worst in the perimenopausal period, partly due to hormonal changes during this period [47]. Psychosocial and cognitive changes during menopause might contribute to menopausal mood disorders [48]. Symptoms of depression and anxiety have been associated with hot flashes: perhaps through hormonal changes [49] or sleeping disturbances [48] as the underlying mechanism.

Although estrogen is expected to improve and stabilize mood during menopause, partly by improving vasomotor symptoms, research shows no effect of HRT on depression [50]. Exercise, cognitive behavioral therapy, and non-hormonal medication seem effective treatment solutions for menopausal depression and anxiety [48,51,52].

11. Vasomotor symptoms or hot flashes

During and after the menopausal transition, 55–79% of women experience vasomotor symptoms or hot flashes to some degree. Variable rates are likely to be influenced by factors such as climate, diet, lifestyle, women’s role and attitudes [53]. Hot flashes involve a sudden sensation of mild to intense heat that may be accompanied by anxiety, palpitations, sweating, and facial flushing [54,55]. Origins of hot flashes can be found in the changing levels of circulatory estrogen. Risk factors are race and ethnicity, smoking, socio-economic status, BMI, physical activity and genetics [48]. Vasomotor symptoms are associated with a less favorable cardiovascular risk profile [56]. HRT appears to be the most effective treatment for menopause-related hot flashes. Alternative treatments include exercise, acupuncture, complementary medicine and non-hormonal pharmaceutical treatment. There is some evidence for non-hormonal pharmaceutical agents such as selective serotonin reuptake inhibitors (SSRI’s), serotonin–norepinephrine reuptake inhibitors (SNRI’s) and gabapentin (Neurontin) [57]. Evidence for other treatments, however, is either weak or contradictory [48].

12. Menopause raises the risk of sleep disturbances

With increasing age, quantity and quality of sleep deteriorates and sleep disturbances become more common in menopausal women. Studies report a prevalence of sleep disturbances at about 50% [58]. Postmenopausal women tend to report higher incidences of sleep difficulties compared to pre- or perimenopausal women [59]. Prevalence of sleep-disordered breathing or sleep apnea increases during and after menopause [48]. Sleep disturbances have detrimental effects on quality of life (daytime sleepiness, decreased concentration, mood disorders [60]), physiological functioning, including metabolic flexibility and insulin resistance, and lead to increased risk of CVD and CHD [7,61]. In a cross-sectional study, sleep fragmentation and sleep deprivation in older adults was associated with the incidence of Alzheimer’s disease and with the rate of cognitive decline [37]. Diagnosis and treatment of sleeping problems, however, is difficult. Hormonal influences, psychological factors, inactivity and comorbidity can contribute to sleeping difficulties in menopausal women [59,62]. Likewise, treatment strategies vary from hormonal treatment and medications to lifestyle and behavioral modification [59,63].

13. Migraine affects women throughout life

Migraine is a complex disorder characterized by recurrent episodes of headaches. 75% of migraine sufferers are women (17.1% prevalence among US women) [64]. In childhood, boys suffer from migraine at the same rate as girls, but after puberty through adolescence and into mid-adulthood migraine is more frequent in women. Through menopause, prevalence decreases among women [65]. Migraine accounts for 1.4% of disability in women aged 50–69 and for 0.3% of deaths in 70+ women [3]. Migraine is considered a vascular and neurogenic process, and it has a genetic component. Approximately 70% of patients have a first-degree relative with a history of migraine. A variety of environmental and behavioral factors may precipitate migraine attacks in predisposed persons. Although several factors including stress, sleep, smoking, exercise, fasting, and diet are thought to trigger migraine, no strong evidence was found for causal relationships in longitudinal studies [66,67].

Migraine treatment involves acute and preventive therapy, either pharmacological or non-pharmacological (patient education, biofeedback, cognitive-behavioral and relaxation therapy). Evidence for treatment options regarding diet and activity is weak [68,69]. Migraine sufferers have a higher risk of CVD, including ischemic stroke [70]. Migraine is associated with depression [71], however its association with subsequent cognitive decline and dementia remains unknown. Migraines have been attributed to the absence of variations in estrogen levels. Tailored HRT to minimize hormonal imbalance, might be effective to reduce migraine in the perimenopausal period [72], however it has been associated with higher rates of migraine at postmenopause [73]. Caution with regard to HRT is needed [74,75]. Beyond this, usual lifestyle factors and other nutritional recommendations (e.g. coffee, chocolate and alcohol consumption) remain key in management and prevention of migraine.

14. Multimorbidity and frailty

Nearly 60% of elderly women suffer from multiple disorders: hypertension, osteoarthritis, diabetes and osteoporosis being among the most prevalent. Health issues in women are thus likely to coexist, elevating risk of death, disability, poor quality of life, and adverse drug events [76,77]. Multimorbidity and age, furthermore, predict frailty, a common geriatric syndrome that embodies an elevated risk of decline in health and function among older adults [78]. Frailty prevalence is particularly high in individuals over 75 years.

15. Common solutions: lifestyle and nutrition

In menopause many, if not all, health issues are connected to changing estrogen levels. Consequently, stabilizing hormonal levels seems an obvious strategy to prevent and treat menopausal health issues. But not only do changing estrogen levels lead to metabolic changes in menopausal women causing a variety of health conditions in middle-aged and elderly women, so do lifestyle and nutritional experiences accumulated until that age. Indeed, HRT to stabilize hormonal levels, might significantly reduce menopause related symptoms. However, because of significant adverse effects regarding increased risk of venous thromboembolism, stroke and (breast) cancer, its use is still
open for debate. Rather than prescribing HRT, most guidelines for health problems affecting menopausal women describe optimizing/improving nutrition and lifestyle as – the first-option for prevention and treatment. In particular, poor diet, physical inactivity, alcohol and smoking are related to negative outcomes on most of the described conditions. Furthermore, specific food groups and nutrients such as soy, calcium and vitamin D are linked to positive health outcomes. It is recognized that postmenopausal women are often less physically active than during their premenopausal years, suggesting a possible benefit for interventions that address physical activity and exercise in the perimenopausal period [79]. Apart from nutritional and lifestyle changes, some health problems may also benefit from specific interventions, ranging from non-hormonal drug treatment in migraine and hot flashes to screening and vaccination for cervical cancer and psychological therapy in mood disorders and sleep disturbances. As hormonal and lifestyle risk factors lead to multimorbidity, hormonal and lifestyle interventions would lead to multiple improvements at multiple levels contributing synergistically to women’s health and quality of life. This is even more the case for lifestyle interventions compared to pharmacological or other medical interventions.

In this review, we focused on health issues in developed countries. In developing countries, middle-aged and elderly women suffer more frequently from communicable disease including HIV and pulmonary infections. Although lifestyle changes are indeed important in preventing these diseases, care approaches differ. However, obesity and diseases arising from metabolic risk factors are also an overwhelming challenge in developing countries [80]. The prevalence of obesity is rising and so are its related diseases such as diabetes and CVD, asking for a global approach focusing on nutrition and lifestyle.

Even with recent insights of women’s health issues, putative risk factors and promising care approaches, improving women’s health remains a challenge. Future research should manage contradictory findings in prior studies and should extensively focus on the role of nutrition and lifestyle in postmenopausal health issues. Of particular interest is the role of multimorbidity on health outcomes in postmenopausal women and on frailty. Interconnection of diseases, particularly in mood disorders, hot flashes and sleep disturbances, and in migraine, dementia, depressions and cardiovascular diseases are potentially an interesting topic of future research. Furthermore, attention should be given to genetic predisposition, not only for CVD and diabetes, but for other health issues. Understanding genetic predisposition to specific health conditions and knowledge of nutrition and lifestyle modifications that influence the potential for diseases is necessary to improve health. All research findings, then, should be actively translated into care approaches for middle-aged and elderly women worldwide, taking multimorbidity and global differences and similarities into account.

Contributors

All authors contributed actively at all stages of preparation of the manuscript.

Competing interests

None.

Funding

Maryam Kavousi is supported by the AXA Research Fund. G.M. van Dijk, J. Troup and O.H. Franco work in ErasmusAG, a center for aging research across the life course funded by Nestlé Nutrition (Nestec Ltd.); Metagenics Inc.; and AXA. Nestlé Nutrition (Nestec Ltd.); Metagenics Inc.; and AXA had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review or approval of the manuscript.

Provenance and peer review

Not commissioned; externally peer reviewed.

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