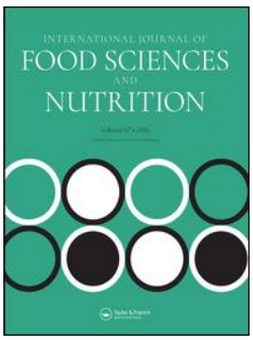

International Journal of Food Sciences and Nutrition

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/iijf20

A practical nutritional guide for the management of sleep disturbances in menopause

Daniela Laudisio , Luigi Barrea , Gabriella Pugliese , Sara Aprano , Bianca Castellucci , Silvia Savastano , Annamaria Colao & Giovanna Muscogiuri

To cite this article: Daniela Laudisio , Luigi Barrea , Gabriella Pugliese , Sara Aprano , Bianca Castellucci , Silvia Savastano , Annamaria Colao & Giovanna Muscogiuri (2020): A practical nutritional guide for the management of sleep disturbances in menopause, International Journal of Food Sciences and Nutrition, DOI: 10.1080/09637486.2020.1851658

To link to this article: https://doi.org/10.1080/09637486.2020.1851658

Published online: 30 Nov 2020.

INTERNATIONAL JOURNAL OF FOOD SCIENCES AND NUTRITION
https://doi.org/10.1080/09637486.2020.1851658

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

A practical nutritional guide for the management of sleep disturbances in menopause

Daniela Laudisio[a,b]*, Luigi Barrea[a,b]*, Gabriella Pugliese[a,b], Sara Aprano[a,b], Bianca Castellucci[a,b], Silvia Savastano[a,b], Annamaria Colao[a,b,c] and Giovanna Muscogiuri[a,b]

[a]Dipartimento di Medicina Clinica e Chirurgia, Unit of Endocrinology, Federico II University Medical School of Naples, Naples, Italy; [b]Centro Italiano per la cura e il Benessere del paziente con Obesità (C.I.B.O), Department of Clinical Medicine and Surgery, Endocrinology Unit, University Medical School of Naples, Naples, Italy; [c]Cattedra Unesco "Educazione alla salute e allo sviluppo sostenibile", University Federico II, Naples, Italy

ABSTRACT

Sleep disturbances (SD) represent one of the main symptoms of menopause and they are caused by several factors. Hormonal changes such as the reduction of oestrogen levels and the consequent vasomotor symptoms (VMS) along with psychiatric disorders such as depression and anxiety could contribute to the onset of SD. Furthermore, obesity *per sè* or through the obstructive sleep apnoea (OSA) could blunt sleep. Moreover, in menopause is usual a reduction in melatonin, that could contribute to SD. Nutritional strategies are paramount because they could contribute to manage menopause-related SD, in particular tackling obesity and overweight. Furthermore, some foods, such as soy, fish, whole grains, vegetables and fruit could decrease symptoms like depression and VMS, correlated with SD in postmenopausal women. Therefore, the aim of this review is to provide an overview of the current evidence on SD in menopause and to provide nutritional strategies for managing SD in this context.

ARTICLE HISTORY
Received 10 June 2020
Revised 3 November 2020
Accepted 12 November 2020

KEYWORDS
Sleep disturbances; menopause; diet; nutritionist; obesity; vasomotor symptoms

Introduction

Currently, sleep disturbances (SD) represent a common concern among the general population; in fact, about 35% of individuals have problems falling asleep, staying asleep, awakening early, or not feeling refreshed after sleep. SD have a significant impact on quality of life and are associated with numerous adverse health outcomes. In fact, SD and the consequent sleep loss may have detrimental effects on the cardiovascular, endocrine and nervous systems, determining an increased risk of cardiovascular diseases, hypertension, obesity, type 2 diabetes and impaired glucose tolerance, anxiety and depression (Barrea, Pugliese, Framondi et al. 2020; Leger and Bayon 2010; Kohli et al. 2011; Vogtmann et al. 2013; Thurston et al. 2017). Among SD, insomnia, characterised by difficulty falling asleep or staying asleep, accompanied by daytime impairment of mental and/or physical function and irritability (Bianchi 2017) is estimated to be more frequent in women (Ohayon 2002; Krystal 2003). Furthermore, the prevalence of SD among women is variable and increases with age (Kravitz and Joffe 2011). It ranges from 16% to 42% in premenopausal women, from 39% to 47% in perimenopausal women, and, it affects 35% to 60% in postmenopausal women (Kravitz and Joffe 2011). Menopause is a physiological event in the woman's life characterised by the cessation of spontaneous menstrual cycles caused by a reduction in the sex hormones oestrogen and progesterone and a consequent increase of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which occurs when the ovarian reserve ends (Nelson 2008). In addition to insomnia, the most commonly SD founded in menopausal women, include nocturnal breathing disturbances, of which obstructive sleep apnoea (OSA) is the most common, restless leg syndrome, periodic limb movement syndrome, depression and anxiety (Guidozzi 2013). The aetiology for SD in menopausal women is still unknown, but, however, it seems that are caused by the contribution of several risk factors that commonly occur in menopause such as decreased oestrogen levels and the consequent vasomotor symptoms (VMS), depression, weight gain (mostly the increase of

CONTACT Giovanna Muscogiuri giovanna.muscogiuri@gmail.com Dipartimento di Medicina Clinica e Chirurgia, Unit of Endocrinology, Federico II University Medical School of Naples, Via Sergio Pansini 5, Naples 80131, Italy
*These authors have equally contributed to this manuscript.

visceral adiposity) (Guidozzi 2013). Several studies showed an improvement of VMS after phytoestrogens intake (Hachul et al. 2011; Franco et al. 2016). This could be due to their chemical structure that is similar to that of oestradiol, therefore, mimicking oestrogen-like properties and relieving menopausal symptoms (Britt et al. 2005; Cano et al. 2010; Lambert et al. 2017); also, evidence indicates that high fibre and low glycemic index foods intakes may be associated with a reduced risk of depression (Gangwisch et al. 2015; Daneshzad et al. 2020). In fact, postprandial hyperglycaemia and resultant compensatory hyperinsulinemia from high dietary glycemic load can result in reactive hypoglycaemia (Seaquist et al. 2013), triggering the secretion of autonomic counterregulatory hormones such as adrenaline, cortisol, glucagon, and growth hormone, and these hormones responses can cause symptoms such as depression and anxiety (Ludwig 2002). Moreover, high fibre and low glycemic index foods intakes, could contribute to weight loss and to reduction of waist circumference (WC; Appling et al. 2007; Dormire and Howharn 2007). In particular, visceral adipose tissue is an important source of pro-inflammatory cytokines could be associated with the sleep regulation (Perrini et al. 2017; Muscogiuri et al. 2019). Furthermore, a high intake of omega-3 has been reported to decrease depression and anxiety that in turn could contribute to worsen VMS. In fact, omega-3 play a role in mental health as it reduces neuronal damage by oxidative stress, hindering inflammatory processes and diminishing cytokine circulation and cellular infiltration and also may improve tryptophan transport, a serotonin precursor (Laye et al. 2018; Liao et al. 2019; Tsujiguchi et al. 2019; Godos, Currenti et al. 2020). Thus, the aim of this review is to provide an overview of the current evidence on SD in menopause and to provide nutritional strategies for managing SD in this context.

Menopause and sleep disturbances

Ovarian hormonal changes: oestrogen decrease

The female post-reproductive lifespan is characterised by very low oestrogen levels, exclusively arising from peripheral conversion of testosterone into oestrogens, as there is no longer any ovarian production. The effect of oestrogen levels on SD is complex, because oestrogens clearly have a wide range of potentially effects which impact on sleep, through several mechanisms (Baker et al. 2018). Oestrogens play a role in the metabolism of norepinephrine, serotonin, and acetylcholine-neurotransmitters that in turn affect sleep control (Guidozzi 2013). In fact, oestrogens have been reported to reduce sleep latency and increase total sleep time, to reduce the frequency of awakening after sleep and cyclic spontaneous arousals (Guidozzi 2013). Oestrogens have also an impact on mood thank to their effect on norepinephrine activity in the brain and serotonin response and uptake, thus allowing to hypothesise that oestrogens could have an antidepressant effect (Eichling and Sahni 2005). Indeed, the low oestrogen levels that are usually detected in menopause could account for depression in postmenopausal women (Parry et al. 2006). The most common symptoms related to low oestrogen levels are represented by VMS, commonly called hot flashes (HF). VMS are defined as a sudden sense of body heat or redness around the face and neck, often accompanying by sweating and tachycardia usually lasting less than 30 minutes. These symptoms are the most common in midlife women and are reported by 75% to 85% of postmenopausal women (Gold, Colvin et al. 2006; Al-Safi and Santoro 2014). Several studies reported an association of VMS with SD in postmenopausal women (Ensrud et al. 2009; Lampio et al. 2014). Ensrud et al. conducted a randomised trial in 217 healthy postmenopausal women aged 40–60 years with VMS (Ensrud et al. 2009). The women with a higher frequency of moderate to severe HF were more likely to have insomnia, probably, due to a major of disrupted sleep and a greater night-time wakefulness by numerous arousals. (Ensrud et al. 2009). More recently, in a cross-sectional study, Lampio et al. recruited 158 healthy women (107 premenopausal and 51 postmenopausal) aiming to investigate sleep quality and its association with night sweats and HF (Lampio et al. 2014). Postmenopausal women had poorer general sleep quality, slept more restlessly, and had more nocturnal awakenings compared to premenopausal women. SD were mostly associated to the night sweats and HF (Lampio et al. 2014).

In summary, the ovarian hormonal changes occurring in menopause mostly characterised by the decrease in oestrogen levels could account for the onset of SD in this stage of life. The effects of oestrogen reduction are summarised in Figure 1.

Overweight and obesity

Overweight and obesity are a common finding in postmenopausal women (Dasgupta et al. 2012), mostly due to the changes in reproductive hormone levels; in fact, there is evidence that oestrogen reduction affects fat distribution, leading to an increased proportion of

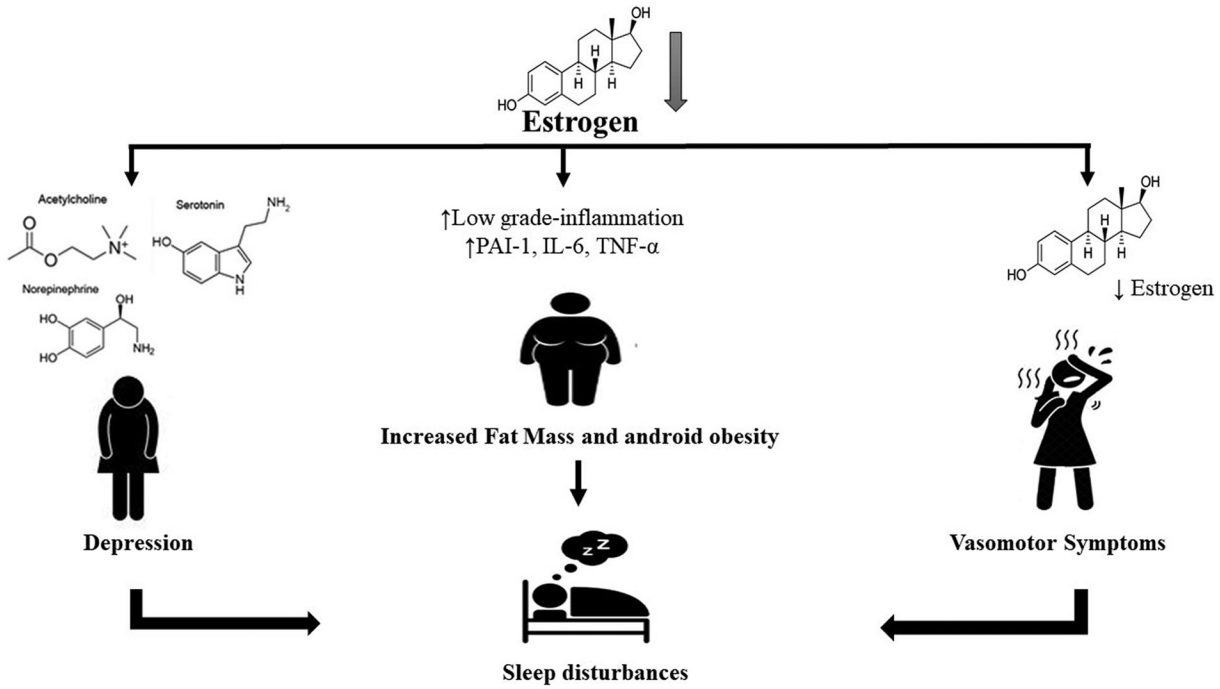

Figure 1. Reduction of oestrogen in menopausal women causes depression, VMS and visceral obesity. Oestrogen play a role in the metabolism of norepinephrine, serotonin, and acetylcholine-neurotransmitters and have an impact on mood, decrease in oestrogen determines depression. Oestrogen reduction affects fat distribution, leading to an increased proportion of abdominal fat in postmenopausal women, visceral adipose tissue is an important font of inflammatory adipocytokines. The most common symptoms related to low oestrogen levels are represented by VMS.

abdominal fat in postmenopausal women (Toth et al. 2000a, 2000b; Abdulnour et al. 2012; Davis et al. 2012; Barrea et al. 2019). The oestrogens, in fact, increase lipolysis and influence adipose tissue lipoprotein lipase activity (Mastorakos et al. 2010); in particular, the oestradiol can indirectly affect lipolysis by inducing the lipolytic enzyme hormone-sensitive lipase or directly by increasing the lipolytic effects of epinephrine (Palin et al. 2003), thus menopause is associated with an increase in fat mass. Moreover, the drop in oestrogen levels may also have a direct effect on muscle tissue; indeed, oestrogen receptors (ER) are present in human muscles under the form of ERα and ERβ in the nuclei of muscle fibres (Lemoine et al. 2003; Wiik et al. 2009) and the oestrogens have been reported to have an anabolic effect on muscle mass. In fact, the oestrogens reduce the inflammation in muscle and limit the muscle damage. In addiction, 17β-oestradiol regulate antioxidant proteins such as superoxide dismutases and glutathione peroxidase through ER (Strehlow et al. 2003; Vina et al. 2008). Therefore, the improving of reduction–oxidation state in fibres and thus keeping muscle proteins like myosin free from posttranslational oxidative modifications could contribute to the maintenance of protein structure–function and ultimately strength (Lowe et al. 2010). Besides, the oestrogens have an effect on muscle tissue, also due to a cross-stimulation by the stimulation of IGF-1 receptors, in particular, ER can be also activated through IGF-1 that acts in stimulating their transcriptional activity (Klotz et al. 2002). Indeed, ERs could take part in muscle strength increase through the effect of both oestrogen and IGF-1. However, both oestrogen and IGF-1 drop at menopause, which is likely to affect muscle mass and strength (Maltais et al. 2009; Agostini et al. 2018). In fact, with the menopause approaches, a rapid loss of both muscle mass and strength occurs with a reduction of 0.6%–1% of muscle mass per year postmenopause and a 21% reduction in muscle strength between ages 25 and 55, occurring at a rate of 1.5% *per* year (Maltais et al. 2009). This loss in muscle mass results in loss of muscle strength and power which (Lang et al. 2010) determines the increases the prevalence of sarcopenia in menopausal women (Messier et al. 2011). Moreover, the aging of skeletal muscle and increase of the adipocyte number determine an infiltration of the muscle fibres by lipids. This condition of sarcopenia could determine adverse clinical outcomes such as mobility limitations and increase of fractures in menopausal women.

It is known that visceral adipose tissue is an important source of inflammatory adipocytokines such as plasminogen activator inhibitor-1 (PAI)-1,

interleukin 6 (IL-6); tumour necrosis factor α (TNF-α), and leptin and lower levels of adiponectin (He et al. 2003; Winkler et al. 2003; Tilg and Moschen 2006; Harman-Boehm et al. 2007; Maury et al. 2007; Pugliese et al. 2020). These pro-inflammatory cytokines could be associated with the sleep regulation and classified as "*sleep-regulatory substances*" (Perrini et al. 2017; Muscogiuri et al. 2019). In agreement with this, WC, an indirect measure of visceral adipose tissue, has been reported to be associated to SD (Davidson and Patel 2008), and these results were confirmed also in postmenopausal women. Indeed, Morfeno-Vicino et al. performed a study in 463 community-dwelling older Spanish women, reporting a significant positive correlation between SD and WC (Moreno-Vecino et al. 2017). Among SD in menopause, OSA was a common finding (Moreno-Vecino et al. 2017). In a cross-sectional study, Polesel et al. investigated the occurrence of OSA across the stages of reproductive lifespan such as premenopause, early postmenopause (in menopause for up to 5 years) and late postmenopause (in menopause for >5 years) (Polesel et al. 2015). They enrolled 407 women: 268 premenopausal women, 139 postmenopausal (43 early postmenopause; 96 late postmenopause). They found that 68.4% of women affected by severe OSA belonged to the late postmenopause group and that a 1 cm increase in WC increased the likelihood of developing moderate to severe OSA by 5% in postmenopausal women (Polesel et al. 2015). Similar results were found in a study carried out by Naufel et al. investigating the association between obesity and SD in postmenopausal women (Naufel et al. 2018). Fifty-three postmenopausal women were enrolled and underwent to anthropometric measurements and full-night polysomnography. As expected, respiratory disturbance index and apnoea–hypopnea index values were worsen in women with obesity (Naufel et al. 2018). In summary, the body composition changes occurring in menopause, in particular, characterised by increase of proportion of abdominal fat could account for the onset of SD in postmenopausal acting directly through the secretion of cytokines or indirectly through OSA.

Melatonin reduction

Melatonin is a hormone synthesised and secreted principally by the pineal gland at night under normal light/dark conditions which play a very important role in circadian rhythm, especially in sleep onset and in sleep maintenance through block arousal mechanism (Conti et al. 2000). Melatonin levels decrease with aging after the age of 50 (Bellipanni et al. 2001). *Melatonin age-related* decline is correlated with a decreased melatonin biosynthesis and release by the pineal gland, which is considered due to decreased retinal light perception and the changing nature of the vitreous body, which transmits less light (Rohr and Herold 2002). Thus, the reduction of melatonin levels usually occurs contemporarily to menopause age (Fernandez et al. 1990). In a group of 79 healthy women, Fernandez et al. have evaluated the morning levels of serum melatonin, FSH, LH, prolactin, progesterone and oestradiol. The women were subdivided in three groups by different reproductive stages (fertile stage, perimenopausal and menopausal period). Serum melatonin levels decreased with age, attaining minimum levels in menopause. Indeed, in a prospective study, Toffo et al. showed that the duration of secretion and concentration of melatonin tended to be lower in postmenopausal women (aged 58–71 years) than in perimenopausal (Toffo et al. 2014).

In conclusion, the decline of melatonin secretion which physiologically occurs with age could be a further player that could contribute to SD in menopause.

Nutritional advices for the management of sleep disturbances in menopause

Phytoestrogens

Phytoestrogens are a biologically active plant-derived compounds with oestrogen-like properties (Cano et al. 2010), and isoflavones (genisten and diadzein) and lignans are the principal source of dietary phytoestrogens. Isoflavones can be abundantly found in soybeans, instead, lignans are found in legumes, vegetables, fruits, flaxseed and whole grains (Rizzo and Baroni 2018). It has been demonstrated that the soy have oestrogenic effects in humans because of the presence of polyphenolic isoflavones, which have oestrogen receptor agonist and antagonist activity (Taylor 2015). The isoflavones have a chemical structure similar to that of oestradiol and therefore also they have oestrogen-like properties. In particular, there are two types of ER: ERα and ERβ. ERα is predominant in the breast and uterus, instead ERβ is predominant in the cardiovascular system, urogenital tract and bone. The affinity of isofolavones to ERβ is more higher than the ERα. Isoflavones act as oestrogens by binding at ER and thus exerciting oestrogen-like effects and relieving menopausal symptoms (Russell et al. 2002; Britt et al. 2005; Lambert et al. 2017). As previously mentioned, oestrogen is drastically reduced with menopause, and the most common symptoms related

to low oestrogen levels are represented by VMS. Thus, the intake of isoflavone could represent in this sense a tool to relieve VMS (Gold, Colvin et al. 2006; Al-Safi and Santoro 2014). Epidemiological studies suggested that in populations that consume dietary soya there is a low incidence of VMS. Soy intake is four to nine times greater in Asian countries than in Western countries and postmenopausal women in Asian countries report a much lower incidence of HF (10–25%) compared to women in Western countries (60–90%) (Reed et al. 2013). A recent meta-analysis of 21 randomised controlled trial (RCTs) evaluated the association overall use of phytoestrogens therapies with menopausal symptoms, including VMS (Franco et al. 2016). The authors showed a significant improvement in daily VMS with isoflavones use, from either dietary sources or use of supplements and extracts (Franco et al. 2016). In particular, the different types of interventions included soy isoflavones (dietetic, supplements and extracts, and red clover isoflavones) showed an association of overall phytoestrogen use with a decrease in the number of daily VMS (Franco et al. 2016). In a clinical trial Hachul et al. demonstrated the beneficial effects of isoflavone treatment on SD in postmenopausal women. The study included two groups of postmenopausal women with insomnia: the first received 80 mg isoflavones (dry extract of the soybean) daily for four months, and the second received a placebo for the same period (Hachul et al. 2011). In postmenopausal women with insomnia, isoflavone treatment was effective in reducing insomnia symptoms, with a significant increase in sleep efficiency in this group (from 77.9% to 83.9%) when compared with the placebo group (from 77.6% to 81.2%); furthermore, isoflavones induced a decrease in the intensity and number of VMS and the frequency of insomnia (from 89.5% to 36.9%) (Hachul et al., 2011). Moreover, it has been suggested that phytoestrogens, in particular isoflavones, with their similar structural to 17-β-oestradiol by binding to ER, has been associated with a decreased risk of hormone-related cancers such as breast cancer (BC) (Verheus et al. 2007; Goodman et al. 2009; Zhu et al. 2011). There are several mechanisms by which isoflavones seem to exert their anticarcinogenic effects, one of is via their antioxidant capacity, in particular, they have the ability to decrease lipid peroxidation as well as oxidative DNA damage (Omoni and Aluko 2005; Griffiths et al. 2014). Moreover, soy phytoestrogens seem to inhibiting cell proliferation and angiogenesis, and also to inducing cell apoptosis (Adlercreutz 1995; Magee and Rowland 2004). However, the phytoestrogens can also exert oestrogenic effects, and in particular, has been showed that physiological concentrations of dietary genistein induce growth of ER (+) BC cells in both *in vitro* and *in vivo* models (Ju et al. 2001; Allred et al. 2004). However, the findings from several reports indicate that soy isoflavones can improve prognosis in BC patients (Chi et al. 2013). Zhang et al. showed that genistein intake imitating Asian consumption patterns improved the response of BC to tamoxifen therapy (Zhang et al. 2017). Similarly, Guha et al. observed reduced BC recurrence with increasing amounts of daidzein consumption in a prospective cohort study of postmenopausal women in treatment with tamoxifen (Guha et al. 2009). In human studies, the implementation of dietary isoflavones for BC patients and BC risk is yet controversial, by their dual nature (i.e. oestrogenic and antiestrogenic actions), but, the higher phytoestrogen consumption seem to predispose to a reduced risk of developing BC, and a better prognosis in women diagnosed with BC (Chen et al. 2014; Wu et al. 2015; Messina 2016). Besides, the European Food Safety Authority recently concluded that in postmenopausal women, isoflavones do not adversely affect breast tissue, thyroid function, or the uterus (EFSA 2015). Therefore, considering this, the medical community could recommend soy foods to postmenopausal patients.

Low glycemic index foods, fibre, fruits, vegetables and whole grains

One of the mechanisms hypothesised thought which low oestrogen levels in menopause could induce VMS is the blunted blood glucose transport across the blood–brain barrier (Cheng et al. 2001). When oestrogen levels decrease in menopause, the responsiveness of glucose transporter 1 (GLUT 1) production to the demands of increased glucose transport needs, such as during an increased neuronal activity or lowered blood glucose levels, is reduced (Dormire 2009). The HF represents a counter-regulatory neurovascular response resulting in vasodilation with consequent increased blood flow to aid delivery of glucose and oxygen delivery to meet the metabolic needs associated with neuronal activation (Dormire and Howharn 2007). Therefore, the optimal blood glucose concentrations may contribute to a lower risk of VMS (Dormire and Howharn 2007). Low glycemic index foods cause lower postprandial glucose concentrations; therefore, blood glucose concentrations are more likely to be kept within limits. Few studies have been carried out on the relationship of dietary fibre with

VMS (Gold, Flatt et al. 2006; Kroenke et al. 2012). Kroenke et al. showed that an increased intake of fruit, vegetables, and whole grains has a protective effect on VMS (Kroenke et al. 2012). The study included 17,473 postmenopausal women, ages 50–79 who participated in the Women's Health Initiative Dietary Modification (Kroenke et al. 2012). The women were randomly assigned to a dietary intervention (40%) or control arm (60%). The dietary intervention provided an increased intake of fruits and vegetables (5 servings *per* day) and whole grains (6 servings *per* day) and an intensive behavioural modification program. Moreover, specialised nutritionists, gaved regular meetings to assist the women in achieving the dietary intervention goals. The controls received a copy of the Dietary Guidelines or Americans and other health-related materials with appropriate advices about nutrition and behaviour. In multivariate-adjusted analyzes, assignment to dietary intervention *vs* control arm was significantly related to a higher likelihood of disappearance of symptoms in women with VMS (Kroenke et al. 2012). In a one cross-sectional study of women with prior early stage BC fibres have been reported to have a protective effect on VMS (Gold, Flatt et al. 2006). In the Women's Healthy Eating and Living randomised, controlled trial of a high vegetable, high fibre, reduced fat diet, 2,198 women with early-stage BC were enrolled (Gold, Flatt et al. 2006). The reduction in the severity of symptoms at 12 months was significantly associated with a high intake of dietary fibre (Gold, Flatt et al. 2006). Although the studies carried out on this topic were few, however, they provided promising results on nutritional approach for the management of VMS.

Polyunsaturated fatty acids

Epidemiologic studies have linked the intake of dietary polyunsaturated fatty acids (PUFA) in the pathophysiology of mood disorders (Group et al. 2008; McNamara 2015; Barrea, Muscogiuri et al. 2020; Godos, Currenti et al. 2020). In particular, dietary intake of food rich in omega-3 (e.g. fish, seafood, and nuts) is associated with reduced prevalence of major depression (Grosso et al. 2014; Laye et al. 2018). Omega-3 play a role in mental health as it reduces neuronal damage by oxidative stress, hindering inflammatory processes and diminishing cytokine circulation and cellular infiltration (Simonetto et al. 2019). Furthermore, omega-3 could improve tryptophan transport, a serotonin precursor, and could also contribute to the maintenance of type 2 serotonergic receptors, mainly responsible for mood regulation (Laye et al. 2018; Godos, Currenti et al. 2020). Recently, Liao et al. conducted a meta-analysis of double-blind randomised placebo-controlled trials to estimate the efficacy of omega-3, especially docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) in the management of depression (Liao et al. 2019). The authors showed an overall beneficial effect of omega-3 on depression symptoms and in particular compared with placebo, EPA has demonstrated clinical benefits when administered at dosage $\leq$1 g/d, whereas DHA formulations did not provide such benefits (Liao et al. 2019). In a cross-sectional study Abshirini et al. evaluated a dietary intake by a validated 147-item food frequency questionnaire (FFQ) to assess the habitual diet of participants during the previous year, and menopausal symptoms by the menopause rating scale (MRS) questionnaire in 393 Iranian postmenopausal women. The authors reported that, the quartile with the highest omega-3 intake had a lower odds ratio (OR) for both somatic and psychological symptoms, such as impaired memory, lack of concentration, nervousness, depression, insomnia (Abshirini et al. 2019). The relationship between omega-3 deficiencies and depressive states, in postmenopausal women, has been demonstrated in a recent population study (Tsujiguchi et al. 2019). Tsujiguchi et al. analysed cross-sectional data from the Shika study and investigated the associations between the intake of omega-3 and depression among people according to sex and weight status (Tsujiguchi et al. 2019). The depressive state has been evaluated by the Japanese short version of the Geriatric Depression Scale and the intake of omega-3 evaluated by the validated food FFQ. The results demonstrated a relationship between omega-3 deficiencies and depressive states in woman, particularly accentuated in women with overweight or obesity (Tsujiguchi et al. 2019).

High glycemic index foods: carbohydrate, sugars, refined cereals

The type and amount of carbohydrates in the diet may also influence the onset and/or the worsening of depression which is a known disease occurring in menopause. Diets with high glycaemic load carbohydrates could contribute to depression through repeated acute spikes and troughs of blood glucose. In insulin resistance states, postprandial hyperglycaemia and resultant compensatory hyperinsulinemia from high dietary glycaemic load can result in reactive hypoglycaemia (Seaquist et al. 2013), triggering the secretion of autonomic counterregulatory hormones

such as adrenaline, cortisol, glucagon and growth hormone (Ludwig 2002). Counterregulatory hormone responses can cause symptoms such as anxiety, irritability and hunger (Ludwig 2002). The results of the Women's Health Initiative Observational Study carried out on, approximately, 70,000 postmenopausal women, showed that the intake of high dietary glycaemic index (added sugars, total sugars, glucose, sucrose, fructose, starch, carbohydrate) and foods such as nonwhole/refined grain consumption were associated with increasing OR of incident depression. Conversely, higher consumption fibre, nonjuice fruit and vegetables was significantly associated with lower OR of incident depression (Gangwisch et al. 2015). Daneshzad et al. in a cross-sectional study, investigated the association among low carbohydrate diet, sleep status, depression, anxiety and stress score among 265 diabetic women in postmenopausal women (Daneshzad et al. 2020). A validated and reliable 168-item semi-quantitative FFQ was used to obtain dietary intakes of women through the past year. This study showed that lower consumption of carbohydrates was associated with an improvement of sleep and decrease the risk of psychological disorders including depressive symptoms, and anxiety level among postmenopausal women (Daneshzad et al. 2020). The high amounts of refined carbohydrates and sugar could be associated with increased risk of depression through increased levels of inflammatory cytokines such as IL-6 and c-reactive protein (CRP) levels (Lucas et al. 2014). Moreover, inflammatory cytokines may have an adverse effect on neurotransmitters, and inflammatory status and endothelial dysfunction could impair the expression of brain-derived neurotrophic factor (BDNF) (Sanchez-Villegas & Martinez-Gonzalez 2013). Liu et al. in a cross-sectional study, conducted among 906 postmenopausal women, explored the association of diet with depression (Liu et al. 2016). The authors reported that the whole plant food intake (rich in whole grains, fruits, and vegetables) was negatively associated with depression score and processed food intake (rich in refined cereals, sweets, preserved food) was positively associated with perceived stress and depression (Liu et al. 2016). Furthermore, diets characterised by high glycaemic load could contribute to the onset of obesity and thus to the increase in visceral adiposity. In fact, a high glycaemic response, promoting postprandial carbohydrate oxidation at the expense of fat oxidation, thus blunting fuel partitioning giving rise to body fat gain (Gangwisch et al. 2020). Of course, weight gain could be associated to changes of body composition mainly characterised by the increase in visceral adipose tissue that plays an important role in the pathogenesis of SD in postmenopausal women. Conversely, diets characterised by low glycaemic load, in particular with a high intake of fibre, may promote satiety, minimise postprandial insulin secretion, and reduce the risk of developing overweight and obesity (Gangwisch et al. 2020).

The intake of whole plant in addition to reducing the glycaemic load, reduce the levels of inflammatory also, by high quantities of vitamins C, E, B, folate, carotenes, polyphenols and various phytochemicals. In fact, these compounds may modulate inflammation and stimulate the immune system by acting as an antioxidant or a neuroprotective agent (Leonard 2005; Ng et al. 2008; Pasco et al. 2010; Godos, Ferri et al. 2020), determining the suppression of neuronal apoptosis, modulating of signalling pathways implicated in neuron survival, and stimulating of adult neurogenesis (Dias et al. 2012; Kurauchi et al. 2012; Moghadam et al. 2018).

Tryptophan

Currently, it is known that tryptophan, an essential component of the diet, is an essential amino acid in humans that is absorbed in the small intestine from protein-rich foods and plays a key role in protein synthesis, and is a precursor of biologically active compounds such as serotonin and melatonin (Wyatt et al. 1970). Tryptophan it is absorbed into the capillaries in the intestinal wall. A small amount of the amino acid remains free while the majority of it (roughly 80%–90%) is transported bound to albumin through the blood and into the brain, and it is converted into melatonin via the serotonin pathway (Paredes et al. 2009; Halson 2014). Dietary sources of tryptophan include milk, turkey, chicken, fish, eggs, pumpkin seeds, beans, peanuts, cheese and leafy green vegetables (some food products containing tryptophan are presented in Table 1). Some studies showed an

Table 1. Tryptophan amount per 100 g in common foods.

Milk	42 mg
Wheat flour	110 mg
Eggs	165 mg
Sausage	93 mg
Potato	28 mg
Cheese	325 mg
Beef	230 mg
Banana	10 mg
Soybeans	160 mg
Bread, oat bran, toasted	140 mg
Chia seeds, dried	440 mg
Chicken, breast, skinless, boneless, meat only	400 mg
Cocoa	290 mg

improvements in sleep parameters following the consumption of tryptophan (Bravo et al. 2013; Mohajeri et al. 2015). In a case control study, Bravo et al. showed an increase in total sleep time and sleep efficiency after a week of tryptophan-rich (60 mg) cereals consumption in older adults (Bravo et al. 2013). The study was carried out in 35 elderly volunteers aged 55–75 years (26 females and 9 males) who suffered from SD. The consumption of cereals with the major dose of tryptophan showed an increased sleep efficiency (sleep percentage while the volunteer is in bed), actual sleep time (assumed sleep minus awake time), and decreased total nocturnal activity and sleep latency (Bravo et al. 2013). In a randomised, placebo-controlled, parallel trial, Mohajeri et al. investigated the effects of a tryptophan-rich, bioavailable dietary supplement from egg protein hydrolysate on cognitive and sleep quality, in fifty-nine mentally and physically healthy women aged 45–65 years (Mohajeri et al. 2015). Thirty women received placebo and 29 the supplement (both as 0·5 g twice per d) for 19 d. Daily consumption of a low-dose supplement containing bioavailable tryptophan may have beneficial effects on emotional and sleep quality. the quality of sleep tended to improve over the duration of the treatment after the test drink compared with the control drink (Mohajeri et al. 2015).

Thus, the consumption of food rich in tryptophan could be suitable in postmenopausal women with SD.

Nutritional assessment of postmenopausal women with sleep disturbances

As previously reported, body composition changes occurring in menopause, in particular characterised by an increase of proportion of abdominal fat that could account for the onset of SD in postmenopausal. The nutritionist taking care of postmenopausal women with overweight or obesity should routinely screen them for SD and should set an appropriate weight management up, which includes, also, appropriate nutritional treatment for the management of menopause-related SD.

Clinical evaluation of body composition

In all postmenopausal women, nutritionists should calculate the body mass index (BMI), using the formula weight in kilograms divided by the square of the height in metres, in order to make diagnosis of obesity. However, BMI is only a screening tool used to screen population at risk of overweight/obesity, in fact, BMI not distinguishes fat mass from the lean or bone mass thus not providing information on metabolic and cardiovascular risk (De Lorenzo et al. 2013). WC, as indirect parameter of fat distribution is recommended in clinical practice, due to its tight correlation with visceral fat (Bosy-Westphal et al. 2010) which represents the main source of low grade inflammation in obesity (Jensen 2008). Additionally, to further investigate the body composition, it would be appropriate to perform bioelectrical impedance analysis (BIA) (Xie et al. 1999; Ross 2003; Fakhrawi et al. 2009; Manios et al. 2013; Tanaka et al. 2015). This technique allows to evaluate the volume and mass of different body compartments such as adipose tissue in the subcutaneous and visceral, fat mass (FM) and fat-free mass (FFM) (Karlsson et al. 2013; Neamat-Allah et al. 2014). The BIA estimates of total body water (TBW), determined by impedance, from which prediction models are used to estimate FFM (Fakhrawi et al. 2009). BIA is a technique quick, safe, non-invasive and relatively inexpensive, and it is validated in healthy subjects (Barrea et al. 2017) and in different diseases (Barrea et al. 2016, 2018, 2019).

Clinical evaluation of sleep disturbances

To date, there are many measurements to evaluate the sleep quality, including objective measurements and subjective measurements (Cronlein et al. 2013). Objective measurements can distinguish the sleep and wake more accurately; among them, polysomnography is considered the gold standard for the detection of specific sleep and sleep–wake rhythm objectivity, and it is particularly useful to diagnose OSA (Erwin and Marsh 1990; Nixon and Brouillette 2002; Van de Water et al. 2011). However, polysomnography is not routinely recommended for the initial assessment of SD, and subjective measurements such as a validated questionnaire, can be a helpful tool for the assessment of SD in outpatient clinic. The Pittsburgh Sleep Quality Index (PSQI) is the most commonly used subjective measure of SD (Mollayeva et al. 2016). PSQI distinguished "poor" from "good" sleep using seven domains: 1) subjective sleep quality; 2) sleep latency; 3) sleep duration; 4) habitual sleep efficiency; 5) sleep disturbances; 6) use of sleep medication; and 7) daytime dysfunction over the last month. Scoring of the answers is based on a 0–3 scale, and 3 reflects the negative extreme on the Likert Scale. Higher scores indicate worse sleep quality, and a global sum of "5" or greater indicates a "poor" sleeper (Buysse et al. 1989; Carole Smyth MSN n.d.). Moreover, a PSQI total score of 5 or more has great sensitivity and specificity for distinguishing people with sleep

impairment or not (Cole et al. 2006). Thus, the administration of the PSQI by an expert nutritionist could represent a valid tool for individuals SD in postmenopausal women (Prather et al. 2014; Blümel et al. 2015; Muscogiuri et al. 2020).

Dietetic intervention

The guidelines for the management of obesity consider that an intensive lifestyle intervention and weight loss program should expect to result in a mean weight loss of about 6% to 8% in 6 to 12 months and weight loss of 5% or more is considered clinically significant (Jensen et al. 2014). Moreover, guidelines and the American obesity society recommend a daily caloric deficit of 500–750 kcal, calculated on estimate daily energy requirement, which translates to a caloric intake of 1200–1500 kcal/d for most middle aged women and is expected to result in an average weight loss of 0.5–0.75 kg/week (American Heart et al. 2014; Jensen et al. 2014; Koliaki et al. 2018). It is also necessary to consider that the total energy requirements decrease as age progresses, therefore, menopausal women need to restrict the total energy intake and increase physical activity to maintain body weight compared to premenopausal women (Barrea, Pugliese, Laudisio et al. 2020; Brończyk-Puzoń et al. 2015). Besides, in postmenopausal women, also the loss of skeletal muscle and gain of adipose tissue induces an age-related slowdown in the basal metabolic rate (Lazzer et al. 2010).

Particular attention should be paid to particular dietary rules:

1. It is recommended adequate protein intake for the maintenance of muscle mass and strength and for the prevention of sarcopenia. The current DRI is 0.8 g protein/kg body weight (Trumbo et al. 2002; Morais et al. 2006; Arentson-Lantz et al. 2015). It is recommended the high consumption of animal protein alternatives such as legumes, tofu and soybeans, and it is recommended at least 3 servings of fish per week and lean cuts of meat;
2. It is recommended intake of phytoestrogens, in particular, isoflavones can be abundantly found in soybeans, instead, lignans are found in legumes, vegetables such as carrots and cabbage, fruits such as strawberries, nuts, flax seeds and whole grains;
3. Fish rich in PUFA omega-3 is preferable, such as: anchovies, herring, mackerel, salmon, sardines, sturgeon, trout and tuna;
4. It is recommended intake of complex carbohydrates such as fibre, nonjuice fruit, vegetables and whole grain and limit intake of carbohydrates with high glycaemic index such as: sugars, glucose, sucrose, fructose, starch;
5. Prefer fruit and vegetables rich in vitamins C, E, B and folate, such as: strawberries, lemon, kiwi, avocado, artichokes, broccoli, asparagus, spinach, chard, black cabbage, endive, lettuce, beetroot, brussels sprouts;
6. It is recommended intake of foods rich in tryptophan (Table 1); estimated to be between 250 mg and 425 mg, which results in a dietary intake of 3.5–6.0 mg/kg of body weight *per* day (Richard et al. 2009).

Conclusions

The menopause is associated with an increase SD such as insomnia or difficulty falling asleep, which negatively impacts quality of life. The aetiology for SD in menopausal women is still controversial, but, the key players seem to be the decrease of oestrogens levels that in turn contribute to the onset of depression, VMS, weight gain and mostly the increase of visceral adiposity could account for the onset of SD in postmenopausal acting directly through the secretion of cytokines or indirectly through OSA. Moreover, melatonin plays a very important role in circadian rhythm, especially in sleep onset and in sleep maintenance. The decline of melatonin secretion which physiologically occurs with age could be a further player that could contribute to SD in menopause. Although data available on SD and nutrition in postmenopausal women are few, they overall suggest that nutritional management strategies could represent a useful tool to treat SD in postmenopausal women. Therefore, adequate management of SD seems to be essential, and it should involve dietary. Increased intake of phytoestrogens could relieve menopausal symptoms in particular VMS, high intake of fibre and low glycemic index foods may be associated with a reduced risk of VMS besides, high intake of fibre could contribute to weight loss and to reduction of waist circumference. Furthermore, a high intake of omega-3 has been reported to decrease depression and anxiety that in turn could contribute to worsen SD. Consumption of tryptophan, a precur sor of melatonin, could improvements in sleep parameters. Therefore, adequate nutritional management and a Clinical evaluation of SD should be mandatory in the clinical practice, and it should involve a tailored diet based on the patient's habits.

Considering that, there are no specific dietary guidelines that are directly related to menopause and SD, this manuscript provides a practical guideline that could be useful for the management of SD in menopause.

Acknowledgements

The assistance of the staff is gratefully appreciated.

Author contributions

The authors' responsibilities were as follows: DL and GM: were responsible for the concept of this paper and drafted the manuscript; DL, LB, GM: provided a critical review of the paper. All authors contributed to and agreed on the final version of the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

ORCID

Daniela Laudisio https://orcid.org/0000-0001-8177-0901
Giovanna Muscogiuri https://orcid.org/0000-0002-8809-4931

References

Abdulnour J, Doucet É, Brochu M, Lavoie J-M, Strychar I, Rabasa-Lhoret R, Prud'homme D. 2012. The effect of the menopausal transition on body composition and cardiometabolic risk factors: a Montreal-Ottawa New Emerging Team group study. Menopause. 19(7):760–767.

Abshirini M, Siassi F, Koohdani F, Qorbani M, Khosravi S, Aslani Z, Pak N, Sotoudeh G. 2019. Higher intake of dietary n-3 PUFA and lower MUFA are associated with fewer menopausal symptoms. Climacteric. 22(2):195–201.

Adlercreutz H. 1995. Phytoestrogens: epidemiology and a possible role in cancer protection. Environ Health Perspect. 103 (Suppl 7):103–112.

Agostini D, Zeppa Donati S, Lucertini F, Annibalini G, Gervasi M, Ferri Marini C, Piccoli G, Stocchi V, Barbieri E, Sestili P. 2018. Muscle and bone health in postmenopausal women: role of protein and vitamin D supplementation combined with exercise training. Nutrients. 10(8): 1103.

Al-Safi ZA, Santoro N. 2014. Menopausal hormone therapy and menopausal symptoms. Fertil Steril. 101(4):905–915.

Allred CD, Allred KF, Ju YH, Clausen LM, Doerge DR, Schantz SL, Korol DL, Wallig MA, Helferich WG. 2004. Dietary genistein results in larger MNU-induced, estrogen-dependent mammary tumors following ovariectomy of Sprague-Dawley rats. Carcinogenesis. 25(2):211–218.

American Heart A, American College Of C, Obesity S. 2014. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults. J Am Pharm Assoc. 54:e3.

Appling S, Paez K, Allen J. 2007. Ethnicity and vasomotor symptoms in postmenopausal women. J Womens Health (Larchmt). 16(8):1130–1138.

Arentson-Lantz E, Clairmont S, Paddon-Jones D, Tremblay A, Elango R. 2015. Protein: a nutrient in focus. Appl Physiol Nutr Metab. 40(8):755–761.

Baker FC, Lampio L, Saaresranta T, Polo-Kantola P. 2018. Sleep and sleep disorders in the menopausal transition. Sleep Med Clin. 13(3):443–456.

Barrea L, Arnone A, Annunziata G, Muscogiuri G, Laudisio D, Salzano C, Pugliese G, Colao A, Savastano S. 2019. Adherence to the mediterranean diet, dietary patterns and body composition in women with polycystic ovary syndrome (PCOS). Nutrients. 11(10):2278.

Barrea L, Fabbrocini G, Annunziata G, Muscogiuri G, Donnarumma M, Marasca C, Colao A, Savastano S. 2018. Role of nutrition and adherence to the mediterranean diet in the multidisciplinary approach of hidradenitis suppurativa: evaluation of nutritional status and its association with severity of disease. Nutrients. 11(1):57.

Barrea L, Macchia PE, D, Somma C, Napolitano M, Balato A, Falco A, Savanelli MC, Balato N, Colao A, Savastano S. 2016. Bioelectrical phase angle and psoriasis: a novel association with psoriasis severity, quality of life and metabolic syndrome. J Transl Med. 14(1):130.

Barrea L, Muscogiuri G, Frias-Toral E, Laudisio D, Pugliese G, Castellucci B, Garcia-Velasquez E, Savastano S, Colao A. 2020. Nutrition and immune system: from the Mediterranean diet to dietary supplementary through the microbiota. Crit Rev Food Sci Nutr. 1–25.doi: 10.1080/10408398.2020.1792826.

Barrea L, Muscogiuri G, Macchia PE, Di Somma C, Falco A, Savanelli MC, Colao A, Savastano S. 2017. Mediterranean diet and phase angle in a sample of adult population: results of a pilot study. Nutrients. 9(2):151.

Barrea L, Pugliese G, Framondi L, Di Matteo R, Laudisio D, Savastano S, Colao A, Muscogiuri G. 2020. Does Sars-Cov-2 threaten our dreams? Effect of quarantine on sleep quality and body mass index. J Transl Med. 18(1):318.

Barrea L, Pugliese G, Laudisio D, Colao A, Savastano S, Muscogiuri G. 2020. Mediterranean diet as medical prescription in menopausal women with obesity: a practical guide for nutritionists. Crit Rev Food Sci Nutr. 1–11.doi: 10.1080/10408398.2020.1755220.

Bellipanni G, Bianchi P, Pierpaoli W, Bulian D, Ilyia E. 2001. Effects of melatonin in perimenopausal and menopausal women: a randomized and placebo controlled study. Exp Gerontol. 36(2):297–310.

Bianchi MT. 2017. Chronic insomnia. Semin Neurol. 37(4): 433–438.

Blümel JE, Chedraui P, Aedo S, Fica J, Mezones-Holguín E, Barón G, Bencosme A, Benítez Z, Bravo LM, Calle A, et al. 2015. Obesity and its relation to depressive symptoms and sedentary lifestyle in middle-aged women. Maturitas. 80(1):100–105.

Bosy-Westphal A, Booke C-A, BlöCker T, Kossel E, Goele K, Later W, Hitze B, Heller M, GlüEr C-C, MüLler MJ, 2010. Measurement site for waist circumference affects its accuracy as an index of visceral and abdominal

subcutaneous fat in a Caucasian population. J Nutr. 140(5):954–961.
Bravo R, Matito S, Cubero J, Paredes SD, Franco L, Rivero M, Rodriguez AB, Barriga C. 2013. Tryptophan-enriched cereal intake improves nocturnal sleep, melatonin, serotonin, and total antioxidant capacity levels and mood in elderly humans. Age (Dordr). 35(4):1277–1285.
Britt KL, Simpson ER, Findlay JK. 2005. Effects of phytoestrogens on the ovarian and pituitary phenotypes of estrogen-deficient female aromatase knockout mice. Menopause. 12(2):174–185.
Brończyk-Puzoń A, Piecha D, Nowak J, Koszowska A, Kulik-Kupka K, Dittfeld A, Zubelewicz-Szkodzińska B. 2015. Guidelines for dietary management of menopausal women with simple obesity. Prz Menopauzalny. 14(1): 48–52.
Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. 1989. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 28(2):193–213.
Cano A, Garcia-Perez MA, Tarin JJ. 2010. Isoflavones and cardiovascular disease. Maturitas. 67(3):219–226.
Carole Smyth MSN, Marie B, Sherry AG, Montefiore Medical Center. N.d. The Pittsburgh Sleep Quality Index (PSQI). New York University College of Nursing.
Chen M, Rao Y, Zheng Y, Wei S, Li Y, Guo T, Yin P. 2014. Association between soy isoflavone intake and breast cancer risk for pre- and post-menopausal women: a meta-analysis of epidemiological studies. PLoS One. 9(2): e89288.
Cheng CM, Cohen M, Wang J, Bondy CA. 2001. Estrogen augments glucose transporter and IGF1 expression in primate cerebral cortex. FASEB J. 15(6):907–915.
Chi F, Wu R, Zeng YC, Xing R, Liu Y, Xu ZG. 2013. Post-diagnosis soy food intake and breast cancer survival: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 14(4):2407–2412.
Cole JC, Motivala SJ, Buysse DJ, Oxman MN, Levin MJ, Irwin MR. 2006. Validation of a 3-factor scoring model for the Pittsburgh sleep quality index in older adults. Sleep. 29(1):112–116.
Conti A, Conconi S, Hertens E, Skwarlo-Sonta K, Markowska M, Maestroni JM. 2000. Evidence for melatonin synthesis in mouse and human bone marrow cells. J Pineal Res. 28(4):193–202.
Cronlein T, Langguth B, Popp R, Lukesch H, Pieh C, Hajak G, Geisler P. 2013. Regensburg Insomnia Scale (RIS): a new short rating scale for the assessment of psychological symptoms and sleep in insomnia; study design: development and validation of a new short self-rating scale in a sample of 218 patients suffering from insomnia and 94 healthy controls. Health Qual Life Outcomes. 11:65.
Daneshzad E, Keshavarz SA, Qorbani M, Larijani B, Azadbakht L. 2020. Association between a low-carbohydrate diet and sleep status, depression, anxiety, and stress score. J Sci Food Agric. 100(7):2946–2952.
Dasgupta S, Salman M, Lokesh S, Xaviour D, Saheb SY, Prasad BV, Sarkar B. 2012. Menopause versus aging: the predictor of obesity and metabolic aberrations among menopausal women of Karnataka, South India. J Midlife Health. 3(1):24–30.
Davidson TM, Patel MR. 2008. Waist circumference and sleep disordered breathing. Laryngoscope. 118(2): 339–347.
Davis SR, Castelo-Branco C, Chedraui P, Lumsden MA, Nappi RE, Shah D, Villaseca P, Writing Group of the IMS, For World MD, Writing Group of the International Menopause Society for World Menopause Day 2012. 2012. Understanding weight gain at menopause. Climacteric. 15(5):419–429.
De Lorenzo A, Bianchi A, Maroni P, Iannarelli A, Di Daniele N, Iacopino L, Di Renzo L. 2013. Adiposity rather than BMI determines metabolic risk. Int J Cardiol. 166(1):111–117.
Dias GP, Cavegn N, Nix A, do Nascimento Bevilaqua MC, Stangl D, Zainuddin MS, Nardi AE, Gardino PF, Thuret S. 2012. The role of dietary polyphenols on adult hippocampal neurogenesis: molecular mechanisms and behavioural effects on depression and anxiety. Oxid Med Cell Longev. 2012:541971.
Dormire S, Howharn C. 2007. The effect of dietary intake on hot flashes in menopausal women. J Obstet Gynecol Neonatal Nurs. 36(3):255–262.
Dormire SL. 2009. The potential role of glucose transport changes in hot flash physiology: a hypothesis. Biol Res Nurs. 10(3):241–247.
EFSA Risk assessment for peri- and post-menopausal women taking food supplements containing isolated isoflavones. 2015. [accessed 2020 Sep 10]. https://www.efsa.europa.eu/en/efsajournal/pub/4246.
Eichling PS, Sahni J. 2005. Menopause related sleep disorders. J Clin Sleep Med. 1(3):291–300.
Ensrud KE, Stone KL, Blackwell TL, Sawaya GF, Tagliaferri M, Diem SJ, Grady D. 2009. Frequency and severity of hot flashes and sleep disturbance in postmenopausal women with hot flashes. Menopause. 16(2):286–292.
Erwin CW, Marsh GR. 1990. Ambulatory polysomnography in the study of patients with disorders of initiating and maintaining sleep. Semin Neurol. 10(2):123–130.
Fakhrawi DH, Beeson L, Libanati C, Feleke D, Kim H, Quansah A, Darnell A, Lammi-Keefe CJ, Cordero-MacIntyre Z. 2009. Comparison of body composition by bioelectrical impedance and dual-energy x-ray absorptiometry in overweight/obese postmenopausal women. J Clin Densitom. 12(2):238–244.
Fernandez B, Malde JL, Montero A, Acuna D. 1990. Relationship between adenohypophyseal and steroid hormones and variations in serum and urinary melatonin levels during the ovarian cycle, perimenopause and menopause in healthy women. J Steroid Biochem. 35(2): 257–262.
Franco OH, Chowdhury R, Troup J, Voortman T, Kunutsor S, Kavousi M, Oliver-Williams C, Muka T. 2016. Use of plant-based therapies and menopausal symptoms: a systematic review and meta-analysis. JAMA. 315(23): 2554–2563.
Gangwisch JE, Hale L, Garcia L, Malaspina D, Opler MG, Payne ME, Rossom RC, Lane D. 2015. High glycemic index diet as a risk factor for depression: analyses from the Women's Health Initiative. Am J Clin Nutr. 102(2): 454–463.
Gangwisch JE, Hale L, St-Onge M-P, Choi L, LeBlanc ES, Malaspina D, Opler MG, Shadyab AH, Shikany JM,

Snetselaar L, et al. 2020. High glycemic index and glycemic load diets as risk factors for insomnia: analyses from the Women's Health Initiative. Am J Clin Nutr. 111(2):429–439.
Godos J, Currenti W, Angelino D, Mena P, Castellano S, Caraci F, Galvano F, Del Rio D, Ferri R, Grosso G. 2020. Diet and mental health: review of the recent updates on molecular mechanisms. Antioxidants (Basel). 9(4):346.
Godos J, Ferri R, Castellano S, Angelino D, Mena P, Del Rio D, Caraci F, Galvano F, Grosso G. 2020. Specific dietary (poly)phenols are associated with sleep quality in a cohort of Italian adults. Nutrients. 12(5):1226.
Gold EB, Colvin A, Avis N, Bromberger J, Greendale GA, Powell L, Sternfeld B, Matthews K. 2006. Longitudinal analysis of the association between vasomotor symptoms and race/ethnicity across the menopausal transition: study of women's health across the nation. Am J Public Health. 96(7):1226–1235.
Gold EB, Flatt SW, Pierce JP, Bardwell WA, Hajek RA, Newman VA, Rock CL, Stefanick ML. 2006. Dietary factors and vasomotor symptoms in breast cancer survivors: the WHEL study. Menopause. 13(3):423–433.
Goodman MT, Shvetsov YB, Wilkens LR, Franke AA, Le Marchand L, Kakazu KK, Nomura AM, Henderson BE, Kolonel LN. 2009. Urinary phytoestrogen excretion and postmenopausal breast cancer risk: the multiethnic cohort study. Cancer Prev Res (Phila). 2(10):887–894.
Griffiths K, Wilson DW, Singh RB, De Meester F. 2014. Effect of dietary phytoestrogens on human growth regulation: imprinting in health & disease. Indian J Med Res. 140(Suppl):S82–S90.
Grosso G, Galvano F, Marventano S, Malaguarnera M, Bucolo C, Drago F, Caraci F. 2014. Omega-3 fatty acids and depression: scientific evidence and biological mechanisms. Oxid Med Cell Longev. 2014:313570.
Group ADC, Bentham P, Gray R, Sellwood E, Hills R, Crome P, Raftery J. 2008. Aspirin in Alzheimer's disease (AD2000): a randomised open-label trial. Lancet Neurol. 7:41–49.
Guha N, Kwan ML, Quesenberry CP, Jr, Weltzien EK, Castillo AL, Caan BJ. 2009. Soy isoflavones and risk of cancer recurrence in a cohort of breast cancer survivors: the Life After Cancer Epidemiology study. Breast Cancer Res Treat. 118(2):395–405.
Guidozzi F. 2013. Sleep and sleep disorders in menopausal women. Climacteric. 16(2):214–219.
Hachul H, Brandao LC, D'Almeida V, Bittencourt LR, Baracat EC, Tufik S. 2011. Isoflavones decrease insomnia in postmenopause. Menopause. 18(2):178–184.
Halson SL. 2014. Sleep in elite athletes and nutritional interventions to enhance sleep. Sports Med. 44(Suppl 1): S13–S23.
Harman-Boehm I, BlüHer M, Redel H, Sion-Vardy N, Ovadia S, Avinoach E, Shai I, KlöTing N, Stumvoll M, Bashan N, et al. 2007. Macrophage infiltration into omental versus subcutaneous fat across different populations: effect of regional adiposity and the comorbidities of obesity. J Clin Endocrinol Metab. 92(6):2240–2247.
He G, Pedersen SB, Bruun JM, Lihn AS, Jensen PF, Richelsen B. 2003. Differences in plasminogen activator inhibitor 1 in subcutaneous versus omental adipose tissue in non-obese and obese subjects. Horm Metab Res. 35(3): 178–182.
Jensen MD. 2008. Role of body fat distribution and the metabolic complications of obesity. J Clin Endocrinol Metab. 93(11 Suppl 1):S57–S63.
Jensen MD, Ryan DH, Apovian CM, Ard JD, Comuzzie AG, Donato KA, Hu FB, Hubbard VS, Jakicic JM, Kushner RF, et al.; American College of Cardiology/American Heart Association Task Force on Practice Guidelines and Obesity Society. 2014. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. Circulation. 129(25 Suppl 2):S102–S138.
Ju YH, Allred CD, Allred KF, Karko KL, Doerge DR, Helferich WG. 2001. Physiological concentrations of dietary genistein dose-dependently stimulate growth of estrogen-dependent human breast cancer (MCF-7) tumors implanted in athymic nude mice. J Nutr. 131(11): 2957–2962.
Karlsson AK, Kullberg J, Stokland E, Allvin K, Gronowitz E, Svensson PA, Dahlgren J. 2013. Measurements of total and regional body composition in preschool children: a comparison of MRI, DXA, and anthropometric data. Obesity (Silver Spring). 21(5):1018–1024.
Klotz DM, Hewitt SC, Ciana P, Raviscioni M, Lindzey JK, Foley J, Maggi A, DiAugustine RP, Korach KS. 2002. Requirement of estrogen receptor-alpha in insulin-like growth factor-1 (IGF-1)-induced uterine responses and in vivo evidence for IGF-1/estrogen receptor cross-talk. J Biol Chem. 277(10):8531–8537.
Kohli P, Balachandran JS, Malhotra A. 2011. Obstructive sleep apnea and the risk for cardiovascular disease. Curr Atheroscler Rep. 13(2):138–146.
Koliaki C, Spinos T, Spinou M, Brinia ME, Mitsopoulou D, Katsilambros N. 2018. Defining the optimal dietary approach for safe, effective and sustainable weight loss in overweight and obese adults. Healthcare (Basel). 6:73.
Kravitz HM, Joffe H. 2011. Sleep during the perimenopause: a SWAN story. Obstet Gynecol Clin North Am. 38(3): 567–586.
Kroenke CH, Caan BJ, Stefanick ML, Anderson G, Brzyski R, Johnson KC, LeBlanc E, Lee C, La Croix AZ, Park HL, et al. 2012. Effects of a dietary intervention and weight change on vasomotor symptoms in the Women's Health Initiative. Menopause. 19:980–988.
Krystal AD. 2003. Insomnia in women. Clin Cornerstone. 5(3):41–50.
Kurauchi Y, Hisatsune A, Isohama Y, Mishima S, Katsuki H. 2012. Caffeic acid phenethyl ester protects nigral dopaminergic neurons via dual mechanisms involving haem oxygenase-1 and brain-derived neurotrophic factor. Br J Pharmacol. 166(3):1151–1168.
Lambert MNT, Thorup AC, Hansen ESS, Jeppesen PB. 2017. Combined Red Clover isoflavones and probiotics potently reduce menopausal vasomotor symptoms. PLoS One. 12(6):e0176590.
Lampio L, Polo-Kantola P, Polo O, Kauko T, Aittokallio J, Saaresranta T. 2014. Sleep in midlife women: effects of menopause, vasomotor symptoms, and depressive symptoms. Menopause. 21(11):1217–1224.

Lang T, Streeper T, Cawthon P, Baldwin K, Taaffe DR, Harris TB. 2010. Sarcopenia: etiology, clinical consequences, intervention, and assessment. Osteoporos Int. 21(4): 543–559.

Laye S, Nadjar A, Joffre C, Bazinet RP. 2018. Anti-inflammatory effects of omega-3 fatty acids in the brain: physiological mechanisms and relevance to pharmacology. Pharmacol Rev. 70(1):12–38.

Lazzer S, Bedogni G, Lafortuna CL, Marazzi N, Busti C, Galli R, De Col A, Agosti F, Sartorio A. 2010. Relationship between basal metabolic rate, gender, age, and body composition in 8,780 white obese subjects. Obesity (Silver Spring). 18(1):71–78.

Leger D, Bayon V. 2010. Societal costs of insomnia. Sleep Med Rev. 14(6):379–389.

Lemoine S, Granier P, Tiffoche C, Rannou-Bekono F, Thieulant ML, Delamarche P. 2003. Estrogen receptor alpha mRNA in human skeletal muscles. Med Sci Sports Exerc. 35(3):439–443.

Leonard BE. 2005. The HPA and immune axes in stress: the involvement of the serotonergic system. Eur Psychiatry. 20 (Suppl 3):S302–S306.

Liao Y, Xie B, Zhang H, He Q, Guo L, Subramaniapillai M, Fan B, Lu C, McLntyer RS. 2019. Efficacy of omega-3 PUFAs in depression: a meta-analysis. Transl Psychiatry. 9(1):190.

Liu ZM, Ho SC, Xie YJ, Chen YJ, Chen YM, Chen B, Wong SY, Chan D, Wong CK, He Q, et al. 2016. Associations between dietary patterns and psychological factors: a cross-sectional study among Chinese postmenopausal women. Menopause. 23(12):1294–1302.

Lowe DA, Baltgalvis KA, Greising SM. 2010. Mechanisms behind estrogen's beneficial effect on muscle strength in females. Exerc Sport Sci Rev. 38(2):61–67.

Lucas M, Chocano-Bedoya P, Shulze MB, Mirzaei F, O'Reilly ÉJ, Okereke OI, Hu FB, Willett WC, Ascherio A. 2014. Inflammatory dietary pattern and risk of depression among women. Brain Behav Immun. 36:46–53.

Ludwig DS. 2002. The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. JAMA. 287(18):2414–2423.

Magee PJ, Rowland IR. 2004. Phyto-oestrogens, their mechanism of action: current evidence for a role in breast and prostate cancer. Br J Nutr. 91(4):513–531.

Maltais ML, Desroches J, Dionne IJ. 2009. Changes in muscle mass and strength after menopause. J Musculoskelet Neuronal Interact. 9(4):186–197.

Manios Y, Kanellakis S, Moschonis G, Pipidis I, Skoufas E, Zafiropulos V. 2013. Estimation of abdominal fat mass: validity of abdominal bioelectrical impedance analysis and a new model based on anthropometry compared with dual-energy x-ray absorptiometry. Menopause. 20(12):1280–1283.

Mastorakos G, Valsamakis G, Paltoglou G, Creatsas G. 2010. Management of obesity in menopause: diet, exercise, pharmacotherapy and bariatric surgery. Maturitas. 65(3):219–224.

Maury E, Ehala-Aleksejev K, Guiot Y, Detry R, Vandenhooft A, Brichard SM. 2007. Adipokines oversecreted by omental adipose tissue in human obesity. Am J Physiol Endocrinol Metab. 293(3):E656–665.

McNamara RK. 2015. Mitigation of inflammation-induced mood dysregulation by long-chain omega-3 fatty acids. J Am Coll Nutr. 34(Suppl 1):48–55.

Messier V, Rabasa-Lhoret R, Barbat-Artigas S, Elisha B, Karelis AD, Aubertin-Leheudre M. 2011. Menopause and sarcopenia: a potential role for sex hormones. Maturitas. 68(4):331–336.

Messina M. 2016. Impact of soy foods on the development of breast cancer and the prognosis of breast cancer patients. Forsch Komplementmed. 23(2):75–80.

Moghadam FH, Mesbah-Ardakani M, Nasr-Esfahani MH. 2018. Ferulic acid exerts concentration-dependent anti-apoptotic and neuronal differentiation-inducing effects in PC12 and mouse neural stem cells. Eur J Pharmacol. 841: 104–112.

Mohajeri MH, Wittwer J, Vargas K, Hogan E, Holmes A, Rogers PJ, Goralczyk R, Gibson EL. 2015. Chronic treatment with a tryptophan-rich protein hydrolysate improves emotional processing, mental energy levels and reaction time in middle-aged women. Br J Nutr. 113(2): 350–365.

Mollayeva T, Thurairajah P, Burton K, Mollayeva S, Shapiro CM, Colantonio A. 2016. The Pittsburgh sleep quality index as a screening tool for sleep dysfunction in clinical and non-clinical samples: a systematic review and meta-analysis. Sleep Med Rev. 25:52–73.

Morais JA, Chevalier S, Gougeon R. 2006. Protein turnover and requirements in the healthy and frail elderly. J Nutr Health Aging. 10(4):272–283.

Moreno-Vecino B, Arija-Blazquez A, Pedrero-Chamizo R, Gomez-Cabello A, Alegre LM, Perez-Lopez FR, Gonzalez-Gross M, Casajus JA, AI, Group E, on behalf of the EXERNET Group. 2017. Sleep disturbance, obesity, physical fitness and quality of life in older women: EXERNET study group. Climacteric. 20(1):72–79.

Muscogiuri G, Barrea L, Annunziata G, Di Somma C, Laudisio D, Colao A, Savastano S. 2019. Obesity and sleep disturbance: the chicken or the egg? Crit Rev Food Sci Nutr. 59(13):2158–2165.

Muscogiuri G, Barrea L, Aprano S, Framondi L, Di Matteo R, Laudisio D, Pugliese G, Savastano S, Colao A. and on behalf of the OPERA PREVENTION Project. 2020. Sleep quality in obesity: does adherence to the Mediterranean diet matter. Nutrients. 12(5):1364.

Naufel MF, Frange C, Andersen ML, Girao M, Tufik S, Beraldi Ribeiro E, Hachul H. 2018. Association between obesity and sleep disorders in postmenopausal women. Menopause. 25:139–144.

Neamat-Allah J, Wald D, Hüsing A, Teucher B, Wendt A, Delorme S, Dinkel J, Vigl M, Bergmann MM, Feller S, et al. 2014. Validation of anthropometric indices of adiposity against whole-body magnetic resonance imaging-a study within the German European Prospective Investigation into Cancer and Nutrition (EPIC) cohorts. PLoS One. 9(3):e91586.

Nelson HD. 2008. Menopause. Lancet. 371(9614):760–770.

Ng F, Berk M, Dean O, Bush AI. 2008. Oxidative stress in psychiatric disorders: evidence base and therapeutic implications. Int J Neuropsychopharmacol. 11(6): 851–876.

Nixon GM, Brouillette RT. 2002. Diagnostic techniques for obstructive sleep apnoea: is polysomnography necessary? Paediatr Respir Rev. 3(1):18–24.

Ohayon MM. 2002. Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev. 6(2):97–111.

Omoni AO, Aluko RE. 2005. Soybean foods and their benefits: potential mechanisms of action. Nutr Rev. 63(8): 272–283.

Palin SL, McTernan PG, Anderson LA, Sturdee DW, Barnett AH, Kumar S. 2003. 17Beta-estradiol and anti-estrogen ICI:compound 182,780 regulate expression of lipoprotein lipase and hormone-sensitive lipase in isolated subcutaneous abdominal adipocytes. Metabolism. 52(4):383–388.

Paredes SD, Barriga C, Reiter RJ, Rodriguez AB. 2009. Assessment of the potential role of tryptophan as the precursor of serotonin and melatonin for the aged sleep-wake cycle and immune function: Streptopelia risoria as a model. Int J Tryptophan Res. 2:23–36.

Parry BL, F, Martinez L, Maurer EL, Lopez AM, Sorenson D, Meliska CJ. 2006. Sleep, rhythms and women's mood. Part II. Menopause. Sleep Med Rev. 10(3):197–208.

Pasco JA, Nicholson GC, Williams LJ, Jacka FN, Henry MJ, Kotowicz MA, Schneider HG, Leonard BE, Berk M. 2010. Association of high-sensitivity C-reactive protein with de novo major depression. Br J Psychiatry. 197(5):372–377.

Perrini S, Cignarelli A, Quaranta VN, Falcone VA, Kounaki S, Porro S, Ciavarella A, Ficarella R, Barbaro M, Genchi VA, et al. 2017. Correction of intermittent hypoxia reduces inflammation in obese subjects with obstructive sleep apnea. JCI Insight. 2(17):e94379.

Polesel DN, Hirotsu C, Nozoe KT, Boin AC, Bittencourt L, Tufik S, Andersen ML, Hachul H. 2015. Waist circumference and postmenopause stages as the main associated factors for sleep apnea in women: a cross-sectional population-based study. Menopause. 22(8):835–844.

Prather AA, Puterman E, Epel ES, Dhabhar FS. 2014. Poor sleep quality potentiates stress-induced cytokine reactivity in postmenopausal women with high visceral abdominal adiposity. Brain Behav Immun. 35:155–162.

Pugliese G, Barrea L, Laudisio D, Salzano C, Aprano S, Colao A, Savastano S, Muscogiuri G. 2020. Sleep apnea, obesity, and disturbed glucose homeostasis: epidemiologic evidence, biologic insights, and therapeutic strategies. Curr Obes Rep. 9(1):30–38.

Reed SD, Lampe JW, Qu C, Gundersen G, Fuller S, Copeland WK, Newton KM. 2013. Self-reported menopausal symptoms in a racially diverse population and soy food consumption. Maturitas. 75(2):152–158.

Richard DM, Dawes MA, Mathias CW, Acheson A, Hill-Kapturczak N, Dougherty DM. 2009. L-Tryptophan: basic metabolic functions, behavioral research and therapeutic indications. Int J Tryptophan Res. 2:45–60.

Rizzo G, Baroni L. 2018. Soy, soy foods and their role in vegetarian diets. Nutrients. 10(1):43.

Rohr UD, Herold J. 2002. Melatonin deficiencies in women. Maturitas. 41(Suppl 1):S85–S104.

Ross R. 2003. Advances in the application of imaging methods in applied and clinical physiology. Acta Diabetol. 40(Suppl 1):S45–S50.

Russell L, Hicks GS, Low AK, Shepherd JM, Brown CA. 2002. Phytoestrogens: a viable option? Am J Med Sci. 324(4):185–188.

Sanchez-Villegas A, Martinez-Gonzalez MA. 2013. Diet, a new target to prevent depression? BMC Med. 11:3

Seaquist ER, Anderson J, Childs B, Cryer P, Dagogo-Jack S, Fish L, Heller SR, Rodriguez H, Rosenzweig J, Vigersky R. 2013. Hypoglycemia and diabetes: a report of a workgroup of the American Diabetes Association and the Endocrine Society. Diabetes Care. 36(5):1384–1395.

Simonetto M, Infante M, Sacco RL, Rundek T, Della-Morte D. 2019. A novel anti-inflammatory role of omega-3 PUFAs in prevention and treatment of atherosclerosis and vascular cognitive impairment and dementia. Nutrients. 11(10):2279.

Strehlow K, Rotter S, Wassmann S, Adam O, Grohe C, Laufs K, Bohm M, Nickenig G. 2003. Modulation of antioxidant enzyme expression and function by estrogen. Circ Res. 93(2):170–177.

Tanaka NI, Hanawa S, Murakami H, Cao ZB, Tanimoto M, Sanada K, Miyachi M. 2015. Accuracy of segmental bioelectrical impedance analysis for predicting body composition in pre- and postmenopausal women. J Clin Densitom. 18(2):252–259.

Taylor M. 2015. Complementary and alternative approaches to menopause. Endocrinol Metab Clin North Am. 44(3): 619–648.

Thurston RC, Chang Y, von Kanel R, Barinas-Mitchell E, Jennings JR, Hall MH, Santoro N, Buysse DJ, Matthews KA. 2017. Sleep characteristics and carotid atherosclerosis among midlife women. Sleep. 40:zsw052.

Tilg H, Moschen AR. 2006. Adipocytokines: mediators linking adipose tissue, inflammation and immunity. Nat Rev Immunol. 6(10):772–783.

Toffo E, Kalleinen N, Haukka J, Vakkuri O, Partonen T, Polo-Kantola P. 2014. Melatonin in perimenopausal and postmenopausal women: associations with mood, sleep, climacteric symptoms, and quality of life. Menopause. 21: 493–500.

Toth MJ, Tchernof A, Sites CK, Poehlman ET. 2000a. Effect of menopausal status on body composition and abdominal fat distribution. Int J Obes. 24(2):226–231.

Toth MJ, Tchernof A, Sites CK, Poehlman ET. 2000b. Menopause-related changes in body fat distribution. Ann N Y Acad Sci. 904(1):502–506.

Trumbo P, Schlicker S, Yates AA, Poos M. Food and Nutrition Board of the Institute of Medicine, The National Academies. 2002. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids. J Am Diet Assoc. 102(11): 1621–1630.

Tsujiguchi H, Thi Thu Nguyen T, Goto D, Miyagi S, Kambayashi Y, Hara A, Yamada Y, Nakamura H, Shimizu Y, Hori D, et al. 2019. Relationship between the intake of n-3 polyunsaturated fatty acids and depressive symptoms in elderly Japanese people: differences according to sex and weight status. Nutrients. 11(4):775.

Van de Water AT, Holmes A, Hurley DA. 2011. Objective measurements of sleep for non-laboratory settings as alternatives to polysomnography - a systematic review. J Sleep Res. 20(1 Pt 2):183–200.

Verheus M, van Gils CH, Keinan-Boker L, Grace PB, Bingham SA, Peeters PH. 2007. Plasma phytoestrogens and subsequent breast cancer risk. J Clin Oncol. 25(6): 648–655.

Vina J, Sastre J, Pallardo FV, Gambini J, Borras C. 2008. Modulation of longevity-associated genes by estrogens or phytoestrogens. Biol Chem. 389(3):273–277.

Vogtmann E, Levitan EB, Hale L, Shikany JM, Shah NA, Endeshaw Y, Lewis CE, Manson JE, Chlebowski RT. 2013. Association between sleep and breast cancer incidence among postmenopausal women in the Women's Health Initiative. Sleep. 36(10):1437–1444.

Wiik A, Ekman M, Johansson O, Jansson E, Esbjornsson M. 2009. Expression of both oestrogen receptor alpha and beta in human skeletal muscle tissue. Histochem Cell Biol. 131(2):181–189.

Winkler G, Kiss S, Keszthelyi L, Sapi Z, Ory I, Salamon F, Kovacs M, Vargha P, Szekeres O, Speer G, et al. 2003. Expression of tumor necrosis factor (TNF)-alpha protein in the subcutaneous and visceral adipose tissue in correlation with adipocyte cell volume, serum TNF-alpha, soluble serum TNF-receptor-2 concentrations and C-peptide level. Eur J Endocrinol. 149:129–135.

Wu AH, Spicer D, Garcia A, Tseng CC, Hovanessian-Larsen L, Sheth P, Martin SE, Hawes D, Russell C, MacDonald H, et al. 2015. Double-blind randomized 12-month soy intervention had no effects on breast MRI fibroglandular tissue density or mammographic density. Cancer Prev Res (Phila). 8(10):942–951.

Wyatt RJ, Engelman K, Kupfer DJ, Fram DH, Sjoerdsma A, Snyder F. 1970. Effects of L-tryptophan (a natural sedative) on human sleep. Lancet. 2(7678):842–846.

Xie X, Kolthoff N, Barenholt O, Nielsen SP. 1999. Validation of a leg-to-leg bioimpedance analysis system in assessing body composition in postmenopausal women. Int J Obes Relat Metab Disord. 23(10): 1079–1084.

Zhang X, Cook KL, Warri A, Cruz IM, Rosim M, Riskin J, Helferich W, Doerge D, Clarke R, Hilakivi-Clarke L. 2017. Lifetime genistein intake increases the response of mammary tumors to tamoxifen in rats. Clin Cancer Res. 23(3):814–824.

Zhu YY, Zhou L, Jiao SC, Xu LZ. 2011. Relationship between soy food intake and breast cancer in China. Asian Pac J Cancer Prev. 12(11):2837–2840.