

Klaudia Pałucka, PhD, <https://orcid.org/0000-0002-6467-9118>  
*Independent Public Health Care Centre  
in Turek*

Agnieszka Bałanda-Bałdyga, PhD, <https://orcid.org/0000-0001-5351-8063>  
*Faculty of Medicine  
Cardinal Stefan Wyszyński University  
in Warsaw*

Assistant Professor Anna B. Pilewska-Kozak, PhD, hab., <https://orcid.org/0000-0003-4562-2295>  
*Department of Obstetrics and Gynaecology Nursing  
Medical University of Lublin*

## Health problems of postmenopausal women Problemy zdrowotne kobiet w okresie pomenopauzalnym<sup>1</sup>

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**Abstract:** The postmenopausal period is the final stage of the transition from the procreative period to the senium period. It is also a time of many complex biological transformations. The changes that occur, associated with the gradual expiration of the endocrine function of the ovaries, can affect the appearance of many psychophysical ailments. Low estrogen values, which are physiologically observed in the postmenopausal period, result in the appearance of various health problems. Clinical signs are divided into early (short-term) and late (long-term). This work discusses the definition and course of postmenopause and the health problems and consequences of sex hormone deficiencies on a woman's body systems. Being aware of the changes taking place during this period of women's lives can help improve and/or create new prophylactic programs. This knowledge seems essential in the daily practice of health professionals, in particular gynaecologists and midwives.

**Keywords:** menopause, postmenopause, climacteric syndrome

**Abstrakt:** Okres pomenopauzalny jest ostatnim etapem przejścia od okresu prokreacyjnego do okresu senium. Jest zarazem czasem wielu skomplikowanych przemian biologicznych. Zachodzące zmiany, związane ze stopniowym wygasaniem funkcji endokrynnej jajników, mogą wpływać na pojawienie się wielu dolegliwości psychofizycznych. Niskie wartości estrogenów, jakie fizjologicznie obserwuje się w okresie pomenopauzalnym, skutkują pojawieniem się różnych problemów zdrowotnych. Objawy kliniczne dzieli się na wczesne (krótkoterminowe) i późne (długoterminowe). W niniejszej pracy omówiono definicję i przebieg postmenopauzy oraz problemy zdrowotne i konsekwencje niedoborów hormonów płciowych na poszczególne układy organizmu. Świadomość zmian zachodzących w tym okresie życia kobiet, może pomóc w poprawie lub /i tworzeniu nowych programów profikatycznych. Wiedza ta wydaje się niezbędną w codziennej praktyce pracowników ochrony zdrowia, w szczególności lekarzy ginekologów i położnych.  
Słowa kluczowe: menopauza, postmenopauza, zespół klimakteryczny

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<sup>1</sup> Polska wersja: <https://stowarzyszeniefidesetratio.pl/Presentations0/2021-3-Palu.pdf>

## Introduction

Postmenopause is the final stage of the transition from the reproductive period to the senile period. It is also a period of many complex biological transformations. The ongoing changes associated with the gradual cessation of endocrine functions of the ovaries may contribute to many psychic and physical ailments. The risk of metabolic and cancer diseases also increases during this period (Kózka et al., 2013; Woods et al., 2016). These diseases are frequently related to a biologically determined predisposition to gaining body fat (Davis et al., 2012). For many years, breast cancer and cancers of the reproductive organs have caused high incidence rate and high mortality rate in Polish women (Kollątaj et al., 2016).

### 1. Postmenopause – definition and course

Postmenopause begins 12 months after the last ever menstrual period. Literature usually divides postmenopause into early (up to 5 years after the last menstrual period) and late (more than 5 years) postmenopause. According to some reports, postmenopause lasts for the rest of a woman's life (Męczekalski & Katulski, 2016). By convention, however, a woman aged over 65 years enters the *senile period* (Dmoch-Gajzlerska and Rabiej, 2007).

Postmenopause is a continuation of intense hormonal changes that have already been initiated in the premenopausal period. It is a period after the irreversible cessation of endocrine functions of the ovaries. The woman no longer experiences menstrual cycles, resulting in the end of her procreative function (Kaczmarek, 2014). The greatest changes in hormonal profile are in estrogen levels. These hormones regulate a variety of physiological functions. They are thus a key regulator of the metabolic system of the female body. Their mechanism of action mainly involves binding to  $\alpha$ - and  $\beta$ -estrogen receptors (ER- $\alpha$  and ER- $\beta$ ) (Rettberg et al., 2014). These receptors are present in most body systems. Hormones act genomically (by regulating gene transcription) and non-genomically (by affecting calcium and potassium channels in a direct way) (Pinkas et al., 2016; Zielniok et al., 2014). After menopause there is a significant decrease in estradiol levels that are usually lower than 80 pmol/l. Estrone becomes the main estrogen. It is produced especially by aromatisation of adrenal androgens found in adipose tissue, reaching the levels of approximately 100 pmol/l. Higher levels of this hormone are observed in obese women (Męczekalski and Katulski, 2016; WHO, 1996).

Follicle-stimulating hormone (FSH) secretion increases in postmenopausal women by 10-15-fold and luteinizing hormone (LH) secretion by 3-fold, compared to their profile for the procreative period (WHO, 1996). FSH has a longer half-life thus there are significant differences between FSH and LH levels (Petkowicz et al., 2013). Prolactin secretion is slightly

decreased (Meczalsky and Katulski., 2016). Approximately 3-4 years after menopause, estrogen reaches its lowest levels while FSH reaches its peak levels (WHO, 1996).

Biosynthesis of androgens in the female body takes place in the ovaries, adrenal cortex and under the influence of peripheral conversion. In postmenopause, the production of these hormones occurs mostly at the extra-ovarian level. The ovaries are involved in the production of 20% androstendione and 40% testosterone. Total testosterone levels may slightly increase, while free testosterone levels remain the same. This is associated with an increase in SHBG (sex hormone-binding globulin) levels. The androstendione levels are decreased. As the female body ages, the secretion of DHEA (dehydroepiandrosterone) and DHEAS (dehydroepiandrosterone sulfate) is reduced. Moreover, GH (growth hormone) levels decrease in postmenopause while insulin resistance increases (Petkowicz et al., 2013; Pinkas et al., 2016). TSH (thyrotropic hormone) and ACTH (adrenocorticotrophic hormone) levels remain at the same level (Meczalski and Katulski., 2016).

## **2. Climacteric syndrome**

The low estrogen levels, which are physiologically observed during postmenopause, result in various health problems (Pinkas et al., 2016). Clinical symptoms are divided into early (short-term) and late (long-term) symptoms. Early symptoms form the climacteric syndrome, alternately called menopausal syndrome. The climacteric syndrome is a set of complaints occurring in the peri-menopausal period that are directly related to endocrine disorders. Psychosocial and environmental factors may also influence these complaints (Sarri et al., 2015). The symptoms of the climacteric syndrome affect the somatic, mental and sexual spheres (Gartoulla et al., 2014). Key symptoms include hot flushes, night sweats, irritability, fatigue, low mood, cognitive impairment and difficulty sleeping (Meczalski & Katulski, 2016). Vasomotor symptoms are considered the most bothersome, i.e. hot flushes and night sweats (Woods et al., 2014). According to current reports, menopausal symptoms can affect more than 80% of women. The period of the onset of climacteric symptoms may be different for every woman, however, they are most strongly felt in the postmenopausal period (Stachoń et al., 2013). The severity of climacteric syndrome is assessed using the Greene Climacteric Scale (GCS) and Kupperman Index (KI) (Bojar et al., 2016).

## **3. Metabolic syndrome**

Late symptoms include problems arising in prolonged exposure to low levels of sex hormones (Sarri et al., 2015). Metabolic syndrome, also called insulin resistance syndrome, syndrome X or dysmetabolic syndrome, is one of these problems. It is a disorder that leads to the development of type 2 diabetes (T2D) and cardiovascular diseases. Metabolic syndrome

is a combination of central obesity, dyslipidemia, hypertension, hypertriglyceridemia and insulin resistance (Coyoy et al., 2016). The prevalence of this syndrome in postmenopausal women ranges from 31% to 60% according to different parts of the world (Sharma et al., 2016).

Estrogen deficiency appears to have a negative effect on the inner layer of the arterial wall, which contributes to a decrease in blood vessel elasticity. The effect of altering the androgen/estrogen ratio on the increase in LDL (low-density lipoprotein) levels and the decrease in HDL (high-density lipoprotein) levels is observed, which is typical of the atherosclerotic profile. Postmenopause is also believed to contribute to changes in the renin-angiotensin system, leading to elevated blood pressure (De Marchi et al., 2017).

Moreover, appetite is frequently increased in the postmenopausal period. Estrogen and progesterone deficiencies accelerate stomach motility. Low levels of serotonin lead to stimulation of hunger and satiety centres that are located in the hypothalamus. On the other hand, melatonin deficiency coexisting with sleep disorders stimulates the development of hyperalimentation syndrome and the occurrence of night time hunger. The aforementioned disorders lead to the development of overweight and obesity (Coyoy et al., 2016; Yalocha et al., 2014).

Postmenopausal weight gain is observed in approximately 60% of Polish women (Pinkas et al., 2016). It is characterised by unfavorable redistribution of body fat. This mainly concerns the fat mass to fat-free mass ratio, where the latter is significantly less. Visceral fat increases by 40% and subcutaneous fat located within the abdominal area by approximately 20%. An increase in visceral fat leads to the central obesity that, in turn, contributes to the development of metabolic syndrome (Janiszewska et al., 2015 B). Decreased levels of estradiol, progesterone, GH, leptin, galanin and neuropeptide Y are considered the main cause of the increase in visceral fat. The causes of the abnormal weight to height ratio should also be sought in unfavorable lifestyles, including low physical activity and poor dietary habits (Pinkas et al., 2016).

#### **4. The consequences of estrogen deficiency in various body systems**

##### **4.1. Central nervous system (CNS)**

The neuroprotective effects of estrogen are particularly important in brain areas such as the hippocampus. In the ventral hippocampus (vHPC), through connections with the hypothalamus and amygdala, they modulate affective processes, i.e. responses to stress and emotions, while the dorsal hippocampus influences cognitive function (Mott et al., 2014). Estrogens stimulate spinogenesis (the development of dendritic spines in neurons) and synaptogenesis (the process of forming synapses). Animal studies have shown that low levels of 17 $\beta$ -estradiol lead to loss of synapses and decreased connectivity between neurons

(Au et al., 2016). Their neuroendocrine effects on cholinergic, serotonergic and GABAergic systems are also recognised (Bojar et al., 2011; Wang et al., 2016). As a result of changes in the functioning of CNS, cognitive impairment occurs in the postmenopausal period. Impaired perception of touch, smell, hearing, and vision, impaired memory and balance, impaired divided attention, as well as impaired spatial intelligence and learning ability are observed (Bojar et al., 2013; Janicka, 2014). Postmenopausal women are found to achieve worse results in psychomotor speed tests, visuospatial ability tests and reaction time tests (Bojar et al., 2014).

Postmenopausal age is a period of increased risk for depression that affects approximately 20-30% of women (Lewicka et al., 2013). Vulnerability to depressive disorders is related not only to changes in CNS, but also to the subjective perception of somatic symptoms of climacteric syndrome and psychosocial problems (Jagtab et al., 2016).

#### **4.2. Cardiovascular system**

Cardiovascular diseases (CVDs) belong to a group of conditions that are divided into three basic disease entities, i.e. peripheral artery disease (PAD), ischemic cerebral infarction and ischemic heart disease (IHD). For many years, the problem was thought to affect mainly men, hence the CVD incidence in women was not considered on such a large scale. Although symptoms of CVDs appear approximately 10 years later than in men, women suffer from more adverse complications (Sobieszczanska, 2011). It is estimated that approximately 22% of European women die from coronary heart disease alone. In contrast, 52% of European women die from other cardiovascular diseases (Schierbeck et al., 2015).

Risk factors, as well as their prevalence, increase significantly in the postmenopausal period. Significant metabolic changes occur in the female body due to losing the cardioprotective effects of estrogens. The abnormal lipid profile, thrombotic lesions in the vessels and central obesity are observed (Pinkas et al., 2016; Van Dijk et al., 2015). Numerous modifiable risk factors for atherosclerosis and heart diseases are identified in women, with the highest severity observed in the postmenopausal period (Piskorz et al., 2015). The following adverse lifestyle changes, which are quite typical for postmenopausal women, are also mentioned as predictors of CVD: poor diet, decreased physical activity and difficulty sleeping (Van Dijk et al. 2015).

#### **4.3. Genitourinary system**

Physiological estradiol deficiency leads to atrophy in the genitourinary system. Its symptoms can significantly affect postmenopausal women's comfort and quality of life. As some reports show, however, only few postmenopausal women report these symptoms to a doctor, thus the problem seems to be under-diagnosed (Gandhi et al, 2016; Parnan Emamverdikhani et al,2016; Varella et al, 2016).

Many degenerative changes occur within reproductive organs. The uterus, ovaries and fallopian tubes gradually decrease in size. The vulva decreases in thickness and is less vascularised. The atrophy affects the skin around the vulva, resulting in its thinning, flaccidity and sagging of the labia majora. There are involution processes within the clitoris and labia minora, as well as lipoatrophy (loss of adipose tissue) within the labia majora. The vulva loses pigmentation and typical pubic hair. There is also mucosal thinning at the vaginal area (Gardziejewska et al., 2014; Skrzypulec-Plinta et al., 2013).

Vaginal atrophy affects up to approximately 75% of women. It results in the appearance of many symptoms, i.e. decreased vaginal tone and elasticity, vaginal dryness and/or vaginosis as well as dyspareunia and bleeding after sexual intercourse. A gradual decrease in vaginal wall elasticity is associated with a decline in the number of collagen and elastin fibers (Parnan Emamverdikhan et al., 2016). In addition, the following symptoms are also observed: impairment of keratinocyte proliferation, initiation of degenerative changes in tissues and inhibition of regenerative processes. This results in epithelial atrophy, damage to the vaginal rugae and reduction of the vaginal vestibule (Gardziejewska et al., 2014; Skrzypulec-Plinta et al., 2013).

On the other hand, vaginal dryness is caused by a decrease in the secretion of cervical mucus and Bartholin's secretion. There are also changes in the vaginal bacterial flora that become deficient in lactic acid bacilli. At the same time, the vagina's pH level increases compared to the procreative period. This leads to itching, burning, redness and more frequent inflammation of reproductive organs, especially bacterial vaginitis (Magon et al., 2012; Skrzypulec - Plinta et al., 2013).

The aforementioned changes within reproductive organs lead to dyspareunia, i.e. pain and burning during sexual intercourse. Based on current reports, up to 25-50% of postmenopausal women report discomfort during sexual activity. Pain can occur in various regions of reproductive organs. It can either be felt within the vulva, vagina or small pelvis. However, most women experience pain in the vaginal vestibule because of its rich innervation. In addition to endocrine disorders, psychosocial factors and chronic disease comorbidities may influence its occurrence (Parnan Emamverdikhan et al., 2016; Stec et al., 2014).

There are atrophic processes in the urinary system, especially within the urinary bladder and urethra. There is also a weakening of the pelvic floor muscles due to a decrease in elastin and collagen fibers found in the connective tissue. This leads to the development of urinary incontinence (UI). According to some scientific reports, UI affects up to 20% of postmenopausal women (Gandhi et al., 2016). Moreover, there is the problem of polyuria and nycturia (excessive urination at night). UI is a urinary control disorder that causes numerous hygienic and social problems (Stadnicka et al., 2015). In the postmenopausal period, the problem of stress urinary incontinence (SUI) and urgency urinary incontinence

(UUI) may arise. The former occurs most commonly. A woman may experience involuntary loss of small amounts of urine, without a sense of urinary urgency, due to coughing or exercising. On the other hand, UUI refers to the situation where involuntary urination occurs together with a sense of urinary urgency and it is accompanied by nycturia (Fiodorenko-Dumas et al., 2014; Varella et al., 2016).

#### **4.4. Skeletal system**

Osteoporosis belongs to the group of primary involuntional pathologies and is responsible for 80% of metabolic bone diseases (Von Mach-Szczypinski et al., 2016). It affects 30% of European women aged over 50 years (Janiszewska et al., 2015 A). The main cause of this disease is the predominance of bone resorption processes over bone formation (ossification). In the postmenopausal age, this disease is called type 1 involuntional osteoporosis. It is associated with  $17\beta$  estradiol deficiency that decreases bone mineral density (Opala and Rabiega-Gmyrek, 2016). This results in bone mass loss and inhibition of the microdamage repair process. This is associated with an increased risk of osteoporotic fractures (Janiszewska et al., 2015).

Osteoporosis is a disease without significant symptoms. Clinical symptoms manifest as a consequence of fractures. In the postmenopausal period, the spinal vertebrae and the femoral neck are mainly affected. These fractures are described as low-energy ones due to their occurrence as a result of a minor injury that would not normally cause such severe consequences (Janiszewska et al., 2015 A; Opala et al., 2016).

#### **4.5. Neoplastic diseases**

Malignant neoplasms usually require a long latency period to fully develop. This period begins with the first exposure to a carcinogen. Healthy cells turn into cancer cells through the process of genetic mutation (DNA changes). Cancer also occurs due to spontaneous mutations, caused by a genetic predisposition. Before the first clinical symptoms occur, however, the pathologically altered cell goes through a system of defense genes, ultimately leading to persistent mutations and the development of a full-blown tumorigenesis. Therefore, the risk of cancer increases with age due to the prolonged effect of mutagenic agents on the aging body (Zatonski et al., 2015). The postmenopausal age is a particularly vulnerable period for carcinogenesis. Breast cancer, colorectal cancer and lung cancer are most commonly observed neoplasms in Polish women (Ostrowska., 2015 A). The most common gynaecological cancers include endometrial cancer, ovarian cancer, cervical cancer and, the least common, vulvar cancer (Singh et al., 2017).

Breast cancer is a major public health problem worldwide, especially in wealthy countries. The disease is most commonly diagnosed in the 50-69 age group (Szkiela et al., 2014). Major risk factors include early menarche and late menopause, confirming a hormone-

dependent type of cancer. It is believed that long-term hormone replacement therapy (HRT) may also contribute, albeit slightly, to the disease. Furthermore, anti-health behaviours such as strong alcohol consumption and low physical activity are considered important pathogenic factors. The impact of mutations in the BRCA1 and BRCA2 genes is also fully recognised (Szkiela et al., 2014). Furthermore, tall and obese women or those who have experienced significant weight gain may be at risk (Jaworski et al., 2015). The most important clinical sign of cancer is a hard and usually painless tumor, irregular in outline and with a demarcation line around nearby tissues. Cancer may also be accompanied by dermatological lesions, i.e. redness, peau d'orange (orange peel skin), retraction of skin and swelling (Piaszczyk et al., 2015). The chance of making a full recovery depends on various factors, i.e. a histological type, tumour grade, tumour size, existing lymph node metastases and a hormonal status of the tumour (Bobek-Billewicz et al., 2014). The high mortality rate in breast cancer is mainly due to its relapse after therapeutic interventions. The tumour recurrence occurs due to the spread of local and/or disseminated residual cancer cells that have survived treatment – minimal residual disease (Havas et al., 2017).

Genital bleeding episodes in postmenopause raise suspicions of neoplastic lesions taking place within the endometrium (Inal et al., 2017; Munro et al., 2014). The etiopathogenesis of endometrial cancer is not fully understood. It is thought that hyperestrogenism may be the cause of oncologic lesions within the endometrium. People with genetic mutations are more likely to get the disease. Endometrial cancer may be associated with Lynch syndrome and hereditary nonpolyposis colorectal cancer syndrome (Colombo et al., 2015). Most women suffering from endometrial cancer live in highly developed countries, where menopause occurs later. Therefore, these women experience a longer estrogenic effect on their genital organs. Endometrial cancer is usually diagnosed around 60 years of age. Major risk factors, in addition to early menarche, late menopause and genetic factors, include diabetes and obesity (Szubert et al, 2014; Tang et al, 2017; Wilczynski et al, 2015).

There are two types of endometrial cancer, i.e. type I (estrogen-dependent) endometrial cancer and type 2 (estrogen-independent) endometrial cancer. Type 1 endometrial cancer is the most common and it usually has a benign course. The affected woman has every chance of making a full recovery (Markowska et al., 2015). Early-stage endometrial cancer, limited only to the endometrial stripe, is nearly 80% of all cases and a five-year survival rate is very high (Bendifallah et al., 2015).

Ovarian cancer has the highest mortality rate out of all gynaecological cancers (Jayson et al., 2014; Niemi et al., 2017). It particularly affects female residents of developed countries [Siegel et al., 2015]. The greatest increase in ovarian cancer incidence is observed after 50 years of age. Currently, there are no screening tests for ovarian cancer due to the lack of identified precancerous stages and the lack of sufficiently sensitive and specific biomarkers.



Advances in treatment yield only marginal differences in terms of overall survival (McAlpine et al., 2014). The ovarian cancer exhibits high invasiveness (Li et al., 2017). Its aggressive development and untypical symptoms mean that it is usually diagnosed at its advanced stage – stage III-IV according to the FIGO staging system. At this stage, complete recovery is very difficult (Schüler-Toprak et al., 2017). The vast majority of cancers are epithelial in nature, and their earliest evidence is usually found in the fimbriae of the uterine tube. Risk factors include hereditary breast and ovarian cancer syndromes, mutations in the BRCA1 and BRCA2 genes, Lynch syndrome, childlessness, ovarian hyperstimulation and failed IVF (in vitro fertilisation) attempts. The diagnosis may be preceded by non-specific dyspeptic symptoms of several months' duration, i.e. abdominal pain and bloating (Jayson et al., 2014).

Cervical cancer is still the leading cause of cancer-related mortality in women worldwide. Given the morbidity and several year survival time, Poland is in the lead among highly developed countries. This disease affects women aged 45-64 years on average (Stanislawska et al., 2016). The main cause of cervical cancer is chronic HPV infection (human papillomavirus). Risk factors include early sexual initiation, multiple children, promiscuity (engaging in sexual activity frequently with different partners), heavy smoking and low socioeconomic status (Nowak-Markwitz, 2016). Early-stage cervical cancer is asymptomatic (Ashtarian et al., 2017). Women with advanced cervical cancer may suffer from bleeding from the reproductive organs and vaginal discharge with an unpleasant odour. Cervical cancer is one of the few cancers that can be effectively prevented through screening. This cancer has long-term development and well-described precancerous stages (Palucka et al., 2017).

Vulvar cancer is one of the least common cancers of the reproductive organs. However, the vulvar cancer incidence increases with age. The mean age of onset is 52 years of age (Singh et al., 2017). There are several histological types of vulvar cancer, with squamous cell carcinoma as the most common (Alkatout et al., 2015). The affected area is the labia majora (Singh et al., 2016). The full recovery is very possible if this cancer is diagnosed at its early stage – this greatly reduces the disease progression. A significant aspect of medical care in vulvar cancer patients is to determine the most conservative treatment possible. During the recovery process, women often require psychosexual support (Alkatout et al., 2015).

### **Summary**

The issues discussed highlight the complexity of postmenopause and its serious implications for women's physical and mental health. The knowledge of biological and

environmental mechanisms of postmenopause should contribute to increased medical personnel's concern for the health of women during menopausal transition.

### **Bibliography:**

- Alkatout, I., Schubert, M., Garbrecht, N., Weigel, M. T., Jonat, W., Mundhenke, C., Günther, V. (2015). Vulvar cancer: epidemiology, clinical presentation, and management options, *International Journal of Women's Health*, 7, 305-313.
- Ashtarian, H., Mirzabeigi, E., Mahmoodi, E., Khezeli, M. (2017). Knowledge about cervical cancer and pap smear and the factors influencing the pap test screening among women, *International Journal of Community Based Nursing and Midwifery*, 5 (2), 188-195.
- Au, A., Feher, A., McPhee, L., Jessa, A., Oh, S., Einstein, G. (2016). Estrogens, inflammation and cognition, *Frontiers of Neuroendocrinology*, 40, 87-100.
- Bendifallah, S., Canlorbe, G., Collinet, P., Arsene, E., Huguet, F., Coutant, C., Hudry, D., Graesslin, O., Raimond, E., Touboul, C., Darai, E. Ballester, M. (2015), Just how accurate are the major risk stratification systems for early-stage endometrial cancer ? *British Journal of Cancer*, 112 (5), 793-801.
- Bojar, I., Lyubinets, O, Novotny, J., Stanchak, Y., Tiszczenko, E., Owoc, A., Raczkiwicz, D. (2016). Intensification of menopausal symptoms among female inhabitants of East European countries, *Annales of Agricultural and Environmental Medicine*, 23 (3), 517-24.
- Colombo, N., Creutzberg, C., Amant, F., Bosse, T., González-Martín, A., Ledermann, J., Marth, C., Nout, R., Querleu, D., Mirza, M.R., Sessa, C. (2015), ESMO-ESGO-ESTRO consensus conference on endometrial cancer: diagnosis, treatment and follow-up, *Annals of Oncology*, 27 (1),16-41.
- Coyoy, A., Guerra-Araiza, C., Camacho - Arroyo, I. (2016). Metabolism regulation by estrogens and their receptors in their central nervous system before and after menopause, *Hormone and Metabolic Research*, 48 (8), 489-96.
- Davis, S.R., Castelo-Branco, C., Chedraui, P., Lumsden, M.A., Nappi, R.E., Shah, D., Villaseca, P. (2012). Understanding weight gain at menopause, *Climacteric*, 15 (5), 419-429.
- De Marchi, R., Dell'Agno, C.M., Romeiro Lopez, T.C., França Gravena, A.A., De Oliveira Demitto, M., Rocha Brischiliari, S.C., Borghesan, D.H., Carvalho, M.D., Pelloso, S.M. (2017). Prevalence of metabolic syndrome in pre - and postmenopausal women, *Archives of Endocrinology Metabolism*, 61 (2),160-166.
- Dmoch-Gajzlerska E., Rabiej M. (2007). Niepokojące objawy zmuszające kobiety do wizyty u lekarza ginekologa w okresie pomenopauzalnym - doniesienie wstępne, *Gerontologia Polska*, 15 (4), 149-152.
- Fiodorenko-Dumas, Z., Paprocka-Borowicz, M. (2014). Postępowanie fizjoterapeutyczne w nietrzymaniu moczu, *Medycyna Ogólna i Nauki o Zdrowiu*, 20 (1), 12-16.

- Gandhi, J., Chen, A., Dagur, G., Suh, Y., Smith, N., Cali, B., Ali, Khan S. (2016). Genitourinary syndrome of menopause: an overview of clinical manifestations, pathophysiology, etiology, evaluation, and management, *American Journal of Obstetrics and Gynecology*, 215 (6), 704-711.
- Gardziejewska, A., Różańska-Kohsek, A., Zalewski, M., Heimrath, J., Zalewski, J. (2014). Seksualność kobiet w okresie klimakterium, *Medycyna Ogólna i Nauki o Zdrowiu*, 20 (4), 400-404.
- Gartoulla, P., Islam, M. R., Bell, R. J., Davis, S. R. (2014). Prevalence of menopausal symptoms in Australian women at midlife: a systematic review, *Climacteric*, 17(5), 529-539.
- Havas, K. M., Milchevskaya, V., Radic, K., Alladin, A., Kafkia, E., Garcia, M., Stolte, J., Klaus, B., Rotmensz, N., Gibson, T.J., Burwinkel, B., Schneeweiss, A., Pruneri, G., Patil, K.R., Sotillo, R., Jechlinger, M., Burwinkel, B. (2017): Metabolic shifts in residual breast cancer drive tumor recurrence, *The Journal of Clinical Investigation*, 127 (6), 2091-2105.
- Inal, Z. O., Inal, H. A., Kucukosmanoglu, I., Kucukkendirici, H. (2017). Assessment of Endometrial Sampling and Histopathological Results: Analysis of 4, 247 Cases, *The Eurasian Journal of Medicine*, 49 (1), 44-47.
- Jagtab, B.L., Prasad, B.S., Chaudhury, S. (2016). Psychiatric morbidity in perimenopausal women, *Industrial Psychiatry Journal*, 25 (1), 86-92.
- Jałocha, W., Wachowska-Kelly, P., Stępień, A., Wojtkiewicz, P., Walecka-Kapica, E., Chojnacki, J., Klupińska, G. (2014). Wydzielanie serotoniny i melaniny oraz mioelektryczna i motoryczna czynność żołądka u kobiet po menopauzie, *Folia Medica Lodziensia*, 41 (2), 155-167.
- Janiszewska, M., Kulik, T., Dziedzic, M., Żołnierczuk-Kieliszek, D., Barańska, A. (2015a). Osteoporoza jako problem społeczny - patogeneza, objawy i czynniki ryzyka osteoporozy pomenopauzalnej, *Problemy Higieny i Epidemiologii*, 96 (1), 106-114.
- Janiszewska, R., Orawiec, R., Nowak, S. (2015b). Ocena składu ciała, odłuszczenia ogólnego i dystrybucji tkanki tłuszczowej u kobiet w procesie starzenia, *Problemy Higieny i Epidemiologii*, 96 (2), 517-522.
- Jaworski, P., Binda, A., Tarnowski, W. (2015). Wpływ otyłości na rozwój choroby nowotworowej, *Postępy Nauk Medycznych*, 28 (9), 673-676.
- Jayson, G.C., Kohn, E.C., Kitchener, H.C., Ledermann, J.A. (2014). Ovarian cancer, *The Lancet*, 384 (9951), 1376-1388.
- Kaczmarek M. (2014). Koncepcja menopauzy w ujęciu ewolucyjnym, *Poznańskie Studia z Filozofii Nauki*, 23 (2), 119-144.
- Kołątaj, W., Karwat, I.D., Kołątaj, B., Pieciewicz-Szczęsna, H., Sowa, M. (2016). Profilaktyka nowotworów u kobiet w Polsce. Sukces, czy niepowodzenie? Opinie pacjentów,

- lekarzy i instytucji odpowiedzialnych za stan zdrowia - metaanaliza, *Journal of Education Health and Sport*, 6 (6), 318-328.
- Kózka, M., Prażmowska, B., Dziedzic, M., Semczak, M. (2013). Styl życia kobiet w okresie menopauzalnym - badania wstępne, *Przegląd Medyczny Uniwersytetu Rzeszowskiego i Narodowego Instytutu Leków w Warszawie*, 1, 61-74.
- Lewicka, M., Sulima, M., Grabowiec, J., Stawarz, B., Makara-Studzińska, M. (2013), Zaburzenia nastroju u kobiet w okresie okołomenopauzalnym, *Journal of Public Health Nursing and Medical Rescue*, 1, 9-15.
- Li, H., Liu, C., Lu, Z., Chen, L., Wang, J., Li, Y., Ma, H. (2017), Upregulation of the long non-coding RNA SPRY4-IT1 indicates a poor prognosis and promotes tumorigenesis in ovarian cancer, *Biomedicine Pharmacotherapy*, 88, 529-534.
- Magon, N., Chauhan, M., Malik, S., Shah, D. (2012). Sexuality in midlife: Where the passion goes? *Journal of Midlife Health*, 3 (2), 61-65.
- Markowska, A., Pawałowska, M., Korcyl, M., Markowska, J. (2015). Rak endometrium typu I i II - nowe spojrzenie na etiologię i przebieg kliniczny, *Current Gynecologic Oncology*, 13 (1), 5-10.
- McAlpine, J.N., Hanley, G.E., Woo, M.M., Tone, A.A., Rozenberg, N., Swenerton, K.D., Blake Gilks, C., Finlayson, S.J., Huntsman, D.G., Miller, D.M. (2014). Opportunistic salpingectomy: uptake, risks, and complications of a regional initiative for ovarian cancer prevention, *American Journal of Obstetrics and Gynecology*, 210 (5), 471-e1.
- Męczekalski, B., Katulski, K. (2016). Okres menopauzy, (w:) G. Bręborowicz (red.), *Położnictwo i Ginekologia*, Wyd. II, 2, 131-135, Warszawa: Wyd. Lek. PZWL.
- Mott, N.N., Pinceti, E., Rao, Y.S., Przybycien-Szymanska, M.M., Prins, S.A., Shults, C.L. Yang, X., Glucksman, M.J., Roberts, J.L., Pak, T.R. (2014), Age-dependent effects of 17 $\beta$ -estradiol on the dynamics of estrogen receptor  $\beta$  (ER $\beta$ ) protein-protein interactions in the ventral hippocampus, *Molecular and Cellular Proteomics*, 13 (3), 760-779.
- Munro, M. G. (2014). Investigation of women with postmenopausal uterine bleeding: clinical practice recommendations, *The Permanente Journal*, 18 (1), 55-70.
- Niemi, R.J., Saarelainen, S.K., Luukkaala, T.H., Mäenpää, J.U. (2017). Reliability of preoperative evaluation of postmenopausal ovarian tumors, *Journal of Ovarian Research*, 10 (15), <https://doi.org/10.1186/s13048-017-0309-4>.
- Opala, T., Rabięga-Gmyrek, D. (2016). Osteoporoza, (w:) B. Bręborowicz (red.). *Położnictwo i Ginekologia*, Wyd. II, tom I, 254-264, Warszawa: Wyd. Lek. PZWL.
- Ostrowska, A. (2015a). Stan zdrowia kobiet - zagrożenia, społeczne uwarunkowania, *Zeszyty Naukowe Ochrony Zdrowia Publicznego i Zarządzanie*, 13 (4), 337-343.
- Pałucka, K., Pilewska-Kozak, A.B., Łepecka-Klusek, C. (2017). Profilaktyczna opieka ginekologiczna w okresie pomenopauzalnym, (w:) M. Szklarczyk, K. Maciąg (red.),

- Najnowsze doniesienia z zakresu medycyny i nauk pokrewnych, 244-252, Lublin: Wyd. Tygiel.
- Parnan Emamverdikhan, A., Golmakani, N., Tabassi, S.A., Hassanzadeh, M., Sharifi, N., Shakeri, M.T. (2016), A survey of the therapeutic effects of vitamin E suppositories on vaginal atrophy in postmenopausal women, *Iranian Journal of Nursing Midwifery Research*, 21 (5), 475-481.
- Petkowicz, B., Piotrkowicz, J., Szeszko, Ł., Banakiewicz, K., Zieliński, P. (2013). Wybrane aspekty zmian chorobowych jamy ustnej kobiet w wieku menopauzalnym, *Przegląd Menopauzalny*, 12 (4), 352-357.
- Piaszczyk, D., Ignaciuk, S., Kosińska, B., Karczewski, J. (2015). Poziom wiedzy studentów Państwowej Szkoły Wyższej w Białej Podlaskiej na temat profilaktyki raka piersi, *Medycyna Ogólna i Nauki o Zdrowiu*, 21 (3), 260-265.
- Pinkas, J., Gujski, M., Wierzińska-Stępnik, A., Owoc, A., Bojar, I. (2016). The polymorphism of estrogen receptor alpha is important for metabolic consequences associated with menopause, *Endokrynologia Polska*, 67 (6), 608-614.
- Piskorz, A., Brzostek, T., Piórecka, B. (2015). Występowanie wybranych czynników ryzyka chorób układu krążenia w grupie kobiet w okresie przed- i pomenopauzalnym - analiza porównawcza, *Hygeia Public Health*, 50 (1), 127-135.
- Rettberg, J.R., Yao, J., Brinton, RD. (2014). Estrogen: a master regulator of bioenergetic systems in the brain and body, *Frontiers of Neuroendocrinology*, 35 (1). 8-30.
- Sarri G., Davies M., Lumsden M.A., Guideline Development Group. (2015). Diagnosis and management of menopause, *British Medical Journal*, 351, 30-32.
- Schierbeck, L. (2015). Primary prevention of cardiovascular disease with hormone replacement therapy, *Climacteric*, 18 (4), 482-497.
- Schüler-Toprak, S., Moehle, C., Skrzypczak, M., Ortmann, O., Treeck, O. (2017), Effect of estrogen receptor  $\beta$  agonists on proliferation and gene expression of ovarian cancer cells, *BMC Cancer*, 17 (1), <https://doi.org/10.1186/s12885-017-3246-0>.
- Sharma, S., Aggarwal, N., Josh, B., Suri, V., Badada, S. (2016). Prevalence of metabolic syndrome in pre- and post-menopausal women: a prospective study from apex institute for North India, *Journal of Midlife Health*, 7 (4), 169-174.
- Siegel, R.L., Miller, K.D., Jemal, A. (2015). Cancer statistics, 2015. CA, *Cancer Journal of Clinicians*, 65 (1), 5-29.
- Singh, B.N., Prateeksha Rawat, A.K.S., Bhagat, R.M., Singh, B.R. (2017): Black tea: Phytochemicals, cancer chemoprevention, and clinical studies, *Critical Reviews in Food Science and Nutrition*, 57 (7), 1394-1410.
- Singh, N., Negi, N., Srivastava, K., Agarwal, G. (2016): A cohort study of vulvar cancer over a period of 10 years and review of literature, *Indian Journal of Cancer*, 53 (3), 412-415.

- Skrzypulec-Plinta, V., Drosdzol-Cop, A., Skwara-Guzikowska, K. (2013). Zdrowa pochwa w okresie menopauzy - czy tylko estrogeny? *Przegląd Menopauzalny*, 12 (1), 40-42.
- Stachoń, A.J. (2013). Ocena odczuwania wybranych objawów w zależności od fazy klimakterium i charakteru menopauzy, *Przegląd Menopauzalny*, 12 (4), 315-320.
- Stadnicka, G., Łepecka-Klusek, C., Pilewska-Kozak, A. B., Jakiel, G. (2015). Psychosocial problems of women with stress urinary incontinence. *Annals of Agricultural Environmental Medicine*, 22 (3), 499-503.
- Stanisławska, J., Janikowska, K., Stachowska, M., Talarska, D., Drozd-Gajdus, E., Szewczyczak, M. (2016). Ocena wiedzy kobiet w zakresie profilaktyki raka piersi i raka szyjki macicy, *Problemy Higieny i Epidemiologii*, 97 (1), 38-44.
- Stec, M., Studzińska, N. (2014). Menopauza a problemy seksualne kobiet, *European Journal of Medical Technologies*, 1 (2), 54-59.
- Szkiela, M., Worach-Kardas, H., Marcinkowski, J.T. (2014). Nowotwór złośliwy piersi - epidemiologia, czynniki ryzyka, znaczenie profilaktyki pierwotnej i wtórnej, *Problemy Higieny i Epidemiologii*, 95 (2), 292-302.
- Szubert, M., Kwiatkowska-Wypych, P., Sikora, M., Szwalski, J., Suzin, J., Kowalczyk-Amico, K. (2014). Gruczołowy rak szyjki macicy czy rak endometrium-trudności w diagnostyce, *Current Gynecologic Oncology*, 12 (3), 239-244.
- Tang, Y.L., Zhu, L.Y., Li, Y., Yu, J., Wang, J., Zeng, X.X., Hu, K.X., Liu, J.Y., Xu, J.X. (2017). Metformin use is associated with reduced incidence and improved survival of endometrial cancer: a meta-analysis, *Bio Med Research International*, <https://doi.org/10.1155/2017/5905384>.
- Van Dijk, G.M., Kavousi, M., Troup, J., Franco, O.H. (2015). Health issues for menopausal women: the top 11 conditions have common solutions, *Maturitas*, 80 (1), 24-30.
- Varella, L.R, Bezerra da Silva, R., Eugênia de Oliveira, M.C., Melo, P.H., Maranhão, T.M., Micussi, MT. (2016). Assessment of lower urinary tract symptoms in different stages of menopause, *The Journal of Physical Therapy Science*, 28 (11), 3116-3121.
- Von Mach-Szczypiński, J., Stanosz, S., Kościuszkiewicz, J., Safranow, K. (2016). New aspects of postmenopausal osteoporosis treatment with micronized estradiol and progesterone, *Ginekologia Polska*, 87 (11), 739-744.
- Wang, Z., Zhang, A., Zhao, B., Gan, J., Wang, G., Gao, F., Liu, B., Gong, T., Liu, W., Edden, R.A. (2016): GABA+ levels in postmenopausal women with mild-to-moderate depression: A preliminary study, *Medicine (Baltimore)*, 95 (39), e4918, <https://doi.org/10.1097/MD.0000000000004918>.
- Wilczyński, M., Danielska, J., Dzieńiecka, M., Malinowski, A. (2015). The role of mRNA in endometrial cancer-with special consideration of mRNA 205, *Ginekologia Polska*, 86 (11), 856-861.

- Winczura, P., Senkus-Konefka, E., Jassem, J. (2013): Polish and international recommendations on the treatment of breast cancer. *Nowotwory, Journal of Oncology*, 63 (1), 58-65.
- Wojnowska, D. (2013): How to prevent menopausal consequences for skin? *Przegląd Menopauzalny*, 12 (1), 69-77.
- Woods, N.F., Mitchell, E.S. (2016). The Seattle Midlife Women's Health Study: a longitudinal prospective study of women during the menopausal transition and early postmenopause, *Women's Midlife Health*, 2 (1), 1-16.
- World Health Organization. (1996). Research on the menopause in the 1990s. Report of a WHO Scientific Group. *Technical Report Series 866*, Genewa.
- Zatoński, W. A., Sulkowska, U., Didkowska, J. (2015), Cancer epidemiology in Poland. *Nowotwory, Journal of Oncology*, 65 (3), 179-196.
- Zielniok, K., Gajewska, M., Motyl, T. (2014). Molekularne aspekty działania  $17\beta$ -estradiolu i progesteronu w komórkowych szlakach sygnałowych, *Postępy Higieny i Medycyny Doświadczalnej*, 68, 777-792.