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ABSTRACTS OF INTEREST

WOMENS HEALTH

#1 | 2025

HT is associated with reduced fracture risk after total hip arthroplasty

In postmenopausal women who are estrogen deficient, hormone therapy (HT) has been shown to improve fragility fracture risk. Because few studies have examined the relationship between HT and periprosthetic fracture (PPF) risk after total hip arthroplasty (THA), investigators retrospectively reviewed data from a large national database to determine the impact of HT use on 10-year PPF risk following THA. Women who underwent elective THA were identified and stratified based on preoperative (< 6 months) HT use. Those taking HT were propensity score matched at a 1:2 ratio to those who did not have a history of HT use based on age and Charlson Comorbidity Index score. In total, 21 220 patients were included.

Patients who were taking HT before THA, demonstrated a lower risk of PPF (hazard ratio, HR 0.8; 95%CI 0.6 to 0.9) within 10 years of THA, but a similar risk of all-cause revision surgery and revision for aseptic loosening. The HT cohort demonstrated lower odds of deep vein thrombosis (odds ratio, OR 0.7; 95%CI 0.6 to 1.0) and similar rates of pulmonary embolism.

Given these results, appropriate HT usage in patients may play a role in reducing periprosthetic fracture after THA.

Reference: Zhao AY, et al. Hormone Replacement Therapy in Postmenopausal Women Undergoing Total Hip Arthroplasty is Associated With Reduced 10-Year Periprosthetic Femoral Fracture Rate. J Arthroplasty 2024 Dec 21:S0883-5403(24)01323-8. http://doi.org/10.1016/j.arth.2024.12.020. Online ahead of print.

Review of menopause and management of menopausal symptoms

Menopause marks a significant transition in a woman's life, typically occurring between the ages of 46 and 55 years. It is characterised by the cessation of menstruation and a decline in ovarian function. This article provides a comprehensive overview of menopause, examining its physiological, psychological, and social dimensions. It explores the hormonal changes, including decreased levels of estrogen and progesterone, and how these changes contribute to common symptoms such as hot flushes, sleep disturbances, and mood fluctuations. Additionally, it highlights contemporary approaches to management, including lifestyle modifications and hormonal and non-hormonal therapies.

The article is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11663262/

Reference: Strelow B, et al. Menopause Decoded: What's Happening and How to Manage It. J Prim Care Community Health 2024 Jan-Dec:15:21501319241307460. http://doi.org/10.1177/21501319241307460.

Guideline on management of premature ovarian insufficiency

Premature ovarian insufficiency (POI) has a prevalence of approximately 3.5%. It presents a significant challenge to women's health, with far-reaching implications, both physically and emotionally. The potential implications include adverse effects on quality of life, on fertility, and on bone, cardiovascular, and cognitive health. Although hormone therapy (HT) can mitigate some of these effects, many questions still remain regarding the optimal management of POI. This document is an update of the previous guideline for the management of POI published in 2015. It provides recommendations on diagnosis; the different sequelae, including bone, cardiovascular, neurological and sexual function, fertility and general well-being; as well as treatment options, including HT. New recommendations have been added regarding the role of anti-Müllerian hormone (AMH) in the diagnosis of POI, fertility preservation, muscle health, and specific considerations for HT in iatrogenic POI. Additionally, the topic on complementary treatments was extended with specific focus on non-hormonal treatments and lifestyle management options. Significant changes from the previous 2015 guideline include the recommendations that only one elevated FSH >25 IU is required for diagnosis of POI, and guidance that AMH testing, repeat FSH measurement, and/or AMH may be required where there is diagnostic uncertainty. Recommendations were also updated regarding genetic testing, estrogen doses and regimens, use of the combined oral contraceptive and testosterone therapy. Women with lived experience of POI provided the recommendations on provision of care.

The guideline is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11631070

Reference: Panay N, et al. Evidence-based guideline: premature ovarian insufficiency. Climacteric 2024; 27(6):510-520.

No evidence of increased venous thromboembolism (VTE) risk associated with hormone therapy (HT)

There is little contemporary data from randomised clinical trials focusing on the effect of oral HT on VTE in women aged 50-60 years. Consequently, investigators retrospectively reviewed data from a

universal health insurance program in Taiwan and applied a target trial emulation framework to evaluate the association between HT and the risk of developing VTE among women of menopausal age.

They emulated a sequence of trials in which women aged 50-60 years with no previous history of HT, hysterectomy, gynaecologic disorders, or cardiovascular events were enrolled. Eligibility and HT use were evaluated monthly from 2011 to 2019. Eligible women were classified as either HT initiators or non-initiators for each consecutive month.

Of the 150 686 148 eligible person-trials (3 001 112 women), 192 215 initiators and 768 860 propensity score-matched non-initiators were included in the analysis. The average duration of the HT was 1.25 years. Over a median follow-up of 5.83 years, 3 334 women developed VTE. The estimated hazard ratio (HR) was 0.96 (95%CI 0.88 to 1.04) in the intention-to-treat analysis and 0.66 (95%CI 0.41 to 1.05) in per-protocol analysis. Thus, in the contemporary clinical setting, the study did not demonstrate an increased VTE risk associated with HT in women aged 50-60 years.

Reference: Yeh Y-C, et al. Hormone therapy and venous thromboembolism risk in women of menopausal age: a target trial emulation. Eur J Epidemiol 2024 Dec;39(12):1341-1351. http://doi.org/10.1007/s10654-024-01181-x.

Prior HT use is associated with better prognosis in women with breast cancer

To examine the characteristics and prognosis of breast cancer (BC) in patients who had received hormone therapy (HT), investigators analysed data from a total of 17 355 postmenopausal patients with BC included in the Korea Breast Cancer Society database (2000-2014). Among them, 21% had a history of HT use before BC diagnosis (HT group), while 79% had never received HT (non-HT group). The HT group exhibited an earlier pathologic stage, lower histologic and nuclear grades, and a higher rate of breast conservation surgery compared to the non-HT group. Furthermore, this group had a higher rate of screening participation and a greater proportion of patients with a normal or overweight body mass index (BMI). The prognosis of the HT group was significantly better than that of the non-HT group, with a 5-year overall survival rate of 94% versus 92%, respectively (hazard ratio, HR 0.7; 95%CI 0.61 to 0.81). Increased screening participation, longer HT duration, and a normal or overweight BMI as seen in the HT group were associated with a better prognosis.

The article is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11710908/

Reference: Kim CW, et al. Characteristics and Prognosis of Breast Cancer Patients With Prior Hormone Replacement Therapy: Insights From the Korean Breast Cancer Society Registry. J Breast Cancer 2024 Dec;27(6):383-394. http://doi.org/10.4048/jbc.2024.0186.

Review of oral health and management of oral conditions occurring due to menopause

Menopause, occurring typically between the ages of 45 and 55 years, marks the end of a woman's reproductive years and is characterised by the cessation of menstruation and a significant decline in estrogen and progesterone production. These hormonal changes impact various aspects of health, including oral health. This review explores the clinical implications of menopause on oral health and outlines preventive strategies.

Hormonal changes during menopause can lead to xerostomia (dry mouth), periodontal disease, burning mouth syndrome (BMS), oral mucosal changes, altered taste sensation, and osteoporosis-related oral health issues. Xerostomia results from decreased salivary flow, increasing the risk of dental caries and oral infections. Periodontal disease is exacerbated by estrogen deficiency, leading to bone loss and increased tooth mobility. BMS, characterised by a chronic burning sensation, and oral mucosal atrophy are linked to hormonal fluctuations. In addition, altered taste perception and osteoporosis further complicate oral health management.

Effective prevention and management strategies include regular dental check-ups, good oral hygiene practices, and tailored treatments such as fluoride treatments, saliva substitutes, and hormone therapy. Nonpharmacological approaches, such as stress management and lifestyle modifications, also play a role. This review emphasises the importance of a multidisciplinary approach, involving dental and medical professionals, to address the complex oral health challenges faced by menopausal women. Understanding the underlying mechanisms and implementing evidence-based preventive measures can significantly enhance the oral health and overall well-being of menopausal women.

The article is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11601932/

Reference: Shrivastava S. Menopause and Oral Health: Clinical Implications and Preventive Strategies. J Midlife Health 2024 Jul-Sep;15(3):135-141. http://doi.org/10.4103/jmh.jmh_125_24.

EMAS Guideline for management of CKD after menopause

The risk of kidney disease increases with age. After menopause, ovarian senescence and the loss of estrogen's renoprotective effects are directly associated with a decline in renal function and indirectly with an accumulation of cardiometabolic risk factors. The latter can predispose to the development of chronic kidney disease (CKD). Conversely, CKD diagnosed during reproductive life adversely affects ovarian function. Both menopause and CKD have a significant impact on cardiovascular and bone health. This position statement from the European Menopause and Andropause Society (EMAS) aims to guide clinicians in providing an individualised approach to menopause management in women with CKD.

Menopause hormone therapy (HT) can be given to women with CKD. The main indication for HT is vasomotor symptoms, but protection of kidney function could be considered as an additional indication for HT in women with primary ovarian insufficiency or early menopause. The regimen should be selected on the basis of patient preference and the individual's cardiovascular risk. Topical, rather than systemic, estrogens are preferred for women at high or very high cardiovascular risk.

No HT dosing studies are available for women with CKD or renal transplant recipients and so the dose of hormonal and non-hormonal preparations should be adjusted in accordance with the patient's creatinine clearance. However, recommended doses of systemic estradiol for women with CKD are 50% to 70% lower than for those with normal kidney function. Women treated with calcineurin inhibitors such as cyclosporine and tacrolimus should

have their estradiol levels closely monitored after initiation of HT.

The management of a postmenopausal woman with CKD should focus on lifestyle advice as well as regular monitoring of the main cardiovascular risk factors and evaluation of bone mineral density. Tailored multidisciplinary advice should be given to women with comorbidities such as diabetes, dyslipidaemia, and hypertension. Management of osteoporosis should be based on the severity of the CKD. Non-hormonal treatments for hot flushes and osteoporosis are not contraindicated in women with CKD.

The guideline is available at https://www.maturitas.org/article/S0378-5122(24)00240-8/fulltext

Reference: Cevik EC, et al. Chronic kidney disease and menopausal health: An EMAS clinical guide. Maturitas 2025 Jan:192:108145. http://doi.org/10.1016/j.maturitas.2024.108145.

Does menopausal HT reduce the risk of dementia?

Despite a large preclinical literature demonstrating neuroprotective effects of estrogen, use of menopausal hormone therapy (HT) to reduce the risk of Alzheimer's disease (AD) has been controversial. Investigators conducted a systematic review and meta-analysis of HT effects on AD and dementia risk which included data from 6 randomised clinical trials (RCTs) with 21 065 treated and 20 997 placebo participants and 45 observational reports with 768 866 patient cases and 5.5 million controls.

RCTs trials conducted in postmenopausal women ages 65 and older show an increased risk of dementia with HT use compared with placebo (relative risk, RR 1.38, 95%CI 1.16 to 1.64). This was driven by estrogen plus progestogen therapy (EPT) (RR 1.64, 95%CI 1.20 to 2.25), whereas there was no significant association between estrogen-only therapy (ET) and dementia (RR 1.19, 95%CI 0.92 to 1.54). Conversely, observational studies indicated a significant 22% reduced risk of AD (RR 0.78, 95%CI 0.64 to 0.95) and 19% reduced risk of all-cause dementia (RR 0.81, 95%CI 0.70 to 0.94) with HT use, with protective effects noted with ET (RR 0.86, 95%CI 0.77 to 0.95), but not with EPT (RR 0.91, 95%CI 0.78 to 1.07). Stratified analysis of pooled estimates indicates a 32% reduced risk of dementia with midlife ET (RR 0.68, 95%CI 0.51 to 0.92) and non-significant reductions with midlife EPT (RR 0.78, 95%CI 0.47 to 1.27). Late-life HT use was associated with a signal for increased risk, which was not statistically significant (EPT: RR 1.32, 95%CI 0.98 to 1.79; ET: RR 1.07, 95%CI 0.10 to 1.14).

The article is available at https://www.frontiersin.org/journals/aging-neuroscience/articles/10.3389/fnagi.2023.1260427/full

Reference: Nerattini M, et al. Systematic review and meta-analysis of the effects of menopause hormone therapy on risk of Alzheimer's disease and dementia. Front Aging Neurosci 2023 Oct 23:15:1260427. http://doi.org/10.3389/fnagi.2023.1260427.

Does menopausal HT affect cognitive function?

Findings from the Kronos Early Estrogen Prevention Study (KEEPS)-Cog trial suggested no cognitive benefit or harm after 48 months of menopausal hormone therapy (HT) initiated within 3 years of final menstrual period. To clarify the long-term effects of HT initiated in early postmenopause, the observational KEEPS Continuation Study re-evaluated cognition, mood, and neuroimaging effects in participants enrolled in the KEEPS-Cog and its parent study the KEEPS approximately 10 years after trial completion. The investigators hypothesised that women randomised to transdermal estradiol (tE2) during early postmenopause would show cognitive benefits, while oral conjugated equine estrogens (oCEE) would show no effect, compared to placebo over the 10 years following randomisation in the KEEPS trial.

The KEEPS-Cog (2005-2008) was an ancillary study to the KEEPS, in which participants were randomised into 3 groups: oCEE (0.45 mg/day), tE2 (50 µg/day) both with micronized progesterone (200 mg/day for 12 days per month) or placebo pills and patch for 48 months. KEEPS Continuation (2017-2022), an observational, longitudinal cohort study of KEEPS clinical trial, involved recontacting KEEPS participants approximately 10 years after the completion of the 4-year clinical trial to attend in-person research visits. Seven of the original 9 sites participated in the KEEPS Continuation, resulting in 622 women of original 727 being invited to return for a visit, with 299 enrolling across the 7 sites. KEEPS Continuation participants repeated the original KEEPS-Cog test battery, which was analysed using 4 cognitive factor scores and a global cognitive score. Cognitive data from both KEEPS and KEEPS Continuation were available for 275 participants. Statistical models were used to assess whether baseline cognition and cognitive changes during KEEPS predicted cognitive performance at follow-up, and whether randomisation to HT modified these relationships, after adjusting for covariates. Similar health characteristics were observed at KEEPS randomization for KEEPS Continuation participants and nonparticipants (i.e., women not returning for the KEEPS Continuation).

Analysis of the cognitive performance data indicated that, across almost all domains, cognitive factor scores changed over time. Tests assessing the effects of HT allocation on cognitive outcomes during the KEEPS and across all years of follow-up including the KEEPS Continuation visit were all statistically nonsignificant. The KEEPS Continuation study found no long-term cognitive effects of HT, with baseline cognition and changes during KEEPS being the strongest predictors of later performance. Cross-sectional comparisons confirmed that participants assigned to HT in KEEPS (oCEE and tE2 groups) performed similarly on cognitive measures to those randomised to placebo, approximately 10 years after completion of the randomised treatments. These findings suggest that short-term exposure to HT started in early menopause poses no long-term cognitive harm; conversely, it provides no cognitive benefit or protective effects against cognitive decline.

The article is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11581397/

Reference: Gleason CE, et al. Long-term cognitive effects of menopausal hormone therapy: Findings from the KEEPS Continuation Study. PLoS Med 2024 Nov 21;21(11):e1004435. http://doi.org/10.1371/journal.pmed.1004435.

Review of pathophysiology and treatment of osteoporosis due to hormone deficiency

Primary osteoporosis is closely linked to hormone deficiency, which disrupts the balance of bone remodelling. It affects postmenopausal women, but also significantly impacts older men. Estrogen can promote the production of osteoprotegerin, a decoy receptor for RANKL, thereby preventing RANKL from

activating osteoclasts. Furthermore, estrogen promotes osteoblast survival and function via activation of the Wnt signalling pathway. Likewise, androgens play a critical role in bone metabolism, primarily through their conversion to estrogen in men. Estrogen deficiency accelerates bone resorption through a rise in pro-inflammatory cytokines (IL-1, IL-6, TNF-α) and RANKL, which promote osteoclastogenesis. In the classic genomic pathway, estrogen binds to estrogen receptors in the cytoplasm, forming a complex that migrates to the nucleus and binds to estrogen response elements on DNA, regulating gene transcription. Androgens can be defined as high-affinity ligands for the androgen receptor; their combination can serve as a ligand-inducible transcription factor.

Hormone therapy has shown promise, but comes with associated risks and side effects. In contrast, the non-genomic pathway involves rapid signalling cascades initiated at the cell membrane, influencing cellular functions without directly altering gene expression. Therefore, the ligand-independent actions and rapid signalling pathways of estrogen and androgen receptors can be harnessed to develop new drugs that provide bone protection without the side effects of traditional hormone therapies. To manage primary osteoporosis, other pharmacological treatments (bisphosphonates, teriparatide, RANKL inhibitors, sclerostin inhibitors, SERMs, and calcitonin salmon) can ameliorate osteoporosis and improve bone mineral density via actions on different pathways. Non-pharmacological treatments include nutritional support and exercise, as well as the dietary intake of antioxidants and natural products.

This article reviews the processes of bone remodelling, hormone actions, hormone receptor status, and therapeutic targets of primary osteoporosis.

The article is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11593909/

Reference: Hsu S-H, et al. Primary Osteoporosis Induced by Androgen and Estrogen Deficiency: The Molecular and Cellular Perspective on Pathophysiological Mechanisms and Treatments. Int J Mol Sci 2024 Nov 12;25(22):12139. http://doi.org/10.3390/ijms252212139.

What is the optimum blood pressure for older women?

The relationship between systolic blood pressure (SBP) and longevity is not fully understood. To determine which SBP levels in women ≥65 years of age with or without blood pressure medication were associated with the highest probability of surviving to 90 years of age, investigators examined results from 16 570 participants enrolled in the Women's Health Initiative who were eligible to survive to 90 years of age by February, 2020, without a history of cardiovascular disease, diabetes, or cancer. Blood pressure was measured at baseline (between 1993 and 1998) and then annually until 2005. The outcome was defined as survival to 90 years of age with follow-up.

During a median follow-up of 19.8 years, 59% of the women survived to 90 years of age. Women with an SBP between 110 and 130 mmHg at attained ages of 65, 70, 75, and 80 years had a 38%, 54%, 66%, or 75% absolute probability to survive to 90 years of age, respectively. The probability of surviving to 90 years of age was lower for higher SBP levels. Women at the attained age of 80 years with 0%, 20%, 40%, 60%, 80%, or 100% time in therapeutic range (defined as an SBP between 110 and 130 mmHg) had a 66%, 68%, 71%, 73%, 75%, or 77% absolute survival probability to 90 years of age.

In conclusion, for women older than 65 years of age with low cardiovascular disease and other chronic disease risk, an SBP level <130 mmHg was found to be associated with longevity. These findings reinforce current guidelines targeting an SBP target <130 mmHg in older women.

Reference: Haring B, et al. Systolic Blood Pressure and Survival to Very Old Age: Results From the Women's Health Initiative. Circulation 2024 May 14;149(20):1568-1577. http://doi.org/10.1161/CIRCULATIONAHA.123.067302.

Postmenopausal women taking antidepressants have worse physical function

To examine cross-sectional and longitudinal relationships of psychotropic medications with physical function after menopause, investigators analysed data from 4 557 postmenopausal women participating in the Women's Health Initiative Long Life Study (WHI-LLS). The mean age at enrolment into the study (during 1993-1998) was 62.8 years. Antidepressant, anxiolytic, and sedative/hypnotic medications were evaluated at WHI enrolment and at 3-year follow-up visits. Performance-based physical function (Short Physical Performance Battery [SPPB]) was assessed at the 2012-2013 WHI-LLS visit. Self-reported physical function (RAND-36) was examined at WHI enrolment and the last available follow-up visit, was at an average of 22 [±2.8] (range: 12-27) years post-enrolment. Results were adjusted to control for confounders, including socio-demographic, lifestyle, and health characteristics.

Anxiolytics were not related to physical function. Antidepressant use at WHI enrolment was cross-sectionally related to worse self-reported physical function at enrolment, and also with worse performance-based physical function (SPPB) at the 2012-2013 WHI-LLS visit some 20 years later. Compared to non-users, those using sedative/hypnotics at WHI enrolment but not at the 3-year follow-up visit reported a faster decline in physical function between WHI enrolment and follow-up visits. The significance of this latter finding is uncertain.

Reference: Beydoun HA, et al. Relationship of psychotropic medication use with physical function among postmenopausal women. Geroscience 2024 Dec;46(6):5797-5817. http://doi.org/10.1007/s11357-024-01141-z.

What are the benefits of calcium and vitamin D supplementation in postmenopausal women?

Although calcium and vitamin D (CaD) supplementation may affect chronic disease in older women, evidence of long-term effects on health outcomes is limited. Therefore, investigators did a post-hoc analysis of long-term post-intervention follow-up of the 7-year randomised intervention trial of CaD in the Women's Health Initiative CaD trial. In this study, 36 282 postmenopausal women with no history of breast or colorectal cancer were randomly assigned to 1 000 mg of calcium carbonate (400 mg of elemental calcium) with 400 IU of vitamin D3 daily or placebo. Outcomes of interest included incidence of colorectal, invasive breast, and total cancer; disease-specific and all-cause mortality; total cardiovascular disease (CVD); and hip fracture.

In comparison to those taking placebo, after a median cumulative follow-up of 22.3

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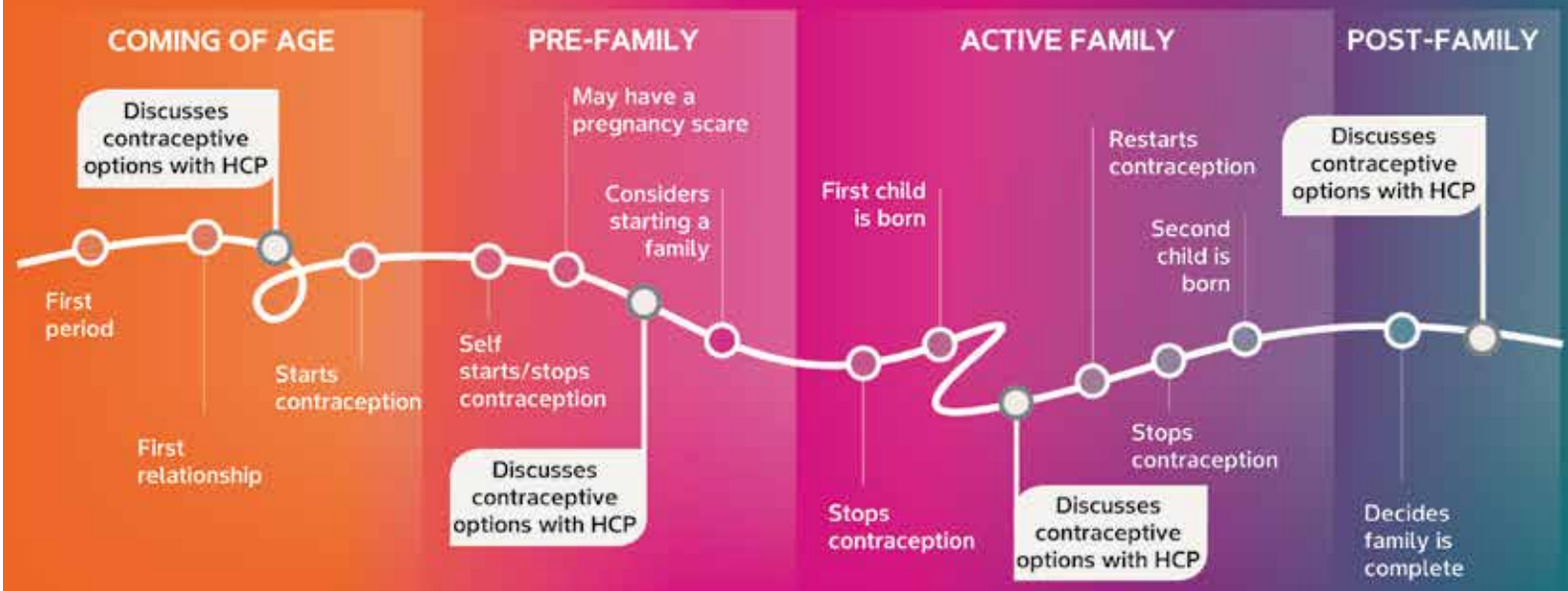

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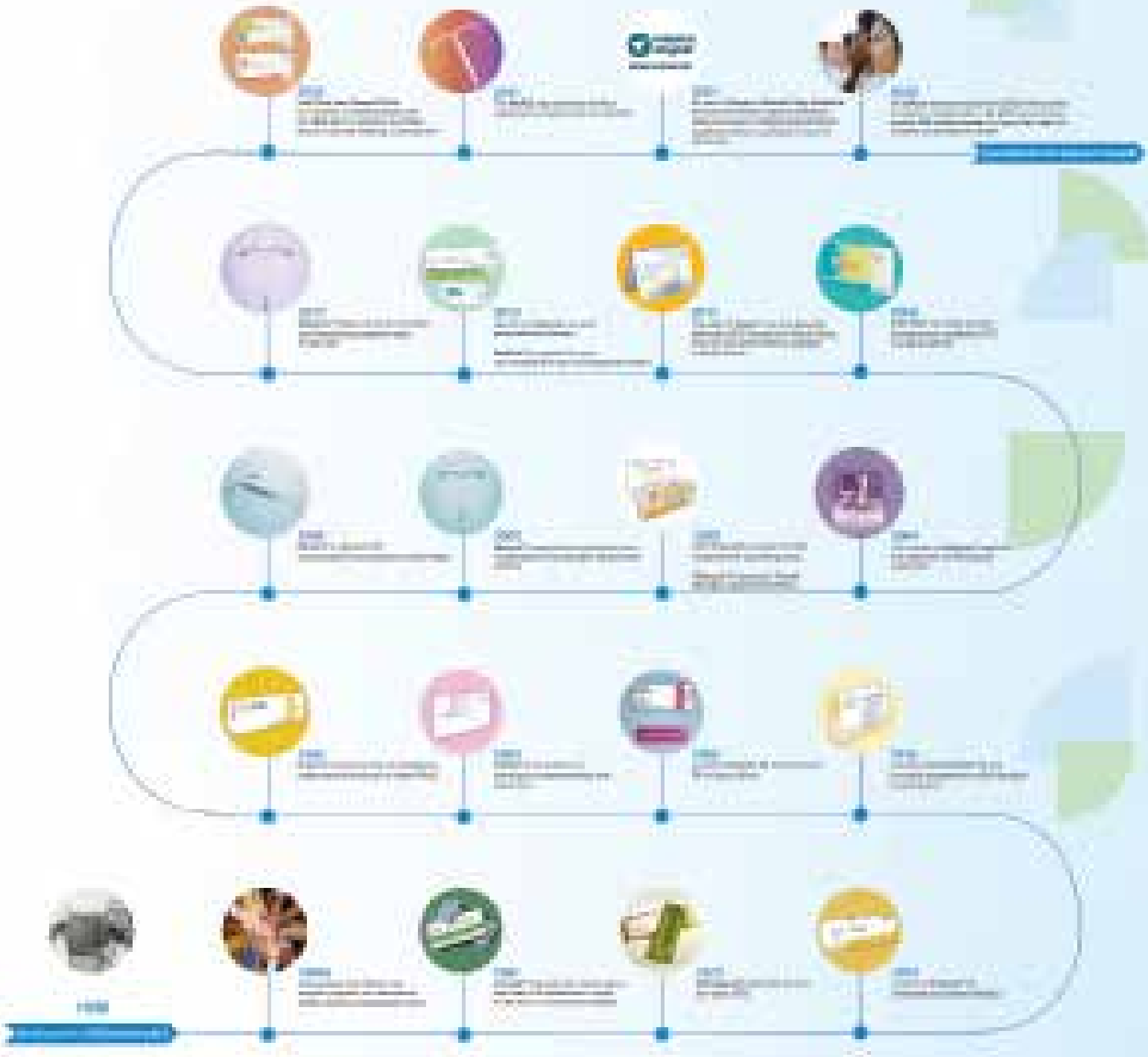

years, women assigned to CaD had a significant 7% reduction in cancer mortality (1 817 vs. 1 943 deaths; hazard ratio, HR 0.93, 95%CI 0.87 to 0.99), along with a 6% increase in CVD mortality (2 621 vs. 2 420 deaths; HR 1.06, 95%CI 1.01 to 1.12). There was no overall effect on other measures, including all-cause mortality. Estimates for cancer incidence varied widely when stratified by whether participants reported supplement use before randomisation, whereas estimates on mortality did not vary, except for CVD mortality.

In conclusion, calcium and vitamin D supplements seemed to reduce cancer mortality and increase CVD mortality after more than 20 years of follow-up among postmenopausal women, with no effect on all-cause mortality.

Reference: Thomson CA, et al. Long-Term Effect of Randomization to Calcium and Vitamin D Supplementation on Health in Older Women: Postintervention Follow-up of a Randomized Clinical Trial. Ann Intern Med 2024 Apr;177(4):428-438. http://doi.org/10.7326/M23-2598.

Review on HT in menopausal women and its relationship to pulmonary hypertension

Pulmonary hypertension (PH) is a multifactorial condition that encompasses a group of diseases characterised by a progressive increase in pulmonary vascular resistance and pulmonary arterial pressure, ultimately leading to right heart failure and death. It occurs more frequently in females than in males, yet women tend to exhibit better outcomes and survival rates. The primary goals of PH treatment are to lower pulmonary arterial pressure, alleviate symptoms such as shortness of breath and chest pain, address modifiable risk factors, and manage the underlying cause, often a common advanced disease like chronic obstructive lung disease or left heart disease. While sex is an unchangeable risk factor for PH development, the presence or absence of estrogens has a significant influence on its progression. Hormone therapy (HT) is the recommended form of estrogen therapy for postmenopausal women, but only in carefully selected cases. However, a paradox arises for women with PH, because some studies emphasise the detrimental effects of estrogen in HT, suggesting that it may contribute to the progression of PH, while others highlight its beneficial role in promoting right ventricle dilation and improving lung vasculature. While preliminary studies have shown promising data indicating that HT may improve outcomes in women with PH, there is currently a lack of placebo-controlled or randomised controlled trials comparing standard therapies with HT. Consequently, no consensus has been established regarding the use of HT in this context. This review provides a comprehensive analysis of the literature on the role of HT in PH.

The article is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11576071

Reference: Gill NK, et al. Hormone Replacement Therapy and Pulmonary Hypertension: A Review of the Literature. Cureus 2024 Oct 20;16(10):e71908. http://doi.org/10.7759/cureus.71908.

Does the type of progestin affect efficacy and tolerability of oral contraceptives when coadministered with psychotropic drugs?

To assess the risk of contraceptive failure and adverse events associated with the type of progestin when coadministered with psychotropic drugs within a routine clinical practice setting, investigators performed a pooled analysis of four large, prospective, multinational cohort studies including women with a new prescription of combined oral contraceptives (COCs) and concomitant psychotropic drug use from 13 European countries and the United States. They evaluated the frequency of contraceptive failures and adverse events within 6 months after COC initiation by progestin type in a total of 7 679 COC users reporting psychotropic drug use at baseline. Results were corrected for potential confounders including age, body mass index, smoking, medical history, history of hormonal contraceptive use, and education level.

The most common progestin type was drospirenone (30%) followed by norethisterone acetate/norethindrone acetate (21%), levonorgestrel (17%), norgestimate (12%), norethindrone (6%), nomegestrol/nomegestrol acetate (6%), desogestrel (5%), and dienogest (4%). Overall, 39 (0.5%) contraceptive failures and 156 (2.0%) adverse events occurred within the first 6 months of follow-up. Comparisons of the different progestins using levonorgestrel as the reference showed a significantly lower risk of adverse events with drospirenone (weighted incidence rate ratio 0.5, 95%CI 0.3 to 0.9), while no difference was observed for other progestins.

In conclusion, among women using psychotropic drugs, drospirenone was associated with a lower risk of adverse events compared to levonorgestrel, while other progestins showed no significant differences. The number of contraceptive failures was low across progestins.

Reference: Boehnke T, et al. Impact of progestin type on the risk of drug interactions between combined oral contraceptives and psychotropic drugs: A pooled analysis of real-world data. Contraception 2024 Dec 19:110786. http://doi.org/10.1016/j.contraception.2024.110786. Online ahead of print.

Education and support are essential to assist women to quit smoking

Smoking while using contraception containing ethinylestradiol increases the risk of cardiovascular diseases. Therefore, it is especially important to encourage women who use these contraceptives to quit smoking. This study aimed to examine the role of risk perception and coping in relation to the intention of women to quit smoking. Sixty eight women completed an online survey which evaluated the relationship between risk perception, coping assessment, and intention to quit smoking. After that, fifteen in-depth semi-structured interviews were conducted to understand how women appraised risk and coping strategies during their quit attempt(s).

Results from the survey showed that risk perception induces the intention to quit smoking. More specifically, a high level of perceived vulnerability, high education level and using the contraceptive method specifically to control the menstrual cycle were associated with greater intention to quit. The interviews showed that women were largely unfamiliar with the combined risks associated with smoking and contraception use, although they did acknowledge the health risks of smoking. In the survey, women seemed to perceive themselves as self-efficacious. Wanting to improve their physical condition, and improve smell and taste were mentioned as reasons for wanting to quit. However, interview participants mentioned that they encountered many difficulties. Social events, withdrawal symptoms and stressful moments at work were identified as specific challenges to successful quitting. Maintaining abstinence from smoking was perceived as easier if there was a good

reason to quit smoking, such as being pregnant or having medical issues. Some ways that the women had found had enhanced their sense of self-efficacy included enlisting support from others, using distractions, chewing gum or sucking sweets, acupuncture, nicotine patches and e-cigarettes.

The findings of this study are that women are largely unaware of the synergetic risk of contraception use and smoking. Education to increase knowledge about these health risks might help women to create the intention to quit smoking. However, to turn this intention into behaviour, providing women with concrete tools to assist them with smoking cessation would be helpful to promote successful quitting and sustained abstinence from smoking.

The article is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11653449

Reference: Hilverda F, et al. Smoking and contracep tion containing ethinylestradiol: A mixed-methods study into women's intentions to quit smoking. Womens Health (Lond) 2024 Jan-Dec:20:17455057241307085. http://doi.org/10.1177/17455057241307085.

Short-term adherence to a ketogenic diet might be helpful for patients with PCOS

To evaluate the clinical effects of a ketogenic diet versus a traditional comprehensive intervention, including lifestyle changes and oral contraceptives, in women with polycystic ovary syndrome (PCOS) who were overweight or obese, investigators performed a retrospective analysis of data from 70 patients with body mass index (BMI) ≥24 kg/m^2 who had received treatment for PCOS. The patients were categorised into two groups based on their past treatment modality: Group 1 received treatment with a ketogenic diet (N = 35), and Group 2 underwent comprehensive intervention (N = 35), with both treatments lasting 3 months. Changes in body weight, BMI, sex hormone levels, glucose-lipid metabolism indicators, and liver and kidney function were compared.

Both groups experienced significant reductions in body weight and BMI after treatment, with the ketogenic diet group showing a greater reduction. Luteinizing hormone (LH), LH/follicle-stimulating hormone (FSH), and total testosterone levels decreased significantly in both groups. The ketogenic diet treatment led to significant reductions in fasting blood glucose, fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), triglyceride, alanine aminotransferase (ALT), and aspartate aminotransferase (AST), while the comprehensive intervention resulted in decreased fasting blood glucose and ALT, and increased high-density lipoprotein-cholesterol. In addition, the ketogenic diet group had a greater reduction in fasting blood glucose, and showed decreases in triglycerides and AST, which remained unchanged in the comprehensive intervention group.

The study indicates that the short-term ketogenic diet treatment provides significant weight loss and effectively improves hormone regulation and glucose-lipid metabolism in overweight or obese PCOS patients, offering a valuable therapeutic option for managing the condition.

Reference: Li M, et al. Impact of short-term ketogenic diet on sex hormones and glucose-lipid metabolism in overweight or obese patients with polycystic ovary syndrome. J Obstet Gynaecol Res 2025 Jan;51(1):e16178. http://doi.org/10.1111/jog.16178.

Review on comparative VTE risk with contraceptives and patient management

Hormonal contraceptive therapy (estrogens and/or progestogens) includes different formulations associated with varying venous thromboembolism (VTE) risks. The thrombogenicity of combined hormonal contraceptives (CHCs) is due at least in part to multiple changes in clotting factors and the vasculature and is dependent on both estrogen dose and type of progestin. Transdermal patch and vaginal ring users have similar or higher VTE risk than women using combined oral contraceptives. Progestin-only agents have varying VTE risk. While depot medroxyprogesterone acetate appears to increase VTE risk, the levonorgestrel-based intrauterine system and low-dose progestin-only pills have no additional VTE risk. There are less data for the subdermal progestin-only implant. This article reviews contraceptive-related VTE risk by agent and by clinical scenario, including in patients with inherited thrombophilia, systemic lupus erythematosus with or without antiphospholipid antibodies or antiphospholipid syndrome, and sickle cell disease. Relevant clinical practice guidelines are reviewed. A multidisciplinary approach to counselling is needed for patient-focused decision-making.

The article is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11665608/

Reference: Skeith L, Bates SM. Estrogen, progestin, and beyond: thrombotic risk and contraceptive choices. Hematology Am Soc Hematol Educ Program 2024 Dec 6;2024(1):644-651. http://doi.org/10.1182/hematology.2024000591.

Contraceptives and reproductive cancer risk

Contraceptives play a crucial role in women's reproductive health, their hormonal components may be linked to cancer risks, specifically breast and gynaecological cancers. Given the high usage rates of hormonal contraceptives, it is vital to systematically evaluate their potential impact on cancer outcomes, especially among women with a family history of gynaecological cancers. To evaluate the evidence on the association between modern contraceptive use and the risk of breast and reproductive cancers (ovarian, endometrial, and cervical cancer) among women of reproductive age, investigators performed a systematic review and meta-analysis using data from 51 studies (2 randomised controlled studies and 49 observational studies).

The review identified a significant reduction in ovarian and endometrial cancer incidence among contraceptive users. Hormonal contraceptive users had a 36% lower risk of ovarian cancer (relative risk, RR 0.64, 95%CI 0.60 to 0.68), with specific reductions associated with combined oral contraceptives (RR 0.62, 95%CI 0.57 to 0.68) and hormonal intra-uterine devices (IUD) (RR 0.68, 95%CI 0.48 to 0.96). When the results were pooled, the rate ratio of cervical cancer was higher among non-users compared to those using hormonal contraceptives (RR 1.28, 95% CI 1.21 to 1.35). However, stratification of the results indicated a significant increased risk of cervical cancer associated with oral contraceptives (RR 1.43, 95%CI 1.31 to 1.56) and any users of oral and non-oral contraceptives (RR 1.19, 95%CI 1.10 to 1.29). There was no apparent association between cervical cancer risk and the IUD (RR = 0.76, 95% CI 0.52 to 1.11). In a comparison between non-users and hormonal IUD users, the risk ratio was 0.58 (95%CI 0.42 to 0.79).

No significant association was found between contraceptive use and breast cancer risk among healthy women (RR 1.00, 95% CI 0.94 to 1.06). However, there was an increased risk of breast cancer among BRCA1/2 mutation carriers using oral contraceptives (hazard ratio, HR 1.39, 95% CI 1.15 to 1.67).

This systematic review highlights the protective effects of modern contraceptives against ovarian and endometrial cancers while identifying a potentially increased risk of cervical cancer. No significant breast cancer risk was found for healthy women, but BRCA1/2 mutation carriers faced increased risks. These findings underscore the need for personalised contraceptive counselling that considers cancer risk factors.

The article is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11599208/

Reference: Jahanfar S, et al. Assessing the impact of contraceptive use on reproductive cancer risk among women of reproductive age-a systematic review. Front Glob Womens Health 2024 Nov 13:5:1487820. http://doi.org/10.3389/fgwh.2024.1487820.

Review of hormonal therapies for management of acne

Acne impairs quality of life, often leads to permanent scars, and causes psychological distress. This review is a comprehensive update on the Federal Drug Administration (FDA)-approved and off-label use of combined oral contraceptives (COC), clascoterone, spironolactone, and emerging hormonal therapies for acne treatment, and it discusses common patient concerns, barriers to care, and individualised care needs.

Hormonal therapies are essential strategies to treat acne. Acne treatment tailored to patient preferences and comorbidity profiles will promote treatment adherence and the safe use of hormonal therapies. Different brands and doses of COC have generally similar efficacy in treating acne. Clinicians should discuss contraceptive options and provide individualised shared decision-making with patients based on their preferences, contraceptive needs, comorbidity profile, access, and cost. Spironolactone is an effective acne treatment with clinical trial data to support its use as a first-line acne treatment for women with acne. Potassium monitoring is of low value for patients on spironolactone unless patients have specific risk factors for hyperkalaemia. Clascoterone is a safe and effective topical anti-androgen for the treatment of acne in men and women with limited systemic effects on reproductive hormones.

The article is available at https://link.springer.com/article/10.1007/s13555-024-01324-8

Reference: Smith CA, et al. Hormonal Therapies for Acne: A Comprehensive Update for Dermatologists. Dermatol Ther (Heidelb) 2025 Jan 3. 15:45-59. http://doi. org/10.1007/s13555-024-01324-8. Online ahead of print.

How do the copper IUD and levonorgestrel IUS compare in terms of efficacy and safety?

Globally, approximately 19% of women of reproductive age use intrauterine contraception, encompassing both copper intrauterine devices (Cu-IUDs) and levonorgestrel intrauterine systems (LNG-IUDs). Despite current guidelines endorsing intrauterine contraception as a primary method, there remains debate regarding device selection. Notably, the lack of data regarding reasons for discontinuation has limited previous meta-analyses. Consequently, to comprehensively evaluate the potential differences between intrauterine devices using available multinational data, investigators performed a systematic review and meta-analysis of data from 20 randomised controlled trials comparing Cu-IUDs and LNG-IUDs. The primary outcome was pregnancy, with secondary outcomes encompassing continuation, reasons for discontinuation, expulsion, satisfaction, and other adverse events.

Compared to Cu-IUDs, LNG-IUDs were associated with lower risks of pregnancy (Risk Ratio, RR 0.22, 95%CI 0.12 to 0.39), ectopic pregnancy (RR 0.12, 95%CI 0.03 to 0.47), discontinuation due to increased bleeding (RR 0.49, 95%CI 0.28 to 0.85), increased bleeding (RR 0.42, 95%CI 0.25 to 0.7), heavy bleeding (RR 0.41, 95%CI 0.22 to 0.75), and dysmenorrhea (RR 0.41, 95%CI 0.34 to 0.48). However, LNG-IUDs were associated with a higher risk of discontinuation due to amenorrhea (RR 21.05, 95%CI 8.83 to 50.00). When comparing LNG (52 mg) IUD with copper (380 mm^2) IUD, the LNG-IUD showed a lower risk of discontinuation due to increased bleeding (RR 0.68, 95%CI 0.55 to 0.58) and dysmenorrhea (RR 0.42, 95%CI 0.34 to 0.53), but a higher risk of discontinuation due to bleeding issues (RR 2.83, 95%CI 2.47 to 3.25) and amenorrhea (RR 5.92, 95%CI 2.81 to 12.49). There were no significant differences between the two in terms of continuation, expulsion, non-medical reasons for discontinuation, satisfaction, and other adverse outcomes.

The study indicates that LNG-IUDs and Cu-IUDs are both highly effective contraceptive methods. Compared to Cu-IUDs, LNG-IUDs were associated with a lower risk of pregnancy and adverse reactions. However, LNG-IUDs carry a higher risk of amenorrhea. When recommending contraceptive methods, healthcare providers should fully inform patients of these potential risks and consider their preferences.

The article is available at https://pmc.ncbi.nlm.nih.gov/articles/PMC11602564/

Reference: Liu P, et al. Contraception with levonorge strel-releasing intrauterine system versus copper in trauterine device: a meta-analysis of randomized con trolled trials. EClinicalMedicine 2024 Nov 12:78:102926. http://doi.org/10.1016/j.eclinm.2024.102926.

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JOURNAL SURVEILLANCE NETWORK WOMENS HEALTH

CPD QUESTIONNAIRE #1 2025

UNIVERSITY OF PRETORIA ACCREDITATION NUMBER: PENDING - ? POINTS

CHOOSE WHICH OF THE FOLLOWING STATEMENTS IS MOST CORRECT

1. **Among postmenopausal women who underwent total hip arthroplasty, compared with those who did not receive hormone therapy (HT), those who did receive HT had**
   a. A lower risk of periprosthetic fracture, but no difference in risk of all-cause revision surgery.
   b. A lower risk of periprosthetic fracture, and increased risk of aseptic loosening.
   c. No difference in risk of periprosthetic fracture, but lower risk of aseptic loosening.
   d. A lower risk of all-cause revision surgery.

2. **Diagnosis of premature ovarian insufficiency requires**
   a. One test to demonstrate elevated FSH >25 IU.
   b. One test to demonstrate elevated testosterone and low estrogen.
   c. At least two tests on two occasions one month apart to demonstrate elevated FSH >5 IU.
   d. At least three tests, each at different stages of a single ovulatory cycle.

3. **Among women with breast cancer, compared to those who did not receive postmenopausal HT, those who did receive postmenopausal HT exhibited**
   a. Later pathologic stage.
   b. Lower histologic grade.
   c. Higher nuclear grade.
   d. Lower rate of breast conservation surgery.

4. **Which of the following is true of menopausal HT in women with CKD?**
   a. HT is contraindicated in women with CKD.
   b. In women with primary ovarian insufficiency, HT is considered to be renoprotective.
   c. Oral HT is preferred in women with CKD at very high CV risk.
   d. Recommended doses of systemic estradiol for women with CKD are the same as for those with normal kidney function.

5. **In observational studies,**
   a. Estrogen-only hormone therapy (EHT) and estrogen plus progestogen therapy (EPT) were associated with significantly reduced risks of AD and all-cause dementia.
   b. ET and EPT were associated with significantly increased risks of AD and all-cause dementia.
   c. ET, but not EPT was associated with significantly reduced risks of AD and all-cause dementia.
   d. EPT, but not ET was associated with significantly reduced risks of AD and all-cause dementia.

6. **Short-term exposure to HT started in early menopause poses no long-term cognitive harm; conversely, it provides no cognitive benefit or protective effects against cognitive decline.**
   a. True.
   b. False.

7. **Which of the following is true of hormones and bone health?**
   a. Estrogen can promote the production of osteoprotegerin.
   b. Estrogen inhibits osteoblast survival and function via activation of the Wnt signalling pathway.
   c. Estrogen deficiency inhibits bone resorption.
   d. HT promotes production of IL 1, which is an anti-inflammatory cytokine.

8. **Which SBP threshold was found to be associated with longevity in older women?**
   a. SBP <110 mmHg.
   b. SBP <130 mmHg.
   c. SBP between 110 mmHg and 140 mmHg.
   d. SBP between 120 mmHg and 140 mmHg.

9. **In postmenopausal women**
   a. Use of anxiolytics was associated with worse self-reported physical function.
   b. Use of anxiolytics was associated with improved self-reported physical function.
   c. Use of antidepressants was associated with worse self-reported physical function.
   d. Use of antidepressants was associated with improved self-reported physical function.

10. **In comparison to those taking placebo, after a median cumulative follow-up of 22.3 years, postmenopausal women taking calcium and vitamin D supplementation had a significant**
    a. Reduction in cancer mortality and CVD mortality.
    b. Reduction in cancer mortality and increase in CVD mortality.
    c. Increase in cancer mortality and reduction in CVD mortality.
    d. Increase in cancer mortality and CVD mortality.

11. **In women taking psychotropic drugs and COCs, which of the following progestins was associated with a lower risk of adverse events than levonorgestrel?**
    a. Norethisterone acetate/norethindrone acetate.
    b. Norgestimate.
    c. Drospirenone.
    d. Dienogest.

12. **Some ways that women had found had enhanced their sense of self-efficacy when they tried to stop smoking were as follows:**
    a. Enlisting support from others was helpful, but using distractions was not helpful.
    b. Chewing gum or sucking sweets was helpful, but e-cigarettes were not helpful.
    c. Chewing gum or sucking sweets was helpful, but acupuncture was not helpful.
    d. Nicotine patches and e-cigarettes were helpful.

13. **In women with polycystic ovary syndrome who were overweight or obese, adhering to a ketogenic diet was associated with significant reductions in**
    a. Fasting blood glucose, but not triglycerides.
    b. Fasting insulin, but not triglycerides.
    c. Insulin resistance, but not ALT.
    d. Triglycerides, ALT and AST.

14. **No significant association was found between hormonal contraceptive use and breast cancer risk among healthy women.**
    a. True.
    b. False.

15. **Topical clascoterone cream is used to treat**
    a. Labial herpes.
    b. Acne.
    c. Impetigo.
    d. Basal cell carcinoma.

PP-PF-WHC-ALL-0434-1 | PP-PF-WHC-ZA-0171-1

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