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DHEA

Cardiovascular Health

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Abdominal Fat and Insulin

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Bone Health

Labrie, F., Diamond, P., Cusan, L., Gomez, J., Bélanger, A., & Candas, B. (1997). Effect of 12-Month Dehydroepiandrosterone Replacement Therapy on Bone, Vagina, and Endometrium in Postmenopausal Women. *The Journal of Clinical Endocrinology & Metabolism*, 82(10), 3498–3505. <https://doi.org/10.1210/jcem.82.10.4306>

Genitourinary Symptoms

Labrie, F., Archer, D. F., Koltun, W., Vachon, A., Young, D., Frenette, L., Portman, D., Montesino, M., Côté, I., Parent, J., Lavoie, L., BSc, A. B., Martel, C., Vaillancourt, M., Balser, J., & Moyneur, É. (2018). Efficacy of intravaginal dehydroepiandrosterone (DHEA) on moderate to severe dyspareunia and vaginal dryness, symptoms of vulvovaginal atrophy, and of the genitourinary syndrome of menopause. *Menopause the Journal of the North American Menopause Society*, 25(11), 1339–1353.
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Mood and Fatigue

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<https://doi.org/10.1210/jc.85.12.4650>

Depression and Libido

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Cancer

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neck cancer Stem-Like cells by downregulation of WNT signaling. *Frontiers in Oncology*, 12, 775541. <https://doi.org/10.3389/fonc.2022.775541>

Lupus

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Immune Function

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Chronic Disease

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Estradiol in Men

Effects of blocking estradiol

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Brain Health

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Bone Health

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Sexual Function

Finkelstein, J. S., Lee, H., Burnett-Bowie, S. M., Pallais, J. C., Yu, E. W., Borges, L. F., Jones, B. F., Barry, C. V., Wulczyn, K. E., Thomas, B. J., & Leder, B. Z. (2013). Gonadal steroids and body composition, strength, and sexual function in men. *New England Journal of Medicine*, 369(11), 1011–1022. <https://doi.org/10.1056/nejmoa1206168>

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Estradiol in Women

Cardiovascular Health

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Brain Health

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Sexual Function

Nathorst-Böös, J., Wiklund, I., Mattsson, L., Sandin, K., & Von Schoultz, B. (1993). Is sexual life influenced by transdermal estrogen therapy? *Acta Obstetrica Et Gynecologica Scandinavica*, 72(8), 656–660. <https://doi.org/10.3109/00016349309021160>

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Joint Pain

Chlebowski, R. T., Cirillo, D. J., Eaton, C. B., Stefanick, M. L., Pettinger, M., Carbone, L. D., Johnson, K. C., Simon, M. S., Woods, N. F., & Wactawski-Wende, J. (2013). Estrogen alone and joint symptoms in the Women's Health Initiative randomized trial. *Menopause the Journal of the North American Menopause Society*, 20(6), 600–608. <https://doi.org/10.1097/gme.0b013e31828392c4>

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Colon Cancer Prevention

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Breast Cancer

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Skin and Eyes

Affinito, P., Di Spiezio Sardo, A., Di Carlo, C., Sammartino, A., Tommaselli, G. A., Bifulco, G., Loffredo, A., Loffredo, M., & Nappi, C. (2003). Effects of hormone replacement therapy on ocular function in postmenopause. *Menopause the Journal of the North American Menopause Society*, 10(5), 482–487. <https://doi.org/10.1097/01.gme.0000063568.84134.35>

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Vasomotor Symptoms and Sleep

Polo-Kantola, P., Erkkola, R., Irjala, K., Pullinen, S., Virtanen, I., & Polo, O. (1999). Effect of short-term transdermal estrogen replacement therapy on sleep: a randomized, double-blind crossover trial in postmenopausal women. *Fertility and Sterility*, 71(5), 873–880. [https://doi.org/10.1016/s0015-0282\(99\)00062-x](https://doi.org/10.1016/s0015-0282(99)00062-x)

Savolainen-Peltonen, H., Hautamäki, H., Tuomikoski, P., Ylikorkala, O., & Mikkola, T. S. (2013). Health-related quality of life in women with or without hot flashes. *Menopause the Journal of the North American Menopause Society*, 21(7), 732–739. <https://doi.org/10.1097/gme.0000000000000120>

Genitourinary Symptoms

Fernandes, T., Costa-Paiva, L. H., Pedro, A. O., Baccaro, L. F. C., & Pinto-Neto, A. M. (2016). Efficacy of vaginally applied estrogen, testosterone, or polyacrylic acid on vaginal atrophy: a randomized controlled trial. *Menopause the Journal of the North American Menopause Society*, 23(7), 792–798. <https://doi.org/10.1097/gme.0000000000000613>

Ferrante, K. L., Wasenda, E. J., Jung, C. E., Adams-Piper, E. R., & Lukacz, E. S. (2019). Vaginal estrogen for the prevention of recurrent urinary tract infection in postmenopausal women: a randomized clinical trial. *Female Pelvic Medicine & Reconstructive Surgery*, 27(2), 112–117. <https://doi.org/10.1097/spv.0000000000000749>

Kim, H., Kang, S., Chung, Y., Kim, J., & Kim, M. (2015). The recent review of the genitourinary syndrome of menopause. *Journal of Menopausal Medicine*, 21(2), 65. <https://doi.org/10.6118/jmm.2015.21.2.65>

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Landmark Studies

Nurses' Health Study 1976

Romieu, I., Willett, W. C., Colditz, G. A., Stampfer, M. J., Rosner, B., Hennekens, C. H., & Speizer, F. E. (1989). Prospective study of oral contraceptive use and risk of breast cancer in women. *JNCI Journal of the National Cancer Institute*, 81(17), 1313–1321. <https://doi.org/10.1093/jnci/81.17.1313>

Danish Osteoporosis Prevention Study (DOPS) 2000

Mosekilde, L., Beck-Nielsen, H., Sørensen, O. H., Nielsen, S. P., Charles, P., Vestergaard, P., Hermann, A. P., Gram, J., Hansen, T. B., Abrahamsen, B., Ebbesen, E. N., Stilgren, L., Jensen, L. B., Brot, C., Hansen, B., Tofteng, C. L., Eiken, P., & Kolthoff, N. (2000). Hormonal replacement therapy reduces forearm fracture incidence in recent postmenopausal women — results of the Danish Osteoporosis Prevention Study. *Maturitas*, 36(3), 181–193. [https://doi.org/10.1016/s0378-5122\(00\)00158-4](https://doi.org/10.1016/s0378-5122(00)00158-4)

PEPI Trial 1997

Barrett-Connor, E., Slone, S., Greendale, G., Kritz-Silverstein, D., Espeland, M., Johnson, S. R., Waclawiw, M., & Fineberg, S. (1997). The postmenopausal estrogen/progestin interventions study: primary outcomes in adherent women. *Maturitas*, 27(3), 261–274. [https://doi.org/10.1016/s0378-5122\(97\)00041-8](https://doi.org/10.1016/s0378-5122(97)00041-8)

Heart and Estrogen/Progestin Replacement Study (HERS) 1998

Hulley, S., Grady D, Bush T., Furberg C., Herrington D., Riggs B., Vittinghoff E. (1998). Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. *JAMA*, 280(7), 605. <https://doi.org/10.1001/jama.280.7.605>

Coronary Risk Factors for Atherosclerosis (CORA) Study 2007

Windler, E., Zyriax, B., Eidenmüller, B., & Boeing, H. (2007). Hormone replacement therapy and risk for coronary heart disease. *Maturitas*, 57(3), 239–246. <https://doi.org/10.1016/j.maturitas.2007.01.004>

EPAT Study 2001

Hodis, H. N., Mack, W. J., Lobo, R. A., Shoupe, D., Sevanian, A., Mahrer, P. R., Selzer, R. H., Liu, C., Liu, C., & Azen, S. P. (2001). Estrogen in the prevention of atherosclerosis. *Annals of Internal Medicine*, 135(11), 939–953. <https://doi.org/10.7326/0003-4819-135-11-200112040-00005>

E3N Study 2007

Fournier, A., Berrino, F., & Clavel-Chapelon, F. (2007). Unequal risks for breast cancer associated with different hormone replacement therapies: results from the E3N cohort

study. *Breast Cancer Research and Treatment*, 107(1), 103–111.
<https://doi.org/10.1007/s10549-007-9523-x>

Women's Health Initiative (WHI) Study 2002:

The conclusions of this study resulted in the rapid decline of HRT use. Despite the subsequent studies and follow-up analyses of the WHI data that refute the WHI conclusions, wrongly held beliefs about risks associated with hormone therapy are prevalent amongst healthcare providers and patients.

Investigators, W. G. F. T. W. H. I. (2002). Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA*, 288(3), 321–333.
<https://doi.org/10.1001/jama.288.3.321>

KEEPS 2014:

Oral conjugated equine estrogen (CEE), compared with estradiol patch, improve lipid profiles. Both have no impact on carotid intima thickness. Although, the study length of 4 years may have been too short to see the full cardiovascular benefits.

Harman, S. M., Black, D. M., Naftolin, F., Brinton, E. A., Budoff, M. J., Cedars, M. I., Hopkins, P. N., Lobo, R. A., Manson, J. E., Merriam, G. R., Miller, V. M., Neal-Perry, G., Santoro, N., Taylor, H. S., Vittinghoff, E., Yan, M., & Hodis, H. N. (2014). Arterial imaging outcomes and cardiovascular risk factors in recently menopausal women. *Annals of Internal Medicine*, 161(4), 249–260. <https://doi.org/10.7326/m14-0353>

ELITE 2016:

Oral estradiol does not increase risk for plaque rupture and heart attack. Starting hormone therapy within 6 years of menopause decreases atherosclerosis progression.

Hodis, H. N., Mack, W. J., Henderson, V. W., Shoupe, D., Budoff, M. J., Hwang-Levine, J., Li, Y., Feng, M., Dustin, L., Kono, N., Stanczyk, F. Z., Selzer, R. H., & Azen, S. P. (2016). Vascular Effects of Early versus Late Postmenopausal Treatment with Estradiol. *New England Journal of Medicine*, 374(13), 1221–1231.
<https://doi.org/10.1056/nejmoa1505241>

Role of Testosterone and Estrogen in Men 2013:

Blocking estrogen in men on testosterone therapy can lead to increased body fat and visceral fat as well as sexual dysfunction.

Finkelstein, J. S., Lee, H., Burnett-Bowie, S. M., Pallais, J. C., Yu, E. W., Borges, L. F., Jones, B. F., Barry, C. V., Wulczyn, K. E., Thomas, B. J., & Leder, B. Z. (2013). Gonadal steroids and body composition, strength, and sexual function in men. *New England Journal of Medicine*, 369(11), 1011–1022. <https://doi.org/10.1056/nejmoa1206168>

REPLENISH Trial 2019:

First RCT to show that combined bioidentical oral estradiol and oral micronized progesterone is effective and safe for treating vasomotor symptoms in postmenopausal women.

Simon, J. A., Kaunitz, A. M., Kroll, R., Graham, S., Bernick, B., & Mirkin, S. (2018). Oral 17 β -estradiol/progesterone (TX-001HR) and quality of life in postmenopausal women with vasomotor symptoms. *Menopause the Journal of the North American Menopause Society*, 26(5), 506–512. <https://doi.org/10.1097/gme.0000000000001271>

TRAVERSE Trial 2023:

Testosterone therapy in men does not increase risk of heart attack, stroke, or prostate cancer, especially in men at high risk or history of cardiovascular disease.

Lincoff, A. M., Bhasin, S., Flevaris, P., Mitchell, L. M., Basaria, S., Boden, W. E., Cunningham, G. R., Granger, C. B., Khera, M., Thompson, I. M., Wang, Q., Wolski, K., Davey, D., Kalahasti, V., Khan, N., Miller, M. G., Snabes, M. C., Chan, A., Dubcenco, E., . . . Nissen, S. E. (2023). Cardiovascular safety of Testosterone-Replacement therapy. *New England Journal of Medicine*, 389(2), 107–117. <https://doi.org/10.1056/nejmoa2215025>

Melatonin

Jet Lag

Herxheimer, A., & Petrie, K. J. (2002). Melatonin for the prevention and treatment of jet lag. *Cochrane Database of Systematic Reviews*, 2010(1), CD001520. <https://doi.org/10.1002/14651858.cd001520>

REM Sleep

Kunz, D., Mahlberg, R., Müller, C., Tilmann, A., & Bes, F. (2004). Melatonin in Patients with Reduced REM Sleep Duration: Two Randomized Controlled Trials. *The Journal of Clinical Endocrinology & Metabolism*, 89(1), 128–134. <https://doi.org/10.1210/jc.2002-021057>

Nocturia

Batla, A., Simeoni, S., Uchiyama, T., deMin, L., Baldwin, J., Melbourne, C., Islam, S., Bhatia, K. P., Pakzad, M., Eriksson, S., & Panicker, J. N. (2021a). Exploratory pilot study of exogenous sustained-release melatonin on nocturia in Parkinson's disease. *European Journal of Neurology*, 28(6), 1884–1892. <https://doi.org/10.1111/ene.14774>

Blood Pressure

Scheer, F. A., Van Montfrans, G. A., Van Someren, E. J., Mairuhu, G., & Buijs, R. M. (2004). Daily nighttime melatonin reduces blood pressure in male patients with essential hypertension. *Hypertension*, 43(2), 192–197. <https://doi.org/10.1161/01.hyp.0000113293.15186.3b>

Antioxidant

Reiter, R. J., Mayo, J. C., Tan, D., Sainz, R. M., Alatorre-Jimenez, M., & Qin, L. (2016). Melatonin as an antioxidant: under promises but over delivers. *Journal of Pineal Research*, 61(3), 253–278. <https://doi.org/10.1111/jpi.12360>

Immune Booster

Srinivasan, V., Maestroni, G., Cardinali, D., Esquifino, A., Perumal, S. P., & Miller, S. (2005). Melatonin, immune function and aging. *Immunity & Ageing*, 2(1), 17. <https://doi.org/10.1186/1742-4933-2-17>

Cancer

Li, Y., Li, S., Zhou, Y., Meng, X., Zhang, J., Xu, D., & Li, H. (2017). Melatonin for the prevention and treatment of cancer. *Oncotarget*, 8(24), 39896–39921. <https://doi.org/10.18632/oncotarget.16379>

Migraines

Long, R., Zhu, Y., & Zhou, S. (2019). Therapeutic role of melatonin in migraine prophylaxis. *Medicine*, 98(3), e14099. <https://doi.org/10.1097/md.00000000000014099>

Progesterone in Women

Progesterone and Progestin

Schumacher, M., Guennoun, R., Ghoumari, A., Massaad, C., Robert, F., El-Etr, M., Akwa, Y., Rajkowski, K., & Baulieu, E. (2007). Novel Perspectives for Progesterone in Hormone Replacement Therapy, with Special Reference to the Nervous System. *Endocrine Reviews*, 28(4), 387–439. <https://doi.org/10.1210/er.2006-0050>

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Cardiovascular Health

Thomas, P., & Pang, Y. (2013). Protective actions of progesterone in the cardiovascular system: Potential role of membrane progesterone receptors (mPRs) in mediating rapid effects. *Steroids*, 78(6), 583–588. <https://doi.org/10.1016/j.steroids.2013.01.003>

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Premenstrual Syndrome

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randomised, placebo-controlled, phase 3 trials. *The Lancet*, 392(10152), 1058–1070.
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Testosterone in Men

Cardiovascular Health

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Lincoff, A. M., Bhasin, S., Flevaris, P., Mitchell, L. M., Basaria, S., Boden, W. E., Cunningham, G. R., Granger, C. B., Khera, M., Thompson, I. M., Wang, Q., Wolski, K., Davey, D., Kalahasti, V., Khan, N., Miller, M. G., Snabes, M. C., Chan, A., Dubcenco, E., . . . Nissen, S. E. (2023). Cardiovascular safety of Testosterone-Replacement therapy. *New England Journal of Medicine*, 389(2), 107–117. <https://doi.org/10.1056/nejmoa2215025>

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Brain Health

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Bone Health

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Muscle and Strength

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Metabolic Health

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Lower Urinary Tract Symptoms

Okada, K., Miyake, H., Ishida, T., Sumii, K., Enatsu, N., Chiba, K., Matsushita, K., & Fujisawa, M. (2016). Improved lower urinary tract symptoms associated with testosterone replacement therapy in Japanese men with Late-Onset hypogonadism. *American Journal of Men S Health*, 12(5), 1403–1408. <https://doi.org/10.1177/1557988316652843>

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Testosterone in Women

Cardiovascular Health

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Brain Health

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