Independent Research & further reading

Guest: Dr Sarah Gottfried

Disclaimer 1: The literature presented here, directly (or as closely as possible), looks at statements made by the guest. In order to fully understand each topic mentioned, an extensive literature review (beyond the scope of this document) would be required.

Disclaimer 2: The information provided in this podcast and any associated materials is not intended to replace professional medical advice. For any medical concerns, it is essential to consult a qualified health professional.

Contents

Cortisol and mitochondria	3
Treating high cholesterol and preventing cardiovascular events	3
Percentage of preventable diseases	4
ACE scores	4
Prevalence of highly sensitive people	5
Adverse childhood experiences and risk of diabetes	6
Perceived stress and heart rate variability	6
Diabetes and lifestyle	7
Cortisol and blood sugar	7
Cortisol and depression	7
Cortisol, suicide and brain volume	8
Cortisol and stress/trauma	9
Endocrine disrupters	10

Vitamin D 11
Prevalence of dysregulated cortisol levels 11
Cortisol levels and meditation 12
Ashwagandha and phosphatidylserine: effect on cortisol levels 12
Testosterone levels on men and women 13
Symptoms of low testosterone 14
PCOS 15
Cortisol and testosterone 15
Diet and testosterone levels 16
Ketogenic diet 16
Estrogen and bone health in men 18
Women and insulin resistance 18
Hormone therapy 19
Dietary fibre 19
Microbiome 20
Menopause symptoms management 21
Birth control pills 21
U Bend: psychological well-being 22
Rates of autoimmune diseases in women 23
Cancer rates 24
References 27

Cortisol and mitochondria

> *“cortisol, either making too much of it or too little or even both within the same day, and it affects energy. It affects mitochondria.”*

Cortisol may affect mitochondrial function by potentially altering energy metabolism, oxidative phosphorylation, calcium binding, and mitochondrial trafficking (1-5).

Treating high cholesterol and preventing cardiovascular events

> *“Say a high cholesterol. And you get treated with a pharmaceutical. And what we know is that we have to treat about 100 to 200 people for one person to benefit. So that I would define as imprecision medicine.”*

The "Number Needed to Treat" (NNT) is a measure used to evaluate the effectiveness of statins in preventing cardiovascular events. It represents the average number of patients who need to be treated with statins to prevent one additional adverse cardiovascular event. The NNT for statins varies significantly based on the risk level of the population. In lower-risk populations, the 5-year NNT to prevent one Coronary Heart Disease event is 146, while in higher-risk populations, it is 53. It is important to note, as reported by a study, that statins significantly reduce all-cause mortality, coronary heart disease mortality, and nonfatal myocardial infarction in elderly patients with existing coronary heart disease, with an NNT of 28 to save one life over five years.

References 6-10.

Percentage of preventable diseases

> *"70 percent of the diseases we're facing right now are utterly preventable with lifestyle medicine"*

- Up to 80% of heart disease, stroke, and diabetes, and 40% of cancers are preventable through lifestyle changes and public health interventions (11).
- A literature review reported that approximately 90-95% of cancer cases are attributed to environmental and lifestyle factors, such as smoking, diet, and physical inactivity, making them largely preventable (12).
- In England, about 40% of morbidity and mortality is considered preventable, with smoking and poor diet being major contributors (13).

ACE scores

> *"You're not quite yet middle aged. But for people who are middle aged, 40 to 65, they found that people who had higher ACE scores, one or higher, they then had a greater risk of 45 different chronic diseases."*

Research shows that individuals with higher ACE scores (typically ≥4) have a significantly increased risk of developing chronic conditions such as cardiovascular disease, chronic obstructive pulmonary disease, diabetes, and depression. However, the health impact of ACEs is evident even at lower scores. One study found that individuals with at least one chronic disease were nearly three times more likely to have four or more ACEs.

References 14-17.

“So, if you know that you have an elevated ACE score, and there's a lot of people who have a score of zero, about 40 percent of men, about 30 percent of women, and what we know is that if you've got this greater risk for 45 different chronic conditions, there's a way that those ACEs are living on in your body.”

Overall, around 40-42% of both children and adults are estimated to have an ACE score of zero. The percentage of women with an ACE score of zero varies significantly across different studies and populations, ranging from as low as 5% in high-risk groups to around 36% in more general populations.

References 18-21.

“People who have adverse childhood experiences, are more likely to have disordered eating.”

Research indicates that a higher number of ACEs is associated with an increased risk of developing disordered eating behaviours. For instance, adolescents with four or more ACEs are significantly more likely to be at high risk for eating disorders compared to those without ACEs. Studies have found that women report higher ACE scores than men, and these scores are associated with a range of disordered eating behaviours. Emotional abuse, physical neglect, and emotional neglect are modestly associated with disordered eating behaviours in women, while emotional abuse is more consistently related to these behaviours in men.

References 22-25.

Prevalence of highly sensitive people

“about 20 percent of the population is highly sensitive”

Highly sensitive individuals make up about 20-30% of the population. They are more reactive to environmental influences, experiencing both negative and positive stimuli more intensely.

References 26-28.

Adverse childhood experiences and risk of diabetes

> *“We know that adverse childhood experiences link to blood sugar problems and a greater risk of prediabetes and diabetes”*

Meta-analyses have shown that exposure to ACEs is linked to a higher likelihood of developing type-2 diabetes.

References 29-31.

Perceived stress and heart rate variability

> *“We know that they link to chronic stress and cortisol problems, high perceived stress, whether the stress is there or not. It also led to, as I started using wearables, Low heart rate variability. The time between each of my heartbeats. And that's a measure of the sympathetic system”*

Multiple studies have found an inverse relationship between perceived stress and HRV. Higher levels of perceived stress are associated with reduced HRV, indicating increased sympathetic nervous system activity and decreased parasympathetic activity.

References 32-36.

Diabetes and lifestyle

> *“if you have blood sugar problems, if you've got prediabetes and diabetes, the treatment is lifestyle. It's the most effective to change the food that you're eating, to increase your exercise, to um, manage your stress in a different way.”*

Intensive lifestyle changes, including diet and exercise, are effective in reducing the progression from prediabetes to type 2 diabetes. These interventions have shown to lower the risk of diabetes incidence and promote regression to normoglycemia.

References 37-41.

Cortisol and blood sugar

> *“cortisol is It's critical for your immune function, it raises your blood sugar”*

Cortisol increases fasting plasma glucose levels, with a modest rise in individuals without diabetes and a more significant increase in those with diabetes. It also raises blood glucose by stimulating gluconeogenesis, the liver's process of producing glucose from non-carbohydrate sources.

References 42, 43.

Cortisol and depression

> *“50 percent of people with depression have high cortisol.”*

Research shows that increased plasma cortisol is found in 24% of depressed women (44).

Cortisol, suicide and brain volume

> *“used by some psychiatrists as a suicide marker. It's associated with more belly fat. And so, the fat receptors, the fat cells in your belly have increased receptors for cortisol. So it's a way of growing your belly fat. We know that it shrinks the brain in women, but not men. Starting in midlife, starting in your 40s, it's not an old age thing.”*

Suicide

The association between cortisol levels and suicidal behaviour appears to vary with age. In individuals under 40, higher cortisol levels are associated with suicide attempts, whereas in those 40 and older, lower cortisol levels are linked to such behaviour. Despite the potential of cortisol as a biomarker, the variability in findings across studies highlights the need for further research to clarify the mechanisms linking cortisol dysregulation to suicidality.

References 45-48.

Abdominal fat

The relationship between cortisol and abdominal fat is complex. Cortisol is known to influence energy homeostasis by increasing the consumption of high-fat and high-sugar foods, which can lead to weight gain and obesity. Additionally, research indicates that individuals with higher levels of abdominal fat often exhibit increased cortisol secretion. This is particularly evident in those with a high waist-to-hip ratio, which is associated with elevated cortisol levels and a hyperactive hypothalamic-pituitary-adrenal (HPA) axis.

References 49-52.

Brain volume

Higher cortisol levels have been associated with lower total cerebral brain volume, particularly in women. This inverse relationship was significant in women but not in men, suggesting

a sex-specific vulnerability to cortisol's effects on brain structure. In men, higher cortisol levels were linked to worse cognitive performance but not necessarily to brain atrophy.

References 53-56.

> *"There was a study from the University of Texas in San Antonio showing that women in their 40s with high cortisol have a shrinkage of total brain volume. And then Lisa Moscone at Cornell also just showed in a study looking at men and women that women with high cortisol also have shrinkage of their total brain volume."*

References 57, 58.

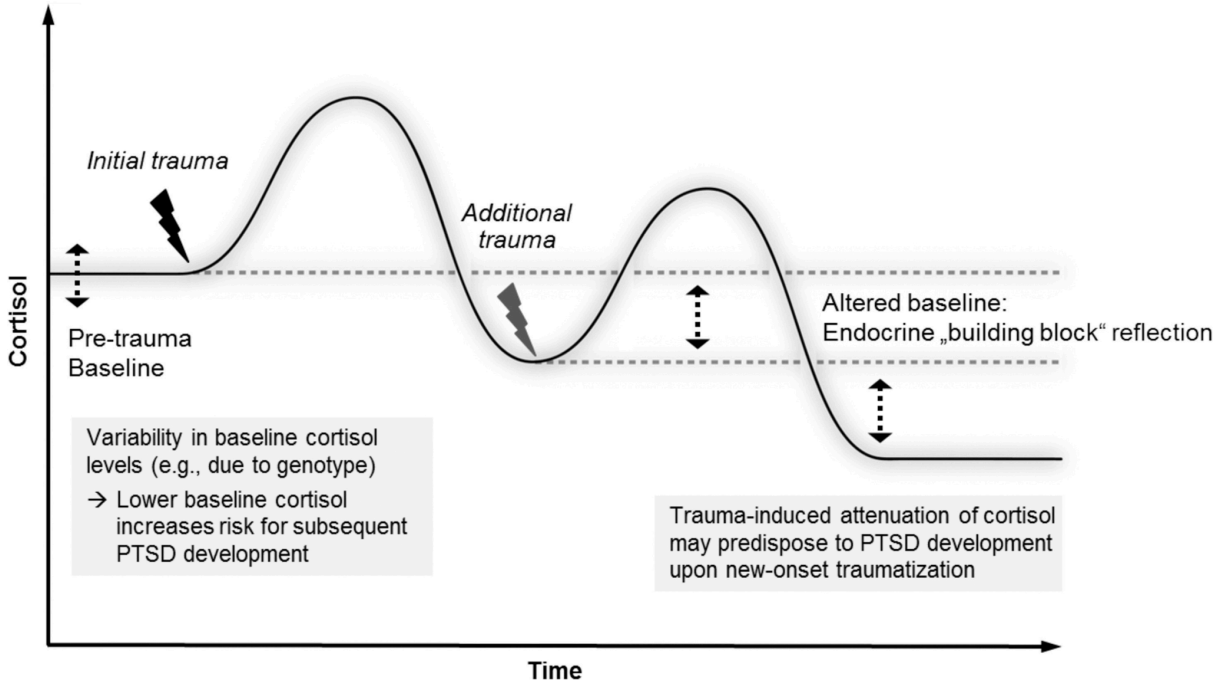
Cortisol and stress/trauma

> *"For people who experience toxic stress or trauma, what typically happens is cortisol goes up."*

> *"More serious exposure to trauma, and they have post traumatic stress disorder. Those people have probably gone through a period of high cortisol, and now they can't keep up anymore. And they are in a low cortisol state."*

In individuals with PTSD, exposure to trauma reminders can trigger an increase in cortisol levels. Although studies suggest that overall cortisol levels may not differ significantly between those with and without PTSD, lower cortisol levels have been observed in certain groups, including women and individuals with a history of physical or sexual abuse.

References 59-64.



An integrative model links long-term cortisol secretion, trauma exposure, and PTSD development. Source: Steudte-Schmiedgen et al. (2016)–reference 64.

Endocrine disrupters

“I would say toxin exposure. So there's endocrine disruptors. There's more than 700 known endocrine disruptors. Things like bisphenol A, um, Like the plastic lining that you see in cans or in plastic containers, water containers. There's skincare products, which women are exposed to more. Things like moisturizer and makeup and other things that contain endocrine disruptors like parabens and there's flame retardants.”

BPA, or bisphenol A, is a well-documented endocrine disruptor with significant effects on hormonal, reproductive, and metabolic health. Studies have also shown associations between paraben exposure and altered reproductive hormone levels, which may contribute to infertility and other reproductive health issues.

References 65-72.

Vitamin D

> *“somewhere around 70 to 80 percent of people don't have enough vitamin D”*

A pooled analysis found that 76.6% of people have serum 25-hydroxyvitamin D levels below 75 nmol/L, indicating widespread insufficiency. In the United States, nearly 80% of the population has vitamin D levels below the optimal range.

References 73-76.

Prevalence of dysregulated cortisol levels

> *“So, the number is high. If I had to look at the general population, it would be a total speculation, I would say somewhere around 30 to 50%.”*

According to the research, approximately 25% of individuals with stress-related disorders experience hypocortisolemia, which is characterised by consistently low cortisol levels following a period of elevated cortisol. This condition, along with hypercortisolemia (consistently elevated cortisol levels), is linked to various health issues, including depression, anxiety, and an increased risk of heart disease.

Reference 77.

Cortisol levels and meditation

> *“How can I leverage that to work with us? And then there's more of a bottom up approach, which is using your senses to create safety and to change. the cortisol signal, kind of the alarm and the way that it goes off in the body. So breath work is really important for that. Meditation, um, different forms of movement, dancing, you know, rhythmic movements, walking, hiking…”*

Meditation practices, including mindfulness and focused attention, have been found to reduce cortisol levels, indicating a decrease in physiological stress markers.

References 78-81.

Ashwagandha and phosphatidylserine: effect on cortisol levels

> *“Cortisol Manager, which is a supplement that includes ashwagandha and phosphatidylserine, and it's been shown to lower cortisol levels.”*

Cortitrol, similar to Cortisol Manager, seems to help reduce cortisol levels and associated oxidative stress during both rest and physical stress. This suggests that supplements containing ingredients like ashwagandha and phosphatidylserine may be beneficial for managing stress-induced cortisol elevation. Ashwagandha, also known as Withania somnifera, has been shown to significantly reduce cortisol levels in several studies. In addition, phosphatidylserine (PS) supplementation has been found to blunt cortisol responses to physical stress. Studies show that both acute and chronic administration of PS can significantly reduce cortisol levels during physical exercise.

References 82-90.

> *“Rhodiola is an adaptogen. So it's, uh, it's an herbal therapy that's been shown to help with cortisol.”*

Rhodiola has been shown to interact with the hypothalamic-pituitary-adrenal (HPA) axis, which is responsible for cortisol production. Studies indicate that Rhodiola can reduce cortisol levels, thereby potentially alleviating stress. While combined supplementation studies show mixed results regarding cortisol, Rhodiola consistently improves subjective stress and mood, suggesting its efficacy as a stress-relieving adaptogen. Further research is needed to fully understand its mechanisms and effects on cortisol.

References 91-96.

Testosterone levels on men and women

> *"I think earlier that men just have 10 times more. Men have more, but it's the most abundant hormone in the female body. Women are exquisitely sensitive to it. It's the most abundant hormone? Yes. Higher concentration than estrogen or progesterone."*

Women secrete greater amounts of androgens, including testosterone, than estrogens. Testosterone is a significant hormone in women, with its levels being higher than those of estradiol (97, 98).

> *"About 15 in a woman? I read on WebMD. Yes, that's, that's a pretty good level. And in men? 300 to 1, 000 nanograms? Yes, I like to see it somewhere around 500 to 1, 000."*

In healthy, non-obese men aged 19 to 39, the established normal range for testosterone levels is between 264 and 916 ng/dL. In women with normal menstrual cycles, serum testosterone levels typically range from 14 to 59 ng/dL, with an average of 34.6 ng/dL, according to one study. Another study reports a reference range of 15 to 46 ng/dL, based on the 5th and 95th percentiles for a typical 30-year-old woman, covering the range for most women.

Symptoms of low testosterone

"And what would be a sign that I had low testosterone if I'm a man? Belly fat, gynecomastia. What's that? That's when you get breast development. Okay. Um, mood changes, mood swings, uh, irritability, uh, depression, cardiovascular changes, erectile dysfunction, decreased libido."

References 102-107.

"If a woman has low testosterone, what are the symptoms we see in a woman? They're similar. So, um, both sexes have fatigue. That's very common. Um, decreased libido, they might be working out at the gym and not seeing a response, they might have some hair loss, um, and testosterone in women has a few unique features, like one of the things we've seen looking at MBA students, students who are getting a master's in business administration, is that the women with higher testosterone tend to be more comfortable with financial risk. I believe it also tracks with confidence and agency."

References 108-111.

<u>Hair</u>

A study found that women with diffuse hair loss had significantly lower levels of sex-hormone binding globulin (SHBG), although their testosterone levels were normal. This suggests that factors other than low testosterone might contribute to hair loss. While low testosterone is not directly linked to hair loss in women, hormonal imbalances, including androgen excess or deficiencies in other steroid hormones, can influence hair health.

Reference 112.

PCOS

> *“So high testosterone tends to track with polycystic ovary syndrome. It's the most common hormone imbalance that women have. It leads to infertility. Um, it leads to increased hair growth in places that you don't want it. So that can include like your chin and between your breasts. It can lead to, um, insulin resistance. In some, but not all, but somewhere around 70 percent of people with PCOS have insulin resistance. So it leads to symptoms of excess androgen, acne, hirsutism.”*

Women with PCOS typically exhibit higher levels of total and free testosterone compared to healthy controls. This elevation is a significant marker for diagnosing PCOS and is associated with symptoms such as hirsutism (excessive hair growth), infertility and menstrual irregularities.

References 113-116.

Insulin resistance is common in women with PCOS, occurring independently of obesity. It is linked to defects in insulin receptor signaling, particularly affecting metabolic pathways while maintaining steroidogenesis, which contributes to hyperandrogenism.

References 117, 118.

Cortisol and testosterone

> *“if you're someone who's making a lot of cortisol, you're going to make less testosterone”*

Cortisol and testosterone interact in complex ways that affect behaviour, stress responses, and physical performance. Cortisol can both inhibit and enhance testosterone's effects depending on the context, such as stress levels and physical activity.

References 119-122.

Diet and testosterone levels

> *"by eating a lower carbohydrate diet, you can change your testosterone level. So you can lower it significantly"*

Some studies suggested that low-carbohydrate diets, such as the ketogenic or Mediterranean diet, which are rich in high-quality fats, increased testosterone levels (123-125). However, a pilot study found that while carbohydrates had little direct effect on testosterone, polyunsaturated and monounsaturated fats significantly reduced its production (126). Other research showed that high-carbohydrate diets increased testosterone levels compared to high-protein diets (127), whereas low-carbohydrate diets—particularly those high in protein—led to a decline in testosterone, with the effect being more pronounced in high-protein, low-carbohydrate diets (128). Additionally, a 12-week study comparing high-fat and high-carb diets in men undergoing strength training found no significant changes in testosterone levels (129). Overall, the relationship between carbohydrates and testosterone remained complex, influenced by factors such as diet composition, metabolic health, and individual variability.

Ketogenic diet

> *"ketogenic diet, what we typically see is that insulin levels are lower, so it does seem to help with metabolic health. It can cause some thyroid dysfunction, so it's worth tracking thyroid. We know that People on a ketogenic diet sometimes have increased inflammation. There's some people who are super responders, and they just do super well with a ketogenic diet. But some people have about a 10 percent change in their LDL"*

<u>Insulin resistance</u>

The ketogenic diet shows promise in improving insulin sensitivity and glycemic control, particularly in individuals with obesity and type 2 diabetes. However, the benefits are often intertwined with weight loss, and the direct effects of ketosis remain a topic of ongoing research.

Further studies are needed to fully understand the mechanisms and long-term implications of KD on insulin function and metabolic health.

References 130-137.

Thyroid dysfunction

The ketogenic diet can significantly alter thyroid hormone levels, particularly by reducing T3 and increasing T4 concentrations. These changes highlight the need for careful monitoring of thyroid function in individuals adopting a ketogenic diet, especially those with existing thyroid issues or on medications that influence thyroid hormones.

References 138-141.

LDL cholesterol

While the ketogenic diet can be effective for weight loss and other health benefits, its impact on LDL cholesterol varies significantly among individuals. Genetic predispositions and individual metabolic responses play crucial roles in determining the extent of LDL cholesterol changes and more research is needed.

References 142-144.

The quickest gender to enter ketosis

> *" So women tend to have more issues with the ketogenic diet. It takes them longer to get into ketosis than it does a man. Even if you, the average man, if they fast for somewhere around 14 to 16 hours, They start to produce ketones. And for women it takes longer. It takes more like 18 to 20 hours. So, probably that's related to fertility and evolutionarily there's some pressure for us to not go into a ketogenic state. "*

Women tend to enter ketosis faster than men, particularly during fasting conditions. This difference is likely due to higher availability of nonesterified fatty acids (NEFA) in women, which enhances ketone production during fasting.

References 145, 146.

Estrogen and bone health in men

> *“ in men, it's a little bit different. The dynamic range is more narrow. And what we generally want with men is for you to have enough estrogen to serve some of these bodily functions, like with Keeping your bones strong, um, but not too much”*

References 147, 148.

Women and insulin resistance

> *“one of the things that happens for women over the age of 40 is that they typically become insulin resistant. Their cells become numb to insulin.”*

While women over 40 may experience increased insulin resistance, it is influenced by a combination of factors such as body fat distribution, reproductive history, physical activity, and psychological health, and not just solely due to age. For example, changes in body fat distribution, particularly increased trunk fat, are linked to higher insulin resistance in middle-aged women.

References 149-152.

Hormone therapy

> *"73 to 75 percent of women do not get the treatment for perimenopause and menopause that they deserve. They're not being offered, for instance, hormone therapy. And that has to change, but hormone therapy can help to reverse this. So that you are more likely to, um, not have some of these body composition changes as you get older."*

Hormone therapy in women, particularly postmenopausal, has complex effects on insulin resistance. While certain therapies can improve insulin sensitivity and reduce diabetes risk, others may exacerbate insulin resistance. The choice of therapy, whether oral or transdermal, and the specific hormonal components used, play crucial roles in these outcomes. Further research is needed to optimise hormone therapy regimens to mitigate insulin resistance while maximising therapeutic benefits.

References 153-159.

Dietary fibre

> *"average American gets somewhere around 14 grams of fiber a day, and we're meant to have about 30 to 35, 40 grams a day. Our Paleolithic ancestors got even more than that, 50 to 100 grams a day. So we are not getting enough fiber. It's critical for blood sugar stabilization, so is protein intake."*

Adequate intake for dietary fibre is 25 to 38 grams per day for adults, but the average intake is around 14 to 17 grams per day, which is less than half of the recommended amount (160-165).

Microbiome

“We know from the microbiome studies that you want about 25 to 35 different species of fruits and vegetables in a week to be able to feed your microbiome.

And what role is the microbiome playing in my hormone function?

It's playing a huge role, so your microbiome is one of the control functions for estrogen levels and maybe testosterone levels. So there's a bi directional relationship, Steve, where there are three bacteria in the gut that can, um, take estrogen and make it keep recirculating. So you're meant to produce estrogen and then use it and then either poop or pee it out. But what happens with some people, if they've got these bacteria, is they keep recirculating the estrogen like bad karma. And so those people tend to have higher estrogen levels. It tends to be associated in men with this greater risk of, um, metabolic dysfunction, prostate cancer. And in women, it's associated with more breast cancer and endometrial cancer. And that, a lot of that starts and is caused by the gut microbiome.”

To support a healthy gut microbiome, consuming a diverse range of fruits and vegetables is beneficial. While specific numbers of species are not universally agreed upon, increasing both the quantity and botanical diversity of fruits and vegetables in your diet can positively influence gut microbiota (165-167).

The gut microbiome plays a crucial role in regulating estrogen metabolism through the "estrobolome", a collection of bacterial genes that encode enzymes like β-glucuronidases, which deconjugate estrogens into their active forms. This process influences circulating estrogen levels and can impact various estrogen-related conditions. Further research is needed to explore therapeutic interventions targeting the microbiome to modulate estrogen levels effectively.

References 168-170.

Interestingly, a high intake of dietary fibre (which promotes a healthy microbiome) has been associated with a reduced risk of several types of cancer, including esophageal, gastric, colon, rectal, colorectal adenoma, breast, endometrial, ovarian, renal cell, prostate, and pancreatic cancers (171). Higher dietary fibre consumption has been associated with a 22% lower cancer risk and also lower mortality (172, 173).

Menopause symptoms management

> *"You believe that many of the symptoms of menopause are avoidable? Yes. Yes, and by that I mean using hormone therapy and using lifestyle medicine as early as possible to manage that transition."*

While menopause symptoms cannot be entirely avoided, a combination of lifestyle changes, dietary adjustments, and both hormonal and non-hormonal treatments can effectively manage and alleviate symptoms (174-178).

Birth control pills

> *"What do you think of birth control pills? I think if they help you avoid surgery, they can be beneficial. But I think they're way overused in our culture. And most people who agree to a birth control pill don't receive full informed consent. They're not told that it'll raise the inflammation in your body by two to three fold. It increases your risk of autoimmune disease, especially Crohn's disease. It makes your control system for your hormones less flexible. It can rob you of testosterone. It can lower your free testosterone. It can shrink your clitoris by up to 20%."*

<u>Inflammation</u>

Hormonal contraceptives can increase inflammation markers such as CRP, potentially raising inflammation levels in the body. The extent of this effect can vary depending on the type of contraceptive and individual responses to stress.

References 179-182.

Autoimmune diseases

There is evidence linking hormonal contraceptive use to an increased risk of developing autoimmune diseases, particularly Crohn's disease. The risk appears to be influenced by the type, duration, and recency of contraceptive use. Individuals considering hormonal contraceptives should be informed of these potential risks, especially if they have a predisposition to autoimmune conditions.

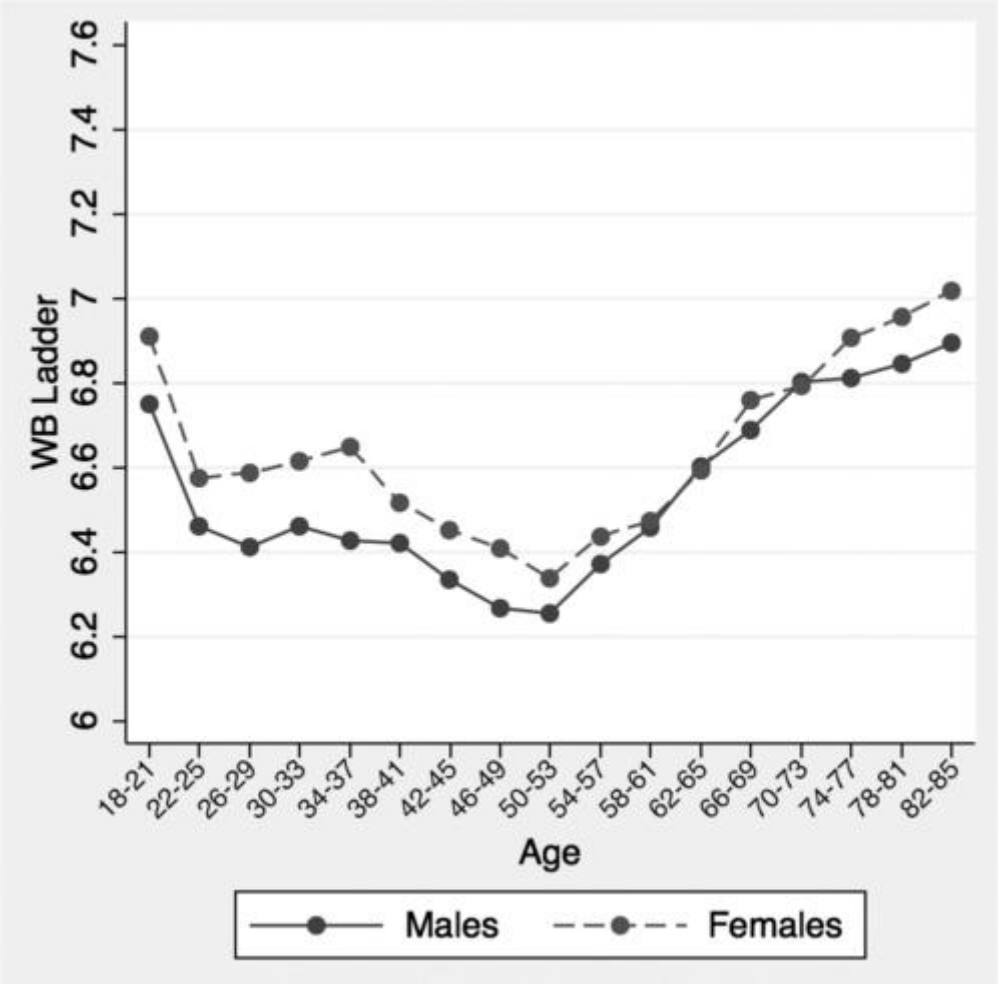
References 183-187.

Clitoris volume

A study found that hormonal contraceptives, specifically oral contraceptives and contraceptive vaginal rings, led to a decrease in clitoral volume in women (188). However, the study does not specify the extent of this reduction, and there is no mention of a 20% decrease.

U Bend: psychological well-being

> *“There's this really interesting study that, um, is called the U Bend. And it looks at psychological well being for adults. It's highest in your 20s and the very start of your 30s. And then there's this U shape where your psychological well being goes down. I know you're 32, so I'm a little sorry to break the news to you. And then it goes back up, right around 50.”*



Well-being in the United States by age. Source: Stone et al. (2010)–reference 189.

Rates of autoimmune diseases in women

> *"Do you see higher rates of autoimmune diseases in women or men? Women. 4X. 4X? Yes. 400 percent more autoimmune diseases? Yes. And what are these autoimmune diseases?"*

A study revealed that women experienced a 60% higher incidence of 32 autoimmune diseases compared to men. Female predominance was seen in 18 of these diseases, while the remaining diseases showed either no difference or were more common in men. In particular,

Sjögren's syndrome was found to be 8 times more common in women, and systemic lupus erythematosus occurred 4 times more frequently in women than in men.

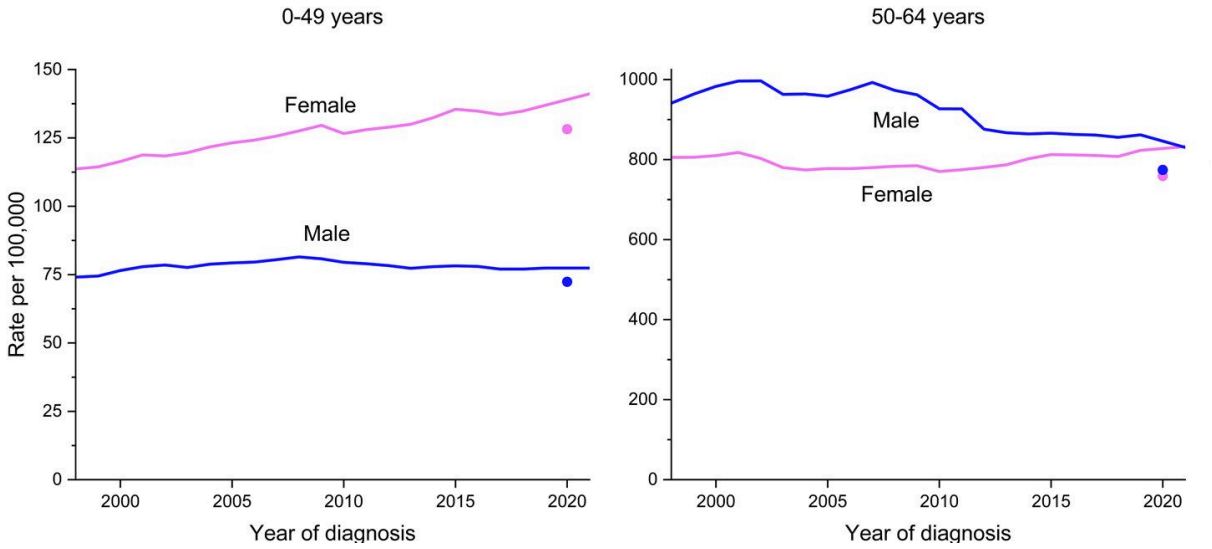
References 190, 191.

> *“they also experienced trauma at an earlier age compared to men. They have much more sexual violence. There are 14 times more likely to be raped than a man.”*

Almost 1 in 5 women and 1 in 71 men have been raped in their lifetime, according to a report (191).

Cancer rates

> *“I saw a graph yesterday which showed the rise in breast cancer amongst women. And actually, I think it was actually, no, it was the rise in all cancers amongst women versus men. And the men graph was pretty flat. But there was this significant rise in women getting more and more forms of cancer. And I was looking through some of the research as to why that would happen. And one of them, one of the points of research said that because women are having children later, that this is causing a rise in cancer.*
>
> *That has been studied with, for instance, breast cancer. Okay. So we know, you know, there's a lot of different factors that can increase a woman's risk of breast cancer. One of them is the age at which you have your first baby. And so the way that we think of this is that it's related to estrogen exposure. So women who get pregnant and maybe they breastfeed for a year, that's often a period of time, like a year and nine months. Where they're not exposed to as much estrogen than they would be if they were menstruating during that time. And so, having babies later seems to be associated with a greater risk of breast cancer.”*



Cancer rates over the years, divided by gender. Source: American Cancer Association; ACS Slide Set: Adapted from Cancer Facts & Figures 2025, slide 6 (192)–reference 193.

Breast cancer

The age at first pregnancy is a significant determinant of breast cancer risk, with early first pregnancies offering a protective effect, particularly against certain breast cancer subtypes. This effect is influenced by genetic factors, parity, and breastfeeding practices.

References 194-196.

"We can talk about separating ejaculation from orgasm in a minute, but in women it's more complicated. So that was the Masterson Johnson way of thinking about the sexual response. Masterson Johnson. And now we know. Masterson Johnson, they were sexologists that published this particular model. And it wasn't until maybe 15, 20 years ago that Rosemary Basson at the University of British Columbia found that women have a different response. They need to have sex in order to feel emotionally connected. Women actually need the emotional connection first to be receptive to sexuality."

Reference 197.

> *“And I just was looking at the data on morning sun. Because I didn't quite believe it. Like it, supposedly it helps you with your circadian rhythm. It helps you with sleeping better. It helps you with melatonin production. It helps you with mood. ”*

The morning sun is a vital component in the regulation of circadian rhythms, impacting various aspects of health and well-being (198-201).

References

1. Xie, X., Shen, Q., Yu, C., Xiao, Q., Zhou, J., Xiong, Z., Li, Z., & Fu, Z. (2020). Depression-like behaviors are accompanied by disrupted mitochondrial energy metabolism in chronic corticosterone-induced mice. The Journal of Steroid Biochemistry and Molecular Biology, 200.

2. Davies, K., Smith, D., El-Bacha, T., Wooding, P., Forhead, A., Murray, A., Fowden, A., & Camm, E. (2022). Cortisol Regulates Cerebral Mitochondrial Oxidative Phosphorylation and Morphology of the Brain in a Region-Specific Manner in the Ovine Fetus. Biomolecules, 12.

3. Kimberg, D., & Goldstein, S. (1966). Binding of calcium by liver mitochondria of rats treated with steroid hormones.. The Journal of biological chemistry, 241 1, 95-103.

4. Li, D., & Sewer, M. (2010). RhoA and DIAPH1 mediate adrenocorticotropin-stimulated cortisol biosynthesis by regulating mitochondrial trafficking.. Endocrinology, 151 9, 4313-23.

5. Du, J., Zhu, M., Bao, H., Li, B., Dong, Y., Xiao, C., Zhang, G., Henter, I., Rudorfer, M., & Vitiello, B. (2016). The Role of Nutrients in Protecting Mitochondrial Function and Neurotransmitter Signaling: Implications for the Treatment of Depression, PTSD, and Suicidal Behaviors. Critical Reviews in Food Science and Nutrition, 56, 2560 - 2578.

6. Rossignol, M., Labrecque, M., Cauchon, M., Breton, M., & Poirier, P. (2018). Number of patients needed to prescribe statins in primary cardiovascular prevention: mirage and reality. Family Practice, 35, 376–382.

7. Afilalo, J., Duque, G., Steele, R., Jukema, J., De Craen, A., & Eisenberg, M. (2008). Statins for secondary prevention in elderly patients: a hierarchical bayesian meta-analysis.. Journal of the American College of Cardiology, 51 1, 37-45 .

8. Blazi, J.et al. (2019). Efficacy and safety of statin therapy in older people: a meta-analysis of individual participant data from 28 randomised controlled trials. Lancet (London, England), 393, 407 - 415.

9. Teng, M., Lin, L., Zhao, Y., Khoo, A., Davis, B., Yong, Q., Yeo, T., & Lim, B. (2015). Statins for Primary Prevention of Cardiovascular Disease in Elderly Patients: Systematic Review and Meta-Analysis. Drugs & Aging, 32, 649-661.

10. Ponce, O., Larrea-Mantilla, L., Hemmingsen, B., Serrano, V., Rodríguez-Gutiérrez, R., Spencer-Bonilla, G., Álvarez-Villalobos, N., Benkhadra, K., Haddad, A., Gionfriddo, M., Prokop, L., Brito, J., & Murad, M. (2019). Lipid-Lowering Agents in Older Individuals: A Systematic Review and Meta-Analysis of Randomized Clinical Trials.. The Journal of clinical endocrinology and metabolism, 104 5, 1585-1594 .

11. Fried, L. (2016). Confronting Global Chronic Disease: The Role for Schools of Public Health.. Global heart, 11 4, 409-412.

12. Anand, P., Kunnumakara, A., Sundaram, C., Harikumar, K., Tharakan, S., Lai, O., Sung, B., & Aggarwal, B. (2008). Cancer is a Preventable Disease that Requires Major Lifestyle Changes. Pharmaceutical Research, 25, 2097 - 2116.

13. Amies, B. (2017). General practice should hold government to account on disease prevention.. The British journal of general practice : the journal of the Royal College of General Practitioners, 67 665, 559.

14. Sanderson, M., Mouton, C. P., Cook, M., Liu, J., Blot, W. J., & Hargreaves, M. K. (2021). Adverse Childhood Experiences and Chronic Disease Risk in the Southern Community Cohort Study. Journal of health care for the poor and underserved, 32(3), 1384–1402.

15. Sonu, S., Post, S., & Feinglass, J. (2019). Adverse childhood experiences and the onset of chronic disease in young adulthood. Preventive medicine, 123, 163–170.

16. Alhowaymel, F. M., Kalmakis, K. A., Chiodo, L. M., Kent, N. M., & Almuneef, M. (2023). Adverse Childhood Experiences and Chronic Diseases: Identifying a Cut-Point for ACE Scores. International journal of environmental research and public health, 20(2), 1651.

17. Campbell, J. A., Walker, R. J., & Egede, L. E. (2016). Associations Between Adverse Childhood Experiences, High-Risk Behaviors, and Morbidity in Adulthood. American journal of preventive medicine, 50(3), 344–352.

18. Kapoor, E., Okuno, M., Miller, V., Rocca, L., Rocca, W., Kling, J., Kuhle, C., Mara, K., Enders, F., & Faubion, S. (2021). Association of adverse childhood experiences with menopausal symptoms: Results from the Data Registry on Experiences of Aging, Menopause and Sexuality (DREAMS).. Maturitas, 143, 209-215.

19. Rifas-Shiman, S., Hivert, M., Chavarro, J., Rich-Edwards, J., & Oken, E. (2023). Abstract P259: Associations of Adverse Childhood Experiences With Cardiovascular Health (Life's Essential 8) Among Women in Midlife. Circulation.

20. Gannon, M., Short, V., LaNoue, M., & Abatemarco, D. (2020). Prevalence of Adverse Childhood Experiences of Parenting Women in Drug Treatment for Opioid Use Disorder. Community Mental Health Journal, 57, 872 - 879.

21. Hillis, S., Anda, R., Dube, S., Felitti, V., Marchbanks, P., & Marks, J. (2004). The association between adverse childhood experiences and adolescent pregnancy, long-term psychosocial consequences, and fetal death. Pediatrics, 113 2, 320-7 .

22. Yoon, C., Mason, S., Loth, K., & Jacobs, D. (2022). Adverse childhood experiences and disordered eating among middle-aged adults: Findings from the coronary artery risk development in young adults study.. Preventive medicine, 107124 .

23. Rienecke, R., Johnson, C., Mehler, P., Grange, L., Manwaring, J., Duffy, A., McClanahan, S., & Blalock, D. (2022). Adverse childhood experiences among a treatment-seeking sample of adults with eating disorders.. European eating disorders review : the journal of the Eating Disorders Association.

24. Kovács-Tóth, B., Oláh, B., Szabó, I., & Túry, F. (2022). Adverse childhood experiences increase the risk for eating disorders among adolescents. Frontiers in Psychology, 13.

25. Ghaffari, A., Graves, K., Hogans-Mathews, S., Flowers, K., & Harman, J. (2024). Associations of adverse childhood events with disordered eating behaviors among US adolescents.. Eating behaviors, 55, 101929 .

26. Friedrich, C., & Lomas, T. (2024). Embodied superpower: A qualitative study of the experience of highly sensitive wellbeing practitioners. International Journal of Wellbeing.

27. Rajić, I. (2024). Sensory Processing Sensitivity. Psiholoska istrazivanja.

28. Acevedo, B. P., Aron, E. N., Aron, A., Sangster, M. D., Collins, N., & Brown, L. L. (2014). The highly sensitive brain: an fMRI study of sensory processing sensitivity and response to others' emotions. Brain and behavior, 4(4), 580–594.

29. Huang, H., Yan, P., Shan, Z., Chen, S., Li, M., Luo, C., Gao, H., Hao, L., & Liu, L. (2015). Adverse childhood experiences and risk of type 2 diabetes: A systematic review and meta-analysis. Metabolism: clinical and experimental, 64(11), 1408–1418.

30. Zhang, Y., Yin, Y., Zhang, X., Ye, J., & Zhang, J. (2022). Association of adverse childhood experiences with diabetes: A systematic review and meta-analysis. Journal of diabetes and its complications, 36(10), 108289.

31. Barman, N., Islam, A. B. M. M. K., & Haque, M. A. (2024). Association between adverse childhood experiences and type 2 diabetes mellitus in later life: A case-control study. PLOS global public health, 4(6), e0002715.

32. Kim, H., Cheon, E., Bai, D., Lee, Y., & Koo, B. (2018). Stress and Heart Rate Variability: A Meta-Analysis and Review of the Literature. Psychiatry Investigation, 15, 235 - 245.

33. Kim, J., Foo, J., Murata, T., & Togo, F. (2024). Reduced heart rate variability is related to fluctuations in psychological stress levels in daily life.. Stress and health : journal of the International Society for the Investigation of Stress, e3447 .

34. Lombardo, D., & Vick, R. (2019). Relationship Between Heart Rate Variability and Perceived Stress in Healthy College-Aged Adults. The FASEB Journal, 33.

35. Tripska, K., Draessler, J., & Pokladnikova, J. (2022). Heart rate variability, perceived stress and willingness to seek counselling in undergraduate students.. Journal of psychosomatic research, 160, 110972 .

36. Silva, A., Araújo, D., Costa, A., Dias, B., Fregonezi, G., & Dias, F. (2015). Increase in perceived stress is correlated to lower heart rate variability in healthy young subjects. Acta Scientiarum. Health Science, 37, 7-10.

37. Glechner, A., Keuchel, L., Affengruber, L., Titscher, V., Sommer, I., Matyas, N., Wagner, G., Kien, C., Klerings, I., & Gartlehner, G. (2018). Effects of lifestyle changes on adults with prediabetes: A systematic review and meta-analysis.. Primary care diabetes, 12 5, 393-408 .

38. Galaviz, K., Weber, M., Suvada, K., Gujral, U., Wei, J., Merchant, R., Dharanendra, S., Haw, J., Narayan, K., & Ali, M. (2022). Interventions for Reversing Prediabetes: A Systematic Review and Meta-Analysis.. American journal of preventive medicine.

39. Chai, X., Wang, Y., Yin, X., Gong, Q., Zhang, J., Shao, R., & Li, G. (2025). Effects of lifestyle interventions on the prevention of type 2 diabetes and reversion to normoglycemia by prediabetes phenotype: A systematic review and meta-analysis of randomized controlled trials.. Diabetes & metabolic syndrome, 19 1, 103184 .

40. Jayedi, A., Soltani, S., Emadi, A., Najafi, A., & Zargar, M. (2024). Efficacy of lifestyle weight loss interventions on regression to normoglycemia and progression to type 2 diabetes in individuals with prediabetes: a systematic review and pairwise and dose-response meta-analyses.. The American journal of clinical nutrition.

41. Wang, Y., Chai, X., Wang, Y., Yin, X., Huang, X., Gong, Q., Zhang, J., Shao, R., & Li, G. (2025). Effectiveness of Different Intervention Modes in Lifestyle Intervention for the Prevention of Type 2 Diabetes and the Reversion to Normoglycemia in Adults With Prediabetes: Systematic Review and Meta-Analysis of Randomized Controlled Trials.. Journal of medical Internet research, 27, e63975 .

42. Ortiz, R., Kluwe, B., Odei, J. B., Echouffo Tcheugui, J. B., Sims, M., Kalyani, R. R., Bertoni, A. G., Golden, S. H., & Joseph, J. J. (2019). The association of morning serum cortisol with glucose metabolism and diabetes: The Jackson Heart Study. Psychoneuroendocrinology, 103, 25–32.

43. Khani, S., & Tayek, J.A. (2001). Cortisol increases gluconeogenesis in humans: its role in the metabolic syndrome. Clinical science, 101 6, 739-47 .

44. Young, E., Carlson, N., & Brown, M. (2001). Twenty-Four-Hour ACTH and Cortisol Pulsatility in Depressed Women. Neuropsychopharmacology, 25, 267-276..

45. O'Connor, D., Ferguson, E., Green, J., O'Carroll, R., & O'Connor, R. (2015). Cortisol levels and suicidal behavior: A meta-analysis. Psychoneuroendocrinology, 63, 370-379.

46. O'Connor, D., Green, J., Ferguson, E., O'Carroll, R., & O'Connor, R. (2017). Cortisol reactivity and suicidal behavior: Investigating the role of hypothalamic-pituitary-adrenal axis responses to stress in suicide attempters and ideators. Psychoneuroendocrinology, 75, 183-191.

47. Herzog, S., Galfalvy, H., Keilp, J., Mann, J., Sublette, M., Burke, A., Oquendo, M., & Stanley, B. (2023). Relationship of stress-reactive cortisol to suicidal intent of prior attempts in major depression. Psychiatry Research, 327.

48. Shalev, A., Porta, G., Biernesser, C., Zelazny, J., Walker-Payne, M., Melhem, N., & Brent, D. (2019). Cortisol response to stress as a predictor for suicidal ideation in youth.. Journal of affective disorders, 257, 10-16 .

49. Mårin, P., Darín, N., Amemiya, T., Andersson, B., Jern, S., & Björntorp, P. (1992). Cortisol secretion in relation to body fat distribution in obese premenopausal women.. Metabolism: clinical and experimental, 41 8, 882-6.

50. Hewagalamulage, S., Lee, T., Clarke, I., & Henry, B. (2016). Stress, cortisol, and obesity: a role for cortisol responsiveness in identifying individuals prone to obesity.. Domestic animal endocrinology, 56 Suppl, S112-20.

51. Björntorp, P. (1995). Endocrine abnormalities of obesity.. Metabolism: clinical and experimental, 44 9 Suppl 3, 21-3 .

52. Pasquali, R., Cantobelli, S., Casimirri, F., Capelli, M., Bortoluzzi, L., Flamia, R., Labate, A., & Barbara, L. (1993). The hypothalamic-pituitary-adrenal axis in obese women with different patterns of body fat distribution.. The Journal of clinical endocrinology and metabolism, 77 2, 341-6 .

53. Echouffo-Tcheugui, J., Conner, S., Himali, J., Maillard, P., DeCarli, C., Beiser, A., Vasan, R., & Seshadri, S. (2018). Circulating cortisol and cognitive and structural brain measures. Neurology, 91, e1961 - e1970.

54. MacLullich, A., Deary, I., Starr, J., Ferguson, K., Wardlaw, J., & Seckl, J. (2005). Plasma cortisol levels, brain volumes and cognition in healthy elderly men. Psychoneuroendocrinology, 30, 505-515.

55. Wolf, O., Convit, A., De Leon, M., Caraos, C., & Qadri, S. (2002). Basal Hypothalamo-Pituitary-Adrenal Axis Activity and Corticotropin Feedback in Young and Older Men: Relationships to Magnetic Resonance Imaging-Derived Hippocampus and Cingulate Gyrus Volumes. Neuroendocrinology, 75, 241 - 249.

56. Klinger-König, J., Frenzel, S., Hannemann, A., Wittfeld, K., Bülow, R., Friedrich, N., Nauck, M., Völzke, H., & Grabe, H. (2021). Sex differences in the association between basal serum cortisol concentrations and cortical thickness. Neurobiology of Stress, 15.

57. Echouffo-Tcheugui, J. B., Conner, S. C., Himali, J. J., Maillard, P., DeCarli, C. S., Beiser, A. S., Vasan, R. S., & Seshadri, S. (2018). Circulating cortisol and cognitive and structural brain measures: The Framingham Heart Study. Neurology, 91(21), e1961–e1970.

58. Mosconi, L., Williams, S., Carlton, C., Zarate, C., Boneu, C., Fauci, F., Ajila, T., Nerattini, M., Jett, S., Andy, C., Battista, M., Pahlajani, S., Osborne, J., Brinton, R. D., & Dyke, J. P. (2024). Sex-specific associations of serum cortisol with brain biomarkers of Alzheimer's risk. Scientific reports, 14(1), 5519.

59. Gola, H., Engler, H., Schauer, M., Adenauer, H., Riether, C., Kolassa, S., Elbert, T., & Kolassa, I. (2012). Victims of rape show increased cortisol responses to trauma reminders: A study in individuals with war- and torture-related PTSD. Psychoneuroendocrinology, 37, 213-220.

60. Elzinga, B.M., Schmahl, C., Vermetten, E., van Dyck, R., & Bremner, J.D. (2003). Higher Cortisol Levels Following Exposure to Traumatic Reminders in Abuse-Related PTSD. Neuropsychopharmacology, 28, 1656-1665.

61. Meewisse, M.L., Reitsma, J.B., de Vries, G., Gersons, B.P., & Olff, M. (2007). Cortisol and post-traumatic stress disorder in adults. British Journal of Psychiatry, 191, 387 - 392.

62. Steudte-Schmiedgen, S., Kirschbaum, C., Alexander, N.C., & Stalder, T. (2016). An integrative model linking traumatization, cortisol dysregulation and posttraumatic stress disorder: Insight from recent hair cortisol findings. Neuroscience & Biobehavioral Reviews, 69, 124-135.

63. O'Connor, D.B., Branley-Bell, D., Green, J., Ferguson, E., O'Carroll, R.E., & O'Connor, R.C. (2019). Effects of childhood trauma, daily stress, and emotions on daily cortisol levels in individuals vulnerable to suicide. Journal of abnormal psychology.

64. Steudte-Schmiedgen, S., Kirschbaum, C., Alexander, N.C., & Stalder, T. (2016). An integrative model linking traumatization, cortisol dysregulation and posttraumatic stress disorder: Insight from recent hair cortisol findings. Neuroscience & Biobehavioral Reviews, 69, 124-135.

65. Kitamura, S., Suzuki, T., Sanoh, S., Kohta, R., Jinno, N., Sugihara, K., Yoshihara, S., Fujimoto, N., Watanabe, H., & Ohta, S. (2005). Comparative study of the endocrine-disrupting activity of bisphenol A and 19 related compounds.. Toxicological sciences : an official journal of the Society of Toxicology, 84 2, 249-59.

66. Bonefeld-Jørgensen, E., Long, M., Hofmeister, M., & Vinggaard, A. (2007). Endocrine-Disrupting Potential of Bisphenol A, Bisphenol A Dimethacrylate,

4-n-Nonylphenol, and 4-n-Octylphenol in Vitro: New Data and a Brief Review. Environmental Health Perspectives, 115, 69 - 76.

67. Kawa, I., Masood, A., Fatima, Q., Mir, S., Jeelani, H., Manzoor, S., & Rashid, F. (2021). Endocrine disrupting chemical Bisphenol A and its potential effects on female health.. Diabetes & metabolic syndrome, 15 3, 803-811 .

68. Vandenberg, L., Maffini, M., Sonnenschein, C., Rubin, B., & Soto, A. (2009). Bisphenol-A and the great divide: a review of controversies in the field of endocrine disruption.. Endocrine reviews, 30 1, 75-95 .

69. Arya, S., Dwivedi, A., Alvarado, L., & Kupesic-Plavsic, S. (2020). Exposure of U.S. population to endocrine disruptive chemicals (Parabens, Benzophenone-3, Bisphenol-A and Triclosan) and their associations with female infertility.. Environmental pollution, 265 Pt A, 114763.

70. Giulivo, M., De Alda, L., Capri, E., & Barceló, D. (2016). Human exposure to endocrine disrupting compounds: Their role in reproductive systems, metabolic syndrome and breast cancer. A review.. Environmental research, 151, 251-264 .

71. Aker, A., Watkins, D., Johns, L., Ferguson, K., Soldin, O., Del Toro, L., Alshawabkeh, A., Cordero, J., & Meeker, J. (2016). Phenols and parabens in relation to reproductive and thyroid hormones in pregnant women.. Environmental research, 151, 30-37 .

72. Virant-Klun, I., Imamovic-Kumalic, S., & Pinter, B. (2022). From Oxidative Stress to Male Infertility: Review of the Associations of Endocrine-Disrupting Chemicals (Bisphenols, Phthalates, and Parabens) with Human Semen Quality. Antioxidants, 11.

73. Van Schoor, N., & Lips, P. (2017). Global Overview of Vitamin D Status.. Endocrinology and metabolism clinics of North America, 46 4, 845-870 .

74. G, R., & Gupta, A. (2014). Vitamin D Deficiency in India: Prevalence, Causalities and Interventions. Nutrients, 6, 729 - 775.

75. Adams, J., & Hewison, M. (2010). Update in vitamin D.. The Journal of clinical endocrinology and metabolism, 95 2, 471-8 .

76. Cui, A., Zhang, T., Xiao, P., Fan, Z., Wang, H., & Yan, Z. (2023). Global and regional prevalence of vitamin D deficiency in population-based studies from 2000 to 2022: A pooled analysis of 7.9 million participants. Frontiers in Nutrition, 10.

77. Sharpley, C., Christie, D., Bitsika, V., Agnew, L., Andronicos, N., McMillan, M., & Richards, T. (2017). The use of salivary cortisol as an index of chronic stress that correlates with depression in prostate cancer patients. Psycho-Oncology, 26, 1400 - 1402.

78. Pascoe, M., Thompson, D., Jenkins, Z., & Ski, C. (2017). Mindfulness mediates the physiological markers of stress: Systematic review and meta-analysis.. Journal of psychiatric research, 95, 156-178 .

79. Koncz, Á., Demetrovics, Z., & Takacs, Z. (2020). Meditation interventions efficiently reduce cortisol levels of at-risk samples: a meta-analysis. Health Psychology Review, 15, 56 - 84.

80. Brand, S., Holsboer-Trachsler, E., Naranjo, J., & Schmidt, S. (2012). Influence of Mindfulness Practice on Cortisol and Sleep in Long-Term and Short-Term Meditators. Neuropsychobiology, 65, 109 - 118.

81. Alhawatmeh, H., Rababa, M., Alfaqih, M., Albataineh, R., Hweidi, I., & Awwad, A. (2022). The Benefits of Mindfulness Meditation on Trait Mindfulness, Perceived Stress, Cortisol, and C-Reactive Protein in Nursing Students: A Randomized Controlled Trial. Advances in Medical Education and Practice, 13, 47 - 58.

82. Kraemer, W., French, D., Spiering, B., Volek, J., Sharman, M., Ratamess, N., Judelson, D., Silvestre, R., Watson, G., Gómez, A., & Maresh, C. (2005). Cortitrol supplementation reduces serum cortisol responses to physical stress.. Metabolism: clinical and experimental, 54 5, 657-68 .

83. Della Porta, M., Maier, J., & Cazzola, R. (2023). Effects of Withania somnifera on Cortisol Levels in Stressed Human Subjects: A Systematic Review. Nutrients, 15.

84. Speers, A., Cabey, K., Soumyanath, A., & Wright, K. (2021). Effects of Withania somnifera (Ashwagandha) on Stress and the Stress-Related Neuropsychiatric Disorders Anxiety, Depression, and Insomnia. Current Neuropharmacology, 19, 1468 - 1495.

85. Lopresti, A., Smith, S., & Drummond, P. (2021). Modulation of the hypothalamic–pituitary–adrenal (HPA) axis by plants and phytonutrients: a systematic review of human trials. Nutritional Neuroscience, 25, 1704 - 1730.

86. Gopukumar, K., Thanawala, S., Somepalli, V., Rao, T., Thamatam, V., & Chauhan, S. (2021). Efficacy and Safety of Ashwagandha Root Extract on Cognitive Functions in Healthy, Stressed Adults: A Randomized, Double-Blind, Placebo-Controlled Study. Evidence-based Complementary and Alternative Medicine : eCAM, 2021.

87. Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012). A Prospective, Randomized Double-Blind, Placebo-Controlled Study of Safety and Efficacy of a High-Concentration Full-Spectrum Extract of Ashwagandha Root in Reducing Stress and Anxiety in Adults. Indian Journal of Psychological Medicine, 34, 255 - 262.

88. Monteleone, P., Beinat, L., Tanzillo, C., Maj, M., & Kemali, D. (1990). Effects of phosphatidylserine on the neuroendocrine response to physical stress in humans.. Neuroendocrinology, 52 3, 243-8 .

89. Monteleone, P., Maj, M., Beinat, L., Natale, M., & Kemali, D. (1992). Blunting by chronic phosphatidylserine administration of the stress-induced activation of the hypothalamo-pituitary-adrenal axis in healthy men. European Journal of Clinical Pharmacology, 43, 569.

90. Starks, M., Starks, S., Kingsley, M., Purpura, M., & Jäger, R. (2008). The effects of phosphatidylserine on endocrine response to moderate intensity exercise. Journal of the International Society of Sports Nutrition, 5, 11 - 11.

91. Panossian, A., Wikman, G., Sarris, J., & Sarris, J. (2010). Rosenroot (Rhodiola rosea): traditional use, chemical composition, pharmacology and clinical efficacy.. Phytomedicine : international journal of phytotherapy and phytopharmacology, 17 7, 481-93 .

92. Panossian, A., Hambardzumyan, M., Hovhanissyan, A., & Wikman, G. (2007). The Adaptogens Rhodiola and Schizandra Modify the Response to Immobilization Stress in Rabbits by Suppressing the Increase of Phosphorylated Stress-activated Protein Kinase, Nitric Oxide and Cortisol. Drug Target Insights, 2, 39 - 54.

93. Dinel, A., Guinobert, I., Lucas, C., Blondeau, C., Bardot, V., Ripoche, I., Berthomier, L., Pallet, V., Layé, S., & Joffre, C. (2019). Reduction of acute mild stress corticosterone response and changes in stress-responsive gene expression in male Balb/c mice after repeated administration of a Rhodiola rosea L. root extract. Food Science & Nutrition, 7, 3827 - 3841.

94. Dye, L., Billington, J., Lawton, C., & Boyle, N. (2020). A Combination of Magnesium, B Vitamins, Green Tea and Rhodiola Attenuates the Negative Effects of Acute Psychosocial Stress on Subjective State in Adults. Current Developments in Nutrition.

95. Boyle, N., Billington, J., Lawton, C., Quadt, F., & Dye, L. (2021). A combination of green tea, rhodiola, magnesium and B vitamins modulates brain activity and protects against the effects of induced social stress in healthy volunteers. Nutritional Neuroscience, 25, 1845 - 1859.

96. Pickering, G., Noah, L., Morel, V., Bertin, C., Pouteau, E., Dualé, C., Macian, N., & Pereira, B. (2022). A Combination of Magnesium, B Vitamins, Rhodiola, and Green Tea (L-theanine) Alleviates Chronic Stress in Healthy Volunteers: A Randomized, Placebo-Controlled Study. Current Developments in Nutrition, 6, 805 - 805.

97. Davis, S., & Wåhlin-Jacobsen, S. (2015). Testosterone in women--the clinical significance.. The lancet. Diabetes & endocrinology, 3 12, 980-92 .

98. Burger, H. (2002). Androgen production in women.. Fertility and sterility, 77 Suppl 4, S3-5 .

99. Travison, T., Vesper, H., Orwoll, E., Wu, F., Kaufman, J., Wang, Y., Lapauw, B., Fiers, T., Matsumoto, A., & Bhasin, S. (2017). Harmonized Reference Ranges for Circulating Testosterone Levels in Men of Four Cohort Studies in the United States and Europe. The Journal of Clinical Endocrinology & Metabolism, 102, 1161–1173.

100. Braunstein, G., Reitz, R., Buch, A., Schnell, D., & Caulfield, M. (2011). Testosterone reference ranges in normally cycling healthy premenopausal women.. The journal of sexual medicine, 8 10, 2924-34.

101. Goebelsmann, U., Goebelsmann, U., Arce, J., Arce, J., Thorneycroft, I., Thorneycroft, I., Mishell, D., & Mishell, D. (1974). Serum testosterone concentrations in women throughout the menstrual cycle and following HCG administration.. American journal of obstetrics and gynecology, 119 4, 445-52.

102. Antonio, L., Wu, F., O'neill, T., Pye, S., Carter, E., Finn, J., Laurent, M., Huhtaniemi, I., Rutter, M., Rastrelli, G., Forti, G., Bártfai, G., Casanueva, F., Kula, K., Punab, M., Giwercman, A., Claessens, F., Decallonne, B., & Vanderschueren, D. (2015). Low free testosterone is associated with hypogonadal signs and symptoms in men with normal total testosterone levels: results from the European Male Ageing Study. Archives of Public Health, 73, P10 - P10.

103. Antonio, L., Wu, F., O'Neill, T., Pye, S., Ahern, T., Laurent, M., Huhtaniemi, I., Lean, M., Keevil, B., Rastrelli, G., Forti, G., Bártfai, G., Casanueva, F., Kula, K., Punab, M., Giwercman, A., Claessens, F., Decallonne, B., & Vanderschueren, D. (2016). Low Free Testosterone Is Associated with Hypogonadal Signs and Symptoms in Men with Normal Total Testosterone.. The Journal of clinical endocrinology and metabolism, 101 7, 2647-57.

104. Sternbach, H. (1998). Age-associated testosterone decline in men: clinical issues for psychiatry.. The American journal of psychiatry, 155 10, 1310-8 .

105. García-Cruz, E., Leibar-Tamayo, A., Romero-Otero, J., Asiaín, I., Carrion, A., Castañeda, R., Mateu, L., Luqué, P., Cardeñosa, O., & Alcaraz, A. (2014). Marked testosterone deficiency-related symptoms may be associated to higher metabolic risk in men with low testosterone levels.. The journal of sexual medicine, 11 9, 2292-301.

106. Kloner, R., Carson, C., Dobs, A., Kopecky, S., & Mohler, E. (2016). Testosterone and Cardiovascular Disease.. Journal of the American College of Cardiology, 67 5, 545-57 .

107. Rastrelli, G., Corona, G., & Maggi, M. (2019). Both comorbidity burden and low testosterone can explain symptoms and signs of testosterone deficiency in men consulting for sexual dysfunction. Asian Journal of Andrology, 22, 265 - 273.

108. Scott, A., & Newson, L. (2020). Should we be prescribing testosterone to perimenopausal and menopausal women? A guide to prescribing testosterone for women in primary care.. The British journal of general practice : the journal of the Royal College of General Practitioners, 70 693, 203-204 .

109. Davis, S. (1999). Androgen replacement in women: a commentary.. The Journal of clinical endocrinology and metabolism, 84 6, 1886-91 .

110. Rohr, U. (2002). The impact of testosterone imbalance on depression and women's health.. Maturitas, 41 Suppl 1, S25-46 .

111. Rech, C., Clapauch, R., De Souza, M., & Bouskela, E. (2016). Low testosterone levels are associated with endothelial dysfunction in oophorectomized early postmenopausal women.. European journal of endocrinology, 174 3, 297-306 .

112. Miller, J., Darley, C., Karkavitsas, K., Kirby, J., & Munro, D. (1982). Low sex-hormone binding globulin levels in young women with diffuse hair loss. British Journal of Dermatology, 106.

113. Münzker, J., Hofer, D., Trummer, C., Ulbing, M., Harger, A., Pieber, T., Owen, L., Keevil, B., Brabant, G., Brabant, G., Lerchbaum, E., & Obermayer-Pietsch, B. (2015). Testosterone to dihydrotestosterone ratio as a new biomarker for an adverse metabolic phenotype in the polycystic ovary syndrome.. The Journal of clinical endocrinology and metabolism, 100 2, 653-60 .

114. Abdelazim, I., Alanwar, A., AbuFaza, M., Amer, O., Bekmukhambetov, Y., Zhurabekova, G., Shikanova, S., & Karimova, B. (2020). Elevated and diagnostic androgens of polycystic ovary syndrome. Przeglad Menopauzalny = Menopause Review, 19, 1 - 5.

115. Balen, A. H., Conway, G. S., Kaltsas, G., Techatraisak, K., Manning, P. J., West, C., & Jacobs, H. S. (1995). Androlоgy: Polycystic ovary syndrome: the spectrum of the disorder in 1741 patients. Human Reproduction, 10(8), 2107–2111.

116. Rosenfield, R., & Ehrmann, D. (2016). The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited.. Endocrine reviews, 37 5, 467-520 .

117. Diamanti-Kandarakis, E., & Dunaif, A. (2012). Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications.. Endocrine reviews, 33 6, 981-1030 .

118. Diamanti-Kandarakis, E., & Papavassiliou, A. (2006). Molecular mechanisms of insulin resistance in polycystic ovary syndrome.. Trends in molecular medicine, 12 7, 324-32 .

119. Brownlee, K., Moore, A., & Hackney, A. (2005). Relationship between circulating cortisol and testosterone: influence of physical exercise.. Journal of sports science & medicine, 4 1, 76-83 .

120. Daly, W., Seegers, C., Rubin, D., Dobridge, J., & Hackney, A. (2004). Relationship between stress hormones and testosterone with prolonged endurance exercise. European Journal of Applied Physiology, 93, 375-380.

121. Popma, A., Vermeiren, R., Geluk, C., Rinne, T., Brink, W., Knol, D., Jansen, L., Engeland, H., & Doreleijers, T. (2007). Cortisol Moderates the Relationship between Testosterone and Aggression in Delinquent Male Adolescents. Biological Psychiatry, 61, 405-411.

122. Sherman, G., Lerner, J., Josephs, R., Renshon, J., & Gross, J. (2016). The interaction of testosterone and cortisol is associated with attained status in male executives.. Journal of personality and social psychology, 110 6, 921-9 .

123. Wilson, J., Lowery, R., Roberts, M., Sharp, M., Joy, J., Shields, K., Partl, J., Volek, J., & D'Agostino, D. (2017). The Effects of Ketogenic Dieting on Body Composition, Strength, Power, and Hormonal Profiles in Resistance Training Males.. Journal of strength and conditioning research.

124. Corsetti, V., Notari, T., & Montano, L. (2023). Effects of the low-carb organic Mediterranean diet on testosterone levels and sperm DNA fragmentation. Current Research in Food Science, 7.

125. da Silva Schmitt, C., da Costa, C. M., Souto, J. C. S., Chiogna, L. M., de Albuquerque Santos, Z. E., Rhoden, E. L., & Neto, B. S. (2023). The effects of a low carbohydrate diet on erectile function and serum testosterone levels in hypogonadal men with metabolic syndrome: a randomized clinical trial. BMC endocrine disorders, 23(1), 30.

126. Pearce, K. L., & Tremellen, K. (2019). The Effect of Macronutrients on Reproductive Hormones in Overweight and Obese Men: A Pilot Study. Nutrients, 11(12), 3059.

127. Anderson, K., Rosner, W., Khan, M., New, M., Pang, S., Wissel, P., & Kappas, A. (1987). Diet-hormone interactions: protein/carbohydrate ratio alters reciprocally the plasma levels of testosterone and cortisol and their respective binding globulins in man.. Life sciences, 40 18, 1761-8 .

128. Whittaker, J., & Harris, M. (2022). Low-carbohydrate diets and men's cortisol and testosterone: Systematic review and meta-analysis. Nutrition and Health, 28, 543 - 554.

129. Wrzosek, M., Woźniak, J., & Włodarek, D. (2020). The Combination of a Diversified Intake of Carbohydrates and Fats and Supplementation of Vitamin D in a Diet Does Not Affect the Levels of Hormones (Testosterone, Estradiol, and Cortisol) in Men Practicing Strength Training for the Duration of 12 Weeks. International journal of environmental research and public health, 17(21), 8057.

130. Kumar, S., Behl, T., Sachdeva, M., Sehgal, A., Kumari, S., Kumar, A., Kaur, G., Yadav, H., & Bungău, S. (2020). Implicating the effect of ketogenic diet as a preventive measure to obesity and diabetes mellitus.. Life sciences, 118661 .

131. , Q., Jiang, L., You, Y., Ni, H., , L., Lin, X., Wang, Z., Yan, W., Xiao, X., Li, X., & Jibin, L. (2024). Ketogenic diet ameliorates high-fat diet-induced insulin resistance in mouse skeletal muscle

by alleviating endoplasmic reticulum stress.. Biochemical and biophysical research communications, 702, 149559 .

132. Paoli, A., Bianco, A., Moro, T., Mota, J., & Coelho-Ravagnani, C. (2023). The Effects of Ketogenic Diet on Insulin Sensitivity and Weight Loss, Which Came First: The Chicken or the Egg?. Nutrients, 15.

133. Luong, T., Pedersen, M., Abild, C., Lauritsen, K., Kjærulff, M., Møller, N., Gormsen, L., & Søndergaard, E. (2024). A 3-Week Ketogenic Diet Increases Skeletal Muscle Insulin Sensitivity in Individuals With Obesity: A Randomized Controlled Crossover Trial. Diabetes, 73, 1631 - 1640.

134. Yuan, X., Wang, J., Yang, S., Gao, M., Cao, L., Li, X., Hong, D., Tian, S., & Sun, C. (2020). Effect of the ketogenic diet on glycemic control, insulin resistance, and lipid metabolism in patients with T2DM: a systematic review and meta-analysis. Nutrition & Diabetes, 10.

135. Skow, S., & Jha, R. (2022). A Ketogenic Diet is Effective in Improving Insulin Sensitivity in Individuals with Type 2 Diabetes.. Current diabetes reviews.

136. Aronica, L., Landry, M., Rigdon, J., & Gardner, C. (2023). Weight, insulin resistance, blood lipids, and diet quality changes associated with ketogenic and ultra low-fat dietary patterns: a secondary analysis of the DIETFITS randomized clinical trial. Frontiers in Nutrition, 10.

137. Grandl, G., Straub, L., Rudigier, C., Arnold, M., Wueest, S., Konrad, D., & Wolfrum, C. (2018). Short-term feeding of a ketogenic diet induces more severe hepatic insulin resistance than an obesogenic high-fat diet. The Journal of Physiology, 596, 4597 - 4609.

138. Iacovides, S., Maloney, S., Bhana, S., Angamia, Z., & Meiring, R. (2022). Could the ketogenic diet induce a shift in thyroid function and support a metabolic advantage in healthy participants? A pilot randomized-controlled-crossover trial. PLoS ONE, 17.

139. Molteberg, E., Thorsby, P., Kverneland, M., Iversen, P., Selmer, K., Nakken, K., & Taubøll, E. (2020). Effects of modified Atkins diet on thyroid function in adult patients with pharmacoresistant epilepsy. Epilepsy & Behavior, 111.

140. Majid, B., Khan, M., Maqsood, A., Khalid, M., Ahmad, Z., & Raza, S. (2022). Impact of ketogenic diet on insulin and thyroid hormones in a healthy cohort. International journal of health sciences.

141. Kose, E., Guzel, O., Demir, K., & Arslan, N. (2017). Changes of thyroid hormonal status in patients receiving ketogenic diet due to intractable epilepsy. Journal of Pediatric Endocrinology and Metabolism, 30, 411 - 416.

142. Burén, J., Ericsson, M., Damasceno, N., & Sjödin, A. (2021). A Ketogenic Low-Carbohydrate High-Fat Diet Increases LDL Cholesterol in Healthy, Young, Normal-Weight Women: A Randomized Controlled Feeding Trial. Nutrients, 13.

143. Joo, M., Moon, S., Lee, Y., & Kim, M. (2023). Effects of very low-carbohydrate ketogenic diets on lipid profiles in normal-weight (body mass index < 25 kg/m2) adults: a meta-analysis.. Nutrition reviews.

144. Chen, S., Su, X., Feng, Y., Li, R., Liao, M., Fan, L., Liu, J., Chen, S., Zhang, S., Cai, J., Zhu, S., Niu, J., Ye, Y., Lo, K., & Zeng, F. (2023). Ketogenic Diet and Multiple Health Outcomes: An Umbrella Review of Meta-Analysis. Nutrients, 15.

145. Ruppert, P., & Kersten, S. (2023). Mechanisms of hepatic fatty acid oxidation and ketogenesis during fasting. Trends in Endocrinology & Metabolism, 35, 107-124.

146. Morrow, P., Marshall, W., Kim, H., & Kalkhoff, R. (1981). Metabolic response to starvation. II. Effects of sex steroid administration to pre- and postmenopausal women.. Metabolism: clinical and experimental, 30 3, 274-8 .

147. Khosla, S., Melton, L., & Riggs, B. (2002). Estrogen and the Male Skeleton. The Journal of Clinical Endocrinology and Metabolism, 87, 1443-1450.

148. Khosla, S., Melton, L., & Riggs, B. (2001). Estrogens and Bone Health in Men. Calcified Tissue International, 69, 189-192.

149. Lee, S., Ryu, K., Son, S., Lee, Y., Park, H., & Kim, T. (2022). Body fat distribution and insulin resistance among Korean middle-aged women: a Korean National Health and Nutrition Examination Survey. Obstetrics & Gynecology Science, 65, 468 - 476.

150. Shin, H., Lee, H., & Kwon, Y. (2020). Association between reproductive years and insulin resistance in middle-aged and older women: A 10-year prospective cohort study.. Maturitas, 142, 31-37 .

151. Racette, S., Evans, E., Weiss, E., Hagberg, J., & Holloszy, J. (2006). Abdominal adiposity is a stronger predictor of insulin resistance than fitness among 50-95 year olds.. Diabetes care, 29 3, 673-8 .

152. Racette, S., Evans, E., Weiss, E., Hagberg, J., & Holloszy, J. (2006). Abdominal adiposity is a stronger predictor of insulin resistance than fitness among 50-95 year olds.. Diabetes care, 29 3, 673-8 .

153. Godsland, I., Gangar, K., Walton, C., Cust, M., Whitehead, M., Wynn, V., & Stevenson, J. (1993). Insulin resistance, secretion, and elimination in postmenopausal women receiving oral or transdermal hormone replacement therapy.. Metabolism: clinical and experimental, 42 7, 846-53 .

154. Moghetti, P., Tosi, F., Castello, R., Magnani, C., Negri, C., Brun, E., Furlani, L., Caputo, M., & Muggeo, M. (1996). The insulin resistance in women with hyperandrogenism is partially reversed by antiandrogen treatment: evidence that androgens impair insulin action in women.. The Journal of clinical endocrinology and metabolism, 81 3, 952-60 .

155. Polderman, K., Gooren, L., Asscheman, H., Bakker, A., & Heine, R. (1994). Induction of insulin resistance by androgens and estrogens.. The Journal of clinical endocrinology and metabolism, 79 1, 265-71 .

156. Bitoska, I., Krstevska, B., Milenković, T., Šubeska-Stratrova, S., Petrovski, G., Mishevska, S., Ahmeti, I., & Todorova, B. (2016). Effects of Hormone Replacement Therapy on Insulin Resistance in Postmenopausal Diabetic Women. Open Access Macedonian Journal of Medical Sciences, 4, 83 - 88.

157. Margolis, K., Bonds, D., Rodabough, R., Tinker, L., Phillips, L., Allen, C., Bassford, T., Burke, G., Torréns, J., Howard, B., & Investigators, F. (2004). Effect of oestrogen plus progestin on the incidence of diabetes in postmenopausal women: results from the Women's Health Initiative Hormone Trial. Diabetologia, 47, 1175-1187.

158. Zang, H., Carlström, K., Arner, P., & Hirschberg, A. (2006). Effects of treatment with testosterone alone or in combination with estrogen on insulin sensitivity in postmenopausal women.. Fertility and sterility, 86 1, 136-44 .

159. De Paoli, M., Zakharia, A., & Werstuck, G. (2021). The role of estrogen in insulin resistance: a review of clinical and pre-clinical data.. The American journal of pathology.

160. King, D., Mainous, A., & Lambourne, C. (2012). Trends in dietary fiber intake in the United States, 1999-2008.. Journal of the Academy of Nutrition and Dietetics, 112 5, 642-8 .

161. Dahl, W., & Stewart, M. (2015). Position of the Academy of Nutrition and Dietetics: Health Implications of Dietary Fiber.. Journal of the Academy of Nutrition and Dietetics, 115 11, 1861-70 .

162. Mcgill, C., Fulgoni, V., & Devareddy, L. (2015). Ten-Year Trends in Fiber and Whole Grain Intakes and Food Sources for the United States Population: National Health and Nutrition Examination Survey 2001–2010. Nutrients, 7, 1119 - 1130.

163. Lanza, E., Jones, D., Block, G., & Kessler, L. (1987). Dietary fiber intake in the US population.. The American journal of clinical nutrition, 46 5, 790-7 .

164. Miketinas, D., Tucker, W., Patterson, M., & Douglas, C. (2021). Usual Dietary Fiber Intake in US Adults with Diabetes: NHANES 2013–2018. Current Developments in Nutrition.

165. Klinder, A., Shen, Q., Heppel, S., Lovegrove, J., Rowland, I., & Tuohy, K. (2016). Impact of increasing fruit and vegetables and flavonoid intake on the human gut microbiota.. Food & function, 7 4, 1788-96 .

166. Van Der Merwe, M. (2020). Gut microbiome changes induced by a diet rich in fruits and vegetables. International Journal of Food Sciences and Nutrition, 72, 665 - 669.

167. Frankenfeld, C., Hullar, M., Maskarinec, G., Monroe, K., Shepherd, J., Franke, A., Randolph, T., Wilkens, L., Boushey, C., Marchand, L., Lim, U., & Lampe, J. (2021). The Gut Microbiome Is Associated with Circulating Dietary Biomarkers of Fruit and Vegetable Intake in a Multiethnic Cohort.. Journal of the Academy of Nutrition and Dietetics.

168. Baker, J., Al-Nakkash, L., & Herbst-Kralovetz, M. (2017). Estrogen-gut microbiome axis: Physiological and clinical implications.. Maturitas, 103, 45-53.

169. Kumari, N., Kumari, R., Dua, A., Singh, M., Kumar, R., Singh, P., Duyar-Ayerdi, S., Pradeep, S., Ojesina, A., & Kumar, R. (2024). From Gut to Hormones: Unraveling the Role of Gut Microbiota in (Phyto)Estrogen Modulation in Health and Disease.. Molecular nutrition & food research, e2300688.

170. Hu, S., Ding, Q., Zhang, W., Kang, M., , J., & Zhao, L. (2023). Gut microbial beta-glucuronidase: a vital regulator in female estrogen metabolism. Gut Microbes, 15.

171. Hu, J., Wang, J., Li, Y., Xue, K., & Kan, J. (2023). Use of Dietary Fibers in Reducing the Risk of Several Cancer Types: An Umbrella Review. Nutrients, 15.

172. Arayıcı, M.E., Başbınar, Y., & Ellidokuz, H. (2023). High and low dietary fiber consumption and cancer risk: a comprehensive umbrella review with meta-meta-analysis involving meta-analyses of observational epidemiological studies. Critical reviews in food science and nutrition, 1-14 .

173. Kim, Y., & Je, Y. (2016). Dietary fibre intake and mortality from cardiovascular disease and all cancers: A meta-analysis of prospective cohort studies. Archives of cardiovascular diseases, 109 1, 39-54 .

174. Cicinelli, C., Trojano, A., Alfonso, R., Damiani, G., Romano, I., Vimercati, A., Gennaro, D., Muzzupapa, G., & D'Amato, A. (2024). Non-hormonal options for managing menopause symptoms: a narrative review. Italian Journal of Gynaecology and Obstetrics..

175. Cicinelli, C., Trojano, A., Alfonso, R., Damiani, G., Romano, I., Vimercati, A., Gennaro, D., Muzzupapa, G., & D'Amato, A. (2024). Non-hormonal options for managing menopause symptoms: a narrative review. Italian Journal of Gynaecology and Obstetrics.

176. Kaunitz, A., & Manson, J. (2015). Management of Menopausal Symptoms.. Obstetrics and gynecology, 126 4, 859-76 .

177. Davis, S., Pinkerton, J., Santoro, N., & Simoncini, T. (2023). Menopause—Biology, consequences, supportive care, and therapeutic options. Cell.

178. Yelland, S., Steenson, S., Creedon, A., & Stanner, S. (2023). The role of diet in managing menopausal symptoms: A narrative review.. Nutrition bulletin.

179. Ihalainen, J., Hackney, A., & Taipale, R. (2019). Changes in inflammation markers after a 10-week high-intensity combined strength and endurance training block in women: The effect of hormonal contraceptive use.. Journal of science and medicine in sport.

180. Kangasniemi, M., Haverinen, A., Luiro, K., Hiltunen, J., Komsi, E., Arffman, R., Heikinheimo, O., Tapanainen, J., & Piltonen, T. (2020). Estradiol valerate in COC has more favorable inflammatory profile than synthetic ethinyl estradiol - a randomized trial.. The Journal of clinical endocrinology and metabolism.

181. Mengelkoch, S., Gassen, J., Slavich, G., & Hill, S. (2023). Hormonal contraceptive use is associated with differences in women's inflammatory and psychological reactivity to an acute social stressor. Brain, behavior, and immunity, 115, 747 - 757.

182. Piltonen, T., Puurunen, J., Hedberg, P., Ruokonen, A., Mutt, S., Herzig, K., Nissinen, A., Nissinen, A., Morin-Papunen, L., Tapanainen, J., & Tapanainen, J. (2012). Oral, transdermal and vaginal combined contraceptives induce an increase in markers of chronic inflammation and impair insulin sensitivity in young healthy normal-weight women: a randomized study.. Human reproduction, 27 10, 3046-56 .

183. Williams, W. (2017). Hormonal Contraception and the Development of Autoimmunity: A Review of the Literature. The Linacre Quarterly, 84, 275 - 295.

184. Khalili, H. (2016). Risk of Inflammatory Bowel Disease with Oral Contraceptives and Menopausal Hormone Therapy: Current Evidence and Future Directions. Drug Safety, 39, 193-197.

185. Narula, N., Wong et al. (2022). Associations of Antibiotics, Hormonal Therapies, Oral Contraceptives, and Long-Term NSAIDs with Inflammatory Bowel Disease: Results from the Prospective Urban Rural Epidemiology (PURE) Study.. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association.

186. Lesko, S., Lesko, S., Kaufman, D., Kaufman, D., Rosenberg, L., Rosenberg, L., Helmrich, S., Helmrich, S., Dr, M., Dr, M., Stolley, P., Stolley, P., Shapiro, S., & Shapiro, S. (1985). Evidence for an increased risk of Crohn's disease in oral contraceptive users.. Gastroenterology, 89 5, 1046-9 .

187. Cornish, J., Tan, E., Simillis, C., Clark, S., Teare, J., & Tekkis, P. (2008). The Risk of Oral Contraceptives in the Etiology of Inflammatory Bowel Disease: A Meta-Analysis. The American Journal of Gastroenterology, 103, 2394-2400.

188. Battaglia, C., Morotti, E., Persico, N., Battaglia, B., Busacchi, P., Casadio, P., Paradisi, R., & Venturoli, S. (2014). Clitoral vascularization and sexual behavior in young patients treated with drospirenone-ethinyl estradiol or contraceptive vaginal ring: a prospective, randomized, pilot study.. The journal of sexual medicine, 11 2, 471-80 .

189. Stone, A. A., Schwartz, J. E., Broderick, J. E., & Deaton, A. (2010). A snapshot of the age distribution of psychological well-being in the United States. Proceedings of the National Academy of Sciences of the United States of America, 107(22), 9985–9990.

190. Kronzer, V.L., Bridges, S.L., & Davis, J.M. (2020). Why women have more autoimmune diseases than men: An evolutionary perspective. Evolutionary Applications, 14, 629 - 633

191. Ji, J., Sundquist, J., & Sundquist, K. (2016). Gender-specific incidence of autoimmune diseases from national registers. Journal of autoimmunity, 69, 102–106.

192. Black, M.C., Basile, K.C., Breiding, M.J., Smith, S.G., Walters, M.L., Merrick, M.T., Chen, J., & Stevens, M.R. (2011). The National Intimate Partner and Sexual Violence Survey (NISVS): 2010 Summary Report. Atlanta, GA: National Center for Injury Prevention and Control, Centers for Disease Control and Prevention.

193. Cancer Incidence Rate for Women Under 50 Rises Above Men's (American Cancer Association)

194. Macmahon, B., Cole, P., Lin, T., Lowe, C., Mirra, A., Ravnihar, B., Salber, E., Valaoras, V., & Yuasa, S. (1970). Age at first birth and breast cancer risk.. Bulletin of the World Health Organization, 43 2, 209-21 .

195. Trichopoulos, D., Hsieh, C., Macmahon, B., Lln, T., Lowe, C., Mirra, A., Ravnihar, B., Salber, E., Valaoras, V., & Yuasa, S. (1983). Age at any birth and breast cancer risk. International Journal of Cancer, 31.

196. Ramón, J., Escribal, J., Casas, I., Benet, J., Iglesias, C., Gavaldal, L., Torras, G., & Oromí, J. (1996). Age at first full-term pregnancy, lactation and parity and risk of breast cancer: A case-control study in Spain. European Journal of Epidemiology, 12, 449-453..

197. Basson, R. (2002). Review: Female sexual dysfunctions — the new models. The British Journal of Diabetes & Vascular Disease, 2(4), 267–270.

198. Reinke, H., & Asher, G. (2019). Crosstalk between metabolism and circadian clocks. Nature Reviews Molecular Cell Biology, 20, 227 - 241.

199. Walker, W., Walton, J., DeVries, A., & Nelson, R. (2020). Circadian rhythm disruption and mental health. Translational Psychiatry, 10.

200. Persson, P., & Persson, A. (2018). Light and darkness in circadian rhythms. Acta Physiologica, 222.

201. Revell, V., Burgess, H., Gazda, C., Smith, M., Fogg, L., & Eastman, C. (2006). Advancing human circadian rhythms with afternoon melatonin and morning intermittent bright light.. The Journal of clinical endocrinology and metabolism, 91 1, 54-9 .