Community notes

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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 (not here presented) 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.

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Health span in the United States

“The average lifespan in the United States is 77 years old. The average health span in the United States, believe it or not, is 67 years old. In fact, if you look at the CDC, and they talk about how long you'll live without a disability, it's actually 63 so there's a delta here. There's at least 1015, years where you will be in some kind of disability and cannot live to your fullest.”

The average life expectancy in the United States in 2017 was 78.6 years (1, 2).

Four pillars of “sex span”

“there's things that I can do to make my sex span last as long as my life span. There's many things you can do, and I called it the four pillars. The first is diet, exercise, sleep and stress reduction.”

Unhealthy lifestyles, particularly obesity, smoking, alcohol abuse, and chronic stress, contribute significantly to sexual dysfunctions in both genders (3).

Testosterone supplementation

“Testosterone supplementation can significantly improve a man and a woman's sexual function”

Testosterone supplementation (TS) can improve sexual function in hypogonadal men, but its effects in eugonadal men are uncertain. Testosterone treatment significantly improves sexual function in men with testosterone deficiency. These findings suggest that sexual dysfunction should be considered a key manifestation of testosterone deficiency, as symptoms can be significantly improved with TS.

Multiple studies have demonstrated that adding testosterone to hormone therapy enhances various aspects of sexual functioning, including libido, arousal, and satisfaction. While not FDA-approved for treating sexual dysfunction in women, testosterone therapy has been used off-label for over 40 years. Current evidence supports considering low-dose testosterone therapy for symptomatic androgen-deficient postmenopausal women with sexual desire disorders, provided they are adequately estrogenized.

Medical students' training in sexual medicine

"Only 65% of US medical students get training in sexual medicine, and of those 65, 50% of those students said that the training was terrible"

Erectile dysfunction and depression

"66% of men who come in with Ed have some degree of depression. 66% right? And that's important. Anxiety. 35% is very important."

Studies indicate that men with high depression scores are nearly twice as likely to report ED compared to non-depressed men (13). A recent study (14) found that among men with ED, 68.3% had mild depression, 25% had moderate depression, and 6.7% had moderately severe depression. In another study, 79.82% and 79.56% of erectile dysfunction patients in the study had anxiety and depression, respectively (15). A systematic review found a median prevalence of 20.0% for ED in men with anxiety disorders (16).

Erectile dysfunction and heart attack or stroke

"ED is the first sign of other major adverse medical problems. For example, if a man comes into my office today, 15% of them will have a heart attack or stroke within seven years. 15% the day they get Ed, 15% will have a heart attack or a stroke within seven years. It's the first sign. Other studies, Dr montorsi showed that if a man presents to the emergency room with a heart attack, on average, 39 months earlier, that's when the ED started. So it is the first sign."

Multiple studies have found that men with ED have a significantly higher risk of developing cardiovascular disease (CVD), coronary heart disease (CAD), stroke, and all-cause mortality compared to those without ED (17, 18). A meta-analysis of prospective cohort studies revealed that ED was associated with a 48% increased risk of CVD (1). Another study found that men with ED had a 29% higher risk of stroke within a 5-year follow-up period (19). Importantly, ED may precede CVD events by several years, with one study reporting

that incident ED was associated with a 25% increased risk of subsequent cardiovascular events (20). ED often precedes symptomatic CAD by an average of 2-3 years, with one study reporting a mean interval of 38.8 months (21).

Libido and hormones

"The four hormones that can affect someone's libido are prolactin, estrogen, thyroid and testosterone. (...) So in other words, serotonin, norepinephrine, dopamine, dopamine goes up, libido goes down. Serotonin goes up, libido. Dopamine goes up, libido goes up, serotonin goes up, libido goes down."

On prolactin:

Elevated prolactin levels have been associated with decreased sexual desire and activity in a study on elderly men (22). Hyperprolactinemia has been shown to reduce libido in both sexes, although in men it is also linked to low testosterone levels (23). While hyperprolactinemia affects libido, it does not appear to impact night erections or penile response to visual erotic stimuli, suggesting its effects on sexual behavior may be primarily psychological (24) The relationship between prolactin and sexual function is complex and may involve multiple mechanisms (25).

On estrogen:

Estrogen's effect on libido is complex and context-dependent. In men with normal hormone levels, estrogen may reduce libido, but it can help maintain sexual desire in those with low androgen levels, such as castrated men or transgender women (26). Psychological and social factors often influence libido more than estrogen itself (27). In postmenopausal women, estrogen-androgen therapy may enhance libido and well-being compared to estrogen-only treatments 28). Estrogen receptors in the brain and reproductive organs suggest a role in sexual function (26). In prostate cancer patients undergoing hormone therapy, estrogen may help sustain libido, though risks should be considered (26).

On thyroid:

Hypothyroidism and hyperthyroidism are linked to higher rates of sexual dysfunction, including erectile and ejaculatory issues in men (29). In women, these conditions impact desire, arousal, and satisfaction (30). The connection between thyroid dysfunction and sexual issues seems stronger in men than women (31).

On testosterone:

Research on testosterone's impact on libido shows mixed results. In premenopausal women, testosterone levels don't consistently correlate with libido, and testosterone treatment hasn't clearly improved sexual desire (32). In aging men, testosterone is linked to libido at the population level, but low libido may not always indicate low testosterone (33). Testosterone therapy has shown benefits for women with sexual desire/arousal issues and elderly men with low testosterone (34, 35). However, the long-term risks of testosterone therapy remain unclear, and further research is needed to understand its effects on libido across different populations (32, 35).

On serotonin:

Selective serotonin reuptake inhibitors (SSRIs) are known to cause sexual dysfunction in both men and women, with prevalence estimates ranging widely from a small percentage to over 80% (36). A strong correlation exists between an antidepressant's serotonin transporter (SERT) affinity and the risk of decreased sexual desire, suggesting that higher SERT affinity is associated with a greater risk of libido reduction (37). However, the relationship between serotonin and sexual function is complex.

On norepinephrine:

The effects of norepinephrine (NE) on libido are not directly studied, but some findings are relevant. In women with low sexual desire, NE metabolite levels were slightly lower, but treatment with yohimbine, which increases NE release, didn't improve sexual desire. NE has various physiological effects, but its direct impact on libido remains unclear and needs more research.

On dopamine:

Dopamine plays a key role in sexual function, affecting arousal, motivation, and reward. It also influences sexual behavior and coordination, with some treatments showing increased libido in certain conditions, though the effects can vary.

Finasteride and libido

"For example, a medication that men take for urinary function called finasteride, shuts down their libido."

Cialis/tadalafil

"When you give a man Cialis five milligrams every day, what it does is, essentially, is having that medication on board all the time."

Long-term efficacy:

Daily administration of low-dose tadalafil offers an alternative treatment option that removes the need for temporal linkage between medication intake and sexual activity, potentially benefiting men who anticipate frequent sexual activity.

Effect on tissue structure:

"Cialis, in my opinion, is one of the few things that helps cure Ed if you look at studies, and you look at a penile tissue, and we biopsy the tissue, and then you biopsy three months later on daily Cialis, it physically gets stronger."

Chronic low-dose tadalafil improved erectile function in diabetic rats by enhancing penile tissue structure, increasing smooth muscle and elastic tissue while reducing fibrous tissue. This suggests that structural changes may improve function beyond the drug's direct effects.

Endothelium protection:

"More importantly, daily Cialis protects the endothelium"

Prolonged efficacy of endothelial function:

"Versa, and what he showed was that those patients that stopped taking it after three months versus placebo still had benefit in terms of endothelial function protection and erectile function protection than those people that took placebo"

Adverse effects:

"so on the larger dose, headache stuff, you know, back pain is more common with Cialis and other medications, but it can be reported. Remember, you shouldn't take these medications. If you have you're taking a nitrate, because it can drop your blood pressure."

The most common side effects include headache, dyspepsia, back pain, nasal congestion, myalgia, and flushing (54, 55, 56). In hypertensive patients, especially those with

uncontrolled blood pressure on multiple medications, a higher dose of tadalafil (20 mg) can significantly lower mean ambulatory blood pressure (57). The drug is generally safe for treated hypertensive patients and does not increase the risk of hypotension-related events or major cardiovascular incidents (58). Given the high prevalence of cardiovascular disease in erectile dysfunction patients, a thorough cardiovascular assessment is recommended before prescribing tadalafil (59).

Reduction in cardiac events and mortality

"Dr Cloner published an article recently showing that those men who took daily Cialis had a 13% reduction in cardiac events and a 25% reduction in mortality"

A large retrospective study found that PDE-5i exposure was linked to a 13% reduction in major adverse cardiovascular events (MACE) and a 25% decrease in all-cause mortality. These findings were consistent across various subgroups, including men with cardiovascular risk factors and those with type 2 diabetes.

Viagra

"So I do use Viagra for women, but Viagra for women helps arousal."

Research on sildenafil (Viagra) for women has shown mixed results. While it can increase vaginal vasocongestion in healthy women and improve sexual function in those with antidepressant-induced dysfunction, larger studies found no significant benefits for women with sexual arousal disorders, leading to uncertainty about its clinical effectiveness for female sexual dysfunction.

Female sexual dysfunction

"roughly 43 to 48% of women suffer from female sexual dysfunction"

Premature ejaculation and antidepressants

"So one of the ways I treat premature ejaculation, because I give them an antidepressant, because it delays the orgasm."

SSRIs (antidepressants) are a safe option for treating premature ejaculation (PE), especially when other interventions fail, but their chronic use limits on-demand treatment. Short-acting SSRIs like dapoxetine address this, though further research is needed to refine

treatment strategies. Many men with lifelong PE actually prefer daily medication over on-demand treatments due to the spontaneity it allows in sexual activity. It's important to note that SSRI treatment is associated with a higher incidence of adverse events compared to placebo.

Wellbutrin and sexual function

"So you want your dopamine to go up in men and women, so we use medications like Wellbutrin. Have you heard of Wellbutrin? It's an antidepressant, but that antidepressant increases dopamine. So I use that to help men increase their libido, or women to increase their libido or sexual function."

Wellbutrin may improve sexual function, particularly in women, with studies showing benefits in psychosexual dysfunction and breast cancer patients (71, 72). However, more research is needed to confirm its effects and mechanisms. The most serious adverse effect of bupropion, marked as Wellbutrin is seizures, with an incidence of less than 1 per 1,000 at usual outpatient doses and less than 1 per 100 at inpatient doses (73). Common side effects include agitation, insomnia, headache, dry mouth, and nausea (73).

Trends in frequency of sexual activity in men

"it says a percentage of men between 18 and 24 reporting no sexual activity in the past year increased from 18.9% between 20 reading some stats here from JAMA Network that says the percentage of men between 18 and 24 reporting no sexual activity in the past year increased from roughly 18% to roughly 30% in the space of what looks like just a few years and similar."

Diabetes prevalence

"diabetes, from 1990 to 2022 100% from 7% to 14% of the population, one out of eight people globally are obese, one out of eight people."

The global prevalence of diabetes has risen sharply and is projected to affect 700 million people by 2045 (75). This increase is closely tied to the growing obesity epidemic (76).

Obesity and testosterone

“Obesity significantly drops testosterone levels. So fat cells contain something called aromatase. Aromatase eats up the testosterone and converts it into estrogen. So the more fat you have, the less testosterone you'll have, because you'll convert it into estrogen. Fat cells also secrete something called cortisol and leptin, which shut down your own natural testosterone production.”

Obesity and low testosterone are strongly connected, with obese men often having lower testosterone levels than those who aren’t obese (77, 78). This can create a cycle where low testosterone leads to more weight gain, which further lowers testosterone (79). Losing weight can help boost testosterone, but focusing on healthy lifestyle changes is the best way to address this issue (77, 80).

Adolescence obesity

“the group that's having the greatest rise in obesity is adolescence obesity”

The prevalence of adolescent obesity has risen sharply, becoming a major public health concern as rates have tripled in the United States over the past 30 years (82).

Body weight and testosterone

“If you lose 10% of your body weight, you. Actually gain 85 nanogram per deciliter in serum testosterone”

Studies show that higher BMI is linked to lower testosterone levels in men, with obesity being a risk factor for low testosterone. Maintaining a healthy weight is important for supporting hormonal balance.

Testosterone and women: muscle mass and fat deposition

“Many women report that muscle mass. If you think about testosterone, body builders take testosterone for a reason why it significantly improves muscle mass. It can decrease fat deposition.“

Testosterone plays a complex role in women’s body composition and metabolism. Higher levels are linked to more overall fat in women with PCOS and healthy premenopausal women (85, 86), while in older women, they are associated with stronger bones, more lean

muscle, and higher fat mass (87). Testosterone also affects fat distribution, contributing to upper body fat and muscle distribution in women with PCOS (85).

Testosterone and cognition

“Many patients will import improvements in cognition”

While some studies suggest testosterone supplementation may be beneficial, particularly in cases of hypogonadism or cognitive impairment, larger randomized controlled trials are needed to fully understand the potential of testosterone as a cognitive enhancer.

Decline on testosterone levels over the decades

“the Framingham Heart Study, back in the 70s, testosterone levels were roughly around the seven hundreds. Average men between the ages of 18 and 40 were around the seven hundreds, and every decade, we're starting to see a decline almost by 50 nanograms per deciliter. And so the latest 2015 numbers are roughly in the mid four hundreds, so we've seen almost a 300 nanogram per deciliter decline in serum testosterone“

Studies like the Framingham Heart Study have shown a significant decline in testosterone levels in American men over recent decades, even when accounting for age, obesity, and lifestyle. Testosterone naturally decreases with age, with total levels dropping by about 1.6% per year and bioavailable testosterone by 2-3% per year.

Testosterone and sperm count

“Low testosterone decreases your sperm count.”

Lower testosterone levels are linked to reduced sperm counts, while normal levels support sperm production (92, 93). However, high doses of testosterone, such as in contraceptive treatments, can disrupt sperm production (94).

Lifestyle and fertility

“diet, exercise, sleep have been shown to help improve fertility in men as well. So I say healthier people are more fertile.”

Research shows that diet, exercise, and weight management can improve fertility in both men and women. A healthy diet rich in fruits, vegetables, whole grains, and seafood is

linked to better semen quality in men (95, 96), while weight management through diet and exercise can boost pregnancy and birth rates in women with overweight or obesity (97).

Semen analysis as an indicator of overall health

“semen analysis is a phenomenal predictor of overall health, many studies showing that if your semen analysis today is impaired, it's a predictor of you having comorbid conditions today, like diabetes, obesity, metabolic syndrome. It's also predictor of prostate cancer.”

Recent studies on semen quality and long-term health outcomes in men have produced mixed results. While some suggest that poor semen quality is linked to higher risks of diseases like cardiovascular issues and diabetes (98), other research finds insufficient evidence to support semen analysis as a reliable predictor of long-term health (99, 100). Although male infertility is connected to higher risks of certain health conditions, sperm concentration alone doesn’t reliably predict risks for mortality or major diseases (99). Larger, well-designed studies are needed to clarify these findings.

“Mike Eisenberg once showed a very nice study, men who have low sperm counts can have a 30% increased risk in diabetes, 50% increased risk in ischemic heart disease in the future. Tom Walsh showed those men can have 2.5 times higher risk of high grade prostate cancer in the future.”

Erectile function and diet

“Many studies have shown that that diet can significantly improve erectile function, and one study, the medita trial, actually showed that it improves sexual function in men and women.”

Recent studies have demonstrated a significant association between diet and erectile function. Adherence to a Mediterranean or plant-based diet, rich in fruits, vegetables, nuts, legumes, and fish, has been linked to a lower risk of erectile dysfunction.

Sexual function and sleep

“studies show that if you're getting less than six hours of sleep a night it significantly increases your risk for sexual dysfunction in men and women, right? Your ideal amount of sleep should be seven to eight hours.”

Research shows that sleep quality is closely linked to sexual function. Poor sleep, especially insomnia, is associated with lower sexual satisfaction and higher rates of sexual dysfunction in both men and women (107, 108).

Erectile function and exercise

“I published a very nice study looking at it was a meta analysis on how much exercise one needs and what type of exercise to actually improve erectile function.”

A systematic review and meta-analysis of randomized controlled trials concluded that physical activity and exercise interventions, particularly aerobic exercise with moderate-to-vigorous intensity, improved patient-reported erectile dysfunction.

Erectile dysfunction and diabetes

“men with ED two times more likely to have undiagnosed diabetes, and yet only 50% of men even talk about it, because they're so embarrassed”

Erectile dysfunction (ED) is common in men with diabetes and may signal undiagnosed diabetes or prediabetes. Despite its prevalence, many men with ED do not discuss it with their doctors, highlighting the need for proactive screening by healthcare providers.

Painful intercourse in postmenopausal women

“lot of women talking about her about this idea that the reason they don't like to have sex is because it hurts. (...) in older women, the most common cause is atrophy of the vaginal wall because of the lack of estrogen.”

Postmenopausal dyspareunia, or pain during sex, affects up to 40% of women and is often linked to lower estrogen levels and vaginal changes (114). However, research shows that hormonal treatments don’t always relieve symptoms, and factors like anxiety, depression, and relationship issues can also play a role (115, 116). Treatments typically include low-dose vaginal estrogen, lubricants, and staying sexually active (114).

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