



Independent Research & Further Reading

Guest: Dr David Unwin

Disclaimer 1: The sources presented here, directly (or as closely as possible), look at statements made by the guest in this episode. To report on each topic thoroughly, an extensive search and review (beyond the scope of this document) would be required.

Disclaimer 2: This podcast and its associated materials do not aim to substitute professional medical advice. For any medical concerns, it is essential to consult a qualified health professional.

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Obesity Prevalence Over Time

"When I was a young doctor and just starting off in practice, that was in 1986, a long time ago, just north of Liverpool... Obesity was rare, very rare, and we didn't have a single case of type 2 diabetes in anybody under 55."

Across recent decades, obesity has become a global epidemic, affecting both adults and children and increasingly considered a "twin pandemic" alongside conditions like diabetes and cardiovascular disease. Prevalence has risen in almost every region, with no country yet showing sustained, large-scale success in reversing adult trends.

Worldwide, adult obesity has more than tripled since 1975; age-standardised prevalence rose from about 4–5% in 1980 to around 14% in 2019, with the highest levels in the Americas, Europe, Oceania, and parts of North Africa and the Middle East. Forecasts suggest that by 2050, over half of the world's adults and large shares of children and adolescents will be overweight or obese, with especially rapid growth expected in Asia and sub-Saharan Africa. In the United States and Korea, national data show steadily rising obesity and severe obesity across most age groups since the late 1990s, with especially high and growing burdens among adolescents, young adults, and some racial/ethnic groups.

References 1-14.

Current Rates of Childhood Overweight in UK

"You go to a school now and look at those kids, and about a third of them will be overweight now."

Between the mid-1990s and late 2010s, the proportion of children in England who are overweight or obese rose from about a quarter to around a third, with especially high and fast-growing rates among 11–15-year-olds. The COVID-19 pandemic caused an abrupt spike, especially in 10–11-year-olds, with excess prevalence persisting and concentrated in the most deprived areas. Overall, excess weight has become common in UK childhood, with roughly one in

five to one in three children affected in different age groups and periods, and is now both a major public health problem and a driver of future adult disease and cost.

References 15-20.

Life Expectancy Loss from Poorly Controlled Diabetes

"We know from UK government figures that for every year you have poorly controlled diabetes, Type 2 or Type 1, you're losing a third of your future. So every year that you have poorly controlled Type 2 diabetes, you're losing 100 days of life."

A UK modelling study using National Diabetes Audit and Office for National Statistics data estimated that, for both type 1 and type 2 diabetes, one year with HbA1c > 58 mmol/mol (not just having diabetes itself) was associated with around 100 days of life lost. This is an average, population-level estimate, not a direct observation in individuals, and it links glycated haemoglobin (HbA1c) level to future mortality risk.

Reference 21.

Cancer as Rising Cause of Mortality in Diabetics

"A rising cause of mortality for people with diabetes is cancer. Eight forms of cancer are strongly associated with diabetes."

Large epidemiologic and genetic studies show that diabetes, especially type 2, is associated with increased risk of many different site-specific cancers, but the exact count depends on how strictly "associated" is defined. Across major pooled cohorts and reviews, positive associations are reported for roughly 10–15 cancer sites, with the strongest and most consistent links for liver, pancreas, endometrium, colorectal, breast, kidney, gallbladder/bile duct, and bladder cancers plus several hematologic malignancies. One umbrella review of meta-analyses assessed type 2 diabetes versus cancer incidence at 18 sites, finding robust evidence for colorectal, hepatocellular (liver), gallbladder, breast, endometrial, and pancreatic cancers. Very large prospective datasets in Asia and

in UK/ China reported statistically increased risks of cancer mortality at about a dozen individual sites, including colorectum, liver, bile duct, gallbladder, pancreas, breast, endometrium, ovary, prostate, kidney, thyroid, bladder, and lymphoma.

Reviews summarising the broader literature similarly conclude that diabetes is linked to a higher incidence of pancreatic, liver, colorectal, breast, endometrial, stomach, urinary tract, and bladder cancers, while the risk appears lower for prostate cancer and sometimes melanoma. Overall, current evidence supports diabetes being meaningfully associated with over ten distinct cancer types, with strength of evidence varying by site.

References 22-31.

Glycocalyx Damage Within Six Hours of Hyperglycemia

"There's work to show that a very high blood sugar damages the non-stick lining of your arteries within six hours. It's called a glycocalyx, the non-stick lining, and damage is occurring very quickly."

Hyperglycemia (high blood sugar) repeatedly emerges as a direct, early driver of endothelial glycocalyx damage, which in turn impairs vascular barrier function and blood flow regulation and promotes clotting and inflammation. In healthy volunteers, ~6 hours of experimentally maintained blood glucose around 300 mg/dL reduced systemic glycocalyx volume, increased plasma hyaluronan (a shed component), and activated coagulation, indicating acute glycocalyx loss and endothelial dysfunction.

Across human, animal, and cell studies, both acute and chronic glucose elevations disrupt this protective gel-like layer, linking diabetes and metabolic stress to microvascular complications and organ injury. Even short-term hyperglycemia in healthy humans and mice rapidly reduces glycocalyx volume or increases its permeability, accompanied by endothelial dysfunction, coagulation activation, and reduced capillary perfusion. In kidneys and retina, high glucose alters glycocalyx composition (notably heparan sulphate and proteoglycans like syndecan-1), weakening its protein-restrictive and barrier roles and contributing to albumin leakage and diabetic microangiopathy.

References 32-43.

Insulin Resistance Pathway via Fatty Liver

“Fatty liver interferes with the good work of insulin, so you develop a thing called insulin resistance, which means your insulin is no longer as powerful as it was.”

Hepatic steatosis (fatty liver) and insulin resistance are tightly linked, with each worsening the other and driving metabolic diseases such as type 2 diabetes. Mechanistically, excess liver fat strongly predicts hepatic insulin resistance and explains most of its variability in humans, largely via the activation of protein kinase C ϵ (PKC ϵ), which disrupts insulin signalling.

Long-term hepatic fat accumulation, influenced by genes such as PNPLA3 and TM6SF2, appears causally related to liver injury (inflammation, fibrosis) and to insulin resistance, with its metabolic impact depending on the degree of liver damage. Insulin resistance and hyperinsulinemia increase triglyceride synthesis and de novo lipogenesis, while higher free fatty acids from adipose tissue further burden the liver, leading to lipotoxic intermediates (DAG, ceramides) and oxidative/ER stress that worsen hepatic and systemic insulin resistance.

References 44-57.

Global Prevalence of Fatty Liver Disease

“We have, well, it's a third of everybody in the developed world has fatty liver now.”

Non-alcoholic fatty liver disease (NAFLD), now largely encompassed by metabolic dysfunction-associated steatotic liver disease (MASLD), has become one of the most common chronic liver diseases worldwide and is tightly linked to obesity, type 2 diabetes, and other metabolic disorders. Large meta-analyses and global burden studies estimate that about 30–38% of the world's adult population has NAFLD/MASLD, with prevalence still rising over recent decades.

References 58-65.

Pre-diabetes and Low-Carb Diet

"I can tell you that the people with pre-diabetes in my practice, north of Liverpool, ninety-three percent of them will get a completely normal blood sugar if they go low carb. Ninety-three percent resolution, and that will last for years because I've checked."

In the publication by the guest (Unwin et al., 2020), a single UK general practice offered routine lower-carb diet advice (via brief GP visits plus optional group sessions) to patients with type 2 diabetes (T2D) and prediabetes over 6 years, without strict carb counting. Among 128 T2D patients choosing this approach for a mean of 23 months, median weight fell from 99.7 to 91.4 kg and HbA1c from 65.5 to 48 mmol/mol (both $p < 0.001$), with improvements in lipids and blood pressure and 46% achieving drug-free T2D remission (HbA1c < 48 mmol/mol off diabetes meds); **93% of 71 prediabetes patients normalised HbA1c (< 42 mmol/mol).**

In a separate study (McKenzie et al., 2021), 96 people with prediabetes received remote, continuous care plus carbohydrate-restricted nutrition for 2 years; 75% were retained, about half consistently met ketone-based restriction targets, and the 2-year cumulative incidence of normoglycemia (HbA1c $< 5.7\%$ without meds) was **52.3%**, while only 3% progressed to T2D.

References 66, 67.

Type 2 Diabetes Remission Rates

"If I can get you early, I've got a seventy-three percent chance of you having a normal blood sugar."

"If we wait five years, you only stand a fifty percent chance. So do you see? It goes ninety-three, over seventy percent, fifty percent."

In a UK primary-care low-carb programme (work published by the guest), 51% of 186 patients achieved drug-free remission overall, rising to 77% if diabetes duration was < 1 year (20% if > 15 years), alongside ~ 10 kg weight loss, an HbA1c drop from 63 to 46 mmol/mol, and major prescribing cost savings.

References 68, 69.

Rapid Liver Function Improvement on Low-Carb

"The liver function, though, Steven, I got people who I thought they were drinking alcohol, and I thought their liver problem was due to alcohol, and they'd had abnormal liver function for 10 years. And suddenly, within weeks, the liver function was improving often by a third or 50%."

- An isocaloric low-carb diet in obese people with non-alcoholic fatty liver disease (NAFLD) produced rapid and “dramatic” liver fat reductions, with quantitative work from similar designs showing about 44% average decreases in hepatic triglycerides within 1–2 weeks (Mardinoğlu et al. 2018).
- A meta-analysis of low-carb interventions in NAFLD found an average 11.53% absolute drop in intrahepatic lipid content (Haghighatdoost et al. 2016).
- In randomised trials, ad libitum Mediterranean and low-fat diets (both relatively lower in carbs than a typical Western diet) reduced liver fat by 25.0% and 32.4%, respectively, over 12 weeks with only minimal weight loss (Properzi et al. 2018).
- A 12-week eucaloric ketogenic diet in type 2 diabetes reduced liver fat by 28% compared with a low-fat diet (Gower et al. 2025).
- In NAFLD, 12 weeks of a low-carb high-fat diet cut liver fat by an absolute 7.2%, similar to intermittent fasting and better than standard advice (Holmer et al. 2021).

References 70-74.

Post-meal Blood Sugar Responses

"The potato obviously it depends on its size. That's quite a big one. So that one is one, two, three, four, and there's more, five, six. Is nine (teaspoons of sugar equivalent)."

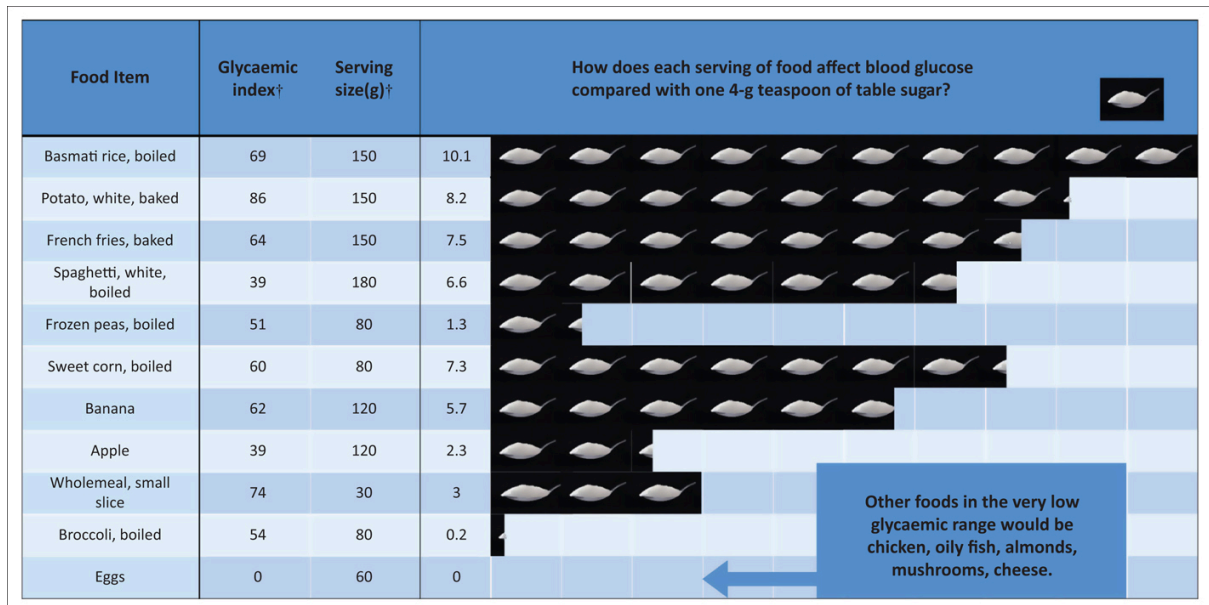
"This is 150 grams of boiled rice. Three, four, five, six, seven, eight, nine, and ten. So that's the winner."

"The banana depends on the size and how ripe it is. A ripe banana has more sugar in it... Let's say that's six 'cause it's a big banana."

"That chocolate bar is actually... is seven and a half. So you, you can give it seven."

"On my teaspoon of sugar equivalent, even a small slice of brown bread is about three teaspoons of sugar."

Common carb foods (bread, rice, potatoes, and biscuits) show very different post-meal blood sugar responses even at equal carbohydrate amounts; portion size can flip which food has the highest glycaemic effect. Large international GI/GL tables now list thousands of foods, showing fruits, legumes, pasta, and many dairy products tend to be lower GI, while cereals and potatoes often have higher and more variable GI values.



Source: Atkinson FS, Foster-Powell K, Brand-Miller JC. International tables of glycemic index and glycemic load values: 2008. Diabetes Care. 2008;31(12):2281–2283. <http://dx.doi.org/10.2337/dc08-1239> Table A1 where the index is greater than zero or for broccoli, which is approximated based on available carbohydrate composition.

FIGURE 1: An improved version of the infographic shared with health professionals to show how the glycaemic index helps inform dietary choices.

Figure from Unwin et al. 2016 (ref 77).

References 75-77.

Glycemic Impact of Bananas

"If I, if I eat a banana, it doubles my blood sugar because I can't regulate my blood sugar... a whole banana is far too much for me and will double my blood sugar."

Bananas are often thought to “spike” blood sugar, but research gives a more nuanced picture. Effects depend on ripeness, amount, timing, and whether you look at a single meal vs long-term intake.

- In Nigerian adults (27 with diabetes), four ripe banana types (each providing 50 g carbohydrate) had a high glycemic index (>70), meaning a clear rise in blood glucose, and were judged “not very appropriate” for strict metabolic control (Adediran et al. 2019).
- In a 12-week study, daily 250–500 g bananas did not worsen fasting glucose in type 2 diabetes and increased adiponectin; changes in glucose were not statistically significant (Cressey et al. 2014).
- In 10 people with type 2 diabetes, a 120 g under-ripe banana caused a much smaller post-meal glucose rise than white bread; an over-ripe banana caused a moderate rise. Glycemic index was ~43 for under-ripe and ~74 for over-ripe banana (Hermansen et al. 1992).

References 78-80.

Magnesium Absorption Declines with Age

"As you get older, you absorb the magnesium less and less. Also, a lot of medication interferes with magnesium absorption, particularly drugs for, um, acidity."

Magnesium status tends to worsen with age due to lower intake, reduced intestinal absorption, increased urinary losses, and frequent use of medications that promote magnesium loss. Mild deficiency is common, often asymptomatic or with vague symptoms such as fatigue, sleep problems, mood changes, and cognitive complaints that can be mistaken for “normal” ageing.

References 81-85.

Different Forms of Magnesium for Different Uses

"If you tend to be a bit constipated, magnesium citrate is very good... If your bowels are not a problem, and particularly if you're wanting better sleep or mood, magnesium glycinate or threonate is actually crosses the blood-brain barrier."

Magnesium citrate, glycinate, and L-threonate are all organic magnesium salts, which generally show higher bioavailability than inorganic forms such as magnesium oxide or carbonate.

Magnesium citrate increases water in the intestines and is widely used as a laxative for constipation and for bowel cleansing (often combined with sodium picosulfate). **In patients with kidney impairment or altered gut anatomy, even standard doses of magnesium can cause hypermagnesaemia, which may lead to lethargy, low blood pressure, and paralytic ileus; dialysis may be required. Magnesium citrate may reduce absorption of levothyroxine by about 7%.**

Magnesium glycinate/bisglycinate provides magnesium in a relatively well-absorbed, generally well-tolerated form. Human trials suggest modest improvements in insomnia symptoms and good safety. Animal and cell studies indicate potential benefits for anxiety, smooth-muscle relaxation (including uterus and gut), and targeted tissue uptake, though these need stronger human confirmation. Chelated/bisglycinate forms are repeatedly described as well tolerated, with less gastric heaviness and less competition with other minerals compared with some other salts.

Magnesium L-threonate is distinguished by its brain bioavailability focus: in adults with self-reported sleep problems, magnesium L-threonate for 21 days improved deep and REM sleep, mood, energy, and daytime productivity versus placebo and was well tolerated.

References 86-102.

Waist-to-Height Ratio Under 0.5 for Metabolic Health

"One recognized way looking at metabolic health is your waist should be less than half your height."

Large systematic reviews and national surveys in adults find that a Waist-to-Height Ratio (WHtR) of ≈ 0.5 is a good global threshold for higher risk, inspiring the message, “keep your waist less than half your height.” In UK adults, $\text{WHtR} \geq 0.5$ identified more people with unfavourable blood pressure, cholesterol, and blood sugar than BMI-waist “risk matrices”. In Saudis and Chinese middle-aged/older adults, $\text{WHtR} \geq 0.5$ was linked to $\sim 2\text{--}4$ -fold higher odds of diabetes, hypertension, or multiple cardiometabolic diseases. Additionally, meta-analyses in youth show that a waist-to-height ratio (WHtR) around 0.5 is associated with approximately 2–4 times higher odds of clustered metabolic risk, although the accuracy of this association varies by region. European and US youths: optimal cutoffs cluster near 0.50. Asian, African, and South American youths: optimal values are often lower (~ 0.46), while some Latin American data suggest higher ($\sim 0.54\text{--}0.55$) cutoffs. Reviews generally recommend WHtR for children ≥ 6 years; it is not validated for preschoolers.

In type 1 diabetes, a higher WHtR (especially ≥ 0.6) is strongly linked to more cardiovascular events and higher 10-year cardiovascular risk. A systematic review in diabetes finds WHtR (with 0.5 as the usual marker) probably predicts cardiovascular risk better than BMI.

References 103-119.

UK Healthy Life Expectancy Decline

“Over the last decade, healthy life expectancy in the UK has fallen by roughly two years.”

Multiple UK and European analyses show that while people have been living longer, the years lived in good health have stopped improving and, in some cases, have fallen. Scotland shows the clearest quantified drop of about two years, with similar adverse patterns across the UK. Across the UK, healthy life years at birth decreased after 2011, while most other EU28 countries saw increases, meaning that more years are now lived in poor health in the UK. For working-age adults in England, healthy life expectancy (no chronic illness or disability) increased more slowly than total life expectancy between 1993 and 2013, supporting an “expansion of morbidity” (more years lived with illness).

References 120-122.

UK Men's and Women's Years of Good Health

"Men in the UK can expect to spend about 60 years in good health."

"Women about 60 years of good health as well."

An Office for National Statistics report for 2008–2010 found that UK males could expect to spend more than 80% of their lives in very good or good health from birth, but it does not give an exact healthy-life-years figure; at age 65, this proportion fell to about 57% of remaining life in good health. Across the EU28, healthy life years (HLY) at birth for UK men were 65.0 years in 2008 and fell to 63.1 years by 2016, indicating a decline rather than stability around 60+ years. For UK women in 2008, healthy life years (HLY) at birth were 66.3 years, falling to 63.1 years in 2016. UK women saw falling healthy life years at birth from 2008 to 2016, while many EU peers improved, implying an expansion of unhealthy life despite overall longevity. Differences by income, education and area deprivation are large: in England, the least-deprived groups can expect around 10 more years of healthy life than the most-deprived.

References 123-127.

Years Lived in Poor Health

"People are now spending roughly up to 23 years at the end of their lives with poor health and in sickness. This means the average person spends nearly a quarter of their life managing chronic illness and/or disability."

Across the Americas, almost one-third of the remaining years after 65 are spent with illness or disability, and this share has stayed roughly constant over three decades despite longer life spans. Globally, added years since 1990 at both birth and age 65 are also disproportionately healthy, but about a quarter to a third are in poor health. In 33 industrialised countries, years lived in poor health at ages 70–74 increased between 1990 and 2019 and now account for about one-quarter to one-third of remaining life.

References 128-131.

US Healthspan-to-Lifespan Gap Worldwide Worst

"Premature death rate that is nearly twice the average of comparable countries."

The United States experiences a very high burden of premature and excess deaths compared with other wealthy countries. From 1999–2020 there were 10,856,851 excess deaths in the US relative to 12 peer nations, including 637,682 excess deaths in 2019, with circulatory diseases alone accounting for 41% of these excess deaths and drug, alcohol, and suicide causes for 13%. Using 21 wealthy countries as a benchmark, the number of these deaths reached 622,534 in 2019, then jumped to 1,009,467 in 2020 and 1,090,103 in 2021, with 49% of these deaths in 2021 occurring before age 65. Applying death rates from five large European countries to the US population implies 400,700 excess US deaths in 2017 and a loss of 13.0 million years of life, a larger annual loss of life than that associated with COVID-19 in 2020. In 2021, the US mortality gap with these European peers increased US deaths by 34.8%, producing 892,491 excess deaths, of which 25.0% (223,266) involved COVID-19 and 48.0% of all deaths at ages 15–64 were excess. Between 2010 and 2018, the gap in life expectancy between the US and other high-income countries widened from 1.88 to 3.05 years, and by 2020 it had grown to 4.69 years, as US life expectancy fell 1.87 years (to 76.87 years), 8.5 times the average decline of 0.22 years in peer countries.

References 132-136.

French Study: Sugary Drinks and Cancer Risk

"A massive French study found that drinking just 100 mil of sugary drinks per day, which could be, you know, a third of a can of soda, is associated with almost 20% increased risk of overall cancer."

A large French cohort study (NutriNet-Santé) followed over 100,000 adults (average age 42) for about 5 years to examine whether drinking sugary beverages is linked to cancer risk. Diet was repeatedly measured using detailed 24-hour food records, and new cancer cases were medically verified and tracked over time.

The study found that **each additional 100 mL per day of sugary drinks (about a third of a typical can of soda) was associated with an 18% higher rate of overall cancer and a 22% higher rate of breast cancer**, after adjusting for age, sex, total calories, other diet factors, BMI, physical activity, smoking, and medical history. No clear association was seen for prostate or colorectal cancer, or for artificially sweetened drinks, though consumption of diet drinks was low, limiting statistical power.

Analyses suggested the sugar content itself (and resulting energy intake and visceral fat) was a key driver of the association. As an observational study, it cannot prove causation, but it supports recommendations to limit sugary drinks, including fruit juice, as a potentially modifiable cancer risk factor.

Reference 137.

Diet Drinks and Early-Onset Colorectal Cancer in Women

"Women who consume two or more dietary drinks daily have over double the risk of early onset colorectal cancer compared to those who drink less than one a week."

This statement refers to a large prospective analysis from the Nurses' Health Study II that followed nearly 100,000 U.S. women to see whether sugar-sweetened beverage (SSB) intake was linked to colorectal cancer diagnosed before age 50. The study included 95,464 female nurses who reported their beverage intake every 4 years from 1991 to 2015 using validated food-frequency questionnaires. Women with prior colorectal cancer, inflammatory bowel disease, or implausible calorie intake were excluded, and 109 early-onset colorectal cancer (EO-CRC) cases were identified during follow-up. Compared with women drinking less than 1 serving of SSB per week, those consuming 2 or more servings per day had a more than doubled risk of EO-CRC (relative risk 2.18; 95% CI 1.10–4.35). Each additional daily serving in adulthood was linked to a 16% higher risk, and each additional daily serving during ages 13–18 was linked to a 32% higher risk. When a serving of SSB in adulthood was hypothetically replaced with artificially sweetened beverages, coffee, reduced-fat milk, or total milk, the estimated EO-CRC risk was 17–36% lower. The authors suggest that cutting SSB consumption in adolescence and young adulthood could be a strategy to help reduce the growing burden of early-onset colorectal cancer.

Multiple other studies link sugary drinks and related diets to colorectal cancer risk in younger adults and the general population. For instance, a Canadian case-control study found EOCRC risk was about three times higher in people consuming ≥ 7 sugary drinks per week versus < 1 per week and was also linked to sedentary time and a westernised diet. A U.S. prospective study in women showed high adolescent intake of simple sugars and sugary drinks was associated with more conventional colorectal adenomas, especially high-risk and rectal adenomas, while adult intake showed no clear association with adenomas. Systematic reviews on EOCRC/early adenomas report higher risk with sugar-sweetened beverages, Western/pro-inflammatory diets, deep-fried and refined foods, sugary desserts, and low fibre/folate, while higher fruit, vegetable, and prudent/healthy diet patterns appear protective.

References 138-144.

Sugary Drinks and Endometrial Cancer Risk

"High consumption of sugary sweetened beverages is linked to a 78% higher risk of estrogen-dependent endometrial cancer in women."

High consumption of sugar-sweetened beverages and other sugary products is consistently linked with a higher risk of several cancers, such as estrogen-dependent (type I) endometrial cancer, in observational research. In the Iowa Women's Health Study of 23,039 postmenopausal women, those with the highest sugar-sweetened beverage (SSB) intake had a 78% higher risk of type I endometrial cancer than nondrinkers, with no association for type II tumours. A Canadian cohort similarly found women in the highest tertile of sugar-containing beverages and fruit juice had about a 60–80% higher risk of overall and type I endometrial cancer. Case-control and cohort work shows higher added sugar, sucrose, and sugary foods (e.g., sweet buns and cookies) are also associated with increased endometrial cancer risk, particularly in women with central obesity.

References 145-148.

Sugary Soda and Telomere Shortening / Biological Aging

"Drinking 20 ounces of sugary soda daily is linked to shortening your telomeres, which are the protective caps on your DNA, equating to 4.6 years of extra biological aging."

This finding comes from a 2014 analysis of US adults linking sugar-sweetened soda intake with shorter leukocyte telomere length, a marker of cellular ageing. The 4.6-year figure comes from the authors' comparison with previously observed associations between telomere length and smoking. They report that the association seen with consuming 20 ounces of sugar-sweetened soda was similar in magnitude to the telomere-length difference associated with smoking, which has been estimated as equivalent to approximately 4.6 years. Therefore, the soda association can be described as comparable in size to the telomere shortening associated with around 4.6 years of ageing.

Reference 149.

Hyperinsulinemia and Apoptosis Inhibition

"High sugar intake causes chronic hyperinsulinemia... Which can inhibit apoptosis, the natural process where damaged or cancerous cells self-destruct."

High-sugar diets can promote insulin resistance, hyperglycemia, and often hyperinsulinemia, especially when sugar intake adds excess calories and weight gain, with strong evidence in animals and more mixed, dose-dependent evidence in humans. Fructose-rich sugar-sweetened beverages, in particular, drive hepatic de novo lipogenesis, inflammation, and hepatic insulin resistance, sometimes even independent of weight gain, whereas sugars in solid foods show weaker links to metabolic disease. Chronic hyperinsulinemia is common in obesity and type 2 diabetes and is increasingly viewed as an active driver of inflammation, ageing, and several cancers rather than a benign compensatory state. At the cellular level, insulin and IGF-1 activate the PI3K/Akt/mTOR pathway, which enhances tumour cell survival, inhibits apoptosis, promotes proliferation, migration, angiogenesis, and therapy resistance in multiple cancer types, including breast, endometrial, and pancreatic cancers.

As a summary, high-sugar diets can promote insulin resistance and elevated insulin, especially with excess calorie intake and weight gain. In turn, hyperinsulinemia and hyperglycemia activate pathways that help cancer cells grow and resist apoptosis. However, the causal chain from everyday sugar intake to a generalised block on damaged cells' self-destruction in humans is more complex and not definitively established.

References 150-163.

Fructose and Tumor Cell Membrane Synthesis

"Fructose is processed in the liver and converted into lipids, which are fats, which is what we were talking about earlier, which recent studies show certain tumors directly consume to build their cell membranes."

Evidence strongly supports that fructose is processed largely in the liver and converted into fatty acids and triglycerides via de novo lipogenesis. Separately, many tumours depend on lipids, which are often taken up from their environment, to build membranes and support their rapid growth. The direct pipeline from fructose to liver fat to tumour membrane lipid is mechanistically consistent with these findings, but it has not been explicitly demonstrated in the studies found.

References 164-176.

Added Sugar and C-Reactive Protein Elevation

"Diets high in added sugars chronically elevate C-reactive proteins called CRPs, an inflammation marker that is heavily correlated with tumor progression and metastasis."

In a large US survey, higher sugar intake was associated with higher High-Sensitivity C-reactive protein (hs-CRP) after adjusting for weight and other factors. Prospective data in European children found a "sweet and processed" pattern (high sugar, low fruits/veg) associated with higher odds of elevated hs-CRP over 2 years. Other studies show mixed or null findings: some child/adolescent studies found no association between added sugar and CRP; an RCT of

sucrose-sweetened drinks in overweight adults showed little effect on CRP. A meta-analysis of trials found total fructose-containing sugars generally had no effect or even modest decreases in CRP, with increases mainly when sugars came from mixed sources including sugar-sweetened beverages.

Elevated CRP reflects chronic inflammation and is associated with a higher incidence of several cancers (breast, colorectal, lung, ovarian, prostate and overall) in large epidemiologic meta-analyses. High CRP is repeatedly linked with worse prognosis, progression, and metastasis across many solid tumours. Experimental and clinical work suggests CRP can actively promote tumour progression and formation of a premetastatic niche, especially in the lungs.

What is not firmly shown is a simple, universal chain where high added sugar intake by itself chronically elevates CRP in all people and, thereby, directly causes metastasis. Other aspects of diet, obesity, and lifestyle also drive inflammation.

References 177-190.

Diet as Second Most Common Cause of Cancer

"After smoking, diet is the next commonest cause of cancer."

Across large national and global studies, tobacco smoking is consistently the leading modifiable cause of cancer. The second most important cause varies slightly but is usually excess body weight (high body mass index).

References 191-193.

Ultra-Processed Food Addiction Prevalence

"She would say about fourteen percent of the population has some aspects of ultra-processed food addiction."

Two recent systematic reviews covering hundreds of studies in 30+ countries estimate global ultra-processed food addiction (UPFA) prevalence at about **14% of adults and 15% of youths**

in the general population. Other narrative reviews and commentaries report similar or slightly broader ranges, typically **14–20% of adults and around 12–15% of children**.

References 194-199.

GLP-1 Drugs Reducing Food Cravings

"I gave him a low dose of the new GLP-1 drugs... The Ozempic helped reduce the noise, the cravings in his head."

Multiple randomised and observational studies find that GLP-1 drugs, especially semaglutide and liraglutide, reduce food cravings and improve control of eating. People report craving fewer foods overall and a lower desire for high-fat, sweet, salty, and savoury items. Emotional eating and eating in response to external cues (seeing/smelling food, situations) also decrease in survey data. In binge eating disorder, early clinical data show fewer binge episodes and decreased cravings, though studies are small and short-term.

GLP-1 drugs act on brain reward regions (insula, orbitofrontal cortex, mesolimbic dopamine system), reducing responses to high-calorie food cues and food anticipation, which is linked to lower cravings and motivation to overeat. They increase pre-meal and post-meal fullness via hypothalamic circuits and slower gastric emptying, which helps people stop eating earlier and feel satisfied longer.

Most craving data are self-reported, often during the weight-loss phase; long-term maintenance effects are unclear. Evidence is strongest for people with obesity and/or diabetes; effects in other groups and in restrictive eating disorders are uncertain.

References 200-210.

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