Casual Friday Series

Advancements in Weight Loss Applications, Pt II

A Biogenetix Clinical Presentation

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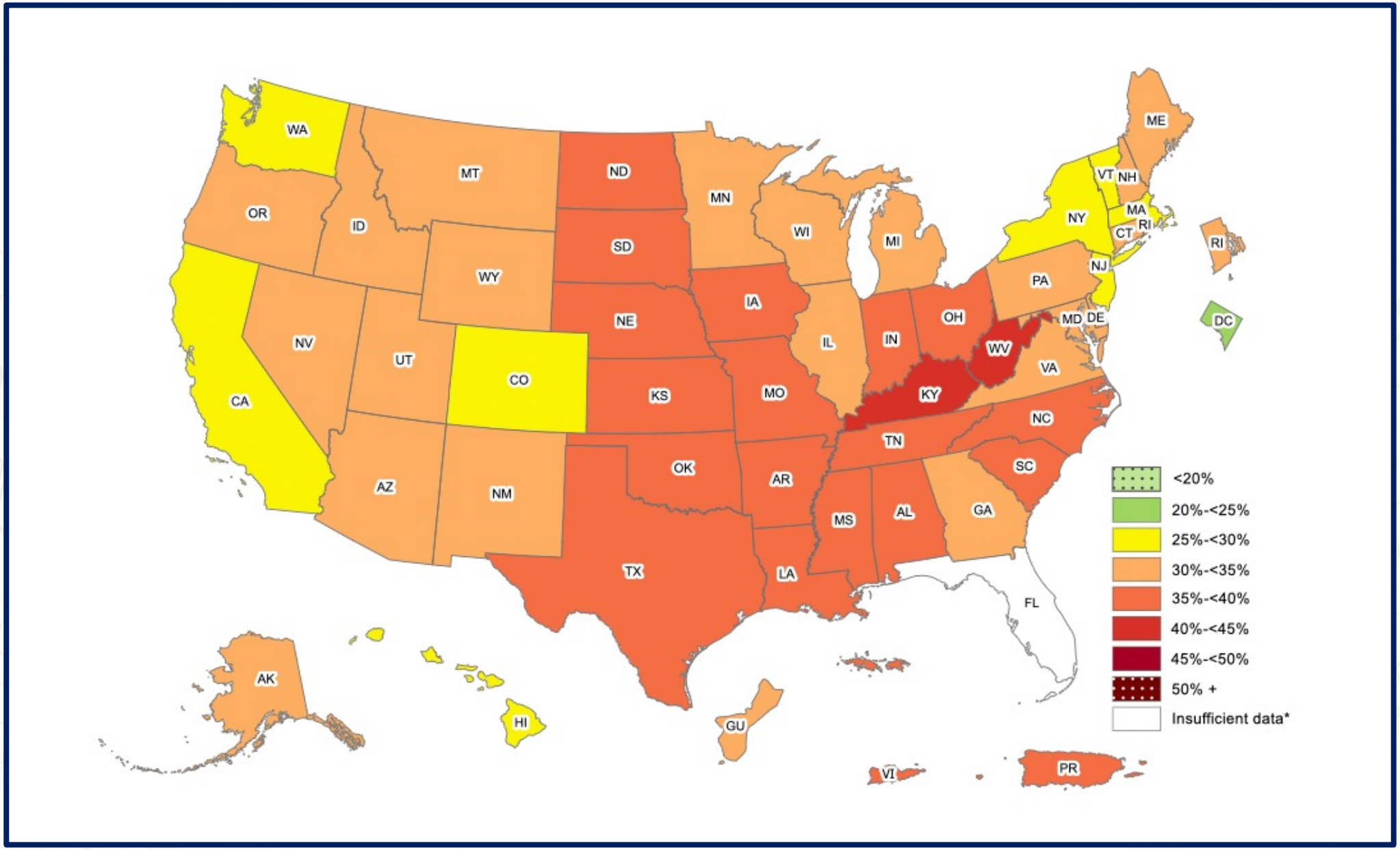
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US Doctors' Group Adopts New Policy on Healthy Weight Assessment

By Nancy Lapid
June 15, 2023

(Reuters) - The American Medical Association (AMA) on Wednesday said it will advise doctors to pay less attention to body mass index (BMI) in determining if a patient is at a healthy weight, saying the measure does not predict disease risk equally well across racial and ethnic groups.

BMI, a ratio of weight to height, has long been used to define underweight, "normal" weight, overweight, obesity and morbid obesity, despite mounting evidence that it is an inaccurate predictor of health risks on an individual level.

At the influential physician group's annual meeting in Chicago, members voted adopt a new policy that says BMI should be just one factor in determining whether a patient is at a healthy weight. Other measures such as body composition, belly fat, waist circumference, and genetic factors are also important, the AMA said.

There have been "issues with using BMI as a measurement due to its historical harm (and) its use for racist exclusion," the AMA said.

Adult BMI Calculator – Results

Recalculate BMI

For the information you entered:

Height: 6 feet, 0 inches

Weight: 225 pounds

Your BMI is **30.5**, indicating your weight is in the **Obesity** category for adults of your height. BMI is a screening measure and is not intended to diagnose disease or illness. For more information, visit About Adult BMI.

Discuss your BMI category with your healthcare provider as BMI may relate to your overall health and well-being. Your healthcare provider might determine possible reasons for obesity and recommend support or treatment. Having obesity can increase risk for chronic conditions, such as high blood pressure, type 2 diabetes, and high cholesterol. Take this 1-minute prediabetes risk test.

Maintaining a weight in the healthy BMI range is one way to support overall health as you age. For more information about lifestyle approaches, visit Healthy Weight.

BMI: Obesity

BMI	Weight Status
Below 18.5	Underweight
18.5—24.9	Healthy Weight
25.0—29.9	Overweight
30.0 and Above	**Obesity**

'Staggering' Weight Loss and Benefits in Body Composition With Tirzepatide

Becky McCall
May 19, 2023

DUBLIN — Substantial reductions in body weight across body mass index (BMI) categories, as well as improved body composition, were achieved with tirzepatide (Mounjaro) in adults for chronic weight management, according to the latest results of the SURMOUNT-1 study.

The new analysis showed that up to 63% of participants achieved a reduction in body weight of at least 20%, and all three tirzepatide doses (5 mg, 10 mg, and 15 mg) led to substantial, clinically meaningful, and sustained body-weight reduction compared with placebo at 72 weeks of follow-up.

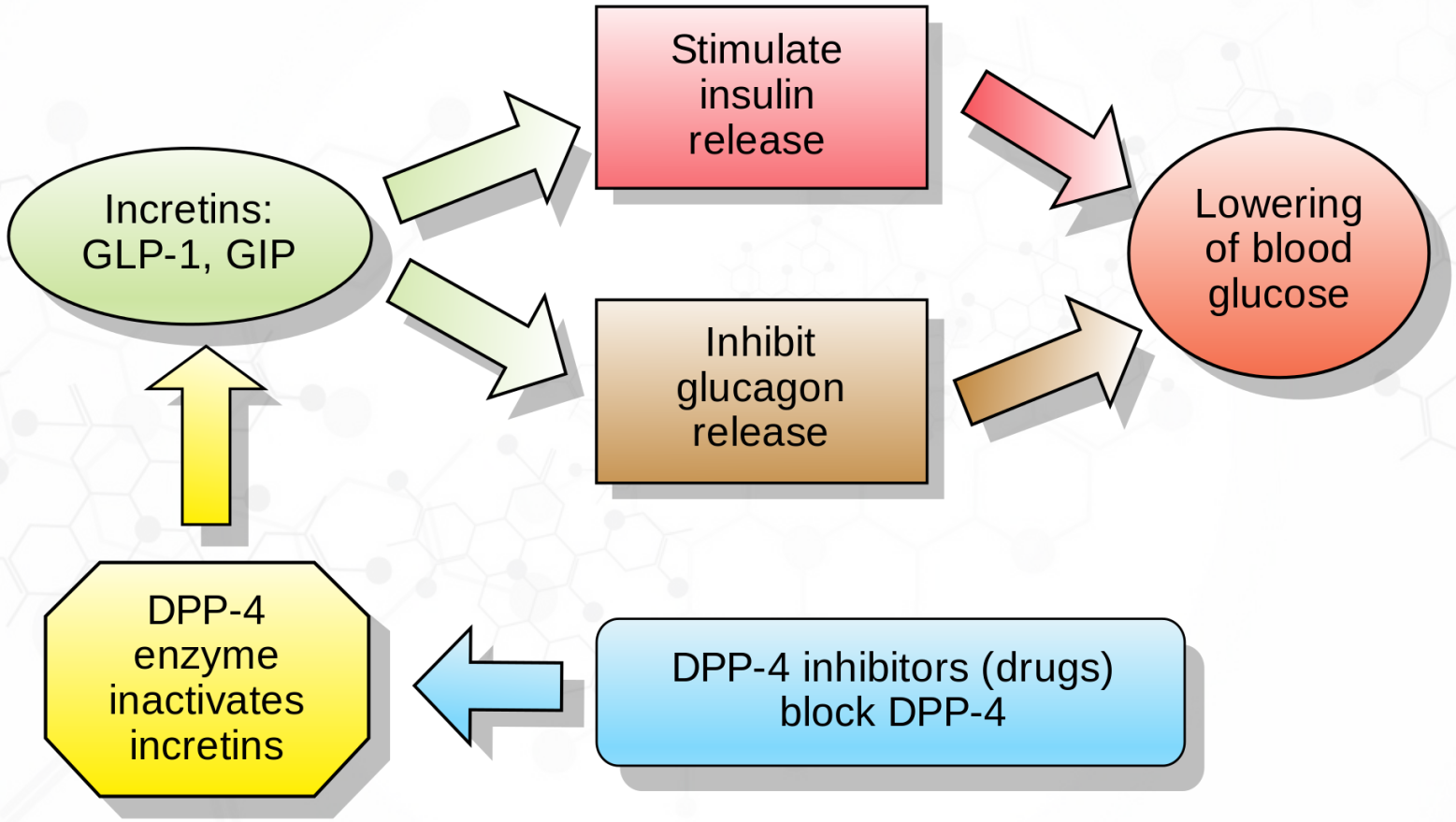
Mean weight loss was –16.0%, –21.4%, and –22.5% with tirzepatide 5 mg, 10 mg, and 15 mg compared with –2.4% for placebo (all $P < .001$ vs placebo). And among participants taking the highest 15-mg dose of tirzepatide, 96%, 90%, and 78% of patients achieved weight reductions of at least 5%, 10%, and 15%.

Mounjaro (tirzepatide) is currently the only class of drug that is both a glucagon-like peptide-1 (GLP-1) and a glucose-dependent insulinotropic polypeptide (GIP) receptor agonist. GLP-1 and GIP are incretins, naturally occurring hormones in your body that stimulate insulin secretion in response to increased blood glucose levels after you eat.

GLP-1 works to slow digestion, causing you to feel fuller longer after eating. Tirzepatide imitates these hormones helping to promote weight loss in patients with obesity.

In comparison, Ozempic is solely a GLP-1 agonist and only activates one hormone receptor.

https://joinfound.com/blogs/posts/mounjaro-vs-ozempic#:~:text=Lilly%27s%20tirzepatide%20imitates%20these%20hormones,only%20activates%20one%20hormone%20receptor.



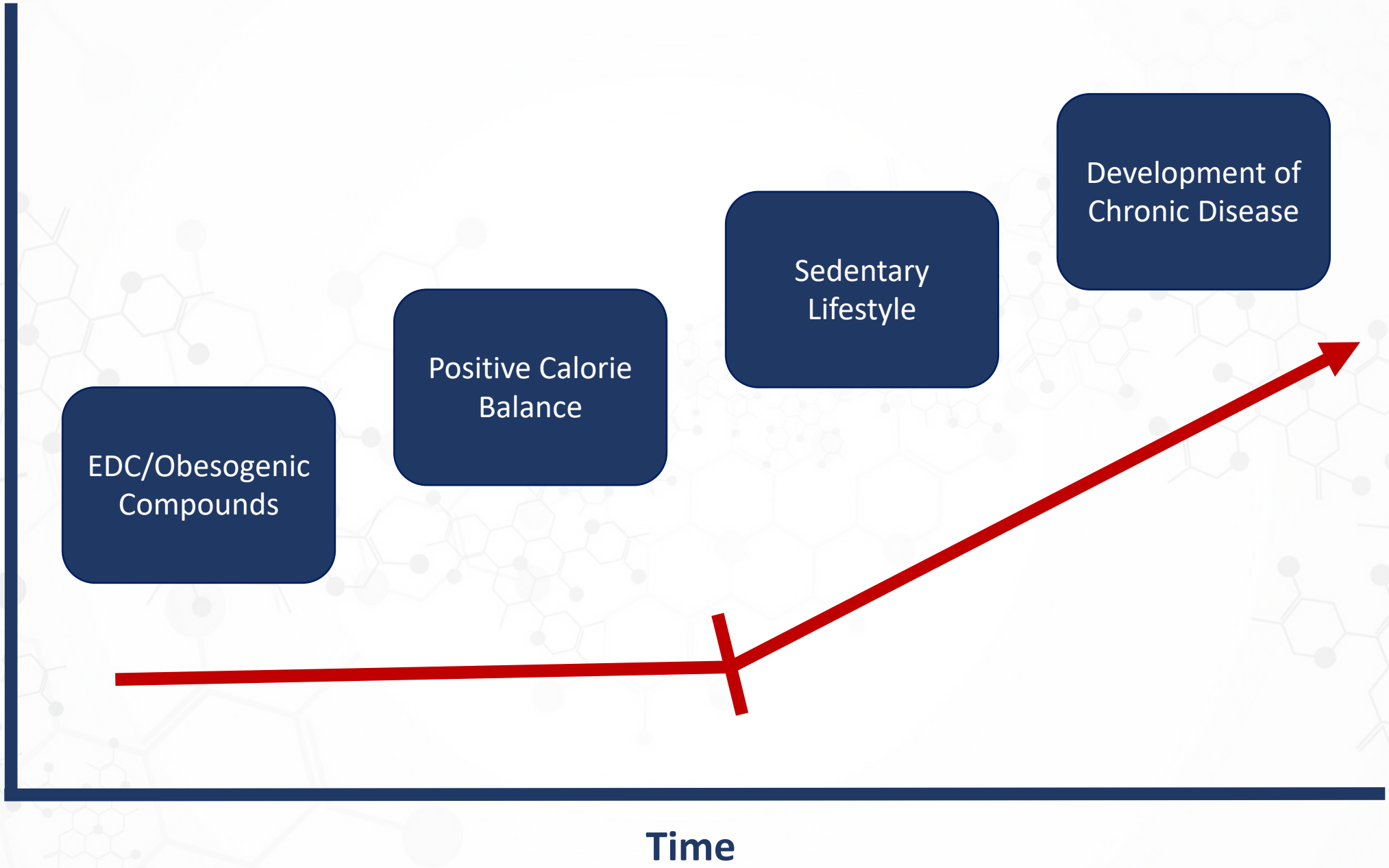
Diabetologia. 2017; 60(8): 1390–1399.
Published online 2017 May 19. doi: 10.1007/s00125-017-4289-0
PMCID: PMC5491562
PMID: 28526920

Effects of semaglutide on beta cell function and glycaemic control in participants with type 2 diabetes: a randomised, double-blind, placebo-controlled trial

Christoph Kapitza,[✉1] Kirsten Dahl,[2] Jacob B. Jacobsen,[2] Mads B. Axelsen,[2] and Anne Flint[2]

This study investigated the effects of 12 weeks of once-weekly s.c. semaglutide treatment on various aspects of beta cell function in participants with type 2 diabetes. It was demonstrated by IVGTT that semaglutide treatment increased first- and second-phase insulin secretion threefold and twofold, respectively, compared with placebo. Correspondingly, levels of glucagon and glucose were decreased with semaglutide vs placebo. Similar findings have been reported for once-daily liraglutide, which significantly increased both first- and second-phase insulin secretion after 14 weeks of treatment in participants with type 2 diabetes [7].

Results from the AST under hyperglycaemic conditions showed that maximal insulin capacity had improved following semaglutide treatment. Despite insulin levels prior to the test being higher in semaglutide-treated participants than in participants receiving placebo, insulin levels increased immediately in response to the stimulus and remained high for the duration of the test. This effect could contribute to the reported efficacy of semaglutide in improving glycaemic control [23], particularly as recent research suggests that individuals with sustained endogenous insulin-secreting capacity may benefit more from GLP-1RA therapy [24].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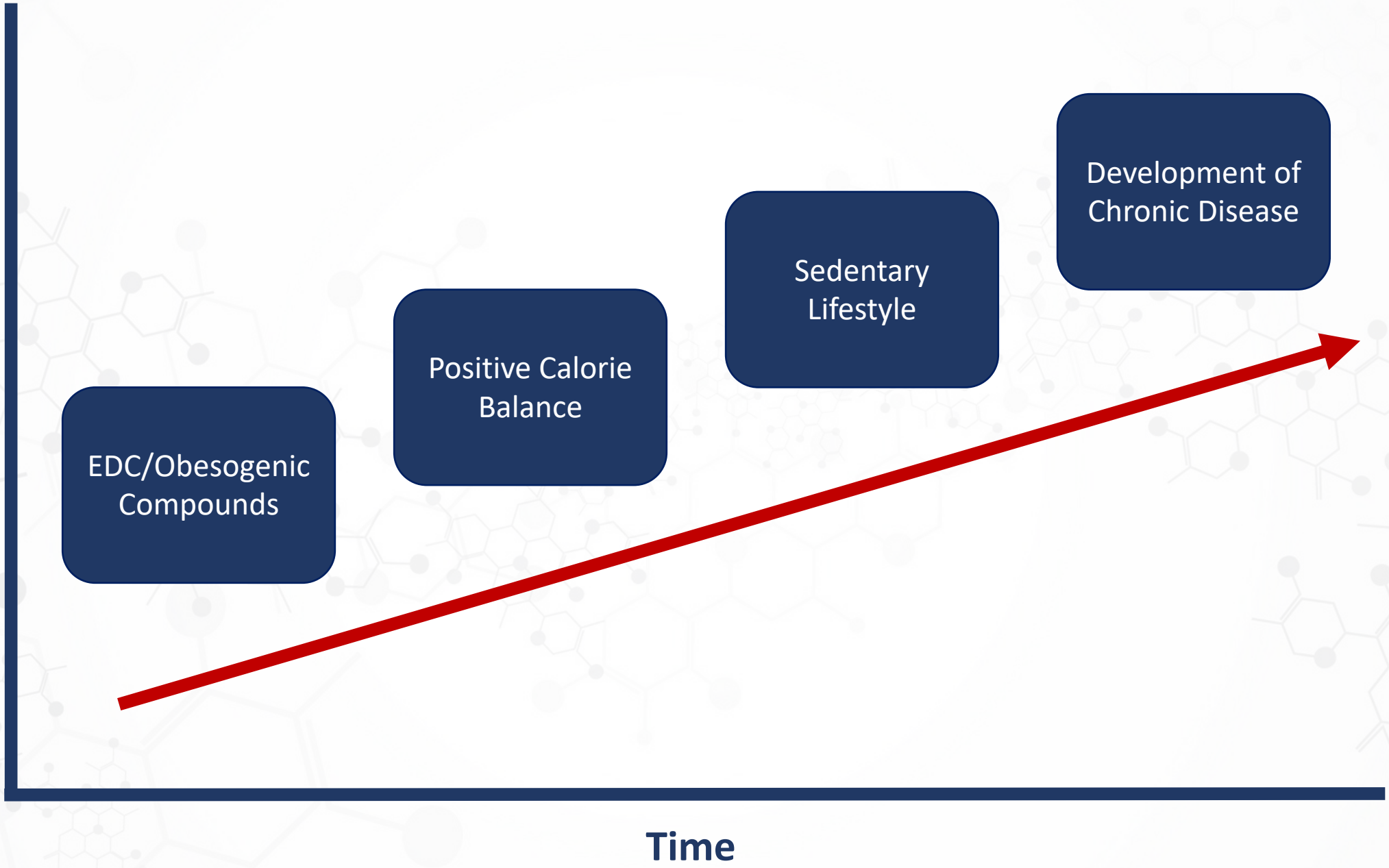
Positive Calorie Balance
Sedentary Lifestyle
Development of Chronic Disease
Time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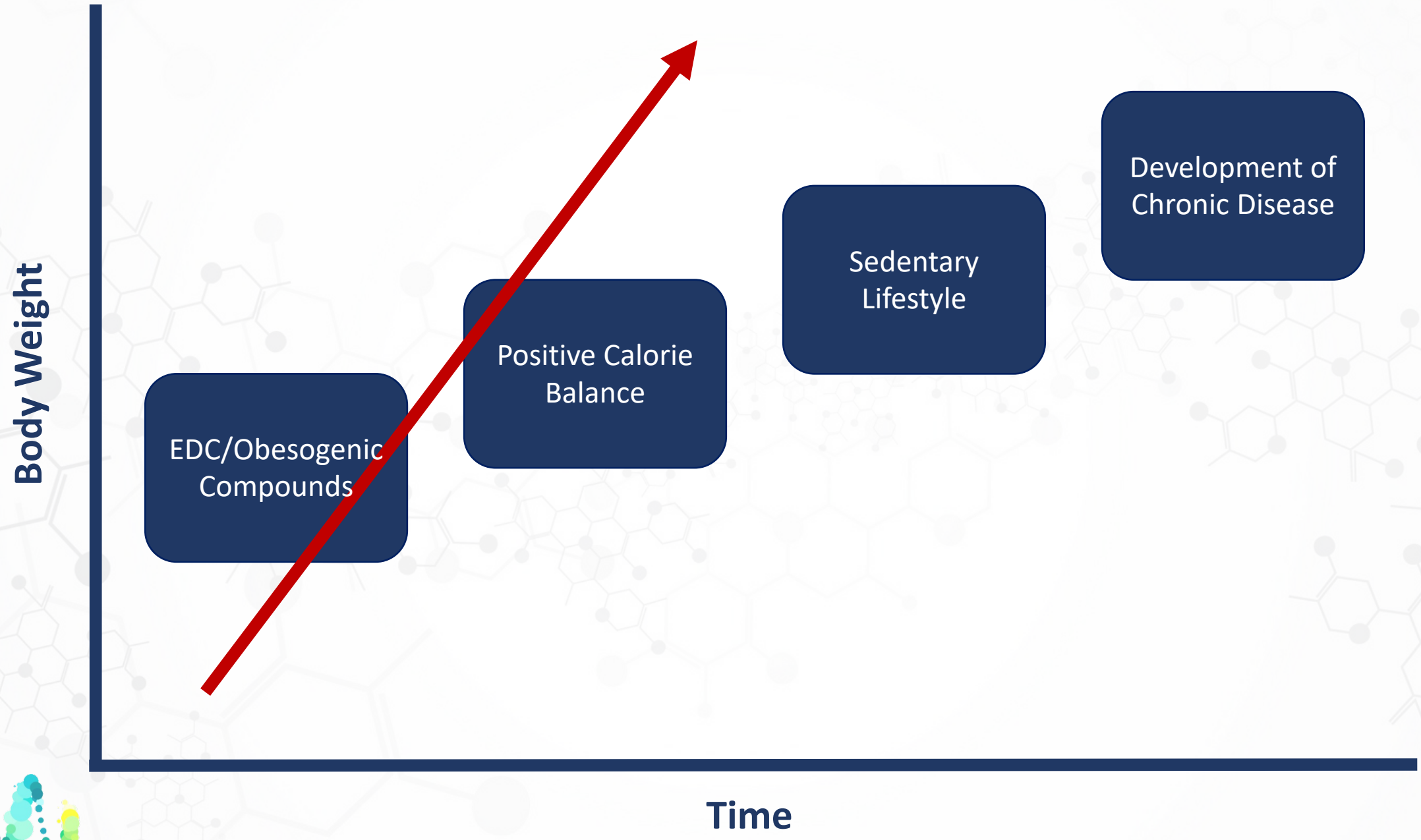
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PMCID: PMC8655100
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Obesogens: How They Are Identified and Molecular Mechanisms Underlying Their Action

Nicole Mohajer, [1] Chrislyn Y. Du, [2] Christian Checkcinco, [2] and Bruce Blumberg[1,2,3,*]

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Obesity has become a present-day pandemic affecting people of all ages across the world. According to the World Health Organization, the prevalence of global obesity has nearly tripled since 1975 with a continued upward trajectory (1). In 2016, the WHO reported more than 1.9 billion adults as overweight, with 650 million of those adults as obese. The prevalence of obesity in children has continued to rise in the U.S alone, despite the nation's efforts to promote better nutrition practices and increase physical activity levels in the educational system (2). In 2019, a staggering 38.2 million children under the age of 5 were reported as overweight or obese, worldwide (1). Comorbidities associated with obesity affect nearly all physiological systems and lead to serious health complications including mortality and a lowered quality of life. Obesity contributes to a growing list of health complications including insulin resistance, cardiovascular diseases, airway dysfunctions, metabolic syndrome, kidney disease, osteoarthritis, skin diseases, reproductive disorders, and cancer (3, 4) and death from COVID-19 (5). In addition to physiological comorbidities, the burden of obesity affects the individual's psychological well-being, leading to higher stress and depression. Obesity often presents together with depression and negative self-image in both children and adults, creating a vicious cycle where the conditions potentiate each other (3, 6). Those who suffer from depression are 58% more likely to develop obesity, and those who are obese are 55% more likely to develop chronic depression (7). Obesity makes it less likely for students to stay in school past the 12th grade, independently of their parent's socioeconomic status (8). Similarly, lower education levels have been linked to higher weight gain and obesity (9). Obesity places a financial and emotional burden on individuals, their families, and the nation at large when loss of productivity and loss of work is considered. The CDC reported the national obesity-related cost to be $147 billion in 2008, however, more recent data from 2014 estimates the cost of obesity and its comorbidities to be closer to $2 trillion dollars (10, 11). It is estimated that the annual cost of obesity in the U.S will rise $48-66 billion each year throughout 2030 (4). Therefore, the severe consequences of obesity on both individual and population-level health demand that urgent attention be paid to this worsening pandemic.

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Some lower income countries have reported a decrease in exercise, other higher income countries, such as the U.S., have reported a consistent or even increased level of exercise over the last 30 years despite the continuous rise in obesity (12, 13). If the population is gaining weight despite recommended physical activity levels, then the problem must also include the nature of the foods ingested as well as energy expenditure. We must consider the *quality* of the calorie being consumed since not all calories are created equal. The quality of the calorie, and whether it is coming from healthy foods or unhealthy foods, influences the types of food we should and shouldn't eat and how our bodies metabolize those calories for maximal benefit. Primates who were given calorically equal meals that only differed in the percentage of cis or trans-fats showed a disparity in weight gain after six years, with the trans-fat group showing an increase in visceral fat (14). The composition of our diets, more so than the caloric count of our daily diets, affects hormonal imbalances, metabolic efficiency, epigenetics, gut health, and fat accumulation (15). According to the carbohydrate-insulin model of obesity, the way we metabolize processed carbohydrates and foods that are higher on the glycemic index (such as starchy, refined, and sugary foods) promotes fat storage in fat cells and is driven by spikes in insulin levels (16). Therefore, eating the same number of calories in candy vs Brussel sprouts will be processed, metabolized, and stored in very different ways. Taken together, the current caloric models of obesity and weight gain are insufficient as stand-alone explanations for the sudden increase in global obesity over the past few decades.

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endocrine disruptors by affecting estrogen receptor-mediated pathways (19). Synthetic EDCs are found in common industrial products such as pesticides, fungicides, flame retardants, plastics, food wrappers, solvents, and metals. Both *in vitro* and *in vivo* studies have shown that synthetic EDCs exert effects on multiple systems including the reproductive system, the central nervous system, the immune system, and on metabolic function (20). In addition to endocrine pathways there are many non-hormonal cellular signaling pathways that could potentially be disrupted by chemical exposures. The concept of "signal toxicity" has been developed to account for this potential disruption of the thousands of cellular signaling pathways that could be targeted (21). Relevant examples of signal toxicity include disruption of neurotransmitter signaling, growth factor signaling pathways, receptor kinase signaling, etc. These should not be ignored in the developing discussion about environmental chemicals and obesity.

The obesogen hypothesis holds that exposure to obesogenic chemicals will lead to increased white adipose tissue (WAT) mass. Adipogenesis is the cellular process by which pluripotent stem cells or preadipocytes commit their fate to differentiating into adipocytes (29). WAT can be found subcutaneously or viscerally, and too much WAT can result in in excess lipid storage, altered adipocyte homeostasis, the disruption of energy balance, and changes in metabolic set points [reviewed in (30)]. In healthy individuals, WAT plays an important role in metabolism and energy homeostasis throughout the body. However, people with obesity and type two diabetes (T2D) experience an inflammatory response in their adipose tissue, particularly in visceral white fat that contains higher levels of reactive oxidative species (29, 31). WAT

In Vitro Studies

Bisphenol A (BPA)	Used in personal products, household care products, and plastics	PPARγ activator	Induces the differentiation of adipocytes	(36, 37)
Parabens	Used as cosmetic preservatives and as bactericides/fungicides	PPARγ activator	Induces the differentiation of adipocytes	(36)
Phthalates	Used in cosmetics, pharmaceuticals, paints, medical equipment, and plastics	PPARγ activator	Induces the differentiation of adipocytes	(36)

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Broadly speaking, there are two major types of adipose tissue found in the human body: white adipose tissue (WAT), which primarily stores lipids and is maintained throughout adulthood, and thermogenic brown adipose tissue (BAT) which "burns" lipids and is primarily found in newborns and infants. BAT was previously thought to be non-existent or very minimal in adult humans but there are indeed brown fat depots found in adults (101). CT and PET-CT scans revealed multiple locations of BAT within the adult body. Brown adipose tissue is found both subcutaneously and viscerally. The major BAT depot in adult humans is subcutaneous in the supraclavicular region with smaller deposits under the clavicles and in the axilla (102). Visceral BAT can be perivascular, perivisceral and around solid organs such as the pancreas, kidney, liver and spleen (102). White adipocytes make up most of our body fat mass and form the visceral and subcutaneous fat tissues that store energy in the form of triglycerides. White adipose cells typically contain a large unilocular lipid droplet while brown adipocytes contain smaller, multilocular droplets that are rich in mitochondria (103). Brown adipocytes exhibit thermogenic activity when uncoupling proteins such as UCP1 are activated in response to environmental stimuli, mainly exposure to cold temperatures (104). Due to their large number of mitochondria, brown adipocytes act as energy generators rather than energy storers and burn calories as heat is expended. In addition to these distinct types of fat cells, a third, hybrid type of fat known as beige or brite adipose tissue, can form past infancy into adulthood. This process, known as "browning" or "beiging", occurs as WAT is exposed to stimuli such as cold temperatures, catecholamines, physical activity, or thiazolidinediones, transforming them into brown-like, mitochondria rich, thermogenic adipocytes (105).

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Table 3

Chemical obesogens and their effects on thermogenic fat and adipose tissue.

Chemical	Source/Use	Proposed Mechanism	Effects	References
Bisphenols (A, F, S)	Chemical used to make polycarbonate plastics and epoxy resins. Found in the lining of food packaging.	Acts as an estrogen receptor agonist androgen, receptor antagonist	Shifts mesenchymal stem cell commitment and differentiation towards adipogenesis	(111, 112)
Dichlorodiphenyltrichloroethane (DDT) & dichlorodiphenyldichloroethylene (DDE)	Found in pesticides. DDE is a metabolite of DDT.	Acts as an estrogen receptor agonist, androgen receptor antagonist.	Induces a loss of BAT thermogenesis and affects the SNS that innervates BAT and WAT.	(77, 111, 113)
Arsenic	Polluted ground water	Lowers the expression of PPARγ, UCP1 and PGC1. Activates Estrogen Receptor	Inhibits the differentiation of BAT.	(115, 116)

50yo female, 5ft 204lbs

High (>95th percentile)

Mycotoxins | Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	REFERENCE
Roridin A	17.82		≤7.6 ng/g
Verrucarin J	19.97		≤9.2 ng/g
2-Hydroxyethyl Mercapturic Acid (HEMA)*	13.21		≤4.75 ug/g

* Indicates NHANES population data reference ranges.

Moderate (75th-95th percentile)

Mycotoxins | Heavy Metals | Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	REFERENCE
Aflatoxin G1	5.64		≤6.53 ng/g
Ochratoxin A (OTA)	6.54		≤6.8 ng/g
Roridin E	1.28		≤1.33 ng/g
Barium*	3.29		≤5.59 ug/g
Tellurium	0.43		≤0.89 ug/g
Bisphenol A (BPA)*	2.2		≤5.09 ug/g
Glyphosate	4.17		≤7.6 ug/g
Mono-ethyl phthalate (MEtP)*	480.44		≤541 ug/g

* Indicates NHANES population data reference ranges.

57yo male, 6ft 270lbs

High (>95th percentile)

Mycotoxins | Heavy Metals | Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
Fumonisins B3	31.53		0 – 6.08 – 10.8	≤10.8 ng/g
Ochratoxin A (OTA)	9.13		0 – 3.83 – 6.8	≤6.8 ng/g
Roridin E	1.88		0 – 0.75 – 1.33	≤1.33 ng/g
Barium*	11.39		0 – 2.33 – 5.59	≤5.59 ug/g
Nickel	14.59		0 – 6.37 – 12.1	≤12.13 ug/g
Glyphosate	29.81		0 – 1.65 – 7.6	≤7.6 ug/g
Mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP)*	33.42		0 – 8.99 – 23.4	≤23.4 ug/g

* Indicates NHANES population data reference ranges.

Moderate (75th-95th percentile)

Mycotoxins | Heavy Metals

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
Aflatoxin B1 (AFB1)	6.61		0 – 3.9 – 6.93	≤6.93 ng/g
Gliotoxin	133.81		0 – 116 – 207	≤207.87 ng/g
Mycophenolic Acid	6.28		0 – 3.6 – 6.4	≤6.4 ng/g
T-2 Toxin	0.18		0 – 0.1 – 0.18	≤0.18 ng/g
Cadmium*	0.64		0 – 0.29 – 0.8	≤0.8 ug/g

* Indicates NHANES population data reference ranges.

57yo female, 5’2 170lbs

High (>95th percentile)

Mycotoxins | Heavy Metals

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
Ochratoxin A (OTA)	10.25		0 – 3.83 – 6.8	≤6.8 ng/g
Satratoxin H	0.25		0 – 0.1 – 0.18	≤0.18 ng/g
Nickel	13.01		0 – 6.37 – 12.1	≤12.13 ug/g

Moderate (75th-95th percentile)

Heavy Metals | Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
Arsenic*	12.72		0 – 11.9 – 52	≤52 ug/g
Bismuth	1.42		0 – 0.58 – 2.53	≤2.53 ug/g
Bisphenol A (BPA)*	2.92		0 – 2.12 – 5.09	≤5.09 ug/g
Glyphosate	3.92		0 – 1.65 – 7.6	≤7.6 ug/g
Methylparaben*	221.1		0 – 180 – 653	≤653 ug/g
Triclosan (TCS)*	279.92		0 – 29.9 – 358	≤358 ug/g

* Indicates NHANES population data reference ranges.

57yo male, 5’6 275lbs

High (>95th percentile)

Mycotoxins · Heavy Metals · Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT	PREVIOUS RESULT	REFERENCE
Diacetoxyscirpenol (DAS)	11.25		0 2.4 4.27		≤4.27 ng/g
Fumonisins B1	6.21		0 3.45 6.13		≤6.13 ng/g
Nickel	18.94		0 6.37 12.1		≤12.13 ug/g
2-Methylhippuric Acid (2MHA)*	319.82		0 77.9 248		≤248 ug/g
Diethylthiophosphate (DETP)*	7.22		0 1.24 3.92		≤3.92 ug/g
Mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP)*	26.57		0 8.99 23.4		≤23.4 ug/g

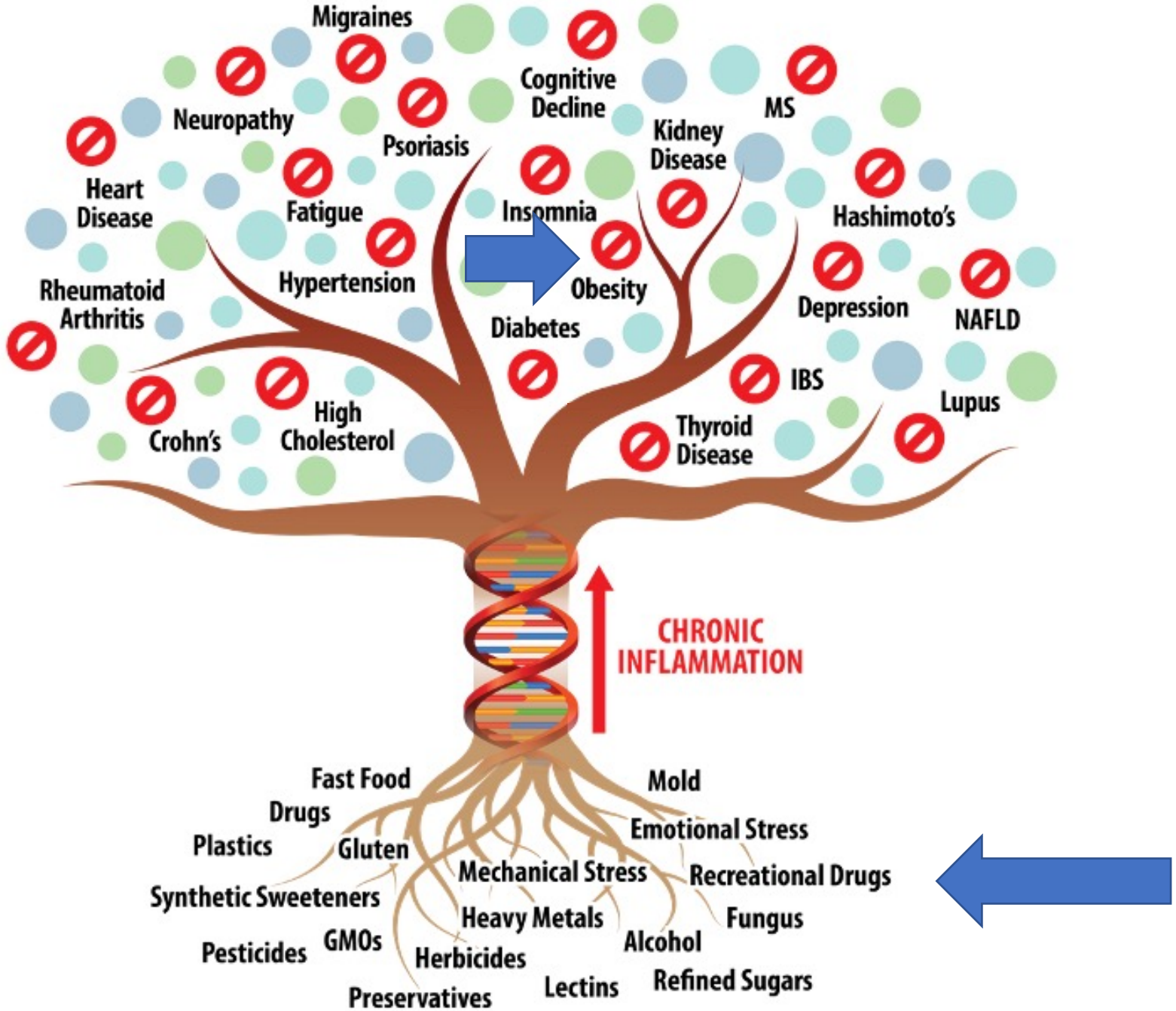
* Indicates NHANES population data reference ranges.

Moderate (75th-95th percentile)

Mycotoxins · Heavy Metals

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT	PREVIOUS RESULT	REFERENCE
Aflatoxin B1 (AFB1)	6.49		0 3.9 6.93		≤6.93 ng/g
Aflatoxin G1	4.25		0 3.68 6.53		≤6.53 ng/g
Fumonisins B3	7.08		0 6.08 10.8		≤10.8 ng/g
Gliotoxin	122.34		0 116 207		≤207.87 ng/g
Ochratoxin A (OTA)	4.48		0 3.83 6.8		≤6.8 ng/g
Barium*	4.73		0 2.33 5.59		≤5.59 ug/g

* Indicates NHANES population data reference ranges.


Migraines
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Hashimoto's
Hypertension
Obesity
Depression
NAFLD
Rheumatoid Arthritis
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
CHRONIC INFLAMMATION
Fast Food
Mold
Drugs
Emotional Stress
Plastics
Gluten
Mechanical Stress
Recreational Drugs
Synthetic Sweeteners
Heavy Metals
Fungus
Pesticides
GMOs
Alcohol
Herbicides
Refined Sugars
Lectins
Preservatives

The Wedge Protocol