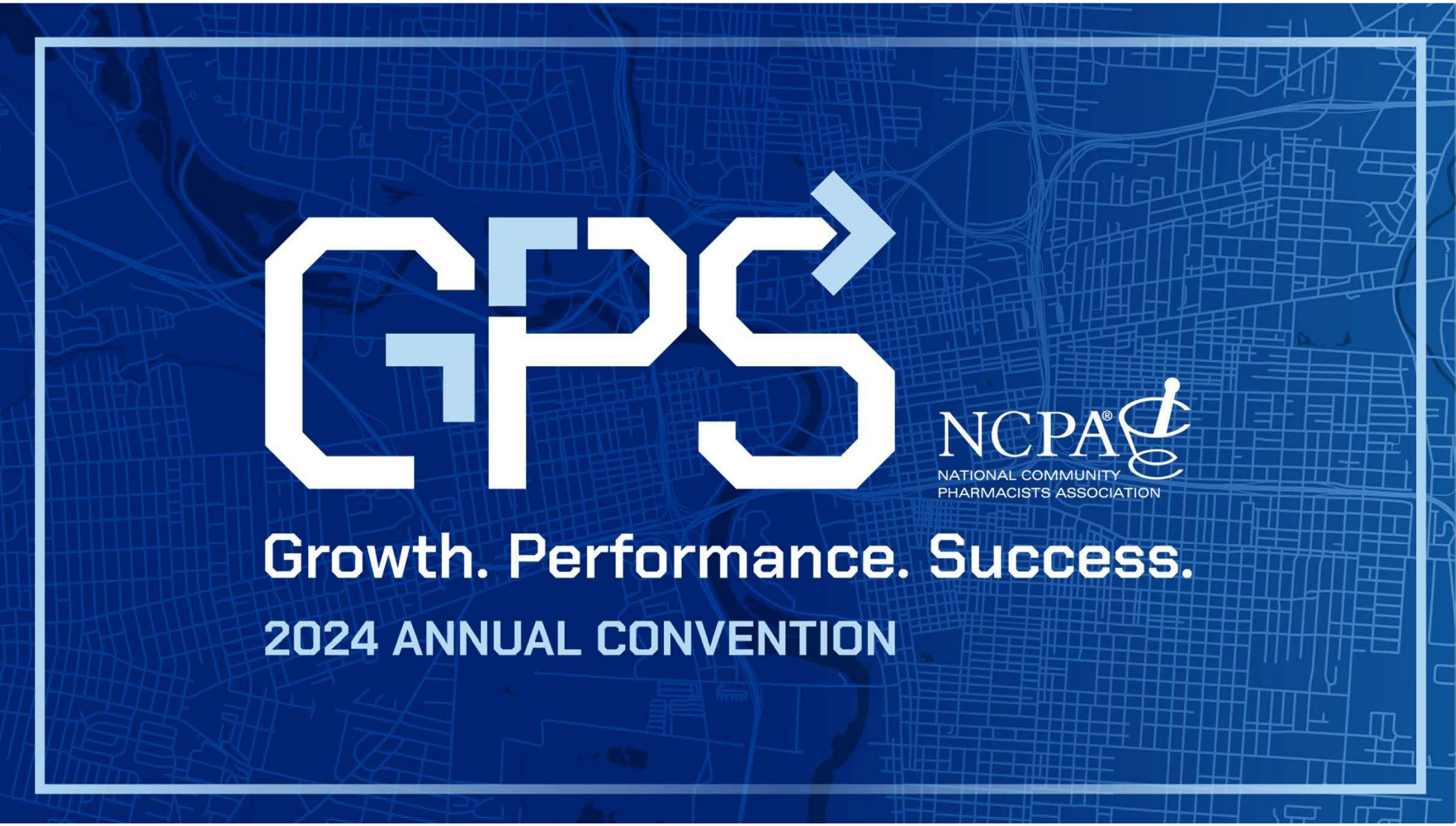
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Weight Loss Beyond GLP-1: A Functional Pharmacist's Approach to Metabolic Health

NCPA 2024 Annual Convention and Expo

Columbus, Ohio

Speaker

Melody Hartzler, PharmD, BCACP, BC-ADM, ABAAHP

CEO & Clinical Pharmacist, PharmToTable, LLC

Director of Patient Care Services, ProferoTeam, LLC

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Disclosure Statement

Dr. Hartzler has a financial interest with NovoNordisk Diabetes, Abbott Diabetes, and owns PharmToTable, LLC and the relationship has been mitigated through peer review of this presentation. There are no relevant financial relationships with ACPE defined commercial interests for anyone else in control of the content of the activity.

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Pharmacist Learning Objectives

1. Review functional medicine principles for supporting metabolic health beyond the use of GLP-1 receptor agonists.
2. Identify key lifestyle, dietary, and micronutrient interventions that can complement or be used in place of pharmacotherapy for weight management.
3. Discuss strategies for pharmacist-led patient education on sustainable weight loss and metabolic optimization through integrative approaches.

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Technician Learning Objectives

1. Review functional medicine principles for supporting metabolic health beyond the use of GLP-1 receptor agonists.
2. List key lifestyle, dietary, and micronutrient interventions that can complement weight management.
3. Identify opportunities to engage pharmacists for pharmacist-led education on sustainable weight loss.

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The Staggering Truth

Nearly 74% of US adults are overweight or obese

1 in 3 children are overweight or obese

$260.6 billion/year medical costs

4 million deaths/year

Worldwide prevalence tripled between 1975 and 2016

State of Obesity 2022: Better Policies for a Healthier America. Trust for America's Health. Accessed September 24, 2023.
Obesity. World Health Organization. Accessed September 24, 2023.

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Obesity

- A state of chronic or low-grade systemic inflammation
- **Metaflammation:** obesity-related chronic low-grade inflammation and subsequent altered metabolism
- "BMI vastly underestimates true obesity"
- For every 5-unit increase in BMI above 25.0 kg/m2:
  - overall mortality increases by 29%
  - vascular mortality by 41%
  - diabetes-related mortality by 210%

BMI (kg/m^2)	Classification
18.5-24.9	Normal weight
25-29.9	Overweight
30-34.9	Class 1 Obesity
35-39.9	Class 2 Obesity
≥ 40	Class 3 Obesity

Versini M, et al. *Autoimmun Rev*. 2014;13(9):981-1000.
Kawai T, et al. *Am J Physiol Cell Physiol*. 2021;320(3):C375-C391.
Monsalve FA, et al. Int J Mol Sci. 2023 Dec 6;24(24):17168.

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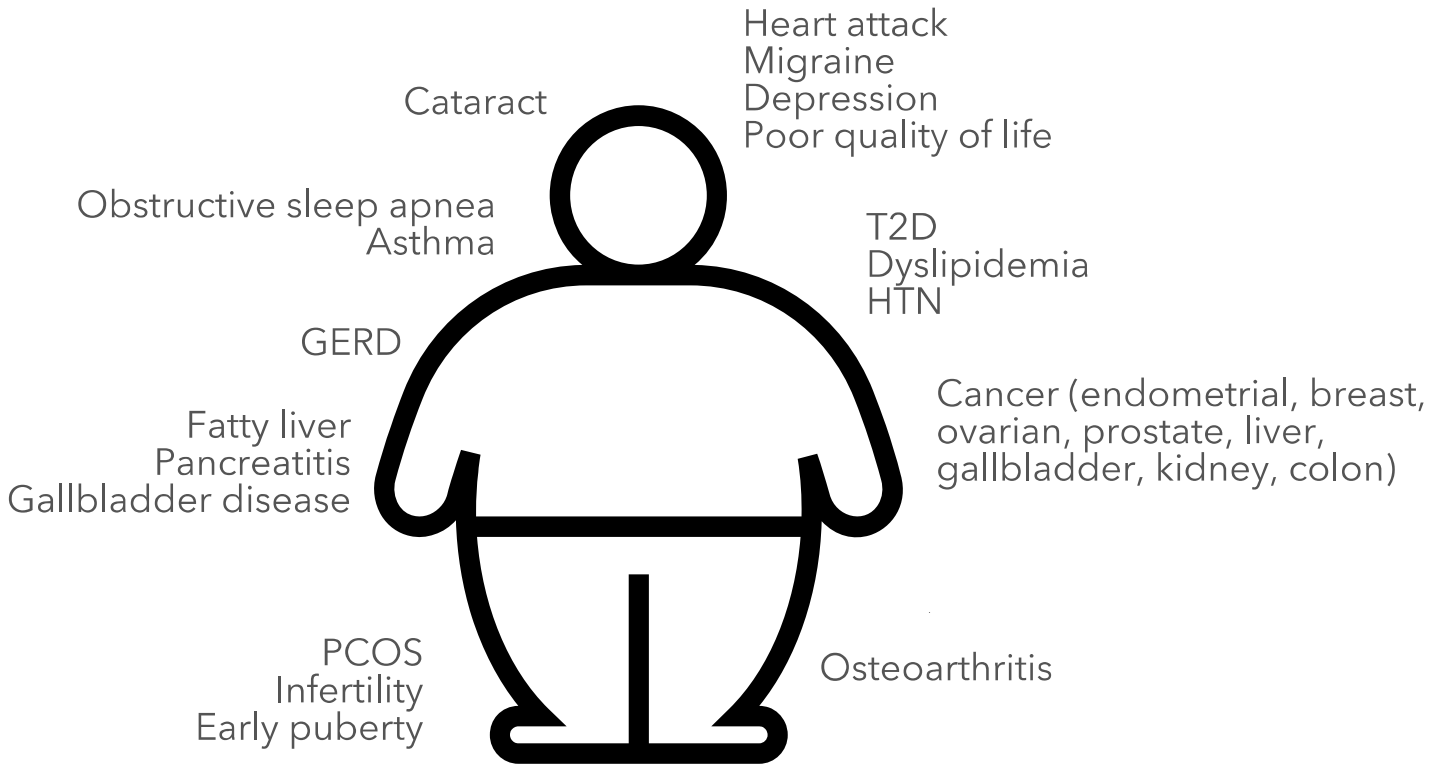
Complications and Comorbidities Associated with Overweight/Obesity



Adapted from Monsalve FA, et al. Int J Mol Sci. 2023 Dec 6;24(24):17168.

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The Need for a Comprehensive Approach

- Nearly 74% of U.S. adults are overweight or obese, contributing to significant health and economic burdens
- Obesity is more than excess weight; it's a state of chronic inflammation, metabolic dysfunction, and hormone imbalance
- Obesity is driven by multiple factors, including poor nutrition, gut health issues, hormonal imbalances, stress, and environmental toxins
- While effective, GLP-1 receptor agonists alone do not address the root causes of metabolic dysfunction

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The Need for a Comprehensive Approach

- Nutrition
- Microbiome
- Insulin Resistance
- Chronic Stress
- Inadequate Sleep
- Circadian Health
- Obesogens
- Hormone Balance
- Nutrient Depletion
- Mental Health/Trauma

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Nutrition

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Nutrition

- Overconsumption of ultra-processed foods
  - Ultra-processed foods represent >1/2 of all calories in the US diet and contribute nearly 90% of all added sugars
  - Increased ultra-processed food consumption is associated with a greater risk of overweight and obesity
- Fewer people prepare meals at home
- Unhealthy food is often cheaper
- Nutrient decline in fruits, vegetables, and grains

Martínez Steele E, et al. BMJ Open. 2016 Mar 9;6(3):e009892.
Monteiro CA, et al. Public Health Nutr. 2018 Jan;21(1):5-17.
Davis DR, et al. J Am Coll Nutr. 2004 Dec;23(6):669-82.
Mendonça RD, et al. Am J Clin Nutr. 2016 Nov;104(5):1433-1440.

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Mediterranean Diet (MD)

- High intake of vegetables, fruits, nuts, cereals, whole grains, and extra-virgin olive oil; moderate consumption of fish and poultry; limited intake of sweets, red meat, and dairy products
- Higher adherence to MD is associated with increased likelihood of weight loss maintenance
- MD can reduce central adiposity and visceral fat
- MD pattern proved to be the most effective in prevention of obesity and obesity-related diseases compared to other diets

Muscogiuri G, et al. Curr Obes Rep. 2022 Dec;11(4):287-304.

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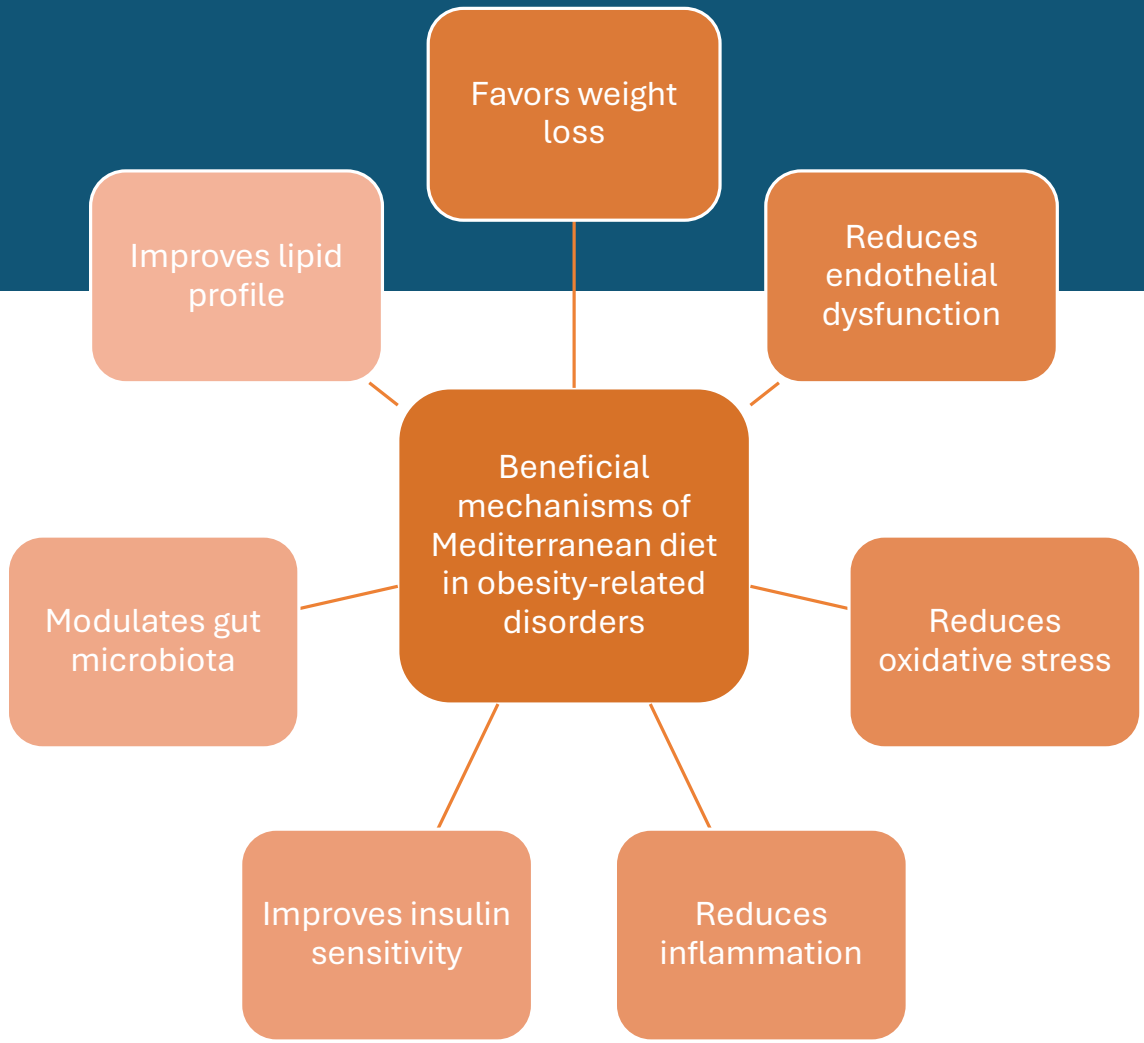

Adapted from Muscogiuri G, et al. Curr Obes Rep. 2022 Dec;11(4):287-304.

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Fasting

- Intermittent fasting (IF): alternates feeding days with fasting days
  - Protocols do not restrict feeding during the feasting days, where people are allowed to eat normally or *ad libitum* and then abstain from eating for one or 2 days
- Time-restricted eating (TRE): restricting the time when meals are consumed within 24 h
  - Most TRE studies range from 4–12 h of eating window without caloric restriction
  - Chrono-nutritional strategy
- Fasting-mimicking diets (FMD): periodic cycles of consecutive days consuming a reduced-calorie diet followed by eating *ad libitum*

Soliman GA. Front Public Health. 2022 Oct 28;10:1017254.

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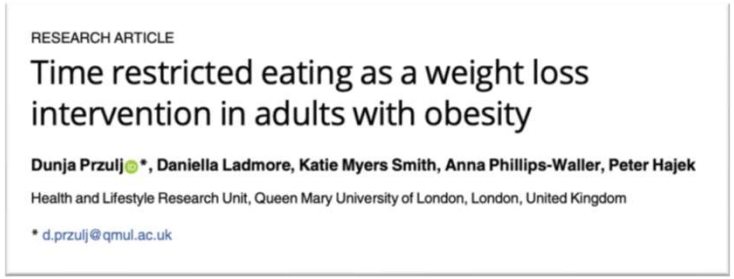
TRE



RESEARCH ARTICLE

Time restricted eating as a weight loss intervention in adults with obesity

Dunja Przulj*, Daniella Ladmore, Katie Myers Smith, Anna Phillips-Waller, Peter Hajek

Health and Lifestyle Research Unit, Queen Mary University of London, London, United Kingdom

* d.przulj@qmul.ac.uk

- n=50
- Mean weight loss:
  - 2.0 kg at 6 weeks
  - 2.6 kg at 12 weeks
- Among participants who provided follow-up data:
  - those who adhered to the intervention for ≥ 5 days/week recorded greater weight loss than those with lower adherence
- The intervention had no effect on blood pressure or lipid profile.

Przulj D, et al. PLoS One. 2021 Jan 28;16(1):e0246186.

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TRE

Effect of time restricted eating on body weight and fasting glucose in participants with obesity: results of a randomized, controlled, virtual clinical trial

Pamela M. Peeke[1], Frank L. Greenway[2], Sonja K. Billes[3], Dachuan Zhang[2] and Ken Fujioka[4]

- 78 randomized participants (60 completed 8 weeks)
- 14:10 (intervention) or 12-h TRE (active control) and prescribed a diet (Jenny Craig® Rapid Results) and exercise program that included weekly customized counseling and support
- Both the 14:10 and 12:12 interventions produced statistically significant and clinically meaningful weight loss of 11 kg and 9 kg, respectively
- 14:10 group also exhibited a statistically significant reduction from baseline in FBG of 8 mg/dl at Week 8

Peeke PM, et al. Nutr Diabetes. 2021 Jan 15;11(1):6.

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Ketogenic diet (KD)

- Originally introduced in 1920
- Fat to carbohydrate ratio is 5:1
- Ketosis occurs as a result of the change in the body's fuel from carbohydrate to fat.
- A KD maintains the body in a state of ketosis, which is characterized by an elevation of D-b-hydroxybutyrate and acetoacetate.

Paoli A. Int J Environ Res Public Health. 2014 Feb 19;11(2):2092-107.

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KD's Weight Loss Effects

- Reduction in appetite due to higher satiety effect of proteins, effects on appetite control hormones and to a possible direct appetite suppressant action of the ketone bodies
- Reduction in lipogenesis and increased lipolysis
- Greater metabolic efficiency in consuming fats highlighted by the reduction in the resting respiratory quotient
- Increased metabolic costs of gluconeogenesis and the thermic effect of proteins
- Other beneficial effects:
  - Ketones may protect from cognitive impairment caused by weight gain and obesity
  - + effects on mood in overweight subjects
- "Attention should be paid to patient's renal function and to the transition phase from ketogenic diet to a normal diet that should be gradual and well controlled"

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Paoli A. Int J Environ Res Public Health. 2014 Feb 19;11(2):2092-107.

KD

Long-term effects of a ketogenic diet in obese patients

Hussein M Dashti MD PhD FICS FACS[1], Thazhumpal C Mathew MSc PhD FRCPath[4], Talib Hussein MB ChB[5], Sami K Asfar MB ChB MD FRCSEd FACS[1], Abdulla Behbahani MB ChB FRCS FACSI PhD FICS FACS[1], Mousa A Khoursheed MB ChB FRCS FICS[1], Hilal M Al-Sayer MD PhD FICS FACS[1], Yousef Y Bo-Abbas MD FRCPC[2], Naji S Al-Zaid BSc PhD[3]

- 83 obese patients
- Objective: To determine the effects of a 24-week ketogenic diet (consisting of 30 g carbohydrate, 1 g/kg body weight protein, 20% saturated fat, and 80% polyunsaturated and monounsaturated fat) in obese patients
- Significant decrease in triglycerides, total cholesterol, LDL and glucose, and a significant increase in HDL cholesterol

Dashti HM, et al. Exp Clin Cardiol. 2004 Fall;9(3):200-5.

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Gut Microbiome

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Healthy Gut Microbiota

- Mainly composed of *Firmicutes, Bacteroides, Proteus, Actinomycetes, Fusobacteria*, and *Verrucomicrobia* (*Firmicutes* and *Bacteroides* dominate)
- Functions:
  - Biodegradation of polysaccharides
  - Production of short-chain fatty acids (SCFAs)
  - Enrichment of specific lipopolysaccharides
  - Production of vitamins and essential amino acids
  - Modulates immune and inflammatory response
- Generally highly diverse
- Dynamic equilibrium

Liu BN, et al. World J Gastroenterol. 2021 Jul 7;27(25):3837-3850.

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Obesity Mechanisms Induced by Gut Microbiota

- Energy absorption
- Central appetite
- Fat storage
- Chronic inflammation
- Circadian rhythm

Liu BN, et al. World J Gastroenterol. 2021 Jul 7;27(25):3837-3850.

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Obese v Lean Microbiome

- Conflicting results on Firmicutes:Bacteroidetes (F:B) ratio in obesity compared to lean people
  - Studies have shown both low and high F:B ratios in obese populations
  - Increased abundance of *Firmicutes* in obese patients improves energy harvesting from the Western diet → promotes better caloric absorption and subsequent weight gain
- Other works have associated obesity with specific bacteria
  - The family Christensenellaceae associated with weight loss, and its relative abundance was inversely related to host BMI
  - Supplementation with *A. muciniphila* improves metabolic parameters in overweight and obese subjects
- Subjects with low microbial gene richness (MGR) often exhibit chronic inflammation, poor insulin sensitivity, higher BMIs, increased adiposity, and dyslipidemia

Amabebe E, et al. Br J Nutr. 2020 May 28;123(10):1127-1137.
Napolitano M, et al. Front Microbiol. 2020 Nov 12;11:590370.
Lahtinen P, et al. JAMA Netw Open. 2022 Dec 1;5(12):e2247226.
Liu BN, et al. World J Gastroenterol. 2021 Jul 7;27(25):3837-3850.

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Two Healthy Diets Modulate Gut Microbial Community Improving Insulin Sensitivity in a Human Obese Population

Carmen Haro, Miguel Montes-Borrego, Oriol A. Rangel-Zúñiga, Juan F. Alcalá-Díaz, Francisco Gómez-Delgado, Pablo Pérez-Martínez, Javier Delgado-Lista, Gracia M. Quintana-Navarro, Francisco J. Tinahones, Blanca B. Landa, José López-Miranda, Antonio Camargo,* and Francisco Pérez-Jiménez*

- Aim was to study the changes in microbiota after 1 year's consumption of a Mediterranean diet (Med diet) or a low-fat, high-complex carbohydrate diet (LFHCC diet) in an obese population
- 20 obese patients (men) within the Coronary Diet Intervention With Olive Oil and Cardiovascular Prevention (CORDIOPREV) study
- Results:
  - LFHCC diet: increase in relative abundance of *Prevotella* and a decrease in *Roseburia* genera
  - Med diet: increased the abundance of the *Roseburia* and *Oscillospira* genera

Haro C, et al. J Clin Endocrinol Metab. 2016 Jan;101(1):233-42.

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Probiotics

- Meta-analysis by Koutnikova et al.
  - Probiotics induced improvements in: body weight, BMI, waist circumference, body fat mass, & visceral adipose tissue mass in overweight but not obese individuals
- Meta-analysis by Tabrizi et al.
  - Probiotic supplementation significantly decreased weight, BMI, FPG, insulin, HOMA-IR, triglycerides, CRP in women with PCOS
- Meta-analysis by Lau et al.
  - Prevalence of obesity and hypertension was lower in the probiotic group

Koutnikova H, et al. BMJ Open. 2019 Mar 30;9(3):e017995.
Tabrizi R, et al. Probiotics Antimicrob Proteins. 2022 Feb;14(1):1-14.
Lau E, et al. Nutrients. 2019 Jun 28;11(7):1482.

Akkermansia muciniphila

- Implicated in the development of obesity
- Converts dietary fiber into short chain fatty acids (SCFAs) that have effects on glucose and lipid homeostasis
- Restores gut barrier function which decreases lipopolysaccharide (LPS)

Xu Y, et al. Front Microbiol. 2020 Feb 21;11:219.

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Supplementation with *Akkermansia muciniphila* in overweight and obese human volunteers: a proof-of-concept exploratory study

Clara Depommier[*,1], Amandine Everard[*,1], Céline Druart[1], Hubert Plovier[1], Matthias Van Hul[1], Sara Vieira-Silva[2,3], Gwen Falony[2,3], Jeroen Raes[2,3], Dominique Maiter[4,5], Nathalie M. Delzenne[6], Marie de Barsy[4,5,9], Audrey Loumaye[4,5,9], Michel P. Hermans[4,5,9], Jean-Paul Thissen[4,5,9], Willem M. de Vos[7,8,9], Patrice D. Cani[#,1]

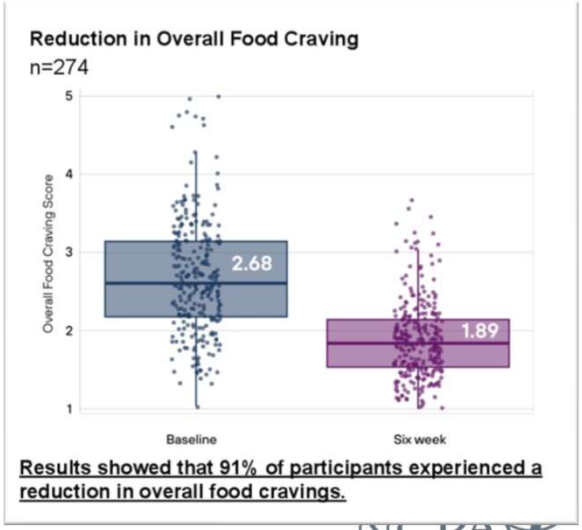
In conclusion, this proof-of-concept study shows that the intervention was safe and well-tolerated and that the supplementation with *A.muciniphila* improves several metabolic parameters (insulin sensitivity, insulinemia, and total cholesterol)

Reduction of Food Cravings Utilizing a Novel Probiotic Containing Akkermansia

M. THOMPSON[1] and T. KARR[1], A. PERLMAN[1]
1 Pendulum Therapeutics, Inc

AIM

The primarily aim of the consumer survey was to explore how the supplementation of GLP-1 Probiotic (*Akkermansia muciniphila* WB-STR-0001, *Clostridium butyricum* WB-STR-0006, and *Bifidobacterium infantis* Bi-26™) affected participants' perceived food cravings over a period of six weeks using a validated questionnaire called the Food-Craving Inventory II (FCI-II).



Results showed that 91% of participants experienced a reduction in overall food cravings.

Depommier C, et al. Nat Med. 2019 Jul;25(7):1096-1103.
Reduction of Food Cravings Utilizing a Novel Probiotic Containing Akkermansia. Adam Perlman. IFM Poster Library. Perlman A. 05/29/2024; 417088; 7 Topic: Other

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Prebiotics

- Study of healthy, non-diabetic individuals that received supplementation with prebiotics (derived from chicory roots) for 2 weeks showed:
  - An increase in plasma GLP-1 and a decrease in postprandial glucose compared to individuals that received the control (dextrin maltose supplementation).
  - Prebiotic supplementation significantly lowered post-meal hunger scores and improved satiety scores.

Cani P, Lecourt E, Delzenne N, et al. *Am J Clin Nutr*. 2009;90(5):1236-1243. doi:10.1016/J.MAM.2012.11.001.

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Address Gut Dysbiosis

Identify & Correct Underlying Causes

- Test

Manage & Treat

- 5R Approach

Reduce Likelihood of Relapse

- Address motility

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5R Gut Protocol

Remove	• Food sensitivities, alcohol, aspirin, NSAIDS from the diet • Use antimicrobials for dysbiosis, infection, and/or parasites
Replace	• Digestive support to improve nutrient absorption and metabolism • May include digestive enzymes, or agents that promote improved motility and regular bowel movements
Reinoculate	• Provide an environment where good bacteria can thrive and where bad ones cannot • Use pre- and probiotics
Repair	• Support of the cellular repair process by providing specific nutritional support for the regeneration of the GI protective barrier • GI mucosa with healing nutrients and botanicals
Rebalance	• Lifestyle factors that influence the gut bacteria such as stress, sleep, exercise and relationships and assure ongoing gut health

Jones DS, et al. Textbook of Functional Medicine 2010.

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Insulin Resistance

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Insulin Resistance (IR)

- IR: decrease in the metabolic response of insulin-response cells to insulin.
- Skeletal Muscle: mutations that reduce the expression of insulin receptor or GLUT4, or any defect in either upstream or downstream signaling pathway would reduce glucose intake into the muscle resulting in a hyperglycemic state
- Adipose Tissue: Insulin acts on adipose tissue in two different ways: (1) stimulating glucose uptake and triglyceride synthesis; and (2) suppressing triglyceride hydrolysis and inducing the uptake of FFA and glycerol from circulation
  - When this tissue becomes resistant, we see increase in FFA

Galicia-Garcia U,et al Int J Mol Sci. 2020;21(17):6275.

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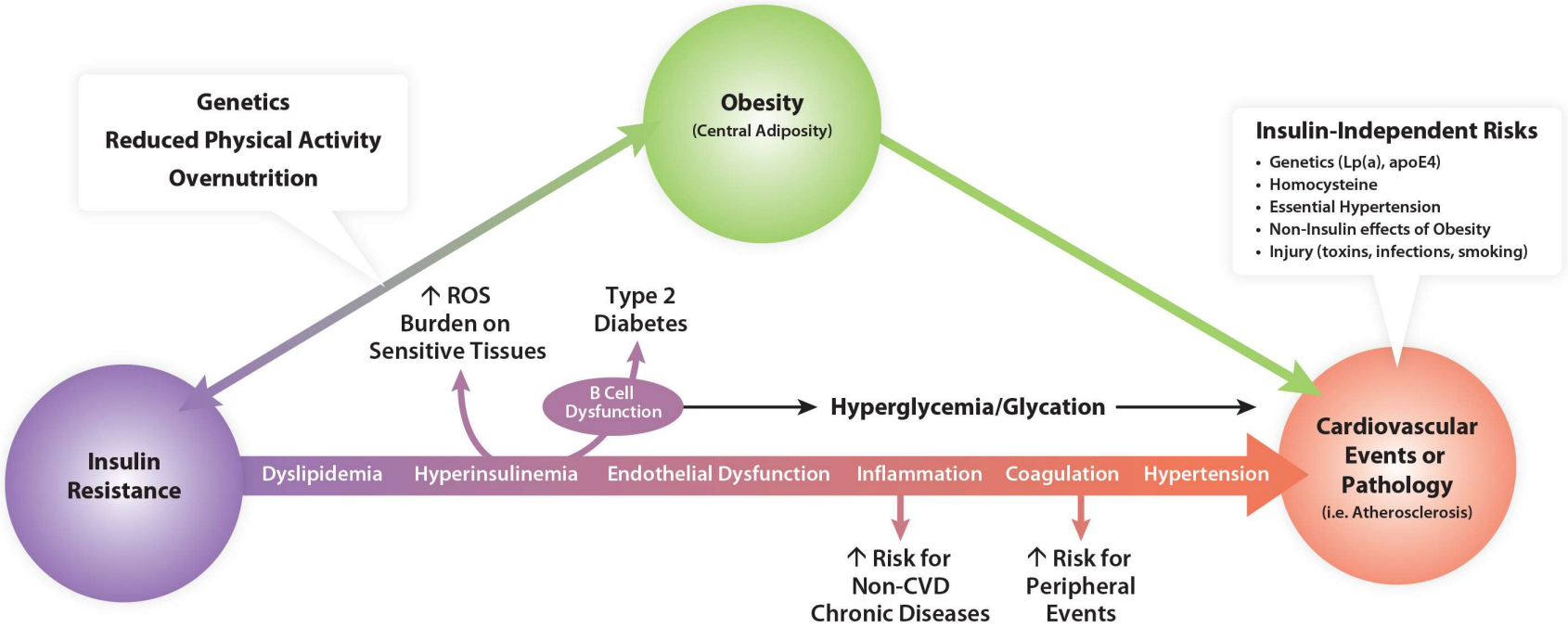
Insulin Resistance & CVD



Reprinted with permission: Figure 4. Guilliams, T. Cardiometabolic Risk Management: A Functional and Lifestyle Approach. The Standard Road Map Series. Pointe Institute 2018.

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Supplements

- Berberine
- Zinc
- Vitamin D
- Magnesium
- Insulin sensitizers: lipoic acid, chromium, vanadium, cinnamon

Xu X, et al. Biomed Pharmacother. 2021 Jan;133:110984.
Ranasinghe P et al. Journal of Diabetes. Accepted Author Manuscript. doi:10.1111/1753-0407.12621
Melguizo-Rodríguez L, et al. Nutrients. 2021 Mar 3;13(3):830.
Nutrients. 2021 Jan 22;13(2):320.
Guilliams, T. Cardiometabolic Risk Management: A Functional and Lifestyle Approach. The Standard Road Map Series. Pointe Institute 2018.
Natural Medicines Comprehensive Database. Natural Medicines [database online]. Stockton, CA: Therapeutic Research Facility; 2019.

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Chronic Stress

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Chronic Stress

- Cortisol
  - Causes a redistribution of white adipose tissue to the abdominal region
  - Increases appetite (“comfort food”)
- Factors that enhance cortisol production
  - Chronic stress
  - Intake of high glycemic foods
  - Lack of sleep
- Obese individuals on average have higher hair cortisol levels
- Hair cortisol concentration (HCC) correlated to a more persistent obesity over time

van der Valk ES, et al. Curr Obes Rep. 2018 Jun;7(2):193-203.

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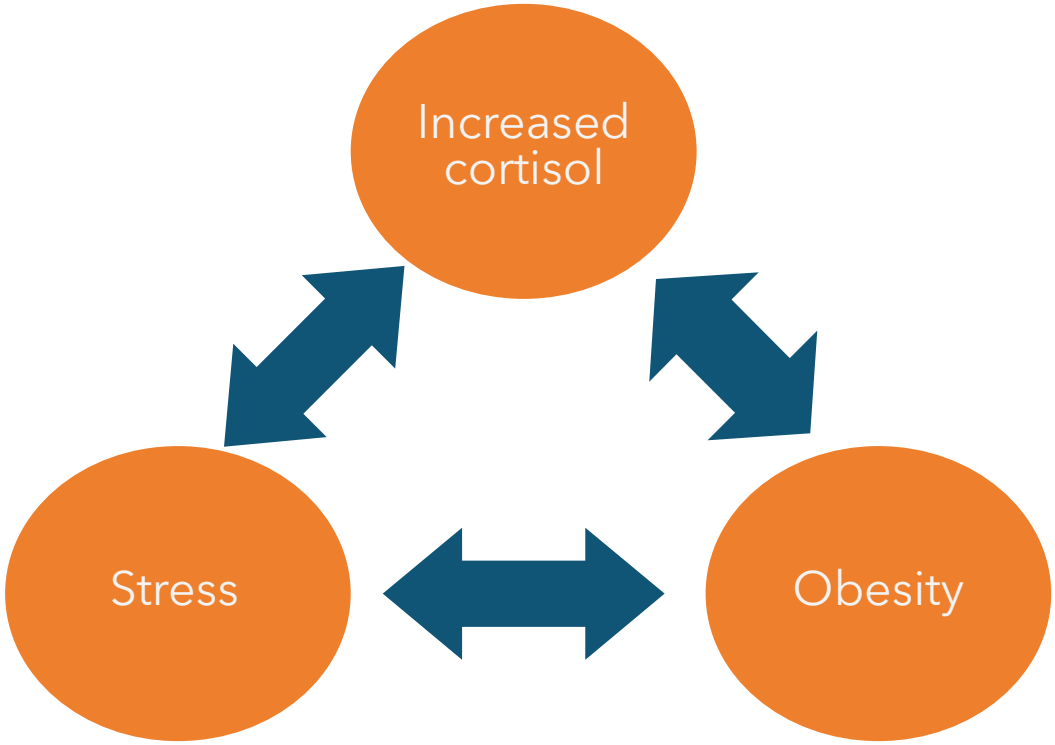
Vicious Cycle



adapted from van der Valk ES, et al. Curr Obes Rep. 2018 Jun;7(2):193-203.

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Possible Mechanisms of Higher Cortisol in Obesity

- Overactivity of the HPA axis
  - Intake of food with a high glycemic index
  - Chronic stress
  - Chronic pain
  - Alcohol
  - Chronic sleep deprivation
  - Night eating syndrome
- Inflammatory markers
- Individual variation in enzymes that are involved in cortisol metabolism

van der Valk ES, et al. Curr Obes Rep. 2018 Jun;7(2):193-203.

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Stress Management

- Overweight and obese women who participated in an 8-week stress management program achieved a significantly larger reduction in BMI compared to control group (along with improved perceived stress and depression levels)
- Overweight and obese children and adolescents that underwent a stress-management intervention, had statistically significant weight loss and decrease in the levels of stress and depression, as well as in internalizing and externalizing problems

Christaki E, et al. J Hum Nutr Diet. 2013 Jul;26 Suppl 1:132-9.
Stavrou S, et al. J Mol Biochem. 2016;5(2):63-70.

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Stress Management Techniques

- Meditation
- Yoga, tai chi, or qigong
- Journaling
- Physical activity
- Breath work
- Social connection
- Connect with nature
- Listen to relaxing music
- Spend time with a pet

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Supplements for Stress/Anxiety Support

- Ashwagandha
- Rhodiola
- Phosphatidylserine
- Eleuthero root extract
- Skullcap
- Probiotics, synbiotics, psychobiotics
- Saffron (*Crocus sativus*)
- Kava kava (*Piper methysticum*)
- Passionflower (*Passiflora incarnate*)
- Valerian (*Valeriana officinalis*)

Yeung KS, et al. Phytother Res. 2018 May;32(5):865-891.
Ferrari S, et al. J Tradit Complement Med. 2024 Mar 21;14(3):237-255.
Kamat D, et al. Int J Environ Res Public Health. 2023 Mar 15;20(6):5171.

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Sleep

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Sleep

- One-third or more adults sleep less than 7 hours per night
- Short sleep duration (<5 or 6 h/day) is associated with a 38% absolute increase in the incidence of obesity compared with normal sleep duration
- Every hour a person must shift their internal clock to match the wakefulness period between weekends and weekdays resulted in an increased odds ratio of 1.3 of having metabolic syndrome in the general population
- Circadian disruption associated with obesity
  - High snacking frequency
  - Reduction in total daily sleep
  - Increased exposure to bright light during the night
- Ghrelin increases with sleep restriction; leptin decreases

Garaulet M, et al. Int J Obes (Lond). 2010 Dec;34(12):1667-83.
Chaput JP, et al. Nat Rev Endocrinol. 2023 Feb;19(2):82-97.

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Improve Sleep Quality & Quantity

- Make sleep a priority!
- Create a relaxing sleep environment
- Go to sleep and wake up at the same time each day
- Avoid blue light in the evening (blue blocker glasses if needed)
- Limit caffeine intake
- Make sure sleep environment is dark and cool
- Get sunlight in the morning to help set circadian rhythm
- Physical activity
- Manage stress

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Circadian Health

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Circadian Disruption and Metabolic Health

- Many metabolic functions demonstrate diurnal rhythmicity
  - enzymes (expression and function) that are important for the regulation of cholesterol, other lipids, glucose and amino acids
  - melatonin receptors are involved in regulating gluconeogenesis, pancreatic β-cell signaling and insulin resistance
- Circadian transcriptional clock present in almost every cell of the body
- Alterations in time of light exposure and food consumption can disrupt circadian rhythms which leads to an inflammatory state and impaired immune system function, promoting the onset of several cardiometabolic diseases
- Consuming calories closer to the onset of melatonin production (near sleep onset) is associated with increased body adiposity
- Consumption of higher calories after ~1900 hours (~4 h before sleep onset) is associated with being less lean
- Low melatonin levels associated with insulin resistance, T2DM and obesity

Bishehsari F, et al. Nat Rev Endocrinol. 2020 Dec;16(12):731-739.
Lotti S, et al. Nutr Metab Cardiovasc Dis. 2023 Aug;33(8):1490-1500.

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The Effects of Light on Metabolism

- Light is the most important stimulus for regulating circadian and behavioral systems
- The deviation from naturally occurring light–dark cycles has introduced adverse effects on human health including disturbance in sleep and circadian rhythm and increased risk for obesity and metabolic disorders
- Melatonin plays a crucial role in regulating energy metabolism and energy balance

Nagai N, et al. Invest Ophthalmol Vis Sci. 2019 Sep 3;60(12):3786-3793.
Ishihara A, et al. Nutrients. 2023 Mar 14;15(6):1391.

Epidemiological Studies on Light and Metabolic Health

- Bedroom brightness significantly associated with an increased risk of high BMI and obesity in women (n = 113,000; 47.2 ± 13.6 yrs)
- In 513 older individuals with and without diabetes, ambient light intensity in the evening before bed from 17.5 to 37.6 lux was associated with a 51% increase in the prevalence of diabetes
- Artificial light at night from indoor and/or outdoor light during sleep was significantly associated with an increased risk of weight gain and obesity in women (n = 43,722; 55.4 ± 8.9 yrs)
- In 528 older Japanese individuals, those sleeping in rooms with >3-lux light tended to have a higher body weight, BMI, waist circumference, triglyceride level, and low-density lipoprotein cholesterol level compared to those sleeping in rooms at <3 lux
- A prospective study suggested that light at night (>5 lux) increases the incidence of diabetes in affected individuals compared to those sleeping with light at <5 lux (n = 678; 70.6 ± 6.6 yrs)
- Mild sleep deprivation combined with nocturnal light exposure during sleep (600 lux) in healthy men (n = 8; 21.1 ± 0.9 yrs) increased post-prandial insulin levels

Ishihara A, et al. Nutrients. 2023 Mar 14;15(6):1391.

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Obesogens

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Obesogens

- Molecules with adverse effects on lipid metabolism and adipogenesis
- 1000+ chemicals reported to have endocrine effects
- Exposure from industrial and household products, pesticides, herbicides, plastics, detergents, flame retardants and personal care products
- 2002: Baillie-Hamilton proposed a link between the obesity epidemic and the increase in new industrial chemicals over the past four decades
- 2006: environmental obesogen hypothesis

Gupta R, et al. Current Research in Green and Sustainable Chemistry. 2020 Jun;3:100009.
Kelishadi R, et al. J Environ Public Health. 2013;2013:896789.

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Common Obesogens

Perfluoroalkyl compounds (PFCs)	Phthalates	Bisphenol A (BPA)	Phytoestrogens (genistein and daidzein)
Organophosphates	Polychlorinated bi-phenyls (PCBs)	Monosodium glutamate	Heavy metals

Gupta R, et al. Current Research in Green and Sustainable Chemistry. 2020 Jun;3:100009.

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Remove and/or Limit Environmental Toxins

- An important first step is to address the topic with patients (many people aren't aware of what they are or where they come from)
- Tips for reducing exposures:
  - Eat organic fruits & vegetables when possible
  - Minimize the use of cosmetics and personal care products (or switch to cleaner brands)
  - Remove artificial sweeteners, high fructose corn syrup, and preservatives from the diet
  - Swap plastic food/drink containers for glass or stainless steel
  - Drink filtered water
  - Get rid of air fresheners and candles in the home

Janesick AS, et al. Am J Obstet Gynecol. 2016 May;214(5):559-65.

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Other Considerations

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Hormone Imbalance

- Hypothyroidism
- PCOS
- Postpartum weight retention
- Menopause

Dabas J, et al. J Health Popul Nutr. 2024 Mar 2;43(1):37.

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Malnutrition in Obesity

- Despite excessive energy consumption, obesity is associated with a shortage of individual microelements
- May be due to:
  - overconsumption of foods high in calories with low-nutrient densities
  - insufficient access to nutrient-rich foods
  - changes in the absorption, distribution, or excretion of nutrients
  - altered micronutrient metabolism resulting from systemic inflammation

Kobylińska M, et al. Obes Facts. 2022;15(1):19-25.

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Prevalence of Deficiency

Micronutrient	Obesity	Type 2 Diabetes
Thiamine (B1)	15-29%	17-79%* includes type 1 data
Pyridoxine (B6)	0-11%	-------
Cobalamin (B12)	3-8%	22%
Folic acid	3-4%	-------
Ascorbic acid (C)	35-45%	Decreased levels reported
Vitamin A	17%	-------
Vitamin D	80-90%	85-90%
Vitamin E	0%	0%
Zinc	14-30%	-------
Chromium	-------	20-40%
Selenium	58%	-------

Adapted from Table 1; Via M. ISRN Endocrinol. 2012;2012:103472.

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Mental Health

- Obesity and depression have a significant and bidirectional association
- Obesity associated with approximately 25% increased risk of developing mood and anxiety disorders
- Adverse Childhood Experiences (ACEs):
  - Potentially traumatic events that occur in childhood (0-17 years)
  - 46% increase in the odds of adult obesity following exposure to multiple ACEs
  - ACEs associated with depression, anxiety, and eating disorders

Rajan TM, et al. J Postgrad Med. 2017 Jul-Sep;63(3):182-190.
Simon GE, et al. Arch Gen Psychiatry. 2006 Jul;63(7):824-30.
Wiss DA, et al. Physiol Behav. 2020 Sep 1;223:112964.
Mares L.S. et al. Traumatology. 2023.

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GLP-1

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Glucagon-like Peptide 1 (GLP-1)

- A gastrointestinal peptide secreted by the intestinal tract that potentiates insulin release and reduces glucagon's concentration in physiological conditions
  - also comes from a-cells in the pancreatic islet and neurons in the nucleus of the solitary tract
- Plays an important role in regulating blood glucose levels and appetite
  - inhibits postprandial gastric emptying and reduce gastric acid secretion
  - inhibits gastric and duodenal peristalsis by inhibiting vagus nerve
  - increases the pressure of pylorus, thus reducing appetite, causing a reduction in body weight and participating in the so-called "ileal braking" effect

Wang JY, et al. Front Endocrinol (Lausanne). 2023 Feb 1;14:1085799.

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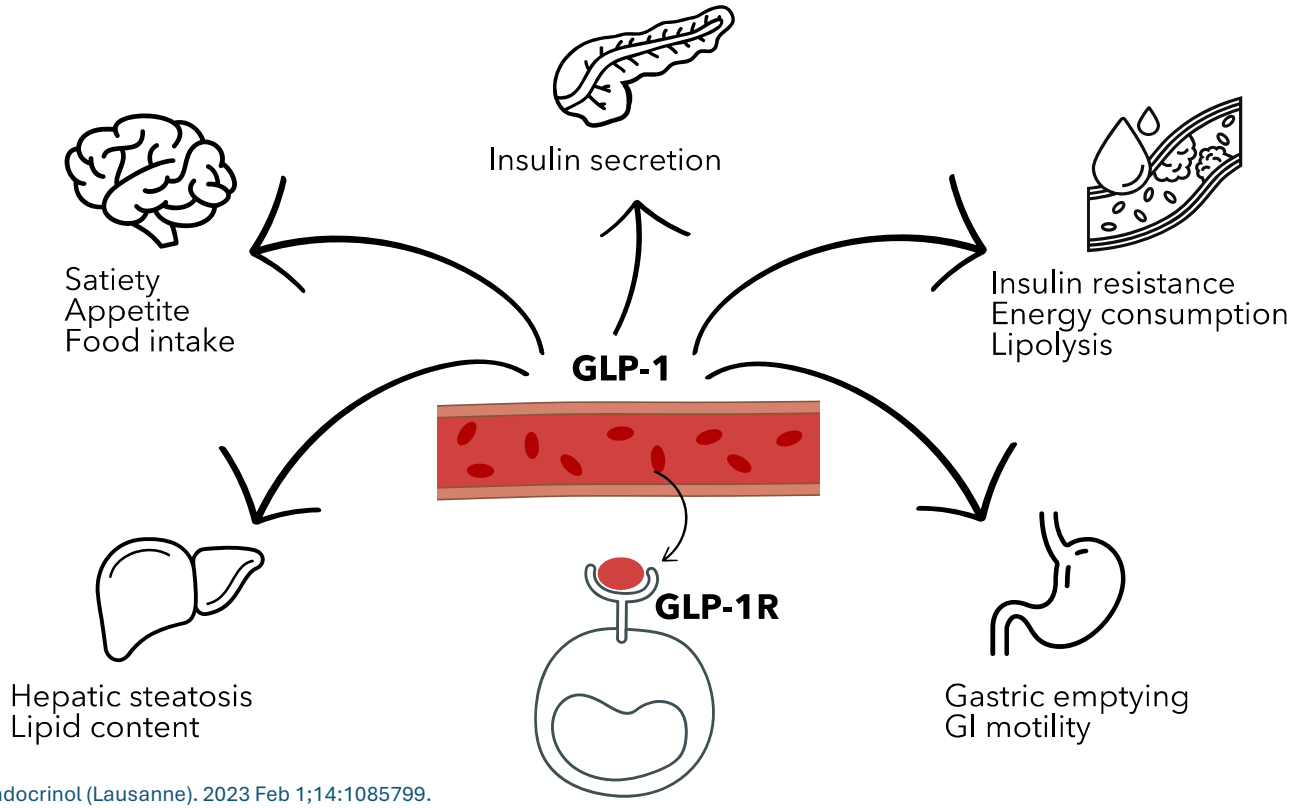
Possible Mechanisms of Weight Loss



Adapted from Wang JY, et al. Front Endocrinol (Lausanne). 2023 Feb 1;14:1085799.

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Boosting GLP-1 with Natural-Based Agents

- Berberine
- Resveratrol
- Cinnamon
- Curcumin
- Tea
- Quercetin
- Ginger

Yaribeygi H, et al. Adv Exp Med Biol. 2021;1328:513-522.

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Strategies for Improving Metabolic Health

Optimize Nutrition	Focus on whole, anti-inflammatory foods and minimize ultra-processed foods.
Enhance Insulin Sensitivity	Incorporate regular exercise and manage carbohydrate intake.
Manage Stress Effectively	Utilize stress reduction techniques like mindfulness and adaptogens.
Support Gut Health	Balance the microbiome with prebiotics, probiotics, and fermented foods.
Balance Hormones	Optimize sleep and consider supplements to support hormonal balance.
Reduce Environmental Toxin Exposure	Limit exposure to obesogens by choosing cleaner food and products.
Prioritize Sleep and Circadian Health	Maintain a consistent sleep schedule and morning sunlight exposure.

Pharmacists' Expanding Role

- Pharmacists are uniquely positioned to provide integrative metabolic care due to their accessibility and expertise in medication management and patient education.
- With skills in monitoring and point-of-care testing, pharmacists can identify early signs of metabolic dysfunction (e.g., elevated glucose, hypertension) and recommend timely interventions.
- Beyond dispensing, pharmacists understand drug-nutrient interactions, side effects, and how medications can impact metabolic health, allowing for comprehensive care adjustments.
- Serve as an essential resource in guiding patients toward healthier lifestyles and better health outcomes.

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Questions?

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