

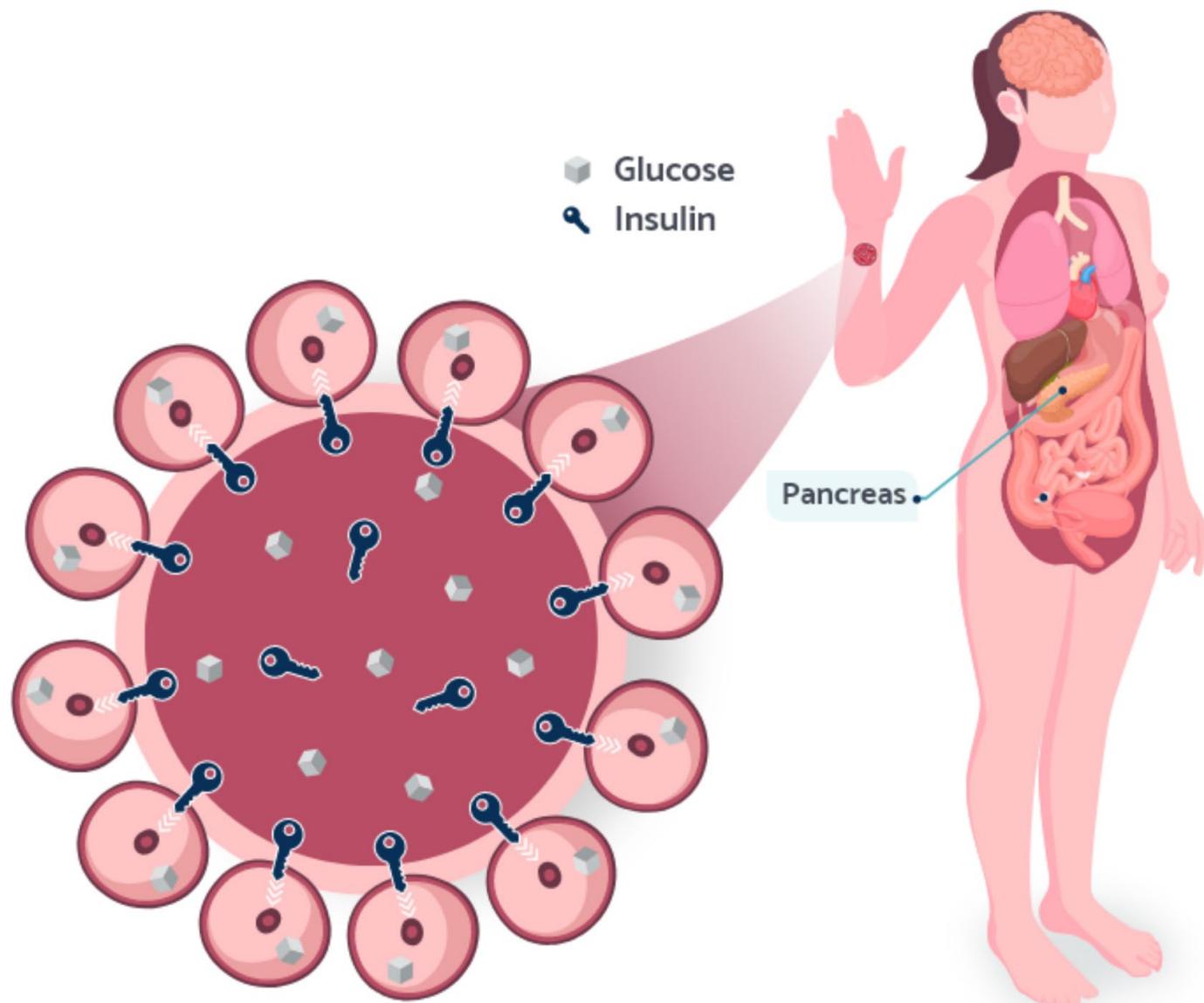
Low Insulin Lifestyle - Audio Book Reference Guide

Contents

CHAPTER 1 – UNDERSTANDING INSULIN AND INSULIN RESISTANCE.....	2
HEALTHY METABOLISM.....	2
INSULIN RESISTANT METABOLISM	3
The Difference Between Insulin Resistance and Type 2 Diabetes.....	4
THE WORK-A-HOLIC PANCREAS	4
THE RETIRED PANCREAS	4
THE LAZY PANCREAS.....	5
Understanding Metabolic Flexibility	5
FLEXIBLE METABOLISM	5
INFLEXIBLE METABOLISM	6
Hyperinsulinemia.....	6
THE VICIOUS CYCLE OF INSULIN RESISTANCE.....	6
CHAPTER 3 - VARIATIONS IN GENETIC PREDISPOSITION TO HIGH INSULIN LEVELS	7
NORMAL MENSTRUAL CYCLE	7
ANOVULATORY MENSTRUAL CYCLE.....	8
HOW HIGH INSULIN LEVELS LEAD TO SYMPTOMS OF PCOS.....	9
CHAPTER 5 – HOW TO LOWER INSULIN LEVELS	10
INSULIN SPIKING EFFECT OF DIFFERENT FOODS.....	10
CHAPTER 7 – THE RESEARCH BEHIND A LOW INSULIN DIET	11
OVERVIEW OF THE RESULTS AFTER 8-WEEK LOW INSULIN LIFESTYLE	11
CHANGE IN GLUCOSE AND INSULIN BEFORE AND AFTER A LOW INSULIN LIFESTYLE.....	12
CHANGE IN TOTAL AND FREE TESTOSTERONE BEFORE AND AFTER A LOW INSULIN LIFESTYLE.....	13
CHANGE IN CHOLESTEROL AND LIPIDS FOLLOWING A LOW INSULIN LIFESTYLE	14
IMPROVEMENTS IN PCOS SYMPTOMS BEFORE AND AFTER A LOW INSULIN LIFESTYLE	15
IMPROVEMENTS IN BINGE EATING BEHAVIORS AFTER A LOW INSULIN LIFESTYLE	16
CHANGE IN FAT OXIDATION.....	16
Replicating the Results.....	17
CHANGE IN FASTING INSULIN BETWEEN THE THREE GROUPS AFTER 8 WEEKS	17
WEIGHT LOSS BETWEEN THE THREE GROUPS AFTER 8 WEEKS	17
REFERENCES	18

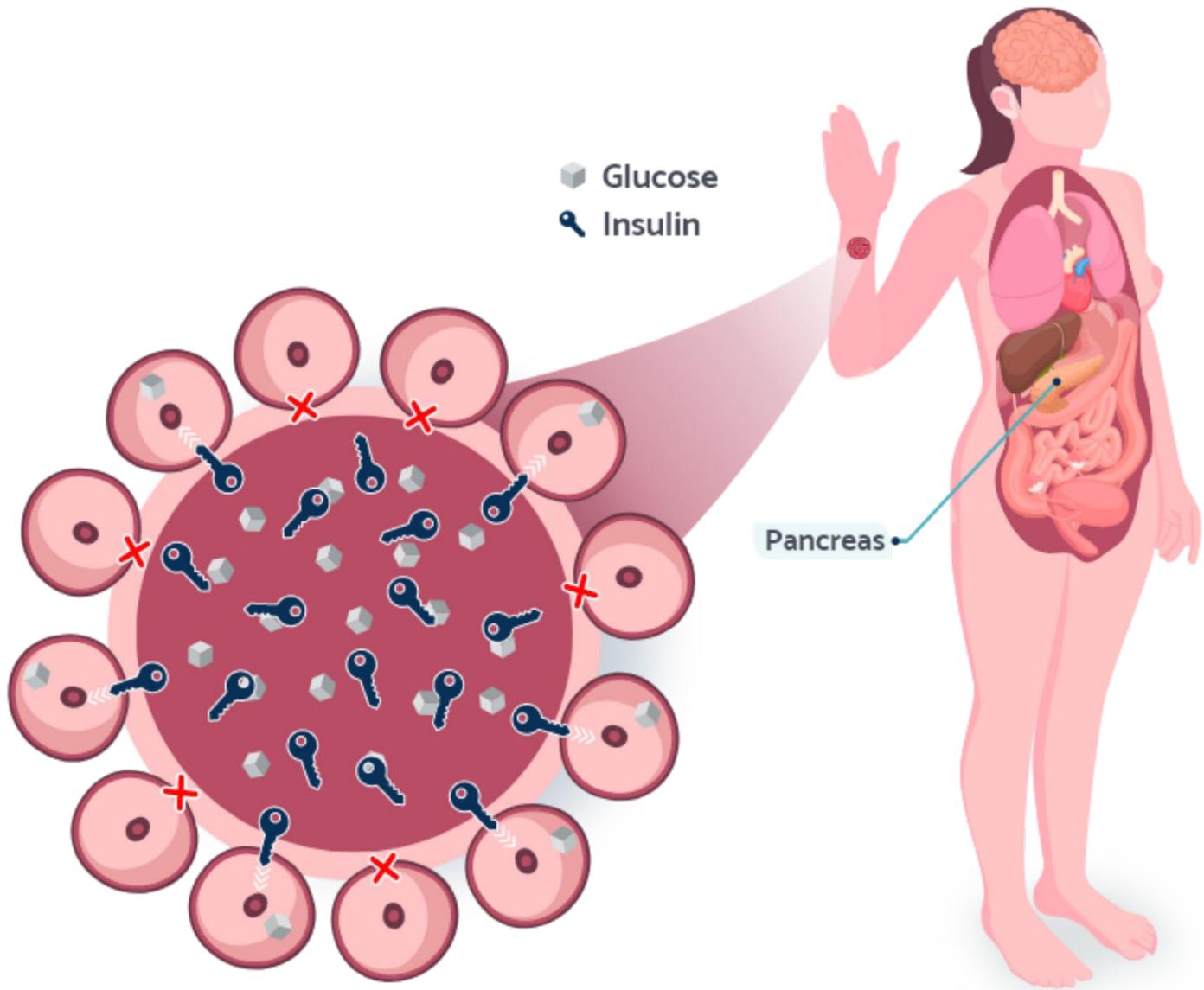
CHAPTER 1 – UNDERSTANDING INSULIN AND INSULIN RESISTANCE

HEALTHY METABOLISM



A healthy metabolism is one where insulin is secreted by the pancreas after a meal, helping to transport glucose into the cells, and then levels in the blood come back down to normal until the next meal. In this figure you can see that insulin (key) is unlocking the cells to allow glucose (sugar cube) to enter. Blood sugar levels in the blood are normal and insulin levels are low.

INSULIN RESISTANT METABOLISM



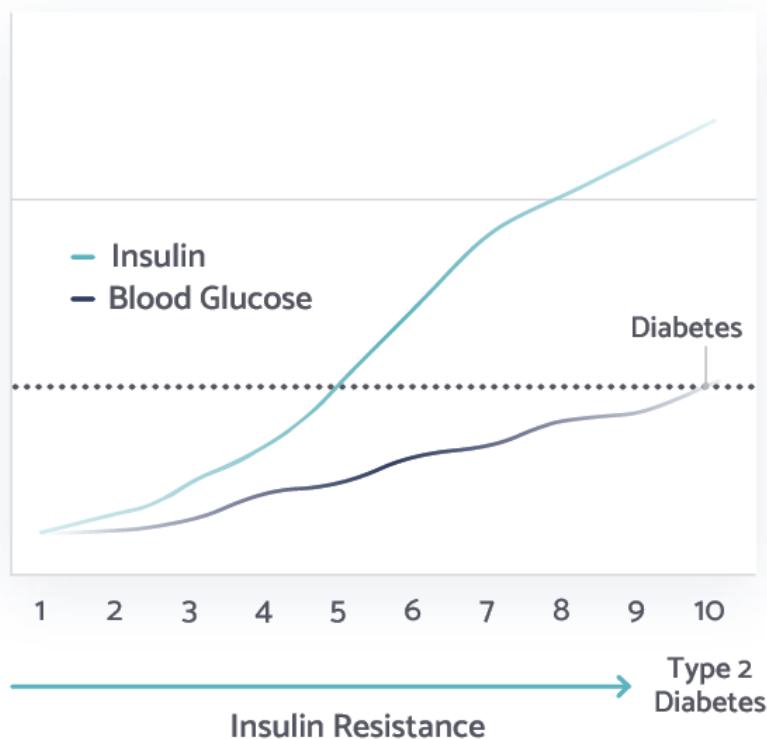
When someone is insulin resistant, the cells don't respond to insulin and it's more difficult to get glucose into the cells. This leads insulin to build up in the blood because the pancreas keeps secreting more insulin to help get glucose into the cells. Someone who is insulin resistant may have normal blood sugar levels because their insulin is still working well enough to get the glucose into the cells – it just takes more insulin to get the same job done.

In the figure you can see that insulin (key) is not working in some of the cells. These cells are resistant (X) to insulin and aren't allowing glucose (sugar cube) to enter. This is a simplified explanation to a highly complex process, but it's meant to give you a visual.

The Difference Between Insulin Resistance and Type 2 Diabetes

THE WORK-A-HOLIC PANCREAS

© Lili Health. All Rights Reserved.



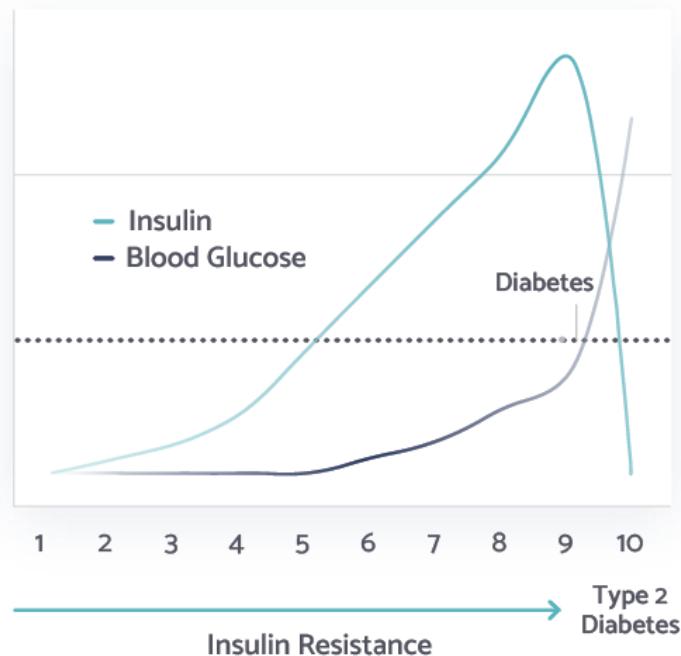
THE WORK-A-HOLIC PANCREAS

The majority of adults have what I like to call a work-a-holic pancreas. Individuals with a work-a-holic pancreas often have high insulin levels for years or even decades before their blood glucose reaches a level that results in a diagnosis of type 2 diabetes. In this graph, the dotted line represents a blood glucose level that would result in a diagnosis of type 2 diabetes.

This graph shows why only testing blood glucose and hemoglobin A1c isn't enough to determine if someone is insulin resistant.

THE RETIRED PANCREAS

© Lili Health. All Rights Reserved.



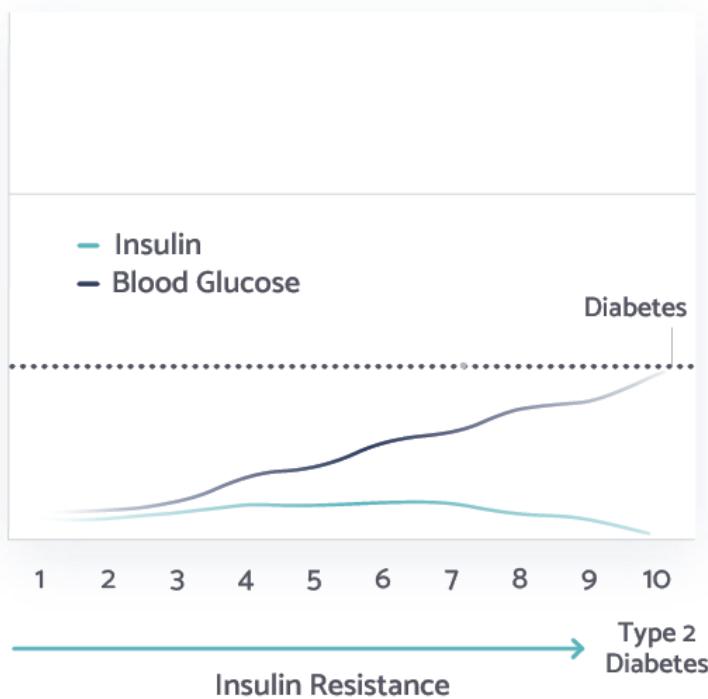
THE RETIRED PANCREAS

Some adults have what I like to call a retired pancreas. This results after years of high insulin levels and excessive demands on the pancreas. Eventually, the pancreas gives out (i.e., retires) and stops secreting enough insulin. Once this happens, blood sugars spike and the person is diagnosed with type 2 diabetes.

This graph shows that if someone has a low fasting insulin but high blood sugar, it probably indicates that their pancreas is nearing retirement.

THE LAZY PANCREAS

© Lili Health. All Rights Reserved.



THE LAZY PANCREAS

Some individuals have what I like to call a lazy pancreas. This is often found in persons of East or Southeast Asian descent and is why type 2 diabetes is common among these populations.

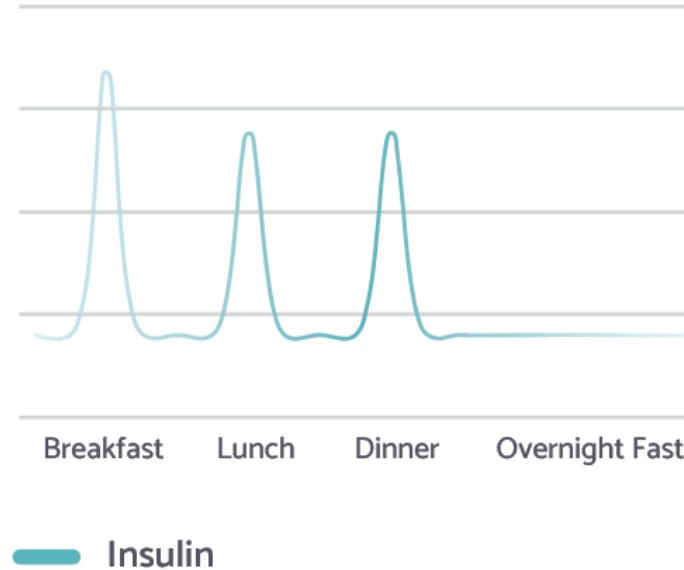
The lazy pancreas just can't keep up, especially when you consider that most Asian populations eat a diet heavy in starch. This results in these individuals having low insulin levels, despite rising blood sugars.

In this graph, you see that insulin levels are always low, but glucose levels continue to rise and rise as insulin levels decline over time.

Understanding Metabolic Flexibility

FLEXIBLE METABOLISM

© Lili Health. All Rights Reserved.



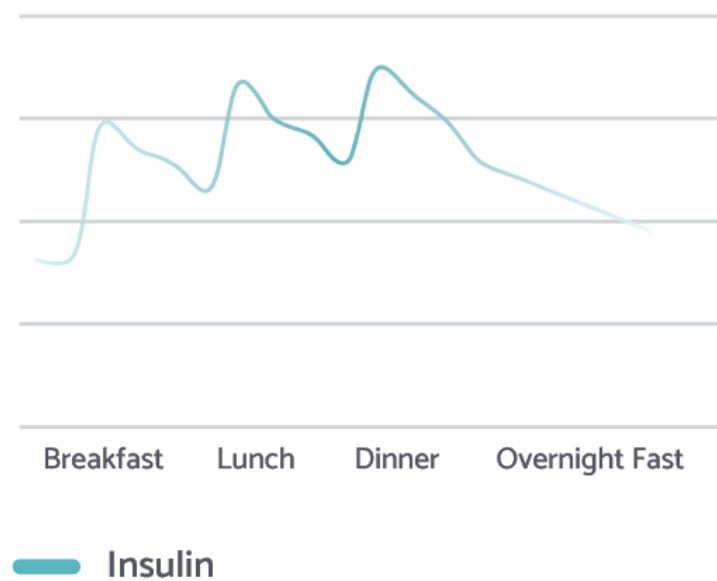
FLEXIBLE METABOLISM

This graph shows the rise and fall of insulin levels over the course of a day in a person who is metabolically flexible. After meals, insulin levels rise and then they come back down to baseline between meals and during an overnight fast.

When insulin levels rise, it allows the body to use glucose from food for energy, and when insulin levels are low, it allows stored body fat to be burned for energy.

INFLEXIBLE METABOLISM

© Lili Health. All Rights Reserved.



INFLEXIBLE METABOLISM

This graph shows a person who has an inflexible metabolism. They start their day with higher-than-normal fasting insulin levels and because insulin levels are so high, they aren't able to come back down to baseline between meals or during the overnight fast. This prevents the body from being able to burn stored body fat for energy.

Overall, hyperinsulinemia can interfere with the body's ability to switch between different fuel sources, leading to metabolic inflexibility.

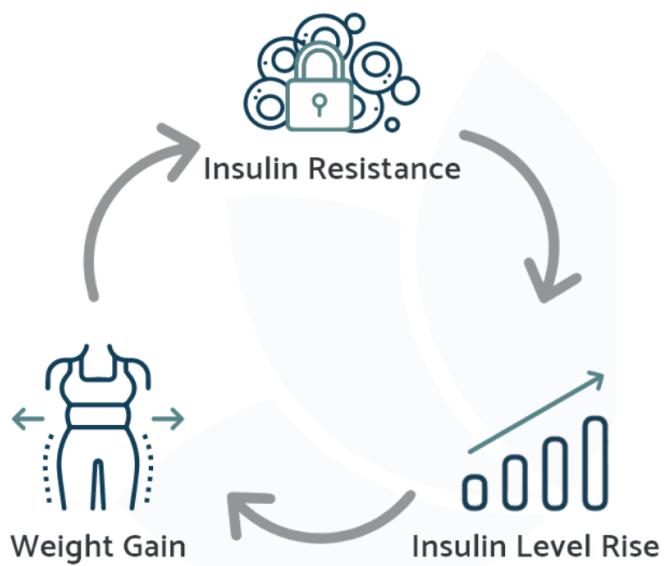
Hyperinsulinemia

THE VICIOUS CYCLE OF INSULIN RESISTANCE



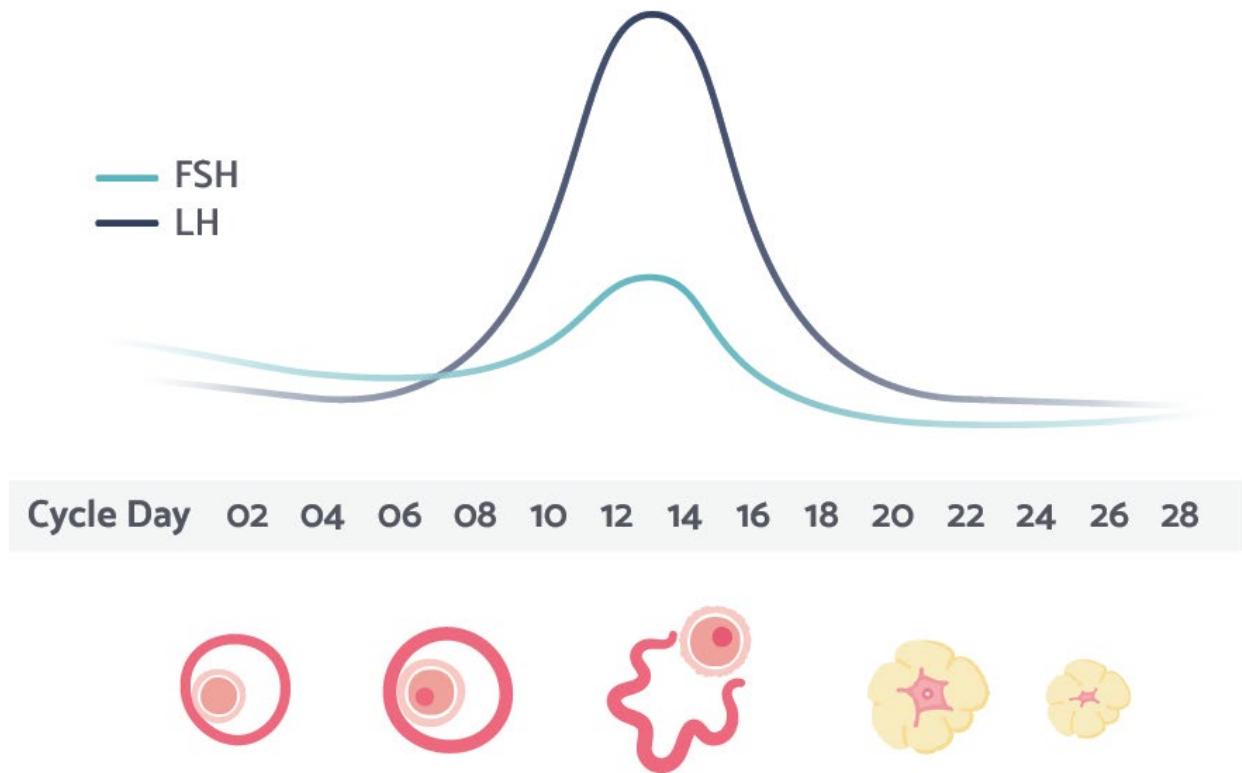
Recurrent Insulin Spikes

>>>



CHAPTER 3 - VARIATIONS IN GENETIC PREDISPOSITION TO HIGH INSULIN LEVELS

NORMAL MENSTRUAL CYCLE



© Lili Health. All Rights Reserved.

ANOVULATORY MENSTRUAL CYCLE

© Lili Health. All Rights Reserved.

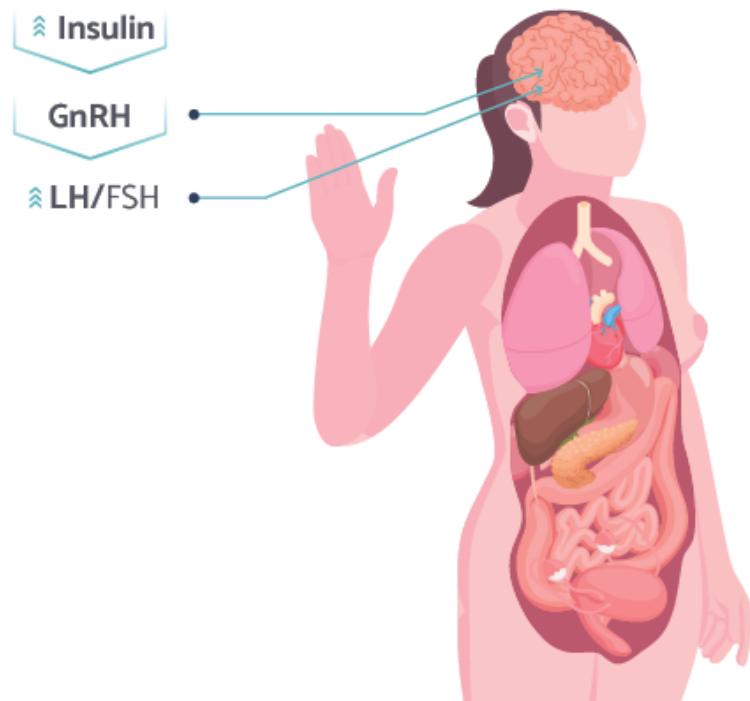
FSH
LH



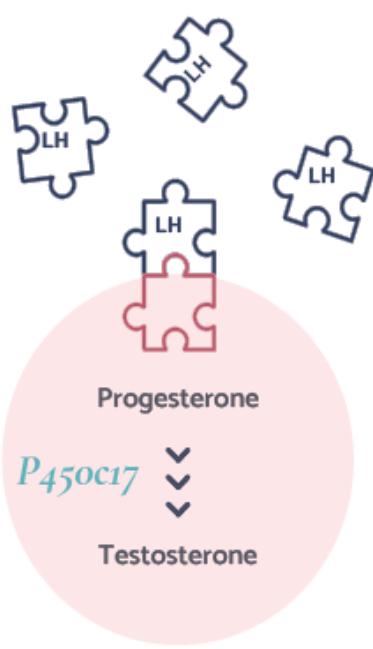
Cycle Day 02 04 06 08 10 12 14 16 18 20 22 24 26 28



HOW HIGH INSULIN LEVELS LEAD TO SYMPTOMS OF PCOS



© Ulli Health. All Rights Reserved.



Irregular
Menstrual Cycles



Hirsutism



Weight Gain



Hair Loss

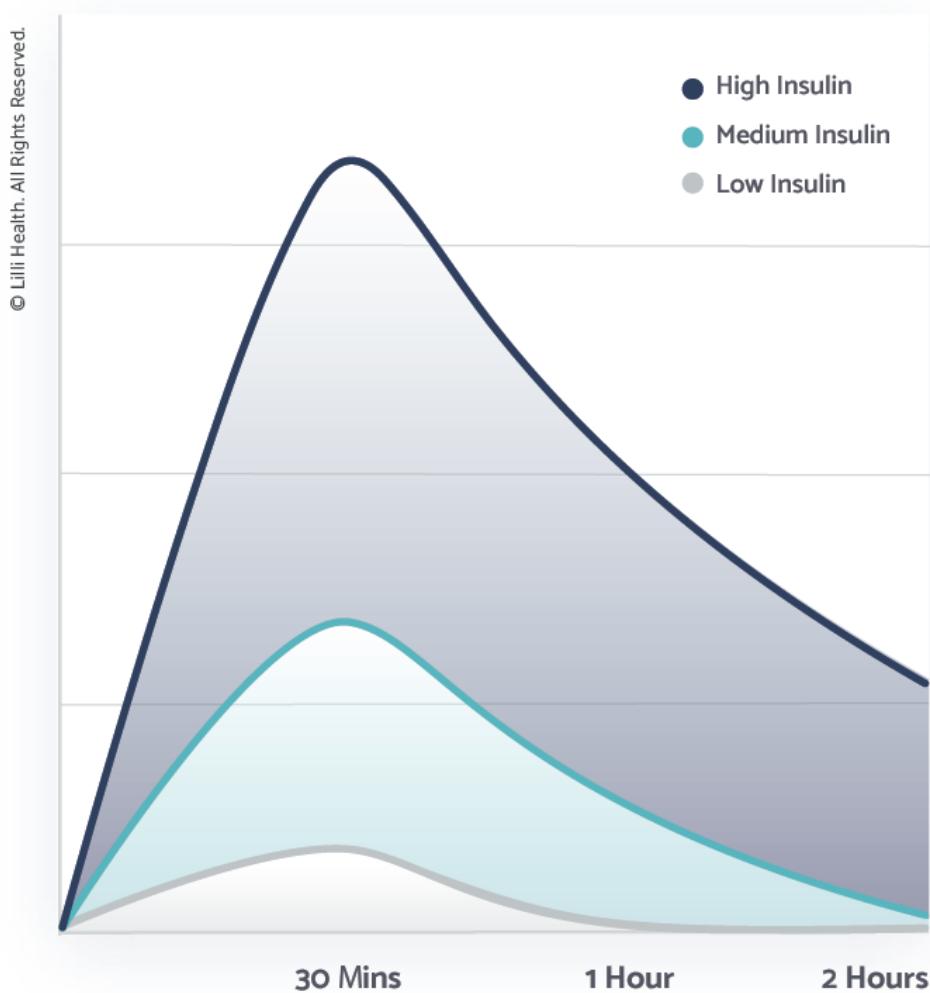


Acne

Ovarian Cysts

CHAPTER 5 – HOW TO LOWER INSULIN LEVELS

INSULIN SPIKING EFFECT OF DIFFERENT FOODS



This graph presents an estimation based on selected studies that show insulin responses to various types of foods. It doesn't represent the exact insulin curve for all individuals and it's simply meant to explain how different foods elicit a different insulin response.

High: starches, dairy, added sugar

Medium: protein, fruit

Low: vegetables, nuts, seeds, healthy oils

CHAPTER 7 – THE RESEARCH BEHIND A LOW INSULIN DIET

OVERVIEW OF THE RESULTS AFTER 8-WEEK LOW INSULIN LIFESTYLE

Lilli Health	Before 8-Week Diet	After 8-Week Diet	Results After Diet	% Change
Weight (lbs)	225.0	206.0	▼ 19.0	▼ 8.5
Waist Circumference (in)	43.2	39.9	▼ 3.3	▼ 7.6
Fasting Glucose (mg/dl)*	95.0	86.0	▼ 8.9	▼ 9.3
2-Hour Glucose (mg/dl)	128.0	114.9	▼ 13.1	▼ 10.2
Fasting Insulin (mIU/ml)	32.7	15.7	▼ 17.0	▼ 52.9
2-Hour Insulin (mIU/ml)	225.8	142.9	▼ 82.8	▼ 36.7
HOMA-IR**	3.9	1.9	▼ 1.9	▼ 48.7
HgbA1c (%)	5.5	5.2	▼ 0.3	▼ 5.4
Total Testosterone (ng/dl)	53.3	43.3	▼ 10.0	▼ 18.7
Free Testosterone (pg/dl)	7.8	6.0	▼ 1.8	▼ 23.1
Triglycerides (mg/dl)	162.8	108.2	▼ 57.0	▼ 35.0

© Lilli Health. All Rights Reserved.

* Patients were not allowed to be in this study if they had confirmed diabetes, thus glucose levels were within the normal range both before and after the study.

** HOMA-IR: Homeostatic model assessment for insulin resistance is used to measure overall insulin resistance. A lower score shows an improvement in insulin resistance.

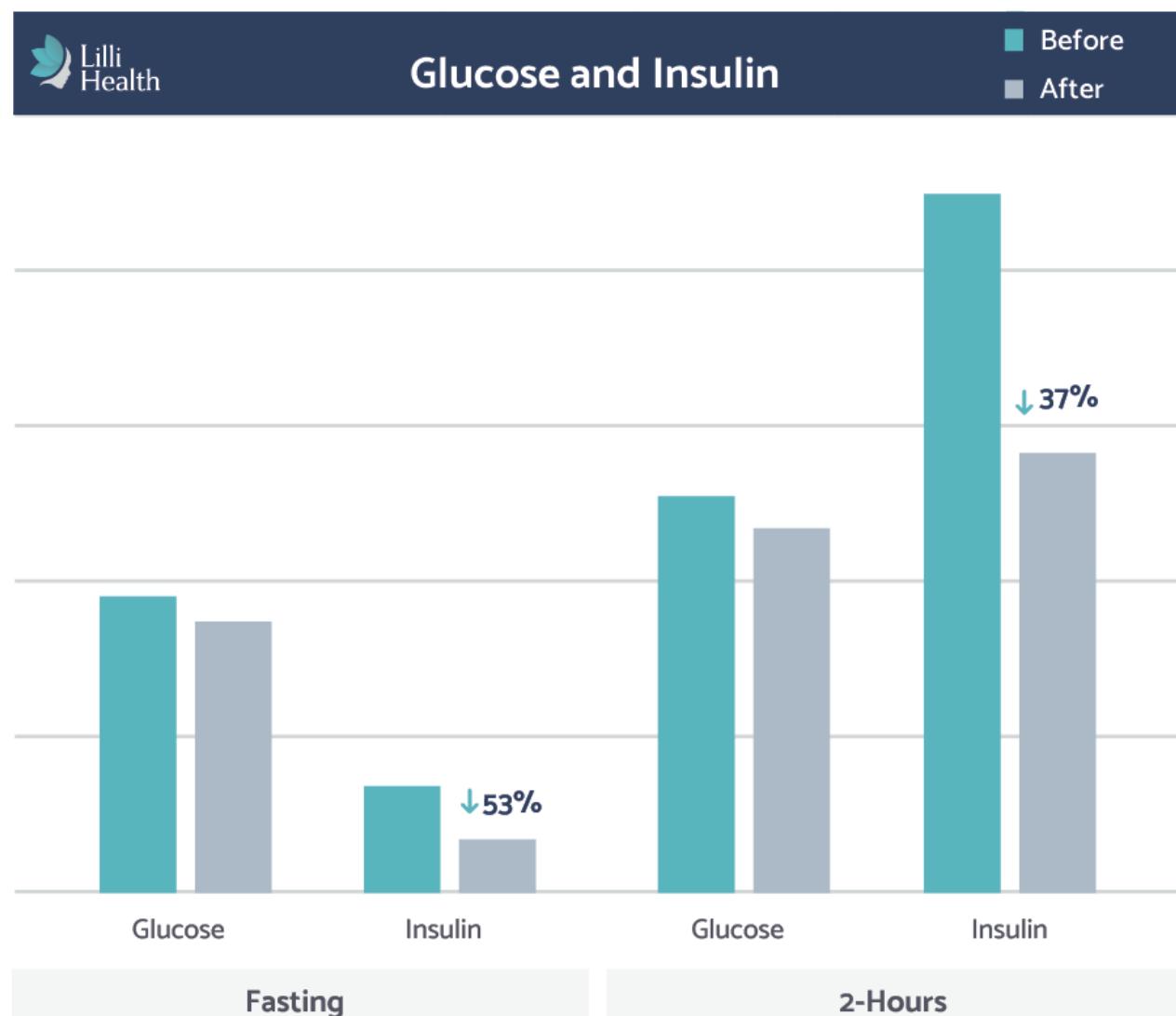
CHANGE IN GLUCOSE AND INSULIN BEFORE AND AFTER A LOW INSULIN LIFESTYLE

Lilli Health	Before	After	Change	% Change
Glucose (fasting) (mg/dl)	95.0	86.0	▼ 8.9	▼ 9.3
Glucose (2-hour) (mg/dl)	128.0	114.9	▼ 13.1	▼ 10.2
Insulin (fasting) (mIU/ml)	32.7	15.7	▼ 17.0	▼ 52.9
Insulin (2-hour) (mIU/ml)	225.8	142.9	▼ 82.8	▼ 36.7
HOMA-IR	3.9	1.9	▼ 1.9	▼ 48.7
HgbA1c (%)	5.5	5.2	▼ 0.3	▼ 5.5

© Lilli Health. All Rights Reserved.

Fasting glucose normal range: <100 mg/dl
 2-hour glucose normal range: <140 mg/dl
 Fasting insulin normal range: 3-8 mIU/ml

2-hour insulin normal range: 16-166 mIU/ml
 HOMA-IR normal range: 1
 HgbA1c normal range: <5.7%

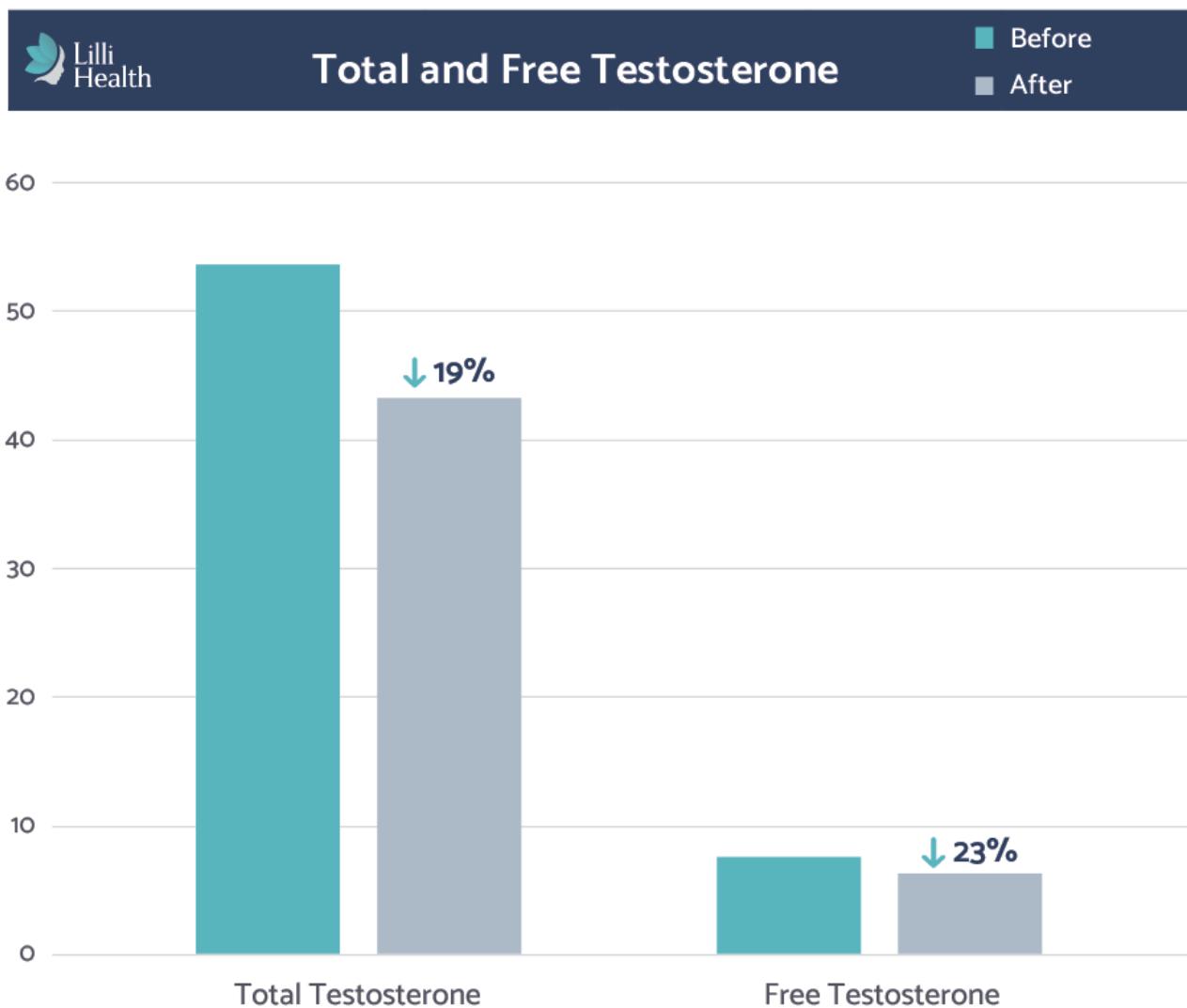


© Lilli Health. All Rights Reserved.

CHANGE IN TOTAL AND FREE TESTOSTERONE BEFORE AND AFTER A LOW INSULIN LIFESTYLE

© Lilli Health. All Rights Reserved

Lilli Health	Before	After	Change	% Change
Testosterone (total) (ng/dl)	53.3	43.3	▼ 10.0	▼ 18.7
Testosterone (free) (pg/dl)	7.8	6.0	▼ 1.8	▼ 23.1



© Lilli Health. All Rights Reserved.

Total testosterone normal range for PCOS: <20 ng/dl

Free testosterone normal range for PCOS: .06-2.57 pg/dl

CHANGE IN CHOLESTEROL AND LIPIDS FOLLOWING A LOW INSULIN LIFESTYLE

Lilli Health	Before	After	Change	% Change
Triglycerides (mg/dl)	162.8	108.2	▼ 57.0	▼ 35.0
Total Cholesterol (mg/dl)	195.9	186.7	▼ 9.3	-
LDL Cholesterol (mg/dl)	127.7	124.7	▼ 2.3	-
HDL Cholesterol (mg/dl)	47.6	41.9	▼ 5.7	-
Vitamin D (ng/mL)	20.3	24.7	▲ 4.4	-

Triglycerides normal range: <150 mg/dl

Total cholesterol normal range: <200 mg/dl

LDL cholesterol normal range: <100 mg/dl

HDL cholesterol normal range: >40 mg/dl

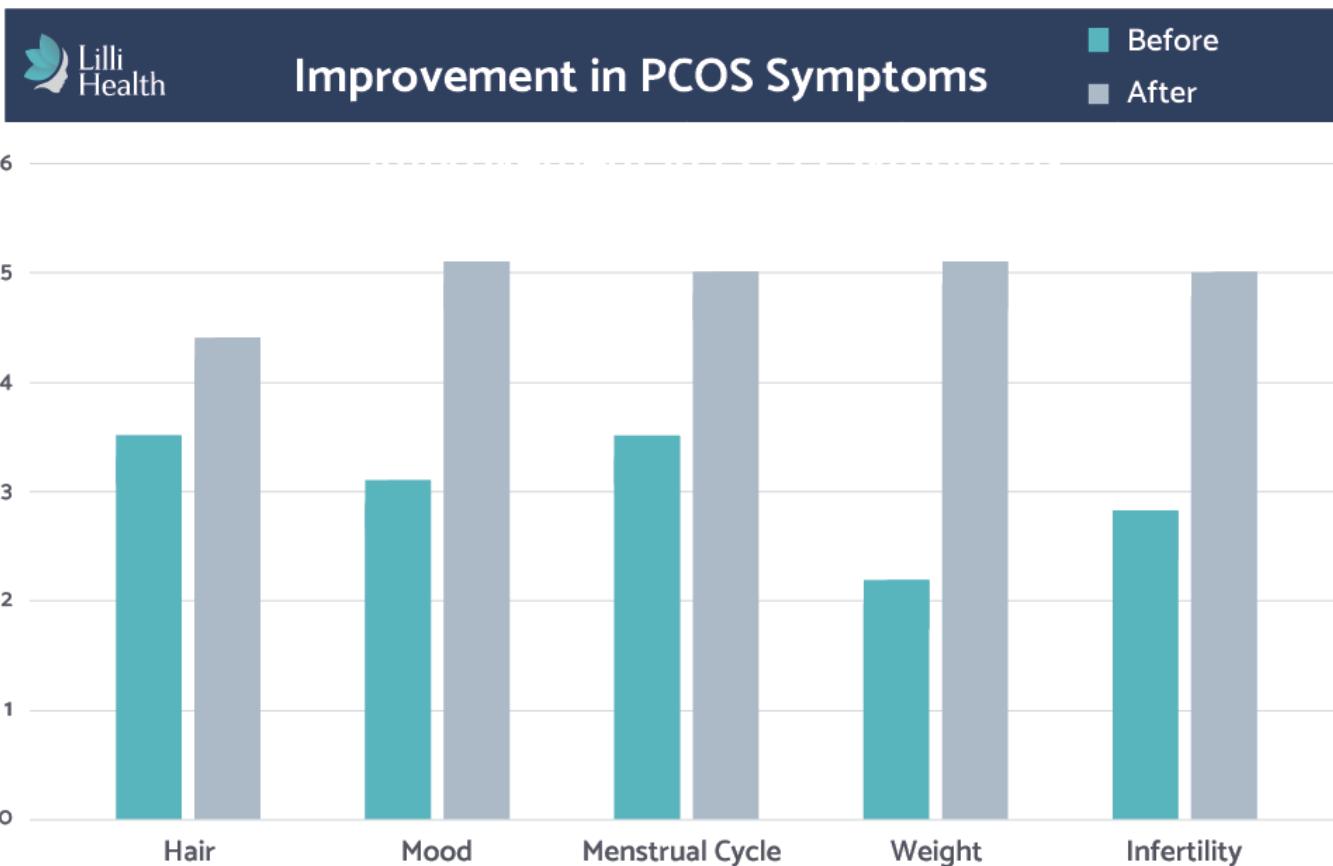
Vitamin D normal range: 20-40 ng/ml

IMPROVEMENTS IN PCOS SYMPTOMS BEFORE AND AFTER A LOW INSULIN LIFESTYLE

© Lilli Health. All Rights Reserved.

Lilli Health	Before	After	Change
Hair	3.5	4.4	▲ 0.9
Mood	3.1	5.1	▲ 2.0
Menstrual Cycle	3.5	5.0	▲ 1.5
Weight	2.2	5.1	▲ 2.9
Infertility	2.8	5.0	▲ 2.2

© Lilli Health. All Rights Reserved.



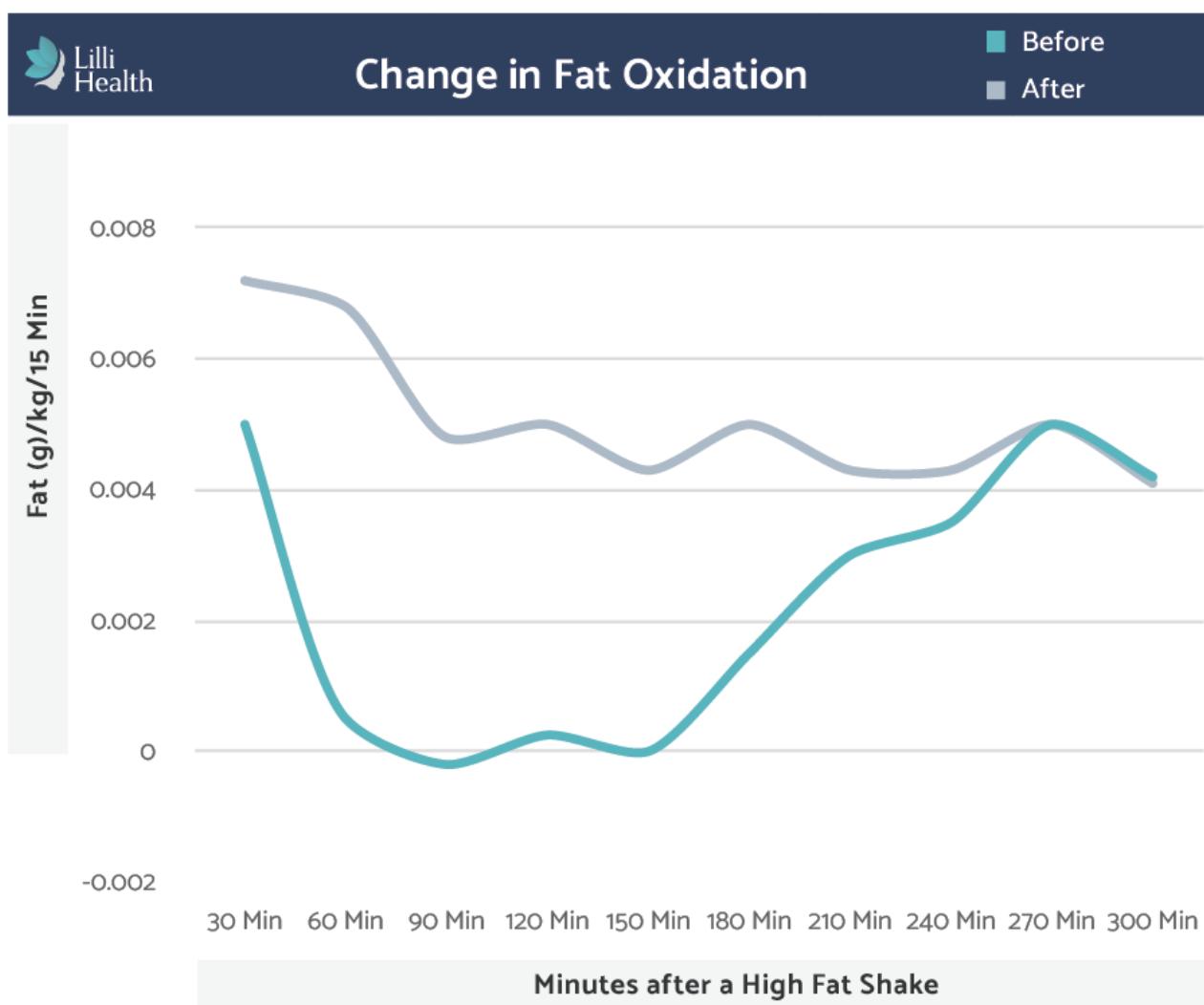
IMPROVEMENTS IN BINGE EATING BEHAVIORS AFTER A LOW INSULIN LIFESTYLE

Improvements in Binge Eating Behaviors After a Low Insulin Lifestyle

Lilli Health	Before	After	Change
Binge Eating Severity	18.0	7.0	▼ 11.0

© Lilli Health. All Rights Reserved.

CHANGE IN FAT OXIDATION



© Lilli Health. All Rights Reserved.

Replicating the Results

CHANGE IN FASTING INSULIN BETWEEN THE THREE GROUPS AFTER 8 WEEKS

Fasting Insulin (μ IU/ml)			
	Pre-Diet	Post-Diet	% Change
Control	21.9	23.2	▲ 5.9
Video Education	20.2	17.6	▼ 12.8
Face-to-Face	32.2	20.6	▼ 36.0

© Lilli Health. All Rights Reserved.

WEIGHT LOSS BETWEEN THE THREE GROUPS AFTER 8 WEEKS

Lilli Health	Weight Loss (lbs)	BMI (kg/m^2)	Waist Circumference (in)	Hip Circumference (in)
Control	▲ 0.4	▲ 0.3	▼ 0.4	▼ 0.5
Video Education	▼ 12.9	▼ 2.2	▼ 1.8	▼ 1.7
Face-to-Face	▼ 17.3	▼ 3.1	▼ 3.2	▼ 3.3

© Lilli Health. All Rights Reserved.

REFERENCES

1. Templeman NM, Skovsø S, Page MM, Lim GE, Johnson JD. A causal role for hyperinsulinemia in obesity. *J Endocrinol.* 2017;232(3):R173-R183. doi:10.1530/JOE-16-0449
2. Ludwig DS, Ebbeling CB. The carbohydrate-insulin model of obesity: Beyond “calories in, calories out.” *JAMA Intern Med.* 2018;178(8):1098-1103. doi:10.1001/jamainternmed.2018.2933
3. Zhang AMY, Wellberg EA, Kopp JL, Johnson JD. Hyperinsulinemia in obesity, inflammation, and cancer. *Diabetes Metab J.* 2021;45(3):285-311. doi:10.4093/DMJ.2020.0250
4. Dankner R, Chetrit A, Shanik MH, Raz I, Roth J. Basal-state hyperinsulinemia in healthy normoglycemic adults is predictive of type 2 diabetes over a 24-year follow-up: A preliminary report. *Diabetes Care.* 2009;32(8):1464-1466. doi:10.2337/dc09-0153
5. Rizza RA, Mandarino LJ, Genest J, Baker BA, Gerich JE. Production of insulin resistance by hyperinsulinaemia in man. *Diabetologia.* 1985;28(2):70-75. doi:10.1007/BF00279918
6. Kolb H, Stumvoll M, Kramer W, Kempf K, Martin S. Insulin translates unfavourable lifestyle into obesity. *BMC Med.* 2018;16(1):232. doi:10.1186/s12916-018-1225-1
7. Shanik MH, Xu Y, Skrha J, Dankner R, Zick Y, Roth J. Insulin resistance and hyperinsulinemia: Is hyperinsulinemia the cart or the horse? *Diabetes Care.* 2008;31(Suppl 2):S262-S268. doi:10.2337/dc08-s264
8. Erion KA, Corkey BE. Hyperinsulinemia: A cause of obesity? *Curr Obes Rep.* 2017;6(2):178-186. doi:10.1007/s13679-017-0261-z
9. Kolb H, Kempf K, Röhling M, Martin S. Insulin: too much of a good thing is bad. *BMC Med.* 2020;18(1):224. doi:10.1186/s12916-020-01688-6
10. Page MM, Johnson JD. Mild suppression of hyperinsulinemia to treat obesity and insulin resistance. *Trends Endocrinol Metab.* 2018;29(6):389-399. doi:10.1016/j.tem.2018.03.018
11. Vergari E, Knudsen JG, Ramracheya R, et al. Insulin inhibits glucagon release by SGLT2-induced stimulation of somatostatin secretion. *Nat Commun.* 2019;10(1):139. doi:10.1038/s41467-018-08193-8
12. Smith RL, Soeters MR, Wüst RCI, Houtkooper RH. Metabolic flexibility as an adaptation to energy resources and requirements in health and disease. *Endocr Rev.* 2018;39(4):489-517. doi:10.1210/er.2017-00211
13. Wang X, Hu Z, Hu J, Du J, Mitch WE. Insulin resistance accelerates muscle protein degradation: Activation of the Ubiquitin-Proteasome pathway by defects in muscle cell signaling. *Endocrinology.* 2006;147(9):4160-4168. doi:10.1210/en.2006-0251
14. Ludwig DS, Apovian CM, Aronne LJ, et al. Competing paradigms of obesity pathogenesis: Energy balance versus carbohydrate-insulin models. *Eur J Clin Nutr.* 2022;76(9):1209-1221. doi:10.1038/s41430-022-01179-2
15. Heller RF, Heller RF. Hyperinsulinemic obesity and carbohydrate addiction: The missing link is the carbohydrate frequency factor. *Med Hypotheses.* 1994;42(5):307-312. doi:10.1016/0306-9877(94)90004-3

16. McAuley KA, Williams SM, Mann JI, et al. Diagnosing insulin resistance in the general population. *Diabetes Care*. 2001;24(3):460-464. doi:10.2337/diacare.24.3.460
17. Bergman RN, Piccinini F, Kabir M, Ader M. Novel aspects of the role of the liver in carbohydrate metabolism. *Metabolism*. 2019;99:119-125. doi:10.1016/j.metabol.2019.05.011
18. Johnson JL, Duick DS, Chui MA, Aldasouqi SA. Identifying prediabetes using fasting insulin levels. *Endocr Pract*. 2010;16(1):47-52. doi:10.4158/EP09031.OR
19. Abdul-Ghani M, DeFronzo RA. Insulin resistance and hyperinsulinemia: The egg and the chicken. *J Clin Endocrinol Metab*. 2021;106(4):e1897-e1899. doi:10.1210/clinem/dgaa364
20. Janssen JAMJL. Hyperinsulinemia and its pivotal role in aging, obesity, type 2 diabetes, cardiovascular disease and cancer. *Int J Mol Sci*. 2021;22(15):7797. doi:10.3390/ijms22157797
21. Lieb W, de Oliveira CMI, Pan S, et al. Clinical correlates of plasma insulin levels over the life course and association with incident type 2 diabetes: The Framingham Heart Study. *BMJ Open Diabetes Res Care*. 2022;10(1). doi:10.1136/bmjdrc-2021-002581
22. Thomas DD, Corkey BE, Istfan NW, Apovian CM. Hyperinsulinemia: An early indicator of metabolic dysfunction. *J Endocr Soc*. 2019;3(9):1727-1747. doi:10.1210/js.2019 -00065
23. Araújo J, Cai J, Stevens J. Prevalence of optimal metabolic health in American adults: National health and nutrition examination survey 2009–2016. *Metab Syndr Relat Disord*. 2019;17(1):46-52. doi:10.1089/met.2018.0105
24. Sung KCC, Seo MHH, Rhee EJJ, Wilson AM. Elevated fasting insulin predicts the future incidence of metabolic syndrome: a 5-year follow-up study. *Cardiovasc Diabetol*. 2011;10(1):108. doi:10.1186/1475-2840-10-108
25. Pohlmeier AM, Phy JL, Watkins P, et al. Effect of a low-starch/low-dairy diet on fat oxidation in overweight and obese women with polycystic ovary syndrome. *Appl Physiol Nutr Metab*. 2014;39(11):1237-1244. doi:10.1139/apnm-2014-0073
26. Phy Jennifer L, Pohlmeier AM, Cooper JA, et al. Low starch/low dairy diet results in successful treatment of obesity and co-morbidities linked to polycystic ovary syndrome (PCOS). *J Obes Weight Loss Ther*. 2015;05(02). doi:10.4172/2165-7904.1000259
27. Wiklund P, Zhang X, Pekkala S, et al. Insulin resistance is associated with altered amino acid metabolism and adipose tissue dysfunction in normoglycemic women. *Sci Rep*. 2016;6(1):24540. doi:10.1038/srep24540
28. Millward DJ. Interactions between growth of muscle and stature: Mechanisms involved and their nutritional sensitivity to dietary protein: The protein-stat revisited. *Nutrients*. 2021;13(3):729. doi:10.3390/nu13030729
29. Hellström A, Ley D, Hansen-Pupp I, et al. Insulin-like growth factor 1 has multisystem effects on foetal and preterm infant development. *Acta Paediatr*. 2016;105(6):576-586. doi:10.1111/apa.13350
30. Manco M, Alterio A, Bugianesi E, et al. Insulin dynamics of breast- or formula-fed overweight and obese children. *J Am Coll Nutr*. 2011;30(1):29-38. doi:10.1080/07315724.2011.10719941

31. Socha P, Grote V, Grusfeld D, et al. Milk protein intake, the metabolic-endocrine response, and growth in infancy: data from a randomized clinical trial. *Am J Clin Nutr.* 2011;94(suppl_6):1776S-1784S. doi:10.3945/ajcn.110.000596
32. Castigliego L, Grifoni G, Rosati R, et al. On the alterations in serum concentration of somatotropin and insulin-like growth factor 1 in lactating cows after the treatment with a little studied recombinant bovine somatotropin. *Res Vet Sci.* 2009;87(1):29-35. doi:10.1016/j.rvsc.2008.10.012
33. Ludwig SKJ, Smits NGE, van der Veer G, Bremer MGEG, Nielsen MWF. Multiple protein biomarker assessment for recombinant bovine somatotropin (rbST) abuse in cattle. *PLoS One.* 2012;7(12):e52917. doi:10.1371/journal.pone.0052917
34. Ludwig SKJ, Tokarski C, Lang SN, et al. Calling biomarkers in milk using a protein microarray on your smartphone. *PLoS One.* 2015;10(8):e0134360. doi:10.1371/journal.pone.0134360
35. Willett WC, Ludwig DS. Milk and Health. *N Engl J Med.* 2020;382(7):644-654. doi:10.1056/NEJMra1903547
36. Simental-Mendía LE, Castañeda-Chacón A, Rodríguez-Morán M, Guerrero-Romero F. Birth-weight, insulin levels, and HOMA-IR in newborns at term. *BMC Pediatr.* 2012;12(1):94. doi:10.1186/1471-2431-12-94
37. Borgoño CA, Hamilton JK, Ye C, et al. Determinants of insulin resistance in infants at age 1 year. *Diabetes Care.* 2012;35(8):1795-1797. doi:10.2337/dc12-0173
38. Madsen AL, Schack-Nielsen L, Larnkaer A, Mølgaard C, Michaelsen KF. Determinants of blood glucose and insulin in healthy 9-month-old term Danish infants: The SKOT cohort. *Diabet Med.* 2010;27(12):1350-1357. doi:10.1111/j.1464-5491.2010.03134.x
39. Cheema AS, Stinson LF, Rea A, et al. Human milk lactose, insulin, and glucose relative to infant body composition during exclusive breastfeeding. *Nutrients.* 2021;13(11):3724. doi:10.3390/nu13113724
40. Hoppe C, Mølgaard C, Juul A, Michaelsen KF. High intakes of skimmed milk, but not meat, increase serum IGF-I and IGFBP-3 in eight-year-old boys. *Eur J Clin Nutr.* 2004;58(9):1211-1216. doi:10.1038/sj.ejcn.1601948
41. Kelsey MM, Zeitler PS. Insulin resistance of puberty. *Curr Diab Rep.* 2016;16(7):64. doi:10.1007/s11892-016-0751-5
42. Huang A, Roth CL. The link between obesity and puberty: what is new? *Curr Opin Pediatr.* 2021;33(4):449-457. doi:10.1097/MOP.0000000000001035
43. Aris IM, Perng W, Dabelea D, et al. Analysis of early-life growth and age at pubertal onset in US children. *JAMA Netw Open.* 2022;5(2):e2146873. doi:10.1001/jamanetworkopen.2021.46873
44. Boucher J, Kleinridders A, Ronald Kahn C. Insulin receptor signaling in normal and insulin-resistant states. *Cold Spring Harb Perspect Biol.* 2014;6(1):a009191. doi:10.1101/cshperspect.a009191
45. Jeffery AN, Metcalf BS, Hosking J, Streeter AJ, Voss LD, Wilkin TJ. Age before stage: Insulin resistance rises before the onset of puberty. *Diabetes Care.* 2012;35(3):536-541. doi:10.2337/dc11-1281

46. Zhou J, Zhang F, Zhang S, et al. Maternal pre-pregnancy body mass index, gestational weight gain, and pubertal timing in daughters: A systematic review and meta analysis of cohort studies. *Obes Rev.* 2022;23(5):e13418. doi:10.1111/obr.13418
47. Hur JH, Park S, Jung MK, et al. Insulin resistance and bone age advancement in girls with central precocious puberty. *Ann Pediatr Endocrinol Metab.* 2017;22(3):176-182. doi:10.6065/apem.2017.22.3.176
48. Bereket A. A critical appraisal of the effect of gonadotropin-releasing hormone analog treatment on adult height of girls with central precocious puberty. *J Clin Res Pediatr Endocrinol.* 2017;9(Suppl 2):33-48. doi:10.4274/jcrpe.2017.S004
49. Moran A, Jacobs DR, Steinberger J, et al. Association between the insulin resistance of puberty and the insulin-like growth factor-I/growth hormone axis. *J Clin Endocrinol Metab.* 2002;87(10):4817-4820. doi:10.1210/jc.2002-020517
50. Chiarelli F, Marcovecchio ML. Insulin resistance and obesity in childhood. *Eur J Endocrinol.* 2008;159(Suppl 1):S67-S74. doi:10.1530/EJE-08-0245
51. Li D, Zheng L, Zhao D, Xu Y, Wang Y. The role of immune cells in recurrent spontaneous abortion. *Reprod Sci.* 2021;28(12):3303-3315. doi:10.1007/s43032-021-00599-y
52. Sonagra AD, Biradar SM, Dattatreya K, Murthy DSJ. Normal pregnancy—A state of insulin resistance. *J Clin Diagn Res.* 2014;8(11):CC01-CC03. doi:10.7860/JCDR/2014/10068.5081
53. Parretti E, Lapolla A, Dalfrà M, et al. Preeclampsia in lean normotensive normotolerant pregnant women can be predicted by simple insulin sensitivity indexes. *Hypertension.* 2006;47(3):449-453. doi:10.1161/01.HYP.0000205122.47333.7f
54. Nagel EM, Kummer L, Jacobs DR, et al. Human milk glucose, leptin, and insulin predict cessation of full breastfeeding and initiation of formula use. *Breastfeed Med.* 2021;16(12):978-986. doi:10.1089/bfm.2021.0131
55. Yan H, Yang W, Zhou F, et al. Estrogen improves insulin sensitivity and suppresses gluconeogenesis via the transcription factor Foxo1. *Diabetes.* 2019;68(2):291-304. doi:10.2337/db18-0638
56. Lorenzo C, Hazuda HP, Haffner SM. Insulin resistance and excess risk of diabetes in Mexican-Americans: The San Antonio heart study. *J Clin Endocrinol Metab.* 2012;97(3):793-799. doi:10.1210/jc.2011-2272
57. Hernández-Jiménez JL, Barrera D, Espinoza-Simón E, et al. Polycystic ovarian syndrome: signs and feedback effects of hyperandrogenism and insulin resistance. *Gynecological Endocrinology.* 2022;38(1). doi:10.1080/09513590.2021.2003326
58. Huang-Doran I, Kinzer AB, Jimenez-Linan M, et al. Ovarian hyperandrogenism and response to gonadotropin-releasing hormone analogues in primary severe insulin resistance. *J Clin Endocrinol Metab.* 2021;106(8). doi:10.1210/clinem/dgab275
59. Tramunt B, Smati S, Grandgeorge N, et al. Sex differences in metabolic regulation and diabetes susceptibility. *Diabetologia.* 2020;63(3):453-461. doi:10.1007/s00125-019-05040-3

60. Baillargeon JP, Carpentier AC. Brothers of women with polycystic ovary syndrome are characterised by impaired glucose tolerance, reduced insulin sensitivity and related metabolic defects. *Diabetologia*. 2007;50(12):2424-2432. doi:10.1007/s00125-007-0831-9
61. Grossmann M, Thomas MC, Panagiotopoulos S, et al. Low testosterone levels are common and associated with insulin resistance in men with diabetes. *J Clin Endocrinol Metab*. 2008;93(5):1834-1840. doi:10.1210/jc.2007-2177
62. Ten S, Maclare N. Insulin Resistance Syndrome in Children. *J Clin Endocrinol Metab*. 2004;89(6):2526-2539. doi:10.1210/jc.2004-0276
63. Wolf W, Wattick R, Kinkade O, Olfert M. Geographical prevalence of polycystic ovary syndrome as determined by region and race/ethnicity. *Int J Environ Res Public Health*. 2018;15(11):2589. doi:10.3390/ijerph15112589
64. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. *J Clin Endocrinol Metab*. 2004;89(6):2745-2749. doi:10.1210/jc.2003-032046
65. Kodama K, Tojjar D, Yamada S, Toda K, Patel CJ, Butte AJ. Ethnic differences in the relationship between insulin sensitivity and insulin response: A systematic review and meta-analysis. *Diabetes Care*. 2013;36(6):1789-1796. doi:10.2337/dc12-1235
66. Gallagher EJ, Fei K, Feldman SM, et al. Insulin resistance contributes to racial disparities in breast cancer prognosis in US women. *Breast Cancer Research*. 2020;22(1). doi:10.1186/s13058-020-01281-y
67. Price JH, Khubchandani J, McKinney M, Braun R. Racial/ethnic disparities in chronic diseases of youths and access to health care in the United States. *Biomed Res Int*. 2013:787616 doi:10.1155/2013/787616
68. Osei K, Schuster DP. Ethnic differences in secretion, sensitivity, and hepatic extraction of insulin in Black and White Americans. *Diabetic Medicine*. 1994;11(8):755-762. doi:10.1111/j.1464-5491.1994.tb00349.x
69. Chan JL, Kar S, Vankay E, et al. Racial and ethnic differences in the prevalence of metabolic syndrome and its components of metabolic syndrome in women with polycystic ovary syndrome: a regional cross-sectional study. *Am J Obstet Gynecol*. 2017;217(2):189.e1-189.e8. doi:10.1016/j.ajog.2017.04.007
70. March WA, Moore VM, Willson KJ, Phillips DIW, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. *Hum Reprod*. 2010;25(2):544-551. doi:10.1093/humrep/dep399
71. Cho YM. Characteristics of the pathophysiology of type 2 diabetes in Asians. *Ann Laparosc Endosc Surg*. 2017;2:14. doi:10.21037/ales.2017.01.03
72. Yabe D, Seino Y. Type 2 diabetes via β -cell dysfunction in east Asian people. *Lancet Diabetes Endocrinol*. 2016;4(1):2-3. doi:10.1016/S2213-8587(15)00389-7
73. Narayan KMV, Kanaya AM. Why are South Asians prone to type 2 diabetes? A hypothesis based on underexplored pathways. *Diabetologia*. 2020;63(6):1103-1109. doi:10.1007/s00125-020-05132-5
74. Li R, Zhang Q, Yang D, et al. Prevalence of polycystic ovary syndrome in women in China: A large community-based study. *Human Reproduction*. 2013;28(9):2562-2569. doi:10.1093/humrep/det262
75. Mani H, Davies MJ, Bodicoat DH, et al. Clinical characteristics of polycystic ovary syndrome: Investigating differences in White and South Asian women. *Clin Endocrinol (Oxf)*. 2015;83(4):542-549. doi:10.1111/cen.12784

76. Rodin DA, Bano G, Bland JM, Taylor K, Nussey SS. Polycystic ovaries and associated metabolic abnormalities in Indian subcontinent Asian women. *Clin Endocrinol (Oxf)*. 1998;49(1):91-99. doi:10.1046/j.1365-2265.1998.00492.x
77. Huang Y, Mark Jacquez G. Identification of a blue zone in a typical chinese longevity region. *Int J Environ Res Public Health*. 2017;14(6):571. doi:10.3390/ijerph14060571
78. Acciai F, Noah AJ, Firebaugh G. Pinpointing the sources of the Asian mortality advantage in the USA. *J Epidemiol Community Health (1978)*. 2015;69(10):1006-1011. doi:10.1136/jech-2015-205623
79. Lucero J, Cedars M. Prevalence of polycystic ovarian syndrome in Jemez-Pueblo Women. *Fertil Steril*. 2005;83(5):S21. doi:10.1016/j.fertnstert.2005.01.049
80. Goins RT, Jones J, Schure M, Winchester B, Bradley V. Type 2 diabetes management among older American Indians: Beliefs, attitudes, and practices. *Ethn Health*. 2020;25(8):1055-1071. doi:10.1080/13557858.2018.1493092
81. Maredia H, Hawley NL, Lambert-Messerlian G, et al. Reproductive health, obesity, and cardiometabolic risk factors among Samoan women. *Am J Hum Biol*. 2018;30(3):e23106. doi:10.1002/ajhb.23106
82. DeBoer MD, Dong L, Gurka MJ. Racial/ethnic and sex differences in the ability of metabolic syndrome criteria to predict elevations in fasting insulin levels in adolescents. *J Pediatr*. 2011;159(6):975-981.e3. doi:10.1016/j.jpeds.2011.05.023
83. Azziz R, Carmina E, Chen Z, et al. Polycystic ovary syndrome. *Nat Rev Dis Primers*. 2016;2:16057. doi:10.1038/nrdp.2016.57
84. Deswal R, Narwal V, Dang A, Pundir C. The prevalence of polycystic ovary syndrome: A brief systematic review. *J Hum Reprod Sci*. 2020;13(4):261. doi:10.4103/jhrs.JHRS_95_18
85. Hoeger KM, Dokras A, Piltonen T. Update on PCOS: Consequences, challenges, and guiding treatment. *J Clin Endocrinol Metab*. 2021;106(3):e1071-e1083. doi:10.1210/clinem/dgaa839
86. Gezer E, Piro B, Cantürk Z, et al. The comparison of gender dysphoria, body image satisfaction and quality of life between treatment-Naive transgender males with and without polycystic ovary syndrome. *Transgend Health*. 2022;7(6):514-520. doi:10.1089/trgh.2021.0061
87. Macut D, Bjekić-Macut J, Rahelić D, Doknić M. Insulin and the polycystic ovary syndrome. *Diabetes Res Clin Pract*. 2017;130:163-170. doi:10.1016/J.DIABRES.2017.06.011
88. Marshall JC, Dunaif A. Should all women with PCOS be treated for insulin resistance? *Fertil Steril*. 2012;97(1):18-22. doi:10.1016/j.fertnstert.2011.11.036
89. Belani M, Deo A, Shah P, Banker M, Singal P, Gupta S. Differential insulin and steroidogenic signaling in insulin resistant and non-insulin resistant human luteinized granulosa cells—A study in PCOS patients. *J Steroid Biochem Mol Biol*. 2018;178:283-292. doi:10.1016/j.jsbmb.2018.01.008
90. Dumesic DA, Abbott DH, Sanchita S, Chazenbalk GD. Endocrine-metabolic dysfunction in polycystic ovary syndrome: An evolutionary perspective. *Curr Opin Endocr Metab Res*. 2020;12:41-48. doi:10.1016/j.coemr.2020.02.013
91. de Medeiros SF, Rodgers RJ, Norman RJ. Adipocyte and steroidogenic cell cross-talk in polycystic ovary syndrome. *Hum Reprod Update*. 2021;27(4):771-796. doi:10.1093/humupd/dmab004

92. Legro, RS, Finegood D, Dunai A. A fasting glucose to insulin ratio is a useful measure of insulin sensitivity in women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 1998;83(8):2694-2698. doi.org/10.1210/jc.83.8.2694
93. Stadtmauer LA, Wong BC, Oehninger S. Should patients with polycystic ovary syndrome be treated with metformin? Benefits of insulin sensitizing drugs in polycystic ovary syndrome - beyond ovulation induction. *Hum Reprod.* 2002;17(12):3016-3026. doi:10.1093/humrep/17.12.3016
94. Kravitz E, Dillawn P, Farr MA, Schutt AK. Utility of the insulin curve in addition to OGTT in detecting hyperinsulinemia in patients with PCOS. *Fertil Steril.* 2021;116(3). doi:10.1016/j.fertnstert.2021.07.346
95. Zhu S, Zhang B, Jiang X, et al. Metabolic disturbances in non-obese women with polycystic ovary syndrome: A systematic review and meta-analysis. *Fertil Steril.* 2019;111(1):168-177. doi:10.1016/j.fertnstert.2018.09.013
96. Tsilchorozidou T, Honour JW, Conway GS. Altered cortisol metabolism in polycystic ovary syndrome: Insulin enhances 5alpha-reduction but not the elevated adrenal steroid production rates. *J Clin Endocrinol Metab.* 2003;88(12):5907-5913. doi:10.1210/jc.2003-030240
97. Grulet H, Hecart AC, Delemer B, et al. Roles of LH and insulin resistance in lean and obese polycystic ovary syndrome. *Clin Endocrinol (Oxf).* 1993;38(6):621-626. doi:10.1111/j.1365-2265.1993.tb02144.x
98. Morciano A, Romani F, Sagnella F, et al. Assessment of insulin resistance in lean women with polycystic ovary syndrome. *Fertil Steril.* 2014;102(1):250-256.e3. doi:10.1016/j.fertnstert.2014.04.004
99. Goodarzi MO, Dumesic DA, Chazenbalk G, Azziz R. Polycystic ovary syndrome: Etiology, pathogenesis and diagnosis. *Nat Rev Endocrinol.* 2011;7(4):219-231. doi:10.1038/nrendo.2010.217
100. Mimouni NEH, Paiva I, Barbotin AL, et al. Polycystic ovary syndrome is transmitted via a transgenerational epigenetic process. *Cell Metab.* 2021;33(3):513-530.e8. doi:10.1016/j.cmet.2021.01.004
101. Zhu Z, Cao F, Li X. Epigenetic programming and fetal metabolic programming. *Front Endocrinol (Lausanne).* 2019;10:764. doi:10.3389/fendo.2019.00764
102. Şanlı E, Kabaran S. Maternal obesity, maternal overnutrition and fetal programming: Effects of epigenetic mechanisms on the development of metabolic disorders. *Curr Genomics.* 2019;20(6):419-427. doi:10.2174/1389202920666191030092225
103. Bell GA, Sundaram R, Mumford SL, et al. Maternal polycystic ovarian syndrome and early offspring development. *Hum Reprod.* 2018;33(7):1307-1315. doi:10.1093/humrep/dey087
104. Pohlmeier A. Effect of a low insulinemic diet on clinical, biochemical, and metabolic outcomes in women with PCOS. Doctoral Dissertation. Texas Tech University; 2013. <https://ttu-ir.tdl.org/handle/2346/58432>
105. Zhang D, Yang X, Li J, Yu J, Wu X. Effect of hyperinsulinaemia and insulin resistance on endocrine, metabolic and fertility outcomes in women with polycystic ovary syndrome undergoing ovulation induction. *Clin Endocrinol (Oxf).* 2019;91(3):440-448. doi:10.1111/cen.14050
106. Nardo LG, Yates AP, Roberts SA, Pemberton P, Laing I. The relationships between AMH, androgens, insulin resistance and basal ovarian follicular status in non-obese subfertile women with and without polycystic ovary syndrome. *Hum Reprod.* 2009;24(11):2917-2923. doi:10.1093/humrep/dep225

107. Qin K nan, Rosenfield RL. Role of cytochrome P450c17 in polycystic ovary syndrome. *Mol Cell Endocrinol.* 1998;145(1-2):111-121. doi:10.1016/S0303-7207(98)00177-4
108. Biernacka-Bartnik A, Kocełak P, Owczarek AJ, et al. Prediction of insulin resistance and impaired fasting glucose based on sex hormone-binding globulin (SHBG) levels in polycystic ovary syndrome. *Int J Endocrinol.* 2022;2022:6498768. doi:10.1155/2022/6498768
109. Carlson LJ, Shaw ND. Development of ovulatory menstrual cycles in adolescent girls. *J Pediatr Adolesc Gynecol.* 2019;32(3):249-253. doi:10.1016/j.jpag.2019.02.119
110. Sun W, Lu J, Wu S, et al. Association of insulin resistance with breast, ovarian, endometrial and cervical cancers in non-diabetic women. *Am J Cancer Res.* 2016;6(10):2334-2344.
111. Gunter MJ, Hoover DR, Yu H, et al. A prospective evaluation of insulin and insulin-like growth factor-I as risk factors for endometrial cancer. *Cancer Epidemiol Biomarkers Prev.* 2008;17(4):921-929. doi:10.1158/1055-9965.EPI-07-2686
112. Kaaks R, Lukanova A, Kurzer MS. Obesity, endogenous hormones, and endometrial cancer risk: A synthetic review. *Cancer Epidemiol Biomarkers Prev.* 2002;11(12):1531-1543.
113. Horvath S, Schreiber CA, Sonalkar S. *Contraception.*; 2000 . Adeyemi-Fowode OA, Bercaw-Pratt JL. Intrauterine devices: Effective contraception with noncontraceptive benefits for adolescents. *J Pediatr Adolesc Gynecol.* 2019;32(5):S2-S6. doi:10.1016/j.jpag.2019.07.001
115. Gainer S, Sharma B. Update on management of polycystic ovarian syndrome for dermatologists. *Indian Dermatol Online J.* 2019;10(2):97-105. doi:10.4103/idoj.IDOJ_249_17
116. Melnik BC. Evidence for acne-promoting effects of milk and other insulinotropic dairy products. *Nestle Nutr Workshop Ser Pediatr Program.* 2011;67:131-145. doi:10.1159/000325580
117. Silverberg NB. Whey protein precipitating moderate to severe acne flares in 5 teenaged athletes. *Cutis.* 2012;90(2):70-72.
118. Simonart T. Acne and whey protein supplementation among bodybuilders. *Dermatology.* 2012;225(3):256-258. doi:10.1159/000345102
119. Spritzer PM, Marchesan LB, Santos BR, Fighera TM. Hirsutism, normal androgens and diagnosis of PCOS. *Diagnostics.* 2022;12(8):1922. doi:10.3390/diagnostics12081922
120. Starace M, Orlando G, Alessandrini A, Piraccini BM. Female androgenetic alopecia: An update on diagnosis and management. *Am J Clin Dermatol.* 2020;21(1):69-84. doi:10.1007/s40257-019-00479-x
121. Shang Y, Zhou H, He R, Lu W. Dietary modification for reproductive health in women with polycystic ovary syndrome: A systematic review and meta-analysis. *Front Endocrinol (Lausanne).* 2021;12:735954. doi:10.3389/fendo.2021.735954
122. Schulte MM, Tsai JH, Moley KH. Obesity and PCOS: The effect of metabolic derangements on endometrial receptivity at the time of implantation. *Reprod Sci.* 2015;22(1):6-14. doi:10.1177/1933719114561552
123. Bellver J, Ayllón Y, Ferrando M, et al. Female obesity impairs in vitro fertilization outcome without affecting embryo quality. *Fertil Steril.* 2010;93(2):447-454. doi:10.1016/j.fertnstert.2008.12.032

124. Niu Z, Lin N, Gu R, Sun Y, Feng Y. Associations between insulin resistance, free fatty acids, and oocyte quality in polycystic ovary syndrome during in vitro fertilization. *J Clin Endocrinol Metab*. 2014;99(11):E2269-E2276. doi:10.1210/jc.2013-3942
125. Vega M, Mauro M, Williams Z. Direct toxicity of insulin on the human placenta and protection by metformin. *Fertil Steril*. 2019;111(3):489-496.e5. doi:10.1016/j.fertnstert.2018.11.032
126. Tian L, Shen H, Lu Q, Norman RJ, Wang J. Insulin resistance increases the risk of spontaneous abortion after assisted reproduction technology treatment. *J Clin Endocrinol Metab*. 2007;92(4):1430-1433. doi:10.1210/jc.2006-1123
127. Sun YF, Zhang J, Xu YM, et al. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: A systematic review and meta-analysis. *Front Endocrinol (Lausanne)*. 2020;11:592495. doi:10.3389/fendo.2020.592495
128. Brutocao C, Zaiem F, Alsawas M, Morrow AS, Murad MH, Javed A. Psychiatric disorders in women with polycystic ovary syndrome: A systematic review and meta-analysis. *Endocrine*. 2018;62(2):318-325. doi:10.1007/s12020-018-1692-3
129. Zou XH, Sun LH, Yang W, Li BJ, Cui RJ. Potential role of insulin on the pathogenesis of depression. *Cell Prolif*. 2020;53(5):e12806. doi:10.1111/cpr.12806
130. Watson KT, Simard JF, Henderson VW, et al. Association of insulin resistance with depression severity and remission status. *JAMA Psychiatry*. 2021;78(4):439-441. doi:10.1001/jamapsychiatry.2020.3669
131. Kleinridders A, Cai W, Cappellucci L, et al. Insulin resistance in brain alters dopamine turnover and causes behavioral disorders. *Proc Natl Acad Sci U S A*. 2015;112(11):3463-3468. doi:10.1073/pnas.1500877112
132. Parcha V, Heindl B, Kalra R, et al. Insulin resistance and cardiometabolic risk profile among nondiabetic American young adults: Insights from NHANES. *J Clin Endocrinol Metab*. 2022;107(1):e25-e37. doi:10.1210/clinem/dgab645
133. Wang G, Divall S, Radovick S, et al. Preterm birth and random plasma insulin levels at birth and in early childhood. *JAMA*. 2014;311(6):587-596. doi:10.1001/jama.2014.1
134. Wei Y, Yang CR, Wei YP, et al. Paternally induced transgenerational inheritance of susceptibility to diabetes in mammals. *Proc Natl Acad Sci U S A*. 2014;111(5):1873-1878. doi:10.1073/pnas.1321195111
135. Masuyama H, Mitsui T, Eguchi T, Tamada S, Hiramatsu Y. The effects of paternal high-fat diet exposure on offspring metabolism with epigenetic changes in the mouse adiponectin and leptin gene promoters. *Am J Physiol Endocrinol Metab*. 2016;311(1):E236-E245. doi:10.1152/ajpendo.00095.2016
136. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nat Rev Endocrinol*. 2018;14(2):88-98. doi:10.1038/nrendo.2017.151
137. Ebrahimi M, Sivaprasad S, Thompson PM, Perry G. Retinal neurodegeneration in euglycemic hyperinsulinemia, prediabetes, and diabetes. *Ophthalmic Res*. Published online December 2, 2022. doi:10.1159/000528503
138. Liu Y, Peng Y, Jin J, et al. Insulin resistance is independently associated with cardiovascular autonomic neuropathy in type 2 diabetes. *J Diabetes Investig*. 2021;12(9):1651-1662. doi:10.1111/jdi.13507

139. Sola D, Rossi L, Schianca GP, et al. Sulfonylureas and their use in clinical practice. *Arch Med Sci.* 2015;11(4):840-848. doi:10.5114/aoms.2015.53304
140. Sweeting A, Wong J, Murphy HR, Ross GP. A clinical update on gestational diabetes mellitus. *Endocr Rev.* 2022;43(5):763-793. doi:10.1210/endrev/bnac003
141. Chu AHY, Godfrey KM. Gestational diabetes mellitus and developmental programming. *Ann Nutr Metab.* 2020;76(Suppl. 3):4-15. doi:10.1159/000509902
142. Blasetti A, Franchini S, Comegna L, Prezioso G, Chiarelli F. Role of nutrition in preventing insulin resistance in children. *J Pediatr Endocrinol Metab.* 2016;29(3):247-257. doi:10.1515/jpem-2015-0189
143. North S, Zinn C, Crofts C. Hyperinsulinemia during pregnancy across varying degrees of glucose tolerance: An examination of the Kraft database. *J Obstet Gynaecol Res.* 2021;47(5):1719-1726. doi:10.1111/jog.14731
144. Perea V, Simó-Servat A, Quirós C, et al. Role of excessive weight gain during gestation in the risk of ADHD in offspring of women with gestational diabetes. *J Clin Endocrinol Metab.* 2022;107(10):e4203-e4211. doi:10.1210/clinem/dgac483
145. Kayemba-Kay's S, Peters C, Geary MPP, Hill NR, Mathews DR, Hindmarsh PC. Maternal hyperinsulinism and glycaemic status in the first trimester of pregnancy are associated with the development of pregnancy-induced hypertension and gestational diabetes. *Eur J Endocrinol.* 2013;168(3):413-418. doi:10.1530/EJE-12-0609
146. Westgate JA, Lindsay RS, Beattie J, et al. Hyperinsulinemia in cord blood in mothers with type 2 diabetes and gestational diabetes mellitus in New Zealand. *Diabetes Care.* 2006;29(6):1345-1350. doi:10.2337/dc05-1677
147. Ladyman SR, Brooks VL. Central actions of insulin during pregnancy and lactation. *J Neuroendocrinol.* 2021;33(4):e12946. doi:10.1111/jne.12946
148. Nommsen-Rivers LA. Does insulin explain the relation between maternal obesity and poor lactation outcomes? An overview of the literature. *Advances in Nutrition.* 2016;7(2):407-414. doi:10.3945/an.115.011007
149. Tsao CW, Aday AW, Almarzooq ZI, et al. Heart disease and stroke statistics-2022 update: A report from the American Heart Association. *Circulation.* 2022;145(8):e153-e639. doi:10.1161/CIR.0000000000001052
150. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. *Cardiovasc Diabetol.* 2018;17(1):122. doi:10.1186/s12933-018-0762-4
151. Iwani NA, Jalaludin MY, Zin RM, et al. Triglyceride to HDL-C ratio is associated with insulin resistance in overweight and obese children. *Sci Rep.* 2017;7:40055. doi:10.1038/srep40055
152. Malhotra A, Redberg RF, Meier P. Saturated fat does not clog the arteries: coronary heart disease is a chronic inflammatory condition, the risk of which can be effectively reduced from healthy lifestyle interventions. *Br J Sports Med.* 2017;51(15):1111-1112. doi:10.1136/bjsports-2016-097285
153. Rocha VZ, Libby P. Obesity, inflammation, and atherosclerosis. *Nat Rev Cardiol.* 2009;6(6):399-409. doi:10.1038/nrcardio.2009.55

154. Pihlajamäki J, Gylling H, Miettinen TA, Laakso M. Insulin resistance is associated with increased cholesterol synthesis and decreased cholesterol absorption in normoglycemic men. *J Lipid Res.* 2004;45(3):507-512. doi:10.1194/jlr.M300368-JLR200
155. Hoenig MR, Sellke FW. Insulin resistance is associated with increased cholesterol synthesis, decreased cholesterol absorption and enhanced lipid response to statin therapy. *Atherosclerosis.* 2010;211(1):260-265. doi:10.1016/j.atherosclerosis.2010.02.029
156. Dong T, Guo M, Zhang P, Sun G, Chen B. The effects of low-carbohydrate diets on cardiovascular risk factors: A meta-analysis. *PLoS One.* 2020;15(1):e0225348. doi:10.1371/journal.pone.0225348
157. O'Connor LE, Kim JE, Clark CM, Zhu W, Campbell WW. Effects of total red meat intake on glycemic control and inflammatory biomarkers: A meta-analysis of randomized controlled trials. *Advances in Nutrition.* 2021;12(1):115-127. doi:10.1093/advances/nmaa096
158. Superko H, Garrett B. Small dense LDL: scientific background, clinical relevance, and recent evidence still a risk even with 'normal' LDL-C levels. *Biomedicines.* 2022;10(4):829. doi:10.3390/biomedicines10040829
159. Fan J, Liu Y, Yin S, et al. Small dense LDL cholesterol is associated with metabolic syndrome traits independently of obesity and inflammation. *Nutr Metab (Lond).* 2019;16(1):7. doi:10.1186/s12986-019-0334-y
160. Lewis GF. Determinants of plasma HDL concentrations and reverse cholesterol transport. *Curr Opin Cardiol.* 2006;21(4):345-352. doi:10.1097/01.hco.0000231405.76930.a0
161. da Silva AA, do Carmo JM, Li X, Wang Z, Mouton AJ, Hall JE. Role of hyperinsulinemia and insulin resistance in hypertension: Metabolic syndrome revisited. *Can J Cardiol.* 2020;36(5):671-682. doi:10.1016/j.cjca.2020.02.066
162. Paoli A, Mancin L, Giacoma MC, Bianco A, Caprio M. Effects of a ketogenic diet in overweight women with polycystic ovary syndrome. *J Transl Med.* 2020;18(1):104. doi:10.1186/s12967-020-02277-0
163. Vigneri R, Sciacca L, Vigneri P. Rethinking the relationship between insulin and cancer. *Trends Endocrinol Metab.* 2020;31(8):551-560. doi:10.1016/j.tem.2020.05.004
164. Perseghin G, Calori G, Lattuada G, et al. Insulin resistance/hyperinsulinemia and cancer mortality: The Cremona study at the 15th year of follow-up. *Acta Diabetol.* 2012;49(6):421-428. doi:10.1007/s00592-011-0361-2
165. Venkateswaran V, Haddad AQ, Fleshner NE, et al. Association of diet-induced hyperinsulinemia with accelerated growth of prostate cancer (LNCaP) xenografts. *J Natl Cancer Inst.* 2007;99(23):1793-1800. doi:10.1093/jnci/djm231
166. di Sebastiano KM, Pinthus JH, Duivenvoorden WCM, Mourtzakis M. Glucose impairments and insulin resistance in prostate cancer: The role of obesity, nutrition and exercise. *Obesity Reviews.* 2018;19(7):1008-1016. doi:10.1111/obr.12674
167. Ellington TD, Miller JW, Henley SJ, Wilson RJ, Wu M, Richardson LC. Trends in breast cancer incidence, by race, ethnicity, and age among women aged ≥ 20 years - United States, 1999-2018. *MMWR Morb Mortal Wkly Rep.* 2022;71(2):43-47. doi:10.15585/mmwr.mm7102a2
168. Dumesic DA, Lobo RA. Cancer risk and PCOS. *Steroids.* 2013;78(8):782-785. doi:10.1016/j.steroids.2013.04.004

169. Wang L, Lu B, He M, Wang Y, Wang Z, Du L. Prostate cancer incidence and mortality: Global status and temporal trends in 89 countries from 2000 to 2019. *Front Public Health*. 2022;10:811044. doi:10.3389/fpubh.2022.811044
170. Haskins C, Cohen J, Kotecha R, Kaiser A. Low carbohydrate diets in cancer therapeutics: Current evidence. *Front Nutr*. 2021;8:662952. doi:10.3389/fnut.2021.662952
171. Bojsen-Møller KN, Lundsgaard AM, Madsbad S, Kiens B, Holst JJ. Hepatic insulin clearance in regulation of systemic insulin concentrations—role of carbohydrate and energy availability. *Diabetes*. 2018;67(11):2129-2136. doi:10.2337/db18-0539
172. Najjar SM, Perdomo G. Hepatic insulin clearance: Mechanism and physiology. *Physiology*. 2019;34(3):198-215. doi:10.1152/physiol.00048.2018
173. Templeman NM, Flibotte S, Chik JHL, et al. Reduced circulating insulin enhances insulin sensitivity in old mice and extends lifespan. *Cell Rep*. 2017;20(2):451-463. doi:10.1016/j.celrep.2017.06.048
174. Fowler CG, Chiasson KB, Colman RJ, Kemnitz JW, Beasley TM, Weindruch RH. Hyperinsulinemia/diabetes, hearing, and aging in the University of Wisconsin calorie restriction monkeys. *Hear Res*. 2015;328:78-86. doi:10.1016/j.heares.2015.07.001
175. Danby FW. Nutrition and aging skin: Sugar and glycation. *Clin Dermatol*. 2010;28(4):409-411. doi:10.1016/j.clindermatol.2010.03.018
176. de la Monte SM. Insulin resistance and neurodegeneration: Progress towards the development of new therapeutics for Alzheimer's disease. *Drugs*. 2017;77(1):47-65. doi:10.1007/s40265-016-0674-0
177. Facchini FS, Hua NW, Reaven GM, Stoohs RA. Hyperinsulinemia: The missing link among oxidative stress and age-related diseases? *Free Radic Biol Med*. 2000;29(12):1302-1306. doi:10.1016/S0891-5849(00)00438-X
178. Basisty N, Meyer JG, Schilling B. Protein turnover in aging and longevity. *Proteomics*. 2018;18(5-6):1700108. doi:10.1002/pmic.201700108
179. Miyagi S, Iwama N, Kawabata T, Hasegawa K. Longevity and diet in Okinawa, Japan: The past, present and future. *Asia Pac J Public Health*. 2003;15:S3-S9. doi:10.1177/101053950301500S03
180. Anisimov VN. Metformin: Do we finally have an anti-aging drug? *Cell Cycle*. 2013;12(22):3483-3489. doi:10.4161/cc.26928
181. Anisimov VN, Bartke A. The key role of growth hormone–insulin–IGF-1 signaling in aging and cancer. *Crit Rev Oncol Hematol*. 2013;87(3):201-223. doi:10.1016/j.critrevonc.2013.01.005
182. Stefanadi EC, Dimitrakakis G, Antoniou CK, et al. Metabolic syndrome and the skin: A more than superficial association. Reviewing the association between skin diseases and metabolic syndrome and a clinical decision algorithm for high risk patients. *Diabetol Metab Syndr*. 2018;10(1):9. doi:10.1186/s13098-018-0311-z
183. Rinnerthaler M, Bischof J, Streubel M, Trost A, Richter K. Oxidative stress in aging human skin. *Biomolecules*. 2015;5(2):545-589. doi:10.3390/biom5020545
184. Mohammed I, Hollenberg MD, Ding H, Triggle CR. A critical review of the evidence that metformin is a putative anti-aging drug that enhances healthspan and extends lifespan. *Front Endocrinol (Lausanne)*. 2021;12:718942. doi:10.3389/fendo.2021.718942

185. Soukas AA, Hao H, Wu L. Metformin as anti-aging therapy: Is it for everyone? *Trends Endocrinol Metab*. 2019;30(10):745-755. doi:10.1016/j.tem.2019.07.015
186. Hölscher C. Insulin signaling impairment in the brain as a risk factor in Alzheimer's disease. *Front Aging Neurosci*. 2019;11:88. doi:10.3389/fnagi.2019.00088
187. Ekblad LL, Rinne JO, Puukka P, et al. Insulin resistance predicts cognitive decline: An 11-year follow-up of a nationally representative adult population sample. *Diabetes Care*. 2017;40(6):751-758. doi:10.2337/dc16-2001
188. Athauda D, Foltynie T. Insulin resistance and Parkinson's disease: A new target for disease modification? *Prog Neurobiol*. 2016;145-146:98-120. doi:10.1016/j.pneurobio.2016.10.001
189. Ruiz-Argüelles A, Méndez-Huerta MA, Lozano CD, Ruiz-Argüelles GJ. Metabolomic profile of insulin resistance in patients with multiple sclerosis is associated to the severity of the disease. *Mult Scler Relat Disord*. 2018;25:316-321. doi:10.1016/j.msard.2018.08.014
190. Manco M, Guerrera S, Ravà L, et al. Cross-sectional investigation of insulin resistance in youths with autism spectrum disorder. Any role for reduced brain glucose metabolism? *Transl Psychiatry*. 2021;11(1). doi:10.1038/s41398-021-01345-3
191. García-Rodríguez D, Giménez-Cassina A. Ketone bodies in the brain beyond fuel metabolism: From excitability to gene expression and cell signaling. *Front Mol Neurosci*. 2021;14:732120. doi:10.3389/fnmol.2021.732120
192. Kim B, Feldman EL. Insulin resistance in the nervous system. *Trends in Endocrinol & Metab*. 2012;23(3):133-141. doi:10.1016/j.tem.2011.12.004
193. Schubert M, Gautam D, Surjo D, et al. Role for neuronal insulin resistance in neurodegenerative diseases. *Proc Natl Acad Sci U S A*. 2004;101(9):3100-3105. doi:10.1073/pnas.0308724101
194. Kullmann S, Kleinridders A, Small DM, et al. Central nervous pathways of insulin action in the control of metabolism and food intake. *Lancet Diabetes Endocrinol*. 2020;8(6):524-534. doi:10.1016/S2213-8587(20)30113-3
195. Krakowiak P, Walker CK, Bremer AA, et al. Maternal metabolic conditions and risk for autism and other neurodevelopmental disorders. *Pediatrics*. 2012;129(5):e1121-e1128. doi:10.1542/peds.2011-2583
196. Dierssen M, Barone E. Editorial: Brain insulin resistance in neurodevelopmental and neurodegenerative disorders: Mind the gap!. *Front Neurosci*. 2021;15:730378. doi:10.3389/fnins.2021.730378
197. Aviel-Shekler K, Hamshawi Y, Sirhan W, et al. Gestational diabetes induces behavioral and brain gene transcription dysregulation in adult offspring. *Transl Psychiatry*. 2020;10(1):412. doi:10.1038/s41398-020-01096-7
198. Watson GS, Craft S. Insulin resistance, inflammation, and cognition in Alzheimer's Disease: Lessons for multiple sclerosis. *J Neurol Sci*. 2006;245(1-2):21-33. doi:10.1016/j.jns.2005.08.017
199. di Majo D, Cacciabaudo F, Accardi G, et al. Ketogenic and modified mediterranean diet as a tool to counteract neuroinflammation in multiple sclerosis: Nutritional suggestions. *Nutrients*. 2022;14(12):2384. doi:10.3390/nu14122384
200. Tay CT, Teede HJ, Hill B, Loxton D, Joham AE. Increased prevalence of eating disorders, low self-esteem, and psychological distress in women with polycystic ovary syndrome: A community-based cohort study. *Fertil Steril*. 2019;112(2):353-361. doi:10.1016/j.fertnstert.2019.03.027

201. Krug I, Giles S, Paganini C. Binge eating in patients with polycystic ovary syndrome: Prevalence, causes, and management strategies. *Neuropsychiatr Dis Treat*. 2019;15:1273-1285. doi:10.2147/NDT.S168944
202. Naessén S, Carlström K, Garoff L, Glant R, Hirschberg AL. Polycystic ovary syndrome in bulimic women – an evaluation based on the new diagnostic criteria. *Gynecol Endocrinol*. 2006;22(7):388-394. doi:10.1080/09513590600847421
203. Ralph AF, Brennan L, Byrne S, et al. Management of eating disorders for people with higher weight: Clinical practice guideline. *J Eat Disord*. 2022;10(1):121. doi:10.1186/s40337-022-00622-w
204. Andriankaja OM, Muñoz-Torres FJ, Vivaldi-Oliver J, et al. Insulin resistance predicts the risk of gingival/periodontal inflammation. *J Periodontol*. 2018;89(5):549-557. doi:10.1002/JPER.17-0384
205. Song IS, Han K, Park YM, et al. Severe periodontitis is associated with insulin resistance in non-abdominal obese adults. *J Clin Endocrinol Metab*. 2016;101(11):4251-4259. doi:10.1210/jc.2016-2061
206. Lyra e Silva N de M, Lam MP, Soares CN, Munoz DP, Milev R, de Felice FG. Insulin resistance as a shared pathogenic mechanism between depression and type 2 diabetes. *Front Psychiatry*. 2019;10:57. doi:10.3389/fpsyg.2019.00057
207. Watson KT, Simard JF, Henderson VW, et al. Incident major depressive disorder predicted by three measures of insulin resistance: A Dutch cohort study. *Am J Psychiatry*. 2021;178(10):914-920. doi:10.1176/appi.ajp.2021.20101479
208. Hamal C, Velugoti LSDR, Tabowei G, et al. Metformin for the improvement of comorbid depression symptoms in diabetic patients: A systematic review. *Cureus*. 2022;14(8):e28609. doi:10.7759/cureus.28609
209. el Massry M, Alaeddine LM, Ali L, Saad C, Eid AA. Metformin: A growing journey from glycemic control to the treatment of Alzheimer's disease and depression. *Curr Med Chem*. 2021;28(12):2328-2345. doi:10.2174/0929867327666200908114902
210. CDC. CDC Rates of Infertility.
211. Mansour R, El-Faissal Y, Kamel A, et al. Increased insulin resistance in men with unexplained infertility. *Reprod Biomed Online*. 2017;35(5):571-575. doi:10.1016/j.rbmo.2017.08.020
212. Wang H, Zhang Y, Fang X, Kwak-Kim J, Wu L. Insulin resistance adversely affect IVF outcomes in lean women without PCOS. *Front Endocrinol (Lausanne)*. 2021;12:734638. doi:10.3389/fendo.2021.734638
213. Sawant S, Bhide P. Fertility treatment options for women with polycystic ovary syndrome. *Clin Med Insights Reprod Health*. 2019;13:1179558119890867. doi:10.1177/1179558119890867
214. Ispasoiu CA, Chicea R, Stamatian FV, Ispasoiu F. High fasting insulin levels and insulin resistance may be linked to idiopathic recurrent pregnancy loss: A case-control study. *Int J Endocrinol*. 2013;2013:576926. doi:10.1155/2013/576926
215. Kamalanathan S, Sahoo J, Sathyapalan T. Pregnancy in polycystic ovary syndrome. *Indian J Endocrinol Metab*. 2013;17(1):37. doi:10.4103/2230-8210.107830
216. Legro RS, Barnhart HX, Schlaff WD, et al. Clomiphene, Metformin, or both for infertility in the polycystic ovary syndrome. *N Engl J Med*. 2007;356(6):551-566. doi:10.1056/NEJMoa063971
217. Bediako PT, BeLue R, Hillemeier MM. A comparison of birth outcomes among black, hispanic, and black hispanic women. *J Racial Ethn Health Disparities*. 2015;2(4):573-582. doi:10.1007/s40615-015-0110-2

218. Menon R. Oxidative stress damage as a detrimental factor in preterm birth pathology. *Front Immunol.* 2014;5:567. doi:10.3389/fimmu.2014.00567
219. Leary C, Leese HJ, Sturmy RG. Human embryos from overweight and obese women display phenotypic and metabolic abnormalities. *Hum Reprod.* 2015;30(1):122-132. doi:10.1093/humrep/deu276
220. Chen S, Wu R, Huang Y, et al. Insulin resistance is an independent determinate of ED in young adult men. *PLoS One.* 2013;8(12):e83951. doi:10.1371/journal.pone.0083951
221. Inman BA, st. Sauver JL, Jacobson DJ, et al. A population-based, longitudinal study of erectile dysfunction and future coronary artery disease. *Mayo Clin Proc.* 2009;84(2):108-113. doi:10.4065/84.2.108
222. Ayad B, Omolaoye TS, Louw N, et al. Oxidative stress and male infertility: Evidence from a research perspective. *Front Reprod Health.* 2022;4:822257. doi:10.3389/frph.2022.822257
223. Basciano H, Federico L, Adeli K. Fructose, insulin resistance, and metabolic dyslipidemia. *Nutr Metab (Lond).* 2005;2(1):5. doi:10.1186/1743-7075-2-5
224. Norton L, Shannon C, Gastaldelli A, DeFronzo RA. Insulin: The master regulator of glucose metabolism. *Metabolism.* 2022;129:155142. doi:10.1016/j.metabol.2022.155142
225. Gannon MC, Nuttall FQ, Westphal SA, Fang S, Ercan-Fang N. Acute metabolic response to high-carbohydrate, high-starch meals compared with moderate-carbohydrate, low-starch meals in subjects with type 2 diabetes. *Diabetes Care.* 1998;21(10):1619-1626. doi:10.2337/diacare.21.10.1619
226. Feng R, Du S, Chen Y, et al. High carbohydrate intake from starchy foods is positively associated with metabolic disorders: A cohort study from a Chinese population. *Sci Rep.* 2015;5:16919. doi:10.1038/srep16919
227. Gannon MC, Nuttall FQ. Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition. *Nutr Metab (Lond).* 2006;3(1):16. doi:10.1186/1743-7075-3-16
228. Kopp W. The atherogenic potential of dietary carbohydrate. *Prev Med (Baltim).* 2006;42(5):336-342. doi:10.1016/j.ypmed.2006.02.003
229. Holm J, Lundquist I, Björck I, Eliasson AC, Asp NG. Degree of starch gelatinization, digestion rate of starch in vitro, and metabolic response in rats. *Am J Clin Nutr.* 1988;47(6):1010-1016. doi:10.1093/ajcn/47.6.1010
230. Krezowski PA, Nuttall FQ, Gannon MC, Billington CJ, Parker S. Insulin and glucose responses to various starch-containing foods in type II diabetic subjects. *Diabetes Care.* 1987;10(2):205-212. doi:10.2337/diacare.10.2.205
231. Kanehara R, Goto A, Sawada N, et al. Association between sugar and starch intakes and type 2 diabetes risk in middle-aged adults in a prospective cohort study. *Eur J Clin Nutr.* 2022;76(5):746-755. doi:10.1038/s41430-021-01005-1
232. Melnik B, Jansen T, Grabbe S. Abuse of anabolic-androgenic steroids and bodybuilding acne: An underestimated health problem. *JDDG.* 2007;5(2):110-117. doi:10.1111/j.1610-0387.2007.06176.x
233. Andreassen M, Raymond I, Kistorp C, Hildebrandt P, Faber J, Kristensen LØ. IGF1 as predictor of all cause mortality and cardiovascular disease in an elderly population. *Eur J Endocrinol.* 2009;160(1):25-31. doi:10.1530/EJE-08-0452

234. Gürgen S, Yücel A, Karakuş A, Çeçen D, Özén G, Koçtürk S. Usage of whey protein may cause liver damage via inflammatory and apoptotic responses. *Hum Exp Toxicol.* 2015;34(7):769-779. doi:10.1177/0960327114556787
235. Smoliga JM, Wilber ZT, Robinson BT. Premature death in bodybuilders: What do we know? *Sports Medicine.* 2023;1-16. doi:10.1007/s40279-022-01801-0
236. Kayapinar O, Ozde C, Koc Ay E, Keskin M, Kaya A. Anterior myocardial infarction in a 26-year-old body builder with concomitant use of whey protein powder and amino acid capsules. *Acta Cardiol Sin.* 2018;34(4):359-362. doi:10.6515/ACS.201807_34(4).20180306A
237. Rencuzogullari I, Börekçi A, Karakoyun S, et al. Coronary thrombosis in three coronary arteries due to whey protein. *Am J Emerg Med.* 2017;35(4):664.e3-664.e4. doi:10.1016/j.ajem.2016.11.002
238. Wolters TLC, Netea MG, Riksen NP, Hermus ARMM, Netea-Maier RT. Acromegaly, inflammation and cardiovascular disease: A review. *Rev Endocr Metab Disord.* 2020;21(4):547-568. doi:10.1007/s11154-020-09560-x
239. Ha K, Kim K, Chun OK, Joung H, Song Y. Differential association of dietary carbohydrate intake with metabolic syndrome in the US and Korean adults: Data from the 2007–2012 NHANES and KNHANES. *Eur J Clin Nutr.* 2018;72(6):848-860. doi:10.1038/s41430-017-0031-8
240. Yang CJ, Samayoa LF, Bradbury PJ, et al. The genetic architecture of teosinte catalyzed and constrained maize domestication. *Proc Natl Acad Sci U S A.* 2019;116(12):5643-5652. doi:10.1073/pnas.1820997116
241. Wright SI, Bi IV, Schroeder SG, et al. The effects of artificial selection on the maize genome. *Science.* 2005;308(5726):1310-1314. doi:10.1126/science.1107891
242. Eckardt NA. Evolution of domesticated bread wheat. *Plant Cell.* 2010;22(4):993-993. doi:10.1105/tpc.110.220410
243. Pourkheirandish M, Dai F, Sakuma S, et al. On the origin of the non-brittle rachis trait of domesticated einkorn wheat. *Front Plant Sci.* 2018;8. doi:10.3389/fpls.2017.02031
244. Bao J, de Jong V, Atkinson F, Petocz P, Brand-Miller JC. Food insulin index: Physiologic basis for predicting insulin demand evoked by composite meals. *Am J Clin Nutr.* 2009;90(4):986-992. doi:10.3945/ajcn.2009.27720
245. Wolever, Meynier, Jenkins, et al. Glycemic index and insulinemic index of foods: An interlaboratory study using the ISO 2010 method. *Nutrients.* 2019;11(9):2218. doi:10.3390/nu11092218
246. Hoyt G, Hickey MS, Cordain L. Dissociation of the glycaemic and insulinaemic responses to whole and skimmed milk. *Br J Nutr.* 2005;93(2):175-177. doi:10.1079/bjn20041304
247. Salehi A, Gunnerud U, Muhammed SJ, et al. The insulinogenic effect of whey protein is partially mediated by a direct effect of amino acids and GIP on β -cells. *Nutr Metab (Lond).* 2012;9(1):48. doi:10.1186/1743-7075-9-48
248. Levine ME, Suarez JA, Brandhorst S, et al. Low protein intake is associated with a major reduction in IGF-1, cancer, and overall mortality in the 65 and younger but not older population. *Cell Metab.* 2014;19(3):407-417. doi:10.1016/j.cmet.2014.02.006

249. Melnik BC, Schmitz G. Pasteurized non-fermented cow's milk but not fermented milk is a promoter of mTORC1-driven aging and increased mortality. *Ageing Res Rev.* 2021;67:101270. doi:10.1016/j.arr.2021.101270
250. Cummings NE, Williams EM, Kasza I, et al. Restoration of metabolic health by decreased consumption of branched-chain amino acids. *J Physiol.* 2018;596(4):623-645. doi:10.1113/JP275075
251. Karusheva Y, Koessler T, Strassburger K, et al. Short-term dietary reduction of branched-chain amino acids reduces meal-induced insulin secretion and modifies microbiome composition in type 2 diabetes: a randomized controlled crossover trial. *Am J Clin Nutr.* 2019;110(5):1098-1107. doi:10.1093/ajcn/nqz191
252. Wolfe RR. Branched-chain amino acids and muscle protein synthesis in humans: Myth or reality?. *J Int Soc Sports Nutr.* 2017;14:30. doi:10.1186/s12970-017-0184-9
253. Melnik BC, John SM, Carrera-Bastos P, et al. The role of cow's milk consumption in breast cancer initiation and progression. *Curr Nutr Rep.* 2023;12(1):122-140. doi:10.1007/s13668-023-00457-0
254. Dhillon J, Lee JY, Mattes RD. The cephalic phase insulin response to nutritive and low-calorie sweeteners in solid and beverage form. *Physiol Behav.* 2017;181:100-109. doi:10.1016/j.physbeh.2017.09.009
255. Witkowski M, Nemet I, Alamri H, et al. The artificial sweetener erythritol and cardiovascular event risk. *Nat Med.* 2023;10.1038/s41591-023-02223-9. doi:10.1038/s41591-023-02223-9
256. Keselman B, Vergara M, Nyberg S, Nystrom FH. A randomized cross-over study of the acute effects of running 5 km on glucose, insulin, metabolic rate, cortisol and Troponin T. *PLoS One.* 2017;12(6):e0179401. doi:10.1371/journal.pone.0179401
257. Niemann MJ, Tucker LA, Bailey BW, Davidson LE. Strength training and insulin resistance: The mediating role of body composition. *J Diabetes Res.* 2020;2020:1-11. doi:10.1155/2020/7694825
258. Heden TD, Liu Y, Park YM, Winn NC, Kanaley JA. Walking reduces postprandial insulin secretion in obese adolescents consuming a high-fructose or high-glucose diet. *J Phys Act Health.* 2015;12(8):1153-1161. doi:10.1123/jpah.2014-0105
259. de Souza JFT, Dátilo M, de Mello MT, Tufik S, Antunes HKM. High-intensity interval training attenuates insulin resistance induced by sleep deprivation in healthy males. *Front Physiol.* 2017;8:992. doi:10.3389/fphys.2017.00992
260. Thind H, Lantini R, Balletto BL, et al. The effects of yoga among adults with type 2 diabetes: A systematic review and meta-analysis. *Prev Med (Baltim).* 2017;105:116-126. doi:10.1016/j.ypmed.2017.08.017
261. Hall KS, Hyde ET, Bassett DR, et al. Systematic review of the prospective association of daily step counts with risk of mortality, cardiovascular disease, and dysglycemia. *Int J Behav Nutr Phys Act.* 2020;17(1):78. doi:10.1186/s12966-020-00978-9
262. Holten MK, Zacho M, Gaster M, Juel C, Wojtaszewski JFP, Dela F. Strength training increases insulin-mediated glucose uptake, GLUT4 content, and insulin signaling in skeletal muscle in patients with type 2 diabetes. *Diabetes.* 2004;53(2):294-305. doi:10.2337/diabetes.53.2.294
263. CAMPBELL WW, KRAUS WE, POWELL KE, et al. High-intensity interval training for cardiometabolic disease prevention. *Med Sci Sports Exerc.* 2019;51(6):1220-1226. doi:10.1249/MSS.0000000000001934

264. Jolleyman C, Yates T, O'Donovan G, et al. The effects of high-intensity interval training on glucose regulation and insulin resistance: A meta-analysis. *Obesity Reviews*. 2015;16(11):942-961. doi:10.1111/obr.12317
265. Putiri A, Close J, Lilly H, Guillaume N, Sun GC. Qigong exercises for the management of type 2 diabetes mellitus. *Medicines*. 2017;4(3):59. doi:10.3390/medicines4030059
266. Chen Z, Ye X, Xia Y, et al. Effect of Pilates on Glucose and Lipids: A systematic review and meta-analysis of randomized controlled trials. *Front Physiol*. 2021;12:641968. doi:10.3389/fphys.2021.641968
267. Drucker DJ, Nauck MA. The incretin system: glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes. *The Lancet*. 2006;368(9548):1696-1705. doi:10.1016/S0140-6736(06)69705-5
268. Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384(11):989-1002. doi:10.1056/NEJMoa2032183
269. Wharton S, Calanna S, Davies M, et al. Gastrointestinal tolerability of once-weekly semaglutide 2.4 mg in adults with overweight or obesity, and the relationship between gastrointestinal adverse events and weight loss. *Diabetes Obes Metab*. 2022;24(1):94-105. doi:10.1111/dom.14551
270. Wilding JPH, Batterham RL, Davies M, et al. Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. *Diabetes Obes Metab*. 2022;24(8):1553-1564. doi:10.1111/dom.14725
271. Fruzzetti F, Perini D, Russo M, Bucci F, Gadducci A. Comparison of two insulin sensitizers, metformin and myo-inositol, in women with polycystic ovary syndrome (PCOS). *Gynecol Endocrinol*. 2017;33(1):39-42. doi:10.1080/09513590.2016.1236078
272. Unfer V, Nestler JE, Kamenov ZA, Prapas N, Facchinetto F. Effects of inositol(s) in women with PCOS: A systematic review of randomized controlled trials. *Int J Endocrinol*. 2016;2016:1849162. doi:10.1155/2016/1849162
273. Volek JS, Phinney SD, Krauss RM, et al. Alternative dietary patterns for Americans: Low-carbohydrate diets. *Nutrients*. 2021;13(10):3299. doi:10.3390/nu13103299
274. Dowis K, Banga S. The potential health benefits of the keto diet: A narrative review. *Nutrients*. 2021;13(5):1654. doi:10.3390/nu13051654
275. Weber DD, Aminzadeh-Gohari S, Tulipan J, Catalano L, Feichtinger RG, Kofler B. Ketogenic diet in the treatment of cancer – where do we stand? *Mol Metab*. 2020;33:102-121. doi:10.1016/j.molmet.2019.06.026
276. Halton TL, Willett WC, Liu S, et al. Low-carbohydrate-diet score and the risk of coronary heart disease in women. *N Engl J Med*. 2006;355(19):1991-2002. doi:10.1056/NEJMoa055317
277. Ebbeling CB, Knapp A, Johnson A, et al. Effects of a low-carbohydrate diet on insulin-resistant dyslipoproteinemia—a randomized controlled feeding trial. *Am J Clin Nutr*. 2022;115(1):154-162. doi:10.1093/ajcn/nqab287
278. Waliłko E, Napierała M, Bryśkiewicz M, Fronczyk A, Majkowska L. High-protein or low glycemic index diet—which energy-restricted diet is better to start a weight loss program? *Nutrients*. 2021;13(4):1086. doi:10.3390/nu13041086

279. Saslow LR, Mason AE, Kim S, et al. An online intervention comparing a very low-carbohydrate ketogenic diet and lifestyle recommendations versus a plate method diet in overweight individuals with type 2 diabetes: A randomized controlled trial. *J Med Internet Res.* 2017;19(2):e36. doi:10.2196/jmir.5806
280. Westman EC, Yancy WS, Mavropoulos JC, Marquart M, McDuffie JR. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. *Nutr Metab (Lond).* 2008;5(1):36. doi:10.1186/1743-7075-5-36
281. Castaldo, Narváez, Izzo, et al. Red Wine Consumption and Cardiovascular Health. *Molecules.* 2019;24(19):3626. doi:10.3390/molecules24193626
282. Gerber PA, Berneis K. Regulation of low-density lipoprotein subfractions by carbohydrates. *Curr Opin Clin Nutr Metab Care.* 2012;15(4):381-385. doi:10.1097/MCO.0b013e3283545a6d
283. Ottolini KM, Andescavage N, Keller S, Limperopoulos C. Nutrition and the developing brain: The road to optimizing early neurodevelopment: A systematic review. *Pediatr Res.* 2020;87(2):194-201. doi:10.1038/s41390-019-0508-3
284. Yuan X, Wang J, Yang S, et al. Effect of intermittent fasting diet on glucose and lipid metabolism and insulin resistance in patients with impaired glucose and lipid metabolism: A systematic review and meta-analysis. *Int J Endocrinol.* 2022;2022:6999907. doi:10.1155/2022/6999907
285. National Institutes of Health. NIH Aim for a Healthy Weight. https://www.nhlbi.nih.gov/health/educational/lose_wt/eat/calories.htm.
286. Kishan R Jackson B, Phy J. Spontaneous Pregnancies in Polycystic Ovary Syndrome (PCOS) Patients with a Low Starch/Low Dairy Diet: A Retrospective Case Series. *J Community Med Public Health.* 2022;6(2). doi:10.29011/2577-2228.100242
287. Ghusn W, De la Rosa A, Sacoto D, et al. Weight loss outcomes associated with semaglutide treatment for patients with overweight or obesity. *JAMA Netw Open.* 2022;5(9):e2231982. doi:10.1001/jamanetworkopen.2022.31982
288. Stadler JT, Marsche G. Obesity-related changes in high-density lipoprotein metabolism and function. *Int J Mol Sci.* 2020;21(23):8985. doi:10.3390/ijms21238985
289. Tzotzas T, Papadopoulou FG, Tziomalos K, et al. Rising serum 25-hydroxy-vitamin D levels after weight loss in obese women correlate with improvement in insulin resistance. *J Clin Endocrinol Metab.* 2010;95(9):4251-4257. doi:10.1210/jc.2010-0757
290. Kelley AS, Smith YR, Padmanabhan V. A narrative review of placental contribution to adverse pregnancy outcomes in women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 2019;104(11):5299-5315. doi:10.1210/jc.2019-00383
291. Chang EM, Han JE, Seok HH, Lee DR, Yoon TK, Lee WS. Insulin resistance does not affect early embryo development but lowers implantation rate in in vitro maturation-in vitro fertilization-embryo transfer cycle. *Clin Endocrinol (Oxf).* 2013;79(1):93-99. doi:10.1111/cen.12099
292. Jackson B, Kishan R, Mullins C, et al. Nutritional education (face-to-face and video instruction) for polycystic ovary syndrome results in greater reduction in BMI and hemoglobin A1C than caloric restriction, exercise and metformin. *Fertil Steril.* 2022;118(4):e95. doi:10.1016/j.fertnstert.2022.08.288
293. Cederroth CR, Zimmermann C, Nef S. Soy, phytoestrogens and their impact on reproductive health. *Mol Cell Endocrinol.* 2012;355(2):192-200. doi:10.1016/j.mce.2011.05.049



Lilli
Health

©Lilli Health. All rights reserved.