Prediabetes is NOT Pre-Problem

The Path of Metabolic Dysregulation

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PRESENTER
Jill Weisenberger, MS, RDN, CDE, CHWC, FAND

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Learning Objectives

1. Describe the disease process from normal blood glucose levels to those in the prediabetes range to the diabetes range and to the stage in which exogenous insulin is required.
2. Identify at least 4 common metabolic abnormalities among people with prediabetes.
3. Identify at least 5 foods that are linked to less insulin resistance and/or the incidence of type 2 diabetes.
4. List and describe at least 5 lifestyle habits that can impact the progression/reversal of prediabetes.

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Disclosures

• Norwegian Seafood Council
• Corteva
• Pyure Organic Stevia
• Calorie Control Council
• 4 books+ by American Diabetes Association

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Scary Numbers ⬆

- 1 in 3 adults
  - 88 million
- 15% diagnosed
  - 85% undiagnosed
- Diabetes
  - 10.5% population
  - 34.2 million people

https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf

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Prediabetes Treatment

- Weight loss
  - 7% body weight
- Physical activity
  - > 150 minutes weekly
- Diet
  - Avoid sugary drinks
- Medication
  - Metformin
- Tobacco cessation

Diabetes Care 2019;42:731–754

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Maria

- 58 years old, upper middle class, well-educated
- Significant family h/o type 2
- BMI: 19
- A1C: 6.2%
- Power walker: 60 – 90 minutes daily
- "Eats clean" & all day
  - Almonds, almond milk, oats, flaxseed, salad, fruit including under-ripe bananas, avocados, crab cakes, sweet potatoes, tofu, lentils, yogurt, pretzels, red wine

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Pathogenesis

Insulin resistance normal
blood glucose   Prediabetes   Diabetes   Diabetes requiring
insulin

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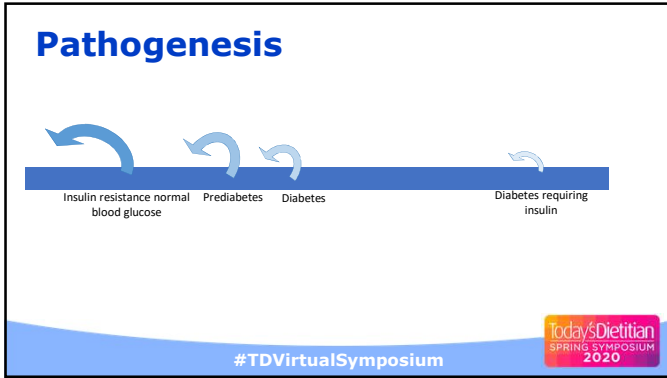
7

Diabetes Prevention Program (DPP)

- 3,234 high-risk people, average 3 years
- Intensive Lifestyle
  - Goal: 7% loss of BW, 150 min physical activity weekly
- Standard Care
  - General diet & exercise advice
- Metformin
  - General diet & exercise advice + metformin BID

https://dppos.bsc.gwu.edu/web/dppos/dppos

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Diabetes Prevention Outcomes Study

	Intensive Lifestyle (%)	Metformin (%)	NOTES
DPP 3-year study	58	31	
DPPOS 10 year data	34	18	Less CVD meds with Lifestyle
DPPOS 15 year data	27	17	B12 deficiency noted

https://dppos.bsc.gwu.edu/web/dppos/dppos

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DPP Strategies

Self-monitor weight	Choose wholesome foods
Track physical activity	Manage stress
Record food intake	Maintain motivation
Decrease calories	Mindset: stop harmful negative thinking

https://www.cdc.gov/diabetes/prevention/lifestyle-program/t2/t2materials.html

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Other Prevention Studies

	Intensive Lifestyle (%)	Notes
Da Qing	39	**Diet:** ↑ veg, ↓ alcohol & sugar **Results:** ↓ all-cause & CVD mortality & microvascular complications
Finnish DPS 13 year	38	**Diet:** ↑ fiber CHO, ↓ SFA **Results:** ↑ fat, ↓CHO = ↑ DM
DPPOS 10 year	34	**Results:** ↓ CVD meds
DPPOS 15 year	27	**Results:** metformin for GDM, starting ↑ FBG & A1C

ADA Standards of Medical Care in Diabetes-2020

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3 Years of Liraglutide vs Placebo

- 1128 participants completed the study
- 3.0 mg liraglutide (Saxenda)
- ↓ calorie, ↑activity, phone & web-based
- Average weight loss: 6%
- Reduced progression to DM: 66%
  - Completers only: 80% risk reduction

Weight Loss Drug Helps Prevent Type 2 Diabetes

Carel W le Roux et al. SC
Lancet. 2017 Apr 8;389(10077

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Diagnostic Criteria

Measurement	Prediabetes	Diabetes
Fasting Plasma Glucose	$\geq$ 100 – 125 mg/dl	$\geq$ 126 mg/dl
2-hour OGTT	$\geq$ 140 – 199 mg/dl	$\geq$ 200 mg/dl
Random Plasma Glucose (+ symptoms)	----	$\geq$ 200 mg/dl
A1C	5.7 – 6.4 %	$\geq$ 6.5%

ADA Standards of Medical Care in Diabetes-2020

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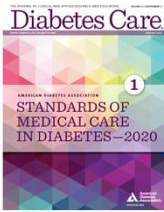
ADA Prevention or Delay of Type 2 Diabetes

- Screen at least annually
- Increased vigilance for CV risk factors
- Refer to DPP or similar program
- Consider metformin, especially for
  - BMI $\geq$ 35
  - H/o GDM
  - $\leq$ 60 years

ADA Standards of Medical Care in Diabetes-2020

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CDC Infographic

Type 2 diabetes

Prediabetes

Heart disease

Stroke

https://www.cdc.gov/diabetes/library/socialMedia/infographics.html

PREDIABETES COULD IT BE YOU?

88 MILLION — 88 million American adults — more than 1 in 3 — have prediabetes

1 IN 3

MORE THAN 8 IN 10 adults with prediabetes don't know they have it
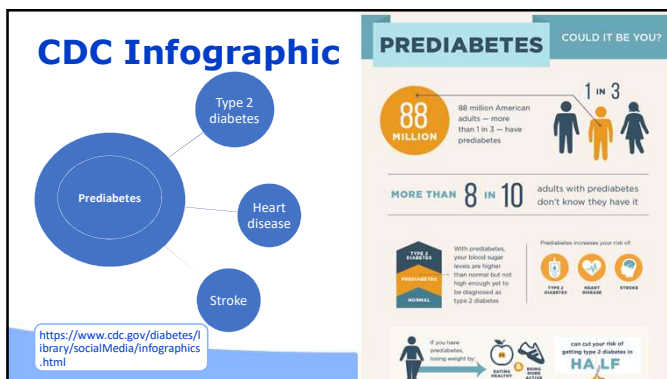
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Traditional View of Type 2 Diabetes:
The Triumverate

Hyperglycemia

Increased Liver Output

Impaired Insulin Secretion

Decreased Muscle Uptake

DeFronzo. Diabetes. 2009; 58(4): 773-795

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Muscle Insulin Resistance

Impaired glucose uptake after eating

- By at least 50%
- Post-prandial hyperglycemia

Exercise (muscle contraction): induced glucose uptake is independent of insulin

DeFronzo. Diabetes. 2009; 58(4): 773-795

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Muscle Insulin Resistance

The muscle resists the action of insulin, so it's slow to allow glucose into the cells. But the muscles welcome glucose during exercise, no matter what.

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Liver Insulin Resistance

Effects post-prandial glucose

- Insulin levels are high after eating, but the liver ignores insulin and sends out more glucose

Effects FBG

- Excess hepatic gluconeogenesis, unrelated to food

DeFronzo. Diabetes. 2009; 58(4): 773-795

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Liver Insulin Resistance

The liver's job is to send out glucose during the night. But with insulin resistance, it dumps out too much. And this is NOT related to what you ate last night

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Decreased β-cell Function

- **Relative** insulin insufficiency
- Fail over time, leading first to high post-prandial BG levels, then to high FBG
- Progressive loss of beta-cell function that determines the rate of disease progression

DeFronzo. Diabetes. 2009; 58(4): 773-795

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Decreased β-cell Function

Your pancreas makes extra insulin to compensate for your cells refusing to use it properly. It used to make enough to keep BG in the normal range. Now your pancreas can't make enough insulin. Blame your pancreas!

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Pathogenesis

Insulin resistance normal blood glucose   Prediabetes   Diabetes   Diabetes requiring insulin

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Insulin resistance

Post-meal blood glucose

Fasting blood glucose

Insulin secretion

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Microvascular Complications

Cardiovascular Complications

-20   -15   -10   -5   0   5   10   15   20   25

Pre DM   Type 2 DM

Onset of Type 2 DM

Ramlo-Halsted. Primary Care: 1999 26(4)
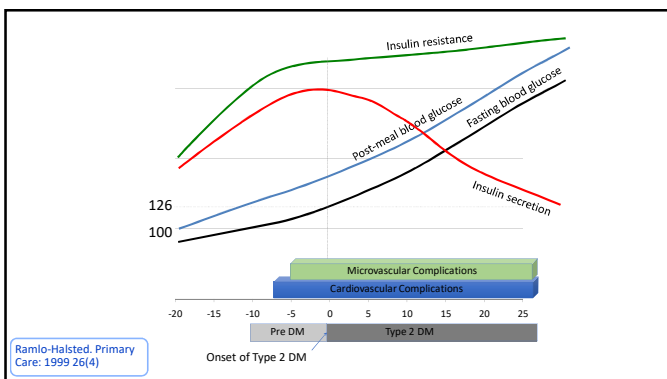
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The Ominous Octet

Stream of FFA

Decreased Incretin Effect

Increased Glucagon Secretion

Increased Appetite

Hyperglycemia

Increased Glucose Reabsorption

Increased Liver Output

Impaired Insulin Secretion

Decreased Muscle Uptake

DeFronzo. Diabetes. 2009; 58(4): 773-795

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Fat Insulin Resistance

Normal insulin action to inhibit TG breakdown is faulty

FFA flood the bloodstream

Muscle IR	Liver IR	Impaired β-cells
Muscle Uptake	Liver Output	Insulin Secretion

DeFronzo. Diabetes. 2009; 58(4): 773-795

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α-Cells of the Pancreas

- Secrete glucagon, counter-regulatory to insulin
  - Excess in type 2 diabetes, likely in prediabetes

- High fasting glucagon levels correlate with high rate of liver glucose production, leading to high FBG

- In type 2 DM, insulin fails to suppress glucagon after eating, leading to high postprandial BG

DeFronzo. Diabetes. 2009; 58(4): 773-795

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α-Cells of the Pancreas

Your liver is leaky and letting out too much glucose.

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Role of Incretin Hormones

GLP-1 And GIP
- Released after eating
- Important for insulin release

Normal Role of GLP-1
- **β-cells:** Enhances glucose-dependent insulin secretion
- **Brain:** Promotes satiety, reduces appetite
- **α-cells:** Reduces glucagon secretion after eating
- **Liver:** Reduces hepatic glucose output (via less glucagon)

DeFronzo. Diabetes. 2009; 58(4): 773-795
AADE Desk -3rd-edition American Association of Diabetes Educators

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Normal Role of GLP-1

Hormones in your gut act nutty, causing you to have higher blood glucose levels and even make you hungrier.

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Insulin Resistance of the Brain

Neurotransmitter dysregulation

- Brain neurotransmitters affect appetite and food intake
- GLP-1 resistance in the brain increases food intake, leading to weight dysregulation
  - Muscle insulin resistance
  - Liver insulin resistance
  - β-cell failure

DeFronzo. Diabetes. 2009; 58(4): 773-795

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Insulin Resistance of the Brain

Problems with your hormones and chemical messengers in your brain can make it harder to regulate your appetite.

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Increased Reabsorption in the Kidneys

- Renal threshold: ~ 180 mg/dl
- Higher in people with **type 2 diabetes**
  - Contributes to the maintenance of hyperglycemia
  - More likely in type 2 diabetes than in prediabetes

DeFronzo. Diabetes. 2009; 58(4): 773-795

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Increased Reabsorption in the Kidneys

Instead of letting you pee out excess blood sugar, your kidneys send it back into your blood...
DIABETES ONLY

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Pathophysiology Summary

- Many years from early IR to prediabetes to type 2 diabetes to complete loss of insulin producing ability

- Prediabetes is multifactorial and affects liver, muscle, fat, pancreas, brain, GI tract

- Underlying cause is IR, thus treatment must include insulin-sensitizing behaviors + in later-stages usually insulin-sensitizing meds

- Consider ALL of insulin's roles

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Cardiometabolic Risk

Age   Genetics   Overweight / Obesity

Abnormal Lipid Metabolism
LDL ↑
ApoB ↑
HDL ↓
TG ↑

Insulin Resistance
Insulin Resistance Syndrome
↑Lipids ↑BP ↑Glucose

Cardiometabolic Risk
Global Diabetes / CVD Risk

Age, Race, Gender, Family History

Smoking
Physical Inactivity
Unhealthy Eating

Hypertension

Inflammation
Hypercoagulation

American Diabetes Association. (2015). Cardiometabolic Risk.Type 2 Diabetes and Cardiovascular Disease.
https://professional.diabetes.org/sites/professional.diabetes.org/files/media/cardiometabolicrisk2015.pdf

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Markers of Insulin Resistance

TG	281
HDL	31
LDL	128

TG: HDL (mg/dl)

Higher value = ●IR and CVD risk[1]

Some experts use 3[2]

1. Diabetes Care 2000; 23(3) 1679-1685
2. McLaughlin et al. 2003; 139(10): 802-809

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Diabetes-Cancer Link: *Expected Higher in Prediabetes*

Cancer Site	Risk Ratio
Liver	2.01
Pancreas	1.94
Endometrium	2.10
Biliary Tract	1.43
Colorectum	1.27
Kidney	1.42
Bladder	1.24
Breast	1.20

Prediabetes and diabetes are also associated with increased death from cancer, even when BMI and other factors are considered.

Shikata et al. Cancer Sci 2013; 104: 9-14

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Maria

A1C 5.5% 2 months later (6.2%)

- 58 years old, upper middle class, well-educated
- Significant family h/o type 2
- **BMI: 19**
- A1C: 6.2%
- **Power walker:** 60-90 minutes daily
- "Eats clean" and all day

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Diet

2018 ADA Standards of Care	Higher intakes of nuts, berries, yogurt, coffee, and tea are associated with reduced diabetes risk. Conversely, red meats and sugar-sweetened beverages are associated with an increased risk.
2020 ADA Standards of Care	An emphasis on whole grains, legumes, nuts, fruits and vegetables, and minimal refined and processed foods is important.

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Dietary Pattern: *Mediterranean*

Meta-analysis from around the world:	23% less likely to develop diabetes
PREDIMED:	52% less likely after 4 years
Food choices	• Seafood, fruits, vegetables, whole grains, olive oil, nuts, other plants • Wine with meals and fruit for dessert

Diabetes Spectr. 2017;(2):72-76.

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Dietary Pattern: *Vegan/Vegetarian*

Adventist Health Study 2	• Vegan diets outperformed vegetarian • All vegetarian diets outperformed nonvegetarian diet
Mechanisms	• More fiber, phytochemicals • Less heme iron

Diabetes Care. 2009; 32:791-796

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Dietary Pattern: *DASH*

Meta-analysis[1]	• 20% reduced risk
PREMIER Study[2]	• Improved fasting insulin, FBG, insulin action
Fruits, vegetables, poultry, fish, nuts, whole grains, nonfat and low-fat dairy	• Lower in fat and higher in animal products compared to Mediterranean

Diabetes Spectr. 2017;(2):76-81
Diabetes Care 2004;27(2):40-347

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Diet

| **2018 ADA Standards of Care** | Higher intakes of nuts, berries, yogurt, coffee, and tea are associated with reduced diabetes risk. |

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Pulses and Other Legumes

FBG (long and short term)

- Magnesium
- Phytonutrients
- Fibers
- Resistant starches

Diabetologia. 2009;52(8):1479-1495

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Berries

Population study-middle aged adults (Finland)

- 35% reduced risk with greatest berry consumption
- Polyphenols
- Fibers

Am J Clin Nutr. 2014:99(2):328-333

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Nuts

Studies show mixed results on diabetes prevention

- Fiber
- Magnesium
- Phytonutrients

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Yogurt

Health Professionals Follow-Up Study, Nurses' Health Study, and Nurses' Health Study II

- Increased 1 serving daily associated with 18% reduced risk
- Probiotics

BMC Medicine. 2014;12:215

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Coffee and Tea

Risk of Diabetes

Daily Cups

Coffee[1]

Regular & decaf Chlorogenic acid Other bioactives	33% ↓isk with 6 cups vs. 0

Tea[2]

Regular & decaf Catechins Other bioactives	15% ↓isk with > 4 cups vs. 0

Diabetes Care Feb 2014, 37 (2) 569-586
Br J Nutr. 2014;111(8):1329-1339

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Oats and Barley

Beta-glucan

- Viscous fiber
  - Improves insulin action, lowers blood glucose
  - Lowers cholesterol levels
- Uncooked oats
  - Resistant starch

J Am Coll Nutr. 2005;24(3)182-188

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Alcohol

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Physical Activity Recommendations

Cardiovascular Exercise

- 3 x weekly, no more than 2 consecutive days without
- ≥ 150 min weekly

Strength Training

- 2-3 sessions on non-consecutive days

Reduce Sedentary Time

- Interrupt prolonged sitting with 3-min breaks every 30 min

Diabetes Care 2016 Nov; 39(11)

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Cardiovascular Exercise

Reduces insulin resistance for 2-48 hours
- Best daily
- 20-minute walk after meals

Non-insulin mediated glucose uptake

Diabetes Care 2016 Nov; 39(11)

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Strength Training

- Reduces insulin resistance as well as CV exercise
  - Effects are additive
- Non-insulin mediated glucose uptake
- Repository for PP BG

Diabetes Care 2016 Nov; 39(11)

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Reduce Sedentary Behavior

Increasing →

Sedentary Behavior:

TV, gaming, driving, etc

Muscle contraction, glucose uptake, venous sufficiency, EE, LPL function, HDL cholesterol

Decreases ↓

Diabetes Care 2016 Nov; 39(11)

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Inactivity Tracker

Day: Monday	Date: February 20	
Time	**Activity**	**Minutes Active or Standing/Total Minutes**
6:00–6:20 A.M.	Wake up, drink coffee, read email	3/20
6:20–6:45 A.M.	Prepare and eat breakfast, pack lunch	4/25
6:45–7:45 A.M.	Jogging and strength training	60/60
7:45–8:20 A.M.	Shower and dress for work	25/35
8:20–9:00 A.M.	Drive to work, arrive to desk	2/40
9:00 A.M. to 12:00 P.M.	Work at desk, bathroom break	3/180
12:00–12:30 P.M.	Lunch break	6/30
12:30–3:00 P.M.	Work at desk, bathroom break	3/150
3:00–3:10 P.M.	Walking break	10/10
3:10–5:30 P.M.	Work at desk, bathroom break	3/140

PREDIABETES: A COMPLETE GUIDE

Your Lifestyle Reset to Stop Prediabetes and Other Chronic Illnesses

JILL WEISENBERGER, MS, RDN, CDE, CHWC, AFMC

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Sleep

Inadequate Sleep[1]

- Linked to weight gain, obesity, diabetes, CVD
- More ghrelin, less leptin
- Decreased insulin resistance
  - Even short term (1 bad night)

U-shaped curve: lowest risk 7-8 hours[2]

JCEM. 2010;95(6):2963-2968
Diabetes Care. 2015;38(3):529-537

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Conclusion: *Overall Healthy Lifestyle*

Eating patterns: more whole foods
- Low carb not required

Physical activity
- Cardio, strength, reduced sedentary behavior

Sleep

Smoking cessation

Weight loss

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Questions?

Jill Weisenberger, MS, RDN, CDE, CHWC, FAND

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