Targeting Hormones for the Management of Obesity and Cardiovascular Diseases

David L. Guarraia, MD, MS, FACC, Dipl ABOM

Associate Professor of Medicine

Medical Director – Preventive Cardiology

Medical Director – Cardiovascular Rehabilitation

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Conflicts of Interest

None

"The doctor of the future will give no medicine, but will interest his patients in the care of the human frame, in diet, and in the cause and prevention of disease."

Thomas Edison

Objectives

1) How did we get here?

2) Current thoughts / models for root causes of obesity

3) Implementing dietary strategies for success

4) Case discussion(s)

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Standard American Diet (SAD)

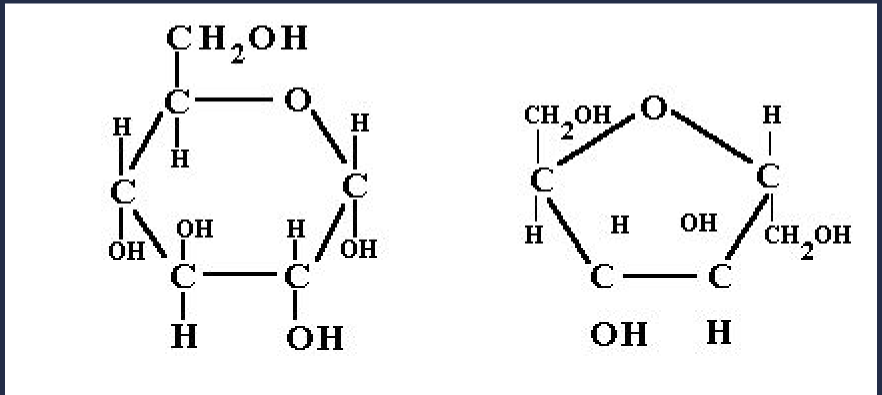
High in sugars (carbohydrates)

Very low in fiber, often low in protein

Hyper-palatable

Low in Cost

Very, very convenient



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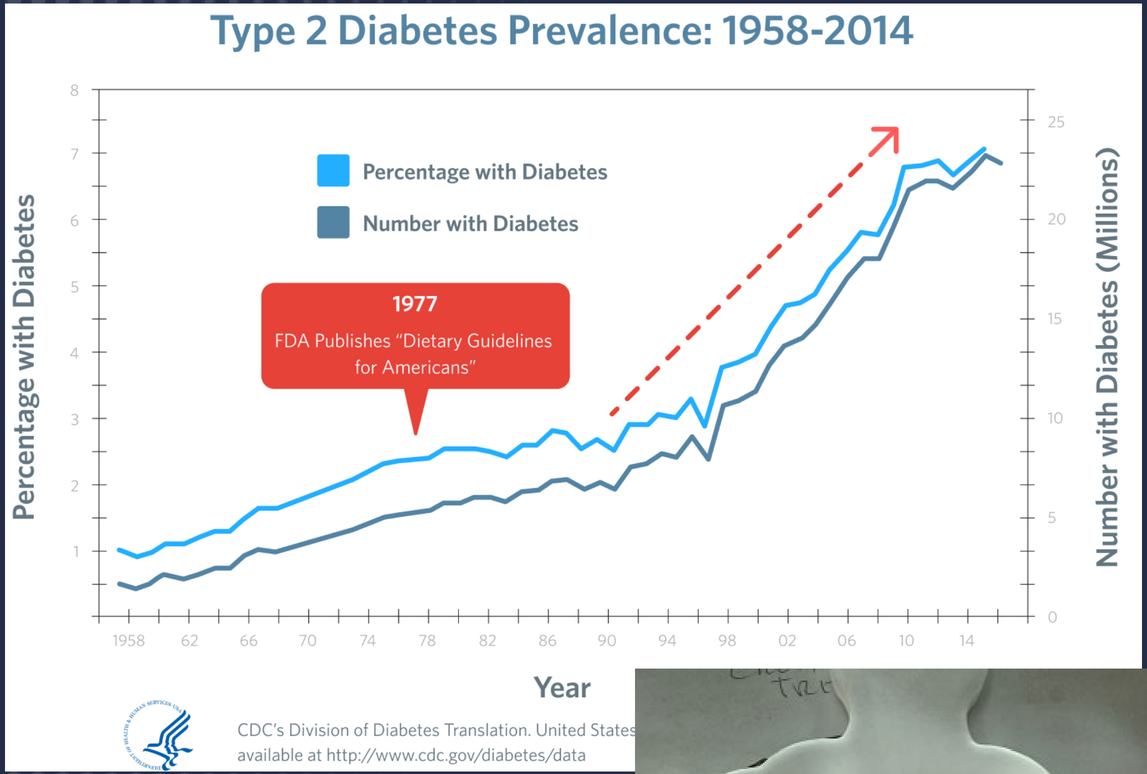

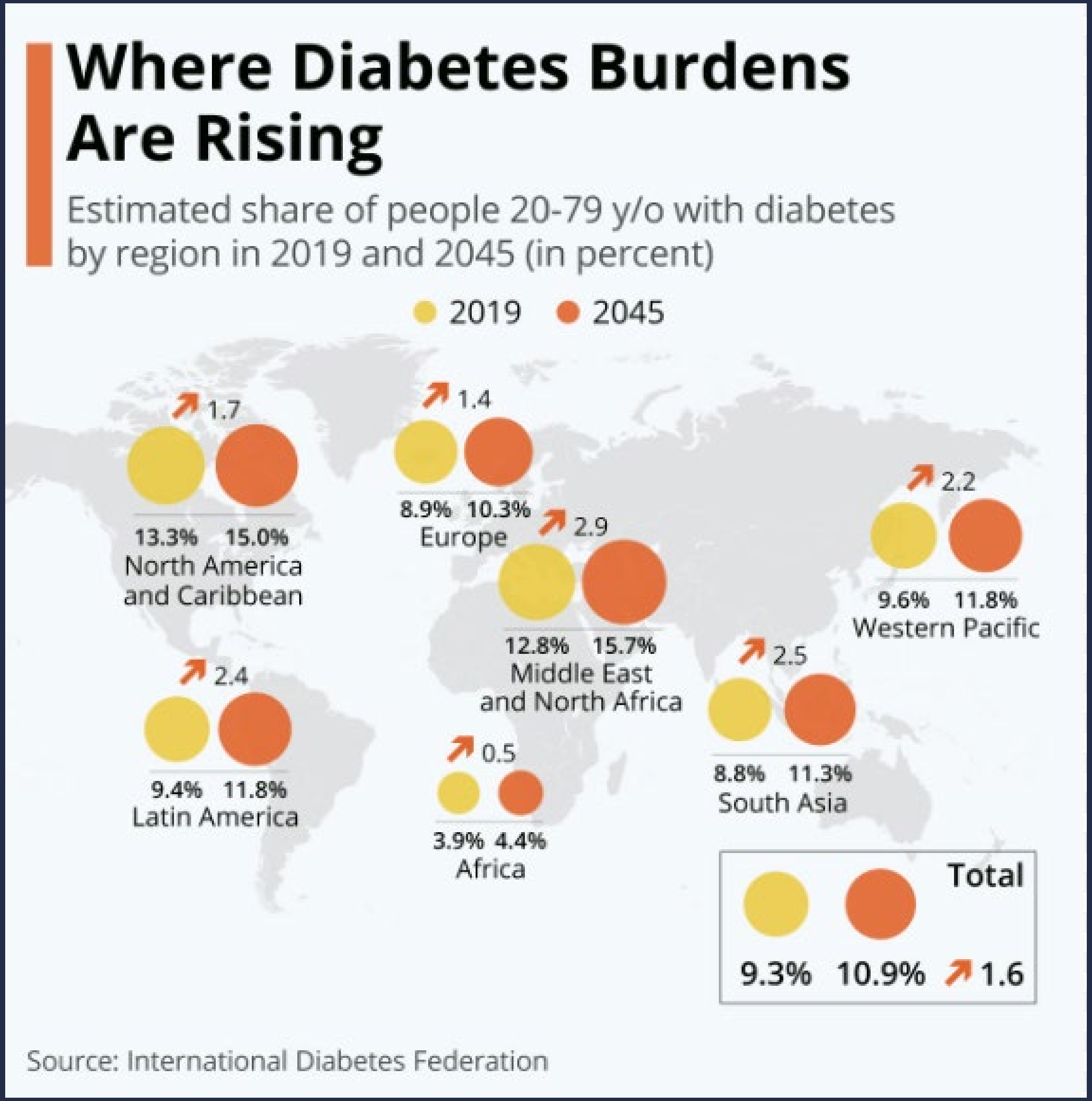

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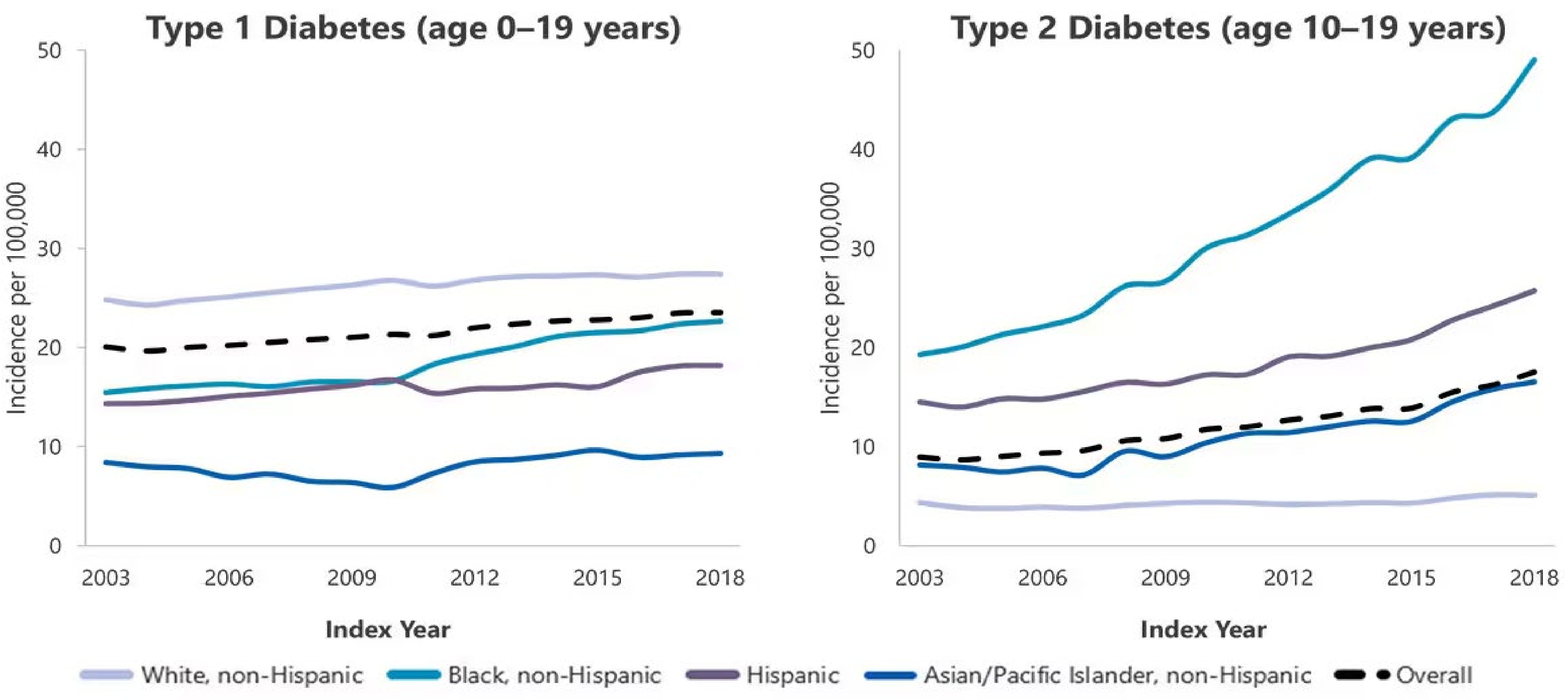

Data source: SEARCH for Diabetes in Youth study.

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METABOLIC SYNDROME AND RELATED DISORDERS
Volume 17, Number 1, 2019

https://doi.org/10.1089/met.2018.0105

Mary Ann Liebert, Inc. publishers

Original Article

Prevalence of Optimal Metabolic Health in American Adults: National Health and Nutrition Examination Survey 2009–2016

Joana Araújo, PhD[1], Jianwen Cai, PhD[2], and June Stevens, PhD[1,3]

Using the most recent guidelines, metabolic health was defined as having optimal levels of:

- waist circumference (WC <102/88 cm for men/women)
- glucose (fasting glucose <100 mg/dL and hemoglobin A1c <5.7%)
- blood pressure (systolic <120 and diastolic <80 mmHg)
- triglycerides (<150 mg/dL)
- high-density lipoprotein cholesterol (≥40/50 mg/dL for men/women)
- not taking any related medication

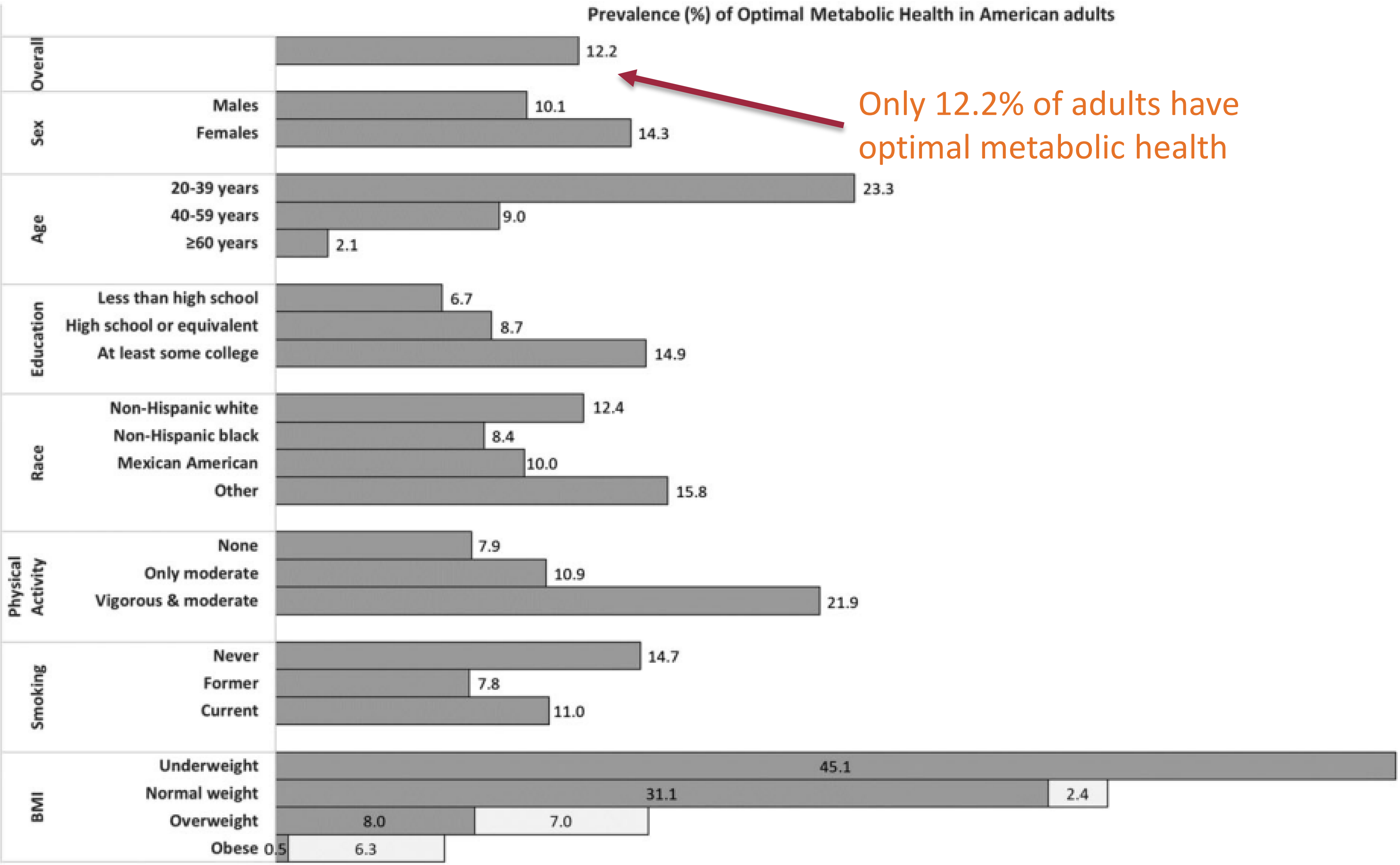

FIG. 1. Population prevalence of optimal metabolic health in American adults, overall and by demographics, physical activity and BMI—NHANES 2009–2016. Hatched segment of bars showing prevalence in BMI categories indicates impact of excluding waist circumference as a criterion. Metabolic health defined as waist circumference <102 cm in men and <88 cm in women; systolic blood pressure <120 mmHg and diastolic blood pressure <80 mmHg; glucose <100 mg/dL and hemoglobin A1c <5.7%; triglycerides <150 mg/dL; high-density lipoprotein cholesterol ≥40 mg/dL in men and ≥50 mg/dL in women; and not taking any lowering medication for blood pressure, glucose, or cholesterol. BMI, body mass index; NHANES, National Health and Nutrition Examination Survey.

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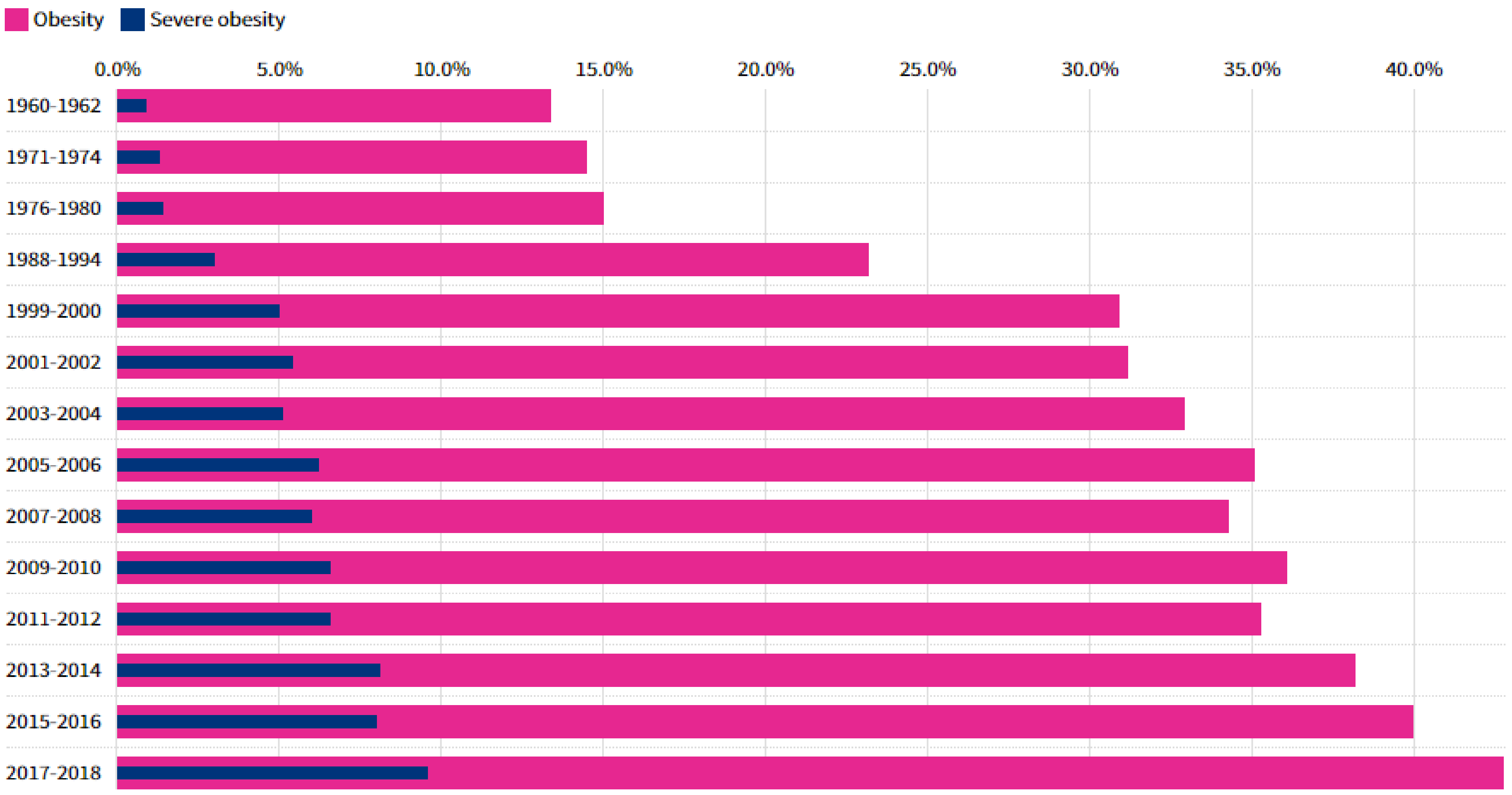
Nationwide obesity rates have more than tripled since the 1960s.

Age-adjusted nationwide obesity and severe obesity rates according to National Health and Nutrition Examination Surveys



This accounts for the population between the ages of 20-74. The obesity category already includes severe obesity.

Source: Centers for Disease Control and Prevention, National Center for Health Statistics • Get the data • Embed • Download image • Download SVG

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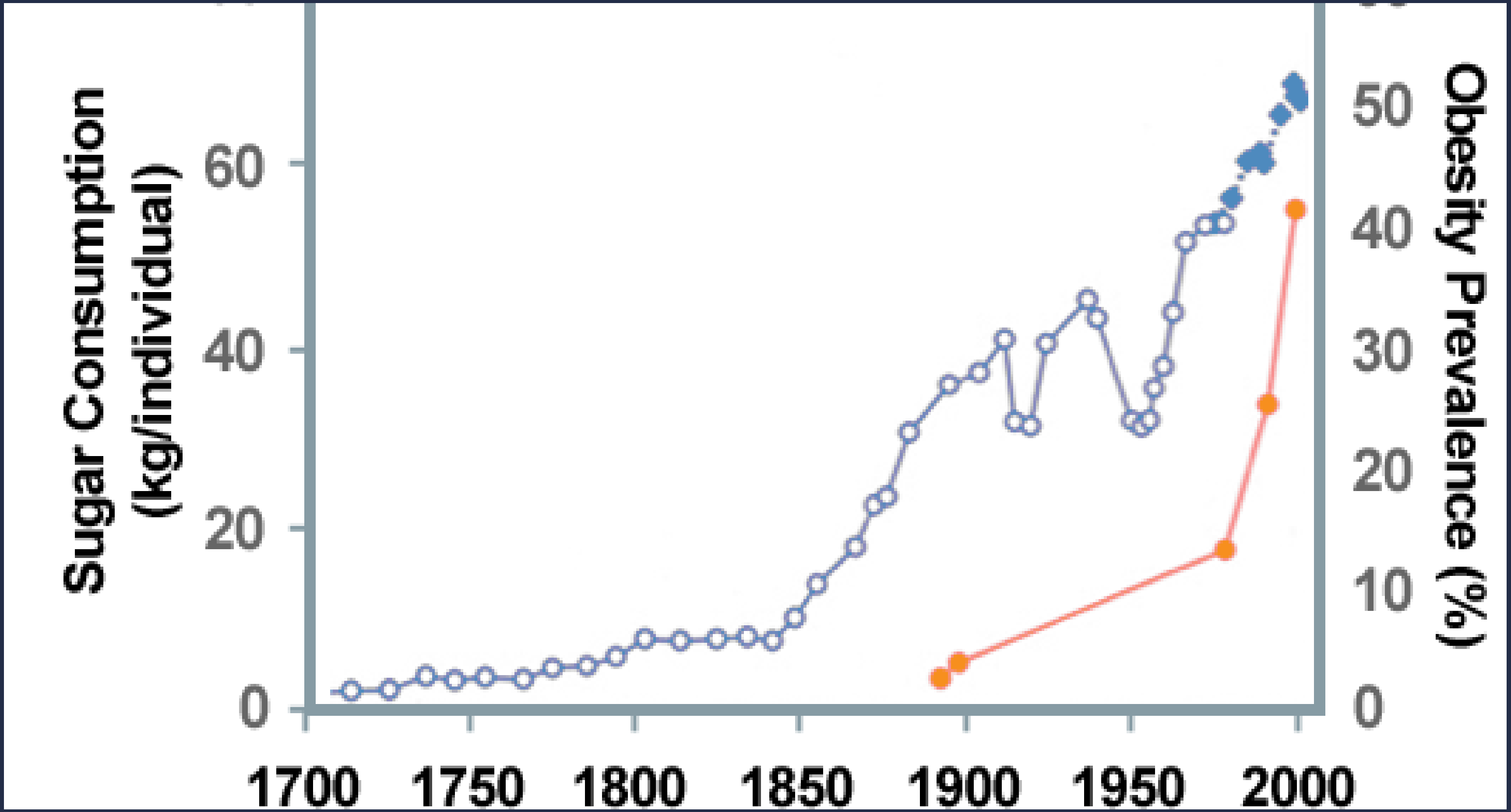

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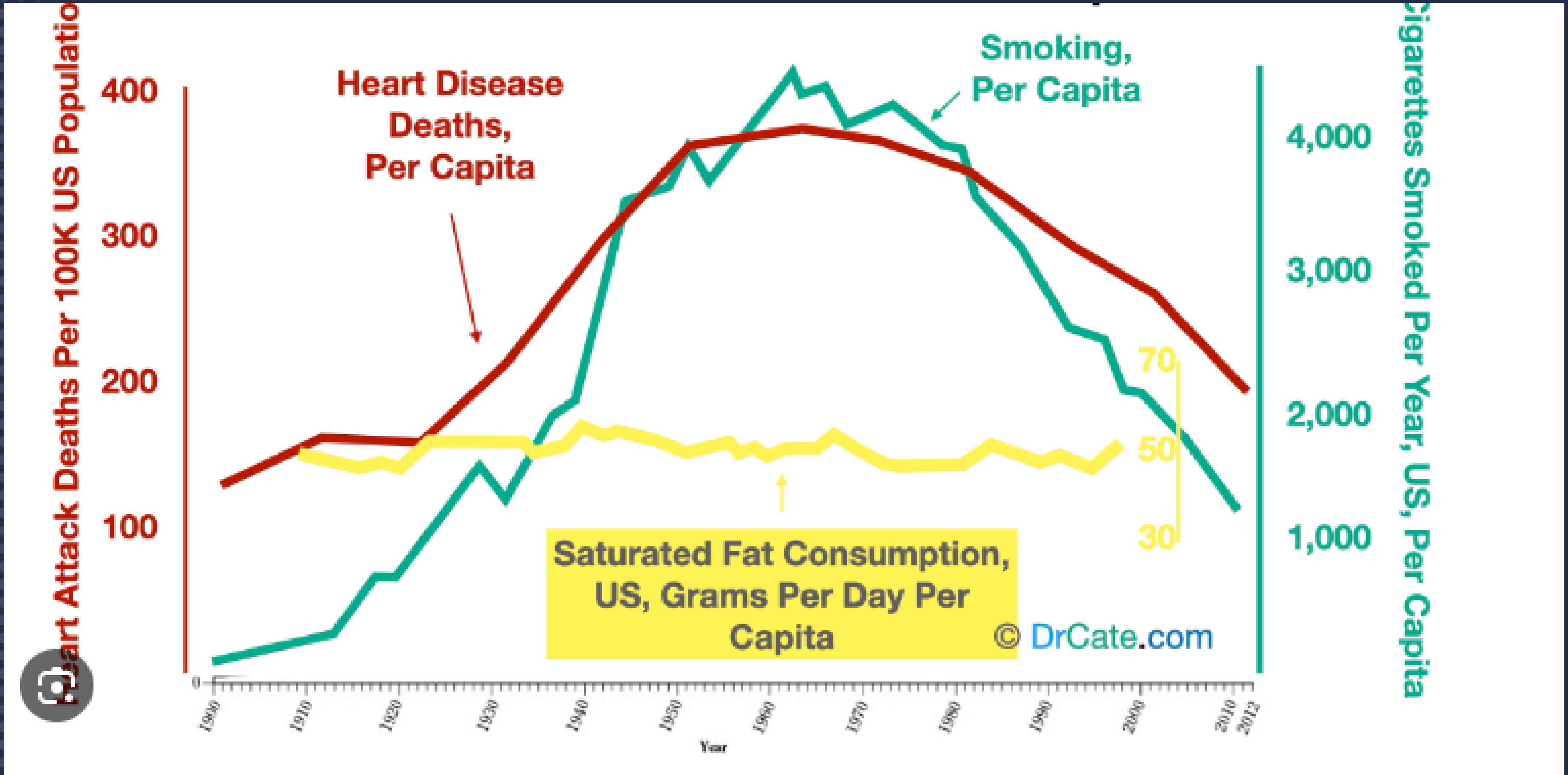

Graph from Dr. Cate Shanahan

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In a healthy adult male of 75 kg (165 lb) with a blood volume of 5 L, a blood glucose level of 5.5 mmol/L (100 mg/dL) amounts to 5 g, equivalent to about a teaspoonful of sugar

USDA National Nutrient Database for Standard Reference, Release 22 (2009)

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To keep all of this in perspective, it's helpful to remember the American Heart Association's recommendations for sugar intake.

- **Men** should consume no more than 9 teaspoons (36 grams or 150 calories) of added sugar per day.

- **Women**, the number is lower: 6 teaspoons (25 grams or 100 calories) per day. Consider that one 12-ounce can of soda contains 8 teaspoons (32 grams) of added sugar! There goes your whole day's allotment in one slurp.

- *Farxiga (dapagliflozin) removes about 75 grams of sugar from blood daily (15 teaspoons)

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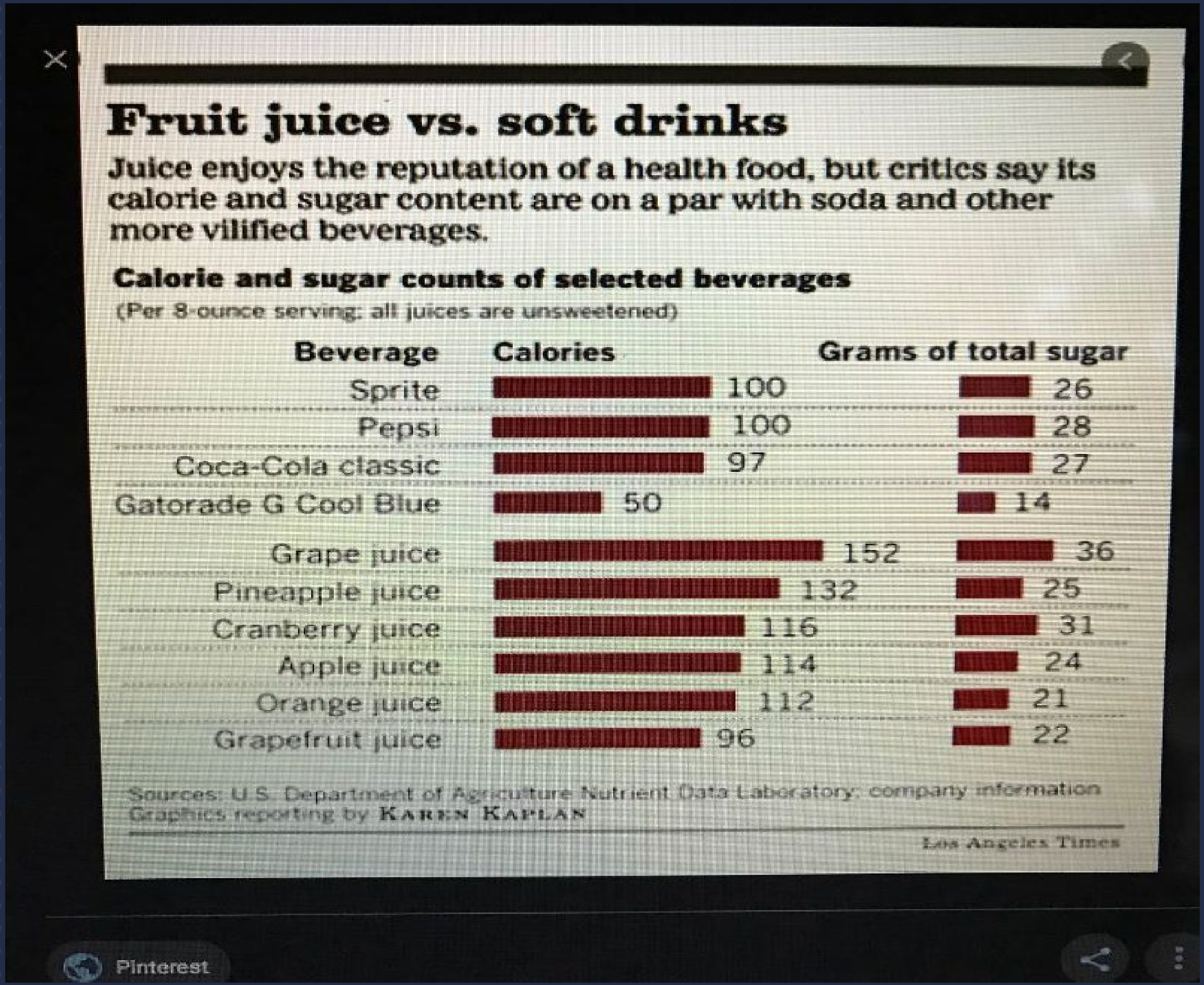
Beverages are the leading category source of added sugars (47% of all added sugars):

•soft drinks – 25%
•fruit drinks – 11%
•sport/energy drinks – 3%
•coffee/tea – 7%

12 oz Drink (*1966) – 16 lbs/year

20 oz drink (*1992) – 26 lbs/year



Fruit juice vs. soft drinks

Juice enjoys the reputation of a health food, but critics say its calorie and sugar content are on a par with soda and other more vilified beverages.

Calorie and sugar counts of selected beverages

(Per 8-ounce serving; all juices are unsweetened)

Beverage	Calories	Grams of total sugar
Sprite	100	26
Pepsi	100	28
Coca-Cola classic	97	27
Gatorade G Cool Blue	50	14
Grape juice	152	36
Pineapple juice	132	25
Cranberry juice	116	31
Apple juice	114	24
Orange juice	112	21
Grapefruit juice	96	22

Sources: U.S. Department of Agriculture Nutrient Data Laboratory; company information
Graphics reporting by KAREN KAPLAN

Los Angeles Times

ms/day of sugar (30 teaspoons)

- 185 grams of sugar (46
4 glazed donuts.

Big Mac - Extra Value Meal

Nutrition Facts

Serving Size 1 Big Mac, 1 large French fries, 1 Large Coke (1,269g)

Amount Per Serving

Calories 1,360 Calories from Fat 520

	% Daily Value*
Total Fat 58g	**89%**
Saturated Fat 12g	**58%**
Trans Fat 1.5g	
Cholesterol 80mg	**26%**
Sodium 1,380mg	**57%**
Total Carbohydrate 190g	**63%**
Dietary Fiber 10g	**40%**
Sugars 95g	
Protein 32g	

Vitamin A 8% • Vitamin C 20%

Calcium 30% • Iron 30%

* Percent Daily Values are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs:

	Calories:	2,000	2,500
Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carb		300g	375g
Dietary Fiber		25g	30g

Microvascular Complications

- **Hyperglycemia:**
- Elevated blood sugar levels, a hallmark of diabetes, directly damage the small blood vessels (microvasculature).

- **Advanced Glycation End Products (AGEs):**
- High glucose levels react with proteins and lipids, forming AGEs, which damage blood vessel walls and impair their function.

- **Oxidative Stress:**
- Hyperglycemia increases the production of reactive oxygen species (ROS), leading to oxidative stress, which damages blood vessels and tissues.

- **Inflammation:**
- Chronic hyperglycemia triggers inflammation in blood vessels, contributing to their damage and dysfunction

Macrovascular Complications

•These include diabetic retinopathy (damage to the retina), nephropathy (kidney damage), heart/peripheral vasculature, and neuropathy (nerve damage).
Macrovascular Disease:

•**Hyperglycemia and Insulin Resistance:**

•These factors contribute to the development of atherosclerosis, a condition where plaque builds up in the large arteries (macrovasculature).

•**AGEs and Oxidative Stress:**

•Similar to microvascular disease, AGEs and oxidative stress play a role in damaging the large arteries and promoting atherosclerosis.

•**Inflammation:**

•Chronic inflammation in the arteries contributes to plaque formation and instability, increasing the risk of cardiovascular events.

•**Impaired Vasodilation:**

•Damage to the endothelium (inner lining of blood vessels) impairs its ability to dilate, leading to increased blood pressure and further cardiovascular damage.

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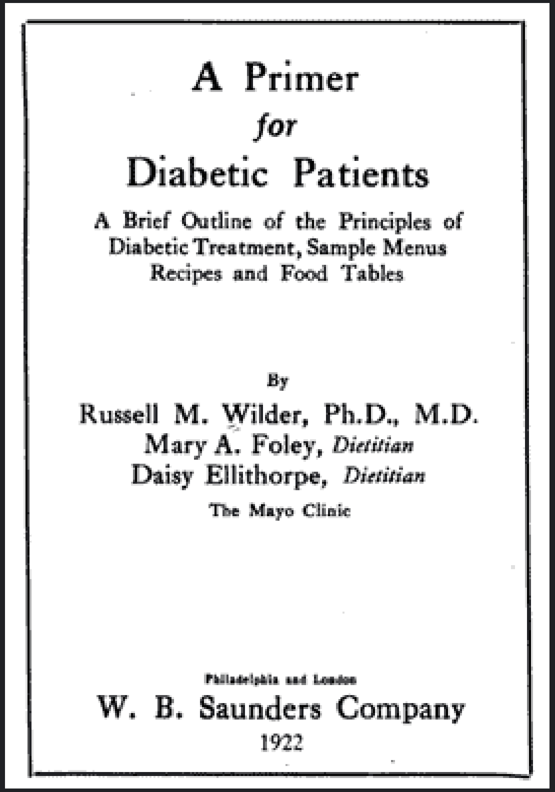


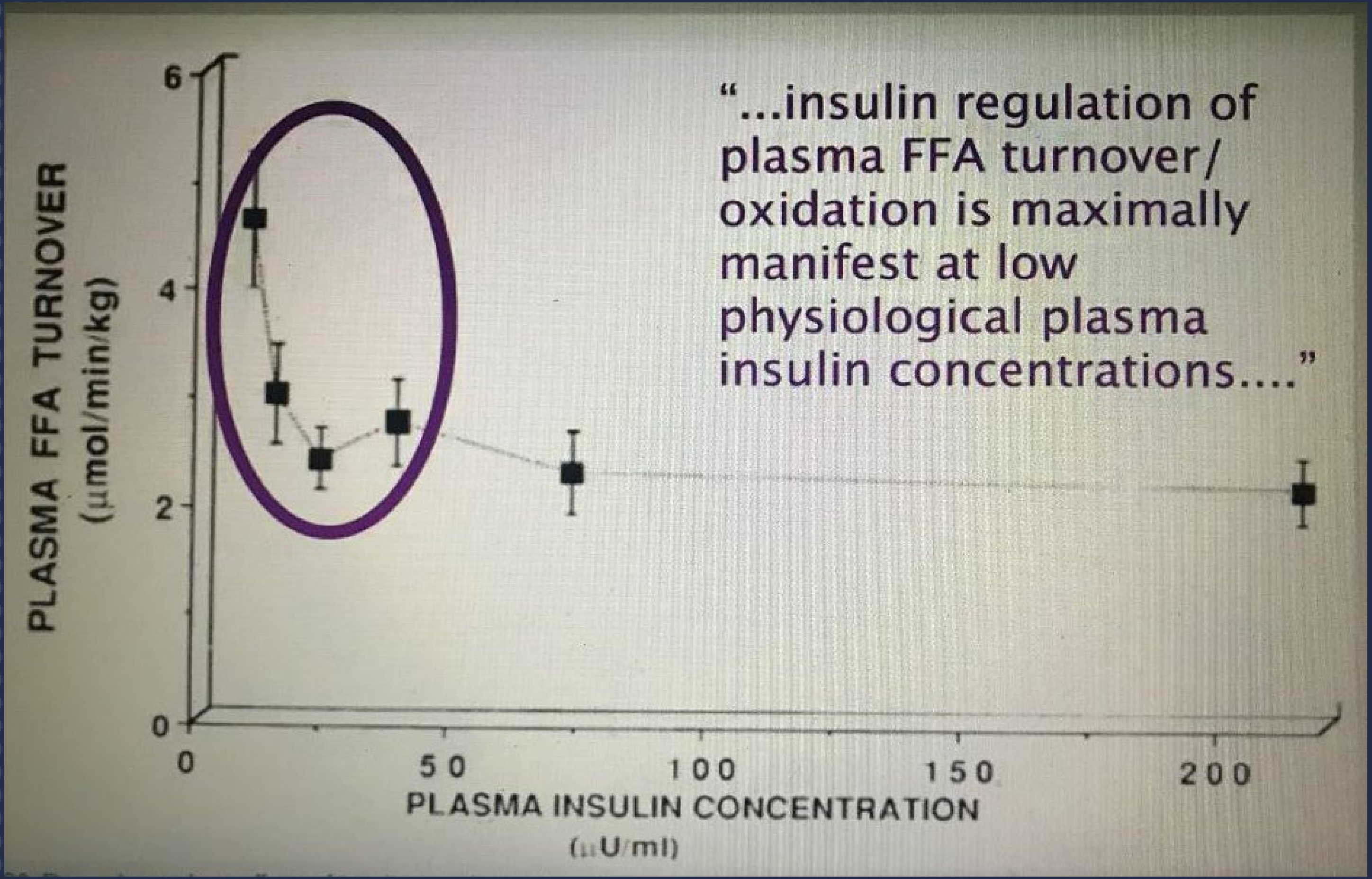
A Primer
for
Diabetic Patients

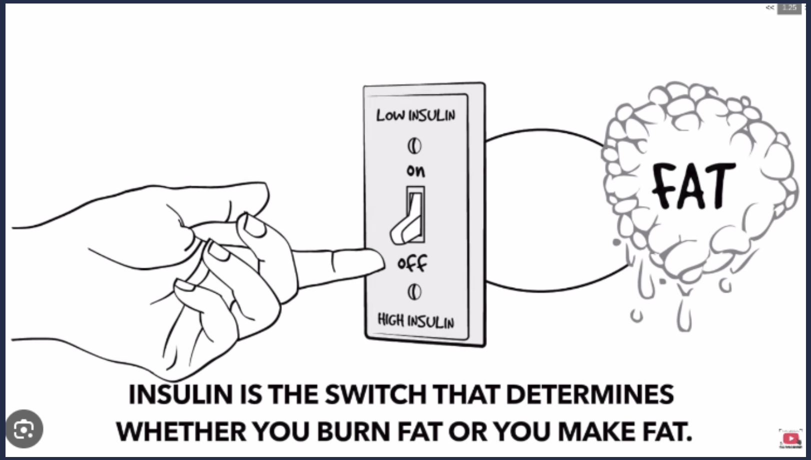
A Brief Outline of the Principles of Diabetic Treatment, Sample Menus Recipes and Food Tables

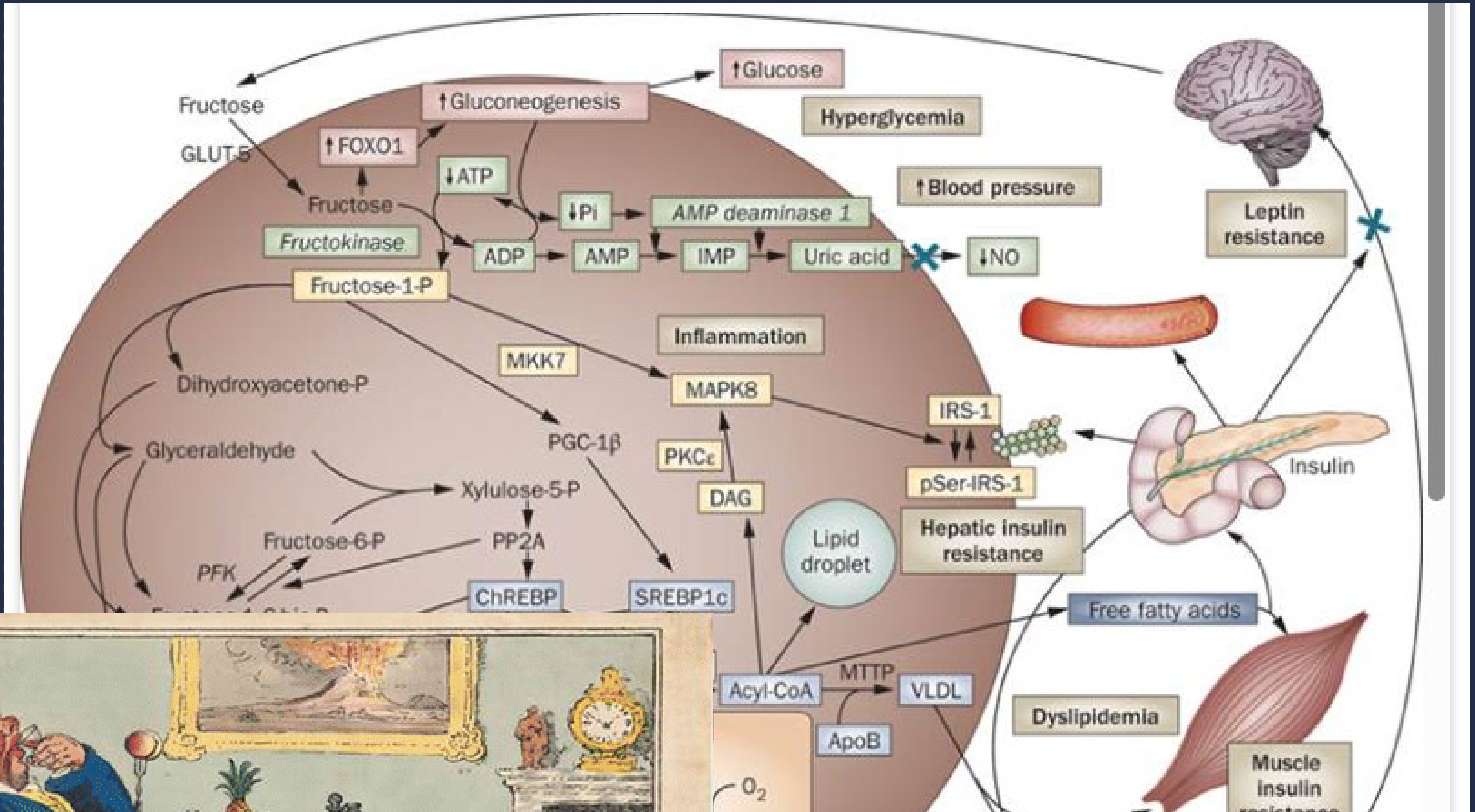
By
Russell M. Wilder, Ph.D., M.D.
Mary A. Foley, *Dietitian*
Daisy Ellithorpe, *Dietitian*
The Mayo Clinic

Philadelphia and London
W. B. Saunders Company
1922

A 100 years ago, this Low Carb Diet was Standard Treatment for Diabetes


"...insulin regulation of plasma FFA turnover/ oxidation is maximally manifest at low physiological plasma insulin concentrations...."
PLASMA FFA TURNOVER
(µmol/min/kg)
0
2
4
6
0
50
100
150
200
PLASMA INSULIN CONCENTRATION
(µU/ml)


LOW INSULIN
ON
OFF
HIGH INSULIN
FAT
INSULIN IS THE SWITCH THAT DETERMINES
WHETHER YOU BURN FAT OR YOU MAKE FAT.



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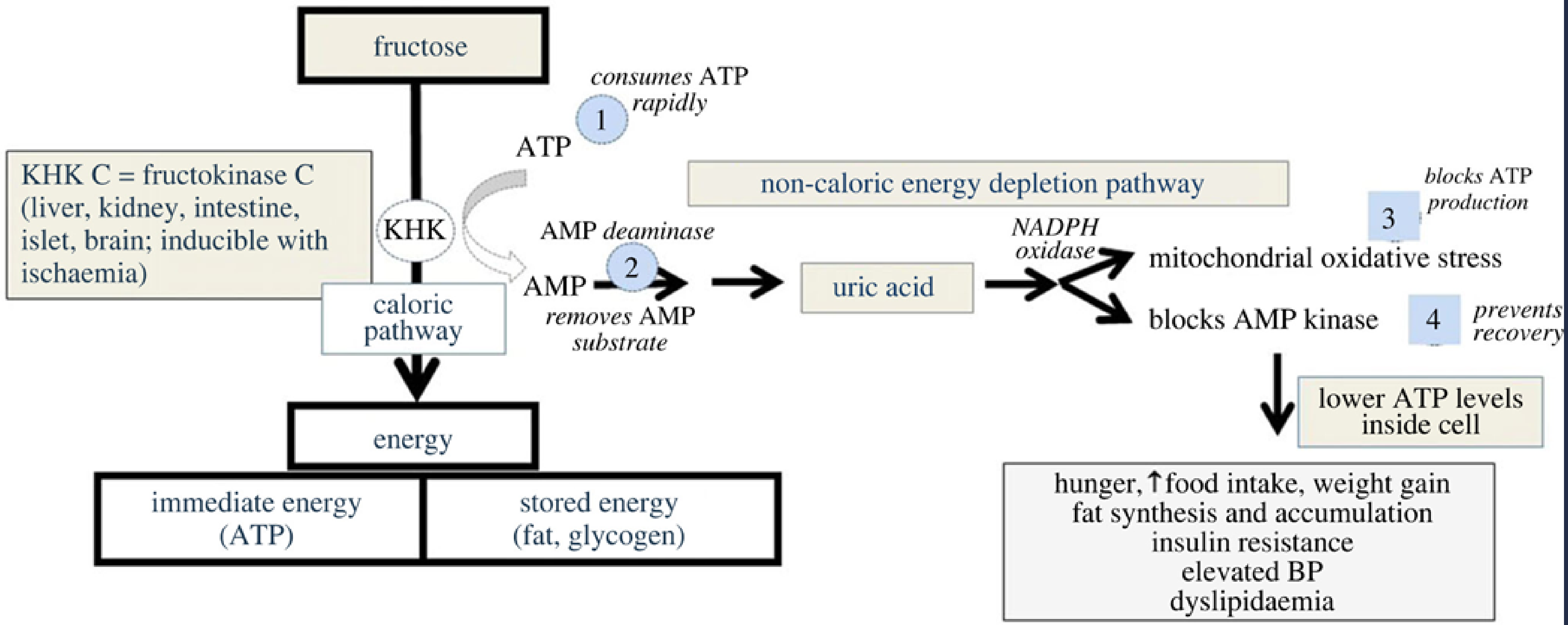

The fructose survival hypothesis for obesity
Richard J. Johnson†, Miguel A. Lanaspa, L. Gabriela Sanchez-Lozada, Dean Tolan, Takahiko Nakagawa, Takuji Ishimoto, Ana Andres-Hernando, Bernardo Rodriguez-Iturbe and Peter Stenvinkel
Published:24 July 2023

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Sugar Industry at Work

Special Communication

November 2016

Sugar Industry and Coronary Heart Disease Research

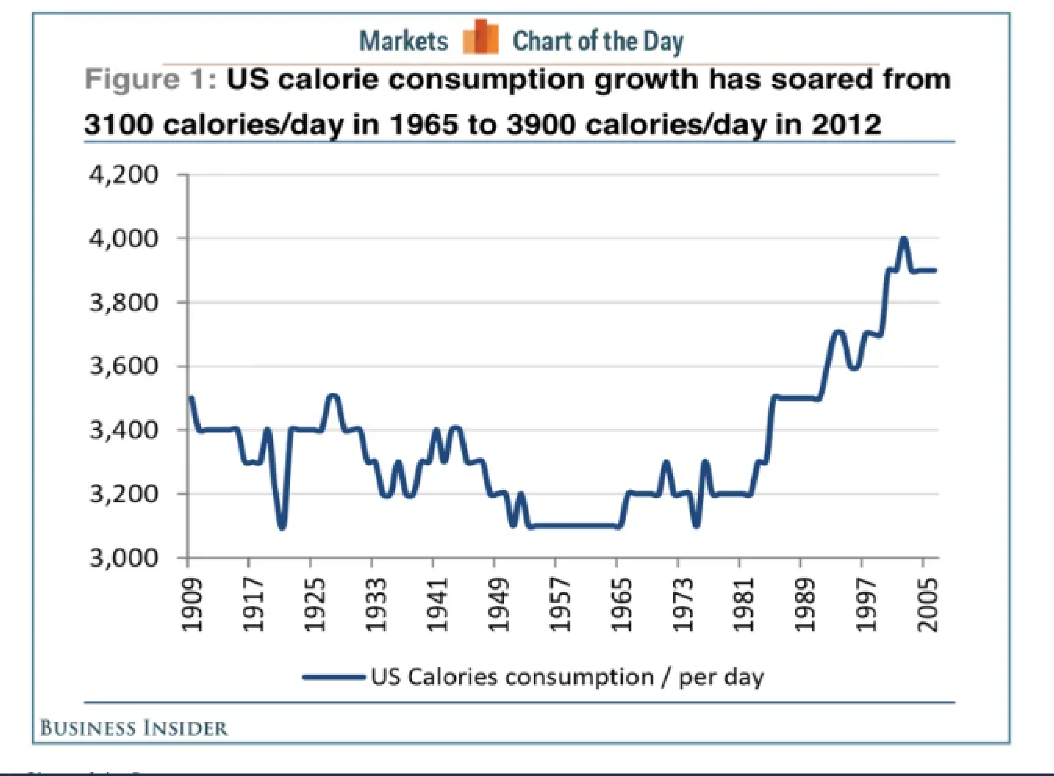
A Historical Analysis of Internal Industry Documents

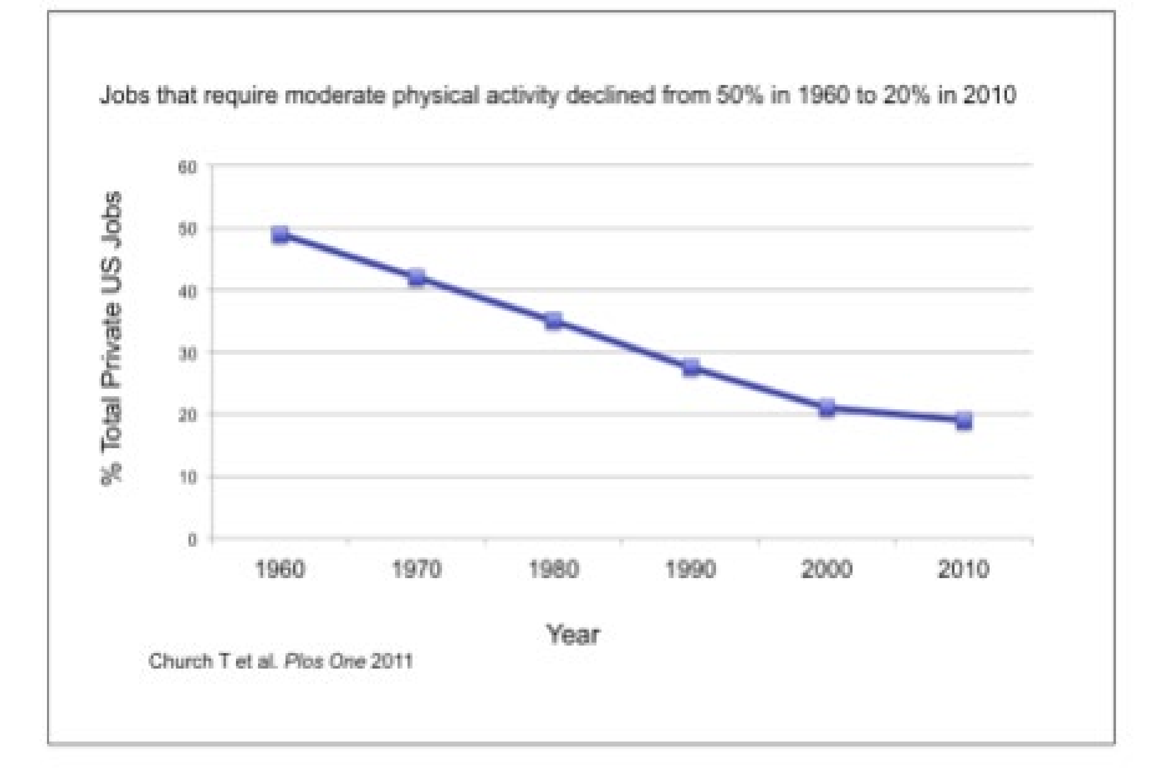
Cristin E. Kearns, DDS, MBA[1,2]; Laura A. Schmidt, PhD, MSW, MPH[1,3,4]; Stanton A. Glantz, PhD[1,5,6,7,8]

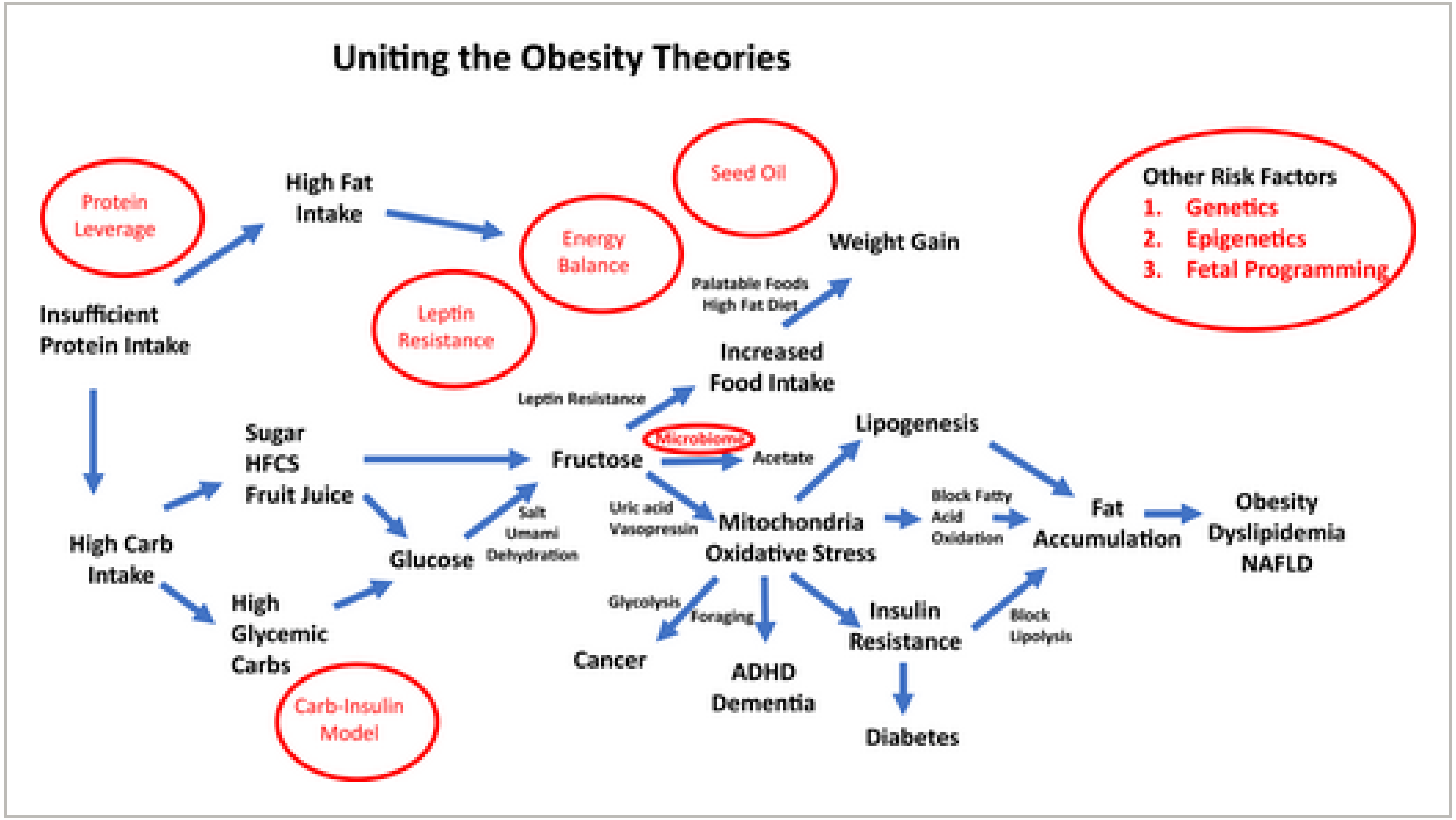
Author Affiliations

JAMA Intern Med. 2016;176(11):1680-1685. doi:10.1001/jamainternmed.2016.5394

"…analyses of sugar industry documents, our findings suggest the industry sponsored a research program in the 1960s and 1970s that successfully cast doubt about the hazards of sucrose while promoting fat as the dietary culprit in CHD."

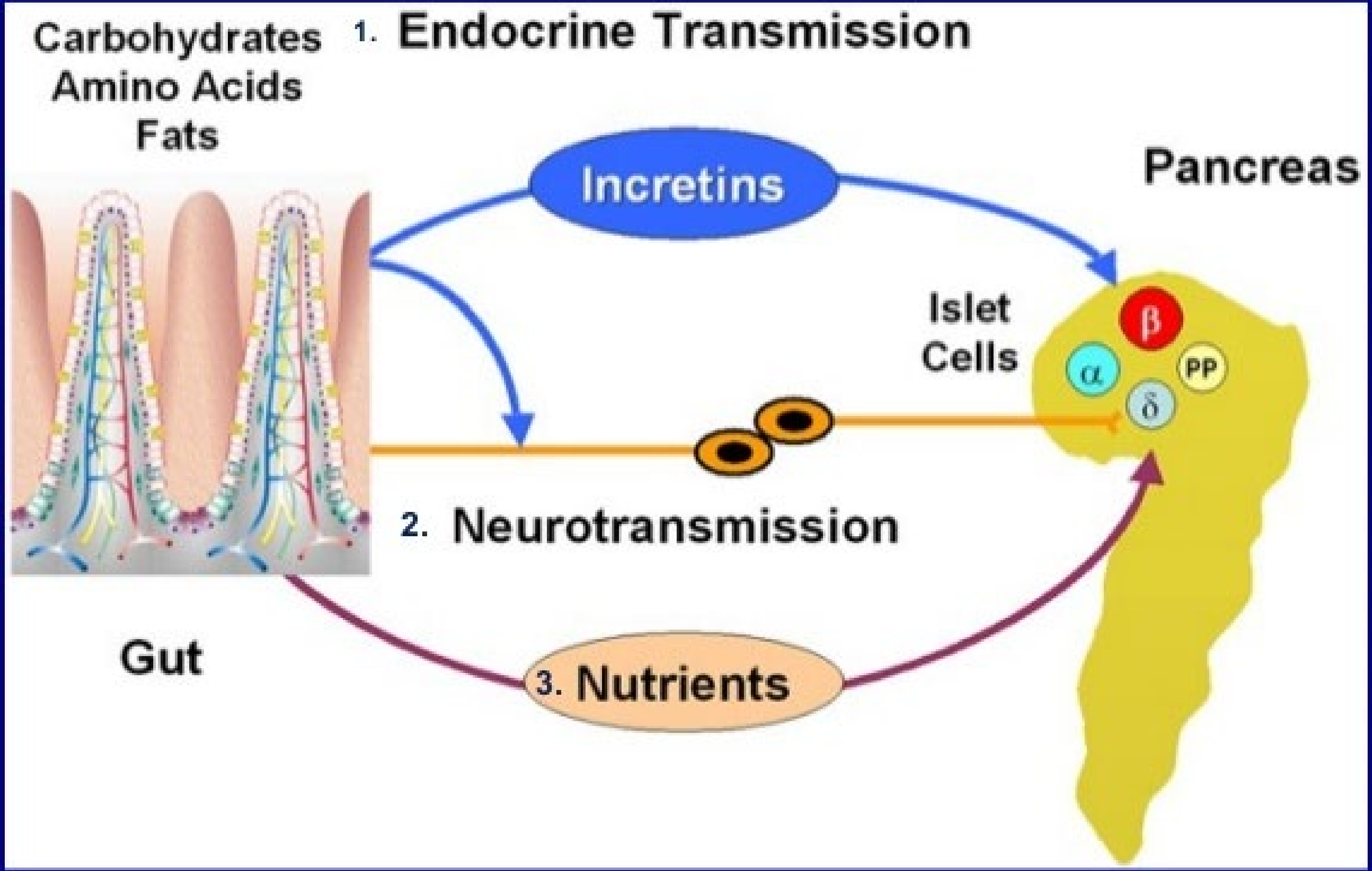

Markets Chart of the Day
Figure 1: US calorie consumption growth has soared from 3100 calories/day in 1965 to 3900 calories/day in 2012
4,200
4,000
3,800
3,600
3,400
3,200
3,000
1909
1917
1925
1933
1941
1949
1957
1965
1973
1981
1989
1997
2005
US Calories consumption / per day
Business Insider


Jobs that require moderate physical activity declined from 50% in 1960 to 20% in 2010
% Total Private US Jobs
60
50
40
30
20
10
0
1960
1970
1980
1990
2000
2010
Year
Church T et al. Plos One 2011

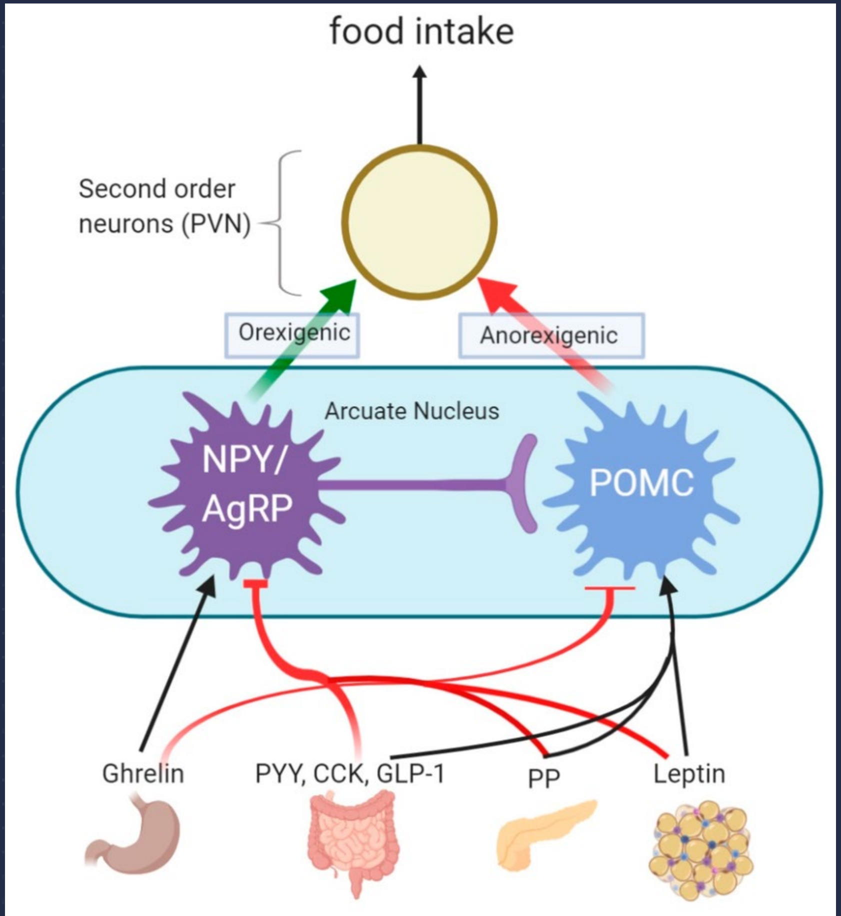


Uniting the Obesity Theories
Protein Leverage
High Fat Intake
Seed Oil
Energy Balance
Leptin Resistance
Weight Gain
Other Risk Factors
1. Genetics
2. Epigenetics
3. Fetal Programming
Palatable Foods
High Fat Diet
Insufficient Protein Intake
Increased Food Intake
Leptin Resistance
Lipogenesis
Sugar
HFCS
Fruit Juice
Microbiome
Fructose
Acetate
Block Fatty Acid Oxidation
Fat Accumulation
Obesity
Dyslipidemia
NAFLD
Salt
Umami
Dehydration
Uric acid
Vasopressin
Mitochondria Oxidative Stress
High Carb Intake
Glucose
Glycolysis
Foraging
Insulin Resistance
Block Lipolysis
High Glycemic Carbs
Cancer
ADHD
Dementia
Carb-Insulin Model
Diabetes

Entero-insular Axis



Hormones involved in satiety and hunger



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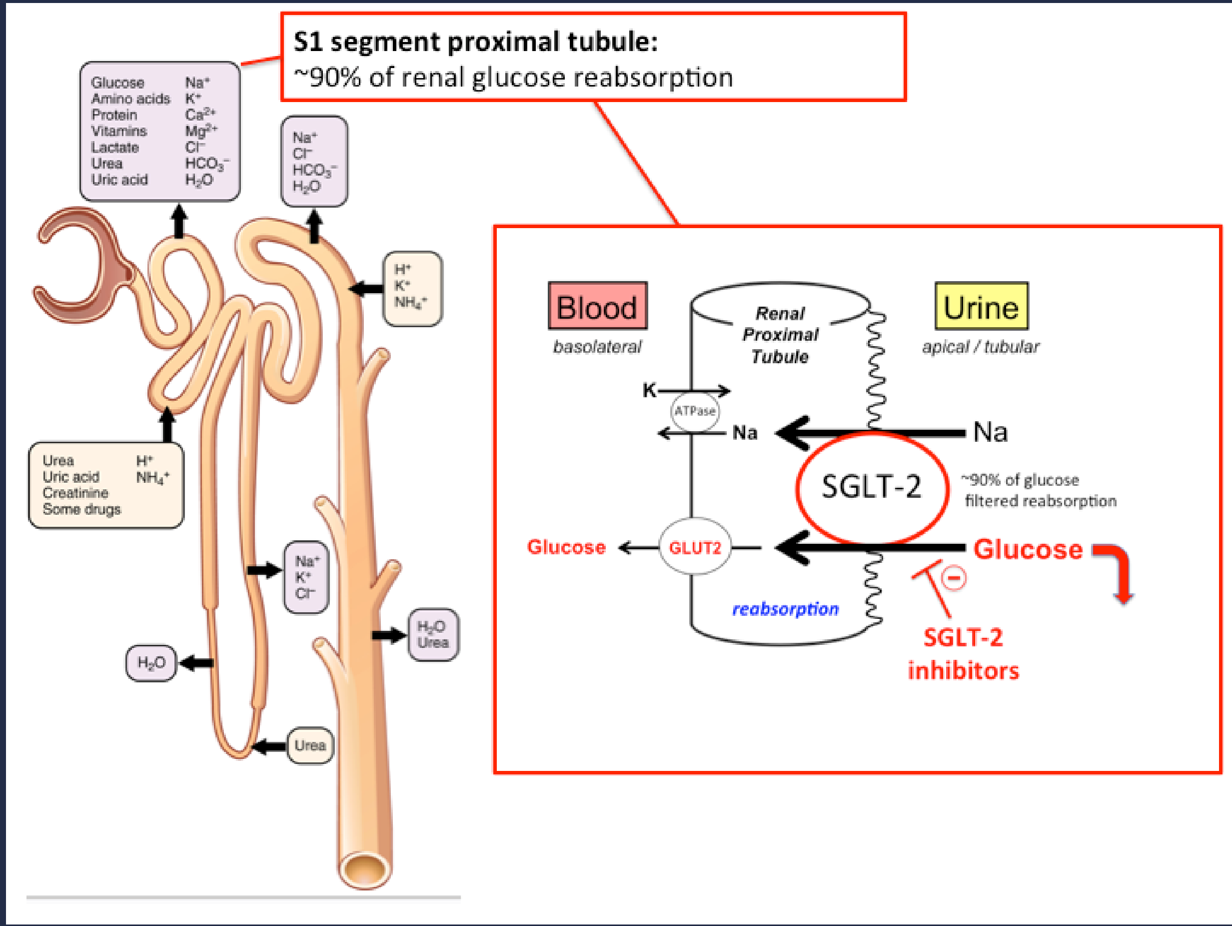
SGLT-2 Inhibitors



SGLT-2 inhibitors

Indirect effects:

Improved glycemic control
Reduced insulin levels
Improved insulin sensitivity
Reduced body weight
Reduced BP
Reduced uric acid level

Direct Effects:

Reduced intra-glomerular pressure
Prevent glomerular and tubuloints. Injury
Reduce toxicity of glc (inflamm/stress)
Prevent renal hypoxia

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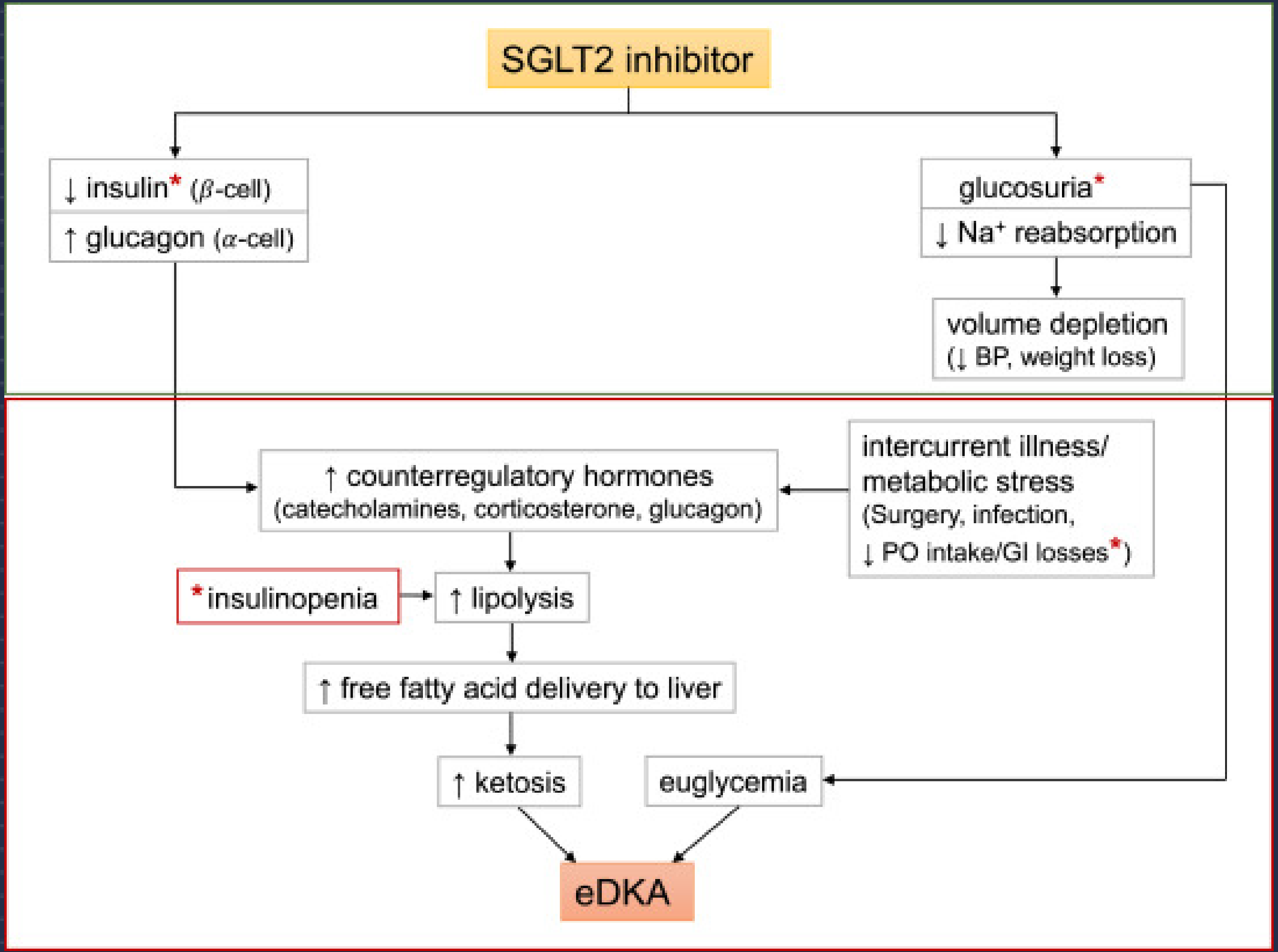
@NWiegley	**EMPA-REG** N= 7020 Cohort: DM2, eGFR 74.1, UACR: ~60% < 30 mg/g Duration: 3.1 years Empaglaflozin vs placebo Event rate %	**CANVAS** N= 10142 Cohort: DM2, eGFR 76.5, UACR: 70% < 30 mg/g Duration: 2.4 years Canagliflozin vs placebo Event rate per 1000 pt-yr	**CREDENCE** N= 4401 Cohort: DM2, eGFR 56.2 +/- 18.2 Mean UACR: 927 mg/g Duration: 2.6 years Canagliflozin vs placebo Event rate per 1000 pt-yr	**DECLARE-TIMI** N= 17160 Cohort: DM2, eGFR 85.4 +/- 16 UACR: NA Duration: 4.2 years Dapagliflozin vs placebo Event rate %	**DAPA-HF** N= 4744 Cohort: DM2 and non-DM, eGFR 66 +/- 19.6; UACR NA Duration: 18.2 months Dapagliflozin vs placebo Event rate %	**DAPA-CKD** N= 4304 Cohort: DM2 & non-DM; eGFR 43.1+/-12.4; UACR 949 mg/g Duration: 2.4 years Dapagliflozin vs placebo Event rate %
Hypoglycemia	**No difference** (1.3 vs 1.5)	**No difference**	**No difference**	**No difference**	**No difference** (0.2 vs 0.2)	More in placebo (0.7 vs 1.3)
DKA	Rare **No Difference** (0.1 vs < 0.1)	Rare **higher in CANA** (0.6 vs 0.3)	Rare **higher in CANA** (2.2 vs 0.2)	Rare **higher in DAPA** (0.3 vs. 0.1)	Rare **3 cases in DAPA** (0.1 vs 0)	Rare 0 in DAPA; 2 in placebo
UTI	**No difference** Complicated (1.7 vs 1.8) Uncomplicated (18.1 vs 18)	**No difference** (40 vs 37)	**No difference** (48 vs 45)	**No difference** (1.5 vs 1.6)	**No difference**	**No difference**
Genital mycotic infections	**Higher in EMPA** (6.4 vs 1.8)	**Higher in CANA** (69 vs 18)	**Higher in CANA** Men (8.4 vs 0.9) Women (12.6 vs 6.1)	**Higher in DAPA** Uncomplicated (0.9 vs 0.1) 6 cases- Fournier gangrene (1 in DAPA; 5 in placebo)	**No difference** (0 vs <0.1%) 1 case- Fournier gangrene (0 in DAPA; 1 in placebo)	**No difference** (0 vs <0.1%) 1 case-m Fournier gangrene (0 in DAPA; 1 in placebo)
Bone fracture	**No difference** (3.8 vs 3.9)	**Higher in CANA** (15.4 vs 11.9)	**No difference** (11.8 vs 12.1)	**No difference** (5.3 vs 5.1)	**No difference** (2.1 vs 2.1)	**Higher in DAPA** (4% vs 3.2%)
Limb amputation	**No difference**	higher in CANA (6.3 vs 3.4)	**No difference** (12.3 vs 11.2)	**No difference** (1.4 vs 1.3)	**No difference** (0.5 vs 0.5)	**No difference** (1.6 vs 1.8)

Euglycemic DKA



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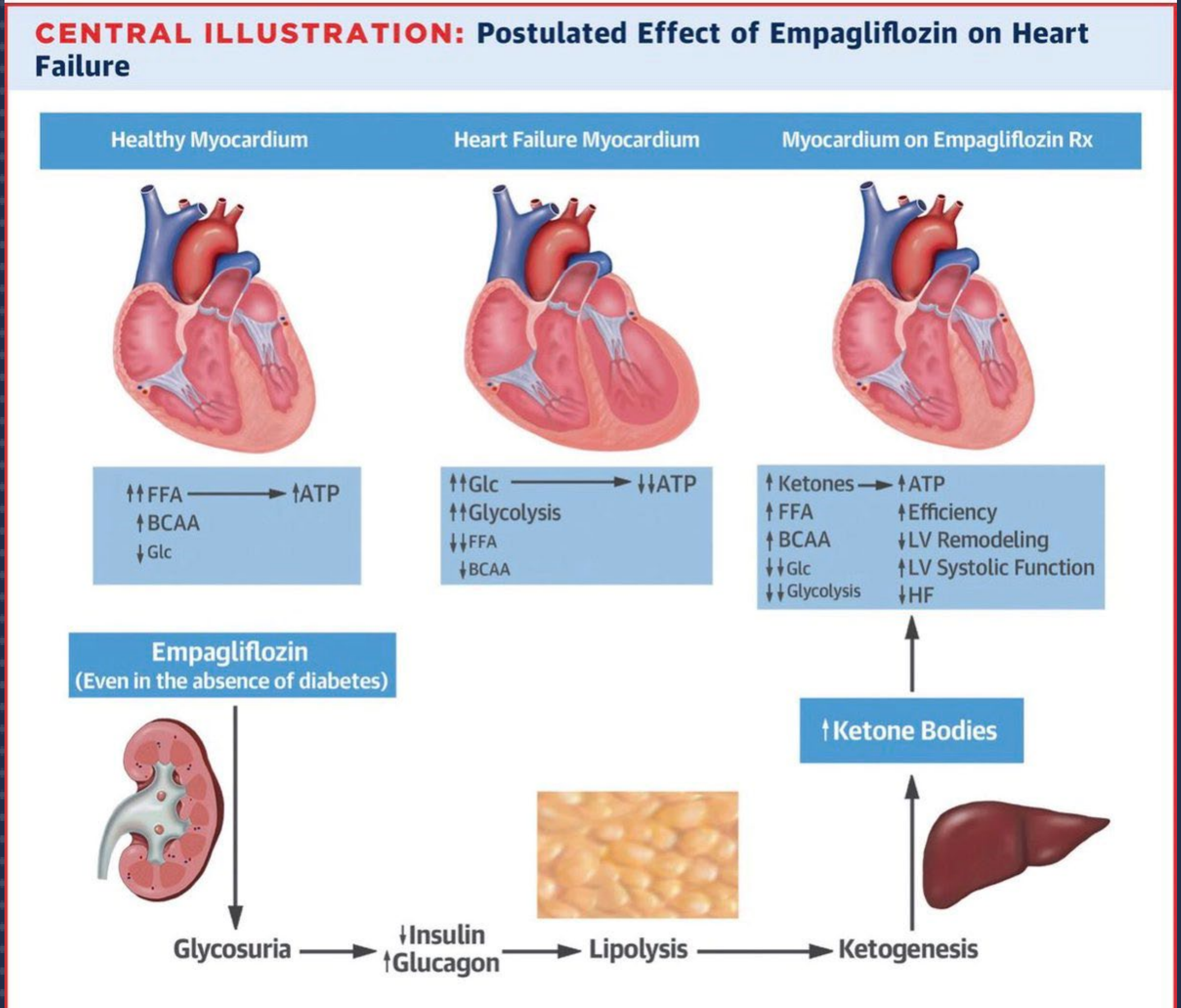

Santos-Gallego, C.G. et al. J Am Coll Cardiol. 2019;73(15):1931-44.

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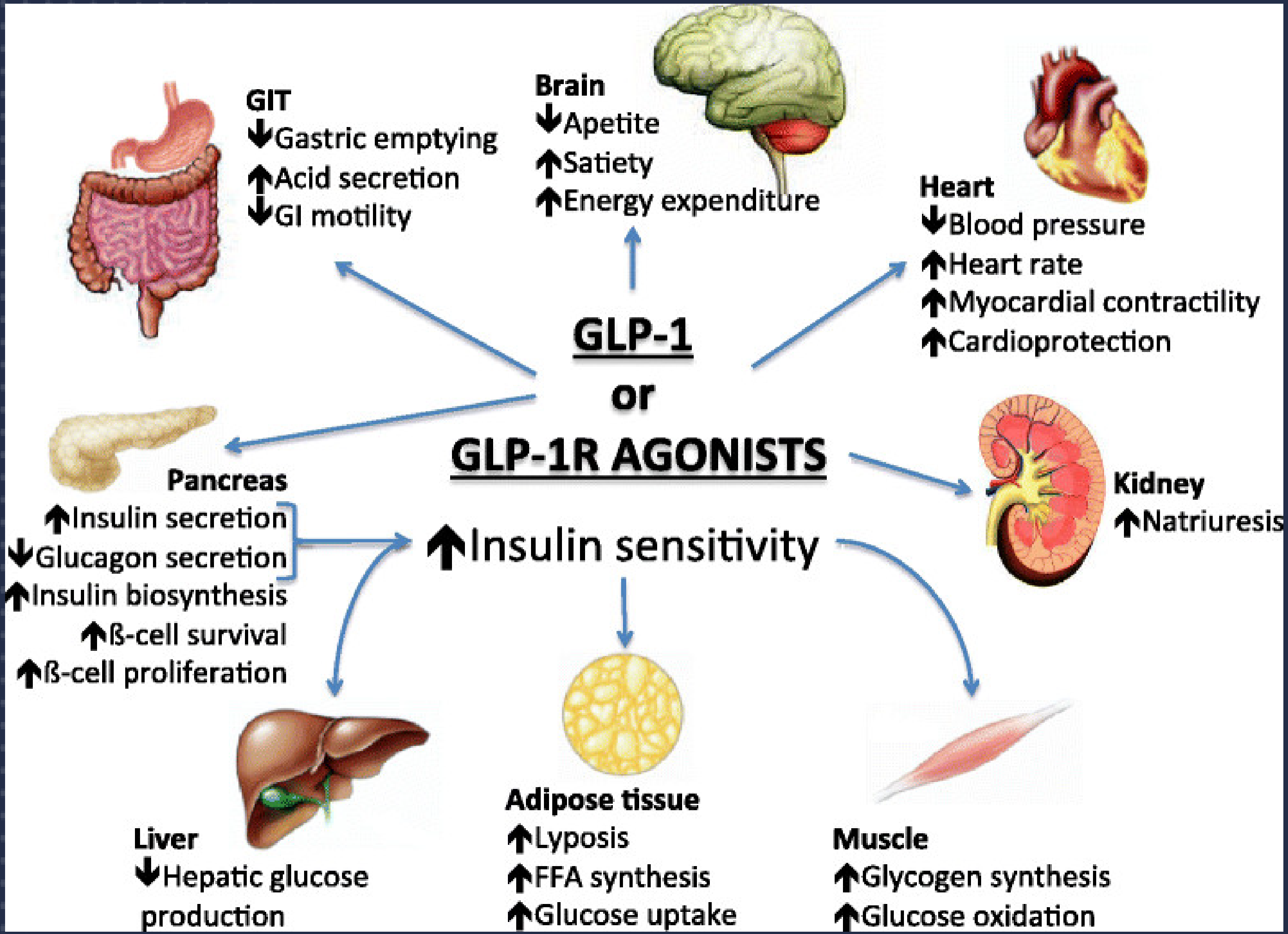
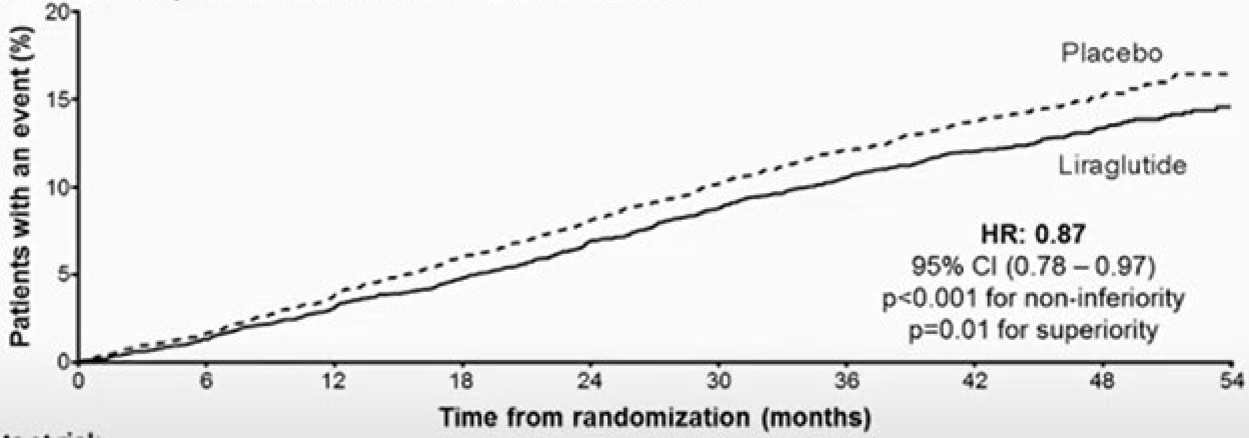
GLP-1


GIT
↓Gastric emptying
↑Acid secretion
↓GI motility
Brain
↓Apetite
↑Satiety
↑Energy expenditure
Heart
↓Blood pressure
↑Heart rate
↑Myocardial contractility
↑Cardioprotection
GLP-1
or
GLP-1R AGONISTS
Pancreas
↑Insulin secretion
↓Glucagon secretion
↑Insulin biosynthesis
↑ß-cell survival
↑ß-cell proliferation
↑Insulin sensitivity
Kidney
↑Natriuresis
Liver
↓Hepatic glucose production
Adipose tissue
↑Lyposis
↑FFA synthesis
↑Glucose uptake
Muscle
↑Glycogen synthesis
↑Glucose oxidation

LEADER: Liralgutide Effect and Action in Diabetes Evaluation of Cardiovascular Outcome Results

Primary outcome

CV death, non-fatal myocardial infarction, or non-fatal stroke



Patients at risk

Liraglutide	4668	4593	4496	4400	4280	4172	4072	3982	1562	424
Placebo	4672	4588	4473	4352	4237	4123	4010	3914	1543	407

The primary composite outcome in the time-to-event analysis was the first occurrence of death from cardiovascular causes, non-fatal myocardial infarction, or non-fatal stroke. The cumulative incidences were estimated with the use of the Kaplan-Meier method, and the hazard ratios with the use of the Cox proportional-hazard regression model. The data analyses are truncated at 54 months, because less than 10% of the patients had an observation time beyond 54 months. CI: confidence interval; CV: cardiovascular; HR: hazard ratio.

Presented at the American Diabetes Association 76th Scientific Sessions, Session 3-CT-SY24. June 13 2016, New Orleans, LA, USA

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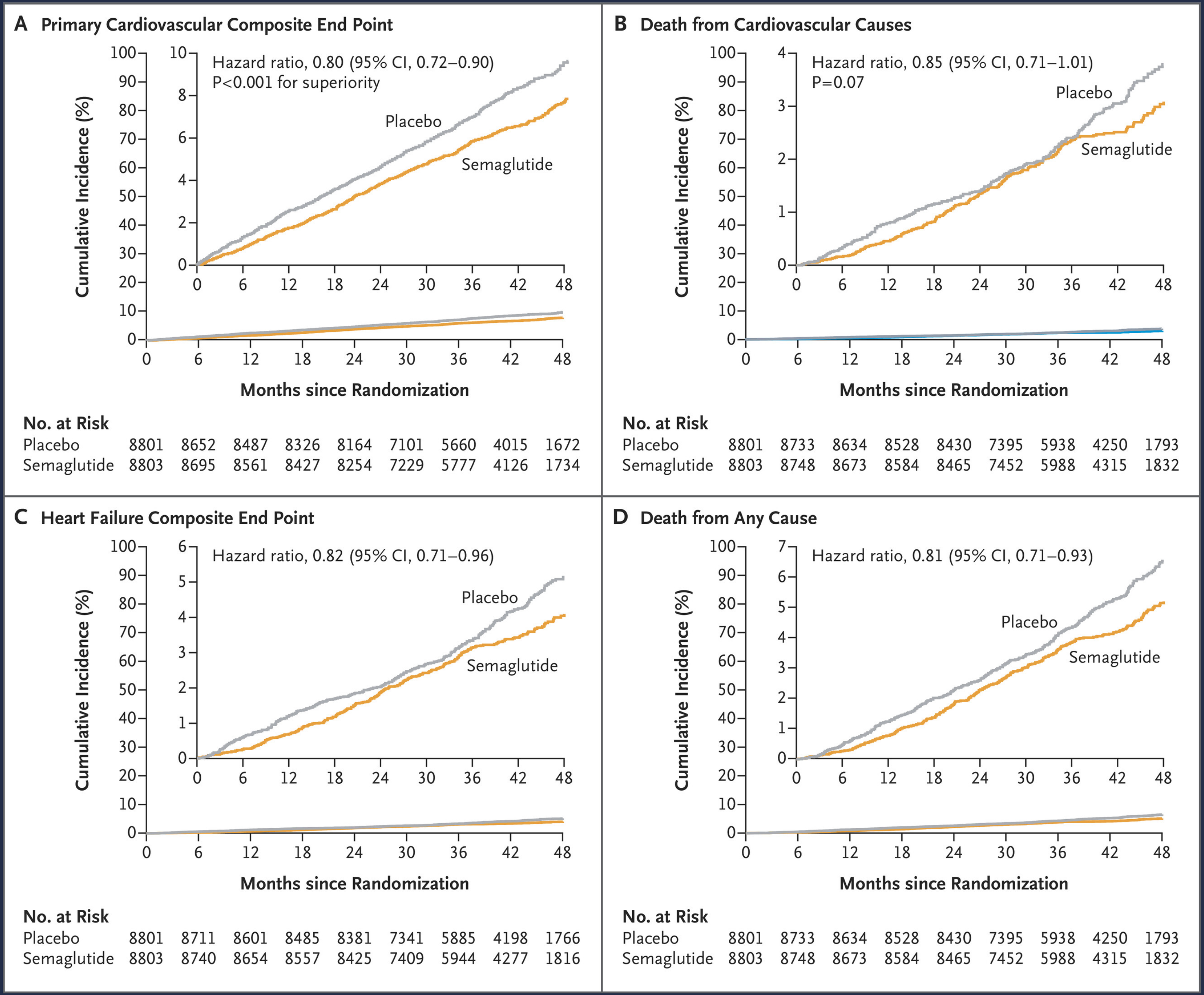
SELECT Trial



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How do we fix this obesity and hyperglycemia?

1) HAVE to identify and eliminate high-fructose containing products without fiber
2) HAVE to reduce glucose which can get converted to fructose when in excess
3) HAVE to maintain lower insulin levels – reduced meal frequency

   1) Reduce or discontinue fructose and glucose- (Low Carb)
   2) Restrict timing of food consumption – (Time Restricted Eating)

Food Guide

Low-Carb Meal Blueprint

FOR RECIPES, CHECK OUT: WWW.DIETDOCTOR.COM

1 LOW CARB VEGETABLES (50% OF PLATE)

leafy greens
beet greens
mustard greens
leaf lettuce
collard greens
dandelion greens
microgreens
bok choy
watercress
romaine
spinach
sprouts
arugula
endive
chard
kale

nightshades
eggplant
*tomatoes
bell peppers

onion family
green onions
onions
shallots
garlic
leeks

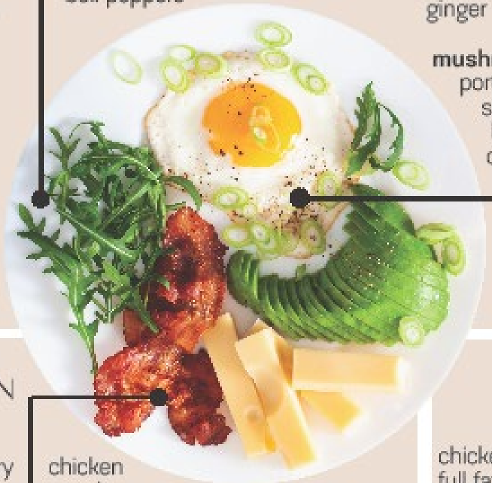
herbs & spices

roots
rutabagas
radishes
celeriac
turnips
daikon
jicama
ginger

crucifers
brussels sprouts
cauliflower
cabbage
broccoli

mushrooms
portobello
shiitake
button
cremini
morel

miscellaneous
green beans
artichokes
asparagus
avocado
cucumber
celery
fennel
spaghetti squash
summer squash
zucchini



2 PALM SIZE PROTEIN

animal
full-fat (FF) dairy
whey protein
hard cheeses
eggs
ground beef
bacon
chuck roast
thighs/breasts
breakfast sausage
kielbasa
bratwurst
polish sausage
beef jerky
pork rinds

chicken
pork
beef
elk
deer
duck
turkey
pork loin
pork ribs
ham steaks
venison
liver

lamb
bison
buffalo
salmon
shrimp
tuna
trout

plant
*nuts
seeds
tempeh
tofu
*peanuts

low sugar fruit & sweeteners
*blueberries
*strawberries
*blackberries
*raspberries
*lemon
*lime
*grapefruit
*stevia
*monkfruit

3 HEALTHY FAT (UNTIL SATISFIED)

chicken stock
full fat yogurt

sugar-free:
-dressings
-sauces
-ranch

cream
fish oil
avocado oil
MCT oil
coconut oil
full-fat dairy
lard + tallow
butter + ghee
peanut butter
sunflower butter
almond butter
greek yogurt
olives (and oil)
bacon (and grease)
nuts + seeds (and oil)
fat from quality protein

***in moderation (Only a handful)**

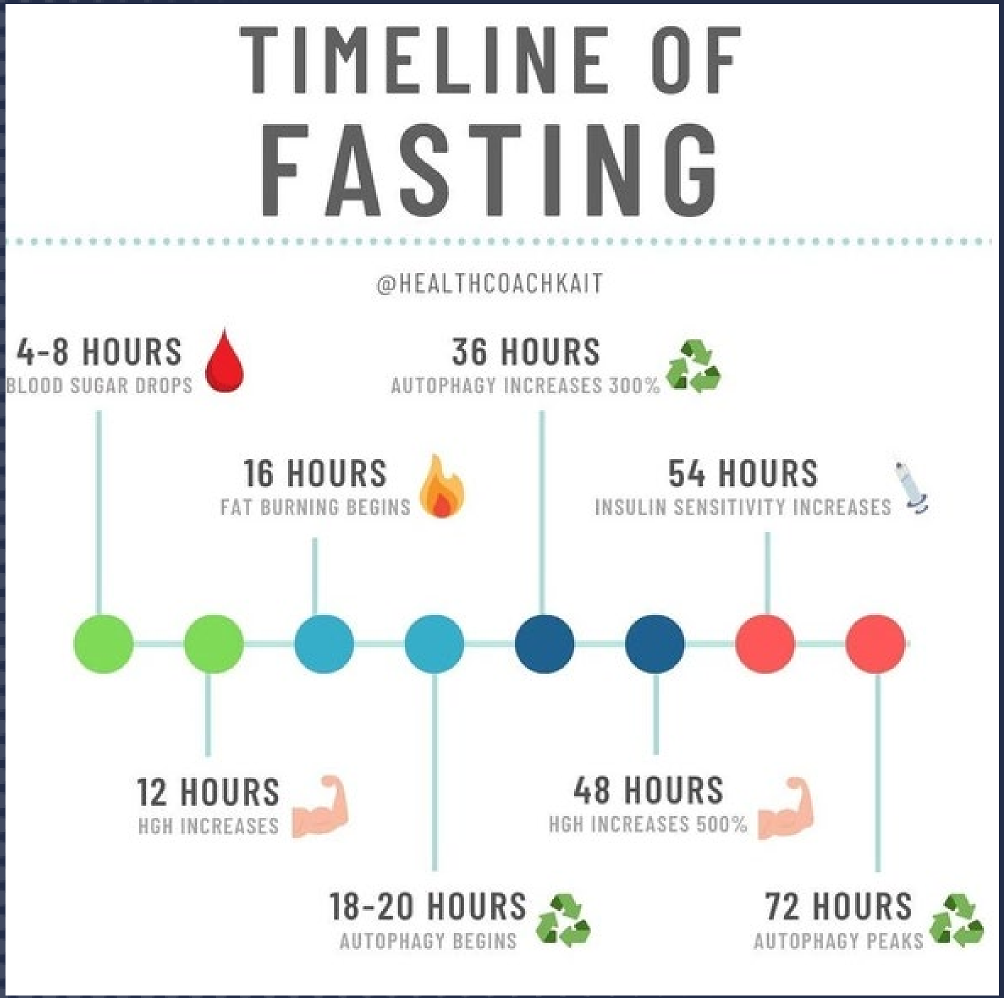
Find the following videos on YouTube:

- Magic Pill
- 23 1/2 hour day
- Tim Noakes- Medical Aspects of Low Carb
- Amber O'Hearn- Ketofest 2017
- Widowmaker

PODCASTS:

- Jason Fung- Obesity Code

Keto at Heart



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Differential Effects of One Meal per Day in the Evening on Metabolic Health and Physical Performance in Lean Individuals

Emma C E Meessen [1], Håvard Andresen [2], Thomas van Barneveld [1], Anne van Riel [1], Egil I Johansen [2], Anders J Kolnes [3], E Marleen Kemper [4], Steven W M Olde Damink [5] [6], Frank G Schaap [5] [6], Johannes A Romijn [7], Jørgen Jensen [2], Maarten R Soeters [1]

Affiliations + expand

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Conclusion: A single meal per day in the evening lowers body weight and adapts metabolic flexibility during exercise via increased fat oxidation whereas physical performance was not affected.

Case 1: Pt GR, 65 yo female with persistent AF, HTN, HFpEF, hyper-insulinemia (fasting insulin 22.7) with normal A1c 5.5, mild coronary calcification (ASCVD – subclinical), BMI 35.88 (Initial visit 2/8/24).

(Follow-up 4/8/24)

8 week follow-up on OMAD (+) Farxiga (+) Low-carb, whole food diet:

Result: 22 lbs weight loss. Fasting Insulin Level: 8.1

BP 10/9/23: Large cuff: 142/80
Regular cuff: 158/88
Her automatic cuff: 157/94

BP 4/8/24 follow-up: 126/64 mmHg

Case 2: RW – 54 y/o female with hypertension, NAFLD, and class II obesity.

Starting weight: 216 lbs (98 kg), BMI: 37.1

Treated with OMAD (+) low-carb

Initial BP: 133/83 mmHg (on HCTZ 25 mg/day)

Results:

Significant weight loss: 12 month follow-up – 167 lbs, (76.1 kg) – BMI 28.8

Dropped from class II obesity to overweight clinical status

Repeating hepatic imaging to reassess steatosis

Consider discontinuation of all anti-hypertensives (BP trend – 108 /66 to 118/70 mmHg only on HCTZ 12.5 mg/day)

Side effects: Had to purchase all new clothes

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Case 3 – SL, 44 yo male with pre-mortem obesity.

Severe HTN on (2) agents (BP's 181/75 mmHg, 145/105 mmHg, and 190/98 mmHg)
Insulin resistance
OSA
BMI-90's
Chronic anemia – Hgb 10, Hct 35.5
Chronic lymphedema with non-healing LE wounds
Chronic hypoxic respiratory failure (requiring home O2 and Eliquis for presumed PE)

Results GLP-1 RA and 27 day fasting protocol:

Overall impact:

1) Net loss of > 120 lbs
2) Significant improvement in perceived mental health
3) Significant improvement in ambulatory ability and walking ability – METS level > 4 without symptoms
4) No evidence of cardiac damage (normal Trop's) and normal BNP (no CHF) and he reached (likely) euvolemic status
5) Off all supplemental O2. Hypercapnic/hypoxemia has corrected
6) Correction in Hgb (without blood products or iron supplementation)
7) Correction of insulin resistance
8) All non-healing wounds on LE have healed
9) Significant change in measured biomorphic data
10) Reduction in LV mass on echo (2 weeks into protocol- final echo pending)
11) Firsts: (first shower in 3 years, regained ability to touch toes on (L) foot, regained ambulatory.
12) Was transitioned for success lap gastric sleeve with Dr. Thomas Shin

As anticipated with fast – Ketones rose and peaked in the 3's and uric acid peaked around 16. We anticipate these to change with re-feeding and may normalize (uric acid) by surgery.

Pre-albumin was not measure prior to fast but is mildly reduced. Albumin remains in target range and has improved / increased during fast. (wish we got this prior to fast)

Hs-crp did go up, but is not as high as it has been in the past. This may be a reflection of chronic MSK issues related to back pain and weight support and increased walking.

LFT's were higher than in the past – but < 3x ULN. Statin was held prior to fast

Born: 1930's -→1990

At 27 yrs old – decided to fast

Goal to achieve weight 180 lbs

Fasted 382 days (lost 22 lbs / month)

Weight: 456→180 lbs (lost 276 lbs)

At time of death 1990 → 196 lbs (16 lbs)

Features of a successful therapeutic fast of 382 days' duration

W. K. STEWART
M.D., F.R.C.P.E., M.R.C.P. Lond.

LAURA W. FLEMING
B.Sc.

University Department of Medicine, Dundee DD1 4HN, Scotland

Summary

A 27-year-old male patient fasted under supervision for 382 days and has subsequently maintained his normal weight. Blood glucose concentrations around 30 mg/100 ml were recorded consistently during the last 8 months, although the patient was ambulant and attending as an out-patient. Responses to glucose and tolbutamide tolerance tests remained normal. The hyperglycaemic response to glucagon was reduced and latterly absent, but promptly returned to normal during carbohydrate refeeding. After an initial decrease was corrected, plasma potassium levels remained normal without supplementation. A temporary period of hypercalcaemia occurred towards the end of the fast. Decreased plasma magnesium concentrations were a consistent feature from the first month onwards. After 100 days of fasting there was a marked and persistent increase in the excretion of urinary cations and inorganic phosphate, which until then had been minimal. These increases may be due to dissolution of excessive soft tissue and skeletal mass. Prolonged fasting in this patient had no ill-effects.

Introduction

Current opinion on fasting therapy for the obese is perhaps best summarized by the view that fasting for relatively short periods is beneficial, whereas longer term fasting (i.e. longer than 40 days) has an element of risk attached (Lawlor & Wells, 1971). It is generally agreed that the long-term outlook for the achievement and maintenance of ideal body weight is poor (MacCuish, Munro & Duncan, 1968; Lawlor & Wells 1971) unless a weight close to the ideal is achieved during the supervised phase (Munro *et al.*, 1970), a process which in the majority of cases would involve a prolonged rather than a short-term fast.

Several years ago a grossly obese young man presented himself for treatment. Initially there was no intention of making his fast a protracted one, but since he adapted so well and was eager to reach his 'ideal' weight, his fast was continued into what is presently the longest recorded fast (*Guinness Book of Records*, 1971). This report describes some of the features which emerged during the 382 days of his fast.

Requests for reprints: Dr W. K. Stewart, Department of Medicine, University, Dundee DD1 4HN, Scotland.

Methods

Patient treatment

Patient A.B. aged 27 years, weighed on admission 456 lb (207 kg). During the 382 days of his fast, vitamin supplements were given daily as 'Multivite' (BDH), vitamin C and yeast for the first 10 months and as 'Paladac' (Parke Davis), for the last 3 months. Non-caloric fluids were allowed *ad libitum*. From Day 93 to Day 162 only, he was given potassium supplements (two effervescent potassium tablets BPC supplying 13 mEq daily) and from Day 345 to Day 355 only he was given sodium supplements (2·5 g sodium chloride daily). No other drug treatment was given. Initially, the patient was treated in hospital but for the greater part of the time he was allowed home, attending regularly as an out-patient for check-up. Twenty-four hour urine collections were made periodically throughout the fast. His mean urinary creatinine excretion was 1541 mg/24 hr, with a ±25% variation, which indicates reasonable collections. No faecal collections were made, but evacuation was in fact infrequent, there being 37–48 days between stools latterly. Venous blood specimens were obtained approximately once a fortnight and tests of carbohydrate metabolism (intravenous glucose tolerance, tolbutamide and glucagon tests) (Marks & Rose, 1965; Oakley, Pyke & Taylor, 1968) were undertaken on nine occasions during the fast. All three tests were carried out consecutively on the same day, following a standard procedure whereby the tolbutamide was given $1\frac{1}{2}$ hr after the glucose infusion, when blood glucose concentrations had returned to normal, and the glucagon was given $1\frac{1}{2}$ hr after the tolbutamide.

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