

Advances in Diabetes Management – Philosophy to Medications to Devices

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Approach to a Patient:
What is Type 2 Diabetes?

... It is **not** about blood sugar

It **is** about insulin resistance

Baseline patient education is very important

Deep/visceral fat around pancreas, liver, etc. prevents the body from using insulin properly.

Essentially your body is resistant to the hormone.

Understanding Insulin Resistance

Visceral fat is directly associated with central obesity

Besides insulin resistance, obesity itself has significant implications for long-term health

Central Obesity

Central Obesity

For example, also associated with:

Death from Influenza

7% increased risk of hospitalization/death with every 5 BMI increase from 22.5 Kg/M²

Cancer risk increased 25%

40% all cancers diagnoses

Earlier onset

13 types associated with obesity

pancreatic, esophageal, gastric, breast, gallbladder, thyroid, ovarian, colorectal, liver, multiple myeloma, kidney, endometrial, meningeal

Abdominal circumference of >102cm in male and >89cm in female are independent risk factors for cardiovascular disease

Leads to cascade of metabolic derangement associated with insulin resistance

Think Metabolic Syndrome, start discussion

Central Obesity

Metabolic Syndrome a continuum

METABOLIC SYNDROME

What is Metabolic Syndrome?
Metabolic syndrome is a cluster of conditions that increase your risk of heart disease, stroke, and type 2 diabetes. These conditions include high blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels. Sometimes insulin resistance that leads to high blood sugar is also present.

Metabolic Syndrome Risk Factors
The following conditions are considered risk factors for metabolic syndrome:
 • High blood pressure
 • High blood sugar
 • High blood cholesterol
 • High triglyceride levels
 • Excess abdominal fat

Obesity
Obesity is a major risk factor for metabolic syndrome. Excess body fat, particularly around the waist, is associated with insulin resistance and other metabolic abnormalities.

High Blood Glucose
High blood glucose levels are a key component of metabolic syndrome. Insulin resistance, a condition where the body's cells do not respond properly to insulin, can lead to high blood sugar.

High Blood Pressure
High blood pressure is another common feature of metabolic syndrome. It is often linked to insulin resistance and excess body fat.

Abnormal Cholesterol Profile (Dyslipidemia)
Metabolic syndrome is associated with an abnormal cholesterol profile, including low levels of HDL cholesterol and high levels of triglycerides.

Medical Conditions Associated with Metabolic Syndrome
 • Insulin Resistance
 • Type 2 Diabetes
 • Non-alcoholic Fatty Liver Disease (NAFLD)
 • Sleep Apnea
 • Atherosclerosis

What Causes Metabolic Syndrome?
The exact cause of metabolic syndrome is not fully understood, but it is believed to be a combination of genetic and lifestyle factors. Insulin resistance is a central feature, and it is often associated with excess body fat, particularly visceral fat.

How is Metabolic Syndrome Treated?
Treatment for metabolic syndrome focuses on lifestyle changes and medication. Lifestyle changes include regular exercise, a healthy diet, and weight loss. Medication may be used to manage blood pressure, blood sugar, and cholesterol levels.

Organs Affected by Untreated Metabolic Syndrome
Untreated metabolic syndrome can lead to serious health complications, including heart disease, stroke, type 2 diabetes, and kidney disease. Excess body fat, particularly around the waist, is associated with insulin resistance and other metabolic abnormalities.

Normal weight
Four women with a BMI of 24 but different fat distribution

Subcutaneous
Visceral

Probability of:
 Less healthy ← | → More healthy

Heart disease	▲ High	▼ Low	▲	▼
Type 2 diabetes	▲	▲	▲	▼
Metabolic disease	▲	▲	▲	▼

Less healthy ← | → More healthy

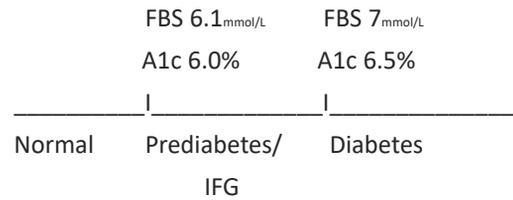
Obese
Four women with a BMI of 32 but different fat distribution

National Geographic Magazine, January 2019

BMI, Weight: bad measures

The Continuum

Insulin resistance takes cumulative toll
 Overproduction of insulin wears out pancreas
 Battle lost early, long before DM2 diagnosis



My Goal

For the new diagnosis or new to me

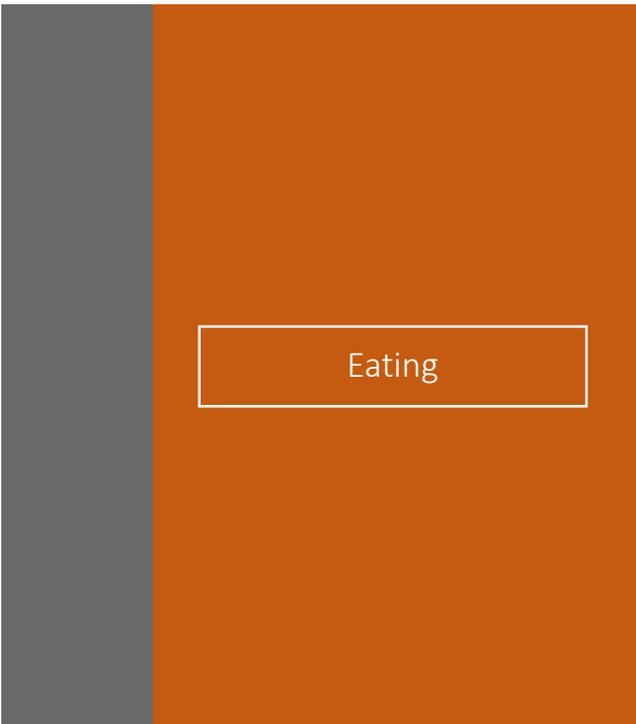
“Statistically speaking, you are most likely to die of a heart attack or stroke. My goal is to have you die from something else.”



Management

Do not set people up to fail!

But be appropriately blunt.



Eating

Offer approach, telling people **what** to eat invites failure

Too much dietary advice can be overly prescriptive, all diets fail

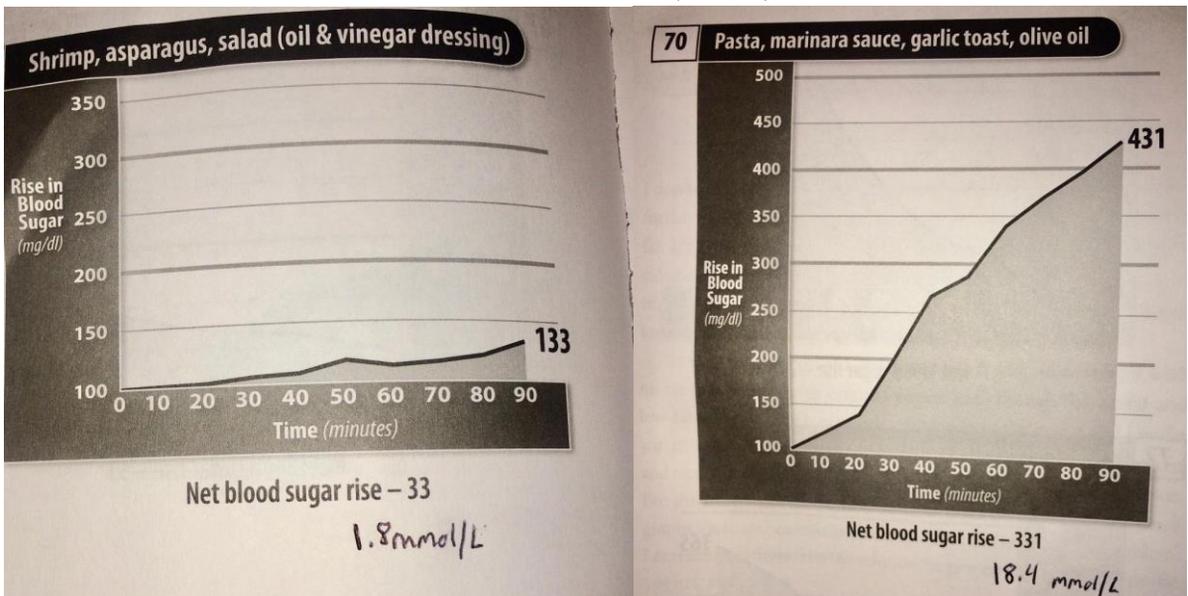
Do not assume sound approach to food, build common base beyond “low fat” mantra

Eating: My Approach

only four things to know...

1. If it has an ingredient label, you probably should not eat it.
2. Bread, pasta, white rice, white potatoes, pasta, crackers, etc. should be considered sugar, minimized

Book: What Should I Eat? by Rick Mystrom



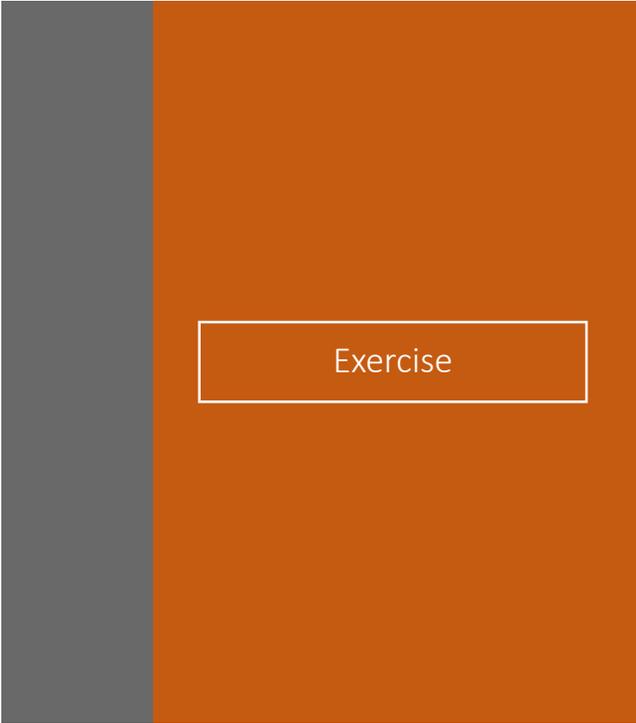
Eating: My Approach
~continued~

3. The French have it figured out.
Eat slowly.

4. Every chain restaurant needs
to be avoided.

Eating: My Approach





Exercise

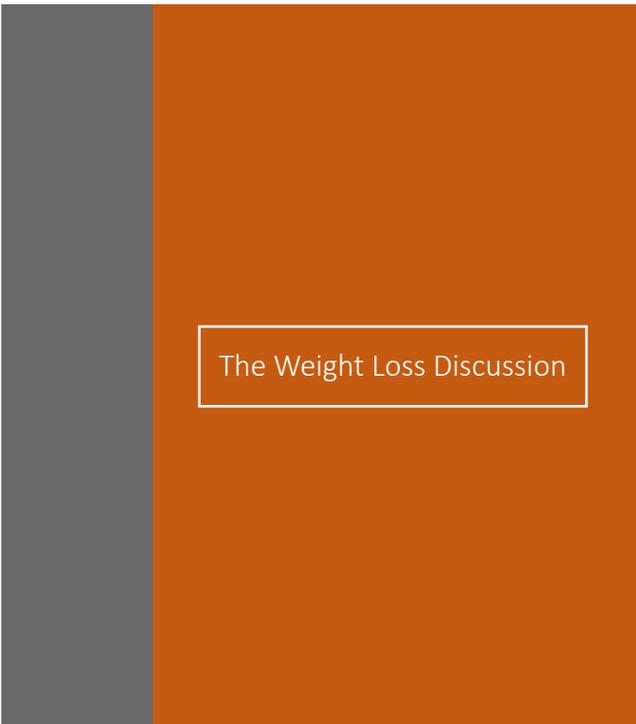
Yes...

Exercise recommendations abound, are they realistic?

Find out where someone is and build slowly from there

Again, do not set people up to fail

But fitness at any weight has benefits (remember body scans)

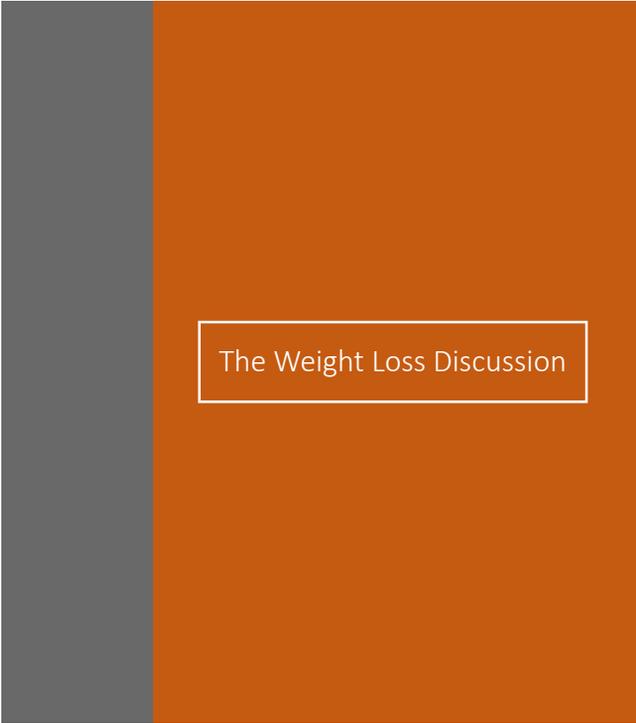


The Weight Loss Discussion

A waste of time, for many reasons

Discuss weight and BMI in generalities only

I do not look at someone's weight or BMI in my diabetes appointments



The Weight Loss Discussion

Losing weight is biologically irresponsible

The body want to be the maximum weight it has ever been

Do not set people up to fail

There is another approach



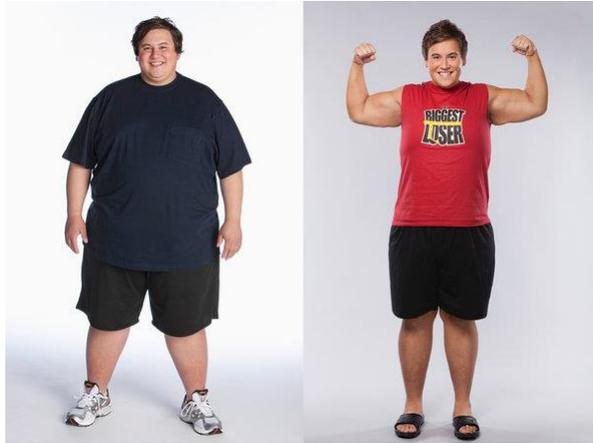
Set Point

Persistent metabolic adaptation 6 years after "The Biggest Loser" competition.
[Obesity](#) 2016 Aug;24(8):1612-9. doi: 10.1002/oby.21538. Epub 2016 May 2.

New York Times May2, 2016
After 'The Biggest Loser,' Their Bodies Fought to Regain Weight

Contestants lost hundreds of pounds during Season 8, but gained them back. A study of their struggles helps explain why so many people fail to keep off the weight they lose.

Sean Algaier
36 yo, Charlotte, NC
Weight before show: 444 lb.
December 2009: 289 lb.
6 years later: 450lb...
Burns 458cal/day less than expected



The Other Approach

Established BMI and weight are not useful

BMI good for population, not for individual

“you must lose weight” ineffective and begs question “what weight should I be, doctor?”

The Other Approach

Measure maximum abdominal girth, think insulin resistance

Benefits:

Allows for non-threatening goals

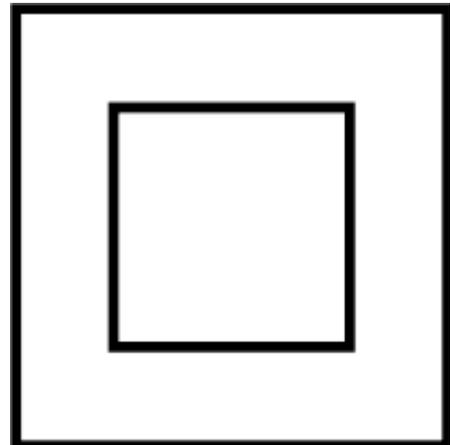
Unique to individual

Easily reproducible, tracked

Not affected by weight gain from exercising

And...

The Other Approach



If you double the circumference, you quadruple the area---
small decreases in maximum circumference exponentially
decreases visceral fat.



The Other Approach

“Sir, you are 130cm around, next year I want be 5cm less.”

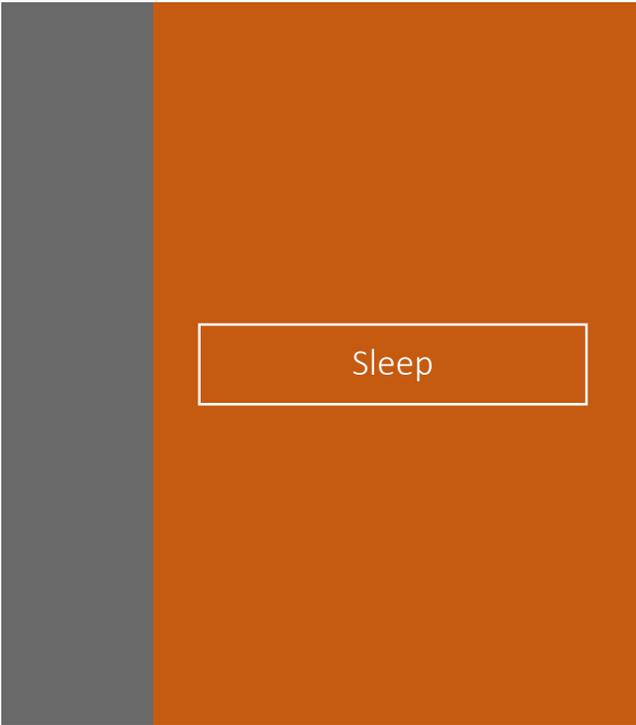
“That’s all? I can do that.”

Goal: arrest growth and ultimately be able to see belt buckle

Subtle changes in approach to eating yields results

Goal is to limit insulin resistance

Fitness at whatever weight



Sleep

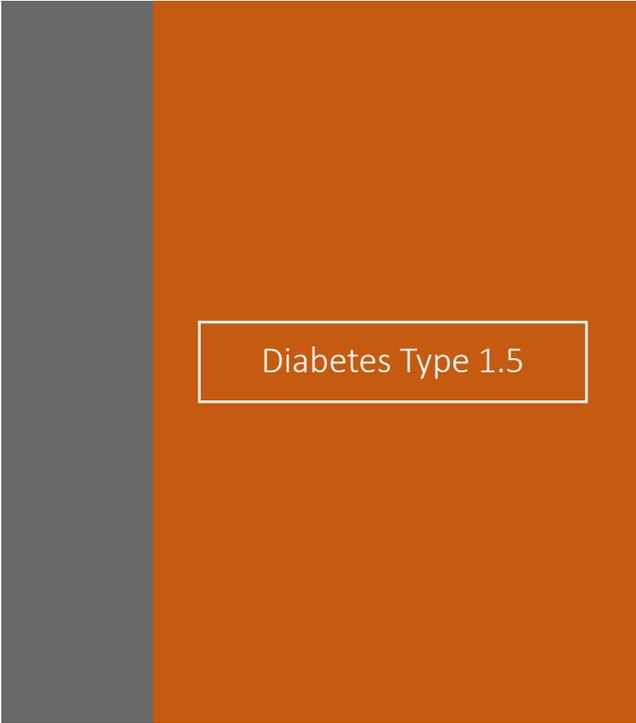
Not optional...

Sleep apnea screening with all physical exams

Validated STOP BANG questionnaire

Untreated sleep apnea increases ghrelin secretion: incr. carb craving, fat storage

Decreased insulin sensitivity...in 5 days of poor sleep



Diabetes Type 1.5

Also...

Latent Autoimmune Diabetes in Adulthood (LADA)

Possibly 20%+

onset not like Type 1

Keep this in mind...euglycemic ketoacidosis



Medications

...it's a great time to have diabetes.

Medications can be overwhelming.

Use dichotomous approach for yourself and for patient education

“Insulin versus glucagon pathways”



Medications

Insulin Pathway

high hypoglycemia potential

weight positive

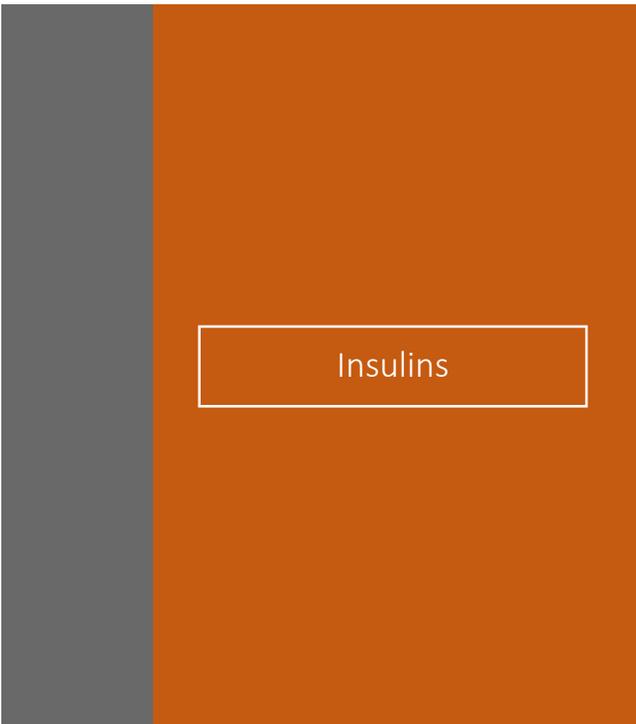
- Insulin
- Sulfonylureas-secretagogues
- Thiazolidinediones-senitzer

“Glucagon” Pathway

low hypoglycemia potential

weight negative

- Metformin
- DPP-4 inhibitors
- GLP-1 agonists
- SGL-2 inhibitors*



Insulins

Basal and meal-time

Quick results, little increased CHF/CVD risk

Removes sugar from blood...
So weight positive and risk of hypoglycemia

Require active monitoring

There IS a dose limit

A slide with a dark grey vertical bar on the left and an orange background. A white-bordered box in the center contains the text "Sulfonylureas".

Sulfonylureas

Secretagogues---flog the pancreas, so must be making insulin

Need to be eating

Work quickly, cheap

Weight gain and risk hypoglycemia

Increase risk of CHF

Glimeperide and glicazide preferable to glyburide

A slide with a dark grey vertical bar on the left and an orange background. A white-bordered box in the center contains the text "Thiazolidinediones".

Thiazolidinediones

Sensitizers

Must be making insulin, in effect 'decreasing' resistance,

Weeks to months to maximum effect, but effective

Weight positive and risk hypoglycemia

Associated with increased risk CHF, edema, pathological fractures and rare bladder cancer



Medications

“Glucagon Pathway”

low hypoglycemia potential

- Metformin
- DPP-4 inhibitors
- GLP-1 agonists
- SGL-2 inhibitors*



Metformin

Cheap effective

For everyone and first line

decreases A1c 0.8-3.1%

Weight negative

Cardioprotective, possibly reduce cancer risk

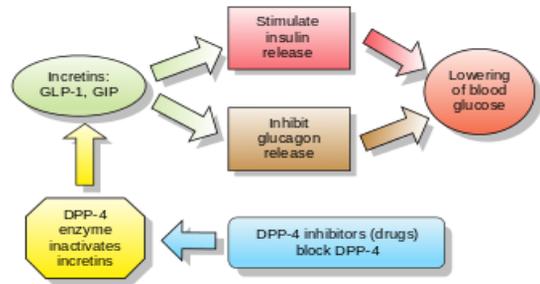
Reduces gluconeogenesis

Very rare hypoglycemia

GI upset common, less with XR, titrate

Incretin

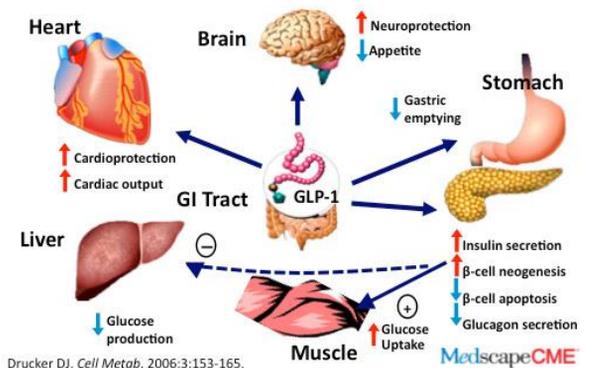
GLP-1 agonist
 Glucose-dependent gut hormone
 regulated by DPP-4



wikipedia.com

Glucagon-Like Peptide 1
 Receptor Agonist

GLP-1 Actions in Peripheral Tissue



Glucagon-Like Peptide 1
Receptor Agonists

Gila monster spit

Incretin released when sugar present

Safe, effective with A1c down +/- 1.5%

Hypoglycemia not an issue

Significant weight loss up to 5 kg
without lifestyle changes

Up to 26% decrease in events

Precautions . . .

Glucagon-Like Peptide 1
Receptor Agonist

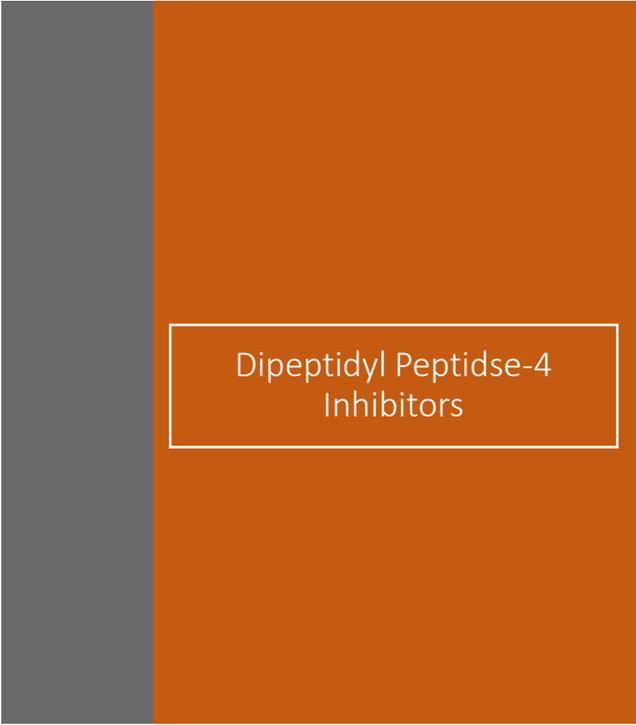
Currently only injectable

Exanatide 2005

Liraglatide 2010-daily
(Victoza/Saxenda)

Dulaglatide 2014-weekly

Semaglutide 2017-weekly



Dipeptidyl Peptidase-4
Inhibitors

DPP-4's

Inhibit the degradation of naturally occurring GLP-1, suppress gluconeogenesis

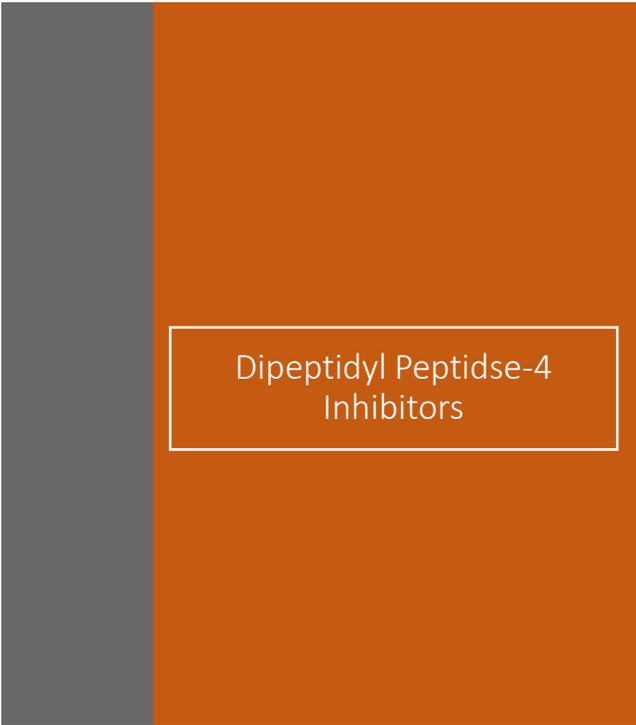
Act when sugar present-rare lows

Decrease A1c <1%

Weight negative

Daily dosing oral medication

Work in gut



Dipeptidyl Peptidase-4
Inhibitors

Sitagliptin

Saxagliptin

Linagliptin

All come in combination with metformin

Overall safe, renal dosing

Do NOT use with GLP-1 RA's

Sodium Glucose co-Transporter 2 Inhibitors

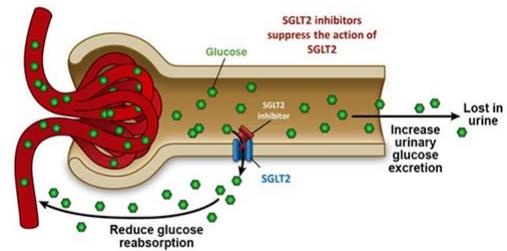
SGLT-2's

Reversing evolution?

Primarily inhibit reabsorption of glucose

Essentially diuresis

The Newest Antihyperglycemic Class SGLT2 Inhibitors



Wright EM, et al. *Physiol Rev.* 2011;91:733-794.

Sodium Glucose co-Transporter 2 Inhibitors

A1c reduction 0.5-0.8%

Work when sugar present

Rare lows

Slight weight negative

Sodium Glucose co- Transporter 2 Inhibitors

The Downsides:

- Increased UTI's/vaginal candidiasis
- Hypotension with high BG
- Euglycemic ketoacidosis
- Monitor renal function/renal dosing
- Caution in elderly
- CHF/CVA events, data mixed

Sodium Glucose co- Transporter 2 Inhibitors

More Downsides:

- Increased risk fracture
- Genital/perineal gangrene?
- Amputations

Names:

- canagliflozin
- dapagliflozin
- empagliflozin

Devices

Glucometers
Continuous Glucose Monitors

Glucometers

Glucometer Improvements

Allowing synchronization

Insulin tracking

Data sharing



Continuous Glucose Monitors

“CGMs”

Advantages:

Reduce finger sticks

Increased monitoring reduces A1c

Disadvantages:

Interstitial, not capillary sampling

Increased cost...but maybe not over time

“CGMs”

Freestyle Libre Pro/Libre

14 day monitoring

Relatively inexpensive

Libre Pro

“blind”

Placed in office/data downloaded in office

Libre

Show trends, programmable alarms

Data sharing

Q5min readings, need finger sticks at extremes

No calibration

Only stores data for 8 hours

Sensor Applicator



Sensor Pack



Sensor (assembled)



Reader



“CGMs”

Eversense

- Works for 90 days
- Need finger sticks at extremes
- Programmable alarms, shows trends
- Implantable/invasive
- Limited data sharing
- Requires twice daily calibration
- Recharge transmitter daily



“CGMs”

Dexcom G6

- Lowered A1c decrease 0.5%, 58% decrease time in hypoglycemia (Type 1)
- Checks up to 288/day
- Shows trends with rate of change
- Programmable alarms
- Data sharing
- No calibration
- Replace every 10 days



Remember

- Goal: minimize insulin resistance
- Offer approach to eating
- Avoid weight/BMI discussions, think maximum girth
- Restorative sleep
- “Diet controlled” diabetes is vestigial
- Good monitoring options emerging
- And think longitudinally



Thank you. Questions?