Get Smart about Diabetes in the Geriatric Patient

David LeVine, M.D. (AKA : Control Agent 125)

American Diabetes Association, *Diabetes Care*. 2022;45(Suppl 1)

AMDA's Diabetic Management in the Post-Acute and Long-Term Care Setting Clinical Practice Guidelines 2015

Management of Diabetes in Long-term Care and Skilled Nursing Facilities: A Position Statement of the American Diabetes Association 2016

DISCLOSURE STATEMENT

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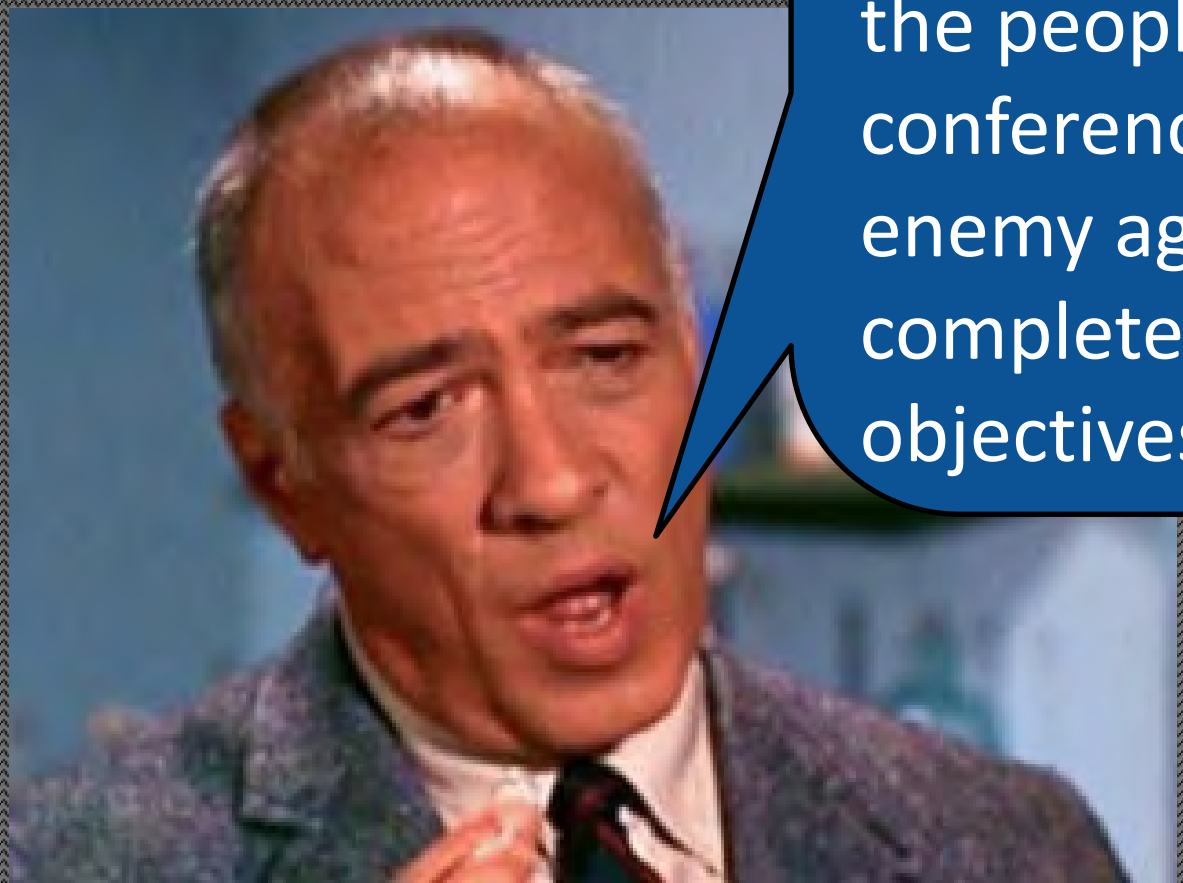
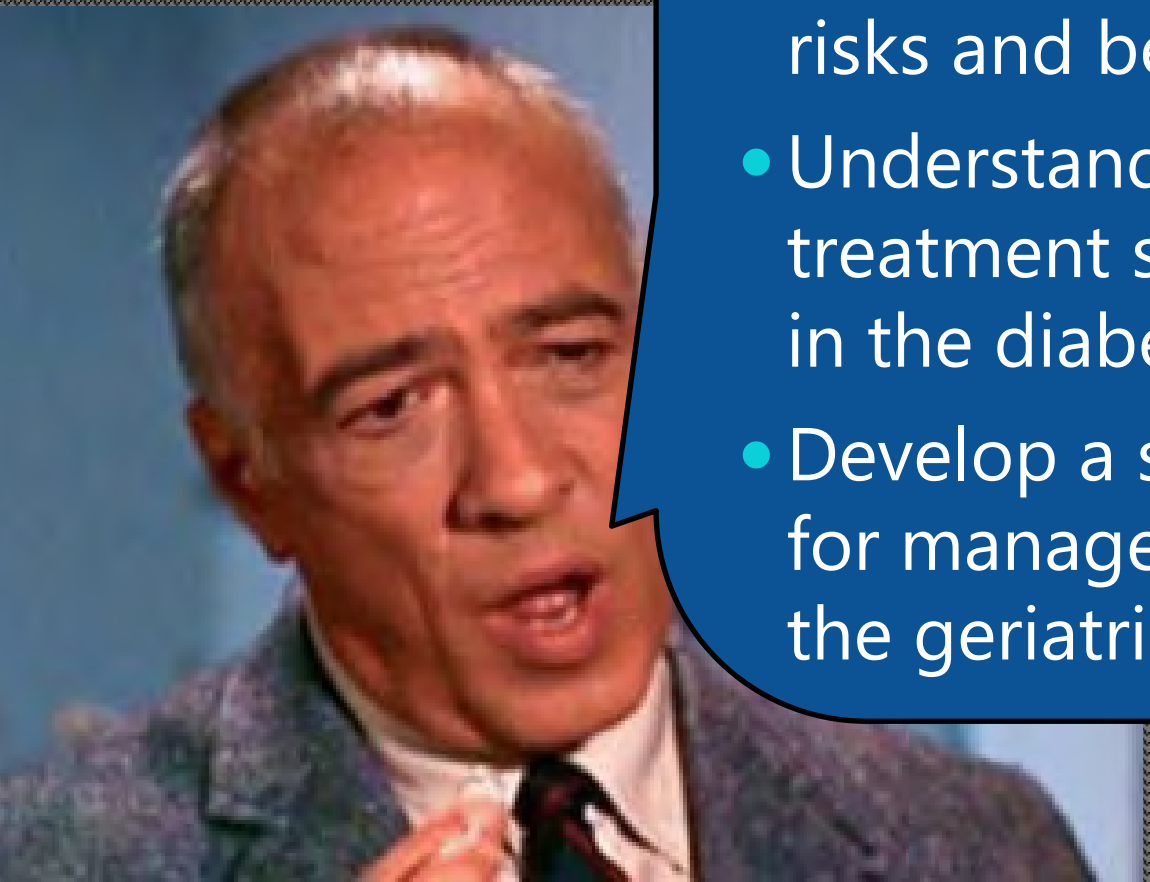


As chief of C.O.N.T.R.O.L., I am giving Dr. LeVine and you, Max, this important mission. You must protect the people in this conference room from enemy agents and complete the following objectives within one hour:



- Review the prevalence and impact of diabetes in the geriatric population
- Discuss the current medications available for diabetes including risks and benefits
- Understand the differences in treatment strategies and goals in the diabetic geriatric patient
- Develop a step-wise approach for management of diabetes in the geriatric patient

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Diabetes Care

WWW.DIABETES.ORG/DIABETESCARE
JANUARY 2022

SUPPLEMENT 1

AMERICAN DIABETES ASSOCIATION

STANDARDS OF MEDICAL CARE IN DIABETES—2022

American Diabetes Association.

ISSN 0149-5992

New guidelines in 2022

- Adults without risk factors be screened for prediabetes and type 2 diabetes starting at age 35. (Previously, the recommended age was 45.)
- All women who are planning to become pregnant be screened for diabetes with a fasting glucose test. (Fasting glucose on 1st visit neonatal visit if not done prior)
- Emphasize the need for individualized treatment plans based on patients' comorbidities and risk of complications. While metformin has long been the first-line therapy for managing diabetes, clinicians can now use GLP-1 receptor agonists or SGLT2 inhibitors instead of, or in addition to, metformin.
- CGM for patients on long-acting insulin also (Previously, the ADA recommended CGM for only individuals taking rapid-acting insulin)
- COVID 19 vaccination

Progression to Type 2 Diabetes

Genetics → Insulin Resistance ← Acquired: Obesity, Sedentary Lifestyle, Aging

Insulin Resistance → Hyperinsulinemia

Hyperinsulinemia → Compensated Insulin Resistance, Normal Glucose Tolerance

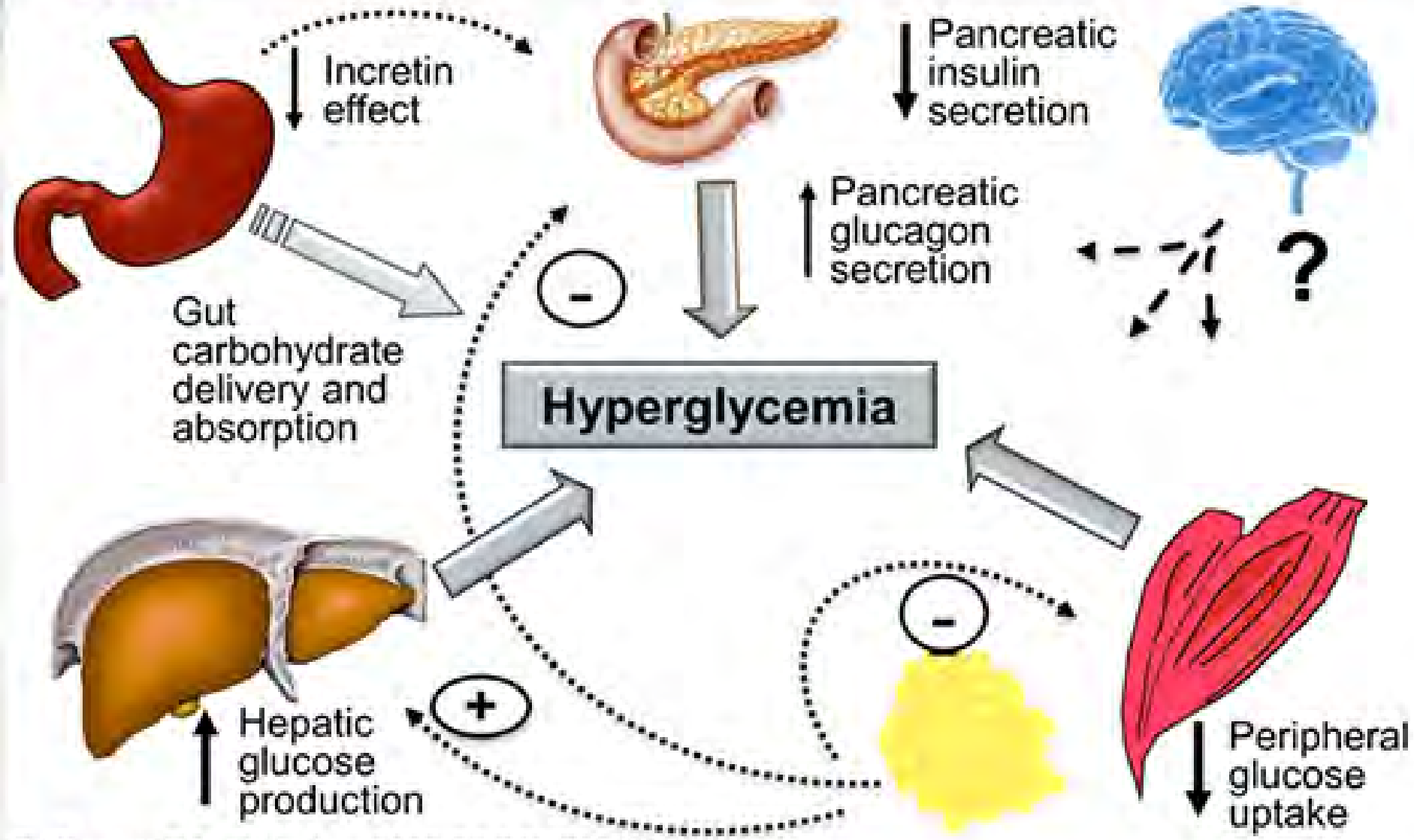
Compensated Insulin Resistance, Normal Glucose Tolerance → Impaired Glucose Tolerance

Impaired Glucose Tolerance → β-Cell "Failure" ← Genetics

β-Cell "Failure" → Type 2 Diabetes

Increased Hepatic Glucose Output → Type 2 Diabetes

Main Pathophysiological Defects in T2D



DeFronzo RA. *Diabetes*. 2009;58:773-795.[15]


Metabolic
Syndrome
HIGH BLOOD GLUCOSE
HIGH BLOOD PRESSURE
HIGH LIPID PROFILE
LARGE WAIST SIZE
LOW HDL LEVELS.

Criteria for the Harmonized Definition of Metabolic Syndrome[3]

Risk Factor	Level That Meets Criteria
Blood pressure*	Systolic ≥130 mm Hg or diastolic ≥85 mm Hg
Fasting plasma glucose*	≥100 mg/dL
Serum triglycerides*	≥150 mg/dL
HDL cholesterol*	Men <40 mg/dL Women <50 mg/dL
Waist circumference	Population-specific thresholds internationally In the United States[1] • **For people of most ancestries** Men ≥40 inches (>102 cm) Women ≥35 inches (≥88 cm) • **For people of Asian ancestry**** Men ≥35 inches (≥90 cm) Women ≥31.5 inches (≥80 cm)

METABOLIC SYNDROME IS DEFINED BY THE PRESENCE OF ANY THREE OF THE FIVE RISK FACTORS.

* BLOOD SUGAR, BLOOD PRESSURE, OR LIPIDS PREVIOUSLY ABNORMAL BUT CONTROLLED BY MEDICATIONS STILL "COUNTS" FOR MEETING THESE CRITERIA.

** THE LOWER CUT-POINT FOR WAIST CIRCUMFERENCE IS BASED ON GREATER VISCERAL ADIPOSITY AT ANY SPECIFIC WAIST CIRCUMFERENCE MEASUREMENT, PARTICULARLY AMONG SOUTH ASIANS COMPARED WITH EUROPEANS. WORK IS IN PROGRESS TO IDENTIFY ADDITIONAL ETHNICITY-BASED WAIST CIRCUMFERENCE CRITERIA.

Metabolic syndrome

- **Metabolic syndrome** is a combination of medical disorders that increase the risk of developing cardiovascular disease and diabetes.
- It affects one in 4 people, and prevalence increases with age.
- Metabolic syndrome AKA **dysmetabolic syndrome**, **metabolic syndrome X**, **cardiometabolic syndrome**, **syndrome X**, **insulin resistance syndrome**, **Reaven's syndrome** (named for Gerald Reaven), and **CHAOS** (in Australia).

CHAOS

CHAOS

C – Coronary Artery Disease
H – Hypertension/Hyperlipidemia
A - Adult Onset Diabetes
O – Obesity
S - Stroke

Why Get Smart?

- Goal is CONTROL
- Normal Fasting Blood Glucose is 99
- Metabolic syndrome a.k.a. CHAOS
- It was one of all time favorite TV shows

Risk Factors

- **Older (>=45y.o.)**
- **Less active**
- **Overweight BMI>=2**
- FHx of diabetes in 1st degree relative
- Being of African, Asian, Native American, Hispanic, or Pacific Islander ancestry
- High blood pressure >=140/90
- High blood levels of triglycerides with low HDL
- History of cardiovascular disease
- Hx of pre-diabetes, metabolic syndrome (CHAOS), impaired glucose tolerance (A1C>5.6 or FBS>99)
- In women, a history of giving birth to large babies (over 9 lbs) and/or diabetes during pregnancy

ADA 2022 Guidelines (in the absence of unequivocal hyperglycemia repeat testing is recommended)

- Hgb A1C >=6.5% (prediabetes 5.7-6.4%)
- Fasting plasma glucose >=126 mg/dl (no calories for >=8 hours) (prediabetes 100-125)
- 2-hour plasma glucose >=200 mg/dl following a 75-g oral glucose tolerance test (prediabetes 140-199)
- A random plasma glucose of >=200mg/dl in a patient with classic symptoms of hyperglycemia

HgbA1C vs. FPG

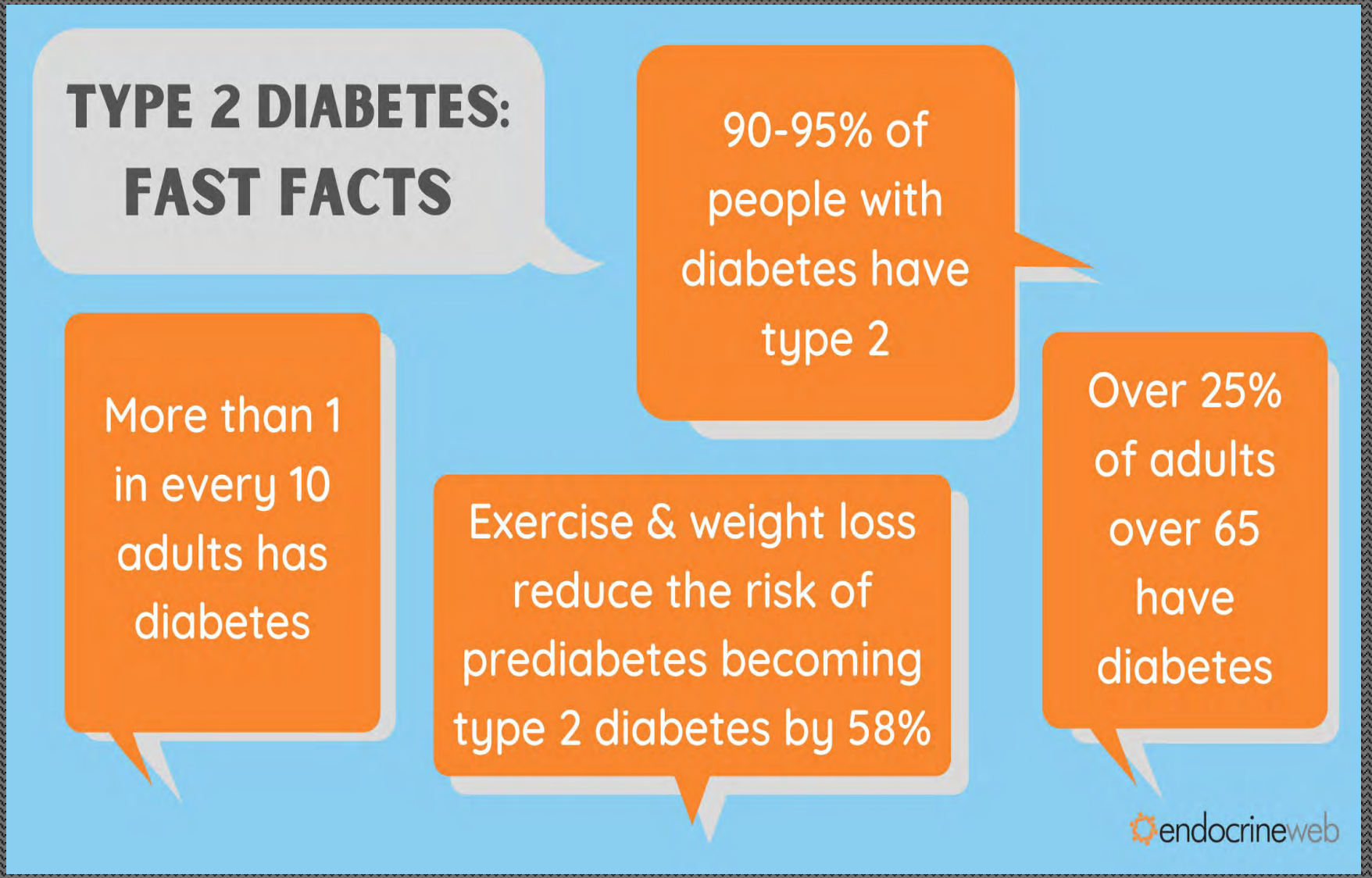
- 1865 community dwelling older patients (70-79y.o.) without diabetes
- 80 (4.3%) met new criterion for diabetes
- Approximately 1/3 had elevated HgbA1c, 1/3 had elevated FPG and 1/3 had both
- 32% met prediabetes criterion with same ratios

HgbA1C vs. OGTT

- Researchers looked at data from 9,000 adults, ages 20 years and older, from the 2005-2014 National Health and Nutrition Examination Survey (NHANES).
- Based on the fasting blood glucose test and the OGTT, 765 patients were diagnosed as having type 2 diabetes (T2D). However, only about 27% of these individuals were classified as having diabetes based on their A1c levels. 73 % of patients would miss out on early intervention and treatment
- The guidelines for diagnosis and treatment of type 2 diabetes from the American Diabetes Association (ADA) already advise against relying solely on A1c although guidelines specify that diabetes can be diagnosed based on fasting plasma glucose (FPG), the OGTT, or the A1c,
- HgbA1c remains the least reliable method for assessing diabetes risk.

Prevalence of diabetes in the elderly

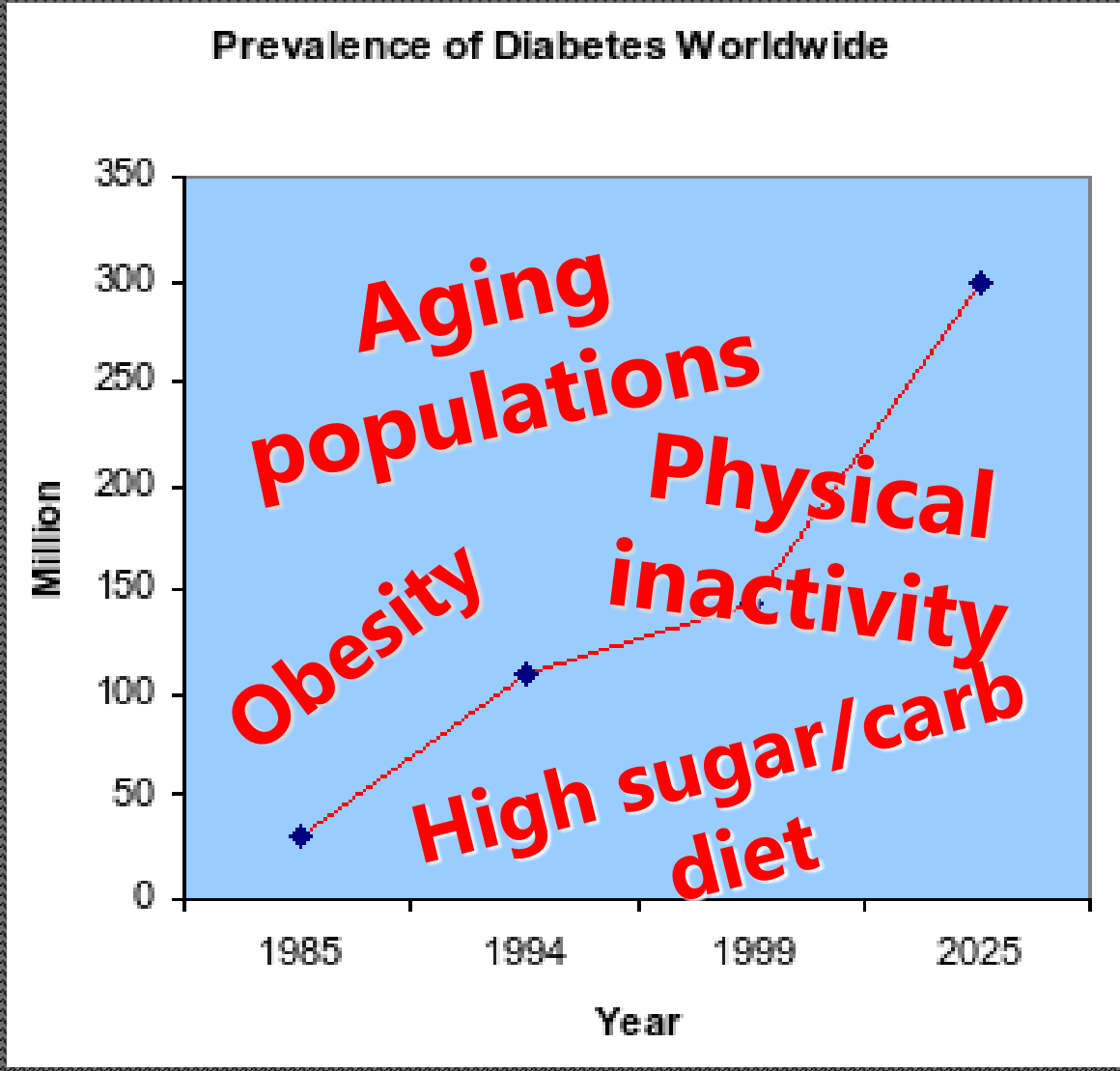
Prevalence of Diabetes



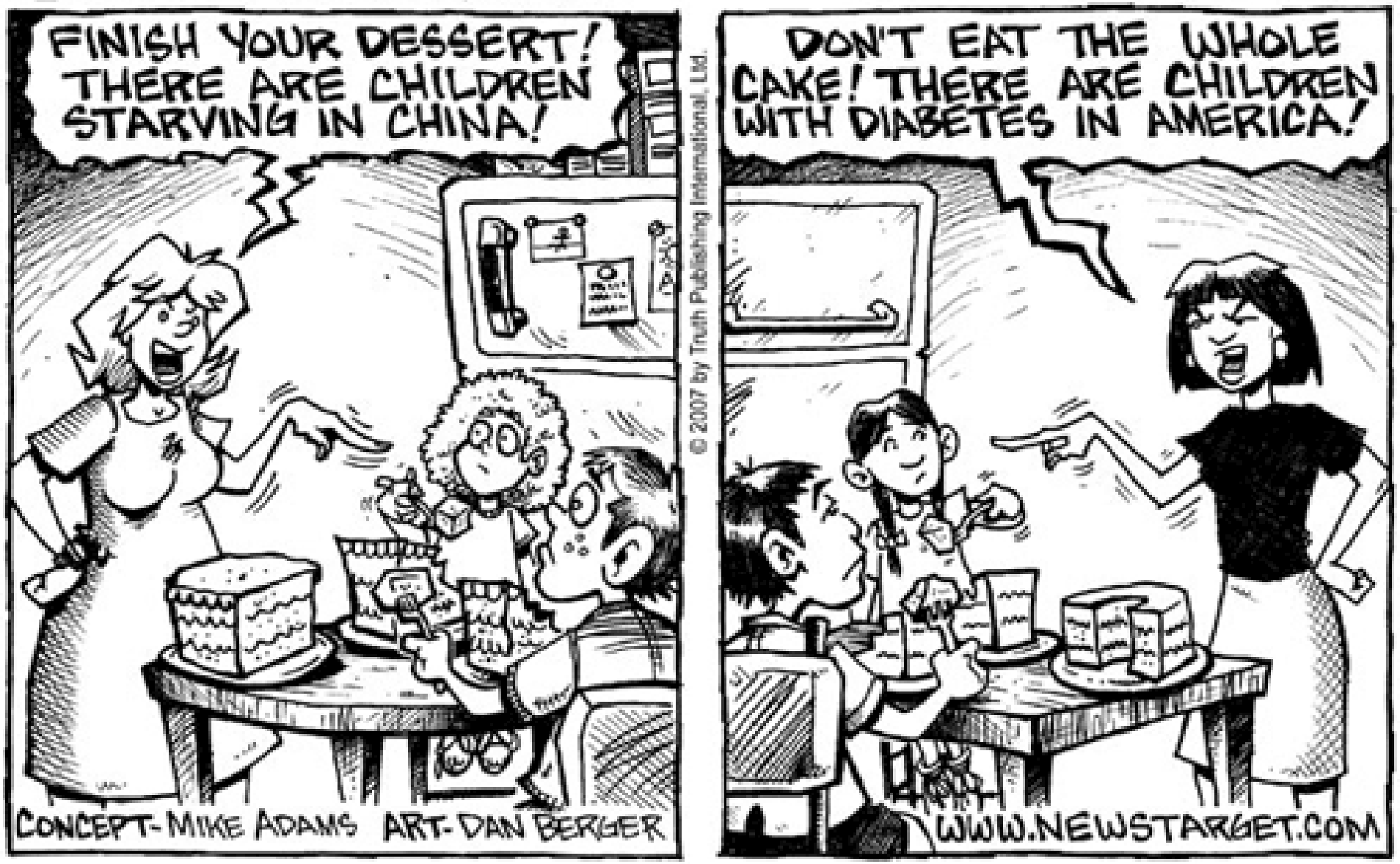
Prevalence of Diabetes in 2022

Diabetes is increasing at an alarming rate in the USA.

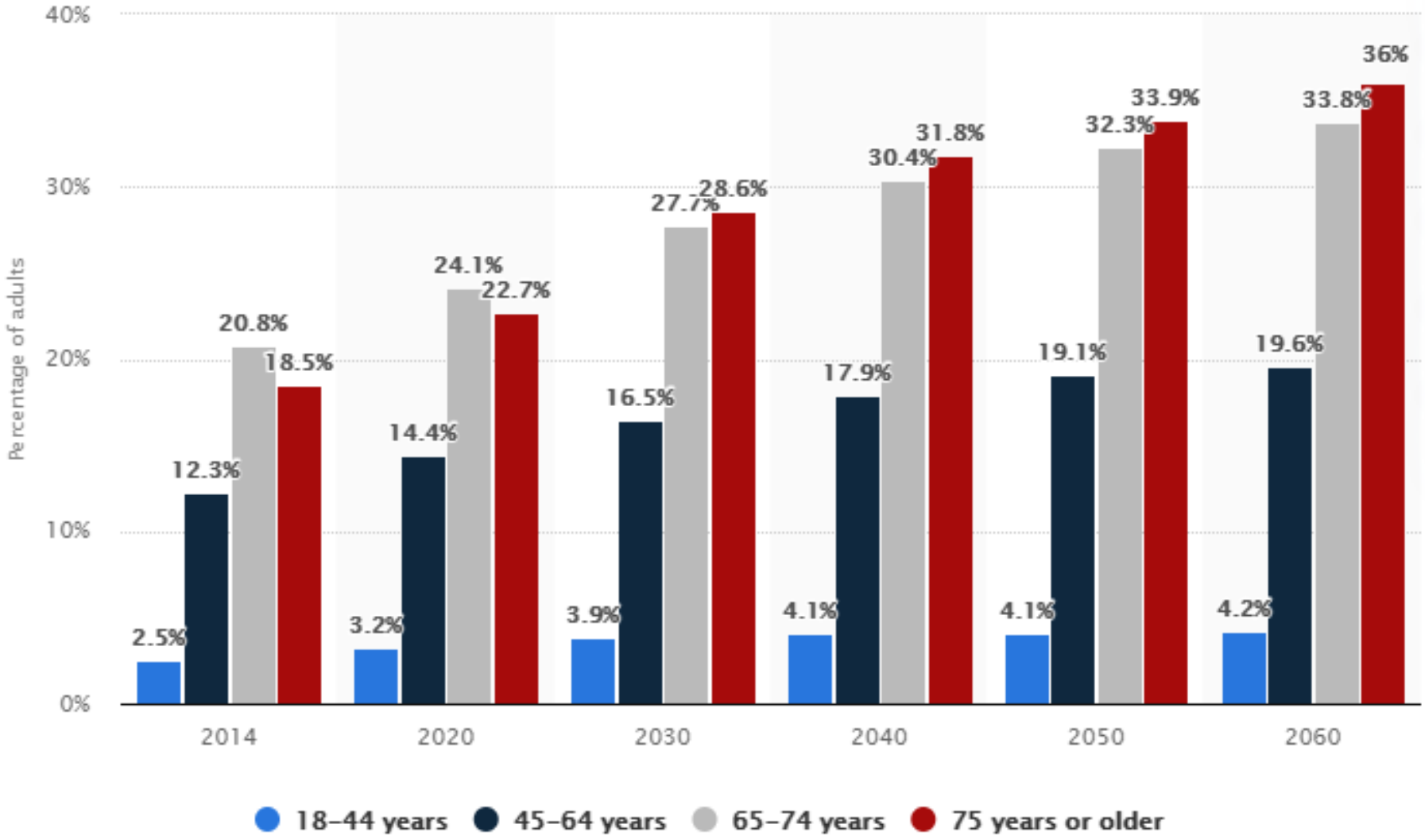
- According to the CDC's National Diabetes Statistics Report for 2022, cases of diabetes have risen to an estimated 37.3 million (11.3%).
- 23% of those U.S. adults with diabetes are undiagnosed.
- An estimated 96 million adults have prediabetes, (38% of the U.S. adult population)
- >8 in 10 adults don't know they have prediabetes
- The percentage of adults with diabetes increased with age, reaching over 26% among those aged 65 years or older
- 26.4 million people aged 65 years or older have prediabetes (48.8%)



COUNTERTHINK



Projected prevalence of diagnosed diabetes in adults in the U.S. for selected years from 2014 to 2060, by age group



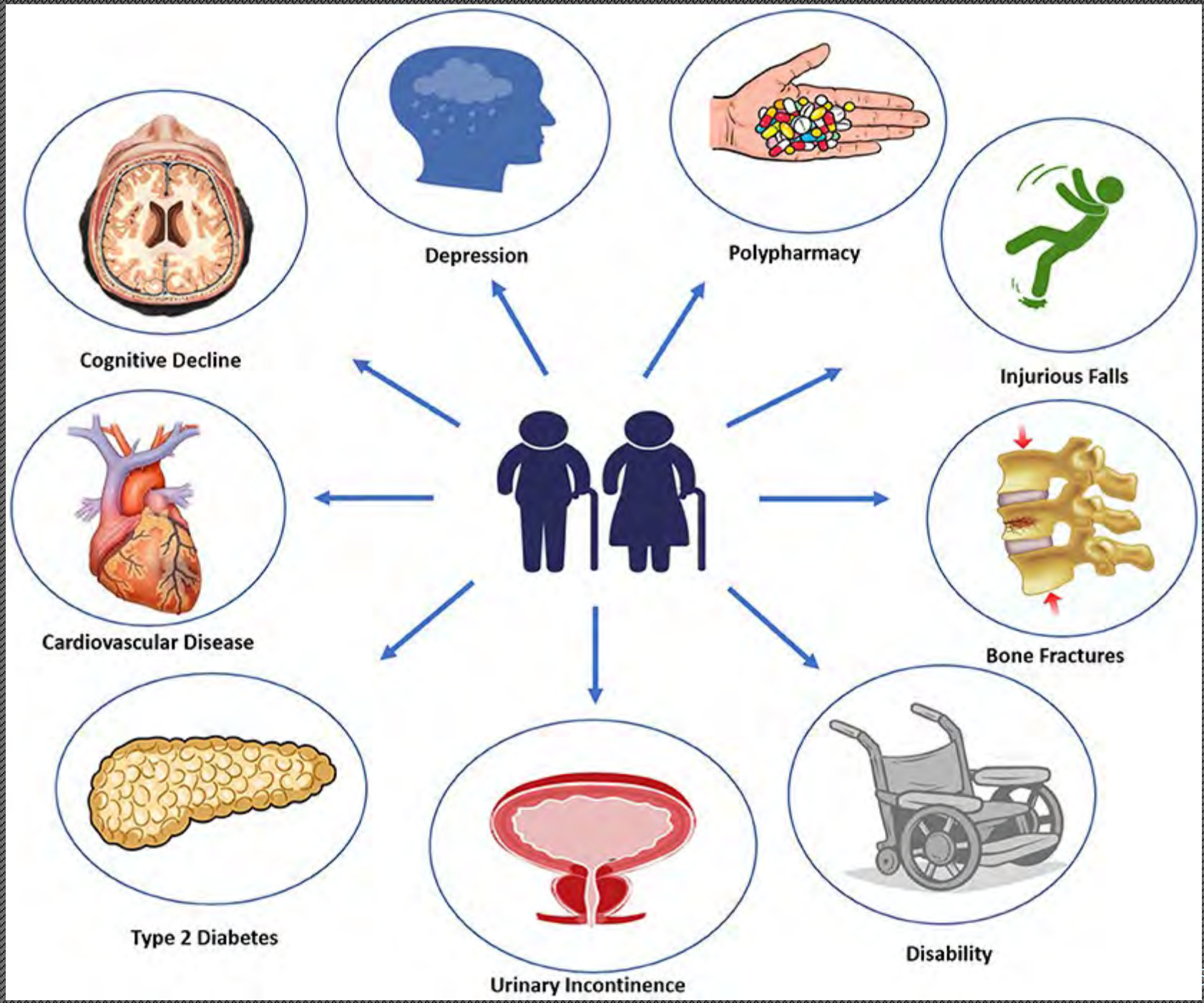
PATHOGENESIS OF HYPERGLYCEMIA IN ELDERLY

Diabetic statistics in the elderly

- In diabetics, 45-74 years of age, diabetes alone was responsible for 43.3% of hospitalizations and 52.1% of nursing home admissions
- Diabetics accounts for 32% of Medicare expenses
- Diabetes is an independent predictor of nursing home placement
- Diabetics in nursing homes have greater co-morbidities especially with cardiovascular issues, depression, and pain and have greater lengths of stay (i.e. > 90 days)

Diabetic statistics in the elderly

- Heart attacks and strokes are 2-4x as frequent in patients with diabetes
- Diabetic nephropathy is the #1 cause of end stage renal failure
- Diabetic retinopathy is one of the leading causes of blindness. DM increases risk of glaucoma 38-40%.
- Increased insulin resistance and diabetes significantly increases risk of cognitive impairment and depression
- Risks of falls, polypharmacy, urinary incontinence, and pain are increased
- Peripheral artery disease and peripheral nephropathy are major risk factors for non-traumatic limb amputations


Depression
Polypharmacy
Cognitive Decline
Injurious Falls
Cardiovascular Disease
Bone Fractures
Type 2 Diabetes
Urinary Incontinence
Disability

Diabetes is the seventh leading cause of death in the United States

Oral Diabetic Medications

Biguanides

metformin

CONTROL

- 1st line therapy!
- No known drug interactions
- Decreases hepatic glucose output
- Decreases insulin resistance
- Increases muscle glucose uptake
- Decreases GI sugar absorption
- Lowers HgbA1C 1.5-2.0%
- Reduces LDL and TG
- Rare hypoglycemia
- Raises GLP levels (glucagon-like peptide)
- Inexpensive
- Weight neutral
- Useful for polycystic ovary synd.

KAOS

- Lactic acidosis although rare (approx 0.03 cases/1000 pt-yrs) is fatal 50% of the times. Higher in diabetics with renal impairment especially if:
  - >80 years old (Monitor GFR!)
  - Acute/unstable CHF
  - Hepatic disease/EtOHism
  - Sepsis /hypoxemia
  - Dehydration
- GI s.e. (diarrhea, nausea, vomiting, indigestion, flatulence)

Metformin

NEJM June 2016

Meta-anaylsis of 204 studies

- Still 1st line therapy in DM2
- Begin metformin at the time of diagnosis w lifestyle changes
- Weight stable or decreased
  - Stable: DDP inh, GLP-1 ag, SGLT-2 inh
  - Increased: sulfonylureas, TZDs, insulin
- Combinations therapy:
  - Lowers A1c similarly except:
  - Met+GLP-1 agonist superior to Met+DPP-4 inhibitors
- As mono tx, low long-term (>2yrs) CV mortality vs sulfonylureas (33-43% increased mortality risk with sulfonylureas than with metformin)
- Low hypoglycemia (sulfonylureas with highest risk of hypoglycemia)
- Metformin was not associated with excessive risk for lactic acidosis

Recently modified FDA restrictions with renal impairment: contraindicated only if GFR <30 and caution if GFR is 30-45

Metformin

Metformin therapy for prevention of type 2 diabetes should be considered in adults with prediabetes, as typified by the Diabetes Prevention Program, especially those aged 25–59 years with BMI ≥35 kg/m^2, higher fasting plasma glucose (e.g., ≥110 mg/dL), and higher A1C (e.g., ≥6.0%), and in women with prior gestational diabetes me

LEVEL OF EVIDENCE: A

Sulfonylureas

2nd generation
glipizide (Glucotrol)
glimepiride (Amaryl)

CONTROL

- >50 years experience
- Inexpensive
- Reduces fasting glucose
- Decreases A1C by 1.5-2.0%

UK Diabetic Cohort Analysis December 4, 2009 stated that sulfonylureas as a drug class were associated with an excess all-cause mortality risk compared to metformin in retrospective analysis of >90,000 diabetic patients

KAOS

- High risk of hypoglycemia
- Weight gain
- Elevated LFTs/Hepatitis
- Cholestatic jaundice
- Photosensitivity/Rash
- Pancytopenia

Anemia
Leukopenia
Thrombocytopenia

- Hyponatremia/SIADH
- May cause prolonged coronary ischemia in MI and angina patients by interfering with K channels
- Avoid glyburide (Diabeta,Glynase,Micronase,Glycron)

1st generation sulfonyureas should not be used in the management of diabetes

REPRESENTATIVE TRADE NAMES

Acetohexamide – Dymelor®

Chlorpropamide – Diabinese®

Tolazamide – Tolinase®

Tolbutamide – Orinase®

An earlier Cochrane review found a statistically significant increase in the risk of cardiovascular death for first generation sulfonylureas relative to placebo(RR 2.63, 95% CI 1.32 to 5.22;P=0.006).

The FDA requires sulfonylureas to carry a label warning regarding increased risk of cardiovascular death.

Meglitinenides

Nateglinide (Starlix), repaglinide (Prandin)

CONTROL

- For patients with Hgb A1C < 8
- Decreases A1C by 0.5-1.0%

Diabetes 12/2004 v.53
"…inhibition of cardiovascular K ATP channels by insulin secretagogues (sulfonyureas and meglitinides) is considered to increase cardiovascular risk

KAOS

- Limited with Hgb A1C>8
- Taken 3-4x daily <=30 minutes before meals
- Hypoglycemia
- Myocardial ischemia
- Weight gain
- GI s.e.(diarrhea, nausea, vomiting, constipation, pancreatitis)
- Not indicated with NPH due to increased CV events

Alpha-glucosidase inhibitors

(acarbose-Precose, miglitol-Glyset)

CONTROL

- Reduces post-prandial glucose absorption
- Lowers HgbA1C .5-.8%
- No risk of hypoglycemia
- No effect on weight gain
- No serious adverse effects

KAOS

- 3 times a day
- ½ regular dose in elderly
- 30% experience GI side effects

Abdominal discomfort

Flatulence, bloating

Diarrhea

- Avoid in IBD, GI obstructon

Thiazolidinediones (AKA: TZDs)

rosiglitazone(Avandia), pioglitazone(Actos)

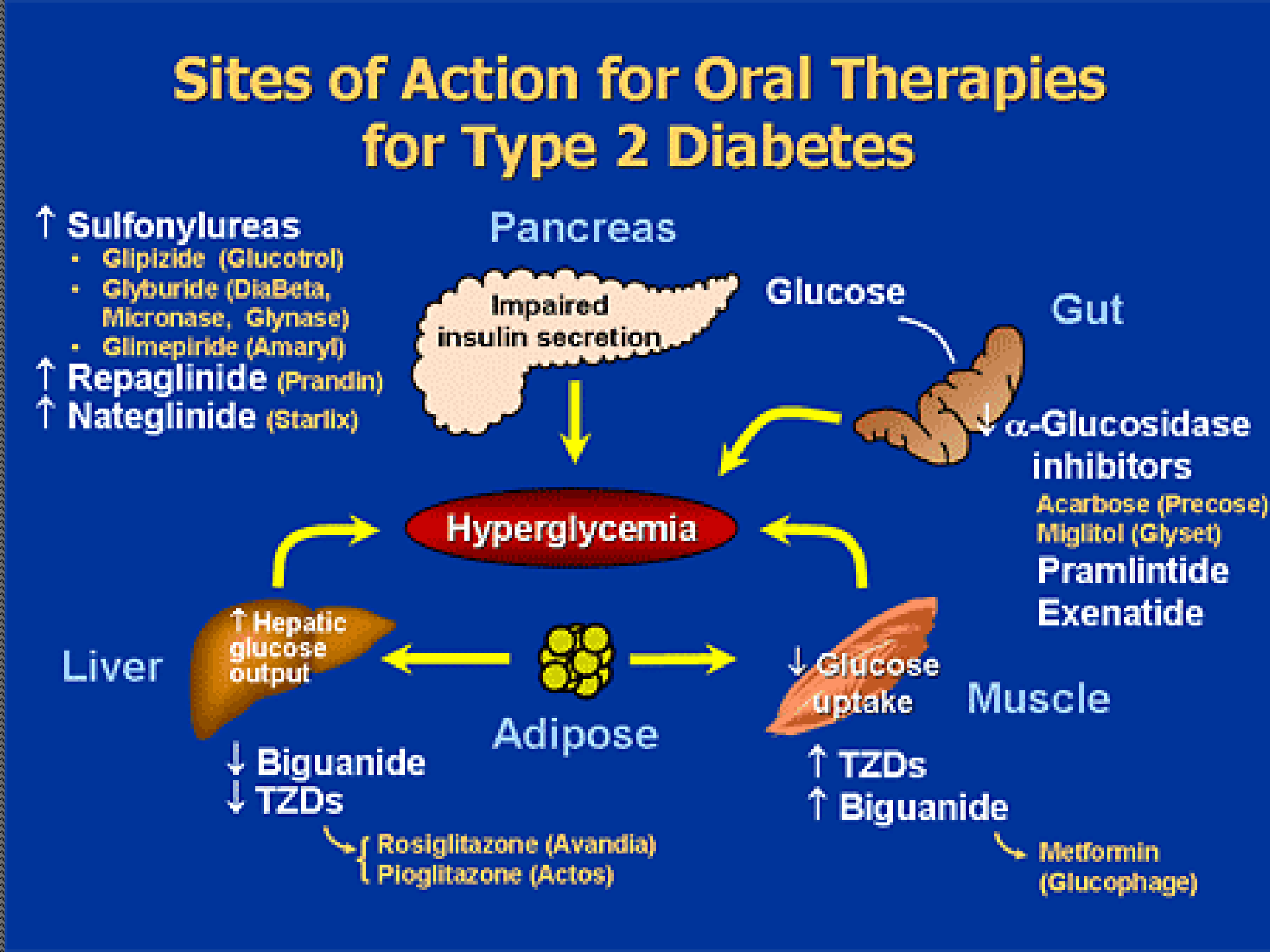
CONTROL

- Decreases insulin resistance
- Decreases hepatic output
- Increases muscle uptake
- Lowers HgbA1C 1.5-2.0%
- No dose reduction in elderly
- No adjustments for CKD
- Rare hypoglycemia (alone)
- Lowers TG and increases HDL
- Reduces hsCRP
- May be taken without regard for meals

KAOS

- Fluid retention and edema
- CHF (contraindicated in NYHA Class III-IV CHF)
- Clearance significantly lower in hepatic impairment (Avoid if LFTs >2.5x higher than normal)
- Fracture risk in females?
- On 9/23/2010 restrictions placed on rosiglitazone in response to data that suggest an elevated risk of CV events such as heart attack and CVA

Sites of Action for Oral Therapies for Type 2 Diabetes



Dipeptyl peptidase-4 (DDP-IV) inhibitors (AKA Gliptins)

sitagliptin(Januvia), linagliptin(Tradjenta), saxagliptin(Onglyza), alogliptin(Nesina)

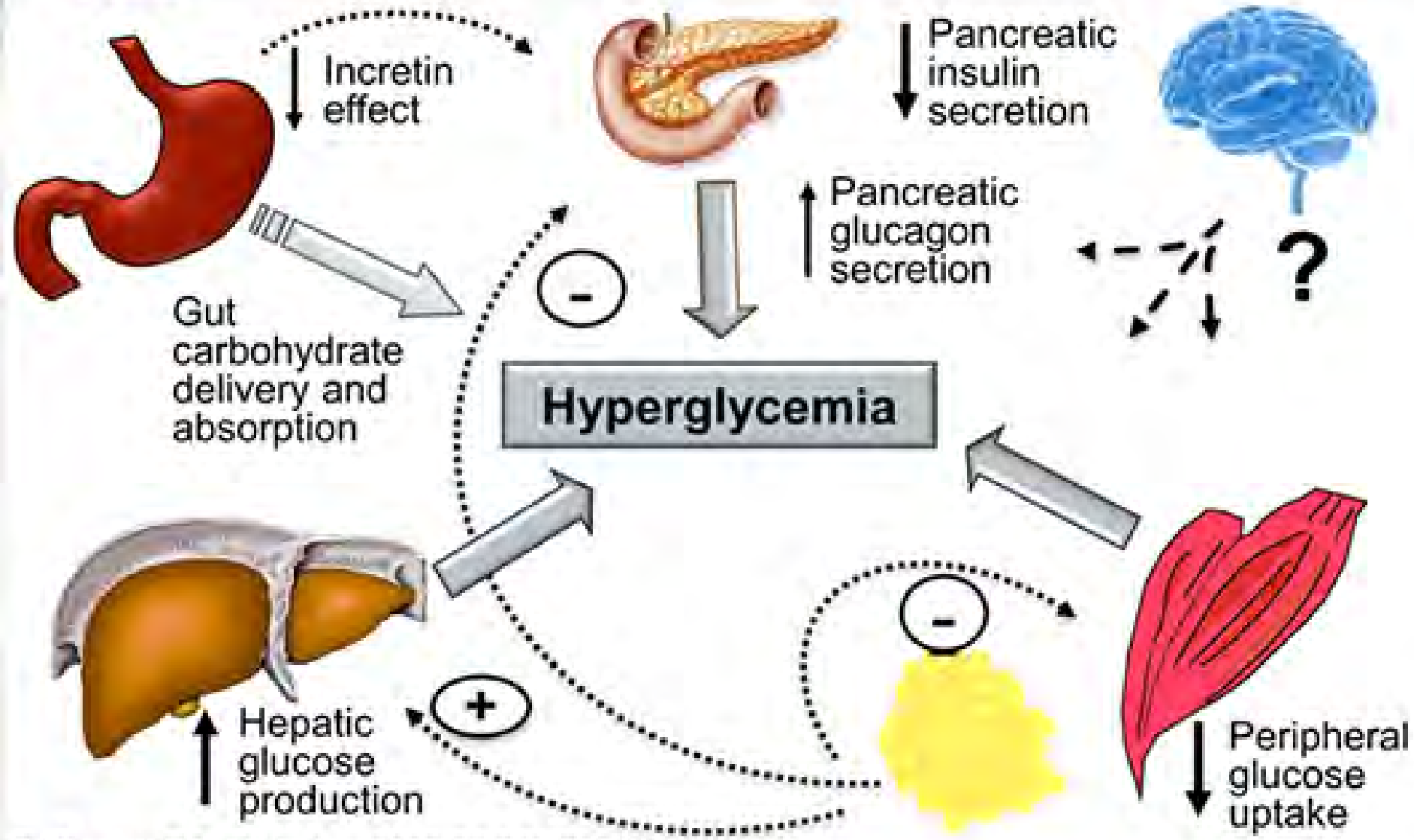
CONTROL

- Prolongs action of GLP-1 & GIP
- Works on both fasting and postprandial blood sugar
- Low risk of hypoglycemia (alone)
- Lowers HgbA1C 1%
- Restores 1st phase insulin response and increases pancreatic insulin output
- Slows glucose absorption from gut by slowing gastric emptying
- Causes early satiety/wt. neutral
- Decreases beta cell apoptosis

KAOS

- Expensive
- Pancreatitis, increased LFTs
- Stevens-Johnson syndrome
- Rash, urticaria, angioedema
- Headache(6.5% vs 5.9% with placebo)
- Monitor renal function periodically and adjust dose for CKD
- Hypoglycemia risk with sulfonylureas

Main Pathophysiological Defects in T2D



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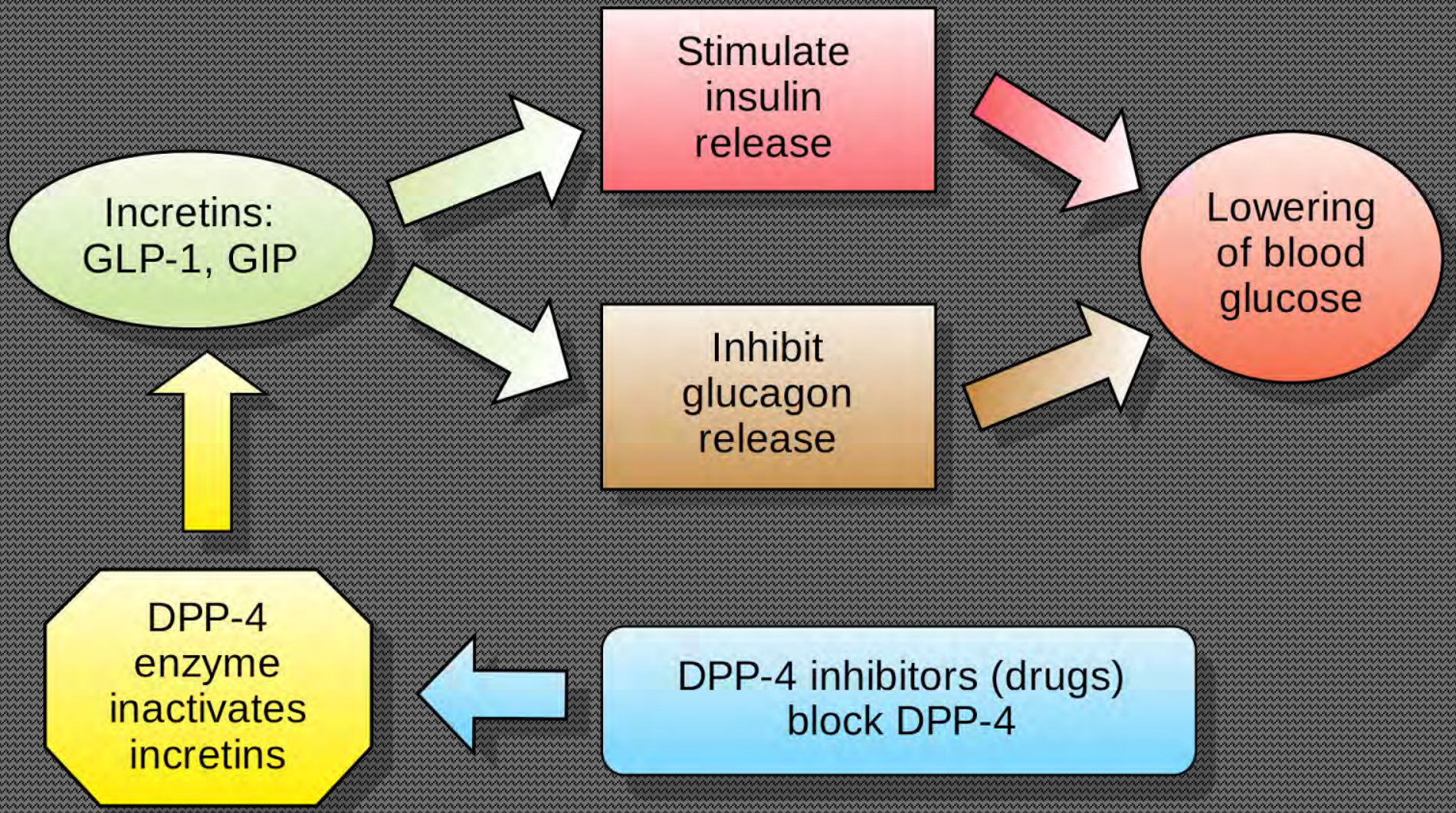
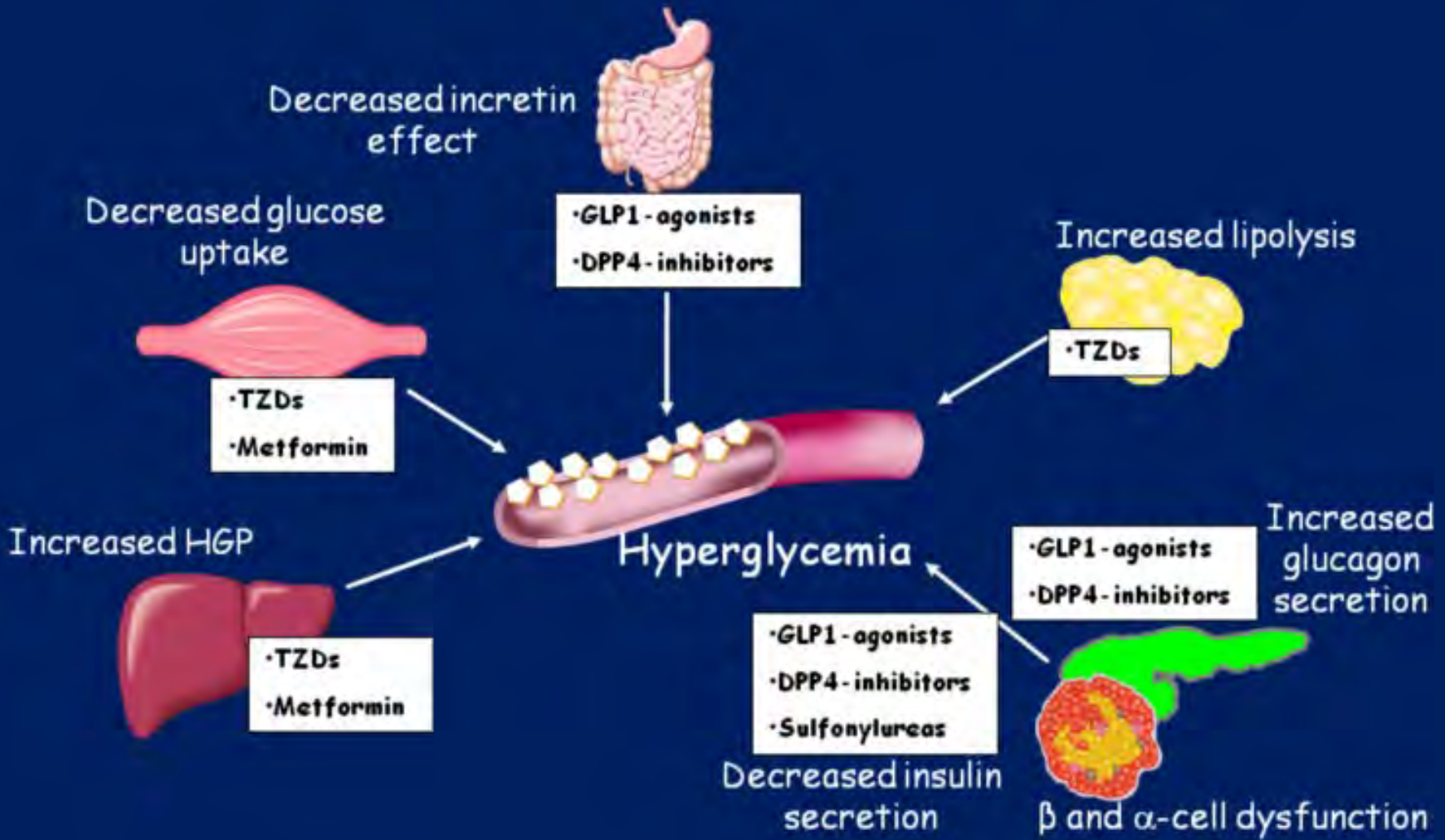

Stimulate insulin release
Incretins: GLP-1, GIP
Lowering of blood glucose
Inhibit glucagon release
DPP-4 enzyme inactivates incretins
DPP-4 inhibitors (drugs) block DPP-4

Patho-physiology of Type 2 diabetes
Site of Action of Available Drugs



Dopamine-2 agonist

Bromocriptine (Cycloset)

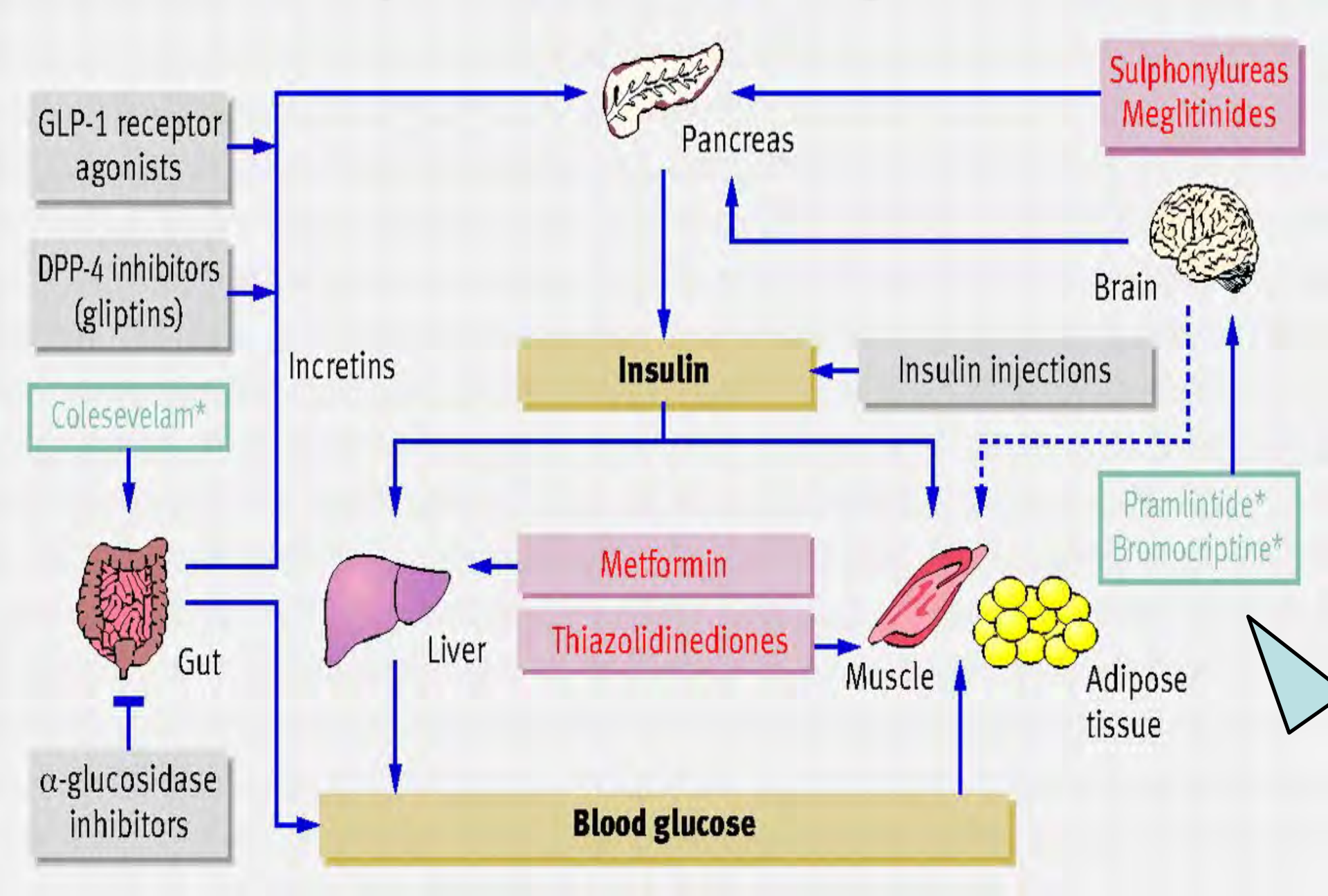
CONTROL

- No weight gain
- Give once daily within 2 hours of waking
- Lowers A1C 0.7%
- Mediates glucose and lipid metabolism centrally, decreasing plasma glucose, triglycerides and FFA levels
- 0.8 mg/day and increase weekly up to 1.6-4.8mg/day

KAOS

- May cause nausea, asthenia, constipation, dizziness, rhinitis (although side effects may be transient)

Dopamine-2 Agonist



Sodium-glucose cotranspoter-2 (SGLT-2) inhibitors

canagliflozin(Invonka),dapagliflozin(Farxiga),empagliflozin(Jardiance),ertugliflozin (Steglatro)

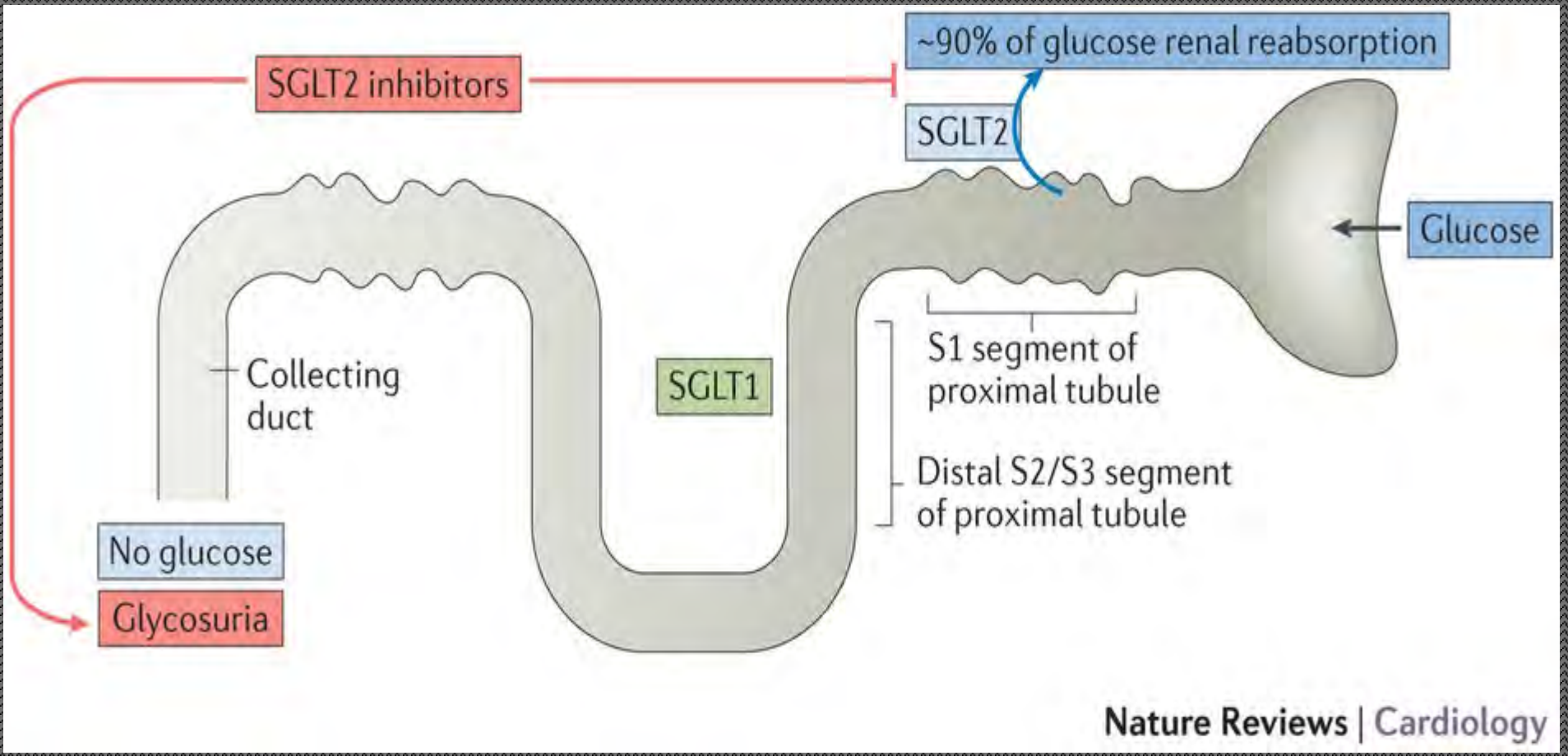
CONTROL

- Blocks glucose reabsorption and increases glucose excretion by the kidney
- Lowers HgbA1C by 0.3%
- No hypoglycemia (alone)
- Weight loss/weight neutral
- Dapagliflozin may prevent renal failure w or w/o DM
- Dapagliflozin may prevent CHF and decrease CV death in very sick pts w EF < 27% w or w/o DM

KAOS

- Expensive ($500/month) for small effect on HgbA1c
- It is a better medicine for advanced CKD (III-IV) and severe CHF (EF<27%) than for DM2
- Contraindicated if low GFR (C<30,D<25, E<45)
- Caution w elderly, alcoholics, uncircumcised
- May increase risk of leg and foot amputation (although Black Box warning removed). Always document foot exam if using.
- Caution w nephrotoxic meds e.g. diuretics, ACEi, ARBs, NSAIDs (Always monitor renal function)
- Hold if decreased fluid intake from fasting/acute illness or fluid loss from GI illness or heat exp
- Highest risk of vaginal yeast infection of DMeds

Sodium-glucose cotransporter-2 inhibitors



Combination diabetic medications since 2014

Glyxambi (Empagliflozin and Linagliptin)
Steglujan (Ertugliflozin and Sitagliptin)
Xigduo XR (Dapagliflozin and Metformin HCI Extended-Release)
Synjardy (Empagliflozin and Metformin)
Segluromet (Ertugliflozin and Metformin)

Kerendia (Finerenone) approved in July 2021 is first-in-class, nonsteroidal mineralocorticoid receptor antagonist (MRA) and is indicated to reduce the progression of chronic kidney disease, risk of kidney failure and risk of cardiovascular disease (and death) in adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D).


If I didn't have to pay for my diabetes meds, I'd be a millionaire now!
Now back to Regis

Parenteral agents

Control

GLP-1 Analogs

Insulin

Amylin Analogs

GLP-1 Agonist

CONTROL

- Stimulates insulin release in the presence of elevated glucose
- Decreases glucagon secretion
- Delays gastric emptying and increases satiety c ass. wt loss
- Lowers HgbA1C .78-1.9%
- Lowers triglycerides & raises HDL
- Lowers blood pressure
- Improves endothelial function
- Reduces CRP & other markers
- Decreases cardiovascular events

KAOS

- Expensive (1st line Rx?)
- Requires injection
- Pancreatitis
- GI s.e. including nausea, vomiting, diarrhea, abdominal pain
- Gastroparesis is a contraindication to use
- Medullary thyroid cancer seen in mice and rats (but not in humans)

Key Characteristics of Currently Available Injectable GLP-1 Receptor Agonists

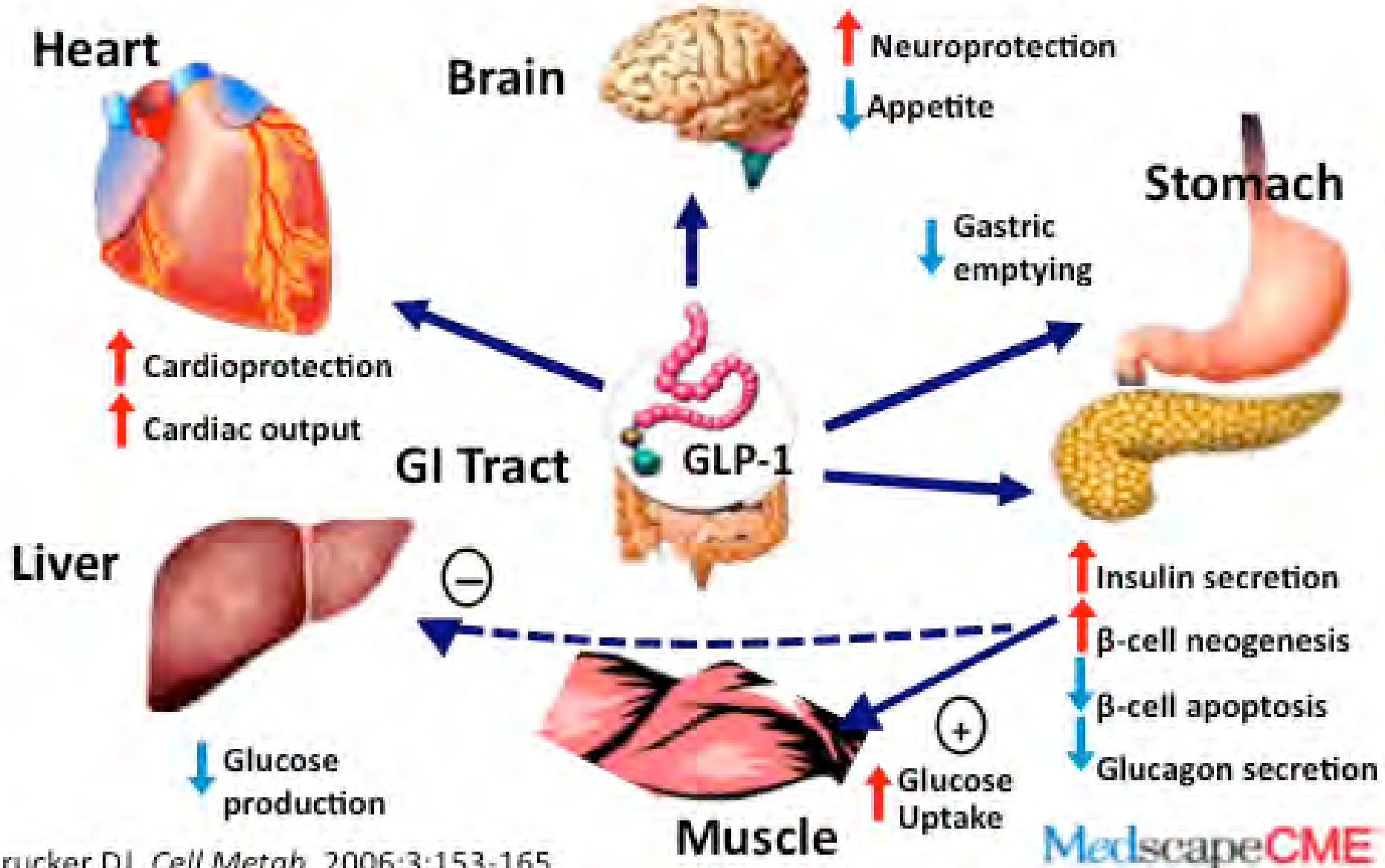
	Exenatide (Byetta)	Liraglutide (Victoza) (Saxenda)	Exenatide ER (Bydureon)	Dulaglutide (Trulicity)	Semaglutide (Ozempic)
Recommended Dosing	Initiate at 5 mcg twice daily; increase to 10 mcg twice daily after 1 month based on clinical response	Initiate at 0.6 mg per day for 1 wk, then increase to 1.2 mg; may increase to 1.8 mg for additional glycemic control	Administer 2 mg once weekly	Initiate at 0.75 mg once weekly; may increase to 1.5 mg for additional glycemic control	Initiate at 0.25 mg once weekly, then after 4 wk increase to 0.5 mg once weekly; may increase to 1 mg for additional glycemic control
Indication(s)	Adjunct to diet and exercise to improve glycemic control in T2DM	• Adjunct to diet and exercise to improve glycemic control in T2DM • To reduce the risk of major adverse CV events in adults with T2DM and established CVD	Adjunct to diet and exercise to improve glycemic control in T2DM	Adjunct to diet and exercise to improve glycemic control in T2DM	Adjunct to diet and exercise to improve glycemic control in T2DM
Administration Frequency	Twice daily	Once daily	Once weekly	Once weekly	Once weekly
GLP-1 RA Type	Short-acting	Long-acting	Long-acting	Long-acting	Long-acting
Hypoglycemia Risk (monotherapy)	Low	Low	Low	Low	Low
Weight Effects	Loss	Loss	Loss	Loss	Loss

lixisenatide(Adlyxin) 20mcg SQ once daily

Oral semaglutide (Rybelsus)

- Rybelsus was approved on September 20, 2019, as the first oral medication in the drug class glucagon-like peptide receptor agonist (GLP-1 RA)
- Rybelsus is not recommended as first-line therapy for patients with type 2 diabetes; rather, metformin is preferred drug for initial treatment.
- The American Diabetes Association (ADA) guidelines recommend the use of a GLP-1 RA, such as semaglutide, to achieve greater blood glucose lowering over initiating insulin for patients whose oral therapy treatments have failed.
- Need to take Rybelsus at least 30 minutes before the first food, beverage, or other oral medication for the day, with no more than 4 oz of plain water.
- The most common adverse effects (AEs) include nausea, diarrhea, vomiting, decreased appetite, indigestion, and constipation. Rybelsus carries a boxed warning regarding the increased risk of thyroid c-cell tumors, and patients who have had medullary thyroid carcinoma (MTC) or a family history of MTC should not take the medication.
- The starting dose of Rybelsus is 3 mg orally once daily for 30 days. After 30 days, the dose should be increased to 7 mg once daily, which may be increased to a maximum of 14 mg once daily if additional blood glucose lowering is needed after at least 30 days on the 7-mg dose.
- The PIONEER 3 randomized clinical trial evaluated the safety and efficacy of oral semaglutide 7 mg/day and 14 mg/day compared with sitagliptin added on to metformin. There were 1864 patients. The study revealed that both doses of semaglutide compared with sitagliptin resulted in statistically significant greater reductions in A1C levels over 26 weeks ($P < 0.001$).

GLP-1 Actions in Peripheral Tissue



Drucker DJ. *Cell Metab*. 2006;3:153-165.

Dual GIP and GLP-1 receptor agonist

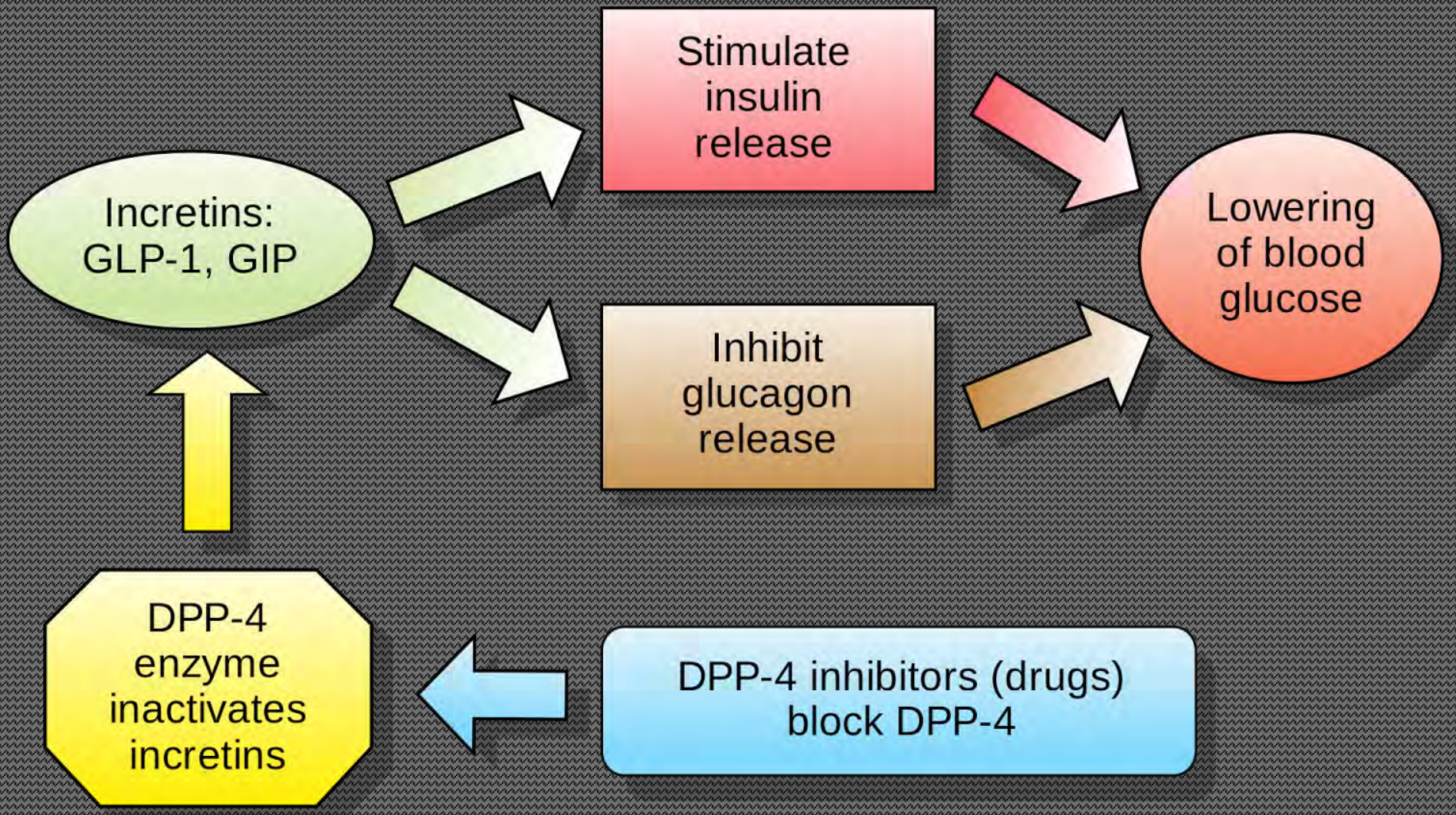
tirzepatide (Mounjaro)

CONTROL

- First in class dual GIP/GLP-1 agonist
- Mimics natural agonists (GIP and GLP-1) and binds to their receptors.
- Delays gastric emptying and up to 20% wt loss at highest dose
- Lowers HgbA1C 1.6-2.3%
- SURPASS trials show superior A1C (+.5%) and weight reduction(+12lbs) at highest dose(15mg/wk) when compared to semaglutide (Ozempic) highest dose (1.5mg/wk) respectively over 40 wks

KAOS

- Expensive ($1539.54/month)
- Requires weekly injection
- GI s.e. including nausea, vomiting, diarrhea, upper abdominal pain
- Gastroparesis is a contraindication to use
- Only for adults with type 2 diabetes as an addition to diet and exercise
- Trial for cardioprotective affect vs dulaglutide ends 10/24


Stimulate insulin release
Incretins: GLP-1, GIP
Lowering of blood glucose
Inhibit glucagon release
DPP-4 enzyme inactivates incretins
DPP-4 inhibitors (drugs) block DPP-4

Amylin Analogs

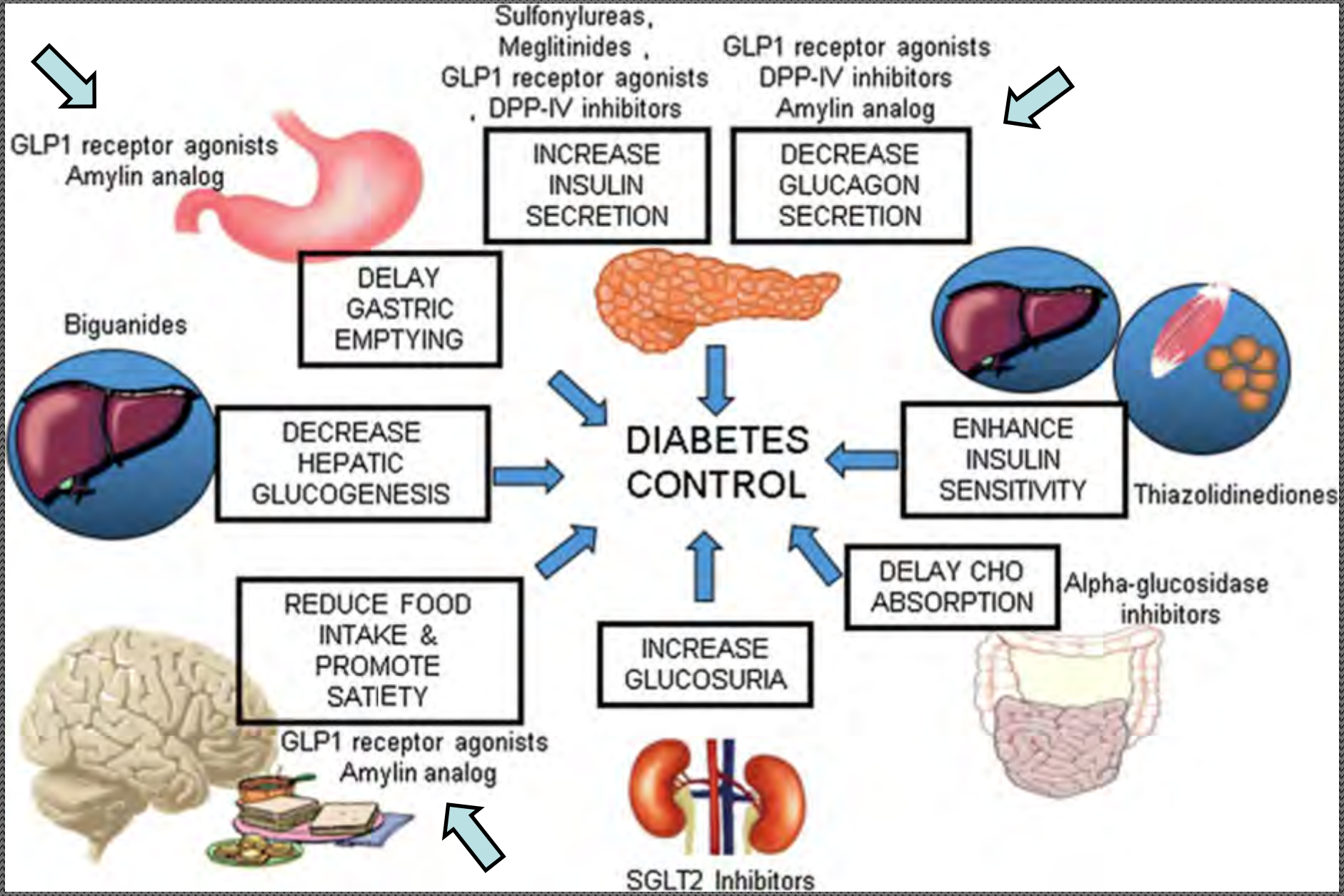
pramlintide (Symlin)

CONTROL

- Lowers insulin requirement
- Lowers A1C 1.5-2%
- Decreases post prandial glucagon production
- Delays gastric emptying
  - Increases satiety
  - Decreased caloric intake
  - Resultant weight loss

KAOS

- Expensive ($977 for 2 pens w GoodRX)
- Requires injection separate from insulin before meals
- Severe hypoglycemia with insulin
- Gastroparesis is a contraindication to use
- Nausea, vomiting, abdominal pain
- Headache
- Dizziness
- Arthralgia
- May reduce absorption of meds


Sulfonylureas,
Meglitinides ,
GLP1 receptor agonists
, DPP-IV inhibitors
GLP1 receptor agonists
DPP-IV inhibitors
Amylin analog
GLP1 receptor agonists
Amylin analog
INCREASE INSULIN SECRETION
DECREASE GLUCAGON SECRETION
DELAY GASTRIC EMPTYING
Biguanides
DECREASE HEPATIC GLUCOGENESIS
DIABETES CONTROL
ENHANCE INSULIN SENSITIVITY
Thiazolidinediones
DELAY CHO ABSORPTION
Alpha-glucosidase inhibitors
REDUCE FOOD INTAKE & PROMOTE SATIETY
INCREASE GLUCOSURIA
GLP1 receptor agonists
Amylin analog
SGLT2 Inhibitors

Insulin

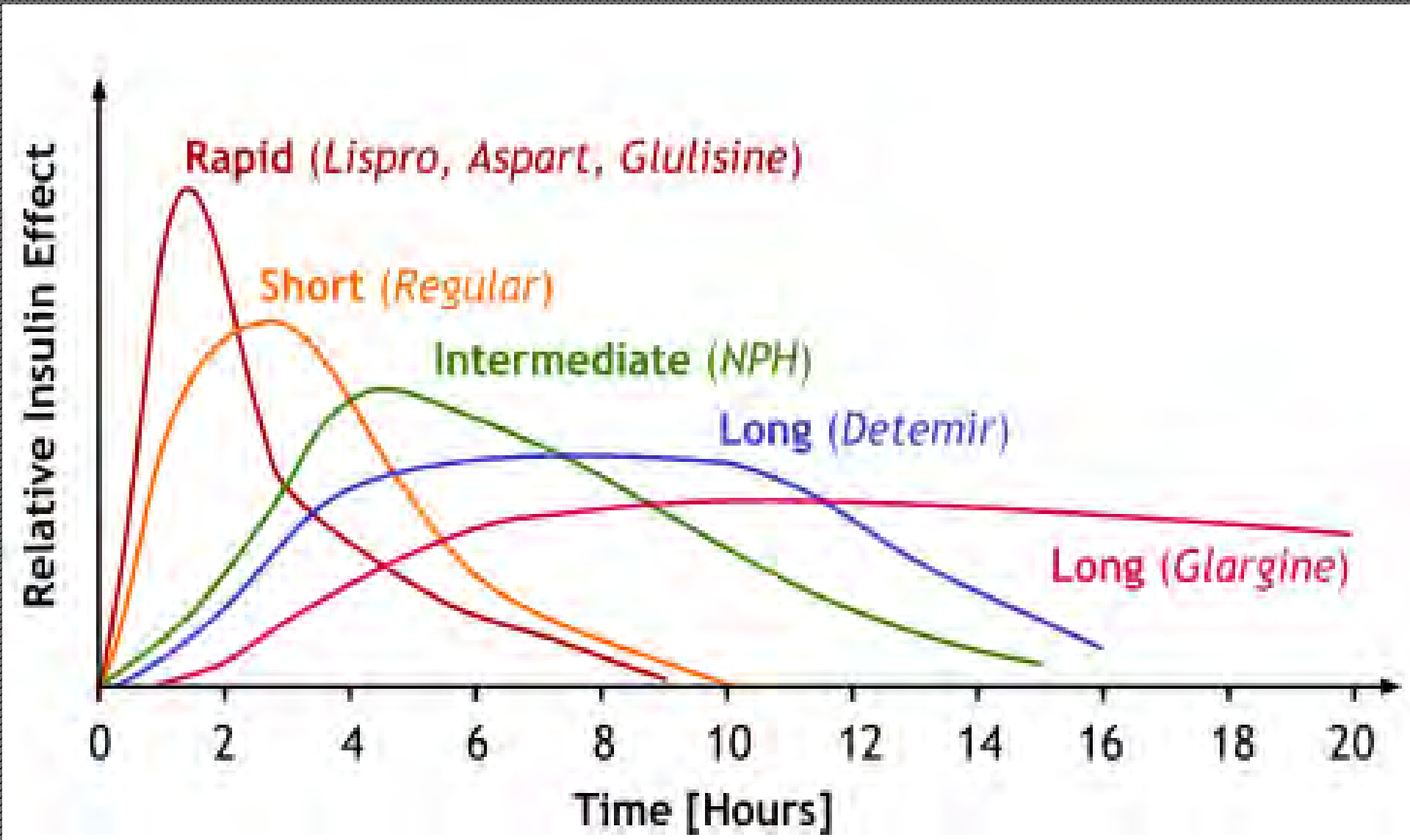
CONTROL

- Relatively inexpensive
- Can lower HgbA1c significantly
- Effective even in late stages
- Available in bottles, pens, pumps and nasal spray

KAOS

- Significant hypoglycemia
- Usually requires injection
- Associated with atherosclerotic weight gain and lipogenesis
- No reduction in CV events per ADVANCE, ACCORD, VADT

Insulin effect and length of action



Insulin Products Comparison Chart

Type of Insulin	Brand Name/ Formulary Status/ Manufacturer	Concentration	May Be Mixed With	Onset	Peak	Duration	Administration in Relation to Meals
Prandial or Correction (Rapid Acting)							
Aspart	Novolog® (F) Novo Nordisk	100 units/mL	NPH	10 to 20 minutes	1 to 3 hours	3 to 5 hours	5 to 10 minutes before meals
Lispro	Humalog® (NF) Lilly	100 units/mL	NPH	15 to 30 minutes	1 to 2 hours	3 to 5 hours	15 minutes before or immediately after meals
Prandial or Correction (Short Acting)							
Regular	Novolin® R (R) Novo Nordisk	100 units/mL	NPH	30 to 60 minutes	2 to 4 hours	4 to 8 hours	30 minutes before meals
Regular	Humulin® R U-500 (F) Lilly	500 units/mL	do not mix with other insulins	30 to 60 minutes	2 to 4 hours	4 to 8 hours	30 minutes before meals
Regular	Humulin® R (NF) Lilly	100 units/mL	NPH	30 to 60 minutes	2 to 4 hours	4 to 8 hours	30 minutes before meals
Basal (Intermediate Acting)							
NPH	Novolin® N (F) Novo Nordisk	100 units/mL	aspart, regular	1 to 2 hours	6 to 14 hours	16 to 24 hours	§see below
NPH	Humulin® N (NF) Lilly	100 units/mL	lispro, regular	1 to 2 hours	6 to 14 hours	16 to 24 hours	§see below
Basal (Long Acting)							
Glargine	Lantus® (F) Aventis	100 units/mL	do not mix with other insulins	1 to 2 hours	no peak	24 hours	without regard to meals

Other basal long acting insulins include: glargine (Lantus, Toujeo, Basaglar), detemir (Levemir) and degludec (Tresiba)

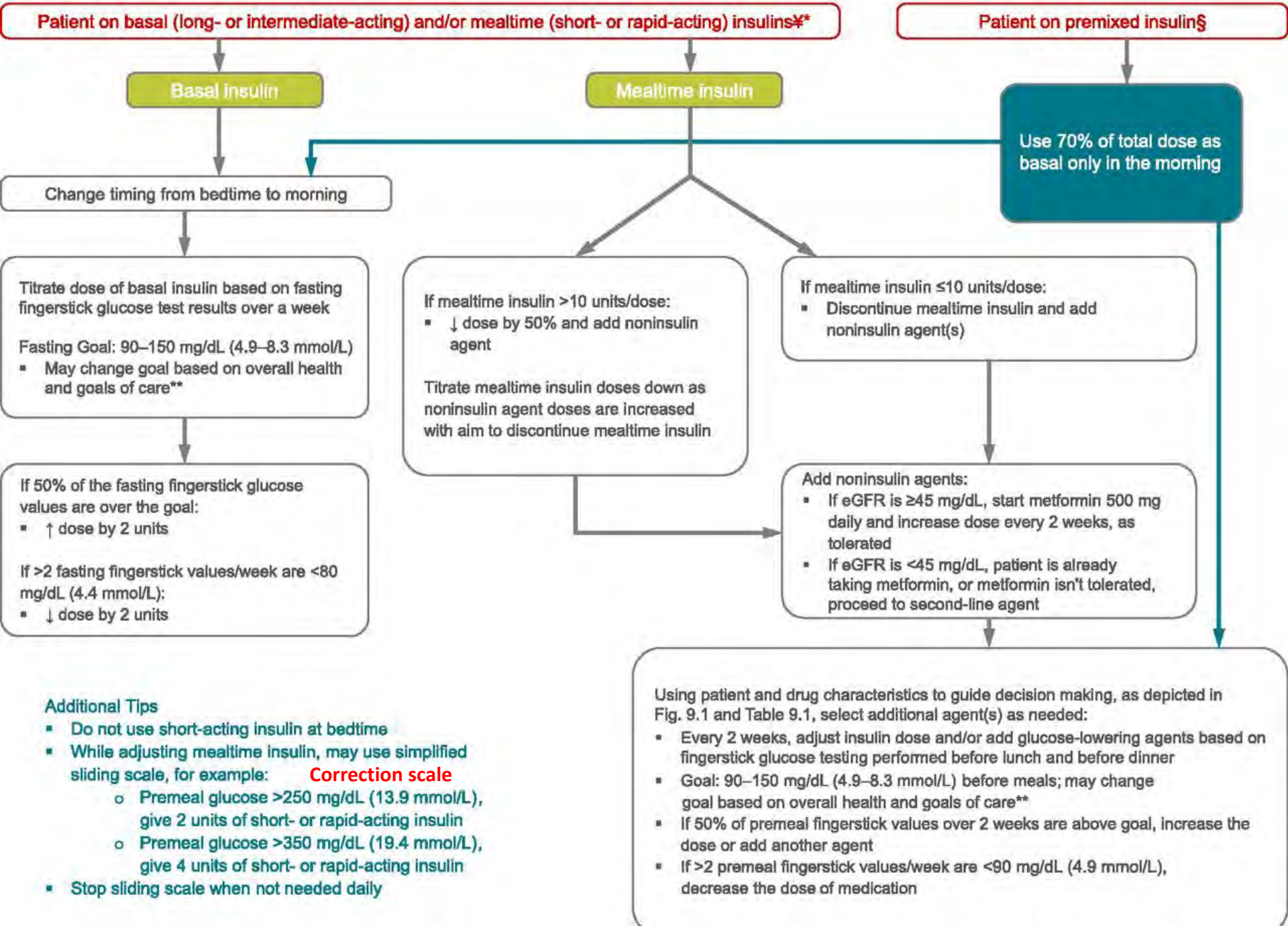
New injectable meds since 2015

- **Tresiba** approved in 2015, is a brand-name version of the drug insulin degludec that lasts up to 42 hours. It's injected once daily.
- **Basaglar and Toujeo** approved 2015 are two new forms of insulin glargine. Both injected once daily similar to another insulin glargine drug called Lantus. (Toujeo is a more concentrated form of insulin glargine)
- **Xultophy** was approved in 2016 combines insulin degludec, a long-acting insulin, and liraglutide, a GLP-1 agonist.
- **Soliqua** was approved in 2016 combines the drug insulin glargine with lixisenatide, a GLP-1 receptor agonist.
- **Adlyxin** (lixisenatide) approved in 2016 is GLP-1 agonist injected once daily.
- **Ryzodeg** was approved in September 2016. It's designed to be used to treat both type 1 and type 2 diabetes. Ryzodeg combines insulin degludec with insulin aspart. It's meant to be injected once or twice daily. (Available in multiple countries but not readily available in US)
- **Ozempic** (semaglutide) approved in late 2017 is a GLP-1 agonist injected once per week (FDA approved semaglutide in oral form in 2019)
- **Semglee** (Insulin Glargine-Yfgn) approved in 2020 is a synthetic, long-lasting insulin medication used to help manage high blood sugar in adults and pediatric patients with type 1 diabetes, as well as adults with type 2 diabetes.
- **Mounjaro** (tirzepatide) approved May 2022 is first in class dual GIP and GLP-1 agonist with significant decreases in HgbA1c and weight reduction benefits.

Inhaled medication for diabetes

Afrezza is a fast-acting insulin approved in 2014 which comes as a powder that you breathe in through your mouth with an inhaler. It is approved for type 1 and type 2 diabetes. Afrezza comes in cartridges that deliver 4 units, 8 units, or 12 units of the drug. It has a black boxed warning for acute bronchospasm in people with asthma or COPD.

Simplification of Complex Insulin Therapy



Basal insulin

Change timing from bedtime to morning

Titrate dose of basal insulin based on fasting fingerstick glucose test results over a week

Fasting Goal: 90–150 mg/dL (4.9–8.3 mmol/L)

- May change goal based on overall health and goals of care**

If 50% of the fasting fingerstick glucose values are over the goal:

- ↑ dose by 2 units

If >2 fasting fingerstick values/week are <80 mg/dL (4.4 mmol/L):

- ↓ dose by 2 units

Mealtime insulin

Use 70% of total dose as basal only in the morning

If mealtime insulin >10 units/dose:

- ↓ dose by 50% and add noninsulin agent

Titrate mealtime insulin doses down as noninsulin agent doses are increased with aim to discontinue mealtime insulin

If mealtime insulin ≤10 units/dose:

- Discontinue mealtime insulin and add noninsulin agent(s)

Add noninsulin agents:

- If eGFR is ≥45 mg/dL, start metformin 500 mg daily and increase dose every 2 weeks, as tolerated
- If eGFR is <45 mg/dL, patient is already taking metformin, or metformin isn't tolerated, proceed to second-line agent

Additional Tips

- Do not use short-acting insulin at bedtime
- While adjusting mealtime insulin, may use simplified sliding scale, for example: **Correction scale**
  - Premeal glucose >250 mg/dL (13.9 mmol/L), give 2 units of short- or rapid-acting insulin
  - Premeal glucose >350 mg/dL (19.4 mmol/L), give 4 units of short- or rapid-acting insulin
- Stop sliding scale when not needed daily

Quick summary on Diabetic medications in the geriatric patient

- Metformin should be first line therapy for most diabetic patients unless GFR<30. Age alone should not be a determining factor. Consider GLP-1 and SGLT2 agents if indicated (heart/kidney dx)
- Addition of basal insulin should be considered early on for safe and effective treatment of diabetes with adjustments determined by fasting blood sugars.
- Glyburide called out by ADA as the worst of the 2nd generation sulfonylureas in terms of hypoglycemic risk for the elderly
- DPP-4 agents are not encouraged due to excessive costs and lower efficacy.
- SGLT-2 agents are essentially ineffective for lowering HgbA1c and very expensive BUT do have a potential role in CHF (EF<27%) and CKD IIIb (GFR >25-45) as long as there is albuminuria, diabetes, or heart failure present.

Diabetes in the Elderly

- Symptoms of hypoglycemia and hyperglycemia are atypical in elderly
- Demented or aphasic patients are unable to communicate their hypoglycemic symptoms
- Hypoglycemic symptoms may be blamed on dementia, psychosis, infection (UTI, sepsis), cardiovascular disease, seizures, stroke, etc. and treated incorrect

Survival as a function of HgbA1c in people with type 2 diabetes: a retrospective cohort study

- All cause mortality was primary outcome
- 47,970 people over 50 years of age followed over 12 years
- Ideal Hgb A1c?
  - 6.5
  - 7.5
  - 10.5

Lancet 375; Issue 9713; page 481-489 2/6/10

Survival as a function of HgbA1c in people with type 2 diabetes: a retrospective cohort study

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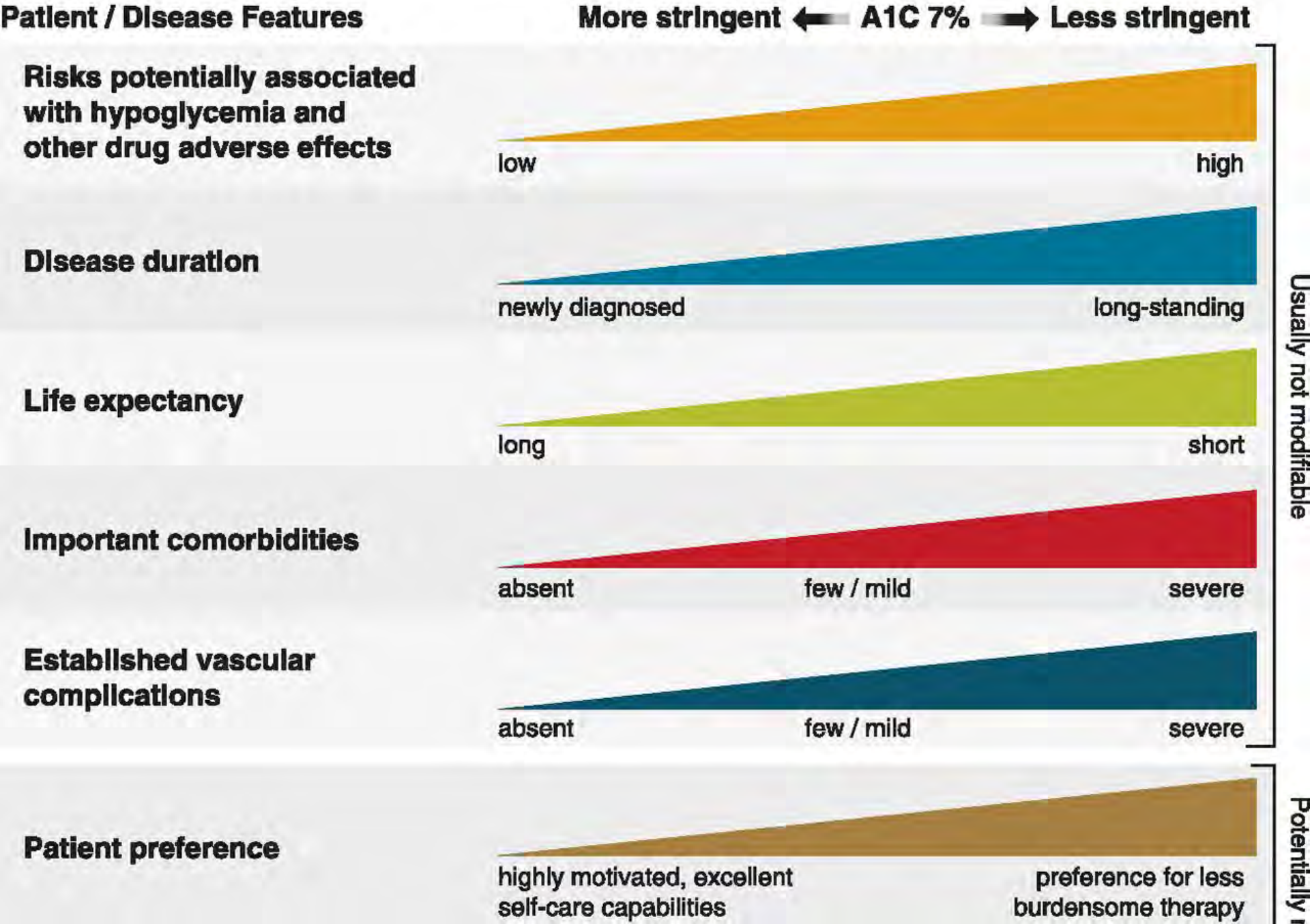
- 47,970 people over 50 years of age followed over 12 years
- Ideal Hgb A1c:
  - 6.5 Hazard Ratio 1.52
  - 7.5 Hazard Ratio 1.0
  - 10.5 Hazard Ratio 1.79

Lancet 375; Issue 9713; page 481-489 2/6/10

Approach to Individualization of Glycemic Targets



Sliding Scale: CHAOS or CONTROL?

- Although sliding-scale insulin (SSI) is widely used in hospitals and LTC facilities, its routine and prolonged use is not recommended

Sliding Scale: CHAOS or CONTROL?

- An insulin sliding scale often generates a roller-coaster pattern of glucose values
- Very high blood glucose values are treated with insulin, sometimes with ensuing hypoglycemia.
- The hypoglycemia is then treated with (often excessive quantities of) carbohydrates and without insulin, with ensuing hyperglycemia.
- Practitioner is often notified when blood glucose level is <60 0r >400

Sliding Scale: CHAOS or CONTROL?

- An insulin sliding scale is reactive, responding to the current blood glucose level, but is not anticipatory or proactive. It does not anticipate carbohydrate intake, metabolic stress or physical activity.
- As usually written, an insulin sliding scale is a device for sustaining hyperglycemia in a patient with uncontrolled diabetes.
- It provides insulin only when the blood glucose is above a threshold value, typically 150-200 mg/dL, and then provides only small doses of insulin, e.g., 2 to 6 units, for values just above that threshold.
- The consequence is that the patient often receives inadequate doses of insulin until the blood glucose level is unacceptably high, often over 300 mg/dL.

Sliding Scale: CHAOS or CONTROL?

- Sliding Scale Insulin results in:
  - Greater patient discomfort (stuck up to 8 times a day)
  - Increased nursing time
  - Interference with daily activities in LTC
  - Compromised quality of life
  - Hyperglycemia and Hypoglycemia

Sliding Scale: CHAOS or CONTROL?

- Studies show that SSI is neither effective nor efficient
- In a prospective randomized trial in 130 hospital patients with type 2 diabetes, a basal-bolus insulin regimen achieved superior control compared with SSI (RABBIT 2 Trial in Diabetes Care 2007;30: 2181-2186)

Intensive Control of Blood Glucose in ICU patients: CHAOS or CONTROL?

- Intensive blood sugar control for 6104 critical care patients with hyperglycemia does not improve outcomes and is associated with a 14% increase in deaths (NICE-SUGAR study NEJM 360:1283-97, 2009)
- Randomized control trial showed that intensive perioperative glucose control did not improve outcomes of open heart surgery patients (Raquel Pei Chen Chan et al. Clinics vol.64 2009)
- Meta analysis of 26 studies (n=13,500) showed that lowering BS with intensive insulin treatment does not affect mortality in critically ill patients (Berge, Mesotten CMAJ April 14,2009)

SSI may be useful to help calculate fixed daily insulin requirement

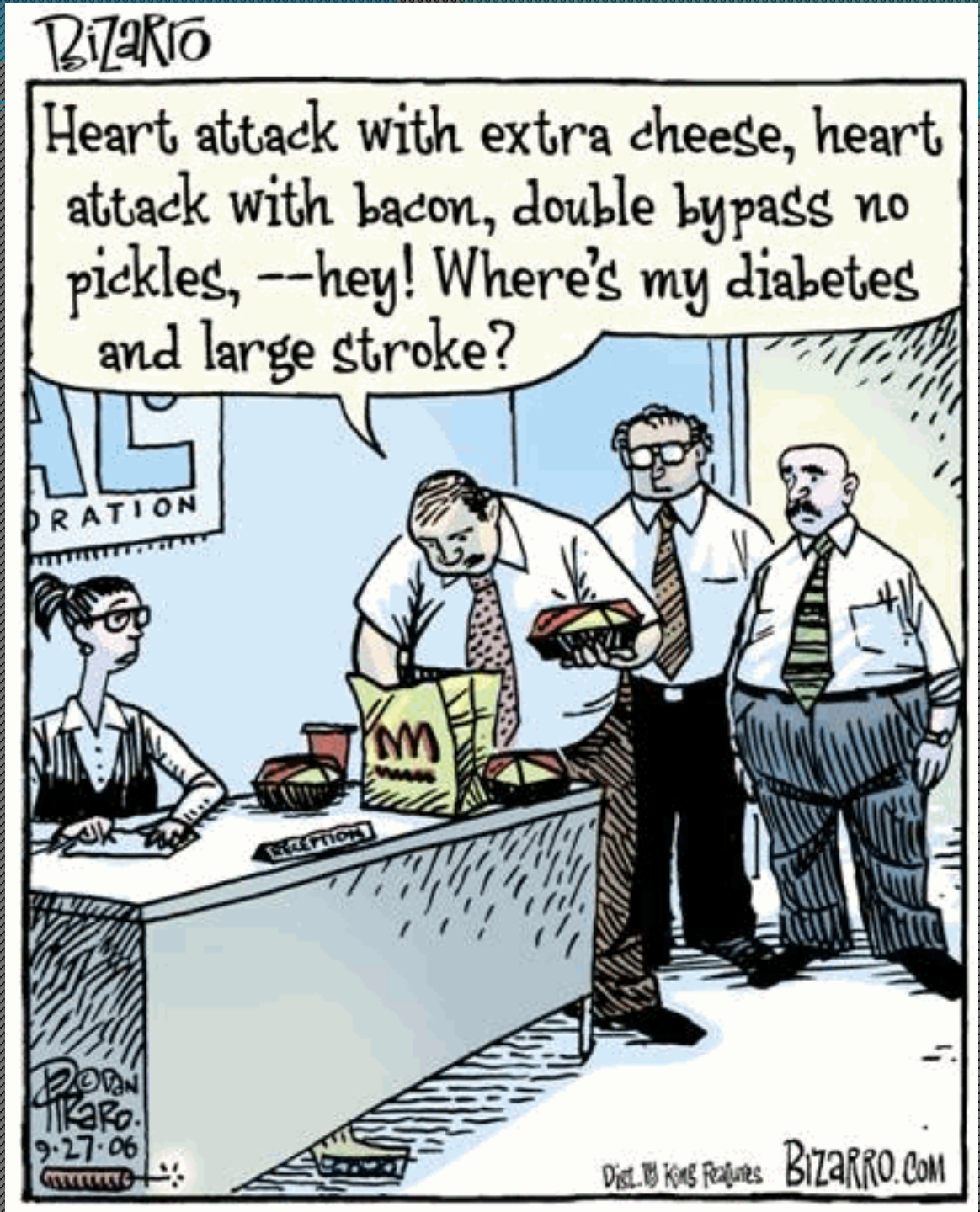
- Newly recognized diabetics
- When insulin requirements are unknown (e.g. acute illness)
- When new therapies are initiated (TF, glucocorticoids)
- SSI (or Correction scale) insulin should be evaluated within 5-7 days and converted to fixed daily insulin which has been shown to provide better control and less hypoglycemia

Be sure to reevaluate or put stop date on SSI to avoid an order remaining in effect indefinitely

The Geriatric Diabetic Diet

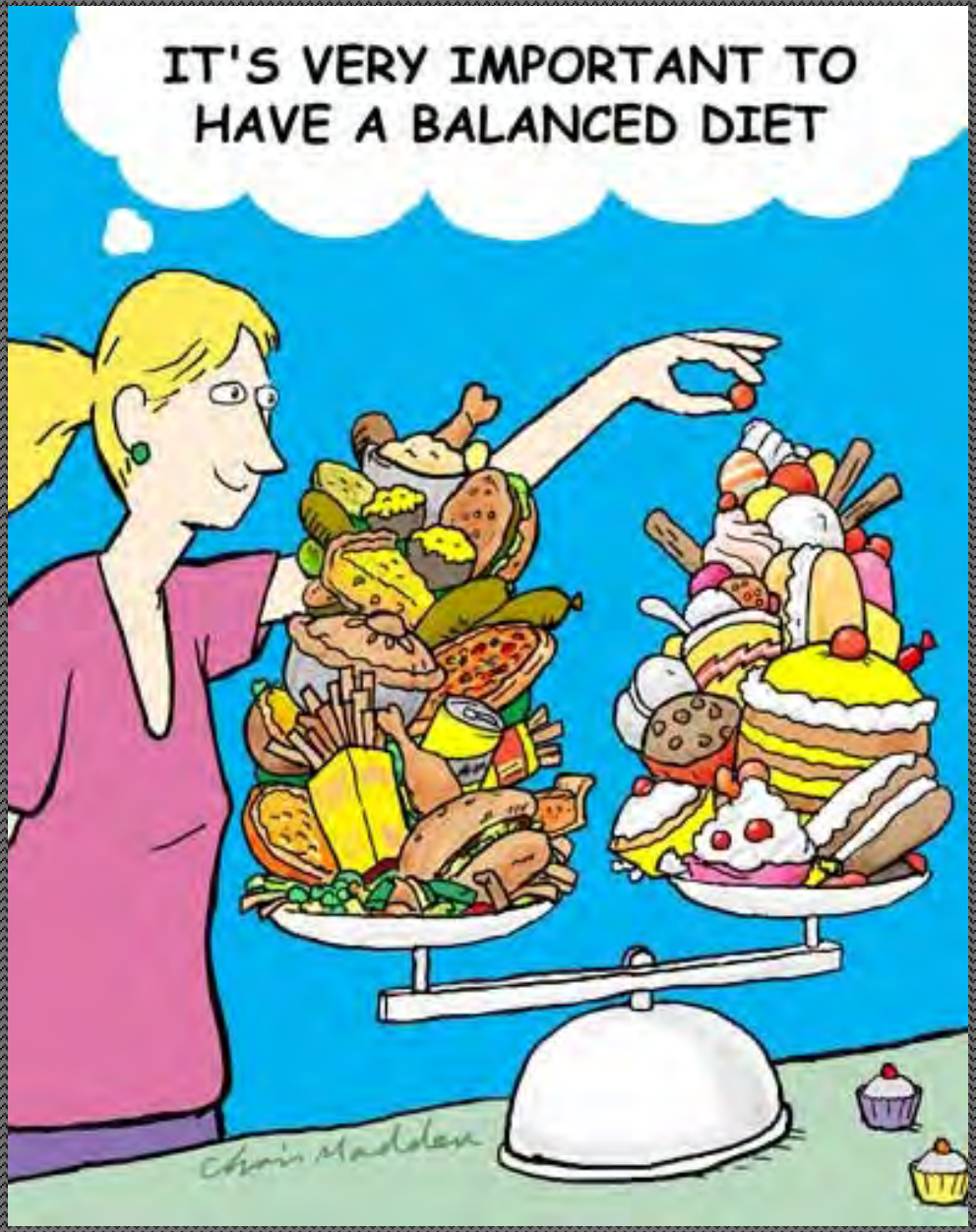
What is the best diet for an 85 year old 110lbs diabetic female in a skilled nursing facility?

- 1800 calorie ADA diet
- Low fat low salt cardiac diet
- Mech. soft diet with small portions
- Fiber rich diet with carbohydrates
- NCS diet (no concentrated sweets)


BIZARRO
Heart attack with extra cheese, heart attack with bacon, double bypass no pickles, --hey! Where's my diabetes and large stroke?
RATION
RECEPTION
DAN PIRARO
9-27-06
Dist. By King Features
BIZARRO.COM

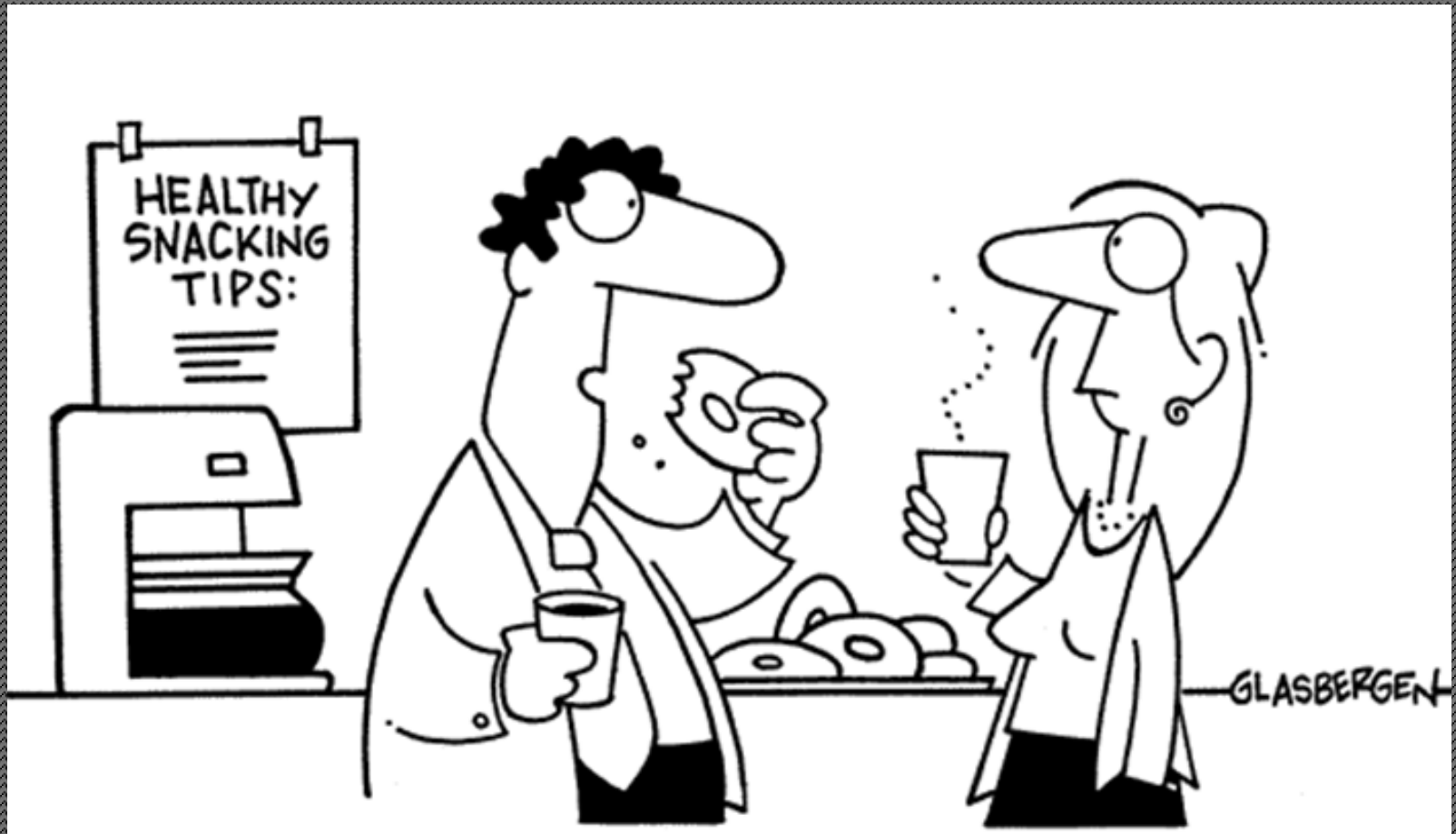
Would you believe?

- 1800 calorie ADA diet
- Low fat low salt cardiac diet
- Mech. soft diet with small portions
- Fiber rich diet with carbohydrates
- NCS (no concentrated sweets) diet


IT'S VERY IMPORTANT TO
HAVE A BALANCED DIET

Diabetic diet rules for geriatrics

- Regular diet with consistent amounts of carbohydrates and adequate fiber
- Consistent meal times
- Time oral agents and insulin to caloric consumption
- Control portion size
- Base caloric need on weight and activity



"The healthiest part of a donut is the hole. Unfortunately, you have to eat through the rest of the donut to get there!"

Avoid strict diets that may result in malnutrition states in patients already at risk

"The more you restrict the diet the more they cheat"

"I try to eat healthy. I never sprinkle salt on ice cream, I only eat decaffeinated pizza and my beer is 100% fat free."

Step One

- Lifestyle modification
- Initiate oral medication
- Basal insulin?

Step Two

- Additional oral agent
- Insulin (basal)

Step Three

- Intensify meds and insulin to establish appropriate goals

Late onset diabetes not equivalent CHD risk factor Archives of Internal Medicine March15, 2011

- Prospective study of 4,000 middle aged men
- Patients 60 years and older with mean diabetes duration of 5 years had a CHD risk ½ that of patients diagnosed before age 60 with diabetes for more than 16 years

Late onset diabetes not equivalent CHD risk factor Archives of Internal Medicine March15, 2011

EVENT	No DM and no prior MI N=3197	Late-onset DM2 N=307	Early-onset DM2 N=107	Men with prior MI and no DM2 N=368
Major Coronary heart Disease	1.0	1.54	2.39	2.51
Major CV disease	1.0	1.37	2.08	2.17
All-cause mortality	1.0	1.31	1.68	1.48

American Diabetes Association Guidelines for Type 2 Diabetes

- Hgb A1C <7.0% ✖ <6.5-7.0
- Fasting glucose 80-130mg/dL
- Postprandial glucose <180mg/dL
- Blood pressure <130/80 ✖ 140/90
- Lipids: LDL<100mg/dL; TG<150 mg/dL
  - ↳ LDL<70 if heart disease
- Yearly:
  - dilated eye exam
  - urinary protein
  - foot exam
  - flu shot
- ASA use and pnemococcal vaccine
  - ↳ aspirin if CVD or prior MI

Guidelines for Type 2 Diabetes in the geriatric patient

- Hgb A1C <7%
- Blood pressure <140/90
- Lipids: LDL<100mg/dl
- ASA
- Diet: ADA diet
- Yearly:
  - Dilated eye exam
  - GFR/urinary protein
  - Podiatric foot exam
  - Flu shot (pneumonia vax)

7.5-8.5% or higher

<150/90

Statin if tolerated

Fiber rich regular diet

Screen for cognitive impairment & depression

Avoid longterm sliding scale insulin

TABLE 1

Evidence-based guidelines for diabetes management in the elderly[3,4]

Health status/patient characteristics	A1C goal (%)	Treatment considerations
Healthy Few coexisting chronic illnesses Intact cognitive and functional status	<7.5	Metformin is the first-line medication if not contraindicated. Patient-specific factors determine which agents are appropriate for dual or triple therapy, if indicated, to achieve glycemic control.
Complex/intermediate Multiple coexisting chronic illnesses Mild to moderate cognitive impairment 2 or more instrumental ADL impairments	<8	For patients with multiple comorbid conditions or a short life expectancy, evaluate the risks and benefits of using antidiabetic medication. Patient-specific factors dictate the choice of medication therapy (if indicated to achieve glycemic control).
Poor Long-term care or end-stage chronic illnesses Moderate to severe cognitive impairment 2 or more ADL dependencies	<8.5	Less aggressive A1C goals may be appropriate for many, and discontinuation of medication may be the proper course of treatment. This group includes those with severe cardiovascular disease, end-stage chronic diseases in addition to diabetes, and life expectancy <5 years.

A1C, glycated hemoglobin; ADL, activities of daily living.

Modify treatment goals in geriatric patients with:

- Poor hypoglycemia awareness
- Recurrent idiopathic hypoglycemia episodes
- Anorexia
- Feeding dependency
- Gangrene
- Malignancy
- Severe dementia
- Life expectancy of less than 5 years

Treatment goals in the geriatric diabetic patient

- Appropriate goals for BS control while avoiding hypoglycemia
- Maintain nutritional status (liberal high fiber diet)
- Physical activity/exercise (150 min/wk) Walking, Tai Chi, Yoga, Dancing, Swimming AND include => 2 days of isometric resistance, strength, and balance training)
- Control pain and depression
- Appropriate blood pressure and lipid management goals (statins not indicated if life expectancy < 2years)
- Reduce lower extremity infections, ulcers, and limb loss
- Individualize and simplify regimens taking into account preferences, life expectancy, and quality of life
- Discuss and document advanced directives

Treatment goals in the elderly diabetic patient

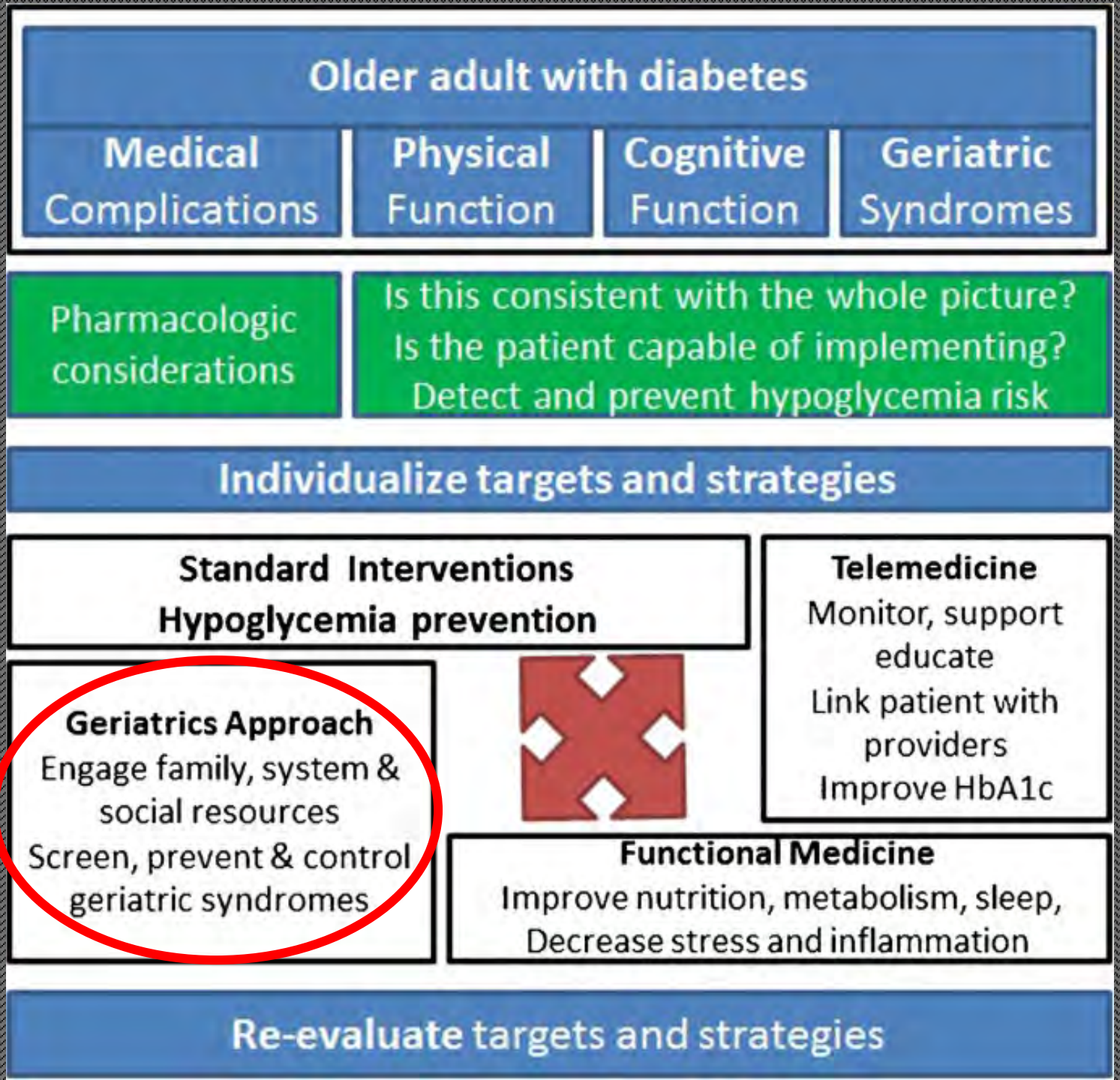
- ADA recommends avoidance of lows at all cost, while avoiding "severe" hyperglycemia.
- ADA calls for Hgb A1C <8.5% but notes that "many conditions" in the LTC patient can interfere with the A1C test.
- In advanced disease, "forget the friggin' A1C" and call for pre-meal glucose of up to 200 as being acceptable.
- For patients at the end of life, the ADA says the A1C, has "no role," and further, that there is "no benefit" of glycemic control at all, except "avoiding symptomatic hyperglycemia."

Considerations in the elderly diabetic patient

- Glycemic goals need to be personalized
- Simplified treatment regimens are preferred
- The "diabetes diet" is "outdated," ineffective, and should be dropped to avoid dehydration, and unintentional weight loss
- The use of sliding scale insulin is to be avoided and use of sliding scale insulin has been added to the American Geriatrics Society (AGS) Beers Criteria for Potentially Inappropriate Medication use in Older Adults,

Considerations in the elderly diabetic patient

Care transitions are extremely important in this population and require close communication between transferring and receiving care teams to ensure patient safety and reduce readmission rates.


Older adult with diabetes
Medical Complications
Physical Function
Cognitive Function
Geriatric Syndromes
Pharmacologic considerations
Is this consistent with the whole picture?
Is the patient capable of implementing?
Detect and prevent hypoglycemia risk
Individualize targets and strategies
Standard Interventions
Hypoglycemia prevention
Telemedicine
Monitor, support educate
Link patient with providers
Improve HbA1c
Geriatrics Approach
Engage family, system & social resources
Screen, prevent & control geriatric syndromes
Functional Medicine
Improve nutrition, metabolism, sleep,
Decrease stress and inflammation
Re-evaluate targets and strategies

Considerations in the elderly diabetic patient

Always remember: First, DO NO HARM!!!

Avoid adverse drug effects and hypoglycemia

THE END

It’s time for questions Max.

I asked you not to tell me that.

questions.