Updates in Youth Onset Type 2 Diabetes

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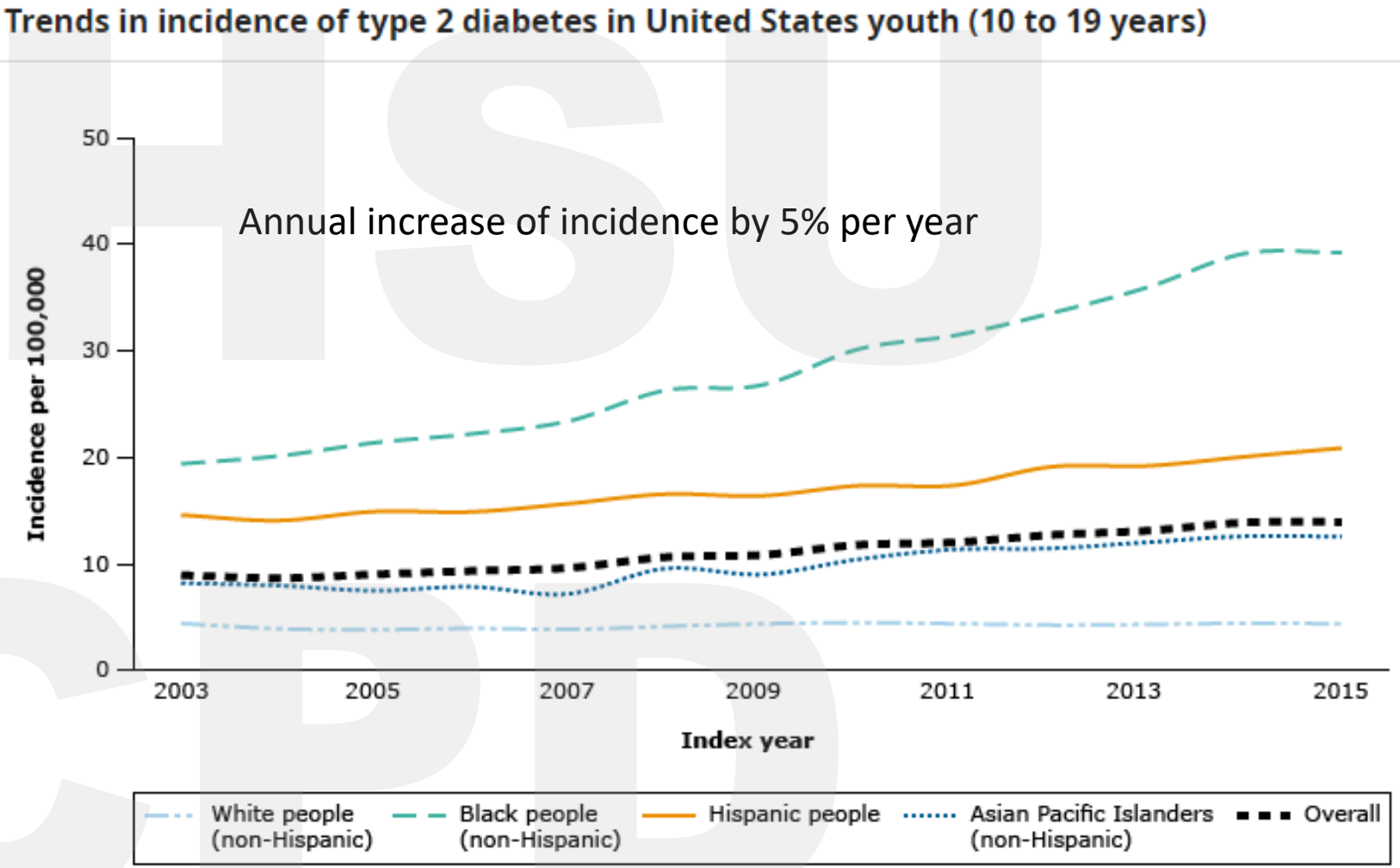
I have no financial disclosures

Outline

- Epidemiology
- Natural History
- Screening
- New Diagnosis Triage
- Treatments and Side effects

Epidemiology: exponential rise in cases in last 2 decades



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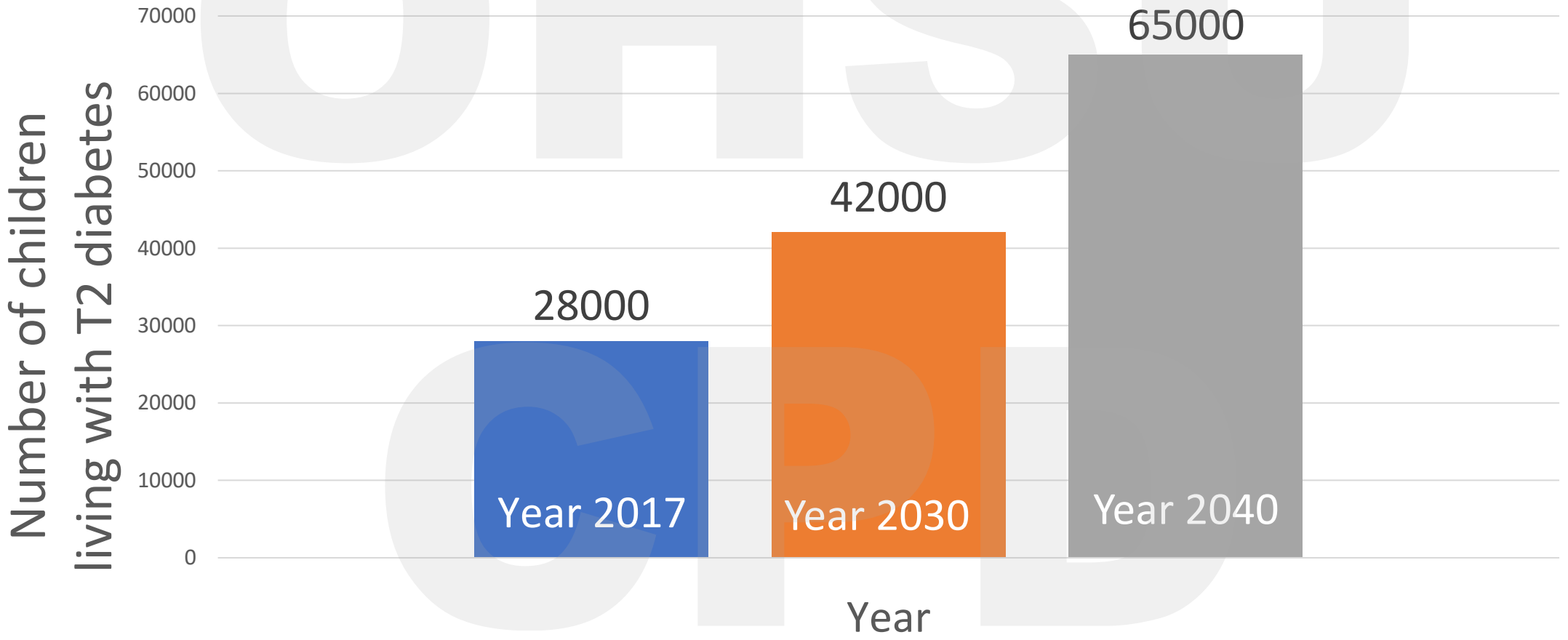
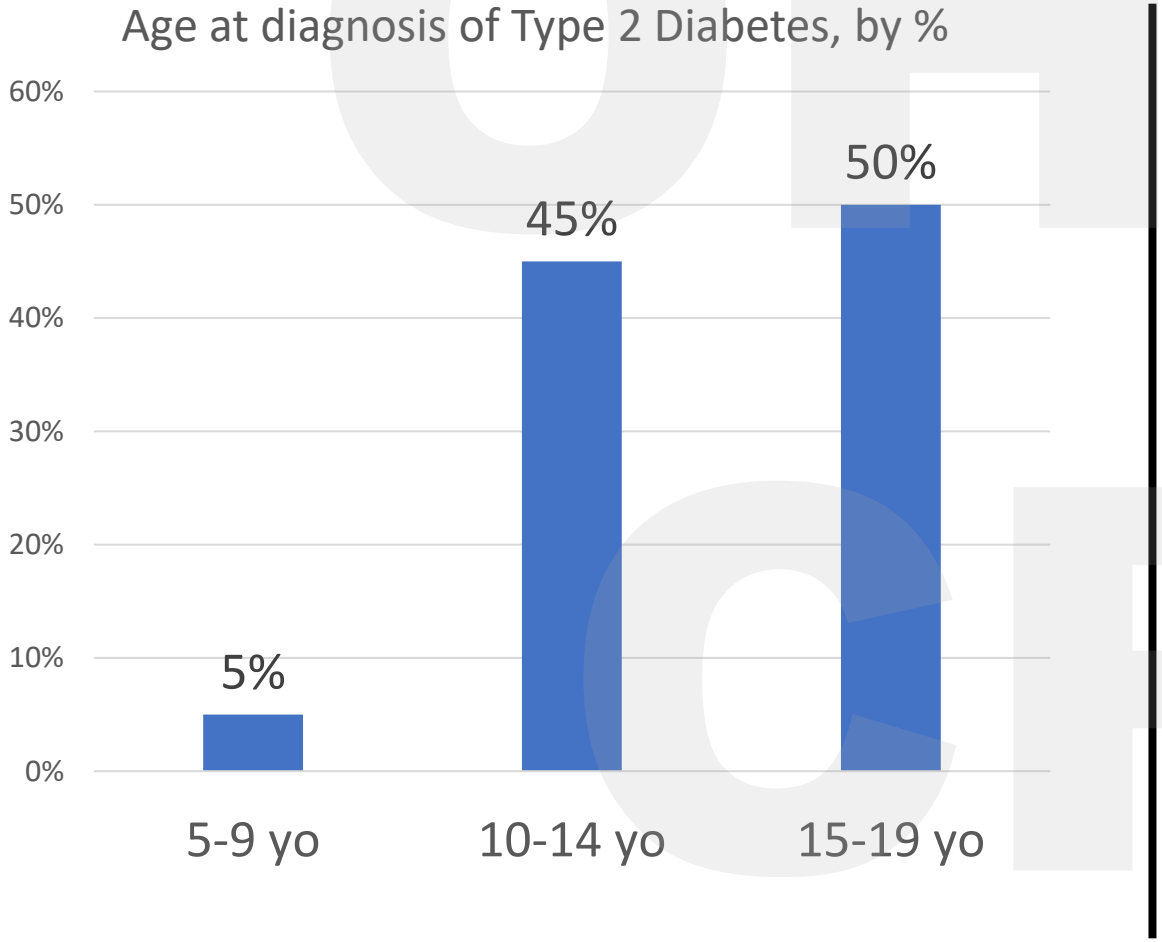
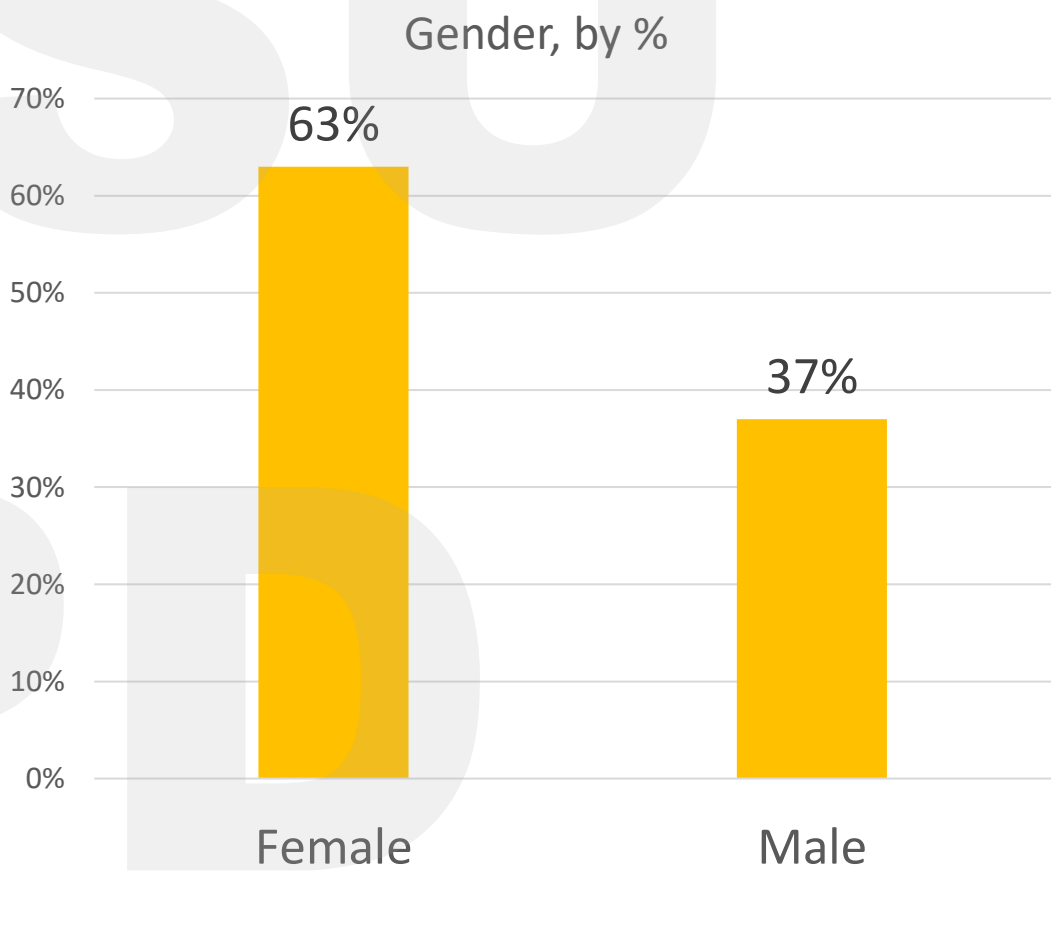
Modeling projections of diabetes burden



PMID 36580405

Characteristics of US youth with T2D 2006-2012





PMID: 31953884

6% of youths with new onset T2D present in DKA

50% of patients are from families making < $25,000 per year

Natural History

- What happens once you have type 2?
- How does this compare to adults?

TODAY study

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 14, 2012 VOL. 366 NO. 24

A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes

TODAY Study Group*

July 2004 -Feb 2009 enrolled

699 participants

- 10- 17 years old
- Type 2 DM < 2 years
- 3 arm RCT

Metformin only

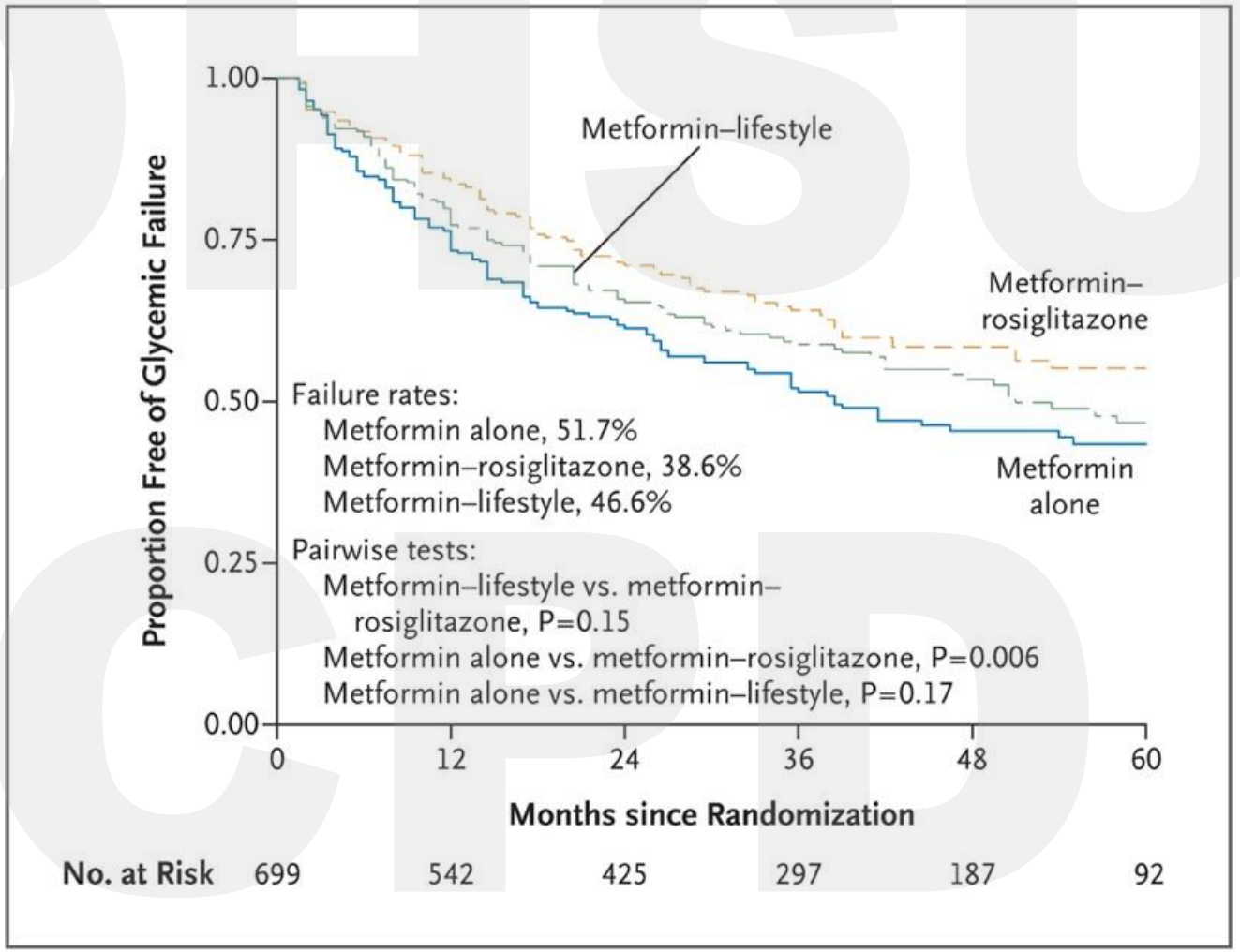
Metformin plus intensive lifestyle

Intensive family-based, behavioral approach to weight loss grounded in social-learning theory

Metformin plus rosiglitazone

Insulin sensitizer, no longer used due to side effects of MI and death in adults

50% of youths on metformin plus intensive lifestyle fail at 5 years

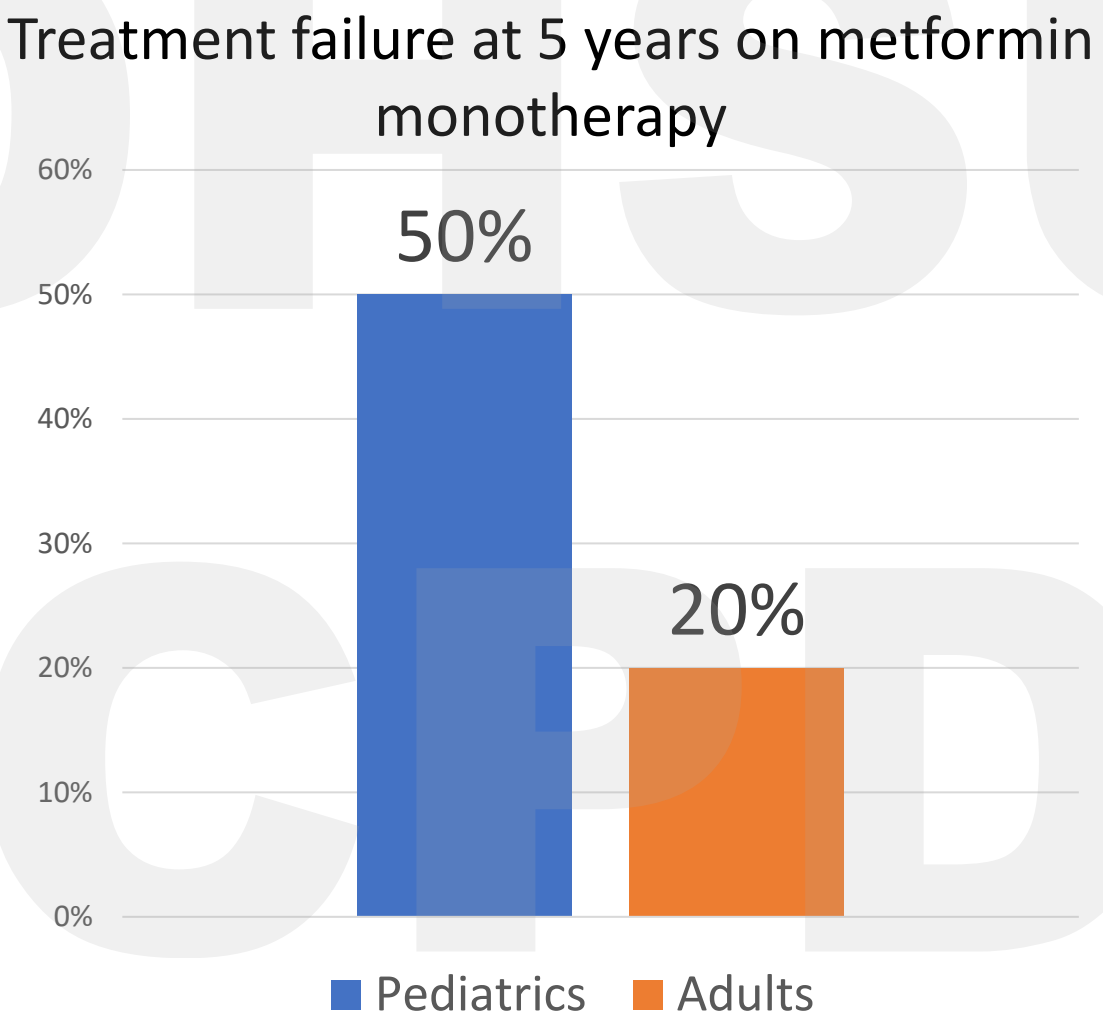


Glycemic failure definition:

- A1c > 8% for 6 months

- inability to wean participant from insulin within 3 months after its initiation due to A1c > 8%

Comparison to adult onset T2D



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August 2022

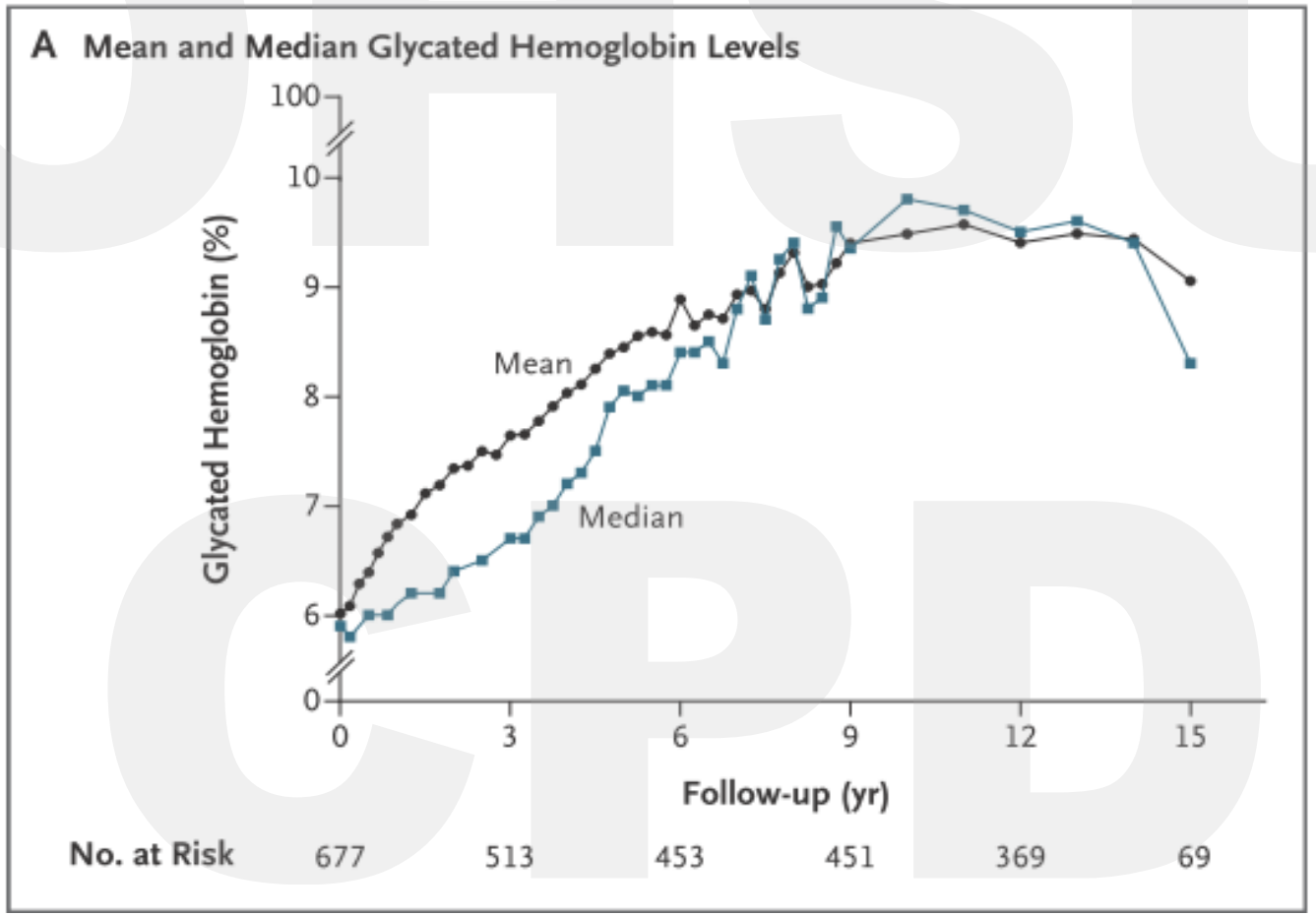
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

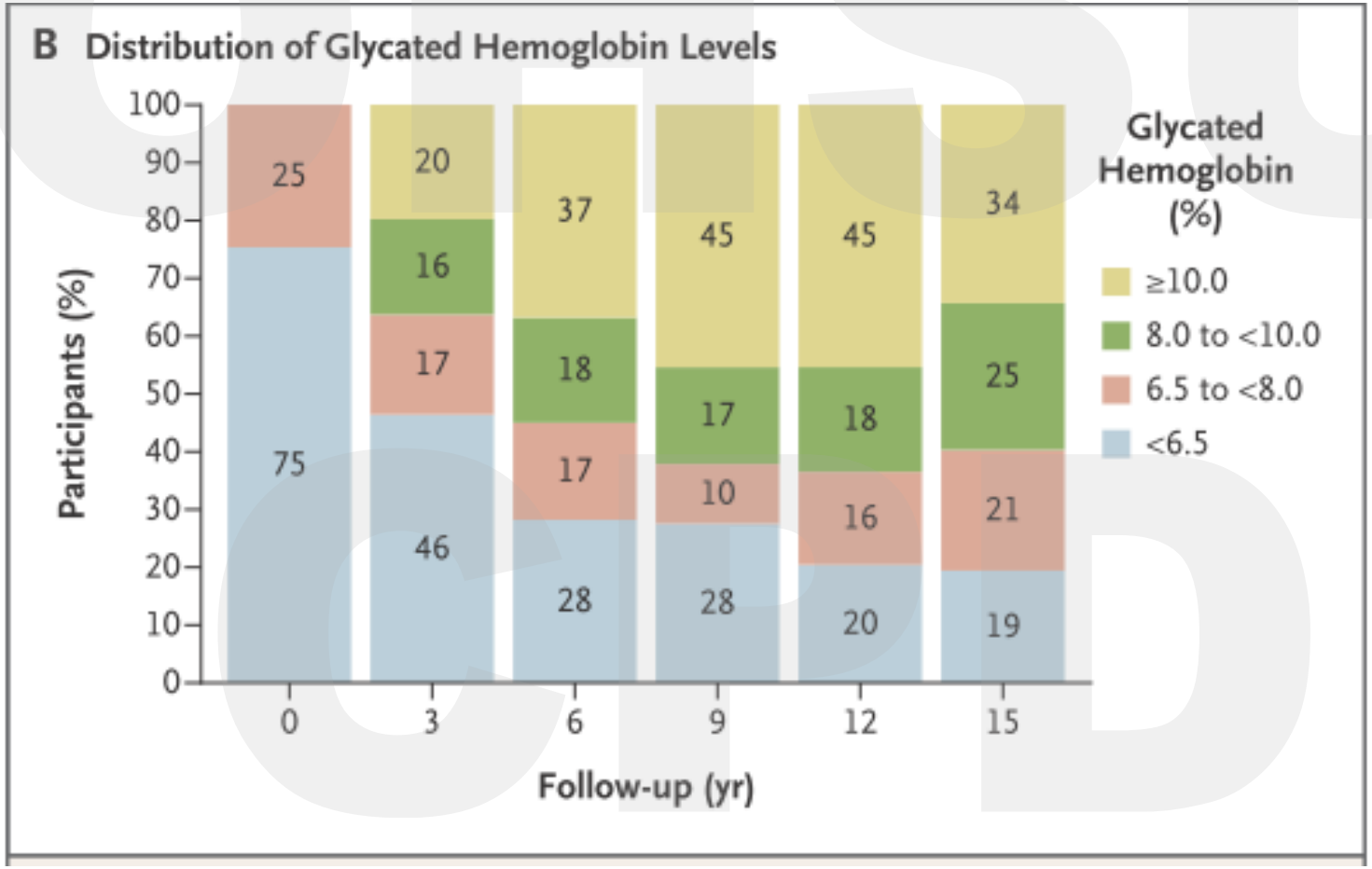
Long-Term Complications in Youth-Onset Type 2 Diabetes

TODAY Study Group*

A1c continues to increase despite treatment



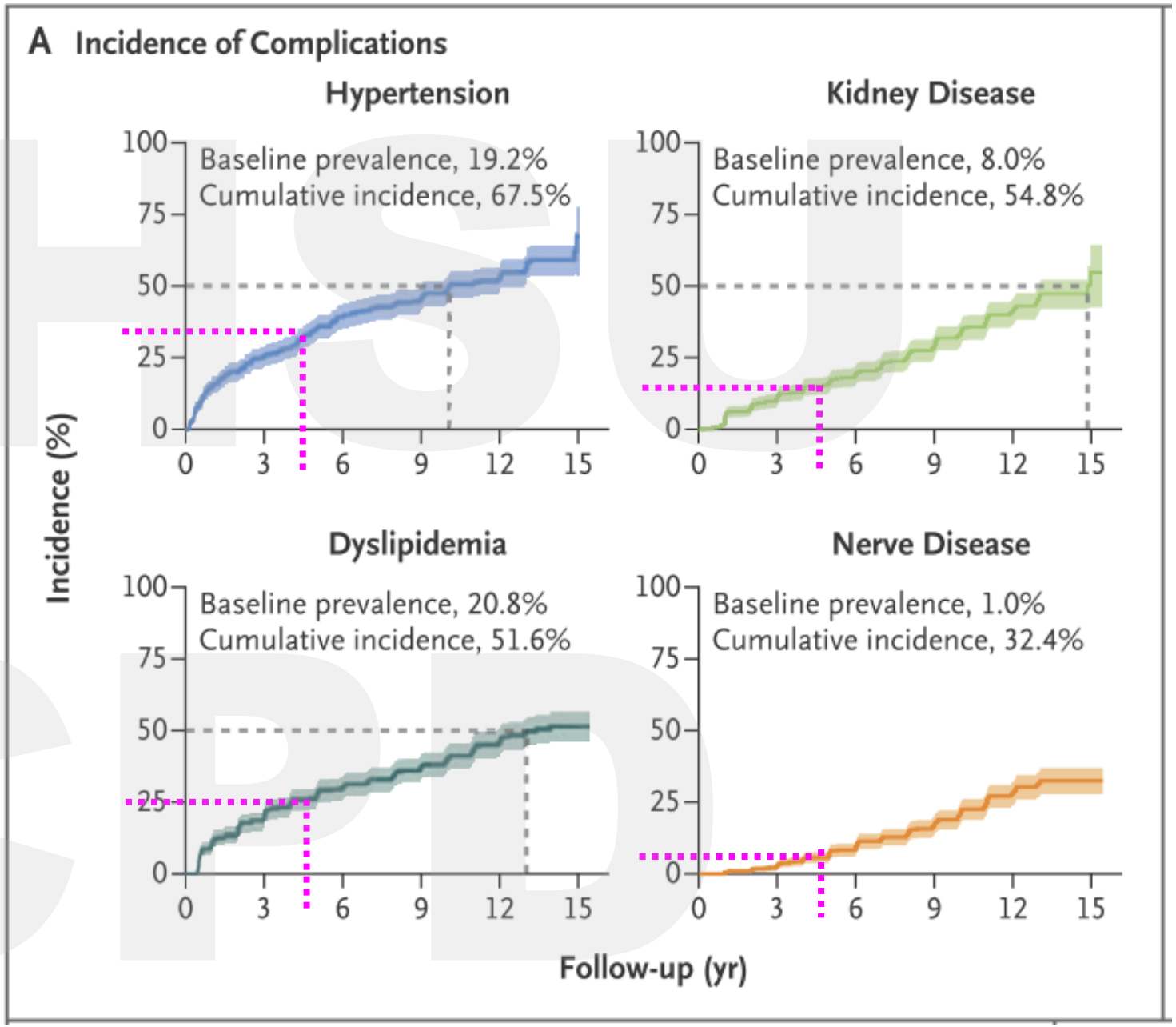
By ~ age 18, only 30% at goal A1c



Standard diabetes care:

Goal A1c < 7% (or 6.5%)

High rates of microvascular complications at an early age



Pink = ~ 5 years after enrollment ~ 18 yo

Grey= number of years to 50% of population

Take home point:

Event	# events	# patients	Event rate per 1000 patient year
CHF	6	6	0.42
MI	4	3	0.58
Stroke	4	3	0.58
ESKD	3	3	0.44
Deaths		6	0.42

Screening

Who?

How?

Testing for type 2 diabetes mellitus in asymptomatic children and adolescents

Overweight or obese:
BMI ≥85th percentile for age and gender
Plus 1 or more of the following additional risk factors*:
Maternal history of diabetes or gestational diabetes mellitus during the child's gestation
Family history of type 2 diabetes mellitus in a first- or second-degree relative
High-risk race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander)
Signs of insulin resistance on physical examination or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small for gestational age birth weight)
Screening frequency
Begin screening at age 10 years, or at onset of puberty if this occurs when the child is <10 years old
Repeat screening every 3 years, or more frequently if BMI is increasing

BMI: body mass index.

American Diabetes Association, 2024

Screening options

A1c

- ≥ 6.5%

Fasting Glucose (potentially less specific)

- BG ≥ 126

Oral glucose tolerance test

- 2 hours BG ≥ 200 after glucose load of 1.75mg/kg (max 75g)

Triage

1. How likely are they to have type 2 diabetes?
2. If likely type 2 diabetes, do they need admission?

How likely are they to have type 2?

History

- T2D- typically very strong family history

Exam

- BMI ≥ 95th%tile
- Possible hypertension
- Acanthosis

Labs

- Urine ketones
  - Moderate or large – unusual but can happen with higher A1c

Do they need admission?

- Unclear if type 1 or type 2
- Acidosis
- Some scenarios of clear type 2 phenotype + ketones would recommend admission

Treatment

ADA Standards of Care 2024

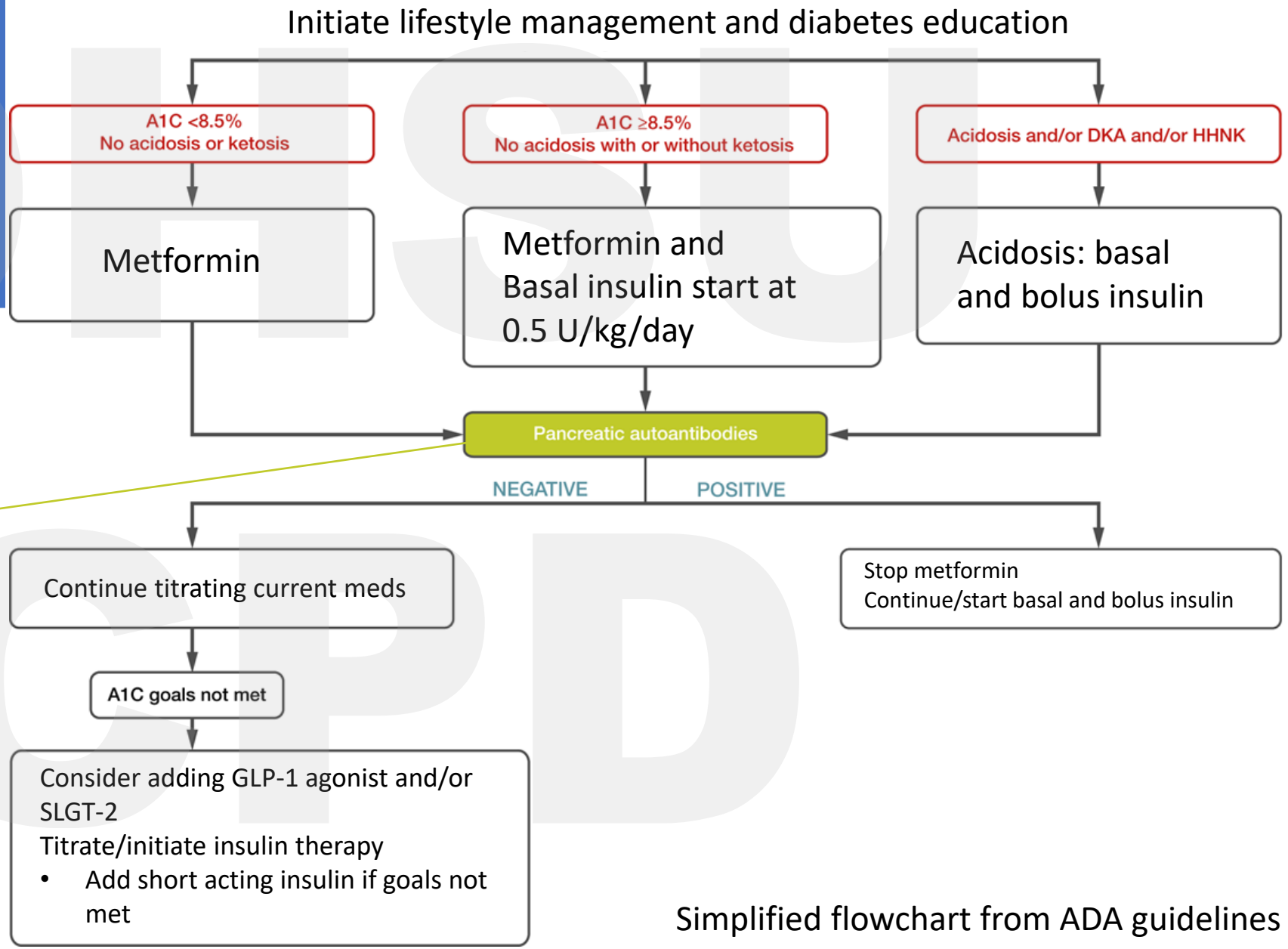
Metformin

GLP-1

SGLT-2

ADA Standards of Care 2024

New- Onset Diabetes in Youth with BMI > 85%tile and Clinical Suspicion of T2D



GAD- 65 Ab
Islet cell Ab
IA-2 Ab
ZNT- 8 Ab

Send first 2 if high suspicion, all 4 if unsure

Simplified flowchart from ADA guidelines

You too can prescribe metformin!

Metformin-

Mechanism of action

Side effects- common! (50%)

- Diarrhea
- Nausea/Vomiting
- Abdominal pain
- Hypoglycemia when used alone would be very unusual

Metformin titration

- Goal: 2000mg per day with tolerable GI side effects
  - Standard metformin needs to be divided BID
  - Extended release can be daily or BID
  - With meals less likely to have GI side effects. But ok to take without food
  - Lower doses than goal can still have glycemic effect

Personal practice: I always use extended release (10% vs 50% incidence of diarrhea)

Example titration:

500mg with dinner x 1 week	1000mg with dinner x 1 week	1500 mg with dinner x 1 week	1000mg with meal BID

Or 2000mg ER daily with meal

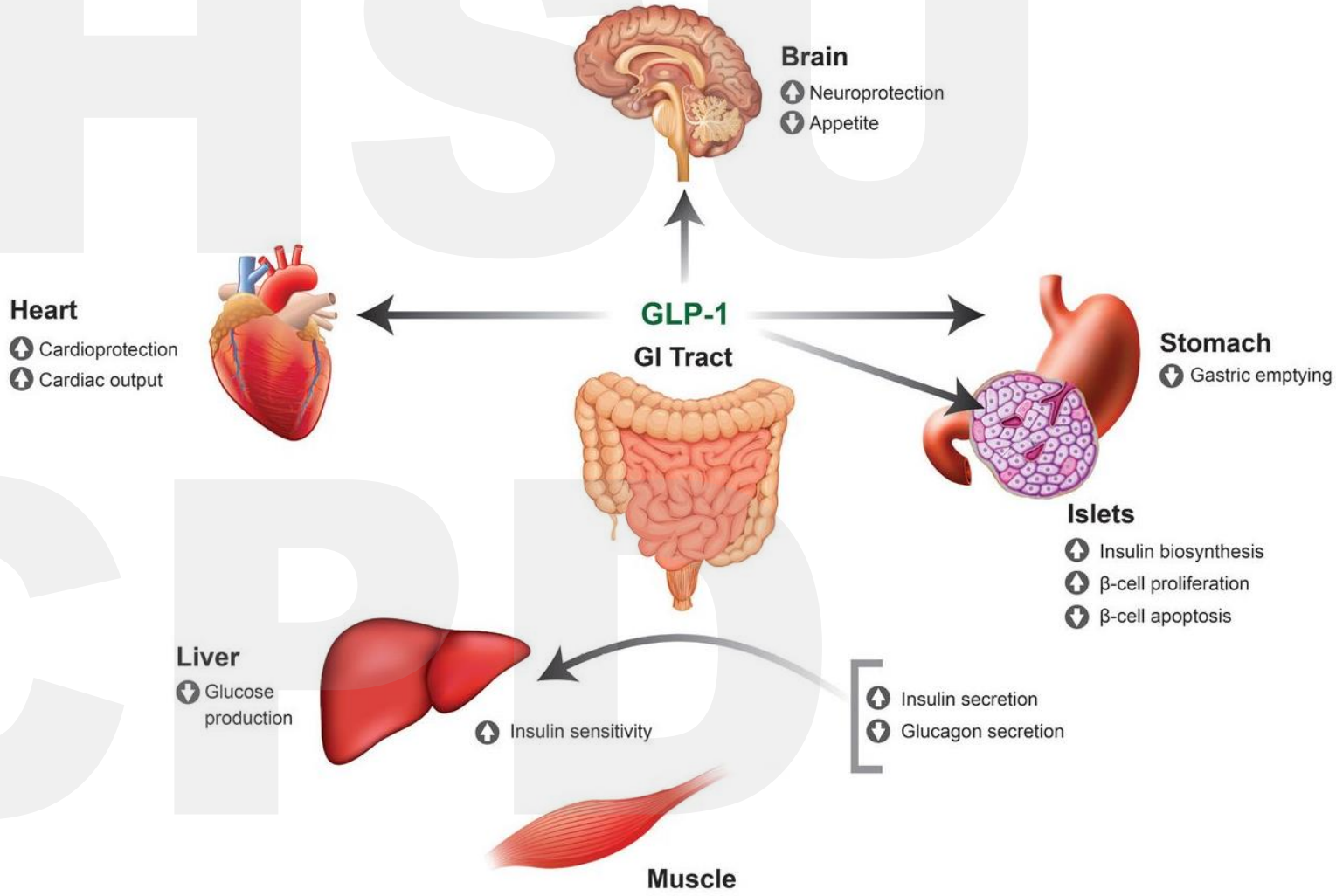
If GI upset, go back to last dose tolerated for 1-2 weeks, then slow uptitration again

GLP-1 agonist (glucagon like peptide-1)

Incretins

- GLP-1 (glucagon like peptide-1)
- GIP (gastric inhibitory peptide)

Hormones produced by the intestinal mucosa in response to eating



FDA approved GLP-1 agonists for children > 10 yo with T2D

Liraglutide (Victoza) –2019

- 0.6, 1.2, 1.8mg
- Daily, injectable

Exenatide (Bydureon) –2021

- 2mg
- Weekly, injectable

Dulaglutide (Trulicity) -- 2022

- 0.75mg, 1.5mg
- Weekly, injectable

What about Ozempic?

Semaglutide (Ozempic)

- 0.25mg, 0.5mg, 1mg, 2mg
- Weekly, injectable
- No pediatric approval. However, semaglutide (Wegovy) is approved for peds weight loss for **> 12 yo** up to 2.4mg per week

Smaller, more frequent meals
Avoid: fatty, spicy, acidic

GLP-1 considerations and side effects

Common side effects

- Nausea, bloating, diarrhea – usually resolves in 2 weeks

Uncommon side effects

- Pancreatitis
- ? AKI, gastroparesis, mental health

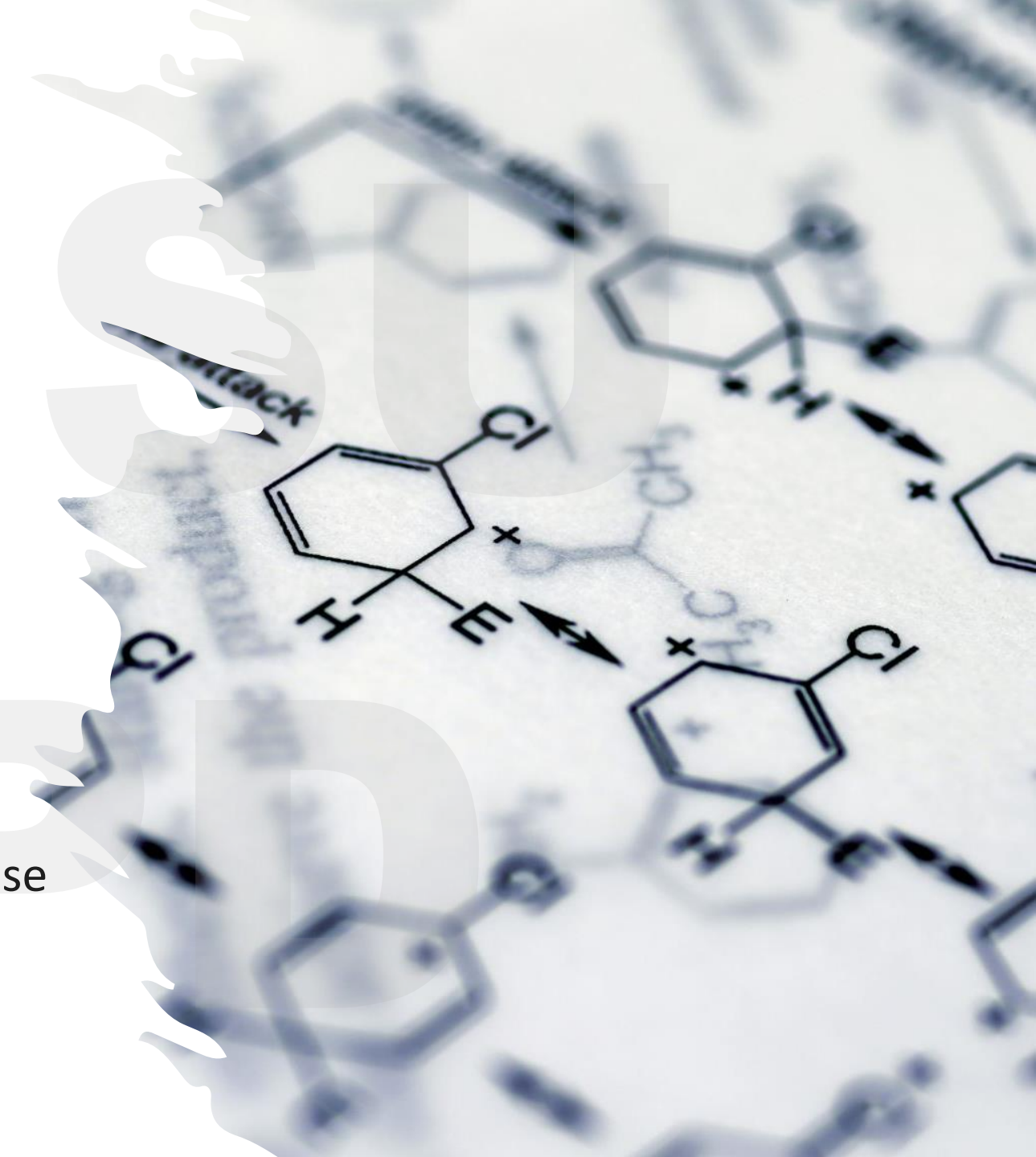
Contraindication

- Family history of medullary thyroid cancer

Surgery considerations

- Theoretical- slower gastric emptying => increased risk of aspiration
- Stop weekly medications 1 week prior
- Stop daily medications 1 day prior

SGLT-2 inhibitor (Sodium-glucose transport protein 2 inhibitor)



Mechanism of action: block glucose reabsorption in the kidney => urinary glucose excretion

FDA approved SGLT-2 inhibitors for children > 10 yo with T2D

Empagliflozin (Jardiance) –2023

- Daily in AM with or without food, oral
- 10mg, 25mg

Dapagliflozin (Farxiga) – 2024

- Daily in AM with or without food, oral
- 5mg, 10mg

SGLT-2 considerations and side effects

Common side effects

- UTI (6%)
- Yeast infection (2%)
- Hypoglycemia (20%)

Uncommon side effects

- Euglycemic DKA (very rare, none in pediatrics yet. Adults 0.1%)
  - Check ketones if abdominal pain, vomiting, illness, SOB
  - Stop medication if not eating for any reason

Contraindication

- Personal practice: A1c > 10%, other risk for ketosis

Surgery considerations

- Increased risk of euglycemic DKA
- Stop 3 days prior

A1c benefit comparisons

Name	A1c
Metformin	1%
Empagliflozin (Jardiance)	0.8%
Exenatide ER (Bydureon BCise)	0.25%
Liraglutide (Victoza)	1.3%
Dulaglutide (Trulicity)	1.5%
Semaglutide (Ozempic)	Adults ~ 1.5%

Blood glucose testing

Very individualized

No insulin

- At least once a week: fasting and 2 hour post prandial
- If families will use more data to inform lifestyle changes, can check every day/meal!

Basal insulin only

- Daily fasting (at least) to monitor for hypoglycemia
- Optimally daily fasting and 2 hour post prandial

Basal + bolus

- Daily before meals and at bedtime

Continuous glucose monitor

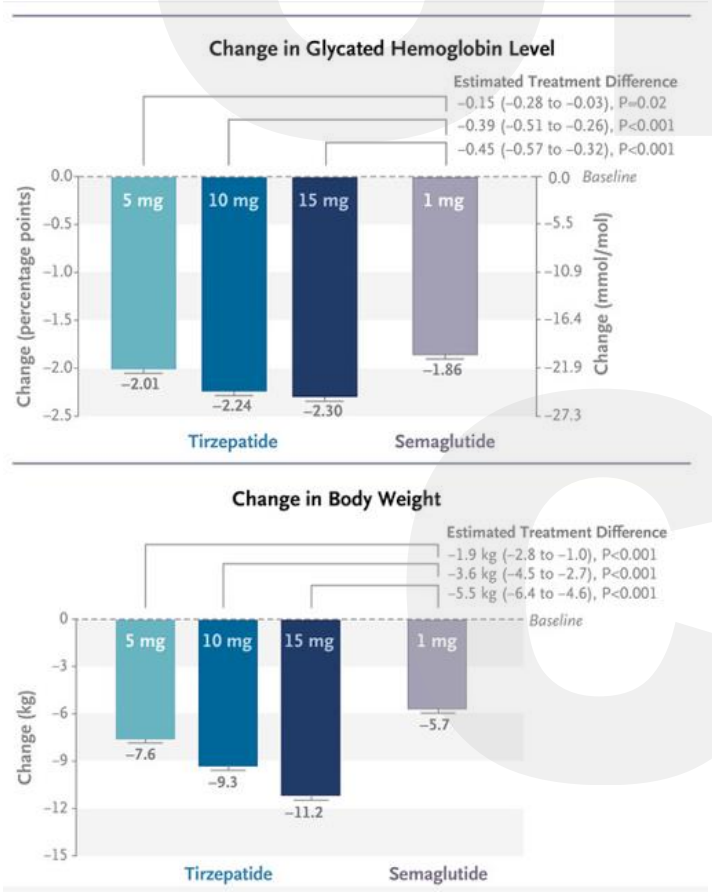
- Awesome if you can get it
- OHP– only approves if on basal + bolus
  - Cash pay: 60-75$ per 14 days for Libre
- If not on insulin can be helpful if patient/family looks at data to understand how food/exercise affects BG
- Makes titrating insulin much easier

Urine ketone testing

- No national consensus
- History of ketones or DKA
- Basal + bolus insulin
- SGLT-2
- Could consider for new diagnosis while awaiting endocrine appointment or confirmatory type 1 diabetes labs

Studies in progress

Adult data



SURPASS- PEDS: tirzepatide GIP-GLP-1 dual agonist

- Status: enrolling, estimated completion date: 2027
- Children's Hospital of LA closest

ST_2OMP

- Non randomized prospective trial
- Vertical sleeve gastrectomy vs advanced medical therapy
- Cincinnati Children's and Children's Hospital of Colorado
- Status: enrolling, estimated completion date: 2025

Take home points

Triaging a new diagnosis

- How likely are they to have type 2?
- 1st step: ketones
- If positive, call a pediatric endocrinologist for help

Make sure it's not type 1 diabetes

- Send antibodies: GAD-65 Ab, Islet cell Ab, (IA-2 Ab, ZNT-8 Ab)
- Glucose, c-peptide, insulin can be helpful too

Treatments

- You too can prescribe metformin!
- Side effects to think about
  - GLP-1 agonist: pancreatitis
  - SGLT-2 inhibitor: UTI, yeast infections, euglycemic DKA

Questions?

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