Updates in Diabetes Management in the Inpatient and Outpatient Setting

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What has changed about diabetes
What has not changed about diabetes

Things which have remained the same

- Insulin is needed for treatment of type 1 DM and prevention of DKA
- Lifestyle modification plays an important roll in management of type 2 diabetes
- Glycemic control reduces risk of microvascular complications
- Glucose monitoring is important particularly for people on medications with hypoglycemia risk

Things which have changed

- Individualized glucose targets and treatment based on patient-specific factors
- Metformin no longer first line for all
- New drugs with more than glycemic benefit alone
- Technology for both insulin delivery and glucose monitoring

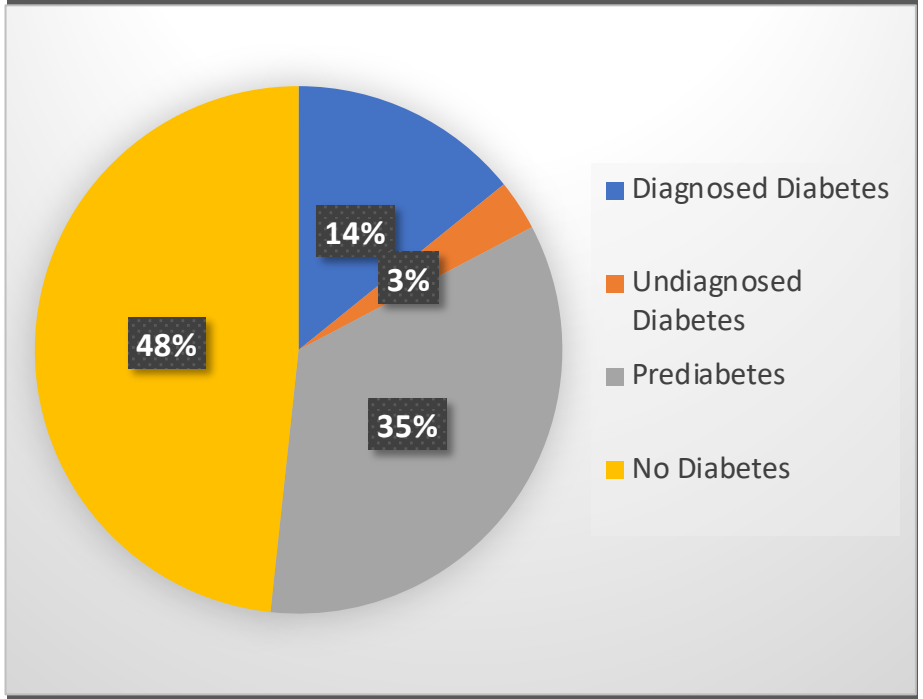
Diabetes Prevalence in Louisiana - 2018 data

Louisiana's diabetes epidemic:

- Approximately **505,468 people in Louisiana**, or 14.2% of the adult population, **have diagnosed diabetes**.
- An additional **113,000 people in Louisiana have diabetes but don't know it**, greatly increasing their health risk.
- There are **1,243,000 people in Louisiana**, 34.4% of the adult population, who have **prediabetes** with blood glucose levels that are higher than normal but not yet high enough to be diagnosed as diabetes.
- **Every year** an estimated **27,282 people in Louisiana** are diagnosed with diabetes.

Diagnosed diabetes costs an estimated $5.7 billion Louisiana each year.

The serious complications include heart disease, stroke, amputation, end-stage kidney disease, blindness—and death.



https://diabetes.org/sites/default/files/2022-04/ADV_2022_State_Fact_sheets_all_rev_LA-4-4-22.pdf

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ADA/EASD Guidelines with focus on Person-Centered Care

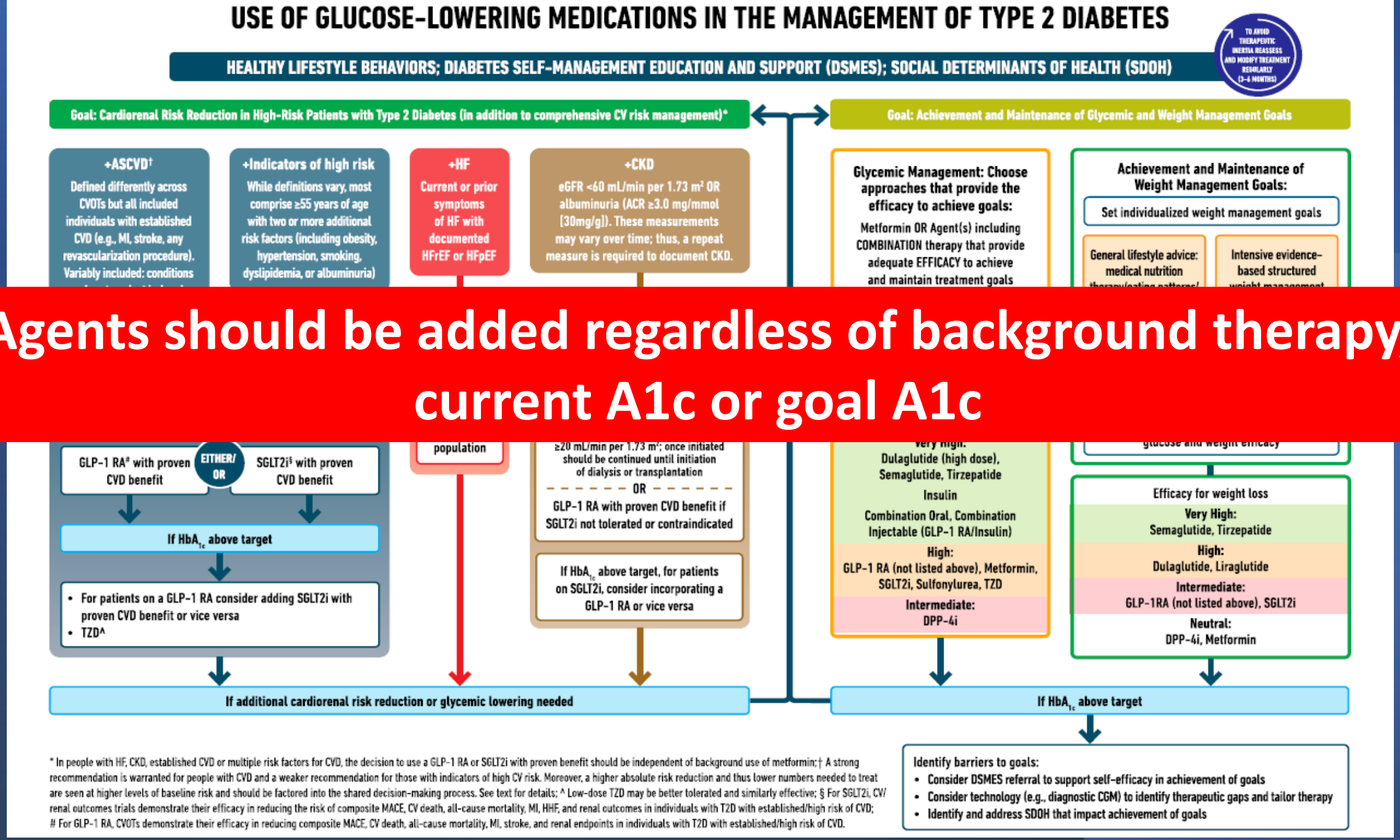
- Weight management
- Cardiovascular disease
- Renal disease
- Glycemic goals
- Healthy lifestyle behaviors
- Diabetes self-management education and support
- Social determinants of health

Previous goals in diabetes care

A1c above goal→ Start metformin

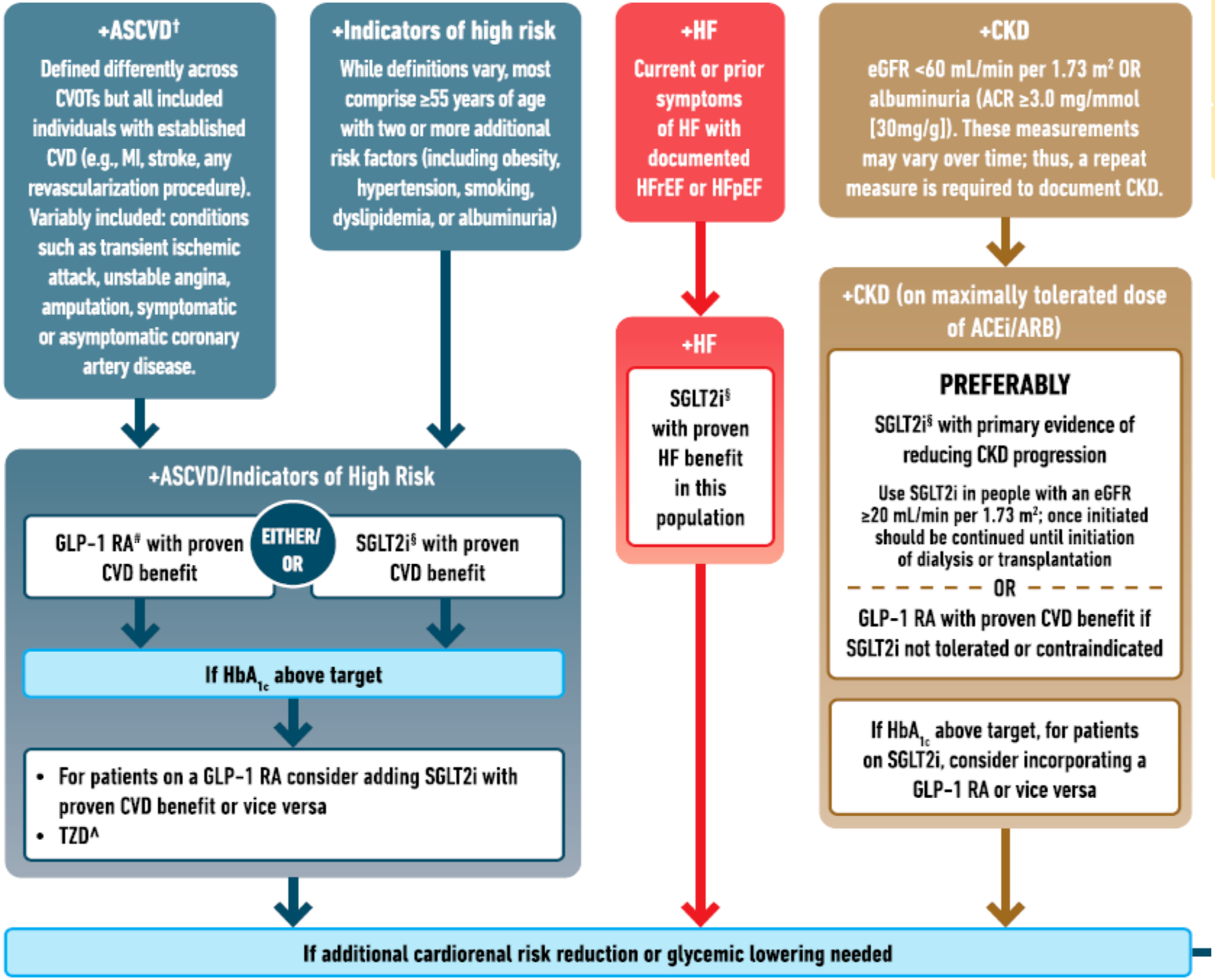
A1c remains above goal → Add more medication

Continue to add medications to get A1c as low as possible



Agents should be added regardless of background therapy, current A1c or goal A1c

Diabetes Care 2023;46(Suppl.1):S140-157



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Metformin

- Approved for use in US in 1995
- For many years was recommended as first line therapy for T2DM and has data for prevention of progression from prediabetes
- Inexpensive, effective and safe
- Possible reduction in CV events and death
- GI intolerance most common side effect
- Should be continued with addition of other agents unless intolerance or fall in GFR <30

First-Line Therapy for Type 2 Diabetes With Sodium–Glucose Cotransporter-2 Inhibitors and Glucagon-Like Peptide-1 Receptor Agonists

A Cost-Effectiveness Study

Jin G. Choi*; Aaron N. Winn, PhD*; M. Reza Skandari, PhD; Melissa I. Franco, MPH; Erin M. Staab, MPH; Jason Alexander, MD; Wen Wan, PhD; Mengqi Zhu, MS; Elbert S. Huang, MD, MPH; Louis Philipson, MD, PhD; and Neda Laiteerapong, MD, MS

- Evaluated lifetime cost-effectiveness of SGLT2i or GLP1RA as first line therapy compared to metformin
- SGLT2i and GLP1RA reduced rates of CHF, MI, stroke but with higher lifetime cost
  - Metformin: $92000
  - SGLT2i: $135000 for the SGLT2 inhibitor
  - GLP1RA: $141000
- Estimated cost would need to be reduced by 70-90% of current to make these drugs cost effective first line options

Ann Intern Med.2022;175:1392-1400. doi:10.7326/M21-2941

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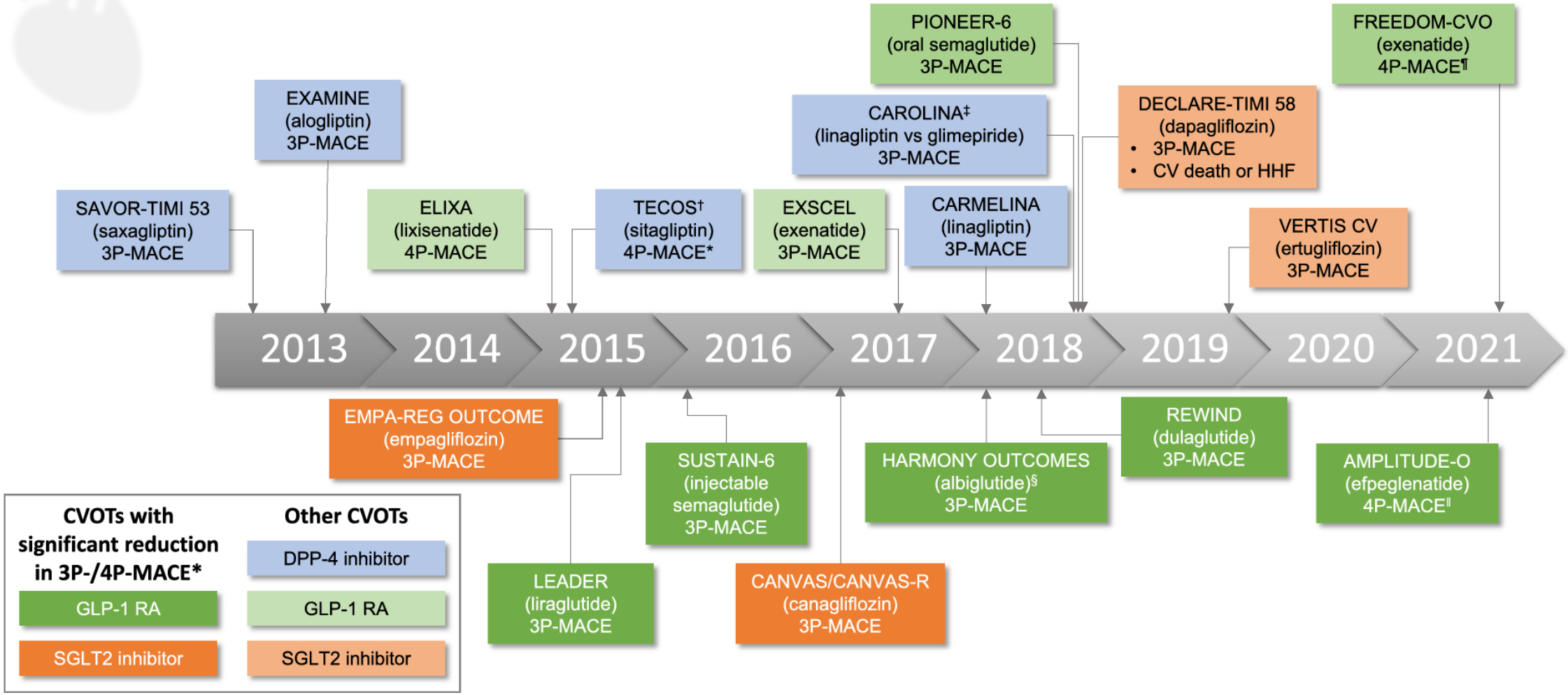
Cardiovascular Outcome Trials



Cardiovascular outcomes trials: a paradigm shift in the current management of type 2 diabetes. *Cardiovasc Diabetol* 2022;21:144

Trial Designs

- Primarily designed to rule-out risk (FDA required)
  - Some powered for superiority if non inferiority demonstrated
- Heterogeneity between trials
- 3 vs 4 point Major Adverse Cardiac Event (MACE)
  - 3 point: CV death, Nonfatal MI, nonfatal stroke
  - 4 point: + Hospitalization for unstable angina
- Secondary or Primary/secondary outcome trial
  - Majority of participants had CVD
  - Longer duration of DM
- Not designed to show A1c control of study drug

Cefalu et al. *Diabetes Care* 2018;41:14-31

Medications with ASCVD Benefit

GLP1 RA

- Dulaglutide (Trulicity)
- Semaglutide SQ (Ozempic)
- Liraglutide (Victoza)
- Albiglutide (Tanzeum)

SGLT2i

- Empagliflozin (Jardiance)
- Canagliflozin (Invokana)

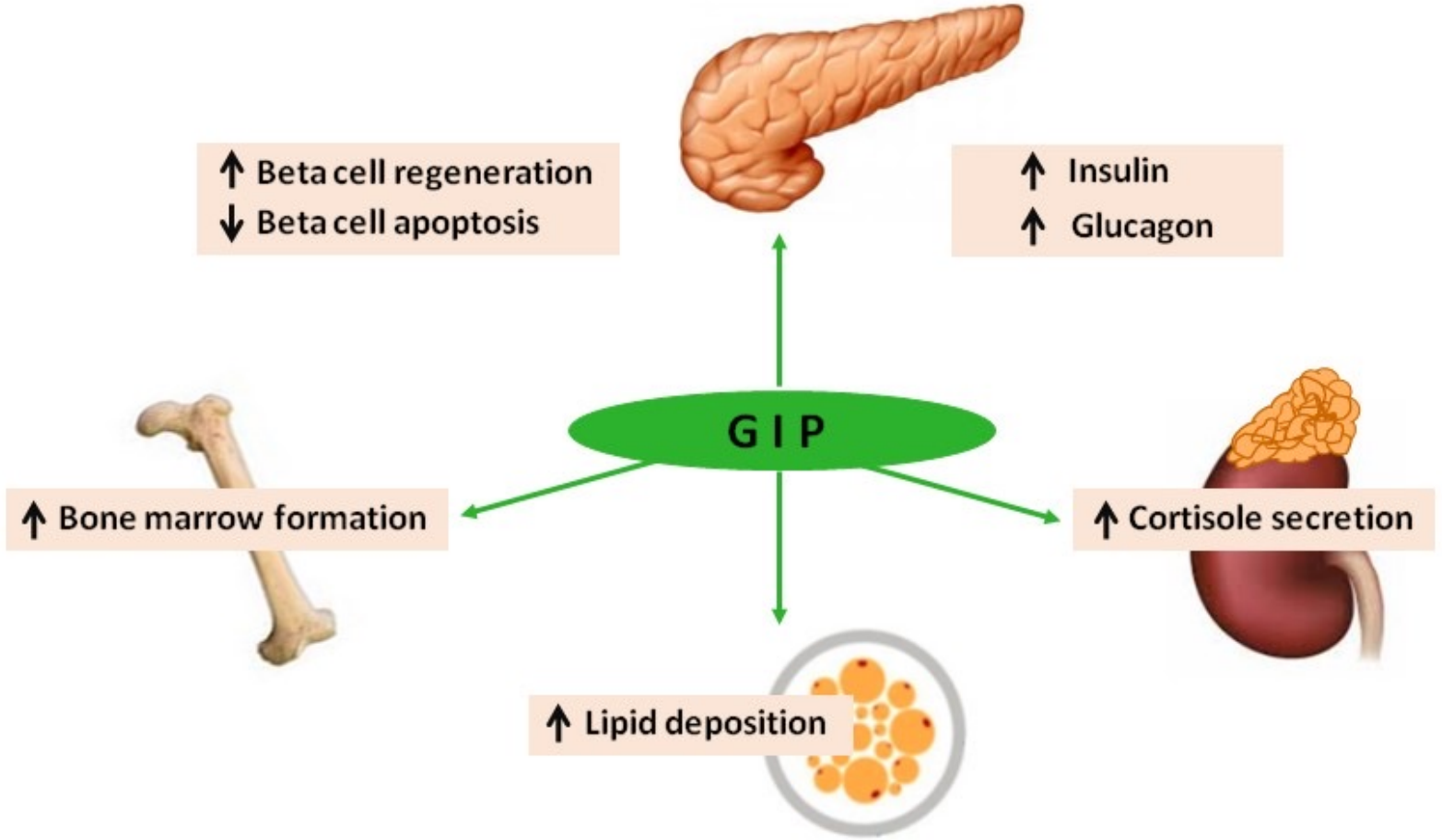
SGLT2i for heart failure and renal disease

	Empagliflozin	Canagliflozin	Dapagliflozin
Glycemic control in T2DM	Yes	Yes	Yes
MACE	Yes	Yes	No
Heart failure hospitalization	Yes	Yes	Yes
Renal disease	Yes	Yes	Yes
GFR cutoffs in trials	>20 mL/min in EMPA-KIDNEY	>30 mL/min in CANVAS	>25 mL/min in DAPA-CKD

***Specific indications vary between drugs and reflect design of individual trials**

Tirzepatide

Dual GIP/GLP1 RA



SURPASS-2: Tirzepetide vs Semaglutide Once Weekly

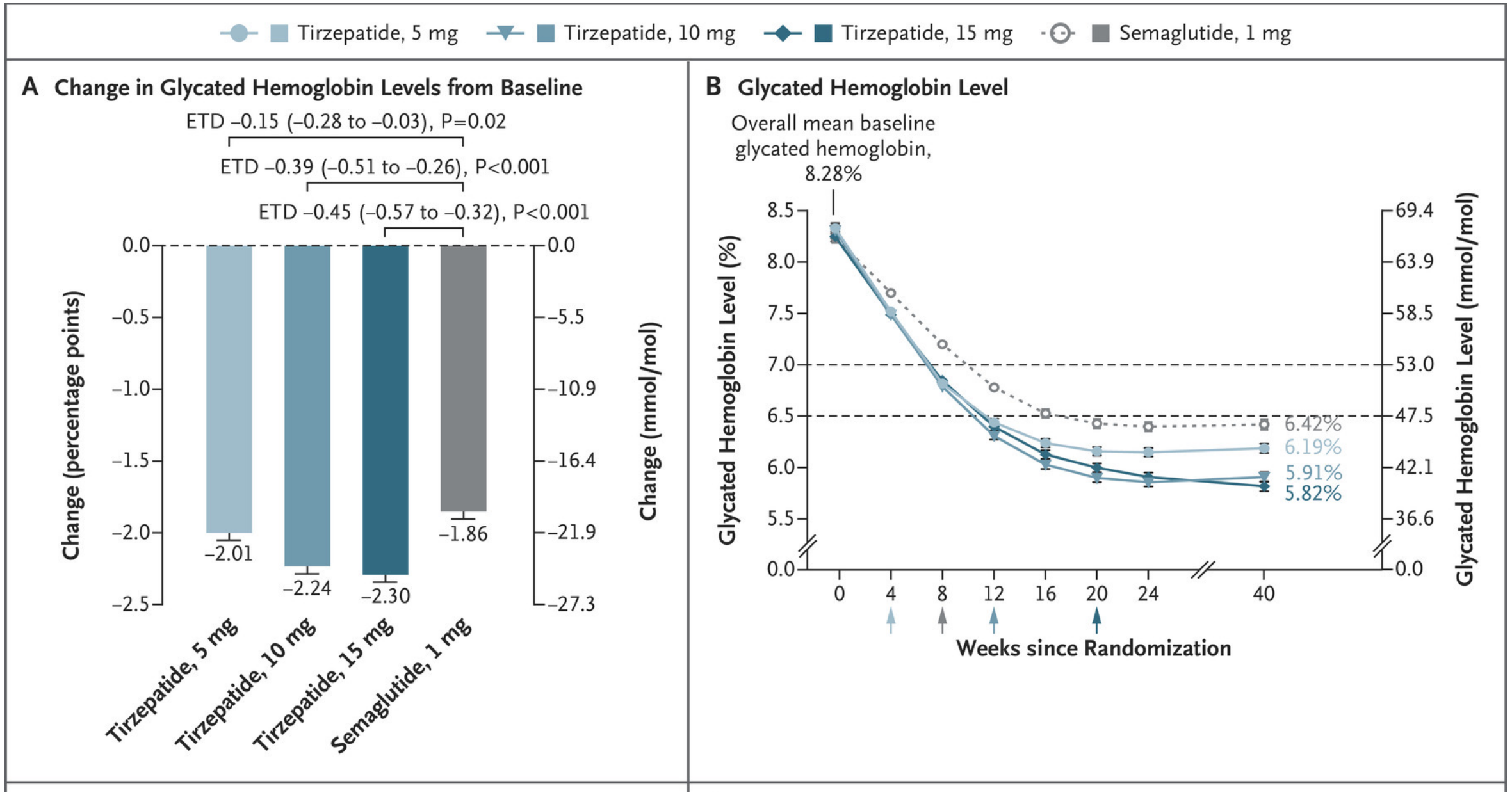
- 40 week, phase 3 randomized trial
- 1879 patients assigned to tirzepatide 5 mg, 10 mg, 15 mg or semaglutide 1 mg weekly
- Inclusion criteria:
  - T2DM
  - 18 years or older
  - On metformin at least 1500 mg daily
  - A1c 7-10.5%
- Primary endpoint was change in HbA1c

Frías JP et al. *N Engl J Med* 2021;385:503-515

SURPASS-2: Tirzepetide vs Semaglutide Once Weekly

- Tirzepatide started at 2.5 mg weekly and increased to assigned dose by 2.5 mg every 4 weeks
- Semaglutide started at 0.25 mg weekly and doubled every 4 weeks to 1 mg
- Dose de-escalation was not allowed

Frías JP et al. *N Engl J Med* 2021;385:503-515



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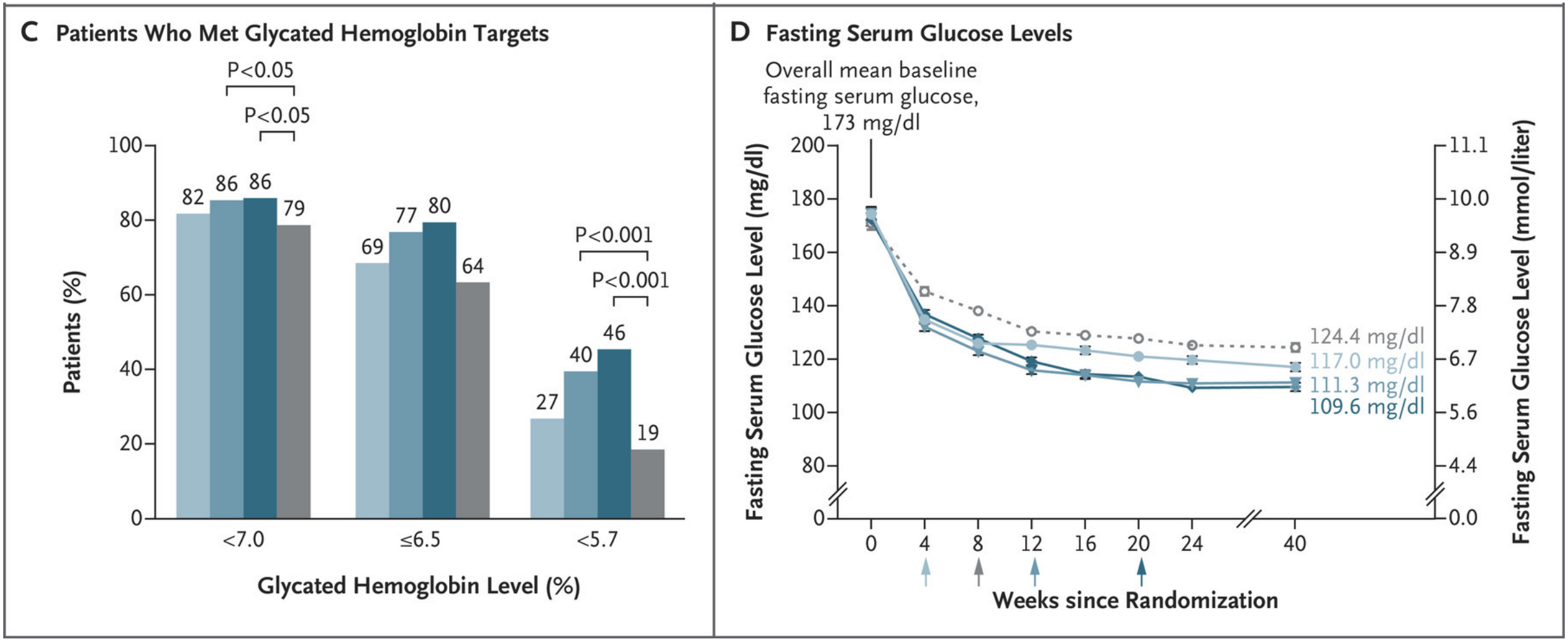

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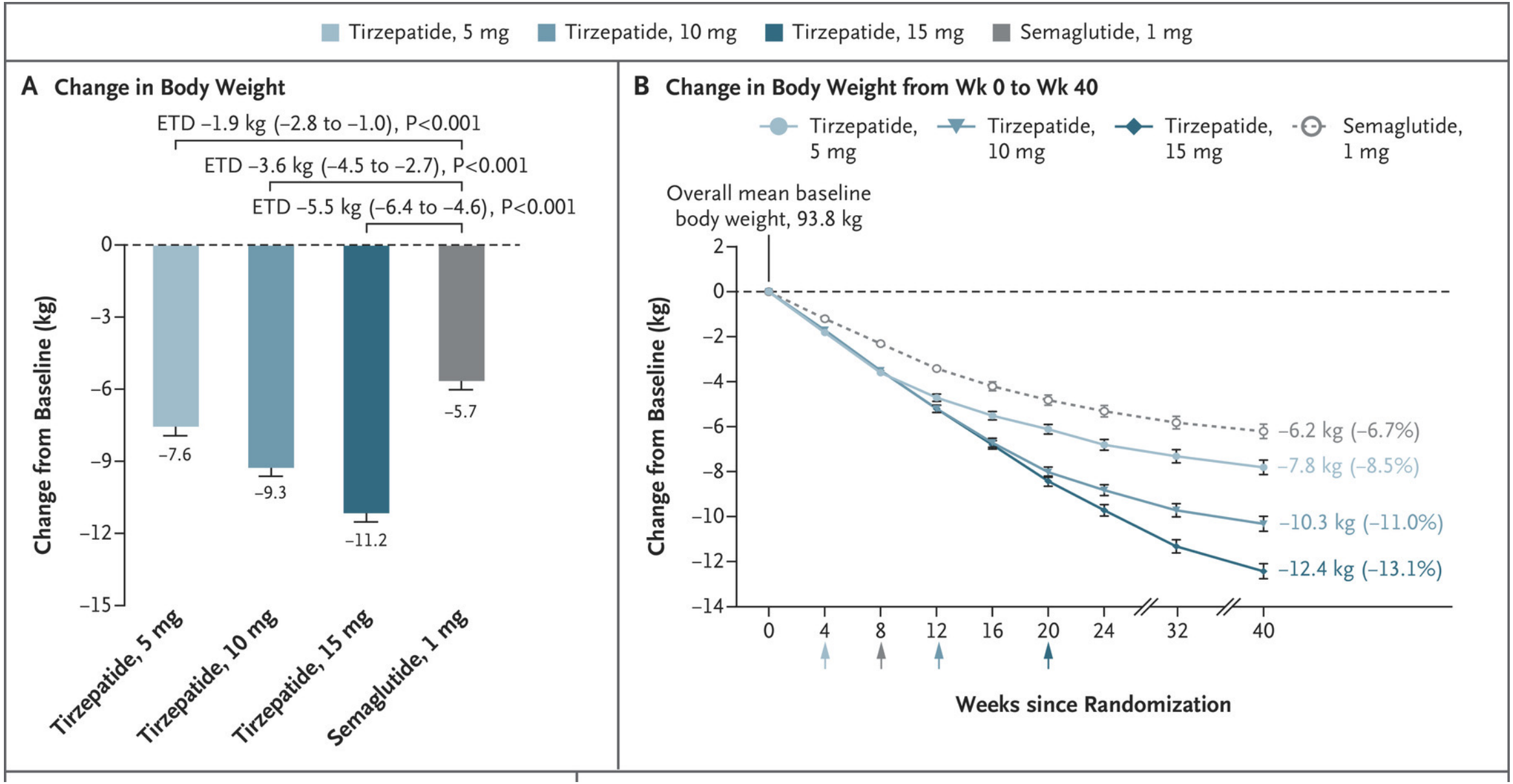

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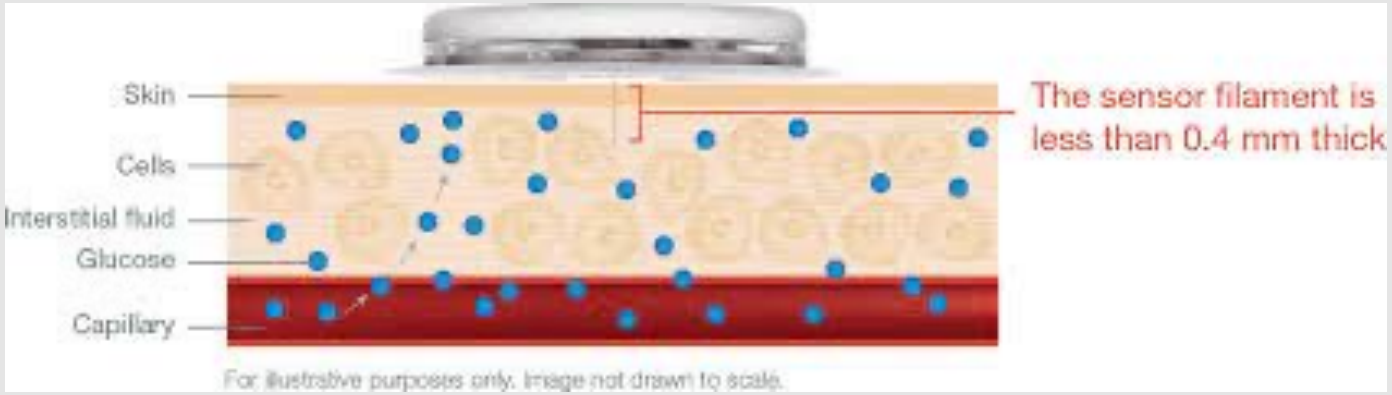
- **Technology for both insulin delivery and glucose monitoring**

Continuous glucose monitors (CGM)



- Continuously monitor glucose in interstitial fluid and send signal to receiving device
- Over time have become smaller, easier to apply and more accurate
- Becoming more widely available to patients

Dexcom G6 and G7

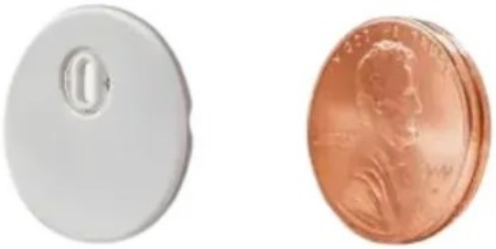
- Real-time CGM which can communicate with receiver, smartphone, smartwatch, insulin pump (Tslim, Omnipod)
- Customizable alerts for low/high glucose as well as rate of change

FreeStyle Libre

Libre 2

- Intermittent scanned-CGM with optional alarms
- Requires patient to scan at least every 8 hours
- Compatible with receiver or smartphone
- Approved for use on upper arm

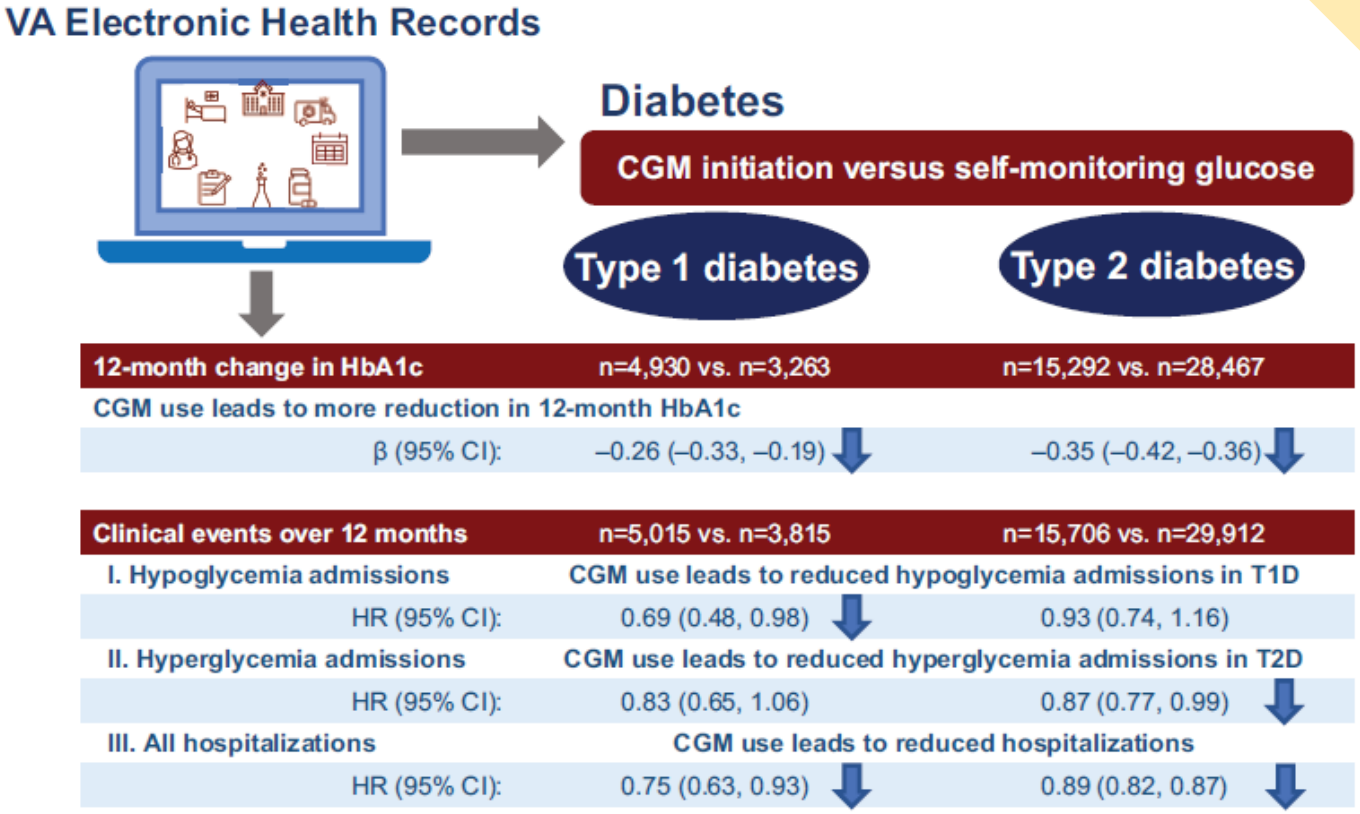
Libre 3



- Real time CGM
- Smaller than previous version
- One piece applicator
- More accurate
- Stronger bluetooth

Data to support use of CGM in a VA population

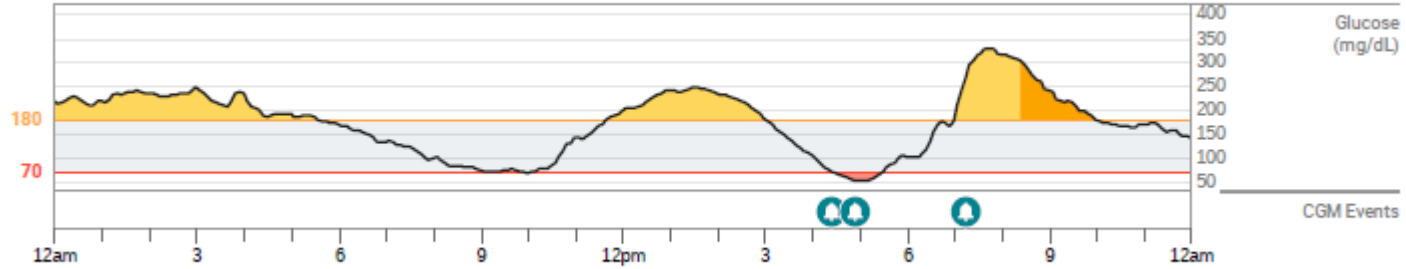
- Retrospective cohort study of patients or insulin in the VA using CGM compared to usual monitoring over 12 month period
- N = 5,015 with T1D and n = 15,706 with T2D
- Users could have Dexcom, FreeStyle Libre or Medtronic sensors
- Demonstrated benefits in both groups for reduction in A1c and all-cause hospitalization
- Fewer admission for hypoglycemia in type 1 group and for hyperglycemia in type 2



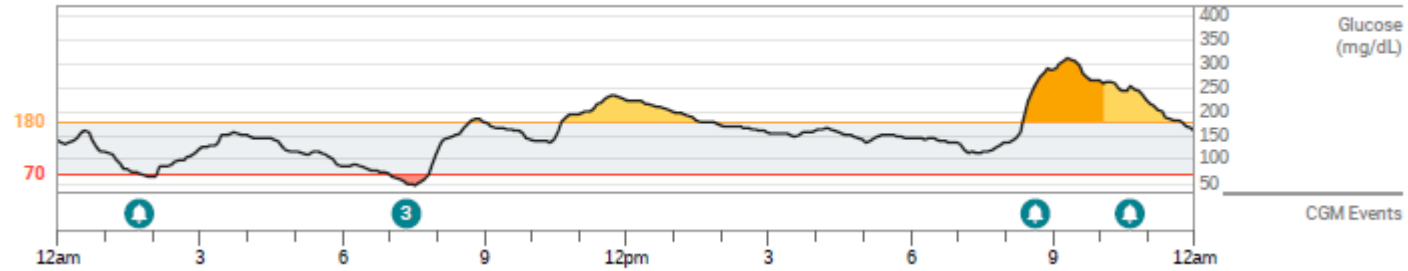
Diabetes Care 2023;46(4):1–10 | https://doi.org/10.2337/dc22-2189

	Over-night	Breakfast		Lunch		Dinner		Bed-time
								
2/9		126						
2/8		78		197				
2/7		105		75		190		
2/6		75		212		138		75
2/5		112		139		266		109
2/4		79		101		97		172
2/3								190

Sat, Feb 4, 2023



Sun, Feb 5, 2023



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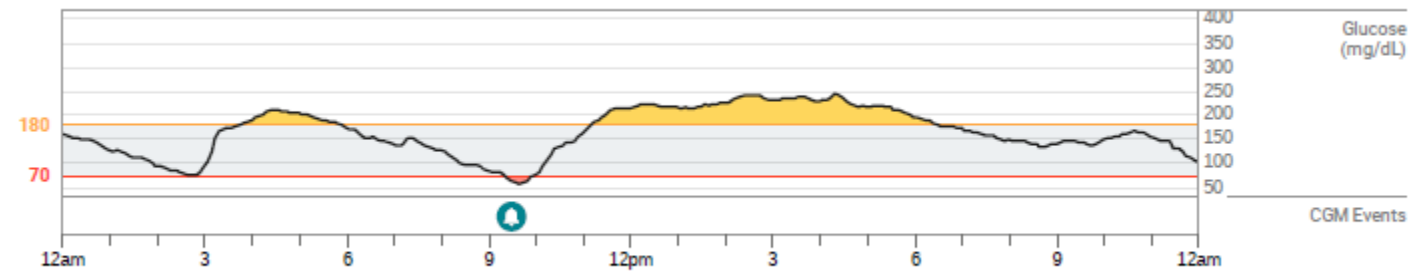


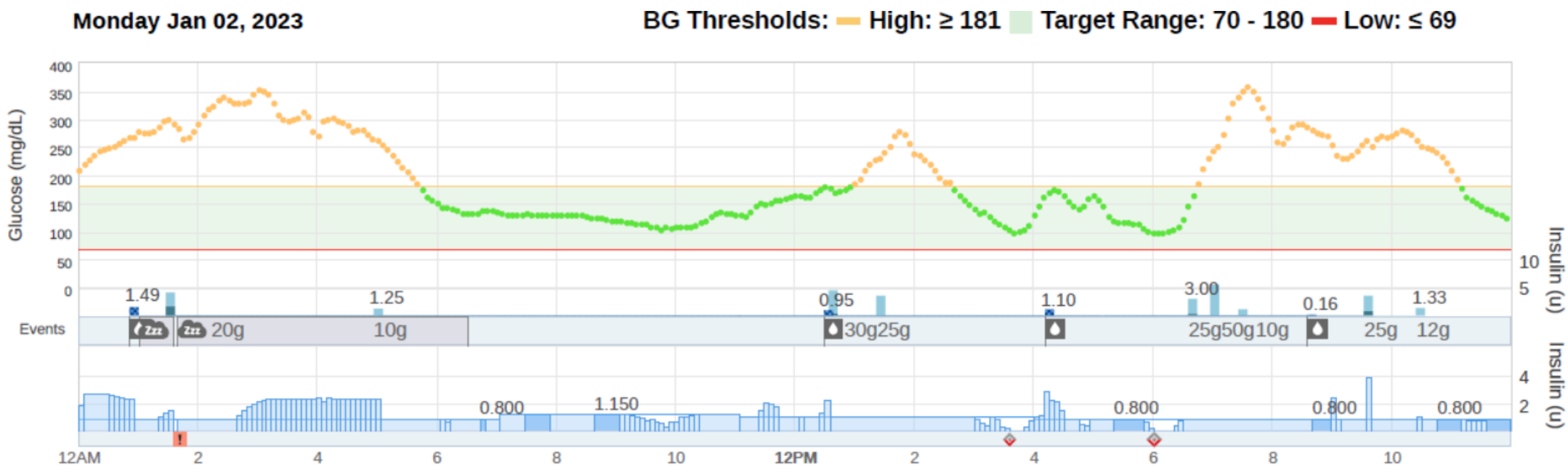
Automated Insulin Delivery Systems

All available insulin pumps now have hybrid closed loop system however algorithms vary

- Tandem Tslim and Dexcom
- Omnipod and Dexcom
- Medtronic with their own sensor

Communication between insulin pump and CGM to titrate basal insulin based on change in glucose

- Algorithm varies between systems
- Will review specifics separately


Monday Jan 02, 2023
BG Thresholds: High: ≥ 181 Target Range: 70 - 180 Low: ≤ 69
Glucose (mg/dL)
400
350
300
250
200
150
100
50
0
Insulin (u)
10
5
Events
1.49
1.25
0.95
1.10
3.00
0.16
1.33
20g
10g
30g25g
25g50g10g
25g
12g
Insulin (u)
4
2
0.800
1.150
0.800
0.800
0.800
12AM
2
4
6
8
10
12PM
2
4
6
8
10

CGM use in the hospital

- No system with FDA approval for inpatient use however the FDA allowed their use as result of the pandemic
- As a result, some hospitals quickly began programs for use of CGM leading to more robust data
- Majority of available data supports use of CGM in inpatient setting
- 2022 Endocrine society Practice guidelines recommend use for CGM for patients at high risk of hypoglycemia and without the following:
  - Hypotension/hypoperfusion
  - Extensive skin infections
  - Interfering medications (high dose acetaminophen, dopamine, vitamin D, hydroxyurea)

Korytkowski MT et al. *J Clin Endocrinol Metab* 2022;107:2101–2128

CGM use in the hospital

Table 2. Resources required for safe implementation of continuous glucose monitoring in the noncritical care hospital setting

Engagement, training, and education of nursing personnel
Patient education regarding care of the device and how to respond to alarms for high or low BG
Purchase of equipment (eg, sensors, transmitters, receivers)
Expertise from healthcare professionals knowledgeable in this technology
Oversight and guidance for CGM use
Integration of CGM data with the hospital electronic medical record
Clarity of assigned responsibility for interpreting and acting on CGM data

Abbreviation: CGM, continuous glucose monitoring
Source: Galindo RJ et al. *J Diabetes Sci Technol*, 2020; (14)4. © Diabetes Technology Society (24).

Correction scale alone is rarely the answer and NEVER appropriate for patients with type 1 DM

regimens

- Basal-bolus regimen
- Continuation of insulin pump therapy
- Insulin infusion

Non-insulin medications

Metformin- not recommended for use

Sulfonylureas- not recommended for use

DPP4i- some data to support use

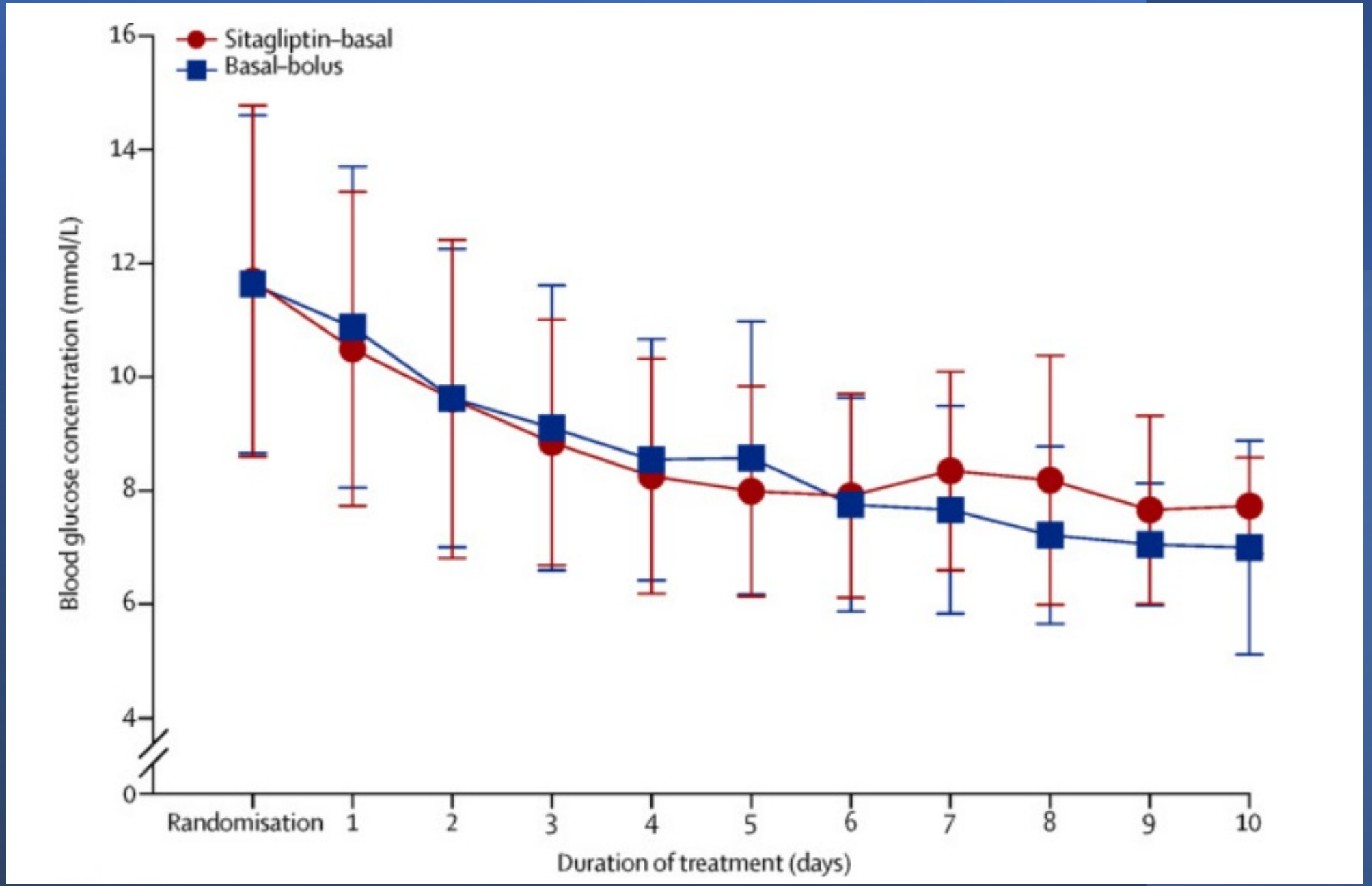
GLP1RA- some data to support use

SGLT2i-not recommended for use due to risk of euglycemic DKA

DPP4 inhibitors in hospital: Sita-Hospital

- Multicenter, prospective, open-label randomized clinical trial
- Patient Population: Patients with T2DM admitted with BG between 140-400 mg/dl, treated with diet, OADs and insulin at TDD < 0.6 Unit/kg
- Treatment Groups
  - Group 1: Sitagliptin plus glargine once daily (n=140)
  - Group 2: Basal bolus regimen with glargine once daily and rapid-acting insulin before meals (n=140)
- Both groups received correction doses of rapid-actin insulin for BG > 140 mg/dl with meals

Pasquel FJ et al. *Lancet Diabetes Endocrinol* 2017;5:125-133

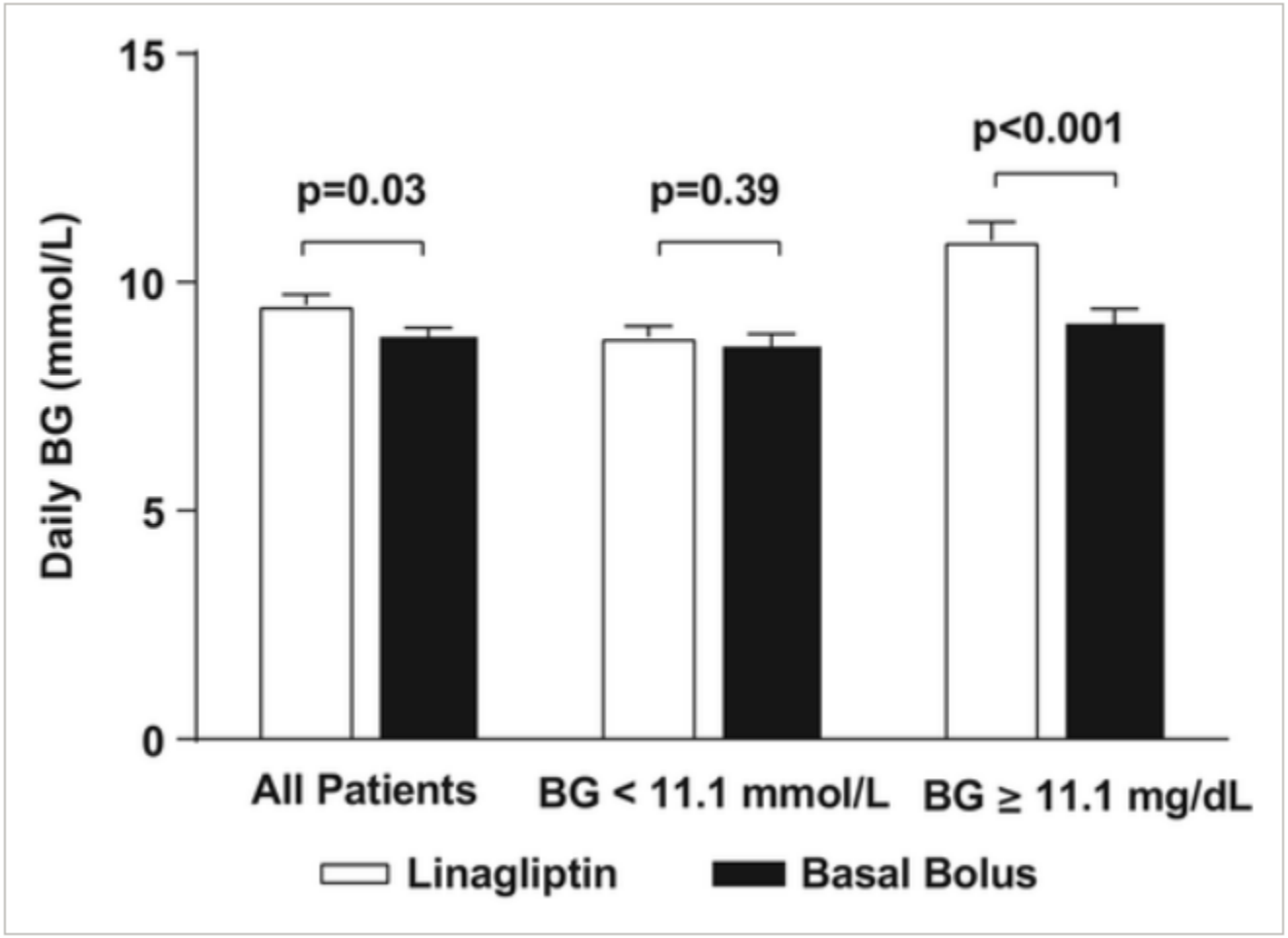


Pasquel FJ et al. *Lancet Diabetes Endocrinol* 2017;5:125-133

	All (n=277)	Sitagliptin–basal (n=138)	Basal–bolus (n=139)	p value *
Treatment failures				
Number of treatment failures	48 (17%)	22 (16%)	26 (19%)	0·54
Day of treatment failure	2·0 (2·0–3·0)	2·0 (2·0–3·0)	2·0 (2·0–3·0)	0·84
Insulin therapy				
Total insulin dose (units per day)	29·1 (18·9)	24·1 (16·2)	34·0 (20·1)	<0·0001
Total daily dose (units per kg)	0·3 (0·2)	0·2 (0·1)	0·3 (0·2)	<0·0001
Total glargine (units per day)	17·3 (11·5)	17·9 (12·5)	16·8 (10·4)	0·94
Total prandial rapid-acting insulin (units per day)	6·1 (8·1)	0·4 (1·9)	11·7 (7·9)	<0·0001
Total supplemental rapid-acting insulin (units per day)	5·7 (5·2)	5·8 (5·7)	5·5 (4·7)	0·91
Number of injections per day during hospital stay	2·7 (1·0)	2·2 (1·1)	2·9 (0·9)	<0·0001
Number of injections per day on days 2–10 of study	2·6 (1·2)	2·1 (1·3)	2·9 (1·1)	<0·0001

Linagliptin surgery trial

- Patients undergoing non-cardiac surgery randomized to linagliptin (n= 137) or basal-bolus insulin (n=143)
- Linagliptin alone inferior in those presenting with BG >200 mg/dL but comparable in those with presenting BG <200 mg/dL
- Significantly lower rates of hypoglycemia in linagliptin group (1.1% vs 11%, *P* = 0.01)
- No differences in LOS, post-surgical complications



Vellanki P et al. *Diabetes Obes Metab* 2019;21:837–843

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Questions which remain

- How do we choose the right drug/tool for the right person?
- How do we provide equal access and cost-effective care?
- Do we have the tools to fight the obesity epidemic?