Diabetes and Hypertension Project ECHO* Clinic

*ECHO: Extension of Community Healthcare Outcomes

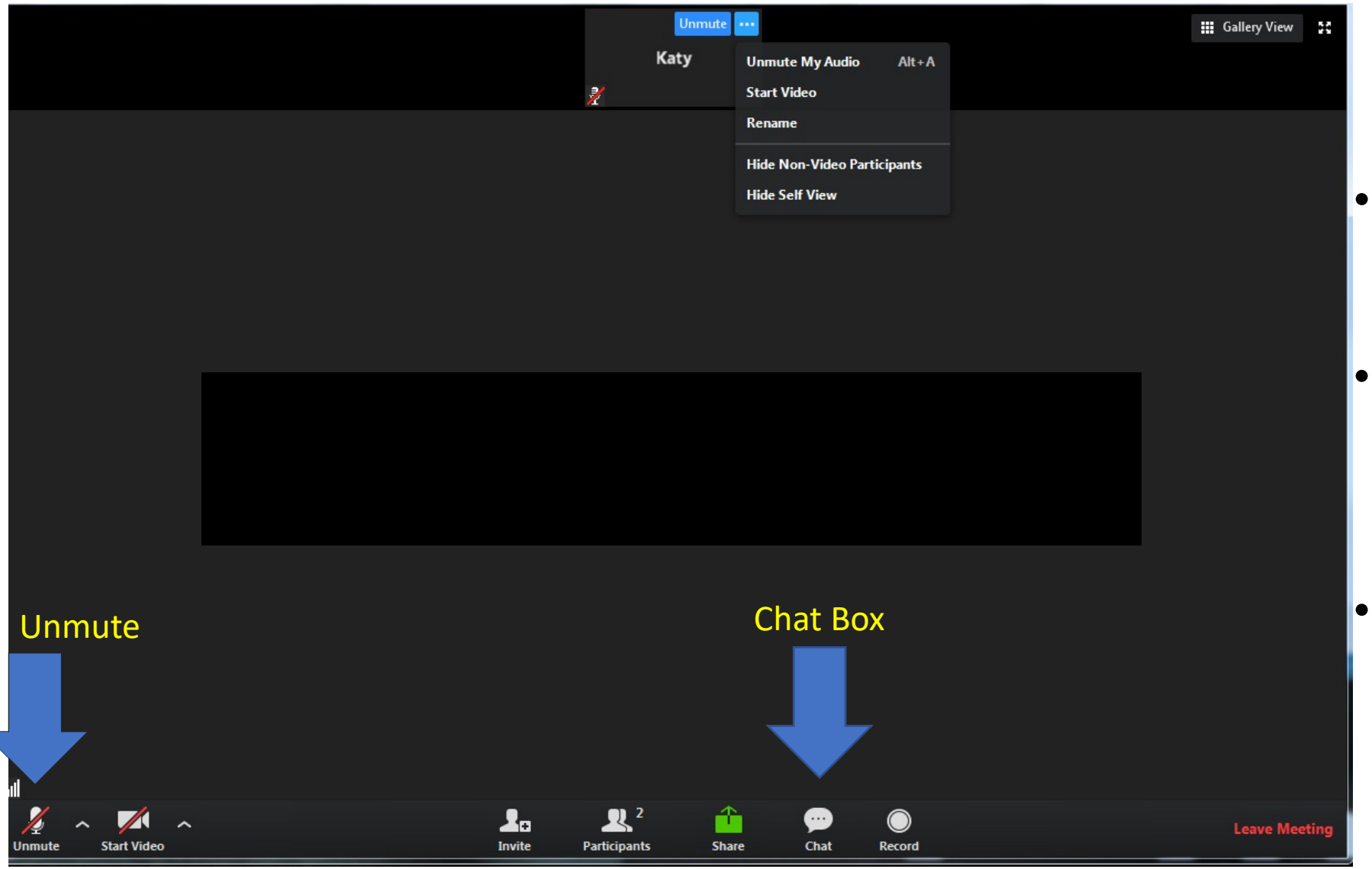
Aug. 12, 2021

Before we begin:

- Rename your Zoom screen with your name and organization
- Claim CE: text 19175-18817 to 804-625-4041
  - Go to **vcuhealth.org/echodmhtn** for instructions on creating your account

The Diabetes and Hypertension ECHO is made possible by funding through CDC Cooperative Agreement NU58DP006620-InnoVAte.

Zoom Reminders



- You are all on mute. Please unmute to talk.
- If joining by telephone audio only, press *6 to mute and unmute.
- Use the chat function to speak with our team or ask questions.

Helpful Reminders

- Please feel free to eat your lunch or step away briefly if needed
- We are recording and can share sessions upon request
  - Each session's slides are available on www.vcuhealth.org/echodmhtn
- Please **do not share any protected health information** in your discussion or the chat box
- Project ECHO operates on the "All Teach, All Learn" model
  - Feel free to ask questions in the chat or unmute to ask questions at designated times
  - We're all here to learn from each other and value each person's input and expertise!

VCU Health Diabetes & Hypertension ECHO Clinics

VCU Hub Team	
Principal Investigator	Dave Dixon, PharmD
Administrative Medical Director ECHO Hub	Vimal Mishra, MD, MMCi
Clinical Experts	Niraj Kothari, MD Trang Le, MD
Project Coordinator/IT Support	Madeleine Wagner

- **NEW: *1-hour*** ECHO clinics on 2nd and 4th Thursdays
- Every ECHO clinic includes a didactic presentation followed by case discussions
- Website: www.vcuhealth.org/echodmhtn
  - Directions for claiming CE can be found here
  - You have up to six days after our session to claim CE by texting **19175-18817** to **804-625-4041**

Disclosures

Trang Le, M.D., has no financial conflicts of interest to disclose.

Niraj Kothari, M.D., has no financial conflicts of interest to disclose.

There is no commercial or in-kind support for this activity.

Use of GLP-1 RAs for Weight Management

Objectives

- Describe approved GLP-1 receptor agonist (RA) agents approved for weight management
- Review GLP-1 RA efficacy data for weight loss
- Discuss dosing regimens and contraindications to GLP-1 RA therapy

Setting expectations:

- In short-term (6 to 12 months) clinical trials evaluating drug therapy, weight loss of 4 to 8 percent is typical[1]

1. not every drug works for every patient

→individual responses vary widely

2. when the maximal therapeutic effect is achieved, a plateau is reached and weight loss ceases.

3. when drug therapy is discontinued, weight gain can be expected.

- Consider using anti-obesity medications longer term for weight loss maintenance if they are well-tolerated and individuals have achieved >5% weight loss on treatment

[1]Khera R et al, JAMA. 2016;315(22):2424Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events: A Systematic Review and Meta-analysis

Goal setting

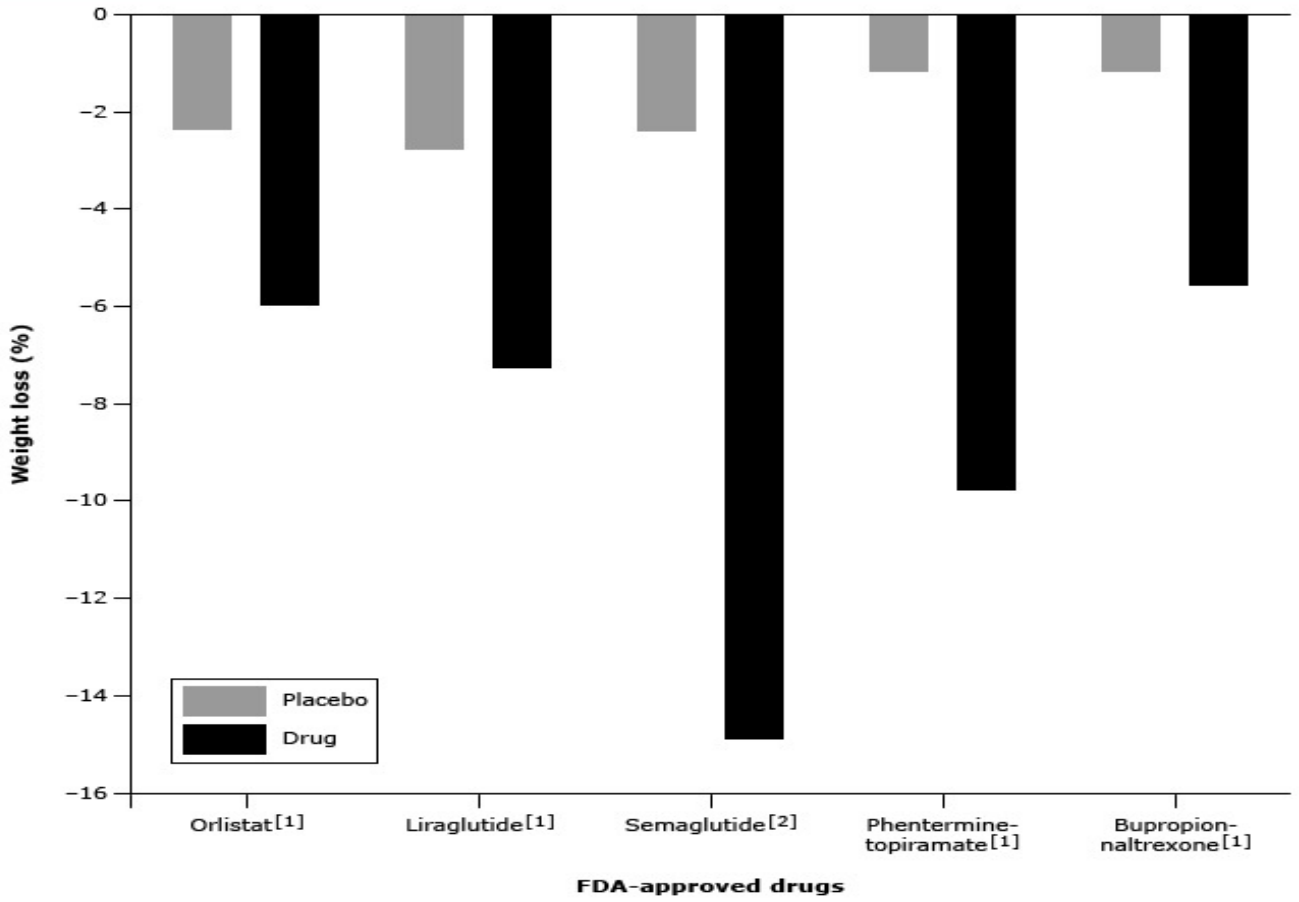
- Weight loss should
  - exceed 2 kg during the first month of drug therapy (~ 1 pound per week),
  - fall > 4-5% below baseline at three to six months, and
  - remain at this level to be considered effective
- A weight loss of 5-10% can substantially reduce the development of diabetes in those with prediabetes

le Roux CW et al, Lancet. 2017;389(10077):1399. Epub 2017 Feb 23
Torgerson JS et al, Diabetes Care. 2004;27(1):155

Candidates for obesity drug therapy

- Body mass index (BMI) ≥30 kg/m^2, OR
- BMI of 27 to 29.9 kg/m^2 with weight-related comorbidities
  (hypertension, dyslipidemia, type 2 diabetes)
- Have not met weight-loss goals (a least 5% of total body weight at 3-6months) with a comprehensive lifestyle intervention alone
- The decision to initiate drug therapy should be individualized weighing the risks and benefits of all treatment options (lifestyle, pharmacologic, device, surgical), COST
- Recommendations for use of drug therapy vary among clinicians

Weight loss outcomes with FDA-approved medications



Weight loss reflects results at 52 weeks, except for semaglutide, which reflects weight loss at 68 weeks.

FDA: US Food and Drug Administration.

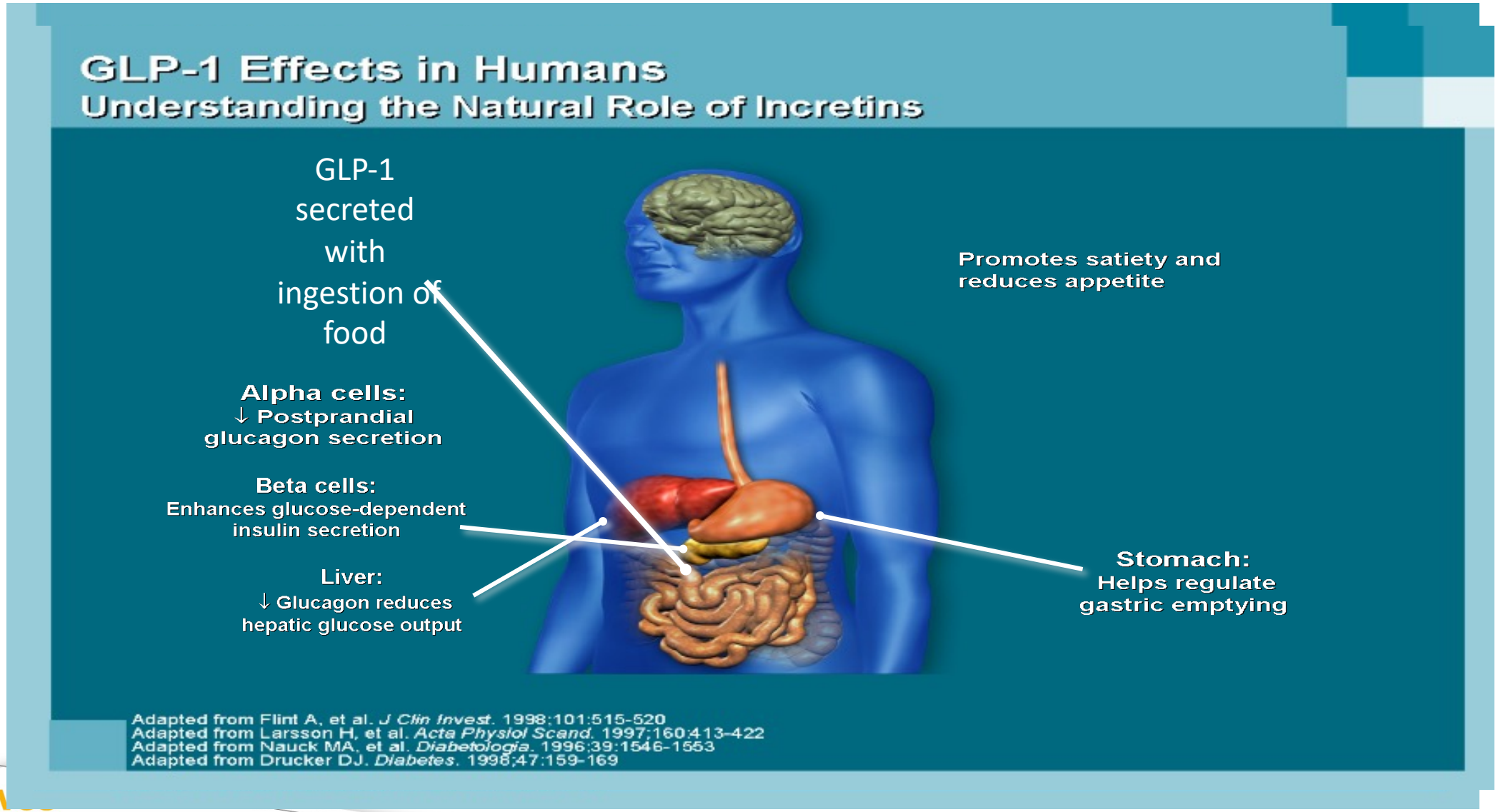
Courtesy of George A Bray, MD.
Data from:

1. *Khera R, Murad MH, Chandar AK, et al. Association of pharmacological treatments for obesity with weight loss and adverse events: A systematic review and meta-analysis. JAMA 2016; 315:2424. doi: 10.1001/jama.2016.7602.*
2. *Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med 2021; 384:989.*

Limitations:

- Short duration of studies
- High attrition rates
- Heterogeneity
- Few head-to-head-trials

GLP-1 Physiology



GLP-1 receptor agonists

- Administered subcutaneously or orally (semaglutide)
- Agents approved for the treatment of obesity in the US include semaglutide (SQ only) and liraglutide.
- For patients with or without diabetes mellitus, some suggest these agents as preferred first-line pharmacotherapy for the treatment of obesity.
- For patients with diabetes in particular, the side effects, need for injections, and expense are balanced by improved glycemia and weight loss.

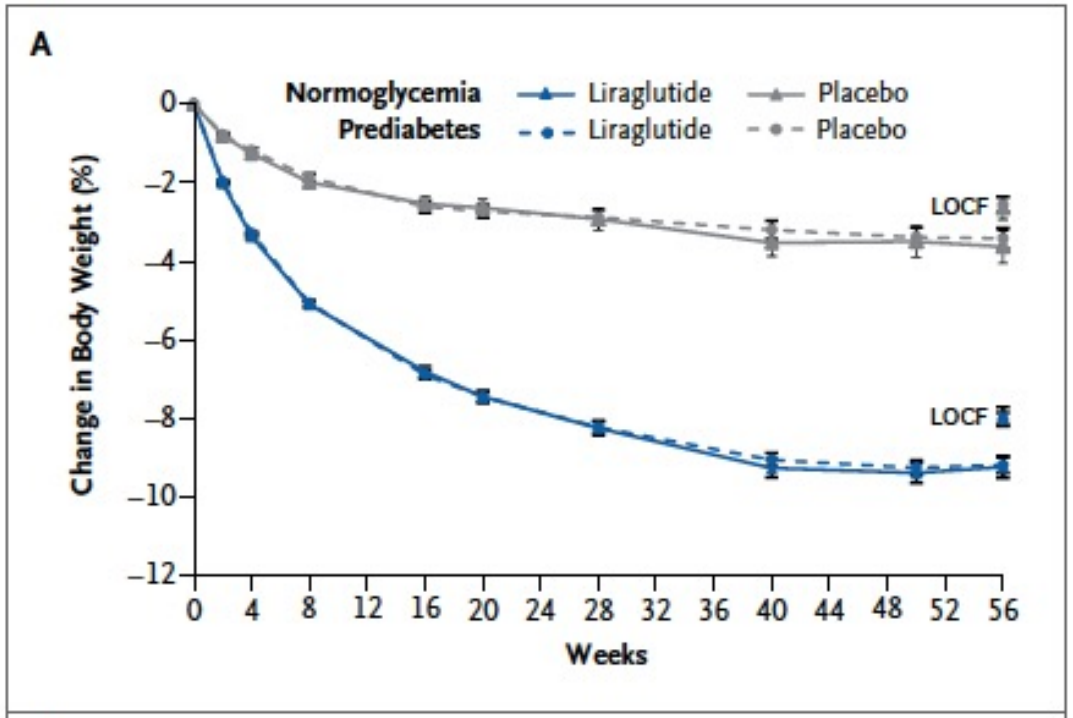
Liraglutide (Saxenda®)

- Dosing: 0.6 mg SQ **once daily**
- Increase by 0.6mg daily in 1 week intervals to target of **3mg daily**

  Pen requires a one-time priming of the device
- Timing of doses is independent of meals
- Need to prescribe pen needles
- FDA approved for diabetes up to a 1.8mg once a day dose (Victoza®)
- Many providers will continue patient on maximum tolerated dose even if goal weight loss is not achieved on that dose

Liraglutide

- Liraglutide has beneficial effects on glycemia in addition to demonstrated efficacy for weight loss.
- May be used in patients with or without diabetes,
- A preferred drug in patients with type 2 diabetes, and particularly in those with cardiovascular disease due to demonstrated reduction of cardiovascular events in this population
- No dosage adjustment necessary with impaired renal function, but limited evidence in hemodialysis and peritoneal dialysis
- Approved for children aged 12 years + for obesity (but aged 10+ for type 2 diabetes)



- 56 weeks, liraglutide 3mg daily vs placebo
- N=3731, BMI≥30 kg/m^2 or ≥27 kg/m^2 with dyslipidemia and/or hypertension,
- mean weight loss was significantly greater in the liraglutide group (-8.0 versus -2.6 kg with placebo)
- cardiometabolic risk factors, hemoglobin A1C, and quality of life all improved modestly but significantly.

Pi-Sunyer X et al, N Engl J Med. 2015;373(1):11.

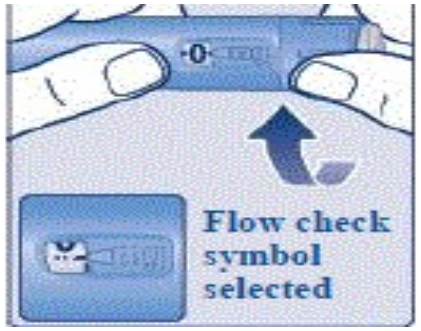
Semaglutide

- once-weekly subcutaneous or once-daily oral dose
- efficacy in weight loss in trials involving patients with and without type 2 diabetes
- In the US, both the oral and injectable preparations are approved for the treatment of type 2 diabetes, whereas only the injectable form is approved for the treatment of obesity

Rosenstock J, et al, JAMA. 2019;321(15):1466
Davies M et al.Lancet. 2021;397(10278):971. Epub 2021 Mar 2.

Semaglutide (Ozempic®) for T2DM

- Injectable Titration dose: 0.25 mg **weekly**
  - Increase to 0.5 mg after **4 weeks**. Max dose 1.0 mg/week
  - 0.25/0.5 mg Pen (2mg/1.5mL Pen) + 6 needles
  - As of April 2021: 2mg/1.5mL pen → 4mg/3mL Pen + 4 needles
    - Pen needles included with the pens
    - Each pen requires a one-time priming step



- Oral (Rybelsus): 3mg daily x 30 days→7mg x 30 days→14mg
  - Give 30 minutes before food / beverages / other meds, in AM

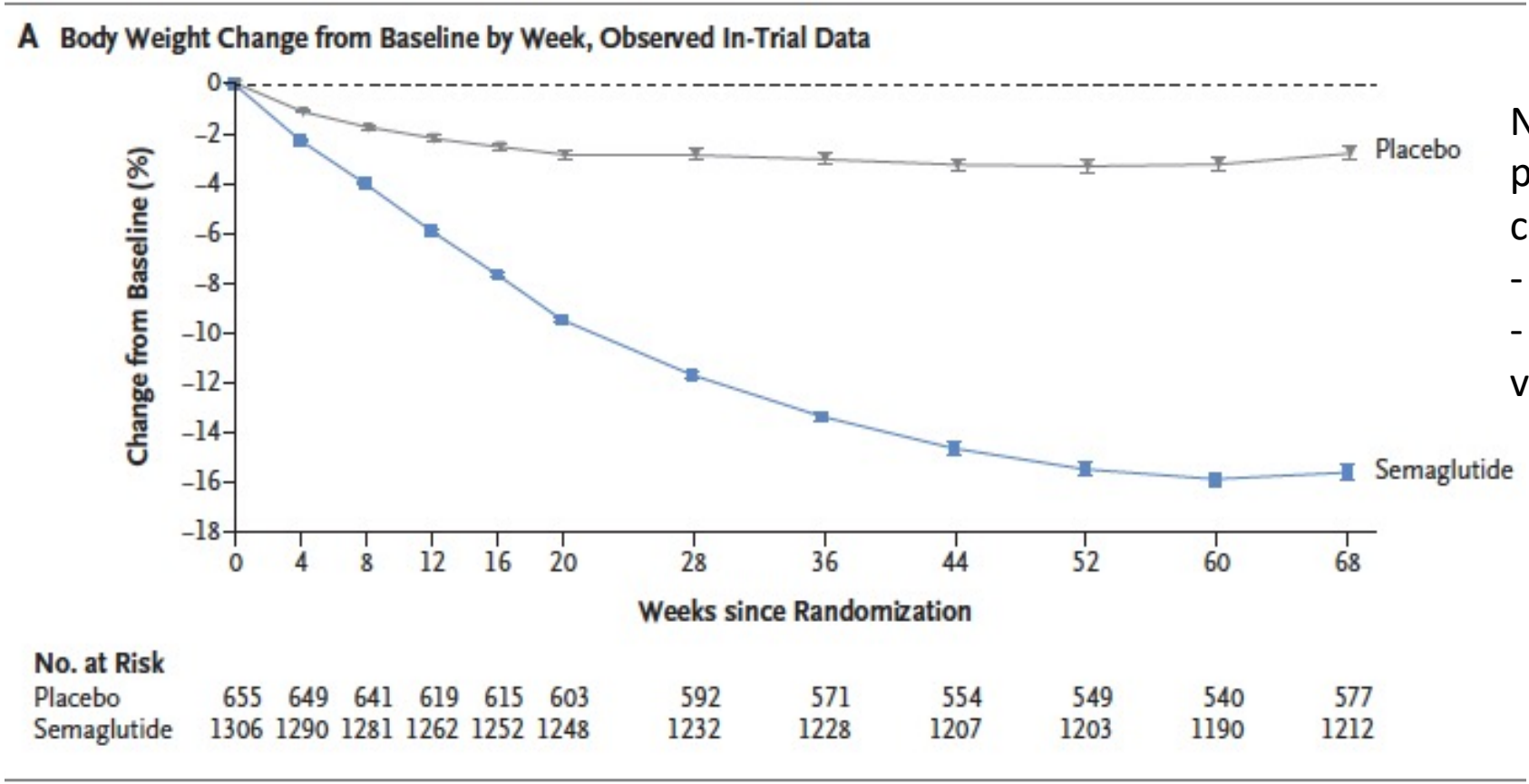
Semaglutide (Wegovy™)

Single use pen, hidden needle

Week 1 through week 4 : 0.25 mg once weekly.
Week 5 through week 8: 0.5 mg once weekly.
Week 9 through week 12: 1 mg once weekly.
Week 13 through week 16: 1.7 mg once weekly.
Week 17 and thereafter (maintenance dosage): 2.4 mg once weekly; if not tolerated, may temporarily decrease dosage to 1.7 mg once weekly for up to 4 additional weeks, then increase to 2.4 mg once weekly.
Note: Discontinue therapy in patients who cannot tolerate the 2.4 mg/week dosage (manufacturer's labeling). Consider discontinuation if at least 5% of baseline body weight loss has not been achieved within 3 months (ADA 2021).

FDA-Approved for weight loss June 4, 2021

Semaglutide 2.4mg, double-blind trial

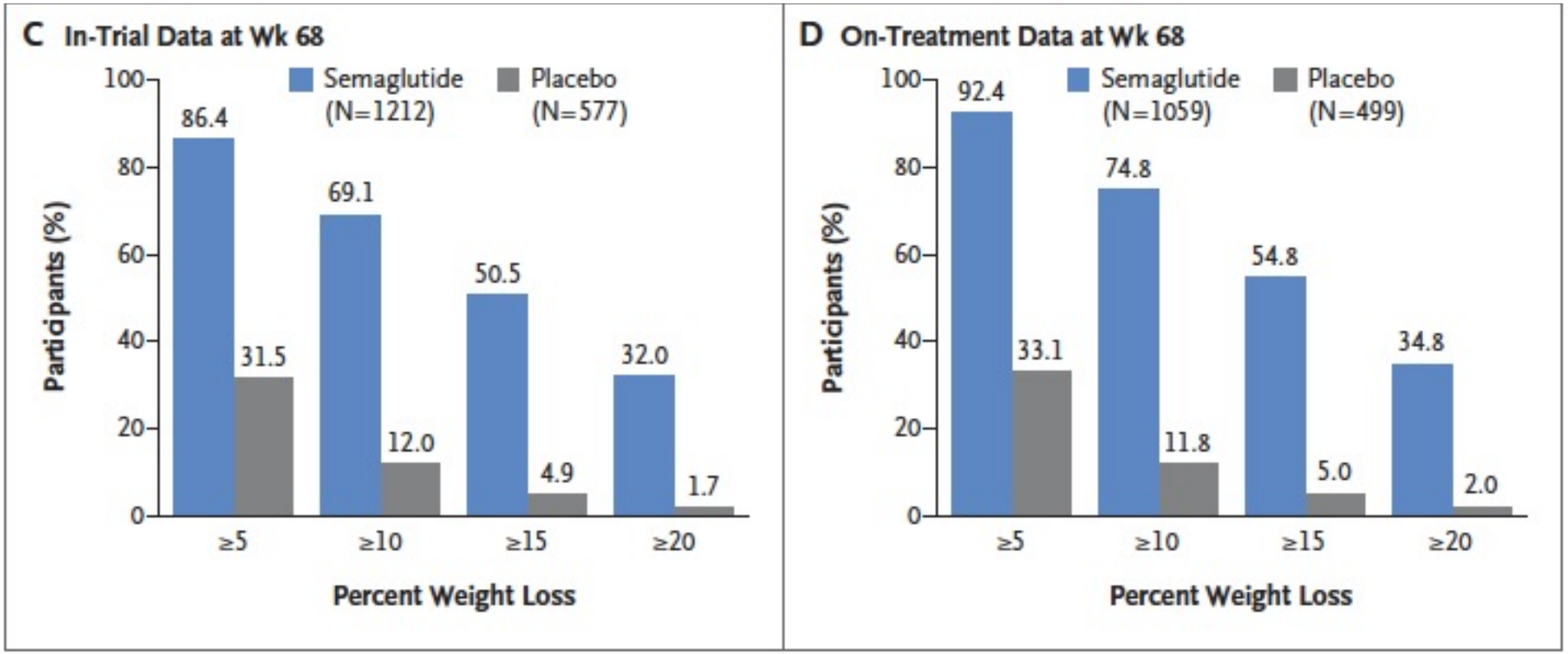


N = 1961 adults BMI ≥ 30 or ≥27 in persons with≥ 1 weight-related coexisting condition) WITHOUT diabetes,
- randomly assigned in a 2:1 ratio
- 68 weeks of treatment semaglutide 2.4 vs placebo, + lifestyle intervention.

Change in body weight =
−15.3 kg semaglutide vs
−2.6 kg in the placebo group

Wilding JPH at al, N Engl J Med. 2021;384(11):989. Epub 2021 Feb 10.

Semaglutide 2.4mg, double-blind trial



Wilding JPH at al, N Engl J Med. 2021;384(11):989. Epub 2021 Feb 10.

Semaglutide

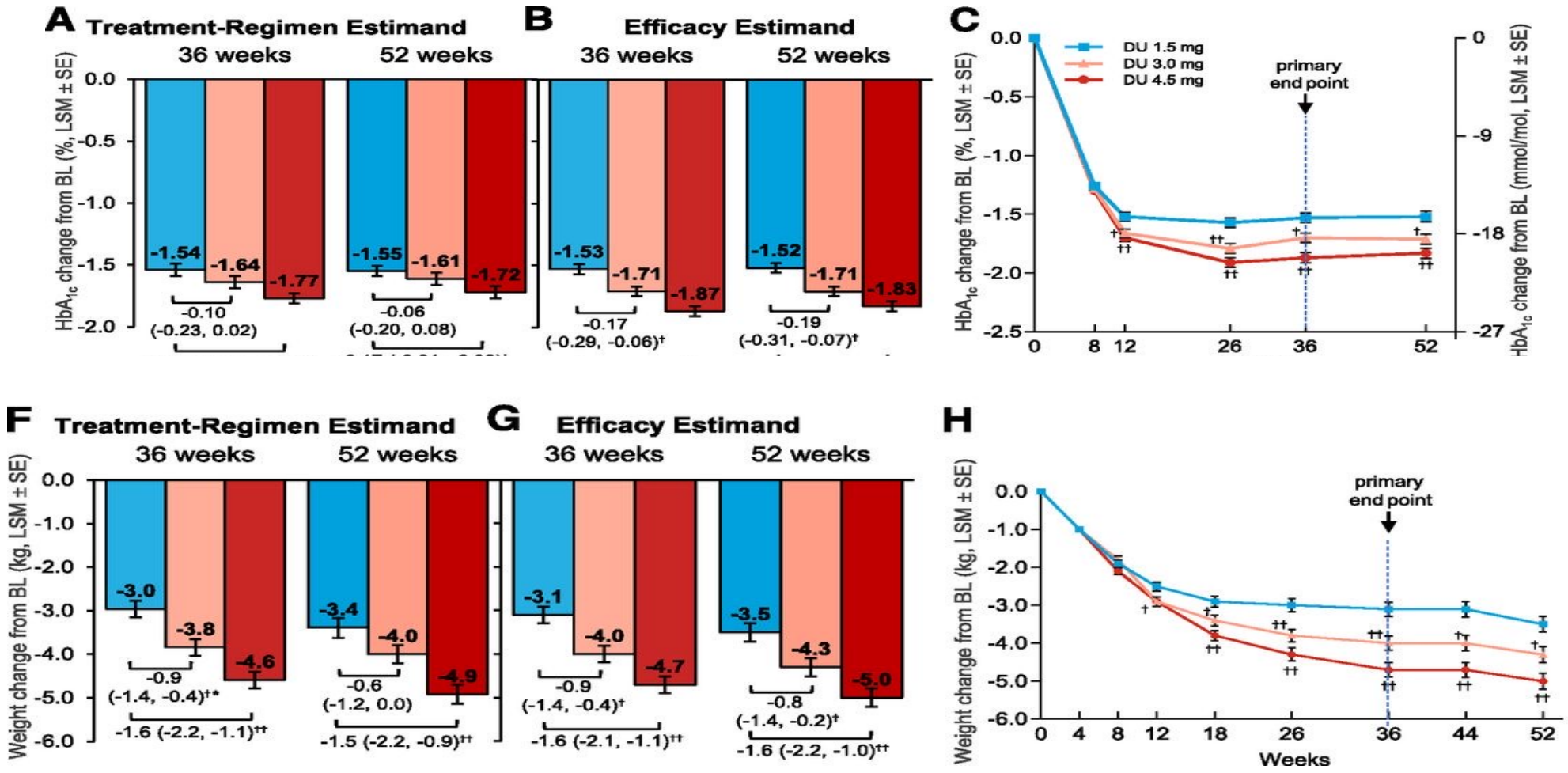
- Shorter duration of treatment is associated with weight regain:
- N=803 participants who were overweight or with obesity were randomly assigned to continue semaglutide treatment or switch to placebo after 20 weeks of initial therapy
- Individuals continuing on semaglutide continued to lose weight, while those switched to placebo regained weight over the subsequent 48 weeks.

Rubino D et al, JAMA. 2021;325(14):1414.

Dulaglutide (Trulicity™)FOR DM

- 0.75-->1.5-->3.0-->4.5 mg SQ **once weekly**
- Each pen is single use

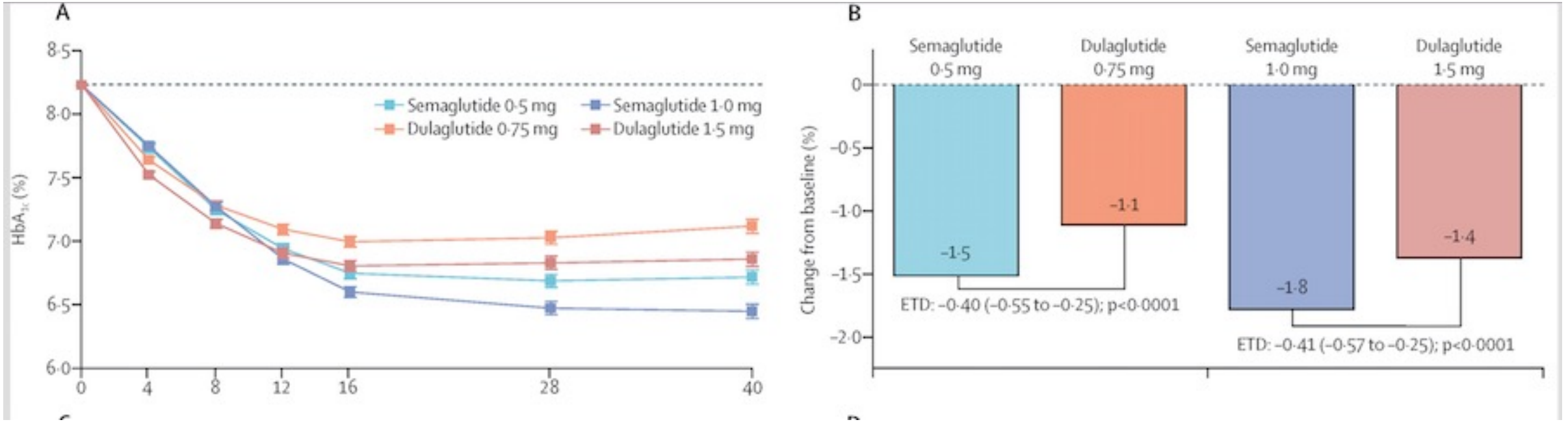
Dulaglutide 3.0 mg and 4.5 mg Versus Dulaglutide 1.5 mg in Metformin-Treated Patients With Type 2 Diabetes



Juan P. Frias et al. Dia Care 2021;44:765-773

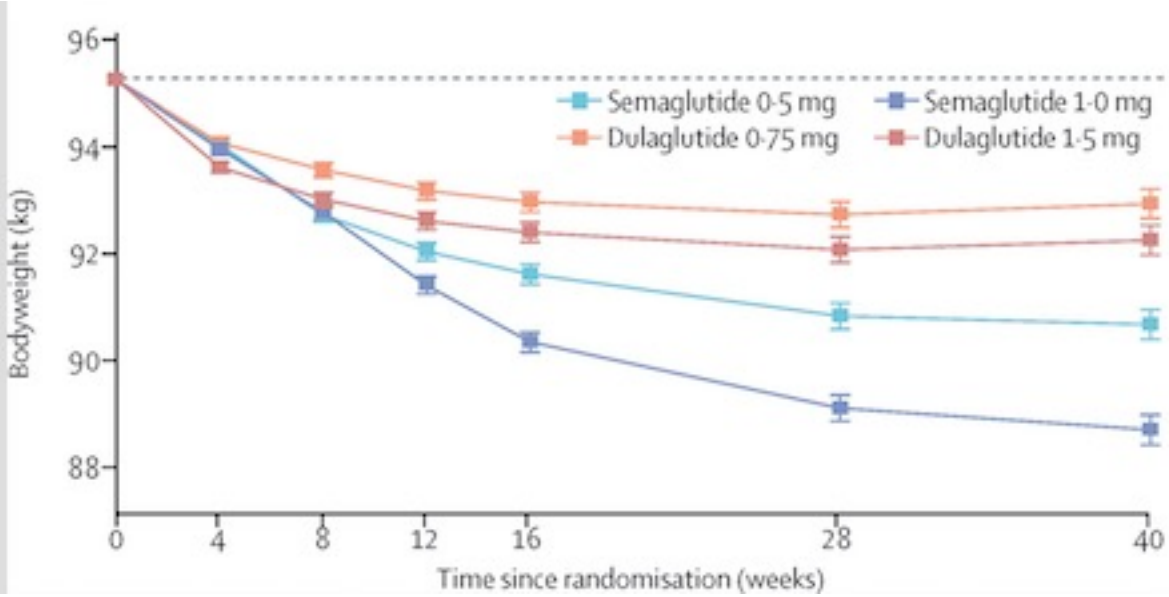
Semaglutide vs dulaglutide

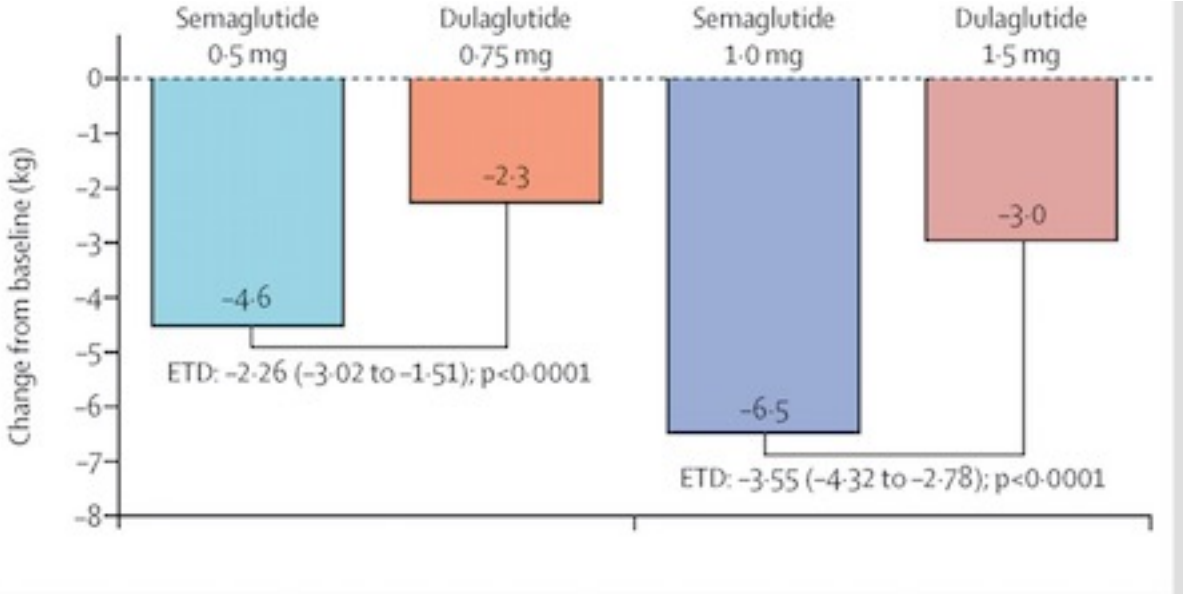
open-label, parallel-group, phase 3b trial
type 2 diabetes with HbA1c 7.0–10.5% on metformin monotherapy



Pratley et al, Lancet Diabetes Endocrinol2018 Apr;6(4):275-286.

Semaglutide vs dulaglutide





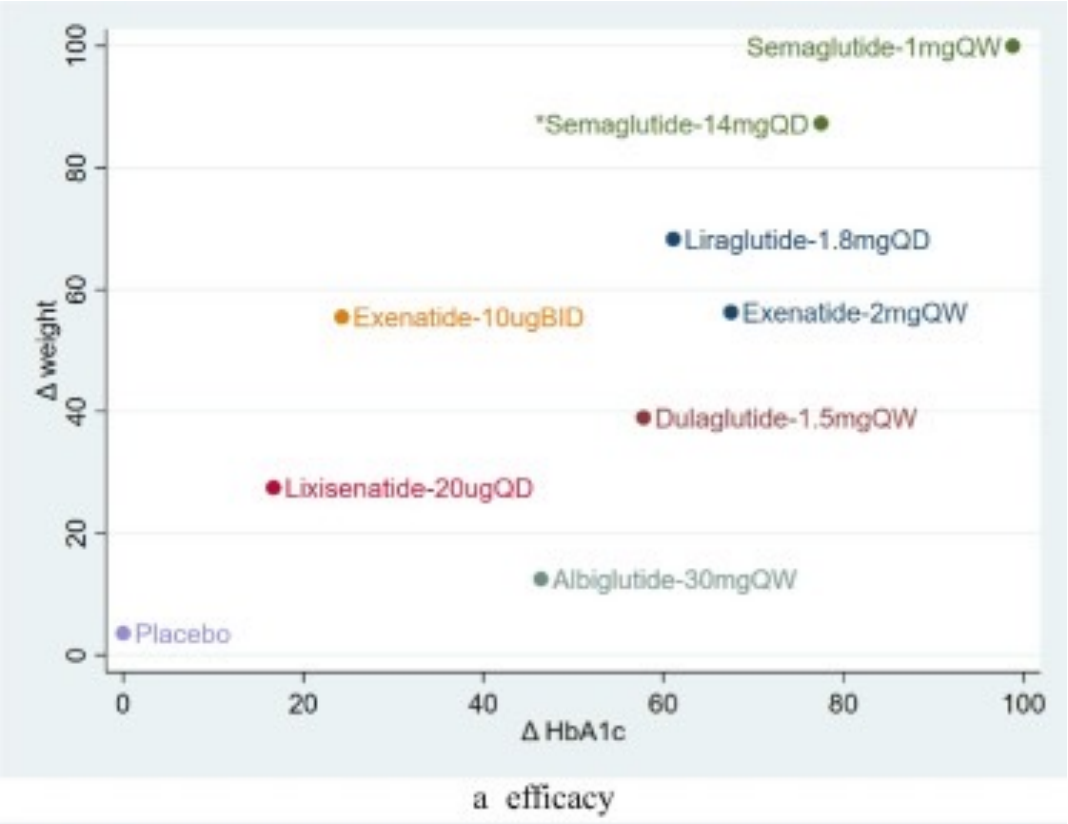
Pratley et al, Lancet Diabetes Endocrinol2018 Apr;6(4):275-286.

GLP-1 agonist adverse effects/contraindications

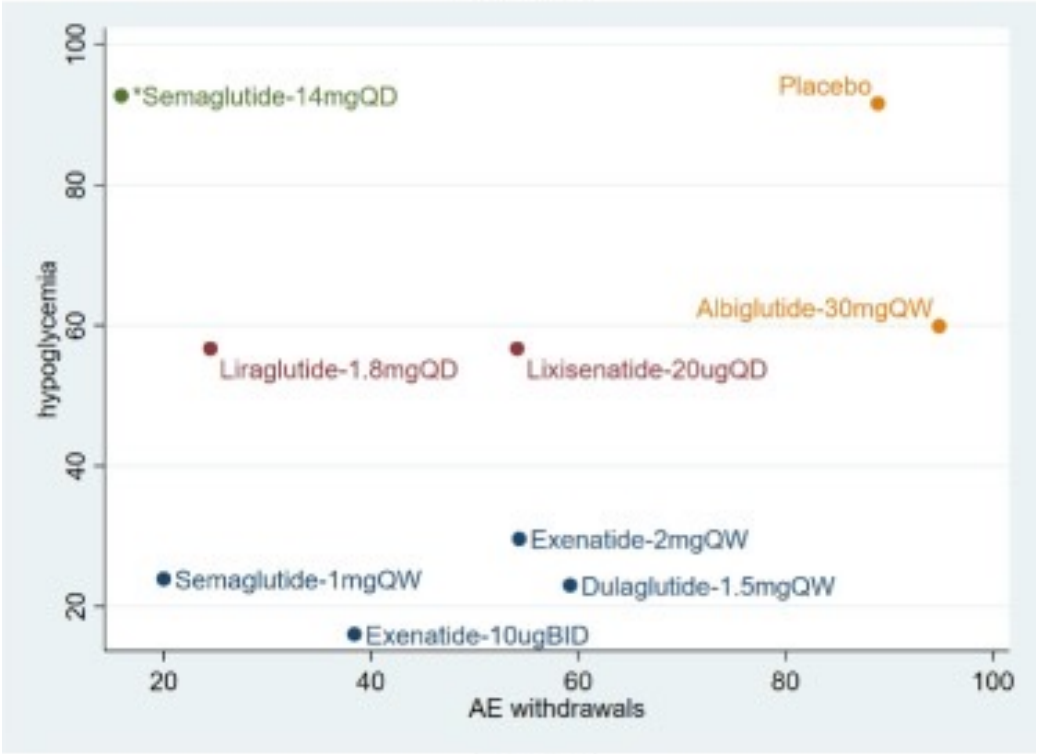
- Adverse Effects
  - Nausea/vomiting, diarrhea
  - Injection site reactions
  - Pancreatitis
- Contraindications/Precautions
  - Gastroparesis
  - History of pancreatitis
  - History of medullary thyroid carcinoma
  - Multiple endocrine neoplasia syndrome 2
  - Monitor for worsening retinopathy

GLP-1 RA in T2DM Meta-analysis, n=11,128

Studies included if (1)enrolled patients with T2D aged 18+, (2) were a randomized clinical trial (RCT); (3) compared GLP-1RA approved by the FDA with a control group



a efficacy



b safety

Xia L et al, Diabetes Res Clin Pract. 2021 Jul;177:108904.

Case Study #1

33 year old lady with T2DM, new patient visit

- Prediabetes in 2016, GDM in 2017 – on insulin (1st pregnancy)
- GDM with 2nd pregnancy in 2019, on insulin, now 9 months postpartum
- Frustrated that she is still on insulin and continuing to gain weight
- States significant stress with 2 young children at home, “I am using insulin as a crutch to eat foods I know I shouldn’t”
- Medications:
  - Metformin 1000mg daily (cannot tolerate higher doses)
  - Lantus 22 units nightly
  - Lispro 18-24 unit with meals, based on rough estimate of carb content

BMI 43.5

Labs: normal renal function, A1c 6.9% postpartum

Case Study #1 (continued)

AGP Report

July 15, 2021 - August 11, 2021 (28 Days)

LibreView

GLUCOSE STATISTICS AND TARGETS

July 15, 2021 - August 11, 2021	**28 Days**
% Time CGM is Active	**44%**

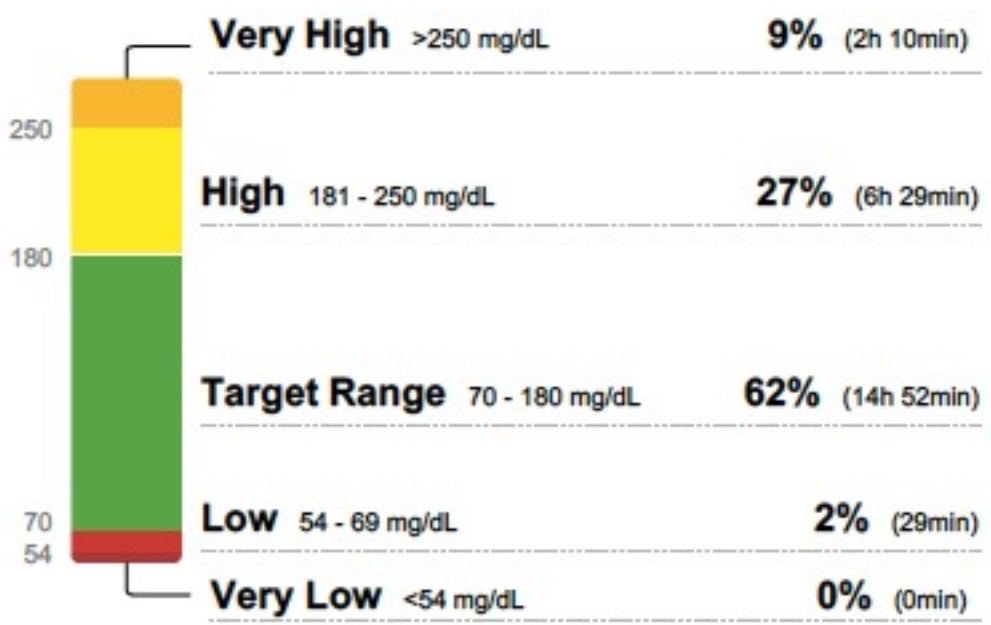
Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges	**Targets** % of Readings (Time/Day)
Target Range 70-180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)

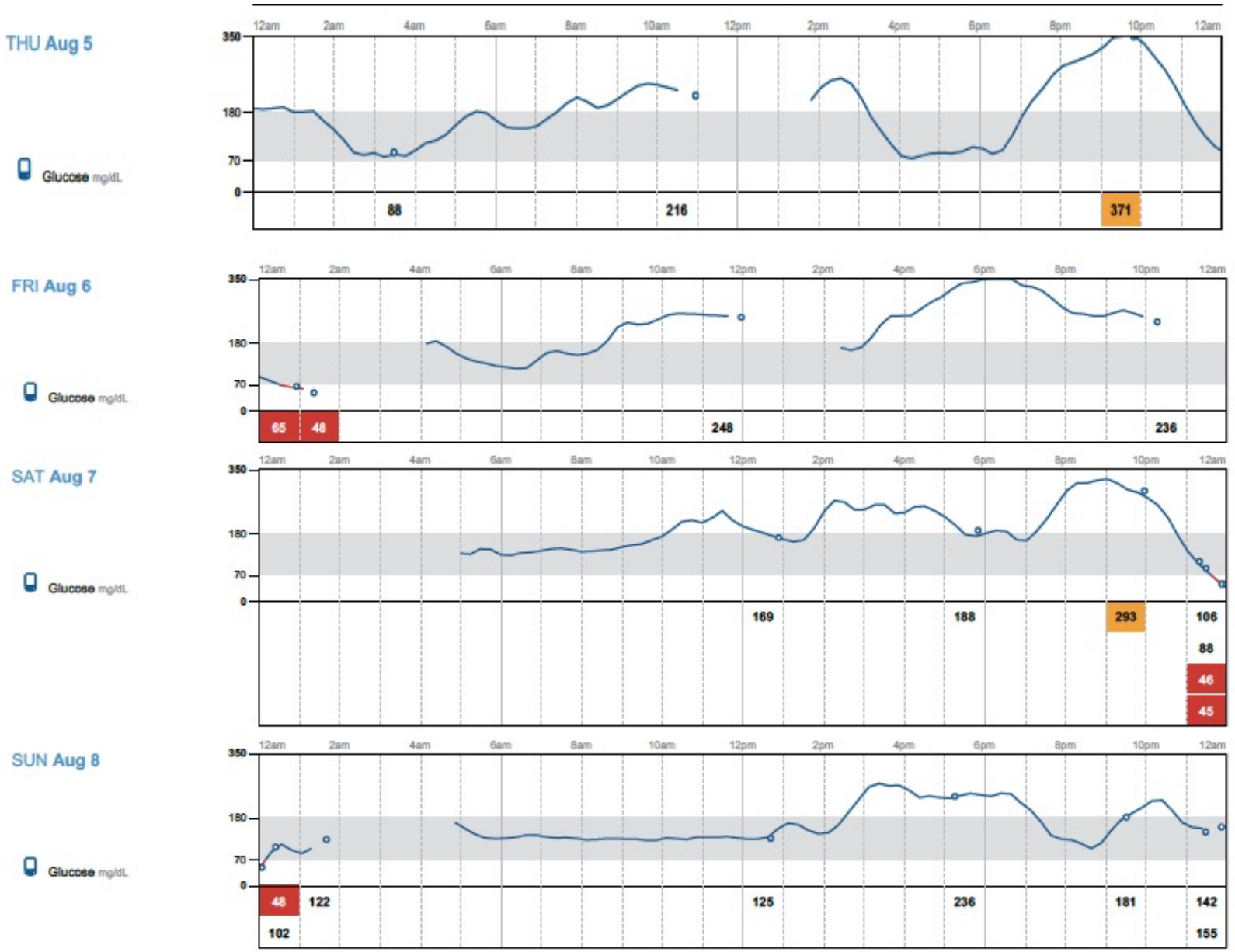
Each 5% increase in time in range (70-180 mg/dL) is clinically beneficial.

Average Glucose	**163** mg/dL
Glucose Management Indicator (GMI)	**7.2%**
Glucose Variability	**36.8%**

Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES





Project ECHO®
Virginia Commonwealth University

VCU

Case Study #2

- 65 year old gentleman with T2DM diagnosed after heart transplant 2009 for nonischemic cardiomyopathy, hyperlipidemia, hypertension,
- A1c 8.9% 3/2020, now 12.2% in 8/2021
- Medications:
  - Meformin 1000mg BID,
  - Lantus 20 units nightly with omission 1-2x per week
  - Lisinopril 20mg daily
  - Mycophenolate mofetil
  - Gabapentin 200mg TID
  - Atorvastatin 40mg daily
  - Amlodipine 10mg daily
  - Carvediolol 3.125mg BID
- labs: glucose 217 fasting AM on day of visit, normal renal function,
- Inquires about a CGM, is reluctant to start mealtime insulin, BMI 29.9

Case Studies

- Anyone can submit cases: www.vcuhealth.org/echodmhtn
- Receive feedback from participants and content experts
- Earn **$150** for submitting and presenting

Provide Feedback

www.vcuhealth.org/echodmhtn

- Feedback
  - Overall feedback related to session content and flow?
  - Ideas for guest speakers?

Access Your Evaluation

vcuhealth.org/services/telehealth/for-providers/education/diabetes-and-hypertension-project-echo

For Providers

- Education
  - **Diabetes and Hypertension Project ECHO**
    - Our Team
    - Curriculum
    - Claiming CE Credit
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  - VCU Nursing Home ECHO
  - VCU Health Palliative Care ECHO
  - Virginia Opioid Addiction ECHO
  - Virginia Sickle Cell Disease ECHO

Diabetes and Hypertension Project ECHO

Welcome to the Diabetes and Hypertension Extension for Community Health Outcomes or ECHO, a virtual network of multidisciplinary diabetes and hypertension experts. An ECHO model connects professionals with each other in real-time collaborative virtual sessions on Zoom. Participants present de-identified cases to one another, share resources, connect to each other, and grow in their expertise. This ECHO will address practice level issues and solutions related to managing complex patients with difficult to control diabetes and hypertension. Register now for an ECHO Session!

Network, Participate and Present

- Engage in a collaborative community with your peers.
- Listen, learn and discuss informational and case presentations in real-time.
- Take the opportunity to submit your de-identified case study for feedback from a team of specialists for diabetes and hypertension.
- Provide valuable feedback.
- Claim CE credit by texting in attendance.

Benefits

VCU Diabetes & Hypertension Project ECHO Clinics

2nd and 4th Thursdays — ***NEW: 12 p.m. to 1 p.m.***

Mark Your Calendars — Upcoming Sessions

Aug. 26: SGLT2is for Chronic Kidney Disease Management

Sept. 9: SGLT2i/GLP1-RA for Cardiovascular Protection

Sept. 23: Diabetic Neuropathy

Please register at www.vcuhealth.org/echodmhtn

Thank you for coming!

Text **19175-18817** to **804-625-4041** for CE credit

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