Diabetes and Hypertension Project ECHO* Clinic

*ECHO: Extension of Community Healthcare Outcomes

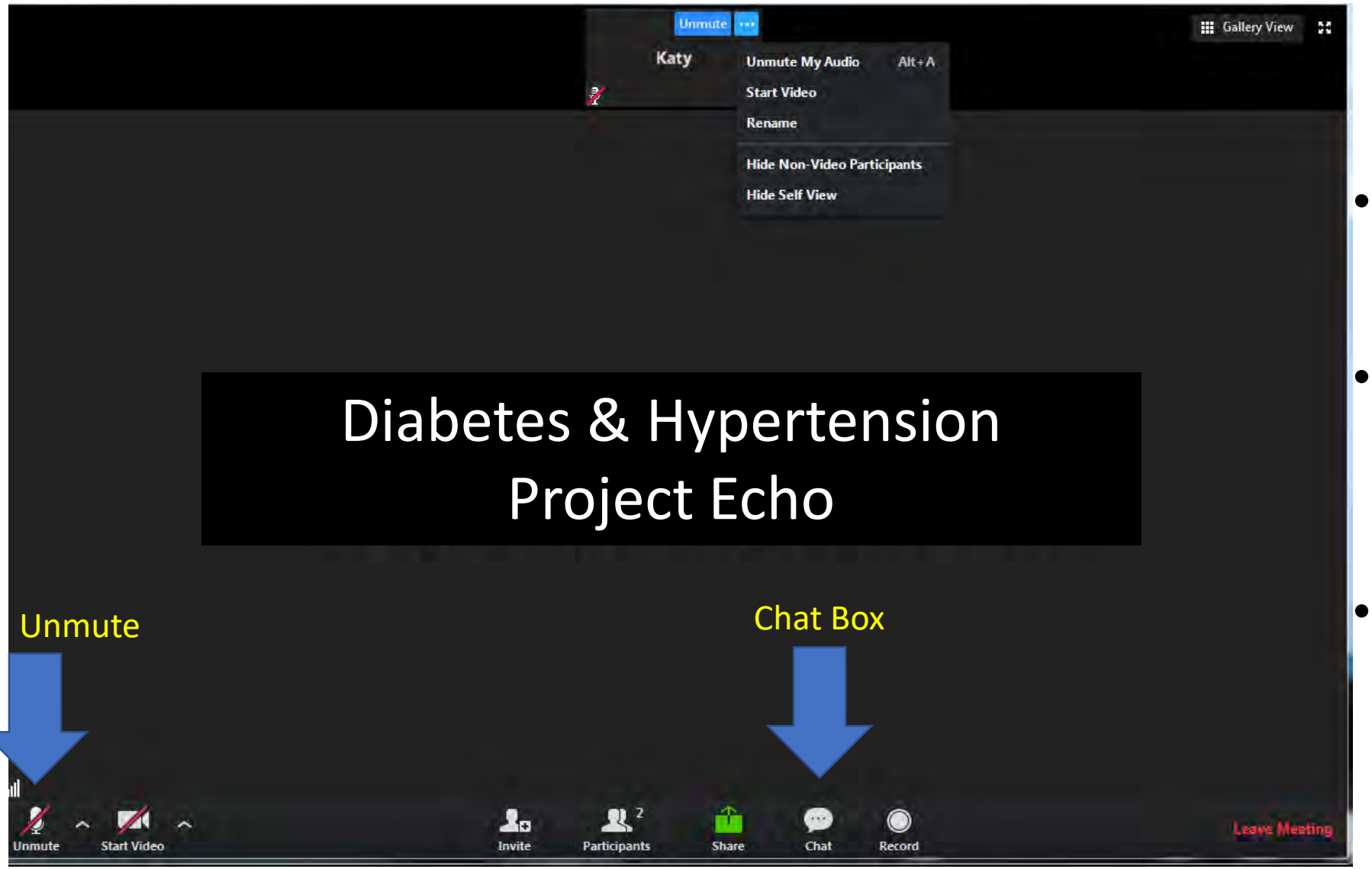
November 10, 2022

Before we begin:

- Rename your Zoom screen with your name and organization
- Claim CE: text 25400-25389 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
Clinical Experts	Niraj Kothari, MD Trang Le, MD
Program Coordinator	Sydney Weber

- One-hour ECHO clinics on 2nd 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 25400 - 25389 to **804-625-4041**

Disclosures

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

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

Diabetes Management in CKD: Updated Guidelines

Learning objectives

- List components of a comprehensive approach to management of T1DM and T2DM with CKD
- Describe preferred agents for glycemic management in diabetes and CKD
- Review safety and monitoring recommendations for preferred medications DM and CKD

Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO)

https://doi.org/10.2337/dci22-0027

Ian H. de Boer,[1] Kamlesh Khunti,[2] Tami Sadusky,[3] Katherine R. Tuttle,[4] Joshua J. Neumiller,[5] Connie M. Rhee,[6] Sylvia E. Rosas,[7] Peter Rossing,[8,9] and George Bakris[10]

[1]Kidney Research Institute, University of Washington, Seattle, WA
[2]Diabetes Research Centre, University of Leicester, Leicester, U.K.
[3]University of Washington, Seattle, WA

Scope of the problem

In the US:

- 1 of every 5 adults with diabetes is not aware of their diagnosis
- 9 of 10 individuals unaware of having underlying CKD
- 2 of 5 individual are unaware of having severe CKD
- In typical practice in the U.S., *less than half of patients* with T2D are screened for albuminuria in a given year
- Diabetes accounts for half of all new cases of kidney failure

Who and when to screen?

T1D Yearly starting 5 years after diagnosis

T2D Yearly starting at diagnosis

How to screen?

Spot urine ACR

and

eGFR

What to do with a positive result?

Repeat and confirm:

- Evaluate possible temporary or spurious causes
- Consider using cystatin C and creatinine to more precisely estimate GFR
- Only persistent abnormalities define CKD

Initiate evidence-based treatments

What defines CKD diagnosis?

Persistent urine ACR ≥30 mg/g

and/or

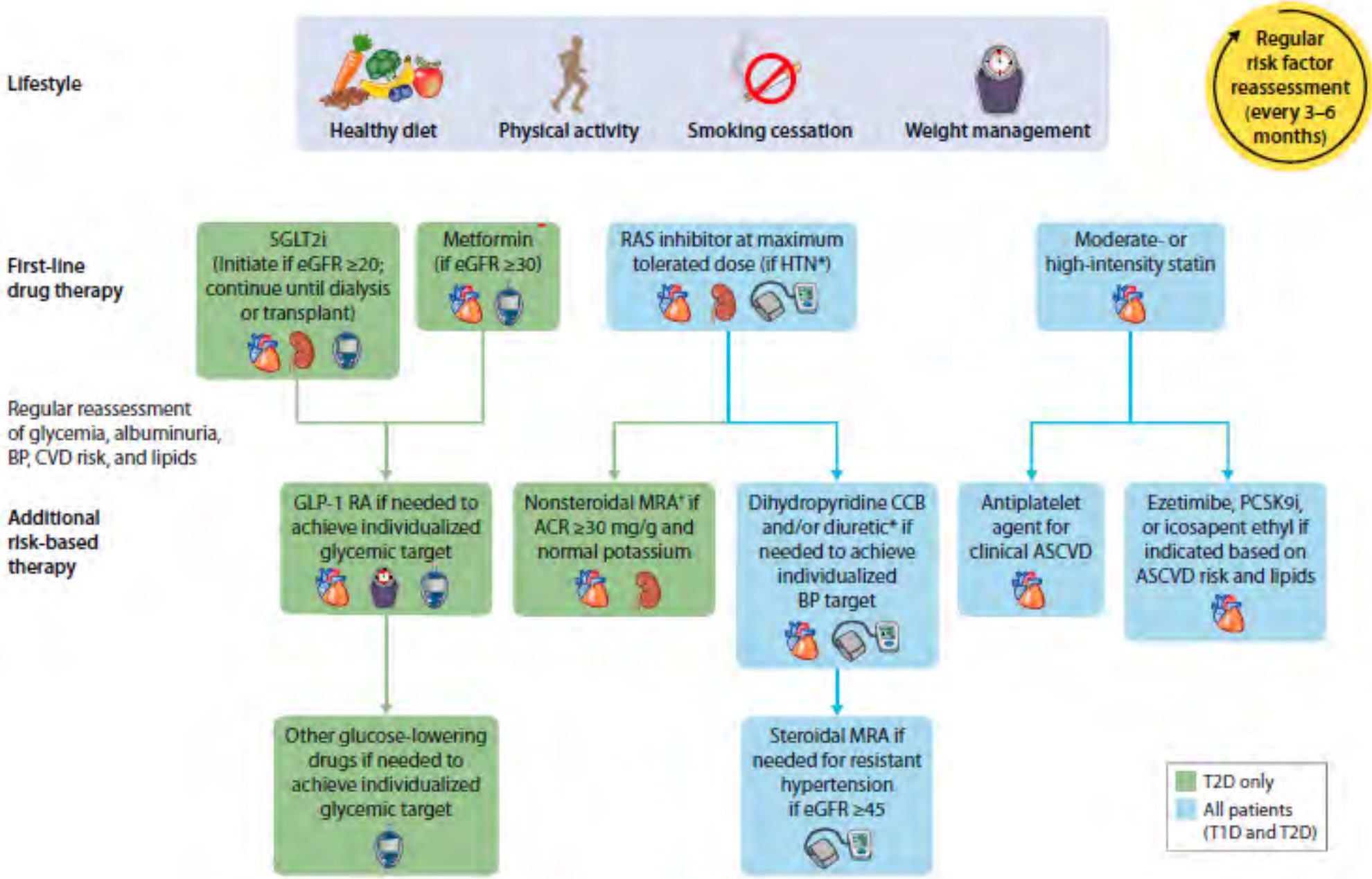
Persistent eGFR <60 mL/min/1.73 m^2

and/or

Other evidence of kidney damage

Emphasis on team-based approach:

- diabetes care and education specialists,
- physicians,
- nurse practitioners,
- physician assistants,
- nurses,
- dietitians,
- exercise specialists,
- pharmacists,
- dentists,
- podiatrists,
- mental health professionals


Lifestyle
Healthy diet
Physical activity
Smoking cessation
Weight management
Regular risk factor reassessment (every 3–6 months)
First-line drug therapy
SGLT2i (Initiate if eGFR ≥20; continue until dialysis or transplant)
Metformin (if eGFR ≥30)
RAS inhibitor at maximum tolerated dose (if HTN*)
Moderate- or high-intensity statin
Regular reassessment of glycemia, albuminuria, BP, CVD risk, and lipids
Additional risk-based therapy
GLP-1 RA if needed to achieve individualized glycemic target
Nonsteroidal MRA† if ACR ≥30 mg/g and normal potassium
Dihydropyridine CCB and/or diuretic* if needed to achieve individualized BP target
Antiplatelet agent for clinical ASCVD
Ezetimibe, PCSK9i, or icosapent ethyl if indicated based on ASCVD risk and lipids
Other glucose-lowering drugs if needed to achieve individualized glycemic target
Steroidal MRA if needed for resistant hypertension if eGFR ≥45
T2D only
All patients (T1D and T2D)

Metformin

- recommended for patients with T2D and CKD - eGFR ≥30mL/min/1.73 m^2
- In case of eGFR 30-44mL/min/1.73 m^2 → reduce dose to 1,000 mg daily
- Also consider 1,000 mg daily if eGFR 45–59mL/min/1.73 m^2 who are at high risk of lactic acidosis
- Monitor B12 levels if > 4 years of treatment
  - Deficiency in 6-30% of patients on long term metformin treatment (n=1111) (Medicine (Baltimore). 2019 Nov; 98(46): e17918)

SGLT2-i

- Recommended in most patients with T2D and CKD with eGFR ≥20 mL/min/1.73 m^2 *independent of HbA1c* or the need for additional glucose lowering
- This recommendation is based on strong evidence that SGLT2i reduce CKD progression, HF, and ASCVD risk in patients with T2D and CKD
- These benefits are independent of glycemia, and an SGLT2i should be used for patients with T2D and CKD *even if glycemic targets are already attained*.
- SGLT2i treatment without metformin may be reasonable for
  - patients with eGFR too low for safe prescription of metformin,
  - metformin intolerance,
  - those who not need metformin to achieve glycemic targets.

SGLT2-i

- Lower limit of eGFR for which initiation of SGLT2i is recommended has changed over time as new data have rapidly become available
- The KDIGO 2022 guideline recommended initiation of an SGLT2i for patients with T2D and CKD and eGFR ≥ 20 mL/min/1.73 m^2 (a change from ≥ 30 mL/min/1.73 m^2 in the 2020 guideline),
- ADA has also updated this threshold to eGFR ≥ 20 mL/ min/1.73 m^2 in its living Standards of Care (from ≥ 25 mL/min/1.73 m^2 in the initial issue of the 2022 Standards of Care).

SGLT2-i

- Initiation is associated with a reversible decline in eGFR, but this generally does *not* require drug discontinuation
- In fact, SGLT2i use appears to protect patients from AKI
- Hypovolemia and hypoglycemia may occur with SGLT2i, but absolute risks are low, especially at low eGFR
- Adjustment of background glycemic therapies is generally not required when initiating an SGLT2i
- Some patients may need closer follow-up to reassess volume status and glycemia
- Euglycemic ketoacidosis with minimal to no elevation in blood glucose may occur in patients taking SGLT2i

  →*Patients with T2D requiring insulin are at particular risk.*

SGLT-i + *euglycemic DKA*

- Maintain at least low-dose insulin and consider pausing SGLT2i treatment during periods of acute illness or stressors
- Blood or urine ketone monitoring may be used for ketosis detection
- Patients with signs, symptoms, or biochemical evidence of ketoacidosis should discontinue SGLT2i therapy and seek immediate medical attention.

GLP-1 receptor agonists

- Reduce albuminuria, and slow eGFR decline, based on
  - secondary outcomes assessed in the cardiovascular outcomes trials clinical trial for glycemic efficacy and safety in patients with T2D and eGFR 15–59 mL
- In cardiovascular outcomes trials, GLP-1 receptor agonists reduced risk of major adverse cardiovascular events (MACE) in patients with T2D
- → MACE risk reduction with liraglutide was significantly greater for those with eGFR <60 mL/ min/1.73 m2 vs those with higher eGFR

Glycemic Management in Advanced CKD

(eGFR <30 mL/min/1.73 m2 ± Kidney Replacement Therapy)

- For T1D, insulin remains the only *approved* therapy.
- Doses are titrated to achieve individualized glycemic goals but may need to be decreased in comparison with earlier stages of CKD due to reduced insulin clearance and other changes in metabolism with advanced CKD

Glycemic Management in Advanced CKD

(eGFR <30 mL/min/1.73 m2 ± Kidney Replacement Therapy)

- In T2D, advanced CKD is a risk factor for hypoglycemia
- When possible, choose drugs that control glycemia without increasing risk of hypoglycemia
- Metformin is contraindicated with eGFR<30 mL/min/1.73 m2 and with dialysis treatment
- SGLT2i can be initiated with eGFR 20–29 mL/min/1.73 m2 and continued at lower eGFR if previously initiated and well tolerated
- However, SGLT2i have minimal effects on glycemia in this range of eGFR and are of use mainly for kidney and cardiovascular benefits not mediated through glycemia.
- Contraindicated in dialysis

Glycemic Management in Advanced CKD

(eGFR <30 mL/min/1.73 m2 ± Kidney Replacement Therapy)

- GLP-1 receptor agonists have been studied with eGFR as low as 15 mL/min/1.73 m2 and retain glucose-lowering potency across the range of eGFR and among dialysis patients.
- GLP-1 receptor agonists reduced ASCVD events and albuminuria in large RCTs and, thus, are theoretically appealing for people with T2D and CKD
  - have not been prospectively tested for cardiovascular efficacy or safety in this population.
- In people with T2D and advanced CKD who have obesity exceeding BMI limits required for kidney transplant listing, ***GLP-1 receptor agonists can be used to aid with weight loss that may facilitate qualification for transplant***

Table 2—Considerations for selecting glucose-lowering agents in patients with T2D and CKD (2,17)

	Progression of CKD	ASCVD	Heart failure	Glucose-lowering efficacy	Hypoglycemia risk	Weight effects	Cost
Metformin	Neutral	Potential benefit	Potential benefit	High	Low	Neutral	Low
SGLT2 inhibitors	Benefit[a]	Benefit[c]	Benefit	Intermediate	Low	Loss	High
GLP-1 receptor agonists	Benefit[b]	Benefit[c]	Potential benefit	High	Low	Loss	High
DPP-4 inhibitors	Neutral	Neutral	Potential risk[c] (saxagliptin)	Intermediate	Low	Neutral	High
Insulin	Neutral	Neutral	Neutral	Highest	High	Gain	High (analogs) Low (human)
Sulfonylureas	Neutral	Neutral	Neutral	High	High	Gain	Low
Thiazolidinediones	Neutral	Potential benefit (pioglitazone)	Increased risk	High	Low	Gain	Low
α-Glucosidase inhibitors	Neutral	Neutral	Neutral	Intermediate	Low	Neutral	Low

Neutral

Potential benefit or intermediate glucose-lowering efficacy

Benefit (organ protection, high efficacy, low hypoglycemia risk, weight loss, or low cost)

Potential risk or high cost to patient

Increased risk for adverse effects

Table 4—Dose adjustments for eGFR <45 mL/min/1.73 m^2 (information presented reflects the package inserts rather than guidance from this consensus report)

	Stage 3b (eGFR 30–44 mL/min/1.73 m^2)	Stage 4 (eGFR 15–29 mL/min/1.73 m^2)	Stage 5 (eGFR <15 mL/min/1.73 m^2)
Metformin	Reduce dose to 1000 mg/day	Contraindicated	
Insulin	Initiate and titrate conservatively to avoid hypoglycemia		
SGLT2 inhibitors*			
Canagliflozin	Maximum 100 mg daily	Initiation not recommended; may continue 100 mg daily if tolerated for kidney and CV benefit until dialysis	
Dapagliflozin	10 mg daily†	Initiation not recommended with eGFR <25 mL/min/1.73 m^2; may continue if tolerated for kidney and CV benefit until dialysis	
Empagliflozin	10 mg daily‡	Initiation not recommended with eGFR <20 mL/min/1.73 m^2; may continue if tolerated for kidney and CV benefit until dialysis	
Ertugliflozin	Use not recommended with eGFR <45 mL/min/1.73 m^2		
GLP-1 receptor agonists§			
Exenatide	Caution initiating or increasing dose; avoid once-weekly formulation	Use not recommended	
Dulaglutide	No dose adjustment required		
Liraglutide	No dose adjustment required		
Lixisenatide	No dose adjustment required		Use not recommended
Semaglutide	No dose adjustment required		

Table 4—Dose adjustments for eGFR <45 mL/min/1.73 m^2 (information presented reflects the package inserts rather than guidance from this consensus report)

	Stage 3b (eGFR 30–44 mL/min/1.73 m^2)	Stage 4 (eGFR 15–29 mL/min/1.73 m^2)	Stage 5 (eGFR <15 mL/min/1.73 m^2)
DPP-4 inhibitors			
Alogliptin	Maximum 12.5 mg daily	Maximum 6.25 mg daily	
Linagliptin	No dose adjustment required		
Saxagliptin	Maximum 2.5 mg daily		
Sitagliptin	Maximum 50 mg daily	Maximum 25 mg once daily	
Sulfonylureas (2nd generation)			
Glimepiride	Initiate conservatively at 1 mg daily and titrate slowly to avoid hypoglycemia		
Glipizide	Initiate conservatively (e.g., 2.5 mg once daily) and titrate slowly to avoid hypoglycemia		
Glyburide	Use not recommended		
Thiazolidinediones			
Pioglitazone	No dose adjustment required		
α-Glucosidase inhibitors			
Acarbose	No dose adjustment required	Use not recommended	
Miglitol	No dose adjustment required	Use not recommended	

Key monitoring and risk mitigation strategies for preferred glucose-lowering agents

Table 3—Key monitoring and risk mitigation strategies for preferred glucose-lowering agents

Medication	Consideration	Monitoring and/or risk mitigation strategies
Metformin	Metformin-associated lactic acidosis	• Monitor eGFR with increasing frequency as eGFR falls to <60 mL/min/1.73 m^2 • Adjust metformin dose as appropriate per eGFR (see Table 4) • Consider dose reduction in the presence of conditions that predispose patients to hypoperfusion and hypoxemia for eGFR 45–59 mL/min/1.73 m^2 • Discontinue for eGFR <30 mL/min/1.73 m^2 • Institute a sick day protocol
	B_{12} malabsorption	• Monitor patients for vitamin B_{12} deficiency when treated with metformin for >4 years
SGLT2i	Genital mycotic infections	• Counsel on genital hygiene
	Volume depletion	• Monitor for hypovolemia and consider proactive dose reduction of diuretics in patients at high risk • Hold SGLT2i during illness
	Diabetic ketoacidosis	• Educate about signs/symptoms to facilitate early recognition • Monitor blood or urine ketones in the case of very high risk • Institute a sick day protocol • Maintain at least low-dose insulin in insulin-requiring individuals
	Hypoglycemia	• Adjust background glucose-lowering agents (e.g., insulin or sulfonylureas) as appropriate
GLP-1 receptor agonists	Nausea/vomiting/diarrhea	• Educate on tolerability and symptom recognition • Start at lowest recommended dose and titrate slowly
	Hypoglycemia	• Adjust background glucose-lowering agents (e.g., insulin or sulfonylureas) as appropriate

Take Home Points

- SGLT2-I with proven kidney or cardiovascular benefit is recommended for patients with T2D, CKD, and eGFR >or = 20 mL/min/1.73 m2 , independent of need for A1c lowering
- Once initiated, the SGLT2i can be continued at lower levels of eGFR (until dialysis or transplant)
- A GLP-1 receptor agonist with proven cardiovascular benefit is recommended for patients with T2D and CKD who do not meet their individualized glycemic target with metformin and/or an SGLT2i or who are unable to use these drugs.
- Caution when starting multiple recommended meds that may have similar hemodynamic effects; dose adjustments in other medications may need to be made to account for additive diuretic or BP effects.
- Initial start of SGLT2i can be associated with a reversible decline in eGFR; consider monitoring rather than discontinuing SGLT2i.

Case Studies

Case 1: 65yo lady, T2DM dx 2009, hyperlipidemia, hypertension, fibromyalgia, presenting for follow up visit

- A1c 7.2%, improved from 9.7% over last 3 years
- BG checks 3-4x daily, range 90-200s, 30 day average 129
- Complications: no neuropathy or retinopathy
- Pertinent medications:
  - Insulin aspart (Novolog) 5 units with high carb meals only – rarely ever using
  - Metformin XR 2000mg daily
  - Dulaglutide 0.75mg SQ weekly, not able to tolerate higher doses
  - Atorvastatin 10mg daily (LDL 88)
  - Irbesartan 75mg daily
- BMI 23.81, BP 129/58

Component	Latest Ref Rng & Units	3/9/2020	9/10/2020	1/25/2022	2/8/2022	3/24/2022	6/20/2022
Sodium	135 - 145 mmol/L	139	141	142	138	141	138
Potassium	3.6 - 5.1 mmol/L	4.3	3.8	4.6	4.4	4.5	4.5
Potassium Comment	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed
Chloride	100 - 110 mmol/L	103	106	105	102	103	105
CO2	21 - 33 mmol/L	29	32	27	25	28	23
Anion Gap	0 - 12 mmol/L	7	3	10	11	10	10
Glucose	65 - 100 mg/dL	**121 (H)**	**121 (H)**	85	**103 (H)**	**166 (H)**	**276 (H)**
BUN	8 - 23 mg/dL	16	11	**25 (H)**	**26 (H)**	17	**26 (H)**
Creatinine	0.50 - 1.00 mg/dL	0.77	0.88	**1.19 (H)**	**1.06 (H)**	**1.05 (H)**	0.98
GFRcr (Estimated)	>=60 mL/min/1.73m2			**51 (L)**	**59 (L)**	**59 (L)**	64
Calcium	8.9 - 10.7 mg/dL	10.4	9.2	10.2	10.0	9.5	9.6

Component	Latest Ref Rng & Units	10/9/2018	9/24/2019	1/13/2021
CREATININE, URINE IN MG/DL	mg/dL	191.8	33.8	**171.8**
Microalb/Creat Ratio	0 - 30 mg/g Crea	17	22	**17**
MICROALBUMIN (MG/DL) IN URINE	mg/L	33.4	7.4	**29.1**

Component	Latest Ref Rng & Units	1/25/2022
Albumin, Ur	mg/L	**42.0**
Creatinine, Urine	mg/dL	**93.9**
Albumin/Creatinine Ratio, Urine	0 - 30 mg/g Crea	**45 (H)**

Questions / suggestions?

Component	Latest Ref Rng & Units	3/9/2020	9/10/2020	1/25/2022	2/8/2022	3/24/2022	6/20/2022	9/23/2022	10/13/2022
Sodium	135 - 145 mmol/L	139	141	142	138	141	138	140	**139**
Potassium	3.6 - 5.1 mmol/L	4.3	3.8	4.6	4.4	4.5	4.5	4.0	**4.0**
Potassium Comment	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed	Not Hemolyzed	**Not Hemolyzed**
Chloride	100 - 110 mmol/L	103	106	105	102	103	105	102	**103**
CO2	21 - 33 mmol/L	29	32	27	25	28	23	29	**27**
Anion Gap	0 - 12 mmol/L	7	3	10	11	10	10	9	**9**
Glucose	65 - 100 mg/dL	**121 (H)**	**121 (H)**	85	**103 (H)**	**166 (H)**	**276 (H)**	**143 (H)**	**105 (H)**
BUN	8 - 23 mg/dL	16	11	**25 (H)**	**26 (H)**	17	**26 (H)**	**32 (H)**	**19**
Creatinine	0.50 - 1.00 mg/dL	0.77	0.88	**1.19 (H)**	**1.06 (H)**	**1.05 (H)**	0.98	**1.63 (H)**	**0.99**
GFRcr (Estimated)	>=60 mL/min/1.73m2			**51 (L)**	**59 (L)**	**59 (L)**	64	**35 (L)**	**63**
Calcium	8.9 - 10.7 mg/dL	10.4	9.2	10.2	10.0	9.5	9.6	9.6	**9.4**

Started SLGT2i

Stopped SLGT2i

Case 2: 47 yo initial visit for T2DM

Chief complaint: “insulin doesn’t work for me”

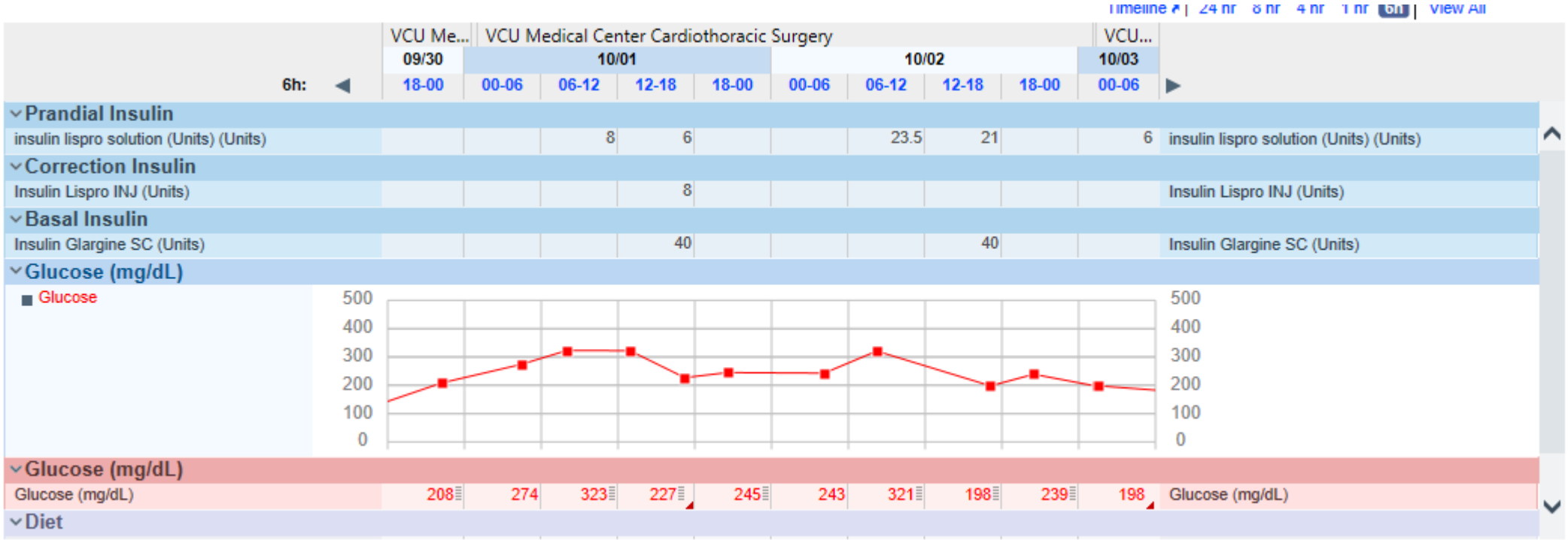
PMHx: sarcoidosis dx 2014, COPD, T2DM, CAD s/p 4v CABG 9/27/2022

DMHx:

- T2DM x 17 years, followed by endocrinology until ~ 2 years ago
- A1c 12.7%, states he was above 14% →7% with glimepiride 4mg BID monotherapy
- Complications: nephropathy, neuropathy, retinopathy
- Reports previous weight was >300 pounds and currently ~200 pounds
- Seen by VCU endocrinology during CABG hospitalization and started on insulin continuous infusion, then transitioned to SQ insulin
- Hospital discharge recs:
  - glargine 40 units daily,
  - lispro 12 units ac meals, 6 units small meals and snacks, and 1:50>150

Insurance: Virginia Premier Medicaid

Inpatient glucose trends



Questions / suggestions?

- "I am going to stop my insulin today. I want to restart glimepiride."

AGP Report

October 25, 2022 - November 7, 2022 (14 Days)

LibreView

GLUCOSE STATISTICS AND TARGETS

October 25, 2022 - November 7, 2022	**14 Days**
% Time CGM is Active	**92%**

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	**151** mg/dL
Glucose Management Indicator (GMI)	**6.9%**
Glucose Variability	**36.2%**

Defined as percent coefficient of variation (%CV)

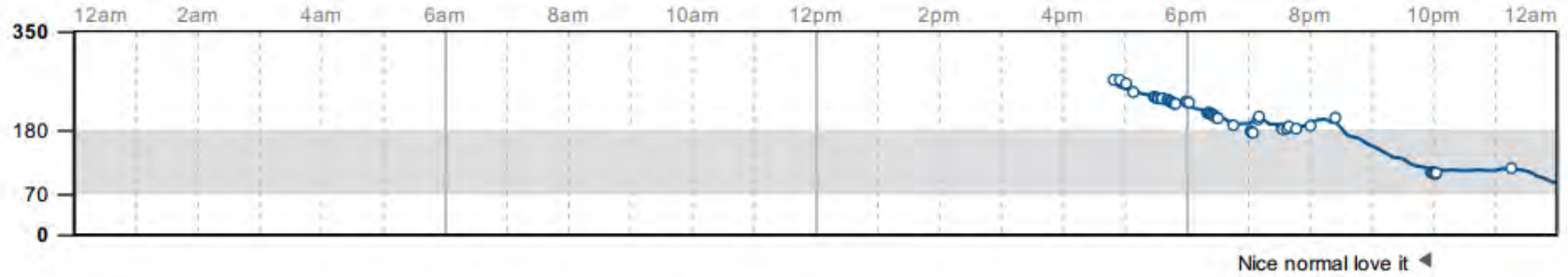
TIME IN RANGES

Very High	>250 mg/dL	**6%**	(1h 26min)
High	181 - 250 mg/dL	**22%**	(5h 17min)
Target Range	70 - 180 mg/dL	**71%**	(17h 3min)
Low	54 - 69 mg/dL	**1%**	(14min)
Very Low	<54 mg/dL	**0%**	(0min)

TUE **Oct 25**

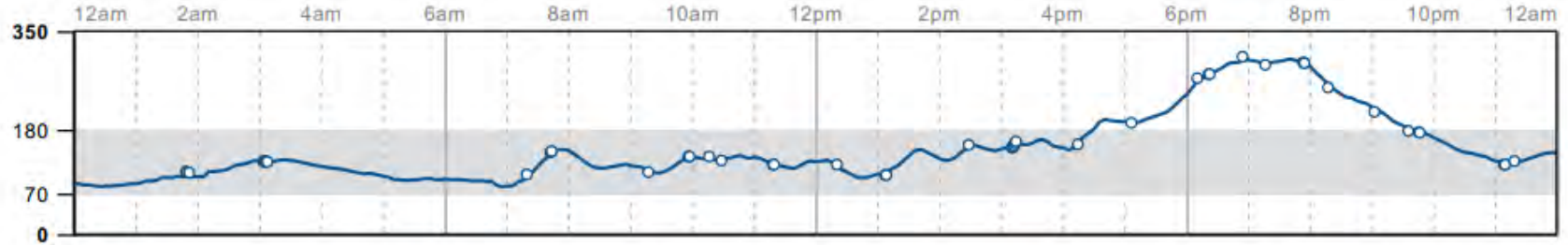
Glucose mg/dL

Notes



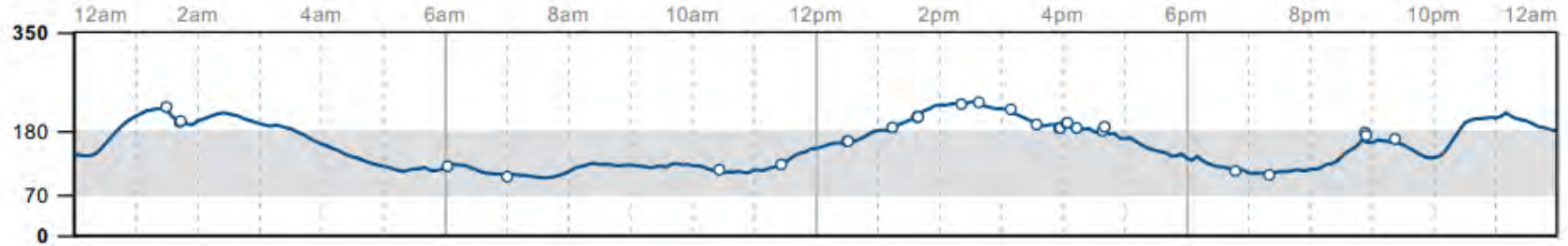
WED **Oct 26**

Glucose mg/dL



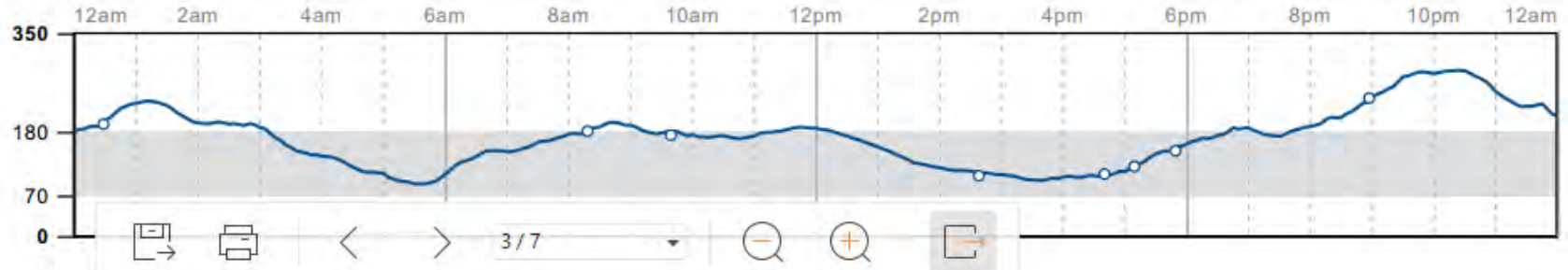
THU **Oct 27**

Glucose mg/dL



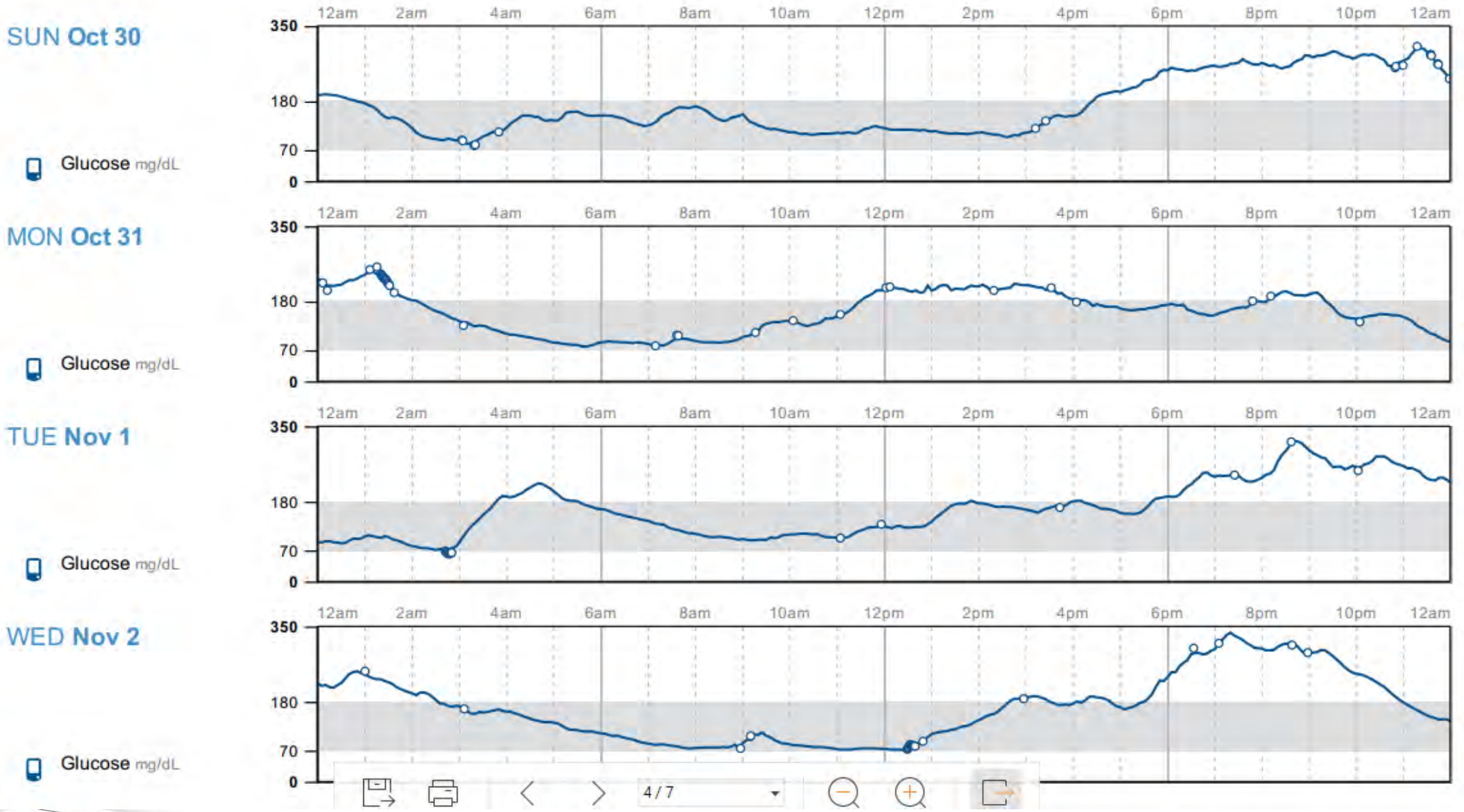
FRI **Oct 28**

Glucose mg/dL



Project ECHO®
Virginia Commonwealth University

VCU


SUN Oct 30
Glucose mg/dL
MON Oct 31
Glucose mg/dL
TUE Nov 1
Glucose mg/dL
WED Nov 2
Glucose mg/dL
12am 2am 4am 6am 8am 10am 12pm 2pm 4pm 6pm 8pm 10pm 12am
350
180
70
0
4 / 7

Questions?

Case Studies

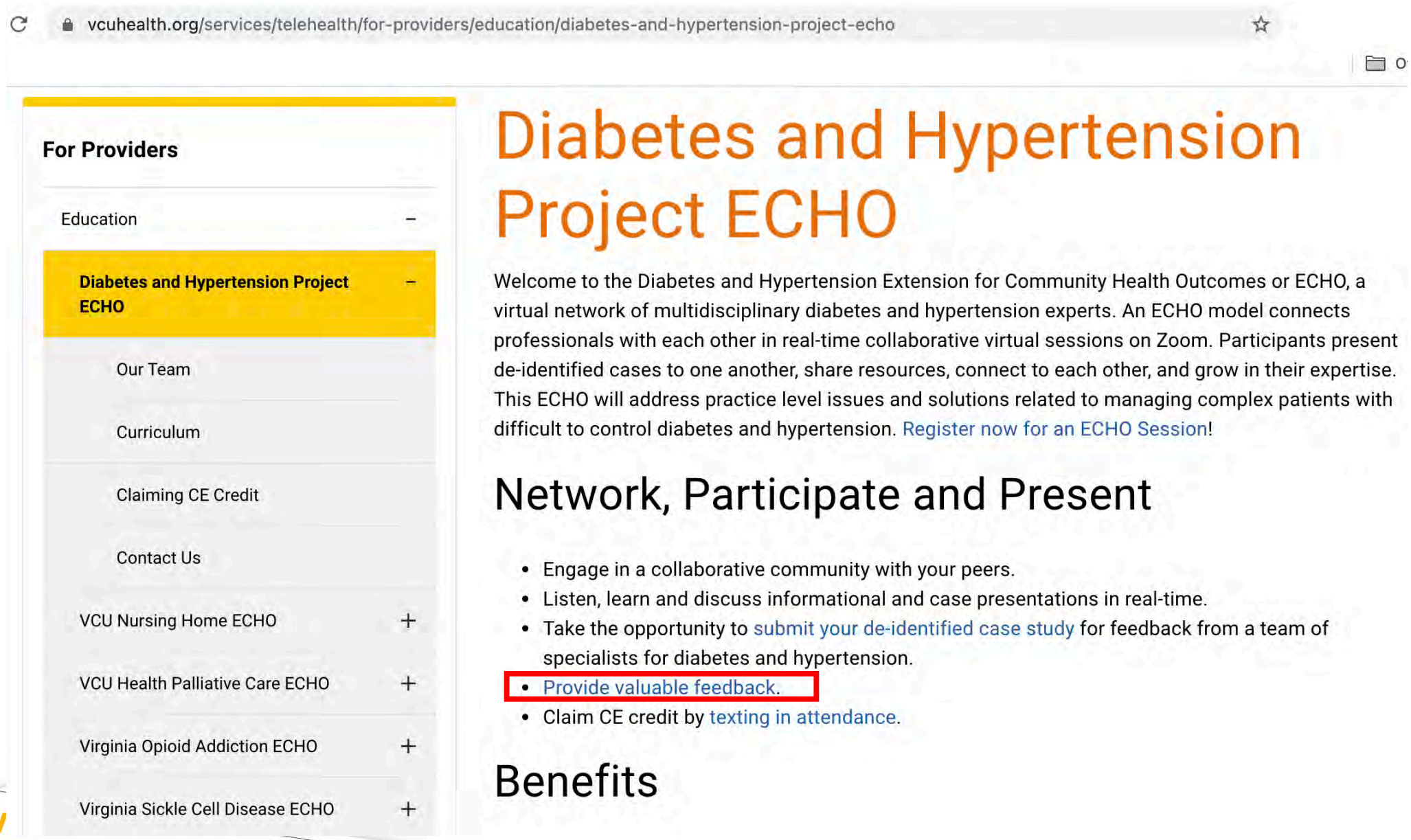
- Anyone can submit cases: www.vcuhealth.org/echodmhtn
- Receive feedback from participants and content experts
- Earn **$150** for submitting and presenting

Provide Feedback

www.vcuhealth.org/echodmhtn

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

Send us your feedback



VCU Diabetes & Hypertension Project ECHO Clinics

2nd Thursdays — 12 p.m. to 1 p.m.

Mark Your Calendars — Upcoming Sessions

December 8, 2022 – TBD

January 12, 2023 – Prediabetes and CKD

February 9, 2023 – Understanding COVID-19's Impact on CKD

Please register at www.vcuhealth.org/echodmhtn

Project ECHO
Virginia Commonwealth University

Thank you for coming!

Text **25400-25389** to **804-625-4041** for CE credit

https://VCU.cloud-cme.com/WebService/SelfAttendScan.aspx?EventID=25400

Reminder: Mute and Unmute to talk
Press *6 for phone audio
Use chat function for questions

VCU