Diabetes and Hypertension Project ECHO* Clinic

*ECHO: Extension of Community Healthcare Outcomes

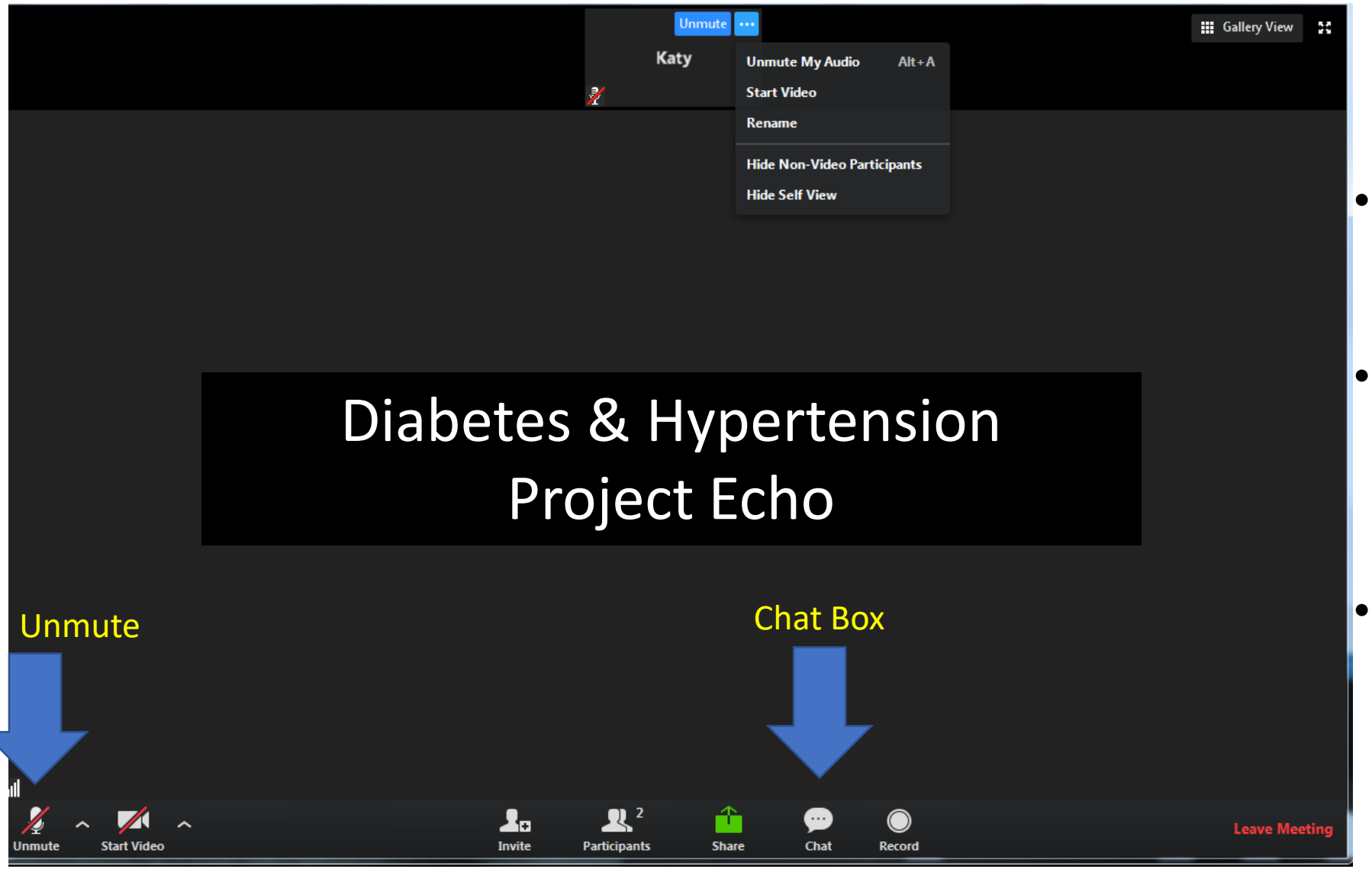
January 12, 2023

Before we begin:

- Rename your Zoom screen with your name and organization
- Claim CE:
- Go to **vcuhealth.org/echodmhtn** for instructions on creatin 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 :

Disclosures

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

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

Prediabetes and Chronic Kidney Disease

Learning objectives

- Describe the epidemiology of renal dysfunction in prediabetes
- Review available data on dysglycemia patterns in prediabetes and correlation with measure of renal function and disease
- Be able to counsel patients appropriately on steps to take in case of prediabetes diagnosis and renal disease

Question

Diabetes dramatically increases the risk of CKD. However,

prediabetes

a. Also dramatically increases the risk of ESRD, just over a longer time frame
b. May result in increased proteinuria before detectable declines in eGFR
c. Has no impact at all on renal disease – it's too early.

If a patient has been diagnosed with prediabetes, the National Kidney Foundation recommends:

a. BMP and eGFR
b. Urine testing for protein
c. Blood pressure monitoring and treatment as indicated
d. All of the above

Analyses of large scale trials have demonstrated:

a. Prediabetes clearly places patients on a spectrum of inexorable progression towards CKD, as compared with normoglycemia

b. The relationship between prediabetes and cardiovascular risk is stronger than the relationship between prediabetes and CKD

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

Scope of the Problem

- Prediabetes is a highly prevalent condition, affecting about one-third of adults in the United States
- Patients with prediabetes have an increased risk for diabetes, with 2% to 10% progressing to diabetes each year
- Although prediabetes is frequently considered an intermediary stage in the progression between normoglycemia and diabetes, many individuals may have prediabetes for several years, while some may never progress.

Scope of the Problem

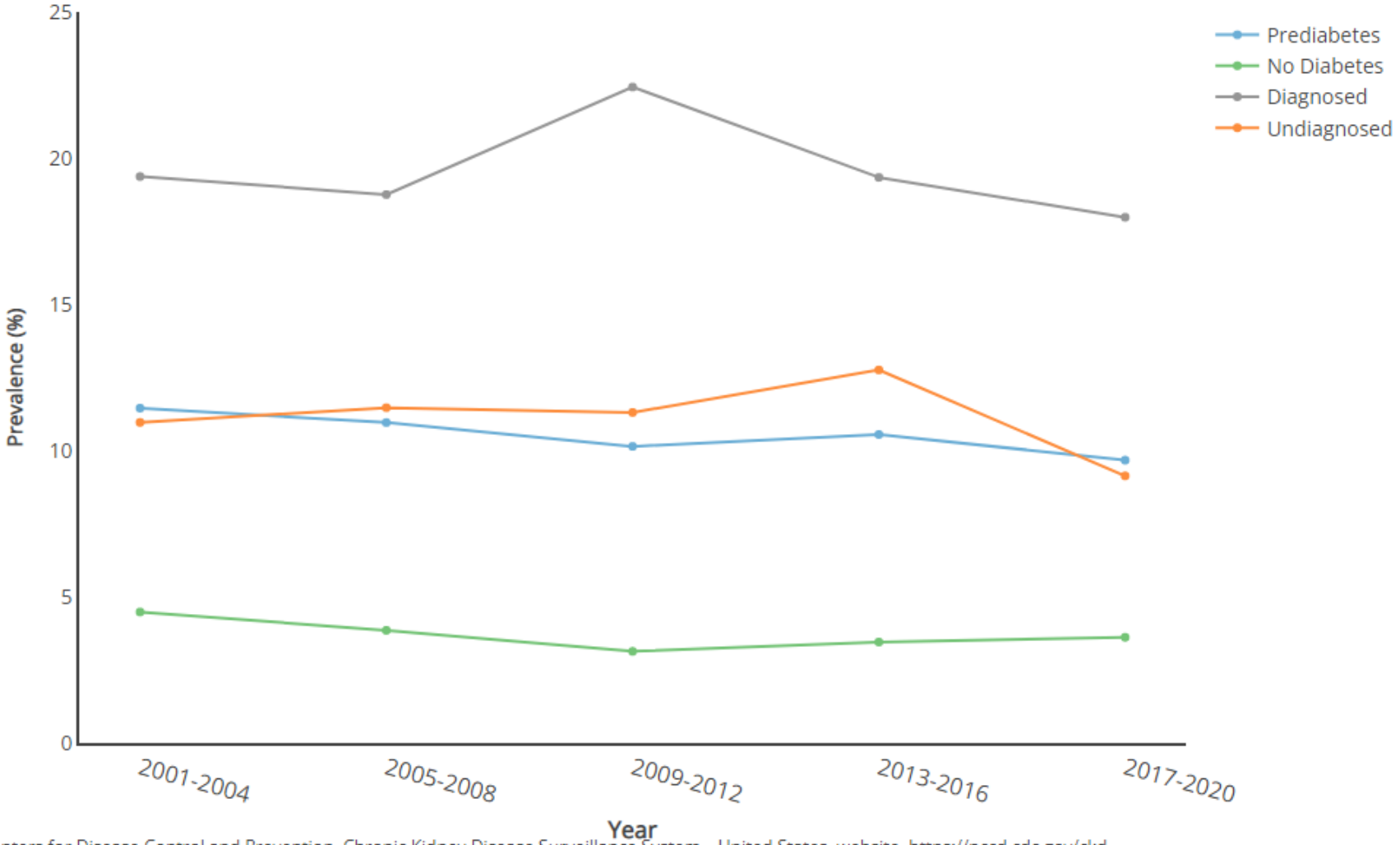
The Cardio-Renal Burdens of Prediabetes in the US:

Data from Serial Cross-sectional Surveys over 1988–2014

- In 2011–2014, adults with prediabetes:
  - >36% were hypertensive;
  - >50% had dyslipidemia;
  - >24% smoked
  - >11% had albuminuria or reduced eGFR;

Lancet Diabetes Endocrinol. 2018 May ; 6(5): 392–403. doi:10.1016/S2213-8587(18)30027-5.

CKD prevalence (Stage 3-4) and Diabetes Status, US NHANES Data



Centers for Disease Control and Prevention. Chronic Kidney Disease Surveillance System—United States. website. https://nccd.cdc.gov/ckd

Scope of the Problem

- Diabetes is an established risk factor for CKD
- What is the prognostic significance of prediabetes in CKD?

Chronic Renal Insufficiency Cohort (CRIC) Study

- Ethnically and racially diverse group of subjects with prevalent CKD across 7 US clinical centers, 2003 to 2008.
- CRIC was designed to elucidate risk factors for progression of CKD, development of ESRD, and development of CV disease among patients with varying stages of CKD,

  →half of whom had diabetes
- Entry criteria included estimated glomerular filtration rate (eGFR) from 20 to 70 mL/min/1.73 m2 and age of 21 to 74 years.

J Clin Endocrinol Metab, Volume 105, Issue 4, April 2020, Pages e1772–e1780, https://doi.org/10.1210/clinem/dgaa017

Secondary analysis of patients with prediabetes at baseline:

- either HbA1c of 5.7% - 6.4% or
- fasting plasma glucose of 100 to 125 mg/dL
- no treatment with antidiabetic drugs
- Diabetes was defined as one of the following: HbA1c ≥ 6.5%, fasting plasma glucose ≥ 126 mg/dL, or treatment with antidiabetic drugs at baseline
- N= 3701 individuals, median follow up: 7.5 years
- At baseline, 23% had prediabetes, 52% had diabetes, 26% had normoglycemia

J Clin Endocrinol Metab, Volume 105, Issue 4, April 2020, Pages e1772–e1780, https://doi.org/10.1210/clinem/dgaa017

Table 2. Association of Prediabetes and Diabetes With Outcomes (HR [95% CI])

	Normoglycemia (n = 945)	Prediabetes (n = 847)	Diabetes (n = 1909)
Composite renal outcome			
No. Events/No. Pts	351/896 (39.2%)	340/800 (42.5%)	1094/1781 (61.4%)
Unadjusted HR	(reference)	1.12 (0.96–1.30)	1.88 (1.66–2.12)
		$P = 0.15$	$P < 0.001$
Model 1 HR	(reference)	1.12 (0.96–1.31)	1.86 (1.64–2.11)
		$P = 0.13$	$P < 0.001$
Model 2 HR	(reference)	1.13 (0.96–1.32)	1.47 (1.27–1.70)
		$P = 0.14$	$P < 0.001$
Composite cardiovascular outcome			
No. Events/No. Pts	93/943 (9.9%)	151/844 (17.9%)	579/1901 (30.5%)
Unadjusted HR	(reference)	1.85 (1.43–2.40)	3.60 (2.89–4.49)
		$P < 0.001$	$P < 0.001$
Model 1 HR	(reference)	1.59 (1.23–2.07)	2.97 (2.37–3.71)
		$P < 0.001$	$P < 0.001$
Model 2 HR	(reference)	1.38 (1.05–1.82)	1.63 (1.27–2.11)
		$P = 0.021$	$P < 0.001$
All-cause mortality			
No. Events/No. Pts	104/945 (11.0%)	151/847 (17.8%)	520/1909 (27.2%)
Unadjusted HR	(reference)	1.63 (1.27–2.09)	2.56 (2.07–3.17)
		$P < 0.001$	$P < 0.001$
Model 1 HR	(reference)	1.36 (1.06–1.76)	2.07 (1.67–2.57)
		$P = 0.016$	$P < 0.001$
Model 2 HR	(reference)	1.28 (0.98–1.66)	1.53 (1.20–1.95)
		$P = 0.071$	$P = 0.001$

Composite renal outcome: Development of ESRD (renal transplantation or dialysis initiation), 50% decline in baseline eGFR (CKD-EPI equation) and eGFR ≤ 15 mL/min/1.73 m^2, or doubling of urine protein to creatinine ratio to ≥ 0.22 g/g creatinine.

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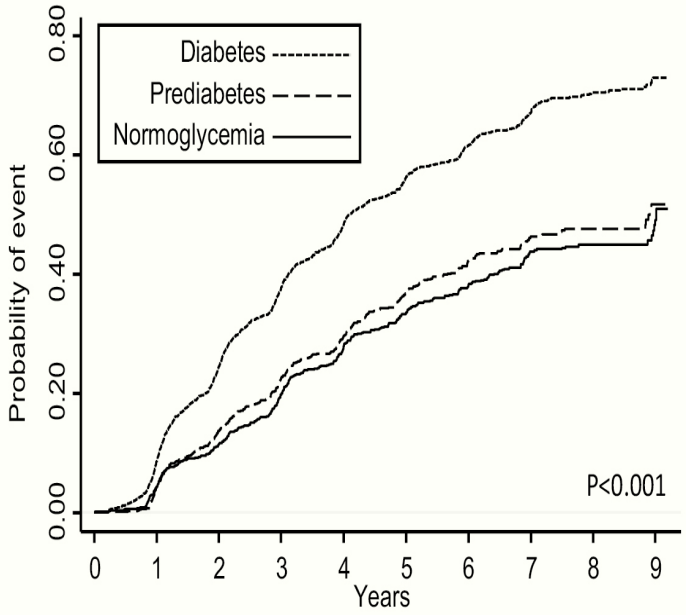
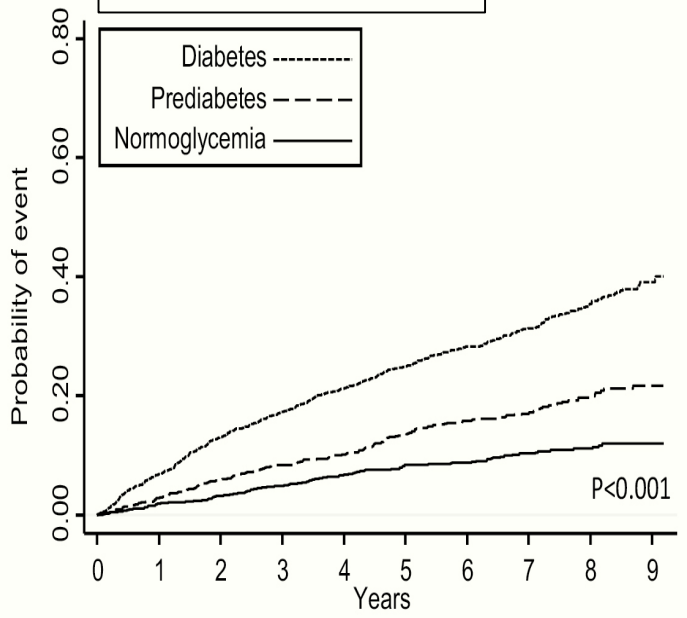
A. Composite renal outcome



Number at risk										
Normoglycemia	896	841	743	646	558	468	416	275	187	57
Prediabetes	800	757	660	570	483	412	354	271	158	48
Diabetes	1781	1605	1262	991	785	619	502	322	175	61

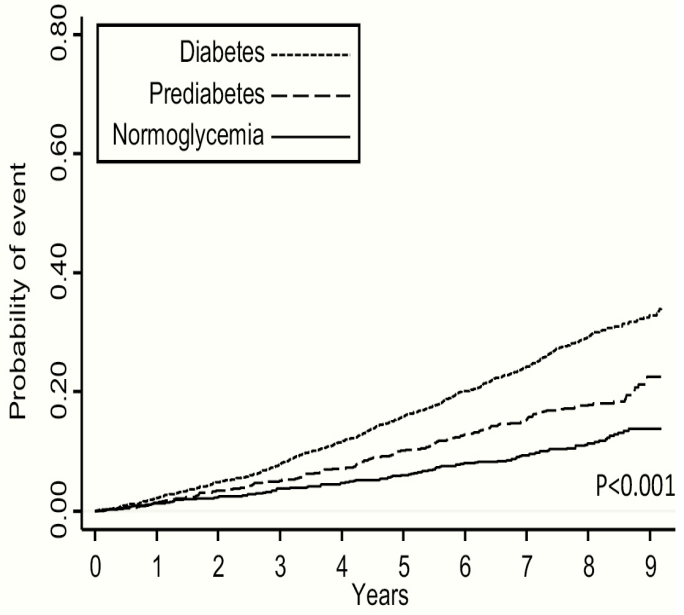
B. Composite cardiovascular outcome

CHF, MI, or stroke



Number at risk										
Normoglycemia	943	903	869	822	781	717	674	484	338	118
Prediabetes	844	803	760	716	680	629	575	469	282	92
Diabetes	1901	1726	1537	1400	1267	1125	987	721	416	148

C. All-cause mortality



Number at risk										
Normoglycemia	945	929	913	890	877	836	787	583	415	145
Prediabetes	847	832	807	787	766	735	693	577	364	119
Diabetes	1909	1858	1780	1705	1624	1509	1366	1040	627	233

Development of ESRD, 50% decline in baseline eGFR, eGFR ≤ 15 mL/min/1.73 m2, or doubling of urine protein to creatinine ratio to ≥ 0.22 g/g creatinine.

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Findings

- prediabetes (versus normoglycemia) was NOT associated with composite renal outcome,
- diabetes WAS associated with an increase of the composite renal outcome (hazard ratio [HR] 1.88; 95% CI (1.66–2.12); $P < 0.001$)
- The pattern of association was similar in adjusted models

J Clin Endocrinol Metab, Volume 105, Issue 4, April 2020, Pages e1772–e1780, https://doi.org/10.1210/clinem/dgaa017

Findings – components of composite renal outcome

- Prediabetes:
  - NOT associated with an increased risk of eGFR decrease or ESRD development,
  - IS associated with proteinuria progression, and an increased risk of adverse CV outcomes.

J Clin Endocrinol Metab, Volume 104, Issue 9, September 2019, Pages 4024–4032, https://doi.org/10.1210/jc.2019-00073

Systolic Blood Pressure Intervention (SPRINT) trial

- multicenter, randomized, controlled trial n= 9361 patients aged ≥ 50 years with hypertension and an increased risk of CV events
- Increased CV risk = at least one of the following:
  - clinical or subclinical CV disease;
  - CKD - eGFR of 20 to 59 mL/min/1.73 m2;
  - a 10-year risk of CV disease of 15% or greateron the basis of the Framingham risk score; or age ≥ 75
- Eligible participants were randomly assigned to SBP target of <140 mm Hg (standard treatment) or <120 mm Hg (intensive treatment)
- Intervention was stopped early after a median follow-up of 3.26 years owing to a significantly lower rate of the primary composite outcome in the intensive-treatment group

J Clin Endocrinol Metab, Volume 104, Issue 9, September 2019, Pages 4024–4032, https://doi.org/10.1210/jc.2019-00073

SPRINT Trial, secondary analysis

- Participants were categorized into two groups according to fasting plasma glucose level at randomization
- ≥100 mg/dL = impaired fasting glucose
- fasting plasma glucose level = normoglycemic

J Clin Endocrinol Metab, Volume 104, Issue 9, September 2019, Pages 4024–4032, https://doi.org/10.1210/jc.2019-00073

SPRINT Trial, secondary analysis

- Composite renal outcome was defined by worsening kidney function or incident albuminuria
- In participants without CKD at baseline, worsening kidney function was defined by a decrease in the eGFR of ≥ 30% to a value of <60 on two consecutive laboratory determinations collected at 3-month intervals.
- In participants with CKD at baseline, worsening kidney function was defined by a decrease in the eGFR of ≥ 50% or the development of ESRD requiring long-term dialysis or kidney transplantation.
- Incident albuminuria was defined for all study participants by a doubling of the urinary albumin/creatinine ratio from <10 mg/g at baseline to >10 mg/g during follow-up.

J Clin Endocrinol Metab, Volume 104, Issue 9, September 2019, Pages 4024–4032, https://doi.org/10.1210/jc.2019-00073

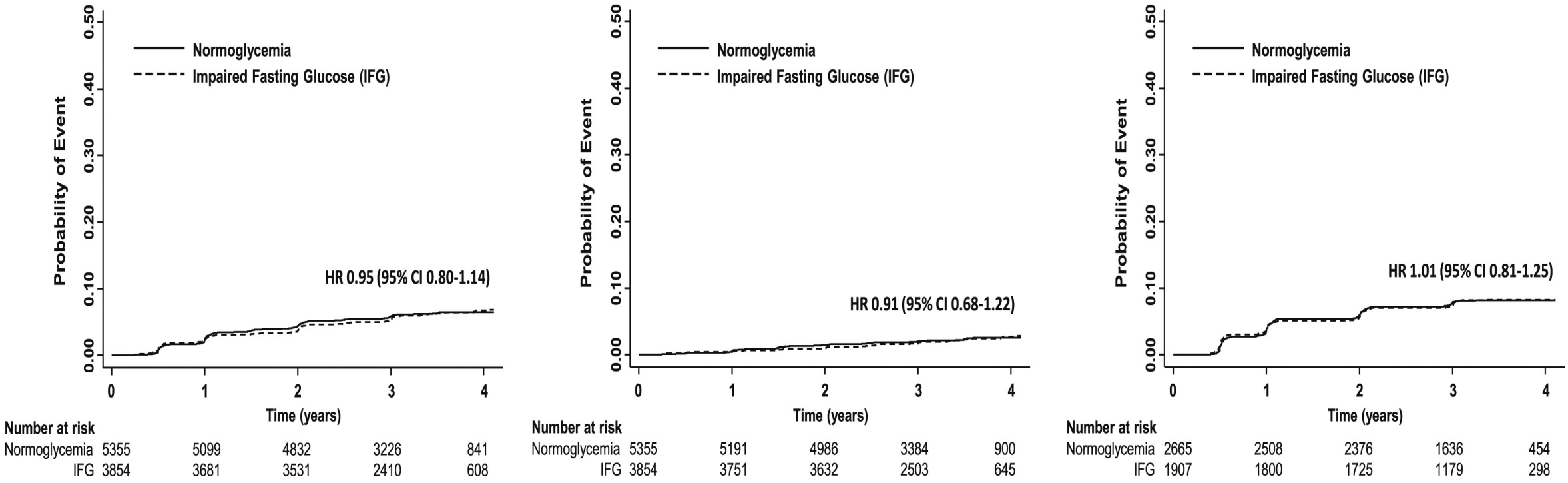
SPRINT Trial, secondary analysis

Table 2. Association of Impaired Fasting Glucose vs Normoglycemia With Outcomes

Outcome	Normoglycemia	Impaired Fasting Glucose	Hazard Ratio (95% CI)
	No. of Events/No. at Risk (%)		
Composite adverse renal outcome[a]	314/5424 (5.8)	221/3897 (5.7)	
Unadjusted model			0.95 (0.80–1.14)
Adjusted model			0.97 (0.81–1.16)
Worsening kidney function[b]	114/5424 (2.1)	79/3897 (2.0)	
Unadjusted model			0.91 (0.68–1.22)
Adjusted model			1.02 (0.75–1.37)
Incident albuminuria[c]	203/2691 (7.5)	147/1928 (7.6)	
Unadjusted model			1.01 (0.81–1.25)
Adjusted model			0.98 (0.78–1.23)

Adjusted model: age, sex, race, smoking status, systolic blood pressure, prior cardiovascular disease, body mass index, statin use, aspirin use, and trial treatment arm.

J Clin Endocrinol Metab, Volume 104, Issue 9, September 2019, Pages 4024–4032, https://doi.org/10.1210/jc.2019-00073



J Clin Endocrinol Metab, Volume 104, Issue 9, September 2019, Pages 4024–4032, https://doi.org/10.1210/jc.2019-00073

Findings:

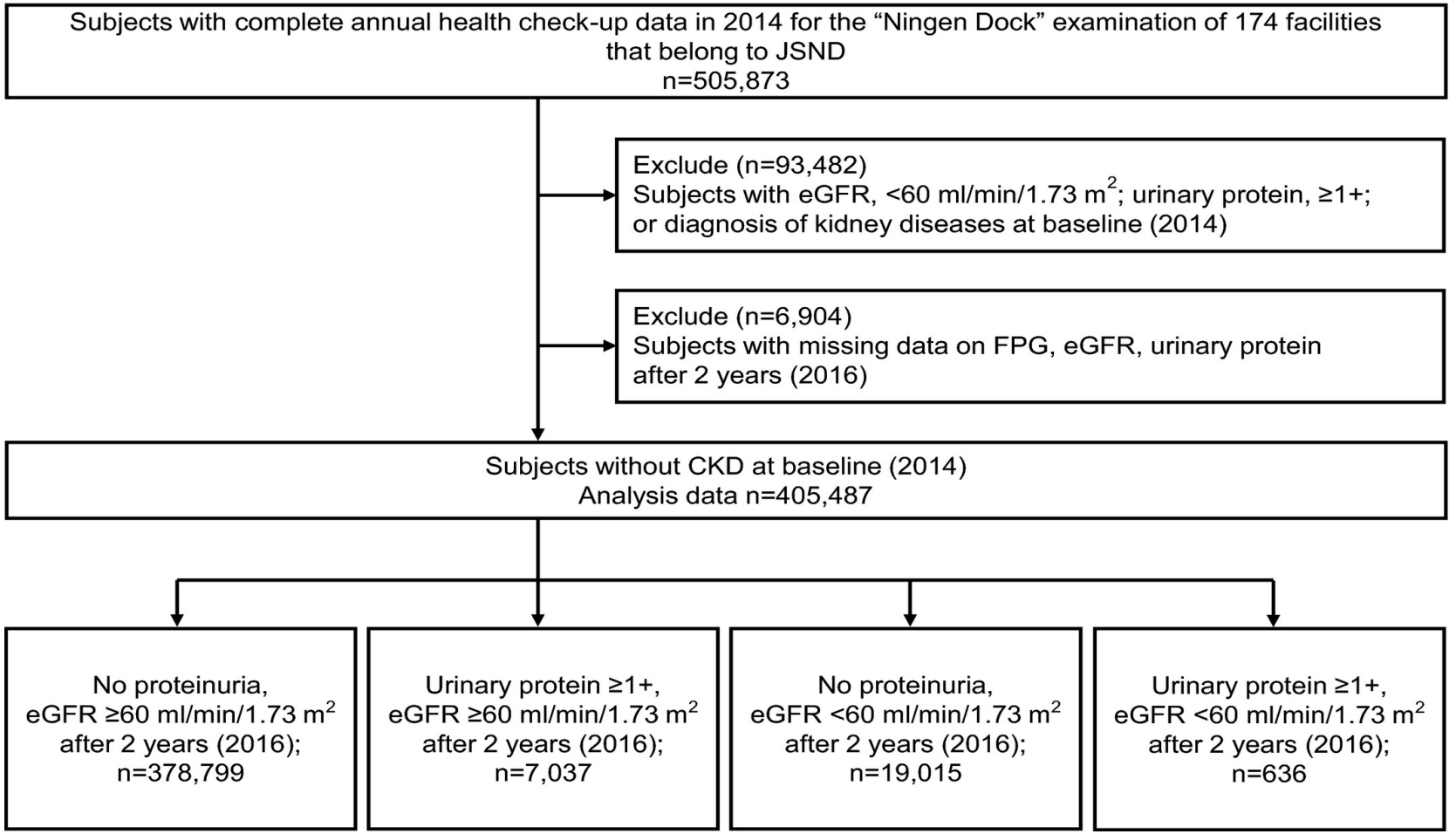
- impaired fasting glucose at baseline was NOT associated with a higher incidence of CKD, worsening kidney function, or incident albuminuria in comparison with normoglycemia.

How might prediabetes affect renal function?

- N= 405,487 participants without CKD (eGFR, ≥60, with negative or trace urinary protein) at baseline were categorized according to fasting plasma glucose as having diabetes (≥126 mg/dl), prediabetes (100–125 mg/dl) or normal glucose level (<100 mg/dl)
- Logistic regression analysis was used to analyze the effects of prediabetes (vs. normal glucose level) on the proteinuria development (urinary protein of ≥1+) and eGFR decline (<60 ml min−1 1.73 m−2) after 2 years.

VCU Diabetic Medicine, Volume: 38, Issue: 8, First published: 25 May 2021, DOI: (10.1111/dme.14607)

Prediabetes is associated with proteinuria development but not with glomerular filtration rate decline: A longitudinal observational study



Diabetic Medicine, Volume: 38, Issue: 8, First published: 25 May 2021, DOI: (10.1111/dme.14607)

Prevalence of Proteinuria after 2 years

	Total	NGL	Prediabetes	Diabetes
	N = 405,487	*N* = 265,708	*N* = 116,951	*N* = 22,828
Proteinuria ≥1+ after 2 years	7037 (1.7%)	3914 (1.5%)	2266 (1.9%)	857 (3.8%)
eGFR <60 ml min^{-1} 1.73 m^{-2} after 2 years	19,015 (4.7%)	11,225 (4.2%)	6492 (5.6%)	1298 (5.7%)
Proteinuria ≥1+ and eGFR <60 ml min^{-1} 1.73 m^{-2} after 2 years	636 (0.2%)	287 (0.1%)	250 (0.2%)	99 (0.4%)

Abbreviations: eGFR, estimated glomerular filtration rate; NGL, normal glucose level.

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Prediabetes and Proteinuria Development

	Unadjusted model		Adjusted model[a]	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Diabetic status (at baseline)				
NGL	Reference		Reference	
Prediabetes	1.369 (1.302–1.439)	<0.001	1.233 (1.170–1.301)	<0.001
Diabetes	2.721 (2.533–2.923)	<0.001	2.241 (2.069–2.428)	<0.001

Abbreviations: CI, confidence intervals; NGL, normal glucose level; OR, odds ratio.

[a]Adjusted for sex, age, BMI, eGFR, hypertension, dyslipidaemia, smoking, past history of cardiac disease and stroke at baseline.

Diabetic Medicine, Volume: 38, Issue: 8, First published: 25 May 2021, DOI: (10.1111/dme.14607)

Prediabetes and eGFR decline

	Unadjusted model		Adjusted model[a]	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Diabetic status (at baseline)				
NGL	Reference		Reference	
Prediabetes	1.351 (1.310–1.393)	<0.001	0.981 (0.947–1.017)	0.294
Diabetes	1.439 (1.359–1.524)	<0.001	1.050 (0.982–1.123)	1.050

Abbreviations: eGFR, estimated glomerular filtration rate; NGL, normal glucose level; OR, odds ratio; CI, confidence intervals.

[a]Adjusted for sex, age, BMI, eGFR, hypertension, dyslipidaemia, smoking, past history of cardiac disease and stroke at baseline.

Diabetic Medicine, Volume: 38, Issue: 8, First published: 25 May 2021, DOI: (10.1111/dme.14607)

Findings

- prediabetes was found to be associated with the proteinuria development but not with eGFR decline in the general population without CKD after 2 years
- Proteinuria in prediabetes might be an earlier detectable renal change, and the screening for prediabetes and evaluation of proteinuria are important for the prevention of CKD.

VCU Diabetic Medicine, Volume: 38, Issue: 8, First published: 25 May 2021, DOI: (10.1111/dme.14607)

Question

Diabetes dramatically increases the risk of CKD. However,

prediabetes

a. Also dramatically increases the risk of ESRD, just over a longer time frame
b. May result in increased proteinuria before detectable declines in eGFR
c. Has no impact at all on renal disease – it's too early.

If a patient has been diagnosed with prediabetes, the National Kidney Foundation recommends:

a. BMP and eGFR
b. Urine testing for protein
c. Blood pressure monitoring and treatment as indicated
d. All of the above

https://www.kidney.org/news/kidneyCare/Summer10/PreDiabetes

Analyses of large scale trials have demonstrated:

a. Prediabetes clearly places patients on a spectrum of progression towards CKD, as compared with normoglycemia

b. The relationship between prediabetes and cardiovascular risk is stronger than the relationship between prediabetes and CKD

Case Studies

Case 1: 62 year old male with emphysema, type 1 diabetes X 40 years complicated by retinopathy, legally blind, gastroparesis, autonomic dysfunction with orthostatic hypotension, microalbuminuria, peripheral vascular disease s/p stent, long-standing tobacco use

- Tresiba (degludec) 9 units daily
- Novolog (aspart), injected 2 hours after eating, 3 units for 150-250, 4 units 251-350, max 7 units
- A1c today 7.3%, Cr 0.86, eGFR 98

30 days | Tue Dec 13, 2022 - Wed Jan 11, 2023

Glucose

Average Glucose

229 mg/dL

Standard Deviation

76 mg/dL

GMI

8.8%

Time in Range

40% Very High

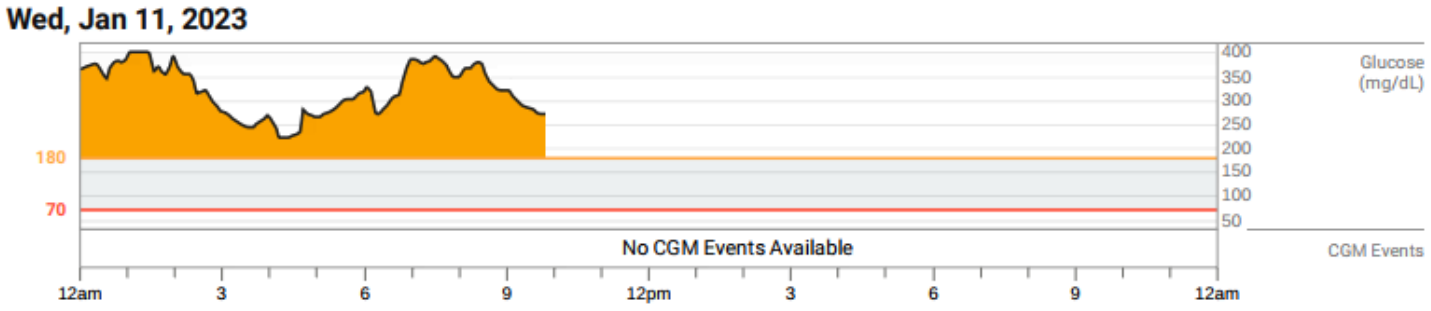
30% High

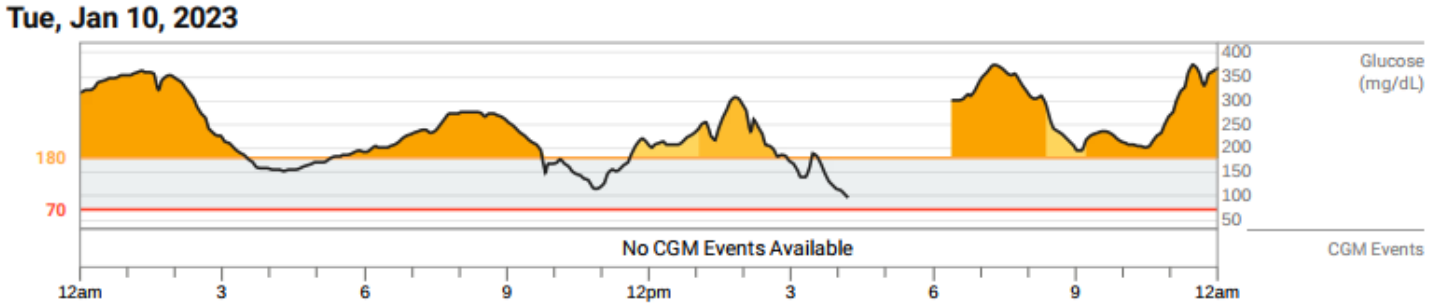
29% In Range

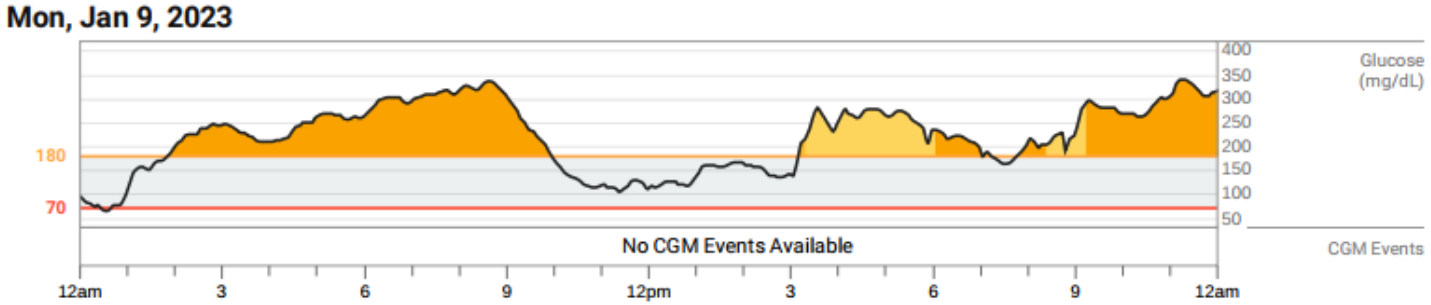
<1% Low

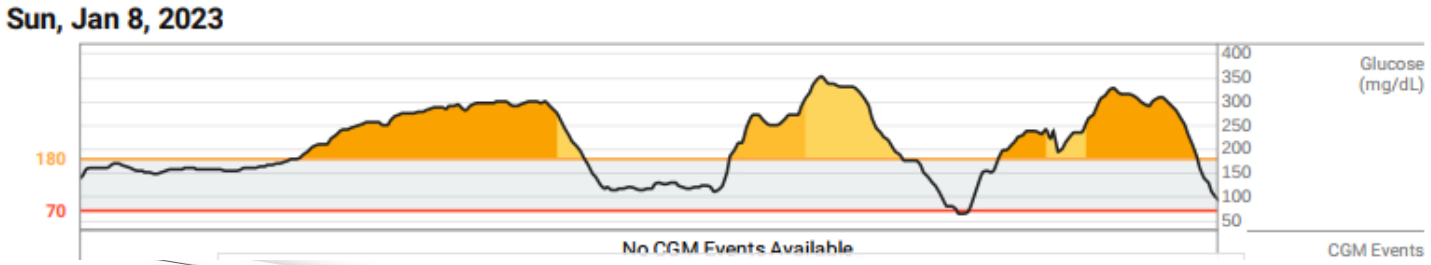
0% Very Low

Target Range:
70-180 mg/dL









- Questions?
- Suggestions?

Case 2: 69-year-old lady with type 2 diabetes, hypertension, hyperlipidemia who presents for follow-up

May 2022: A1c 7.3%

-Lantus (glargine) 30 units 8-9AM

-Trulicity (dulaglutide) 3.0 mg weekly on Wednesdays

-Metformin 1000mg BID

-released to every 6 month follow up in Endocrine clinic

September 2022: A1c 7.9% (was taking metformin 500mg BID, increased to 1000mg BID)

January 2023: A1c 7.4%

-”my pharmacy says Trulicity is out of stock”

- Questions?
- Suggestions?

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

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
    - Contact Us
  - 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 Thursdays — 12 p.m. to 1 p.m.

Mark Your Calendars — Upcoming Sessions

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

March 8, 2923 – American Diabetes Association Standards of Care, 2023 update

Please register at www.vcuhealth.org/echodmhtn

Project ECHO®
Virginia Commonwealth University

Thank you for coming!

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

VCU