Diabetes and Hypertension Project ECHO* Clinic

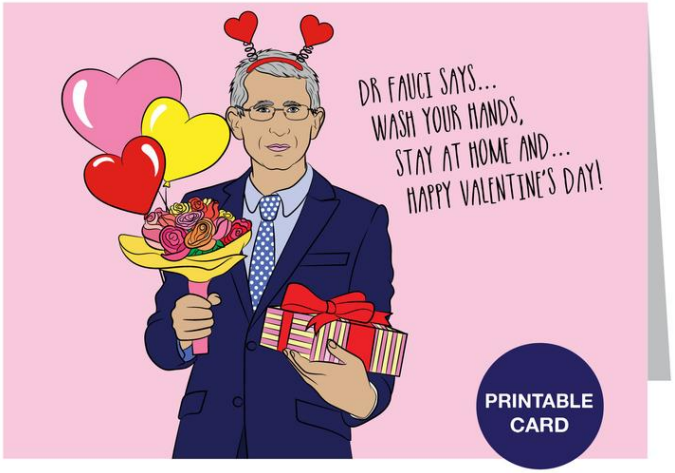
*ECHO: Extension of Community Healthcare Outcomes

February 11, 2021

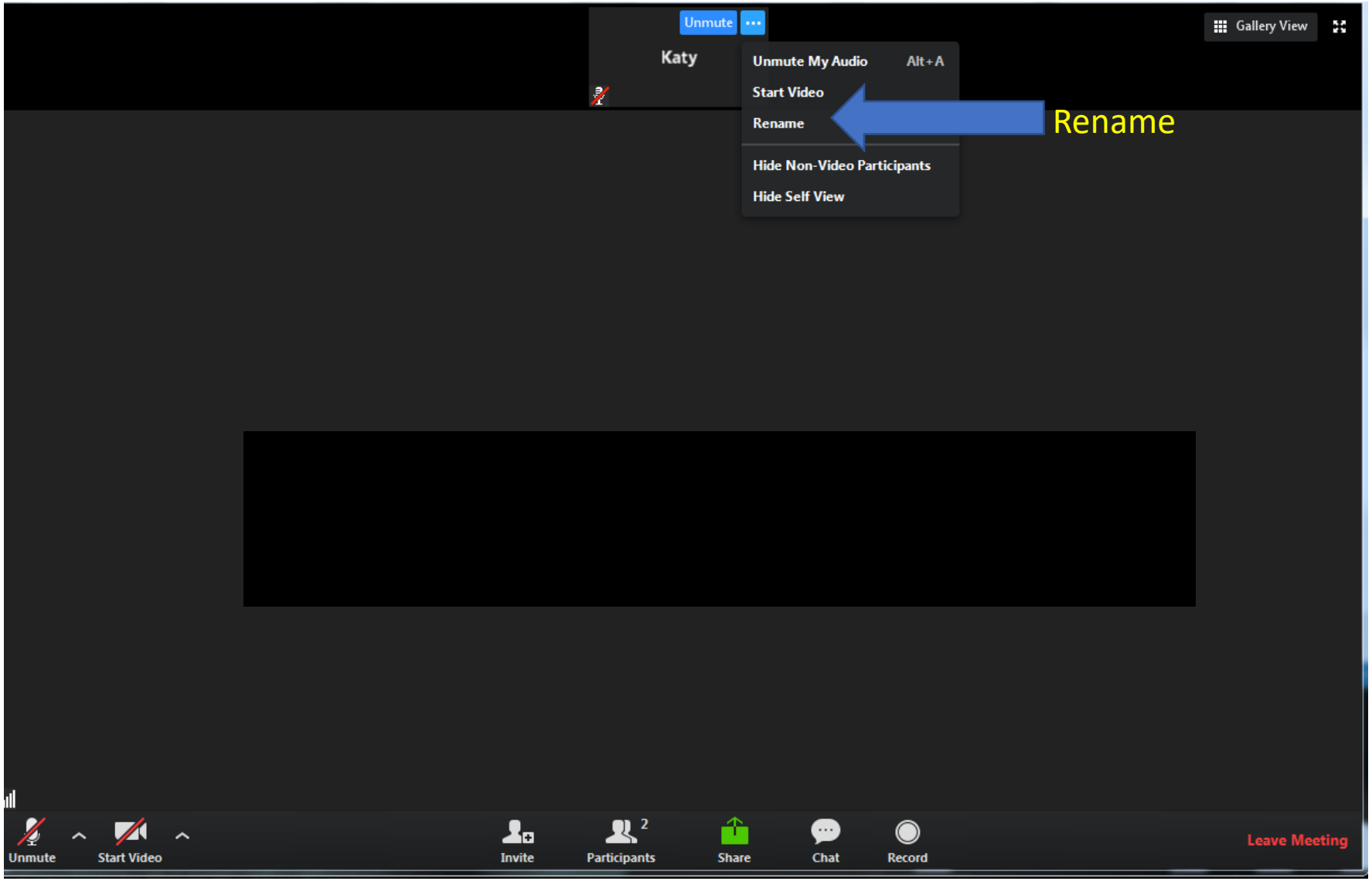
If you have already created your VCU Health CE account, text **19149-18817** to **804-625-4041** to claim CE.

If you haven't, visit **vcuhealth.org/echodmhtn** for instructions on creating your account.

Be thinking of a funny Valentine's Day story to share during introductions!

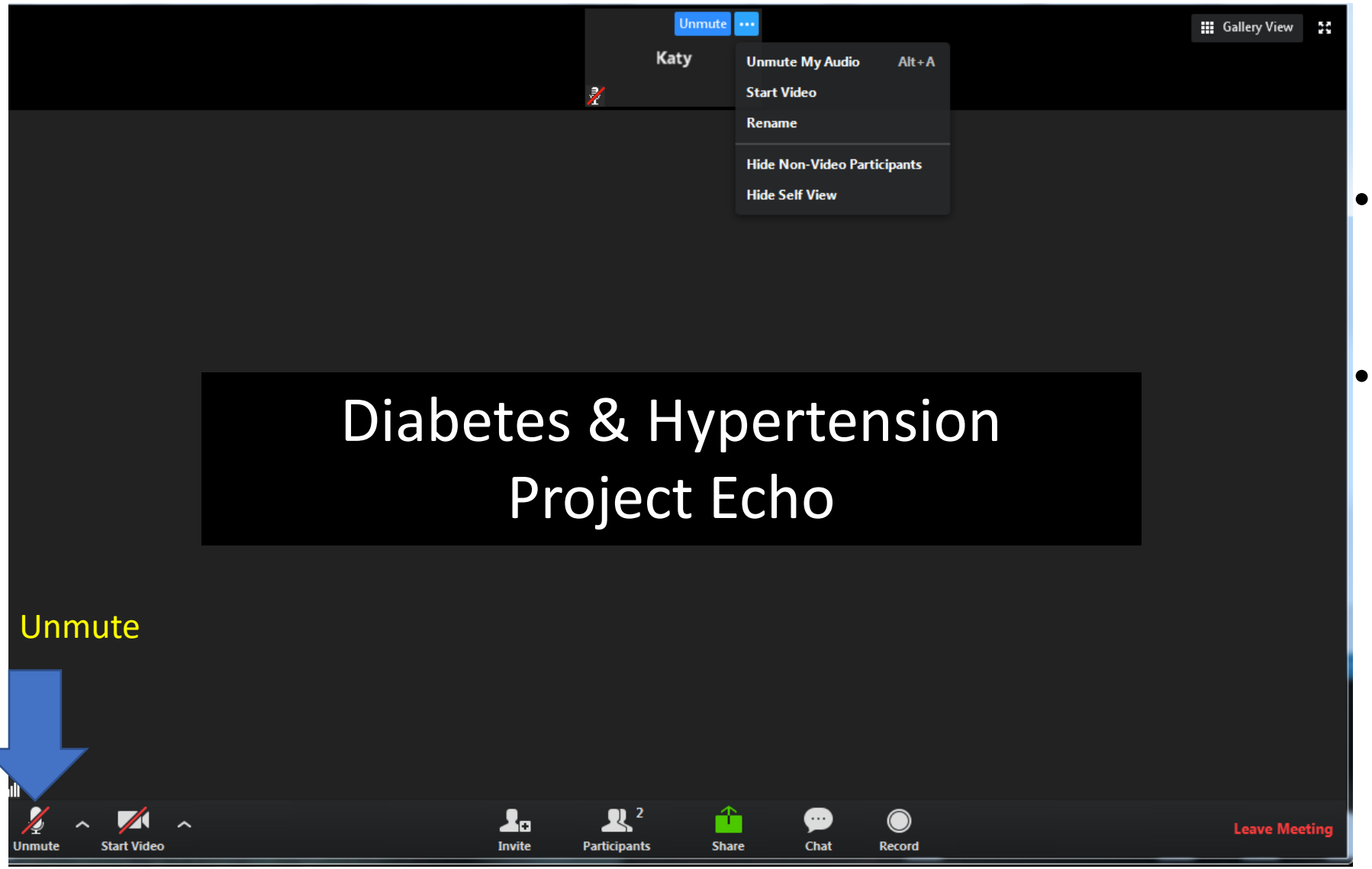


Helpful Reminders



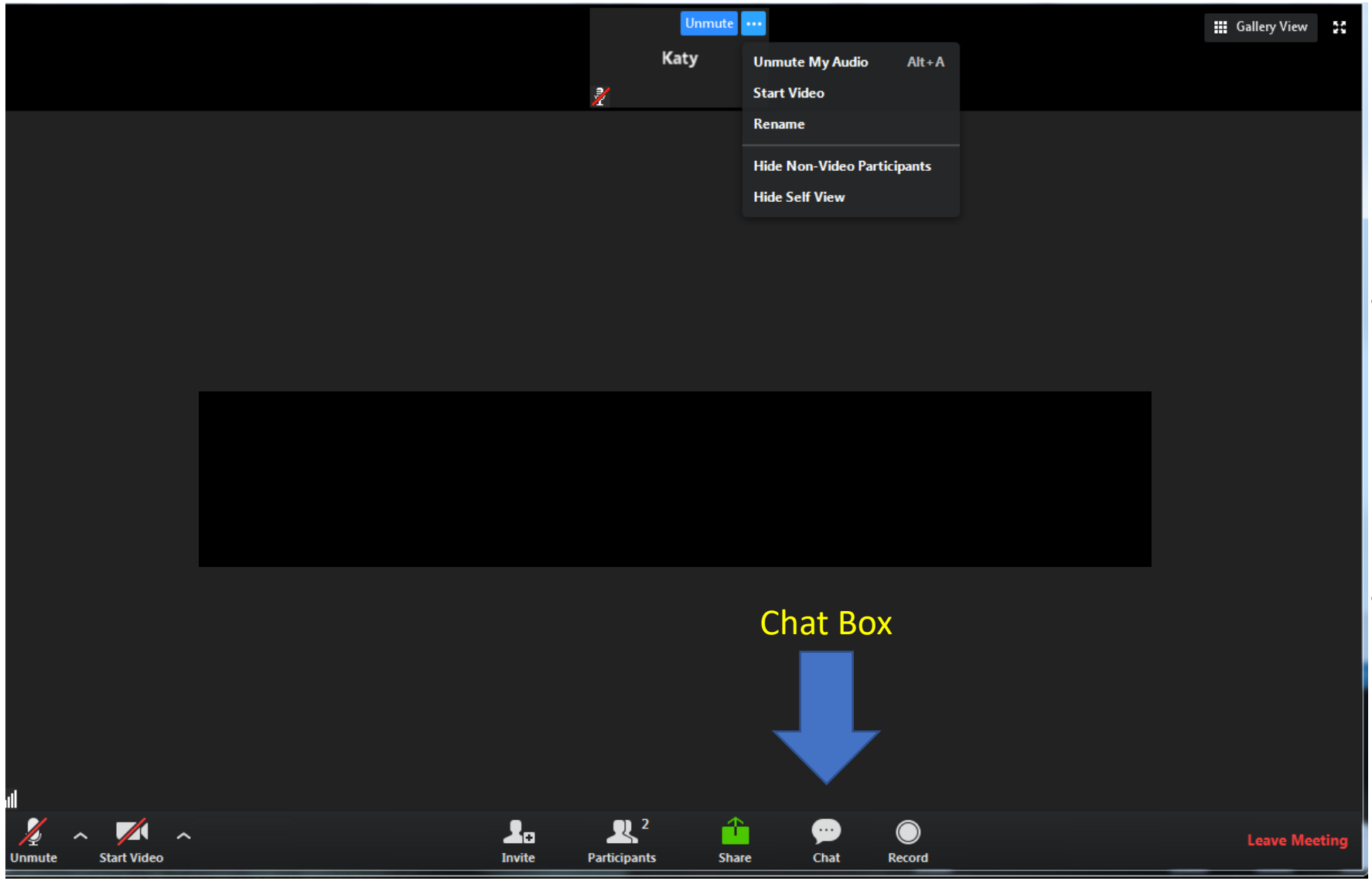
*Rename your Zoom screen with your name and organization

Helpful Reminders



- You are all on mute. Please unmute to talk
- If joining by telephone audio only, press *6 to mute and unmute

Helpful Reminders



- Please type your full name and organization in the chat box
- Use the chat function to speak with our team or ask questions

VCU Health Diabetes & Hypertension ECHO Clinics

- Bimonthly, 1.5-hour tele-ECHO clinics on 2nd and 4th Thursdays
- Every tele-ECHO clinic includes a 30-minute didactic presentation followed by case discussions
- Didactic presentations are developed and delivered by interprofessional experts
- Website: www.vcuhealth.org/echodmhtn
  - Directions for creating an account and claiming CE can be found here also
  - You have up to six days after our session to claim CE by texting **19149-18817** to **804-625-4041**

Hub and Participant Introductions

VCU 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, BA
Program Manager	Bhakti Dave, MPH

- Use chat function for introduction
  - Name
  - Organization

Reminder: Mute and unmute screen to talk or press *6 for phone audio

Share your name, organization, and a funny Valentine's Day story!

Housekeeping items

- 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
  - We encourage you to keep your camera on, but if you are uncomfortable being recorded, feel free to turn it off
- Please **do not share any protected health information** in your discussion or the chat
- 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!

What to Expect

I. Didactic Presentations
    I. Selection of basal insulin regimens
II. Case presentations
    I. Case 1
        I. Case summary
        II. Clarifying questions
        III. Recommendations
    II. Case 2
        I. Case summary
        II. Clarifying questions
        III. Recommendations
III. Closing and questions

Let's get started!

Didactic Presentation

Disclosures

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

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

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

Learning Objectives

- Apply current best practices for comprehensive diabetes and hypertension care to patient case scenarios.
- Recognize best practices for implementing team-based diabetes and hypertension care.
- Demonstrate awareness of opportunities to improve care provided to patients with diabetes and hypertension.

Selection of Basal Insulin Regimens

Learning Objectives

- List differences between currently available basal insulin regimens
- Discuss patient factors that may affect selection of basal insulin injections
- Describe typical approaches towards basal insulin dose conversion or escalation

9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Medical Care in Diabetes—2021*

American Diabetes Association

Diabetes Care 2021;44(Suppl. 1):S111–S124 | https://doi.org/10.2337/dc21-S009

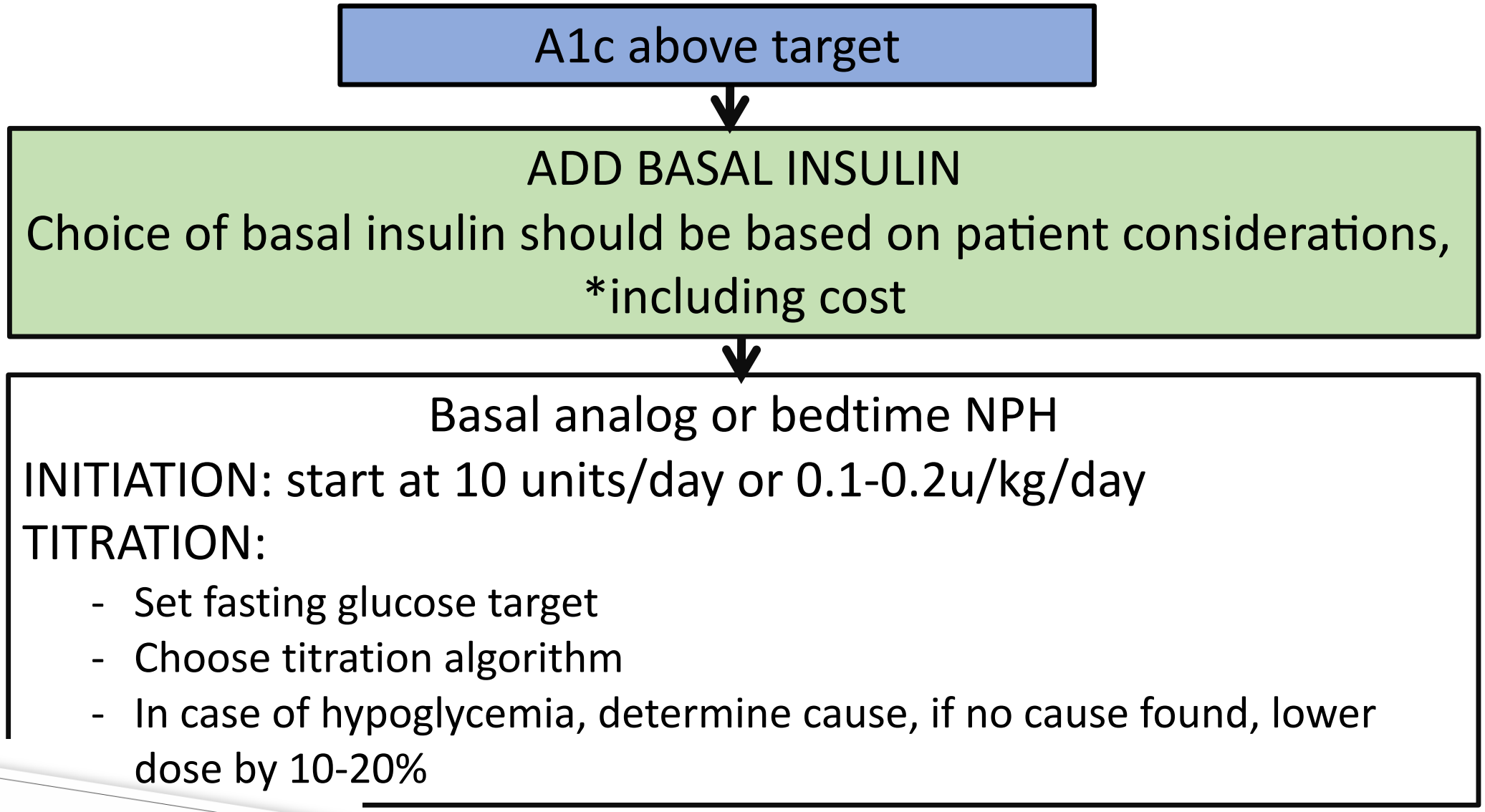
Insulin initiation

- When A1C is ≥1.5% above goal, many patients will require more than monotherapy and lifestyle modifications to reach target A1c
- Insulin is effective where other agents are not and should be considered with
  - Severe hyperglycemia
  - Catabolic features
    - (weight loss, hypertriglyceridemia, ketosis)

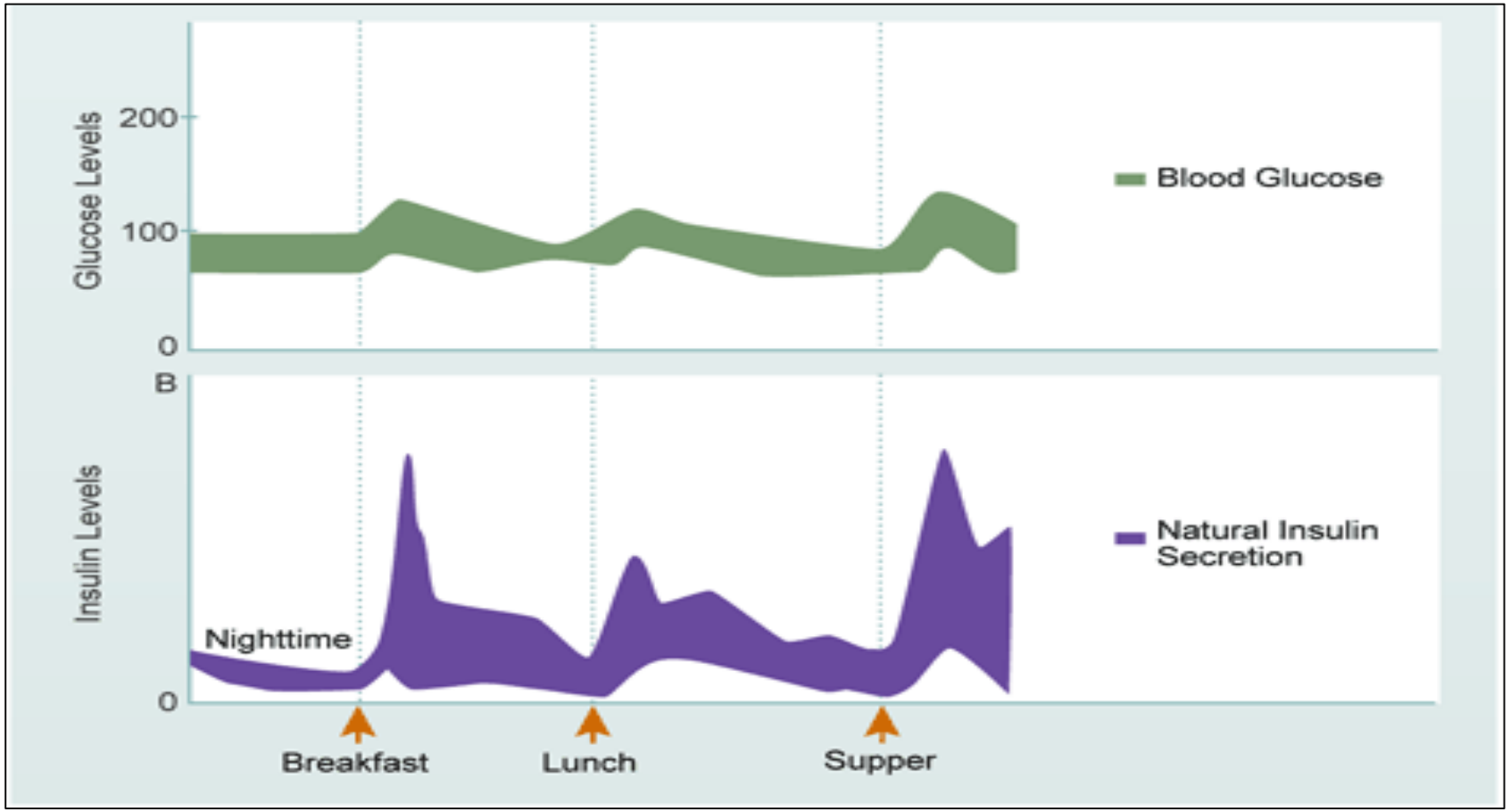
Insulin initiation

- It is common practice to initiate insulin therapy for patients presenting with BG >300mg/dL or if the patient has symptoms of hyperglycemia (i.e., polyuria or polydipsia)
- As glucose toxicity resolves, simplifying the regimen and/or changing to oral agents is often possible

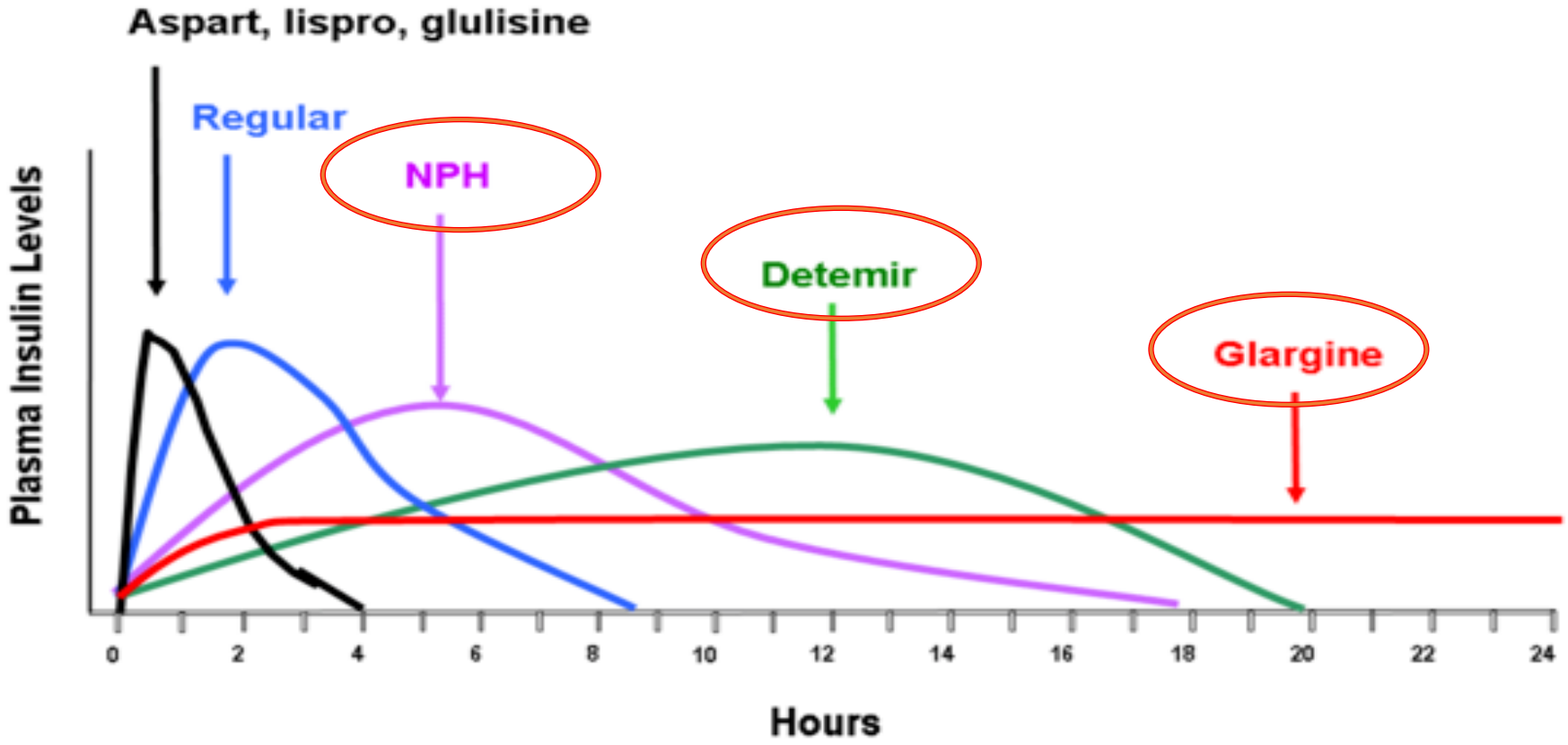
Adding Basal Insulin



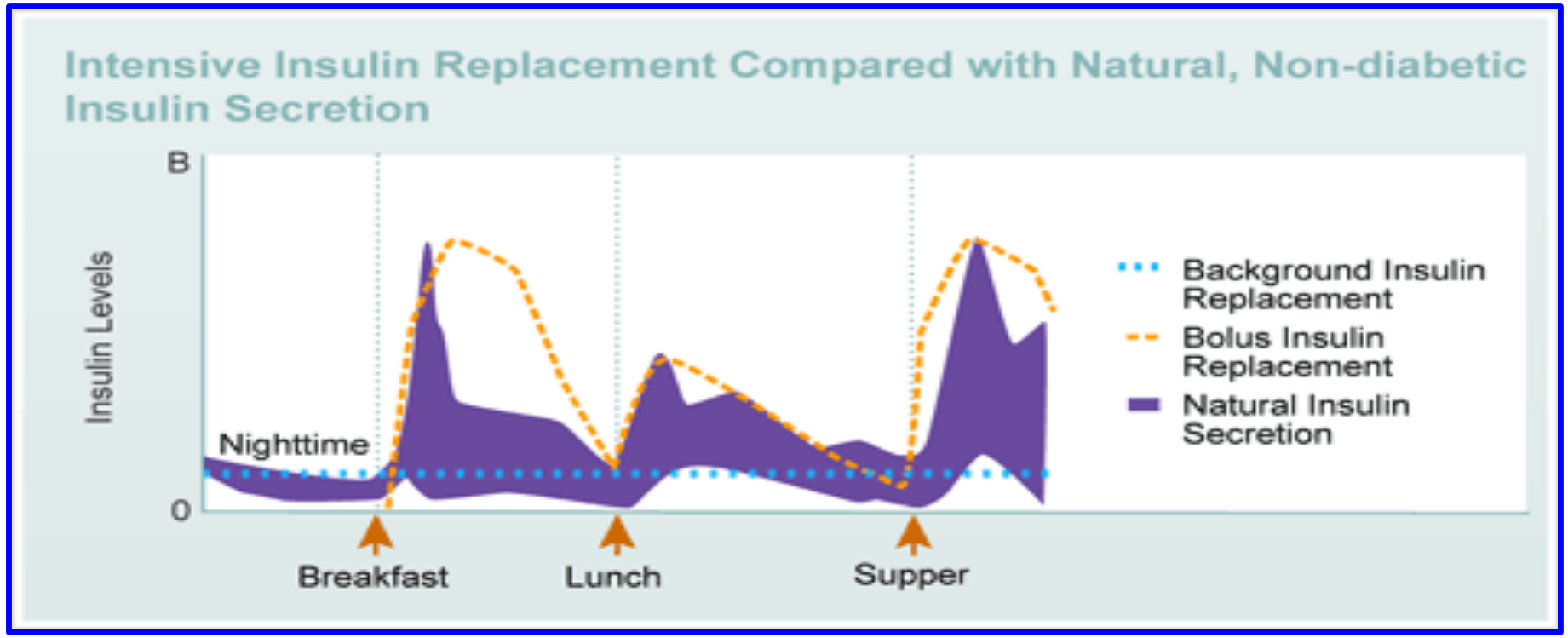
Normal glucose and insulin, 24 hours



Basal-Bolus Insulin Treatment



Basal-Bolus Insulin Treatment



Selection of basal insulin regimen

- Basal insulin alone is the most convenient initial insulin regimen and can be added to metformin and other agents
- Starting doses can be estimated based on
  - body weight - 0.1–0.2 units/kg/day
  - degree of hyperglycemia
- individualized titration over days to weeks as needed

Basal insulin selection

- Goal: ↓ hepatic glucose production and limit hyperglycemia overnight and between meals
- Control of *fasting glucose* can be achieved with human NPH insulin or a long-acting insulin analog
- In clinical trials, long-acting basal analogs (U-100 glargine or detemir) have been demonstrated to reduce the risk of symptomatic and nocturnal hypoglycemia compared with NPH insulin
  - although these advantages are modest and may not persist

Insulin NPH

- Onset 1-2 hours,
- Peak 2-14 hours,
- Duration 14-24 hours
- start at 10 units/day or 0.1-0.2u/kg/day

NPH bedtime, with inadequate control

Consider converting to NPH twice daily

INITIATION:

- Total dose at 80% of bedtime NPH
- 2/3 in AM, 1/3 at bedtime

TITRATION: individualized

Insulin glargine

- Duration of action: 24 hours
- Half life 12 hours,
- “peakless”
- Concentrations: 300U/mL or 100U mL

- What do you tell patients to do if they miss a dose?

What's the best time of day to inject glargine?

A. Morning

B. Bedtime

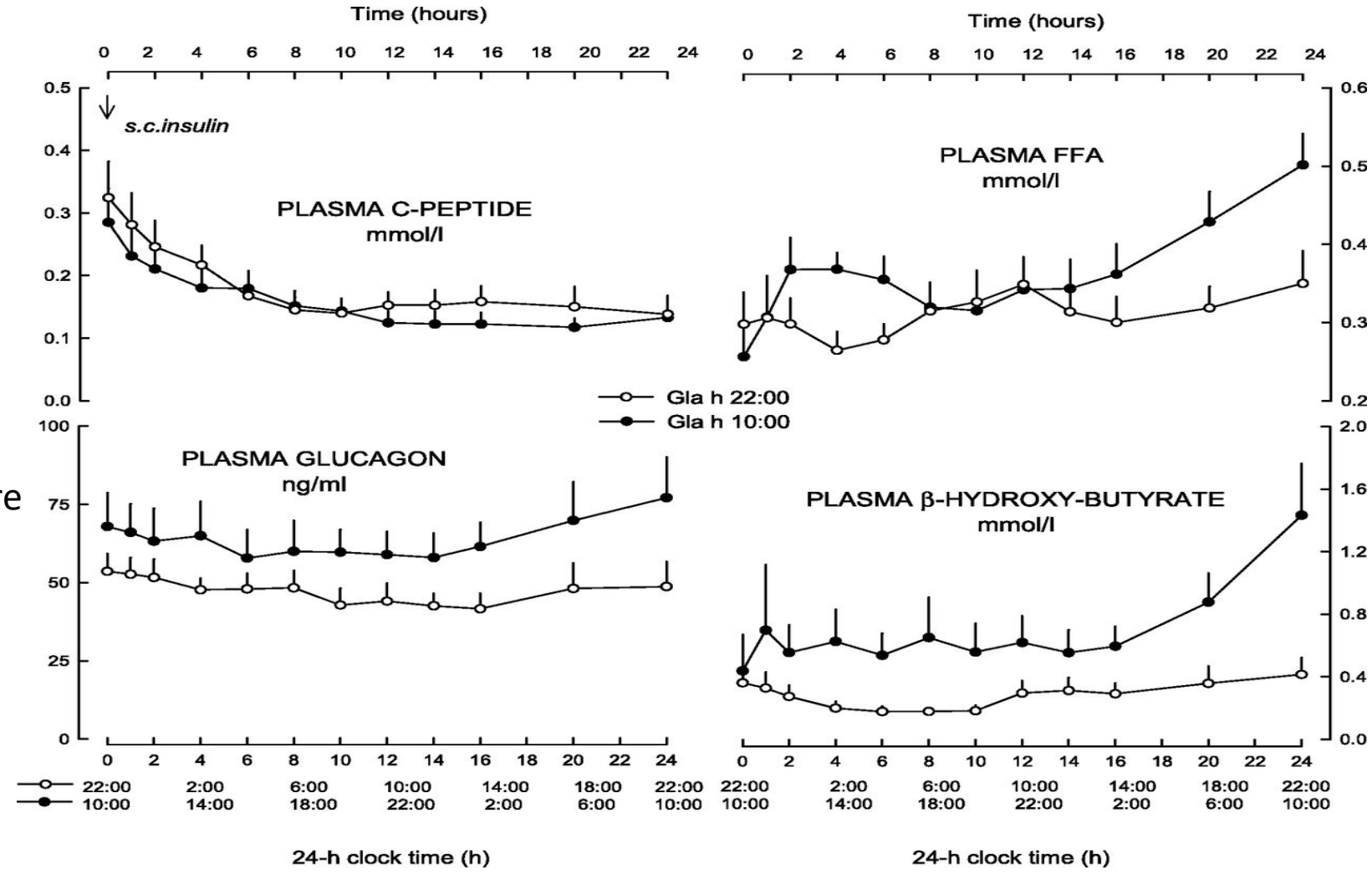
C. Doesn't matter – just every 24 hours

Glucagon

- ↑Hepatic gluconeogenesis / glycogenolysis, fatty acid oxidation (creating ketones)
- ↑insulin resistance

Plasma C-peptide, glucagon, FFAs, and β-OH-butyrate concentrations after SQ injection of 0.4 units/kg insulin glargine (Gla) at either 2200 or 1000 h in 10 subjects with T2DM.

Plasma glucagon concentrations were more suppressed with evening compared with morning dosing



Francesca Porcellati et al. Dia Care 2015;38:503-512

Median cost of insulin products in the U.S. calculated as Average Wholesale Price per 1,000 units of specified dosage form/product

Insulin type	Compounds	Dosage Form / Product	Median AWP, 30-day supply
Intermediate Acting	Human NPH	U-100 vial U-100 prefilled pen	$165 $208
Long Acting	Glargine follow-on	U-100 vial, U-100 prefilled pen	$190
	Glargine	U-100 vial, prefilled pen U-300 prefilled pen	$340 $340
	Detemir	U-100 vial, U-100 prefilled pen	$370
	Degludec	U-100 vial, U-100 prefilled pen, U-200 prefilled pen	$470

*AWP data presented do not include vials of regular human insulin and NPH available at Walmart for approximately $25/vial

What is Follow-On Insulin?

A. Generic insulin
B. Biosimilar insulin
C. The same insulin, just on a different patent

What is Follow-On Insulin?

- Because of the sensitivity of biologic products to the manufacturing process, it is impossible for other manufacturers to produce copies that are identical to the originator biologic product
- Hence, the term *biosimilar* is used and not biogeneric or bioidentical

Term	Definition
Biologic products	Generally large, complex molecules that are often produced through biotechnology in a living system, such as a microorganism, plant cell, or animal cell.
Biosimilar	A biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product. Approved under the Public Health Service Act pathway (see Table 2).
Interchangeable product	A biosimilar product that meets additional requirements outlined by the Biologics Price Competition and Innovation Act, with evidence that it will: • Produce the same clinical result as the reference product in any given patient. • For products administered to a patient more than once that the risk in terms of safety and reduced efficacy of switching back and forth between an interchangeable product and a reference product has been evaluated.
Follow-on product	"Copies" of biologic products approved under the Food, Drug, and Cosmetic Act 505(b)(2) pathway (see Table 2).
Reference product	The single biologic product, already approved by the FDA, against which a proposed biosimilar product is compared.
Originator product	FDA-approved, branded biologic used as a reference product during approval.

Abbreviation: FDA, US Food and Drug Administration.

Journal of Pharmacy Technology 2019, Vol. 35(1) 25–35

Biosimilars ≠ generic copies

- Biosimilars are not generic copies but are biologic products found to be highly similar to the brand (often termed the “originator product”)
- Traditional chemical drugs are generally stable, small molecule compounds
  - well-defined, completely characterized structures, which are identical even when produced by different synthetic pathways
- Biologic products are less straightforward
  - In general, biologic products are large unstable compounds (eg, hormones, interferons, antibodies) with complex, heterogeneous structures that are difficult to fully characterize

Biosimilars ≠ generic copies

- The manufacturing protocols for existing biologic products, including insulins, are the *proprietary* information of the originator pharmaceutical company

→other manufacturers *may not* duplicate the production process

- Thus, it is impossible for other manufacturers to produce copies that are identical to the originator biologic product,
- Hence, the term *biosimilar* is used and not biogeneric or bioidentical

Changing to glargine from NPH

- If changing patients from once-daily NPH insulin to once-daily glargine:

→initial glargine dose is the same as the dose of NPH that is being discontinued

- If changing patients from twice-daily NPH insulin to once-daily glargine:

→initial glargine dosage is 80% of the total NPH dose that is being discontinued (lower the likelihood of hypoglycemia)

Insulin detemir

- half life 5-7 hours
- Peak 3-14 hours,
- Duration up to 24 hours
- SQ injection once or twice daily
- Administer once daily doses with the evening meal or at bedtime.
- For twice daily dosing, administer the evening dose with the evening meal, at bedtime, or 12 hours after the morning dose.
- The recommended starting dose :10 units (or 0.1 units/kg to 0.2 units/kg) given once daily in the evening or divided into a twice daily regimen

Insulin detemir

- If converting from insulin glargine to detemir, the change can be done on a unit-to-unit basis
- If converting from NPH insulin, the change can be done on a unit-to-unit basis.
- However, some patients with type 2 diabetes mellitus may require more detemir than NPH insulin

Insulin degludec

- Duration of action – 42 hours
- Half life 25.4 hours
- “peakless”
- Studied at alternating once-daily dosing intervals of 8 to 40 hours in adult patients
- **What should patients do if they miss a degludec injection?**

Insulin degludec

What should patients do if they miss a degludec injection?

A. Wait until the next day to give the injection
B. Give a half dose immediately upon remembering the missed injection
C. Give the full dose immediately on recognizing the missed injection

Adult patients should wait at least 8 hours between injections

Insulin degludec

- available in 2 concentrations (U-100 pen and vial) and U-200 pen
- Single-patient-use U-200 contains 600 units of
- delivers doses in 2 unit increments and can deliver up to 160 units in a single injection

Insulin degludec

- recommended starting dose in insulin naïve patients with type 2 diabetes mellitus is 10 units once daily*:*
- Start at the same unit dose as the total daily long or intermediate-acting insulin unit dose
- *Pediatric Patients 1 Year of Age and Older with Type 1 or Type 2 Diabetes Mellitus:* Start at 80% of the total daily long or intermediate-acting insulin unit dose to minimize the risk of hypoglycemia

Longer-acting basal analogs

- U-300 glargine or degludec may convey a lower hypoglycemia risk compared with U-100 glargine when used in combination with oral agents
- Despite evidence for reduced hypoglycemia with newer, longer-acting basal insulin analogs in clinical trial settings, in practice these effects may be modest compared with NPH insulin

Monitoring after basal insulin initiation

- Clinicians should be aware of the potential for overbasalization with insulin therapy
- Clinical signals that may prompt evaluation:
  - basal dose greater than 0.5U/kg
  - High bedtime-morning glucose differential >50 mg/dL,
  - hypoglycemia (aware or unaware)
  - high glucose variability

Concentrated insulins

- U-500 regular insulin is, by definition, five times more concentrated than U-100 regular insulin
- Regular U-500 has distinct pharmacokinetics with delayed onset and longer duration of action, has characteristics more like an intermediate-acting (NPH) insulin, and can be used as two or three daily injections

Concentrated insulins

- U-300 glargine and U-200 degludec are three and two times as concentrated as their U-100 formulations and allow higher doses of basal insulin administration per volume used
- U-300 glargine has a longer duration of action than U-100 glargine but modestly lower efficacy per unit administered

True or False?

Patients requiring insulin should be instructed on BOTH pen and vial / syringe technique

Summary

- There are increasing numbers of options for basal insulin regimens, with variable peak / duration of action
- Cost remains a primary driver of basal insulin choice
- Conversion between basal insulins may be helpful in cases of insurance formulary changes

Case presentation #1

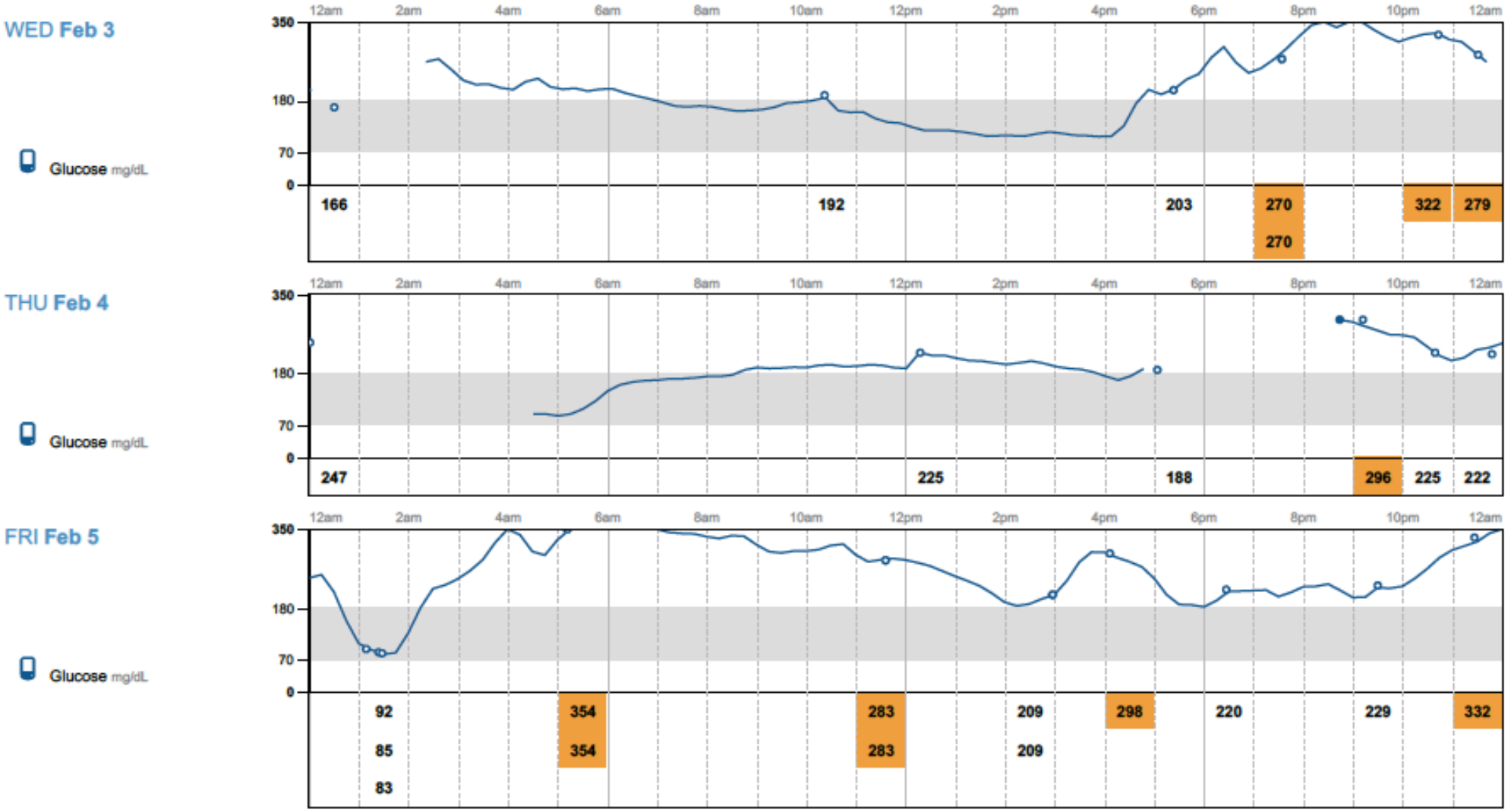
HPI: 23 yo gentleman with T1DM, diagnosed at age 17 years

A1c usually 8.6-10%, estimated at 9% based on CGM readings

Complications: peripheral neuropathy, gastroparesis, malnutrition (BMI usually 16-17)

Medications: Lantus 30 units once daily, usually nightly but varies the time, and misses the dose completely 2x per week, Novolog 1:10g carb ratio, with 2 extra units above 150, and 1:50>200, gabapentin, statin, ACE-I

Gastroparesis is worsening, has missed GI/nutrition follow up evaluations, consumes mainly Glucerna and snacks



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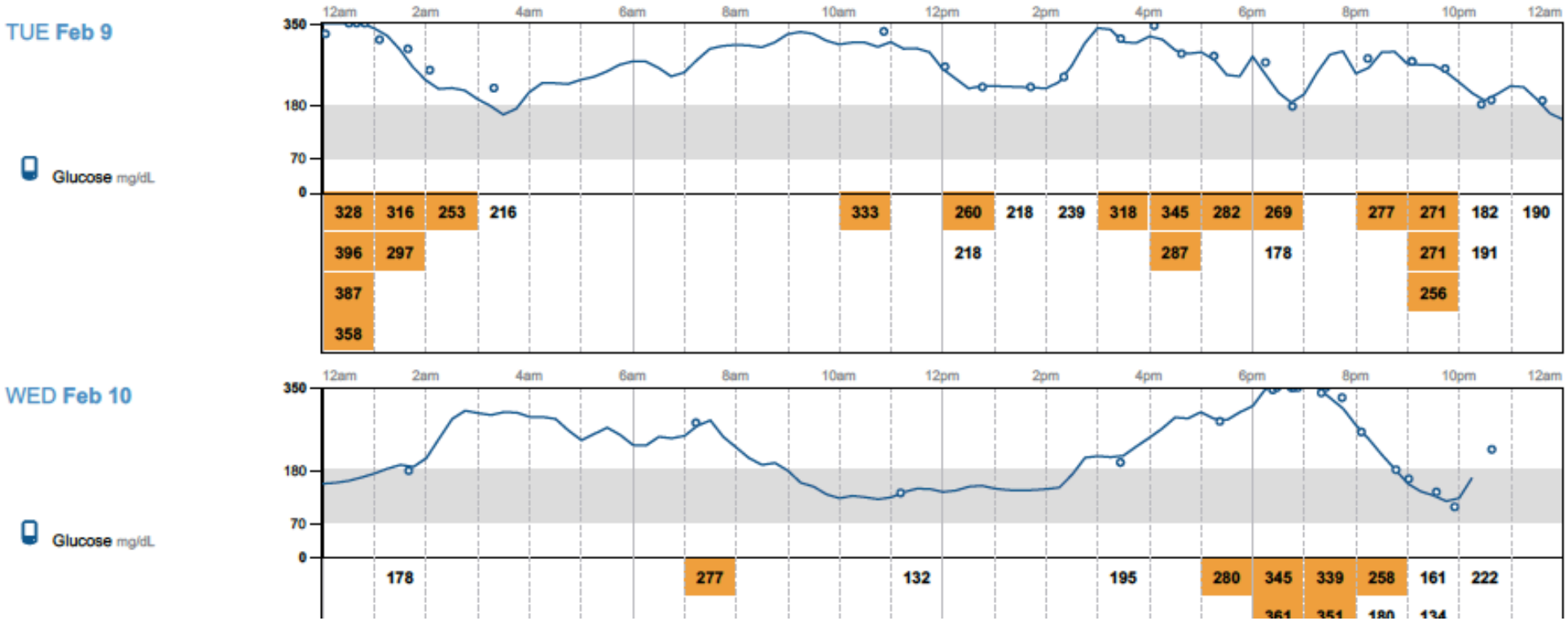

Any clarifying questions?

Any recommendations?

Case presentation #2

52 year old gentleman with renal transplant 8/2015 due to HTN, following up for diabetes diagnosed around time of transplant

Comorbidities: HTN, no neuropathy, mild NPDR, hyperlipidemia

HgA1c = 9.7%, weight = 81kg

Medications:

- NPH 40 in AM, 40 in the evening
- Regular 10 units with meals, 14 if above 200
- Metformin 500mg daily (pre renal transplant team due to concerns of renal function)
- Prednisone 5mg daily

Case presentation #2

- Previous reluctance to change from NPH / regular as he was started on this medication at initial diabetes diagnosis
- Cites cost as a factor in switching to basal bolus insulin
- Concern for daytime hypoglycemia, does not typically check glucose when symptomatic

Case presentation #2

	Breakfast	Lunch	Dinner	Bedtime
6/22/20	**191**			
6/21/20	**149**	209	118	
6/20/20	**159**	309	208	
6/19/20	183	259	327	
6/18/20	109	287	172	
6/17/20	217	114	412	
6/16/20	118	147	99	

Any clarifying questions?

Any recommendations?

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

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  - **Diabetes and Hypertension Project ECHO**
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  - 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 — 12-1:30 p.m.

Mark Your Calendars — Upcoming Sessions

Feb. 25: Secondary Hypertension

March 11: Concentrated Insulins

Please register at www.vcuhealth.org/echodmhtn

THANK YOU!

Text **19149-18817** to **804-625-4041** for CE credit

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