



Diabetes and Hypertension Project ECHO* Clinic

*ECHO: Extension of Community Healthcare Outcomes

March 11, 2021

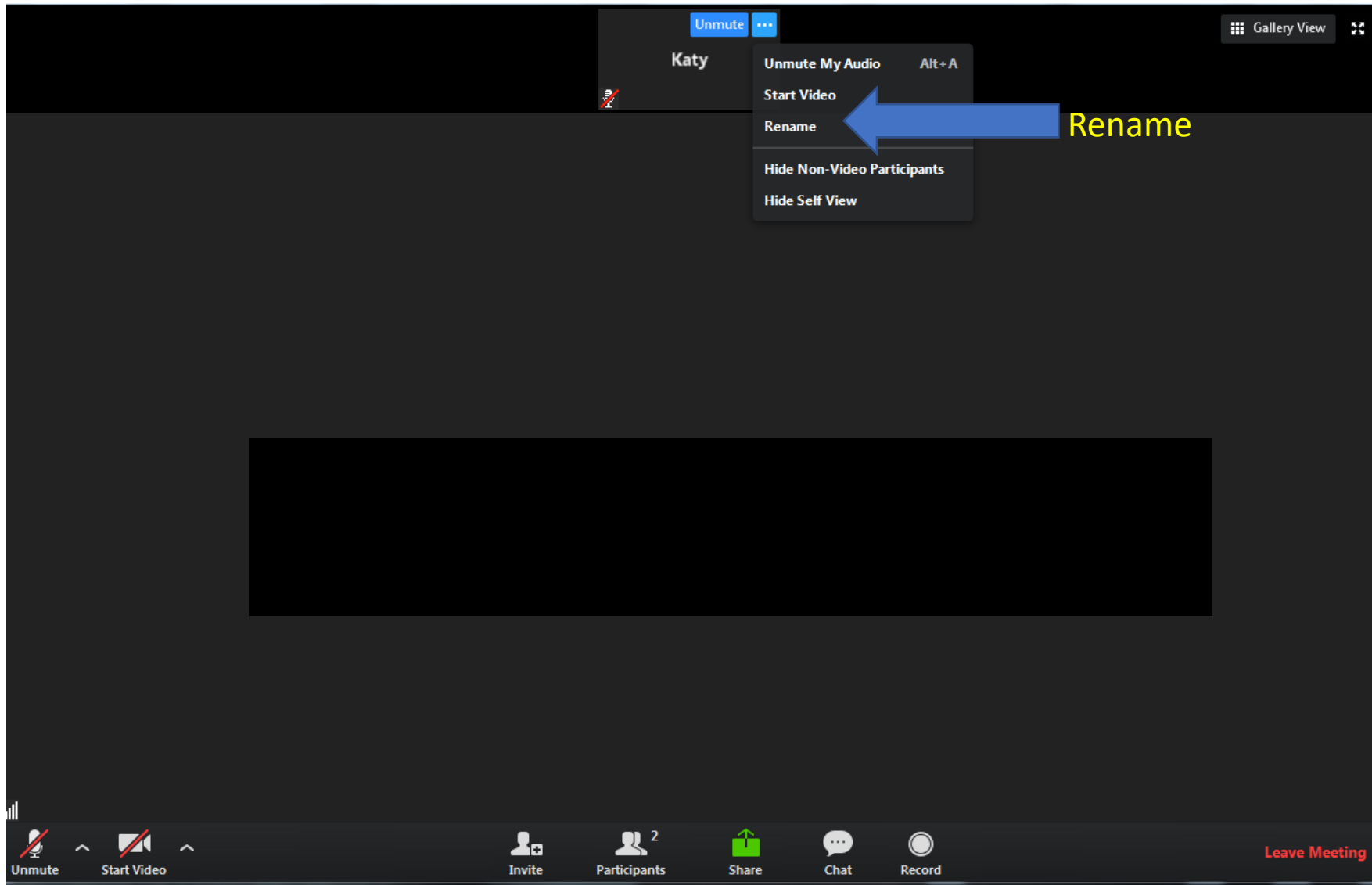
**If you have already created your VCU
Health CE account, text 19153-18817
to 804-625-4041 to claim CE.**

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

Are you doing anything for
St. Paddy's Day? Plan to
share during introductions!



Helpful Reminders



*Rename your Zoom screen with your name and organization

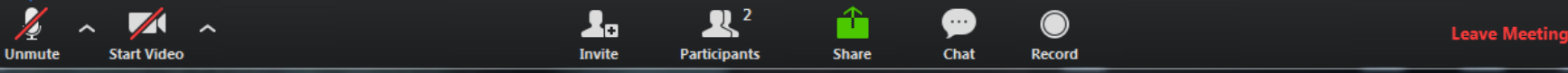
Helpful Reminders



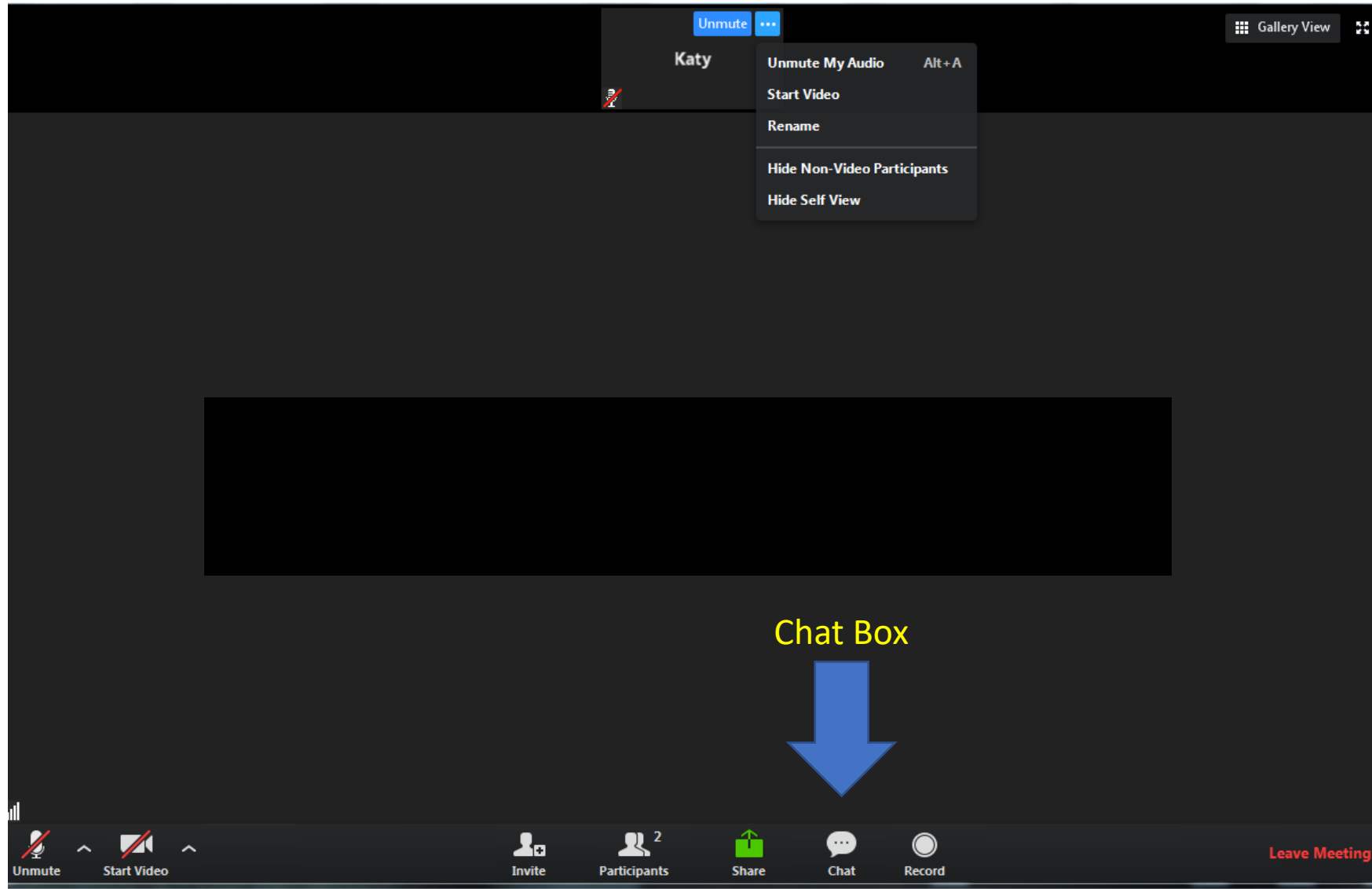
Diabetes & Hypertension Project Echo

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

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 **19153-18817** 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 something you're doing for St. Paddy's Day!

ECHO is all teach, all learn



Interactive



Co-management
of cases



Peer-to-peer
learning



Collaborative
problem solving



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. Concentrated Insulins
- 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.

Concentrated Insulins

Learning Objectives

- List the currently available concentrated insulins
- Describe differences between standard vs concentrated formulations
- Discuss instances when concentrated insulins may be advantageous
- Review tips for converting between insulins

Concerns at high doses of insulin

- Hypoglycemia
- Dosing errors (vial formulations)
- Absorption issues
- Patient insulin variability
- Overbasalization

At high doses of insulin

- When requiring >200 units/day, administration of U100 (100 units/mL) insulin may be problematic:
 - Larger volume injections
 - Multiple injections to deliver a single dose → increased complexity of regimen

Practical benefits of concentrated insulins

- Decreased number of injections
 - Can avoid splitting the dose
- Decreased pain
 - Smaller volumes may be associated with less pain
(?thigh > abdomen)

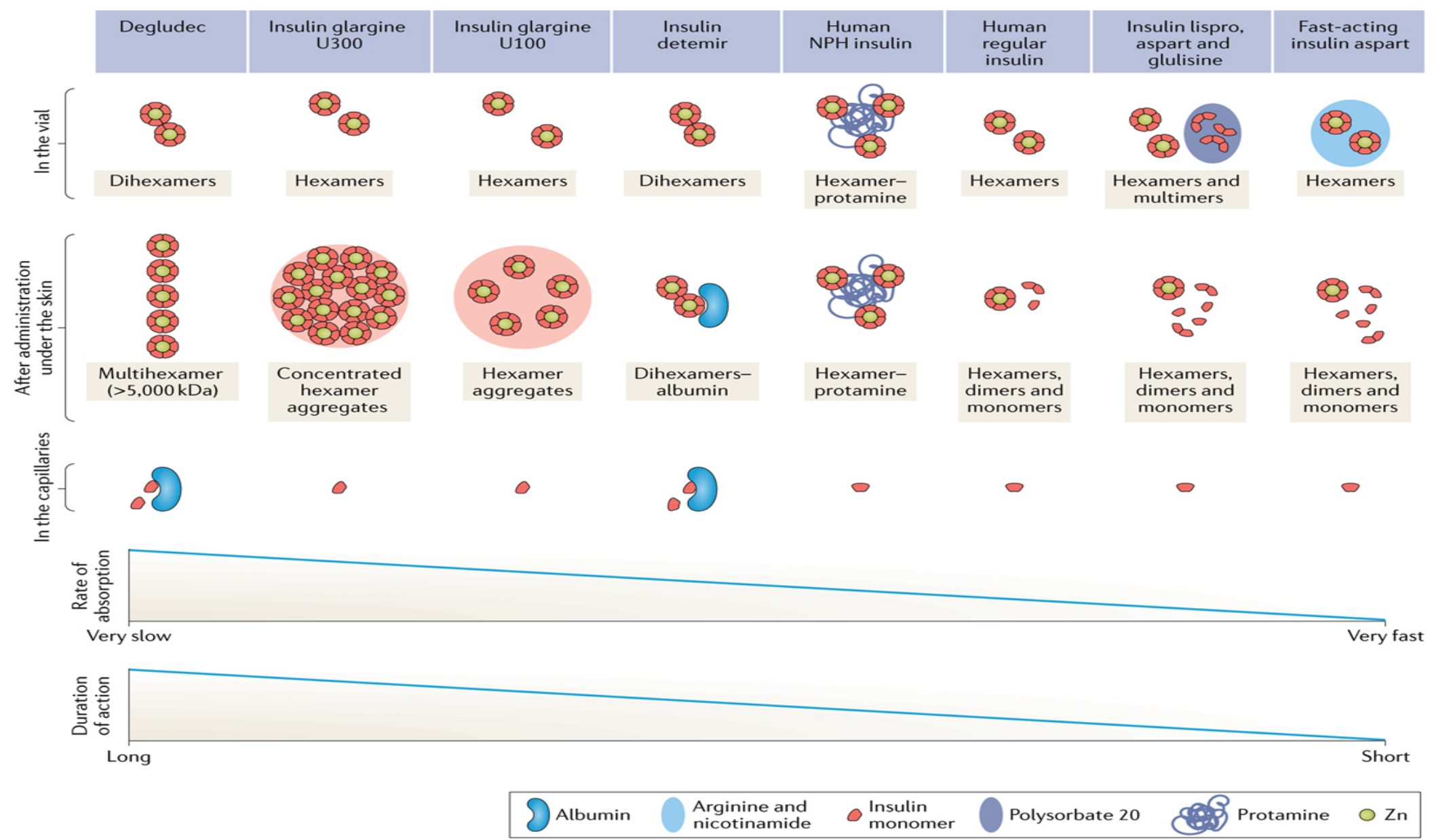
Practical benefits of concentrated insulins

- Less frequent pen changes
 - Be aware of minimum daily doses, related to the shelf-life of the insulin in the pen
- Easier delivery of larger doses
 - Impaired dexterity / thumb reach
 - Time to hold the needle under the skin to allow for full dose delivery

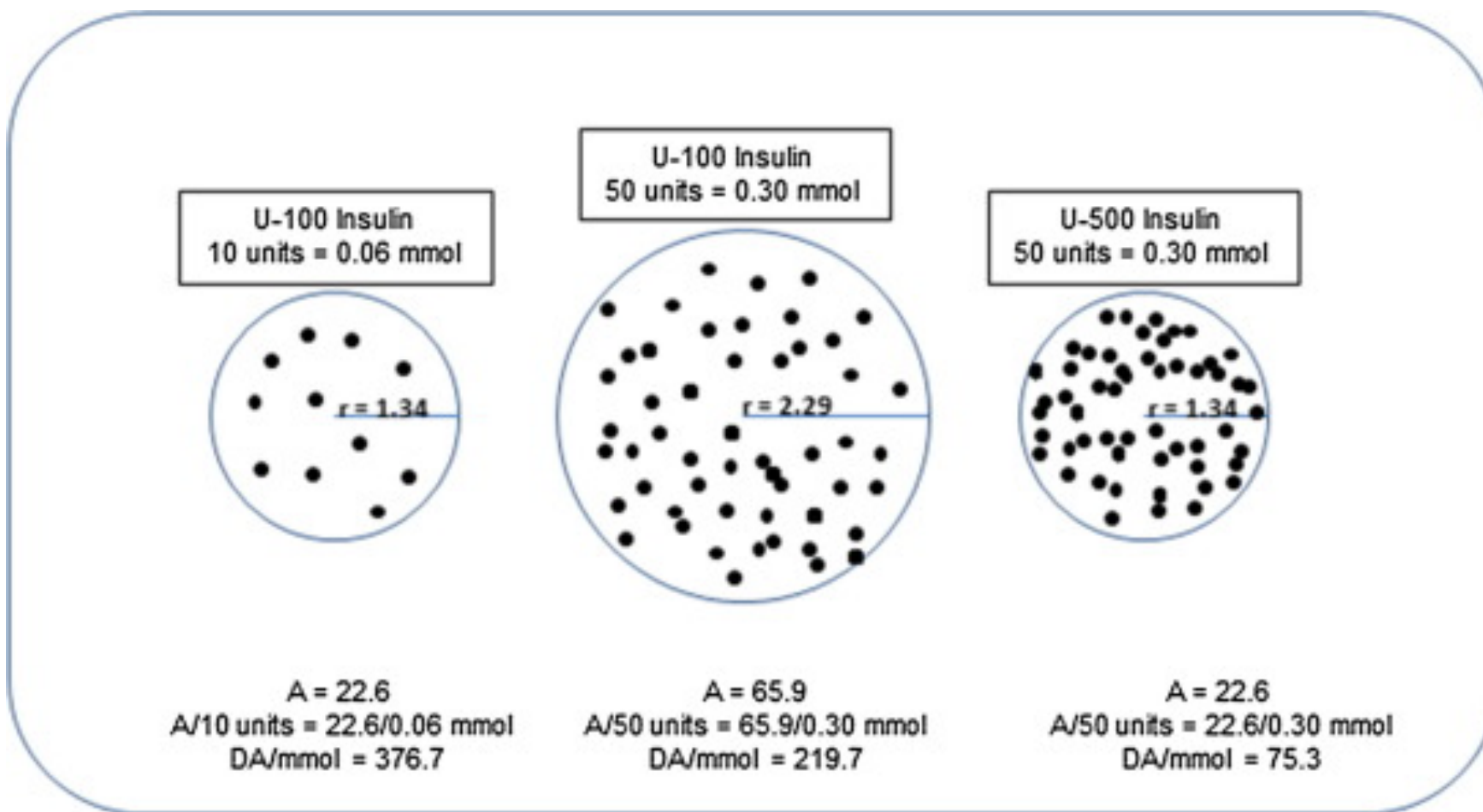


Pharmacokinetic / pharmacodynamic changes

- % of insulin as hexamers is higher at higher concentrations
- Insulin must dissociate into dimers or monomers before being absorbed into capillaries

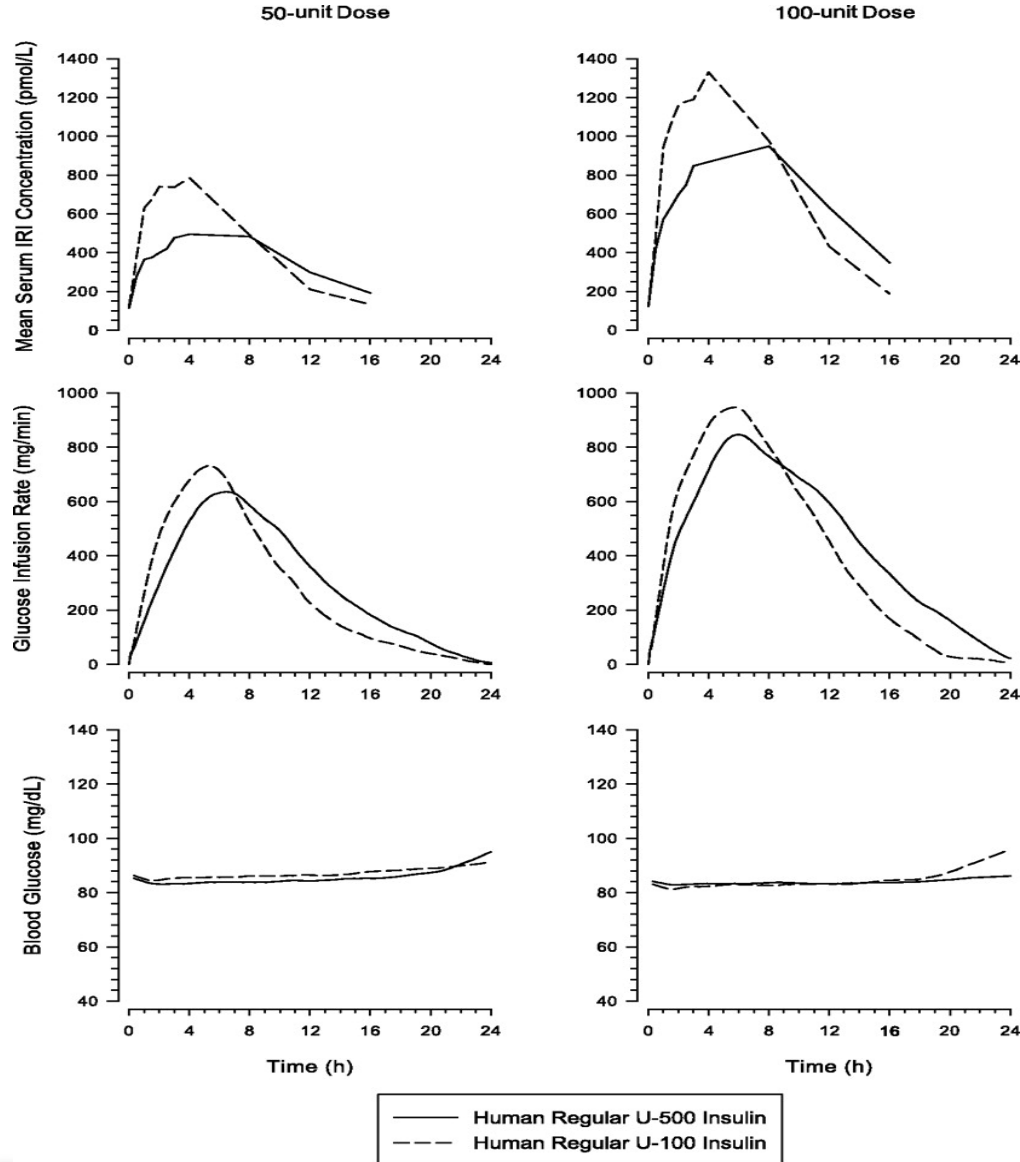


Volume increases by 3 while surface area increases by 2



- SQ administration of increasing human insulin concentrations results in slower absorption and appearance of insulin in the plasma
- The higher the insulin concentration is, the slower its diffusion into tissues
- Similarly, because of the larger surface area per insulin molecule, a smaller dose of the same insulin concentration will be absorbed faster than a larger one

PK and PD profiles, U500 vs U100 regular insulin



→ Delayed and blunted peak insulin concentration / insulin action

Bioequivalence

- Pharmacokinetic term describing formulations with the same active ingredient and similar patterns of absorption into the bloodstream
- Equivalent release of bioequivalent formulations should result in equivalent rate and magnitude of drug absorption

Which of the following are bioequivalent?

- A. Regular U100 and U500
- B. Glargine U100 and Glargine U300
- C. Degludec U100 and Degludec U200
- D. Lispro U100 and Lispro U200

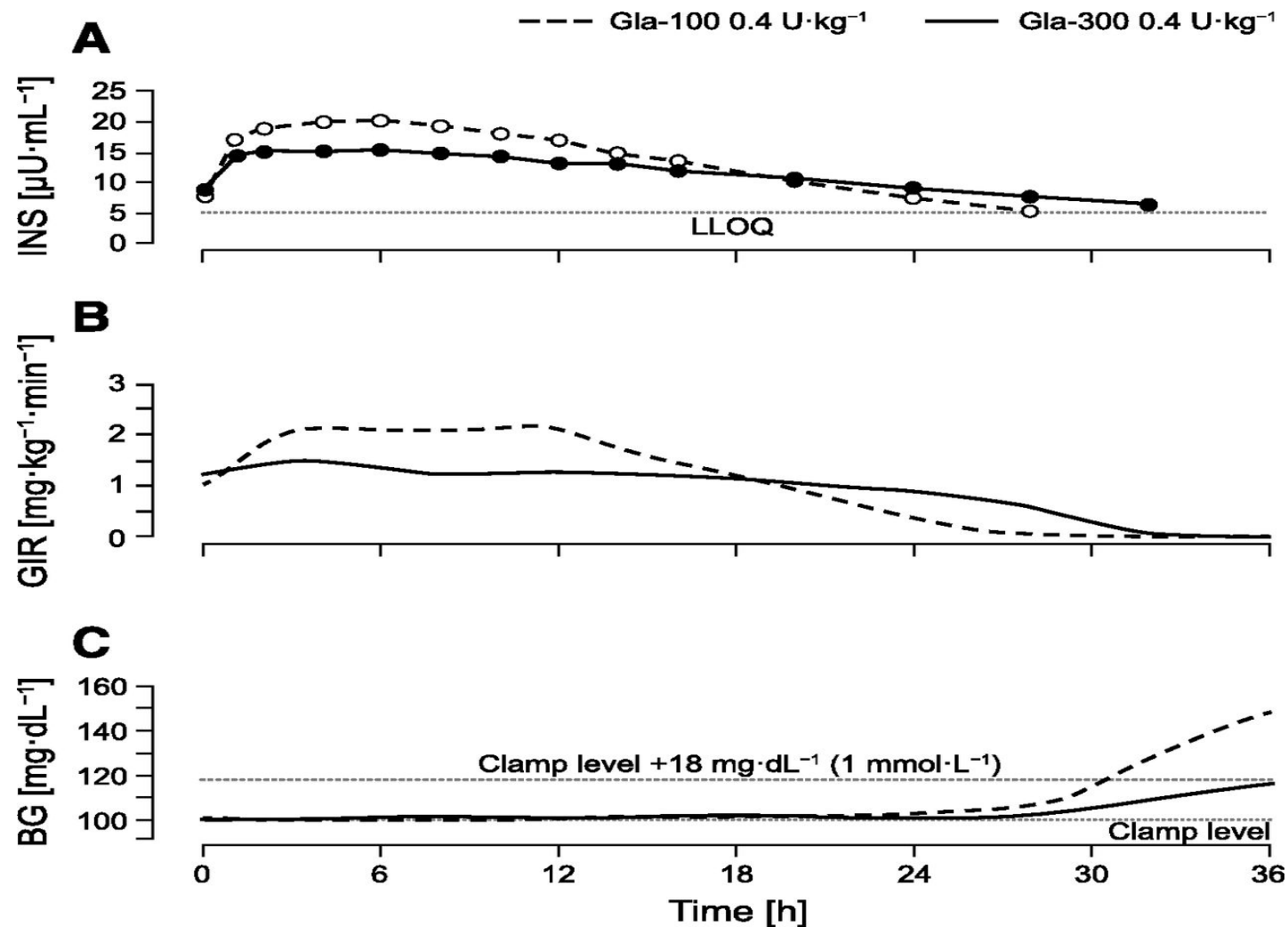
Which of the following are bioequivalent?

- A. Regular U100 and U500
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- C. Degludec U100 and Degludec U200
- D. Lispro U100 and Lispro U200

Concentrated insulins that are NOT bioequivalent

- Regular U100 and U500
- Glargine U100 and Glargine U300

Glargine, U300 vs U100



Reinhard H.A. Becker et al. Dia Care 2015;38:637-643

Glargine U300

- Half-life ~23 hours
- Steady state in 4 days
- Duration of action <36 hours
- 3 pens per box

Glargine U300

- Solostar Pen, 450 units, max single injection dose 80 units
- Max Solostar Pen, 900 units, max single injection dose 160 units
- 2 unit increments
- Stable at room temperature for 42 days
 - Minimum 11 units daily for Solostar
 - Minimum 20 units daily for Max Solostar



Starting dose of glargine U300

- Weight based, 0.2u/kg, if insulin naïve
 - Already on basal insulin → 1:1
 - NPH or insulin detemir → 80%
-
- When converting from U-300 to U-100, 20% reduction is recommended to minimize hypoglycemic risk with the U-100 insulin product

Human Regular U500

- 20mL vial = 10,000 units
- Pen, 1500 units, max 300 units at a time
- 5 unit increments
- Stable at room temp for 28 days (pen) or 40 days (vial)
- Vial – minimum 250 units daily to be used within 40 days
- Pen – minimum 54 units daily before expiration



U100 to U500 insulin

U500 is for patients on > 200 units insulin total daily dose (TDD)

- A1C $< 8\%$: consider empiric reductions of 10-20% TDD
- A1C $> 10\%$: consider empiric increase of 10-20% TDD
- Can try BID or TID dosing

U500 titration

T1D Initial Dose Proportions: 40:30:30¹

INSULIN DOSE TO ADJUST	PLASMA-EQUIVALENT GLUCOSE VALUE*	SMPG (mg/dL)	DOSE TITRATION†
PRE-BREAKFAST	MEDIAN [§] PRE-LUNCH SMPG	≤70 [‡]	-10%
PRE-LUNCH	MEDIAN [§] PRE-DINNER SMPG	71-130	No change in dose
PRE-DINNER	MEDIAN [§] PRE-BREAKFAST SMPG	131-180	+5%
		181-220	+10%
		>220	+15%

<https://www.humulin.com>, accessed 3/10/2021

U500 titration

BID Initial Dose Proportions: 60:40¹

INSULIN DOSE TO ADJUST	PLASMA-EQUIVALENT GLUCOSE VALUE*	SMPG (mg/dL)	DOSE TITRATION†
PRE-BREAKFAST	MEDIAN [§] PRE-DINNER SMPG	≤70 [‡]	-10%
		71-130	No change in dose
PRE-DINNER	MEDIAN [§] PRE-BREAKFAST SMPG	131-180	+5%
		181-220	+10%
		>220	+15%

<https://www.humulin.com>, accessed 3/10/2021

Concentrated insulins that ARE bioequivalent

- Degludec U100 and Degludec U200
- Lispro U100 and Lispro U200
- → related to lysine / proline, destabilization of hexamer formation, and zinc content of the buffering solutions

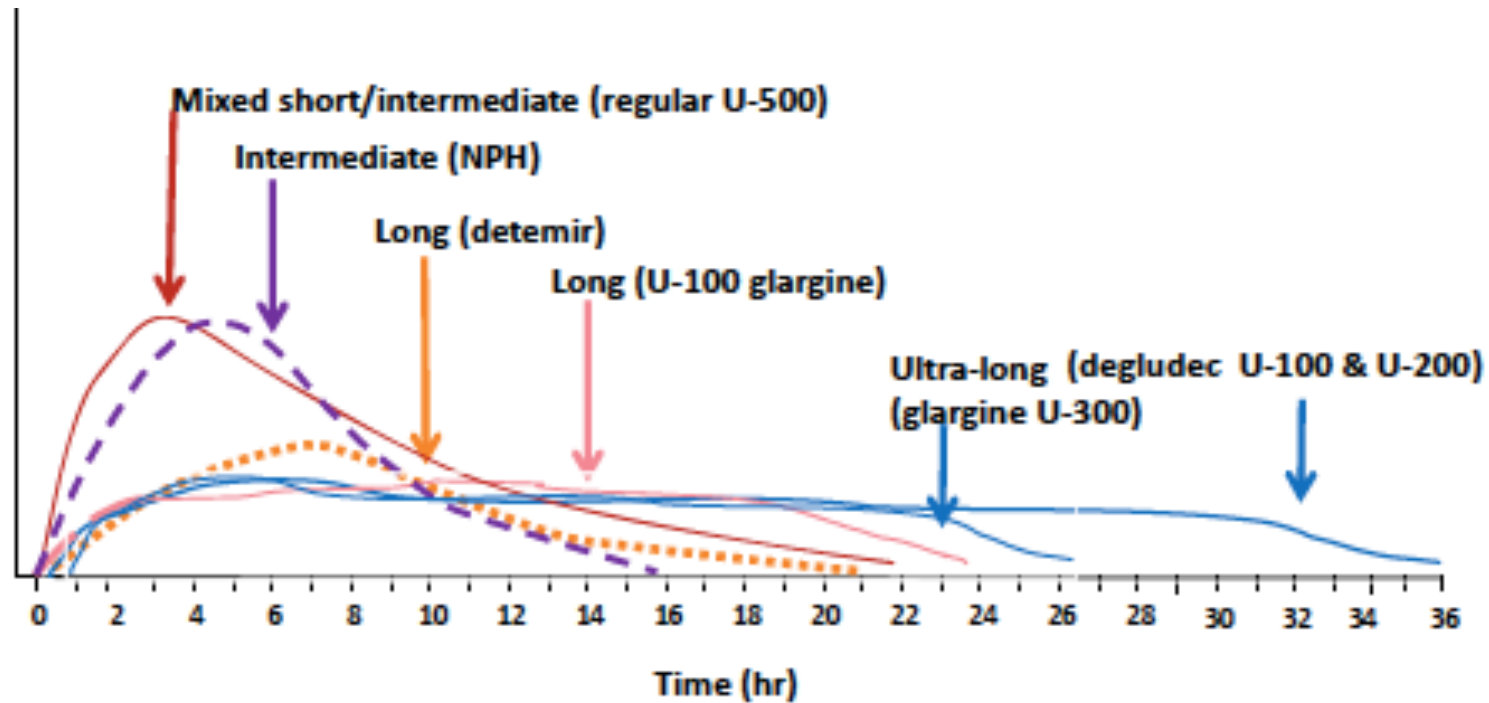
Degludec U200

- 3ml, 600 unit pens
- Up to 160 units per injection
- No need for dose conversion between U200 and U100 degludec (they are bioequivalent)
- U200 stable at room temp for 56 days, so fewer pen changes for people taking minimum of 11 units daily
- Duration of action 42 hours or longer
- Half life ~25 hours
- Steady state 3-4 days



True or false

Regular insulin U500 is a basal insulin



Lispro U200

- 3mL pens, max 60 units per injection, 1 unit increments
- Same unit dose but half the volume
- Stable at room temp x 28 days
- Minimum dose 21 units daily to use the pen contents before expiration



Pen devices

	Regular U500	Glargine U300	Glargine U300	Degludec U200	Lispro U200
Action	Prandial and basal	Basal	Basal	Basal	Prandial
Bioequivalent	No	No	No	Yes	Yes
Unit increments	5	1	2	2	1
Max dose (units)	300	80	160	160	60
Units/pen	1500	450	900	600	600
Expiration (days)	28	42	42	56	28
Minimum daily units	54	11	20	11	21

Useful tips

- Beware of overbasalization
- Address insulin resistance
- Newer, longer-acting basal analogues and higher concentration may have some benefits (more “peakless”, less variability with different administration times)
- Address insulin resistance
- Carefully review shelf life after initial use, dispense sufficient pens to last 30/90 days
- Address insulin resistance

Case Study #1: Dr. Negrón

- Demographic information

- Age: 57
- Male
- Caucasian
- Employed
- Social support: lives with wife and children (3)

- Past medical history:

- Type 1 DM with neuropathy, retinopathy, nephropathy
- CAD with MI, s/p CABG
- CVA (2018)
- CKD s/p renal transplant
- HLD
- GERD
- OSA
- Sarcoidosis

- Current medications (most pertinent):

- amlodipine 10mg daily
- aspirin 81mg daily
- atorvastatin 80mg daily
- furosemide 40mg daily
- hydralazine 50mg BID
- insulin glargine 48U daily
- insulin NovoLog for ICR 1:7 (at home) and 1:8 (at work) and correction 4 units for BG 150-200mg/dL; 6 units for 201-250 mg/dL; 8 units for 251-300 mg/dL; 10 units max if > 300mg/dL
- metoprolol tartrate 25mg BID
- prednisone 5mg daily
- spironolactone 25mg daily
- mycophenolate 500mg daily
- tacrolimus 2mg BID
- ticagrelor 60mg BID

Case Study #1: Dr. Negron (cont.)

- What interventions have you tried up to this point?
 - Insulin doses adjustments
 - Dietitian/nutrition referral
 - Enrollment in Remote Home Monitoring Program (RHMP)
- What is your main concern or challenge (e.g. diagnosis, management, etc.) ?
 - Transition to insulin pump and continuous glucose monitoring (CGM)

Case Study #2: Lauren Harrow, NP

54 year old African American male, married, high school education, insured, disability income with support from cardiac nurse navigator team, lives with wife and children, strong social support at home. Admitted for dyspnea x1 week and plan for right heart catheterization.

Past medical history:

HFrEF LVEF 30% 2/2 NICM s/p CardioMEMs,
type 2 diabetes,
hyperlipidemia,
hypertension,
class 3 obesity,
sleep apnea,
chronic kidney disease

Case Study #2: Lauren Harrow, NP

Labs: Na 138, K 4.1, Cl 107, CO2 22, BUN 32, creatinine 1.62, AM glucose 163 ,
GFR 48, WBC 8.1, a1c 9.9% on admission, Hgb 11.1, Hct 32.7, PLT 169

Meds:

insulin regular U500 180 units AC breakfast and 140 units AC dinner,
allopurinol 400 mg daily,
atorvastatin 40 mg bedtime, fenofibrate 134 mg po daily,
gabapentin 600 mg PO TID,
aspirin 81 mg po daily, carvedilol 3.125 mg po q12hr, duloxetine 90 mg PO daily,
metoclopramide 5 mg PO TID with meals,
sacubitril-valsartan 1 tab q12h

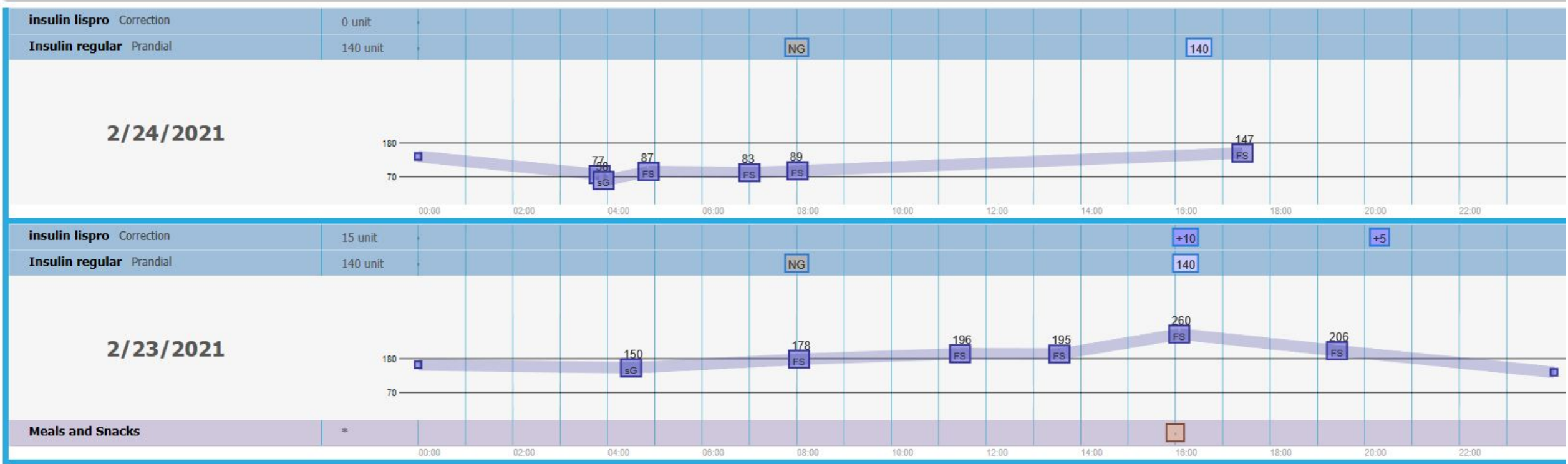
Case Study #2: Lauren Harrow, NP

Barriers to care: wears Dexcom on thigh due to striae of abdomen, nausea x1 week, NPO for upper GI series advised on AM rounds, NPO three days in a row for unexpected procedures

Case Study #1: Lauren Harrow, NP (cont.)

- What interventions have you tried up to this point?
Patient utilizes Dexcom G6 CGM and was placed NPO for upper GI series to r/o gastroparesis.
- Endocrine was not notified of NPO status until the morning of planned test. Patient received 140 units PM dose of U500 the night prior.
- Medication history shows AM U500 dose was held the morning of admission. Patient reports he had nothing to eat on the day of admission until 3pm. Pre-prandial BG at 3pm was 172. Decision was made to hold U500 AM dose and give U500 dose prior to dinner as BG was 163 with arrow straight across on AM fasting BG per Dexcom and was 165 at 10pm the night prior, 163 at dinner the night prior, 162 pre lunch, and 129 AM fasting the day prior. Jardiance was held by cardiology to rule out cause of dizziness creating further glucose excursions.

Glucose Data



Case Study #1: Lauren Harrow, NP (cont.)

- What is your main concern or challenge?
 - Advising patient of dosing recommendations in event of future NPO status. Patient requesting the entire dose be administered to prevent elevated BG as he was monitoring trends with Dexcom Clarity App on his cell phone during hospitalization.
 - In the future, recommend decreasing U500 30% the night prior to procedure and the morning of the procedure to 120 U500 in the AM and 100 units in the PM. BG was 260 after holding U500 AM dose.
 - The patient was very concerned about BG over 180 and this created stress in the patient as he was following Clarity trends closely during hospitalization.
 - Hospital BG goals are a little higher than home BG targets (140-180) creating stress in patient.

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



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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

March 25: Hypertension in Pregnancy

April 8: Combination Therapy for Hypertension

April 22: Diabetes in Pregnancy

Please register at www.vcuhealth.org/echodmhtn

Thank you, and see you in two weeks!



Text **19153-18817** to **804-625-4041** for CE credit

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