

Initiating Insulin in Diabetes

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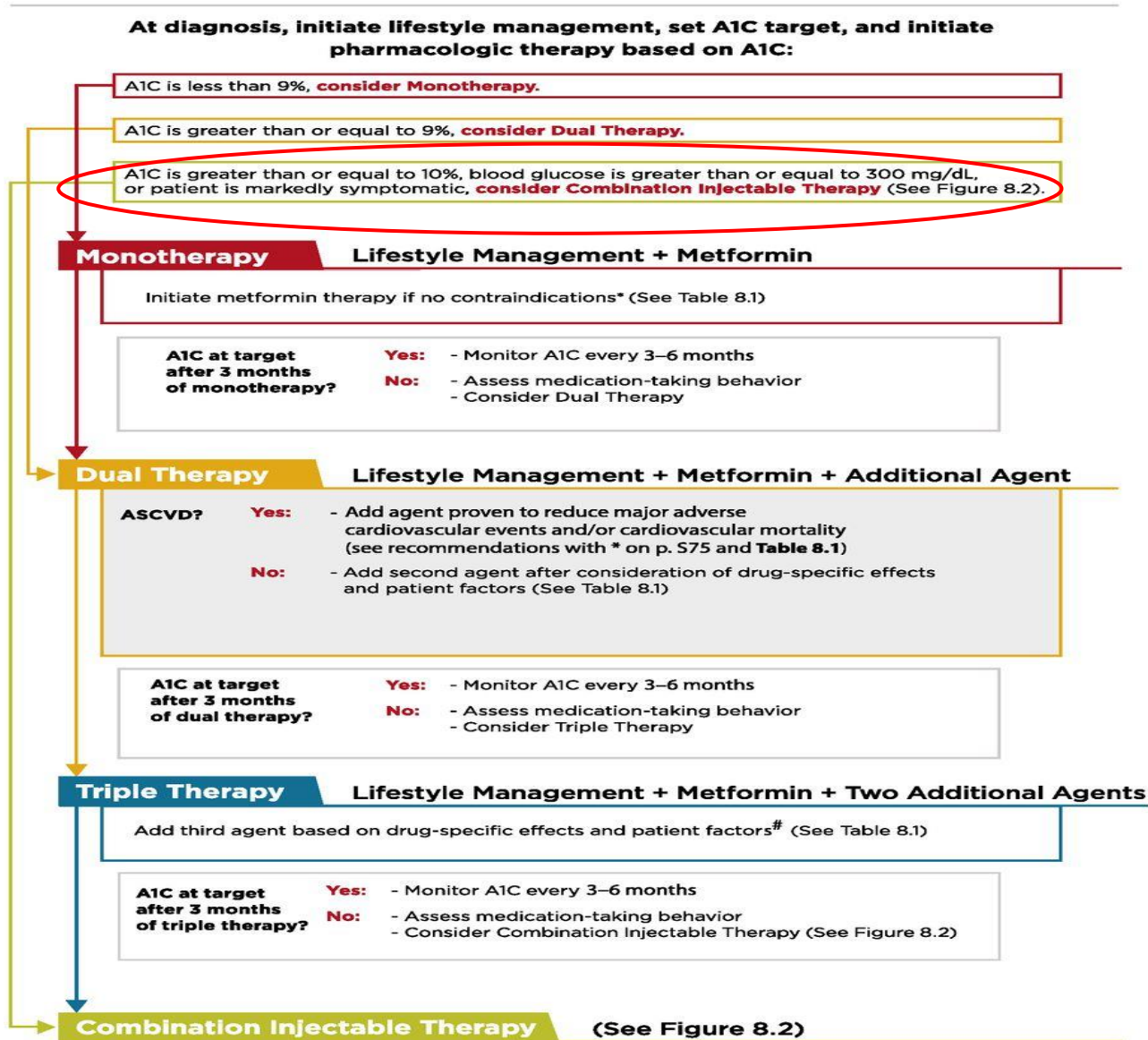
Objectives:

- To understand the terminology of insulin initiation/use
- To be able to select a weight based starting dose of basal insulin based on patient characteristics
- To understand the physiology of insulin and insulin use
- To be able to understand how to use basal/bolus insulin
- To increase knowledge of the newer basal insulins

Insulin Initiation in Diabetes type 2

- **Insulin therapy recommended:**
 - If initial A1C level greater than 10% for symptomatic hyperglycemia
(many people need earlier intervention with insulin than occurs in real world practice)
- **Or diabetes is uncontrolled despite optimal oral glycemc therapy**

Antihyperglycemic Therapy in Adults with Type 2 Diabetes

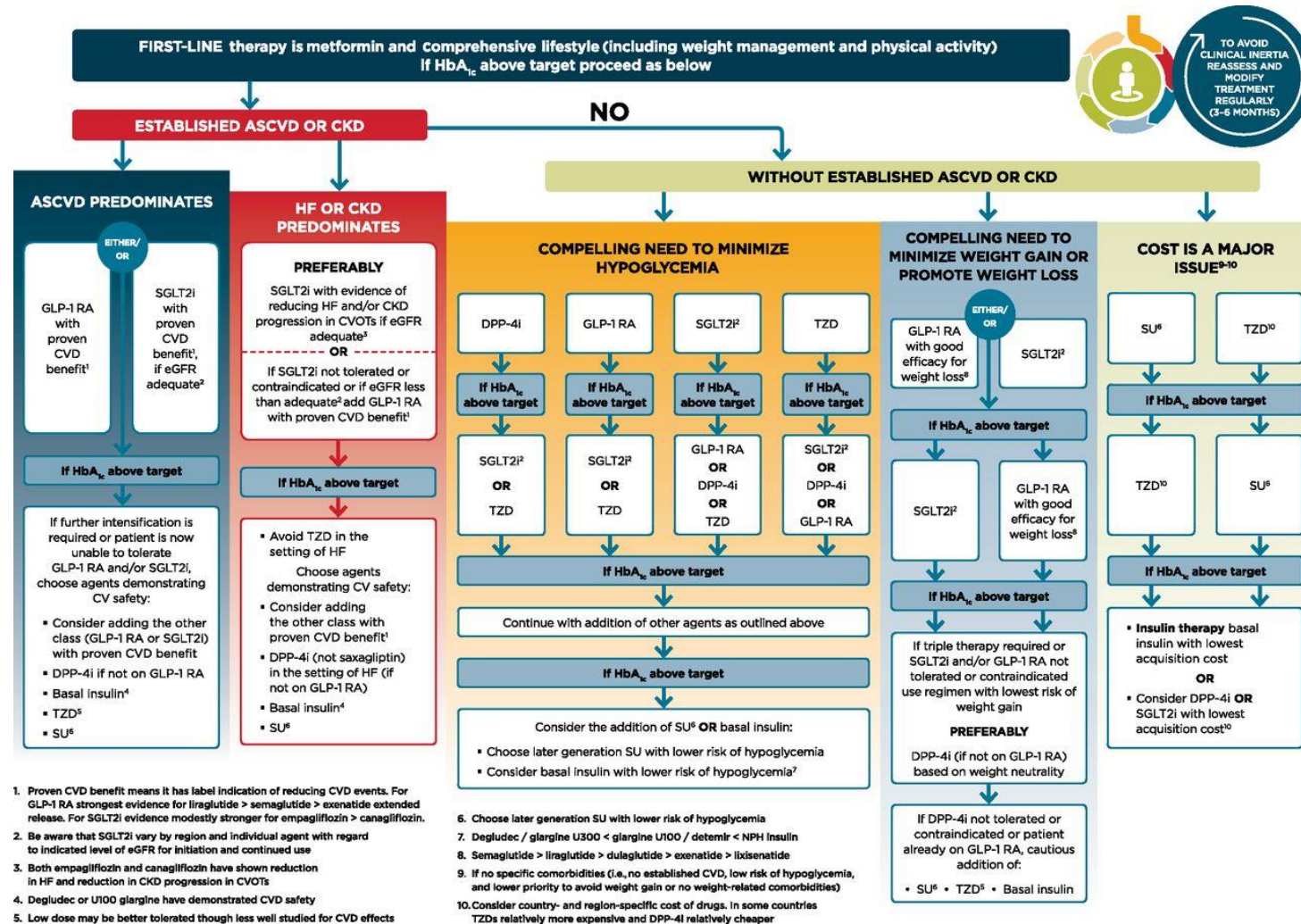


Antihyperglycemic therapy in type 2 diabetes: general recommendations. *If patient does not tolerate or has contraindications to metformin, consider agents from another class in Table 8.1. #GLP-1 receptor agonists and DPP-4 inhibitors should not be prescribed in combination.

American Diabetes Association Dia Care 2018;41:S73-S85



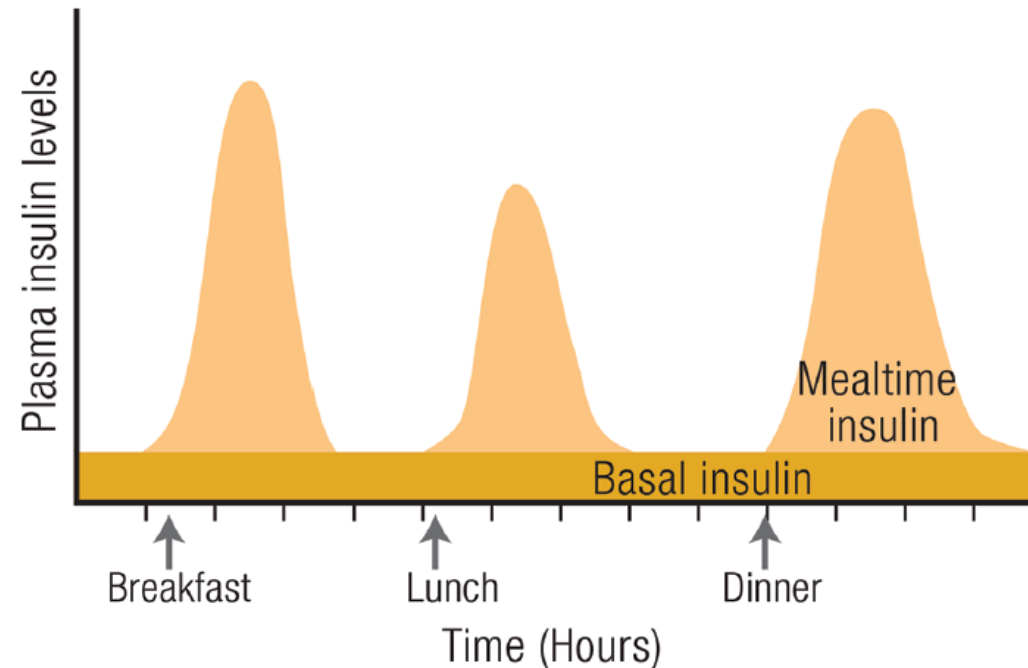
Glucose-lowering medication in type 2 diabetes: overall approach.



American Diabetes Association Dia Care 2019;42:S90-S102

Diabetes/ Insulin Terminology

- **Basal** - long acting insulin dosed once or twice a day
- **Prandial** (before meals) – short acting insulin to prevent hyperglycemia with Carbohydrate(CHO) intake



(Endocrine Reviews 41: 733 – 755, 2020)

Diabetes/ Insulin Terminology



- **Correction/sensitivity** – short acting insulin to correct/lower an elevated glucose
- **Augmentation**- adding insulin typically basal to help with blood sugar control
- **Replacement**- Total Daily Insulin Dose(TDD) used usually divided 50/50 basal and prandial

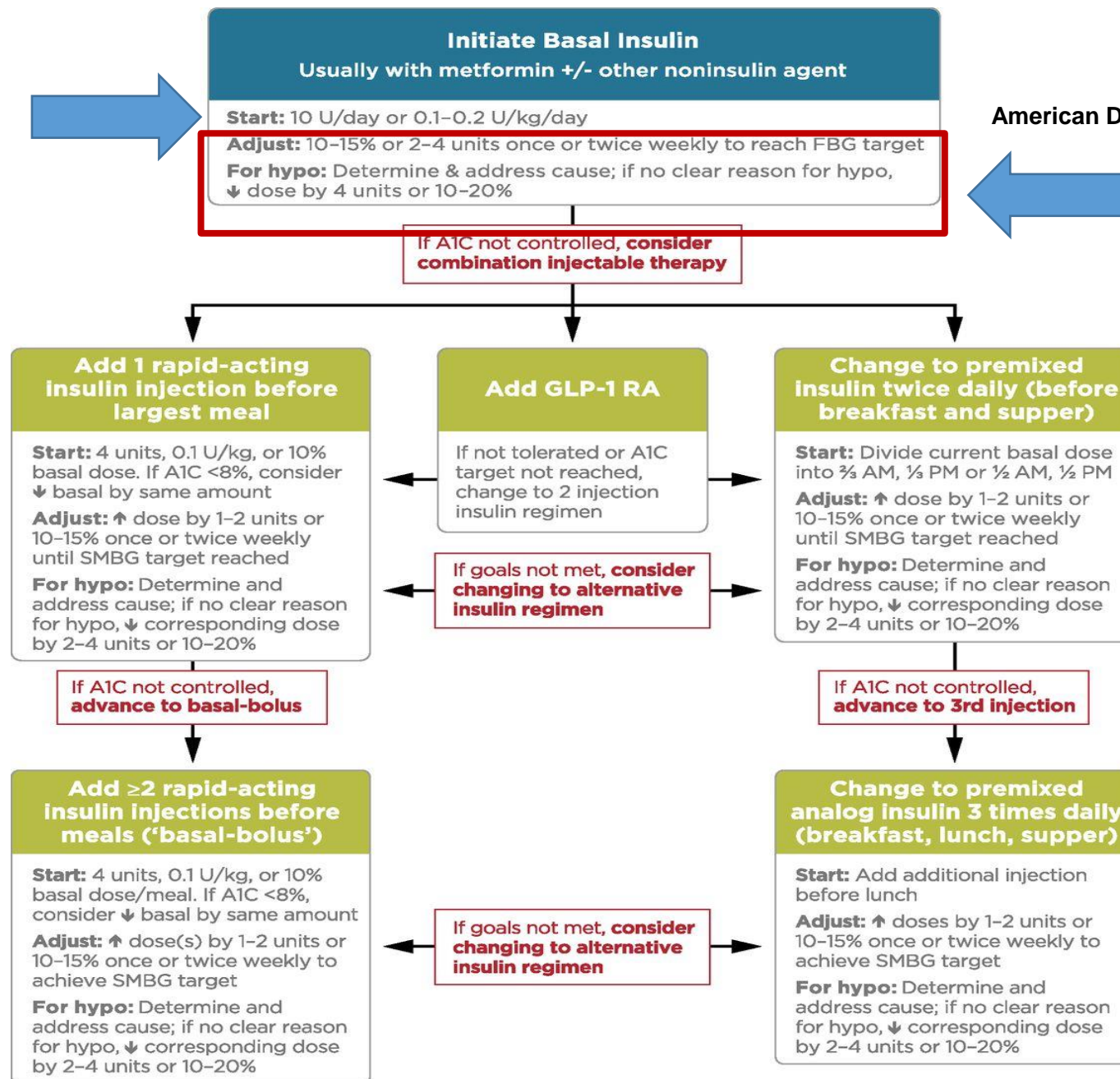
SENSITIVITY/CORRECTION FACTOR

- Represents the drop in glucose (in mg/dl) per 1 unit of short acting insulin
- Example formula:

$$1800-1500/\text{total daily dose (TDD)}$$

Often called (SSI) Sliding Scale Insulin but more appropriate term is correctional scale

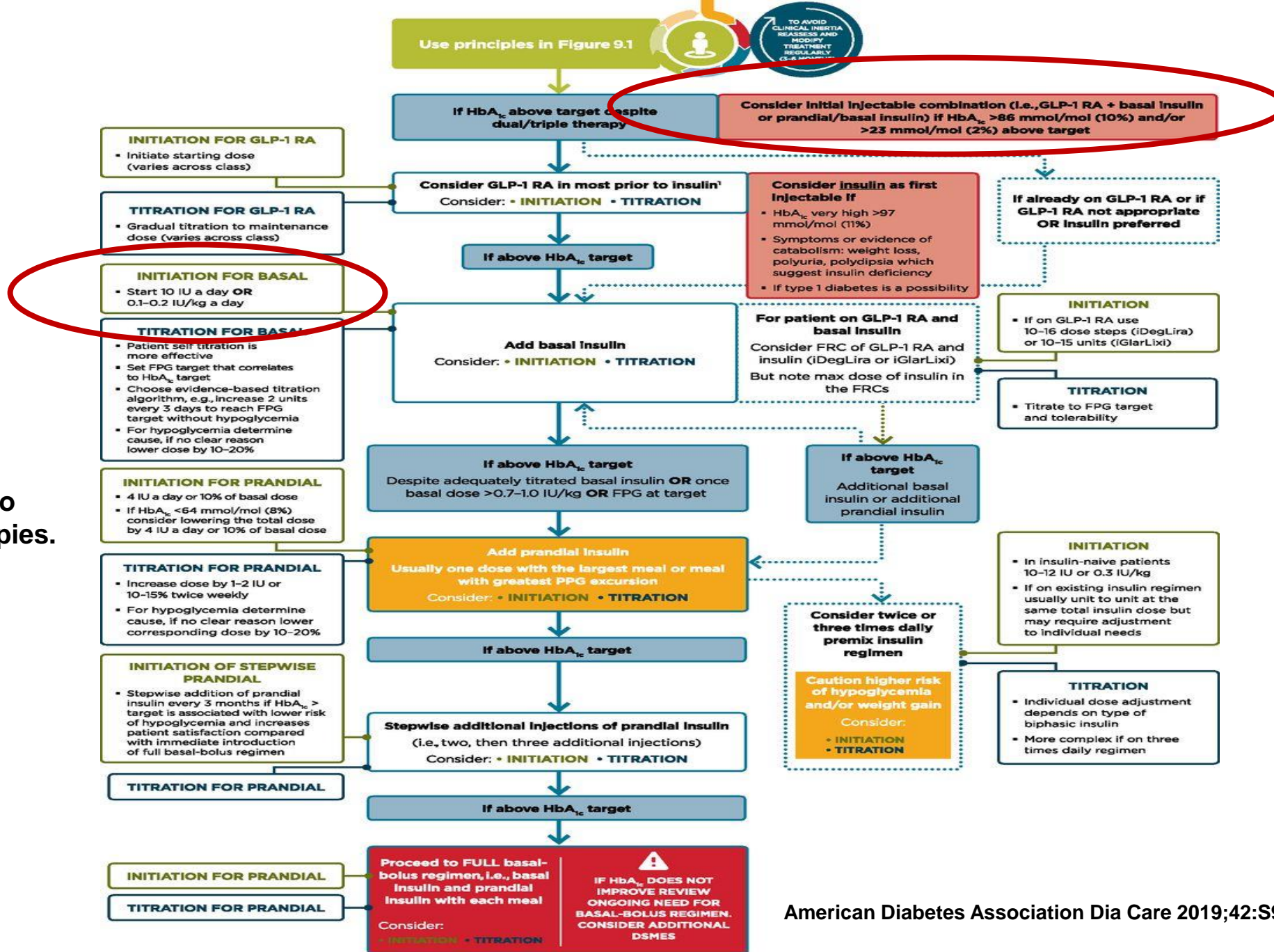
I disagree with starting at such a low dose 10 units on most people.. Lets discuss why!



American Diabetes Association Dia Care 2018;41:S73-S85

I agree with the simple way they recommend titrating insulin

Intensifying to injectable therapies.



American Diabetes Association Dia Care 2019;42:S90-S102



Teaching Points:

- **Basal insulin:**

- Remember objective of basal insulin is to restrain hepatic glucose production and limit fasting hyperglycemia
- Avoid over-basalization : basal doses of > 0.5 units/kg indicate time to add pre meal insulin
- Do not start same amount of insulin on 50Kg person as 100 Kg person
- Consideration to cost must be part of the decision making process in choosing a basal insulin

Insulin Initiation/ understand the concept of replacement

1. Math-start with weight based calculation
2. Individualize based on the patient characteristics
3. ****Your comfort level****

3 STEPS to predicting insulin dose

1. Calculate Total Daily Dose (TDD)
2. Separate TDD into multi-dosing(basal/bolus)
3. Determine Correction factor

Typical insulin dose in type 1 DM vs. Type II

- For insulin sensitive DM patient, the total daily insulin is **~0.4units/kg**
“typical” for type 1 is 0.5-0.7u/kg (0.25-0.35u/kg basal)
- For insulin resistant patient/ D type 2, the total daily insulin ranges
from **~0.5 units /kg – 1.0 +unit/kg** (0.25-0.5u/kg basal)

STEP 1:

WHAT'S THE TOTAL DAILY DOSE (TDD)?

Factors that influence the dose of insulin :

- Age
- Renal function
- Weight
- Medications like steroids

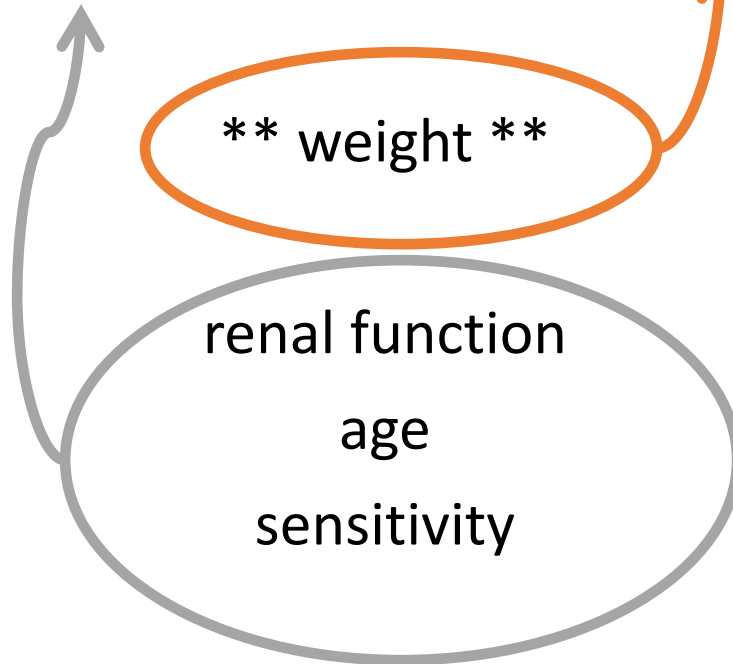
0.2 – 1.0 units * kg

**** weight ****

renal function

age

sensitivity



Estimating starting total daily insulin and dividing TTD by 2: step 2

Need less insulin:

- For BMI <25 (BMI low or at ideal body weight) ~0.4 u/kg (0.2u/kg basal)
- Poor kidney function: Cr>2 /GFR <15 and/or age>70: The total daily insulin is ~0.2 units/kg (.1-.2units /kg basal)
- For a GFR of 15-30: the total daily insulin is ~0.3 u/kg (0.15-0.2u/kg basal)

Type 2 DM insulin initiation

- Patients with type 2 DM are resistant especially with a1c >9-10 they are glucose toxic!!
- Higher BMI= more insulin resistance....(so need to become more comfortable with higher starting doses of insulin)

The challenge:

- Finding **the balance between rapidly improving blood sugar vs. risk for hypoglycemia**

Type 2 DM

- **Another high yield teaching point:** If patient is on $>1.0\text{u/kg}$ insulin

Question if patient taking insulin regularly/as instructed

Compliance may be the issue

As well typically over $.5\text{u/kg}$ for basal no clear benefit for increasing basal. so think about prandial insulin and or intensifying insulin sparing agents

STEP 3: Understand Correction Factor

“Correction Factor (CF)” = estimate of the glucose points dropped per unit of insulin

**When the glucose is too high,
how much extra insulin do you give?**

Use CF to make a *patient-personalized* “correctional” scale

STEP 3:

CORRECTION FACTOR(CF)

Use 1700 (some use 1800 or 1500)

$$CF = 1700 / TDD$$

Pt is on 50 units bid lantus, BMI 35 and wt 100kg

Insulin dose is 1u/kg

$$1700/100= 17$$

Current sugar is 200

then 1 unit of insulin should drop the pt 17 points so to

183

Timeline of insulin development

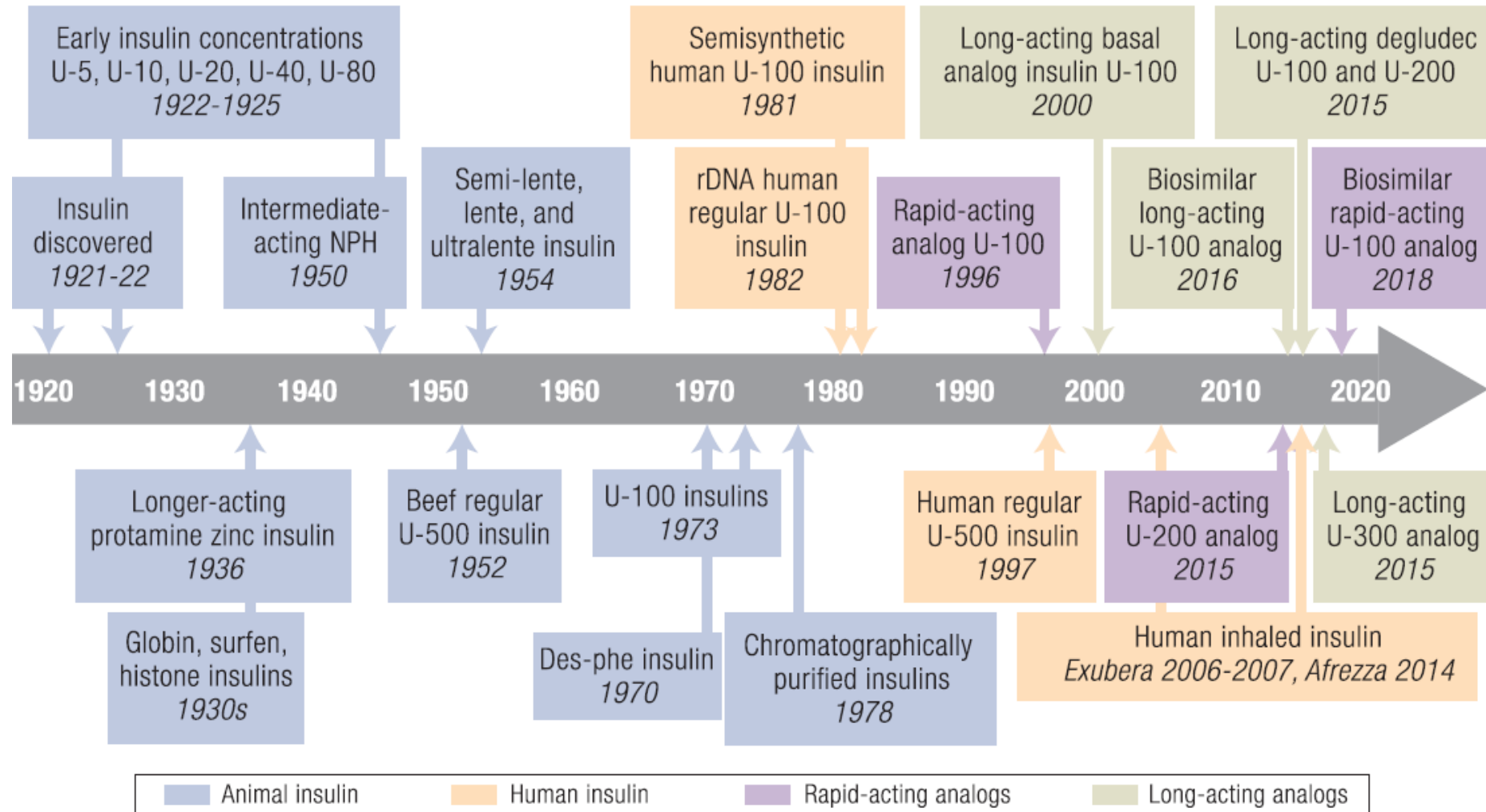


Figure 1. Timeline of insulin development with approximate historical dates. Abbreviations: NPH, neutral protamine Hagedorn; rDNA, recombinant DNA; U = units.

Insulin Types: BASAL INSULIN

<i>INSULIN TYPE</i>	<i>ONSET</i>	<i>PEAK</i>	<i>DURATION</i>
Long-acting			
Detemir (Levemir)	3 to 4 hours	6 to 8 hours	6 to up to 24 hours (18-24 hours average)
Glargine (Lantus)	90 minutes	None	24 hours
Intermediate-acting			
NPH (Humulin N)	1 to 2 hours	4 to 10 hours	14 or more hours
Degludec (Tresiba)*	1 hour	None	<42 hours
Glargine u100/ (Basaglar)	90 minutes	None	24 hours
Glargine/ U300 Toujeo			

Typically needs to be given twice a day. ??slightly less weight gain

Newer Kids on the block

Table 1.
**Pharmacokinetic Profiles
of Insulin Therapies**

Max dose of Basal insulin per injection

- Tresiba(Degludec) u200: FlexTouch[®] is a 160-unit maximum-dose pen
- Lantus(glargine) u100[®] SoloSTAR[®] is an 80-unit maximum-dose pen

Prandial Insulin

Prandial	onset	peak	duration	
Regular*	~0.5-1	~2-3	Up to 8	<ul style="list-style-type: none"> Must be injected 30-45 min before a meal Injection with or after a meal could increase risk for hypoglycemia
Aspart (novolog)	<0.5	~0.5-2.5	~3-5	<ul style="list-style-type: none"> Can be injected 0-15 min before a meal Less risk of postprandial hypoglycemia compared to regular insulin
Glulisine (Apidra)				
Lispro (Humalog)				

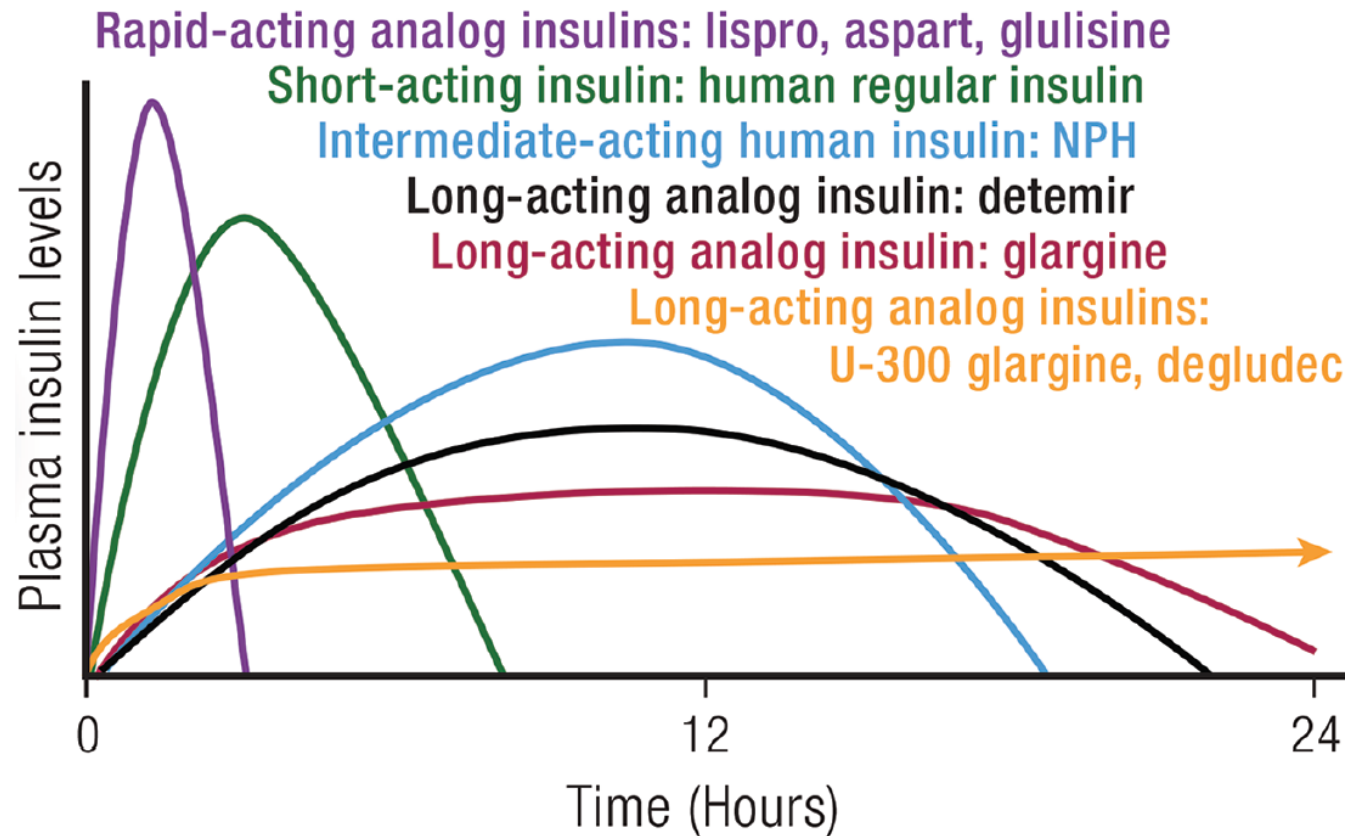
* Exhibits a peak at higher dosages.

† Dose-dependent

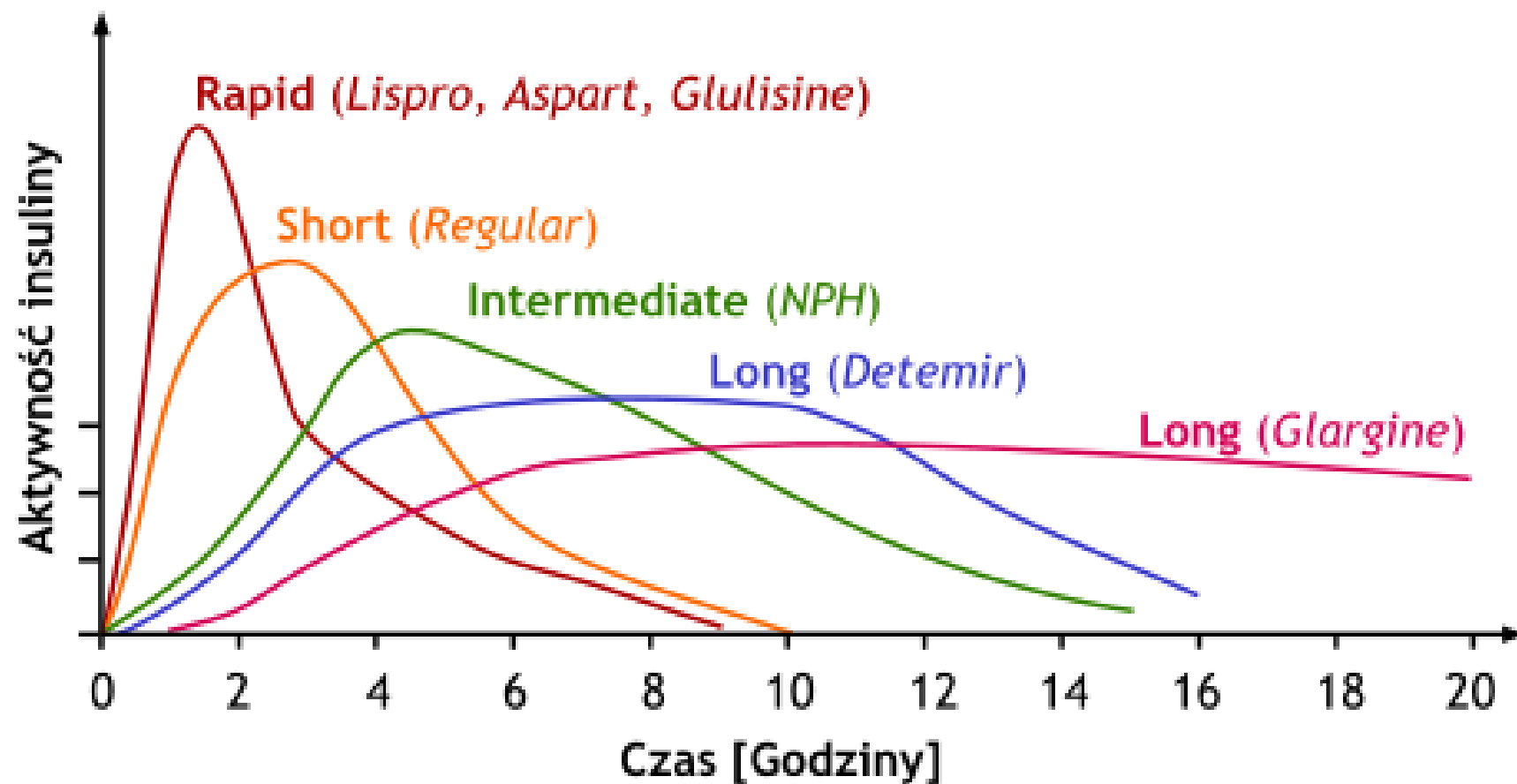
* Over the counter insulin

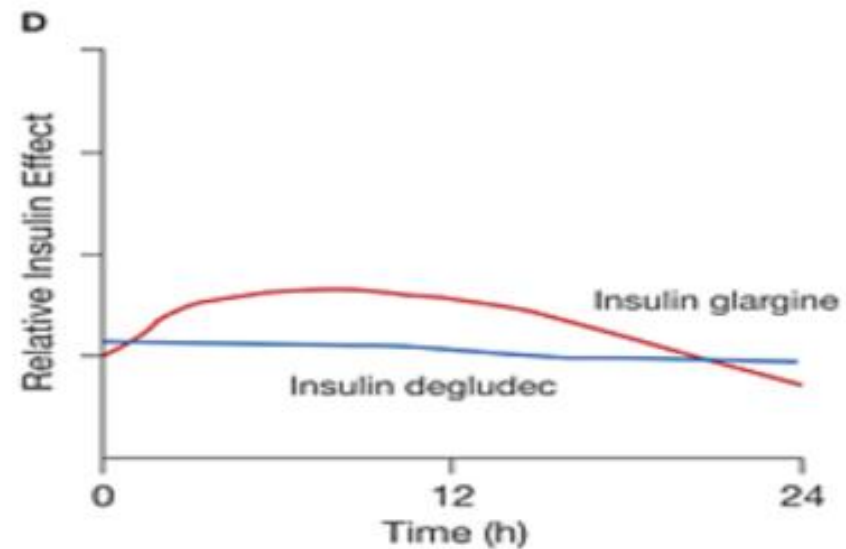
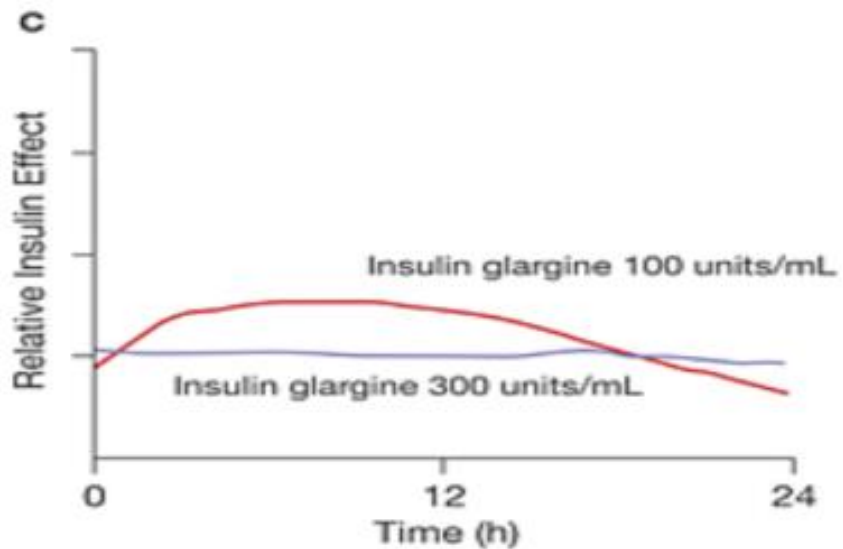
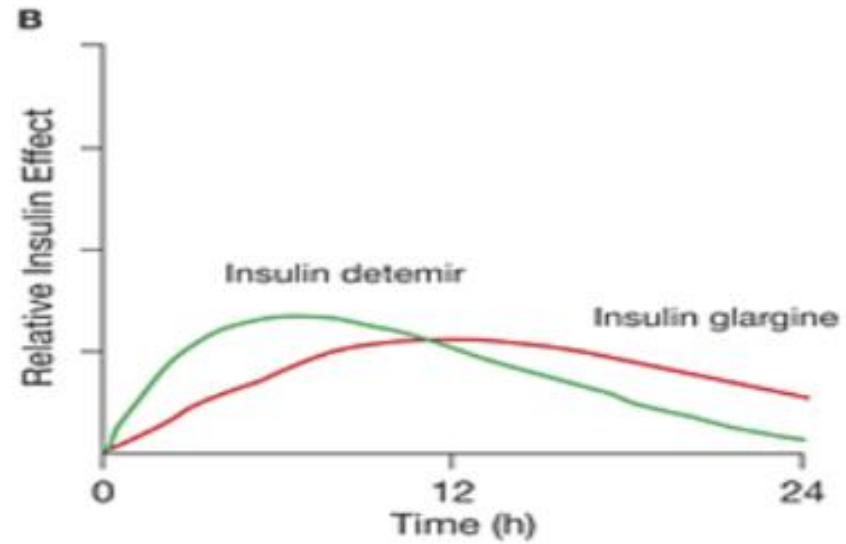
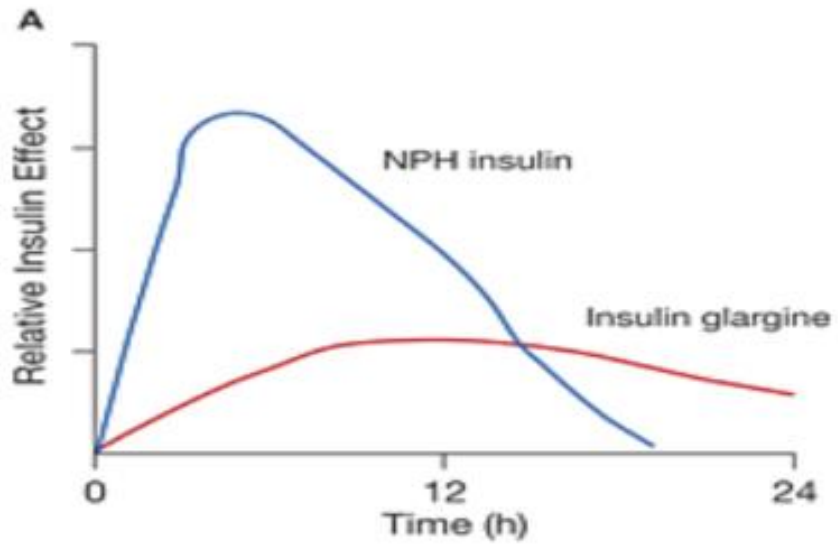
- [ADMELOG® \(insulin lispro - injection\) 100 Units/mL Pen](#)

Duration of Insulin



Duration of Insulin





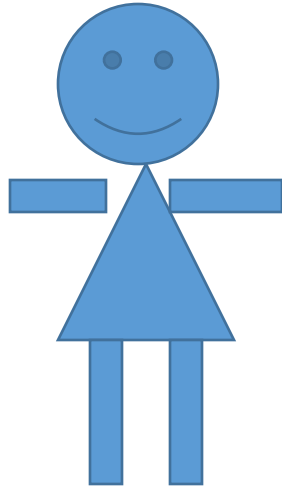
De Groot LJ, Chrousos G, Dungan K, et al., editors.
South Dartmouth (MA): MDText.com, Inc.;

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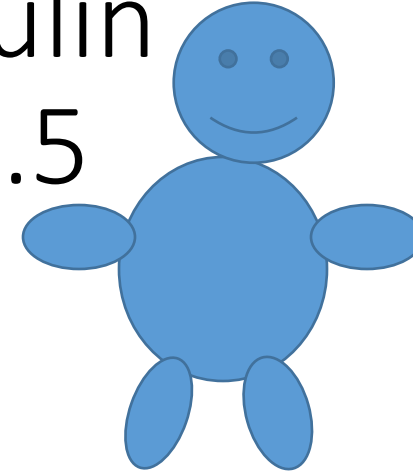
Consider when
TDD >250 units

Required TDD ^b (Units)	Route and Frequency ^{c,d}	U-500 Insulin Dosage ^e
150–300	Twice daily	50/50 or 60/40 before breakfast and supper
	Three times daily	33/33/33 before meals
	CSII	Three mealtime bolus doses = 50% TDD plus 24-hr basal insulin infusion = 50% TDD
300–600	Three times daily	33/33/33 before meals
	Four times daily	30/30/30/10 (mealtimes and bedtime)
	CSII	Three mealtime bolus doses = 50% TDD plus 24-hr basal insulin infusion = 50% TDD
>600	Four times daily	30/30/30/10 (mealtimes and bedtime)

Hello!



Start me on Insulin
My a1c is 10.5



80 kg

72 yo F

Type II DM

GFR 30

Dm for 20 yrs

Conservative !!

110 kg

52 yo

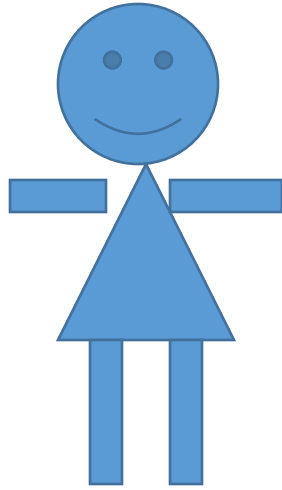
Type II DM

nmI GFR

Dm for 1 yr

Aggressive !!

Hello!



What is her total daily insulin?

0.2-0.4 unit/kg

80 kg

72 yo F

Type II DM

GFR 30

Dm for 20 yrs

Conservative !!

80kg x .1-.2u=8-16 units basal insulin

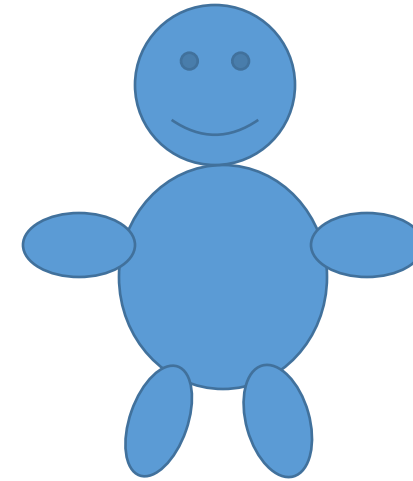
Prandial:

.1-.2u=8-16 bolus /3= 3-5 units with meals

Correction: $1700/20=85$

Hello!

- $110\text{kg} \times .3-.5\text{u}=33-55$ units basal insulin
- How do you titrate up basal insulin?



110 kg

52 yo

Type II DM

nml GFR

Dm for 1 yr

Aggressive !!

Titration of Basal Insulin

Treat-to-Target Trial's Titration Schedule for Basal Insulin in Patients with Diabetes Mellitus

<i>FASTING GLUCOSE LEVEL</i>	<i>INCREASE IN BASAL INSULIN</i>
120 to 140 mg per dL (6.66 to 7.77 mmol per L)	2 units
141 to 160 mg per dL (7.83 to 8.88 mmol per L)	4 units
161 to 180 mg per dL (8.94 to 9.99 mmol per L)	6 units
> 180 mg per dL (9.99 mmol per L)	8 units

Teaching: Adjust Insulin daily

- For blood sugars less than 100, reduce the total daily insulin by 10%
- For blood sugars less than 70, reduce the total daily insulin by 20%
- For fasting blood sugars persistently greater than 180, increase the total daily insulin by 10%
- For fasting blood sugars persistently greater than 200, increase the total daily insulin by 20%

INSULIN ADJUSTMENT:

Type of insulin:_____

Take one shot of insulin at bedtime.

Your starting dose is _____units of insulin.

Take your fasting blood sugar every **day before breakfast**.

You will adjust your insulin to normalize your before breakfast fingerstick blood sugar.

If your morning fingerstick blood sugar remains greater than 150 for 3 days in a row, increase your insulin dose by 2 units.

Continue to increase your dose by 2 units every 3 days until your morning glucose is less than 150

If you experience unexplained low blood sugars (<70) at any time of the day, call your health care provider. **Do not increase your insulin and reduce by 4 units.**

If your blood sugar is less than 100 two mornings in row then Decrease your insulin dose by 2 units.

- **SLIDING SCALE INSULIN**
Use *Regular (R)*, *NovoLog (aspart®)* or *Humalog(Lispro®)* Or *APIDRA®* for the sliding scale.

Check your fingerstick blood sugar _____times a day and record.

Give Reg, NovoLog, Humalog, APIDRA insulin before meals only according to the following scale and premeal directions.

Take _____units prior to breakfast.

Take _____units prior to lunch

Take _____units prior to dinner

<u>Blood sugar reading</u>	<u>Action</u>
<70	Eat or drink 15 gm of carbohydrate (CHO): ½ c of fruit juice, 1 c skim milk, or 3 glucose tablets. You may also have typical meal and <u>take ½ dose of premeal insulin</u>

<u>80</u> - <u>140</u>	No additional premeal insulin
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<u>141</u> - <u>170</u>	Inject 1units
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<u>171</u> - <u>200</u>	Inject 2units
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<u>201</u> - <u>230</u>	inject 3 units
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Etc...

At bedtime do not correct your blood sugars unless >180 then take ½ correction dose

Summary teaching points

- Start at 0.3u/kg or more for basal insulin initiation for those with a1c >9-10, especially in those that are younger and without renal issues
- Start at .1-.2 u/kg if concern for low blood sugars (renal, older age, lower BMI)
- Ensure they understand how to increase or decrease their insulin(ensure they can use a meter and have one and supplies!!)
- Ensure they are taking insulin /have picked up- **call one week after start**
- Partner with them to encourage lifestyle changes as a way to come off insulin and **see them for close follow-up in 1 month** so they are motivated to change....and then consider insulin sparing agents if sugars improved.