

# Introduction to most commonly used approaches for T2 Insulin Treatment

25 February, 2019

# Diabetes Specialist Guidelines for Approaches for T2 Insulin Treatment

[American Diabetes Association | Resources For Professionals  
www.knowdiabetesbyheart.org/professional/guidelines](https://www.knowdiabetesbyheart.org/professional/guidelines)

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**AACE/ACE Clinical Practice Guidelines** for Developing a **Diabetes** Mellitus ... American Association of Clinical Endocrinologists and American **Diabetes** Association. Comprehensive Type 2 Diabetes Management Algorithm

[EASD: https://www.easd.org](https://www.easd.org)

The European Foundation for the Study of Diabetes (EFSD)

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The global advocate for people with diabetes. The mission of **IDF** is to promote diabetes care, prevention and a cure worldwide.

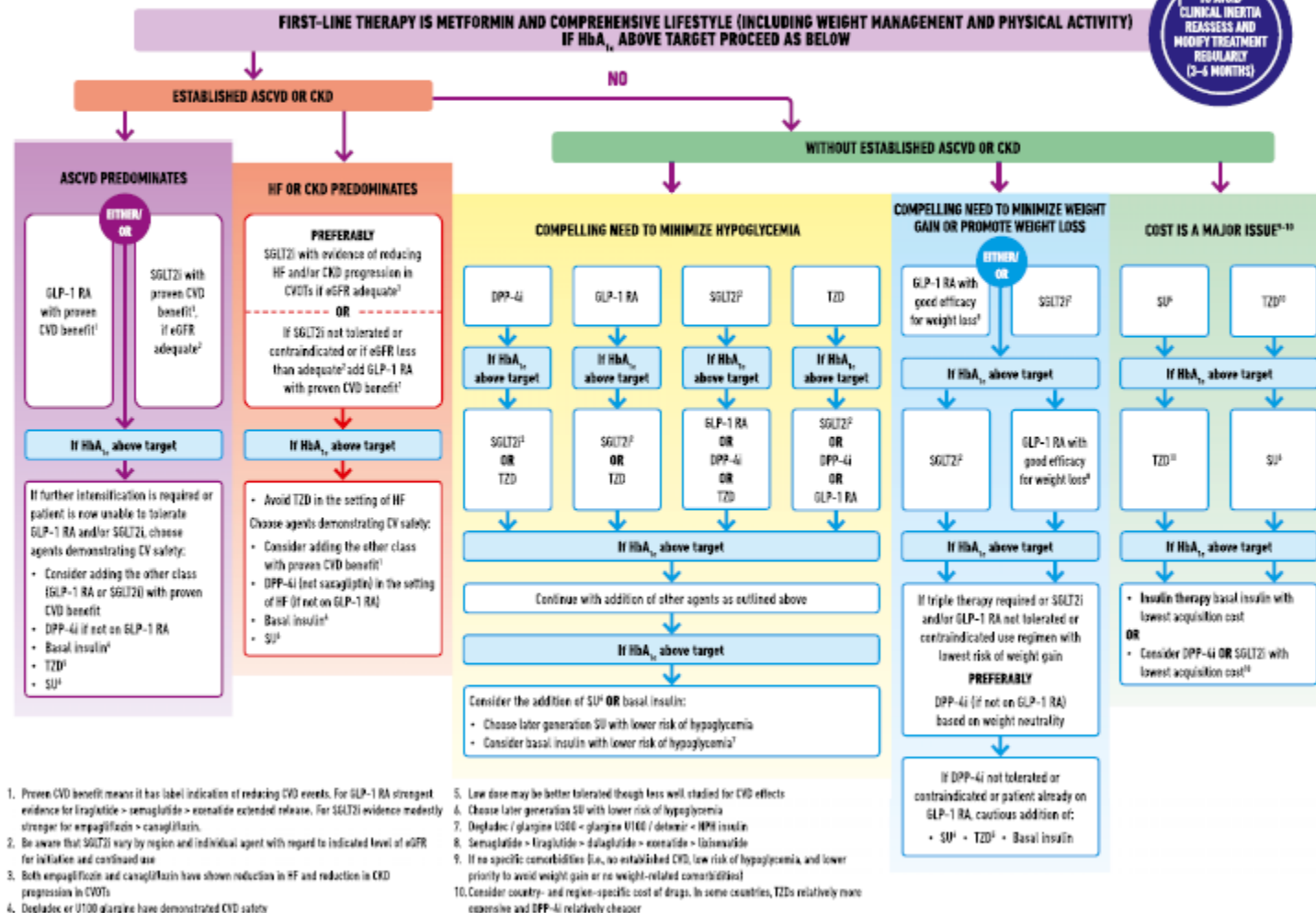
# Insulin Treatment of T2 Diabetes

## A Summary for Clinicians

### Epidemiology

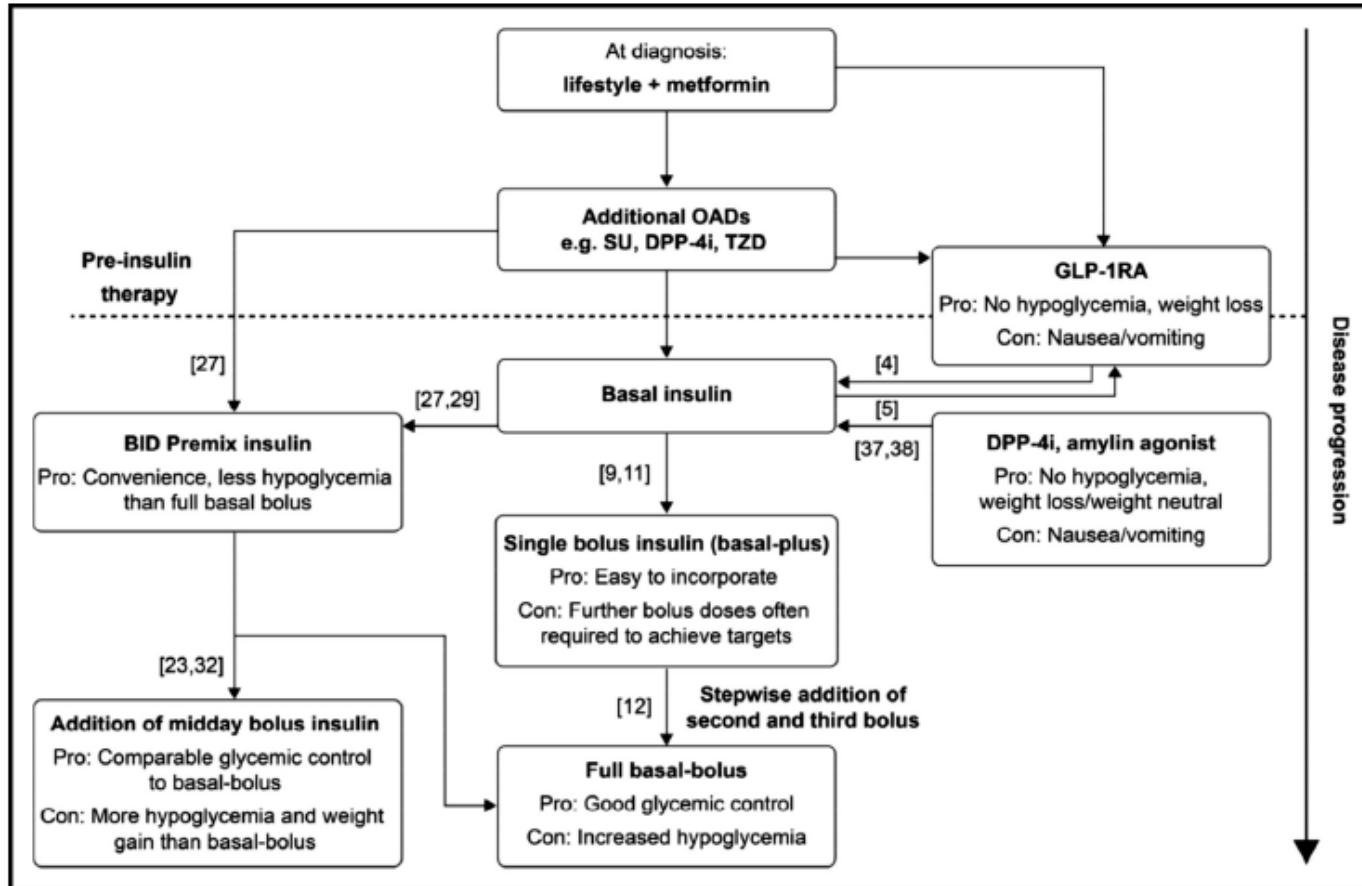
- By 2025 1 in 3 in the U.S.
- At the time of diagnosis, 50% of pancreatic beta cells have died.
- T2 is progressive, so ultimately in 5-10 years, pancreas is not secreting insulin
- 60% have HbA1c > 7%, (where oral treatment usually starts), the population average is 8.1%, range is 6.9% - 13.0%.
- Insulin should be started when HbA1c > 9.0%
- UKPDS showed that lowering HbA1c by 1% reduces Microvascular complications by 37%, lowers risk of Diabetes-related death by 21% and lowers risk of MI by 14%.
- The three stages to insulin therapy include:
  - Initiation
  - Optimization
  - Intensification

# GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



**Figure 2—Glucose-lowering medication in type 2 diabetes: overall approach.** CV, cardiovascular; DPP-4i, dipeptidyl peptidase 4 inhibitor; GLP-1 RA, glucagon-like peptide 1 receptor agonist; SGLT2i, SGLT2 inhibitor; SU, sulfonylurea.

## Suggested Treatment Intensification Routes

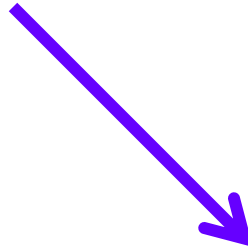


**Figure** Simple flow diagram showing the suggested treatment intensification routes available to patients with T2D as the disease progresses.

BID = twice daily; DPP-4i = dipeptidyl peptidase-4 inhibitor; OAD = oral antidiabetic drug; SU = sulfonylurea; T2D = type 2 diabetes; TZD = thiazolidinedione.

# Oral Diabetes Medications

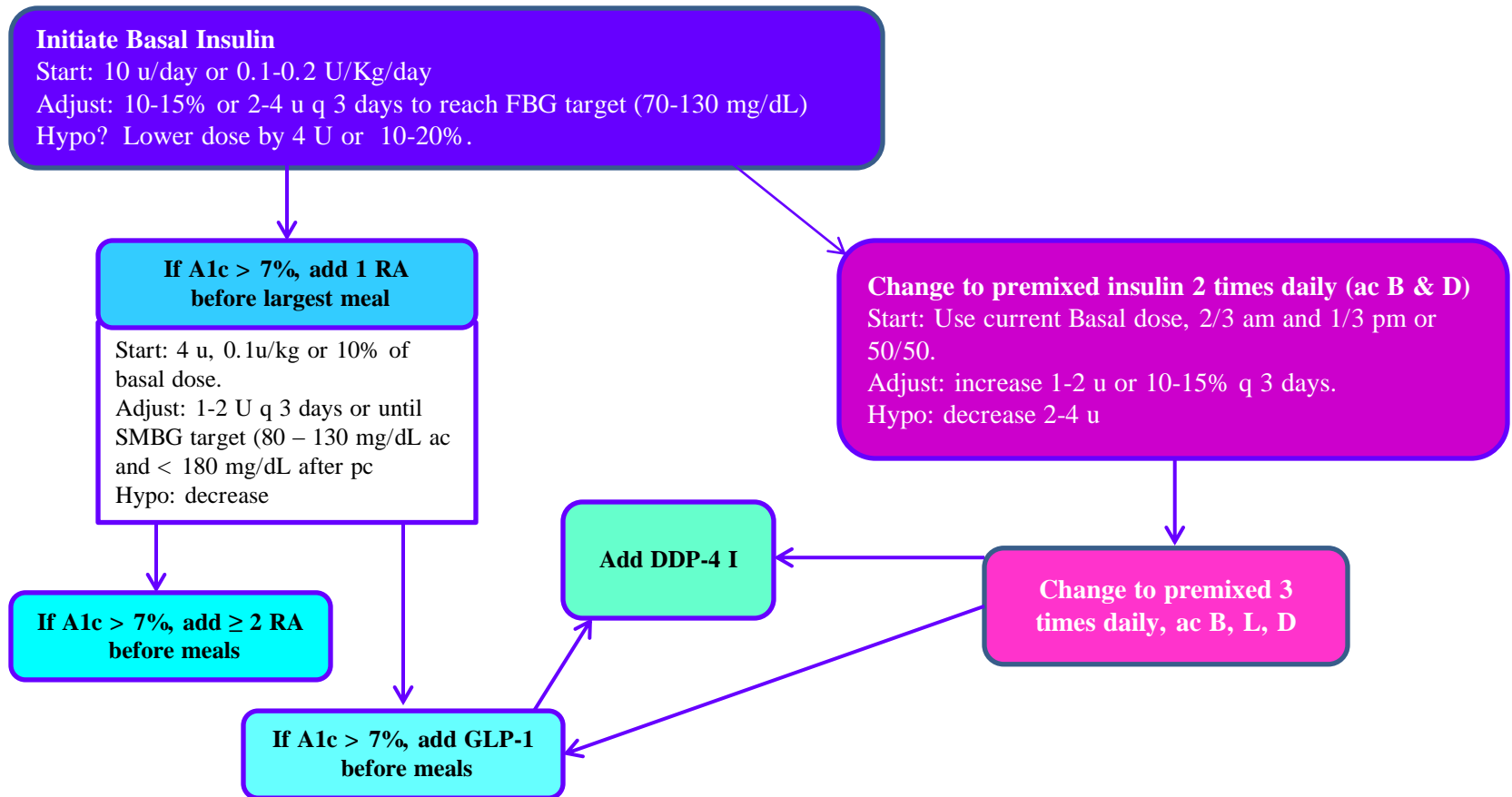
A1c < 9% = Monotherapy (Metformin)  
9-10% = Dual therapy (Met + SGLT2; vs. DPP-4; vs. SFN or  
or Triple therapy ( 3 of above)  
≥ 10% + BG ≥ 300 mg/dL = combination injectable therapy



Initiate Basal Insulin

Diabetes Care 2018; 41(Suppl. 1):S1-S159

# Initiate Insulin Therapy



AJM 2013; 126 (9A):S21-S27.

Diabetes Care 2018; 41(Suppl.1):S1-S159.

# Candidate Methods: Insulin Intensification 1

## Basal/Bolus Insulin Initiation and Titration: Meneghini

### Calculate initial insulin doses:

- Basal insulin dose = subject wt. in kg  $\div$  4
- Prandial insulin dose = subject wt. in kg  $\div$  12

Initiate basal once daily in the evening or at bedtime

Initiate prandial 15 min. before each meal

### Targets:

- FBG = 70 – 120 mg/dL
- Preprandial = 90 – 126 mg/dL

### Adjustments:

- Adjust by  $\pm$  2 units every 4-7 days until target BG levels are achieved.

**Adjust Basal- Use Fasting BG**

**Adjust pre-breakfast- Use pre-lunch BG (prior day)**

**Adjust pre-lunch- Use pre-dinner BG**

**Adjust pre-dinner- Use pre bedtime BG**

AJM 2013; 126 (9A):S21-S27.



# Candidate Methods: Insulin Intensification 1

## Prandial Bolus Initiation and Titration: Meneghini

**Table 4** Insulin Titration Algorithms for the STEPwise Study\*

IDet titration		SimpleSTEP			ExtraSTEP	
Prebreakfast PG Levels (mg/dL)	IDet Dose Adjustment	Premeal PG Levels (mg/dL)	Bedtime PG Levels (mg/dL)	IAsp Dose Adjustment	2-hour Postmeal PG Levels (mg/dL)	IAsp Dose Adjustment
56†	−4 U					
56-71†	−2 U	<72†	<72†	−2 U	<72†	−2 U
72-108	0	72-108	72-144	0	72-144	0
109-144	+2 U	109-162	145-180	+2 U	145-180	+2 U
145-162	+4 U	>162	>180	+4 U	>180	+4 U
>162	+6 U					
IDet titrated based on average of 3 PG measurements before breakfast		IAsp added to largest self-reported meal. Titration based on premeal/bedtime PG levels from 4 daily PG measurements			IAsp added to meal with largest PG increment. Titration based on postmeal PG levels from 6 daily PG measurements	

IAsp = insulin aspart; IDet = insulin detemir; PG = plasma glucose; U = unit.

\*© 2009 AACE, reproduced with permission, from Meneghini et al, *Endocr Pract.* 2011;17:727-736.<sup>14</sup>

†One or more PG values <72 mg/dL (4.0 mmol/L) without obvious explanation.

AJM 2013; 126 (9A):S21-S27.

# Candidate Methods: Insulin Intensification 2

## Basal/Bolus Insulin Initiation and Titration: Bergenstahl

Insulin glargine adjustments: both groups

Mean of last 3-day fasting SMBG mg/dl	Adjustment
>180 mg/dl	Increase 8 units
140–180 mg/dl	Increase 6 units
120–139 mg/dl	Increase 4 units
95–119 mg/dl	Increase 2units
70–94 mg/dl	No change
<70 mg/dl	Decrease by the same number of units as insulin glulisine increase that titration week or up to 10% of total insulin glargine dose

Insulin glulisine adjustments: simple algorithm group

Mealtime dose	Pattern of mealtime blood glucose values below target*	Pattern of mealtime blood glucose values above target†
≤10 units	Decrease by 1 unit	Increase by 1 unit
>11–19 units	Decrease by 2 units	Increase by 2 units
≥20 units	Decrease by 3 units	Increase by 3 units

Insulin glulisine adjustments: carbohydrate counting (insulin-to-carbohydrate ratio) group‡

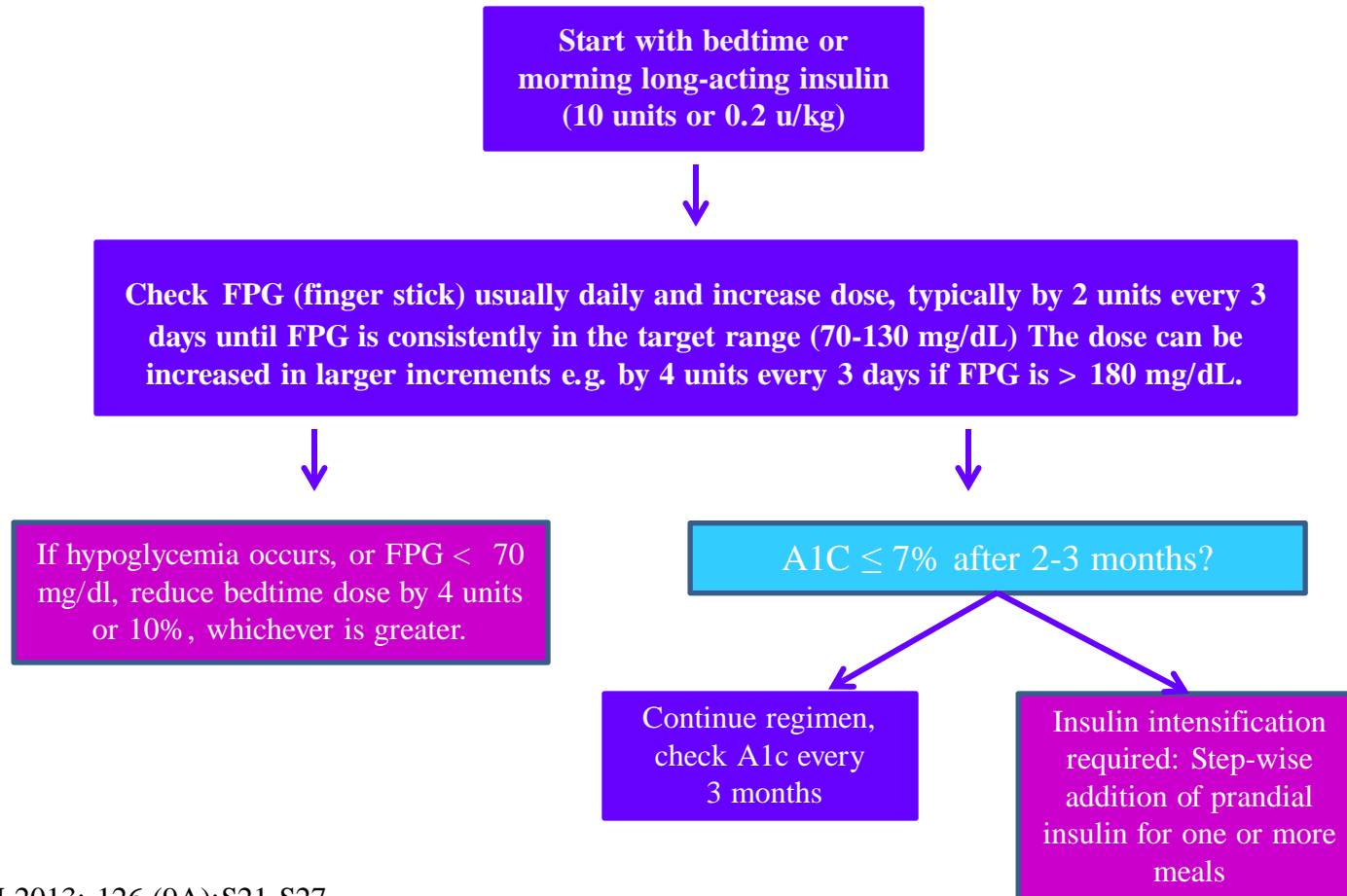
Mealtime dose	Pattern of mealtime blood glucose values below target*	Pattern of mealtime blood glucose values above target†
1 unit/20 g	Decrease to 1 unit/25 g	Increase to 1 unit/15 g
1 unit/15 g	Decrease to 1 unit/20 g	Increase to 1 unit/10 g
1 unit/10 g	Decrease to 1 unit/15 g	Increase to 2 units/15 g
2 units/15 g	Decrease to 1 unit/10 g	Increase to 3 units/15 g
3 units/15 g§	Decrease to 2 units/15 g	Increase to 4 units/15 g

\*If more than one-half of the mealtime blood glucose values for the week were below target. †If more than one-half of the mealtime blood glucose values for the week were above target. ‡Each patient in the carb count group was also given a schedule for a mealtime insulin glulisine correction dose to add a few units if high or subtract a few units if low. §Increase mealtime insulin as needed following this pattern.

Diabetes Care 2008; 31(7):1305-1310.

# Candidate Methods: Insulin Intensification 3

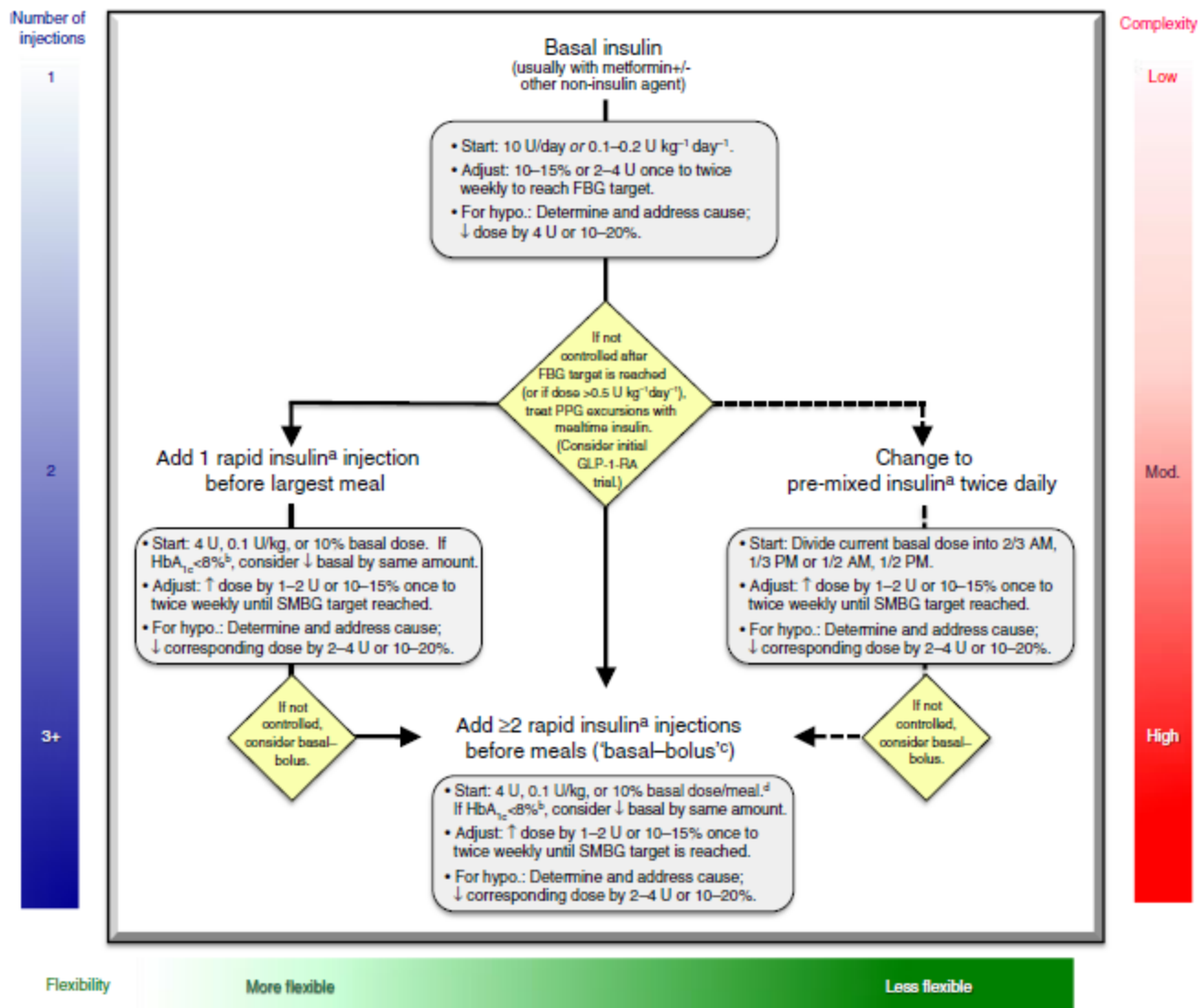
## Basal/Bolus Insulin Initiation and Titration: Scripps\_ADA



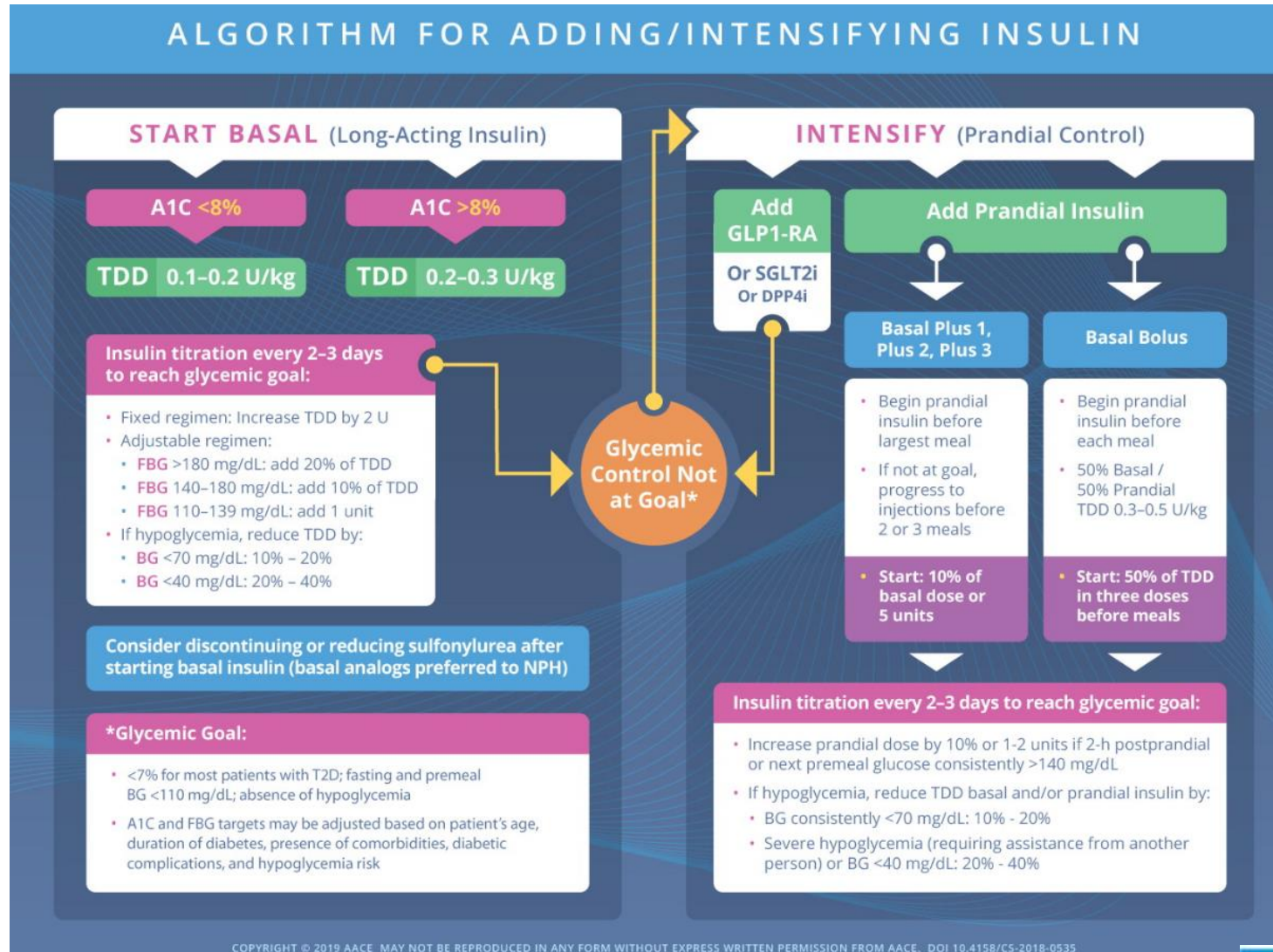
AJM 2013; 126 (9A):S21-S27.

# Candidate Methods: Insulin Intensification 4 – ADA/EASD 2015

Updated  
2018

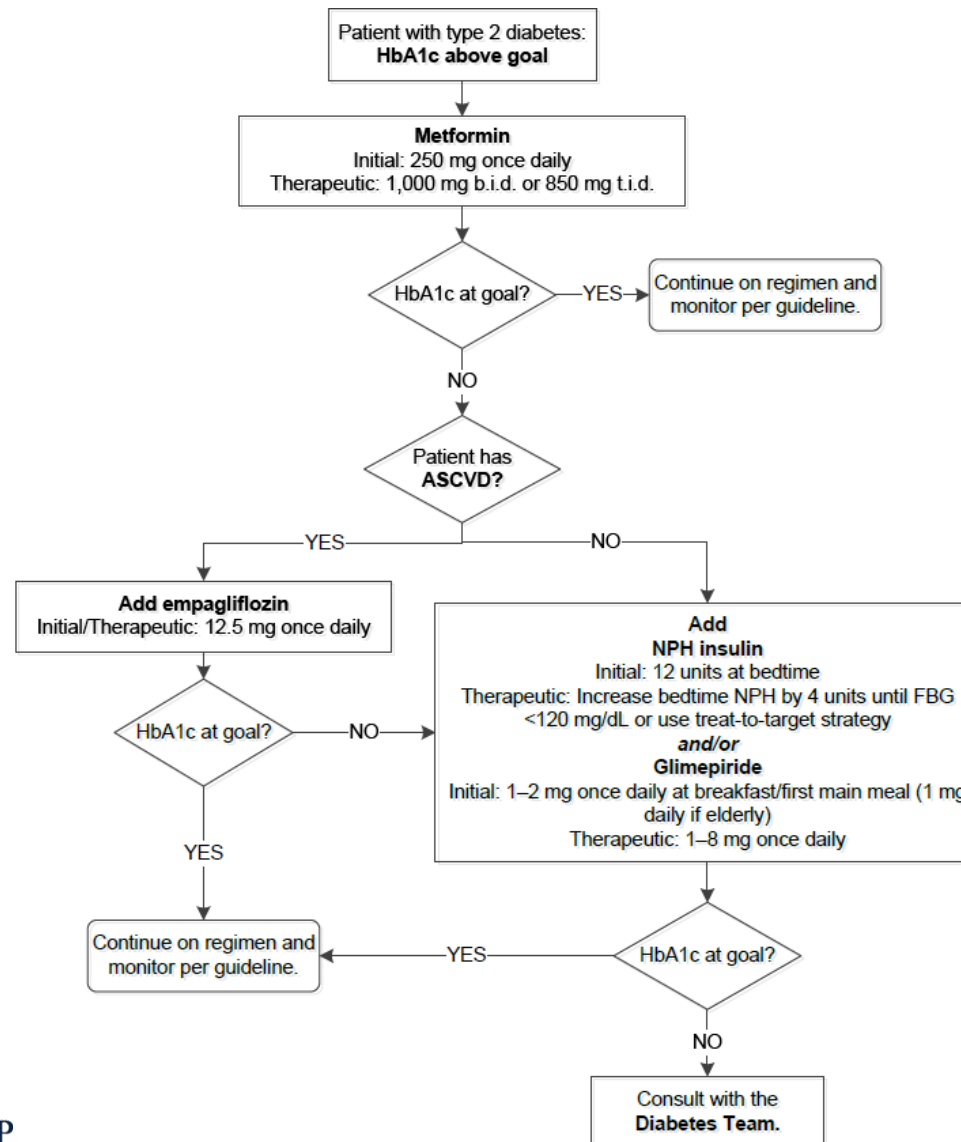


# Candidate Methods: Insulin Initiation/Intensification AACE/ACE



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# Candidate Methods: Insulin Initiation/Intensification: Kaiser



# Approaches to Post-prandial Correction

# Approaches to Using Trend Arrows with Libre

FreeStyle Libre System Trend Arrows		
Reader	Glucose Direction	Change in Glucose
↑	Rising quickly	<b>Glucose is rising quickly</b> Increasing >2 mg/dL/min or >60 mg/dL in 30 minutes
↗	Rising	<b>Glucose is rising</b> Increasing 1–2 mg/dL/min or 30–60 mg/dL in 30 minutes
→	Changing slowly	<b>Glucose is changing slowly</b> Not increasing/decreasing >1 mg/dL/min
↘	Falling	<b>Glucose is falling</b> Decreasing 1–2 mg/dL/min or 30–60 mg/dL in 30 minutes
↓	Falling quickly	<b>Glucose is falling quickly</b> Decreasing >2 mg/dL/min or >60 mg/dL in 30 minutes
No arrow present indicates that the system cannot calculate the velocity and direction of the glucose change.		

Kudva et al, J Endo Society 2018; 2(12):1-18.



# Approaches to Using Trend Arrows with Libre

Insulin Dose Adjustments Using the FreeStyle Libre System Trend Arrows in Adults: Pre-meal and Corrections ≥4 Hours Post-meal				
Insulin Dose Adjustments				
FreeStyle Libre Trend Arrows	Correction Factor* (CF)			
	<25	25–<50	50–<75	≥75
↑	+3.5 units	+2.5 units	+1.5 units	+1.0 units
↗	+2.5 units	+1.5 units	+1.0 units	+0.5 units
→	No adjustment	No adjustment	No adjustment	No adjustment
↘	-2.5 units	-1.5 units	-1.0 units	-0.5 units
↓	-3.5 units	-2.5 units	-1.5 units	-1.0 units
Insulin dose adjustments using trend arrows do not replace standard calculations using ICR and CF. Adjustments are increases or decreases of rapid-acting insulin in addition to calculations using ICR and CF. Adjustments using trend arrows are an additional step to standard care.				
*Correction factor (CF) is in mg/dL and indicates glucose lowering per unit of rapid-acting insulin.				
Considerations				
<p><b>Mealtime is ideal to begin applying insulin dose adjustments using trend arrows.</b> For the 4 hours following a meal, refer to <i>Figure 3</i> for an approach to minimize hypo- and hyperglycemia during this timeframe.</p> <p><b>For rapidly rising sensor glucose</b> (UP arrow; ↑) at pre-meal, consider administering insulin 15–30 minutes before eating.</p> <p><b>For rapidly falling sensor glucose</b> (DOWN arrow; ↓):</p> <ul style="list-style-type: none"> <li>• Pre-meal: consider administering insulin closer to the meal</li> <li>• Near or lower than 150 mg/dL: consider holding pre-meal insulin dose until glucose trends have stabilized</li> </ul> <p><b>For frail or older adults</b>, start conservatively to reduce hypoglycemia risk:</p> <ul style="list-style-type: none"> <li>• Upward arrows: reduce dose increase by at least 50% (e.g., +1.0 units may become +0.5 units or no insulin increase)</li> <li>• Downward arrows: increase dose reduction by at least 50% (e.g., -1.0 units may become -1.5 or -2.0 units)</li> </ul> <p><b>When rounding of insulin dose is needed:</b></p> <ul style="list-style-type: none"> <li>• Calculate total insulin dose using insulin dosing parameters for food intake (if any), correction, and trend arrow adjustment</li> <li>• Round to the nearest whole number or half unit as appropriate</li> <li>• If at a midpoint (i.e., 0.5 units) and needing to round to a whole number: <ul style="list-style-type: none"> <li>◦ Round up when flat or upward arrow is present</li> <li>◦ Round down when downward arrow is present</li> </ul> </li> </ul>				

# Approaches to Using Trend Arrows with Libre

Kudva et al, J Endo Society 2018; 2(12):1-18.

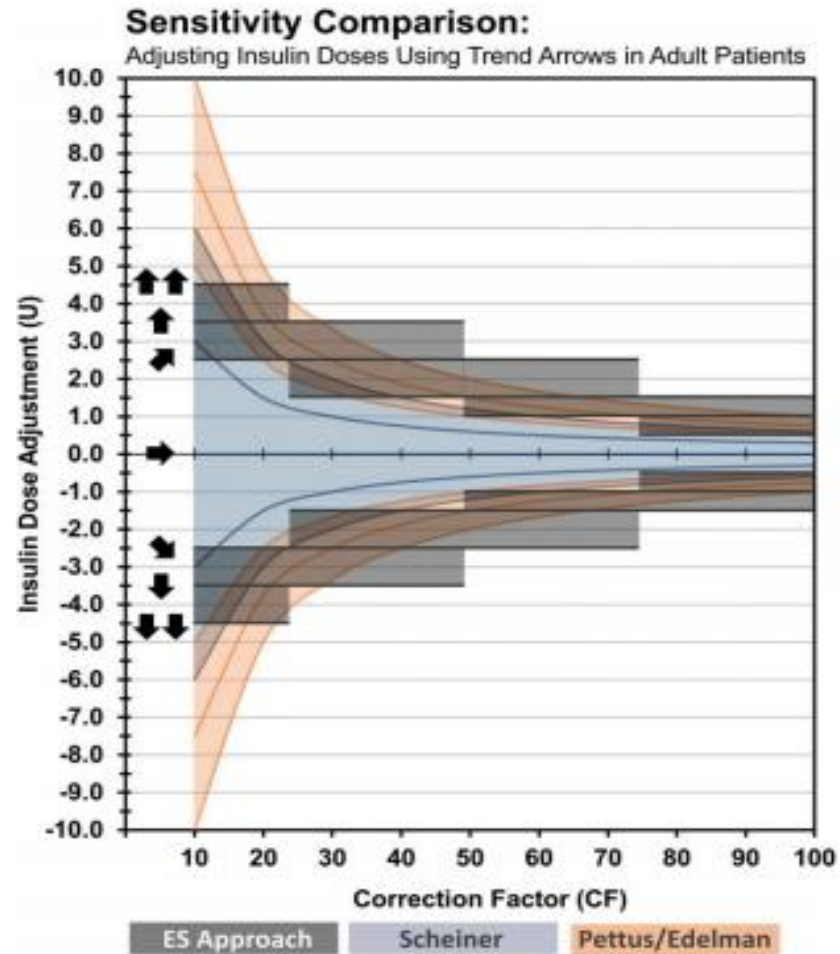
Post-meal Scanning and Treatment Decisions for MDI and CSII-Treated Patients Using the FreeStyle Libre Systems	
During the 4 hours following mealtime bolus, individuals needing corrective action should rely on current sensor glucose and predetermined ICR and CF values. Avoid taking additional bolus insulin doses within the first 2 hours to prevent insulin stacking.	
2–4 hr Post-meal Glucose Concentration	
>250 mg/dL	
FreeStyle Libre Trend Arrows	Action
↑	Take corrective action using bolus insulin dose based on CF. Re-scan in 1 hour. If up arrow persists after additional hour: • Confirm with fingerstick • Change infusion site (if using an insulin pump) • Take additional corrective insulin dose based on CF
↗	Take corrective action using bolus insulin dose based on CF. Re-scan in 1 hour. Avoid additional correction doses for 2 hours,
→	No action needed. Rescan in 1 hour.
↘	No action needed. Rescan in 1 hour,
↓	No action needed. Rescan in 1 hour.
181–250 mg/dL	
↑	Consider corrective action using bolus insulin dose based on CF. Re-scan in 1 hour. Avoid additional correction doses for 2 hours,
↗	Consider corrective action using bolus insulin dose based on CF. Re-scan in 1 hour. Avoid additional correction doses for 2 hours,
→	No action needed. Rescan in 1 hour.
↘	No action needed. Rescan in 30 minutes,
↓	No action needed. Rescan in 30 minutes,
70–180 mg/dL	
↑	No action needed. Rescan in 1 hour.
↗	No action needed. Rescan in 1 hour.
→	No action needed. Rescan in 1 hour.
↘	Ingest 15 g fast-acting carbohydrate, Re-scan in 15–30 min. If sensor glucose ≤70 mg/dL with downward arrow at 30 min, confirm with fingerstick and ingest additional 15 g fast-acting carbohydrate.
↓	Ingest 15 g fast-acting carbohydrate. Re-scan in 15–30 min. If sensor glucose ≤70 mg/dL with downward arrow at 30 min, confirm with fingerstick and ingest additional 15 g fast-acting carbohydrate.
Corrective action is necessary for sensor glucose readings at or below 70 mg/dL when downward arrows are present. Following corrective action, rescanning is needed to ensure the sensor glucose reading is trending toward an acceptable range.	

# Approaches to Using Trend Arrows with Libre

Pre-Exercise Planning for Aerobic and Mixed Exercise Using Trend Arrows in the FreeStyle Libre Systems			
Pre-Exercise Glucose Concentration			
<100 mg/dL	100–180 mg/dL	181–250 mg/dL	>250 mg/dL
<b>DO NOT Exercise</b> <i>Ingest carbohydrate and/or wait until &gt;100 mg/dL</i>	<b>Exercise Carefully</b> <i>Rescan every 30 minutes to avoid hypoglycemia</i>	<b>Exercise</b> <i>Rescan every 30 minutes to avoid hypoglycemia</i>	<b>DO NOT Exercise</b> <i>Correct and/or wait until ≤250 mg/dL</i>
↑ Wait until >100 mg/dL	↑ Rescan in 30 min	↑ Rescan in 30 min	↑ Correct to ≤180 mg/dL
↗ Wait until >100 mg/dL	↗ Rescan in 30 min	↗ Rescan in 30 min	↗ Correct to ≤180 mg/dL
→ Ingest 15 g carbohydrate	→ Consider ingesting 15 g carbohydrate*	→ Rescan in 30 min	→ Correct to ≤180 mg/dL
↘ Ingest 15 g carbohydrate	↘ Consider ingesting 15 g carbohydrate*	↘ Rescan in 30 min	↘ Wait until ≤250 mg/dL
↓ Ingest 30 g carbohydrate	↓ Consider ingesting 30 g carbohydrate*	↓ Consider ingesting 15 g carbohydrate	↓ Wait until ≤250 mg/dL
Considerations			
<ul style="list-style-type: none"> <li>Hypoglycemia is a primary concern for individuals with diabetes during aerobic and mixed exercise, which typically causes glucose concentrations to fall. It is strongly recommended that individuals plan ahead as much as possible prior to exercise and consider both the type and duration of exercise when planning. Individuals are advised to wait 2 hours after a bolus dose to begin exercise to minimize rapid glucose changes. Individuals with the ability to adjust basal insulin delivery should discuss adjustment strategies with their healthcare provider.</li> <li>Patients engaged in anaerobic exercise should consider ingesting less carbohydrate during exercise and refrain from insulin stacking if glucose concentrations rise.</li> <li>Vigilant scanning after exercise is needed to avoid delayed hypoglycemia (6-8 hours following exercise).</li> <li>Strategies for extended duration (&gt;150 min) exercise and/or high-performance athletics should be developed collaboratively with the healthcare provider.</li> <li>Consider ketone testing for readings &gt;250 mg/dL with upward trend arrows.</li> </ul>			
<p>*Aerobic exercise-related hypoglycemia is a serious concern. When in the lower end of normal glucose range, ingest fast-acting carbohydrate prior to starting exercise.</p>			

Kudva et al, J Endo Society 2018; 2(12):1-18.

# Approaches to Using Trend Arrows with Libre



Aleppo et al, J Endo Society 2017; 1(12):1445-1460.

# Approaches to Using Trend Arrows with Libre

Previous Methods to Adjust Insulin Dose Using Trend Arrows				
Trend Arrows	Insulin Adjustment	DirecNet	Scheiner	Pettus/Edelman
↑↑	Increase	20% increase of total dose	Increase to cover current sensor glucose <u>plus</u> 60 mg/dL	Increase to cover current sensor glucose <u>plus</u> 100 mg/dL
↑	Increase	20% increase of total dose	Increase to cover current sensor glucose <u>plus</u> 30 mg/dL	Increase to cover current sensor glucose <u>plus</u> 75 mg/dL
↗	Increase	10% increase of total dose	Cover current sensor glucose	Increase to cover current sensor glucose <u>plus</u> 50 mg/dL
→	No adjustment	0% increase	Cover current sensor glucose	Cover current sensor glucose
↘	Decrease*	10% decrease of total dose	Cover current sensor glucose	Decrease to cover current sensor glucose <u>minus</u> 50 mg/dL
↓	Decrease*	20% decrease of total dose	Decrease to cover current sensor glucose <u>minus</u> 30 mg/dL	Decrease to cover current sensor glucose <u>minus</u> 75 mg/dL
↓↓	Decrease*	20% decrease of total dose	Decrease to cover current sensor glucose <u>minus</u> 60 mg/dL	Decrease to cover current sensor glucose <u>minus</u> 100 mg/dL
*May require suspension or delay of insulin administration and/or remedial action (e.g., carbohydrate intake), depending on current sensor glucose value and potential risk for hypoglycemia.				

Aleppo et al, J Endo Society 2017; 1(12):1445-1460.