Insulin Intensification

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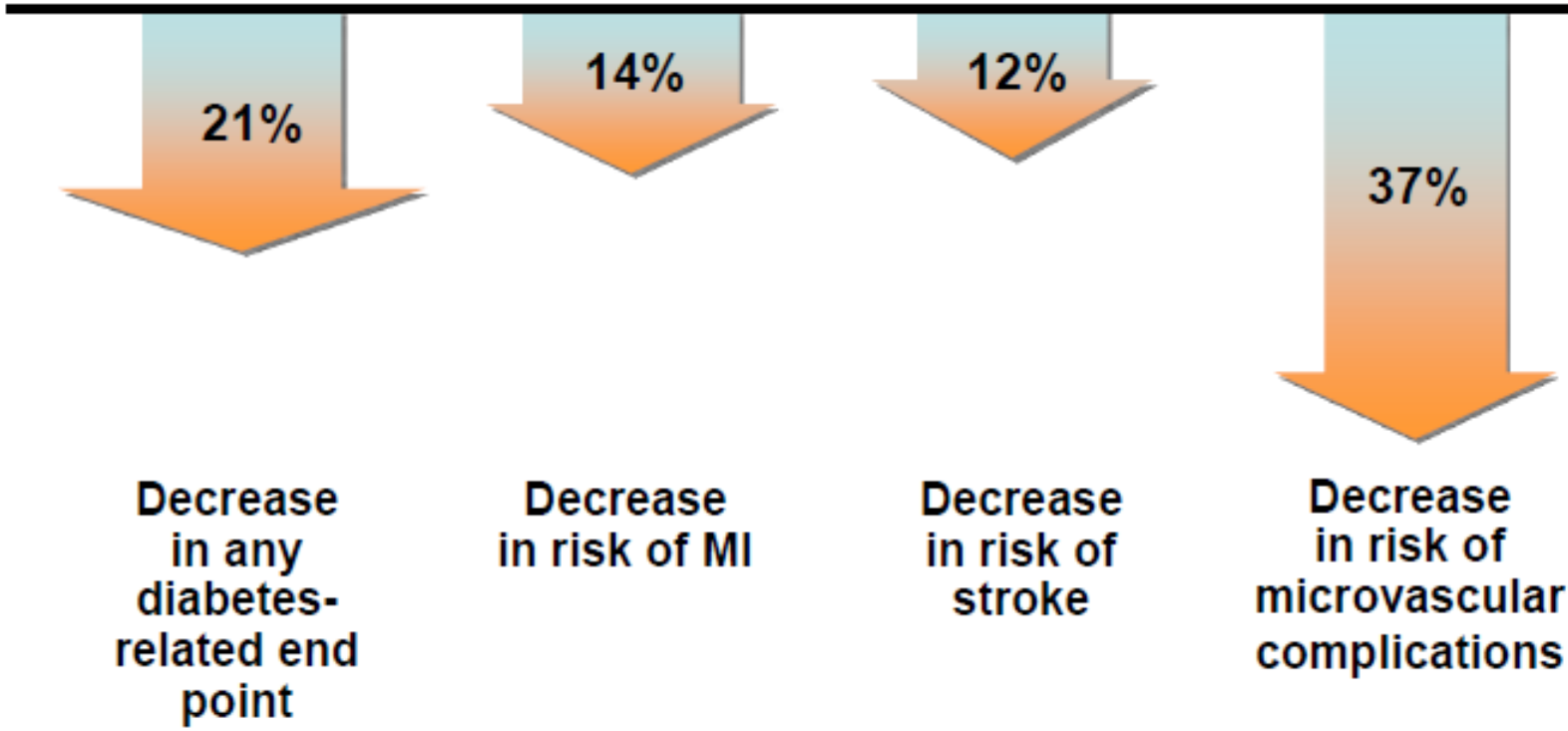
Objectives

- Need for tight control
- Barriers for intensification
- Overbasalization
- How to intensify
- Conclusion

The Need For Tight Glycemic Control

According to the United Kingdom Prospective Diabetes Study (UKPDS) 35, Every 1% Drop in A1C Resulted in:



United Kingdom Prospective Diabetes Study. Stratton IM et al. *BMJ*. 2000;321:405-412.

Insulin Treatment Patterns: common strategies

BID, twice daily; OD, once daily; TID, three times daily

Barriers

- Insulin causes blindness, renal failure, amputations, heart attacks, strokes, or early death
- Sense of personal failure
- Low self-confidence
- Low confidence in therapy
- Injection phobia
- Hypoglycemia concerns
- Feeling that diabetes is a serious cause of concern
- Negative impact on social life and job
- Health care provider inadequately explaining risks/benefits
- Limited insulin self-management training

Some of the physicians' barriers to timely initiate insulin

- Concerns over patients with comorbidities
- Excess weight gain in already overweight patients
- Concerns about patient non-compliance
- Risk of severe hypoglycemia/adverse effects on QoL
- Lack of resources—drug costs, staff, skills
- Patient refusal

“patient-centered” approach

- Individualizing therapy and goals for pts With T2DM
- The individualized targets should take into account not only clinical conditions, such as relevant comorbid conditions, age, duration of diabetes, and history of sever hypoglycemia, but also the patient-specific psycho-socioeconomic context

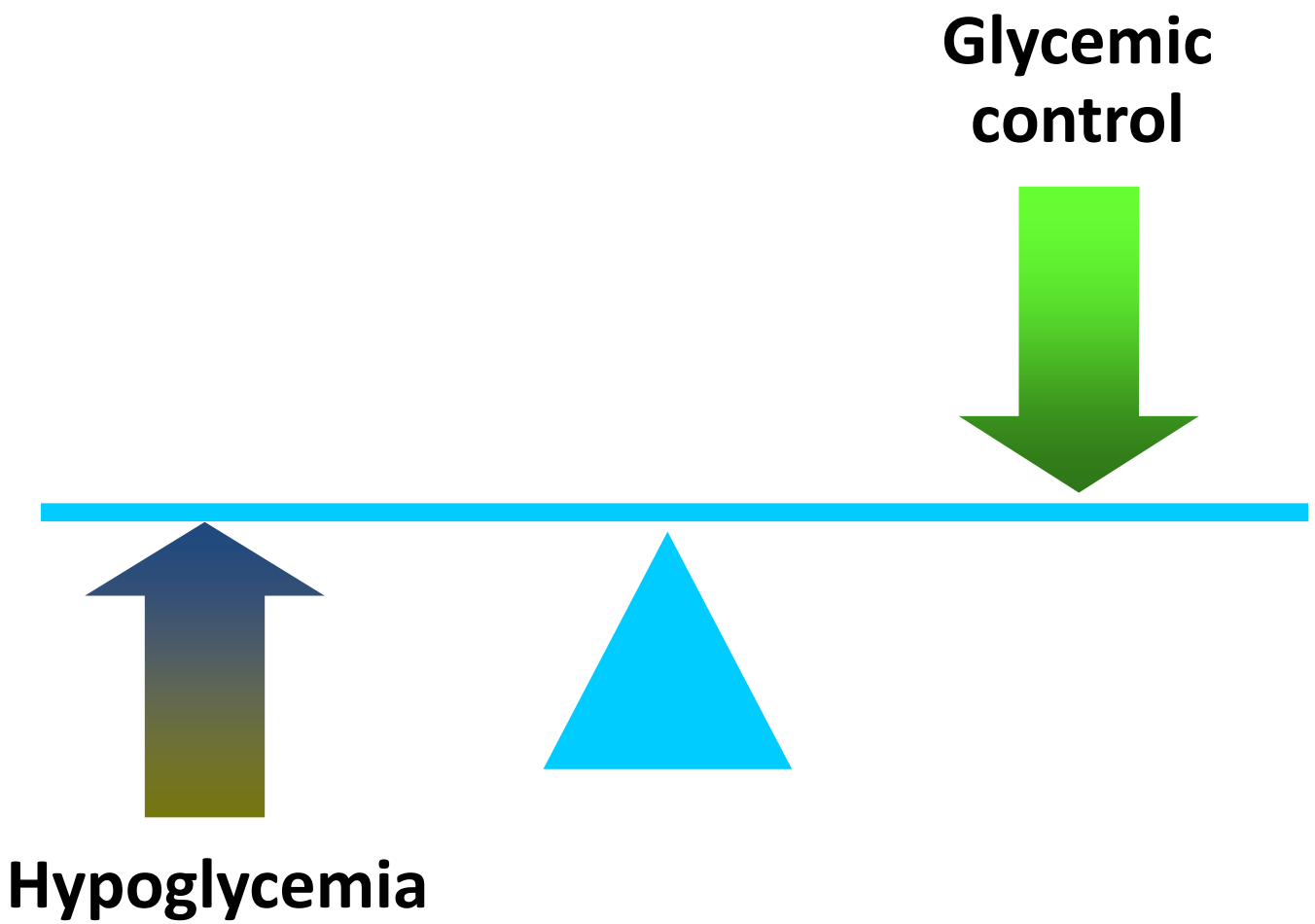
Educating

- The progressive nature of type 2 diabetes should be regularly and objectively explained to patients, and clinicians should avoid using insulin as a threat or describing it as a sign of personal failure or punishment
- Rather, the utility and importance of insulin to maintain glycemic control once progression of the disease overcomes the effect of other agents should be emphasized

Which Insulin for intensification?

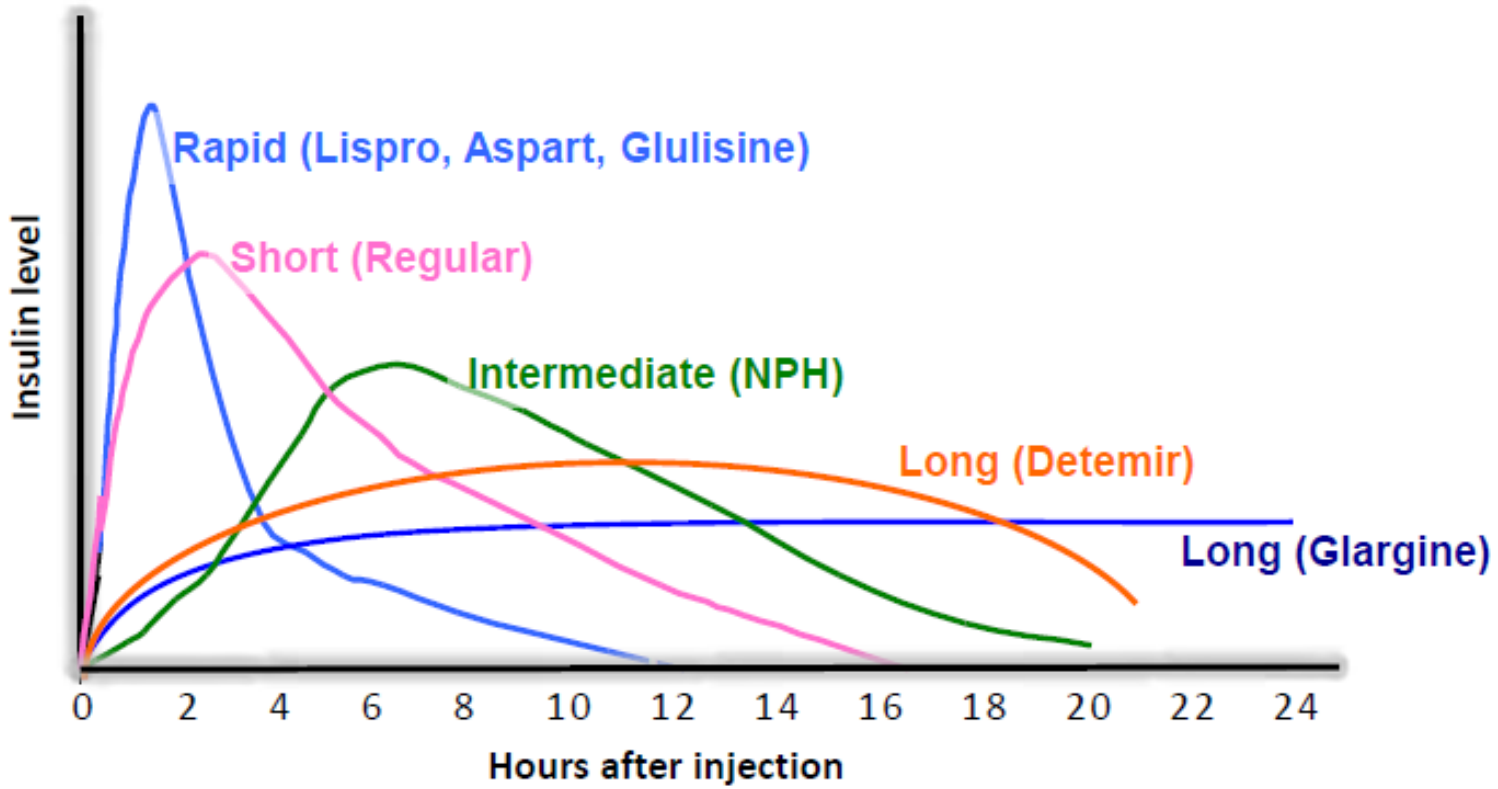
- A major challenge for primary care physicians when initiating and intensifying insulin therapy is choosing when to use each of the many insulins available today
- Rapid-acting, short-acting, intermediate-acting, long-acting, or premixed insulins

Balancing Good Glycemic Control with a Low Risk of Hypoglycemia

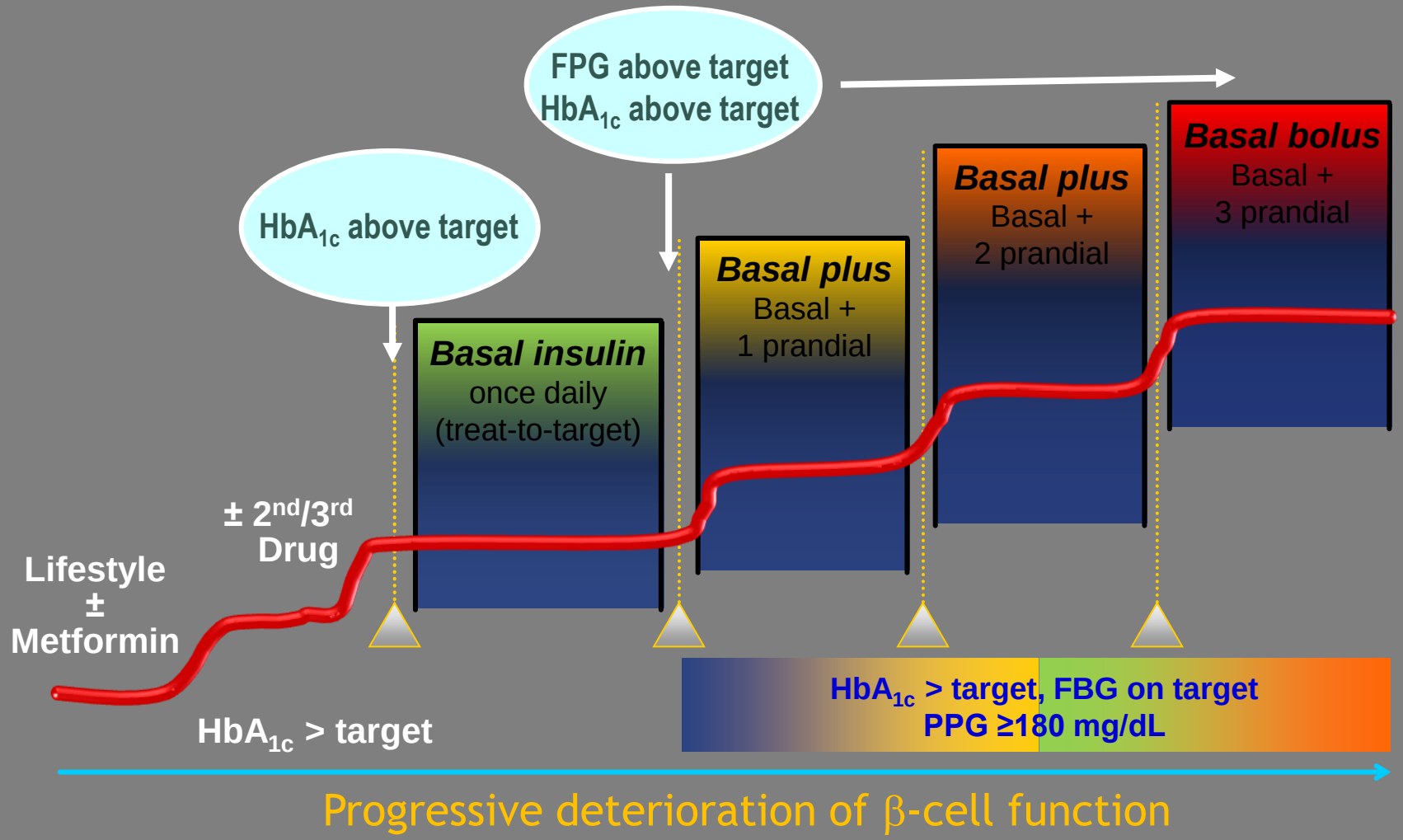


3. ANTI-HYPERGLYCEMIC THERAPY

- Therapeutic options: Insulin



The most precise and flexible prandial coverage is possible with "basal-plus/bolus" therapy



Adapted from Raccah *et al. Diabetes Metab Res Rev* 2007;23:257.

Overbasalization

- Basal dose greater than 0.5 units/kg
- High bedtime–morning blood glucose
- Postpreprandial glucose differential (e.g., bedtime–morning glucose differential ≥ 50 mg/dL)
- Hypoglycemia (aware or unaware)
- High variability

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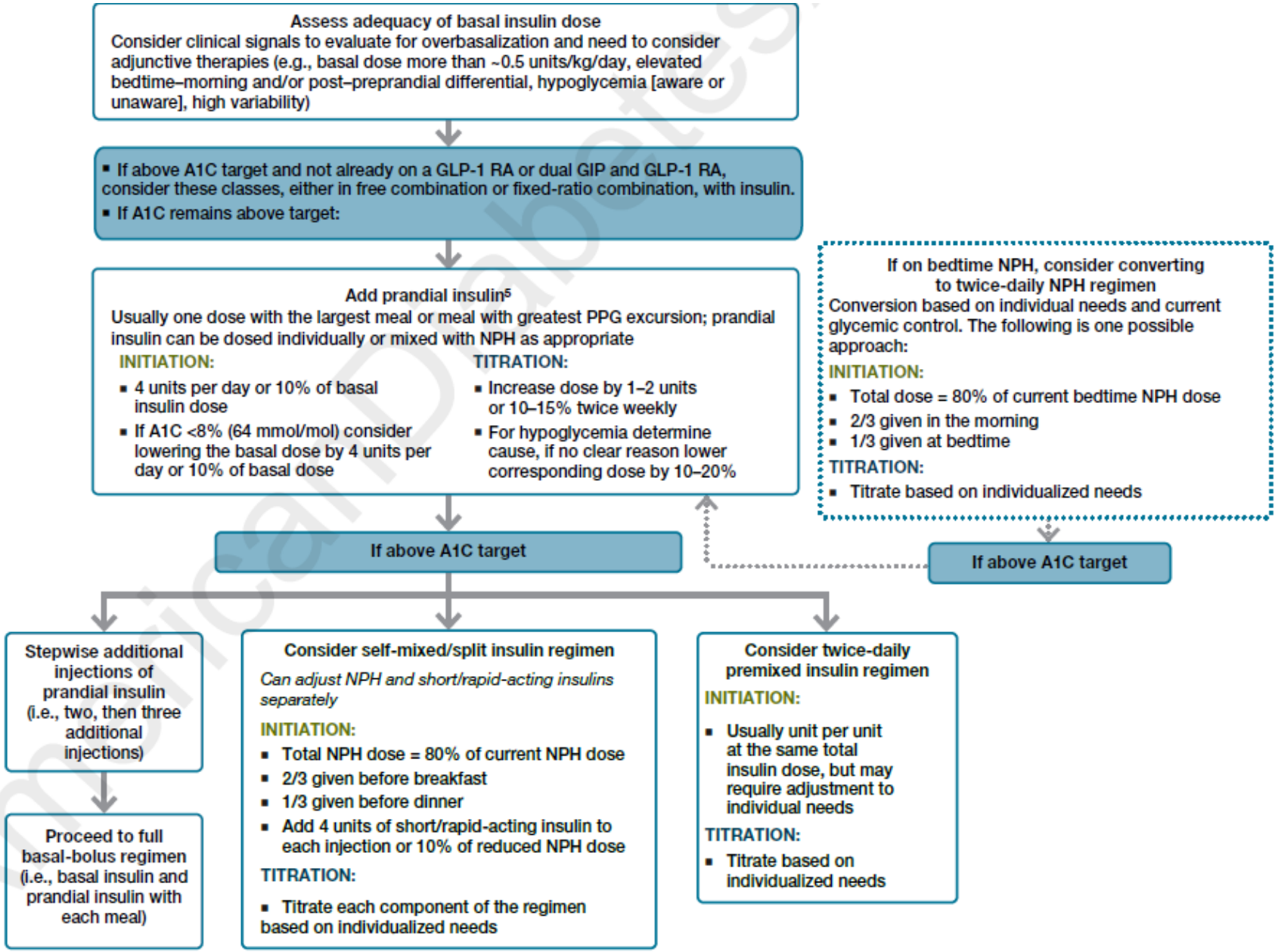

1. Consider insulin as the first injectable if evidence of ongoing catabolism, symptoms of hyperglycemia are present, when A1C levels (>10% [86 mmol/mol]) or blood glucose levels (300 mg/dL [16.7 mmol/L]) are very high, or a diagnosis of type 1 diabetes is a possibility.
2. When selecting GLP-1 RA, consider individual preference, A1C lowering, weight-lowering effect, or fequency of injection. If CVD is present, consider GLP-1 RA with proven CVD benefit. Oral or injectable GLP-1 RA are appropriate.

A common pitfall

- A common pitfall with basal insulin dosing is increasing the dose too much before adding prandial insulin
- Often, providers may note continual “fasting” hyperglycemia and titrate glargine up to 60, 80, or 100 units per day before adding prandial insulin

- A consensus treatment of the American Diabetes Association and the European Association for the study of diabetes. *Diabetes Care* 32:193–203, 2009

Start and stay with NovoMix® 30

Recommended NovoMix® 30 start dose

	Breakfast	Dinner
Once-daily start[3,4]	–	12 units
Twice-daily start[3,5]	6 units	6 units

1. NovoMix® 30 Summary of Product Characteristics.
2. Garber A *et al.* The 1-2-3 study. *Diabetes, Obesity and Metabolism* 2006; 0: 1–10.
3. Raskin P *et al.* On behalf of the INITIATE Study Group. Basal insulin or premix analogue therapy in type 2 diabetes patients. *Euro J Int Med* 2007; 18: 56–62.

Twice/thrice Daily Premix Intensification

Recommendations of Iran Consensus

When intensifying premix analogue therapy from OD to BID, split the OD dose into equal breakfast and dinner doses and titrate further

When intensifying premix analogue from BID to TID, consider adding 2–6 U or 10% of total daily premix insulin dose before lunch which may require down titration of morning dose (-2 to -6 U)

Twice/thrice Daily Premix Insulin for Intensification

Recommendations of Iran Guideline on switching from OD→BD→TID

OD to BID

- **Split the OD dose into equal breakfast and dinner doses (50:50)**
- Titrate the doses preferably once a week according to the algorithm
- Discontinue sulphonylureas
- Continue metformin
- Consider discontinuing TZDs as per local guidelines and practice
- Administer BIAsp 30 just before meals

BID to TID

- Add 2–6 U or 10% of total daily BIAsp 30 dose before lunch
- Down-titration of morning dose (-2 to -6 U) may be needed after adding the lunch dose
- Titrate the doses preferably once a week according to the algorithm
- Continue metformin
- Consider discontinuing TZDs as per local guidelines and practice
- Administer BIAsp 30 just before meals

TZD, thiazolidinedione

Unnikrishnan *et al. Int J Clin Pract* 2009:63(11):1571-7

BIAsp 30: dosage regimen

Dose to titrate	Timing of blood glucose measurements used for dose titration		
	BIAsp 30 OD	**BIAsp 30 BID**	**BIAsp 30 TID**
Breakfast	–	Pre-dinner	Pre-lunch
Lunch	–	–	Pre-dinner
Dinner	Pre-breakfast	Pre-breakfast	Pre-breakfast

BIAsp, biphasic insulin aspart; BID, twice daily; OD, once daily; TID, three-times daily

Garber *et al. Diabetes Obes Metab* 2006;8:58–66; Raskin *et al. Diabetes Care* 2005;28:260–5

Once Daily Premix Insulin for Initiation

Recommendations of Iran Consensus on Titration

* mg/dL Pre-breakfast/pre-dinner value	Dose adjustment (Units) Pre-dinner/pre-breakfast dose change
<80	-2
80–130	0
131–160	+2
161–180	+4
>180	+6

It is recommended to titrate the dose once a week based on pre meal value. It is recommended to modify dose based on the lowest/mean value of the 3 most recent values.

*For patients initiated on pre-breakfast dose, titrate according to pre-dinner values and vice versa

Oral agent?

- When initiating combination injectable therapy, metformin therapy should be maintained, while SUs and DPP-4 inhibitors are typically weaned or discontinued
- In individuals with suboptimal blood glucose control, especially those requiring large insulin doses, adjunctive use of TZDs or an SGLT2I may help to improve control and reduce the amount of insulin needed

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CONCLUSIONS

- The importance of individualizing treatment in pts with T2DM is established
- Note the barriers which are very important
- Intensify insulin as needed
- Titrate appropriately
- Act in the way that be treat to target