

Insulin therapy

Zahra Davoudi and Azam Erfanifar MD,
Department of Endocrinology,
Loghman Hakim Hospital,
Shahid Beheshti University of Medical
Sciences, Tehran, Iran



Case 1

A 62- year- old retired schoolteacher attended the diabetes clinic on a routine follow- up visit.

He had a background history of hypertension and Type 2 DM for 20 years.

He was currently taking zipmet50.1000 (twice daily), diabezid 60 (twice daily), and valsartan , amlodipine (80.5 mg once a day).

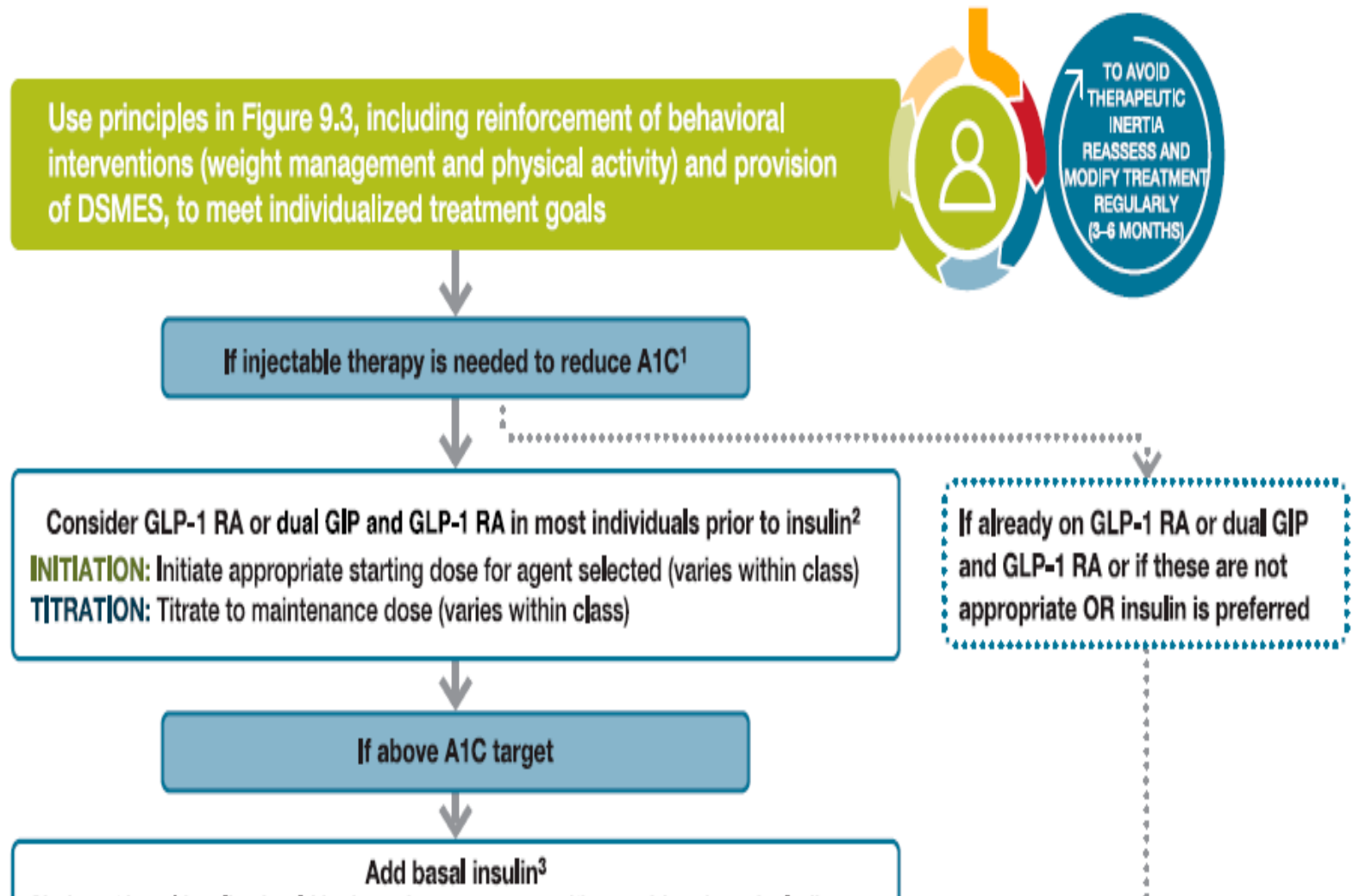
On examination, his BMI was 32 kg/ m2. His blood pressure was 152 /92 mm of Hg.

Investigations:

HbA1c 8:9

The next step ??????????

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- 1. Consider insulin as the first injectable if evidence of ongoing catabolism is present, symptoms of hyperglycemia are present, when A1C or blood glucose levels are very high (i.e., A1C >10% or blood glucose \geq 300 mg/dL)or when a diagnosis of type 1 diabetes is a possibility.**
- 2. When selecting GLP-1 RAs, consider individual preference, A1C lowering, weight-lowering effect, or frequency of injection. If CVO is present. consider GLP-1 RA with proven CVO benefit. Oral or injectable GLP-1 RAs are appropriate.**

case2

A 62- year- old woman with Type 2 DM for over 20 years was reviewed In the diabetes clinic on a routine follow- up visit.

She was on metformin, gliclazid and sitagliptin tablets for Type 2 DM. She was taking

lisinopril and amlodipine tablets for blood pressure (BP) control . She had weight loss during 6 months and recent polyuria , polydipsia ;

On examination, she had a BMI of 23.5 kg/ m². Her BP was 142/ 84 mmHg. She had clinical evidence of peripheral neuropathy.

Investigations:

Urinary albumin creatinine ratio 35 mg/ mmol

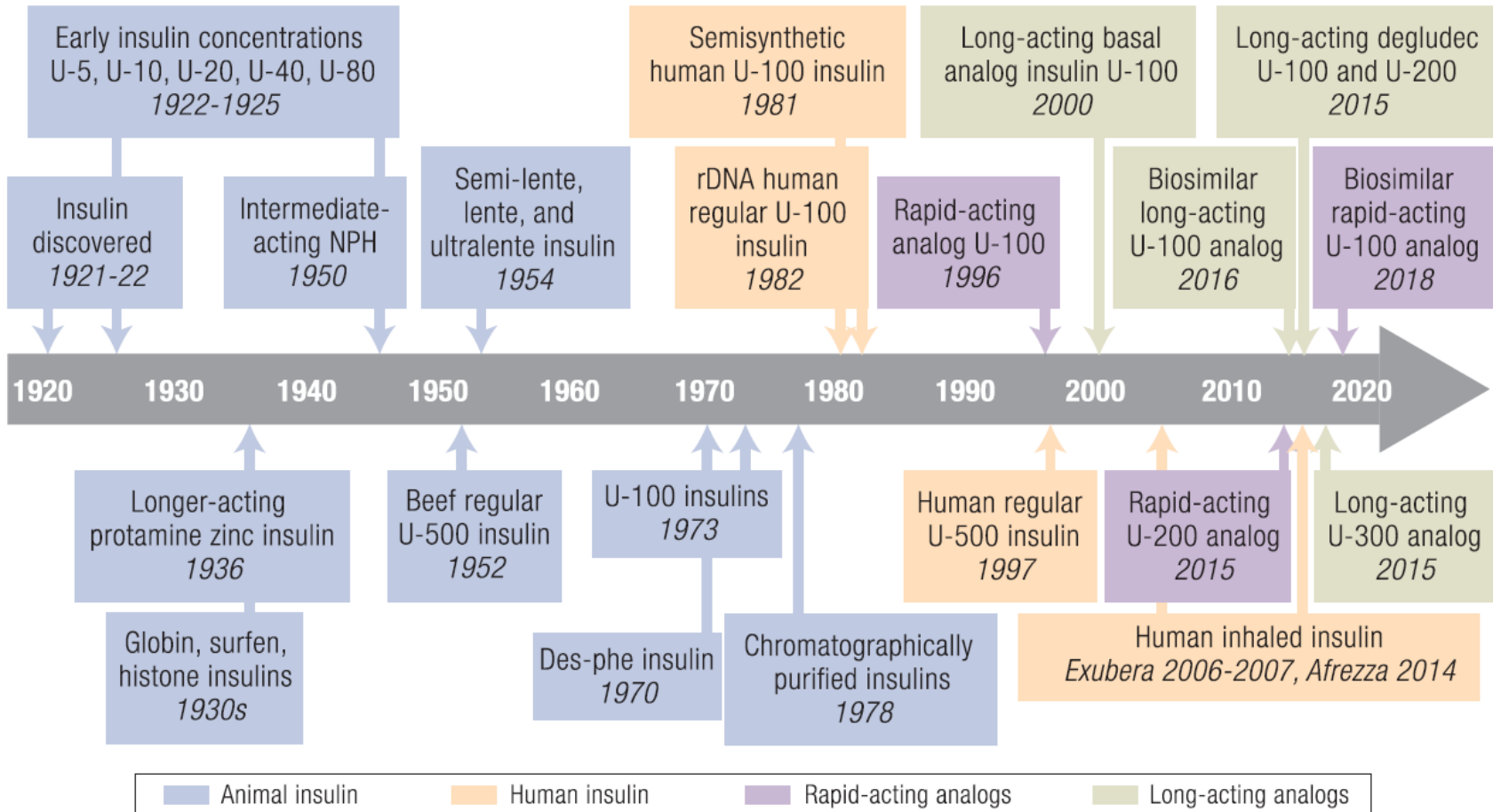
eGFR creatinine 47 ml/ min/ 1.73m²

HbA1c :10.5

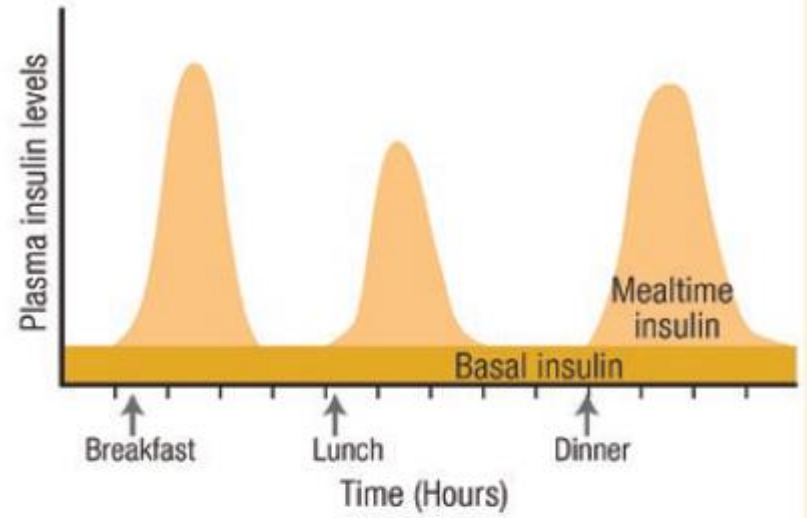
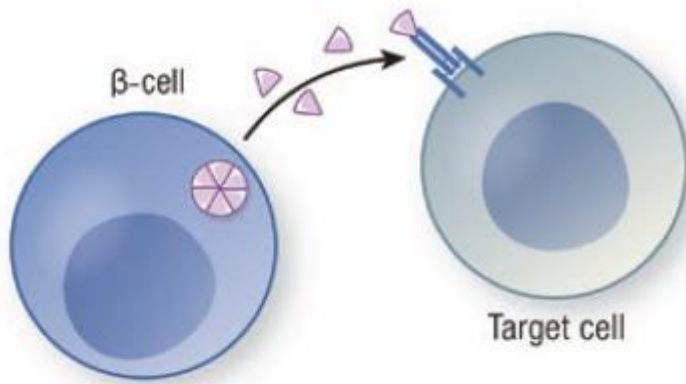
Which one of the following is the most appropriate next step in her further management?

- A. Start SGLT2Inhibitor
- B. Refer to renal clinic
- C. Stop metformin
- D. Start insulin

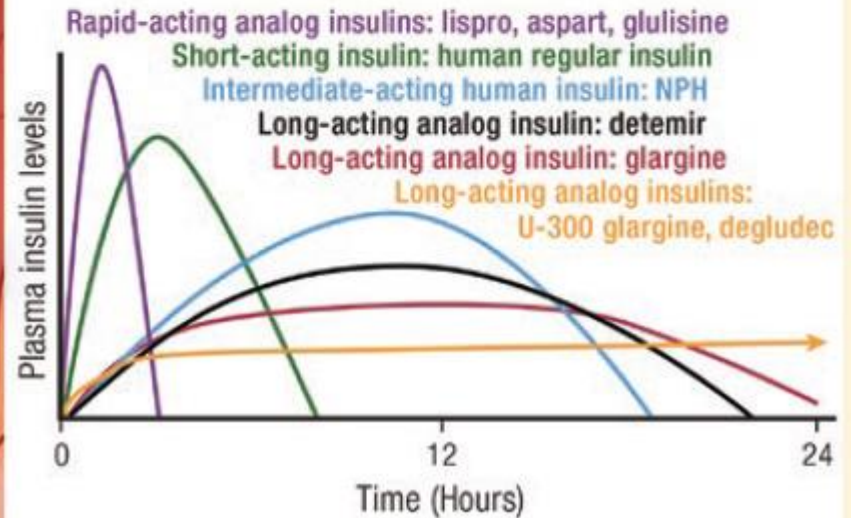
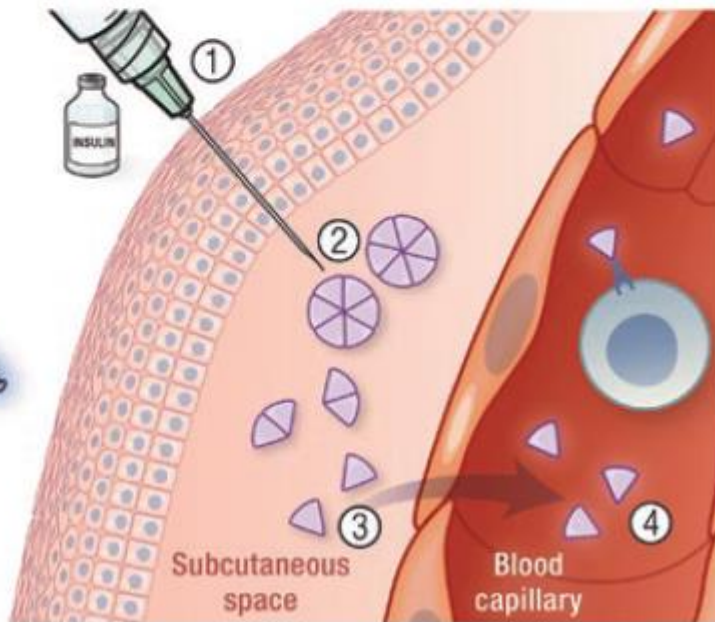
Timeline of insulin development with approximate historical dates



Endogenous insulin



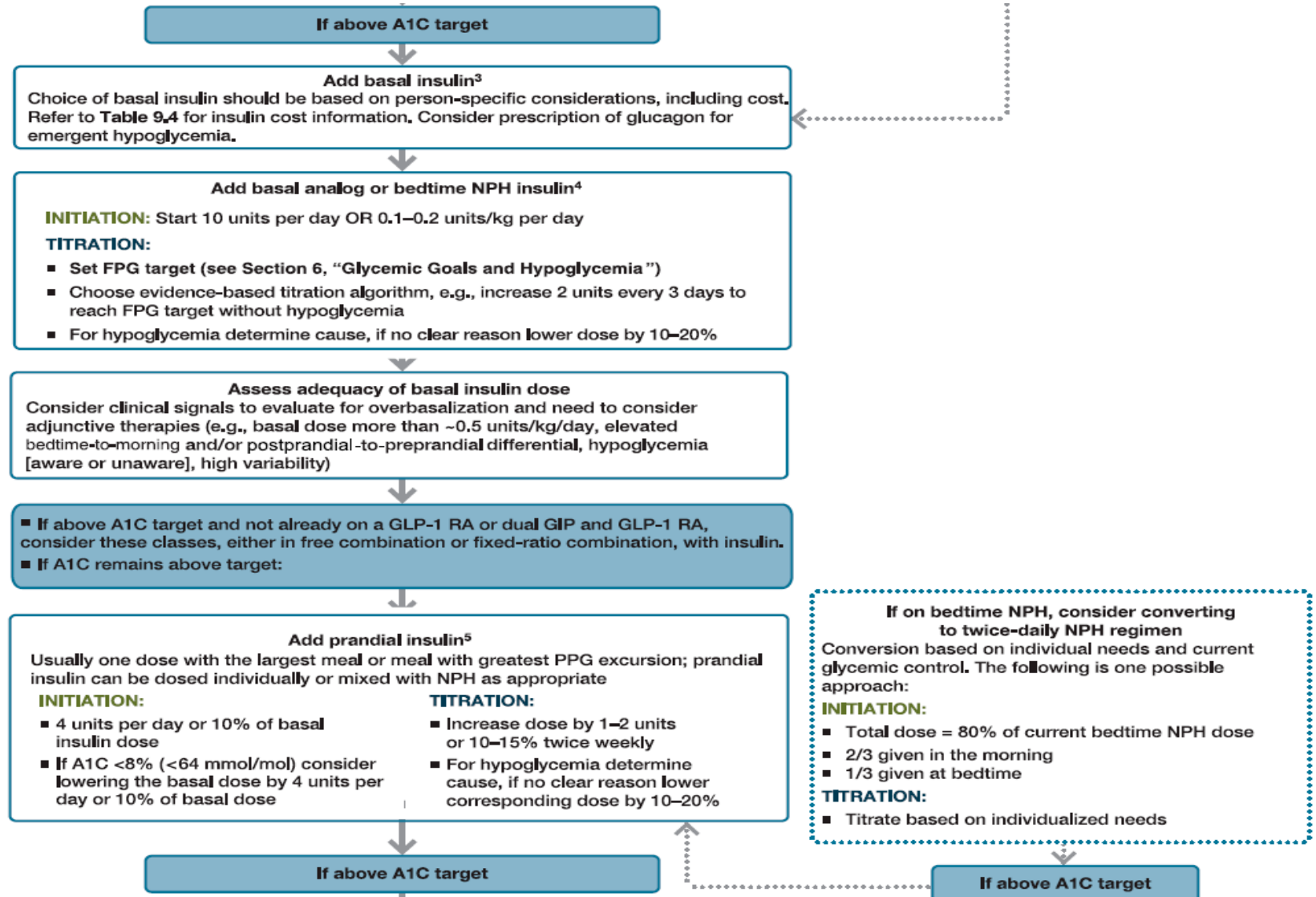
Exogenous insulin

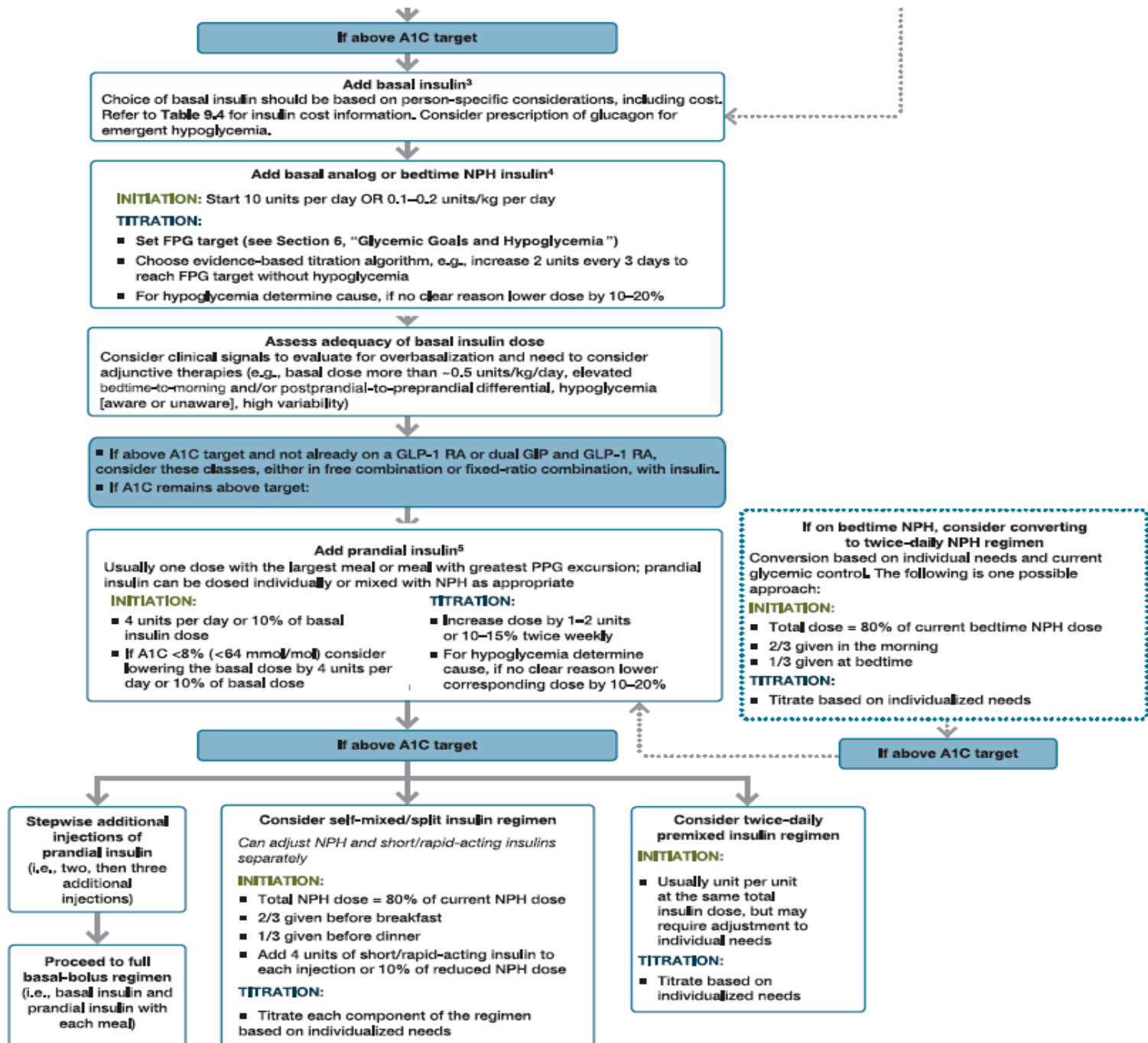


Indications for insulin therapy

- A. In T2 DM , FPG more than 300 mg/dl in **symptomatic patients** with polyuria, polydipsia and weight loss ,(HbA1c>10); Uncontrolled diabetes with oral agents and **catabolic state**
- B. **T1DM and** Latent autoimmune diabetes in adult
- C. **Gestational diabetes**
- D. Physician-patient option wish to receive insulin as initial therapy
- E. Post MI , Renal failure , Hepatic failure ,uncontrolled CHF
- F. Allergy or serious reaction to oral agents

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Insulin

Properties of Insulin Preparations^a

Preparation	Time of Action		
	Onset, h	Peak, h	Effective Duration, h
Short-acting^b			
Aspart	<0.25	0.5–1.5	2–4
Glulisine	<0.25	0.5–1.5	2–4
Lispro ^f	<0.25	0.5–1.5	2–4
Regular ^e	0.5–1.0	2–3	3–6
Inhaled human insulin	0.5–1.0	2–3	3
Long-acting^e			
Degludec	1–9	— ^c	42 ^d
Detemir	1–4	— ^c	12–24 ^d
Glargine ^f	2–4	— ^c	20–24
NPH	2–4	4–10	10–16
Examples of insulin combinations^e			
75/25–75% protamine lispro, 25% lispro	<0.25	Dual ^f	10–16
70/30–70% protamine aspart, 30% aspart	<0.25	Dual ^f	15–18
50/50–50% protamine lispro, 50% lispro	<0.25	Dual ^f	10–16
70/30–70% NPH, 30% regular	0.5–1	Dual ^f	10–16
Combination of long-acting insulin and GLP-1 receptor agonist	See text		



Glargine 100unit/cc



Glargine 300unit/cc



Levemir(Detemir)



Novorapid (aspart)



Apidra (gliulisine)



lispro



NovoMix^{70/30}

NovoMix[®] 30



Humalog Mix50



Humalog Mix25



Ryzodeg



insulin regimens for the treatment of diabetes

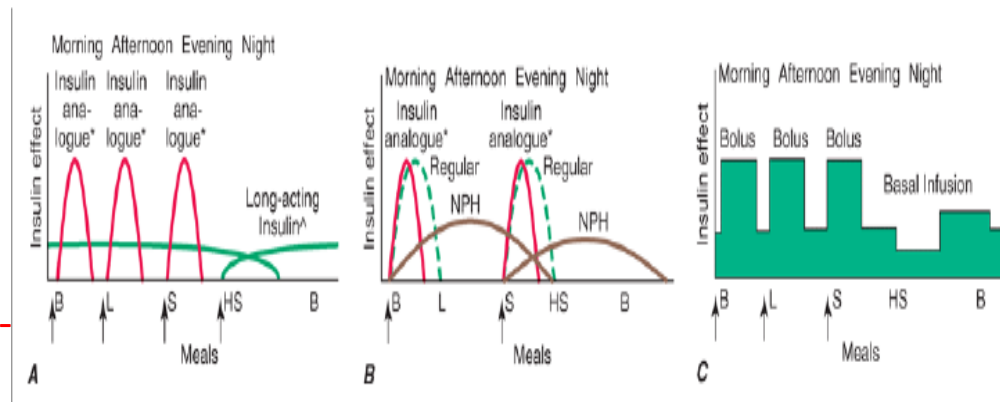
Basal – bolus :

provided by long-acting (NPH insulin, insulin glargine, or insulin detemir) insulin formulations; with short-acting insulin in an attempt to mimic physiologic insulin release with meals.

conventional :mixing of NPH and short-acting insulin formulations is common practice

CSII :continuous subcutaneous insulin infusion

In all regimens, long-acting insulins (NPH, glargine, or detemir) supply basal insulin, whereas regular, insulin aspart, glulisine, or lispro insulin provides prandial insulin. **Short-acting insulin analogues should be injected just before or just after a meal; regular insulin is given 30–45 min prior to a meal**



In practice

- In general, individuals **with type 1 DM require 0.3-0.7 units/kg per day of insulin divided into multiple doses, with approximately 50% of daily insulin given as basal insulin and 50% as prandial insulin.**
- To determine the meal component of the **preprandial insulin dose**, the patient uses an **insulin-to-carbohydrate ratio** (a common ratio for type 1 DM is 1 unit/10–15 g of carbohydrate, but this must be determined for each individual).
- **(450 or 500/total daily dose insulin=carb count ratio)**
- To this insulin dose is added the supplemental or correcting insulin based on the preprandial blood glucose (one formula uses 1 unit of insulin for every 1.6–3.3 mmol/L [30–60 mg/dL] over the preprandial glucose target; **this correction factor** can be estimated from **1500/[total daily insulin dose]**).

In **Type 2 DM** insulin is usually initiated in a single dose of long-acting insulin (0.1–0.3 U/kg per day), given in the evening or just before bedtime (NPH, glargine, detemir, or degludec).

- Because fasting hyperglycemia and increased hepatic glucose production are prominent features of type 2 DM, **bedtime insulin is more effective in clinical trials than a single dose of morning insulin.**
- Glargine given at bedtime has less nocturnal hypoglycemia than NPH insulin.
- Some physicians prefer a relatively low, fixed starting dose of long-acting insulin (5–15 units) or a weight-based dose (0.1 units/kg).
- **The insulin dose may then be adjusted in 10–20% increments as dictated by SMBG results.**
- Both morning and bedtime long-acting insulin may be used in combination with oral glucose-lowering agents.
- **Initially, basal insulin may be sufficient, but often prandial insulin coverage with multiple insulin injections is needed as diabetes progresses .**

Case3

Suboptimal control on oral medications

Low risk for CAD

- **Background**

- 60 year old male
- T2DM since 6 years
- No known micro or macrovascular complications of diabetes
- No other known co-morbid conditions

- **Current Medication**

- Metformin 1000 mg twice daily
- Gliclazide 80 mg BID
- Aspirin 80 mg daily
- Multivitamin daily

- **Life style**

- Has met with nutritionist & is following reasonable meal plan
- Walks 4 days per week for 30 minutes each time
- Testing Glucose once or twice daily
- Not keen to take insulin-thinks has severe disease if has to take insulin

- **Physical Examination**

- Weight: 79.5 kg
- Height: 1.82 m
- BMI: 24 kg/m²
- BP: 125/80
- Examination of all systems normal
- No evidence of micro or macrovascular complications

Case 3

Suboptimal control on oral
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Case 3

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Home glucose monitoring data (mg/dl)

Pre-breakfast	2 hours after breakfast	2 hours after lunch	2 hours after dinner
168	210		
174		175	
158			178
172	196		
182			

HbA_{1c} 9.1%

Laboratory data

Lipids:

- Total cholesterol : 189 mg/dl
- HDL : 55 mg/dl
- TG : 145 mg/dl
- LDL : 95 mg/dl

Creatinine: 0.8 mg/dl

LFTs: normal

What can be done in this case?

- Modification of SU dosage
- Add another OAD
- Add basal insulin (Insulin Detemir)
- Add liraglutide
- Other options

Action

- Continued Metformin with the same dose
- Reduced SU gradually
- Started on Insulin Detemir 10 units at bedtime
- Dose titrated every 3 days by 3 units to achieve fasting glucose of (90-120) mg/dl
- Walking daily
- Watching meal plan more carefully

Follow-up ...

1 week

- FPG: 142mg/dl
- PPG: 171 mg/dl
- No hypoglycemia event

1 month

- FPG: 128 mg/dl
- PPG: 162 mg/dl
- No hypoglycemia event

Follow-up ...

3 months

- SU D/C, 30 units of Insulin Detemir at bedtime
- HbA1c: 7.6%
- FPG: 115 mg/dl, PPG: 155 mg/dL
- No hypoglycemia event
- Follow up 3 months later

Follow-up ...

6 months

Weight : 80 kg

Pre-breakfast	2 hours after breakfast	2 hours after lunch	2 hours after dinner
105	155		
96		168	
101			176
90	149		

HbA_{1c} 6.8%

Special populations

Administration

Pump use

Paediatric	Pregnancy	Hepatic impairment	Renal impairment	Elderly	Pts prone to severe hypoglycaemia	Time	In-use temperature	Reservoir storage	Pre-filled cartridge available
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NovoRapid^{®1,2}	✓ ≥1 year	✓	✓	✓	✓	✓	Immediately before – when necessary soon after meal	<30°C (cold in-use) [†]	6 days	✓
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Insulin glulisine^{3,4}	✓ ≥6 years	Only exposure data	✗	✓	No separate PK/PD studies	No RCT data available	Shortly before – when necessary soon after meal	<25°C	48 hours	✗
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Case 4

**Adjust medications to help with
lower hypoglycaemia events**

Case 3

Background

- 50 year old male
- T2DM since 11 years
- No known micro or macrovascular complications of diabetes

Current Medication

- Metformin 2000 mg daily
- NPH 18 U morning
- NPH 14 U pre-dinner

Case 3

Physical Examination

- Weight: 65 kg
- BMI: 23 kg/m²
- Cr : 1.29 mg/dl
- BP : 130/80
- No evidence of any micro or macrovascular complications
- Complain of nocturnal hypoglycaemia
- Hospitalization due to severe hypoglycaemia

Home glucose monitoring data (mg/dl)

FBS	2 h after breakfast	2 h after lunch	2 h after dinner	03:00 am
110	170	140	160	60
90	165	180	140	

HbA_{1c} 7.5%

What can be done in this case?

- Add another OAD
- Decrease dose of evening NPH
- Change in injection time of evening NPH
- Switch from NPH to once daily of insulin detemir
- Other options

Action

- Continue metformin
 - Switch from NPH to once daily insulin detemir & titrate
 - Twice daily NPH -----> (~ 80% of NPH) total daily dose
- Start dose of insulin detemir : 25 U morning
- Titration algorithm : -3, 0, 3

Follow-up..

- **1 week**

- F: 111mg/dl
- 2 h PPG ~ 160
- Without hypoglycemia event

- **1 month**

- F: 98 mg/dl
- 2 h PPG ~ 148
- Happy that no hypoglycemia event since changing the therapy
- More satisfaction with once daily injection instead of twice daily

Follow-up..

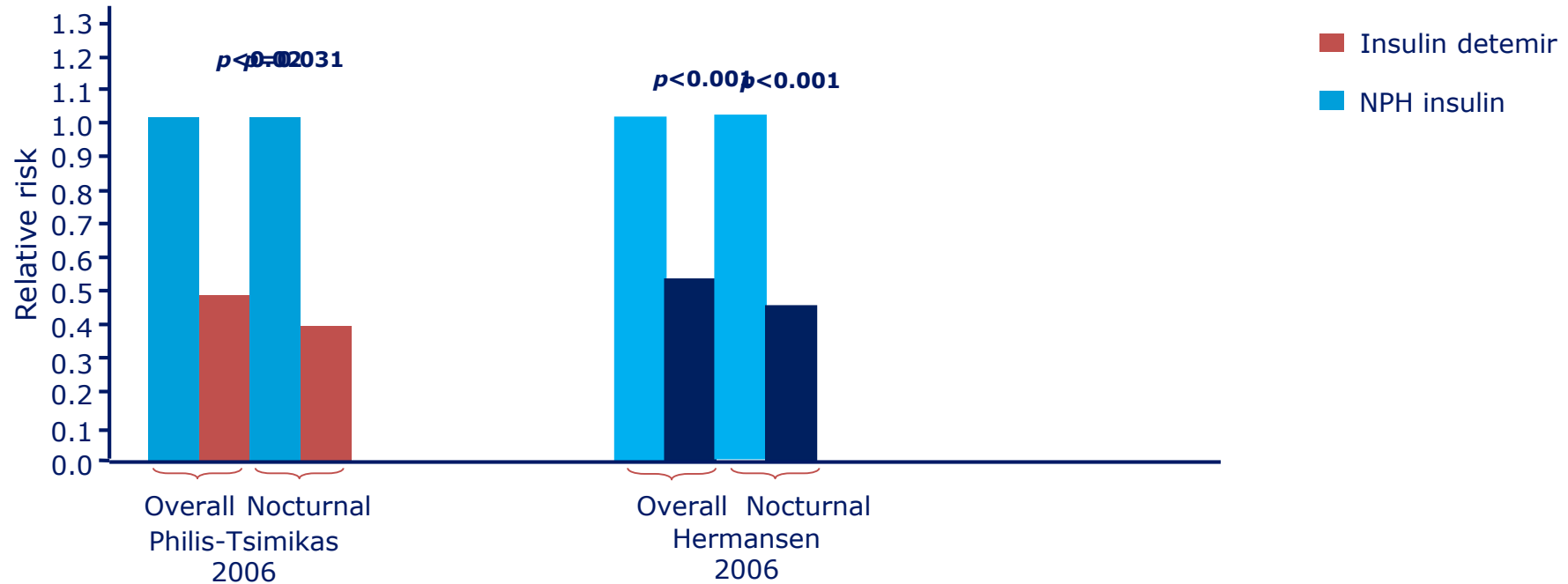
- **3 months later**

- Insulin Detemir 32 U at morning
- Metformin 2000 mg daily
- No hypoglycemia event
- No weight gain

HbA1c: 7.3%
FPG: 95 mg/dl

Type 2 diabetes: basal–oral – hypoglycaemia

Significantly less hypoglycaemia compared with NPH insulin



Based on biochemically confirmed events: plasma glucose <3.1 mmol/L
NPH, neutral protamine Hagedorn; NS, not significant

Case5

Adjust medications to help with
weight loss

Case 4

Background

- 67 year old male
- T2DM since 12 years
- Co-morbid conditions
 - ✓ HTN
 - ✓ Hyperlipidemia
 - ✓ hypothyroidism
- No known micro or macrovascular complications of diabetes

Current Medication

- Metformin 1 g twice daily
- Glibenclamide 5 mg daily
- NPH 15 U morning
- NPH 10 U pre-dinner
- Atorvastatin 40 mg daily
- Lisinopril 40 mg daily
- Levothyroxine 150 mcg daily

Case 4

Physical Examination

- Weight: 112 kg
- Height: 1.78 m
- BMI: 35.5 kg/m²

- BP : 130/80

- No evidence of any micro or macrovascular complications

Home glucose monitoring data (mg/dl)

Pre-breakfast	2 hours after lunch	2 hours after dinner	Bedtime
(80-150)	(130-160)	(150-170)	(110-200)

HbA_{1c} 8.9%

Issues

- Suboptimal glucose control
- Obesity
 - difficulty losing weight
 - not really following a specific meal plan or exercising regularly
- Motivated to make some lifestyle changes
- Plan
 - Weight management programme
 - Review and change medications

Action

- Multidisciplinary weight management programme
 - ✓ Percent of calorie from carbohydrate in the main meals: (40/30/30)%
(most of them complex carb)
 - ✓ Exercise prescription
 - ✓ Change medication
 - Change NPH to Insulin Detemir (decrease dose/ titrate according to FPG target)
- Start dose: 20 U*
- Decrease glibenclamide dose if possible
 - Start liraglutide 0.6 mg

Follow-up..

- **1 week**

- FPG: 135mg/dl
- Nausea
- Reduced appetite
- ↑ liraglutide dose to 1.2 mg
- Titrate insulin detemir according to FPG target

- **1 month**

- FPG: 122 mg/dl
- Nausea still persisting, but better
- Happy that no hypoglycaemia event since changing the therapy
- Decrease glibenclamide dose
- Titrate insulin detemir according to FPG target

Follow-up..

- **3 months later**

- Insulin Detemir 30 U at bedtime
- Liraglutide 1.2 mg
- Metformin 1 g twice daily
- Glibenclamide stopped

Weight 97 kg (Lost 15kg)

BP: 120/70

HbA1c: 7.3%

FPG: 110 mg/dl



Q&A

