Diabetes Treatment

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بسم الله الرحمن الرحیم

Benefits of intensive glycaemic control: UKPDS results

		p value
A. Main results of intensive (sulphonylureas or insulin) versus conventional (diet) therapy[a]		
12%	Any diabetes-related endpoint	0.029
16%	Myocardial infarction	0.052
25%	Microvascular disease	0.0099
21%	Retinopathy at 12 years	0.015
33%	Albuminuria at 12 years	0.000054
B. Results of metformin versus conventional therapy in obese patients[b]		
32%	Any diabetes-related endpoint	0.002
39%	Myocardial infarction	0.01
30%	All macrovascular events	0.02
42%	Diabetes-related death	0.017
36%	All-cause mortality	0.011

[a]Data from: UKPDS 33 (1998a).

[b]Data from: UKPDS 34 (1998b).

Good News for Type 2 Diabetes

Keeping A1c in target range reduces:

Heart attack

as much as 16%

Eye damage

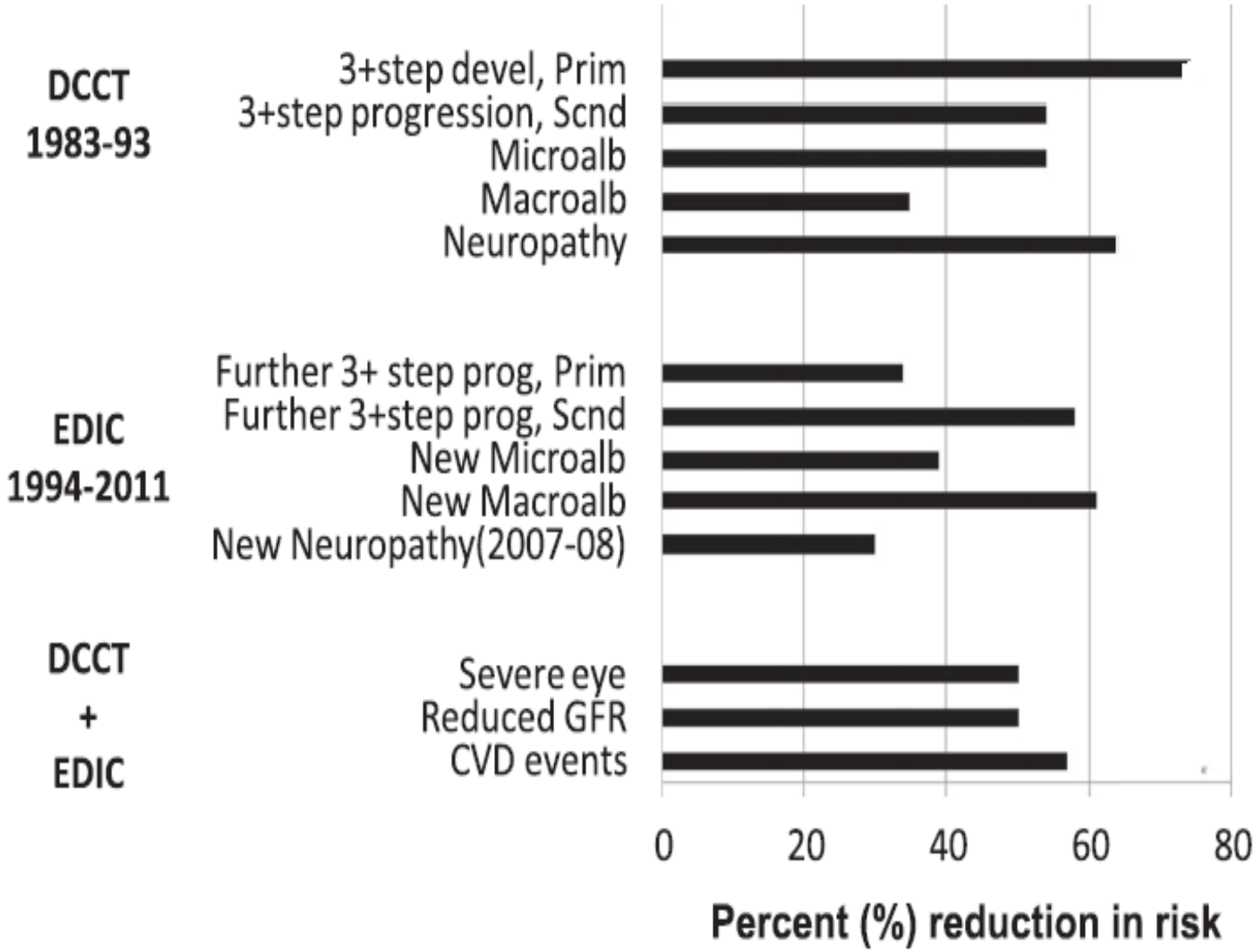
as much as 21%

Kidney disease

as much as 34%

United Kingdom Prospective Diabetes Study

The importance of metabolic control(DCCT,EDIC)

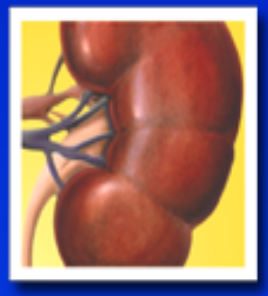


Good News for Type 1 Diabetes

Keeping blood glucose in target range reduces:

Kidney disease

as much as 56%

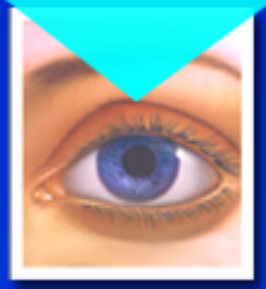


Nerve damage

as much as 60%

Eye disease

as much as 76%



Diabetes Control and Complications Trial

Impact of Intensive Therapy for Diabetes: Summary of Major Clinical Trials

Study	Microvasc		CVD		Mortality	
UKPDS	↓	↓	↔	↓	↔	↓
DCCT / EDIC*	↓	↓	↔	↓	↔	↔
ACCORD	↓		↔		↑	
ADVANCE	↓		↔		↔	
VADT	↓		↔		↔	

Long Term Follow-up

Glycemic target recommendations

Table 5.2—Summary of glycemic recommendations for nonpregnant adults with diabetes

A1C	<7.0% (53 mmol/mol)*
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (10.0 mmol/L)

*More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations.

†Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.

Glycemic target in pediatric group

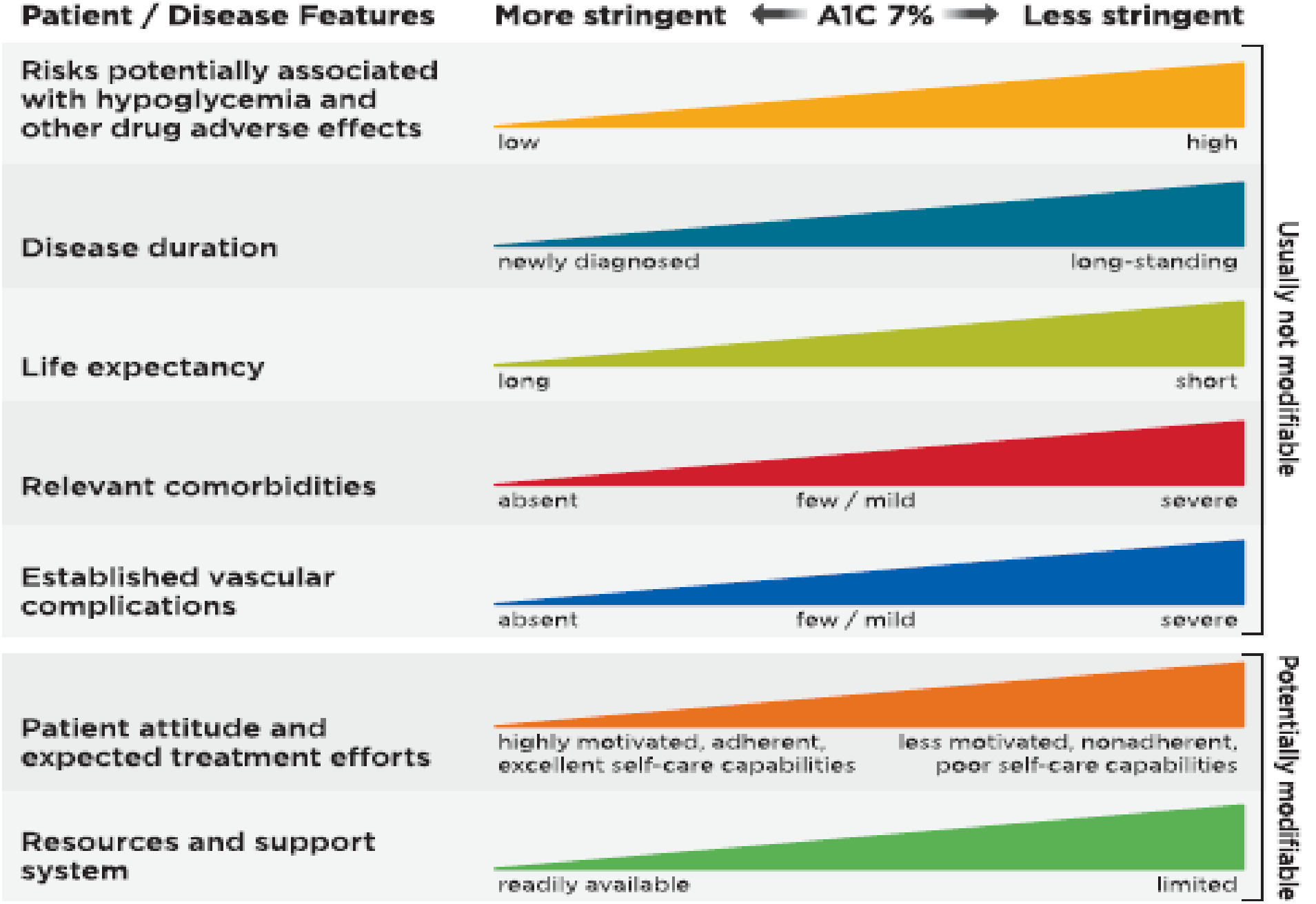
Table 12.1—Blood glucose and A1C goals for children and adolescents with type 1 diabetes

Blood glucose goal range			
Before meals	Bedtime/overnight	A1C	Rationale
90–130 mg/dL (5.0–7.2 mmol/L)	90–150 mg/dL (5.0–8.3 mmol/L)	<7.5% (58 mmol/mol)	A lower goal (<7.0% [53 mmol/mol]) is reasonable if it can be achieved without excessive hypoglycemia

Key concepts in setting glycemic goals:

- Goals should be *individualized*, and lower goals may be reasonable based on a benefit-risk assessment.
- Blood glucose goals should be modified in children with frequent hypoglycemia or hypoglycemia unawareness.
- Postprandial blood glucose values should be measured when there is a discrepancy between preprandial blood glucose values and A1C levels and to assess preprandial insulin doses in those on basal-bolus or pump regimens.

Approach to the Management of Hyperglycemia



Life style Modification

- Diet control
- Exercise
- Smoking cessation

Exercise

Benefits:

- including cardiovascular risk reduction, reduced blood pressure, maintenance of muscle mass, reduction in body fat, and weight loss.

- For individuals with type 1 or type 2 DM, exercise is also useful for lowering plasma glucose (during and following exercise) and increasing insulin sensitivity.

- In patients with diabetes, the ADA recommends 150 min/week (distributed over at least 3 days) of aerobic physical activity.

- In patients with type 2 DM, the exercise regimen should also include resistance training.

- Individuals with type 1 DM are prone to either **hyperglycemia** even DKA or **hypoglycemia** during exercise, depending on the pre-exercise **plasma glucose**, the circulating **insulin level**, and the level of exercise-induced **catecholamines**.

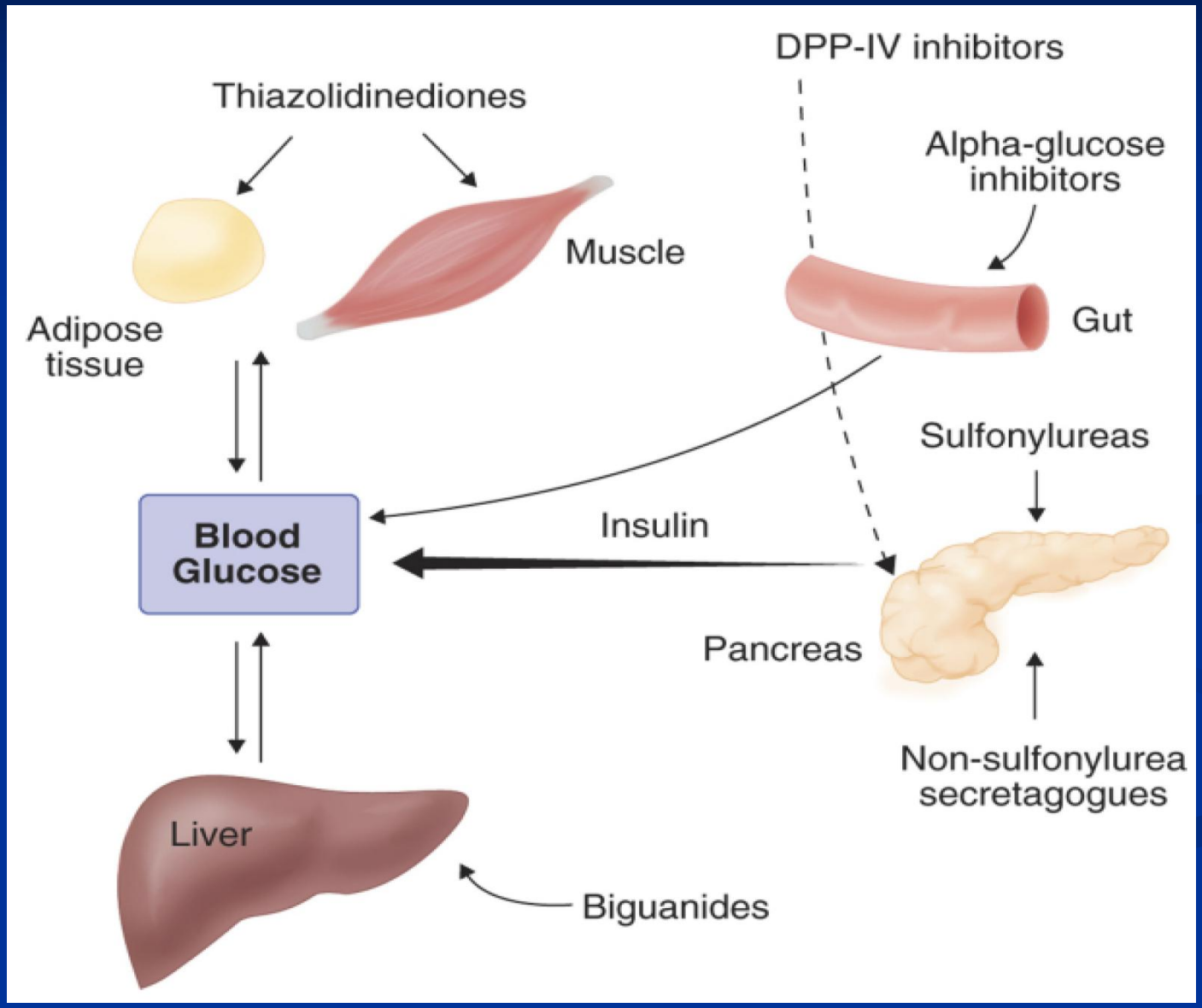
To avoid exercise-related hyper- or hypoglycemia individuals with type 1 DM should:

- (1) monitor blood glucose before, during, and after exercise.
- (2) delay exercise if blood glucose is >14 mmol/L (250 mg/dl) and ketones are present.
- (3) if the blood glucose is <5.6 mmol/L (100 mg/dl), ingest carbohydrate before exercising.

- (4) monitor glucose during exercise and ingest carbohydrate to prevent hypoglycemia.
- (5) decrease insulin doses (based on previous experience) before exercise and inject insulin into a nonexercising area.
- (6) learn individual glucose responses to different types of exercise and increase food intake for up to 24 h after exercise, depending on intensity and duration of exercise.

Oral Hypoglycemic Agents

OHA for DM


DPP-IV inhibitors
Thiazolidinediones
Alpha-glucose inhibitors
Muscle
Adipose tissue
Gut
Sulfonylureas
Blood Glucose
Insulin
Pancreas
Non-sulfonylurea secretagogues
Liver
Biguanides

Biguanides

- **Mode of action:**
  - reduces hepatic glucose production through an undefined mechanism
  - improves peripheral glucose utilization slightly
- Advantage:
  - reduces fasting plasma glucose and insulin levels
  - improves the lipid profile
  - promotes modest weight loss.

Metformin

Adverse effects:

- GI disturbances (20%):nausea, abdominal pain, bloating, anorexia, metallic taste and diarrhea
- Start with a low dose, titrating slowly
- Asymptomatic subnormal B12 levels
- Renal excretion
- Lactic acidosis can occur with the administration of Metformin, but is extremely rare (3 cases per 100,000 pt/yrs)

Table 4. Exclusion Criteria for the Use of Metformin.

Renal impairment: plasma creatinine values ⩾1.5 mg per deciliter (132 μmol per liter) for men and ⩾1.4 mg per deciliter (124 μmol per liter) for women
Cardiac or respiratory insufficiency that is likely to cause central hypoxia or reduced peripheral perfusion
History of lactic acidosis
Severe infection that could lead to decreased tissue perfusion
Liver disease, including alcoholic liver disease, as demonstrated by abnormal liver-function tests
Alcohol abuse with binge drinking sufficient to cause acute hepatic toxicity*
Use of intravenous radiographic contrast agents†

*Moderate alcohol intake is not a contraindication, if liver function is normal.

†It is uncertain whether the reported occurrence of lactic acidosis after the intravenous administration of radiographic contrast agent was due in part to preexisting renal disease and reduced fluid intake before the imaging was performed.

Sulfonylureas

Mechanism of action :

- Increase insulin release from pancreas
- Suppress secretions of Glucagon

Sulfonylureas

Adverse effects

1. Hypoglycemia which occurs in 2 to 4% of patients per yr.
2. Wt gain (approximately 4 to 6 kg)
3. Dermatological reactions (Photosensitivity)
4. Hematological reactions (Aplastic Anemia)
5. GI disturbances

→ The active metabolites can accumulate in pts with Clcr < 30ml/min

→ Glipizide is preferred in pts with mod.- severe renal dysfunction

Meglitinides

- Decrease in HbA1c of 1.4 to 1.8%
- No effect on cholesterol
- May increase body weight
- The incidence of hypoglycemia is less than or equal to sulfonylurea
- Should be administered prior to meals

Acarbose

- Mode of action:
  - Poorly absorbed 1%
  - Inhibits a glucosidase, so inhibits CHO degradation
- Side effects:
  - Flatulence (77%)
  - Diarrhea
  - Abdominal pain (21%)
  - Decreased iron absorption

Thiazolidenedione

- **Mode of action:**
  - Insulin sensitizer (increase insulin sensitivity in muscle, adipose tissue & liver)
  - They are not insulin secretagogues (not insulin releasers)

Thiazolidinedione

Adverse effects:

- ↑ plasma volume (20%) ⇒ edema ⇒ ↑ Wt
- Small ↓ in Hb & Hct
- Should be used with caution in pts with advanced CHF (Class III/IV)
- Pioglitazone may ↓ the concentration of OCPs
- Rosiglitazone may increase MI risk
- ↓ Clearance in pts with mod. to severe liver disease → should not be used if ALT >2.5 × upper limit
- LFT should be monitored every 2 m for 1 year

New drugs

Amylin (Pramlintide)

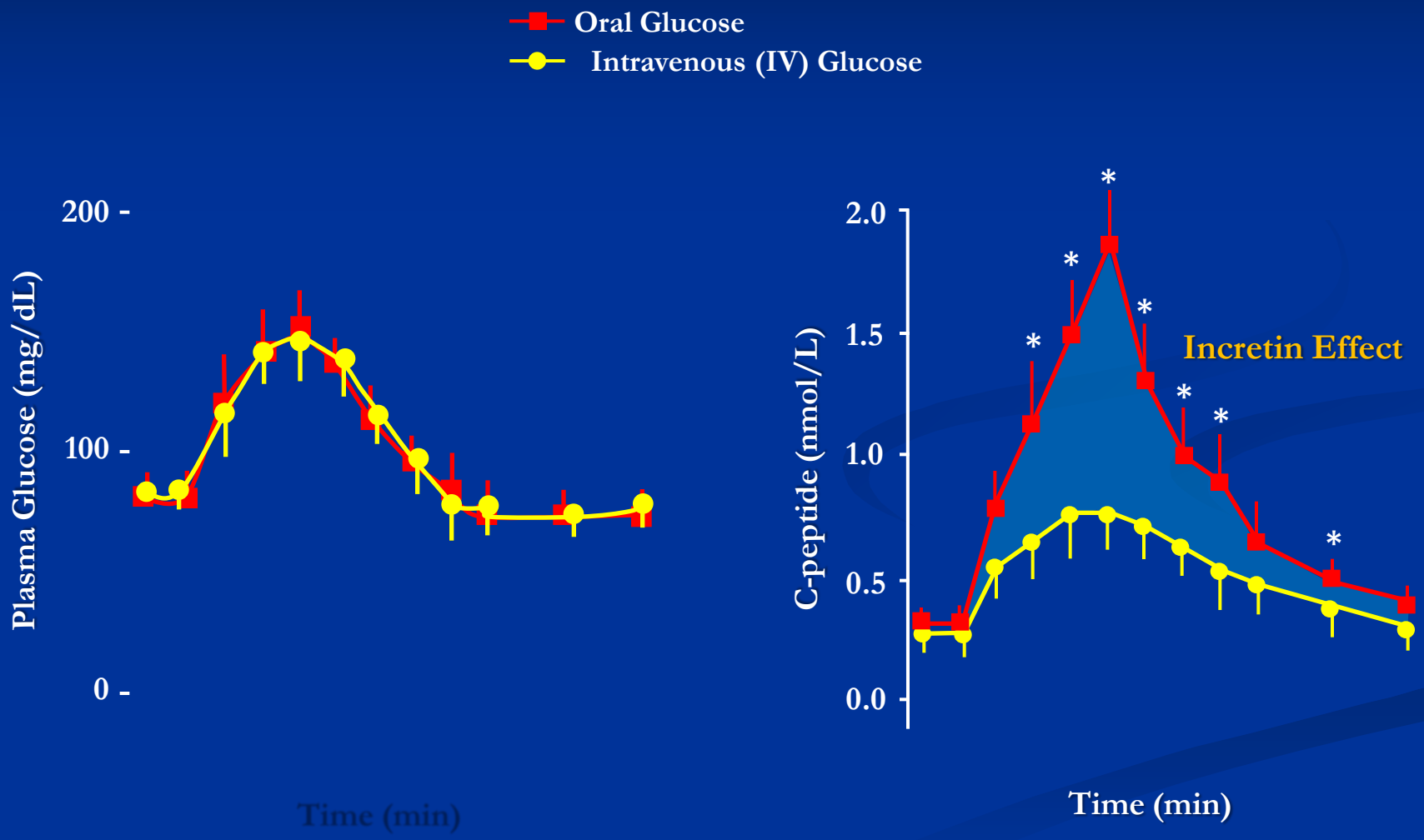
- Mechanisms of action:
  - Lowers postprandial glucagon
  - Slows gastric emptying
  - Suppresses appetite

- Receptors located in the CNS
  - Some of the functions exerted via the vagus nerve
- Both T1DM and T2DM

  - Insulin: involved in glucose disappearance from bloodstream

  - Amylin: controls glucose appearance in the bloodstream (from the stomach and liver)

The Incretin Effect



Nauck MA, et al. *J Clin Endocrinol Metab*. 1986;63:492-498

Incretins

- Gut hormones (members of the superfamily of glucagon-related peptides) that stimulate **insulin secretion** in response to **nutrients**
- Glucose-dependent function
- Two most well-characterized incretins:
  - Glucose-dependent insulinotropic peptide **(GIP)**
  - Glucagon-like peptide-1 **(GLP-1)**

Glucagon-Like Peptide-1 (GLP-1)

1. Stimulates insulin synthesis and secretion
2. Promotes islet cell growth
3. Inhibits glucagon release
4. Delays gastric emptying
5. Induces satiety
6. Extrapancreatic effects on glucose (reduce gluconeogenesis)

Most of these effects act to maintain blood glucose in the post-prandial state.

Incretin-Based Drugs

1. Incretin mimetics (GLP-1 analogs)
   - Resistant to DPP-IV and long-acting
   - Exenatide (Byetta) twice daily S/C injection
     - ½ life 2-4 hours
   - Liraglutide (Victoza) once-daily subcutaneous dosing
     - ½ life 10-12 hours
2. DPP-IV inhibitors (oral)
   - Sitagliptin (Januvia) 100 mg once daily
   - Saxagliptin (Onglyza) 2.5-5 mg once daily

Liraglutide (Victoza)

- Administered as once daily S/C injection
- Weight loss
- Very expensive
- Adverse effects:
  - GI, dose dependent
  - do not cause clinically-significant hypoglycemia
  - ↓ CVD events

DPP-IV inhibitors (sitagliptin)

- Weight neutral with no observed changes in caloric intake
- Significant reduction in HbA1c (-0.6%)
- Hypoglycemia was described in 10% of subjects and was generally mild and often related to missed meals and/or strenuous exercise
- **The greatest potential advantage of DPP-IV inhibitors over GLP-1 agonists is that DPP-IV inhibitors can be given orally**

Sodium-Glucose Cotransporter 2 Inhibitors(SGLT2)

- Canagliflozin, Dapagliflozin, Empagliflozin
- blocking glucose reabsorption in the proximal renal tubule by inhibiting SGLT2.
- provide modest weight loss and BP reduction, ↓ CVD events in type 2 diabetes.
- **Adverse effects:**
  - Euglycemic diabetic ketoacidosis
  - UTI
  - Polyuria
  - Dehydration(↑ Creatinine transiently)

Table 8.2—Median monthly cost of maximum approved daily dose of noninsulin glucose-lowering agents in the U.S. (48)

Class	Compound(s)	Dosage strength/product (if applicable)	Median AWP (min, max)†	Maximum approved daily dose*
Biguanides	• Metformin	500 mg (IR)	$84 ($5, $94)	2,000 mg
		850 mg (IR)	$108 ($5, $108)	2,550 mg
		1,000 mg (IR)	$86 ($4, $87)	2,000 mg
		500 mg (ER)	$90 ($82, $6,672)	2,000 mg
		750 mg (ER)	$72 ($65, $92)	1,500 mg
		1,000 mg (ER)	$1,028 ($1,010, $7,213)	2,000 mg
Sulfonylureas (2nd Gen)	• Glyburide	5 mg	$94 ($64, $103)	20 mg
		6 mg (micronized)	$50 ($48, $71)	12 mg (micronized)
	• Glipizide	10 mg (IR)	$74 ($67, $97)	40 mg (IR)
		10 mg (XL)	$97	20 mg (XL)
	• Glimepiride	4 mg	$74 ($71, $198)	8 mg
Meglitinides (glinides)	• Repaglinide	2 mg	$799 ($163, $878)	16 mg
	• Nateglinide	120 mg	$156	360 mg
TZDs	• Pioglitazone	45 mg	$349 ($348, $349)	45 mg
	• Rosiglitazone	4 mg	$355	8 mg
α-Glucosidase inhibitors	• Acarbose	100 mg	$104 ($104, 105)	300 mg
	• Miglitol	100 mg	$241	300 mg
DPP-4 inhibitors	• Sitagliptin	100 mg	$436	100 mg
	• Saxagliptin	5 mg	$436	5 mg
	• Linagliptin	5 mg	$428	5 mg
	• Alogliptin	25 mg	$436	25 mg
Bile acid sequestrant	• Colesevelam	625 mg tabs	$679	3.75 g
		1.875 g suspension	$1,357	3.75 g
Dopamine-2 agonists	• Bromocriptine	0.8 mg	$719	4.8 mg
SGLT2 inhibitors	• Canagliflozin	300 mg	$470	300 mg
	• Dapagliflozin	10 mg	$470	10 mg
	• Empagliflozin	25 mg	$470	25 mg
GLP-1 receptor agonists	• Exenatide	10 μg pen	$729	20 μg
	• Exenatide (extended-release)	2 mg powder for suspension or pen	$692	2 mg**
	• Liraglutide	18 mg/3 mL pen	$831	1.8 mg
	• Albiglutide	50 mg pen	$527	50 mg**
	• Dulaglutide	1.5/0.5 mL pen	$690	1.5 mg**
Amylin mimetics	• Pramlintide	120 μg pen	$2,124	120 μg/injection††

ER and XL, extended release; IR, immediate release; TZD, thiazolidinedione. †Calculated for 30 day supply (AWP unit price × number of doses required to provide maximum approved daily dose × 30 days); median AWP listed alone when only one product and/or price. *Utilized to calculate median AWP (min, max); generic prices used, if available commercially. **Administered once weekly. ††AWP calculated based on 120 μg three times daily.

PROFILES OF ANTIDIABETIC MEDICATIONS

	MET	GLP-1 RA	SGLT-2i	DPP-4i	AGi	TZD	SU / GLN	COLSVL	BCR-QR	INSULIN	PRAML
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/ Severe / Mild	Neutral	Neutral	Moderate to Severe	Neutral
WEIGHT	Slight Loss	Loss	Loss	Neutral	Neutral	Gain	Gain	Neutral	Neutral	Gain	Loss
RENAL/ GU	Contra-indicated CKD Stage 3B,4,5	Exenatide Contra-indicated CrCl < 30	Genital Mycotic Infections	Dose Adjustment May be Necessary (Except Linagliptin)	Neutral	May Worsen Fluid Retention	More Hypo Risk	Neutral	Neutral	More Hypo Risk & Fluid Retention	Neutral
GI Sx	Moderate	Moderate	Neutral	Neutral	Moderate	Neutral	Neutral	Mild	Moderate	Neutral	Moderate
CHF	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate	Neutral	Neutral	Neutral	Neutral	Neutral
CVD	Benefit		Increased LDL			Neutral	?		Safe		
BONE	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate Bone Loss	Neutral	Neutral	Neutral	Neutral	Neutral

Few adverse events or possible benefits — Use with caution — Likelihood of adverse effects

Insulin

The most powerful agent we have to control glucose

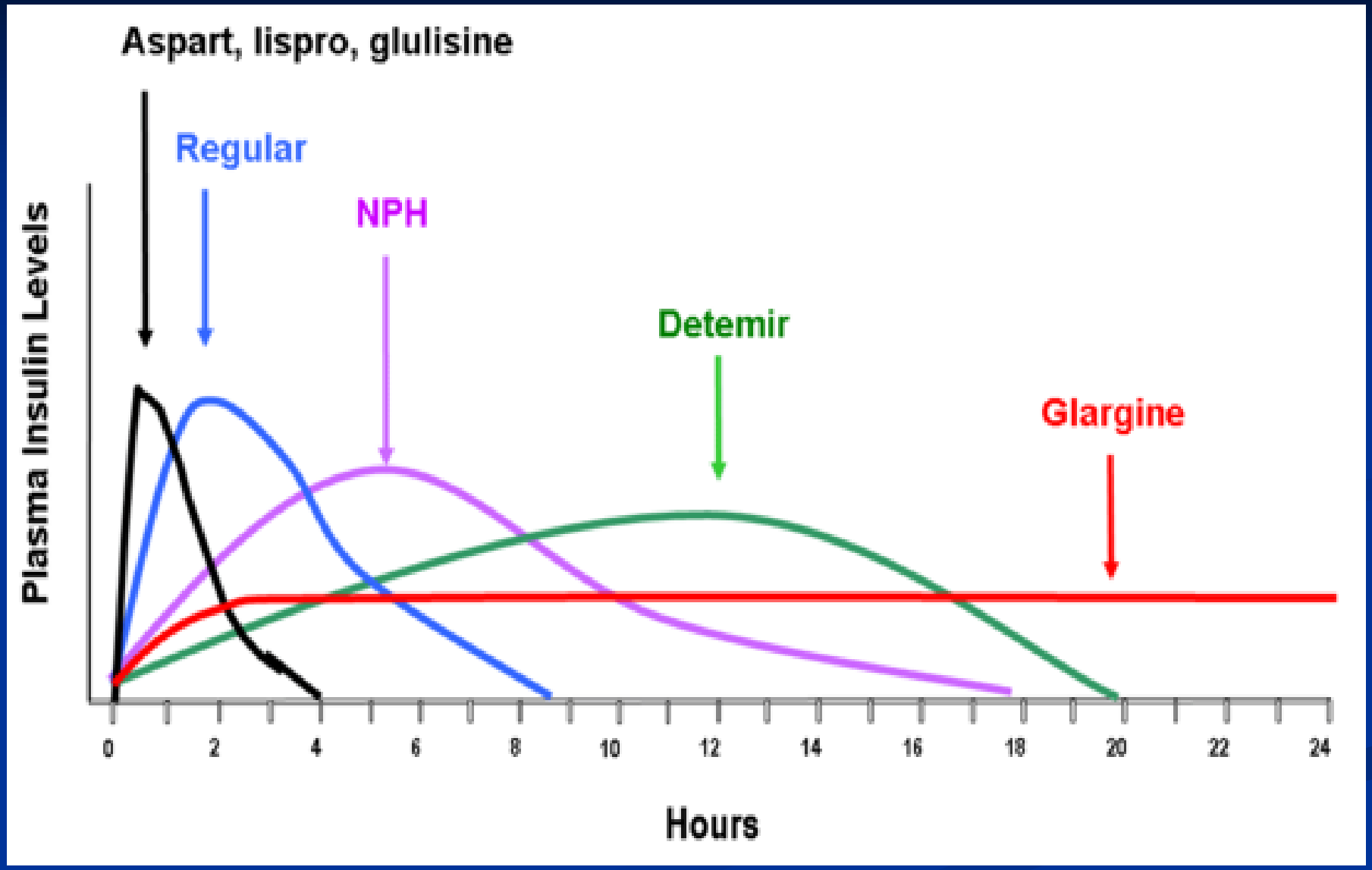
Indication of Insulin therapy

- Type 1 diabetes
- Unstable and complicated diabetes
- Type 2 diabetes failed on OHA
- Pregnancy
- Surgery in diabetic patients
- Development of hyperglycemic crisis

Table 8.3—Median cost of insulins in the U.S. calculated as average wholesale price per 1,000 units of specified dosage form/product (48)

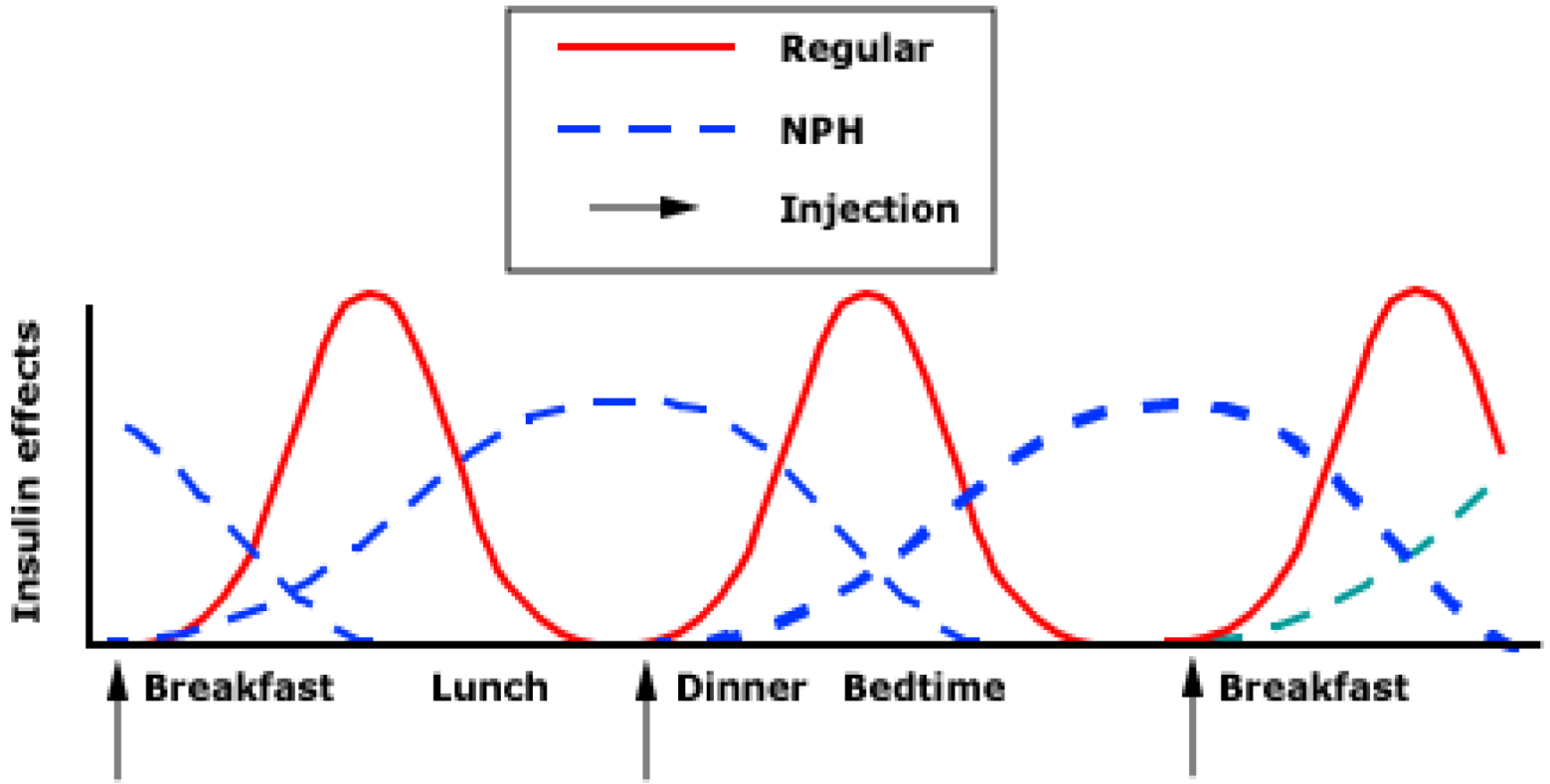
Insulins	Compounds	Dosage form/product	Median AWP package price (min, max)*
Rapid-acting analogs			
	• Lispro	U-100 vial	$306
		U-100 3 mL cartridges	$306 ($306, $379)
		U-100 prefilled pen; U-200 prefilled pen	$394
	• Aspart	U-100 vial	$306
		U-100 3 mL cartridges	$380
		U-100 prefilled pen	$395
	• Glulisine	U-100 vial	$283
		U-100 prefilled pen	$365
	• Inhaled insulin	Inhalation cartridges	$557 ($453, $754)
Short-acting			
	• Human Regular	U-100 vial	$165
Intermediate-acting			
	• Human NPH	U-100 vial	$165
		U-100 prefilled pen	$350
Concentrated Human Regular insulin			
	• U-500 Human Regular insulin	U-500 vial	$165
		U-500 prefilled pen	$213
Basal analogs			
	• Glargine	U-100 vial; U-100 prefilled pen; U-300 prefilled pen	$298
	• Detemir	U-100 vial; U-100 prefilled pen	$323
	• Degludec	U-100 prefilled pen; U-200 prefilled pen	$355
Premixed products			
	• NPH/Regular 70/30	U-100 vial	$165
		U-100 prefilled pen	$350
	• Lispro 50/50	U-100 vial	$317
		U-100 prefilled pen	$394
	• Lispro 75/25	U-100 vial	$317
		U-100 prefilled pen	$394
	• Aspart 70/30	U-100 vial	$318
		U-100 prefilled pen	$395

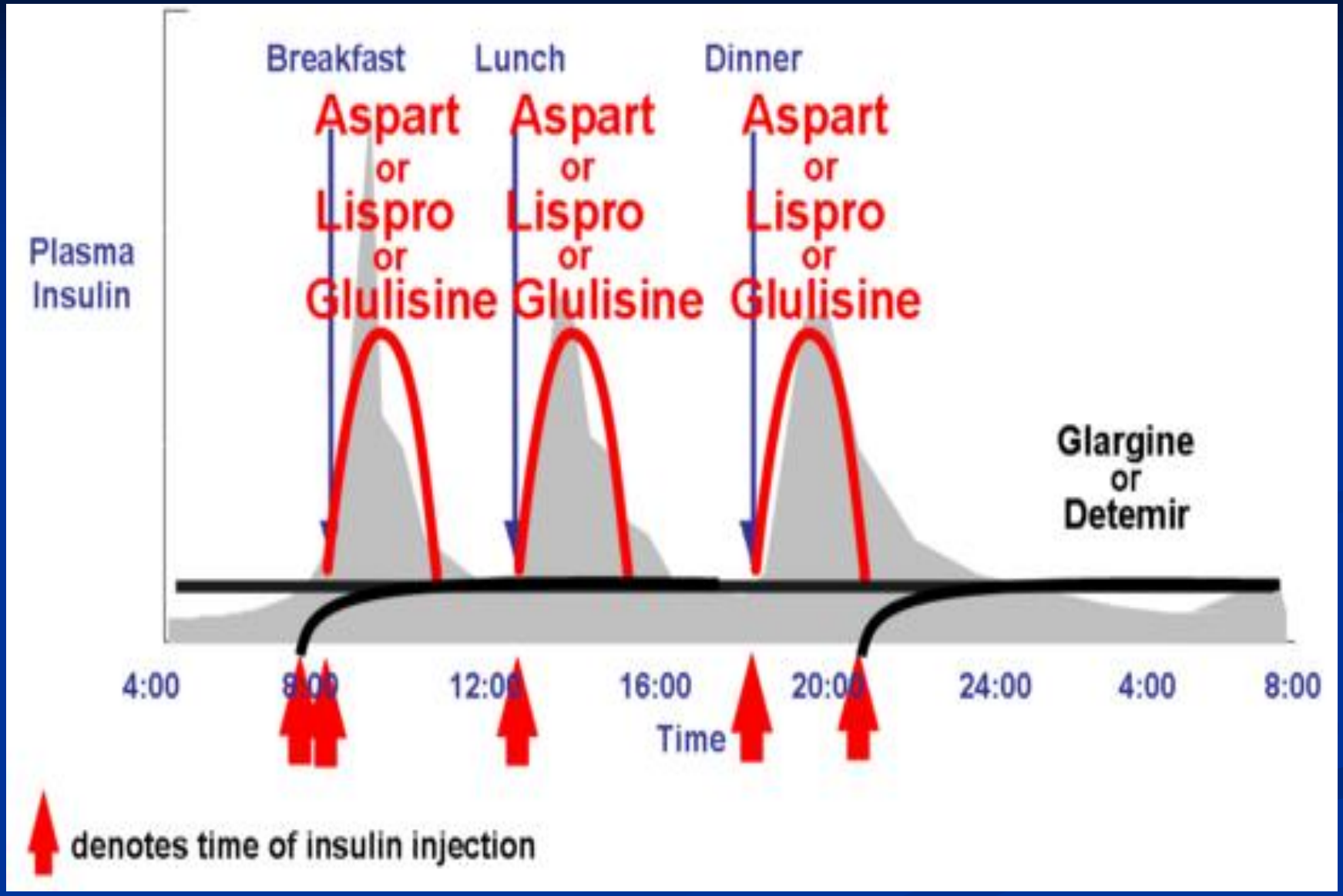
AWP listed alone when only one product and/or price.



Conventional insulin therapy

Effect of twice-daily insulin regimen




Breakfast
Lunch
Dinner
Aspart or Lispro or Glulisine
Aspart or Lispro or Glulisine
Aspart or Lispro or Glulisine
Plasma Insulin
Glargine or Detemir
4:00
8:00
12:00
16:00
20:00
24:00
4:00
8:00
Time
denotes time of insulin injection

Method of Insulin Preparation

- Conventional insulin therapy
- Intensive insulin therapy
  A. *MSI (multi subcutaneous injection)*
  B. *CSII (continues sq insulin injection)*

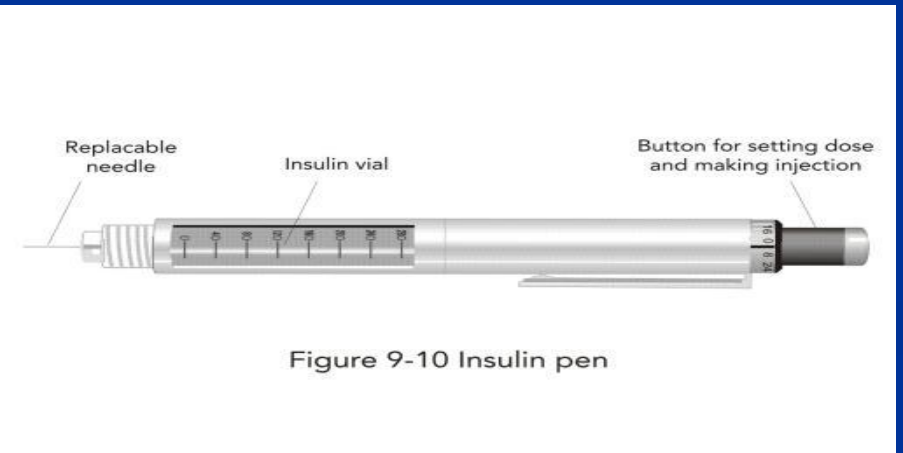
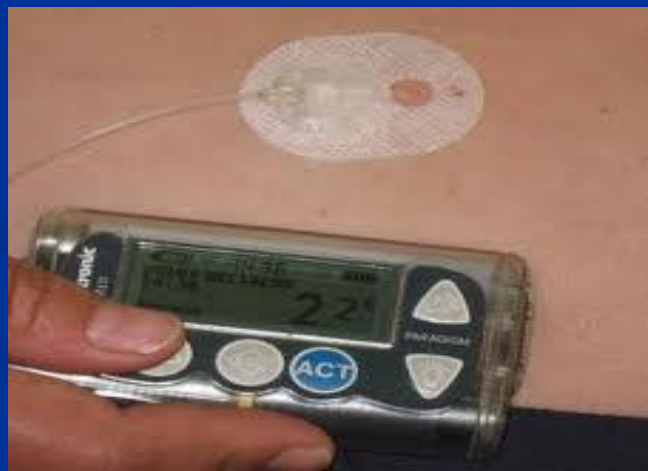


Figure 9-10 Insulin pen



Intensive Management (MDI or CSII)

- Pregnancy
- newly diagnosed patients with type 1
- Renal transplant
- Good compliance
- Possibility

PHARMACOLOGICAL THERAPY FOR TYPE 1 DIABETES

- Pramlintide: FDA approved
- Metformin: may reduce insulin requirements and improve metabolic control in overweight/obese patients with poorly controlled type 1 diabete. BUT Metformin is not FDA-approved
- Incretin-Based Therapies: are not currently FDA approved
- SGLT2: are not FDA approved

Pancreas and Islet Cell Transplantation in type 1

It should be reserved for patients with type 1 diabetes that:

- undergoing simultaneous renal transplantation
- following renal transplantation
- For those with recurrent ketoacidosis
- For those with severe hypoglycemia despite aggressive glycemic management

Start with Monotherapy unless:

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

Monotherapy — Metformin — Lifestyle Management

EFFICACY*	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	GI/lactic acidosis
COSTS*	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Dual Therapy — Metformin + — Lifestyle Management

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Triple Therapy — Metformin + — Lifestyle Management

Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or SGLT2-i	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin§	or GLP-1-RA	or Insulin§	or GLP-1-RA
or Insulin§	or Insulin§		or Insulin§		

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

Combination Injectable Therapy (See Figure 8.2)

Figure 8.1—Antihyperglycemic therapy in type 2 diabetes: general recommendations. The order in the chart was determined by historical availability and the route of administration, with injectables to the right; it is not meant to denote any specific preference. Potential sequences of antihyperglycemic therapy for patients with type 2 diabetes are displayed, with the usual transition moving vertically from top to bottom (although horizontal movement within therapy stages is also possible, depending on the circumstances). DPP-4-i, DPP-4 inhibitor; fxs, fractures; GI, gastrointestinal; GLP-1 RA, GLP-1 receptor agonist; GU, genitourinary; HF, heart failure; Hypo, hypoglycemia; SGLT2-i, SGLT2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione. *See ref. 21 for description of efficacy and cost categorization. §Usually a basal insulin (NPH, glargine, detemir, degludec). Adapted with permission from Inzucchi et al. (21).

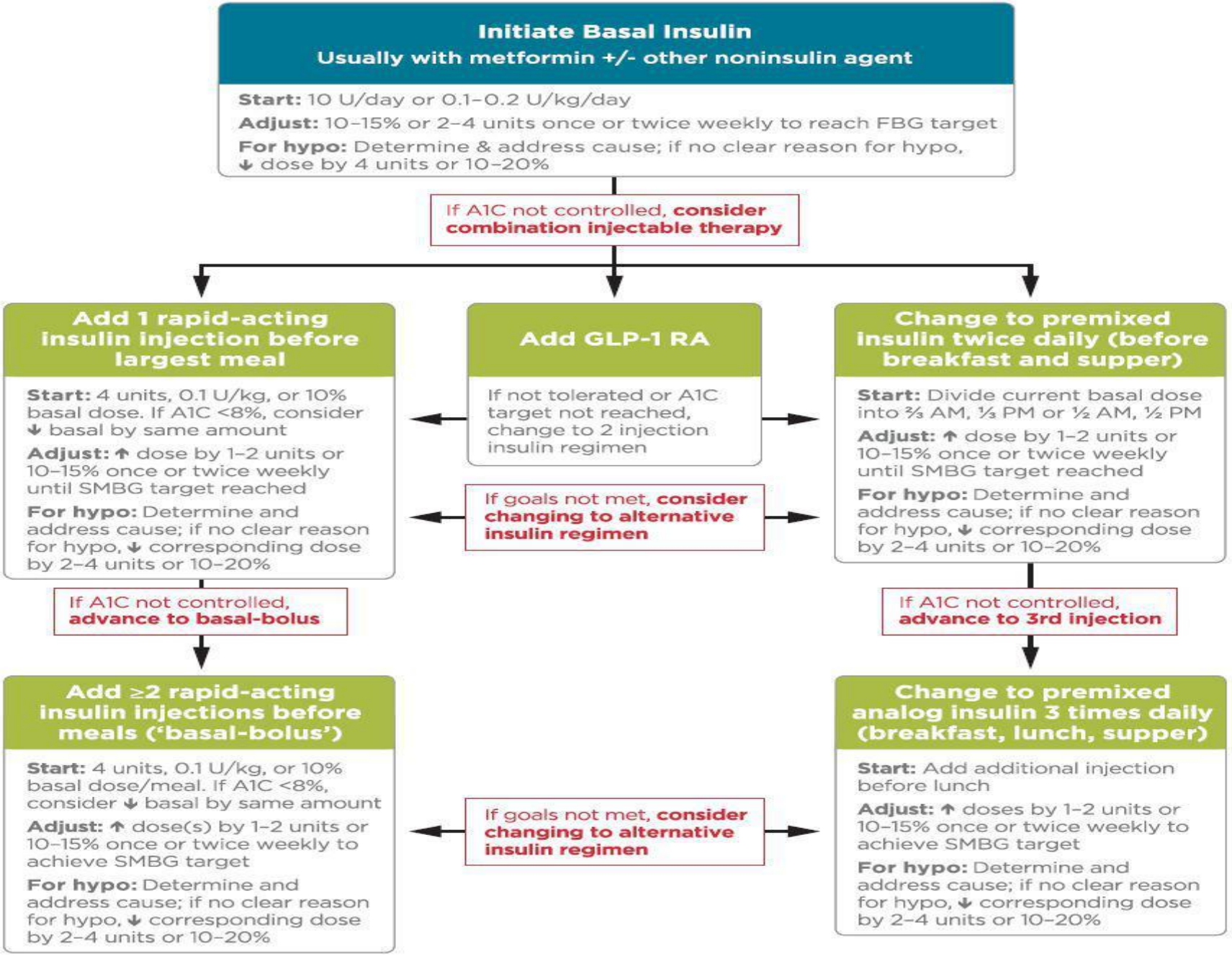


Figure 8.2—Combination injectable therapy for type 2 diabetes. FBG, fasting blood glucose; GLP-1 RA, GLP-1 receptor agonist; hypo, hypoglycemia. Adapted with permission from Inzucchi et al. (21).

Regimen strategy

Minimal Cost Strategy

- For a large proportion of patients, particularly those who are elderly, drug costs are an overwhelming issue.
- Diet and exercise can be extremely effective and almost free.
- The least expensive drugs for the treatment of diabetes are the sulfonylureas; metformin has become available in generic formulations.
- Thus, a minimum cost strategy could start with a sulfonylurea and progress to the addition of generic metformin or bedtime or presupper insulin and finally two or more insulin injections per day if necessary.

Minimum Weight Gain Strategy

- A strategy to minimize weight gain would emphasize diet and exercise and would almost certainly employ metformin or an GLP-1 as initial therapy with the addition of the other agent if one was inadequate.
- As sulfonylureas and repaglinide seem to have a modest weight-sparing effect in combination therapy with insulin, one or the other could be added before insulin administration in such a strategy.

Minimal Injection Strategy

- Too many patients are determined to avoid insulin injections at any cost.
- The minimal injection strategy involves sulfonylureas, metformin, AGIs, DDP 4 inh, and thiazolidinediones, which can be added in any order.
- Insulin, probably as a bedtime or presupper dose to minimize the inconvenience, would be added only if absolutely necessary.
- Most patients require insulin at some point in their lifetime.

Hypoglycemia Avoidance Strategy

- The AGIs have been reported in small studies to reduce "reactive" hypoglycemia.
- Other oral agents could be added in any order with the exception that insulin secretagogues would be added last, their dose minimized, and glyburide avoided.
- Nateglinide in particular among the secretagogues is associated with an exceptionally low risk of significant hypoglycemia.
- The insulin analogues are associated with a lower risk of hypoglycemia than human insulin.

Pregnancy and DM

- Insulin is the preferred medication for treating hyperglycemia in gestational diabetes mellitus, as it does not cross the placenta to a measurable extent.
- Metformin and glyburide may be used, but both cross the placenta to the fetus, with metformin likely crossing to a greater extent than glyburide. All oral agents lack long-term safety data

Glucose targets

- for women with type 1 or type 2 diabetes, and GDM:
  - Fasting ≤95 mg/dL (5.3 mmol/L) and
  - either One-hour postprandial ≤ 140 mg/dL (7.8 mmol/L) or
  - Two-hour postprandial ≤ 120 mg/dL (6.7 mmol/L)
  - A1C ≤ 6–6.5%

TABLE 344-13 Guidelines for Ongoing Medical Care for Patients With Diabetes

- Self-monitoring of blood glucose (individualized frequency)
- A1C testing (2–4 times/year)
- Patient education in diabetes management (annual)
- Medical nutrition therapy and education (annual)
- Eye examination (annual)
- Foot examination (1–2 times/year by physician; daily by patient)
- Screening for diabetic nephropathy (annual; see Fig. 344-11)
- Blood pressure measurement (quarterly)
- Lipid profile and serum creatinine (estimate GFR) (annual)
- Influenza/pneumococcal immunizations
- Consider antiplatelet therapy (see text)

Abbreviation: A1C, hemoglobin A1C.


لبخندی که در چهره ام می بینی معنایش
این نیست که زندگی ام بی نقص
است، بلکه یعنی قدردان داشته هایم
هستم و از خدا بخاطر نعمتهایش
سپاسگزار....