

Management of Hyperglycemia in Type 2 Diabetes, 2015: A Patient-Centered Approach

Update to a Position Statement of the American Diabetes Association (ADA)
and the European Association for the Study of Diabetes (EASD)



Diabetes Care 2015;38:140–149
Diabetologia 2015;58:429–442



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1. PATIENT-CENTERED CARE

2. BACKGROUND

- Epidemiology and health care impact
- Relationship of glycemic control to outcomes
- Overview of the pathogenesis of Type 2 diabetes

3. ANTI-HYPERGLYCEMIC THERAPY

- Glycemic targets
- Therapeutic options
 - Lifestyle
 - UPDATED** - Oral agents & non-insulin injectables
 - Insulin

3. ANTIHYPERGLYCEMIC THERAPY

- Implementation Strategies
 - Initial drug therapy
 - UPDATED** - Advancing to dual combination therapy
 - UPDATED** - Advancing to triple combination therapy
 - UPDATED** - Transitions to and titrations of insulin

4. OTHER CONSIDERATIONS

- Age
- Weight
- Sex/racial/ethnic/genetic differences
- Comorbidities (*CAD, HF, CKD, Liver disease, Hypoglycemia-prone*)

5. FUTURE DIRECTIONS / RESEARCH NEEDS

1. Patient-Centered Approach

“...providing care that is respectful of and responsive to individual patient preferences, needs, and values - ensuring that patient values guide all clinical decisions.”

- Gauge patient’s preferred level of involvement.
- Explore, where possible, therapeutic choices. Consider using decision aids.
- Shared Decision Making – a collaborative process between patient and clinician, using best available evidence and taking into account the patient’s preferences and values
- Final decisions regarding lifestyle choices ultimately lie with the patient.

2. BACKGROUND

- **Relationship of glycemic control to microvascular and macrovascular outcomes.**

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

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

Kendall DM, Bergenstal RM. © International Diabetes Center 2009

UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998;352:854.
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 Moritz T. *N Engl J Med* 2009;361:1024)

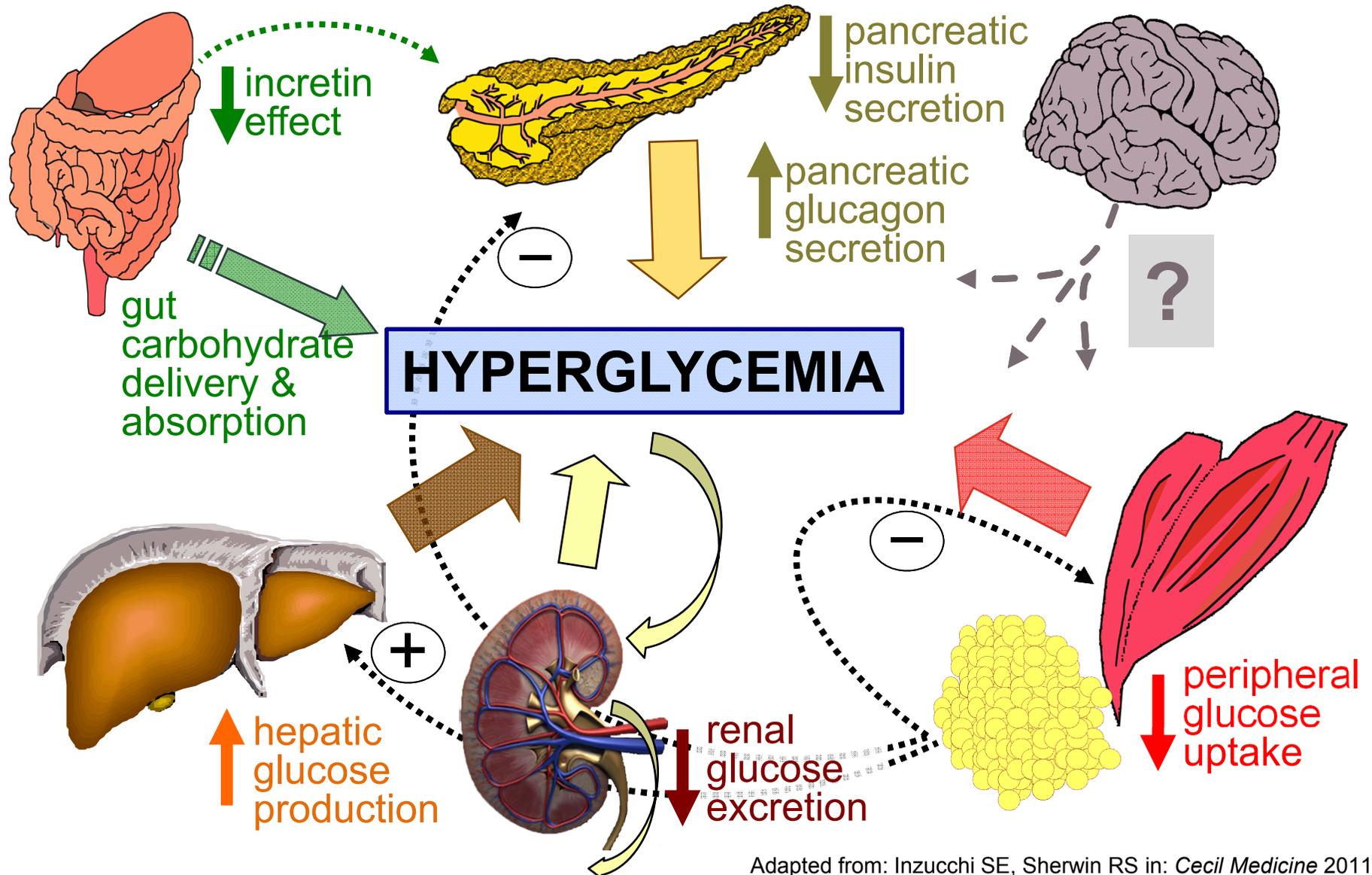
Initial Trial
 Long Term Follow-up

* in T1DM

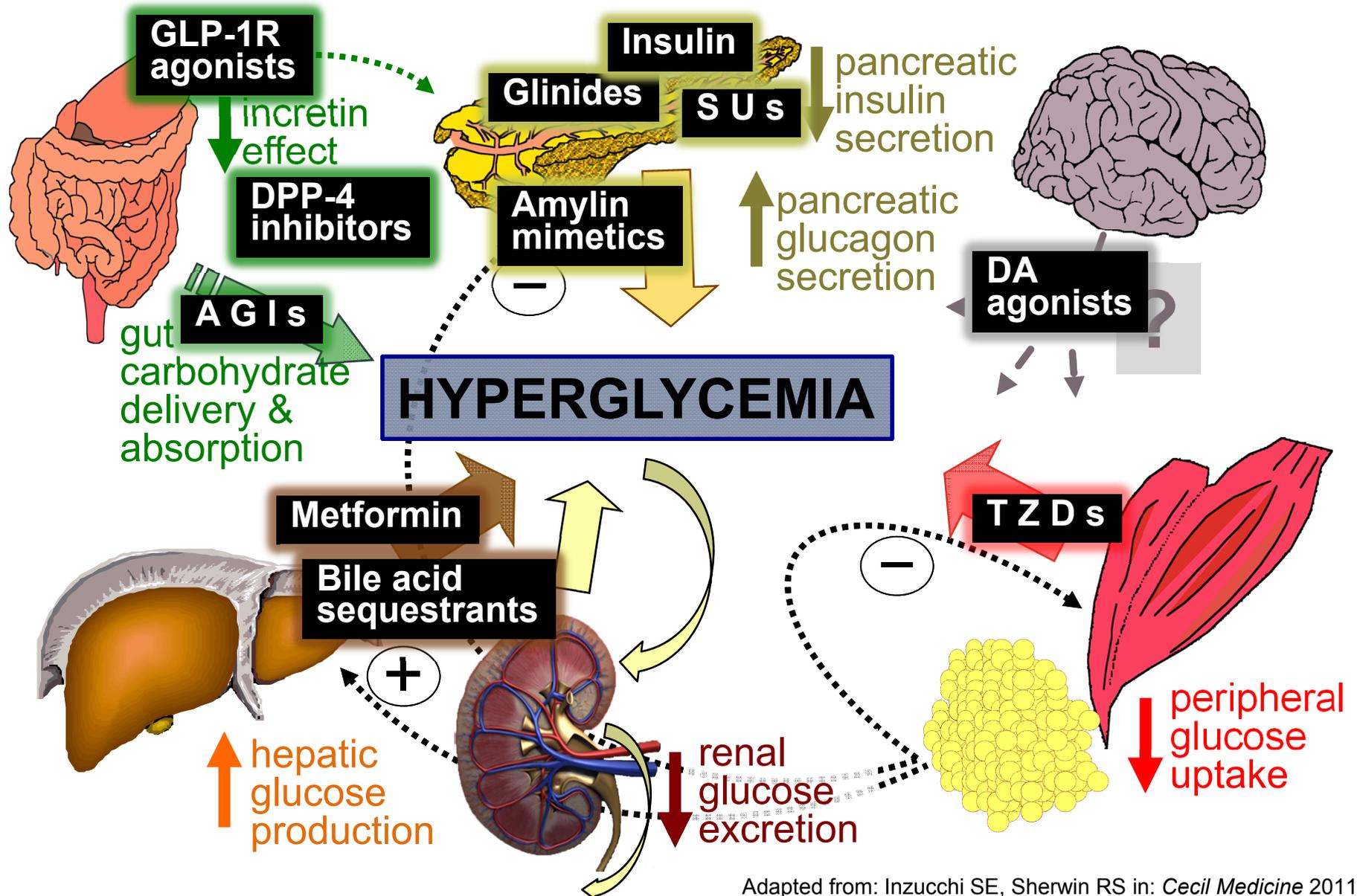
2. BACKGROUND

- **Overview of the pathogenesis of T2DM**
 - **Insulin secretory dysfunction**
 - **Insulin resistance (muscle, fat, liver)**
 - **Increased endogenous glucose production**
 - **Decreased incretin effect**
 - **Deranged adipocyte biology**

Multiple, Complex Pathophysiological Abnormalities in T2DM



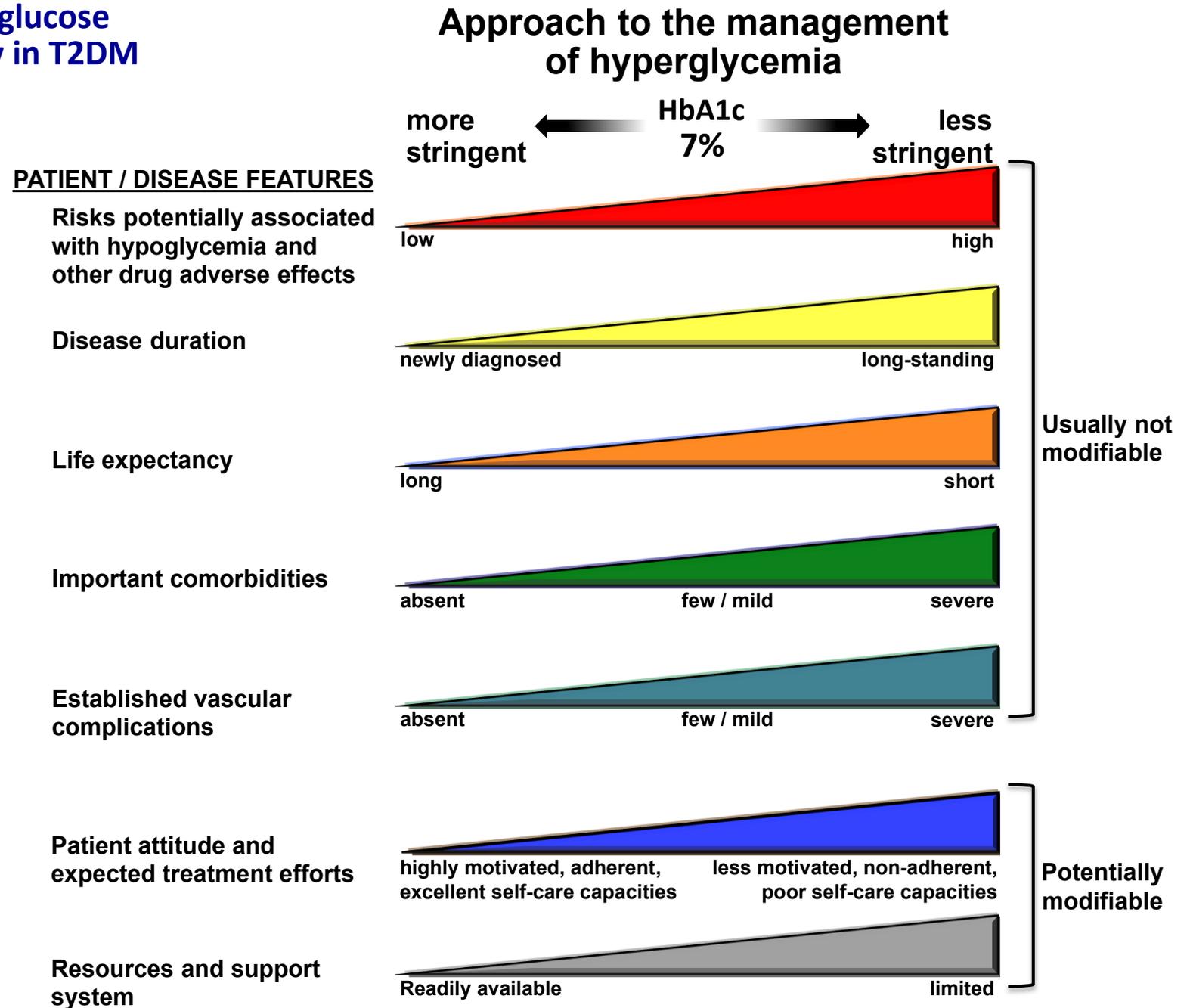
Multiple, Complex Pathophysiological Abnormalities in T2DM



3. ANTI-HYPERGLYCEMIC THERAPY

- **Glycemic targets**
 - **HbA1c < 7.0%** (mean PG ~150-160 mg/dl [8.3-8.9 mmol/l])
 - Pre-prandial PG <130 mg/dl (7.2 mmol/l)
 - Post-prandial PG <180 mg/dl (10.0 mmol/l)
 - ***Individualization*** is key:
 - Tighter targets (6.0 - 6.5%) - younger, healthier
 - Looser targets (7.5 - 8.0%⁺) - older, comorbidities, hypoglycemia prone, etc.
 - Avoidance of hypoglycemia

Figure 1. Modulation of the intensiveness of glucose lowering therapy in T2DM



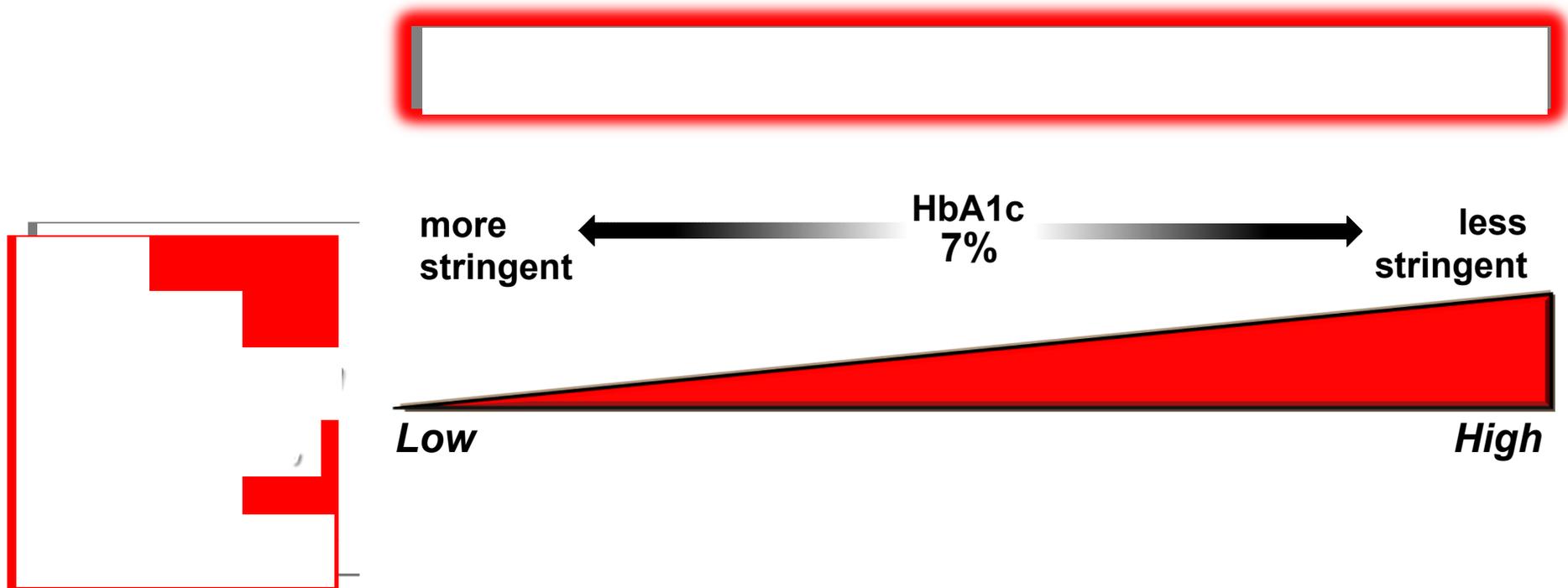


Figure 1. Modulation of the intensiveness of glucose lowering therapy in T2DM

**Disease
duration**

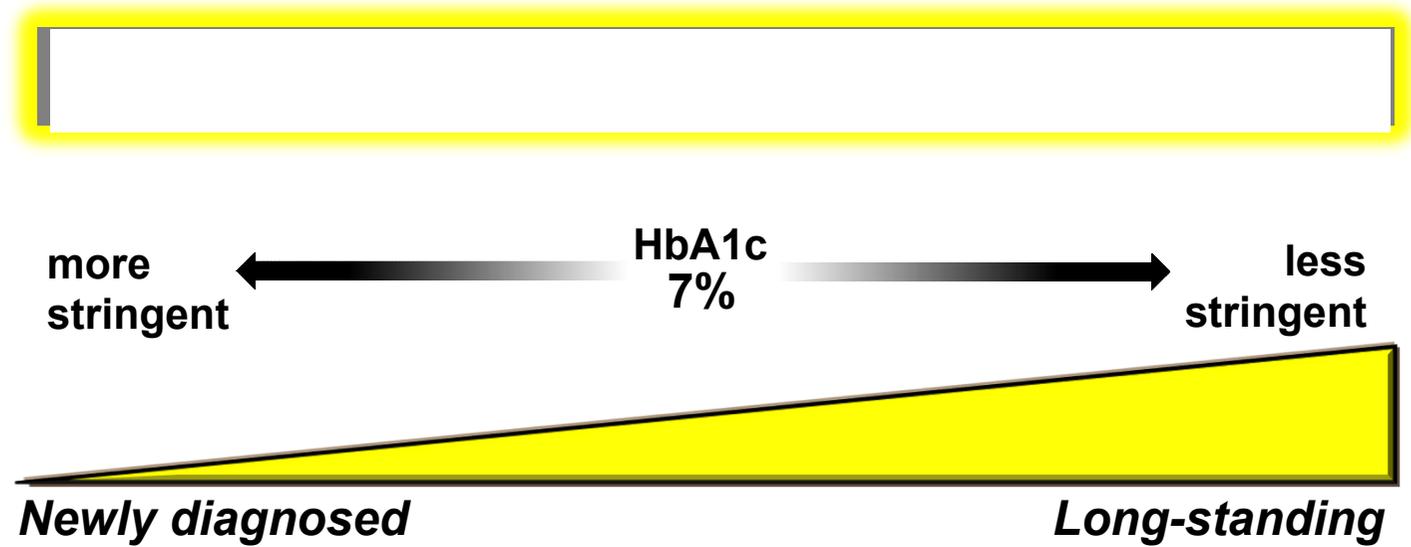


Figure 1. Modulation of the intensiveness of glucose lowering therapy in T2DM

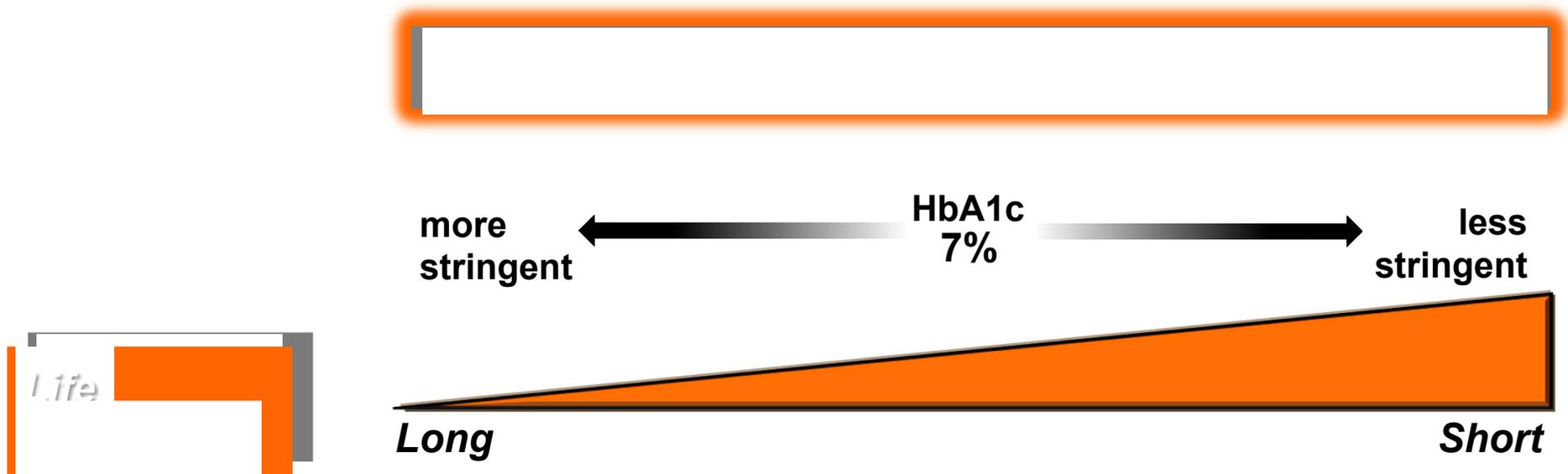


Figure 1. Modulation of the intensiveness of glucose lowering therapy in T2DM

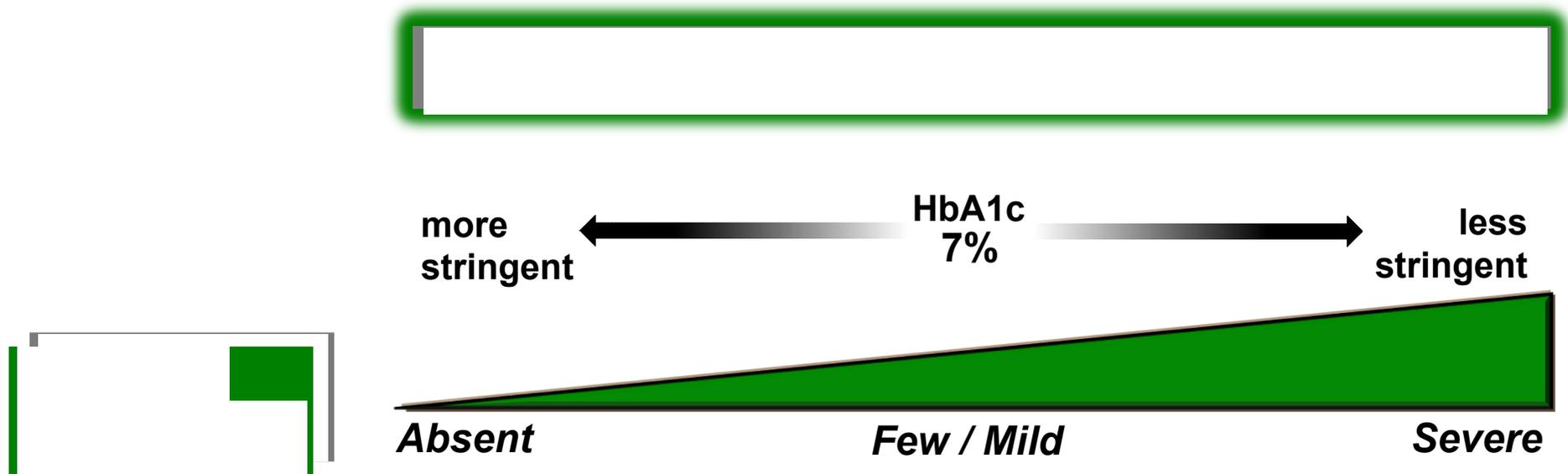


Figure 1. Modulation of the intensiveness of glucose lowering therapy in T2DM

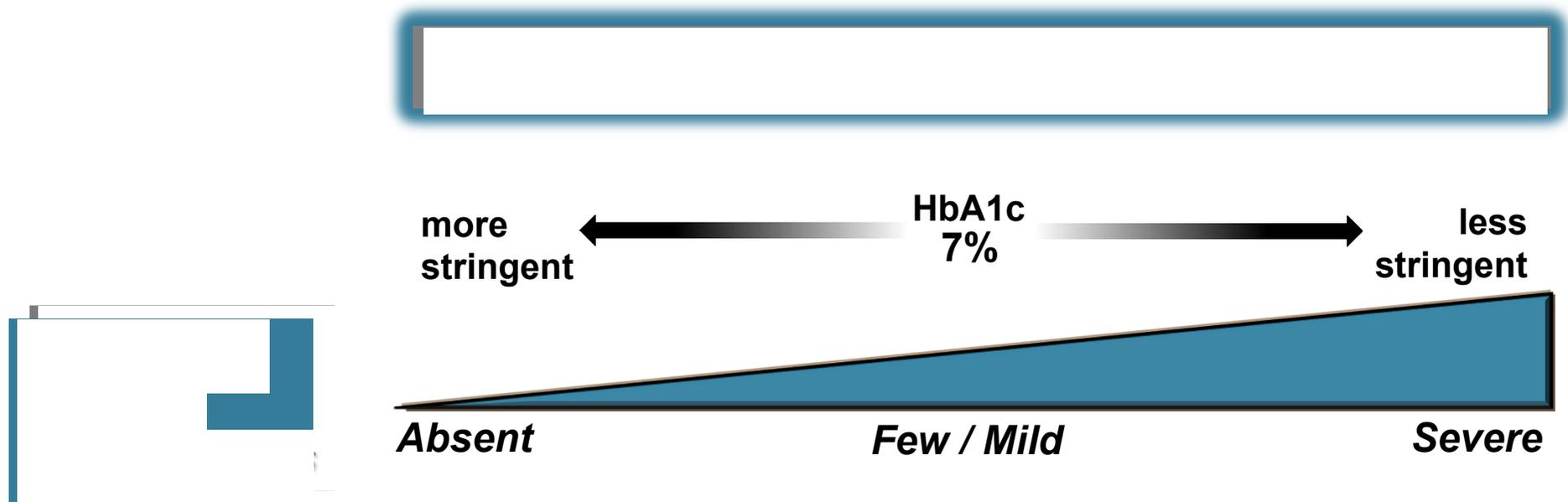


Figure 1. Modulation of the intensiveness of glucose lowering therapy in T2DM

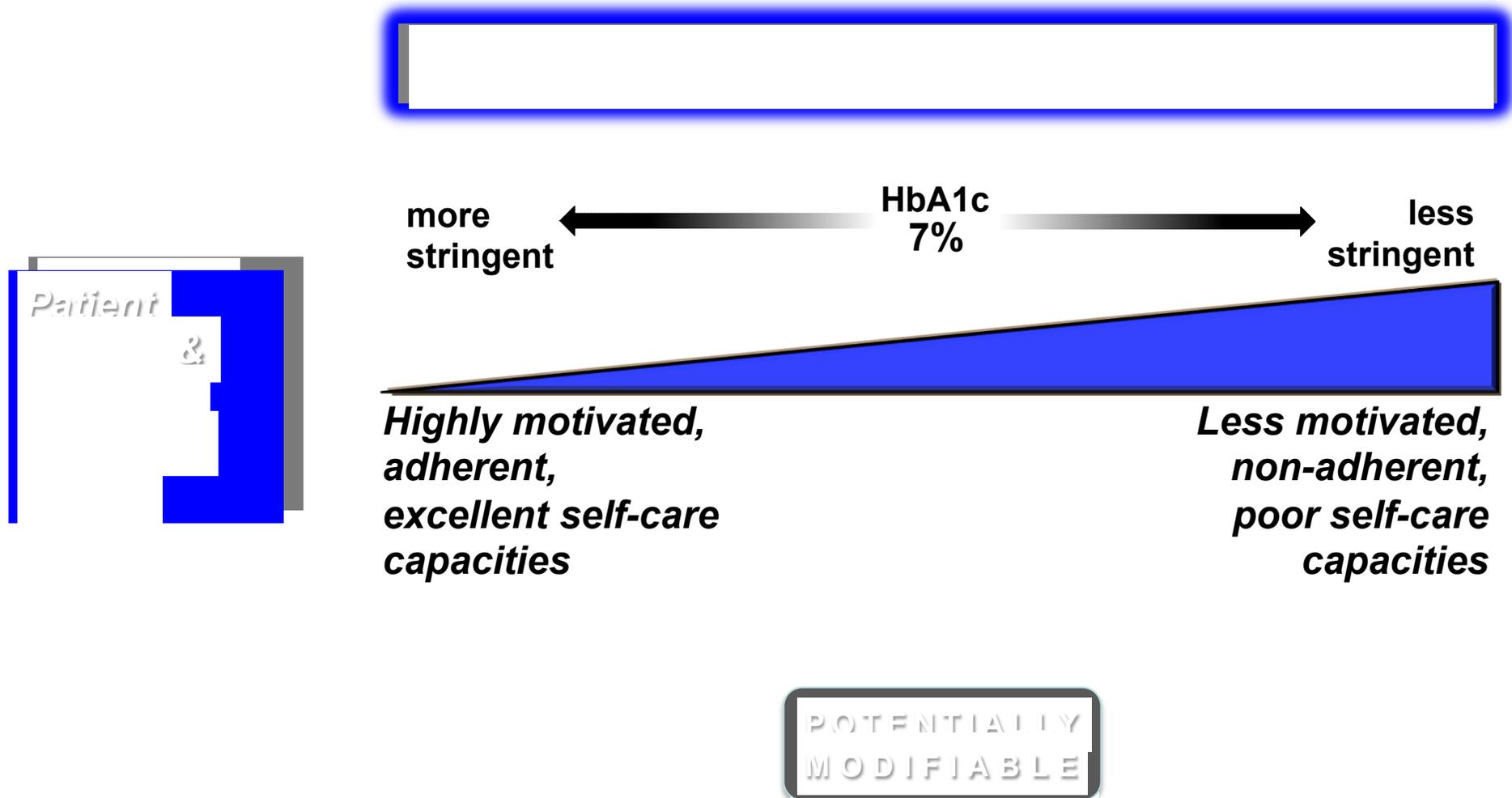


Figure 1. Modulation of the intensiveness of glucose lowering therapy in T2DM

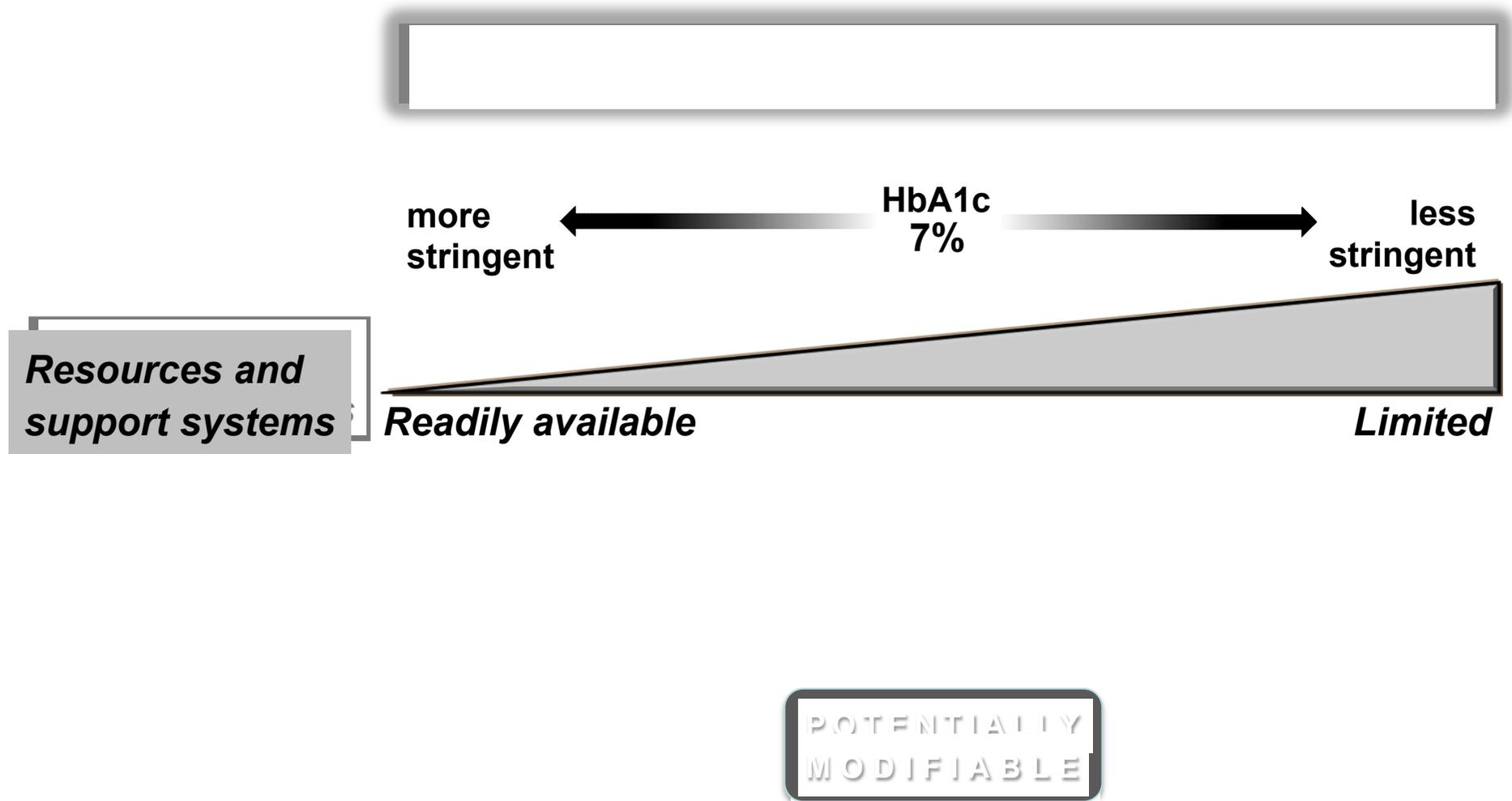
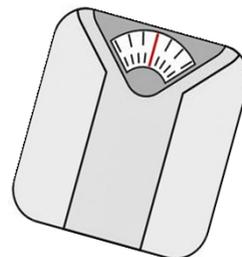


Figure 1. Modulation of the intensiveness of glucose lowering therapy in T2DM

3. ANTI-HYPERGLYCEMIC THERAPY

- Therapeutic options: Lifestyle

- Weight optimization



- Healthy diet

- Increased activity level



3. ANTI-HYPERGLYCEMIC THERAPY

- Therapeutic options:

Oral agents & non-insulin injectables

- Metformin
- Sulfonylureas
- Thiazolidinediones
- DPP-4 inhibitors
- SGLT-2 inhibitors
- GLP-1 receptor agonists
- Meglitinides
- α -glucosidase inhibitors
- Colesevelam
- Dopamine-2 agonists
- Amylin mimetics



Oral Class	Mechanism	Advantages	Disadvantages	Cost
Biguanides	<ul style="list-style-type: none"> • Activates AMP-kinase (?other) • ↓ Hepatic glucose production 	<ul style="list-style-type: none"> • Extensive experience • No hypoglycemia • Weight neutral • ? ↓ CVD 	<ul style="list-style-type: none"> • Gastrointestinal • Lactic acidosis (rare) • B-12 deficiency • Contraindications 	Low
Sulfonylureas	<ul style="list-style-type: none"> • Closes K_{ATP} channels • ↑ Insulin secretion 	<ul style="list-style-type: none"> • Extensive experience • ↓ Microvascular risk 	<ul style="list-style-type: none"> • Hypoglycemia • ↑ Weight • Low durability • ? Blunts ischemic preconditioning 	Low
Meglitinides	<ul style="list-style-type: none"> • Closes K_{ATP} channels • ↑ Insulin secretion 	<ul style="list-style-type: none"> • ↓ Postprandial glucose • Dosing flexibility 	<ul style="list-style-type: none"> • Hypoglycemia • ↑ Weight • ? Blunts ischemic preconditioning • Dosing frequency 	Mod.
TZDs	<ul style="list-style-type: none"> • PPAR-γ activator • ↑ Insulin sensitivity 	<ul style="list-style-type: none"> • No hypoglycemia • Durability • ↓ TGs (pio) • ↑ HDL-C • ? ↓ CVD events (pio) 	<ul style="list-style-type: none"> • ↑ Weight • Edema/heart failure • Bone fractures • ↑ LDL-C (rosi) • ? ↑ MI (rosi) 	Low

Table 1. Properties of anti-hyperglycemic agents

Diabetes Care 2015;38:140-149;
Diabetologia 2015;58:429-442

Oral Class	Mechanism	Advantages	Disadvantages	Cost
α-Glucosidase inhibitors	<ul style="list-style-type: none"> • Inhibits α-glucosidase • Slows carbohydrate digestion / absorption 	<ul style="list-style-type: none"> • No hypoglycemia • Nonsystemic • \downarrow Postprandial glucose • ? \downarrow CVD events 	<ul style="list-style-type: none"> • Gastrointestinal • Dosing frequency • Modest \downarrow A1c 	Mod.
DPP-4 inhibitors	<ul style="list-style-type: none"> • Inhibits DPP-4 • Increases incretin (GLP-1, GIP) levels 	<ul style="list-style-type: none"> • No hypoglycemia • Well tolerated 	<ul style="list-style-type: none"> • Angioedema / urticaria • ? Pancreatitis • ? \uparrow Heart failure 	High
Bile acid sequestrants	<ul style="list-style-type: none"> • Bind bile acids • ? \downarrow Hepatic glucose production 	<ul style="list-style-type: none"> • No hypoglycemia • \downarrow LDL-C 	<ul style="list-style-type: none"> • Gastrointestinal • Modest \downarrow A1c • Dosing frequency 	High
Dopamine-2 agonists	<ul style="list-style-type: none"> • Activates DA receptor • Alters hypothalamic control of metabolism • \uparrow insulin sensitivity 	<ul style="list-style-type: none"> • No hypoglycemia • ? \downarrow CVD events 	<ul style="list-style-type: none"> • Modest \downarrow A1c • Dizziness, fatigue • Nausea • Rhinitis 	High
SGLT2 inhibitors	<ul style="list-style-type: none"> • Inhibits SGLT2 in proximal nephron • Increases glucosuria 	<ul style="list-style-type: none"> • \downarrow Weight • No hypoglycemia • \downarrow BP • Effective at all stages 	<ul style="list-style-type: none"> • GU infections • Polyuria • Volume depletion • \uparrow LDL-C • \uparrowCr (transient) 	High

Table 1. Properties of anti-hyperglycemic agents

Diabetes Care 2015;38:140-149;
Diabetologia 2015;58:429-442

Injectable Class	Mechanism	Advantages	Disadvantages	Cost
Amylin mimetics	<ul style="list-style-type: none"> • Activates amylin receptor • ↓ glucagon • ↓ gastric emptying • ↑ satiety 	<ul style="list-style-type: none"> • ↓ Weight • ↓ Postprandial glucose 	<ul style="list-style-type: none"> • Gastrointestinal • Modest ↓ A1c • Injectable • Hypo if insulin dose not reduced • Dosing frequency • Training requirements 	High
GLP-1 receptor agonists	<ul style="list-style-type: none"> • Activates GLP-1 R • ↑ Insulin, ↓ glucagon • ↓ gastric emptying • ↑ satiety 	<ul style="list-style-type: none"> • ↓ Weight • No hypoglycemia • ↓ Postprandial glucose • ↓ Some CV risk factors 	<ul style="list-style-type: none"> • Gastrointestinal • ? Pancreatitis • ↑ Heart rate • Medullary ca (rodents) • Injectable • Training requirements 	High
Insulin	<ul style="list-style-type: none"> • Activates insulin receptor • Myriad 	<ul style="list-style-type: none"> • Universally effective • Unlimited efficacy • ↓ Microvascular risk 	<ul style="list-style-type: none"> • Hypoglycemia • Weight gain • ? Mitogenicity • Injectable • Patient reluctance • Training requirements 	Variable

Table 1. Properties of anti-hyperglycemic agents

Diabetes Care 2015;38:140-149;
Diabetologia 2015;58:429-442

Healthy eating, weight control, increased physical activity & diabetes education

Mono-therapy

- Efficacy*
- Hypo risk
- Weight
- Side effects
- Costs

Metformin

- high
- low risk
- neutral/loss
- GI / lactic acidosis
- low

Triple therapy



If HbA1c target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-i:



Figure 2. Anti-hyperglycemic therapy in T2DM: General recommendations

Healthy eating, weight control, increased physical activity & diabetes education

Mono-therapy

Efficacy*	high
Hypo risk	low risk
Weight	neutral/loss
Side effects	GI / lactic acidosis
Costs	low

Metformin



If HbA1c target not achieved after ~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 +	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
	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	GI	hypoglycemia
Costs	low	low	high	high	high	variable

Figure 2. Anti-hyperglycemic therapy in T2DM: General recommendations

Healthy eating, weight control, increased physical activity & diabetes education

Mono-therapy

Efficacy*	high
Hypo risk	low risk
Weight	neutral/loss
Side effects	GI / lactic acidosis
Costs	low

Metformin

If HbA1c target not achieved after ~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 + Sulfonylurea	Metformin + Thiazolidinedione	Metformin + DPP-4 inhibitor	Metformin + SGLT2 inhibitor	Metformin + GLP-1 receptor agonist	Metformin + 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	GI	hypoglycemia
Costs	low	low	high	high	high	variable

If HbA1c target not achieved after ~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 + Sulfonylurea	Metformin + Thiazolidinedione	Metformin + DPP-4 Inhibitor	Metformin + SGLT-2 Inhibitor	Metformin + GLP-1 receptor agonist	Metformin + 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 Insulin [§]	or SGLT2-i
or	GLP-1-RA	or GLP-1-RA	or Insulin [§]	or Insulin [§]		or GLP-1-RA
or	Insulin [§]	or Insulin [§]				

Figure 2. Anti-hyperglycemic therapy in T2DM: General recommendations

Healthy eating, weight control, increased physical activity & diabetes education

Mono-therapy

Efficacy*	high
Hypo risk	low risk
Weight	neutral/loss
Side effects	GI / lactic acidosis
Costs	low

Metformin

Dual therapy†

If HbA1c target not achieved after ~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):

	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
	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	GI	hypoglycemia
Costs	low	low	high	high	high	variable

Triple therapy

If HbA1c target not achieved after ~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):

	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
	Sulfonylurea + TZD or DPP-4-i or SGLT2-i or GLP-1-RA or Insulin [§]	Thiazolidinedione + SU or DPP-4-i or SGLT2-i or GLP-1-RA or Insulin [§]	DPP-4 Inhibitor + SU or TZD or SGLT2-i or Insulin [§]	SGLT-2 Inhibitor + SU or TZD or DPP-4-i or Insulin [§]	GLP-1 receptor agonist + SU or TZD or Insulin [§]	Insulin (basal) + TZD or DPP-4-i or SGLT2-i or GLP-1-RA

If HbA1c target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-i:

Combination injectable therapy‡

Metformin +

Basal Insulin +	Mealtime Insulin	or	GLP-1-RA
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Healthy eating, weight control, increased physical activity & diabetes education

Mono-therapy

Efficacy*
Hypo risk
Weight
Side effects

Metformin

high
low risk
neutral/loss
GI / lactic acidosis
low

Metformin intolerance or contraindication

If HbA1c target not achieved after ~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):

Metformin +	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
high	high	intermediate	intermediate	high	highest
moderate risk	low risk	low risk	low risk	low risk	high risk
gain	gain	neutral	loss	loss	gain
hypoglycemia	edema, HF, fxs	rare	GU, dehydration	GI	hypoglycemia
low	low	high	high	high	variable

If HbA1c target not achieved after ~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):

Metformin +	Metformin +				
Sulfonylurea	Thiazolidinedione	DPP-4 Inhibitor	SGLT-2 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 Insulin [§]	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin [§]	or Insulin [§]		or GLP-1-RA
or Insulin [§]	or Insulin [§]				

If HbA1c target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-i:

Metformin +

Basal Insulin +	Mealtime Insulin	or	GLP-1-RA
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Dual therapy[†]

HbA1c ≥9%

Efficacy*
Hypo risk
Weight
Side effects
Costs

Triple therapy

Uncontrolled hyperglycemia (catabolic features, BG ≥300-350 mg/dl, HbA1c ≥10-12%)

Combination injectable therapy[†]

Healthy eating, weight control, increased physical activity & diabetes education

Mono-therapy

Efficacy*
Hypo risk
Weight
Side effects
Costs

Metformin

high
low risk
neutral/loss
GI / lactic acidosis
low

If HbA1c target not achieved after ~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[†]

Efficacy*
Hypo risk
Weight
Side effects
Costs

Metformin +	Metformin +	Metformin +	Metformin +
Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist
high	intermediate	intermediate	high
low risk	low risk	low risk	low risk
gain	neutral	loss	loss
edema, HF, fxs	rare	GU, dehydration	GI
low	high	high	high

If HbA1c target not achieved after ~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 +	Metformin +	Metformin +	Metformin +
Thiazolidinedione	DPP-4 Inhibitor	SGLT-2 Inhibitor	GLP-1 receptor agonist
+	+	+	+
or DPP-4-i	or TZD	or TZD	or TZD
or SGLT2-i	or SGLT2-i	or DPP-4-i	
or GLP-1-RA			

Figure 2A. Anti-hyperglycemic therapy in T2DM:
Avoidance of hypoglycemia

Healthy eating, weight control, increased physical activity & diabetes education

Mono-therapy

Efficacy*
Hypo risk
Weight
Side effects
Costs

Metformin

high
low risk
neutral/loss
GI / lactic acidosis
low

If HbA1c target not achieved after ~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†

Efficacy*
Hypo risk
Weight
Side effects
Costs

	Metformin +	Metformin +	Metformin +
	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist
Efficacy*	intermediate	intermediate	high
Hypo risk	low risk	low risk	low risk
Weight	neutral	loss	loss
Side effects	rare	GU, dehydration	GI
Costs	high	high	high

If HbA1c target not achieved after ~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 +	Metformin +
	DPP-4 Inhibitor +	SGLT-2 Inhibitor +
	or SGLT2-i	or DPP-4-i

Figure 2B. Anti-hyperglycemic therapy in T2DM:
Avoidance of weight gain

Healthy eating, weight control, increased physical activity & diabetes education

Mono-therapy

Efficacy*	high
Hypo risk	low risk
Weight	neutral/loss
Side effects	GI / lactic acidosis
Costs	low

Metformin

Dual therapy†

Efficacy*	high	high	highest
Hypo risk	moderate risk	low risk	high risk
Weight	gain	gain	gain
Side effects	hypoglycemia	edema, HF, fxs	hypoglycemia
Costs	low	low	variable

Triple therapy

Efficacy*	high	high	highest
Hypo risk	moderate risk	low risk	high risk
Weight	gain	gain	gain
Side effects	hypoglycemia	edema, HF, fxs	hypoglycemia
Costs	low	low	variable

If HbA1c target not achieved after ~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):

If HbA1c target not achieved after ~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):



If HbA1c target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGL T2-i:



Figure 2C. Anti-hyperglycemic therapy in T2DM: Minimization of costs

3. ANTI-HYPERGLYCEMIC THERAPY



- **Therapeutic options: *Insulins***

Human Insulins

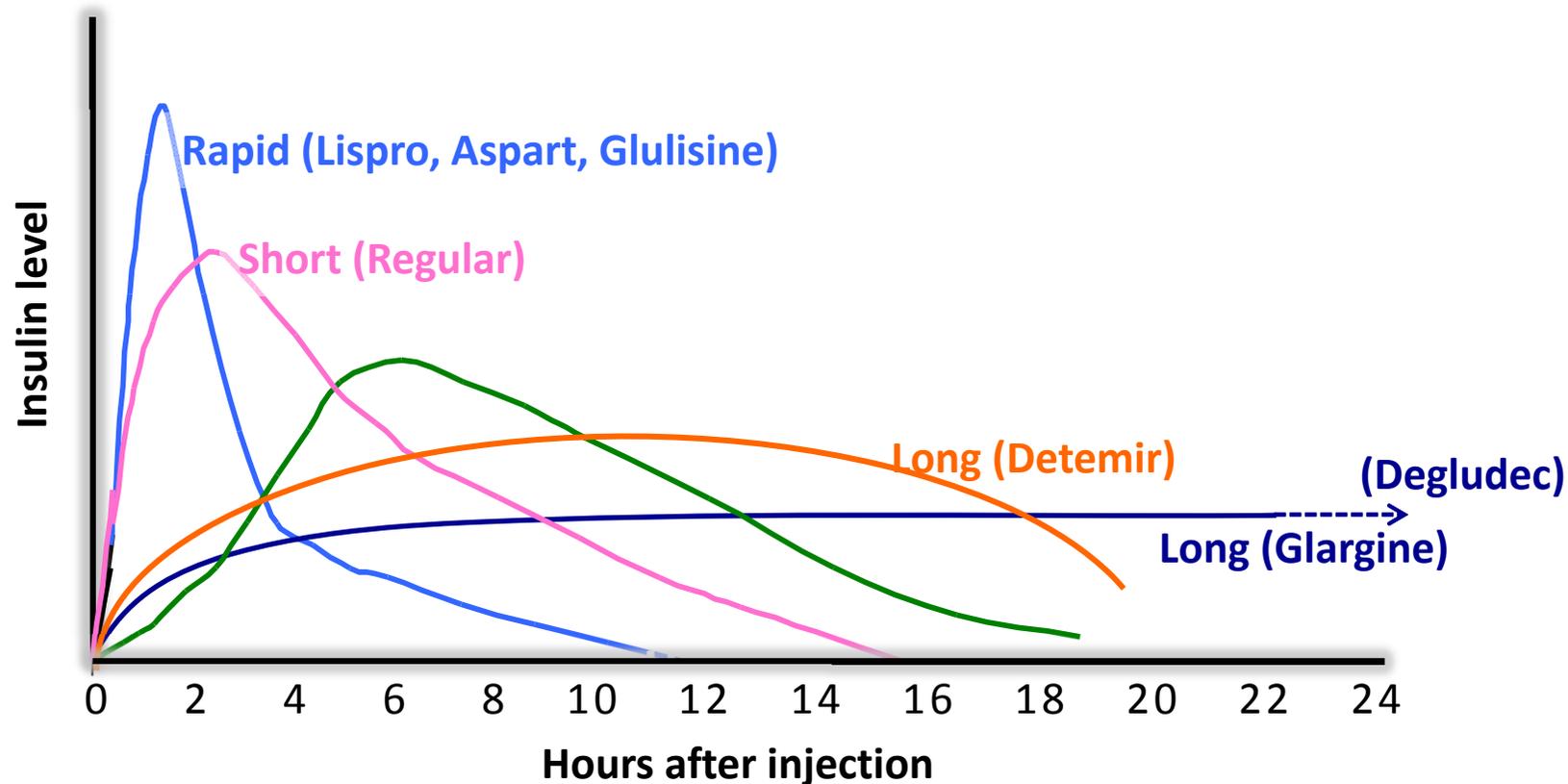
- Neutral protamine Hagedorn (NPH)
- Regular human insulin
- Pre-mixed formulations

Insulin Analogues

- Basal analogues (glargine, detemir, degludec)
- Rapid analogues (lispro, aspart, glulisine)
- Pre-mixed formulations

3. ANTI-HYPERGLYCEMIC THERAPY

- Therapeutic options: *Insulins*



**Figure 3.
Approach
to starting
& adjusting
insulin in
T2DM**

Basal Insulin

(usually with metformin +/-
other non-insulin agent)

- **Start:** 10U/day or 0.1-0.2 U/kg/day
- **Adjust:** 10-15% or 2-4 U once-twice weekly to reach FBG target.
- **For hypo:** Determine & address cause;
↓ dose by 4 units or 10-20%.

Figure 3.
Approach
to starting
& adjusting
insulin in
T2DM

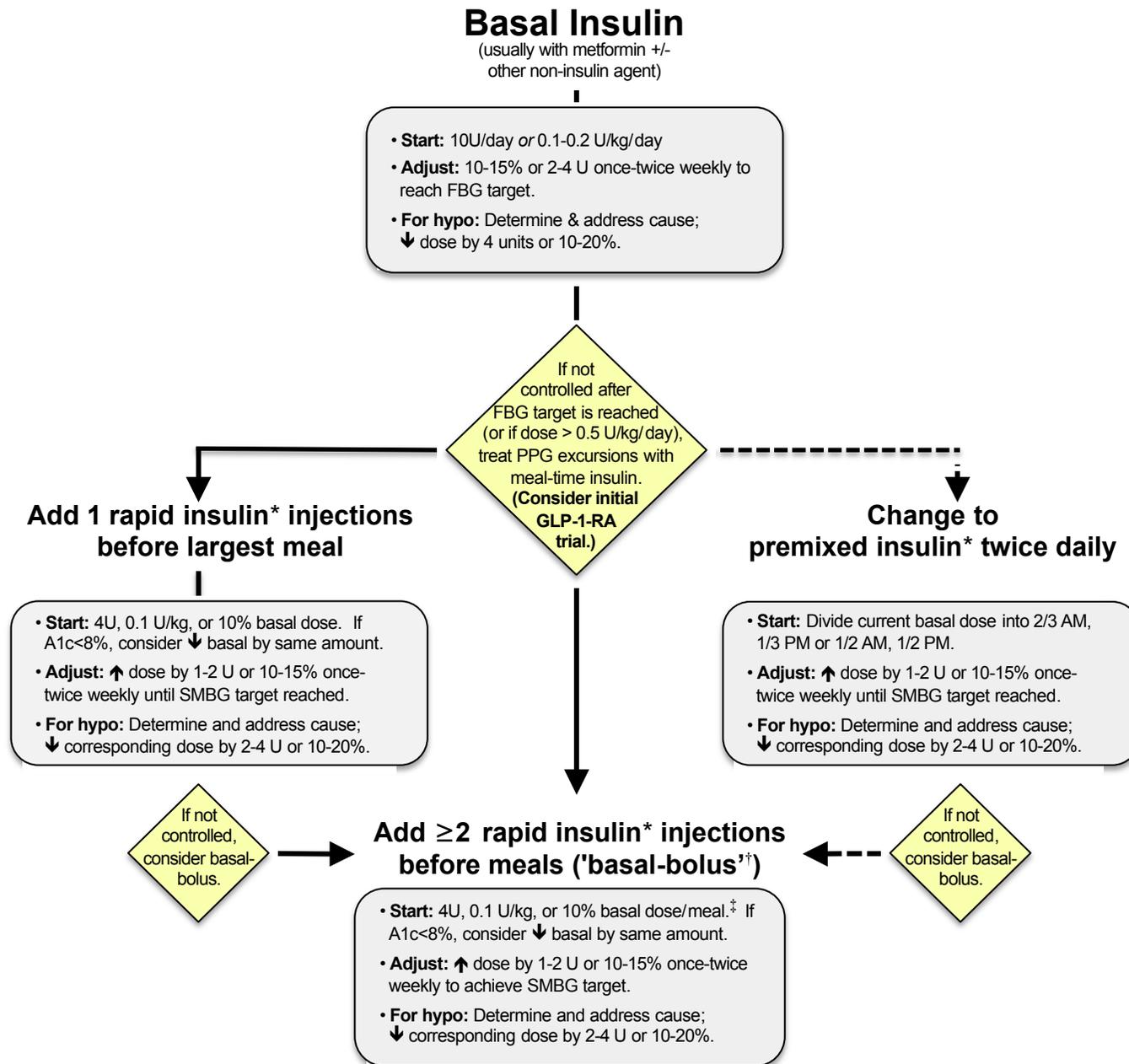
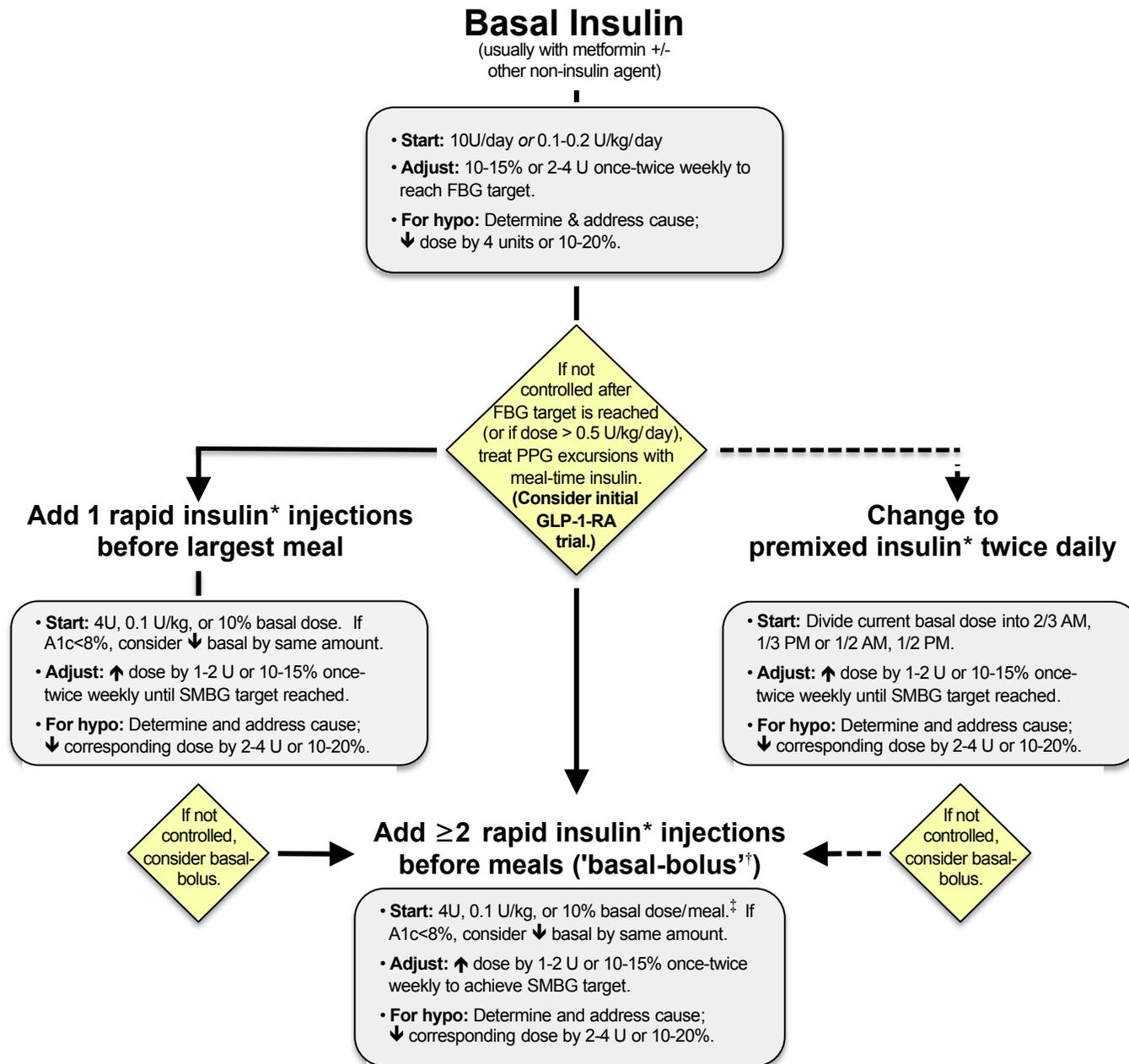


Figure 3.
Approach
to starting
& adjusting
insulin in
T2DM



4. OTHER CONSIDERATIONS

- **Age**
- **Weight**
- **Sex / racial / ethnic / genetic differences**
- **Comorbidities**
 - **Coronary artery disease**
 - **Heart Failure**
 - **Chronic kidney disease**
 - **Liver dysfunction**
 - **Hypoglycemia-prone**

4. FUTURE DIRECTIONS / RESEARCH NEEDS

- **Comparative effectiveness research**
 - Focus on important clinical outcomes
- **Contributions of genomic research**
- **Perpetual need for clinical judgment!**

KEY POINTS

- Glycemic targets & BG-lowering therapies must be individualized, based on a variety of patient and disease characteristics.
- Diet, exercise, & education: foundation of any T2DM therapy program.
- Unless contraindicated, metformin remains the optimal first-line drug.
- After metformin, data are limited. Combination therapy with 1-2 other oral / injectable agents is reasonable. Try to minimize side effects.
- Ultimately, many patients will require insulin therapy alone or in combination with other agents to maintain BG control.
- All treatment decisions should be made in conjunction with the patient (focusing on his or her preferences, needs & values.)
- Comprehensive CV risk reduction - a major focus of therapy.