



Developing Optimal Treatment Plans for Patients with Type 2 Diabetes

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Well-Ahead Louisiana Provider Education Network



Meet the Experts

- Nancy Caddigan, PharmD, RPh



- Jeffery Evans, PharmD, RPh

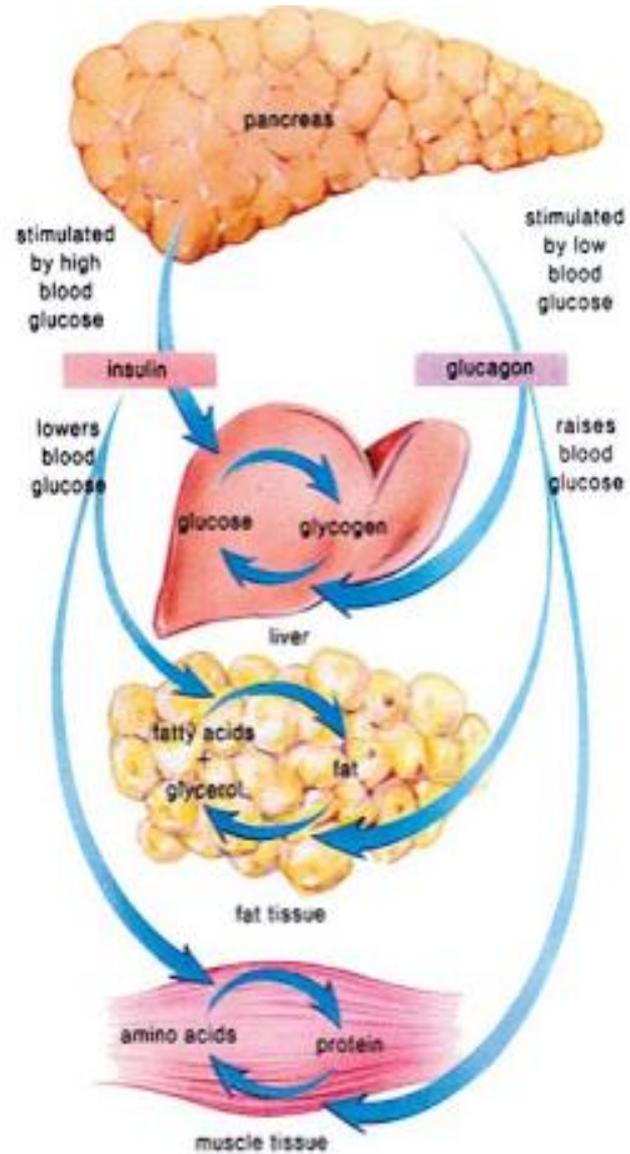


Type 2 Diabetes Review
&
Available Agents for Optimal
Treatment Plans for Patients

Objectives

- At the end of the presentation, the attendee will be able to
 - Describe different non-insulin options for the treatment of type 2 diabetes
 - Develop a plan to treat type 2 diabetes with oral and non-insulin injectable medications

What happens with glucose?



Physiologic Causes of T2DM

Insulin Resistance

Decreased Insulin
Secretion

B-Cell Function Decline

Hyperglycemia

Type 2 Diabetes Mellitus

Factors that impact T2DM

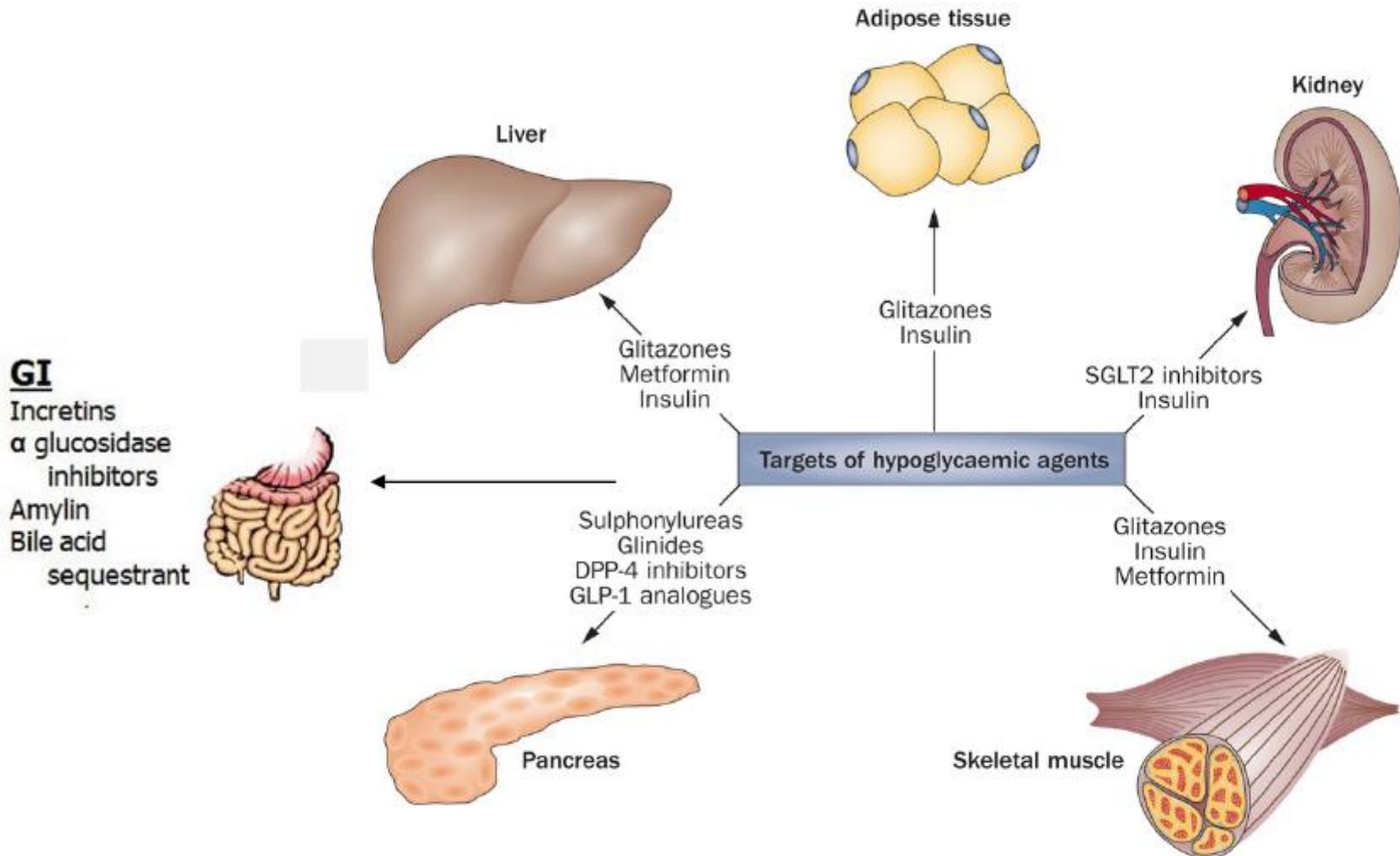
- Older Age
- Family History of DM
- Race
- Ethnicity
- Obesity
- Impaired glucose Metabolism
- Physical Inactivity

Medication Classes

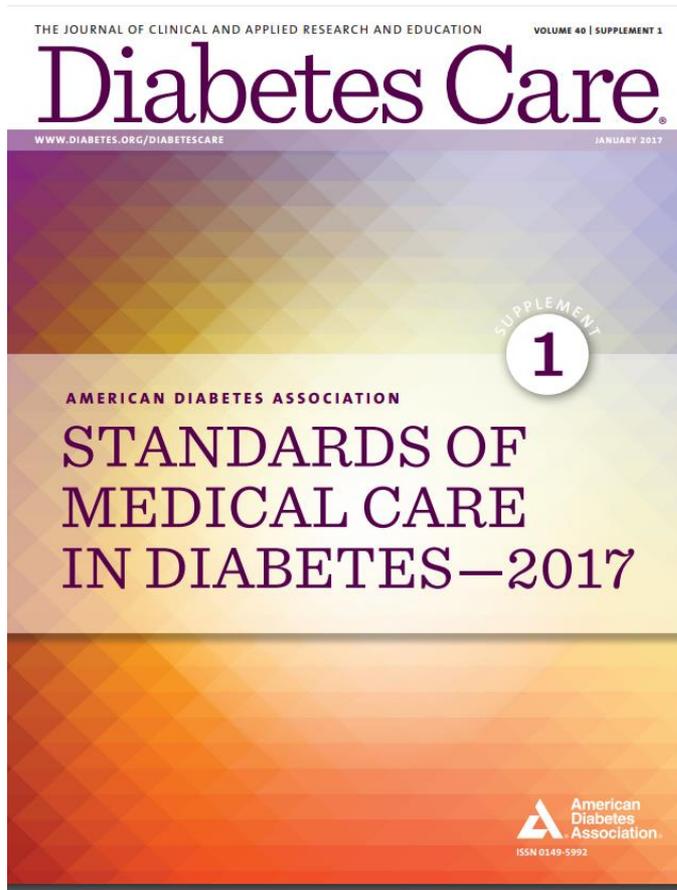
- Biguanides
- Sulfonylureas
 - Second Generation
- Incretin-based Drugs
 - Glucagon Like Peptide-1 (GLP-1) agonists
 - Dipeptidyl Peptidase-4 (DPP4) Inhibitors
- Sodium Glucose Cotransporter-2 (SGLT2) Inhibitors
- Thiazolidinediones (TZDs)
- Meglitinides
- Alpha-Glucosidase Inhibitors

Diabetes Medications

Target Organs



Guidelines for the Treatment of Diabetes Mellitus



AACE/ACE Consensus Statement

CONSENSUS STATEMENT BY THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY ON THE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM – 2017 EXECUTIVE SUMMARY

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This document represents the official position of the American Association of Clinical Endocrinologists and American College of Endocrinology. Where there were no randomized controlled trials or specific U.S. FDA labeling for issues in clinical practice, the participating clinical experts utilized their judgment and experience. Every effort was made to achieve consensus among the committee members. Position statements are meant to provide guidance, but they are not to be considered prescriptive for any individual patient and cannot replace the judgment of a clinician.

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Selection of anti-hyperglycemic agents

- You should consider these factors when selecting a medication:
 - Efficacy
 - Cost
 - Weight Patient
 - Comorbidities
 - Side effects
 - Hypoglycemic Risks
 - Patient Preferences (oral, doses)

Biguanides

- Product on market
 - Metformin (Glucophage) (4 -10\$/month)
- MOA
 - Reduces glucose production in the liver
 - Increases rate of stored glucose
 - Increases lipolysis
 - Notice no indication of HYPOglycemia
- Side effects
 - Weight loss and reduces dyslipidemia
 - Diarrhea with nausea (short term)
 - Lactic Acidosis (Rare)

Metformin, Contraindications

- Renal disease
 - Debate over SrCr limits
- Hepatic disease
- Alcoholism
- Hypoxia
 - Caused by anything
- Hold doses of Metformin
 - Contrast media
 - Severe Infection
 - Shock

Sulfonylureas, Pharmacology

- Mechanism of Action
 - Stimulate the beta cells of the pancreas to release insulin
- Lowers A1c by up to 1%
- First generation sulfonylureas are generally avoided
 - Higher risk of HYPOglycemia
 - Renally eliminated

Sulfonylurea, Side effects

- Risk of Hypoglycemia
- Potential decrease in effectiveness
- Weight gain
- Photosensitivity
 - Sulfa allergy is not really a concern

Reasons to avoid sulfonylureas

- Pregnancy/Breast feeding
- Elderly (risk of HYPOglycemia)
- Liver or kidney disease (drug stays around longer)

Sulfonylureas

- Products on the market

Generic Name	Brand Name	Cost/Month	Dosing
Glimepiride	Amaryl	10 - 20	QD
Glipizide	Glucotrol (XL)	10 - 15 (20 - 35)	BID - TID (QD - BID)
Glyburide	Diabeta	10	BID

Incretins

- Two classes affect this group of hormones
 - GLP-1 Agonists
 - DPP-4 Inhibitors
- Both will increase levels (or effectiveness) of incretins

What happens with incretin?

- When you eat
 - Levels increase and make you feel full
 - And encourage insulin to be released
 - GLP-1 levels increase
 - This result is decreased DRAMATICALLY in patients with Diabetes

So what about GLP1

- GLP -1 actions
 - Slows gastric emptying
 - Regulates appetite in the Hypothalamus
 - Suppresses glucagon release but encourages insulin release

Dipeptidyl-Peptidase-4 (DPP-4) inhibitors

- DPP -4 breaks down GLP – 1 (so blocking it will increase GLP – 1 levels)

GLP – 1 agonist and DPP-4 Inhibitors

Products on the market

- GLP – 1 agonists
 - Exenatide
(Byetta & Bydureon)
 - Liraglutide (Victoza)
 - Dulaglutide (Trulicity)
 - Albiglutide (Tanzeum)
- DPP – 4 Inhibitors
 - Sitagliptin (Januvia)
 - Saxagliptin (Onglyza)
 - Linagliptin (Trajenta)
 - Alogliptin (Nesina)

GLP – 1 agonists and DPP-4 Inhibitors, clinical effects

- GLP – 1
 - Decreases A1c ~1.0%
 - Weight loss
- Dosage
 - Sub – Q administration
 - Daily to weekly administration
- DPP-4 Inhibitors
 - Decreases A1c ~1%
- Dosage
 - Oral administration
 - Once daily

GLP – 1 agonists and DPP-4 Inhibitors, adverse effects

- GLP – 1
 - Nausea
 - Dose Dependent
 - Thyroid C-Cell Tumors
 - Family history of medullary thyroid cancer
 - Pancreatitis
 - Renal Insufficiency
- DPP-4 Inhibitors
 - Debatable
 - Pancreatitis
 - Pancreatic cancer
 - CV benefits
 - Not fully understood

GLP – 1 agonists and DPP-4 Inhibitors, patients of concern

- GLP – 1
 - History of
 - Gastroparesis
 - Pancreatitis
 - Insurance status
 - All are expensive
 - Recommended for patients in need of weight loss
- DPP-4 Inhibitors
 - Hypersensitivity reactions
 - Including SJD
 - Other less serious skin disorders

Pricing

GLP - 1 Inhibitors			
Generic	Brand	Cost/Month	Dosing
Exentide	Byetta	690	Daily
Liraglutide	Victoza	761	
Dulaglutide	Trulicity	641	
Lixsenatide	Adylxin	577	
Albiglutide	Tanzeum	492	

Pricing

DPP - 4 Inhibitors			
Generic	Brand	Price	Dosing
Sitagliptin	Januvia	414	Daily
Linagliptin	Tradjenta	363	
Alogliptin	Nesina	174	
Saxagliptin	Onglyza	372	

Sodium Glucose Cotransporter-2 Inhibitors (SGLT2)

- Products on the market
 - Canagliflozin (Invokana)
 - Dapagliflozin (Farxiga)
 - Empagliflozin (Jardiance)
- Mechanism of Action
 - Bind to the S1/S2 segment of the proximal tubule
 - There they inhibit the reabsorption of glucose
 - This leads increased excretion of glucose
 - That leads to lower blood glucose and A1C

Sodium Glucose Cotransporter-2 Inhibitors (SGLT2)

- Clinical effects
 - Decrease A1c ~0.5% to 1%
 - Should help with weight loss
 - Up to 400 Kcals are lost daily through urine
 - Blood pressure reduction
 - Working as a diuretic
 - Low risk of hypoglycemia

Sodium Glucose Cotransporter-2 Inhibitors (SGLT2)

- Adverse effects
 - More common
 - GI – Constipation, diarrhea and nausea
 - UTI and genitourinary infections
 - Less common
 - Dizziness
 - Sometimes orthostatic hypotension

Pricing

SGLT-2 Inhibitors			
Generic	Brand	Price/Month	Dosing
Canagliflozin	Invokana	443	Daily
Empagliflozin	Jardiance	415	
Dapagliflozin	Farxiga	447	

Thiazolidinediones (TZDs)

- Products on the market
 - Rosiglitazone (Avandia)
 - Pioglitazone (Actos)
- Clinical Effects
 - Sensitizes cells to insulin
 - Lowers A1c by ~1%
 - Has effects on
 - Adipose tissue
 - Muscle
 - Liver

Thiazolidinediones (TZDs)

- Adverse Effects
 - Weight gain
 - Fluid Retention
 - Not for use in NYHA Class III or IV HF
 - Evidence indicates bone fracture risks
 - Rosiglitazone had MI worries, but those are removed
 - Pioglitazone has bladder cancer risks

Pricing

Thiazolidinediones			
Generic	Brand	Cost/Month	Dosage
Rosiglitazone	Avandia	173	Daily
Pioglitazone	Actos	17 - 100	Daily

Meglitinide Analogues (glinides)

- Products on the market
 - Repaglinide (Prandin)
 - Nateglinide (Starlix)
- Clinical Effects
 - Similar effects as sulfonylurea
 - But at a different site than sulfonylurea
 - A1C lowering of ~1%

Meglitinide Analogues (glinides)

- Adverse Effects
 - Better tolerated than sulfonylureas
 - Hypoglycemia
 - Weight gain
 - Contraindicated in liver disease
 - Decrease dose in severe renal dysfunction

Pricing

Glinides			
Generic	Brand	Cost/Month	Dosage
Repaglinide	Prandin	31	With meals
Nateglinide	Starlix	63	With meals

Alpha-Glucosidase Inhibitors

- Products on the Market
 - Acarbose (Precose)
 - Miglitol (Glyset)
- Clinical Effects
 - Inhibits enzymes in the GI tract from breaking down carbohydrates
 - Delays intestinal CHO absorption
 - Delays glucose from entering blood stream
 - Lowers A1C up to 1%

Alpha-Glucosidase Inhibitors

- Adverse Effects
 - GI effects
 - Bloating
 - Nausea
 - Diarrhea
 - Flatulence

Alpha-Glucosidase Inhibitors

- Contraindications
 - Intestinal Obstruction
 - IBS
 - Crohn's disease
 - Cirrhosis
 - Renal Impairment

Pricing

Alpha-Glucosidase Inhibitors			
Generic	Brand	Price/Month	Dosage
Acarbose	Precose	30	
Miglitol	Glyset	241	

Insulin Therapy

Types of Insulin

Rapid or Short Acting

Humalog

\$529

Novolog

\$538

Apidra

\$400

Novolin R

\$24

Novolin N

\$24

Long Acting

Lantus

\$274

Levemir

\$409

Trujeo

\$347

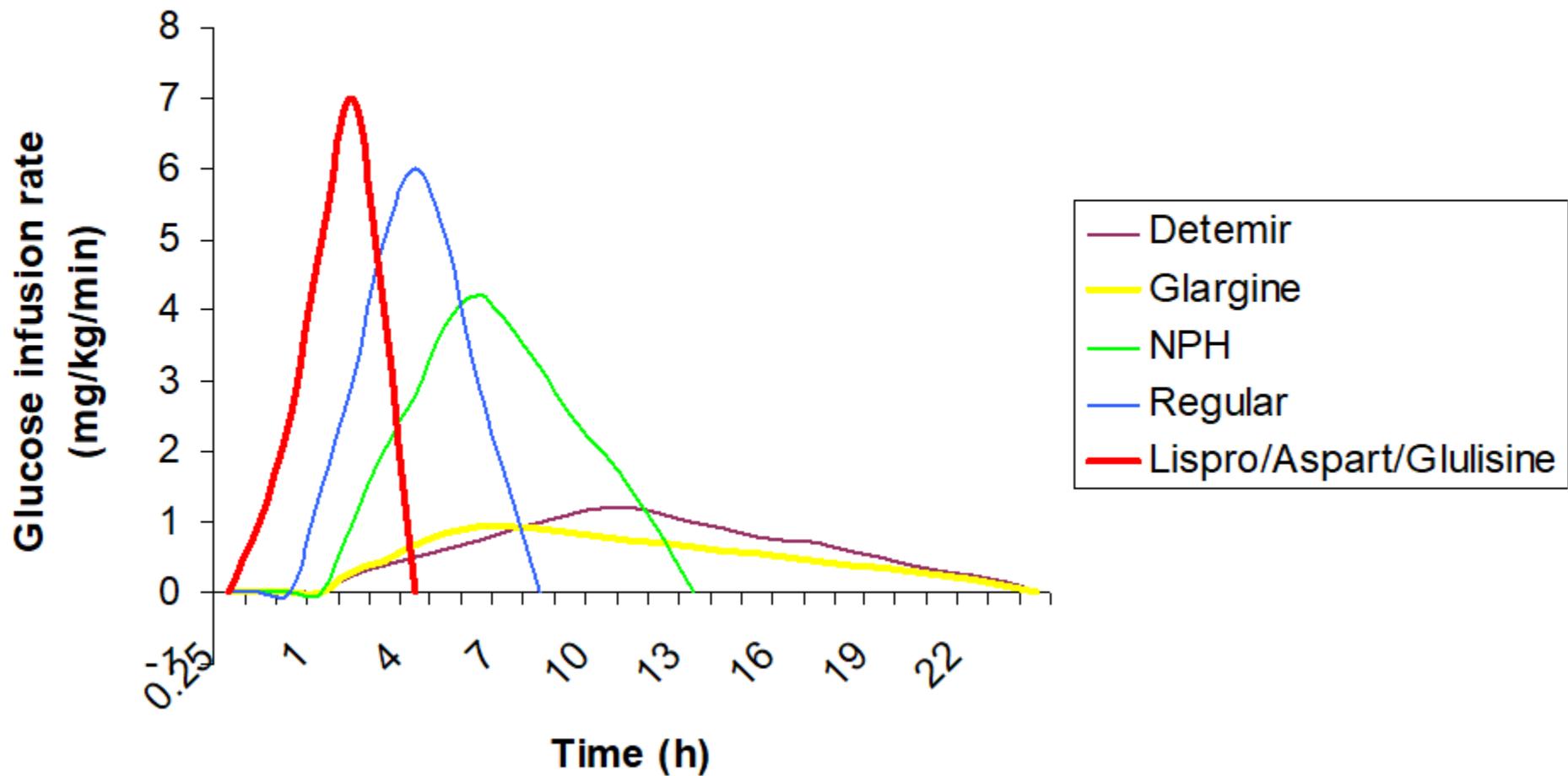
Basaglar

\$227

Tresiba

\$390

Insulin time/activity profiles



Treatment plans

Therapeutic Decision Making Initial and Dual Therapy

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):

Therapeutic Decision Making

Triple Therapy and Adding Intensive Insulin

Triple Therapy

Metformin +

Lifestyle Management

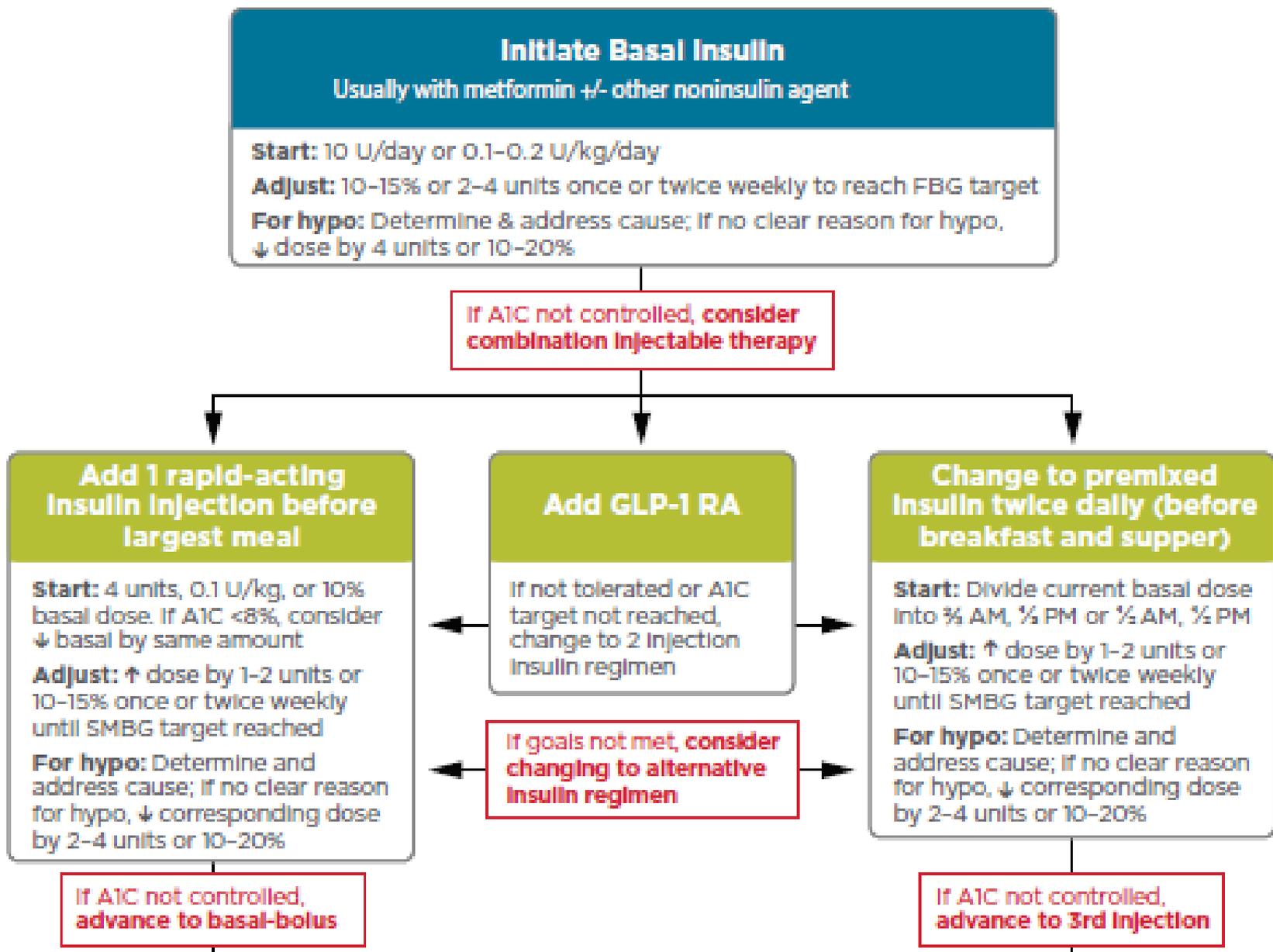
Sulfonylurea +		Thiazolidinedione +		DPP-4 Inhibitor +		SGLT2 Inhibitor +		GLP-1 receptor agonist +		Insulin (basal) +	
	TZD		SU		SU		SU		SU		TZD
or	DPP-4-i	or	DPP-4-i	or	TZD	or	TZD	or	TZD	or	DPP-4-i
or	SGLT2-i	or	SGLT2-i	or	SGLT2-i	or	DPP-4-i	or	SGLT2-i	or	SGLT2-i
or	GLP-1-RA	or	GLP-1-RA	or	Insulin [§]	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 3)

Adding insulin in T2DM



Questions

THANK YOU!

