Medication Management of Type II Diabetes: Bringing Best Practice into Daily Practice

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Disclosures

- Today's presentation is supported by a grant from the Diabetes Regional Health Improvement Program (RHIP).
- I am currently a member of the PacificSource pharmacy and therapeutics committee.
- I have no relationships, financial or otherwise, with any drug manufacturers.

Objectives

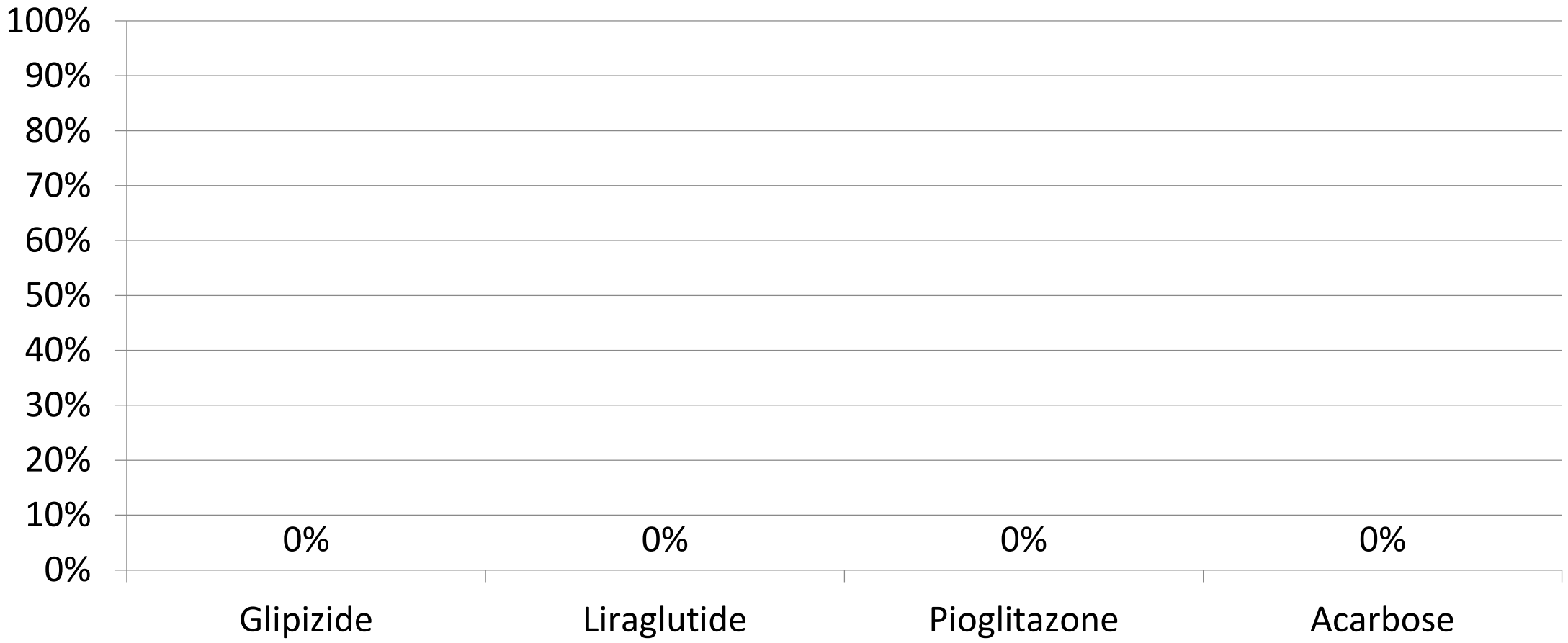
- Be familiar with the strengths and weaknesses of available treatments for diabetes
- Reconcile guideline-supported therapy with common insurance formulary restrictions
- Apply behavioral, psychiatric, and social determinants of health considerations to the treatment plan

Knowledge Check

For a patient with coronary artery disease, A1c above goal, already established on metformin and lifestyle therapy, which is the best next choice:

1. Glipizide
2. Liraglutide
3. Pioglitazone
4. Acarbose

Results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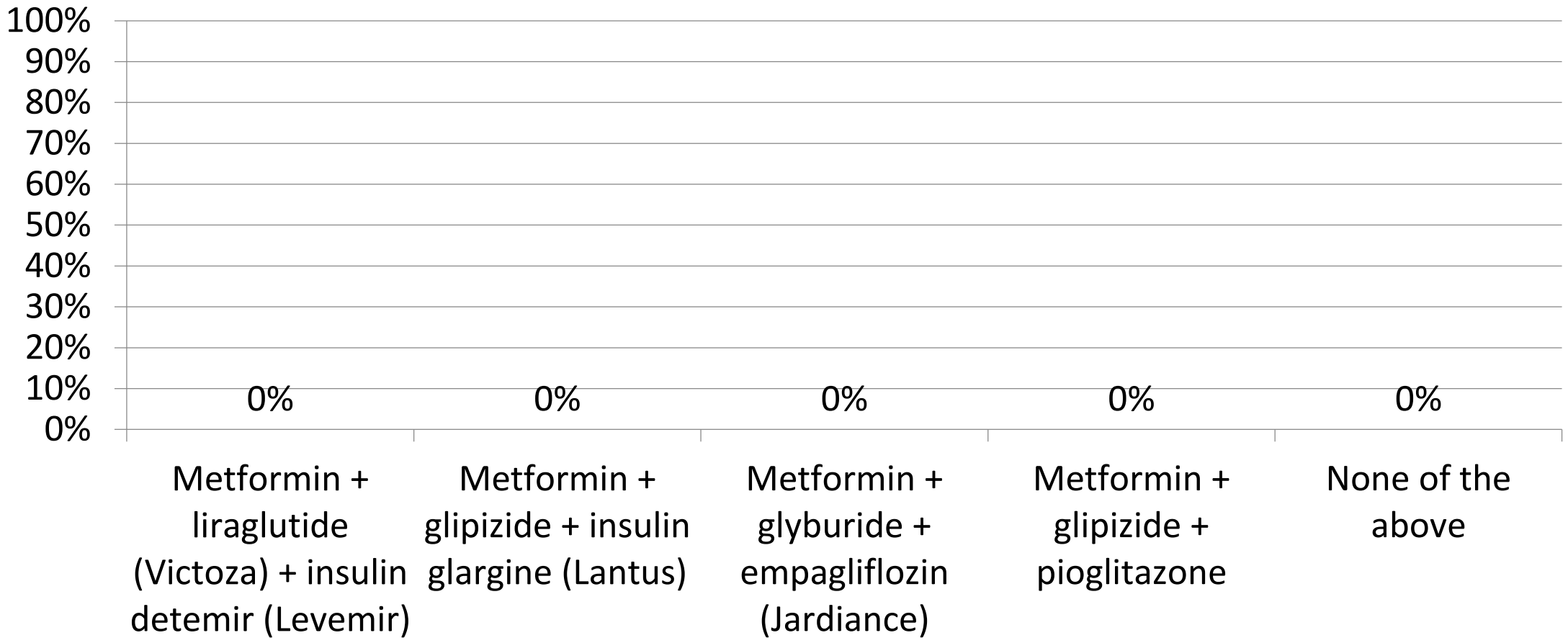
Glipizide
Liraglutide
Pioglitazone
Acarbose

Knowledge Check

For a patient covered by Medicare part D which regimen will be the most affordable? (assuming no extra help)

1. Metformin + liraglutide (Victoza) + insulin detemir (Levemir)
2. Metformin + glipizide + insulin glargine (Lantus)
3. Metformin + glyburide + empagliflozin (Jardiance)
4. Metformin + glipizide + pioglitazone
5. None of the above

Results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Metformin + liraglutide (Victoza) + insulin detemir (Levemir)
Metformin + glipizide + insulin glargine (Lantus)
Metformin + glyburide + empagliflozin (Jardiance)
Metformin + glipizide + pioglitazone
None of the above

Knowledge Check

Clinically Significant Hypoglycemia, as defined by the ADA, is a blood sugar below:

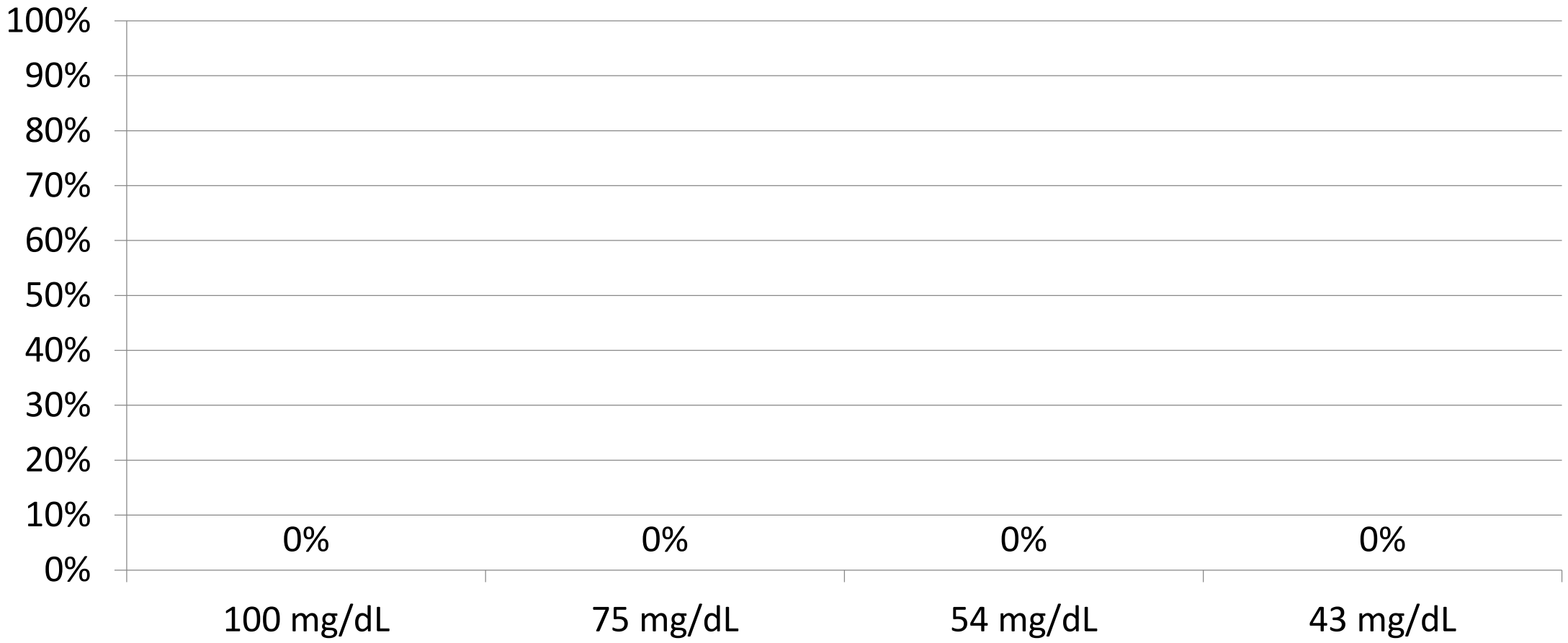
a.100 mg/dL

b.75 mg/dL

c.54 mg/dL

d.43 mg/dL

Results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75 mg/dL
54 mg/dL
43 mg/dL

Natural progression of type 2 diabetes

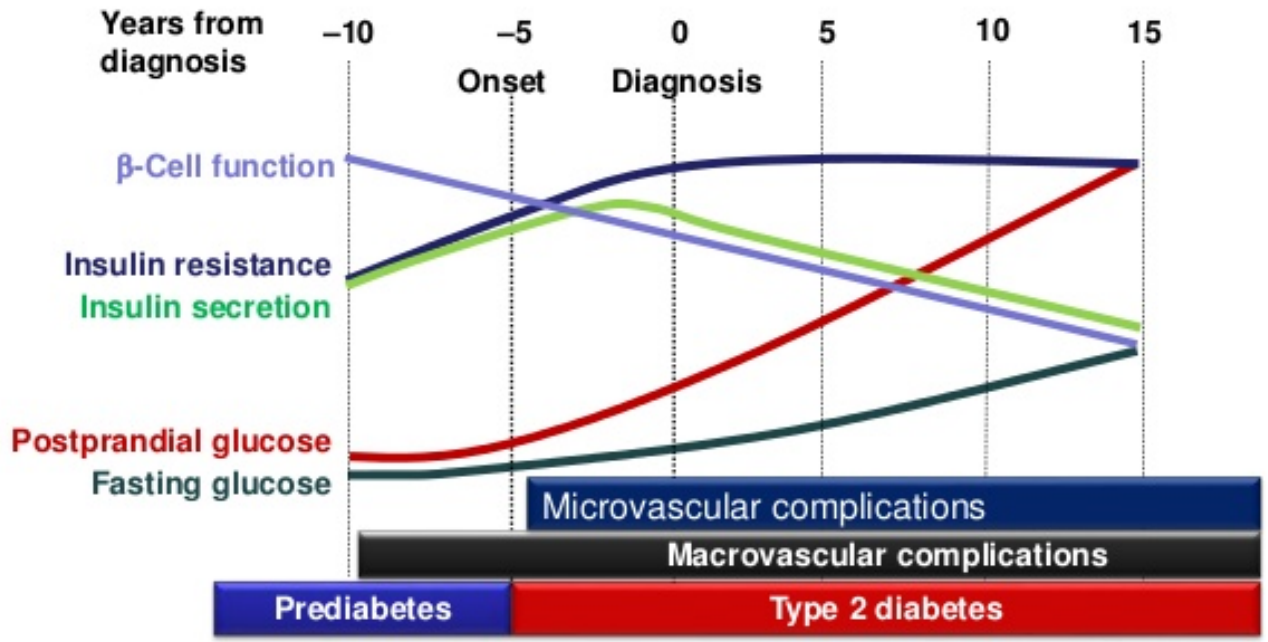
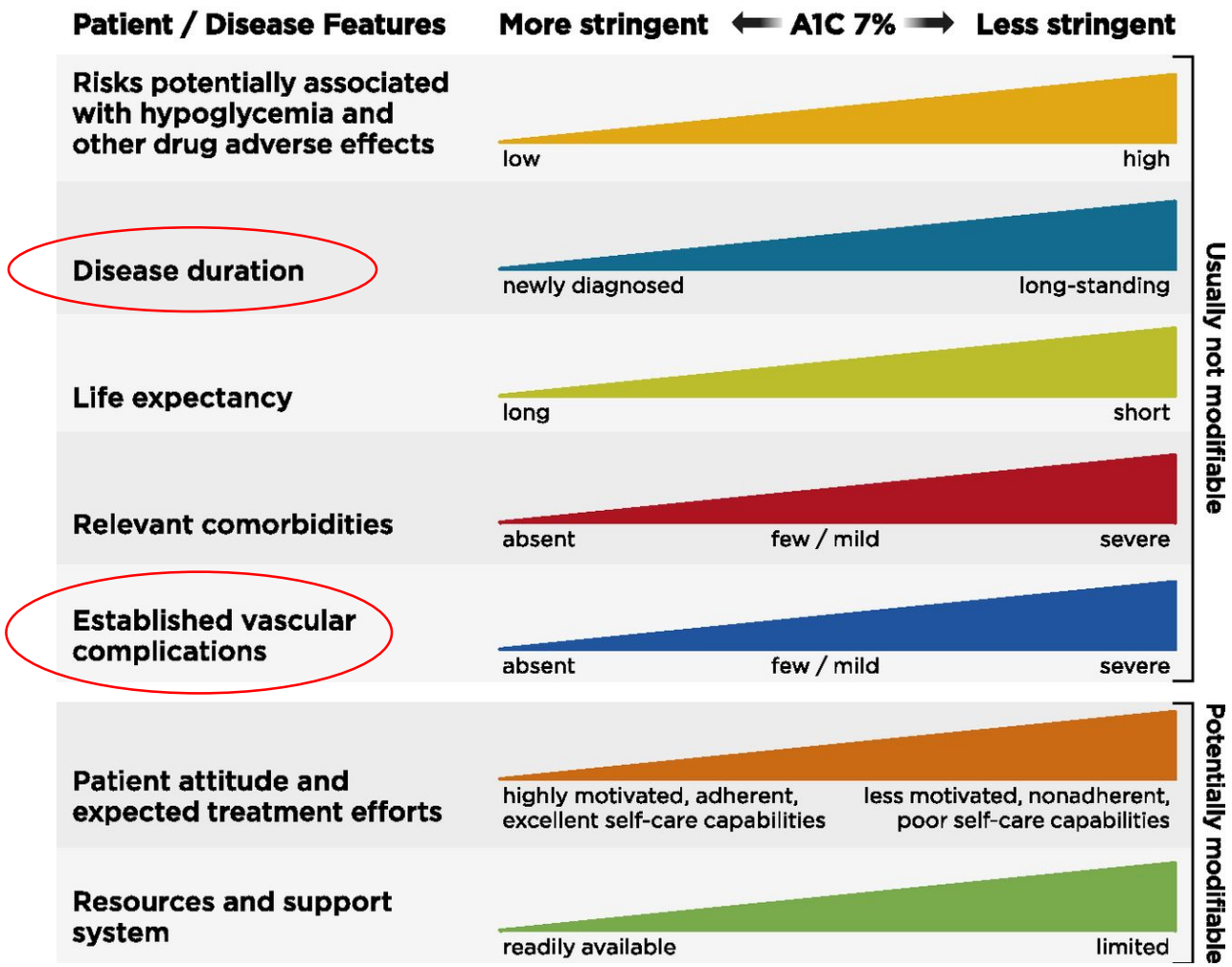


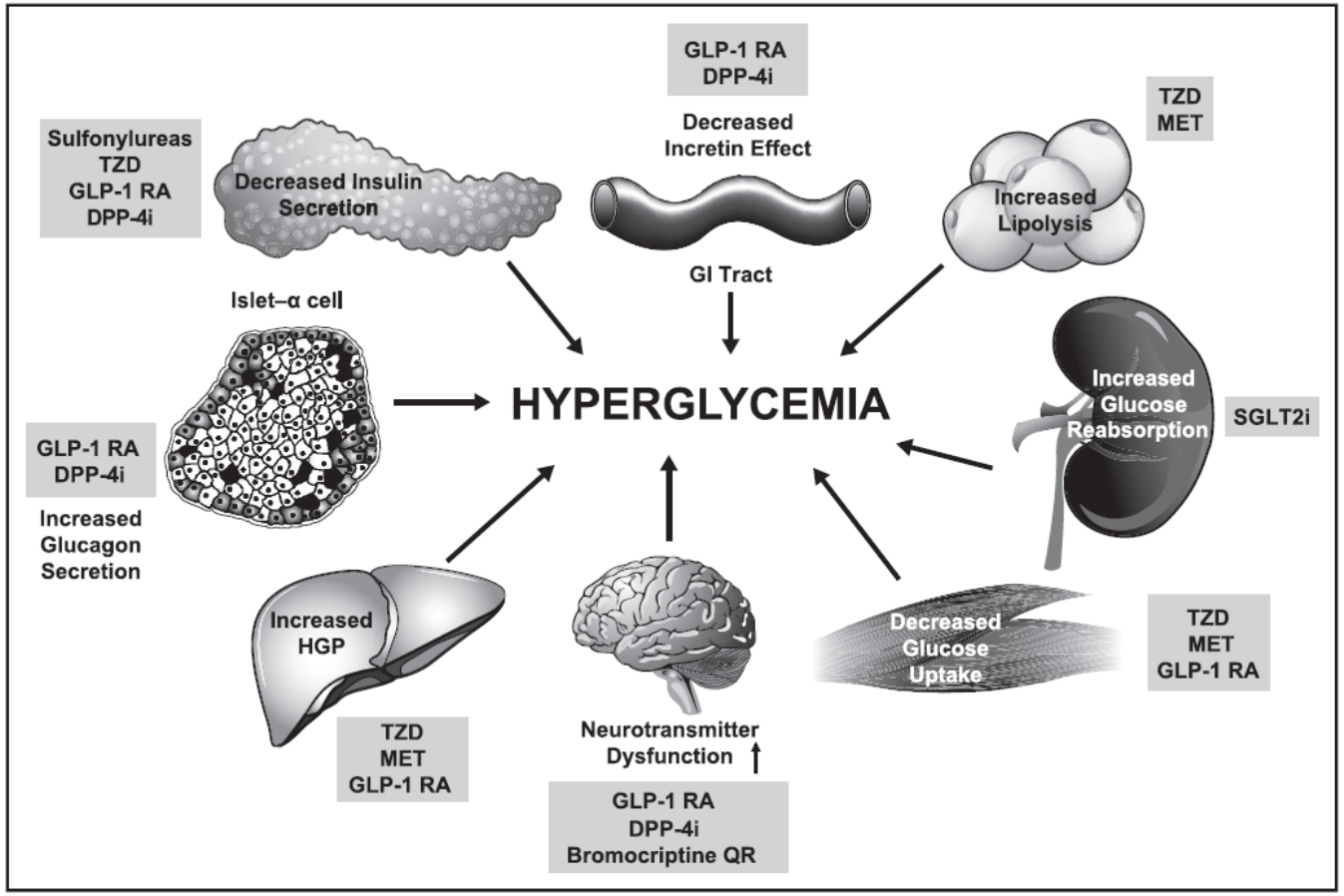
Figure courtesy of the AACE Diabetes Resource Center

Approach to management of hyperglycemia



ADA Standards 2017

Multiple, Complex Pathophysiological Abnormalities in T2DM



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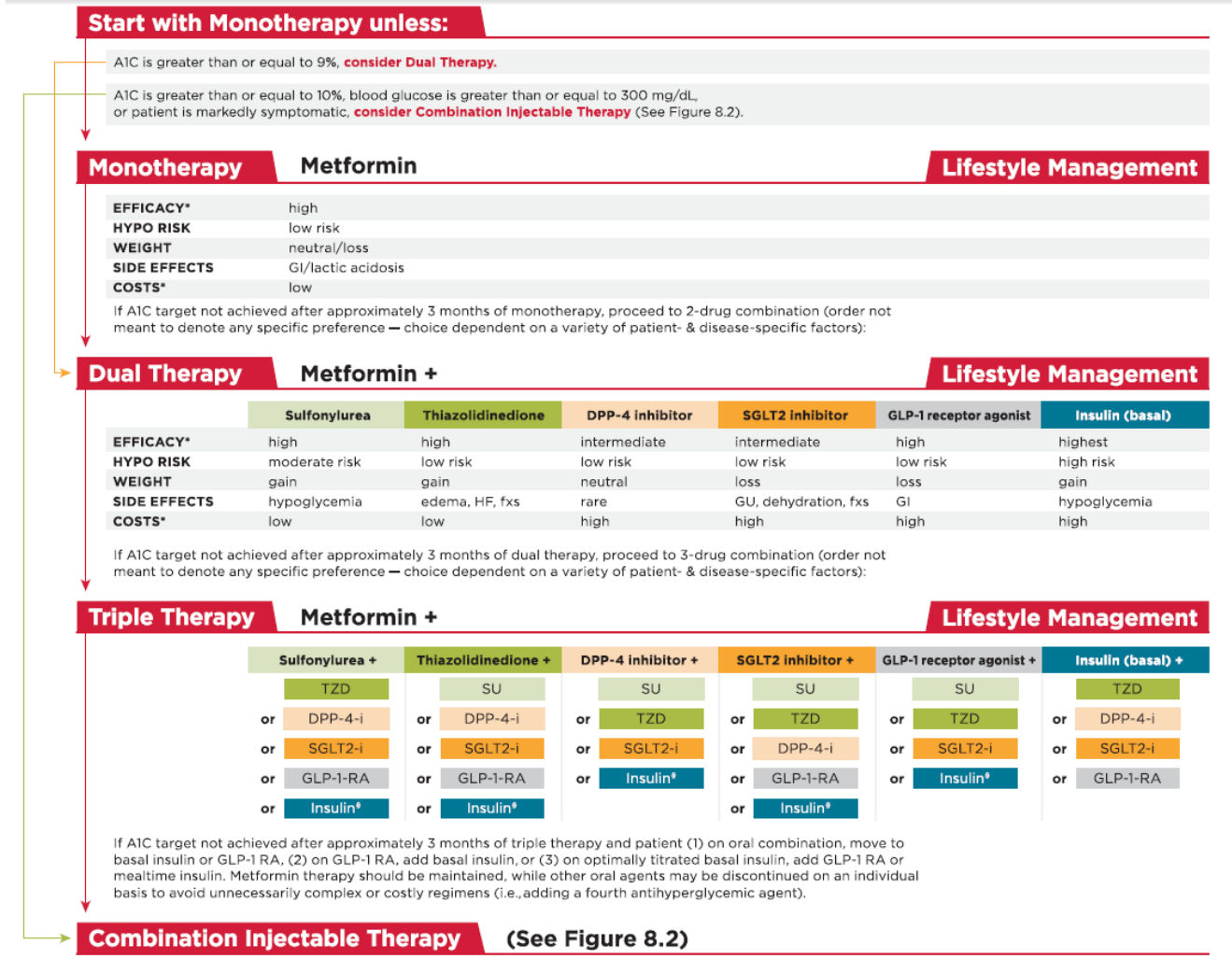
ADA Standards of Care 2017



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)**

Cardiovascular Outcomes Trials (CVOT's)

- Remember Avandia (rosiglitazone)?
  - In 2008 CVOT data became a required element for FDA approval of new diabetes drugs
  - This creates added burden of evidence on drugs in the pipeline
  - Questions have been raised about the clinical applicability of CVOT data
    - Selection bias inherent in designing inclusion criteria to recruit a population in which adequate cardiovascular events will occur in the time-frame of the study
  - FDA approvals have recently also come with specifics about CV risk reduction

Drug Class	Mortality	Myocardial Infarction	Stroke	Heart Failure	Microvascular
DPP-4 Inhibitors	Neutral	Neutral	Neutral	Neutral: Sitagliptin May Increase: Saxagliptin, Alogliptin	Not Reported
SGLT-2 inhibitors (empagliflozin and canagliflozin only)	Reduction (NNT 38/3 yrs)	Neutral	Neutral	Reduction (NNT=71)	Nephrophathy Reduction Amputation increase: canagliflozin
TZD's (pioglitazone only)	Neutral	Neutral/Reduce	Neutral/Reduction	Increase	Not Reported
GLP-1 receptor agonists	Reduction: liraglutide (NNT 45) Neutral: lixisenatide Semaglutide	Reduction: liraglutide Neutral/Reduce: Semaglutide Neutral: Lixisenatide	Reduction: Semaglutide Neutral/Reduce: Liraglutide Neutral: Lixisenatide	Neutral	Renal outcomes reduction: liraglutide, semaglutide Neutral: lixisenatide Retinal outcomes increase: semaglutide

CVOT Findings To Date

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH

FIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY)
IF HbA_{1c} ABOVE TARGET PROCEED AS BELOW

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

ESTABLISHED ASCVD OR CKD

ASCVD PREDOMINATES

EITHER/OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1], if eGFR adequate[2]

If HbA_{1c} above target

If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:

- Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD benefit
- DPP-4i if not on GLP-1 RA
- Basal insulin[4]
- TZD[5]
- SU[6]

HF OR CKD PREDOMINATES

PREFERABLY
SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate[3]

OR

If SGLT2i not tolerated or contraindicated or if eGFR less than adequate[2] add GLP-1 RA with proven CVD benefit[1]

If HbA_{1c} above target

- Avoid TZD in the setting of HF

Choose agents demonstrating CV safety:

- Consider adding the other class with proven CVD benefit[1]
- DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
- Basal insulin[4]
- SU[6]

NO

WITHOUT ESTABLISHED ASCVD OR CKD

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i[2]	TZD
If HbA_{1c} above target			
SGLT2i[2] OR TZD	SGLT2i[2] OR TZD	GLP-1 RA OR DPP-4i OR TZD	SGLT2i[2] OR DPP-4i OR GLP-1 RA

If HbA_{1c} above target

Continue with addition of other agents as outlined above

If HbA_{1c} above target

Consider the addition of SU[6] **OR** basal insulin:

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/OR

- GLP-1 RA with good efficacy for weight loss[8]
- SGLT2i[2]

If HbA_{1c} above target

- SGLT2i[2]
- GLP-1 RA with good efficacy for weight loss[8]

If HbA_{1c} above target

If triple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated use regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA)

COST IS A MAJOR ISSUE[9-10]

- SU[6]
- TZD[10]

If HbA_{1c} above target

- TZD[10]
- SU[6]

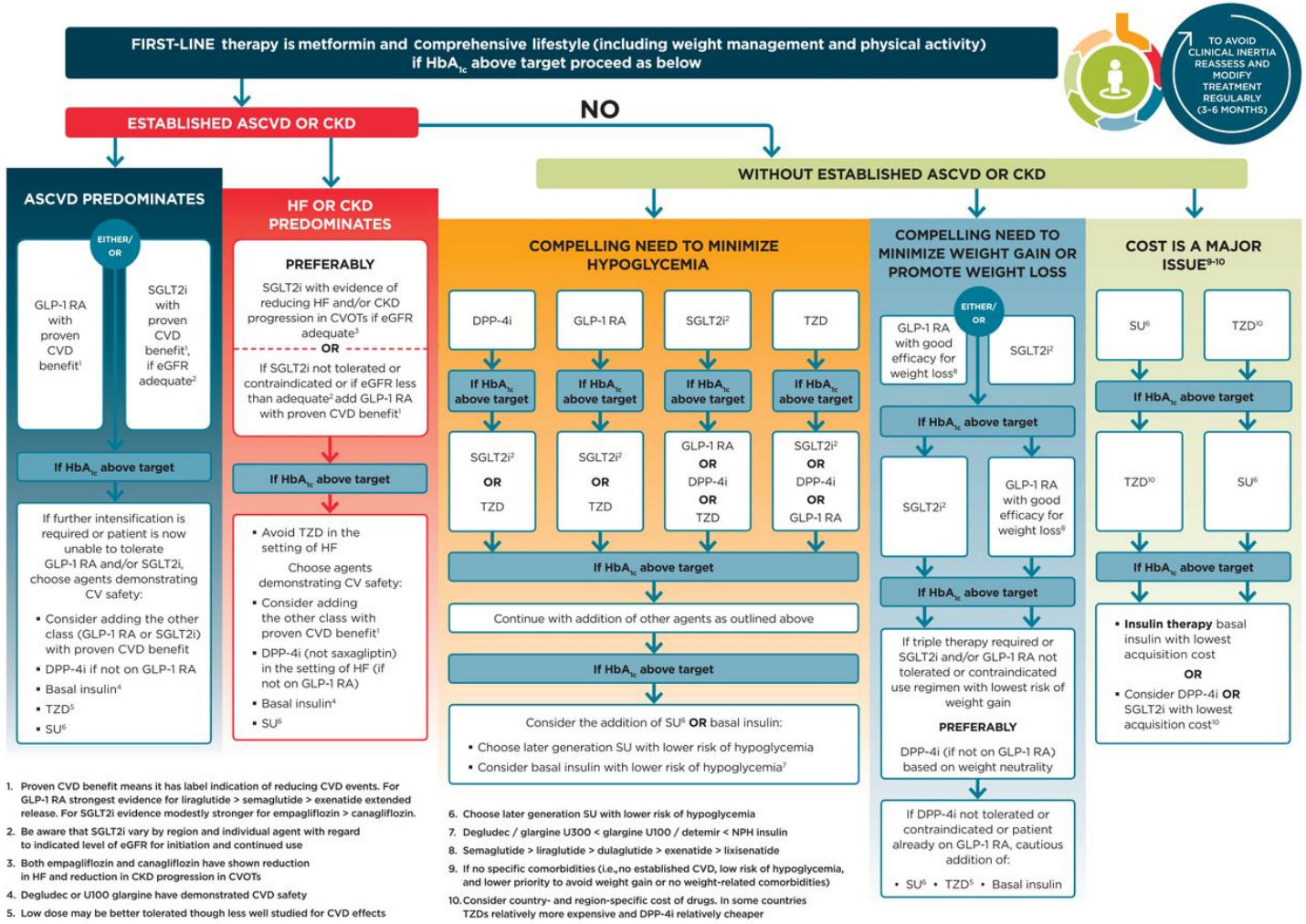
If HbA_{1c} above target

- **Insulin therapy** basal insulin with lowest acquisition cost

OR

- Consider DPP-4i **OR** SGLT2i with lowest acquisition cost[10]

Glucose-lowering medication in type 2 diabetes: overall approach.

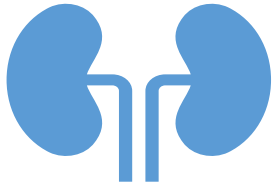


1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU with lower risk of hypoglycemia
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

American Diabetes Association Clin Diabetes 2019;37:11-34

American Diabetes Association.

Non-insulin agent pearls



Metformin –put it in the water already!

Optimize dose to 2000 mg/day as much as possible

Use XR formulation

Modest weight loss, durable benefit,

Use eGFR to determine renal dosing not SCr

Can deplete B12 levels (up to 16% of patients) monitor and supplement where neuropathy or anemia are present.

SFU's (glipizide, glyburide, glimepiride)

Choose glipizide for low cost

Associated with weight gain*

High risk of hypoglycemia

No CVD benefit, and may increase risk of CV harm

What is the impact of SFU on CV outcomes?

Study	N & Duration	Intervention	Findings
Meinert et al 1970 Diabetes **RCT** ***did not control for smoking between groups**	N = 409 5 years	Tolbutamide vs placebo	Increased CV mortality with tolbutamide (12.7% vs 4.9%, NNH = 13) All-cause mortality not significant (14.7% vs 10.2%)
Hong et al 2012 Diabetes Care **RCT** **Participants selected for existing CVD, and mean A1c 7.6% at baseline**	N = 304 5 years	Glyburide vs Metformin	Increased composite CV events with Glyburide (35% vs 25%, NNH = 10, HR 0.54, 95% CI 0.3-0.90, p=0.026)
Kahn et al, 2006 NEJM **RCT** ***40% of participants withdrew prior to completion**	N = 2895 4 years	Glyburide vs Metformin	All-cause mortality not significant (2.2% vs 2.1%) Total CV events not significant (2.9% vs 4.0%)
Vaccaro et al, 2017 Lancet **RCT**	N = 3028 5 years	Metformin + SFU vs Metformin + Pioglitazone	No difference in composite CV outcomes (0.96, 95% CI 0.74-1.26, p=0.79) Hypoglycemia more common in SFU arm (34% vs 10%, p<0.0001, NNH = 5)
Gallwitz et al 2012 Lancet **RCT**	N = 1519 2 year	Metformin + Glimepiride vs Metformin + Linagliptin	A non-inferiority trial, with CV events reported as adverse events: 3.4% vs 1.5%, NNH = 53 (RR 0.46, 95% CI 0.23-0.91, p=0.0213) Hypoglycemia: 36% vs 7%, p<0.0001, NNH 4

Bottom Line: SFU treatment does not reduce CV outcomes, and may increase CV harm.

Non-insulin agent pearls

TZD's (Pioglitazone)

- A good insulin sensitizer for pt's who can't take metformin
- Added to insulin creates edema – just don't do it
- weight gain common & associated with osteopenia/osteoporosis
- Generic = Good option for Medicare patients with high co-pays on other meds (if no CHF or osteopenia/osteoporosis)
- Now on the "$4 list" at Walmart… for $9 per month

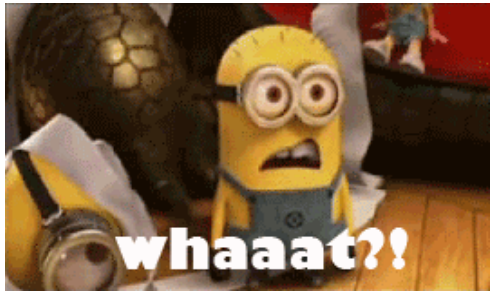
DPP-4 inhibitors ("gliptins" Januvia, Tradjenta, Onglyza, etc)

- costly and not very effective–reserve for those near A1c goal already
- PS Communitysolutions covers Januvia at step-2 after a 30 day trial of metformin or SFU
- Generally cardiac-neutral, avoid saxagliptin or alogliptin in HF

Non-insulin agents continued…

SGLT-2 inhibitors ("flozins" Invokana, Jardiance, Farxiga)

- PS Community Solutions covers Jardiance at step-2 after 30 day trial of metformin or SFU
- Consider for patients with CHF or nephropathy *(EMPA-REG & CANVAS trials)*
- Weight loss and BP reduction –effect is modest for both (~2 kg and 3-4 mmHg)
- Acts on renal sodium channels –check BMP after initiating treatment
- EMPA-REG and CANVAS trials found reduced CVD risk for empagliflozin and canagliflozin. Other trials ongoing/pending.
- Avoid if history of amputation; caution in PVD
- Mycotic genital infection



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Non-insulin agents continued a bit more…

GLP-1 receptor agonists (Victoza, Byetta, Trulicity, Bydureon, etc.)

- Weight reduction generally >2.0 kg
- For A1c reduction: Trulicity=Victoza>Bydureon>Byetta
- Use Trulicity or Bydureon for once-weekly convenience vs Use Victoza for renal impaired or GI sensitive cases
- Once-weekly = stronger effect on fasting BG vs daily = stronger impact on post-prandial BG
- Painful subcutaneous nodules & erratic drug release for some users of Bydureon – better with Bcise pen.
- Avoid if history of thyroid cancer
- Titrate dose slowly to minimize GI side effects

Thrasher, J. Am J Cardiol 2017

Case Study

- 70 year old, weighs 100kg, History of CABG, tobacco, BG 400-500 for past weeks, Insulin 100+ units Lantus at HS (solostar), Oral Meds: Metformin, glipizide,
- Most recent A1c – 11.3%
- Pt can’t afford Lantus insulin pen – what other option?

Step Therapy for Oral Diabetes Meds

POLICY NAME:
ORAL ANTIDIABETIC AGENTS

If the patient has tried a Step 1 drug (at least a 30-day supply in the prior 180 days), then authorization for a Step 2 drug may be given. If the patient has tried a Step 2 drug (at least a 30-day supply in the prior 180 days), then authorization for a Step 3 drug may be given.

Step 1 Drugs: GLIMEPIRIDE TABLET, GLIPIZIDE ER TABLET EXTENDED RELEASE 24 HOUR, GLIPIZIDE TABLET, GLIPIZIDE XL TABLET EXTENDED RELEASE 24 HOUR, GLIPIZIDE-METFORMIN HCL TABLET, GLYBURIDE MICRONIZED TABLET, GLYBURIDE TABLET, GLYBURIDE-METFORMIN TABLET, METFORMIN HCL ER TABLET EXTENDED RELEASE 24 HOUR, METFORMIN HCL TABLET

Step 2 Drugs: JANUMET TABLET, JANUMET XR TABLET EXTENDED RELEASE 24 HOUR, JANUVIA TABLET, JARDIANCE TABLET

Step 3 Drugs: INVOKAMET TABLET, INVOKAMET XR TABLET EXTENDED RELEASE 24 HOUR, INVOKANA TABLET, JENTADUETO TABLET, JENTADUETO XR TABLET EXTENDED RELEASE 24 HOUR, TRADJENTA TABLET

PacificSource Community Solutions Medicaid

Prior-Authorization for GLP-1 Agonist

What's missing? **Basal Insulin**

POLICY NAME:
GLUCAGON-LIKE PEPTIDE-1 AGONISTS
Affected Medications: BYETTA Subcutaneous (Exenatide), BYDUREON Subcutaneous (Exenatide), BYDUREON BCise Subcutaneous (Exenatide), VICTOZA Subcutaneous (Liraglutide), TRULICITY Subcutaneous (dulaglutide)

Covered Uses:	• All FDA-approved indications not otherwise excluded by benefit design.
Required Medical Information:	• The patient is diagnosed as having type-2 diabetes with an HbA1C level greater than 7. • The patient demonstrated an inadequate ~~treatment~~ response, intolerance or contraindication to an adequate trial of: metformin AND an additional oral antidiabetic agent (e.g. sulfonylurea (e.g. glyburide, glimepiride, glipizide), pioglitazone, Dipeptidyl peptidase-4 (DPP4) inhibitor (~~e.g. Januvia~~, Tradjenta), or Sodium-glucose co-transporter 2 (SGLT2) inhibitor (Invokana, Jardiance). • For **reauthorization**, patient ~~demonstrated~~ an expected reduction in hemoglobin A1c (HbA1C) since starting therapy of at least 0.5%

PacificSource Community Solutions Medicaid

DMAP for GLP-1 Agonist Coverage

Glucagon-like Peptide-1 (GLP-1) Receptor Agonists

Goal(s):

- Promote cost-effective and safe step-therapy for management of type 2 diabetes mellitus (T2DM).

Length of Authorization:

- Up to 12 months

Requires PA:

- GLP-1 receptor agonists that are preferred products do not require PA when prescribed as second-line therapy in conjunction with metformin.
- All non-preferred GLP-1 receptor agonists require a PA

Table 121-0030-1 Oregon Fee-for-Service Enforceable Physical Health Preferred Drug List

Effective: April 1, 2019

System	Class		Preferred
Endocrine	Diabetes, GLP-1 Receptor Agonists	exenatide *	PEN INJCTR

DMAP for SGLT-2 Inhibitor Coverage

- SGLT-2's not well covered. Must try all other classes first or have contraindications. Still, some patients will meet these criteria.

Sodium-Glucose Cotransporter-2 Inhibitors (SGLT-2 Inhibitors)

Goal(s):

- Promote cost-effective and safe step-therapy for management of type 2 diabetes mellitus (T2DM).

Length of Authorization:

- Up to 6 months

Requires PA:

- All SGLT-2 inhibitors

4. Has the patient tried and failed metformin and a sulfonylurea, have contraindications to these treatments or is requesting a SGLT-2 inhibitor to be used with metformin and a sulfonylurea?	**Yes:** Go to #5	**No:** Pass to RPh. Deny and recommend trial of metformin or sulfonylurea. See below for metformin titration schedule.
6. Has the patient tried and failed (unable to maintain goal A1c) all of the following drugs, or have contraindications to all of these drugs? 1. Insulin 2. Thiazolidinedione 3. DPP-4 inhibitor 4. GLP-1 receptor agonist	**Yes:** Approve for up to 6 months	**No:** Pass to RPh. Deny and require a trial of insulin, thiazolidinedione, DPP-4 inhibitor, and GLP-1 agonist.

Medicare Plans… A Game of Tiers

Fewer PA restrictions, but more complexity

Preferred Pharmacy Cost-sharing for Essentials Choice Rx 14 What You Pay[1] All formulary drugs may be supplied through in-network mail-order or retail pharmacies.			
Stage One: Yearly Deductible			
Deductible	There is a **$175** yearly deductible on drugs in **Tiers 3, 4, and 5**. During this stage, you pay the full cost of drugs in Tiers 3, 4, and 5 until you have paid the deductible amount above. The deductible does **not** apply to drugs in Tiers 1, 2, and 6.		
	Up to a 30-day supply	**31-day to 60-day supply**	**61-day to 90-day supply**
Stage Two: Initial Coverage			
Tier 1 Preferred Generic	$3 co-pay	$6 co-pay	$6 co-pay Mail-Order $9 co-pay Retail
Tier 2 Generic	$12 co-pay	$24 co-pay	$24 co-pay Mail-Order $36 co-pay Retail
Tier 3 Preferred Brand	$37 co-pay	$74 copay	$74 co-pay Mail-Order $111 co-pay Retail
Tier 4 Non-Preferred Drug	31% co-insurance	31% co-insurance	31% co-insurance
Tier 5 Specialty	29% co-insurance[2]	Not available	Not available
Tier 6 Select Care Drugs	$0 co-pay	$0 co-pay	$0 co-pay

[1] If you have Low Income Co-pay Subsidies you will have varying out-of-pocket expenses.

[2] Limited to a 1-month (30-day) supply through in-network mail-order or retail pharmacies.

Case Study

- 70 year old, weighs 100kg, History of CABG, tobacco, BG 400-500 for past weeks, Insulin 100+ units Lantus at HS (solostar), Oral Meds: Metformin, glipizide,
- Most recent A1c – 11.3%
- Pt can’t afford Lantus insulin pen – what other option?

Extra Help for Medicare Recipients

Extra Help with Medicare Prescription Drug Plan Costs

What help can I receive?

Medicare beneficiaries can qualify for Extra Help with their Medicare prescription drug plan costs. The Extra Help is estimated to be worth about $4,900 per year. To qualify for the Extra Help, a person must be receiving Medicare, have limited resources and income, and reside in one of the 50 States or the District of Columbia.

Call 800-722-4134 (toll free) or contact your local SHIBA office to get information about your plan options.

- https://www.ssa.gov/benefits/medicare/prescriptionhelp/
- https://healthcare.oregon.gov/shiba/pages/index.aspx

When the goal is to minimize cost, go generic (uninsured and Medicare)

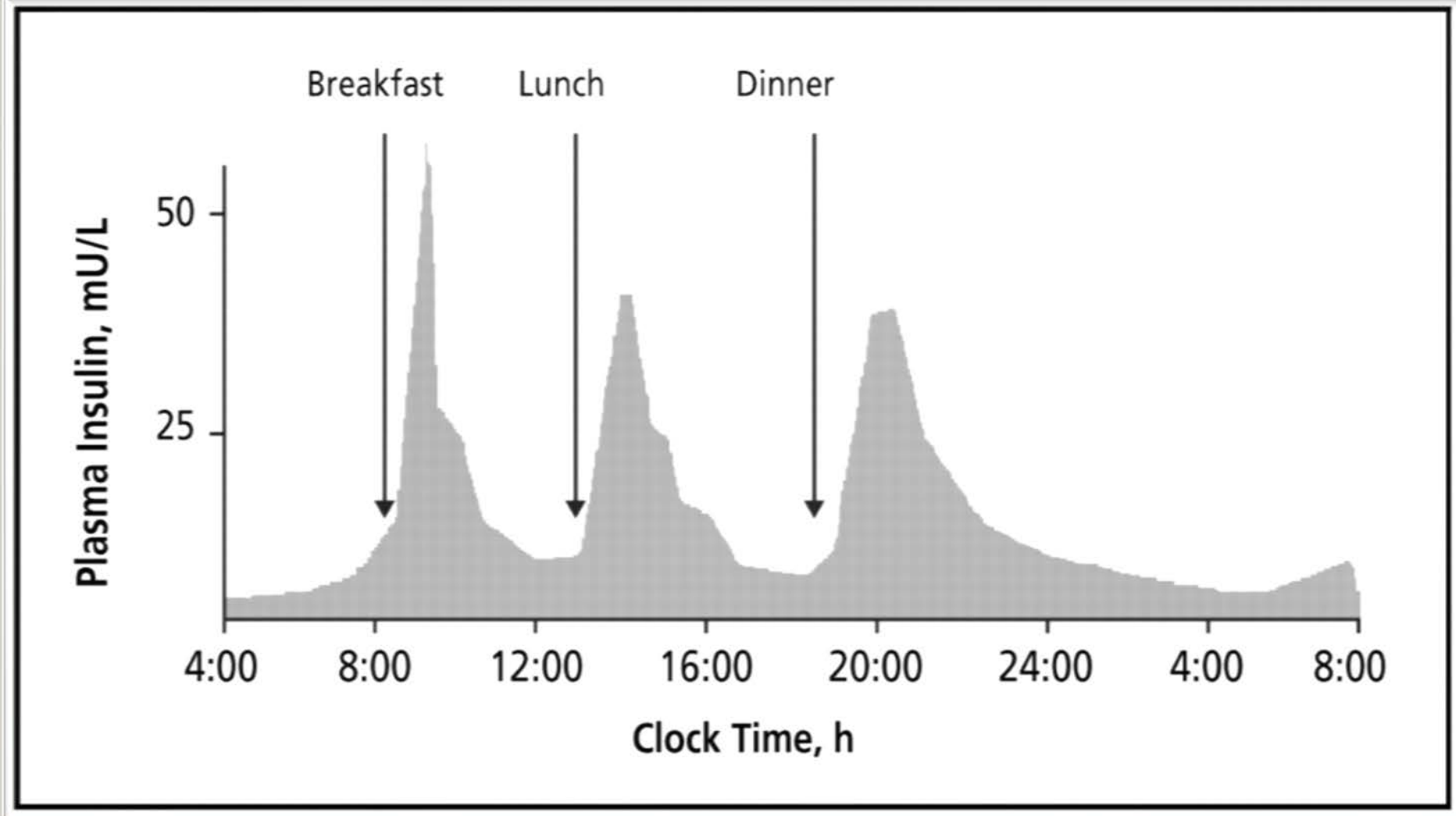
- Oral Meds - Metformin and Sulfonylureas
  - **Walmart** offers 3 month supply of following meds for ~ $10
    - Metformin
    - Metformin XR
    - Glipizide
    - Glyburide
    - Glimepiride
    - Pioglitazone is $9 per month
  - Other pharmacies are competitive now:
    - **Fred Meyer**, Rite Aid, Walgreens (membership programs)
    - **BiMart** ($4.00 list)

Insulin therapy in T2DM

- The progressive nature of T2DM should be regularly & objectively explained to T2DM patients.
- Avoid using insulin as a threat, describing it as a failure or punishment.
- Beware of clinical inertia
  - Give patients a self-titration algorithm
  - Refer to a diabetes educator

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic targets. Diabetes Care 2019

Relative effects of insulin analogs



lispro and regular human insulin. *Diabetes Care.* 2005;28:1077-1082.
Thompson R, Christie D, Hindmarsh PC. The role for insulin analogs in diabetes care, *Current Pediatrics.* 2006;

ALGORITHM FOR ADDING/INTENSIFYING INSULIN

START BASAL (Long-Acting Insulin)

A1C <8%

TDD 0.1–0.2 U/kg

A1C >8%

TDD 0.2–0.3 U/kg

Insulin titration every 2–3 days to reach glycemic goal:

- Fixed regimen: Increase TDD by 2 U
- Adjustable regimen:
  - FBG >180 mg/dL: add 20% of TDD
  - FBG 140–180 mg/dL: add 10% of TDD
  - FBG 110–139 mg/dL: add 1 unit
- If hypoglycemia, reduce TDD by:
  - BG <70 mg/dL: 10% – 20%
  - BG <40 mg/dL: 20% – 40%

Consider discontinuing or reducing sulfonylurea after starting basal insulin (basal analogs preferred to NPH)

***Glycemic Goal:**

- <7% for most patients with T2D; fasting and premeal BG <110 mg/dL; absence of hypoglycemia
- A1C and FBG targets may be adjusted based on patient's age, duration of diabetes, presence of comorbidities, diabetic complications, and hypoglycemia risk

Glycemic Control Not at Goal*

INTENSIFY (Prandial Control)

Add GLP1-RA

Or SGLT2i
Or DPP4i

Add Prandial Insulin

Basal Plus 1, Plus 2, Plus 3

- Begin prandial insulin before largest meal
- If not at goal, progress to injections before 2 or 3 meals
- **Start: 10% of basal dose or 5 units**

Basal Bolus

- Begin prandial insulin before each meal
- 50% Basal / 50% Prandial TDD 0.3–0.5 U/kg
- **Start: 50% of TDD in three doses before meals**

Insulin titration every 2–3 days to reach glycemic goal:

- Increase prandial dose by 10% or 1-2 units if 2-h postprandial or next premeal glucose consistently >140 mg/dL
- If hypoglycemia, reduce TDD basal and/or prandial insulin by:
  - BG consistently <70 mg/dL: 10% - 20%
  - Severe hypoglycemia (requiring assistance from another person) or BG <40 mg/dL: 20% - 40%

 DOI 10.4158/CS-2018-0535

Insulin and OHP (Medicaid)

Basal Insulin Options:	Covered = Novolin N, Lantus, Levemir
	Not covered = Tresiba, Toujeo, Basaglar
Prandial Insulin Options:	Covered = Novolog, Novolin R
	Not covered = Humalog, Apidra, Afrezza
Mixed Insulin Options:	Covered = Novolog 70/30, Novolin 70/30
	Not covered = Humalog 75/25, Humalog 50/50

When the goal is to minimize cost, go generic

Insulins – Oldies but Goodies

- NPH, Regular, 70/30 mix
- $25 a vial at Walmart – ReliOn
- Novolin N is a Q12Hr basal option
- 70/30 offers prandial in a single injection, but higher rates of hypoglycemia
- Tier 1 or 2 on *SOME* Medicare plans

Note: insulin syringes are not necessarily cheaper at Walmart than other pharmacies

	PacificSource Community Solutions (Medicaid)[B]	DMAP OHP (Medicaid)[C]	PacificSource Commercial[B]	Medicare w/supplement[B]	Medicare or Uninsured[D]	VA[C]
Step 1	Metformin ER 500mg	Metformin ER 500mg	Metformin ER 500mg	Metformin ER 500mg	Metformin ER 500mg	Metformin ER 500mg
Step 2	+Jardiance Or +Januvia if near goal	+Januvia if near goal or +Byetta or Bydureon	+Jardiance or Trulicity or Victoza	+DPP4 or GLP1 or SGLT2	+SFU	+Jardiance if CVD present or +Glipizide +TZD*
Step 3	+Januvia if near goal or +Trulicity or Victoza	+Basal insulin, or Glipizide, or TZD*	+Jardiance or Trulicity or Victoza	+DPP4 or GLP1 or SGLT2 or basal insulin	+TZD or Acarbose	+Jardiance, or Nesina if near goal, or TZD*
Step 4	+Basal insulin, or Januvia, or alternative GLP-1	+prandial insulin	+Basal insulin	+basal insulin	+Novolin insulin	+Basal insulin

*Avoid if CHF risk, morbid obesity, osteoporosis risk, or bladder cancer

SFU = Glipizide, Glyburide, Glimepiride; TZD = pioglitazone; GLP1 = Glucagon-Like Peptide 1 agonist (Victoza, Trulicity, Bydureon, Byetta, Ozempic, Adlyxin, Tanzeum); SGLT2 = sodium glucose co-transporter 1 inhibitor (Jardiance, Invokana, Farxiga); DPP4 = dipeptidyl peptidase 4 inhibitor (Januvia, Nesina, Trajenta, Onglyza)

Superscript Guideline/Evidence Alignment, A = fully aligned with guideline/evidence, B = partially aligned, C = not aligned

Case Study

- 33 year old female
- Type 2 DM x4 years, smoking, HTN
- Lantus 40 units/day, metformin, glipizide
- A1c 8.1%, BMI 42
- Insurance: OHP

Adding newer meds to established regimens:

SGLT-2 inhibitors:

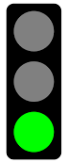
- SFU = reduce dose by 50% or DC
- Metformin, DPP4i, or TZD = no change
- Basal insulin = depending on A1c/EAG reduce dose by up to 50% or no change and monitor closely

GLP-1 agonists:

- SFU or DPP4i = DC redundant
- Metformin or TZD = no change
- Basal insulin = reduce dose by 20-50% then titrate
- Prandial insulin = conditional dosing based on SMBG

When the goal is to avoid weight gain

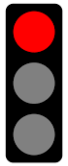
- These meds associated with weight loss:
  - GLP-1 agonists (Byetta, Bydureon, Victoza, Tanzeum, Trulicity)
    - Best evidence with liraglutide (Victoza 1.8 mg dose ~6 lbs more than placebo) https://www.ncbi.nlm.nih.gov/pubmed/26284720



  - SGLT-2 Inhibitors (Invokana, Farxiga, Jardiance)
    - Consider Jardiance for pt's w/heart failure (EMPA-REG)
    - Caution with history of yeast infection or UTI
    - Ave weight loss 2-5% body weight
    - Possibly other metabolic benefits –studies underway

Meininger G, Canovatchel W, Polidori D, Rosenthal N. Canagliflozin for the treatment of adults with Type 2 diabetes. Diabetes Manag. 2015;5:183-201.

When the goal is to avoid weight gain

- These meds are weight neutral:
  - Metformin 
  - DPP-IV Inhibitors: Januvia, Onglyza, Tradjenta, Nesina (low efficacy – I use if A1c is within 0.5 to 1% of goal) 
  - Acarbose (diarrhea is often prohibitive –my approach is to start at 12.5-25 mg with largest meal of the day) 

When the goal is avoid hypoglycemia

The Good:

- Metformin
- Pioglitazone
- Acarbose
- GLP-1 agonists
- SGLT-2 inhibitors

The Bad:

- Sulfonylureas
- Insulin
  - 70/30 > Prandial > Basal

The Particularly vulnerable:

- Those with CKD
- Autonomic nueropathy

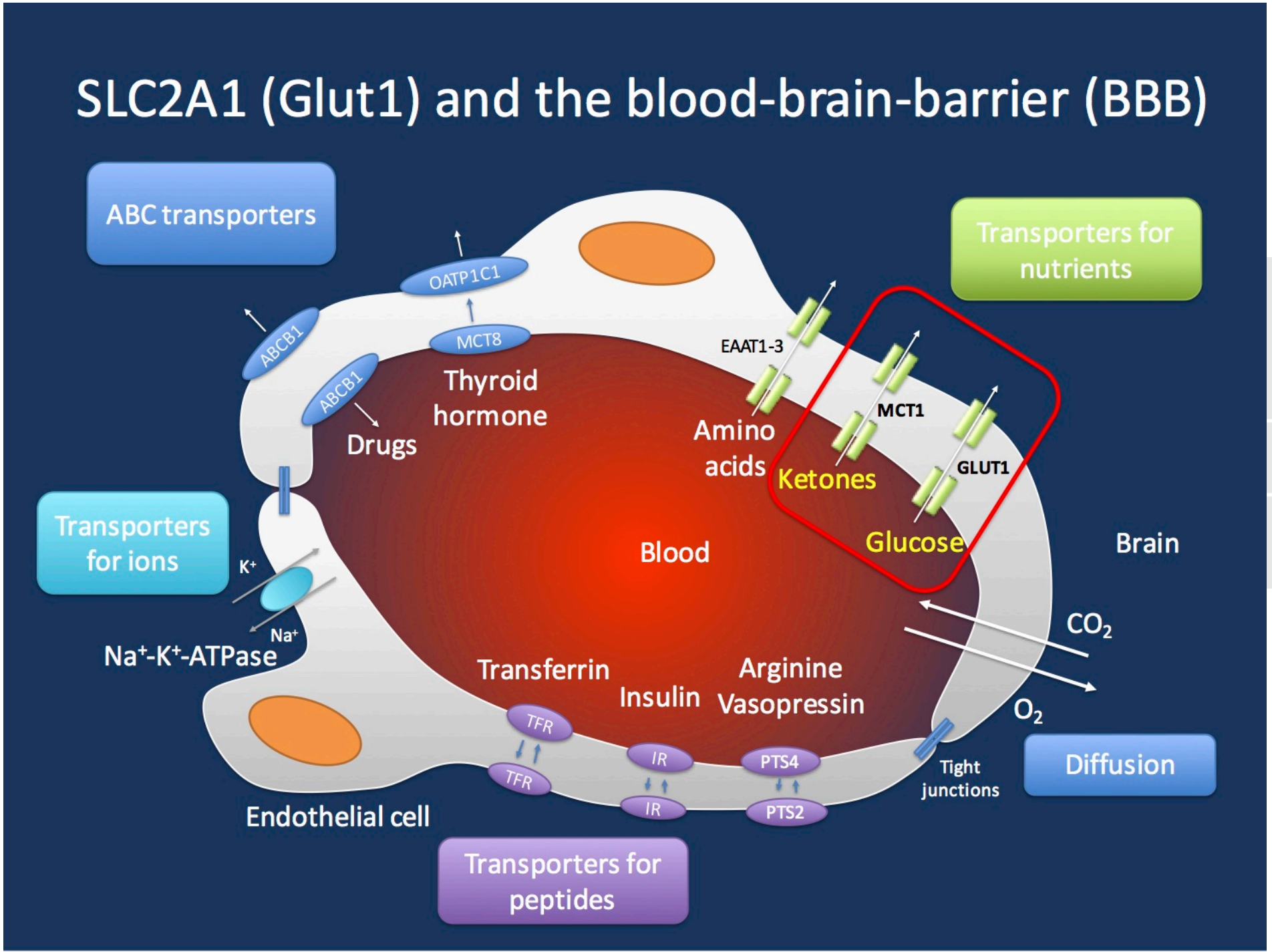
Case Study

- 69 year old male, BMI 31, on Metformin 2000mg a day and Glipizide 40mg a day, Creatinine 1.2, 11 year history of diabetes
- Most recent A1c 9.1%
- Medicare
- In the visit he shares with you that he keeps candy with him at all times

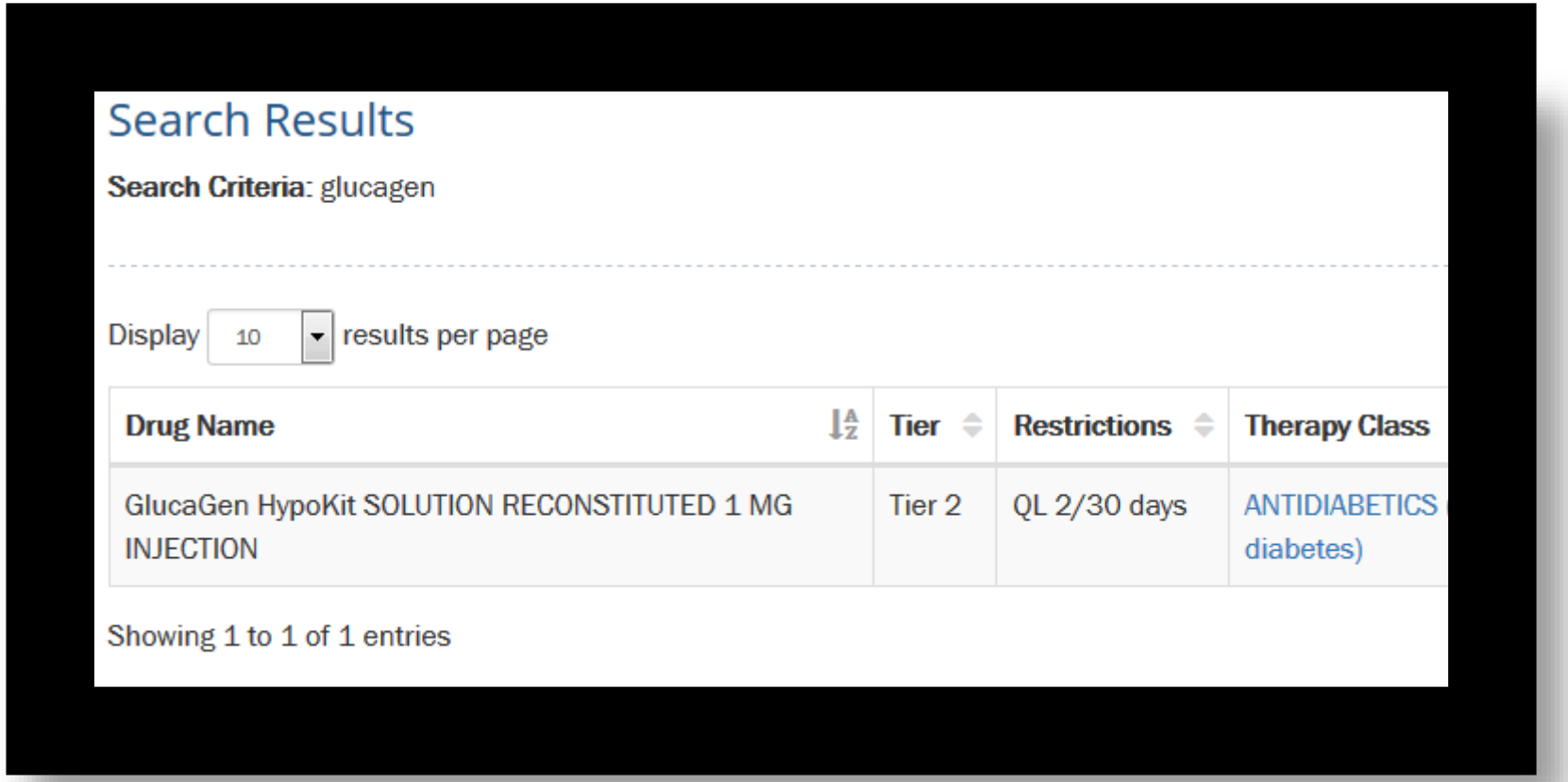
Recommendations: Glycemic Goals in Adults

- A reasonable A1C goal for many nonpregnant adults is <7% (53 mmol/mol).
- Consider more stringent goals (e.g. <6.5%) for select patients if achievable without significant hypos or other adverse effects.
- Consider less stringent goals (e.g. <8%) for patients with a history of severe hypoglycemia, limited life expectancy, or other conditions that make <7% difficult to attain.

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic targets. Diabetes Care 2019


SLC2A1 (Glut1) and the blood-brain-barrier (BBB)
ABC transporters
Transporters for nutrients
Transporters for ions
Transporters for peptides
OATP1C1
ABCB1
ABCB1
MCT8
Thyroid hormone
Drugs
EAAT1-3
Amino acids
MCT1
Ketones
GLUT1
Glucose
Blood
Brain
K+
Na+
Na+-K+-ATPase
CO2
O2
Transferrin
Insulin
Arginine Vasopressin
TFR
TFR
IR
IR
PTS4
PTS2
Tight junctions
Diffusion
Endothelial cell

Recommendations: hypoglycemia



Search Results

Search Criteria: glucagen

Display 10 results per page

Drug Name	Tier	Restrictions	Therapy Class
GlucaGen HypoKit SOLUTION RECONSTITUTED 1 MG INJECTION	Tier 2	QL 2/30 days	ANTIDIABETICS (diabetes)

Showing 1 to 1 of 1 entries

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

Continuous Glucose Monitoring (CGM)

PacificSource Community Solutions

POLICY NAME:
CONTINUOUS GLUCOSE MONITORS
Affected Medications: FREESTYLE LIBRE and DEXCOM G6

Covered Uses:	• All FDA-approved indications not otherwise excluded by benefit design.
Required Medical Information:	1. Diagnosis of Type 1 diabetes currently on an insulin pump 2. Diagnosis of Type 1 diabetes not currently using an insulin pump with one of the following: • Baseline HbA1c Level 8.0% or higher • Frequent or severe hypoglycemia • Impaired awareness of hypoglycemia 3. Pregnant women or actively attempting to conceive and have a diagnosis of Type 1 diabetes 4. Children and adolescents under 21 with a diagnosis of Type 1 diabetes
Appropriate Treatment Regimen & Other Criteria:	
Exclusion Criteria:	• Type 2 diabetes

Key Points

- CV risk reduction - the major focus of therapy for all patients
- Individualize Glycemic targets & BG-lowering
- Diet, exercise, & education: foundation T2DM therapy
- Metformin = optimal 1st-line drug
- After metformin -> Combo therapy should reduce CV/renal risk with minimal weight gain or hypoglycemia
- Ultimately, many T2 patients will require insulin therapy
- All treatment decisions should be made in conjunction with the patient (focus on preferences, needs & values)

Glossary of Acronyms

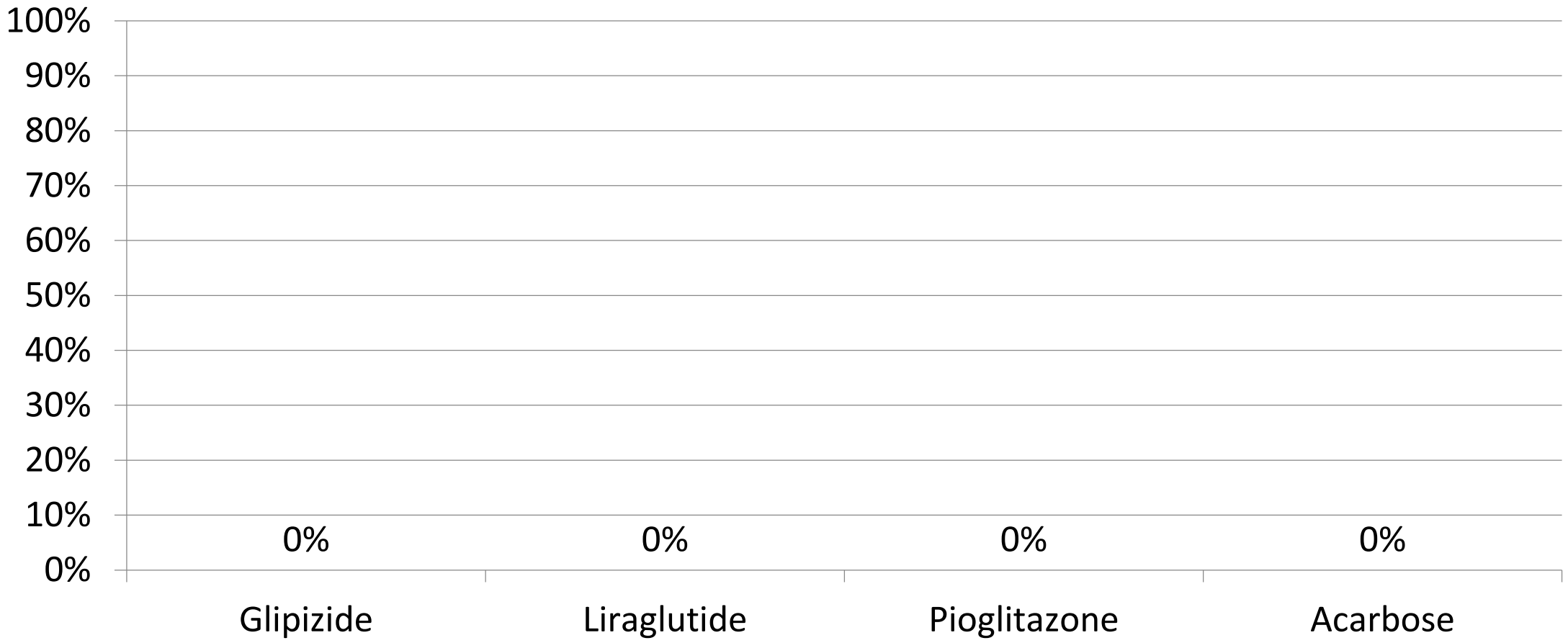
- SMBG = Self Monitoring of Blood Glucose
- SFU = Sulfonylurea
- TZD = Thiazolidinedione
- GLP-1 = Glucagon-Like Peptide 1 agonist
- DPP4 = Dipeptidyl Peptidase 4 Inhibitor
- SGLT-2 = Sodium-Glucose Cotransporter-2 inhibitor
- PSCS = Pacific Source Community Solutions Medicaid
- DMAP = Division of Medical Assistance Programs, aka Open Card, Oregon fee-for-service Medicaid

Knowledge Check

For a patient with coronary artery disease, A1c above goal, already established on metformin and lifestyle therapy, which is the best next choice:

1. Glipizide
2. Liraglutide
3. Pioglitazone
4. Acarbose

Results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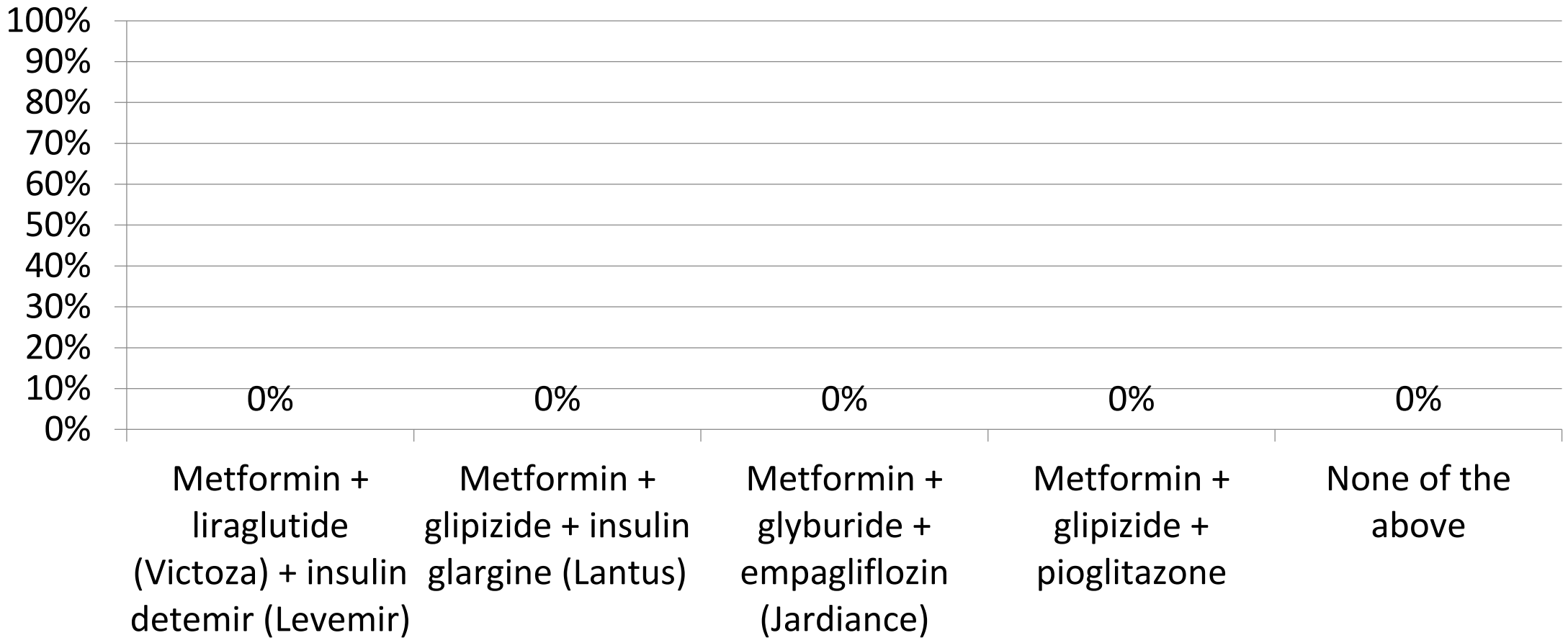
Glipizide
Liraglutide
Pioglitazone
Acarbose

Knowledge Check

For a patient covered by Medicare part D which regimen will be the most affordable? (assuming no extra help)

1. Metformin + liraglutide (Victoza) + insulin detemir (Levemir)
2. Metformin + glipizide + insulin glargine (Lantus)
3. Metformin + glyburide + empagliflozin (Jardiance)
4. Metformin + glipizide + pioglitazone
5. None of the above

Results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Metformin + liraglutide (Victoza) + insulin detemir (Levemir)
Metformin + glipizide + insulin glargine (Lantus)
Metformin + glyburide + empagliflozin (Jardiance)
Metformin + glipizide + pioglitazone
None of the above

Knowledge Check

Clinically Significant Hypoglycemia, as defined by the ADA, is a blood sugar below:

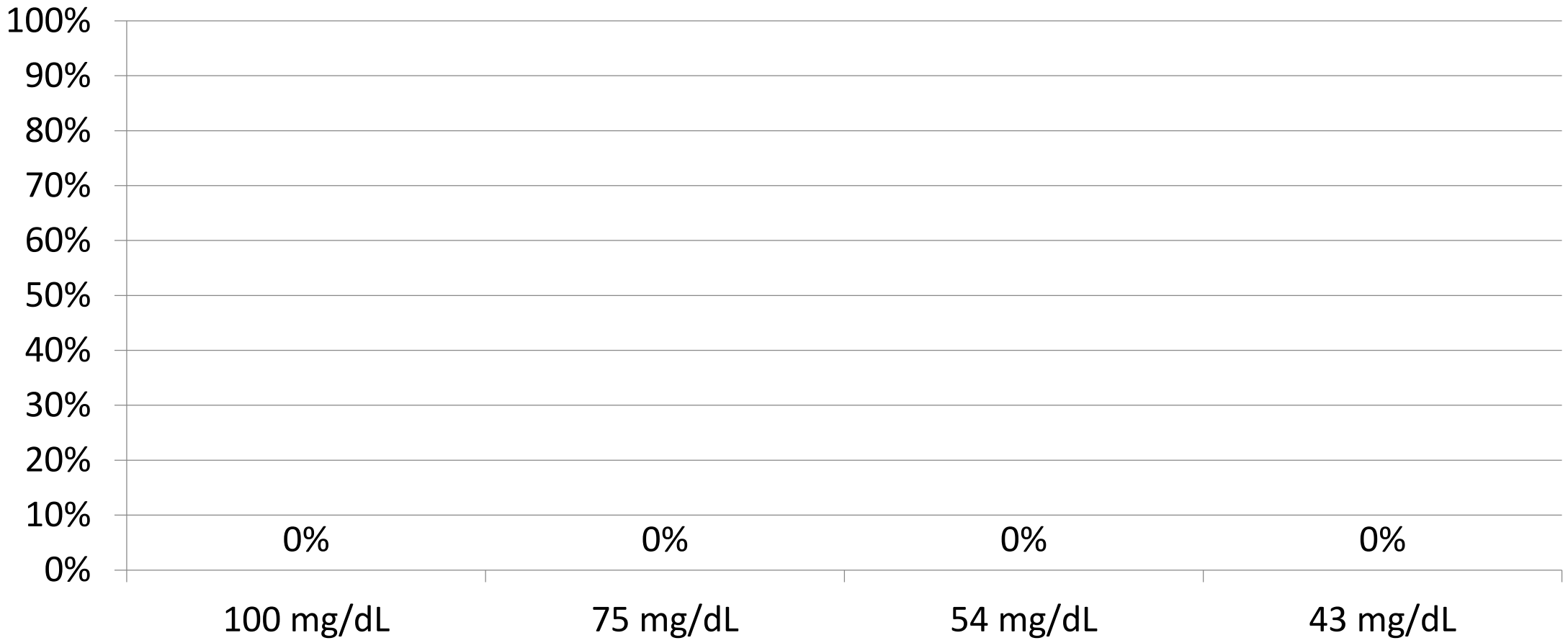
a.100 mg/dL

b.75 mg/dL

c.54 mg/dL

d.43 mg/dL

Results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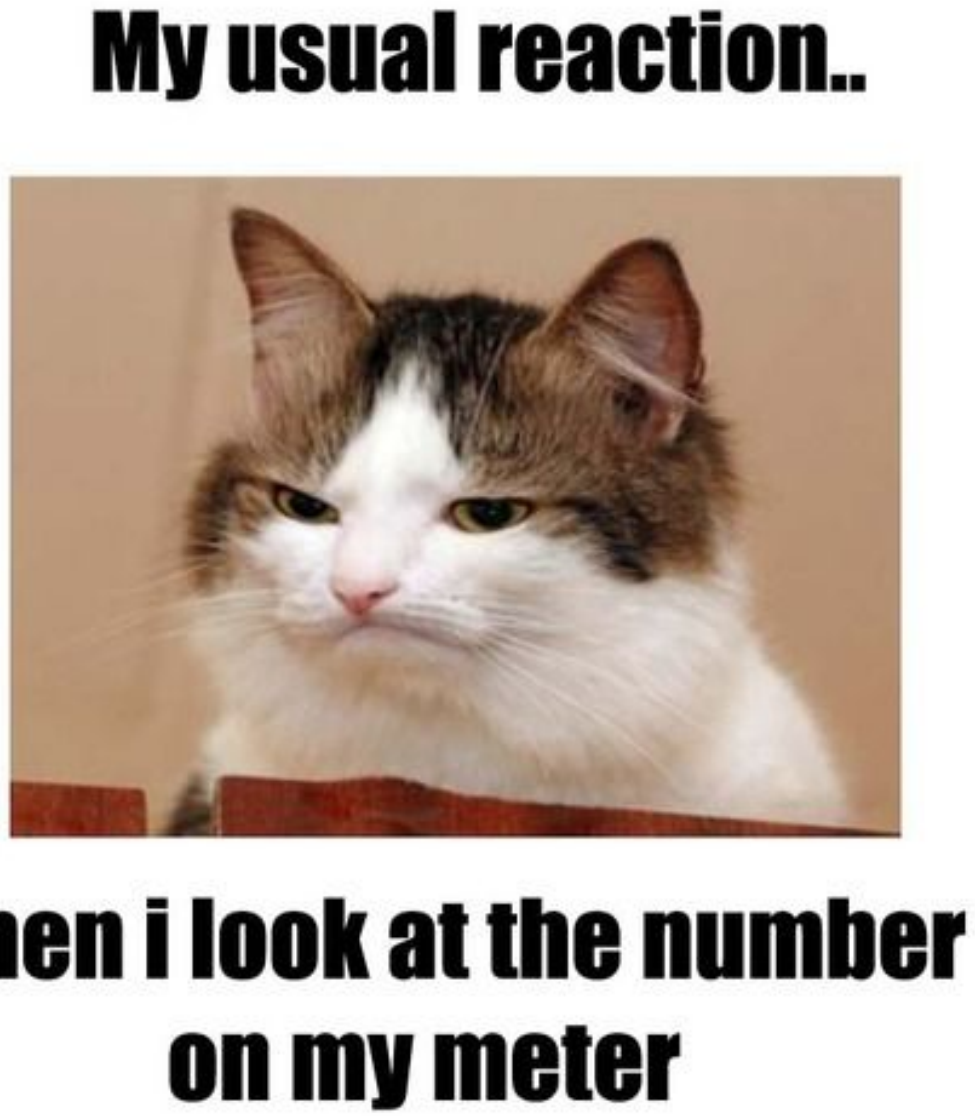
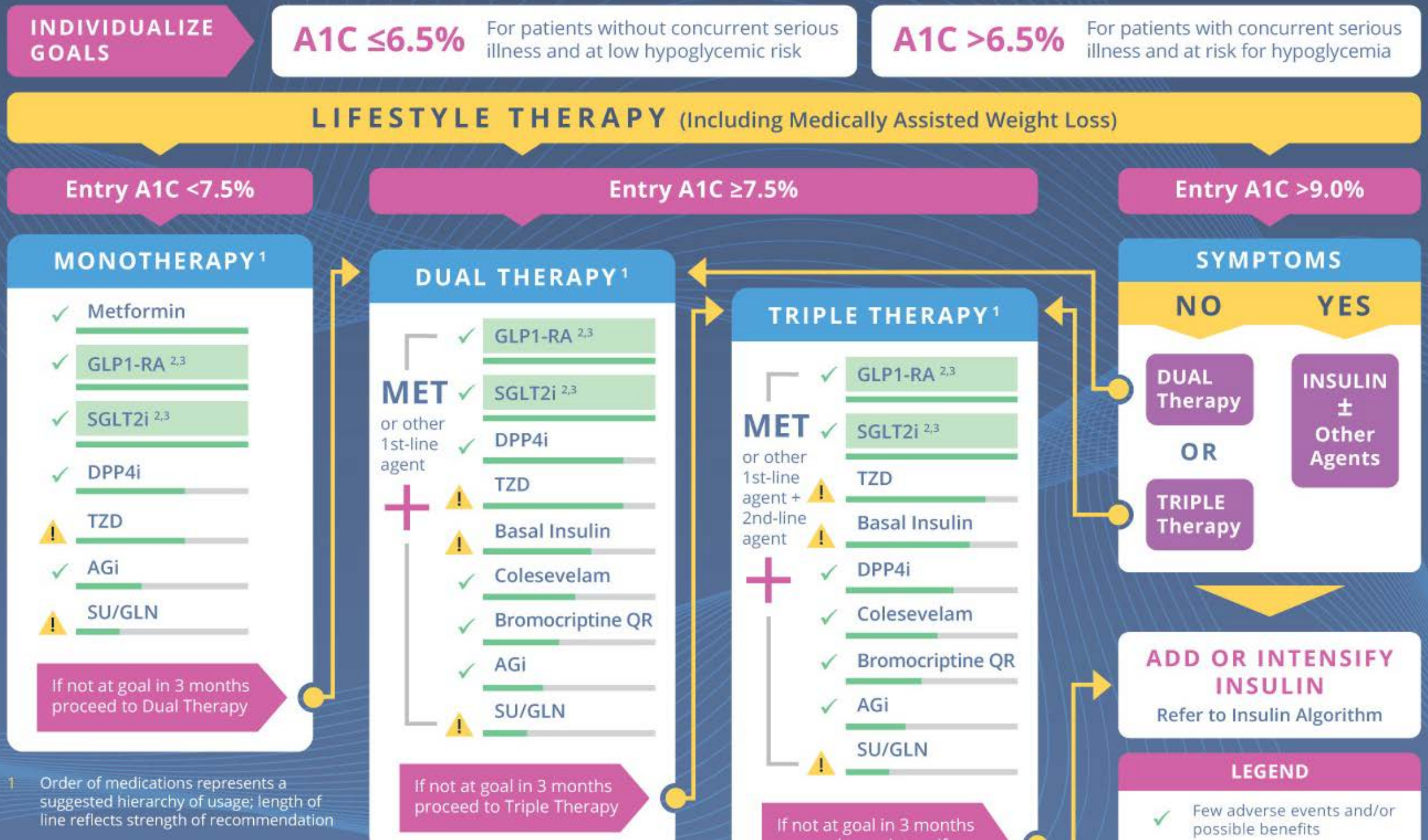
100 mg/dL
75 mg/dL
54 mg/dL
43 mg/dL

Thanks for your attention and participation

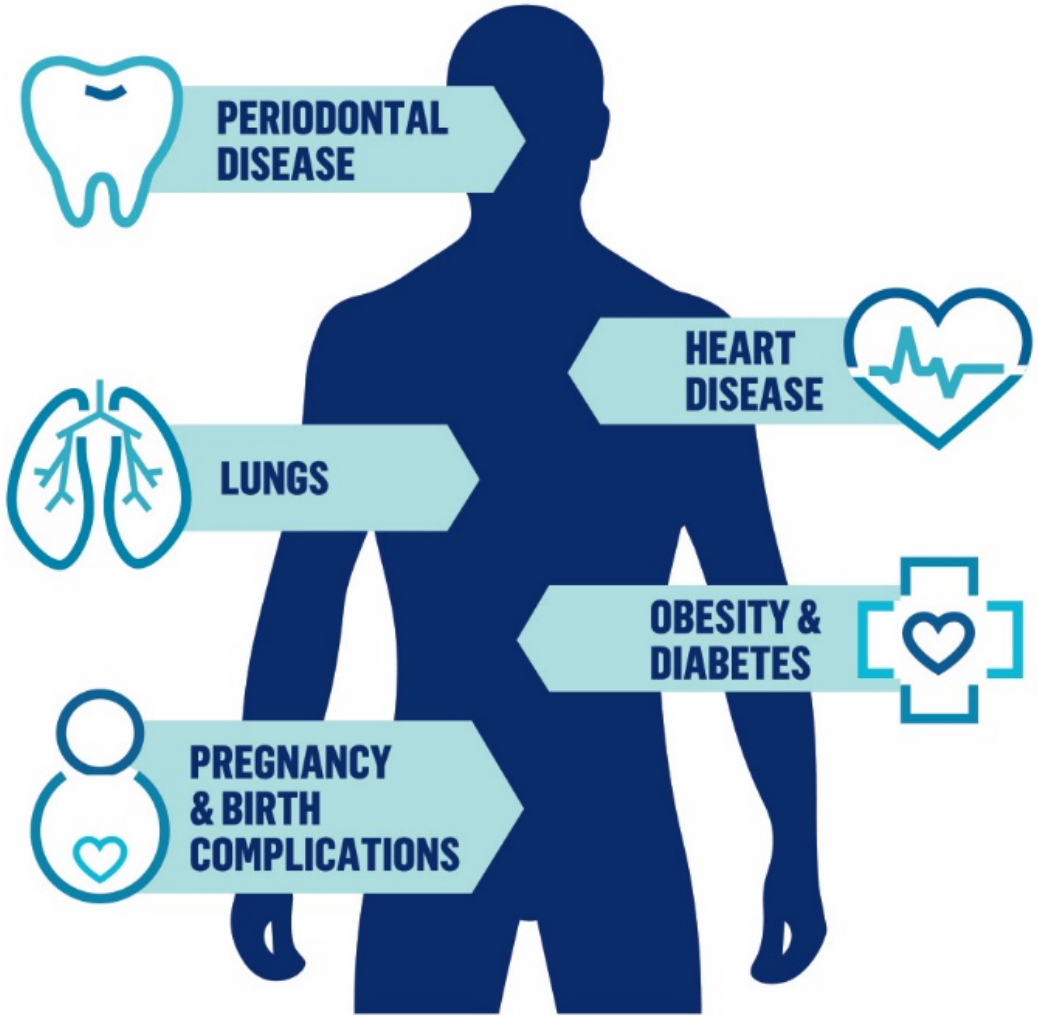




ORAL HEALTH IS IMPORTANT TO OVERALL HEALTH

People with diabetes are at risk for mouth problems, especially gum disease.

- Gum disease can damage the gum and bone that hold your teeth in place and may lead to painful chewing problems and tooth loss.
- Gum disease also makes it hard to control your glucose (blood sugar).



Quality Health Metrics Oral Evaluation for Adults with Diabetes

WHO: OHP Members 18 years and older who have a confirmed diabetes diagnosis.

WHAT: Receives a Comprehensive, Periodic, or periodontal evaluation.

WHEN: Measurement year January 1st – December 31st.

WHERE: Oral evaluations are to be completed in the office by a dentist.

HOW: When a diabetic patient is seen by primary care, ask “Have you seen a dentist this year?”

Nutrition Best Practice: There is no diet.

There is no diabetic diet.

One size does not fit all and meal plans should be individualized.

Overall goal is to work towards sustainable lifestyle changes and avoid fad diets.

Nutrition Best Practice: Structure.

Focus on a structured meal and snack pattern that honors hunger and fullness cues with a goal of stabilizing blood sugar.

Aim for eating 1-2 hours after waking and leave no more than 4-5 hours between eating sessions is a good place to start.

Hunger cues: aim for just satisfied, not overly full or starving.

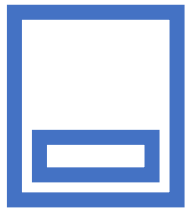
Structure can help reduce mindless eating due to boredom, habit, or emotional eating.

Nutrition Best Practice: Type of carbohydrates.

- Choose complex, nutrient rich carbohydrates such as whole grains, fruit, milk, beans, and sweet potatoes just to name a few.
- Aim for 5 servings of fruits/vegetables per day to increase fiber which will overall be beneficial for blood sugar, weight and heart health. Overall fiber intake should be 25-30 grams per day.
- Reduce simple carbohydrates that have less nutritional value such as soda, cakes, candy, cookies, crackers, chips.
- Practice tools for portion control such as hand method, plate method and carbohydrate counting.
    - For men, aim for 4-5 choices at each meal (3 meals/day) and 1 choice per snack (optional).
    - For women, aim for 3-4 choices at each meal (3 meals/day) and 1 choice for snack (optional).

Nutrition Best Practice: Water.

- Focus on drinking plenty of sugar free beverages such as water.
- 64 ounces a day or eight, 8 oz glasses is a good place to start.
- Avoid sugar-added beverages such as soda, sports drinks, flavored coffee drinks and juice.



Nutrition Best Practice: Movement.

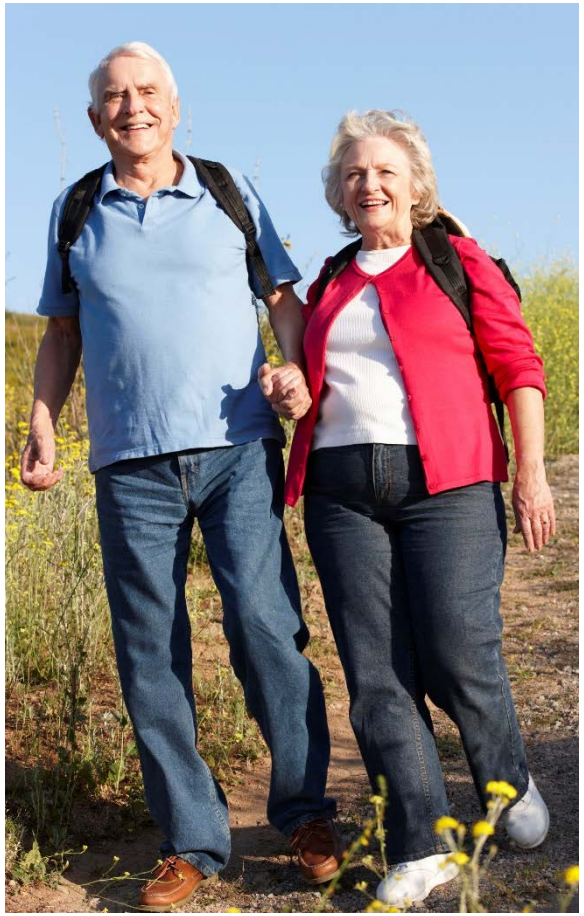
Increase movement. The goal is to sit less and move more!

Aim for 30-60 minutes of movement most days of the week.

A good place to start is moving after meals and snacks.

Movement should be joyful and sustainable!

Case Study



- 54 year old, smoking, eGFR 44 ml/min, BMI 34. Checking BG inconsistently. On Metformin 500mg BID for past 4 months. Had bad experience with hypoglycemia on glyburide.
- Most recent A1c 8.9%
- Insurance
  - Uninsured

Case Study

- 61 year old overweight woman with type 2 diabetes 10 years. Has been trying to control diabetes with diet and exercise and Metformin 2 g/day.
- GFR in 90s.
- Worried about weight gain, BMI 39
- A1c 9.4%
- Insurance
  - OHP