2023 Approach to Diabetes Care in the Elderly

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Objectives

- To review commonly used medications in the treatment of diabetes
- To learn about recently approved/newer diabetes medications and their place in diabetes management
- To gain understanding about diabetes management in the elderly population
- To learn about the benefits and concerns related to continuous glucose monitoring

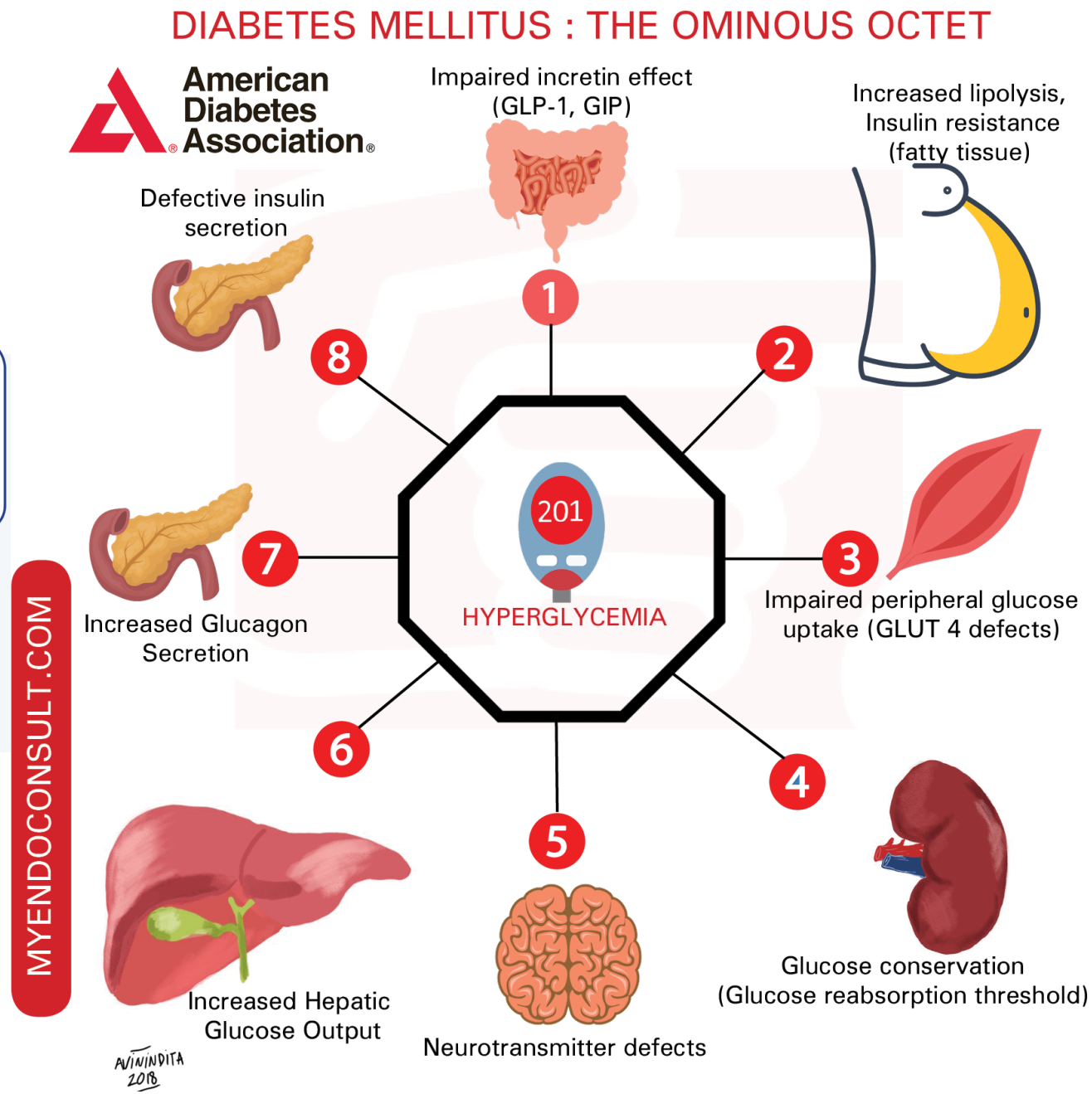
Ominous Octet

- SGLT-2 INHIBITORS — 4
- DPP-4 INHIBITORS — 7
- METFORMIN — 6
- THIAZOLIDINEDIONES — 2 3 6 8
- GLUCAGON-LIKE PEPTIDE 1 AGONISTS — 1 3 5 6 7 8

CLINICAL PEARL

Optimal management of Type 2 Diabetes Mellitus should include early initiation of combination therapy using multiple drugs with different mechanisms of action.

Novel Agents for the Treatment of Type 2 Diabetes. Diabetes Spectr. 2014 May; 27(2): 100–112.



Metformin

Improves glucose tolerance through:

- Decreased hepatic production of glucose
- Decreased sugar absorption in intestines
- Increased insulin sensitivity

- Common side effects: diarrhea, nausea, vomiting, gas, indigestion, vitamin b12 deficiency
- Serious side effects: rare hypoglycemia, lactic acidosis

- Available on its own or in combination with other DM medications
- Low cost

Metformin cont.

- Renal considerations:
  - Lactic acidosis
    - Rare but potentially life threatening
    - Serum lactate >23 mg/dL
  - Increased all-cause mortality in patients with CKD Stage 5

- FDA (9)
  - Obtain eGFR prior to starting
  - Contraindicated if eGFR falls below 30
  - Not recommended to initiate if eGFR 30-45
  - Obtain eGFR annually
    - If less than <45
    - Discontinue if eGFR falls <30

Sulfonylureas

- Bind to sulfonylurea receptors, ultimately leading to the stimulation of insulin release from functioning pancreatic beta cells
- Common side effects: hypoglycemia, dizziness
- Low cost

On to the Newer Agents

Labs to consider

- A1c – to measure average blood glucose over the past three months
- Fructosamine – to measure average blood glucose over the past 2-3 weeks
- C-peptide – to evaluate insulin production by the beta cells in the pancreas
- eGFR – to assess renal function

A1C and Estimated Average Glucose Levels

	A1C Percentage	Estimated Average Glucose (EAG)	
In-range	< 5.7%	< 117 mg/dL	6.5 mmol/L
Prediabetes	5.7-6.4%	117-137 mg/dL	6.5-7.6 mmol/L
Diabetes	> 6.4%	> 137 mg/dL	> 7.6 mmol/L
Increased risk of complications ↓	6.5%	140 mg/dL	7.8 mmol/L
	7.0%	154 mg/dL	8.6 mmol/L
	7.5%	169 mg/dL	9.4 mmol/L
	8.0%	183 mg/dL	10.1 mmol/L
	8.5%	197 mg/dL	10.9 mmol/L
	9.0%	212 mg/dL	11.8 mmol/L
	9.5%	226 mg/dL	12.6 mmol/L
	10%	240 mg/dL	13.4 mmol/L

SGLT2 inhibitors

Sodium-glucose cotransporter-2 inhibitors – prevent the reabsorption of glucose in the kidneys, leading to the removal of glucose from the body through urine

Common brands:

- Brenzavvy™ (bexaglifloxin)
- Invokana® (canagliflozin)
- Farxiga® (dapagliflozin)
- Jardiance® (empagliflozin)
- Steglatro® (ertugliflozin)

SGLT2i Benefits

SLOWS THE PROGRESSION OF KIDNEY DISEASE, REDUCTION IN ONSET OF END STAGE RENAL DISEASE, CARDIOVASCULAR OR RENAL DEATH IN PATIENTS WITH AND WITHOUT DIABETES

REDUCTION IN HEMOGLOBIN A1C LEVELS BY AN AVERAGE OF 0.5%-0.8% WHEN USED AS MONOTHERAPY OR ADD-ON THERAPY (MIKHAIL, 2014)

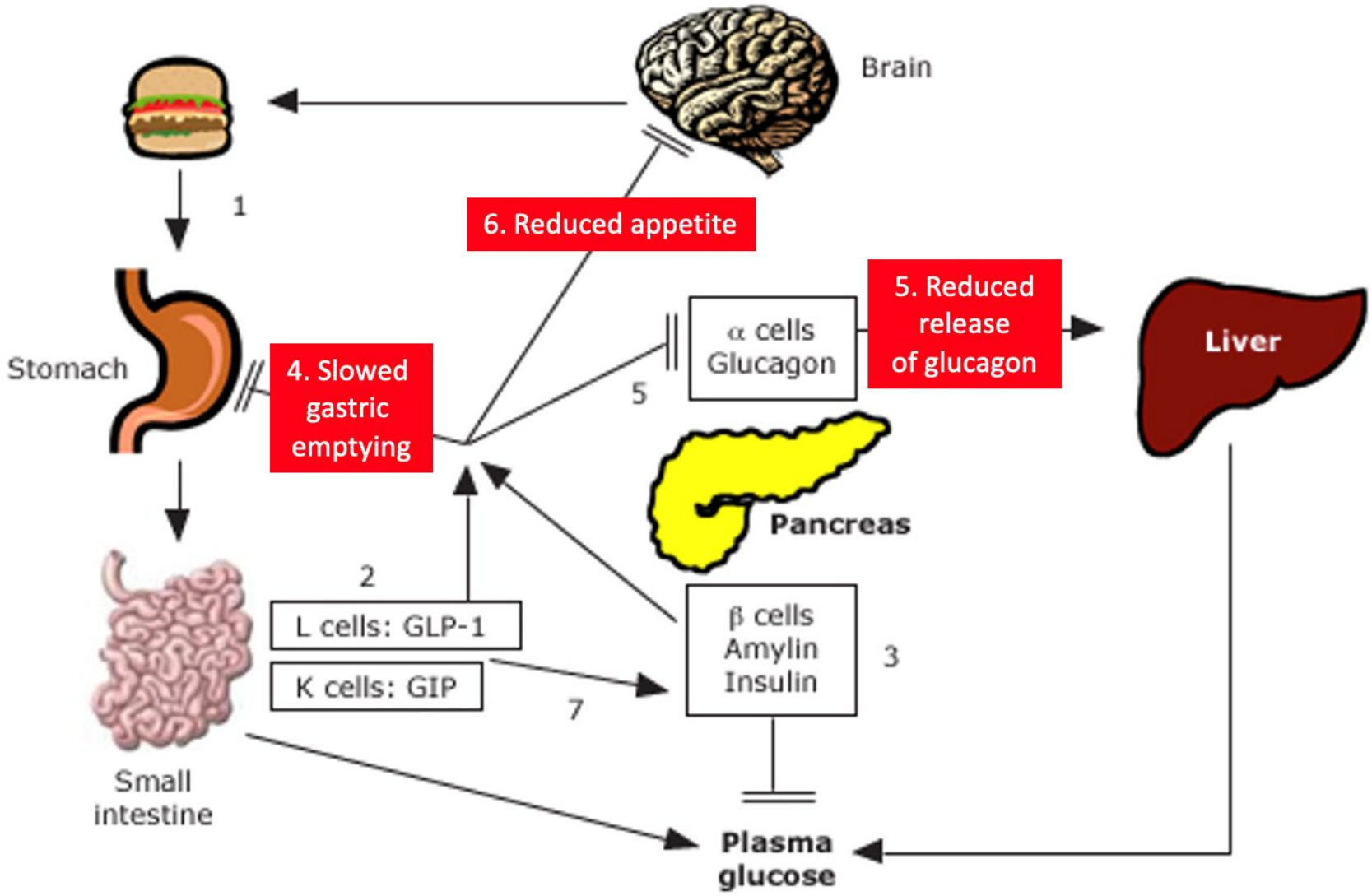
LOWER RISK OF CARDIOVASCULAR MORTALITY, MAJOR ADVERSE CARDIOVASCULAR EVENTS, AND HOSPITALIZATION DUE TO HEART FAILURE (KYRIAKOS, 2020)

SGLT2i concerns

- Common:
  - Increased frequency of urination
  - Urinary tract infectious disease
  - Female genital infection
- Serious:
  - Euglycemic Diabetic Ketoacidosis
  - Hypoglycemia
  - Acute Kidney Injury
  - Sepsis due to UTI
- High cost (~$700/month)

GLP1 receptor agonists

Glucose-Like peptide-1 (GLP1) and Glucose-dependent Insulinotropic Polypeptide (GIP) are gut hormones that are secreted by the body to secrete insulin in response to a meal.



Source: UpToDate

GLP1 RA names

Injection:
- Trulicity® (dulaglutide) – weekly
- Ozempic® (semaglutide) - weekly
- Saxenda®, Victoza® (liraglutide) – daily
- *Bydureon bcise® (exenatide ER) - weekly*
- *Adlyxin® (lixisenatide) – daily*
- *Byetta® (exenatide) – twice daily*

Oral:
- Rybelsus® (semaglutide) - daily

GLP1 RA benefits

Weight loss

A1c reduction by 0.8-1.6%

Cardiovascular benefits in those with diabetes and established atherosclerotic cardiovascular disease (ASCVD, i.e., history of heart attack or stroke)

Renal benefits – prevents albuminuria and slows decline of kidney function towards end stage renal disease in patients with diabetic kidney disease

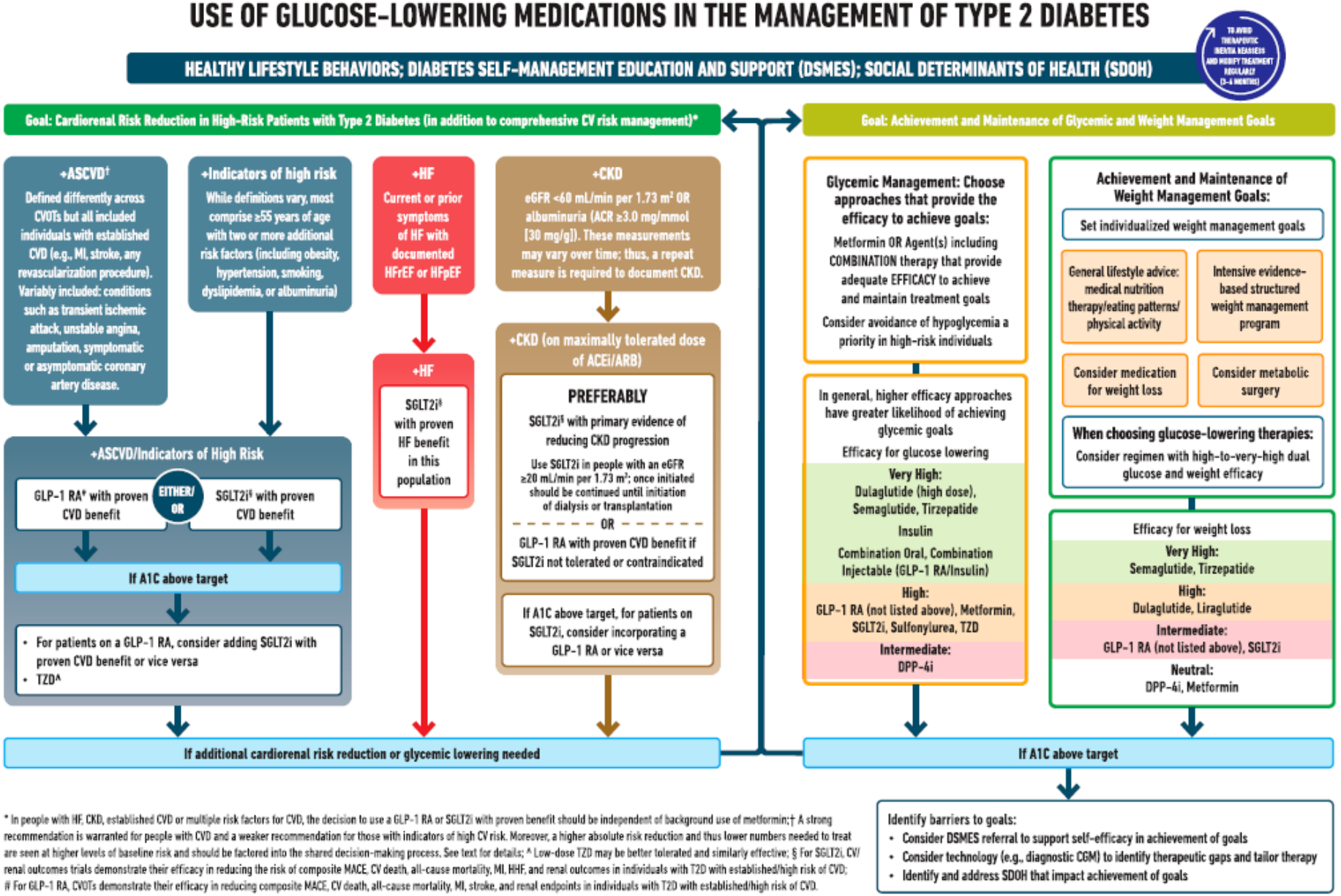
GLP1 agonist concerns

- Common side effects:
  - Nausea, vomiting, diarrhea, constipation, abdominal pain, decreased appetite
- Serious side effects:
  - Pancreatitis
  - Cholecystitis or Cholelithiasis (gall bladder problems)
  - Thyroid cancer
  - Gastroparesis
- High cost (~$1200/month)

Current Guidelines

- American Diabetes Association still recommends Metformin as first line for the treatment of type 2 diabetes.
- GLP1 agonist can be “considered in patients with a contraindication or intolerance to metformin, in patients with a hemoglobin A1c greater than 1.5% over target, or in patients who do not reach their target A1c in three months, particularly in patients with atherosclerosis, heart failure, or chronic kidney disease” (Collins, 2023)

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES



* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin;† A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

Pharmacologic Approaches to Glycemic Management:
Standards of Care in Diabetes - 2023. *Diabetes Care* 2023;46(Suppl. 1):S140-S157

Considerations for the elderly

- If considering sulfonylureas, glipizide has no active metabolites, therefore carries the lowest risk of hypoglycemia. Recommended over glimepiride and glyburide in elderly.
- Jardiance had increased chance of UTI
  - Incidence of 7.6-9.3% in all patients, 15.1-15.7% in 75 years and older
- “In a systematic review and meta-analysis of GLP-1 receptor agonist trials, these agents have been found to reduce major adverse cardiovascular events, cardiovascular deaths, stroke, and myocardial infarction to the same degree for people over and under 65 years of age(104)” (Diabetes Care 2023; 46 (supplement 1):S222)

Pharmacotherapy risks and benefits in the elderly[2-4]

Class/drug	Disadvantages	Advantages	A1C-lowering potential	Cost
Metformin	• Gastrointestinal adverse effects • B12 deficiency • Lactic acidosis (rare) in patients with cardiovascular, renal, or hepatic dysfunction	• Minimal hypoglycemia • Likely reduces both microvascular and macrovascular events • Weight loss	1%-1.5%	Low
Sulfonylureas • Glipizide • Glyburide • Glimepiride	• Hypoglycemia (avoid glyburide) • Weight gain	• Good initial efficacy	1%-2%	Low
TZDs • Pioglitazone • Rosiglitazone	• Weight gain • Edema/heart failure • Increased fracture risk • Increased LDL • Increased risk of bladder cancer (pioglitazone)	• Minimal hypoglycemia • Improved HDL • Reduced triglycerides (pioglitazone)	1%-1.5%	Low
DPP-4 inhibitors • Sitagliptin • Saxagliptin • Linagliptin • Alogliptin	• Associated with pancreatitis • Severe joint pain • New or worsening heart failure	• Minimal hypoglycemia • Well tolerated • Once-daily dosing	0.5%-0.9%	High
GLP-1 RAs • Exenatide • Liraglutide • Dulaglutide • Albiglutide	• Injectable • Gastrointestinal adverse effects • Associated with pancreatitis • Avoid in thyroid cancer	• Minimal hypoglycemia • Weight loss • Liraglutide may offer cardiovascular benefit	1%-1.5%	High
SGLT-2 inhibitors • Canagliflozin • Empagliflozin • Dapagliflozin	• Genitourinary infections • Genital yeast infections • Polyuria • Hyperkalemia • Hypotension • Pancreatitis • Increased LDL	• Minimal hypoglycemia • Weight loss • Decreased blood pressure • Once-daily dosing • Empagliflozin may offer cardiovascular benefit	0.5%-1%	High
Insulin	• Injectable • Hypoglycemia • Requires visual, manual, and cognitive skills	• Effective in all patients	Theoretically unlimited efficacy	High

A1C, glycated hemoglobin; DPP-4, dipeptidyl peptidase-4; GLP-1 RA, glucagon-like peptide-1 receptor agonists; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SGLT-2, sodium glucose cotransporter-2; TZDs, thiazolidinediones.

Keber (2018)

Treatment Goals

Table 13.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.0–7.5% (53–58 mmol/mol)	80–130 mg/dL (4.4–7.2 mmol/L)	80–180 mg/dL (4.4–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or two or more instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or two or more ADL impairments)	Limited remaining life expectancy makes benefit uncertain	Avoid reliance on A1C; glucose control decisions should be based on avoiding hypoglycemia and symptomatic hyperglycemia	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<140/90 mmHg	Consider likelihood of benefit with statin

Diabetes Care 2023; 46 (supplement 1):S220

Addressing Polypharmacy

What are the patient's treatment goals?

Benefits of deprescribing:

- Limit risk of hypoglycemia, improve medication adherence, minimize cost, simplify regimen, reduce risk of drug interactions

Examples:

A patient may be on a basal and bolus insulin regimen requiring four injections/day. If deemed appropriate, this could be simplified to a mixed insulin, only requiring two injections/day.

Table 13.2

Table 13.2—Considerations for treatment regimen simplification and deintensification/deprescribing in older adults with diabetes (93,128)

Patient characteristics/ health status	Reasonable A1C/ treatment goal	Rationale/considerations	When may regimen simplification be required?	When may treatment deintensification/ deprescribing be required?
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	<7.0–7.5% (53–58 mmol/mol)	• Patients can generally perform complex tasks to maintain good glycemic control when health is stable • During acute illness, patients may be more at risk for administration or dosing errors that can result in hypoglycemia, falls, fractures, etc.	• If severe or recurrent hypoglycemia occurs in patients on insulin therapy (regardless of A1C) • If wide glucose excursions are observed • If cognitive or functional decline occurs following acute illness	• If severe or recurrent hypoglycemia occurs in patients on noninsulin therapies with high risk of hypoglycemia (regardless of A1C) • If wide glucose excursions are observed • In the presence of polypharmacy
Complex/intermediate (multiple coexisting chronic illnesses or two or more instrumental ADL impairments or mild-to-moderate cognitive impairment)	<8.0% (64 mmol/mol)	• Comorbidities may affect self-management abilities and capacity to avoid hypoglycemia • Long-acting medication formulations may decrease pill burden and complexity of medication regimen	• If severe or recurrent hypoglycemia occurs in patients on insulin therapy (even if A1C is appropriate) • If unable to manage complexity of an insulin regimen • If there is a significant change in social circumstances, such as loss of caregiver, change in living situation, or financial difficulties	• If severe or recurrent hypoglycemia occurs in patients on noninsulin therapies with high risk of hypoglycemia (even if A1C is appropriate) • If wide glucose excursions are observed • In the presence of polypharmacy
Community-dwelling patients receiving care in a skilled nursing facility for short-term rehabilitation	Avoid reliance on A1C, glucose target 100–200 mg/dL (5.55–11.1 mmol/L)	• Glycemic control is important for recovery, wound healing, hydration, and avoidance of infections • Patients recovering from illness may not have returned to baseline cognitive function at the time of discharge • Consider the type of support the patient will receive at home	• If treatment regimen increased in complexity during hospitalization, it is reasonable, in many cases, to reinstate the prehospitalization medication regimen during the rehabilitation	• If the hospitalization for acute illness resulted in weight loss, anorexia, short-term cognitive decline, and/or loss of physical functioning

Diabetes Care 2023; 46 (supplement 1):S223

Table 13.2 cont.

Table 13.2—Considerations for treatment regimen simplification and deintensification/deprescribing in older adults with diabetes (93,128)

Patient characteristics/ health status	Reasonable A1C/ treatment goal	Rationale/considerations	When may regimen simplification be required?	When may treatment deintensification/ deprescribing be required?
Very complex/poor health (LTC or end-stage chronic illnesses or moderate-to-severe cognitive impairment or two or more ADL impairments)	Avoid reliance on A1C and avoid hypoglycemia and symptomatic hyperglycemia	• No benefits of tight glycemic control in this population • Hypoglycemia should be avoided • Most important outcomes are maintenance of cognitive and functional status	• If on an insulin regimen and the patient would like to decrease the number of injections and fingerstick blood glucose monitoring events each day • If the patient has an inconsistent eating pattern	• If on noninsulin agents with a high hypoglycemia risk in the context of cognitive dysfunction, depression, anorexia, or inconsistent eating pattern • If taking any medications without clear benefits
At the end of life	Avoid hypoglycemia and symptomatic hyperglycemia	• Goal is to provide comfort and avoid tasks or interventions that cause pain or discomfort • Caregivers are important in providing medical care and maintaining quality of life	• If there is pain or discomfort caused by treatment (e.g., injections or finger sticks) • If there is excessive caregiver stress due to treatment complexity	• If taking any medications without clear benefits in improving symptoms and/or comfort

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Continuous Glucose Monitoring

Also known as a CGM, is a medical device that measures blood glucose levels automatically without a manual blood sample.

Benefits:

- Less finger sticks for the patient
- Better monitoring of diabetes control
- Avoid hypoglycemic emergencies by following trends or responding to alarms

Cost:

- Covered through Medicare Part B/Durable Medical Equipment for patients with a diagnosis of diabetes and on insulin – 20% cost share
- Potentially extended coverage for members of Medicare Advantage plans – cost may vary per plan, potentially as low as $0

CGM concerns

- Lag time can lead to “over-bolusing” or skipping basal insulin
- Dexterity issues may impact sensor application
- Sensor falls off early or must be removed before imaging
- Skin irritation due to adhesives
- Alarm fatigue

Table 7.4—Continuous glucose monitoring devices interfering substances

Medication	Systems affected	Effect
Acetaminophen		
>4 g/day	Dexcom G6	Higher sensor readings than actual glucose
Any dose	Medtronic Guardian	Higher sensor readings than actual glucose
Alcohol	Medtronic Guardian	Sensor readings may be higher than actual glucose
Ascorbic acid (vitamin C), >500 mg/day	FreeStyle Libre	Higher sensor readings than actual glucose
Hydroxyurea	Dexcom G6, Medtronic Guardian	Higher sensor readings than actual glucose
Mannitol	Senseonics Eversense	Sensor bias within therapeutic concentration ranges
Tetracycline	Senseonics Eversense	Sensor bias within therapeutic concentration ranges

Diabetes Care 2023; 46 (supplement 1):S117

Patient Case

- Initial assessment in June 2023
  - 83 yo AA Female
  - Morbidly obese (weight 290 lb), lives with daughter, has trouble ambulating uses walker and wheelchair
  - Initial DM regimen: Lantus 30u QD, Humalog 15u TID with meals
  - Has taken Metformin in past but experienced nausea and diarrhea
  - Denies smoking or drinking
  - DM testing: noncompliant to traditional BG monitors
  - Labs (from April 2023):
    - A1c – 9.6%
    - eGFR – 60 mg/mmol

Post Intervention

- Applied for PAP – Tresiba, Novolog, Ozempic
- Prescribed CGM – Freestyle Libre 2 reader and sensors
- Patient was started on sample of Ozempic 0.25/0.5mg QW
- In a matter of weeks, Humalog was discontinued
- Ozempic was gradually increased to 1mg QW, then 2mg QW
- Started Jardiance 25mg daily and eventually Lantus was discontinued
- Final DM regimen: Jardiance 25mg QD, Ozempic 2mg QW

Outcome

- Reduced 4 injections/day to 1 injection/wk
- Lost over 30 lbs, current weight 258 lbs
- A1c – 7.2% in Sept

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Questions?