How to Use the American Diabetes Association's Type 2 Diabetes Algorithm

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Disclosures of Interest

None

Key points to emphasize

New information -- Updated October 5, 2018 at EASD meeting in Berlin

1. Update informed by evidence generated in the past 2 years
2. Greater focus on lifestyle interventions, with increased emphasis on weight loss and obesity management, including metabolic surgery
3. Greater focus on patient related issues and self-management which have a major impact on success of any pharmacological interventions
4. Preferred choices of glucose-lowering agents driven by new evidence from CVOT and consideration of areas of major clinical need (for example weight and risk of hypoglycemia)
5. GLP-1 RAs are preferred to insulin as first injectable

Balancing Risks and Benefits for Personalized Goals

More Stringent Control

- No hypoglycemia
- Less complexity/polypharmacy
- Lifestyle or metformin only
- Short disease duration
- Long life expectancy
- No CVD

Less Stringent Control

- History of severe hypoglycemia
- High burden of therapy
- Longer disease duration
- Limited life expectancy
- Extensive co-morbidity
- CVD

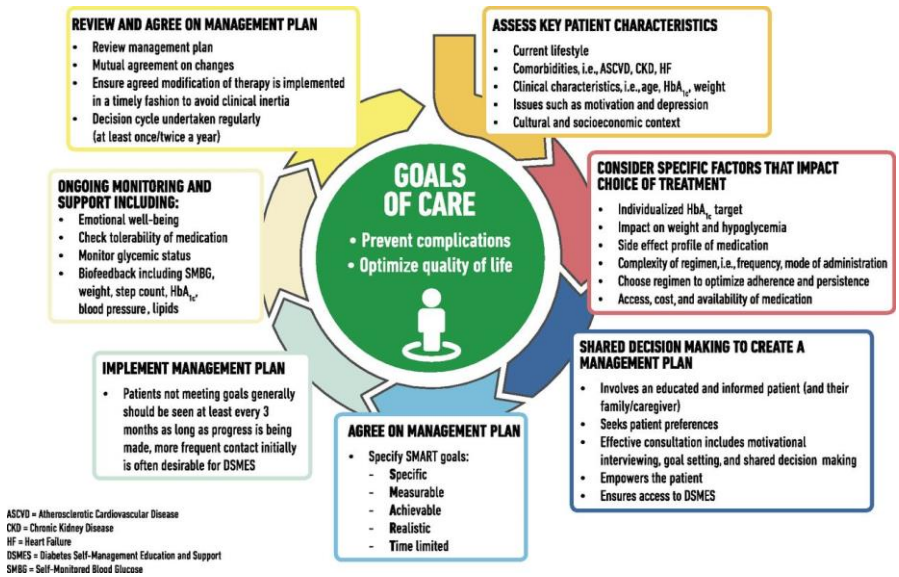
Improving Glycemic Management

- Focus on treatments for glycemic control
  - Behavioral approaches
  - Medications
  - Metabolic surgery

- Addresses increasing complexity of patient centered therapeutic decisions in the context of expanding therapeutic options and new information on benefits and risks

Putting the Patient at the Center of Care

Decision cycle for patient-centered glycemic management in type 2 diabetes.



American Diabetes Association.

American Diabetes Association. 4. Comprehensive medical evaluation and assessment of comorbidities: Standards of Medical Care in Diabetes 2019. Diabetes Care 2019;42(Suppl. 1):S34–S45

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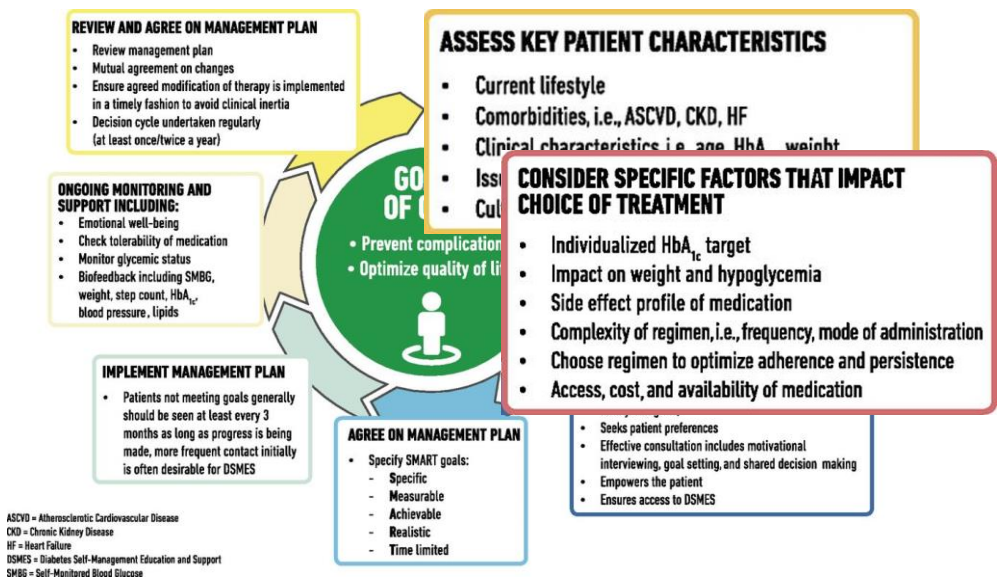

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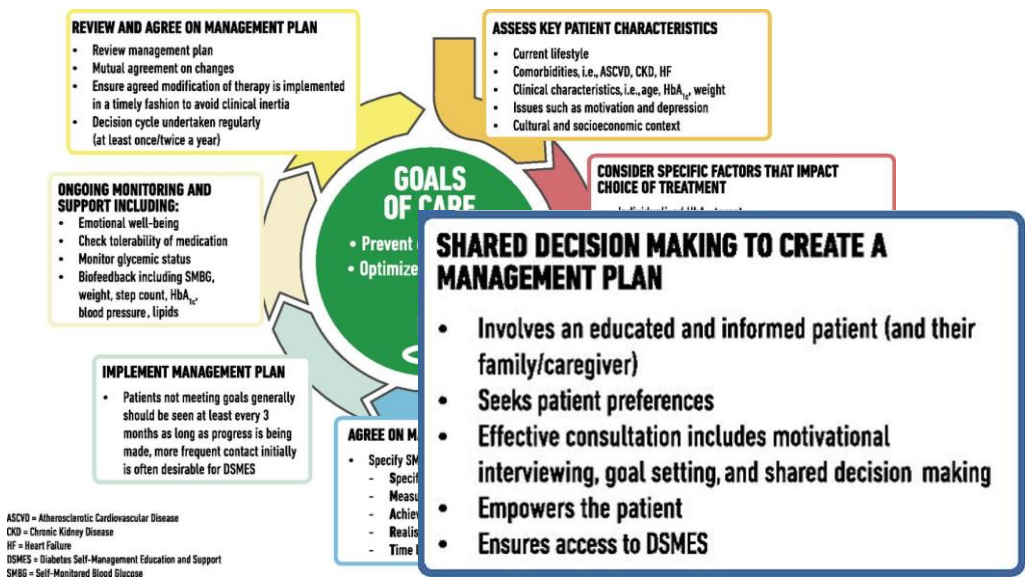
Empathic patient-centered care

- Patients with diabetes often live with multiple chronic conditions
- Providers & health care systems should prioritize the delivery of empathic, individualized patient-centered care
- To determine what is the best management option for each patient, consider each individual's
  - personal, social and biomedical context,
  - his/her values,
  - reasons he/she values the available options, and
  - relative contribution of each option in terms of benefits, harms, costs and inconveniences.

Decision cycle for patient-centered glycemic management in type 2 diabetes.



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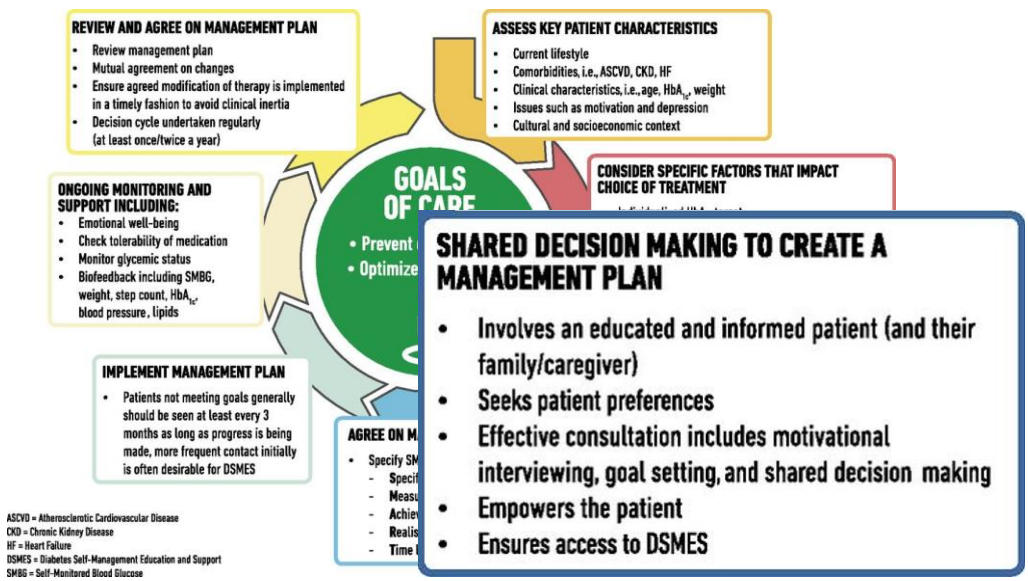
Shared decision making in type 2 diabetes

SDM can improve

- decision quality
- patient knowledge
- patient risk perception

Ethical imperative for support of patients' autonomy

Decision cycle for patient-centered glycemic management in type 2 diabetes.



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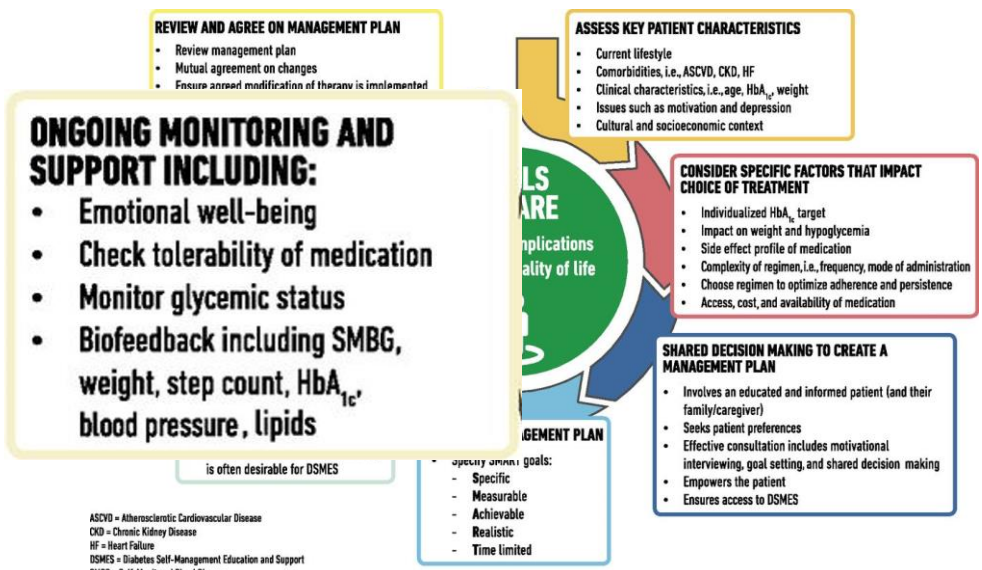
Diabetes Self-Management Education and Support (DSMES)

- Is available to patients at critical times
- Individualized to the needs of the person, including language and culture
- Structured theory-driven written curriculum with supporting materials
- Delivered in group or individual settings by trained educators
- Promote healthy eating, physical activity, good medication-taking behavior, and increase self-efficacy
- Supports person and their family in developing attitudes, beliefs, knowledge and skills to self-manage diabetes
- Includes core content and monitoring of patient progress, including health status, quality of life.
- Evidence-based

Decision cycle for patient-centered glycemic management in type 2 diabetes.



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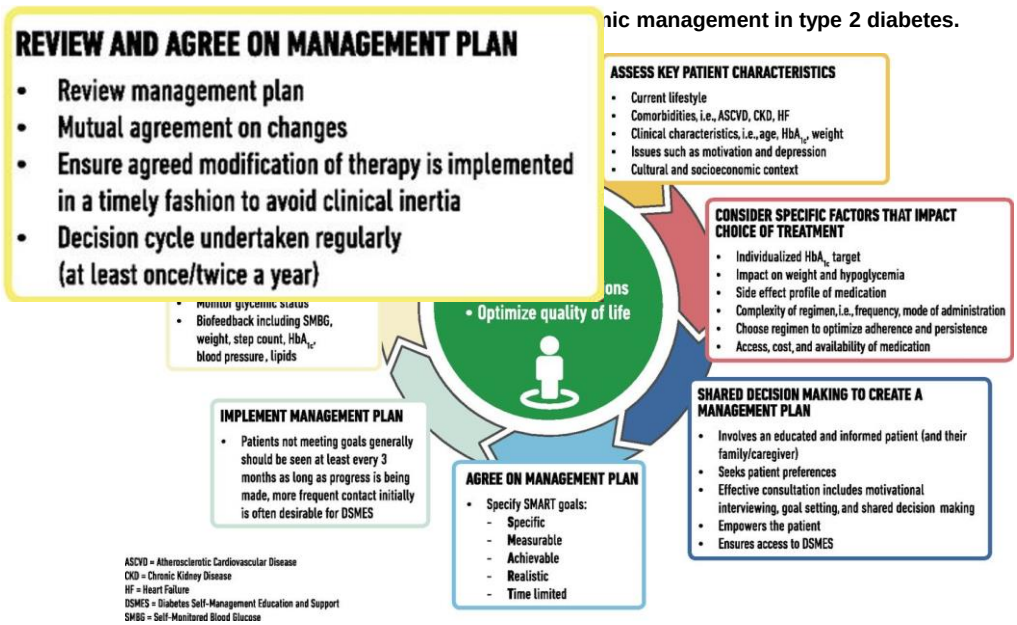
Persistence and medication adherence

- Mean medication adherence rate ≈ 75%, average proportion of patients adherent to medication < 70%.
- Adherence slightly varies between orals vs injectable therapy and individual classes
- Discontinuation rates range from 10% to 60% (both in observational studies and in clinical trials)

nic management in type 2 diabetes.



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Clinical Inertia

Clinical inertia: failure of healthcare providers to initiate or intensify therapy when indicated, due to:

- overestimation of care provided
- use of “soft” reasons to avoid intensification of therapy
- lack of education, training, and practice organization aimed at achieving therapeutic goals

Glucose-Lowering Medication in Type 2 diabetes: overall approach

Foundational therapy is metformin and comprehensive lifestyle management (including weight management and physical activity)

Metformin is the preferred initial glucose lowering medication for most people with T2D

This recommendation is based on the efficacy, safety, tolerability, and extensive clinical experience with this medication. Results from UKPDS showed benefits of initial treatment with metformin in clinical outcomes related to diabetes, with less hypoglycemia and weight gain than with insulin or sulfonylureas.

Foundational therapy is metformin and comprehensive lifestyle management (including weight management and physical activity)

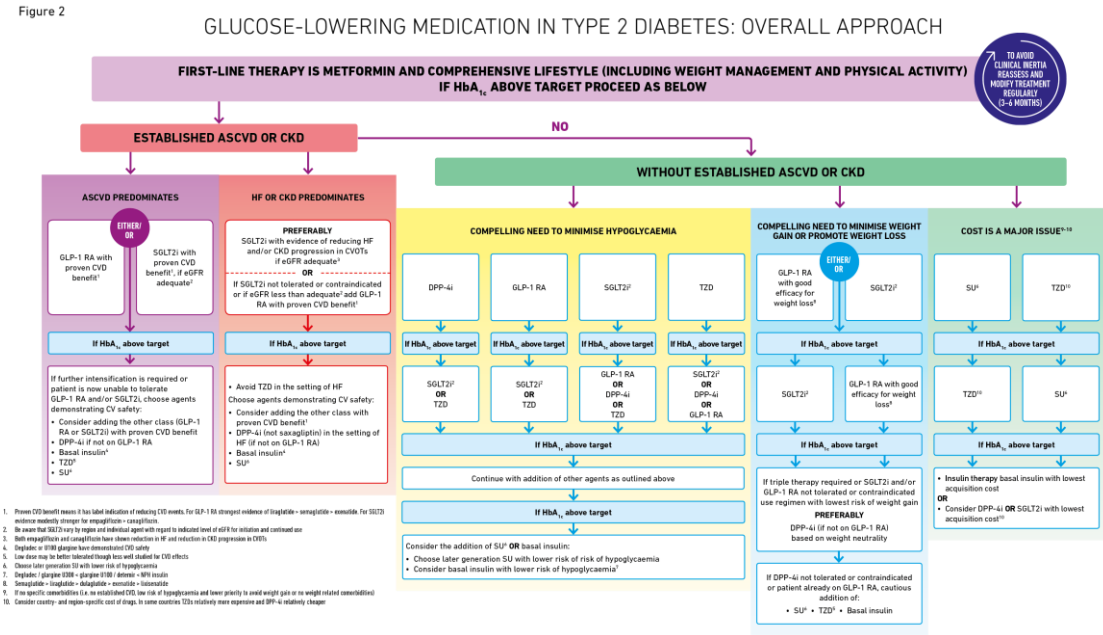
Recommendation:

The stepwise addition of glucose lowering medication is generally preferred to initial combination therapy.

While there is some support for initial combination therapy due to the greater initial reduction of A1C than metformin alone, there is little evidence that this approach is superior to sequential addition of medications for maintaining glycemic control, or slowing the progression of diabetes.

Since the absolute efficacy of most oral medications rarely exceeds 1% reduction in A1C, initial combination therapy should be considered in patients presenting with A1C levels more than 1.5% above their target. Fixed-dose formulations can improve medication-taking behavior when combination therapy is used and may achieve glycemic targets more rapidly.

Figure 2



1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence of liraglutide > semaglutide > exenatide. 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 hypoglycaemia
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 hypoglycaemia and lower priority to avoid weight gain or no weight related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries T2Rs relatively more expensive and DPP-4i relatively cheaper

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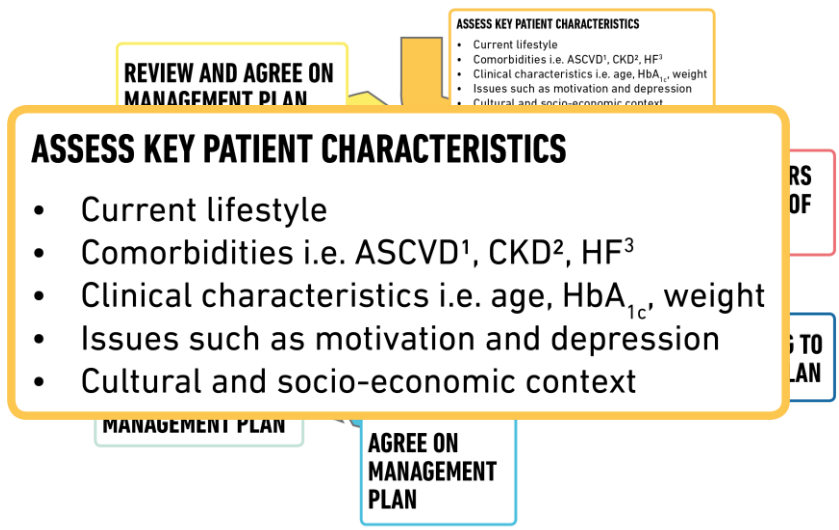
Case 1

- **Patient:** Ms. M
- **Age:** 61
- **Occupation:** Special Needs teacher in Bessemer and grandmother of 2
- **Diabetes Hx:** diagnosed in 2006; no complications; struggles with weight, erratic schedule
- **Current Meds:** metformin and sitagliptin
- **A1C:** 10.4%, anti-GAD negative, eGFR >60 ml/min/1.73m
- **BG pattern:** checks occasionally with range 80 - 201, no hypoglycemia
- **Patient/Provider Goals:** avoid complications, facilitate weight loss, dosing simplicity

Figure 1

DECISION CYCLE FOR PATIENT-CENTRED GLYCAEMIC MANAGEMENT IN TYPE 2 DIABETES



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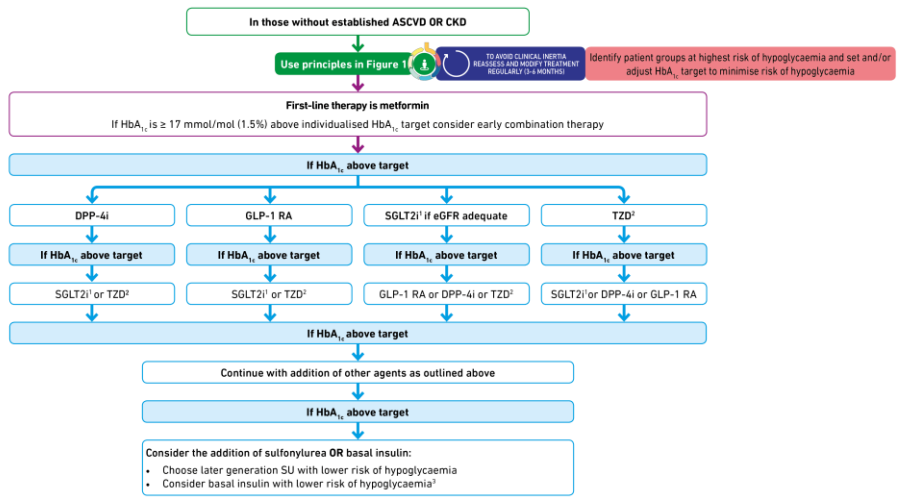
Foundational therapy is metformin and comprehensive lifestyle management (including weight management and physical activity)

CHOOSING GLUCOSE-LOWERING MEDICATION IF COMPELLING NEED TO MINIMISE HYPOGLYCAEMIA



1. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
2. Low dose TZDs are better tolerated
3. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin

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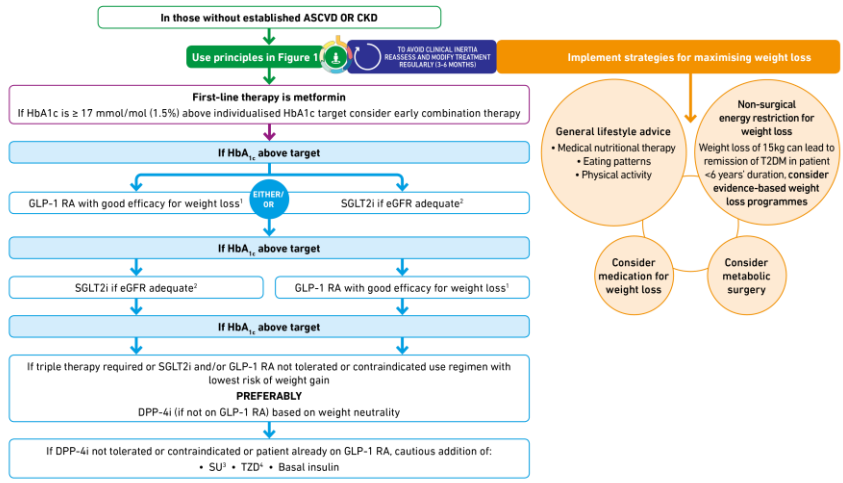
CHOOSING GLUCOSE-LOWERING MEDICATION IF COMPELLING NEED TO MINIMISE WEIGHT GAIN OR PROMOTE WEIGHT LOSS



1. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Choose later generation SU with lower risk of hypoglycaemia
4. Low dose may be better tolerated though less well studied for CVD effects

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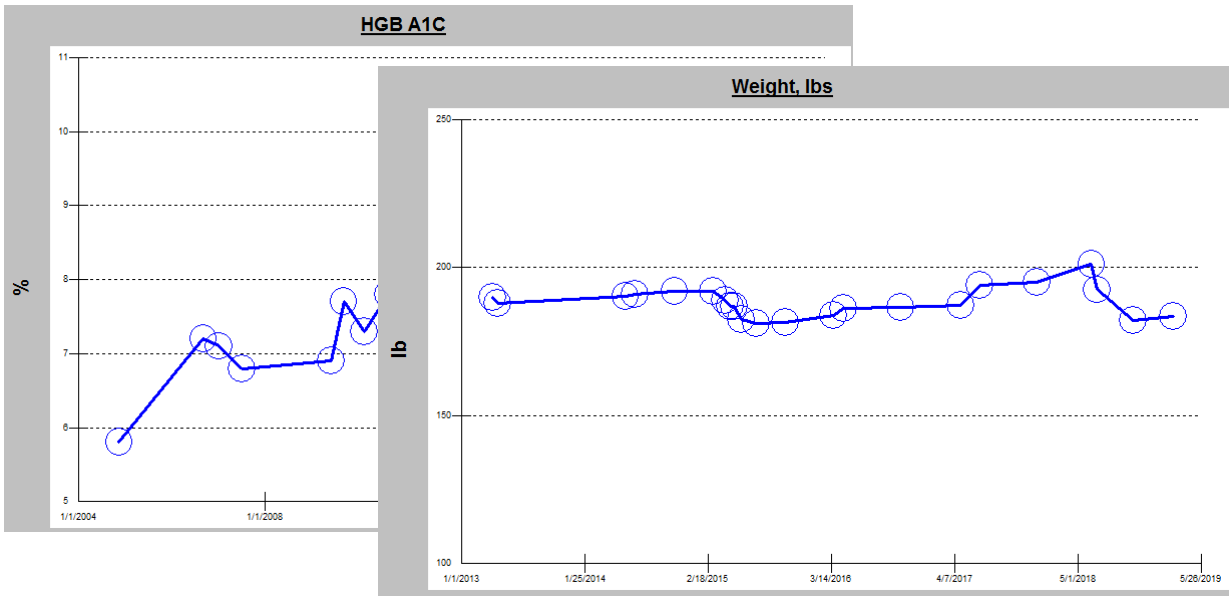

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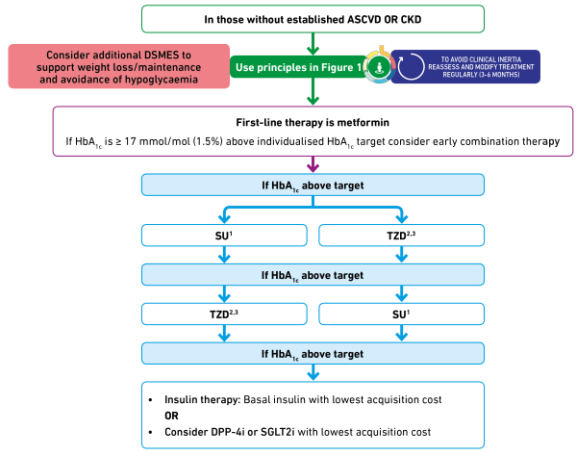
CHOOSING GLUCOSE-LOWERING MEDICATION IF COST IS A MAJOR ISSUE



1. Choose later-generation SU to minimise risk of hypoglycaemia
2. Consider country- and region-specific cost of drugs. In some countries, TZD relatively more expensive and DPP-4i relatively cheaper
3. Low-dose TZDs are better tolerated

Case 2

- **Patient:** Mr. D
- **Age:** 45
- **Occupation:** disabled due to heart disease
- **Diabetes Hx:** since 2005, no retinopathy, no nephropathy, no neuropathy sx; intolerant of metformin
- **Cardiovascular History:** complex CAD, ischemic cardiomyopathy, ~4 admissions per year for angina
- **Current Diabetes Meds:** Levemir BID and Novolog with meals
- **A1C:** 10.8%
- **Glucoses:** no home glucose logs; fear of hypoglycemia
- **Patient/Provider Goals:** avoidance of heart disease progression / same + weight loss

Step 1: Assess cardiovascular disease

Presence of cardiovascular disease is compelling indication

ASCVD predominates 

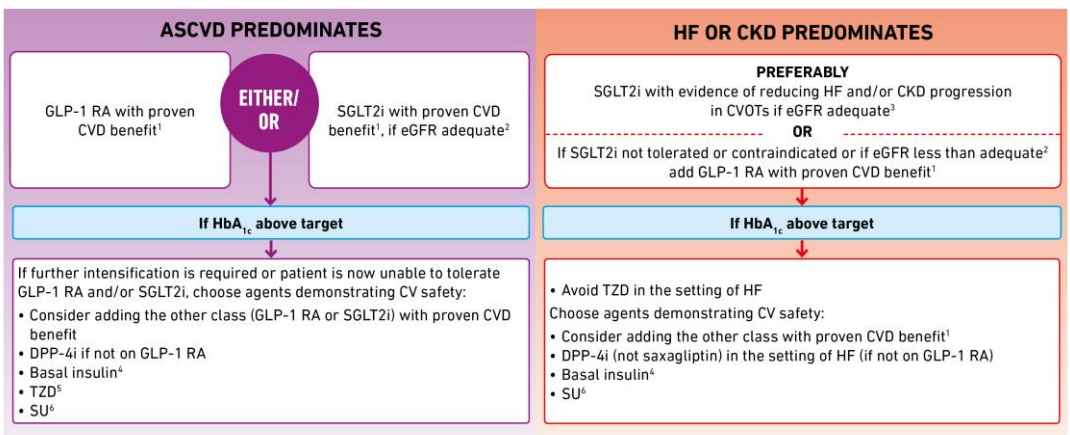
 HF or CKD predominates

Considerations

- ASCVD is defined differently across trials
  - Established CVD (e.g. MI, stroke, revascularization procedure)
  - Very high cardiovascular risk
- Each cardiovascular outcomes trial, while large, is a single experiment
- It is not always clear whether differences in trial findings within a drug class are related to trial design or to true differences in the individual medications
  - Where evidence suggests a hierarchy, this is noted

Recommended Process for Glucose Lowering Medication Selection: Where Does New Evidence From Cardiovascular Outcome Trials Fit In ?

CHOOSING GLUCOSE-LOWERING MEDICATION IN THOSE WITH ESTABLISHED ASCVD OR CKD



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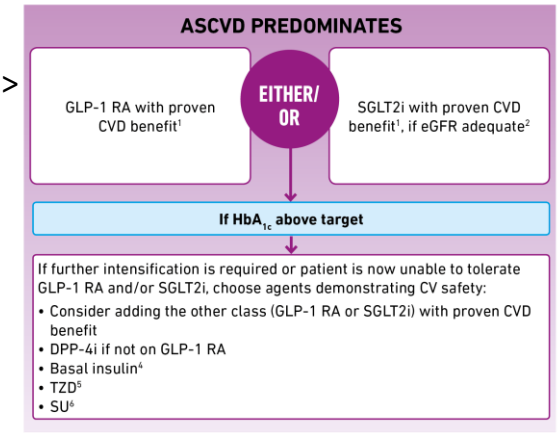
If ASCVD Predominates:

GLP-1 RA *with proven cardiovascular benefit*

- Strongest evidence for liraglutide > semaglutide > exenatide LAR

SGLT2-i *with proven cardiovascular benefit*

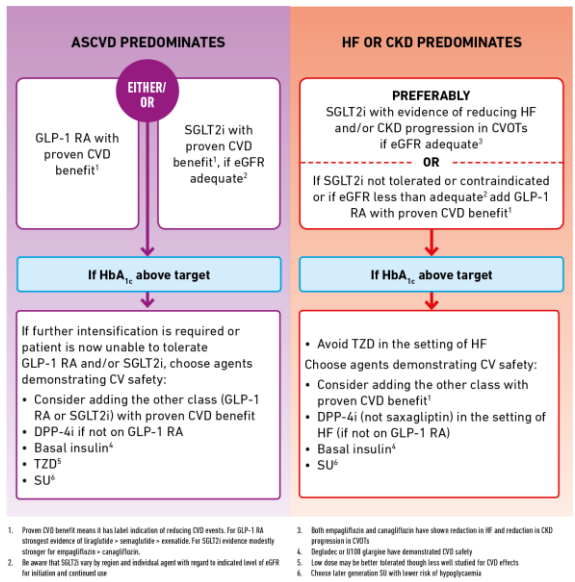
- Modest evidence for empagliflozin > canagliflozin

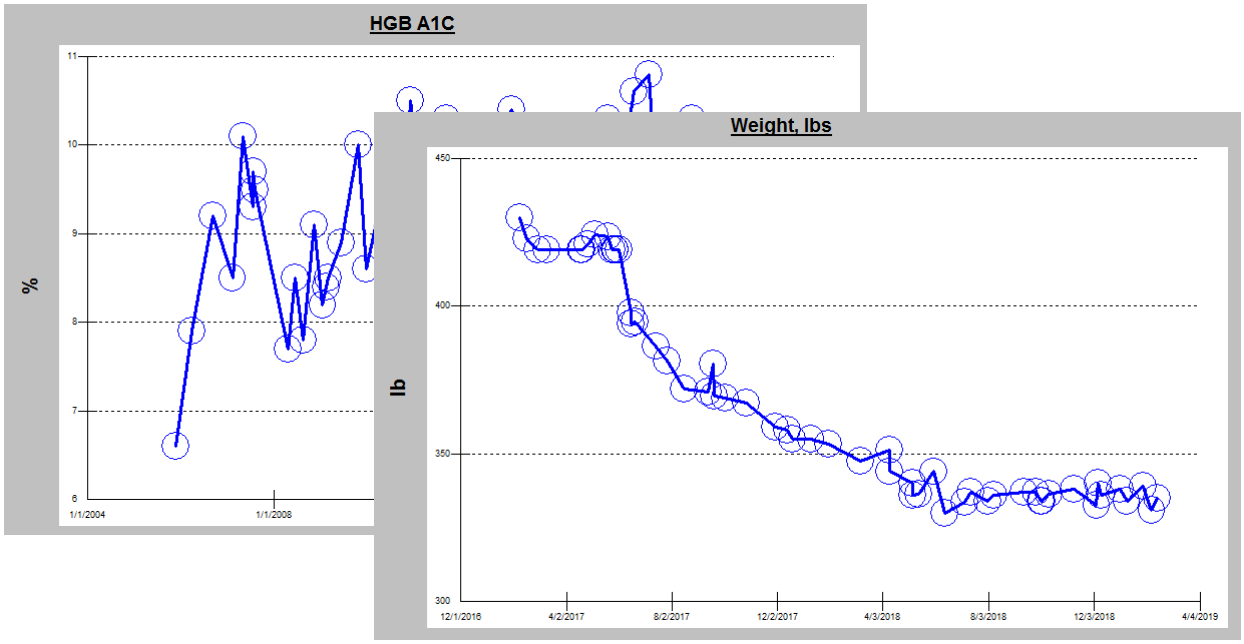


Caveats and Questions

No evidence of CVD benefit in those at lower cardiovascular risk

The combination of SGLT2-i and GLP-1 RA has not been tested in cardiovascular outcome trials





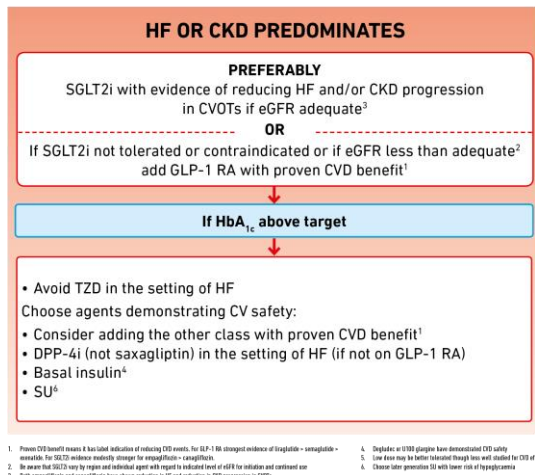
Case 3

- **Patient:** Ms. E
- **Age:** 71
- **Occupation:** Retired
- **Diabetes Hx:** 2012
- **Cardiovascular History:** CVA 1999; CAD with CABG 1993
- **Renal History:** CKD stage 3; GFR 30-40
- **Current Diabetes Meds:** NPH BID, Regular Insulin TIDWM, pioglitazone 30 mg daily
- **Cardiovascular Meds:** atorvastatin, ASA, ACE-i and ARB, ISDN, HCTZ, Lasix, b-bl, plavix
- **BG pattern:** not checking often, no known hypoglycemia but gets “weak” mid-day if she does not eat
- **Patient/Provider Goals:** Overwhelmed, too many problems, cannot do usual ADLs

Step 1: Assess cardiovascular disease

Presence of cardiovascular disease is compelling indication

CHOOSING GLUCOSE-LOWERING MEDICATION IN THOSE WITH ESTABLISHED HF OR CKD



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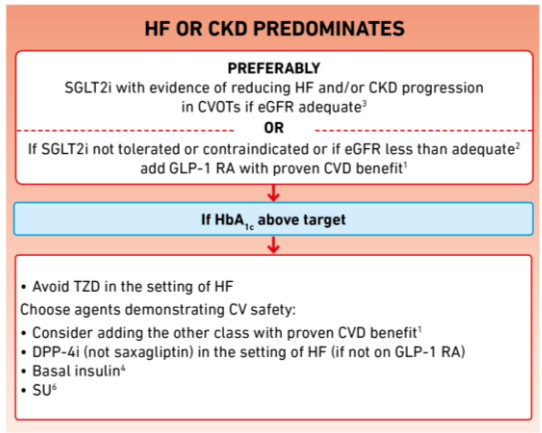
Among patients with ASCVD in whom HF coexists or is of concern, SGLT2 inhibitor are recommended

Rationale: Patients with T2D are at increased risk for heart failure with reduced or preserved ejection fraction

Significant, consistent reductions in hospitalization for heart failure have been seen in SGLT2-i trials

Caveat: trials were not designed to adjudicate heart failure

Majority of patients did not have clinical heart failure at baseline



Recommendation:

For patients with type 2 diabetes and chronic kidney disease, consider use of a sodium–glucose cotransporter 2 inhibitor or glucagon-like peptide 1 receptor agonist shown to reduce risk of chronic kidney disease progression, cardiovascular events, or both. **C**

Several of these medications have demonstrated renal benefit and cardiovascular benefit and should be considered as part of treatment.

American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes 2019. Diabetes Care 2019;42(Suppl. 1):S90–S102

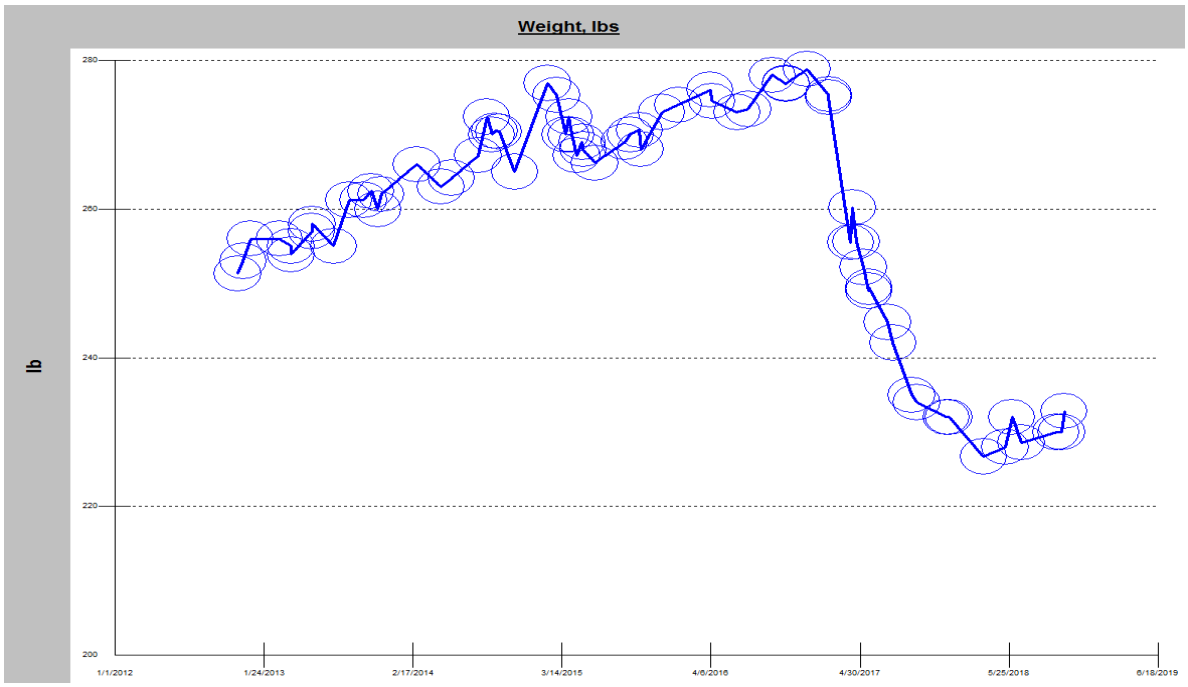
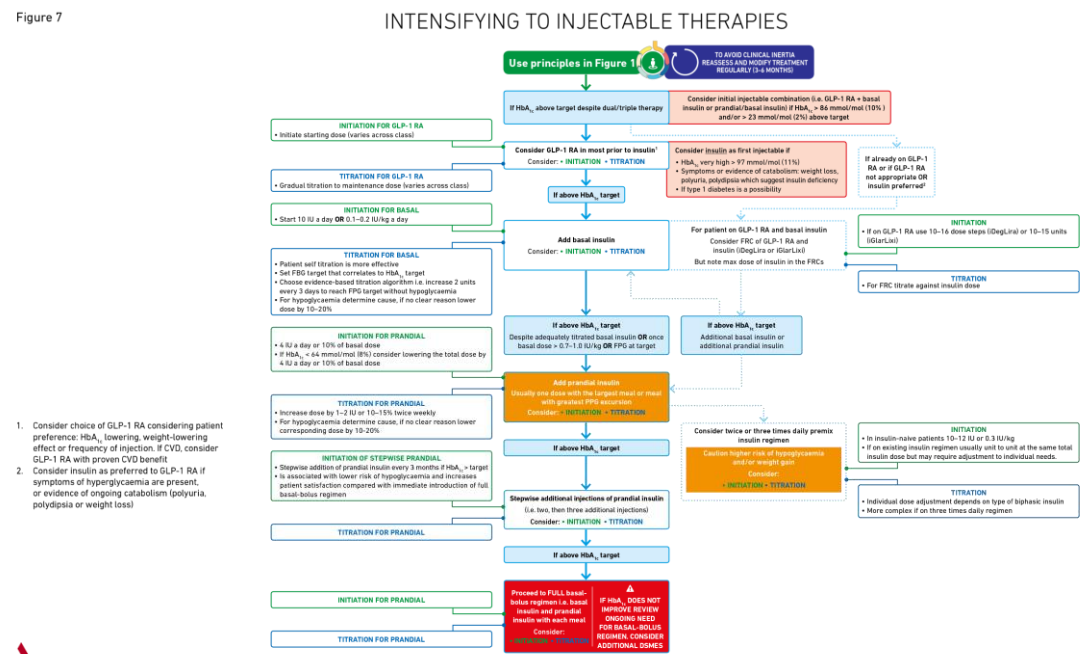


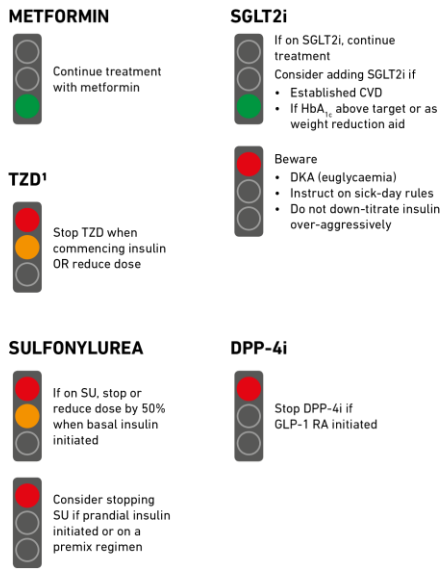
Figure 7



1. Consider choice of GLP-1 RA considering patient preference: HbA_{1c} lowering, weight-lowering effect or frequency of injection. If CVD, consider GLP-1 RA with proven CVD benefit
2. Consider insulin as preferred to GLP-1 RA if symptoms of hyperglycaemia are present, or evidence of ongoing catabolism (polyuria, polydipsia or weight loss)

Figure 8

CONSIDERING ORAL THERAPY IN COMBINATION WITH INJECTABLE THERAPIES



1. Contraindicated in some countries, consider lower dose. This combination has a high risk of fluid retention and weight gain

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Recommendations

In most patients who need the greater glucose-lowering effect of an injectable medication, glucagon-like peptide 1 receptor agonists are preferred to insulin. **B**

Intensification of treatment for patients with type 2 diabetes not meeting treatment goals should not be delayed. **B**

The medication regimen should be reevaluated at regular intervals (every 3–6 months) and adjusted as needed to incorporate new patient factors. **E**

American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes 2019. Diabetes Care 2019;42(Suppl. 1):S90–S102

Conclusions

An important early step in this new approach: consider the presence or absence of ASCVD, CKD, and heart failure.

In patients with ASCVD, some GLP-1 RA and SGLT2-i are recommended in these patients.

Conclusions

Among patients with atherosclerotic cardiovascular disease at high risk of heart failure or in whom heart failure coexists, sodium–glucose cotransporter 2 inhibitors are preferred.

For patients with type 2 diabetes and chronic kidney disease, consider use of a sodium–glucose cotransporter 2 inhibitor or glucagon-like peptide 1 receptor agonist shown to reduce risk of chronic kidney disease progression, cardiovascular events, or both.

- Studies of HF or CKD as primary outcome are ongoing with SGLT2-i.

Summary

Consider the presence or absence of ASCVD, CKD and HF

Start with metformin if tolerated, then:

In patients with ASCVD a GLP-1 RA or SGLT2-i is recommended

In patients with HF SGLT2-i is recommended

In patients with CKD, with or without ASCVD consider an SGLT2-i

Agents with proven benefit are preferred

ASCVD, CKD and HF affects choice of additional glucose lowering medication

Thank you

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