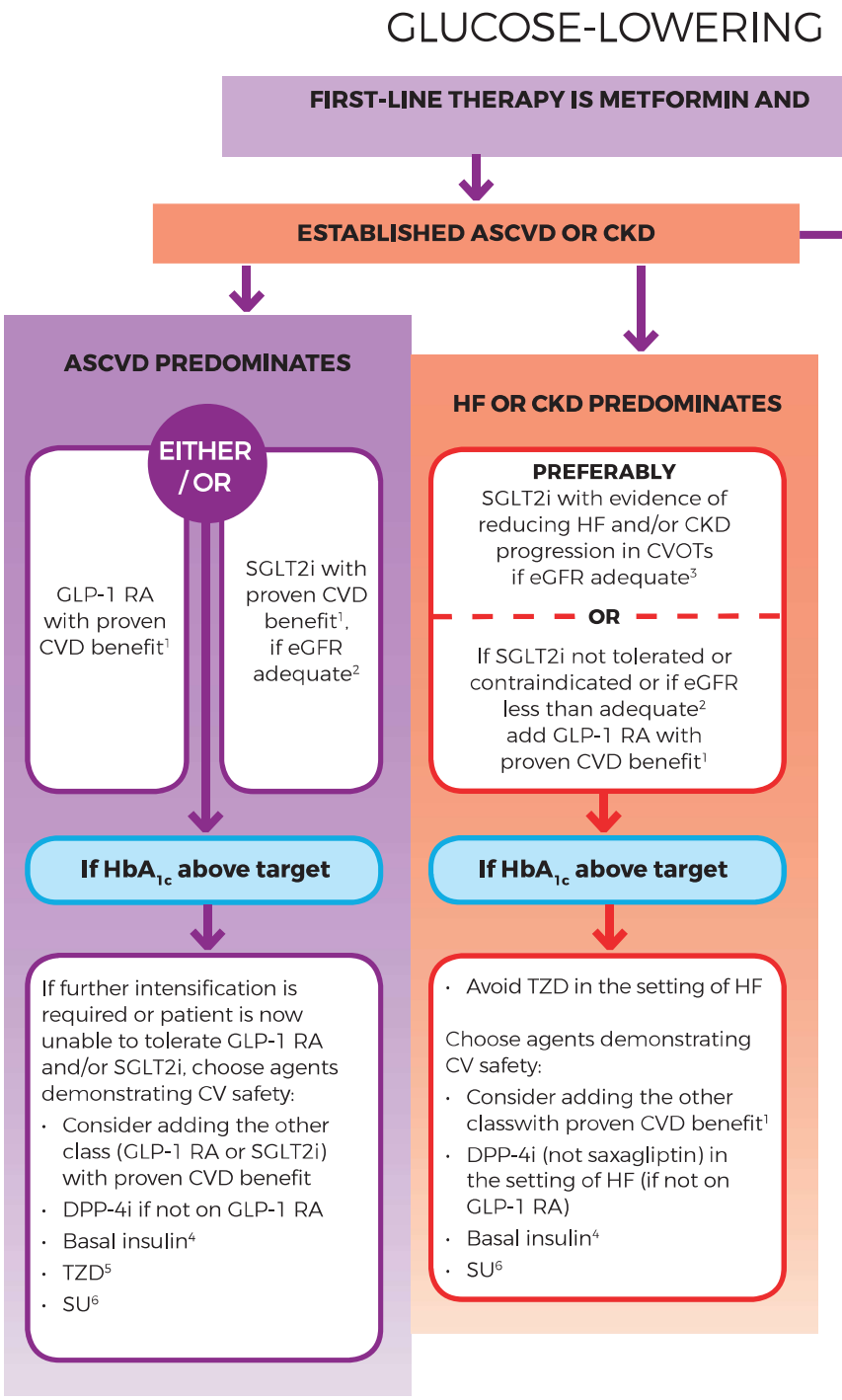
GLUCOSE-LOWERING MEDICATION: **DECISION FLOW CHART**

Dr Justin Coleman reviewed the ADA/EASD 2018 consensus report on management of hyperglycaemia in T2D and found a useful tool to assist in the increasingly complex decision making process for the selection of glucose-lowering medication.

In the preceding article *Living Evidence* (p14-16), the Living Evidence for Diabetes Consortium predict the Australian living evidence for the therapeutic control of blood glucose in adults with T2D will be launched by the end of March 2020.

In the meantime DMJ has been granted approval to reproduce the following flow chart from *Management of hyperglycaemia in type 2 diabetes: the 2018 consensus report by the American Diabetes Association (ADA) / European Association for the Study of Diabetes (EASD)*[1].

The report updates position statements from 2012 and 2015. Prof. MJ Davies, co-author of the report, commented that the rapidly evolving evidence base, particularly the cardiovascular outcome trials (CVOTs), required a more structured review of literature. The resulting position statement places greater emphasis on a patient-centred approach to care and lifestyle interventions. The main pharmacological changes resulted from the CVOTs evidence but have also included the new approach of highlighting particular needs such as weight or hypoglycaemia management.[2]



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

MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH

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)

NO

WITHOUT ESTABLISHED ASCVD OR CKD

COMPELLING NEED TO MINIMISE HYPOGLYCAEMIA

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 SU6 OR basal insulin:
- Choose later generation SU with lower risk of hypoglycaemia
- Consider basal insulin with lower risk of hypoglycaemia[7]

COMPELLING NEED TO MINIMISE 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) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:
- SU6 - TZD5 - Basal insulin

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]

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 TZDs relatively more expensive and DPP-4i relatively cheaper.

Reprinted by permission from Springer Nature: Diabetologia, Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Melanie J. Davies, David A. D'Alessio, Judith Fradkin et al. Jan 1, 2018