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

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Disclosures of Interest

None

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al·go·rithm

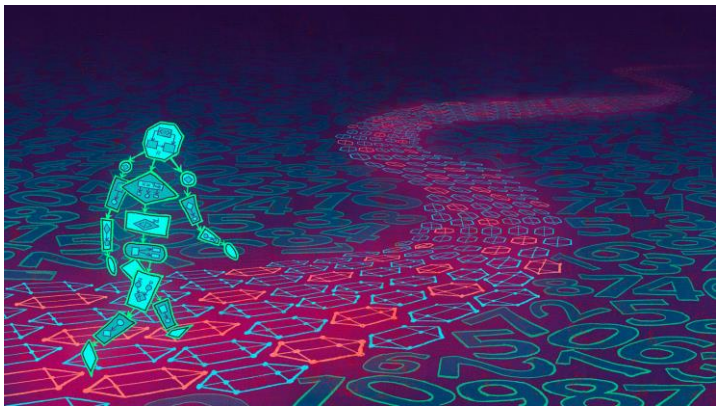
/ˈalgəˌriT͟Həm/

noun

noun: **algorithm**; plural noun: **algorithms**

a process or set of rules to be followed in calculations or other problem-solving operations, especially by a computer.

"a basic **algorithm for** division"



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

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Publications

Diabetologia https://doi.org/10.1007/s00125-018-4729-5

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)

Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Diabetes Care 2018;41:1-33 https//:doi.org/10.2337/dci18-0033

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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

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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

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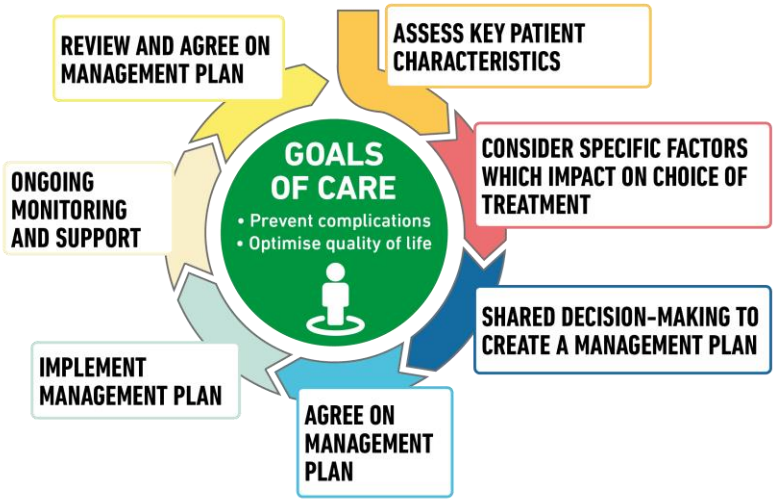
Figure 1 DECISION CYCLE FOR PATIENT-CENTRED GLYCAEMIC MANAGEMENT IN TYPE 2 DIABETES



Shared decision making in type 2 diabetes

SDM can improve

- decision quality
- patient knowledge
- patient risk perception

Ethical imperative for support of patients' autonomy

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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

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.

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Persistence and medication adherence

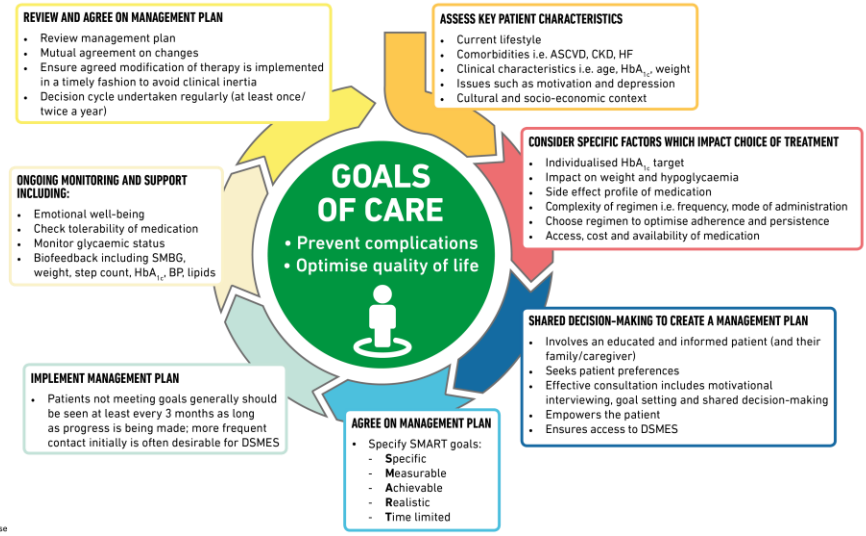
- Mean medication adherence rate ≈ 75%, average proportion of patients adherent to medication < 70%.
- Adherence slightly varies between orals vs injectable therapy and individual classes
- Discontinuation rates range from 10% to 60% (both in observational studies and in clinical trials)

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

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



ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self-Monitored Blood Glucose

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

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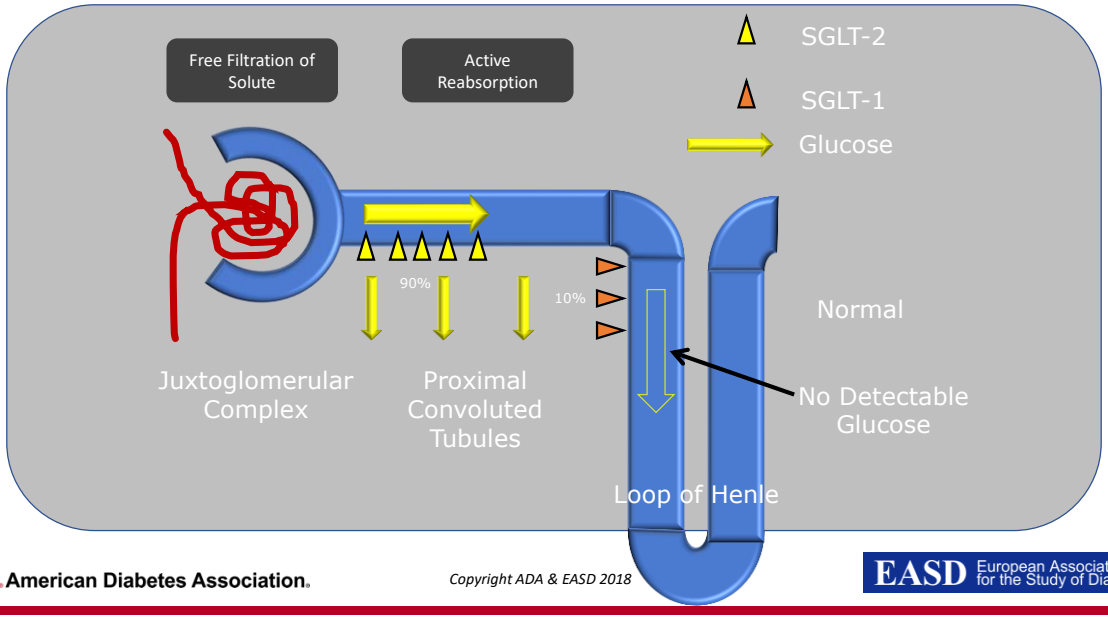
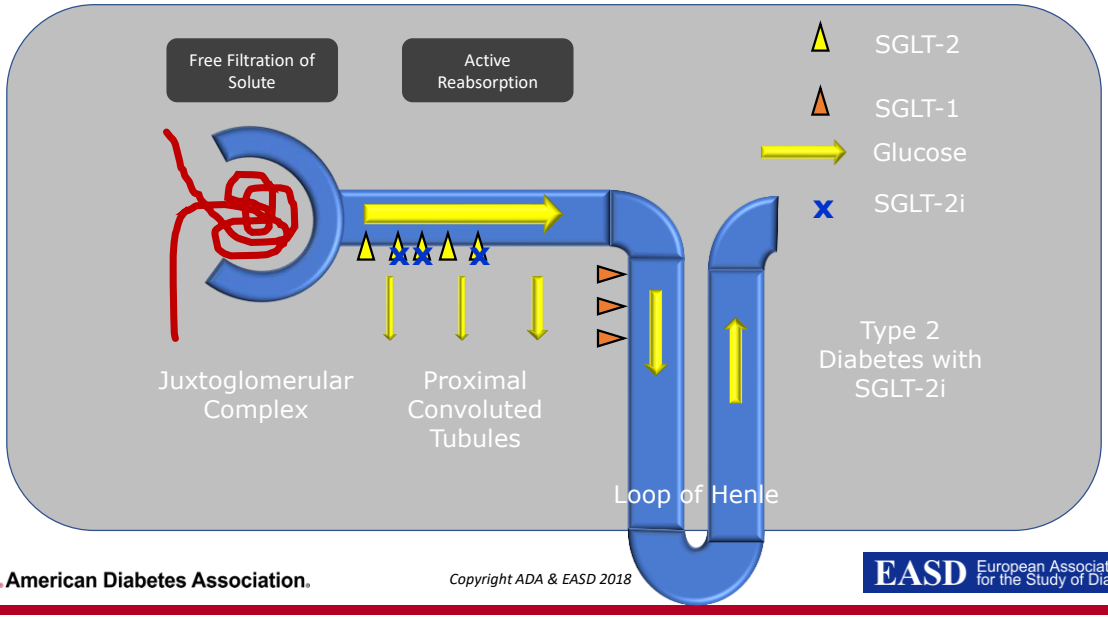
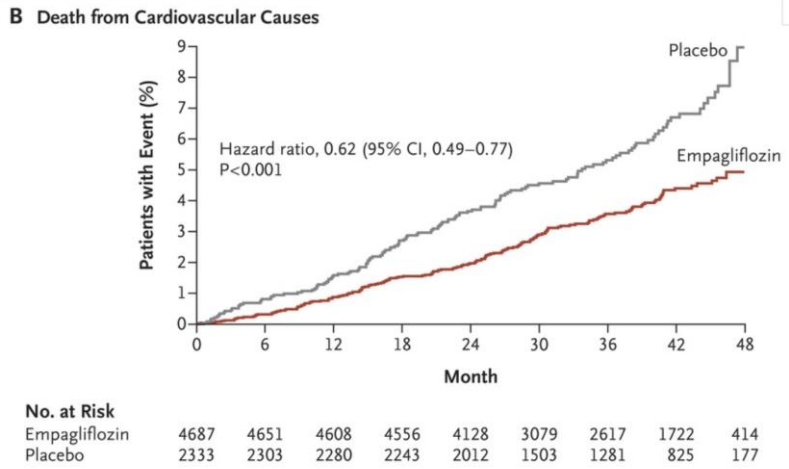
SGLT-2 Inhibitors: Mechanism of Action



SGLT-2 Inhibitors: Mechanism of Action *(cont)*

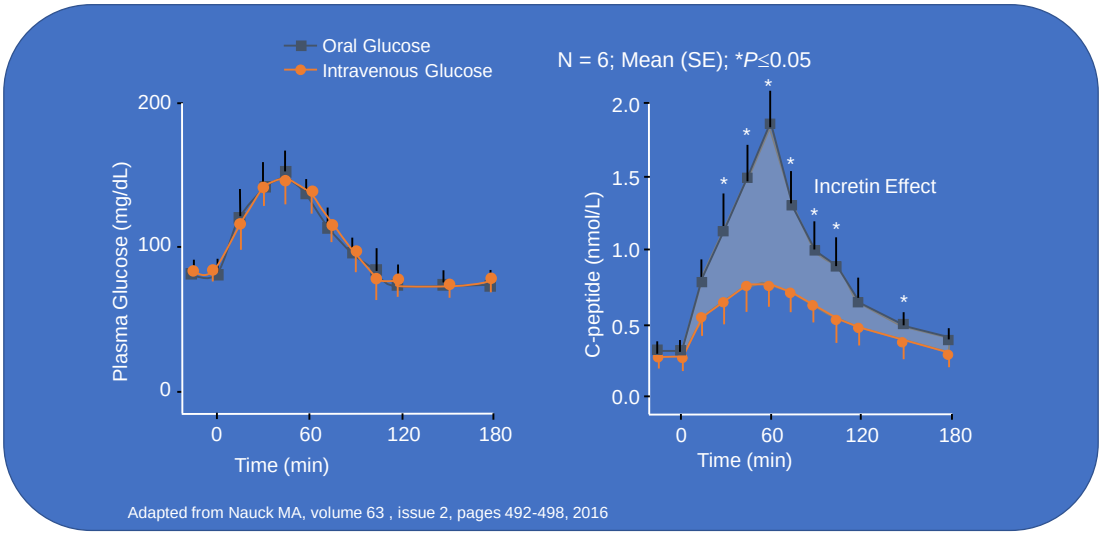


Death from cardiovascular cause: empagliflozin



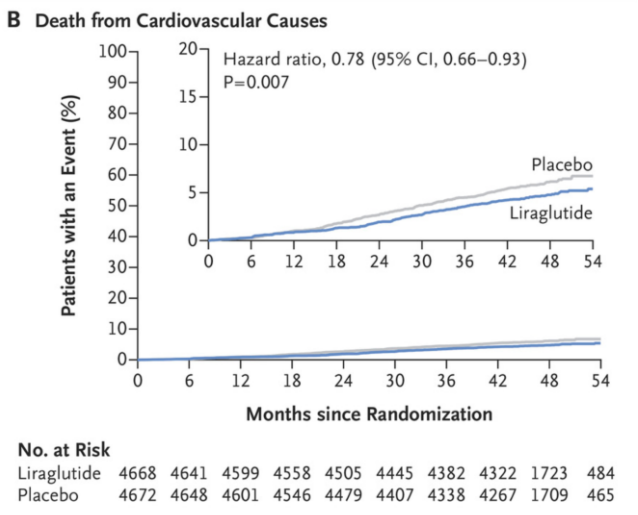
Zinman B et al. N Engl J Med 2015; 373:2117-2128

The Incretin Effect



Adapted from Nauck MA, volume 63 , issue 2, pages 492-498, 2016

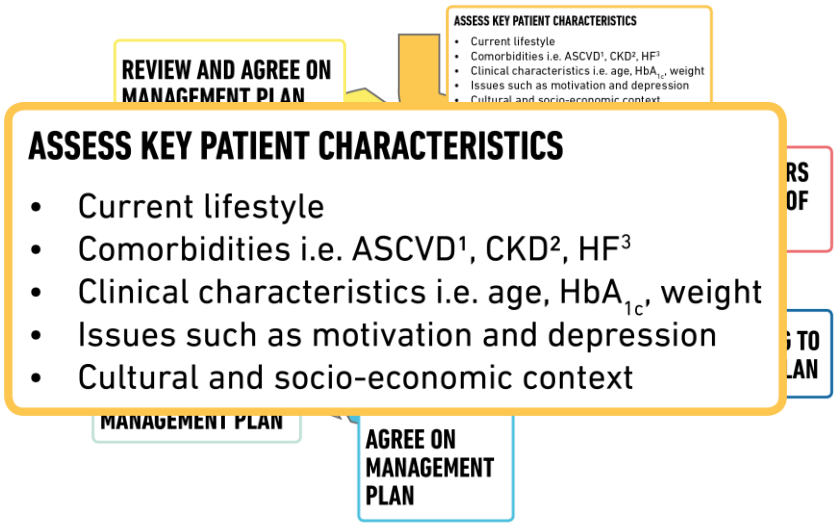
Death from cardiovascular cause: liraglutide



Marso SP et al. N Engl J Med 2016; 375:311-322

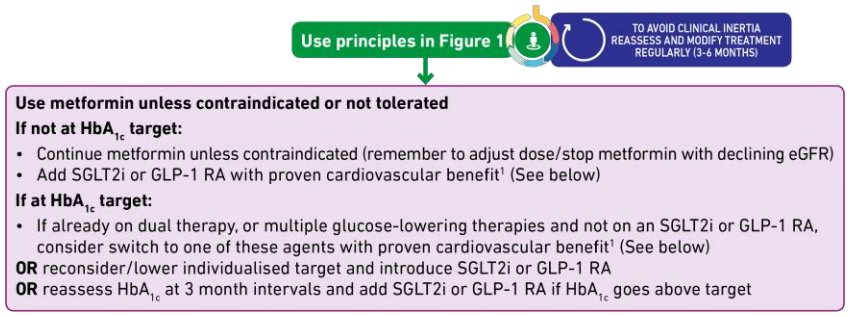
Figure 1

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



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

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



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Step 1: Assess cardiovascular disease

Presence of cardiovascular disease is compelling indication

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

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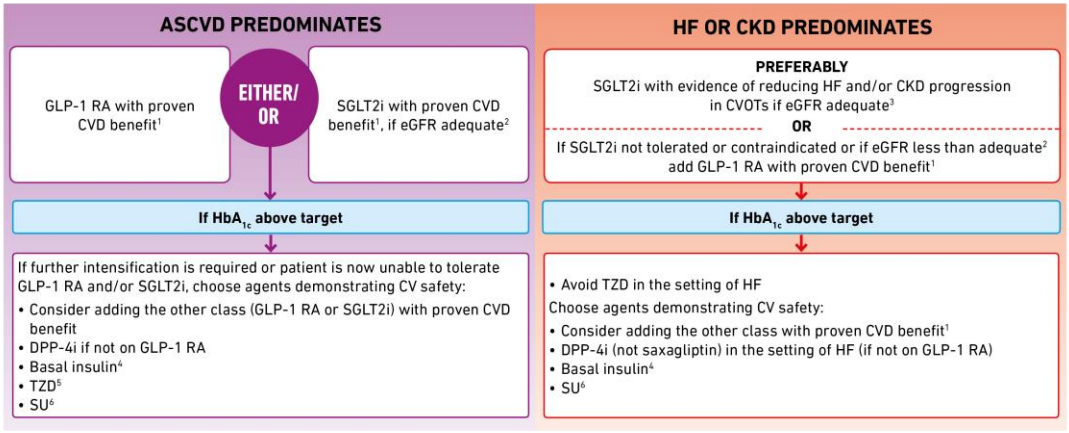
CHOOSING GLUCOSE-LOWERING MEDICATION IN THOSE WITH ESTABLISHED ASCVD OR CKD

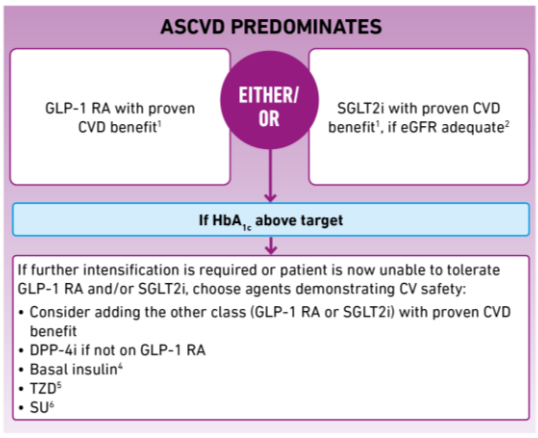


1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence of liraglutide > semaglutide > exenatide. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated 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

If ASCVD Predominates:

GLP-1 RA *with proven cardiovascular benefit*
- liraglutide > semaglutide > exenatide LAR
- recent data for dulaglutide (lower risk population)

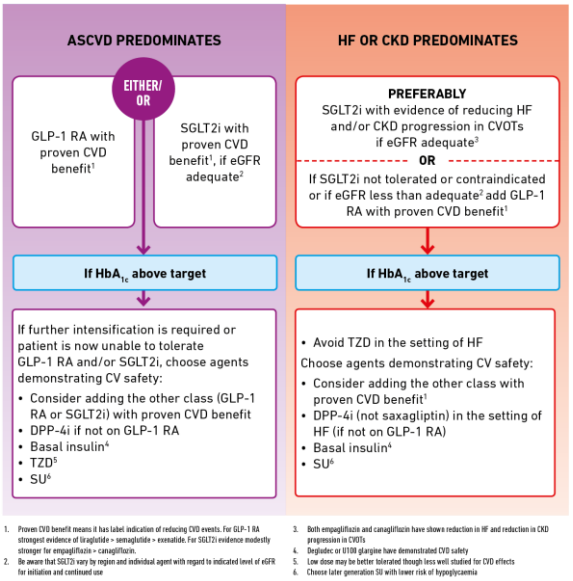
SGLT2-i *with proven cardiovascular benefit*
- empagliflozin > canagliflozin
- recent data for dapagliflozin (lower risk population, heart failure hospitalization benefit)



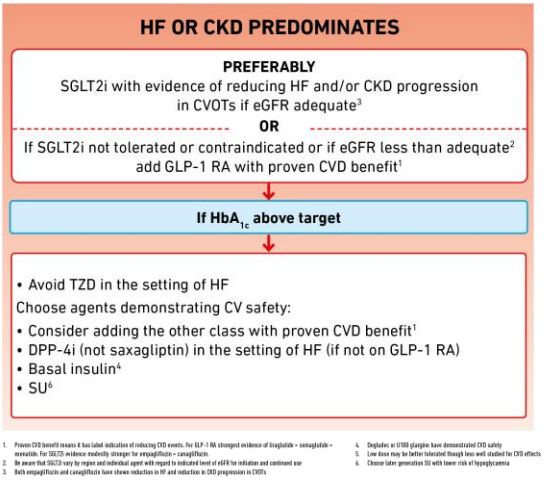
Caveats and Questions

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



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



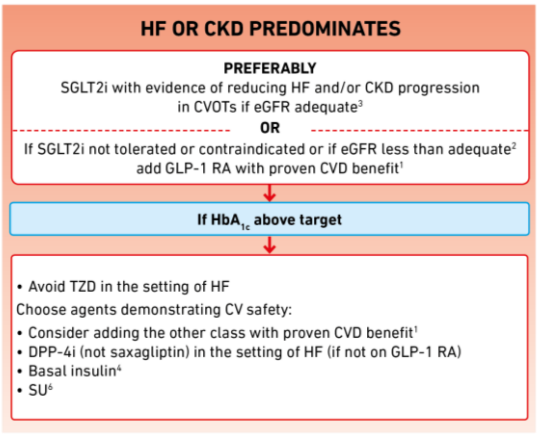
Among patients with ASCVD in whom HF coexists or is of concern, SGLT2 inhibitor are recommended

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 (except recent dapagliflozin study)

Majority of patients did not have clinical heart failure at baseline



Consensus Recommendation:

For patients with type 2 diabetes and CKD, with or without cardiovascular disease, consider the use of an SGLT2-i shown to reduce CKD progression or, if contraindicated or not preferred, a GLP-1 RA shown to reduce CKD progression

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

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CKD Considerations

- For SGLT2-i, adequate eGFR differs between countries and compounds
- SGLT2-i are registered as glucose-lowering agents to be started if eGFR>45-60 ml/min/1.73m^2 and stopped at eGFR 45-60, as glucose-lowering effect declines with eGFR
- SGLT2-i CVOTs included patients with eGFR>30, and there were no excess adverse events in subjects with eGFR<60
- For GLP-1 RA, GI side effects increase with declining renal function
- GLP-1 RA are not recommended in end stage renal disease due to limited experience

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.

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Conclusions

Hospitalization for heart failure

- reduced consistently with SGLT2-i in two trials but was a secondary outcome
- reduced in a third trial as a co-primary end point

For patients with type 2 diabetes and CKD, with or without cardiovascular disease, consider the use of an SGLT2-i shown to reduce CKD progression or, if contraindicated or not preferred, a GLP-1 RA shown to reduce CKD progression

- 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 ASCVD and 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

Age: 62
Occupation: Sales manager
Diabetes Hx: 10 years, mild neuropathy symptoms, normal dilated eye exam 6 months ago
Cardiovascular Hx: M.I. 3 years ago, s/p CABG, EF 43%
Current Diabetes Meds: metformin ER 1000 mg BID, glimepiride 4 mg once daily
Cardiovascular Meds: statin, ARB, beta blocker, diuretic, ASA
A1C: 7.9%, microalbumin/creatinine ratio 156 µg/mg, eGFR 52 ml/min/1.73m^2
BG pattern: fasting average 132 mg/dL, post-meal average 200s mg/dL, hypoglycemia when playing golf
Patient/Provider Goals: avoid further complications, stabilize renal dysfunction, reduce post-meal BGs, dosing simplicity, play golf without hypoglycemia

Mark

Age: 51
Occupation: delivery man
Diabetes Hx: 8 years, microalbumin/creatinine ratio not detected, NPR, active, eats out every day
Cardiovascular History: CVA last year (slurred speech, left-sided weakness) w/ full recovery, stopped smoking
Current Diabetes Meds: metformin 500 mg ER 3 tabs per day, pioglitazone 30 mg daily
Cardiovascular Meds: blood pressure, statin, ASA
A1C: 9.5%, anti-GAD negative, eGFR >60 ml/min/1.73m^2
BG pattern: fasting average 135 mg/dL, post-meal average 221 mg/dL, no hypoglycemia
Patient/Provider Goals: avoid complications, support healthy eating

Jerry

The Full Range Of Therapeutic Options—Lifestyle Management, Medication and Obesity Management

Outline

The Foundation of Hyperglycemic Management

Lifestyle
- Medical Nutrition Therapy
- Physical activity

Medications

Metabolic Surgery

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For Details on Each Medication Please See . . .

Table 2—Glucose-lowering medications and therapies available in the U.S. or Europe and specific characteristics that may guide individualized treatment choices in nonpregnant adults with type 2 diabetes

Class	Medications/therapies in class	Primary physiological action(s)	Advantages	Disadvantages/adverse effects	Efficacy
	• Low carbohydrate • Vegetarian • Others			• Requires lifelong behavioral change • Social barriers may exist	
Physical activity	• Running, walking • Bicycling (including stationary) • Swimming • Resistance training • Yoga • Tai chi • Many others	• Energy expenditure • Weight management • ↑ Insulin sensitivity	• Inexpensive • ↓ Fall risk by increasing balance/strength • ? Improves mental health • ↑ Bone density • ↓ Blood pressure • ↓ Weight • Improves ASCVD risk factors	• Risk of musculoskeletal injury • Requires motivation • Risk of foot trauma in patients with neuropathy • Requires lifelong behavioral change	Intermediate
Energy restriction	• Individual energy restriction with or without energy tracking • Programs with counseling • Food substitution programs	• Energy restriction • Weight management • ↓ Hepatic and pancreatic fat • ↑ Insulin sensitivity	• Lowers glycemia • Reduces need for diabetes and other medications • No serious side effects • Improves ASCVD risk factors	• Requires motivation • Requires lifelong behavioral change	Variable, with potential for very high efficacy; often intermediate
Oral medications					
Biguanides	• Metformin	• ↓ Hepatic glucose production • Multiple other non-insulin-mediated mechanisms	• Extensive experience • No hypoglycemia • Inexpensive	• GI symptoms • Vitamin B_{12} deficiency • Use with caution or dose adjustment for CKD stage 3B (eGFR 30–44 mL·min^{-1} [1.73 m]$^{-2}$) • Lactic acidosis (rare)	High
SGLT2 inhibitors	• Canagliflozin • Dapagliflozin • Empagliflozin • Ertugliflozin	• Blocks glucose reabsorption by the kidney, increasing glucosuria • ? Other tubulo-glomerular effects	• No hypoglycemia • ↓ Weight • ↓ Blood pressure • Effective at all stages of T2DM with preserved glomerular function • ↓ MACE, HF, CKD with some agents (see text)	• Genital infections • UTI • Polyuria • Volume depletion/hypotension/dizziness • ↑ LDL-C • ↑ Creatinine (transient) • Dose adjustment/avoidance for renal disease • ↑ Risk for amputation (canagliflozin) • ↑ Risk for fracture (canagliflozin)	Intermediate–high (dependent on GFR)

New Since 2014

Metformin

US and EU Labels were revised in 2016 for use when eGFR is reduced

Insulins

Degludec (long acting) approved in the US (approved earlier in EU)
Fast-acting insulin aspart approved in US and EU
Biosimilars have become available for glargine and lispro
Concentrated forms of several have become available
Inhaled insulin (US)

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New Since 2014

SGLT2 Inhibitors

- Ertugliflozin approved in US and EU
- Combination products approved (with metformin or DPP4 inhibitors)
- CVOTs with empagliflozin, canagliflozin (and dapagliflozin) complete with broad benefits on cardiorenal outcomes

GLP-1 Receptor Agonists

- Two agents were approved: lixisenatide (in US 2016, EU 2013), semaglutide
- Combination products approved (with long-acting insulins)
- CVOTs with liraglutide, semaglutide and exenatide extended-release complete with cardiovascular benefits
- New safety data is reassuring regarding pancreatitis and pancreatic cancer

Outline

Lifestyle

- Medical Nutrition Therapy
- Physical activity

Medications

Metabolic Surgery

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Summary

Lifestyle is the foundation*

- Highly effective in motivated, adherent patients

Medications

- Lots of choices
- We hope to make it easier to navigate them
- Safety, efficacy, cost and convenience

Metabolic surgery*

- Consider it as very effective salvage therapy

*The only choices that can lead to disease remission

Putting It All Together: Strategies for Implementation

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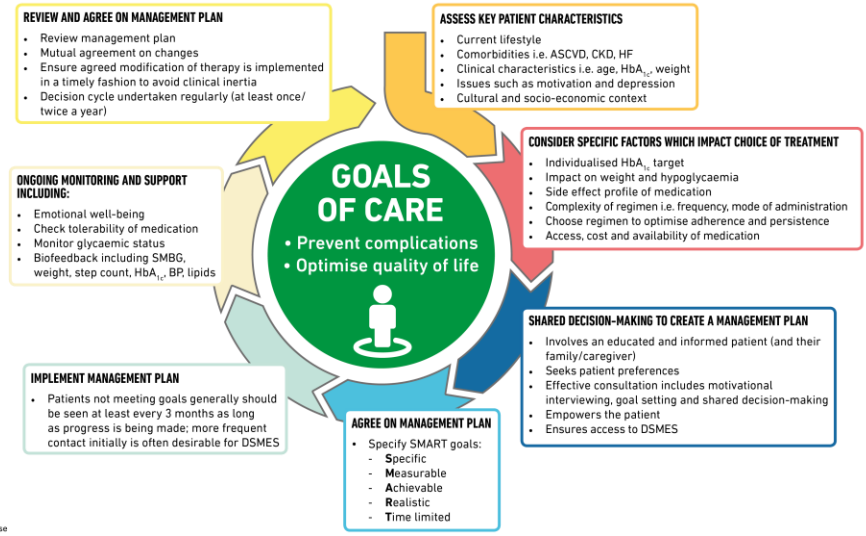
DECISION CYCLE FOR PATIENT-CENTRED GLYCAEMIC MANAGEMENT IN TYPE 2 DIABETES



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CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self-Monitored Blood Glucose

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Glucose-Lowering Medication in Type 2 diabetes: overall approach

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

***Consensus Recommendation*:**

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 (UKPDS 34).

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

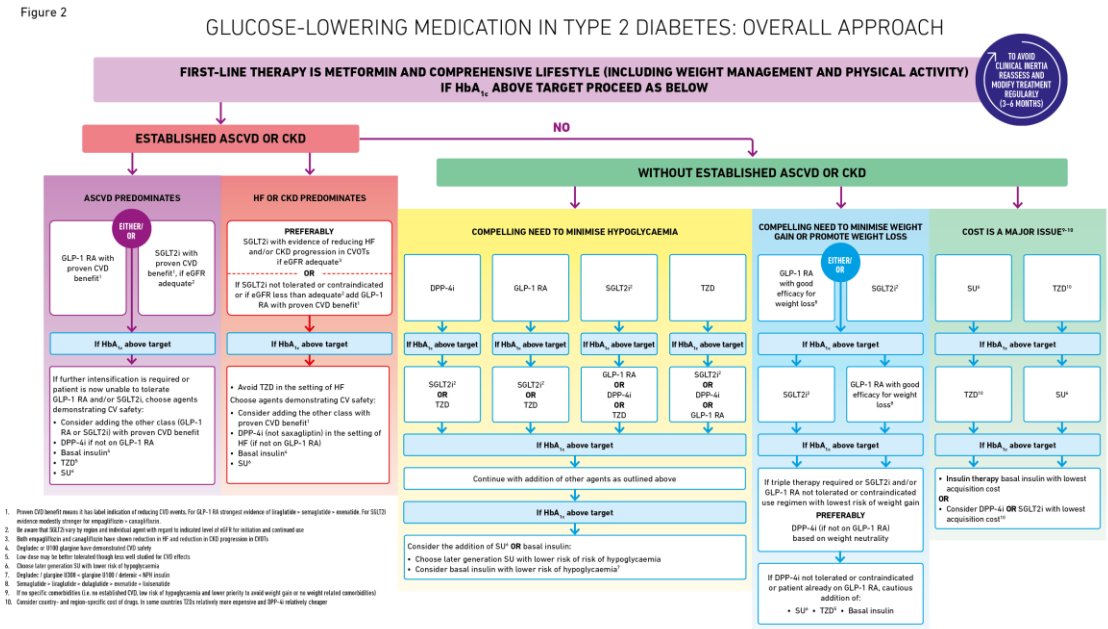
Consensus Recommendation:

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

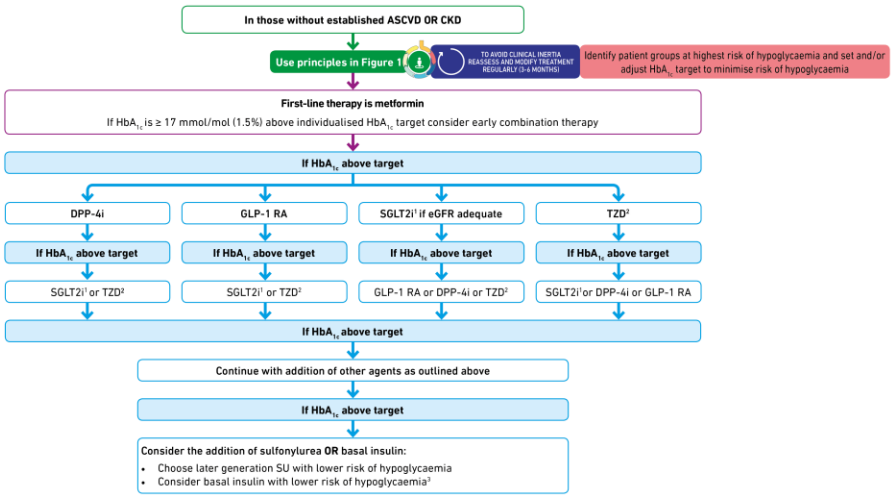


Glucose-Lowering Medication in Type 2 Diabetes: Overall Approach

***Consensus Recommendation*:**
The choice of medication added to metformin is based on patient preference and clinical characteristics. Important clinical characteristics include the presence of established **ASCVD**, other co-morbidities such as HF or CKD, and risk for specific adverse medication effects, particularly **hypoglycemia** and **weight gain**, as well as safety, tolerability, and **cost**.

Consensus Recommendation:
Intensification of treatment **beyond** dual therapy to maintain glycemic targets requires consideration of the impact of medication side effects on co-morbidities, as well as the burden of treatment and cost.

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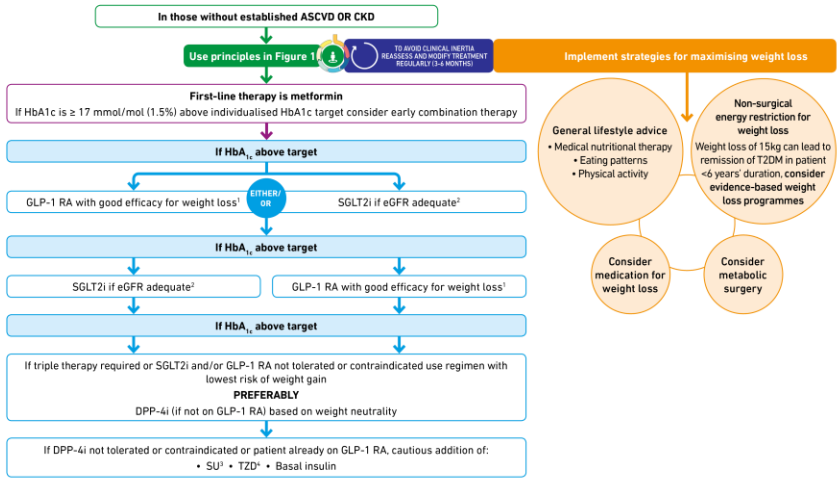
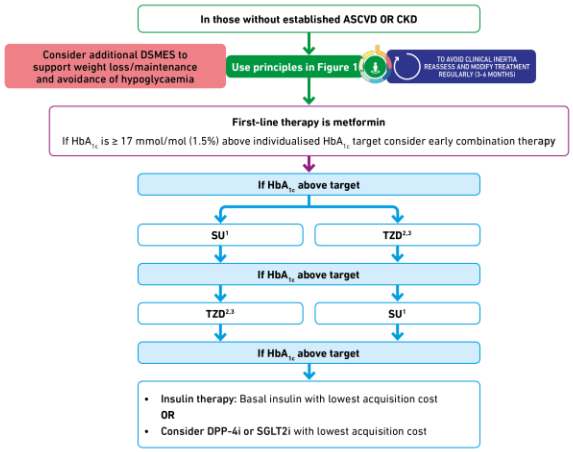
CHOOSING GLUCOSE-LOWERING MEDICATION IF COMPELLING NEED TO MINIMISE WEIGHT GAIN OR PROMOTE WEIGHT LOSS



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

CHOOSING GLUCOSE-LOWERING MEDICATION IF COST IS A MAJOR ISSUE



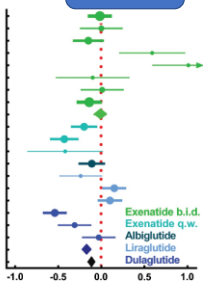
1. Choose later-generation SU to minimise risk of hypoglycaemia
2. Consider country- and region-specific cost of drugs. In some countries, TZD relatively more expensive and DPP-4i relatively cheaper
3. Low-dose TZDs are better tolerated

Consensus Recommendation: In patients who need the greater glucose-lowering effect of an injectable medication, **GLP-1 receptor agonists are the preferred choice to insulin** . For patients with extreme and symptomatic hyperglycaemia, insulin is recommended.

HbA1c

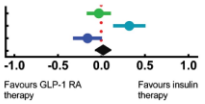
GLP-1 RA versus insulin treatment (OGLM background)

Study	Duration of action	Difference in means	Lower Limit	Upper Limit	Z-value	p-value
Heine et al. 2005 [44]	short	-0.02	-0.16	0.12	-0.24	0.81
Barnett et al. 2007 [33]	short	0.00	-0.25	0.25	0.00	1.00
Nauck et al. 2007 [47]	short	-0.15	-0.33	0.03	-1.63	0.10
Bergenstal et al. 2009 a [34]	short	0.59	0.21	0.97	3.02	0.0026
Bergenstal et al. 2009 b [34]	short	1.01	0.59	1.43	4.72	< 0.0001
Bunck et al. 2009 [35]	short	-0.10	-0.53	0.33	-0.46	0.65
Davies et al. 2009 [38]	short	0.01	-0.24	0.26	0.08	0.94
Gallwitz et al. 2011 [41]	short	-0.14	-0.29	0.01	-1.87	0.061
All short-acting GLP-1 RAs		**-0.02**	**-0.09**	**0.06**	**-0.39**	**0.70**
Diamant et al. 2010 [40]	long	-0.20	-0.35	-0.05	-2.57	0.010
Inagaki et al. 2012 [45]	long	-0.43	-0.60	-0.26	-5.08	< 0.0001
Davies et al. 2013 [37]	long	-0.42	-0.86	0.02	-1.87	0.061
Weissman et al. 2014 [50]	long	-0.11	-0.27	0.05	-1.39	0.16
Russell-Jones et al. 2009 [49]	long	-0.24	-0.49	0.01	-1.89	0.059
D'Alessio et al. 2015 [36]	long	0.15	0.01	0.29	2.12	0.034
Gough et al. 2015 [43]	long	0.10	-0.04	0.24	1.37	0.17
Araki et al. 2015 [32]	long	-0.54	-0.68	-0.40	-7.66	< 0.0001
Giorgino et al. 2015 a [42]	long	-0.31	-0.50	-0.12	-3.13	0.0018
Giorgino et al. 2015 b [42]	long	-0.03	-0.22	0.16	-0.30	0.76
All long-acting GLP-1 RAs		**-0.17**	**-0.22**	**-0.12**	**-6.24**	**< 0.0001**
All GLP-1 RAs		**-0.12**	**-0.16**	**-0.07**	**-5.30**	**< 0.0001**



GLP-1 RA versus rapid-acting insulin (basal insulin + OGLM background)

Study	Duration of action	Difference in means	Lower Limit	Upper Limit	Z-value	p-value
Diamant et al. 2014 [39]	short	-0.03	-0.17	0.11	-0.42	0.67
Mathieu et al. 2014 [46]	long	0.32	0.13	0.51	3.37	0.0008
Rosenstock et al. 2014 [48]	long	-0.16	-0.33	0.01	-1.89	0.059
All GLP-1 RAs		**0.02**	**-0.08**	**0.11**	**0.34**	**0.73**



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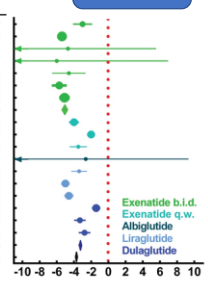
Weight

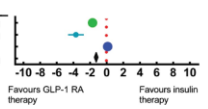
GLP-1 RA versus insulin treatment (OGLM background)

Study	Duration of action	Difference in means	Lower Limit	Upper Limit	Z-value	p-value
Barnett et al. 2007 [33]	short	-3.00	-4.11	-1.89	-5.30	< 0.0001
Nauck et al. 2007 [47]	short	-5.40	-5.95	-4.85	-19.09	< 0.0001
Bergenstal et al. 2009 a [34]	short	-4.70	-14.96	5.56	-0.90	0.37
Bergenstal et al. 2009 b [34]	short	-6.00	-18.94	6.94	-0.91	0.36
Bunck et al. 2009 [35]	short	-4.60	-6.54	-2.66	-4.65	< 0.0001
Davies et al. 2009 [38]	short	-5.71	-6.57	-4.85	-13.03	< 0.0001
Gallwitz et al. 2011 [41]	short	-5.10	-5.71	-4.49	-16.39	< 0.0001
All short-acting GLP-1 RAs		**-5.10**	**-5.44**	**-4.75**	**-28.93**	**< 0.0001**
Diamant et al. 2010 [40]	long	-4.00	-4.56	-3.45	-14.13	< 0.0001
Inagaki et al. 2012 [45]	long	-2.01	-2.48	-1.54	-8.36	< 0.0001
Davies et al. 2013 [37]	long	-3.50	-4.50	-2.50	-6.85	< 0.0001
Weissman et al. 2014 [50]	long	-2.63	-14.58	9.32	-0.43	0.67
Russell-Jones et al. 2009 [49]	long	-3.40	-4.32	-2.49	-7.29	< 0.0001
D'Alessio et al. 2015 [36]	long	-5.00	-5.48	-4.52	-20.41	< 0.0001
Gough et al. 2015 [43]	long	-4.60	-5.11	-4.09	-17.60	< 0.0001
Araki et al. 2015 [32]	long	-1.42	-1.89	-0.95	-5.90	< 0.0001
Giorgino et al. 2015 a [42]	long	-3.31	-3.98	-2.64	-9.75	< 0.0001
Giorgino et al. 2015 b [42]	long	-2.77	-3.44	-2.11	-8.16	< 0.0001
All long-acting GLP-1 RAs		**-3.28**	**-3.47**	**-3.09**	**-33.48**	**< 0.0001**
All GLP-1 RAs		**-3.71**	**-3.88**	**-3.54**	**-43.32**	**< 0.0001**



GLP-1 RA versus rapid-acting insulin (basal insulin + OGLM background)

Study	Duration of action	Difference in means	Lower Limit	Upper Limit	Z-value	p-value
Diamant et al. 2014 [39]	short	-1.70	-1.98	-1.42	-12.02	< 0.0001
Mathieu et al. 2014 [46]	long	3.70	4.65	-2.75	-7.66	< 0.0001
Rosenstock et al. 2014 [48]	long	0.12	-0.29	0.53	0.57	0.57
All GLP-1 RAs		**-1.28**	**-1.50**	**-1.05**	**-11.19**	**< 0.0001**

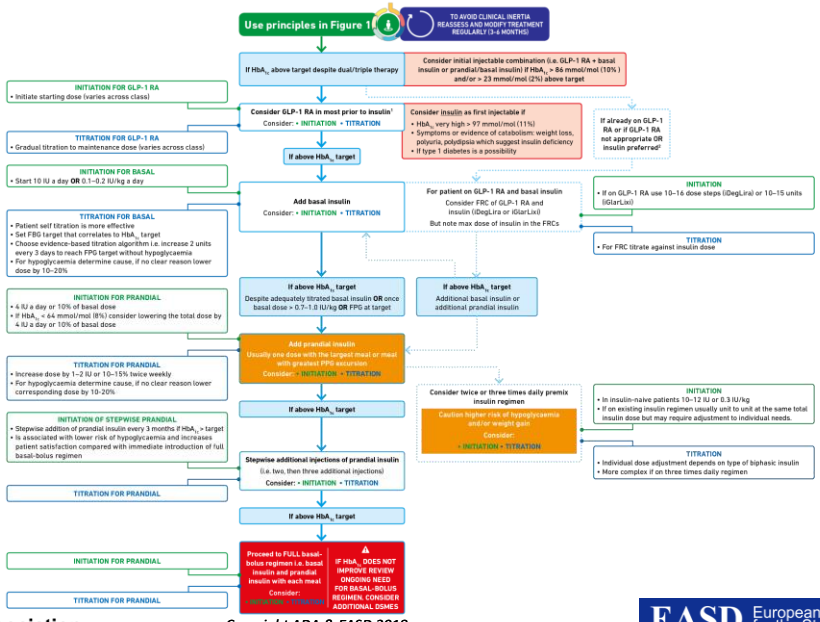


Age: 77
Occupation: retired teacher
Diabetes Hx: 12 years, no retinopathy, no nephropathy, no neuropathy sx, SU caused hypoglycemia, SGLT2-i yeast infections, pioglitazone edema
Cardiovascular History: none
Current Diabetes Meds: metformin 500mg BID, pioglitazone 30 mg daily
A1C: 8.3%
Cardiovascular Meds: none
BG pattern: fasting average 145 mg/dL, post-meal average 200 mg/dL, infrequent hypoglycemia
Patient/Provider Goals: healthy aging

Jennice

Figure 7

INTENSIFYING TO INJECTABLE THERAPIES



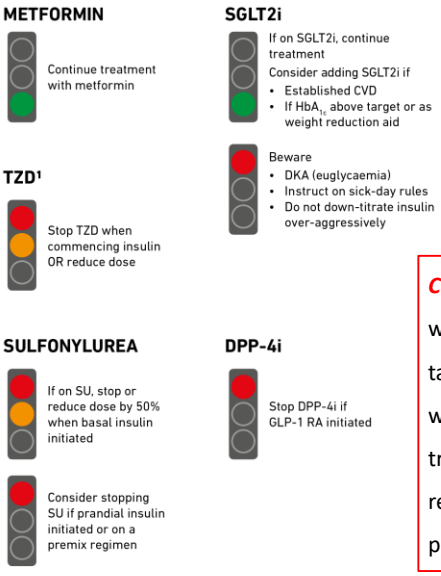
1. Consider choice of GLP-1 RA considering patient preference: HbA_{1c} lowering, weight-lowering effect or frequency of injection. If CVD, consider GLP-1 RA with proven CVD benefit
2. Consider insulin as preferred to GLP-1 RA if symptoms of hyperglycaemia are present, or evidence of ongoing catabolism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

American Diabetes Association.

EASD European Association for the Study of Diabetes

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

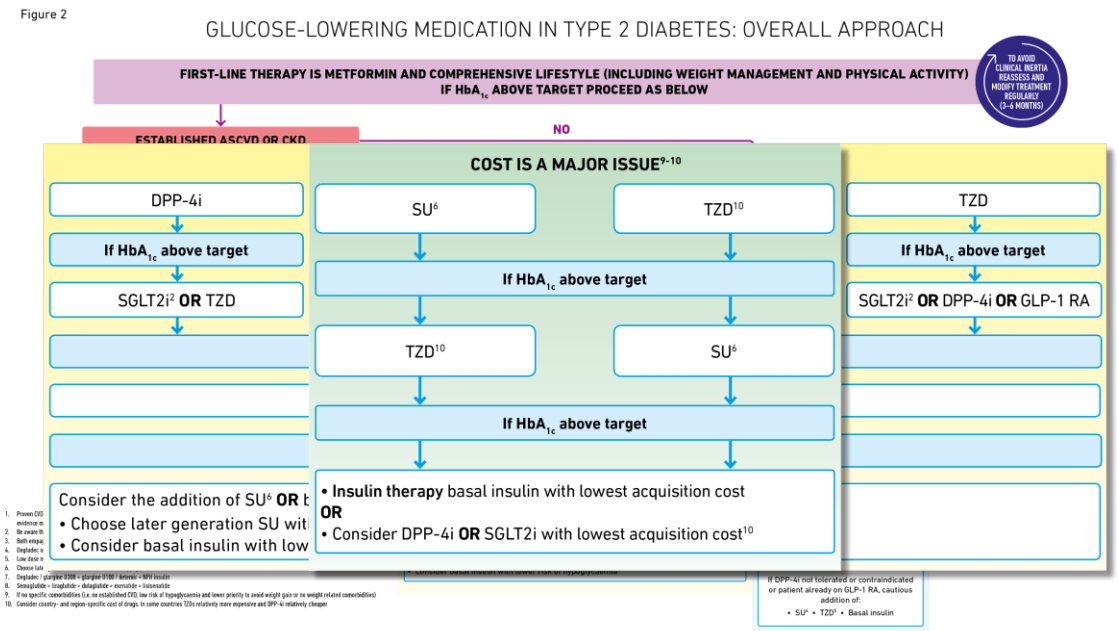
Consensus Recommendation: Patients who are unable to maintain glycemic targets on basal insulin in combination with oral medications can have treatment intensified with GLP-1 receptor agonists, SGLT2 inhibitors, or prandial insulin.

American Diabetes Association.

EASD European Association for the Study of Diabetes

Glucose-lowering Medication in Type 2 Diabetes: Overall Approach

Consensus Recommendation: The choice of medication added to metformin is based on patient preference and clinical characteristics. Important clinical characteristics include the presence of established **ASCVD**, other co-morbidities such as HF or CKD, and risk for specific adverse medication effects, particularly **hypoglycemia** and **weight gain**, as well as safety, tolerability, and **cost**.



Age: 57
Occupation: CEO of local non-for-profit
Diabetes Hx: 6 years, no cx; struggles with weight, eating out, daily schedule
Current Meds: metformin, saxagliptin, insulin detemir 36 units
A1C: 8.1%, anti-GAD negative, eGFR >60 ml/min/1.73m
BG pattern: fasting average 142 mg/dL, post-meal average 207 mg/dL, no hypoglycemia
Patient/Provider Goals: avoid complications, facilitate weight loss, dosing simplicity

Lise

Overall Summary

- The management of hyperglycemia in type 2 diabetes has become complex with the number of glucose-lowering medications now available.
- Patient-centered decision-making and support and consistent efforts at improving diet and exercise remain the foundation of all glycemic management.
- Initial use of metformin, followed by addition of glucose-lowering medications based on patient co-morbidities and concerns is recommended as we await answers to the many questions that remain.

The position statement is available

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Thank you