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

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American Diabetes Association

Disclosures of Interest

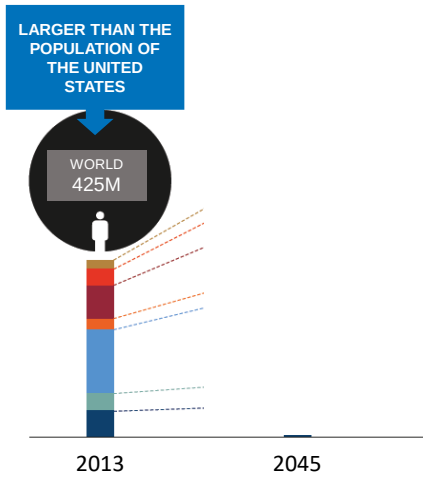
No disclosures to report

American Diabetes Association.

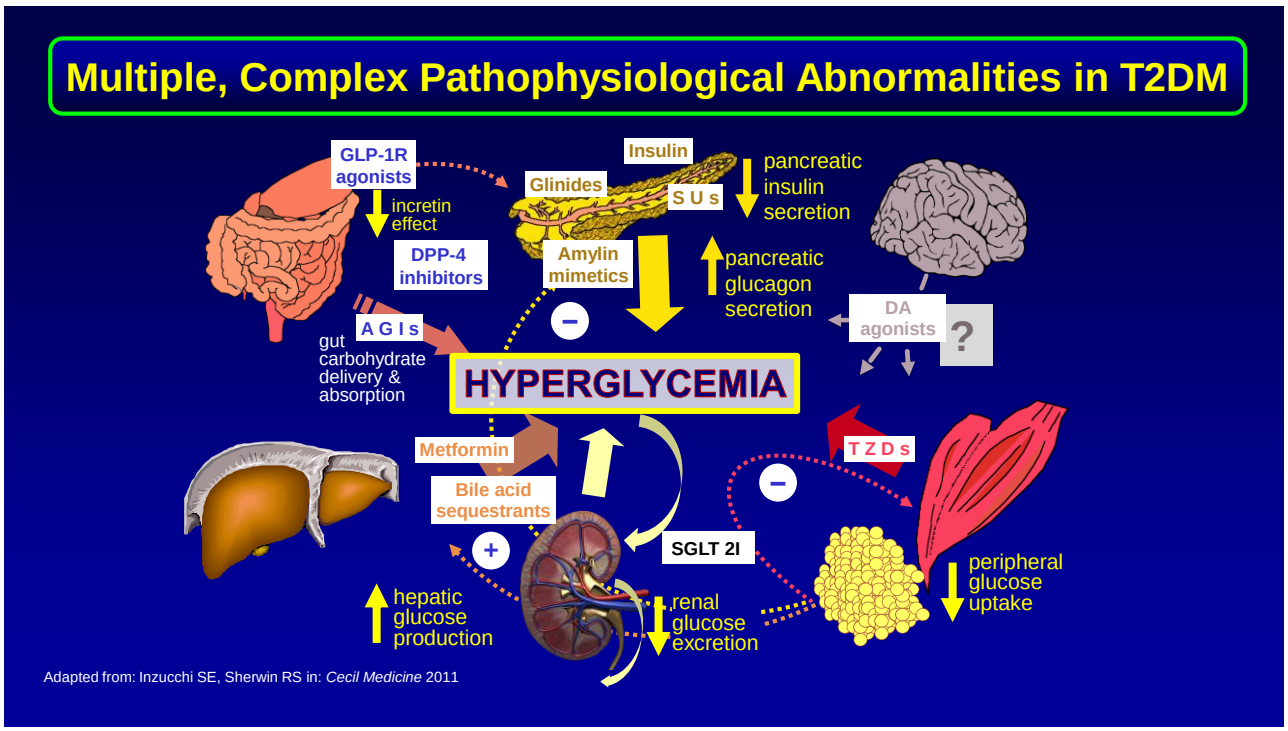
GLOBAL PREVALENCE EXPECTED TO INCREASE *48%* BY 2045[1]

2017 Statistics:

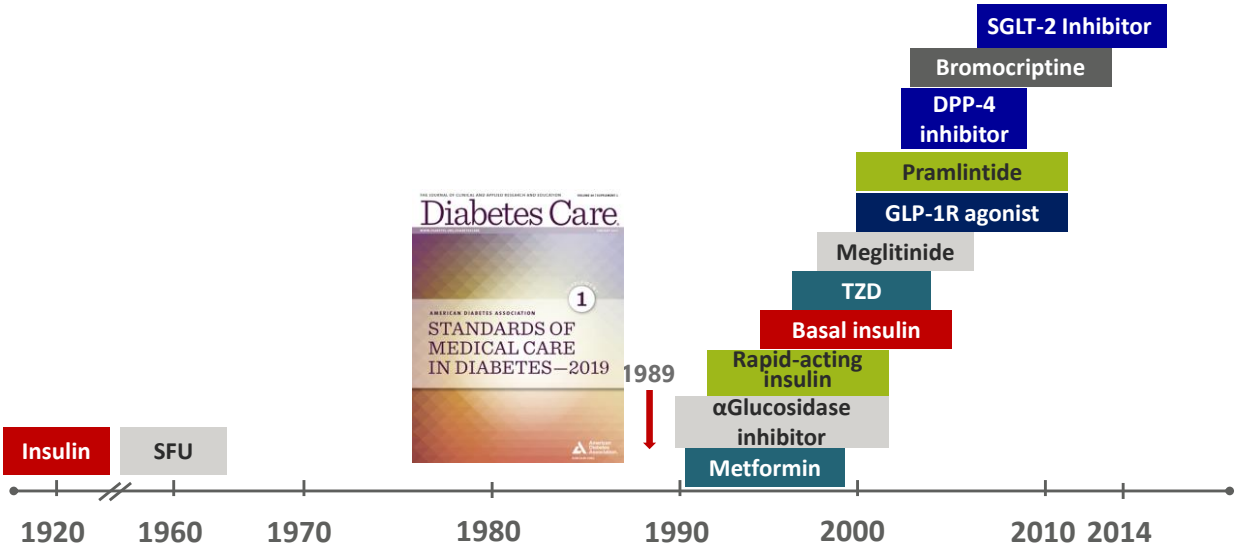
- Over 11% prevalence in US
- Type 2 diabetes accounts for 90 to 95% of all diabetes cases
- 325 Million globally at risk
- 4 Million deaths attributable to diabetes
- $727 billion (USD) in health expenditure



1.IDF Diabetes Atlas, 8th edition. 2017. International Diabetes Foundation.
2.http://www.cdc.gov/chronicdisease/resources/publications/aag/ddt.htm.



Therapeutic Advances Over Past 20 Years



Update on Latest Treatment Recommendations

- Appropriate glycemic target?
  - Considering the "company it keeps!"
- Clinical approach to arrive at the target?
  - Concept of "metabolic memory"
  - Overcoming clinical inertia
- CV consequences of diabetes?
- New Algoritm to achieve individualized goals.

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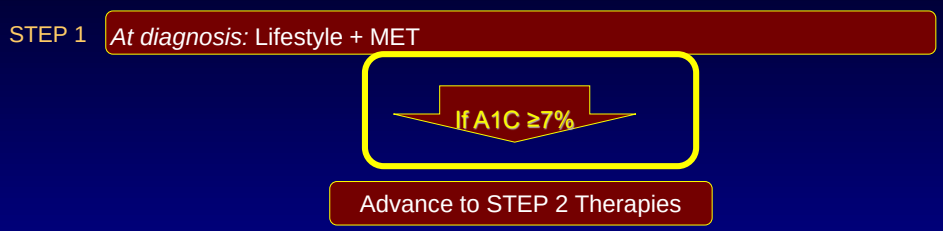
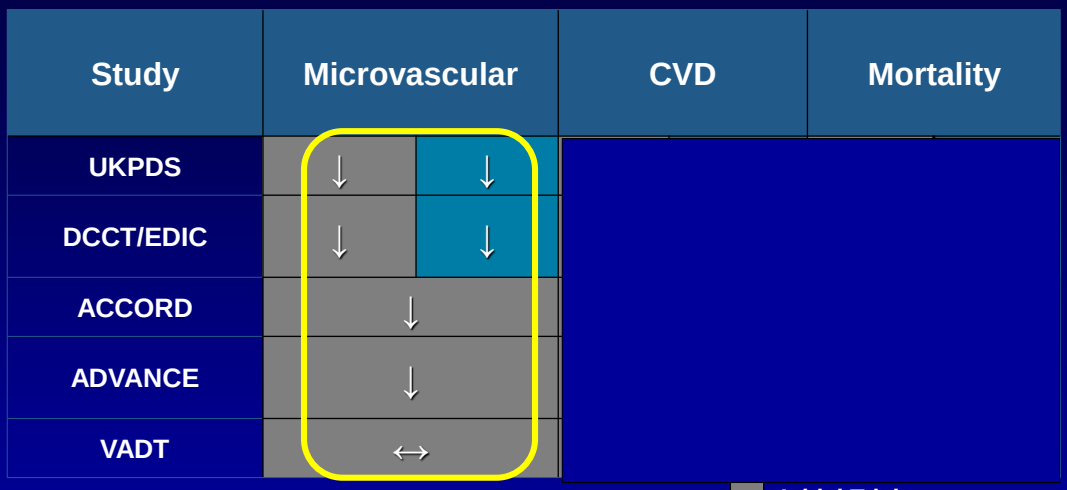
Consensus Statement for the Management of Type 2 Diabetes



*Validation based on clinical trials and clinical judgment.
Adapted from Nathan DM, et al. *Diabetes Care*. 2008;31(1):173-175.

A Broad View of Glycemia and Complications



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Nathan DM, *et al. N Engl J Med*. 2005;353:2643-53. Gerstein HC, *et al*. *N Engl J Med*. 2008;358:2545-59.
Patel A, *et al*. *N Engl J Med*. 2008;358:2560-72. Duckworth W, *et al. N Engl J Med*. 2009;360:129-39.
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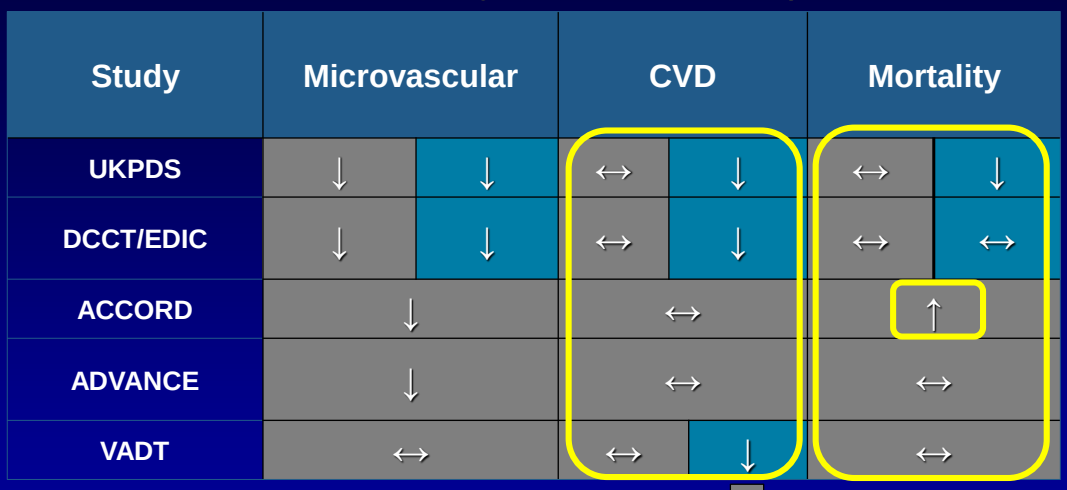

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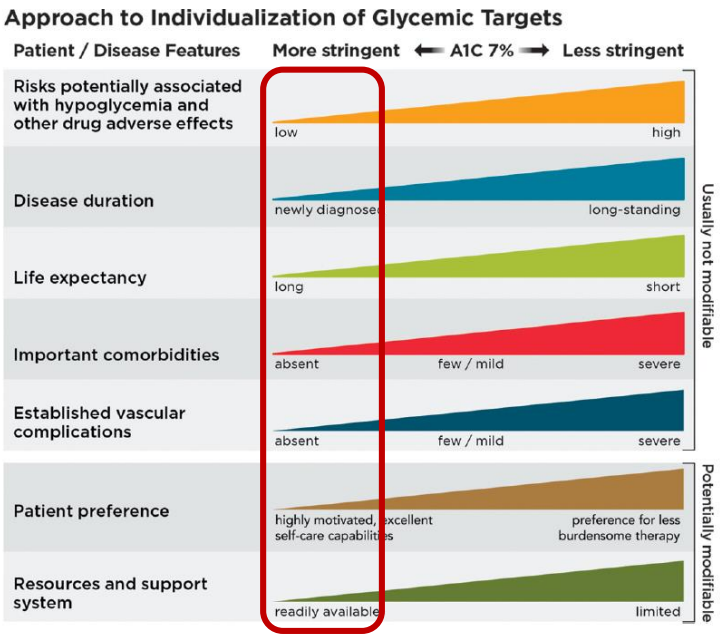


American Diabetes Association.

American Diabetes Association. 6. Glycemic targets. Standards of Medical Care in Diabetes - 2019. *Diabetes Care* 2019;42(Suppl. 1):S61-S70

HbA1C Goal is not "One-size-fits-all"

More Stringent (as close to 6% as possible)

ADA < 7%
AACE ≤ 6.5%

Less Stringent (< 8%)

No broad agreement on A1C targets

American Association of Clinical Endocrinologists ≤ 6.5%

American Diabetes Association <7%

American College of Physicians <8%

ACP American College of Physicians℠
Leading Internal Medicine, Improving Lives

CLINICAL GUIDELINE

Hemoglobin A_{1c} Targets for Glycemic Control With Pharmacologic Therapy for Nonpregnant Adults With Type 2 Diabetes Mellitus: A Guidance Statement Update From the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Timothy J. Wilt, MD, MPH; Devan Kansagara, MD, MCR; Carrie Horwitch, MD, MPH; Michael J. Barry, MD; and Mary Ann Forciea, MD; for the Clinical Guidelines Committee of the American College of Physicians*

Doctors' Group Issues Controversial Advice for Type-2 Diabetes

American College of Physicians ups A1c limit to 8%

diabetes.

TREATMENTS

Major Medical Associations Feud Over Diabetes Guidelines

March 5, 2018 · 5:01 PM ET

Ann Intern Med. 6 March 2018

Annals of Internal Medicine

IDEAS AND OPINIONS

Guidelines Versus Guidelines: What's Best for the Patient?

Boris Draznin, MD, PhD; David M. Nathan, MD; Mary T. Korytkowski, MD; Marie E. McDonnell, MD; Sherita Hill Golden, MD, MHS; Mark H. Schutta, MD; and William T. Cefalu, MD

A1C Targets Should Be Personalized to Maximize Benefits While Limiting Risks

Matthew C. Riddle,[1] Hertzel C. Gerstein,[2] Rury R. Holman,[3] Silvio E. Inzucchi,[4] Bernard Zinman,[5] Sophia Zoungas,[6] and William T. Cefalu[7]

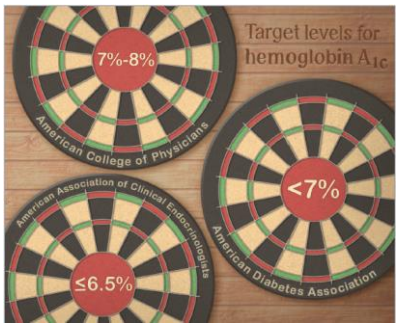
Diabetes Care 2018;41:1121–1124 | https://doi.org/10.2337/dci18-0018

Medical News & Perspectives

For Patients With Type 2 Diabetes, What's the Best Target Hemoglobin A_{1C}?

Jennifer Abbasi

JAMA Published online May 30, 2018



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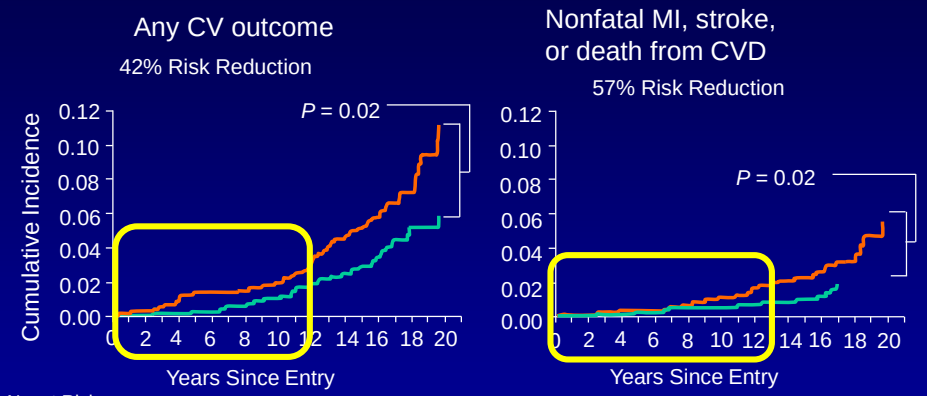
Glycemic Control Reduces Long-Term Risk of Macrovascular Complications: DCCT-EDIC

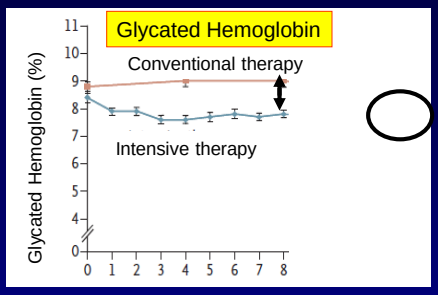


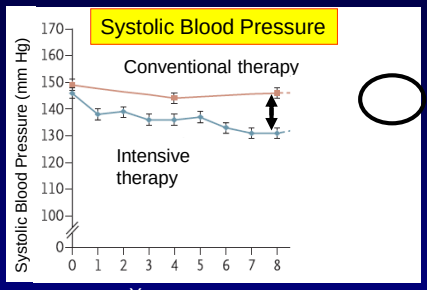
No. at Risk								
Conventional	714	688	618	92	721	694	637	96
Intensive	705	683	629	113	705	686	640	118

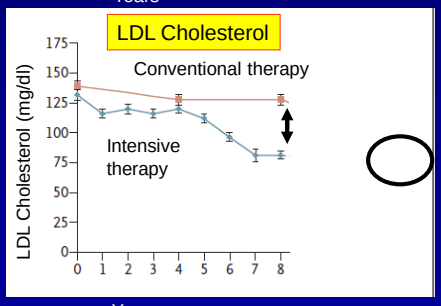
DCCT = Diabetes Control and Complications Trial.

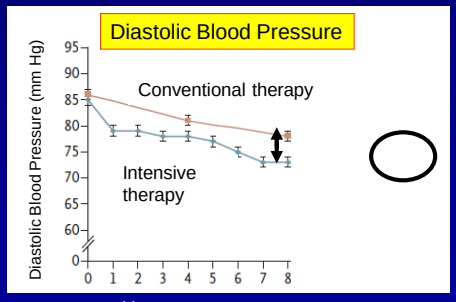
DCCT-EDIC Study Research Group. *N Engl J Med.* 2005;353:2643-2653.

Steno-2 Follow-Up







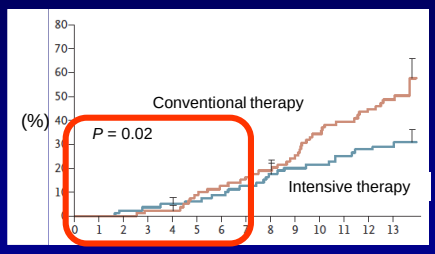


Gaede P, et al. *N Engl J Med*. 2008;358(6):580-591.

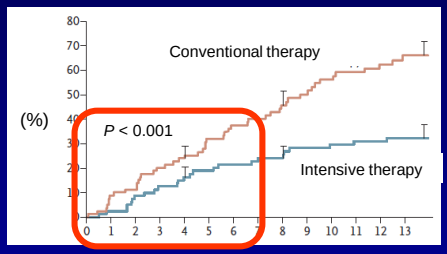
Steno-2 Follow-Up Years: Cardiovascular Events

Metabolic Memory?

Cumulative Incidence of Death



Cumulative Incidence of Any Cardiovascular Event



No. at Risk

Intensive Therapy	80	78	75	72	65	62	57	39
Conventional Therapy	80	80	77	69	63	51	43	30

No. at Risk

Intensive Therapy	80	72	65	61	56	50	47	31
Conventional Therapy	80	70	60	46	38	29	25	14

Gaede P, et al. *N Engl J Med*. 2008;358(6):580-591.

Metabolic Memory: ACCORD Follow-on Study

Persistent Effects of Intensive Glycemic Control on Retinopathy in Type 2 Diabetes in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) Follow-On Study

*The Action to Control Cardiovascular Risk in Diabetes Follow-On (ACCORDION) Eye Study Group and the Action to Control Cardiovascular Risk in Diabetes Follow-On (ACCORDION) Study Group**

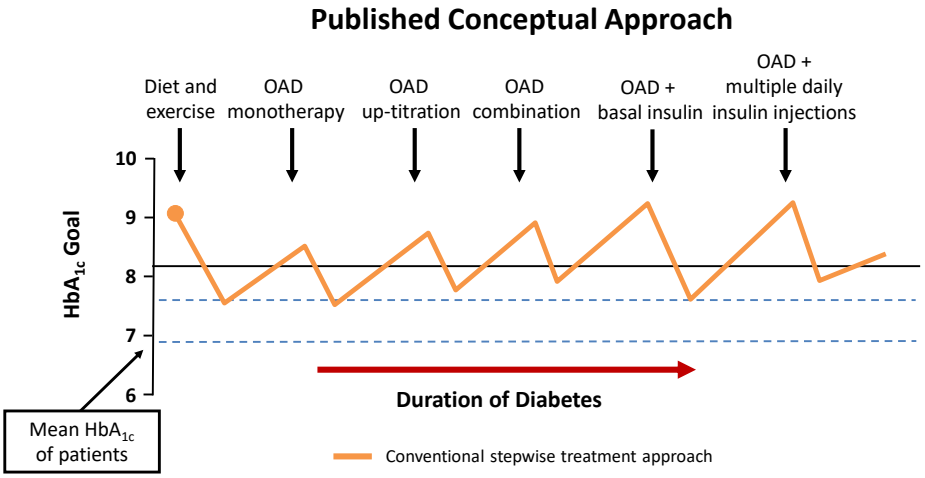
Diabetes Care 2016;39:1089–1100 | DOI: 10.2337/dc16-0024

Big Picture Messages

- Type 1 and type 2 diabetes: ***early*** meticulous glucose control can prevent microvascular and neuropathic complications
- Type 1 and type 2 diabetes: ***early*** meticulous glucose control appears to prevent CVD many years later ("*metabolic memory*" and "*legacy effect*")

"The ADA recommends that a reasonable A1C goal for many nonpregnant adults with type 2 diabetes is less than 7 percent based on the available evidence to date and incorporated into ADA's Standards of Care".

Overcoming Therapeutic Intertia



OAD = oral anti-hyperglycemic agent.
Adapted from Campbell IW. *Br J Cardiol*. 2000;7(10):625-631. Del Prato S, et al. *Int J Clin Pract*. 2005;59:1345-1355.

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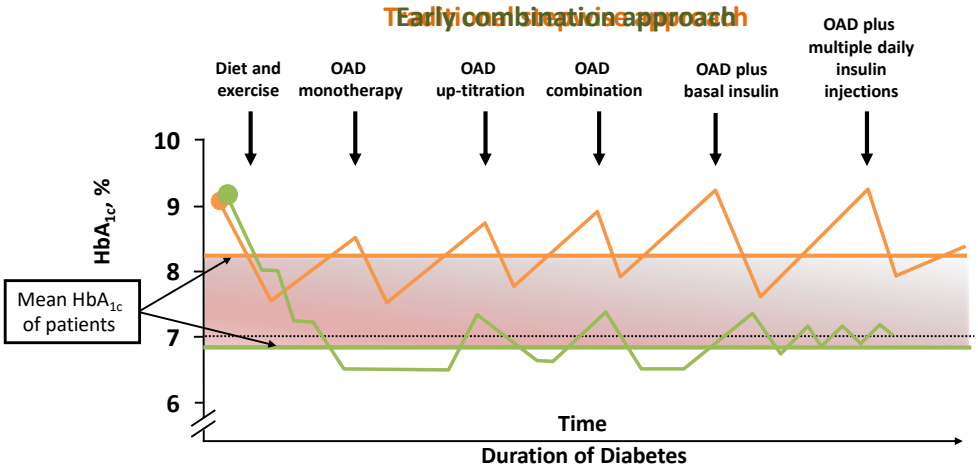

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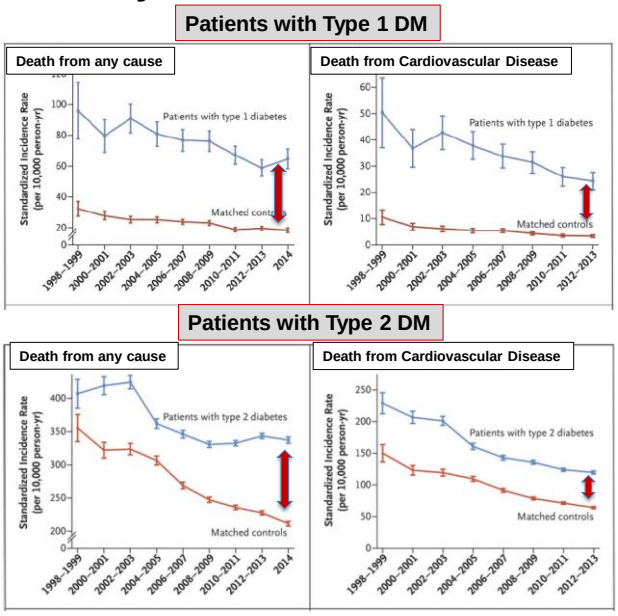
Mortality and Cardiovascular Disease in Type 1 and Type 2 Diabetes



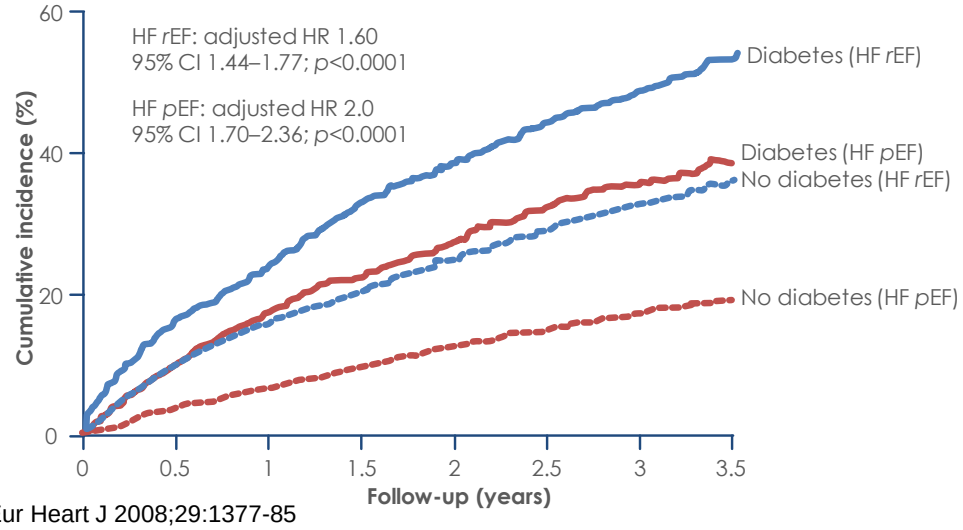
"…data from 1998 to 2014 showed marked reductions in mortality and in the incidence of cardiovascular complications among adults with either type 1 diabetes or type 2 diabetes".

"Residual Risk"

"There remains a substantial excess overall rate of all outcomes analyzed among persons with either type 1 diabetes or type 2 diabetes as compared with the general population.

Rawshani A, Rawshani A, Franzén S, et al. **N Engl J Med**. 2017 Apr 13;376(15):1407-1418.

Diabetes & Risk of Heart Failure Hosp/Death



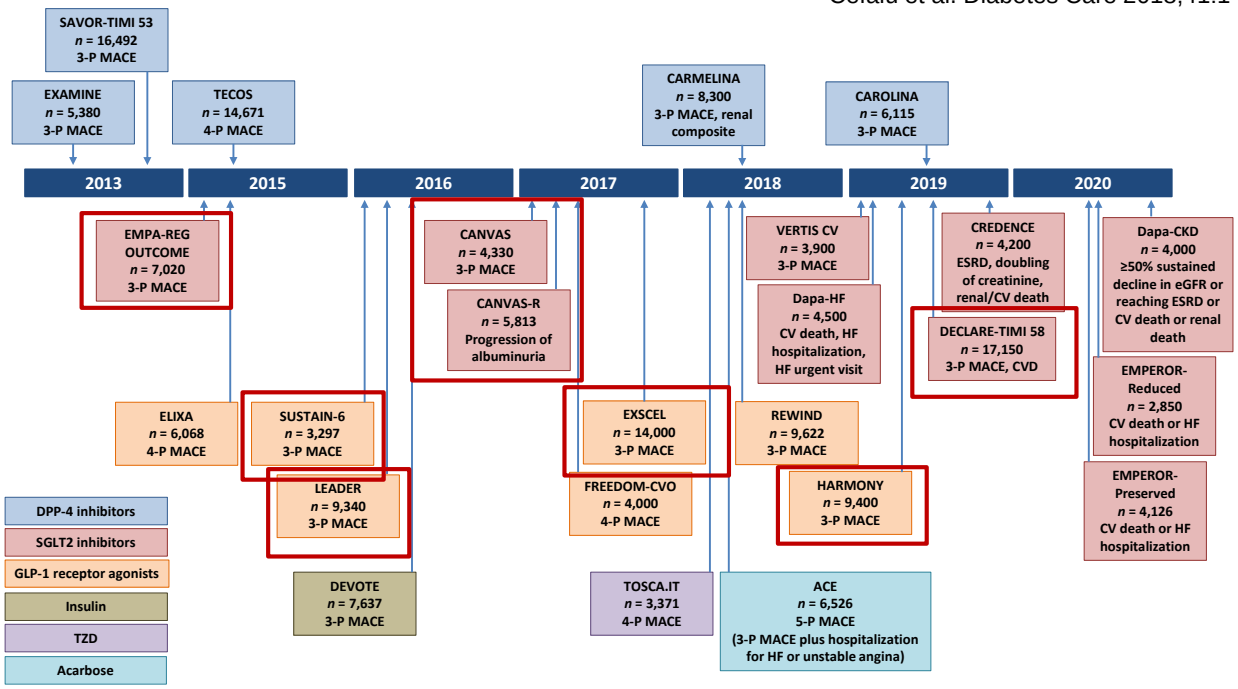
MacDonald et al. Eur Heart J 2008;29:1377-85

Cardiovascular Outcomes Trials in Type 2 Diabetes: Where Do We Go From Here? Reflections From a *Diabetes Care* Editors' Expert Forum

William T. Cefalu,[1] Sanjay Kaul,[2] Hertzel C. Gerstein,[3] Rury R. Holman,[4] Bernard Zinman,[5] Jay S. Skyler,[6] Jennifer B. Green,[7] John B. Buse,[8] Silvio E. Inzucchi,[9] Lawrence A. Leiter,[10] Itamar Raz,[11] Julio Rosenstock,[12] and Matthew C. Riddle[13]

Diabetes Care 2018;41:14–31 | https://doi.org/10.2337/dci17-0057

Cefalu et al. Diabetes Care 2018;41:14



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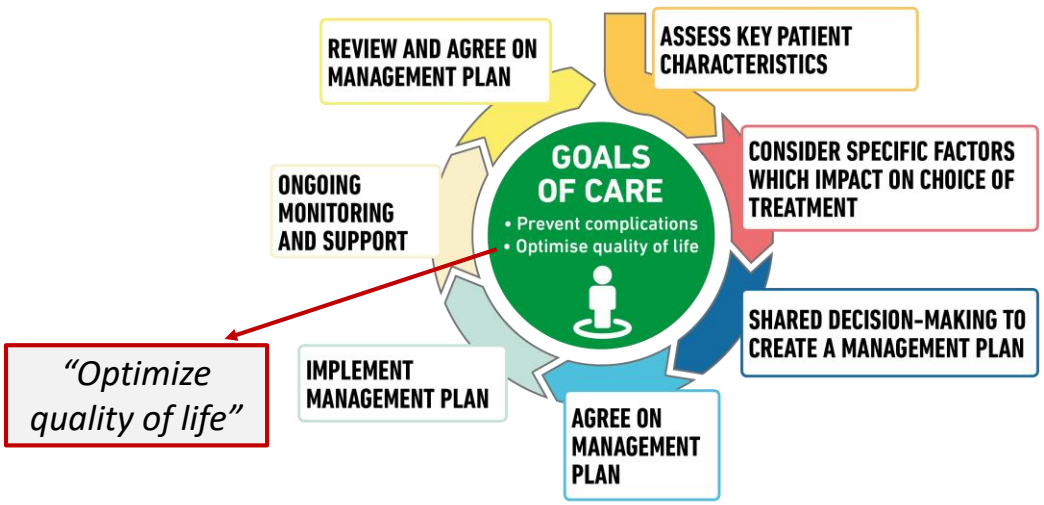
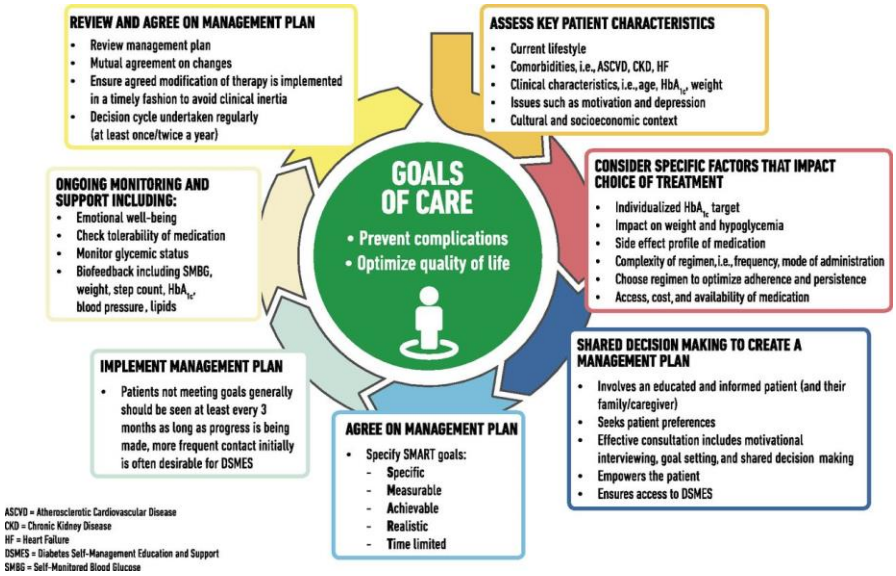
Putting the Patient at the Center of Care

Figure 1

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



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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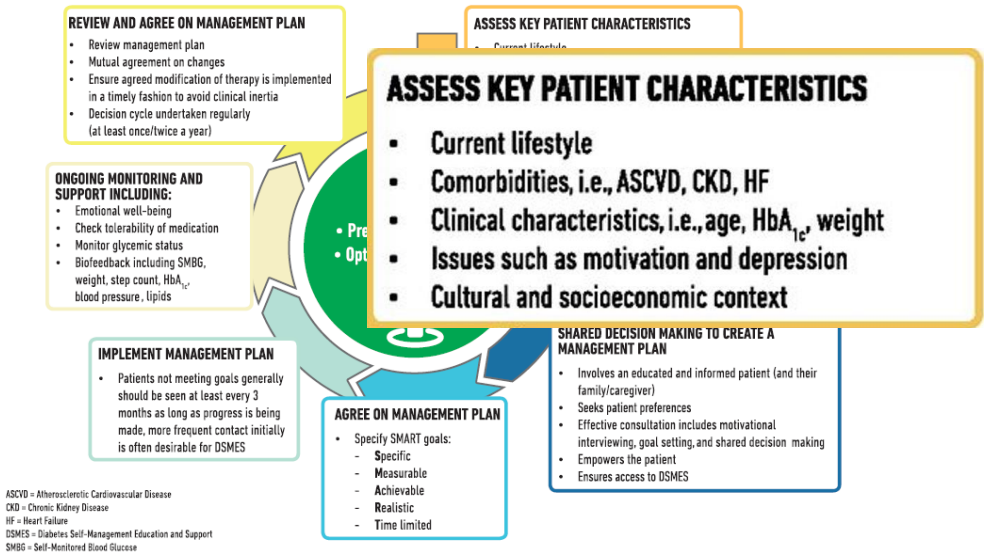

American Diabetes Association.

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

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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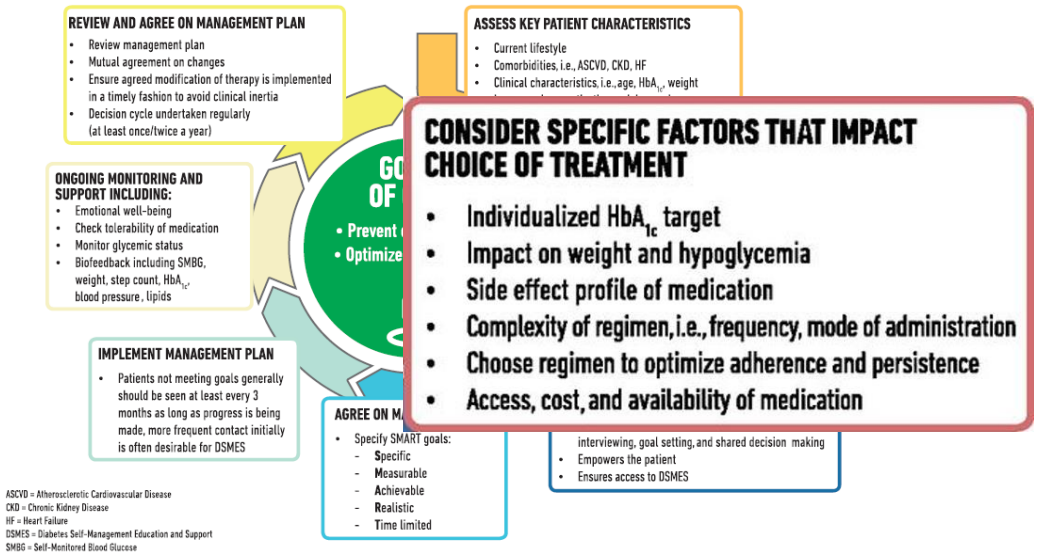

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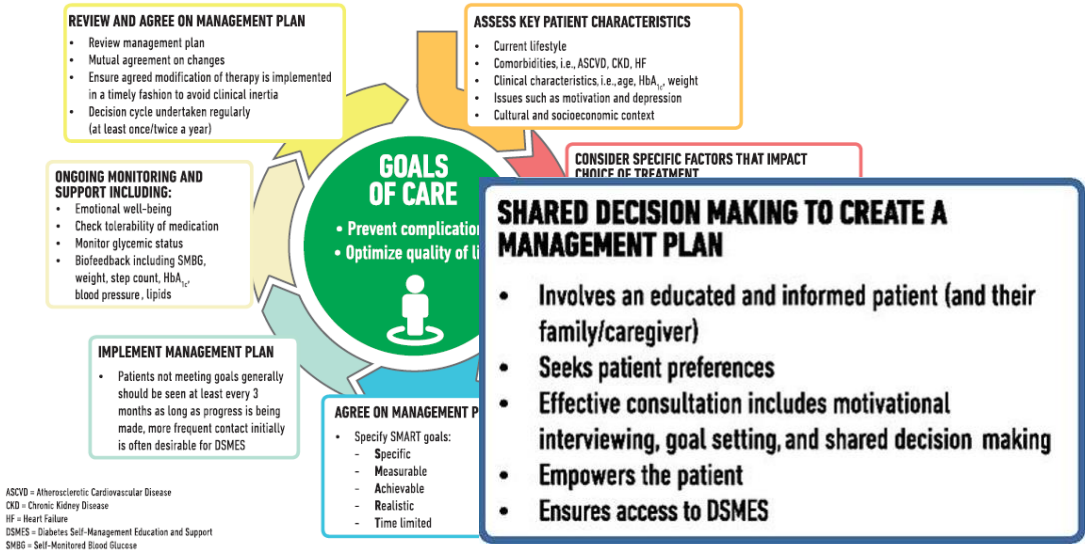

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Shared decision making in type 2 diabetes

SDM can improve

- decision quality
- patient knowledge
- patient risk perception

Ethical imperative for support of patients' autonomy

Use of Empowering Language.

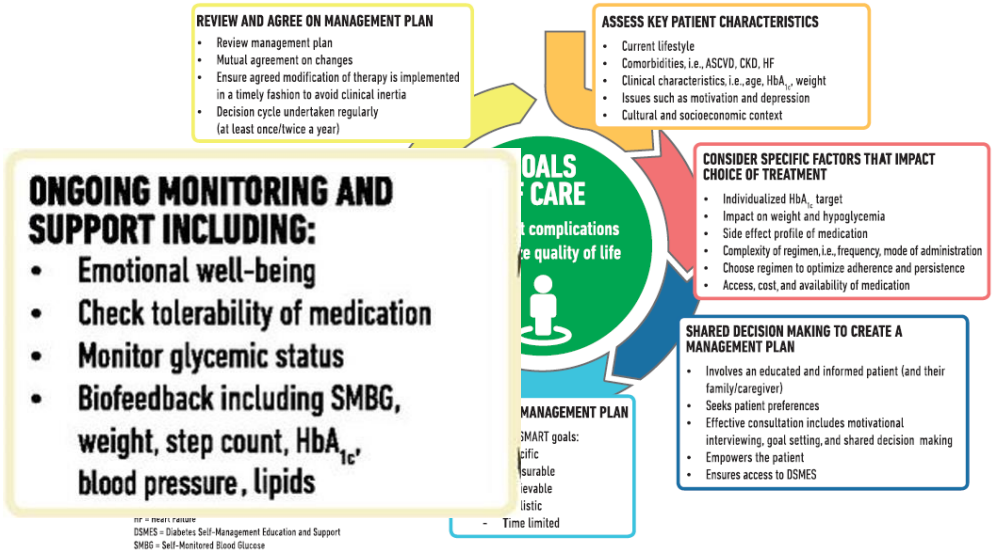
Five key consensus recommendations for language use:

1. Use language that is neutral, nonjudgmental, and based on facts, actions, or physiology/biology;
2. Use language that is free from stigma;
3. Use language that is strength based, respectful, and inclusive and that imparts hope;
4. Use language that fosters collaboration between patients and providers;
5. Use language that is person centered (e.g., “person with diabetes” is preferred over “diabetic”).

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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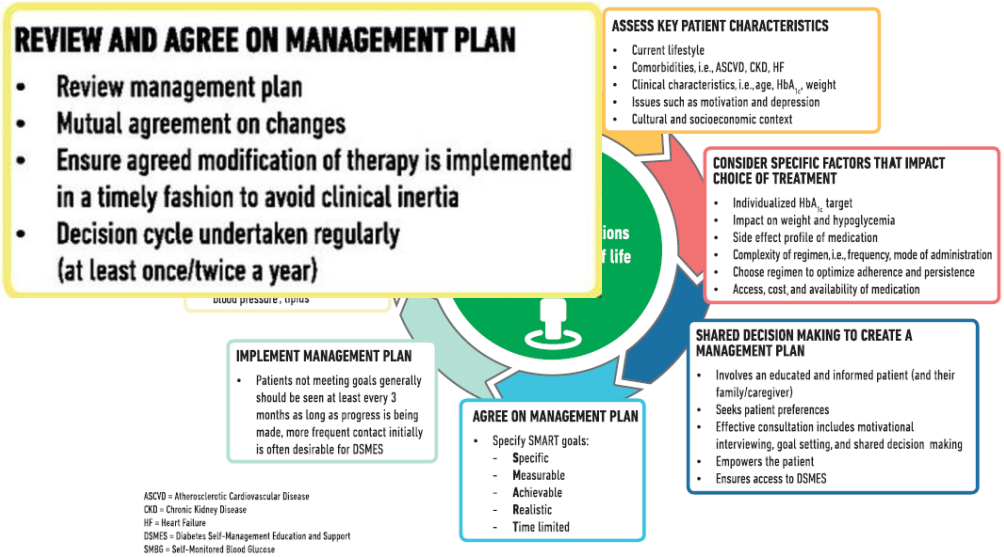

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Glucose Lowering Drug Categories

- Sulfonylureas
- Metformin
- Acarbose
- Meglitinides
- Insulin
- TZDs
- DPP4 inhibitors
- GLP-1 receptor agonists
- SGLT-2 inhibitors
- Other drugs
  - Colesevalam
  - Bromocriptine
  - Pramlintide

ADA. Diabetes Care 2018; 41(Supp 1): S1-S153

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

Step 1: Assess cardiovascular disease

Presence of cardiovascular disease is compelling indication

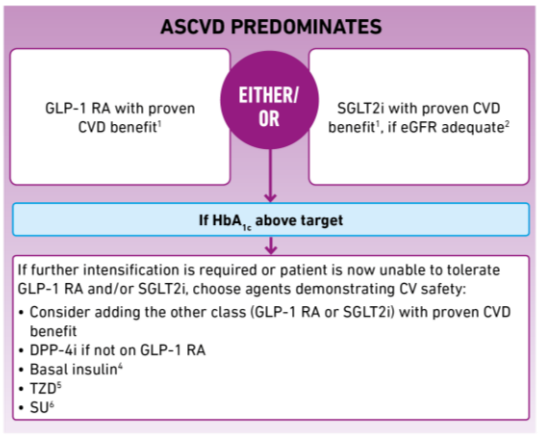
If ASCVD Predominates:

<u>GLP-1 receptor</u> agonist *with proven cardiovascular benefit*

- Liraglutide > semaglutide > exenatide LAR

<u>SGLT2 inhibitor</u> *with proven cardiovascular benefit*

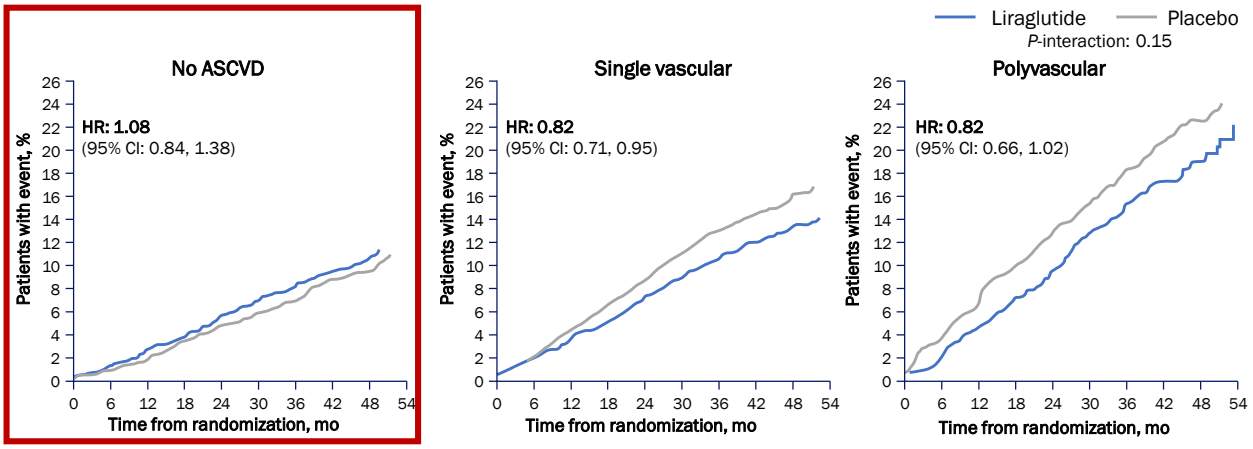
- Empagliflozin > canagliflozin



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

American Diabetes Association.

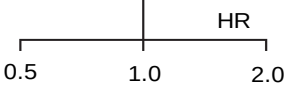
LEADER: Kaplan–Meier Estimates of Time to First MACE
Primary MACE: Stratified By Vascular Territory



- Kaplan–Meier estimates (based on number of vascular territories involved at baseline) of time to first primary MACE (composite of cardiovascular death, non-fatal myocardial infarction or non-fatal stroke); HRs and 95% CIs are based on Cox regression analyses.
- Verma S, et al. *Circulation.* 2018;137:2179-2183. Courtesy of John Buse

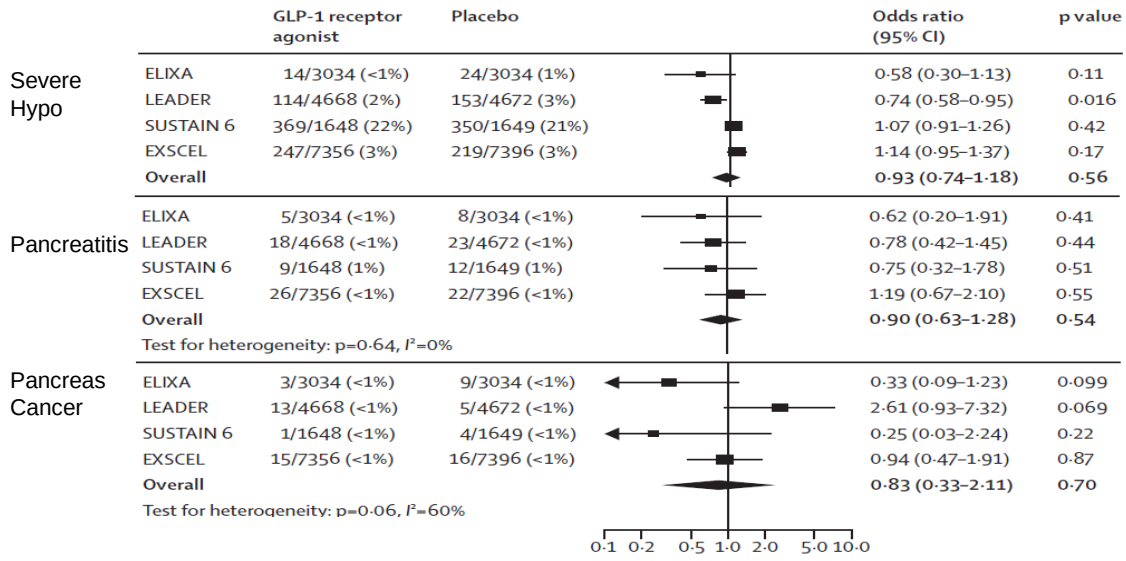
GLP1RA CVOTs: Meta-Analysis
Bethel et al. Lancet 2018; 6:105

		GLP-1 receptor agonist	Placebo	Hazard ratio (95% CI)	p value
3 Point MACE	ELIXA	400/3034 (13%)	392/3034 (13%)	1·02 (0·89–1·17)	0·776
	LEADER	608/4668 (13%)	694/4672 (15%)	0·87 (0·78–0·97)	0·015
	SUSTAIN 6	108/1648 (7%)	146/1649 (9%)	0·74 (0·58–0·95)	0·016
	EXSCEL	839/7356 (11%)	905/7396 (12%)	0·91 (0·83–1·00)	0·061
	Overall			**0·90 (0·82–0·99)**	**0·033**
	Test for heterogeneity: p=0·11, I^2=50%				
Mortality	ELIXA	211/3034 (7%)	223/3034 (7%)	0·94 (0·78–1·13)	0·50
	LEADER	381/4668 (8%)	447/4672 (10%)	0·85 (0·74–0·97)	0·020
	SUSTAIN 6	62/1648 (4%)	60/1649 (4%)	1·05 (0·74–1·50)	0·79
	EXSCEL	507/7356 (7%)	584/7396 (8%)	0·86 (0·77–0·97)	0·016*
	Overall			**0·88 (0·81–0·95)**	**0·002**
	Test for heterogeneity: p=0·63, I^2=0%				



GLP1RA CVOTs: Meta-Analysis

Bethel et al. Lancet 2018; 6:105



SGLT2i CVOTs: Meta-Analysis

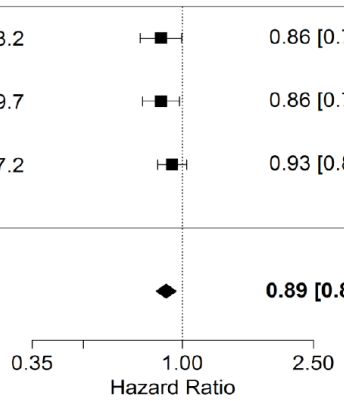
Zelniker et al. Lancet 2018; Online

	EMPA-REG OUTCOME[1]	CANVAS Program[2]	DECLARE-TIMI 58[3]
Drug	Empagliflozin	Canagliflozin	Dapagliflozin
Doses analysed	10 mg, 25 mg (once daily)	100 mg, 300 mg (once daily)	10 mg (once daily)
Median follow-up time, years	3·1	2·4	4·2
Trial participants	7020	10 142	17 160
Age, mean	63·1	63·3	63·9
Women	2004 (28·5%)	3633 (35·8%)	6422 (37·4%)
Patients with established atherosclerotic cardiovascular disease	7020 (100%)	6656 (65·6%)	6974 (40·6%)
Patients with a history of heart failure	706 (10·1%)	1461 (14·4%)	1724 (10·0%)
Patients with eGFR <60 mL/min per 1·73 m²	1819 (25·9%)	2039 (20·1%)	1265 (7·4%)

SGLT2i CVOTs: Meta-Analysis

Zelniker et al. Lancet 2018; Online

MI/Stroke, or CV Death	Patients	Events	Treatment Events per 1000 pt-yrs	Placebo Events per 1000 pt-yrs	Weights (%)	HR [95% CI]
EMPA-REG OUTCOME	7020	772	37.4	43.9	23.2	0.86 [0.74, 0.99]
CANVAS Program	10142	1011	26.9	31.5	29.7	0.86 [0.75, 0.97]
DECLARE-TIMI 58	17160	1559	22.6	24.2	47.2	0.93 [0.84, 1.03]
FE Model (P-value = 0.0014)						**0.89 [0.83, 0.96]**

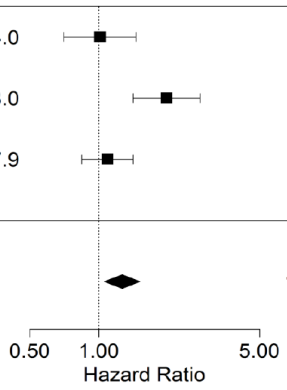


Q statistic = 1·20, p=0·55, I^2= 0%

SGLT2i CVOTs: Meta-Analysis – Side Effects

Zelniker et al. Lancet 2018; Online

Amputations	Patients	Events	Treatment Events per 1000 pt-yrs	Placebo Events per 1000 pt-yrs	Weights (%)	HR [95% CI]
EMPA-REG OUTCOME	7020	131	6.5	6.5	24.0	1.01 [0.70, 1.44]
CANVAS Program	10142	187	6.3	3.4	28.0	1.97 [1.41, 2.75]
DECLARE-TIMI 58	17143	236	3.6	3.3	47.9	1.09 [0.84, 1.40]
FE Model (P-value = 0.0096)						**1.26 [1.06, 1.51]**



Q statistic = 9·56, p=0·0084, I^2= 79·1%

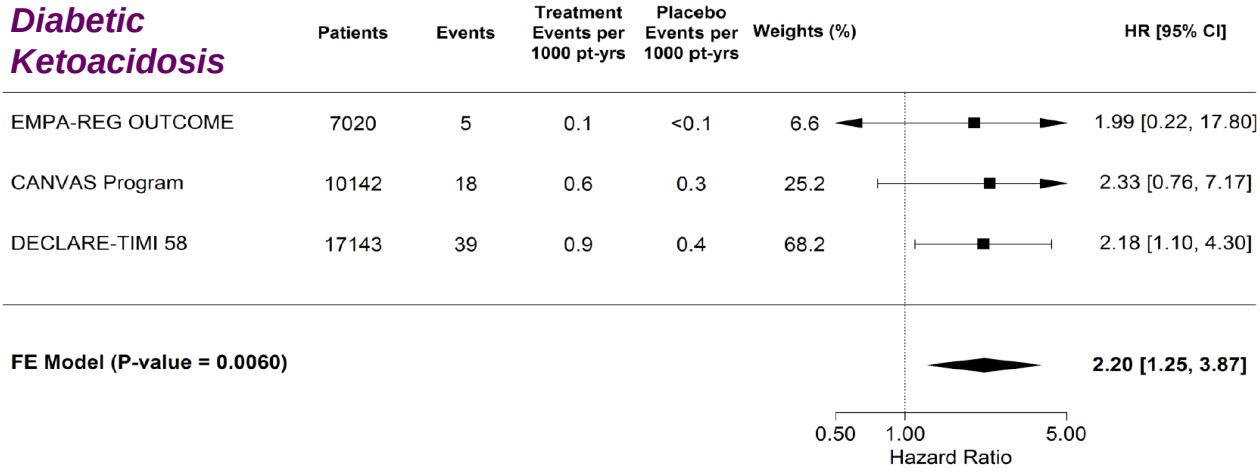
SGLT2i CVOTs: Meta-Analysis – Side Effects

Zelniker et al. Lancet 2018; Online

Q statistic = 9·16, p=0·0102, I^2= 78·2%

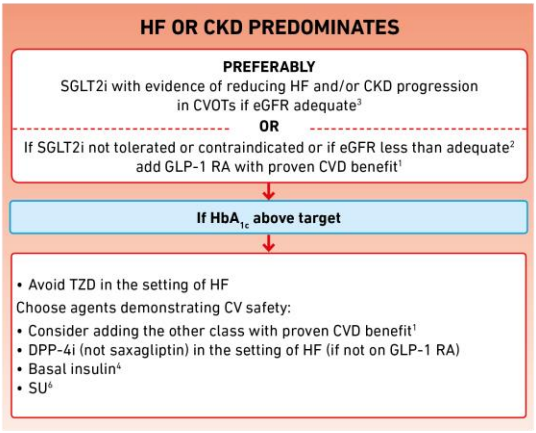
SGLT2i CVOTs: Meta-Analysis – Side Effects

Zelniker et al. Lancet 2018; Online



Q statistic = 0·02, p=0·99, I^2= 0%

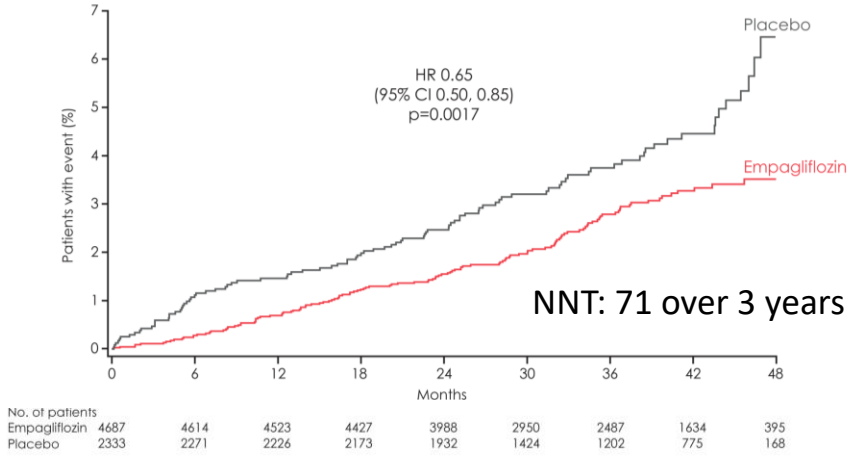
CHOOSING GLUCOSE-LOWERING MEDICATION IN THOSE WITH ESTABLISHED HF OR CKD



American Diabetes Association.

EMPA-REG

Hospitalization for heart failure, secondary outcome



Cumulative incidence function. HR, hazard ratio

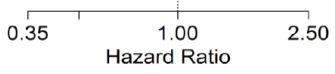
Zinman *et al. N Engl J Med* 2015;373:2117–28

American Diabetes Association.

SGLT2i CVOTs: Meta-Analysis – CV Outcomes

Zelniker et al. Lancet 2018; Online

Heart Failure Hospitalization	Patients	Events	Treatment Events per 1000 pt-yrs	Placebo Events per 1000 pt-yrs	Weights (%)	HR [95% CI]
EMPA-REG OUTCOME	7020	221	9.4	14.5	24.0	0.65 [0.50, 0.85]
CANVAS Program	10142	243	5.5	8.7	25.6	0.67 [0.52, 0.87]
DECLARE-TIMI 58	17160	498	6.2	8.5	50.4	0.73 [0.61, 0.88]
FE Model (P-value <0.0001)						**0.69 [0.61, 0.79]**

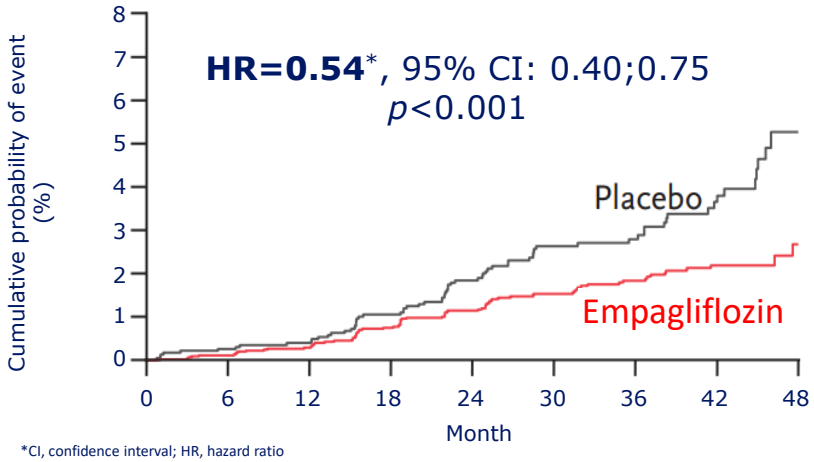


Q statistic = 0·60, p=0·74, I^2= 0%

EMPA-REG

Time to first renal event (secondary outcome)

Doubling of the serum creatinine level, the initiation of renal-replacement therapy, or death from renal disease



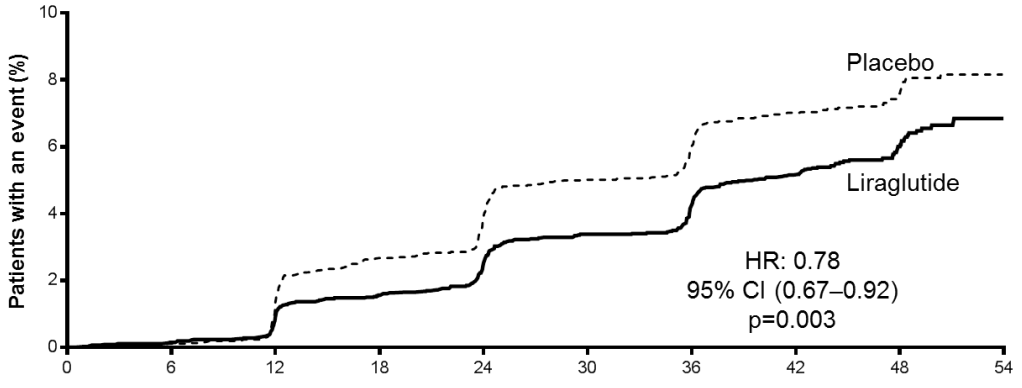
*CI, confidence interval; HR, hazard ratio

Wanner *et al. N Engl J Med* 2016;375:323-34

LEADER

Time to first renal event (secondary outcome)

Macroalbuminuria, doubling of serum creatinine, ESRD, renal death



Patients at risk										
Liraglutide	4668	4635	4561	4492	4400	4304	4210	4114	1632	454
Placebo	4672	4643	4540	4428	4316	4196	4094	3990	1613	433

The cumulative incidences were estimated with the use of the Kaplan–Meier method, and the hazard ratios with the use of the Cox proportional-hazard regression model. The data analyses are truncated at 54 months, because less than 10% of the patients had an observation time beyond 54 months. CI: confidence interval; ESRD: end-stage renal disease; HR: hazard ratio.

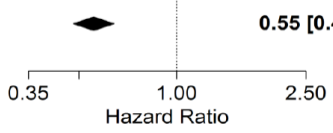
Marso SP et al. *N Engl J Med* 2016;375:311–322

American Diabetes Association.

SGLT2i CVOTs: Meta-Analysis – Renal

Zelniker et al. Lancet 2018; Online

↓ *Renal Fⁿ/ESRD Renal Death*	Patients	Events	Treatment Events per 1000 pt-yrs	Placebo Events per 1000 pt-yrs	Weights (%)	HR [95% CI]
EMPA-REG OUTCOME	7020	152	6.3	11.5	20.9	0.54 [0.40, 0.75]
CANVAS Program	10142	249	5.5	9.0	34.0	0.60 [0.47, 0.77]
DECLARE-TIMI 58	17160	365	3.7	7.0	45.1	0.53 [0.43, 0.66]
FE Model (P-value <0.0001)						**0.55 [0.48, 0.64]**



Q statistic = 0.59, p=0.74, I^2= 0%

Considerations for Therapy: HF and CKD

- **HEART FAILURE**: Hospitalization for **heart failure** was reduced consistently with SGLT2-i in two trials but was a secondary outcome

- **CHRONIC KIDNEY DISEASE:** For patients with type 2 diabetes and **CKD**, with or without cardiovascular disease, consider the use of an SGLT2 inhibitor shown to reduce CKD progression or..

  …..if contraindicated or not preferred, a GLP-1 receptor agonist shown to reduce CKD progression

American Diabetes Association.

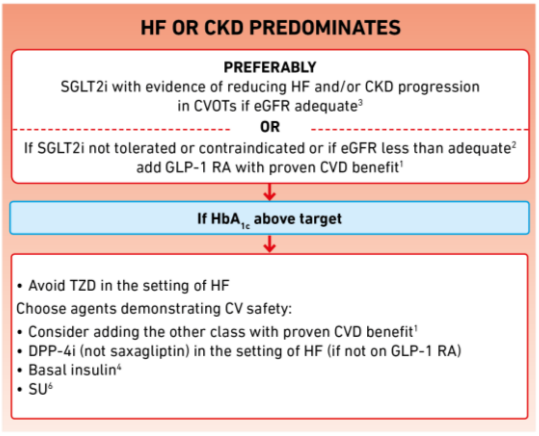
Among patients with ASCVD in whom HF coexists or is of concern, SGLT2 inhibitor are recommended

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 inhibitor trials

Caveat: trials were not designed to adjudicate heart failure

Majority of patients did not have clinical heart failure at baseline



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. Dapluxtec 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

American Diabetes Association.

Considerations for Therapy: HF and CKD

- 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 gastrointestinal side effects increase with declining renal function are not recommended in end stage renal disease due to limited experience

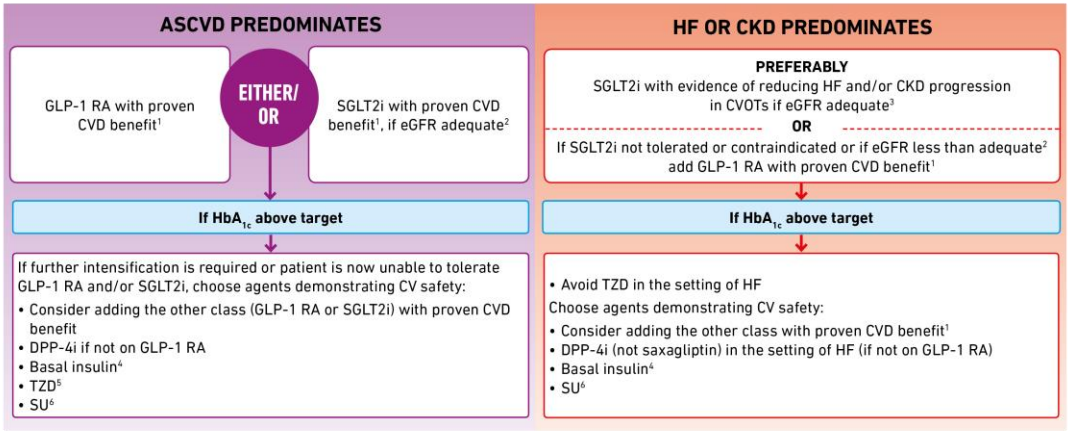
American Diabetes Association.

SGLT2i CVOTs: Meta-Analysis – Role of eGFR

Zelniker et al. Lancet 2018; Online

eGFR	↓Renal F^n, ESRD or Renal Death	Heart Failure Hospitalization	MI, Stroke, or CV Death
<60	0.67 (051, 0.89)	0.60 (0.47, 0.77)	0.82 (0.70, 0.95)
60-89	0.56 (0.46, 0.70)	0.69 (0.57, 0.83)	0.91 (0.82, 1.00)
> 90	0.44 (0,32, 0,59)	0.88 (0,68, 1.13)	0.94 (0.82, 1.07)
P Trend	0.026	0.007	0.2
As eGFR Falls…	Less effective	More effective	More effective

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



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5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU with lower risk of hypoglycaemia

American Diabetes Association.

Summarizing the Approach to Management

*Balancing **Risks** and **Benefits** for Personalized Goals*

More Stringent Control

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

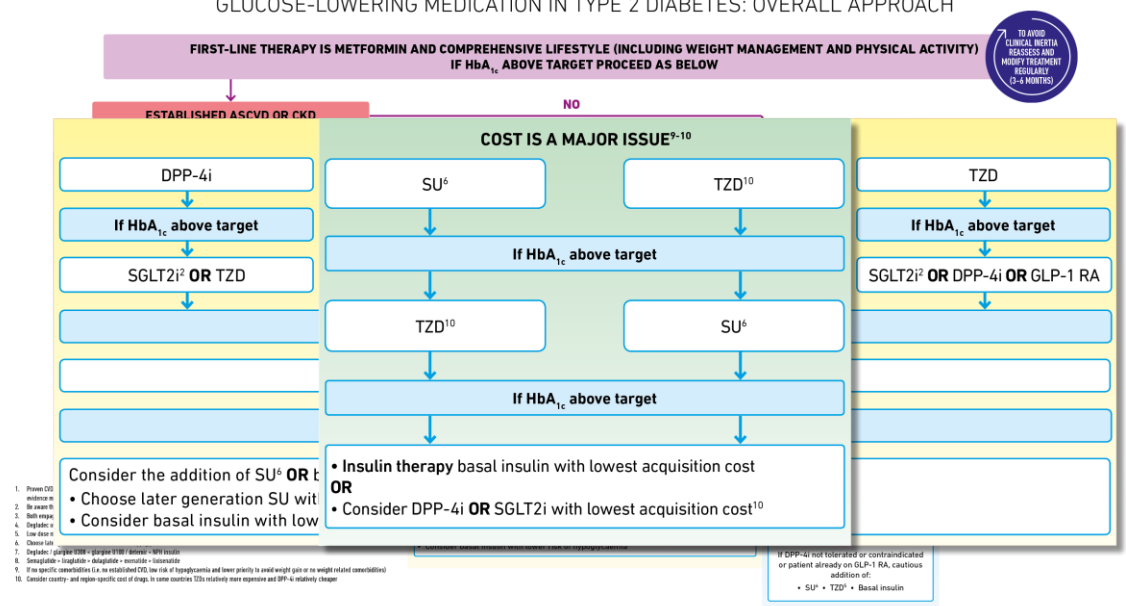
Less Stringent Control

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

American Diabetes Association.

Figure 2

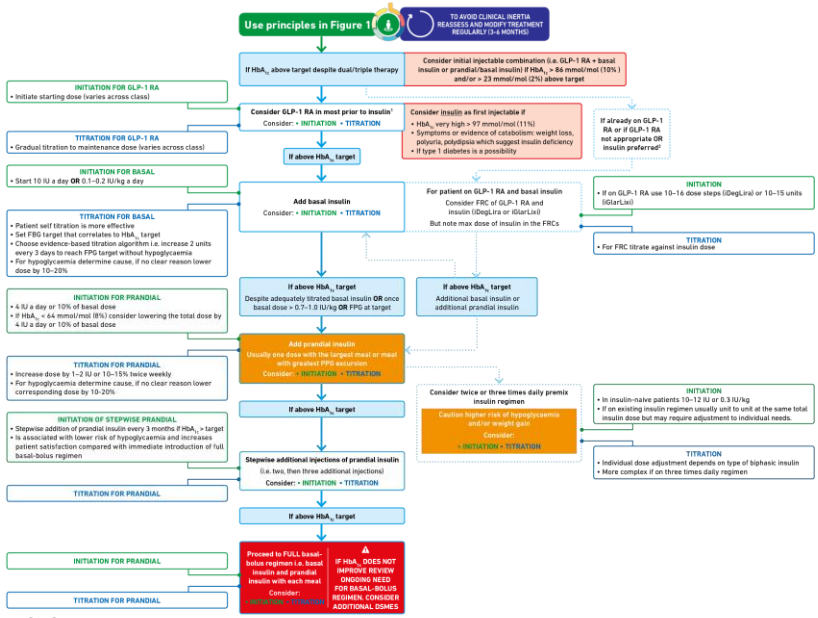
GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



American Diabetes Association.

Figure 7

INTENSIFYING TO INJECTABLE THERAPIES



1. Consider choice of GLP-1 RA considering patient preference: HbA1c 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.

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**

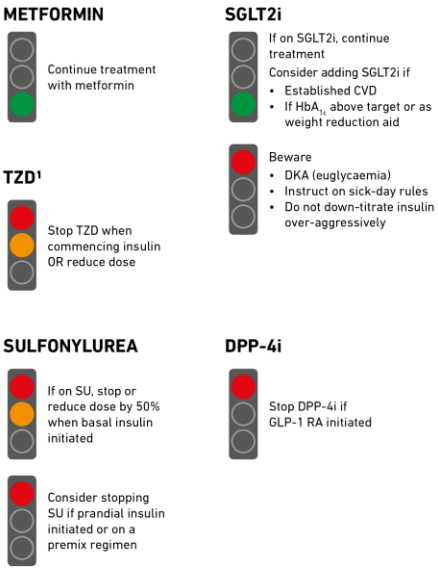
The medication regimen should be reevaluated at regular intervals (every 3–6 months) and adjusted as needed to incorporate new patient factors. **E**

American Diabetes Association.

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 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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New Onset Patient With Type 2 DM

53-year-old male patient, a college teacher, recently diagnosed with type 2 diabetes during a routine physical. The HbA1c was 7.1 %. His BMI is 32 kg/m2.

He is moderately active and walks approx. 3 miles a day 3 to 4 days a week.

Renal function is normal (estimated glomerular filtration rate [eGFR] of 79 mL/min/1.73 m2). Microalbumin was normal

He has mild dyslipidemia controlled with a statin and hypertension controlled with an angiotensin II receptor blocker (blood pressure ≤140/90 mm Hg).

Eye exam normal, rest of physical is normal with exception of central obesity.

He questions whether medication is appropriate and really wants to lose weight, but without success.

Metformin Failure

A 65-year-old female patient with 8-year history of T2DM presents with an HbA1c of 7.3 %despite receiving metformin (2000 mg/d) for the last 12 months. Her BMI is 31 kg/m2.

Blood pressure is at target on ACE-I, LDL < 70 mg/dl on statin.

She is asymptomatic, normal renal and hepatic function. FBG: 150-200, mg/dl

Eye exam normal, Central obesity present, diminished sensation to pinprick noted in lower extremities.

Failure of Metformin and DPP-4 Inhibitor

67-year-old male patient with a 10-year history of T2DM presents with an HbA1c of 9.0% despite receiving metformin (2000 mg/d) plus a DPP-4 inhibitor for the last 12 months. His BMI is 37 kg/m2.

Renal function (estimated glomerular filtration rate [eGFR] of 59 mL/min/1.73 m2). ACR was 150 µg albumin/mg creatinine.

He has dyslipidemia (LDL of 120 mg/dl) on low dose statin and hypertension (145/90) while on an angiotensin II receptor blocker and HCTZ.

He has a history of MI 5 years ago. He is not active and complains of fatigue and tiredness during afternoon walks. So, he curtails his walks.

He remains concerned with hypoglycemia, and on initial discussion, desires to avoid insulin.

Type 2 DM, Poorly Controlled, Limited Resources

45-year old male works part time in odd jobs and as a waiter.
Married and one child. Diagnosed 2 years ago, currently on metformin 1000 mg BID.

Hypertension history, but on ACE-I with good control, BP < 130/80 mmHg.
No known history of CAD.

BMI = 31, Cr 1.0, AST 29, ALT 30

No medical insurance and does not qualify for Medicaid. Due to resources, only self monitors home blood glucose twice weekly.

A1c 8.5%

Type 2 DM, Elderly, Visually impaired

80-year old retired librarian, type 2 DM for 17 years.

Hypertensive on ACE-I (BP 150/95 mmHg). LDL 110 mg/dl on moderate dose statin. Past history of angioplasty, MI approx. ten years ago, eGFR 44 mL/min/1.73 m2, AST/ALT 28/31.

The patient lives alone in a senior retirement community and uses a walker. She eats dinner in community dining room and prepares breakfast and lunch herself.

Has decreased vision and past laser surgery and current vision is 20/100. Currently on metformin 500 mg BID, She take 35 units of Glargine at night.

A1c = 8.6%

Summary of Approach

- 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

Take Away Messages

- *We have an incredible arsenal of medications and new options at our disposal*
- *Decisions on strategy and needs to be patient centered*
- *We are entering a new era where **all** co-morbidities (ASCVD, HF, CKD) needs to be considered*
- *The time is now for now for individualizing goals for the patient and recommending evidenced based strategies*

Thanks!!!