HbA1c Poor Control: Pharmacists on the care team

Presenters:

Andrew J. Ahmann M.D., Professor of Medicine, Division of Endocrinology, Diabetes and Clinical Nutrition School of Medicine and Harold Schnitzer Director of the Harold Schnitzer Diabetes Health Center

Sarah Wetherson, MA, Transformation Analyst, Oregon Health Authority

Hosted by:
Oregon Health Authority Transformation Center

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Oregon Health Authority

Financial relationship disclosures

Andrew Ahmann, MD: see table below.
Nancy Elder, MD, MSPH: no disclosures
Sarah Wetherson: no disclosures.

Name of commercial interest	Who has the relationship?	What is the relationship?		What was received?	Please provide a brief explanation of how this relationship does not cause a conflict of interest.
Novo Nordisk	myself	Consultant		Consulting Fees	The programs will be evidence based and use no brand names. Recommendations for therapy will emphasize classes of medications and strictly adhere to national guidelines (e.g. American Diabetes Association guidelines.
Lilly	myself	Consultant		Consulting Fees	The programs will be evidence based and use no brand names. Recommendations for therapy will emphasize classes of medications and strictly adhere to national guidelines (e.g. American Diabetes Association guidelines.
Dexcom	myself	Investigator	local PI for research studiies developing continuous glucose monitoring advances	Grant Support	CGM is not part of the discussion topics.
Medtronic	myself	Consultant	Expert advisory board	Consulting Fees	Relationship unrelated to subject matter of this program. Insulin pumps will not be addressed.

Getting CME credit

- After this webinar, we'll send a link to the post-test and evaluation
- Please complete the post-test and evaluation by Monday, February 24
- Certificates will come from OHSU within the next 8 weeks

Addressing Poor HbA1c Control: Clinic-based Solutions

Pharmacists As Part Of The Care Team

PRESENTED BY: Andrew Ahmann, MD

Conflict of Interest

- I have the following Conflicts of Interest to report
  - ✧ Grants/Research
    - Lilly, Dexcom
  - ✧ Consultant
    - Lilly, Novo Nordisk, Medtronic

- Any non-approved medication use will be identified.

Reviewing the importance of controlling diabetes.

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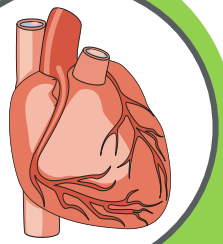
Diabetes Statistics

- 30.3 millions have diabetes in the US
  - 9.4% of the population
  - 12.2% of adults
- Rates higher for American Indians, Blacks and Hispanic
- 33.9% of US adults have prediabetes
- 2017 costs estimated at $327 billion in US
  - Costs are increasing rapidly (26% from 2012-2017)
- Costly complications of diabetes are decreasing but rates remain much higher than the general population.

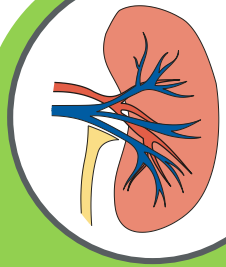
National Diabetes Statistics Report, 2017 (CDC)
American Diabetes Association, Diabetes Care 2018; 41:917-928

Clinical Impact of Diabetes

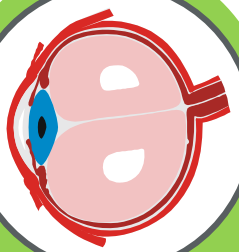
Diabetes



2- to 4-fold increase in cardio-vascular disease



Leading cause of new cases of kidney failure



Leading cause of new cases of blindness in working-aged adults

Leading cause of lower extremity amputations

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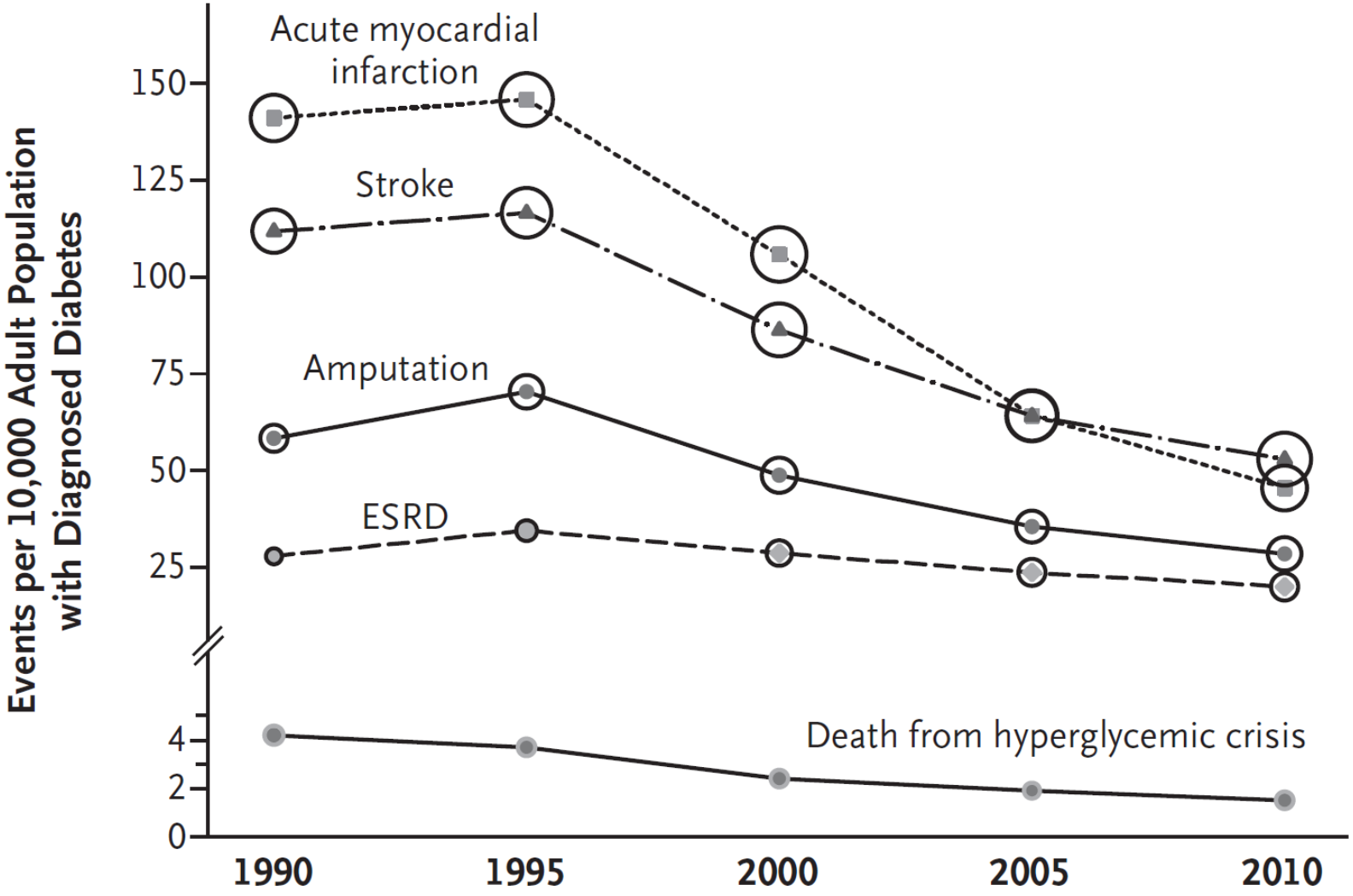
Changes in Diabetes Related Complications from 1990-2010



Gregg EW et al. N Engl J Med 2014; 370:514-523

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Changes in Diabetes Complication Rates

Complication	% Reduction	Relative Rate
MI with DM	**- 67.8**	1.8
MI without DM	-31.2	
Stroke with DM	**-52.7**	1.5
Stroke without DM	- 5.5	
LEA with DM	**- 57.4**	2.7
LEA without DM	- 12.9	
ESRD with DM	**- 28.3**	6.1
ESRD without DM	+ 65	

- Data from National Health Interview Survery, National Hospital Discharge Survey, US Renal Data System and US National Vital Statistics System
- 1990-2010

Gregg EW et al. N Engl J Med 2014; 370: 514-523

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What We Know About Benefit of Glucose Control In Type 2 Diabetes

- **Microvascular complications** (including neuropathy)
  - Benefit with early intervention
    - UKPDS
  - Benefit from later improvements in glucose control
    - ACCORD
    - ADVANCE
    - VADT
- **Macrovascular complications**
  - Long-term benefit with early intervention
    - UKPDS, confirmed on extension
  - No significant benefit shown in those intensified later
    - ACCORD, ADVANCE

Gerstein HC, et al. *NEJM.* 2008;358:2545-2559. Patel A, et al. *NEJM.* 2008;358:2560-2572. Duckworth W, et al. *NEJM* 2009;360:129-139. UKPDS Group. *Lancet.* 1998;352:837-853. Ismail-Geigi F, et al. *Ann Intern Med.* 2011;154:554-559.

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Diabetes Management is More Than Glucose Control

Standard vs Intensive Therapy in T2DM – Steno 2 Study

Table 1. Treatment Goals for the Conventional-Therapy Group and the Intensive-Therapy Group.*

Variable	Conventional Therapy		Intensive Therapy	
	1993–1999	2000–2001	1993–1999	2000–2001
Systolic blood pressure (mm Hg)	<160	<135	<140	<130
Diastolic blood pressure (mm Hg)	<95	<85	<85	<80
Glycosylated hemoglobin (%)	<7.5	<6.5	<6.5	<6.5
Fasting serum total cholesterol (mg/dl)	<250	<190	<190	<175
Fasting serum triglycerides (mg/dl)	<195	<180	<150	<150
Treatment with ACE inhibitor irrespective of blood pressure	No	Yes	Yes	Yes
Aspirin therapy				
For patients with known ischemia	Yes	Yes	Yes	Yes
For patients with peripheral vascular disease	No	No	Yes	Yes
For patients without coronary heart disease or peripheral vascular disease	No	No	No	Yes

Differences at Analysis

- ↑ CHO
- ↓ Fat
- ↑ Exercise
- ↓ A1C (0.7%)
- ↓ LDL
- ↓ Urine Albumin
- ↓ BP

Gaede P et al. NEJM 2003; 348:383-393

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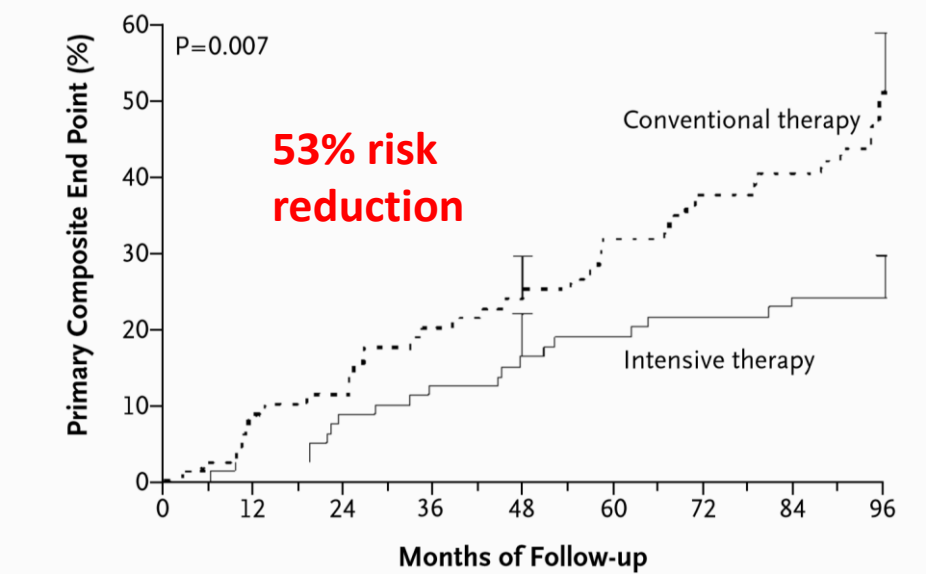
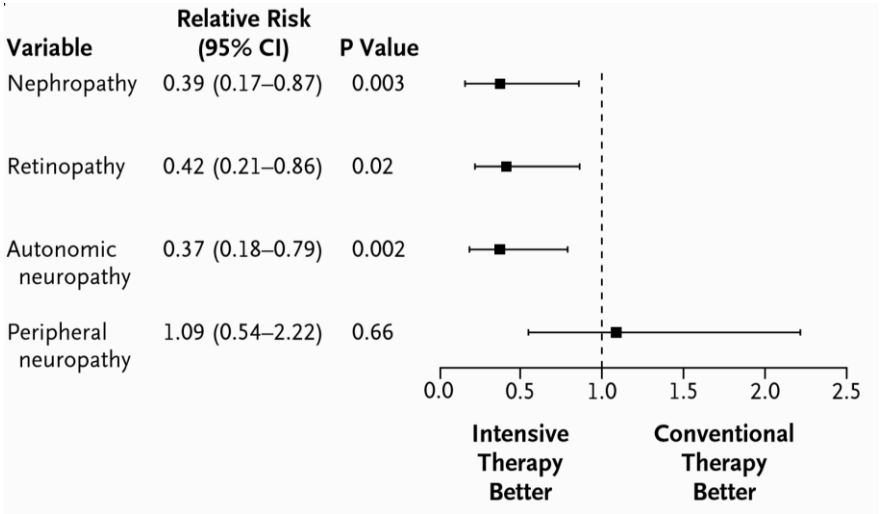
Steno-2 Study Results

Comprehensive Therapy Is Important





Primary Outcome: 5 point MACE

CV death, nonfatal MI, nonfatal stroke, revascularization, amputation

A 21 year follow-up also showed an almost 8 year longer life.

Gaede P et al. NEJM 2003; 348: 383-393

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ADA Standards of Care 1989

- First published standards of care
- Publication was 4 pages long
- No specific recommendations for:
  - Glucose control
  - BP control
  - Lipid management
  - Eye care (only referral to ophthalmology)
  - Foot exam
  - Kidney evaluation or management

Diabetes Care 1989; 12:365-368

ADA Standards of Care 2020

- Now 212 pages in 16 sections
- Population health:
  - Team approach with collaborative effort including patient
  - Treatment decisions must be evidence based
  - Employ Chronic Care Model, use registries, decisions support tools
  - Utilize lay health coaches and community health workers
  - Always assess social context
  - Identify patients with pre-diabetes
    - Refer to a Diabetes Prevention Program

Diabetes Care 2020; 43(Suppl 1): S1-S212

ADA Standards of Care 2020

- Important to have diabetes self-management education and support
  - Patient centered
  - Should be reimbursed
  - Nutrition recommendations are individualized
  - Most adults should get 150 minutes of moderate intensity exercise per week
- Individualize A1C goals
  - Depends on age, co-morbidities, complications, risk of hypoglycemia.

Diabetes Care 2020; 43(Suppl 1): S1-S212

ADA Standards of Care 2020

- Check A1C at least twice yearly
  - Target depends on age, co-morbidities, complications, risk of hypoglycemia.
- Ask about hypoglycemia any time the patient is on an agent that can cause hypoglycemia
- Patient glucose monitoring depending on agents and intensity of insulin therapy

Diabetes Care 2020; 43(Suppl 1): S1-S212

ADA Standards of Care 2020

- Monitor blood pressure
  - Usually treat with medication if ≥140/ 90
  - Goal is ≤ 130/80 for those with high CV risk
    - 10-year CV risk ≥ 15%
- CVD Prevention beyond BP
  - Moderate intensity statin in patients without CV disease age 40-75
  - If patient has CV disease or very high risk ►high dose
  - If 10 year risk ≥ 20% and LDL ≥ 70 mg/dl or LDL decrease >50%
    - Add ezetimibe or PCSK9 inhibitors
  - T2DM w ASCVD, SGLT2i or GLP-1 RA if A1C elevated
- ASA for secondary prevention

Diabetes Care 2020; 43(Suppl 1): S1-S212

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ADA Standards of Care 2020

- Screening for microvascular complications
  - Microalbumin:creatinine ratio yearly (repeat if +)
  - Eye exam yearly
  - Comprehensive foot exam yearly
- Treat microvascular complications
  - Nephropathy - - ACEI/ARB, BP ↓, A1C ↓, SGLT2 inh
  - Eyes - - Glucose control, laser Tx, VEGF
  - Neuropathy - - A1C ↓, special footwear for highest risk
- For older adults:
  - Screen for cognitive deficits
  - High priority to avoid hypoglycemia

Diabetes Care 2020; 43(Suppl 1): S1-S212

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What is Accomplished in a Visit

- Review interim history
  - Success in accomplishing previously stated goals
  - Any changes in diet or activity or stressors
  - ROS focusing on diabetes complications / comobidities
- Review of diabetes specific health maintenance
- Pertinent physical exam (e.g. feet)
- Review of data:
  - A1C, BGs, Lipids, microalbumin
- Allow patient to ask questions
- Discuss potential changes in therapy or goals
  - Involve patient in the decision.

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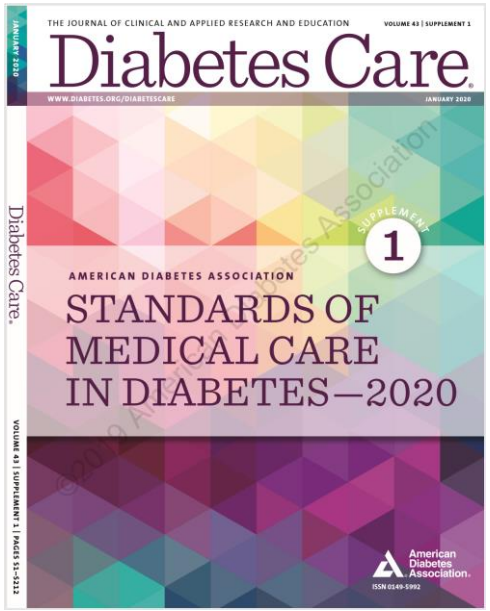
Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Melanie J. Davies,[1,2] David A. D'Alessio,[3] Judith Fradkin,[4] Walter N. Kernan,[5] Chantal Mathieu,[6] Geltrude Mingrone,[7,8] Peter Rossing,[9,10] Apostolos Tsapas,[11] Deborah J. Wexler,[12,13] and John B. Buse[14]

Diabetes Care 2018;41:2669–2701 | https://doi.org/10.2337/dci18-0033

Incorporated into the ADA Standards of Care in the January 2020 supplement of *Diabetes Care*



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Successful Diabetes Care is a Team Effort

- Diabetes educator (multiple training backgrounds)
- Pharmacist
- RD
- Care Coordinator
- Physician or APP
- Podiatrist
- Psychologists or social workers
- Ophthalmologist
- Specialists to manage complications

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Barriers To Successful Diabetes Management

- Provider inertia - - Delay in progression of therapy to reach target
- Behavioral barriers
- Non-adherence
- Hypoglycemia
- Weight gain
- Lack of knowledge
- Physical disability
- Cultural factors and language barriers
- Personal health beliefs
- Costs/ financial resources

Adapted from Funnell MM. *Clinical Diabetes*. 2007;25(1):36-38. Derr RL, et al. *Diabetes Spectrum*. 2007; 20(3):177-185. Karter AJ, et al. *Diabetes Care.* 2010;33(4):733-735.

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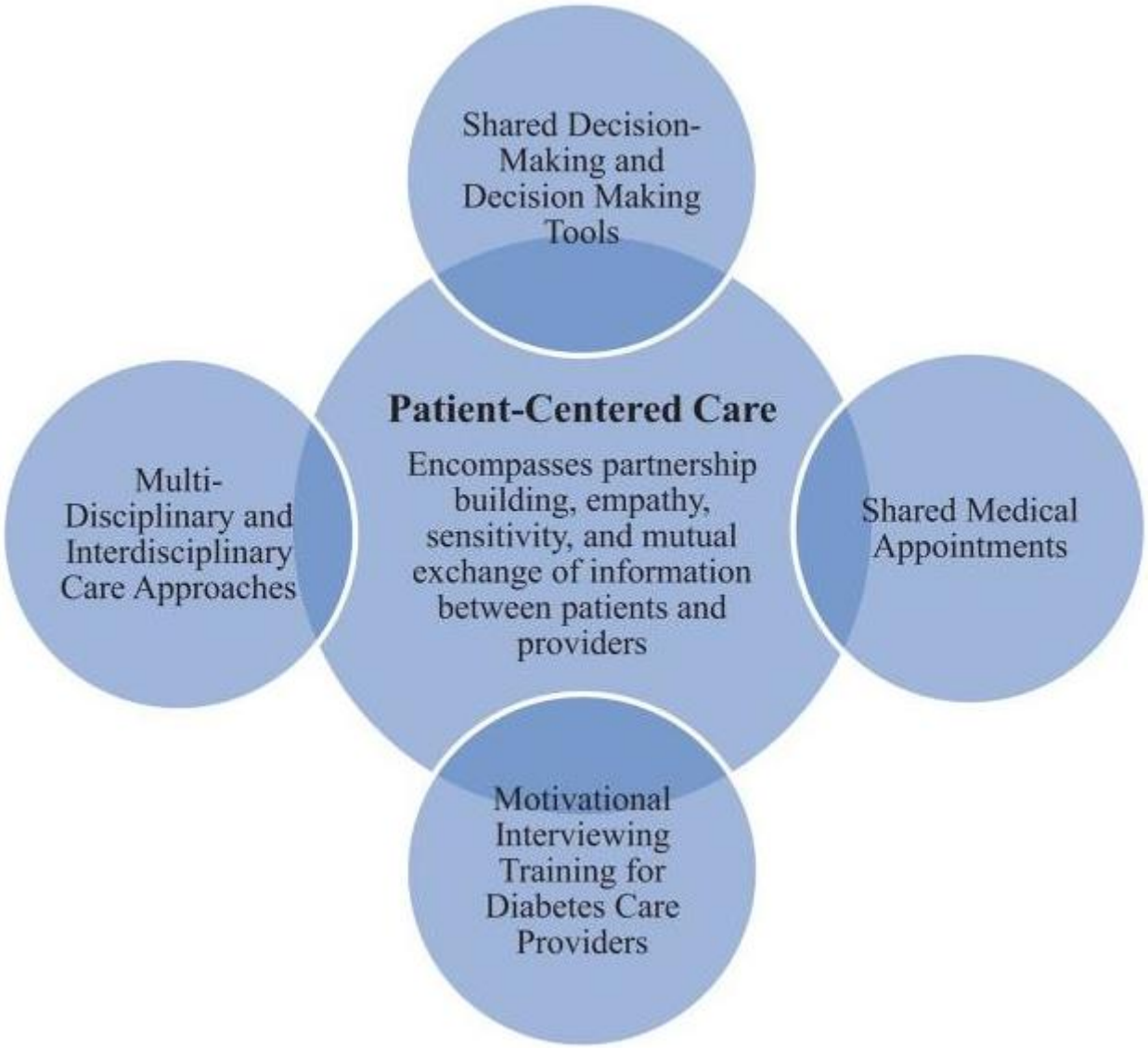

Powell PW et al Curr Diabetes rev 2015; 11:222-230

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Figure 1

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

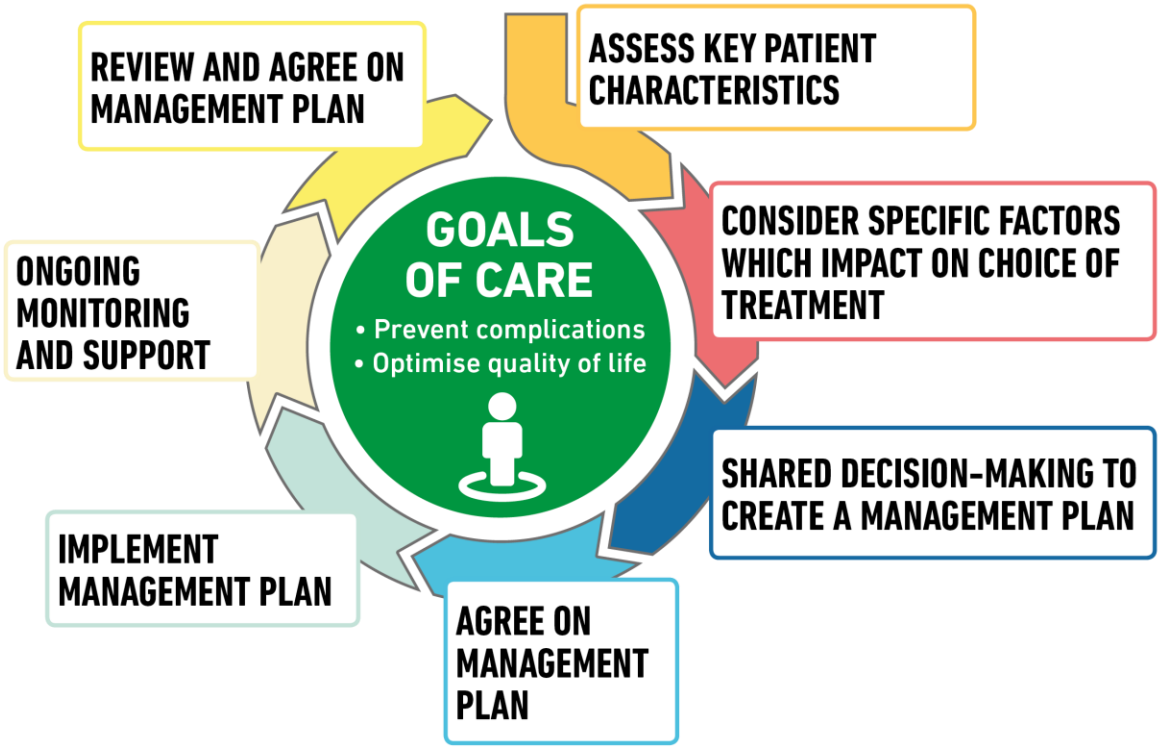

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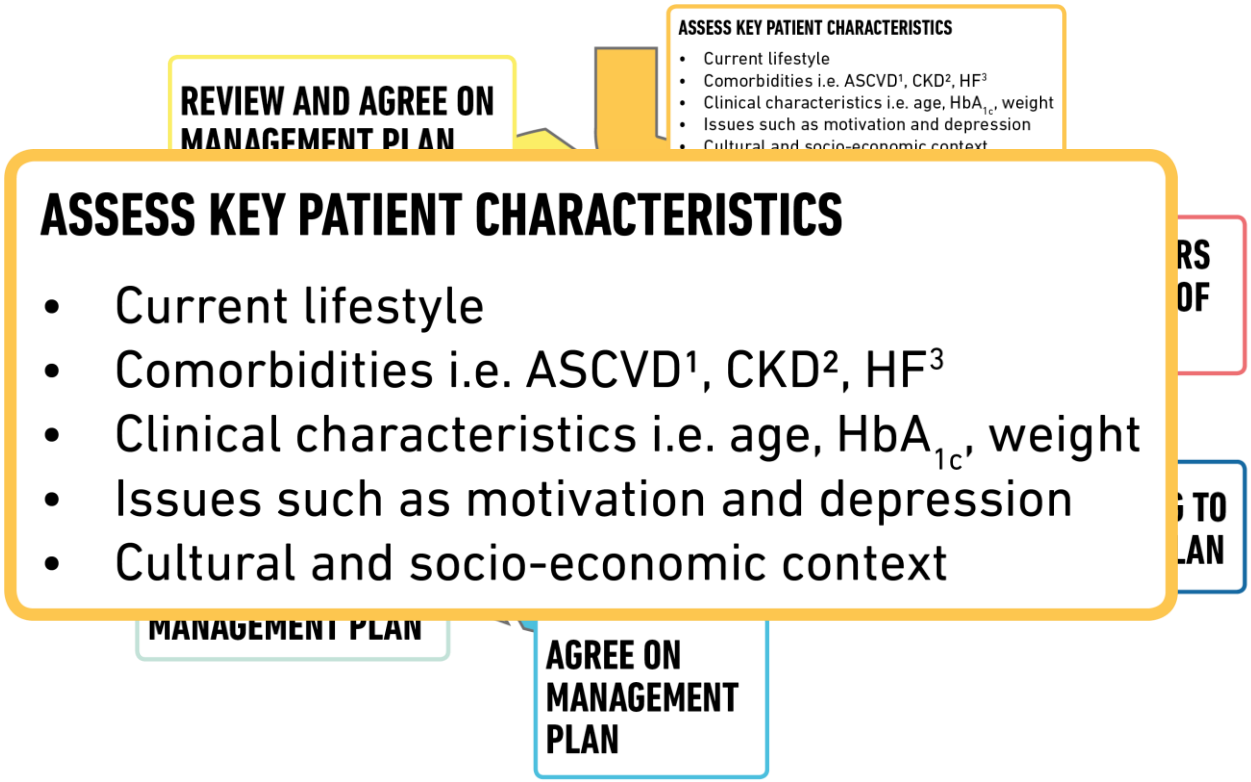
Figure 1

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



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

- A1C Goal for most nonpregnant adults is < 7.0%
- Goal is set with patient and should be higher for some (e.g. 7-8%)

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

Components of Hyperglycemic Management

Lifestyle

- Medical Nutrition Therapy
- Physical activity

Medications

Metabolic Surgery

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Diabetes Self-Management Education and Support: Delivery.

Four critical time points for DSMES delivery:

1. At diagnosis;
2. Annually for assessment of education, nutrition, and emotional needs;
3. When new complicating factors (health conditions, physical limitations, emotional factors, or basic living needs) arise that influence self-management; and
4. When transitions in care occur such as new meds or progressive renal insufficiency

DSMES is among the recommended standards of care that is most overlooked.

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Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report

Diabetes Care 2019;42:731–754 | https://doi.org/10.2337/dci19-0014

Alison B. Evert,[1] Michelle Dennison,[2] Christopher D. Gardner,[3] W. Timothy Garvey,[4,5] Ka Hei Karen Lau,[6] Janice MacLeod,[7] Joanna Mitri,[8] Raquel F. Pereira,[9] Kelly Rawlings,[10] Shamera Robinson,[11] Laura Saslow,[12] Sacha Uelmen,[11] Patricia B. Urbanski,[13] and William S. Yancy Jr.[14,15]

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For Details on Each Medication Please See . . . .

Table 9.1—Drug-specific and patient factors to consider when selecting antihyperglycemic treatment in adults with type 2 diabetes

	Efficacy	Hypoglycemia	Weight change	CV effects		Cost	Oral/SQ	Renal effects		Additional considerations
				ASCVD	CHF			Progression of DKD	Dosing/use considerations*	
Metformin	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Low	Oral	Neutral	▪ Contraindicated with eGFR <30	▪ Gastrointestinal side effects common (diarrhea, nausea) ▪ Potential for B12 deficiency
SGLT-2 inhibitors	Intermediate	No	Loss	Benefit: empagliflozin†, canagliflozin	Benefit: empagliflozin†, canagliflozin	High	Oral	Benefit: canagliflozin, empagliflozin	▪ Renal dose adjustment required (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin)	▪ **FDA Black Box:** Risk of amputation (**canagliflozin**) ▪ Risk of bone fractures (canagliflozin) ▪ DKA risk (all agents, rare in T2DM) ▪ Genitourinary infections ▪ Risk of volume depletion, hypotension ▪ ↑LDL cholesterol ▪ Risk of Fournier's gangrene
GLP-1 RAs	High	No	Loss	Neutral: lixisenatide Benefit: liraglutide† > semaglutide > exenatide extended release	Neutral	High	SQ	Benefit: liraglutide	▪ Renal dose adjustment required (exenatide, lixisenatide) ▪ Caution when initiating or increasing dose due to potential risk of acute kidney injury	▪ **FDA Black Box:** Risk of thyroid C-cell tumors (**liraglutide, albiglutide, dulaglutide, exenatide extended release**) ▪ Gastrointestinal side effects common (nausea, vomiting, diarrhea) ▪ Injection site reactions ▪ ?Acute pancreatitis risk
DPP-4 inhibitors	Intermediate	No	Neutral	Neutral	Potential risk: saxagliptin, alogliptin	High	Oral	Neutral	▪ Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment ▪ No dose adjustment required for linagliptin	▪ Potential risk of acute pancreatitis ▪ Joint pain
Thiazolidinediones	High	No	Gain	Potential benefit: pioglitazone	Increased risk	Low	Oral	Neutral	▪ No dose adjustment required ▪ Generally not recommended in renal impairment due to potential for fluid retention	▪ **FDA Black Box:** Congestive heart failure (**pioglitazone, rosiglitazone**) ▪ Fluid retention (edema; heart failure) ▪ Benefit in NASH ▪ Risk of bone fractures ▪ Bladder cancer (pioglitazone) ▪ ↑LDL cholesterol (rosiglitazone)
Sulfonylureas (2nd generation)	High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	▪ Glyburide: not recommended ▪ Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia	▪ FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)
Insulin — Human Insulin	Highest	Yes	Gain	Neutral	Neutral	Low	SQ	Neutral	▪ Lower insulin doses required with a decrease in eGFR; titrate per clinical response	▪ Injection site reactions ▪ Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs
Insulin — Analogs						High	SQ			

*For agent-specific dosing recommendations, please refer to the manufacturers' prescribing information. †FDA approved for CVD benefit. CHF, congestive heart failure; CV, cardiovascular; DPP-4, dipeptidyl peptidase 4; DKA, diabetic ketoacidosis; DKD, diabetic kidney disease; GLP-1 RAs, glucagon-like peptide 1 receptor agonists; NASH, nonalcoholic steatohepatitis; SGLT2, sodium–glucose cotransporter 2; SQ, subcutaneous; T2DM, type 2 diabetes.

ADA Standards of Care in Diabetes Care 2020; 43(suppl 1): S101

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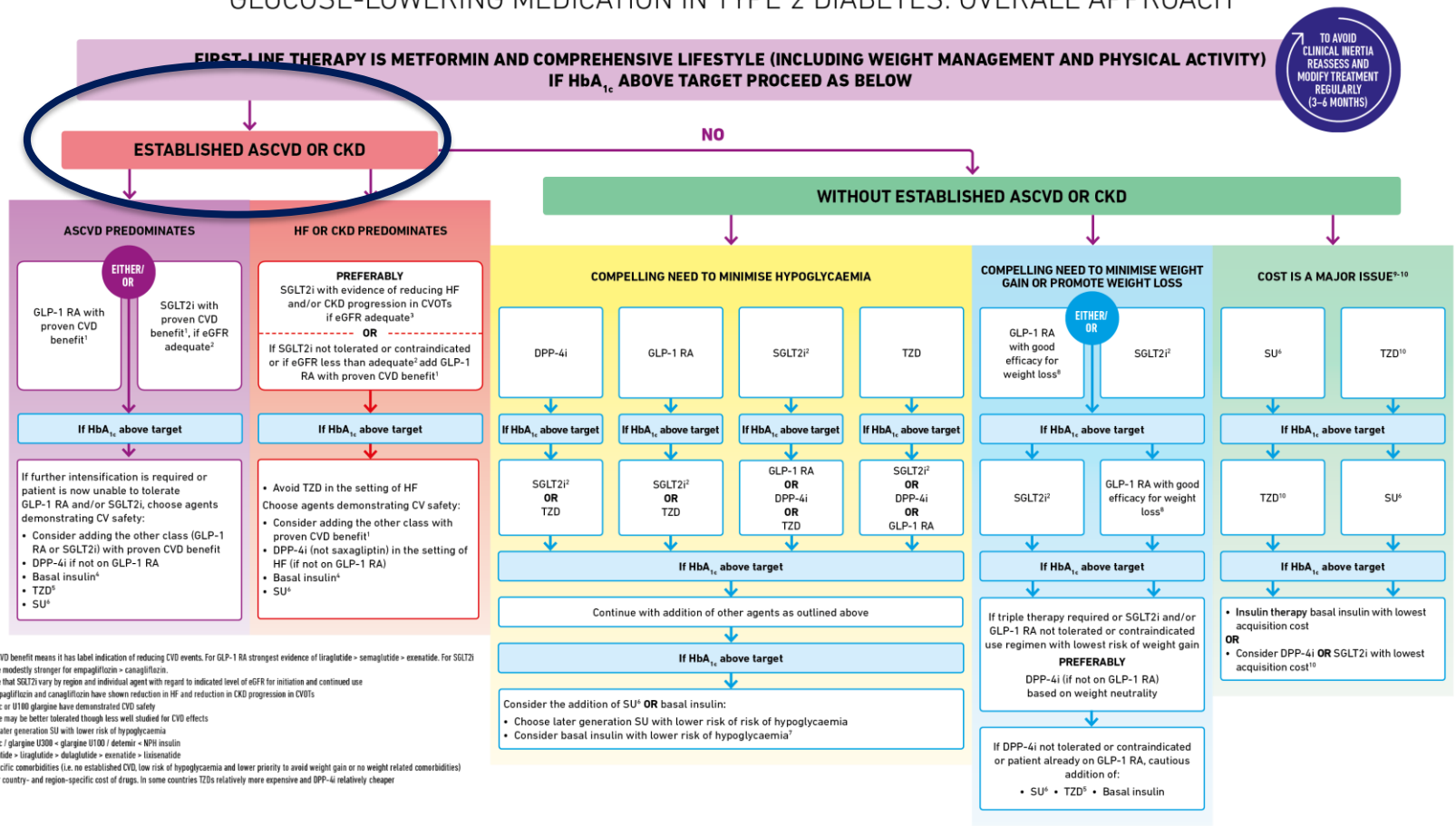
Figure 2

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



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 TZDs relatively more expensive and DPP-4i relatively cheaper

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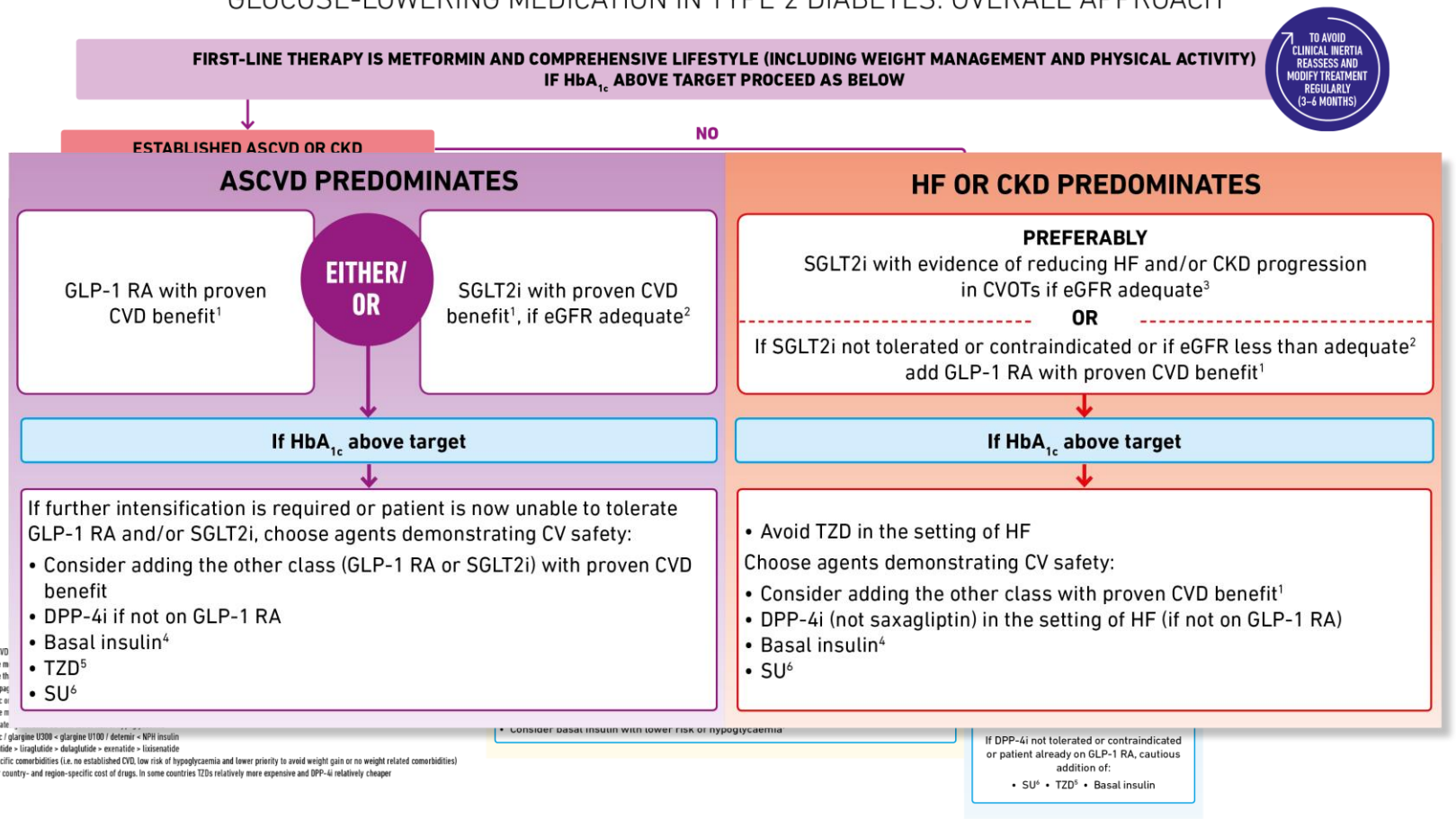
Figure 2

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



Effects of Newer DM Medications: MACE (Major Cardiovascular Events)

Drug Class	LEADER	REWIND	SUSTAIN-6*	EXSCEL
GLP-1 Long acting agonists	Beneficial	Beneficial	Beneficial	Neutral
	EMPA-REG	**CANVAS**	**DECLARE**	**CREDENCE**
SGLT2-Inhibitor	Beneficial	Beneficial	Neutral	Beneficial

MACE = Major Adverse Cardiovascular Events: CV death, MI, stroke.
* Statistical testing for superiority not prespecified in SUSTAIN-6

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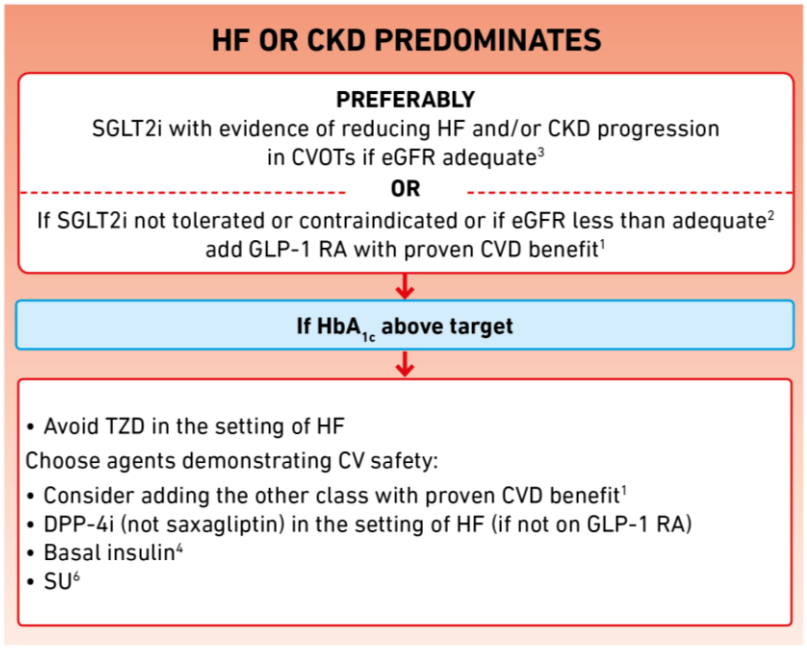
Among patients with ASCVD in whom HF coexists or is of concern, SGLT2 inhibitor are recommended

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 inhibitor trials

Caveat: trials were not designed to adjudicate heart failure

Majority of patients did not have clinical heart failure at baseline



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Effects of Newer DM Medications: Heart Failure

Drug Class	LEADER	REWIND	SUSTAIN-6*	EXSCEL
GLP-1 Long acting agonists	Neutral	Neutral	Neutral	Neutral
	EMPA-REG	**CANVAS**	**DECLARE**	**CREDENCE**
SGLT2-Inhibitor	 Beneficial	 Beneficial	 Beneficial	 Beneficial

MACE = Major Adverse Cardiovascular Events: CV death, MI, stroke.
* Statistical testing for superiority not prespecified in SUSTAIN-6

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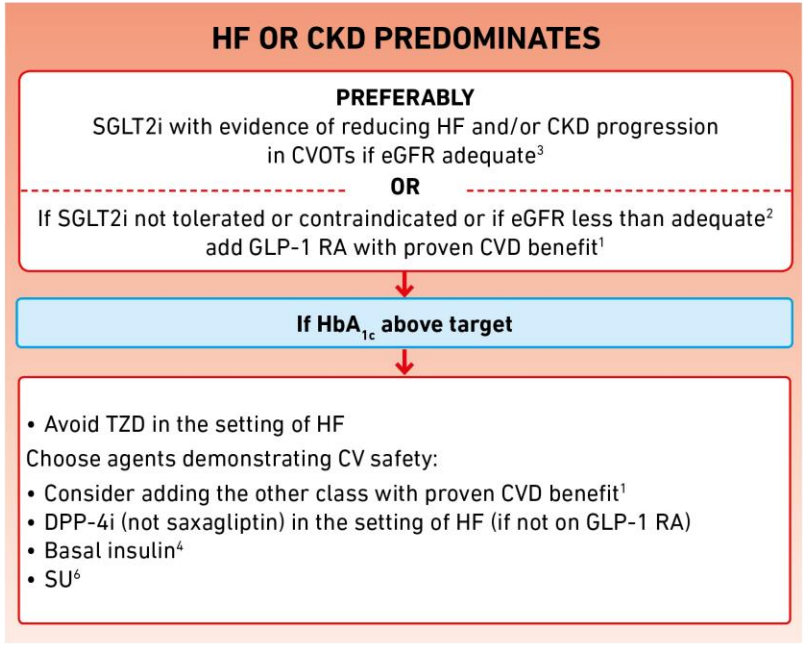
CHOOSING GLUCOSE-LOWERING MEDICATION IN THOSE WITH ESTABLISHED HF OR CKD



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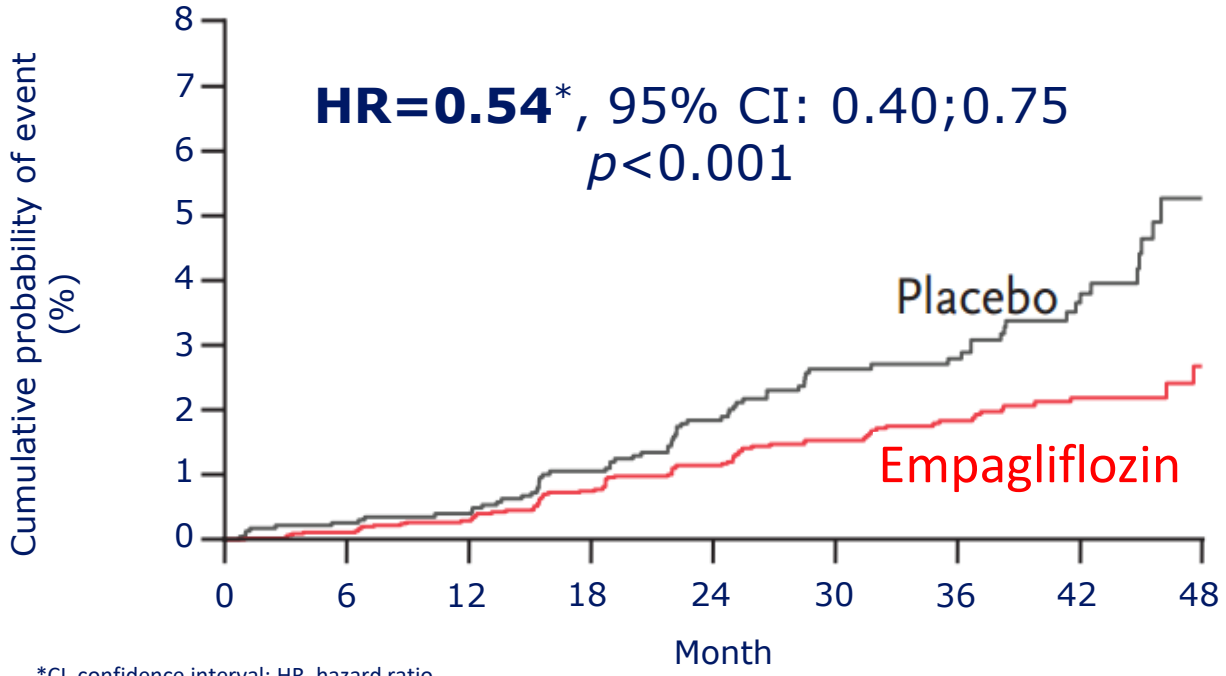
EMPA-REG

Time to first renal event (secondary outcome) with empagliflozin

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

46% reduction in progression of kidney disease in high CV risk patients

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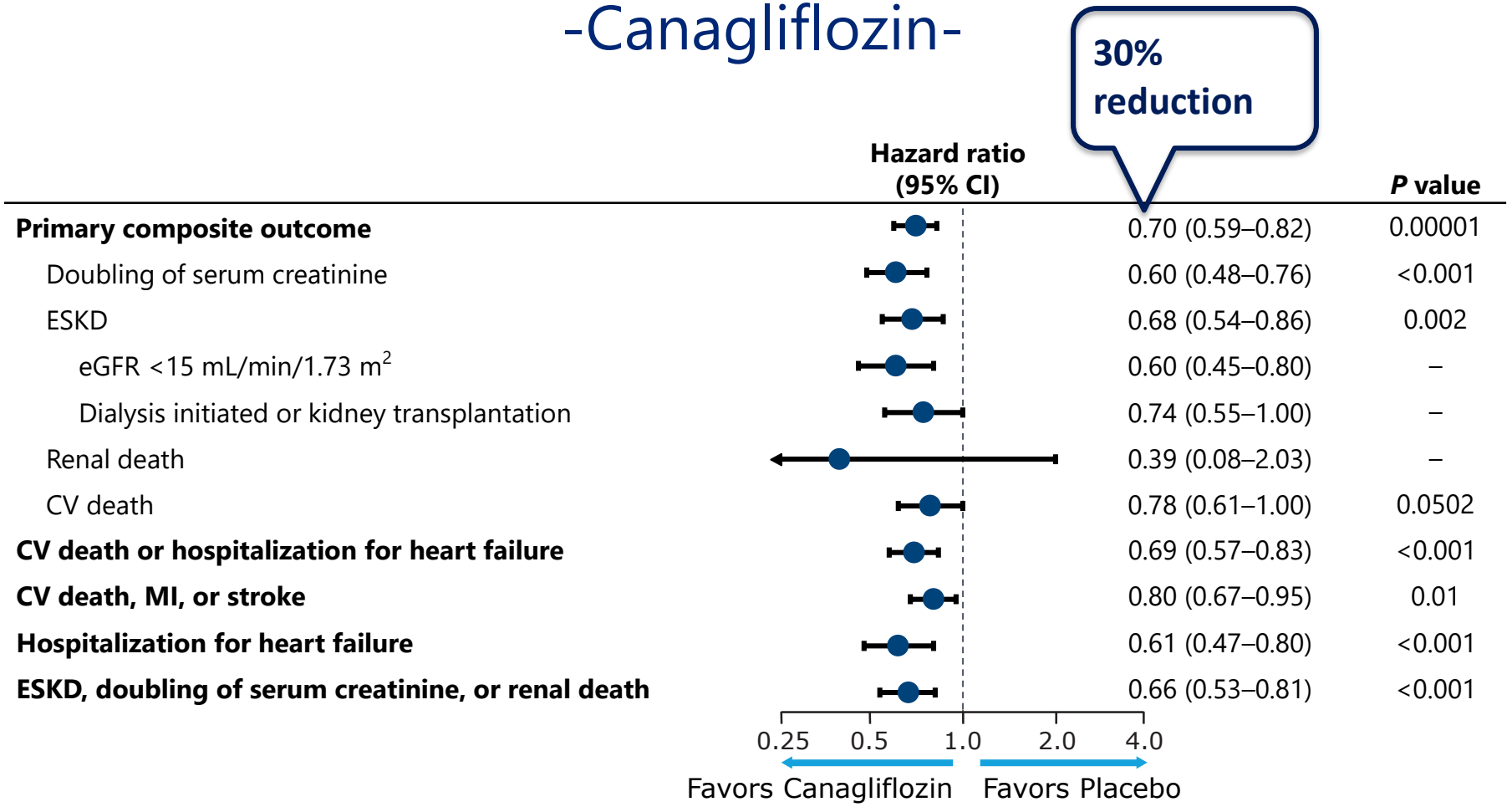
CREDENCE: Summary Of Results

Primary Outcome Renal Rather Than CV

-Canagliflozin-



Primary outcome was positive even in the subgroup with eGFR 30-45 ml/min

Perkovic V et al. NEJM 2019; 380:2295-2306

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CKD Considerations

SGLT2-i are registered as glucose-lowering agents to be started if eGFR>45/min/1.73m^2

SGLT2-I are generally stopped at eGFR < 45, 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

GLP-1 RA are not recommended in end stage renal disease due to limited experience

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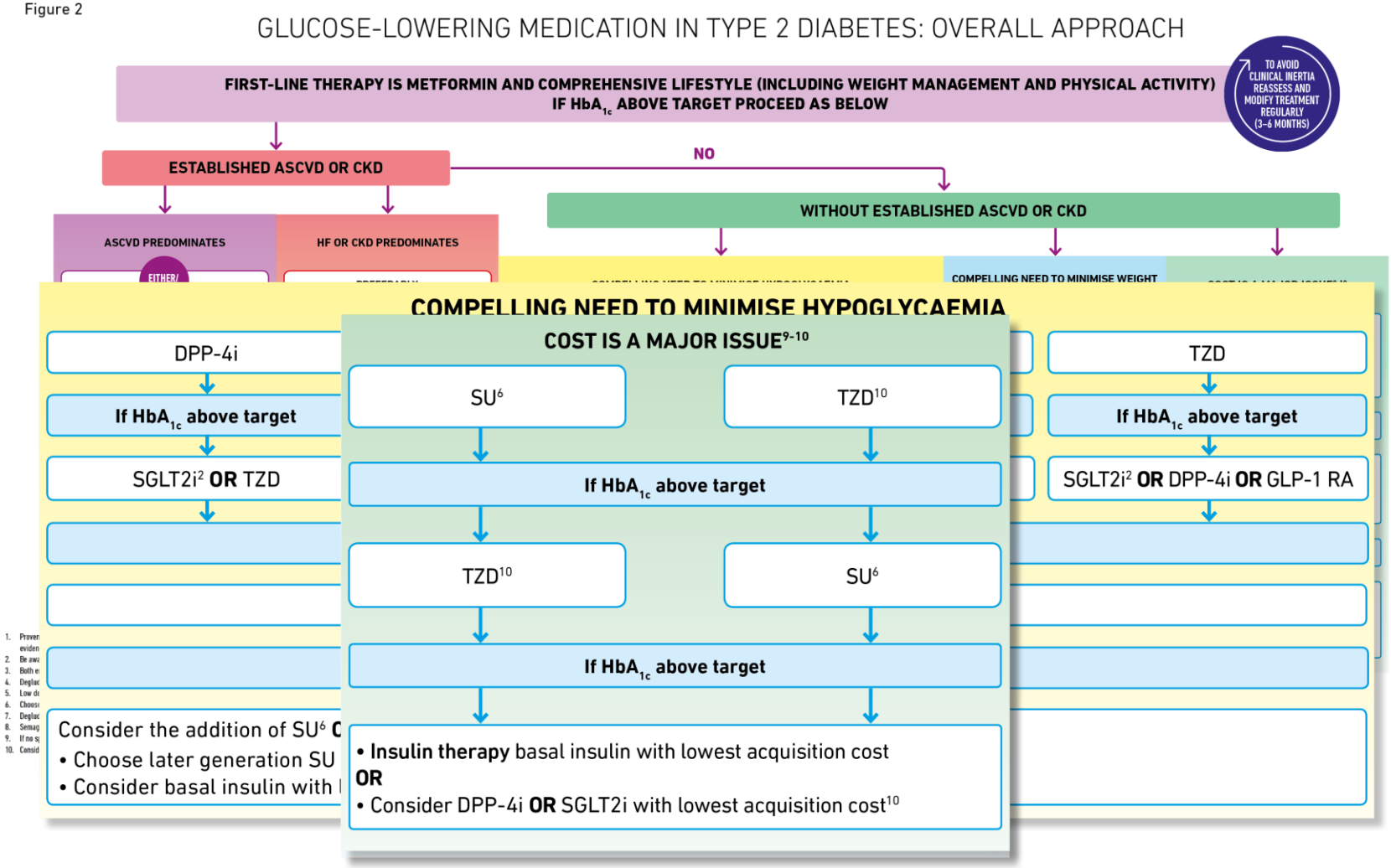
Figure 2


GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH
FIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY)
IF HbA1c ABOVE TARGET PROCEED AS BELOW
TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)
ESTABLISHED ASCVD OR CKD
NO
WITHOUT ESTABLISHED ASCVD OR CKD
ASCVD PREDOMINATES
HF OR CKD PREDOMINATES
COMPELLING NEED TO MINIMISE WEIGHT
COMPELLING NEED TO MINIMISE HYPOGLYCAEMIA
COST IS A MAJOR ISSUE9-10
DPP-4i
If HbA1c above target
SGLT2i2 OR TZD
SU6
TZD10
If HbA1c above target
TZD10
SU6
If HbA1c above target
• Insulin therapy basal insulin with lowest acquisition cost
OR
• Consider DPP-4i OR SGLT2i with lowest acquisition cost10
TZD
If HbA1c above target
SGLT2i2 OR DPP-4i OR GLP-1 RA
Consider the addition of SU6
• Choose later generation SU
• Consider basal insulin with

Diabetes Medications Can Be Costly

Table 9.2—Median monthly cost of maximum approved daily dose of noninsulin glucose-lowering agents in the U.S.

Class	Compound(s)	Dosage strength/product (if applicable)	Median AWP (min, max)†	Median NADAC (min, max)†	Maximum approved daily dose*
Biguanides	• Metformin	500 mg (IR)	$84 ($4, $93)	$2	2,000 mg
		850 mg (IR)	$108 ($6, $109)	$3	2,550 mg
		1,000 mg (IR)	$87 ($4, $88)	$2	2,000 mg
		500 mg (ER)	$89 ($82, $6,671)	$4 ($4, $1,267)	2,000 mg
		750 mg (ER)	$72 ($65, $92)	$4	1,500 mg
		1,000 mg (ER)	$1,028 ($1,028, $7,214)	$311 ($311, $1,321)	2,000 mg
Sulfonylureas (2nd generation)	• Glimepiride	4 mg	$71 ($71, $198)	$4	8 mg
	• Glipizide	10 mg (IR)	$75 ($67, $97)	$5	40 mg (IR)
		10 mg (XL)	$48	$15	20 mg (XL)
	• Glyburide	6 mg (micronized)	$50 ($48, $71)	$10	12 mg (micronized)
		5 mg	$93 ($63, $103)	$13	20 mg
Thiazolidinediones	• Pioglitazone	45 mg	$348 ($283, $349)	$4	45 mg
	• Rosiglitazone	4 mg	$407	$329	8 mg
α-Glucosidase inhibitors	• Acarbose	100 mg	$106 ($104, $106)	$23	300 mg
	• Miglitol	100 mg	$241	$311	300 mg
Meglitinides (glinides)	• Nateglinide	120 mg	$155	$46	360 mg
	• Repaglinide	2 mg	$878 ($162, $898)	$48	16 mg
DPP-4 inhibitors	• Alogliptin	25 mg	$234	$170	25 mg
	• Saxagliptin	5 mg	$490 ($462, $490)	$392	5 mg
	• Linagliptin	5 mg	$494	$395	5 mg
	• Sitagliptin	100 mg	$516	$413	100 mg
SGLT2 inhibitors	• Ertugliflozin	15 mg	$322	$257	15 mg
	• Dapagliflozin	10 mg	$557	$446	10 mg
	• Canagliflozin	300 mg	$558	$446	300 mg
	• Empagliflozin	25 mg	$558	$448	25 mg
GLP-1 receptor agonists	• Exenatide (extended release)	2 mg powder for suspension or pen	$792	$634	2 mg**
	• Exenatide	10 μg pen	$850	$680	20 μg
	• Dulaglutide	1.5/0.5 mL pen	$876	$702	1.5 mg**
	• Semaglutide	1 mg pen	$875	$704	1 mg**
	• Liraglutide	18 mg/3 mL pen	$1,044	$835	1.8 mg
Bile acid sequestrants	• Colesevelam	625 mg tabs	$712 ($674, $712)	$354	3.75 g
		3.75 g suspension	$674	$598	3.75 g
Dopamine-2 agonists	• Bromocriptine	0.8 mg	$855	$685	4.8 mg
Amylin mimetics	• Pramlintide	120 μg pen	$2,547	$2,036	120 μg/injection†††

AWP, average wholesale price; DPP-4, dipeptidyl peptidase 4; ER and XL, extended release; GLP-1, glucagon-like peptide 1; IR, immediate release; NADAC, National Average Drug Acquisition Cost; SGLT2, sodium–glucose cotransporter 2. †Calculated for 30-day supply (AWP [44] or NADAC [45] unit price × number of doses required to provide maximum approved daily dose × 30 days); median AWP or NADAC listed alone when only one product and/or price. *Utilized to calculate median AWP and NADAC (min, max); generic prices used, if available commercially. **Administered

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CAROLINA Study
- Shows SU has CV Safety-

- Part of the CVOT on linagliptin using an active comparator
  - 5 mg linagliptin vs up to 4 mg glimepiride
- 6033 subjects with T2DM over mean 6.3 years
- Primary Outcome =

  MACE with CV Death, nonfatal MI or nonfatal stroke
- Results:
  - **No difference in primary outcome with HR 0.98** (95% CI 0.84-1.14)
  - No difference in CV morality (HR = 1.0)
  - No difference in A1C (glimepiride lower early but higher later)
  - 1.5 Kg lower weight with linagliptin
  - Much lower hypoglycemia with linagliptin

Presented at 79th ADA Scientific Sessions June 10, 2019 San Francisco

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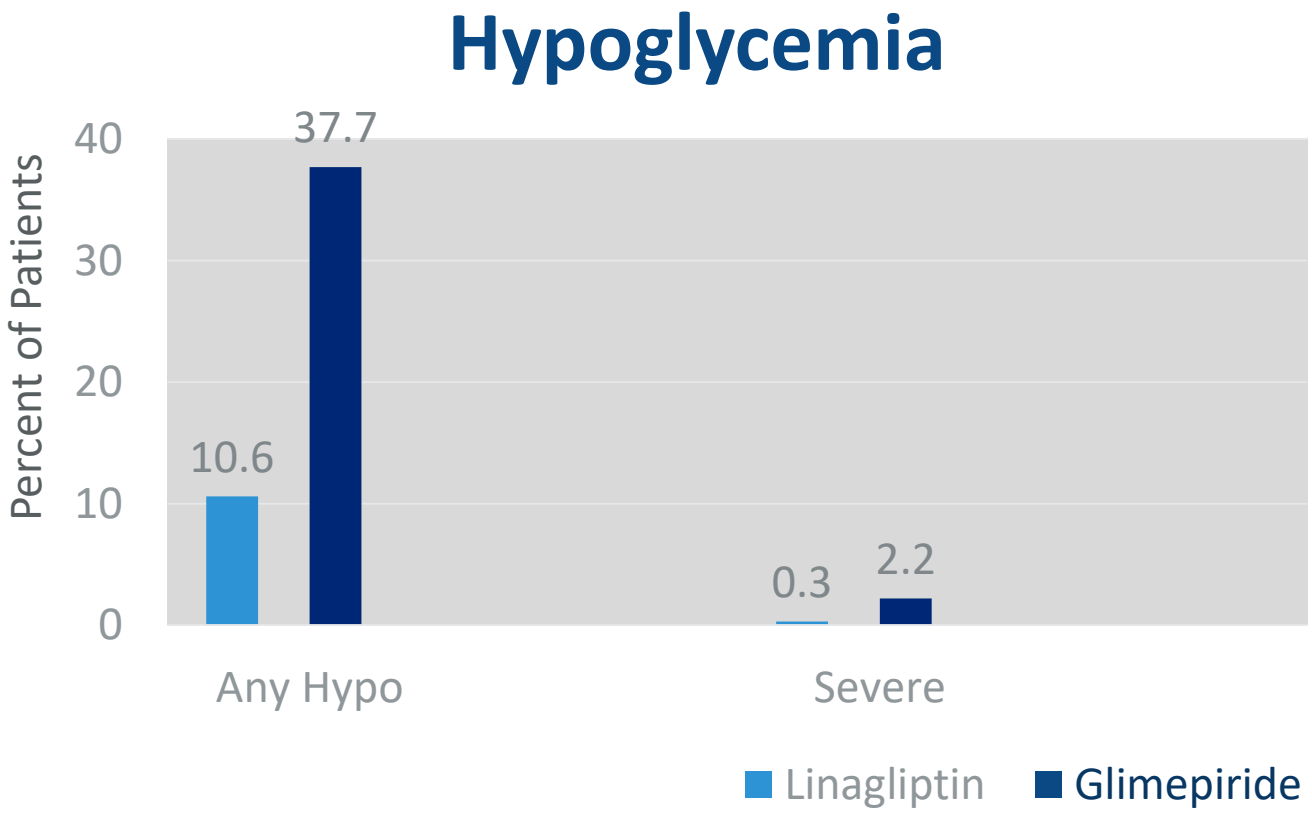
CAROLINA Study

- Linagliptin vs Glimepiride -



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Summary of ADA/EASD Consensus on T2DM Management

- It is important to have a patient centered approach
  - Shared decision making
  - Diabetes education is important periodically
- Metformin and lifestyle change are the foundation therapy for all patients.
- When the A1C no longer reaches the individual's goal, consider the cardiovascular and renal status
  - GLP-1 RA or SGLT2 inh if CVD is present
  - Prefer SGLT2 inh if HF or kidney disease are present
- Specific patient characteristics and circumstances guide therapy when heart disease is not a factor.
- GLP-1 RA are preferred as first injectable and before prandial insulin if patient is on basal insulin

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Pharmacists Play Many Roles

- Medication management
  - Insulin initiation and titration
  - **Special understanding of medication adherence**
- Full visit management
- Education
  - General diabetes and medication education
- Drug information
- Diabetes technology management
- Remote outreach
  - Telemedicine or mobile clinics

Hughes JD et al. Integrated Pharmacy Res & Practice 2017; 6:15-27. Ayadurai S et al J Diab Res 2016. Moreno G et al J Am Pham Ass 2017 57:686

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Medication Adherence in Diabetes

- Varies with population but 35-45% of patients are not adherent (< 80% of doses taken) over time
- Poor adherence is documented to correlate with higher morbidity, mortality and hospitalization
- Adherence varies by ethnicity
  - e.g. lower in Latinos, particularly if limited English proficiency
- Is often overlooked by clinicians
  - e.g. insulin doses are increased without consideration of missed dose causing the higher A1C

Khunti K et al Diabetes Care 2017; 40:1588. Huber CA et al Medicine 2016; 95:26. Capoccia K et al Diab Educator 2016; 42:34

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Factors Influencing Adherence

- Knowledge
- Patient involvement in goal setting and treatment decisions
- Socioeconomic factors
- Cultural factors
- Frequency of visits/ communications (cadence)
- Number of medications
- Frequency of dosing - - < vs > twice daily
- Hypoglycemia / side effects
- Weight gain
- Disabilities
- Satisfaction with their care

Khunti K et al Diabetes Care 2017; 40:1588. Huber CA et al Medicine 2016; 95:26.
Capoccia K et al Diab Educator 2016; 42:34

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Overcoming the Barriers to Insulin Therapy

- Avoid using insulin as a “threat,” but a solution and discuss it as an option early
- Use insulin pens and regimens that offer maximum flexibility
- **Give a “limited” trial of insulin**
- Tell patient injection is less painful than finger stick and give an injection in the office
- **Teach patient to recognize and treat hypoglycemia, and use basal analog insulins to minimize hypoglycemia risk**
- Meet with dietitian before initiation of insulin

Kruger D, et al. *Diabetes Educ*. 2010;36(suppl 3):44S-72S. Funnell MM. *Clinical Diabetes*. 2007;25(1):36-38. Derr RL, et al. *Diabetes Spectrum*. 2007; 20(3):177-185.

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Summary

- Diabetes management is complex and requires a collaborative effort
  - Multidisciplinary team (includes the pharmacist)
  - The patient at the center
- Team members must be aware of standards of care
- Goals and treatments need to be individualized.
- Many meds are available with different mechanisms
  - Selections of agents is affected by CV status
- Adherence to lifestyle modification and medications is a major factor in success.

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Thank You!

Thank you!

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- For more information about this presentation, contact Transformation.Center@state.or.us
- Find more resources for diabetes care here: https://www.oregon.gov/oha/HPA/dsi-tc/Pages/Diabetes.aspx
- Sign up for the Transformation Center's technical assistance newsletter: https://www.surveymonkey.com/r/OHATransformationCenterTA