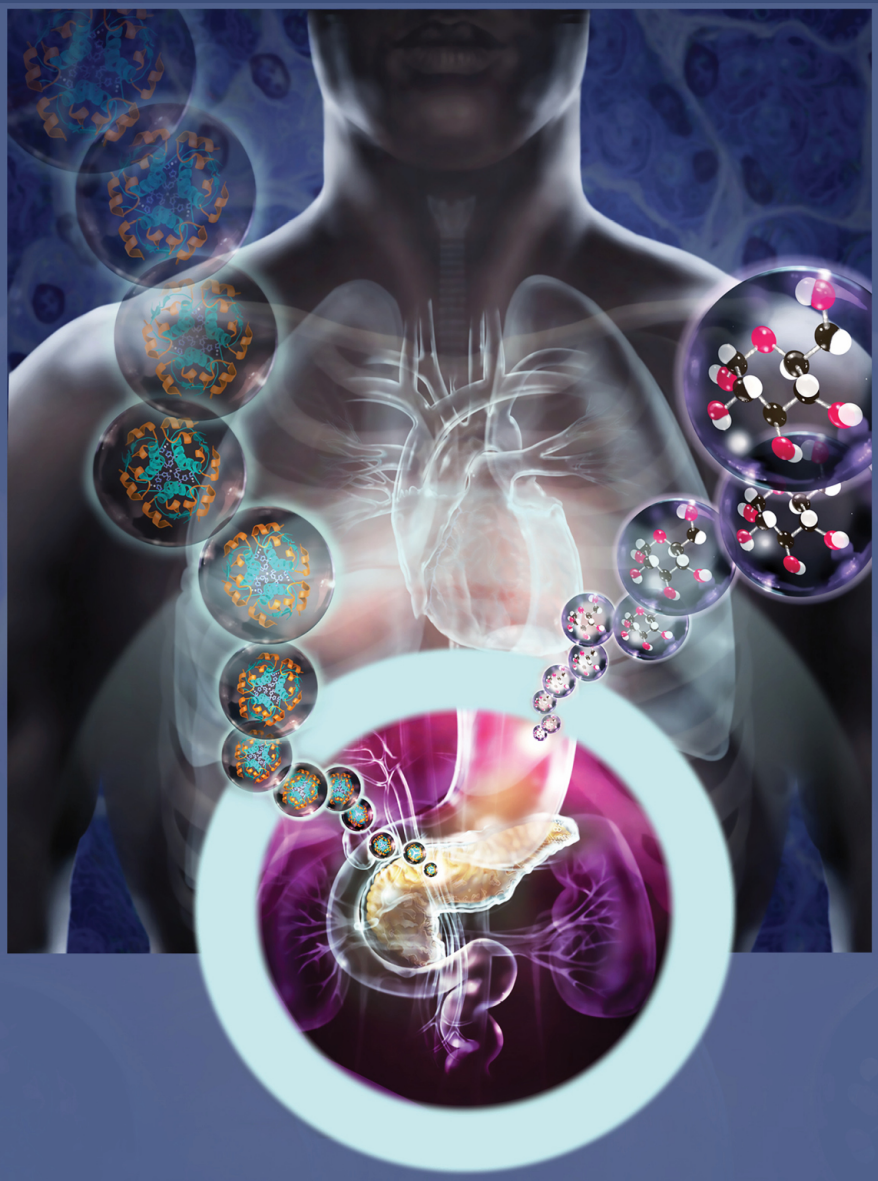

Reducing Atherosclerotic Cardiovascular Disease *in* Patients with Type 2 Diabetes: TeleECHO Series

FACULTY PRESENTER
Silvio E. Inzucchi, MD
Yale School of Medicine
Yale-New Haven Hospital
New Haven, CT

This activity is provided by Med Learning Group.
This activity is co-provided by Complete Conference Management (CCM).
This activity is supported by an educational grant from Lilly.

I. **Diabetes Overview**
   a. Epidemiology
   b. Disease burden of diabetes and associated co-morbidities
   c. Healthcare costs
   d. Risk factors for CVD
   e. Lack of efficacy of traditional interventions to overcome CV risk

II. **Role of GLP-1 Receptor Agonists and SGLT2 Inhibitors in Reducing CV Risk**
   a. Place in therapy
   b. Clinical trial data on the efficacy, safety and CV risk reduction of:
      i. SGLT2 inhibitors
      ii. GLP-1 receptor agonists

III. **Current Treatment Guidelines for Primary and Secondary Prevention of CVD in Diabetes**
   a. Hypertension
   b. Lipid Management
   c. Antiplatelet therapy
   d. Cardiovascular disease
   e. Current treatment guidelines for glycemic control

IV. **Patient-Centered Approaches to Glycemic Control**
   a. Setting glycemic goals
   b. Age considerations
   c. Communication strategies and techniques for facilitating adherence

V. **Case Study**

VI. **Conclusion**

VII. **Questions and answers**

Reducing Atherosclerotic Cardiovascular Disease in Patients with Type 2 Diabetes: TeleECHO Series

Chair

Silvio E Inzucchi, MD
Director, Yale Medicine Diabetes Center
Professor of Medicine, Endocrinology
Yale University School of Medicine
New Haven, CT

Faculty

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Endocrinology, Diabetes & Metabolism

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Clinical Pharmacy Specialist - Endocrine

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Samuel E. Crockett Chair in Diabetes Research

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Senior Investigator and Diabetes Program Lead

Translational Research Institute for Metabolism and Diabetes

Orlando, FL

Learning Objectives

- Discuss current treatment recommendations for primary and secondary prevention of atherosclerotic cardiovascular disease in patients with type 2 diabetes
- Evaluate clinical trial data on the use of GLP-1 receptor agonists and SGLT2 inhibitors to reduce cardiovascular events in patient with type 2 diabetes
- Review updated treatment guidelines that incorporate patient-specific factors and evidence from recent cardiovascular outcome trials to improve glycemic control and reduce cardiovascular risk in patients with type 2 diabetes

Target Audience

This educational activity is intended for primary care physicians in the United States who treat adults with type 2 diabetes.

ACCREDITATION AND DESIGNATION STATEMENTS

Accreditation Statement

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Credit Designation Statement

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Nursing Credit Information

Purpose: This program would be beneficial for nurses involved in the care of patients with type 2 diabetes mellitus.

Credits: 1.0 ANCC Contact Hour(s)

Accreditation Statement

Ultimate Medical Academy/CCM is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. Awarded 1.0 contact hour(s) of continuing nursing education of RNs and APNs.

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Dr. Pratley disclosed speaker & consulting fees from AstraZeneca; consulting fees from Boehringer-Ingelheim; consulting fees from Eisai, Inc.; consulting fees from GlaxoSmithKline; consulting fees from Glytec, LLC; consulting fees from Janssen; grants from Lexicon Pharmaceuticals; grants & consulting fees from Ligand Pharmaceuticals, Inc;, grants & consulting fees from Lilly; grants & consulting fees from Merck; consulting fees from Mundipharma; grants, speaker fees and consulting fees from Novo Nordisk; consulting fees from Pfizer; grants & consulting fees from Sanofi; grants, speaker fees & consulting fees from Takeda; personal consulting fees from Sanofi US Services, Inc., outside the submitted work. Except for consulting fees in June 2018 from Sanofi US Services, Inc., Dr. Richard Pratley's services were paid for directly to AdventHealth, a nonprofit organization.

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1. Read the CME/CNE information and faculty disclosures.
2. Participate in the web-based live activity.
3. Complete and submit the evaluation form to Med Learning Group.

You will receive your certificate after the web-based live activity.

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- Remember to direct all questions to the "co-host." There is a toggle button above the typing space that allows you to specify the location of your message delivery.

Reducing Atherosclerotic Cardiovascular Disease in Patients with Type 2 Diabetes: TeleECHO Series

Silvio E. Inzucchi, MD
Yale School of Medicine
Yale-New Haven Hospital
New Haven, CT

Disclosures

- **Dr. Silvio Inzucchi** is a consultant for Boehringer Ingelheim, AstraZeneca, Sanofi/Lexicon, Novo Nordisk, Merck, vTv Pharmaceuticals, Zafgen, Abbott/Alere, and Eisai (TIMI). He has also received salary from Elsevier, McGraw-Hill, and UpToDate.
- During the course of this lecture, the faculty may mention the use of medications for both FDA-approved and non-approved indications.

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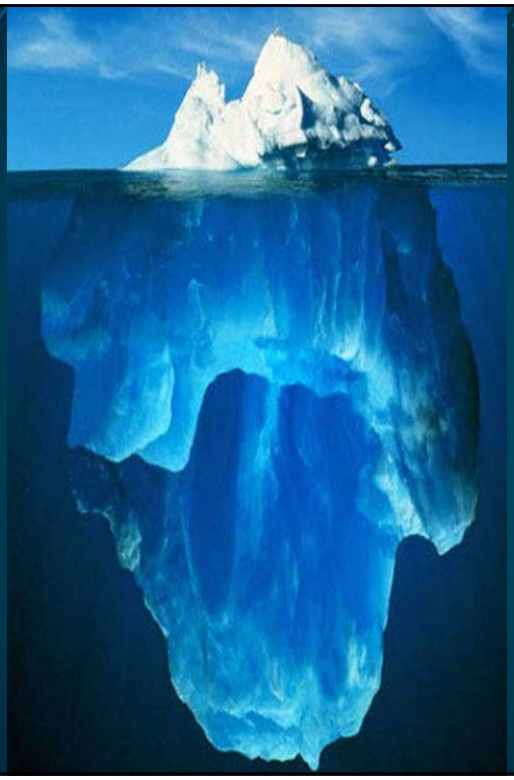
Educational Objectives

- Discuss current treatment recommendations for primary and secondary prevention of atherosclerotic cardiovascular disease in patients with type 2 diabetes
- Evaluate clinical trial data on the use of GLP-1 receptor agonists and SGLT2 inhibitors to reduce cardiovascular events in patient with type 2 diabetes
- Review updated treatment guidelines that incorporate patient-specific factors and evidence from recent cardiovascular outcome trials to improve glycemic control and reduce cardiovascular risk in patients with type 2 diabetes



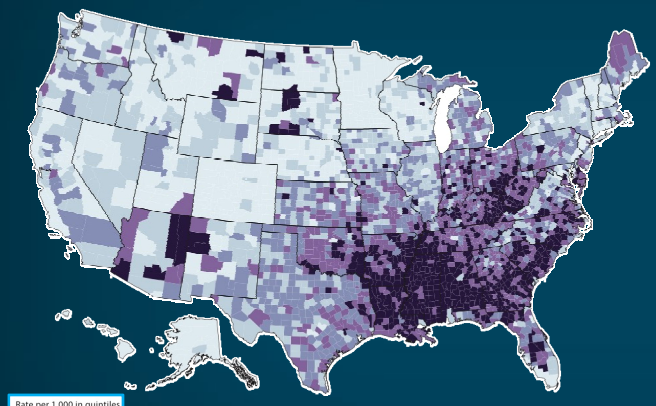
34.2 million with diabetes

88 million with prediabetes

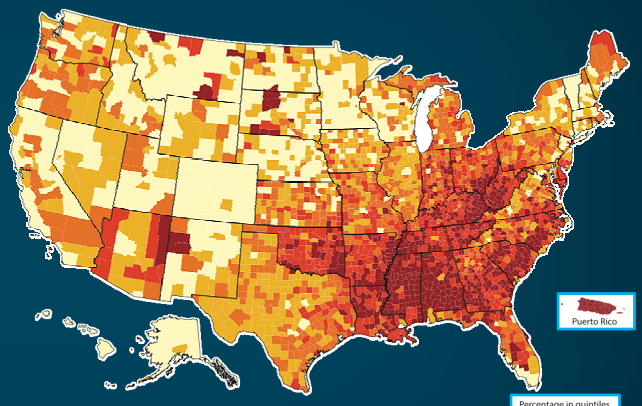
Centers for Disease Control and Prevention (CDC). National Diabetes Statistics Report—2020 (www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf). Accessed 2/19/2020.

Incidence and Prevalence of Diabetes in United States by Region

Diagnosed diabetes incidence (2013)



Diagnosed diabetes prevalence (2013)

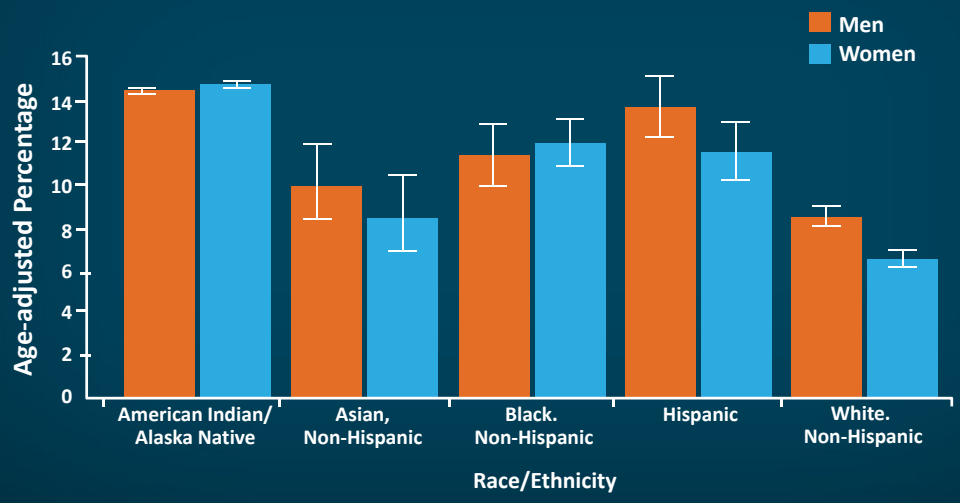


Counties in the *southern and Appalachian regions* of the United States tend to have the highest rates of **incidence** and **prevalence**.

CDC. National Diabetes Statistics Report—2017 (https://nationaldppcsc.cdc.gov/servlet/fileField?entityId=ka1t0000000CcBsAAK&field=Attachment__Body__s). Accessed 2/19/2020.

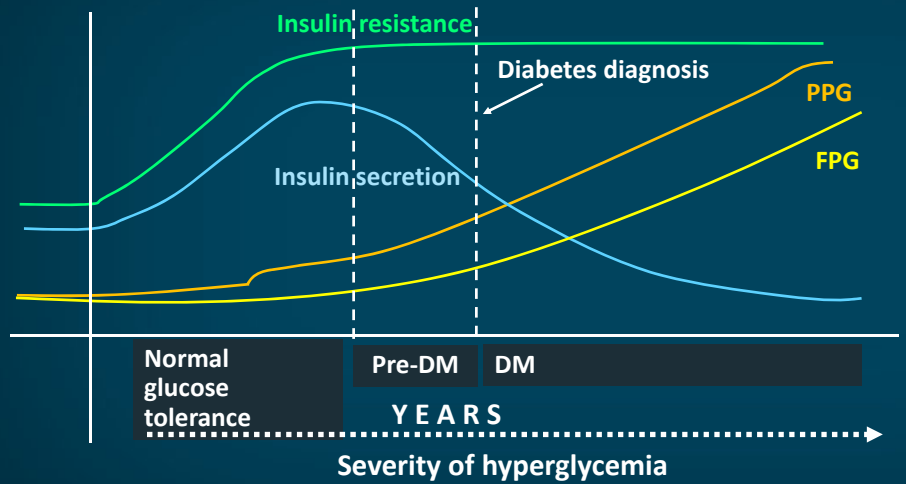
Prevalence of Diabetes by Ethnicity

Estimated age-adjusted adult prevalence of diagnosed diabetes by race/ethnicity (2017–2018)



CDC. National Diabetes Statistics Report—2020 (https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf). Accessed 2/21/2020.

Progressive β-Cell Dysfunction Is Key Driver of Progressive Dysglycemia in T2DM

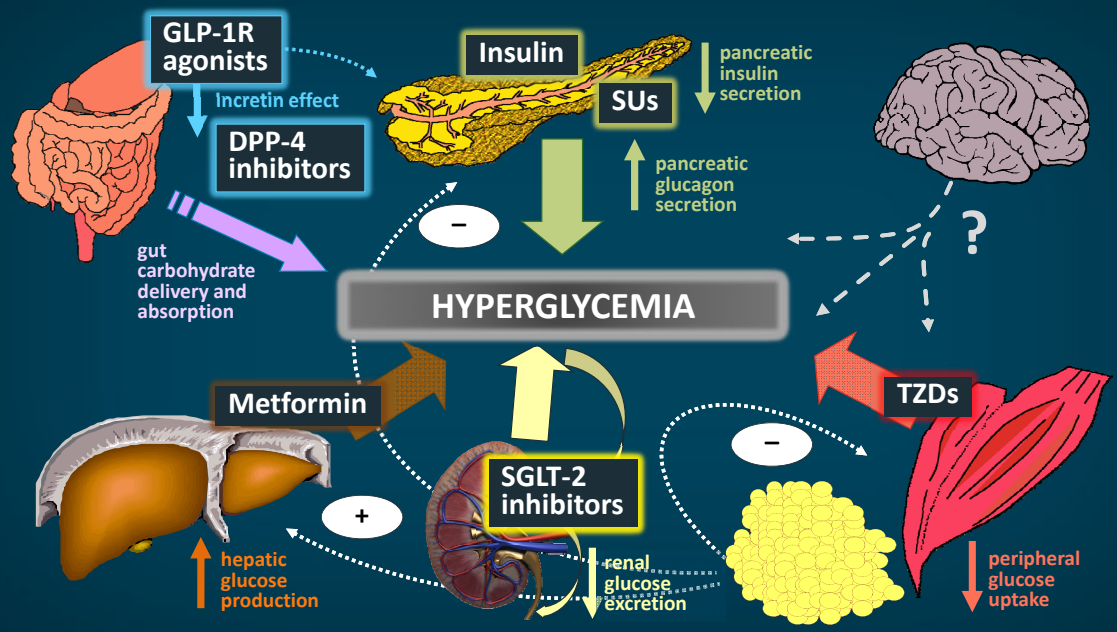


By time of diabetes diagnosis, up to 80% of β-cell function may be lost.

T2DM = type 2 diabetes mellitus; DM = diabetes mellitus; PPG = postprandial plasma glucose; FPG = fasting plasma glucose.

Defronzo RA. *Diabetes*. 2009;58:773-795. Fehse F et al. *J Clin Endocrinol Metab.* 2005;90:5991-5997. Figure adapted from Kendall DM et al. *Am J Med*. 2009;122(6 suppl):S37-S50.

Major Pathophysiologically Based T2DM Therapies



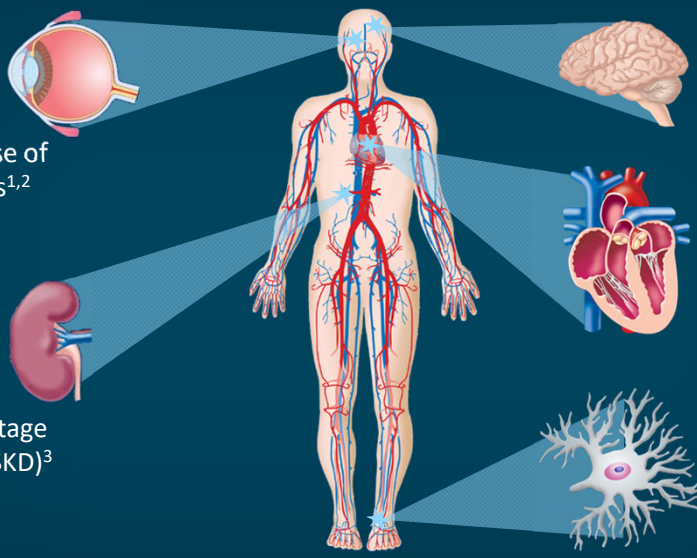
GLP-1R = glucagon-like peptide-1 receptor; DPP = dipeptidyl peptidase; SU = sulfonylurea; SGLT = sodium-glucose transporter; TZD = thiazolidinedione.

Adapted from Inzucchi SE, Sherwin RS. Type 2 diabetes mellitus. In: Goldman L, Schafer AI (eds). *Goldman's Cecil Medicine,* 24th edition. WB Saunders, 2011.

Complications of Diabetes

Diabetic retinopathy
An important cause of blindness in adults[1,2]

Diabetic nephropathy
Leading cause of chronic and end-stage kidney disease (ESKD)[3]



Stroke
Hypertension in ~20–60%, increasing risk of stroke[4]

Cardiovascular disease
CVD is major cause of morbidity and mortality in T2DM[5]

Diabetic neuropathy
Leading cause of non-traumatic lower extremity amputations[6,7]

CVD = cardiovascular disease.

1. Klein R, Klein BE. Chapter 21. In: *Diabetes in America, 3rd edition*. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), 2016. 2. Fong DS et al. *Diabetes Care.* 2003;26(suppl 1):S99-S102. 3. Afkarian M et al. *JAMA.* 2016;316:602-610. 4. Arauz-Pacheco C et al. *Diabetes Care.* 2003;26(suppl 1):S80-S82. 5. Barrett-Connor E et al. Chapter 18. In: *Diabetes in America, 3rd edition.* NIDDK, 2016. 6. Mayfield JA et al. *Diabetes Care.* 2003;26(suppl 1):S78-S79. 7. ADA. *Diabetes Care.* 2019;42(suppl 1):S124-S138.

Disease Burden of Diabetes

Hospitalizations with diabetes-associated conditions can include:

Condition	Age-Adjusted Rate (per 1000)
Congestive heart failure (CHF)	9.4
Stroke	6.0
Myocardial infarction (MI)	5.6
Lower extremity amputations	3.4
Hyperosmolar hyperglycemic nonketotic syndrome (HHNK)	1.3
Diabetic ketoacidosis (DKA)	17.1
Hypoglycemia	3.0

Medicare data for beneficiaries aged 65 years and older with diabetes demonstrated overall *prevalence* of multiple cardiovascular diseases, including:

Condition	Age-Adjusted Rate (per 100)
Coronary heart disease	46.8
CHF	26.2
Chronic kidney disease (CKD)	31.0
Peripheral vascular disease	20.7

CDC. Diabetes Health Burden Toolkit (https://nccd.cdc.gov/Toolkit/DiabetesBurden/Home/Health). (Hospitalizations data from 2016 and Medicare data from 2013). Accessed 2/19/2020.

Healthcare Cost of Diabetes

Annual Total Costs Attributable to Diabetes, United States (2013)

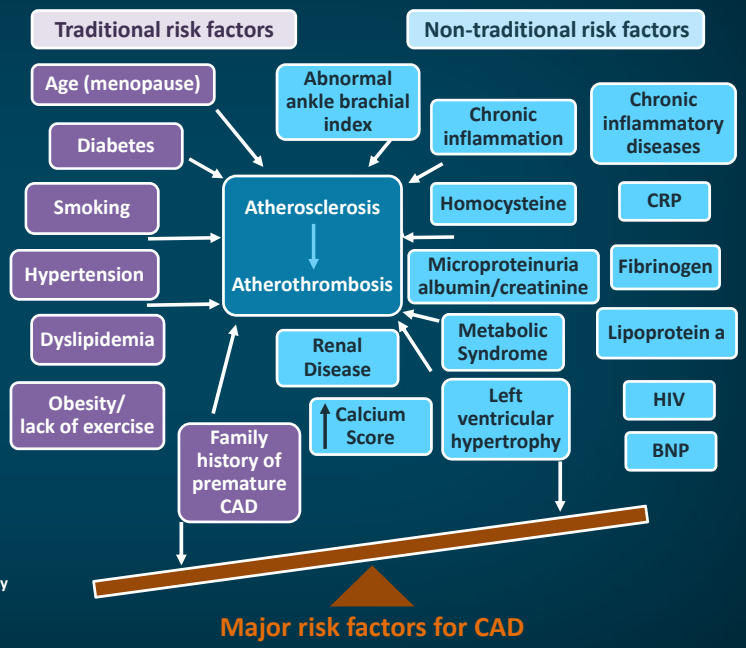
	Age Group (in years)	Direct Cost ($ in Millions)	Indirect Cost ($ in Millions)	Total Cost ($ in Millions)	Total Cost per Person with Diabetes ($)
Overall	19-64	107,250.8	193,148.5	300,399.3	20,181
	65+	84,228.9	36,969.9	121,198.8	11,647
	Total	191,479.7	230,118.4	421,598.0	16,670

Indirect costs include **inability to work** (1.2 million persons, with annual cost of 77.5 million) and **premature mortality** (240,250 persons, resulting in mortality cost of 68.7 million in work productivity and 33.5 million in household productivity).

CDC. Diabetes Health Burden Toolkit (https://nccd.cdc.gov/Toolkit/DiabetesBurden/Home/Economic). (Healthcare cost data from 2013). Accessed 2/19/2020.

Risk Factors for CVD in Diabetes

- Age: men ≥45 years; women ≥ 55 years
- Family history of premature CAD
  - CAD in male 1st-degree relative at <65 years
- Hypertension
  - BP >140/90 mmHg or on anti-HTN medication
- Cigarette smoking
- Diabetes
- Hypercholesterolemia
- Low HDL (<40 mg/dL)
- Hypertriglyceridemia (>200 mg/dl)
- Obesity



BP = blood pressure; HTN = hypertension; HDL = high-density lipoprotein; CAD = coronary artery disease; CRP = C-reactive protein; HIV = human Immunodeficiency virus; BNP = B-type natriuretic peptide.

Boudi FB, Ahsan CH. Medscape eMedicine, 2019 (https://emedicine.medscape.com/article/164163-overview). Accessed 2/19/2020.

AHA: Top 10 Take-Home Messages for the *Primary* Prevention of CVD

1. **Most important preventative modality is *promotion of a healthy lifestyle***
2. Team-based care approaches; social determinants of health (SHOC) assessment to edify treatment decisions
3. 10-year ASCVD risk estimation/discussion prior to pharmacological therapy (adults 40–75 years)
4. Healthy diet (vegetables, fruits, nuts, whole grains, lean protein and fish), and weight loss for overweight/obese
5. Physical activity (150 min/week moderate-intensity, 75 min/week vigorous)
6. **Lifestyle changes in T2DM are *crucial*; if pharmacotherapy is indicated,** metformin is 1st line, followed by consideration of **SGLT2-i or GLP-1 RA**
7. Tobacco cessation
8. Use ASA **infrequently**—lack of net benefit
9. Statins are 1st-line therapy for ASCVD prevention in people with elevated LDL (≥190 mg/dL), DM patients 40–75 years, and those identified at sufficient ASCVD risk
10. Non-pharmacologic interventions for all adults with elevated BP or hypertension; target BP <130/80 with pharmacotherapy

AHA = American Heart Association; GLP-1 RA = GLP-1 receptor agonist; ASCVD = atherosclerotic cardiovascular disease; ASA = aspirin.

Arnett DK, et al. *J Am Coll Cardiol.* 2019;74:e177-e232 (https://www.ahajournals.org/doi/10.1161/CIR.0000000000000677).

AHA Life's Simple 7®

- Ideal cardiovascular health based on 7 of the 10 most costly risk factors—**Life's Simple 7**—that can be improved through lifestyle changes
- Studies have shown:
  - Annual employer healthcare cost were $2021 less with at least 6 risk factors in optimal ranges.
  - 78% risk reduction for heart-related death with at least 5 risk factors in optimal ranges

Stop smoking | Eat better | Get active | Manage weight | Manage BP | Lipid control | Reduce BG

BG = blood glucose.

AHA. Life's simple 7, 2020 (www.heart.org/en/professional/workplace-health/lifes-simple-7). Accessed 2/19/2020.

Major Glucose-Lowering Drugs Classes

Class	Generic Names	↓ A1c	Mechanism(s)	Positive(s)	Negative(s)	Cost
Insulin	Degludec, glargine, detemir, NPH, regular, lispro, aspart, glulisine	No limit	Replaces deficient insulin supply	No ceiling; most titratable agent	Hypo, weight gain	highly variable
SU	Glyburide, glipizide, glimepiride	1–1.5%	↑ endogenous insulin production	Extensive experience	Hypo, weight gain	$
Metformin	Metformin	1–1.5%	↓ hepatic glucose production (? others)	±Wt loss, no hypo, ↓ CV events (?)	GI, lactic acidosis, B-12 deficiency	$
TZD	Rosiglitazone, pioglitazone	1–1.5%	Enhances peripheral insulin sensitivity	Durability, no hypo, ↓ CV events*, ↓ NASH	Weight gain, edema, HF, bone fxs, ? bladder ca*	$–$$$
DPP-4 i	Sitagliptin, saxagliptin, alogliptin, linagliptin	0.5–1%	↓ DPP-4 activity and ↑ incretins (GLP1, GIP)	Well-tolerated; no hypo	Urticaria, ? pancreatitis, ? HF*	$$$$
GLP-1 RA	Exenatide, liraglutide, dulaglutide, lixisenatide, semaglutide	1–1.5%	↑ insulin & ↓ glucagon, ↓ gastromotility, hunger	Wt loss, no hypo, ↓ BP, ↓ MACE*	GI, ? pancreatic disease,? thyroid, medullary ca	$$$$
SGLT2-i	Canagliflozin, dapagliflozin, empagliflozin, ertugliflozin	0.5–1%	↑ urinary glucose excretion	Wt loss, no hypo, ↓s BP, ↓ MACE*, ↓ HF†, ↓ CKD#	Polyuria, GU, DKA; bone fxs*, amputations*	$$$$

Reducing CV Risk

Role of GLP-1 Receptor Agonists and SGLT2 Inhibitors

ADA Standards of Medical Care in Diabetes—2019

Glycemic Treatment Goals for Older Adults

Health Status	Rationale	HbA1c Goal	Glucose (mg/dL)		BP (mmHg)
			Fasting/ preprandial	Bedtime	
Healthy (few coexisting illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5%	90–130	90–150	<140/90
Complex/intermediate health (multiple coexisting chronic illnesses, 2+ ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0%	90–150	100–180	<140/90
Very complex/poor health (LTC or end-stage chronic illness, or moderate-to-severe cognitive impairment, or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain.	<8.5%	100–180	110–200	<150/90

HbA1c = glycosylated hemoglobin; ADL = activities of daily living; LTC = long-term care.

ADA. *Diabetes Care*. 2019;42(suppl 1):S139-S147.

Summary of 25 Years of Diabetes Clinical Trials Linking Glucose Control to Vascular Complications

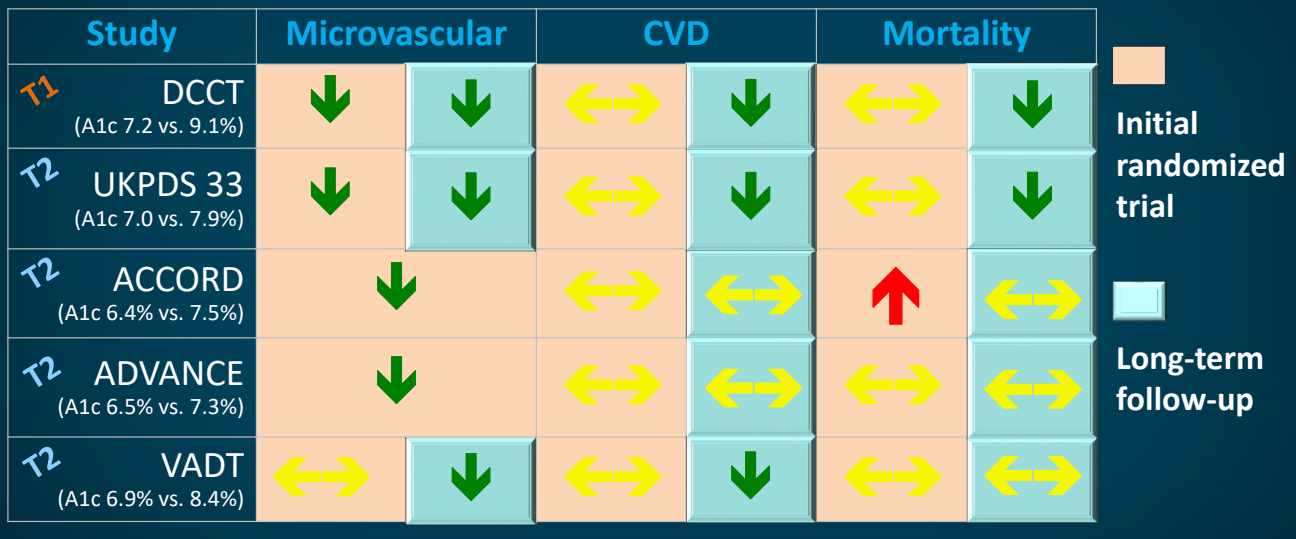
1. **Glycemic control** (**HbA1c ~7%, perhaps even lower**) reduces ***micro***vascular complications in both T1DM and T2DM, with relative risk reduction (RRR) in the 25–60% range.

2. However, the **impact** of glycemic control itself on ***macro***vascular complications in T2DM is **small to nonexistent**. Any benefit is on the order of a RRR of ~15%. This is mainly for non-fatal MI (not CV death), and seems to require long-term efforts before it can be appreciated. (Benefit may be larger in T1DM.)

T1DM = type 1 diabetes mellitus; CV = cardiovascular.

Inzucchi S. Update on Diabetes Drugs and CVD Risk. ADA 2017 (https://professional.diabetes.org/sites/professional.diabetes.org/files/media/inzucchi_update_on_diabetes_drugs_and_cvd_risk_final.pdf). Accessed 2/19/2020.

Impact of Intensive Glucose-Lowering Therapy in DM
Summary of Major RCTs



DCCT Group. *N Engl J Med.* 1993;329: 977-986. Nathan DM, et al. *N Engl J Med.* 2005;353:2643-2653. DCCT Group. *JAMA* 2015;313:45-53. UKPDS Group. *Lancet.* 1998;352:854-865. Holman RR, et al. *N Engl J Med.* 2008;359:1577-1589. Gerstein HC, et al. *N Engl J Med.* 2008;358:2545-2559. Patel A, et al. *N Engl J Med.* 2008;358:2560-2572. Duckworth W, et al. *N Engl J Med.* 2009;360:129-139 (erratum:361:1024). Kendall DM, Bergenstal RM. ©International Diabetes Center 2009, 2015.

FDA-Mandated CV Outcomes Non-insulin Trials in T2DM

Study	SAVOR[1]	EXAMINE[2]	TECOS[3]	CARMELINA[4]	CAROLINA[5]
DPP4-i	saxagliptin	alogliptin	sitagliptin	linagliptin	linagliptin
Comparator	plac	plac	plac	placel	glimepi U)
N	792	5	71	3	03
Results	2013	2013	2015	2018	2018

NEUTRAL

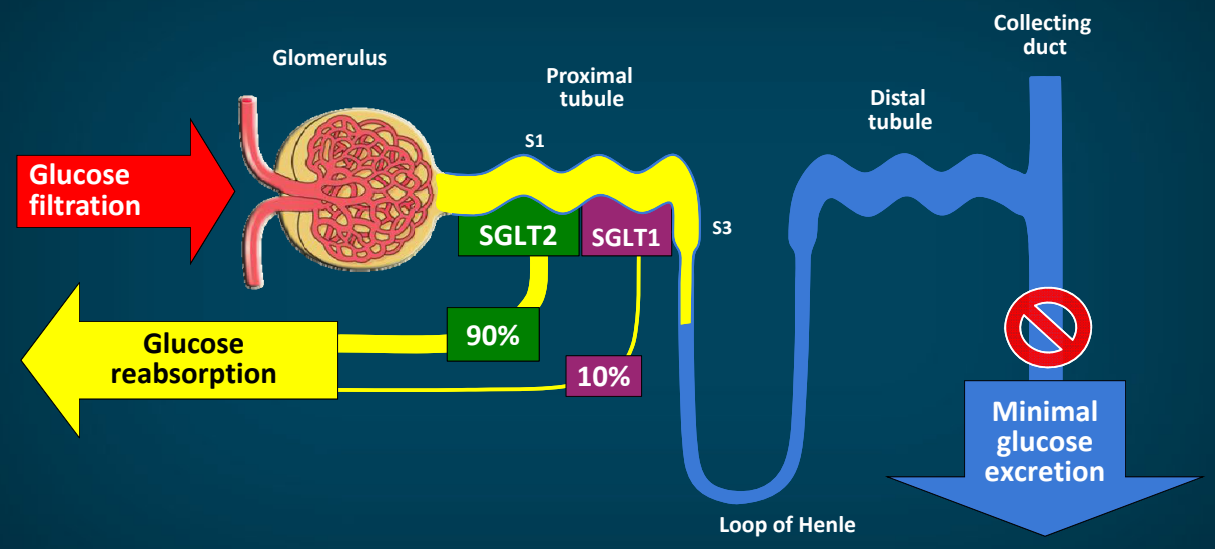
Study	ELIXA[6]	LEADER[7]	SUSTAIN 6[8]	EXSCEL[9]	REWIND[10]	HARMONY[11]
GLP1-RA	lixisenatide	liraglutide	semaglutide	exenatide LR	dulaglutide	albiglutide
Comparator	pl	placebo	placebo	placebo	placebo	placebo
N	68	9340	3297	14,752	9901	9463
Results	2015	2015	2016	2017	2018	2018

NEUTRAL

Study	EMPA-REG[12]	CANVAS[13]	(CREDENCE[14])	DECLARE[15]	VERTIS CV[16]
SGLT2-i	empagliflozin	canagliflozin	canagliflozin	dapagliflozin	ertugliflozin
Comparator	placebo	placebo	placebo	placebo	placebo
N	7020	4330	4401	17,160	8246
Results	2015	2017	2018	2018	2020

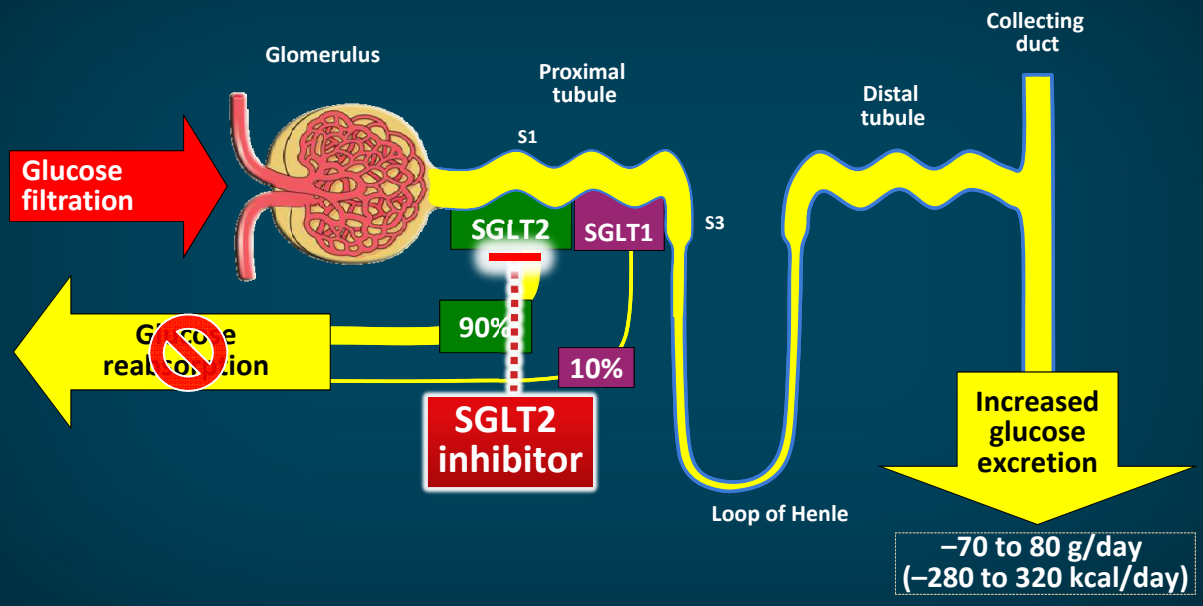
1. NCT01107886 (SAVOR). 2. NCT00968708 (EXAMINE). 3. NCT00790205 (TECOS). 4. NCT01897532 (CARMELINA). 5. NCT01243424 (CAROLINA). 6. NCT01147250 (ELIXA). 7. NCT01179048 (LEADER). 8. NCT01720446 (SUSTAIN 6). 9. NCT01144338 (EXSCEL). 10. NCT01394952 (REWIND). 11. NCT02465515 (HARMONY). 12. NCT01131676 (EMPA-REG). 13. NCT01032629 (CANVAS). 14. NCT02065791 (CREDENCE). 15. NCT01730534 (DECLARE). 16. NCT01986881 (VERTIS CV).

Normal Physiology of Renal Glucose Homeostasis



Wright EM. *Am J Physiol Renal Physiol.* 2001;280:F10-F18. Lee YJ, et al. *Kidney Int Suppl.* 2007;106:S27-S35. Han S, et al. *Diabetes.* 2008;57:1723-1729.

SGLT2 Inhibition Reduces Renal Glucose Reabsorption



Wright EM. *Am J Physiol Renal Physiol.* 2001;280:F10-F18. Lee YJ, et al. *Kidney Int Suppl.* 2007;106:S27-S35. Han S, et al. *Diabetes.* 2008;57:1723-1729. Inzucchi SE, et al. *Diabetes Care.* 2015;38:140-149.

SGLT2 Inhibitors

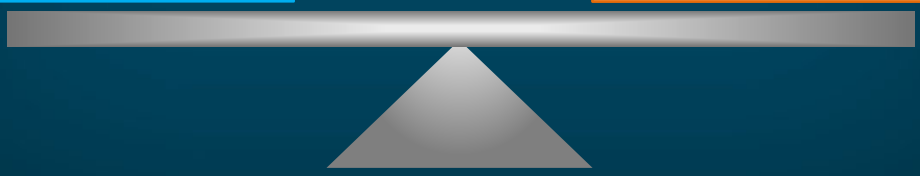
Risk-to-Benefit Ratio Prior to CV Outcome Trials

BENEFITS

- ↓HbA1c ~0.6–0.9%
- Low hypoglycemia risk
- Modest ↓ weight
- Modest ↓ BP
- ↓ Albuminuria
- Small ↓ TGs
- Small ↑ HDL-C

RISKS

- Polyuria/dehydration
- Genital mycotic infections
- ? UTIs
- Small ↓ GFR (reversible)
- Diabetic ketoacidosis (DKA)
- Small ↑ LDL-C
- ? ↑ Fracture risk

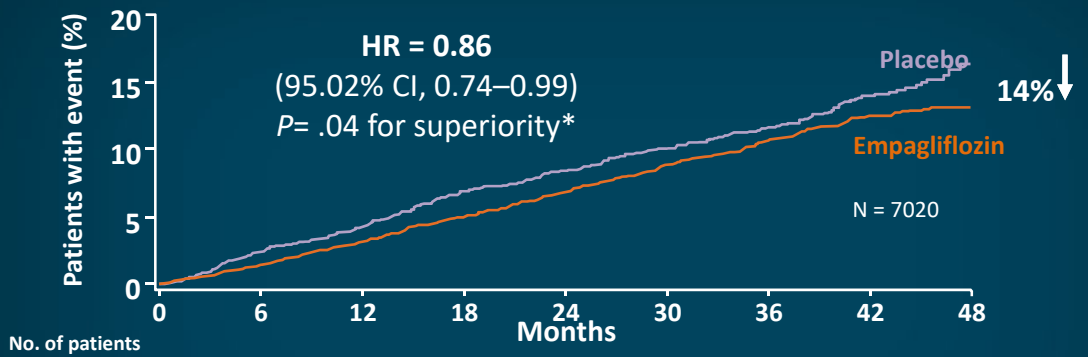


TG = triglycerides; UTI = urinary tract infection; GFR = glomerular filtration rate; LDL-C = low-density lipoprotein-cholesterol.

Kim Y, Babu AR. *Diabetes Metab Syndr Obes.* 2012;5:313-327. Inzucchi SE, et al. *Diabetes Care.* 2015;38:140-149. Burke KR, et al. *Pharmacotherapy.* 2017;37:187-194.

EMPA-REG: Primary Outcome

Cumulative Incidence of 3-Point MACE (CV death, nonfatal MI, or nonfatal stroke)



No. of patients									
Empagliflozin	4687	4580	4455	4328	3851	2821	2359	1534	370
Placebo	2333	2256	2194	2112	1875	1380	1161	741	166

Primary outcome (composite of death from CV causes, nonfatal MI, or nonfatal stroke) occurred in a significantly lower percentage of patients in empagliflozin group (10.5%) vs placebo (12.1%).

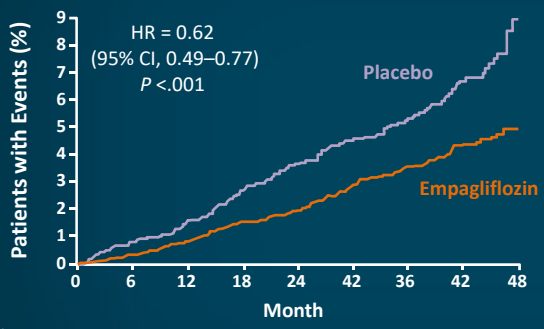
*Two-sided tests for superiority were conducted (statistical significance was indicated if $P \leq .0498$).

MACE = major adverse cardiovascular events; HR = hazard ratio; CI = confidence interval.

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

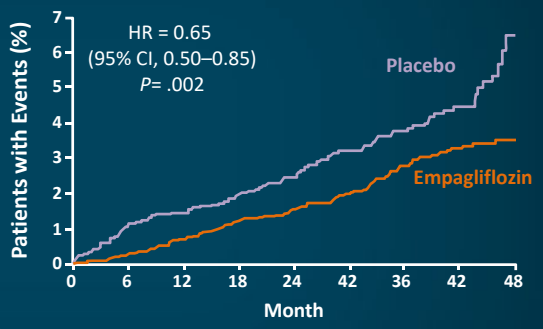
EMPA-REG: CV Death and Heart Failure Hospitalization

Death from CV causes



No. at risk									
Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1772	414
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177

HF Hospitalization



No. at risk									
Empagliflozin	4687	4614	4523	4427	3988	2950	2487	1634	395
Placebo	2333	2271	2226	2173	1932	1424	1202	775	168

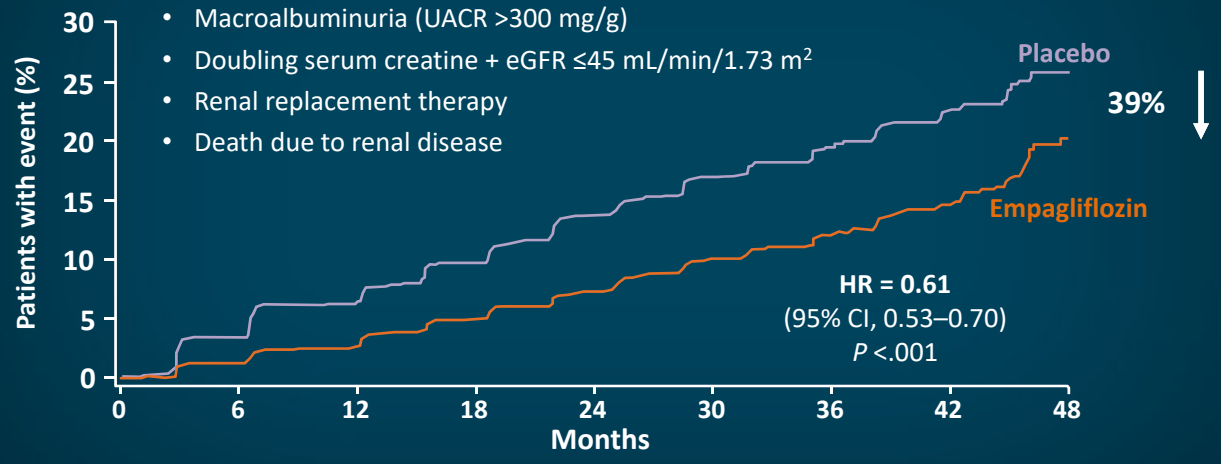
HF = heart failure.

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

EMPA-REG *Secondary* OUTCOME: Cumulative Incidence of Incident or Worsening Nephropathy

Incident or worsening nephropathy

- Macroalbuminuria (UACR >300 mg/g)
- Doubling serum creatine + eGFR ≤45 mL/min/1.73 m^2
- Renal replacement therapy
- Death due to renal disease



Kaplan-Meier estimate. Hazard ratio based on Cox regression analyses.
USCR = urinary albumin-to-creatinine ratio; eGFR = estimated GFR.

Wanner C, et al. *N Engl J Med.* 2016;375:323-334.

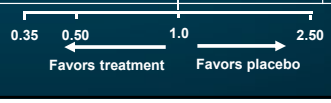
SGLT2i Trial Meta-analysis of Cardiovascular Outcomes

Meta-analysis on MI, stroke, and CV death (MACE)*

	Patients Tx	Patients PBO	Events	Events/1000 PY Tx	Events/1000 PY PBO	Weight (%)	HR (95% CI)
Patients with atherosclerotic cardiovascular disease							
EMPA-REG OUTCOME	4687	2333	772	37.4	43.9	29.4	0.86 (0.74–0.99)
CANVAS Program	3756	2900	796	34.1	41.3	32.4	0.82 (0.72–0.95)
DECLARE-TIMI 58	3474	3500	1020	36.8	41.0	28.2	0.90 (0.79–1.02)
Patients with ASCVD (*P*= .0002)							**0.86 (0.80–0.93)**
Patients with multiple risk factors							
CANVAS Program	2039	1447	215	15.8	15.5	25.9	0.98 (0.74–1.30)
DECLARE-TIMI 58	5108	5078	539	13.4	13.3	74.1	1.01 (0.86–1.20)
Fixed effects model for multiple risk factors (*P*= .98)							**1.00 (0.87–1.16)**

Meta-analysis on HF hospitalizations and CV death*

	Patients Tx	Patients PBO	Events	Events/1000 PY Tx	Events/1000 PY PBO	Weight (%)	HR (95% CI)
Patients with atherosclerotic cardiovascular disease							
EMPA-REG OUTCOME	4687	2333	463	19.7	30.1	30.9	0.66 (0.55–0.79)
CANVAS Program	3756	2900	524	21.0	27.4	32.8	0.77 (0.65–0.92)
DECLARE-TIMI 58	3474	3500	597	19.9	23.9	36.4	0.83 (0.71–0.98)
Patients with ASCVD (*P* <.0001)							**0.76 (0.69–0.84)**
Patients with multiple risk factors							
CANVAS Program	2039	1447	128	8.9	9.8	30.2	0.83 (0.58–1.19)
DECLARE-TIMI 58	5108	5078	316	7.0	8.4	69.8	0.84 (0.67–1.04)
Fixed effects model for multiple risk factors (*P*= .0634)							**0.84 (0.69–1.01)**



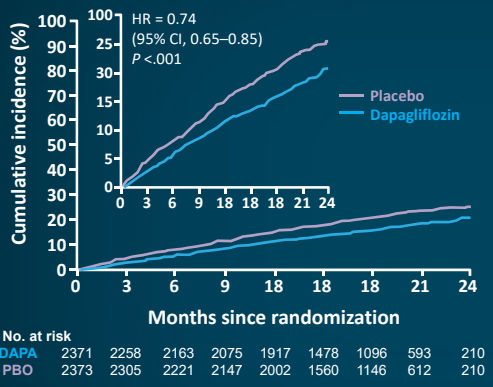
**Stratified by presence of established atherosclerotic disease*

Tx = treatment; PBO = placebo; PY = patient years.

Zelniker TA, et al. *Lancet.* 2019;393:31-39.

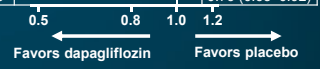
DAPA HF Primary Outcomes: DM vs Non-DM Subgroups

Primary outcome



Primary outcome subgroup analysis

Subgroup	DAPA n = 2373	PBO n = 2371	Hazard Ratio (95% CI)
	Patients/total, no.		
Hospitalization for heart failure			
Yes	195/1124	279/1127	0.67 (0.56–0.80)
No	191/1249	223/1244	0.84 (0.69–1.01)
Type 2 diabetes at baseline			
Yes	215/1075	271/1064	0.75 (0.63–0.90)
No	171/1298	231/1307	0.73 (0.60–0.88)
Afib or flutter on enrollment ECG			
Yes	109/569	126/559	0.82 (0.63–1.06)
No	277/1804	376/1812	0.72 (0.61–0.84)
Main cause of heart failure			
Ischemic	223/1316	289/1358	0.77 (0.65–0.92)
Non-ischemic or unknown	163/1057	213/1013	0.71 (0.58–0.87)
Body-mass index			
<30	259/1537	320/1533	0.78 (0.66–0.92)
≥30	127/834	182/838	0.69 (0.55–0.86)
Baseline eGFR (ml/min/1.73m²)			
<60	191/962	254/964	0.72 (0.59–0.86)
≥60	195/1410	248/1406	0.76 (0.63–0.92)



Primary outcome was composite of worsening HF (*hospitalization for HF or urgent visit resulting in IV treatment for HF*) or CV death, which occurred in a significantly lower percentage of patients in dapagliflozin group (16.3%) vs placebo (21.2%).

DAPA = dapagliflozin; AFib = atrial fibrillation; ECG = electrocardiogram; IV = intravenous.

McMurray JJV, et al. *N Engl J Med.* 2019;381:1995-2008.

FDA-Mandated CV Outcomes Non-insulin Trials in T2DM

Study	SAVOR[1]	EXAMINE[2]	TECOS[3]	CARMELINA[4]	CAROLINA[5]
DPP4-i	saxagliptin	alogliptin	sitagliptin	linagliptin	linagliptin
Comparator	plac	plac	plac	placebo	glimepiride
N	16,492	5,380	14,671	6,979	6,033
Results	2013	2013	2015	2018	2018

NEUTRAL NEUTRAL NEUTRAL NEUTRAL "NEUTRAL"

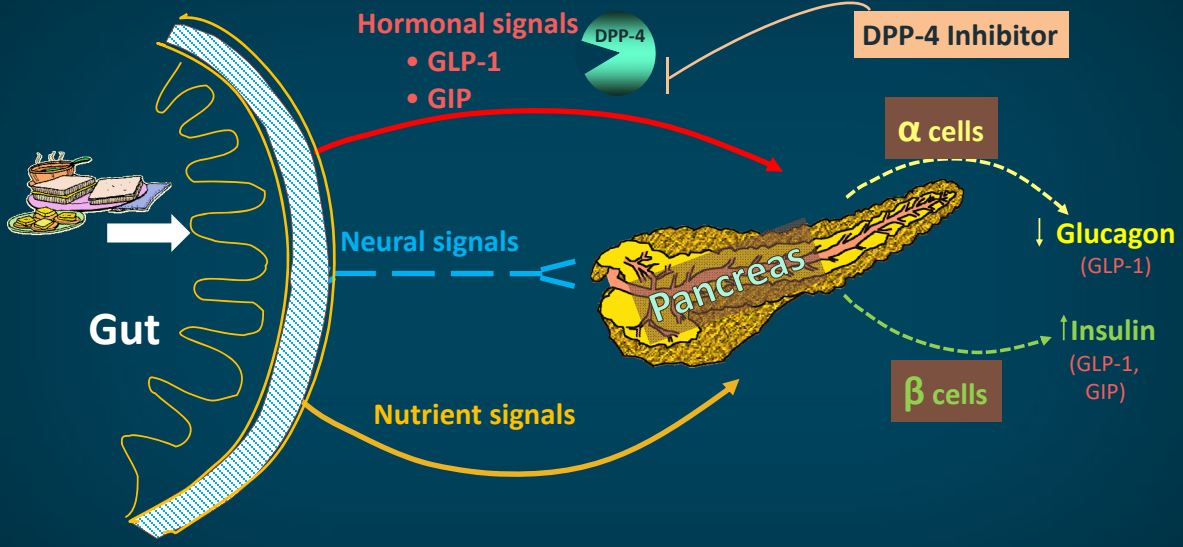
Study	ELIXA[6]	LEADER[7]	SUSTAIN 6[8]	EXSCEL[9]	REWIND[10]	HARMONY[11]
GLP1-RA	lixisenatide	liraglutide	semaglutide	exenatide LR	dulaglutide	albiglutide
Comparator	pl	placebo	placebo	placebo	placebo	placebo
N	6,068	9340	3297	14,752	9901	9463
Results	2015	2015	2016	2017	2018	2018

NEUTRAL

Study	EMPA-REG[12]	CANVAS[13]	(CREDENCE[14])	DECLARE[15]	VERTIS CV[16]
SGLT2-i	empagliflozin	canagliflozin	canagliflozin	dapagliflozin	ertugliflozin
Comparator	placebo	placebo	placebo	placebo	placebo
N	7,020	10,142	4,401	17,160	8246
Results	2015	2017	2018	2018	2020

1. NCT01107886 (SAVOR). 2. NCT00968708 (EXAMINE). 3. NCT00790205 (TECOS). 4. NCT01897532 (CARMELINA). 5. NCT01243424 (CAROLINA). 6. NCT01147250 (ELIXA). 7. NCT01179048 (LEADER). 8. NCT01720446 (SUSTAIN 6). 9. NCT01144338 (EXSCEL). 10. NCT01394952 (REWIND). 11. NCT02465515 (HARMONY). 12. NCT01131676 (EMPA-REG). 13. NCT01032629 (CANVAS). 14. NCT02065791 (CREDENCE). 15. NCT01730534 (DECLARE). 16. NCT01986881 (VERTIS CV).

The Enteroinsular Axis



GIP = glucose-dependent insulinotropic peptide.

Adapted with permission from Creutzfeldt W. *Diabetologia*. 1979;16:75-85. Copyright © 1979 Springer-Verlag. Drucker DJ. *Diabetes Care*. 2003;26:2929-2940. Kieffer TJ, Habener JF. *Endocr Rev*. 1999;20:876-913. Nauck MA, et al. *Diabetologia*. 1993;36:741-744.

GLP-1 Receptor Agonists

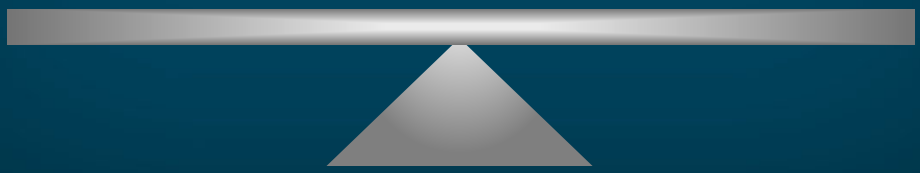
Risk-to-Benefit Ratio Prior to CV Outcome Trials

BENEFITS

- ↓HbA1c ~1.0–1.5%
- Low hypoglycemia risk
- Significant ↓ weight
- Modest ↓ BP
- ↓ Albuminuria
- Modest ↓ LDL-C, TGs
- ↓ Inflammatory markers
- ? Direct cardiac effects

RISKS

- Injectables
- Nausea/vomiting
- ? Pancreatitis risk
- Medullary thyroid cancer (mice)



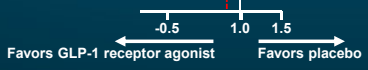
Kim Y, Babu AR. *Diabetes Metab Syndr Obes*. 2012;5:313-327. Inzucchi SE, et al. *Diabetes Care*. 2015;38:140-149. Abdul-Ghani M, DeFronzo RA. *Diabetes Care*. 2017;40:1121-1127. Lee YS, Jun HS. *Mediators of Inflammation*. 2016; article ID 3094642.

GLP-1 RA Trial Meta-analysis of Cardiovascular Outcomes

Meta-analysis on risk of MACE (MI, stroke, and CV death)

	GLP-1 receptor agonist n/N (%)	Placebo n/N (%)	Hazard Ratio (95% CI)
Three-component MACE			
ELIXA	400/3034 (13%)	392/3034 (13%)	1.02 (0.89–1.17)
LEADER	608/4668 (13%)	694/4672 (15%)	0.87 (0.78–0.97)
SUSTAIN-6	108/1648 (7%)	146/1649 (9%)	0.74 (0.58–0.95)
EXSCEL	839/7356 (11%)	905/7396 (12%)	0.91 (0.83–1.00)
Harmony Outcomes	338/4731 (7%)	428/4732 (9%)	0.78 (0.68–0.90)
REWIND	594/4949 (12%)	663/4952 (13%)	0.88 (0.79–0.99)
PIONEER 6	61/1591 (4%)	76/1592 (5%)	0.79 (0.57–1.11)
Overall (I^2=40.9%, *P*= .118)	2948/27,977 (11%)	3304/28,027 (12%)	0.88 (0.82–0.94)
Cardiovascular death			
ELIXA	156/3034 (5%)	158/3034 (5%)	0.98 (0.78–1.22)
LEADER	219/4668 (5%)	278/4672 (6%)	0.78 (0.66–0.93)
SUSTAIN-6	44/1648 (3%)	46/1649 (3%)	0.98 (0.65–1.48)
EXSCEL	340/7356 (5%)	383/7396 (5%)	0.88 (0.76–1.02)
Harmony Outcomes	122/4731 (3%)	130/4732 (3%)	0.93 (0.73–1.19)
REWIND	317/4949 (6%)	346/4952 (7%)	0.91 (0.78–1.06)
PIONEER 6	15/1591 (1%)	30/1592 (2%)	0.49 (0.27–0.92)
Overall (I^2=13.5%, *P*= .327)	1277/27,977 (5%)	1471/28,027 (5%)	0.88 (0.81–0.96)

	GLP-1 receptor agonist n/N (%)	Placebo n/N (%)	Hazard Ratio (95% CI)
Fatal or non-fatal myocardial infarction			
ELIXA	270/3034 (9%)	261/3034 (9%)	1.03 (0.87–1.22)
LEADER	292/4668 (6%)	339/4672 (7%)	0.86 (0.73–1.00)
SUSTAIN-6	54/1648 (3%)	67/1649 (4%)	0.81 (0.57–1.16)
EXSCEL	483/7356 (7%)	493/7396 (7%)	0.97 (0.85–1.10)
Harmony Outcomes	181/4731 (4%)	240/4732 (5%)	0.75 (0.61–0.90)
REWIND	223/4949 (5%)	231/4952 (5%)	0.96 (0.79–1.15)
PIONEER 6*	37/1591 (2%)	31/1592 (2%)	1.18 (0.73–1.90)
Overall (I^2=27.4%, *P*= .219)	1540/27,977 (6%)	1662/28,027 (6%)	0.91 (0.84–1.00)
Fatal or non-fatal stroke			
ELIXA	67/3034 (2%)	60/3034 (2%)	1.12 (0.79–1.58)
LEADER	173/4668 (4%)	199/4672 (4%)	0.86 (0.71–1.06)
SUSTAIN-6	30/1648 (2%)	46/1649 (3%)	0.65 (0.41–1.03)
EXSCEL	187/7356 (3%)	218/7396 (3%)	0.85 (0.70–1.03)
Harmony Outcomes	94/4731 (2%)	108/4732 (2%)	0.86 (0.66–1.14)
REWIND	158/4949 (3%)	205/4952 (4%)	0.76 (0.62–0.94)
PIONEER 6*	12/1591 (1%)	16/1592 (1%)	0.74 (0.35–1.57)
Overall (I^2=0.0%, *P*= .557)	721/27,977 (3%)	852/28,027 (3%)	0.84 (0.76–0.93)



Kristensen SL, et al. *Lancet Diabetes Endocrinol*. 2019;7:776-785.

FDA-Mandated CV Outcomes in Non-insulin Trials in T2DM

Study	SAVOR[1]	EXAMINE[2]	TECOS[3]	CARMELINA[4]	CAROLINA[5]
DPP4-i	saxagliptin	alogliptin	sitagliptin	linagliptin	linagliptin
Comparator	pl[illegible]	pl[illegible]	pl[illegible]	plac[illegible]	glime[illegible]
N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Results	2013	2013	2015	2018	2018

NEUTRAL

Study	ELIXA[6]	LEADER[7]	SUSTAIN 6[8]	EXSCEL[9]	REWIND[10]	HARMONY[11]
GLP1-RA	lixisenatid[illegible]	liraglutide	semaglutide	exenatide [illegible]	dulaglutide	~~albiglutide~~
Comparator	[illegible]	placebo	placebo	[illegible]	placebo	placebo
N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Results	2015	2015	2016	2017	2018	2018

NEUTRAL

Study	EMPA-REG[12]	CANVAS[13]	(CREDENCE[14])	DECLARE[15]	VERTIS CV[16]
SGLT2-i	empagliflozin	canagliflozin	canagliflozin	dapagliflozin	ertugliflozin
Comparator	placebo	placebo	placebo	placebo	placebo
N	[illegible]	[illegible]	[illegible]	[illegible]	8246
Results	2015	2017	2018	2018	2020

1. NCT01107886 (SAVOR). 2. NCT00968708 (EXAMINE). 3. NCT00790205 (TECOS). 4. NCT01897532 (CARMELINA). 5. NCT01243424 (CAROLINA). 6. NCT01147250 (ELIXA). 7. NCT01179048 (LEADER). 8. NCT01720446 (SUSTAIN 6). 9. NCT01144338 (EXSCEL). 10. NCT01394952 (REWIND). 11. NCT02465515 (HARMONY). 12. NCT01131676 (EMPA-REG). 13. NCT01032629 (CANVAS). 14. NCT02065791 (CREDENCE). 15. NCT01730534 (DECLARE). 16. NCT01986881 (VERTIS CV).

FDA Update

- **Dulaglutide** approved for the *reduction of major adverse cardiovascular events* (MACE) in adults with T2DM in both **primary *and* secondary prevention** populations (2/2020)
  - Additional GLP-1 agents with CV indications include liraglutide and semaglutide, both approved for risk reduction of MACE in T2DM adults with ***established*** CVD *(secondary prevention)*
- Dulaglutide indication update based on REWIND outcomes (5.4 years observation):

Time to First Occurrence of:	Dulaglutide N = 4949	Placebo N = 4952	Hazard Ratio (95%CI)
Composite of MACE:	**594 (12.0%)**	**663 (13.4%)**	**.88 (.79, .99)**
Cardiovascular (CV) death	317 (6.4%)	346 (7.0%)	.91 (.78, 1.06)
Non-fatal myocardial infarction (MI)	205 (4.1%)	212 (4.3%)	.96 (.79, 1.16)
Non-fatal stroke	135 (2.7%)	175 (3.5%)	.76 (.61, .95)
Fatal or non-fatal MI	223 (4.5%)	231 (4.7%)	.96 (.79, 1.15)
Fatal or non-fatal stroke	158 (3.2%)	205 (4.1%)	.76 (.62, .94)

AJMC. Press Release: Dulaglutde (https://www.ajmc.com/newsroom/fda-approves-dulaglutide-for-adults-with-t2d-regardless-of-cvd). Accessed March 2, 2020. Dulaglutide (Trulicity®) PI 2020 (http://pi.lilly.com/us/trulicity-uspi.pdf). Accessed February 24, 2020. Liraglutide (Victoza®) PI 2019 (https://www.novo-pi.com/victoza.pdf). Accessed March 2, 2020. Semaglutide (Ozempic®) PI 2020 (https://www.novo-pi.com/ozempic.pdf). Accessed March 2, 2020.

Treatment Guidelines for Primary and Secondary Prevention of CVD in Diabetes

2019 ACC/AHA Guidelines on the Primary Prevention of CVD

Hypertension	Lipids	Antiplatelet therapy	CVD	Glycemic control to reduce CVD risk
Log-linear association of *increasing* systolic BP (SBP) and diastolic BP (DBP) levels and risk of ASCVD	**Primary ASCVD prevention** *requires risk factor assessment* in childhood *Statin therapy indicated in those <19 y with familial dyslipidemia history (hx)*	Low-dose aspirin • *Secondary ASCVD* prevention • **Lack of net benefit** in primary ASCVD prevention (select patient consideration)	Dietary counseling for heart-healthy diet *Lowers CVD events and CVD mortality*	**1st line—metformin** ***Reductions:*** • ***39%*** *MI* • ***36%*** *all-cause mortality* • ***32%*** *DM-related micro- and macrovascular outcomes*
BP increase (20 mm/Hg *SBP or* 10 mm/Hg *DBP*) **doubled death risk** from: • Stroke • Heart disease • Other vascular disease	**Lifetime risk** assessment for young adults (20–39 y) *Consider statins with family hx of premature ASCVD & LDL-C ≥160*		**≥150 minutes/week** moderate-to-vigorous physical activity (aerobic and resistance) *Lowers HbA1c ~ 0.7%*	**SGLT2 inhibitors** *Significant reduction in ASCVD events and heart failure*
BP-lowering meds advised *even at stage 1 HTN* with estimated 10-year ASCVD risk ≥10%			**Quit smoking** • Increases ***all-cause mortality*** risk • Causal for ASCVD	**GLP-1 receptor agonists** *Significant ASCVD event reduction in high-risk T2DM*

It may be reasonable to initiate **SGLT2-i** or **GLP-1 RA** therapy for **primary CVD prevention** in T2DM patients with additional risk factors for CVD.

Arnett DK, et al. *J Am Coll Cardiol*. 2019;74:e177-e232.

CV Risk Factor Reduction Strategies in DM

American Diabetes Association (ADA)

BP (mm/Hg)

- Lifestyle for >120/80; drug therapy for ≥140/90
- Use ACEI*/ARB*, dihydropyridine CCB, or thiazide-like diuretics; target BP <140/90
- Start with 2 drugs if BP ≥160/100
- Multiple drug therapy usually necessary

Lipids (mg/dL)

20–39 years + CVD RFs	40–75 years + CVD RFs	>75 years
Moderate-intensity statin	Moderate-intensity statin	Moderate-intensity statin

- **In adults with diabetes at higher risk:** High-intensity statin if 10-yr ASCVD risk is ≥20%. If overt ASCVD, high-intensity statin and add ezetimibe or PCSK-9i if LDL >70.

TGs >500	TGs 135–499 +ASCVD/other CV risk on statin	TGs 175–499
Treat pharmacologically (fibrates, EPA)	Consider adding icospent ethyl	Address lifestyle, glycemic control, other factors (eg, TG-raising meds)

Aspirin

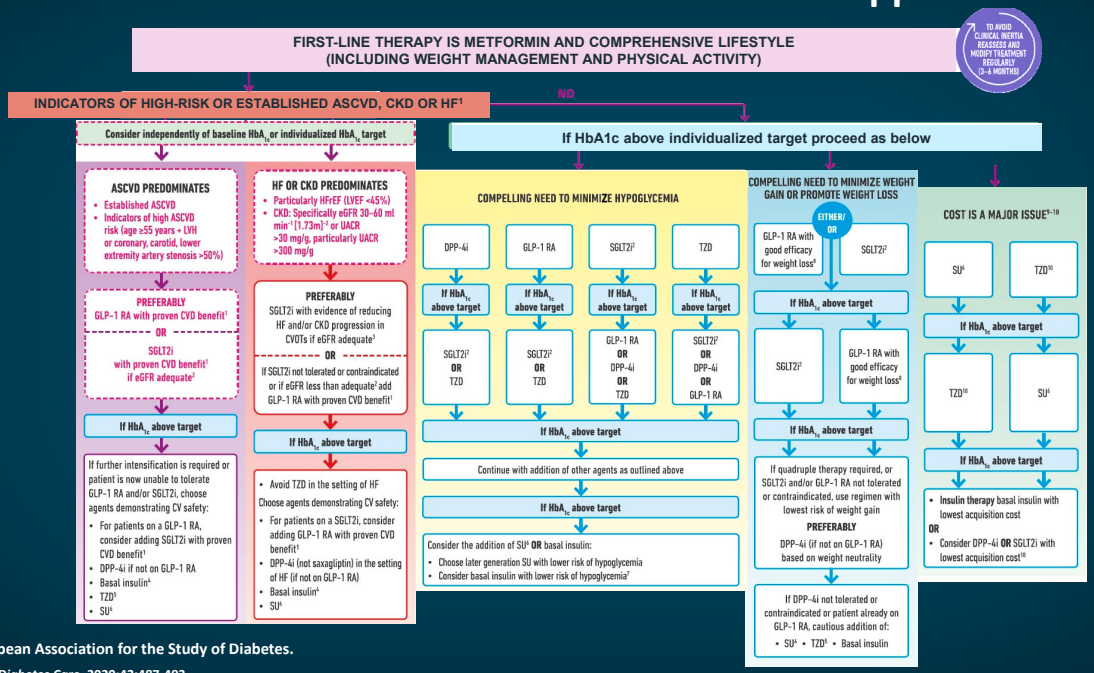
- **+ ASCVD**: ASA 75–162 mg/d for *secondary prevention*
- 'High-risk': Consider ASA 75–162 mg/d for *primary prevention* after weighing risks/benefits

*favored if albuminuria.

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; RF = risk factor; EPA = eicosapentaenoic acid.

ADA. *Diabetes Care*. 2020;43(suppl 1):S111-S134.

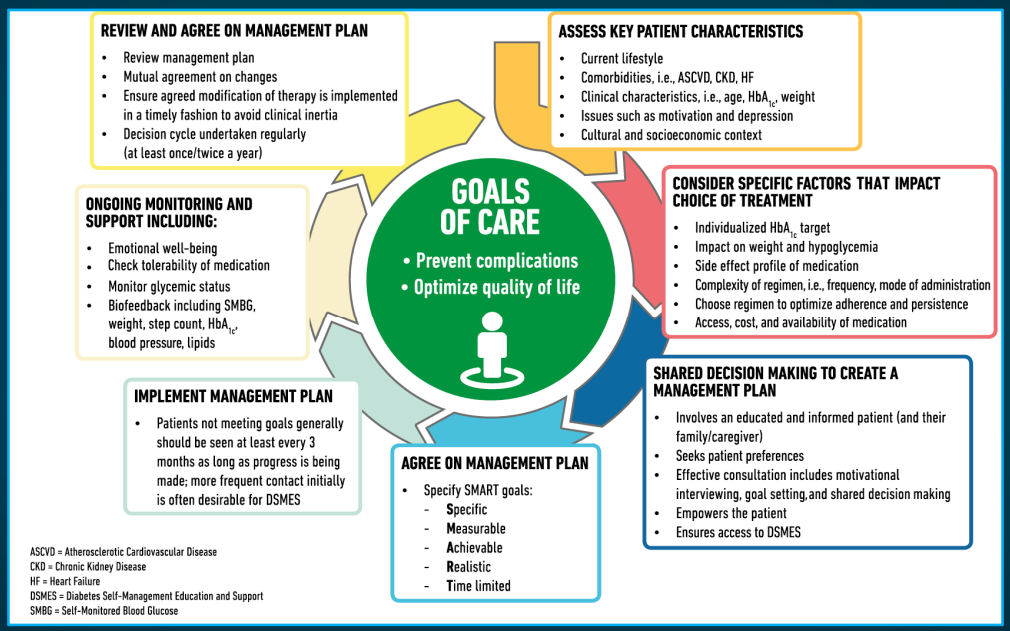
2019 ADA-EASD Consensus T2DM—Overall Approach



EASD = European Association for the Study of Diabetes.

Buse JB, et al. *Diabetes Care*. 2020;43:487-493.

Decision Cycle for Patient-Centered Glycemic Management in T2DM



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

Davies MJ, et al. *Diabetes Care*. 2018;41:2669-2701.

6 *Ps* of *Personalizing* Diabetes Care

1. ***P*athophysiology**	Insulin resistance vs deficiency? Stage of disease?
2. ***P*otency**	Distance from HbA1c target?
3. ***P*recautions**	Side effects, contraindications?
4. "***P*erks"**	Added benefits beyond glucose control? (weight, BP, CV, renal)
5. ***P*racticalities**	Tablets vs injections? Administration frequency? Need for blood glucose monitoring?
6. ***P*rice**	Branded vs generic? Insurance coverage?

Inzucchi SE. *Endocrinol Metab Clin North Am.* 2018;47:137-152.

Characteristics to Consider When Individualizing Therapy in Older Patients With T2DM

- Comorbid conditions (CHF, cancer, etc.)
- Diabetes duration
- Presence of macrovascular disease
- Presence of CKD
  - Decreased drug clearance
  - Associated CVD
- Presence of advanced retinopathy, with impaired vision
- History of severe hypoglycemia
- Psychologic, social, and economic characteristics
  - Safety concerns and support systems
  - Adverse effects of medications (polypharmacy)
  - Psychological/cognitive status
  - Economic considerations
  - Quality of life

ADA. *Diabetes Care.* 2019;42(suppl 1):S139-S147. Moghissi E. *Diabetes Ther.* 2013;4:239-256.

Reducing Atherosclerotic Cardiovascular Disease in T2DM

Summary

1. T2DM has a complex pathogenesis.
2. Glucose-lowering options have expanded markedly over the past 10–15 years.
3. "Foundation therapy" remains **lifestyle** and **metformin**. Several options are available beyond metformin.
4. Recent clinical trials demonstrate that CV (and CKD) risk are reduced with certain glucose-lowering classes of agents, including **SGLT2 inhibitors** and **GLP-1-R agonists**.
5. With any treatment decision, it is important to weigh both the risks and benefits of each agent and design a treatment regimen ***individualized*** to the patient.
6. Also, ***don't forget to address CV risk factors***!

Case Studies

CASE STUDY 1

Healthy, Newly Diagnosed Patient with T2DM

Healthy, Newly Diagnosed Patient with T2DM

- CC: BD is a 44-year-old African-American woman who presents for T2DM evaluation.
- HPI:
  - –She had gestational diabetes during the last 2 of her 3 pregnancies, the first treated with diet and the last needing insulin; her diabetes resolved post-partum.
  - –Her diabetes re-emerged about 6 years after her last delivery with a noted HbA1c of 6.8% within the last 6 months. Because of her history, she had already been watching her diet and trying to be as active as possible.
  - –Despite these measures, her A1c has continued to climb and is now at 7.4%.
  - –Her medical history is otherwise negative, except for frequent vaginal yeast infections and migraine headaches.

CC = chief complaint; HPI = history of present illness.

Healthy, Newly Diagnosed Patient with T2DM
History

Past medical history: migraines, yeast vaginitis x 1 episode yearly for past 3–4 years

Past surgical history: C-section x 2

Social history: nurse practitioner working in a family medicine practice; married, with 3 children (ages 5, 8, and 10); non-smoker; non-drinker; takes 9000 steps per day on pedometer; vegetarian

Family history: sister and mother with T2DM, no CVD

Allergies: NKDA

Medications: metformin 1000 mg BID, rizatriptan, metoclopramide, naproxen prn, fluconazole prn

NKDA = no known drug allergies; BID = twice daily; prn = as needed.

Healthy, Newly Diagnosed Patient with T2DM
Exams, Labs, and Studies

Physical exam

Vitals: weight = 184 lbs, BMI = 30.7 kg/m^2, BP = 128/84, HR = 72, RR = 14

Normal exam except for obesity

Laboratories

- FPG = 123, HbA1c = 7.4%
- Cr = 0.9, eGFR = 104, UACR = 12 mcg/mg Cr
- LDL-C = 164 mg/dL, HDL-C = 81 mg/dL, TGs = 98 mg/dL

Studies

- EKG: normal

BMI = body-mass index; HR = heart rate; RR = respiratory rate; Cr = creatinine.

Cardiovascular risk?

Diagnostic and Therapeutic Recommendations

Healthy, Newly Diagnosed Patient with T2DM
Considerations

Additional interventions to consider:

Studies

- None

Therapeutic management

- How would you address this patient's T2DM?
- How would you address this patient's other CV risk factors

- A1c target <7.0%
- Add one of several agents (SU, TZD, DPP4i, SGLT2i, GLP-1 RA, basal insulin)
- Individualization is key
- DPP4i may be easiest option

- Address LDL-C (when?)

CASE STUDY 2

Add-On Therapy in a T2DM Patient with CAD

Add-On Therapy in a T2DM Patient with CAD

- CC: RA is a 63-year-old woman with a 6-year history of T2DM on metformin monotherapy, who is referred for suboptimal glycemic control in the setting of known CAD.
- HPI:
  - –She presented 6 years ago with a HbA1c of 7.5% after 2–3 years of prediabetes. Metformin was started and titrated to a dose of 1500 mg/day, and her A1c fell to 6.8%. Over the intervening years, A1c has slowly climbed to her most recent result of 7.9%.
  - –During these years, she developed exertional angina with a positive nuclear stress test. Cardiac catherization showed single-vessel disease, for which she received a drug-eluting stent, with resolution of her symptoms. She has known normal left-ventricular function.

Add-On Therapy in a T2DM Patient with CAD

History

Past medical history: hypertension, hyperlipidemia, breast cancer, colonic polyps, primary hypothyroidism (Hashimoto disease), NAFLD, OA knees

Past surgical history: lumpectomy (radiation), polypectomy, arthroscopic meniscal surgery L knee

Social history: high school math teacher; divorced, with one adult child; former smoker; 2 glasses wine most days; inactive; diet high in carbs (sweets)

Family history: + T2DM both parents; mother had stroke, and father had heart failure

Allergies: PCN, sulfa drugs

Medications: losartan 50 mg QD, amlodipine 5 mg QD, chlorthalidone 25 mg QD, lovastatin 20 mg QD, aspirin 81 mg QD, ticagrelor 60 mg BID, anastrozole 1 mg QD

NAFLD = non-alcoholic fatty liver disease; OA = osteoarthritis; PCN = penicillin.

Add-On Therapy in a T2DM Patient with CAD

Exams, Labs, and Studies

Physical exam

Vitals: weight = 181 lbs, BMI = 29.3 kg/m^2, BP = 128/82, HR = 66, RR = 16

No evidence of HF, no retinopathy, no neuropathy

Laboratories

- FPG = 116, HbA1c = 7.9%
- Cr = 0.79, eGFR = 87, UACR = 54 mcg/mg Cr
- AST = 49, ALT = 62
- LDL-C = 190 mg/dL, HDL-C = 44 mg/dL, TGs = 161 mg/dL

Studies

- EKG: normal
- Cardiac echo: normal

AST = aspartate aminotransferase; ALT = alanine aminotransferase.

Cardiovascular risk?

Diagnostic and Therapeutic Recommendations

Add-On Therapy in a T2DM Patient with CAD

Considerations

Additional interventions to consider:

Studies

- None

Therapeutic management

- How would you address this patient's T2DM?
- How would you address this patient's other CV risk factors

- Consider maximizing metformin dose
- Add 2nd agent: SGLT2i or GLP-1 RA
- A1c target <7.5%

- Weight loss
- Increase aerobic activity
- Intensify lipid therapy

Thank you!

Questions and Answers

Reducing CVD in Patients with T2DM Poster Portal

Project ECHO®

Med Learning Group
New York

T2DM.posterprogram.com