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Examining the Impact of Cardiovascular Safety with Emerging Treatments for Type 2 Diabetes

MANAGED CARE REVIEW BOARD®

Jointly provided by

Impact Education LLC

PIM Postgraduate Institute for Medicine

This activity is supported by independent educational grants from Boehringer Ingelheim Pharmaceuticals Inc./ Lilly USA, LLC Alliance, Merck & Co., Inc., and Novo Nordisk, Inc.

AMCP Academy of Managed Care Pharmacy®

Held in conjunction with AMCP Managed Care & Specialty Pharmacy Annual Meeting 2017.

Educational Objectives

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- Recognize the rationale for cardiovascular outcome trials (CVOTs) in T2DM and review data from recent CVOTs of anti-hyperglycemic agents
- Examine alignment of managed care T2DM treatment algorithms with recent CVOT data
- Implement patient-centered strategies to minimize cardiovascular risk in patients treated in a managed care setting
- Discuss the potential impact of CVOT results on benefit design strategies

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Type 2 Diabetes and Cardiovascular Outcomes Trials (CVOTs)

Jennifer Green, MD
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Duke University Medical Center
Chief, Endocrine Section
Durham VA Medical Center

Learning Objective

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- Recognize the rationale for cardiovascular outcomes trials (CVOT) in T2D and review data from recent CVOT of anti-hyperglycemic agents

Diabetes is Associated with Significant Loss of Life Years

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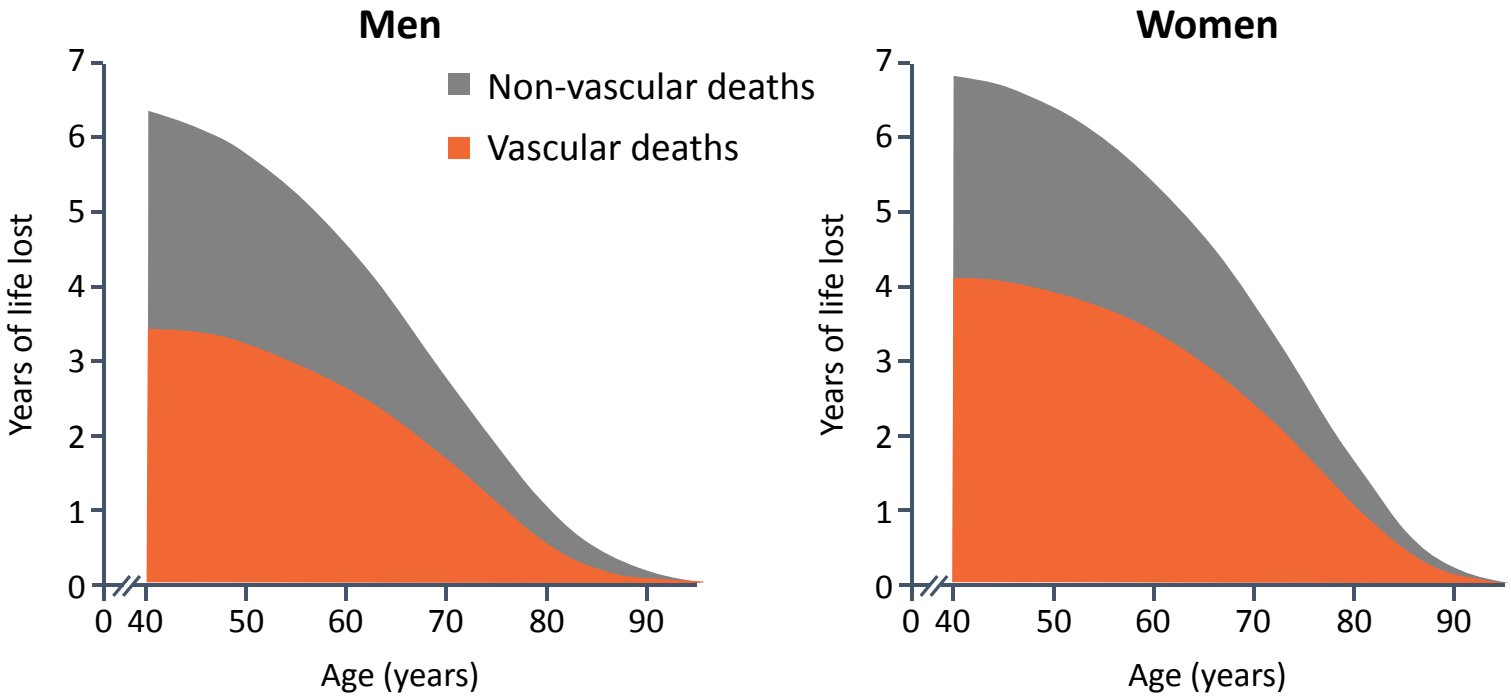

On average, a 50-year-old individual with diabetes and no history of vascular disease will die 6 years earlier compared to someone without diabetes

Seshasai SR, et al. *N Engl J Med*. 2011;364:829-841.

Pathophysiologic Progression of Type 2 Diabetes and Its Vascular Complications

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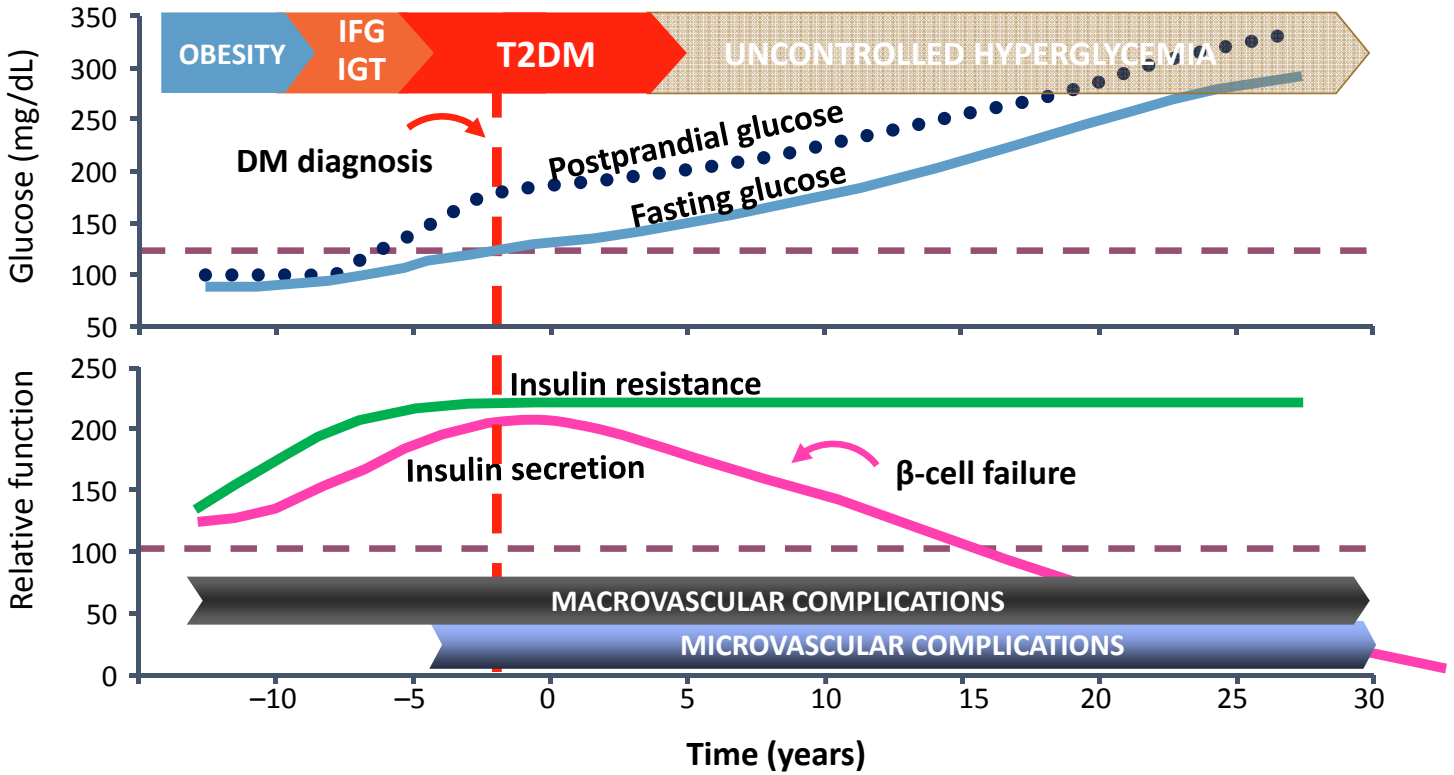

IFG = impaired fasting glucose; IGT = impaired glucose tolerance; T2DM = type 2 diabetes mellitus

Adapted from Ramlo-Halsted BA, et al. *Clin Diabetes.* 2000;18:80-84.

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Cardiovascular Outcomes: Recent Trials

FDA Guidelines for CV Safety Trials for Antihyperglycemic Medications (2008)

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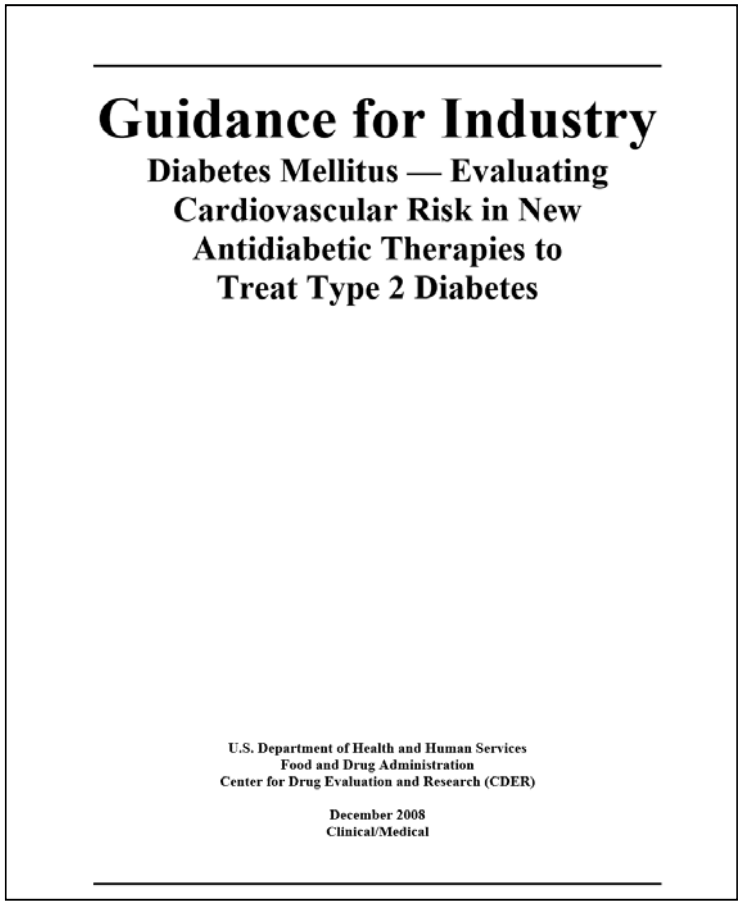

Guidance for Industry

Diabetes Mellitus — Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

December 2008
Clinical/Medical

- As part of the approval process for antidiabetic medications…

"…a postmarketing trial generally will be necessary to definitively show that the ***upper bound of the two-sided 95 percent confidence interval for the estimated risk ratio is less than 1.3****.*

This can be achieved by conducting a single trial that is adequately powered or by combining the results from a premarketing safety trial with a similarly designed postmarketing safety trial. ***This clinical trial will be a required postmarketing safety trial.***

FDA Guidance on Conduct of CVOTs

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- Patient selection
  - Focus on high-risk populations including those with advanced disease, elderly and those with renal impairment
- Duration
  - At least 2 years of CV safety data
- Endpoints
  - A prospective independent adjudication of CV events in phase 2 and 3 studies must also be performed including CV mortality, myocardial infarction (MI) and stroke, and possibly hospitalization for ACS, and urgent revascularization

US Food and Drug Administration. Guidance for industry. 2008. https://www.fda.gov/downloads/Drugs/.../Guidances/ucm071627.pdf. Accessed March 2017.

Possible Statistical Scenarios for Drug Approval Based on CVOT Results

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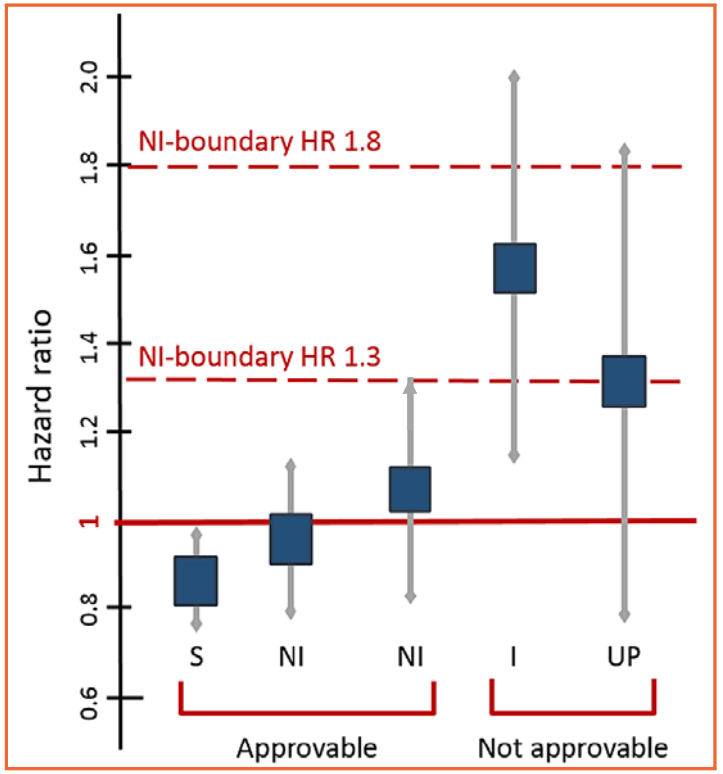
- Possible scenarios for approval of new glucose lowering drugs depending on the hazard ratio (HR) for CV risk
- An upper bound of the two-sided 95% confidence interval (CI) for the estimated increased risk above the non-inferiority (NI) boundary of 1.3 as well as underpowered studies prevents FDA approval



S=superiority; NI=non-inferiority; I=inferiority; UP=underpowered; HR=hazard ratio

Schnell O, et al. *Cardiovasc Diabetol*. 2016; 15:139.

US Food and Drug Administration. Guidance for industry. 2008. https://www.fda.gov/downloads/Drugs/.../Guidances/ucm071627.pdf. Accessed March 2017.

Large CVOTs Are Underway or Recently Completed Since 2008

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Drug Class	Trial	Drug	Primary Endpoint	N
DPP-4 inhibitors	TECOS	Sitagliptin	MACE + UA	14,671
	SAVOR-TIMI 53	Saxagliptin	MACE	16,492
	EXAMINE	Alogliptin	MACE	5,380
	CAROLINA	Linagliptin	MACE + UA	6,000
	CARMELINA	Linagliptin	CV risk	8,300
GLP-1 RA	LEADER	Liraglutide	MACE	9,340
	SUSTAIN-6	Semaglutide	MACE	3,297
	ELIXA	Lixisenatide	MACE	6,068
	EXSCEL	Exenatide	MACE	14,000
	ITCA 650	Exenatide	MACE	4,000
	REWIND	Dulaglutide	MACE	9,622
	HARMONY	Albiglutide	MACE	9,400
SGLT2 inhibitors	EMPA-REG	Empagliflozin	MACE	7,020
	CANVAS	Canagliflozin	MACE	4,407
	DECLARE-TIMI 58	Dapagliflozin	MACE	17,150
	VERTIS CV	Ertugliflozin	MACE	8,000
Insulin	DEVOTE	Degludec	MACE	7,500

MACE = major adverse cardiac events (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke UA= hospitalization for unstable angina

Smith RJ, et al. *Diabetes Care*. 2016; 39:738-742; Jayawardene D, et al. *Heart Lung Circ.* 2014;23:997-1008.

COVT Completion Dates

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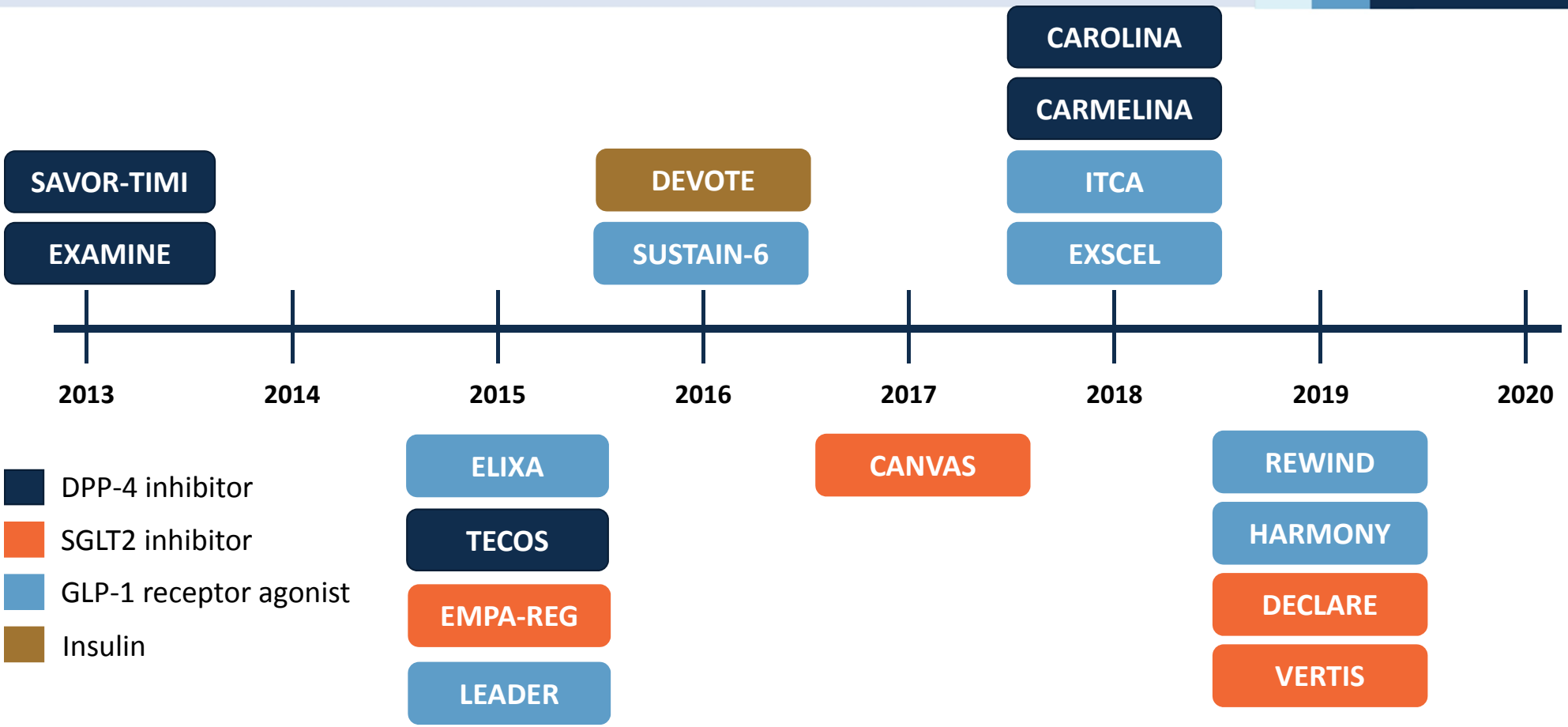

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Results

Interpretation, Comparison and Application of the Results: Caveats and Limitations

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- Results may only be valid for the particular patient groups enrolled in the studies
  - Thus far, focus has been on high CV risk patients with T2DM
- It is unclear how translatable the results are to the general patient population
- Comparison among results is difficult and is limited by significant variation in
  - Study design
  - Patient selection criteria including patient age, disease duration, baseline blood glucose levels
  - Definition of cardiovascular risk and manifestations of CV disease at baseline
  - Baseline and achieved A1C levels
  - Study endpoints
  - Statistical analysis

Schnell O, et al. *Cardiovasc Diabetol*. 2016; 15:139.

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CVOTs:
DPP-4 Inhibitors

SAVOR TIMI-53: Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus-Thrombolysis in MI

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Study Design

- **Patients** with T2D and CVD or CVD risk (n=16,492)
- **Randomization**
  - Saxagliptin: n=8,280
  - Placebo: n=8,212
- **Superiority study** with provision to test for noninferiority
- **Primary endpoint**: Composite of CV death, nonfatal MI, or nonfatal ischemic stroke
- **Secondary endpoint**: CV death, nonfatal MI, nonfatal ischemic stroke, hospitalization for HF, coronary revascularization, or unstable angina

Key Results

- Median follow-up: 2.1 years
- Endpoint A1C
  - Saxagliptin: 7.7% ± 1.4% (P<0.001 vs placebo)
  - Placebo: 7.9% ± 1.5%
- CV outcomes
  - Primary: HR 1.00 (95% CI 0.89 to 1.12); *P*=0.99 for superiority; *P*<0.001 for noninferiority
  - Secondary HR: 1.02 (95% CI 0.94 to 1.11); *P*=0.66 for superiority
- **Higher incidence of HF hospitalization w/saxagliptin**
- No difference between groups in incidence of acute/chronic pancreatitis; fewer cases of pancreatic cancer w/ saxagliptin; more cases of nonfatal angioedema w/saxagliptin (8 vs 1)

CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; MI, myocardial infarction; SAVOR-TIMI, Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus–Thrombolysis in Myocardial Infarction.

Scirica BM, et al. *N Engl J Med*. 2013;369,1317-1326.

SAVOR TIMI-53: Clinical Outcomes

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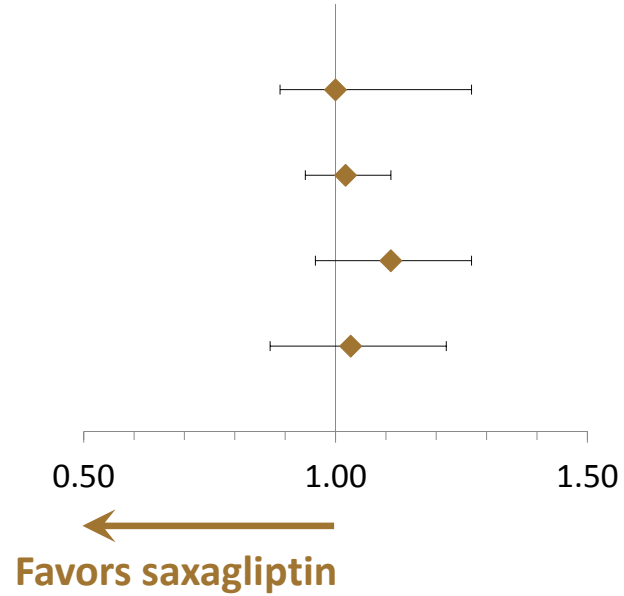
	Hazard ratio (95% CI)	*P* value
Primary composite endpoint*	1.00 (0.89-1.12)	0.99
Secondary composite endpoint†	1.02 (0.94-1.11)	0.66
Death from any cause	1.11 (0.96-1.27)	0.15
CV death	1.03 (0.87-1.22)	0.72



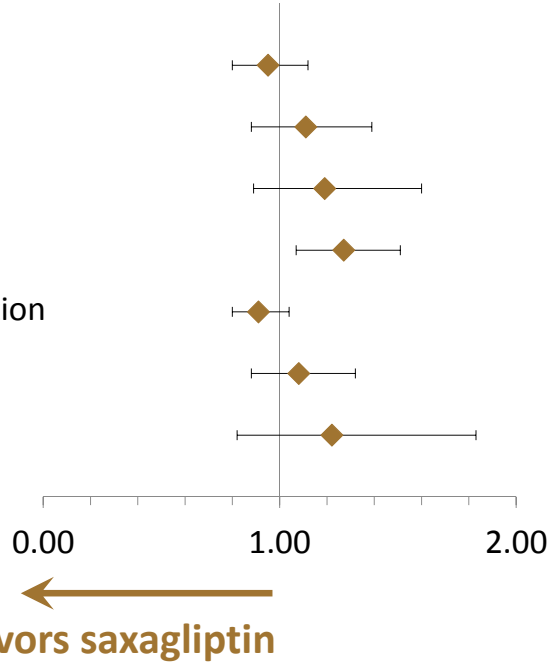
*CV death, nonfatal MI, or nonfatal ischemic stroke; †CV death, nonfatal MI, nonfatal ischemic stroke, hospitalization for HF, coronary revascularization, or unstable angina.

CI, confidence interval; CV, cardiovascular; HF, heart failure; MI, myocardial infarction; SAVOR-TIMI, Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus–Thrombolysis in Myocardial Infarction.

Scirica BM, et al. *N Engl J Med*. 2013;369,1317-1326.

SAVOR TIMI-53: Individual Secondary Outcomes

	Hazard ratio (95% CI)	*P* value
Myocardial infarction	0.95 (0.80-1.12)	0.52
Ischemic stroke	1.11 (0.88-1.39)	0.38
Hospitalization for unstable angina	1.19 (0.89-1.60)	0.24
Hospitalization for heart failure	**1.27 (1.07-1.51)**	**0.007**
Hospitalization for coronary revascularization	0.91 (0.80-1.04)	0.18
Renal endpoint*	1.08 (0.88-1.32)	0.46
Hospitalization for hypoglycemia	1.22 (0.82-1.83)	0.33



*Doubling of creatinine, initiation of dialysis, renal transplantation, or creatinine >6.0 mg/dL

CI, confidence interval; CV, cardiovascular; SAVOR-TIMI, Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus–Thrombolysis in Myocardial Infarction.

Scirica BM, et al. *N Engl J Med*. 2013;369,1317-1326.

SAVOR TIMI-53: Characteristics and Risk of HF Hospitalization

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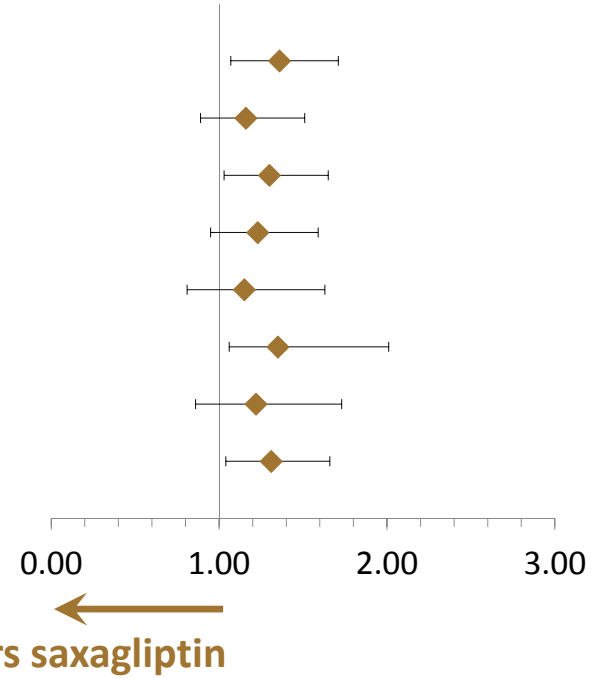
	Hazard ratio (95% CI)	*P* value
eGFR ≤60 mL/min	**1.36 (1.07-1.71)**	**0.01**
eGFR >60 mL/min	1.16 (0.89-1.51)	0.27
No prior heart failure	**1.30 (1.03-1.65)**	**0.03**
Prior heart failure	1.23 (0.94-1.59)	0.13
No risk factors*	**1.15 (0.81-1.63)**	**0.45**
1 risk factor	**1.35 (1.06-1.72)**	**0.02**
2 risk factors	1.22 (0.86-1.73)	0.27
Highest quartile NT-proBNP (333-46,627 pg/mL)	**1.31 (1.04-1.66)**	**0.02**



*eGFR ≤60 mL/min or history of previous HF.

HF, heart failure; NT-proBNP, N-terminal pro B-type natriuretic peptide; Q, quartile; SAVOR-TIMI, Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus–Thrombolysis in Myocardial Infarction.

Scirica BM, et al. *Circulation.* 2014;130:1579-1588.

SAVOR TIMI-53: Risk of Hospitalization for Heart Failure

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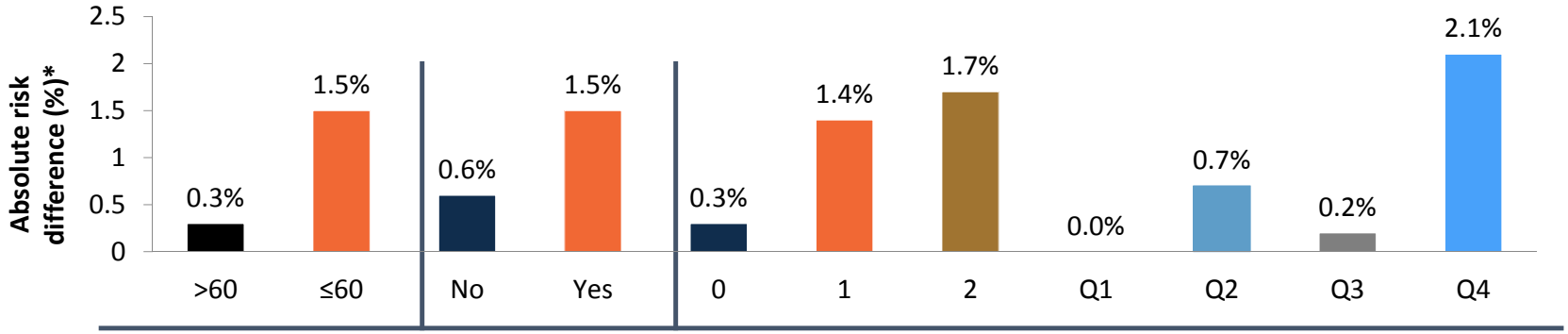

		eGFR (mL/min)		HF history		No. HF risk factors†			NT-proBNP quartiles (pg/mL)			
No. excess HHF events in patients treated with saxagliptin vs placebo per 1000 pt-y									(5-64)	(65-141)	(142-333)	(334-46,627)
	n =	11,637	4,855	14,387	2,105	10,418	5,188	866	3,076	3,076	3,076	3,073
		2	8	3	8	1	7	8	0	4	1	10

*Saxagliptin vs placebo.

†eGFR ≤60 mL/min or history of previous HF.

HF, heart failure; HHF, hospitalizations for heart failure.

Scirica BM, et al. *Circulation*. 2014;130:1579-1588.

EXAMINE: Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care

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Study Design

- **Patients** with T2D and ACS (n=5,380)
- **Randomization**
  - Alogliptin: n=2,701
  - Placebo: n=2,679
- **Noninferiority study**: prespecified HR margin = 1.3 for primary endpoint
- **Primary endpoint**: Composite of CV death, nonfatal MI, or nonfatal stroke
- **Secondary endpoint**: CV death, nonfatal MI, nonfatal stroke, urgent revascularization for unstable angina

*Upper boundary of 1-sided repeated CI, alpha level 0.01.
CI, confidence interval; CV, cardiovascular
White W, et al. *N Engl J Med*. 2013;369:1327-1335.

Key Results

- Median follow-up: 18 months
- Least squares mean difference in A1C: -0.36% (95% CI -0.43 to -0.28; *P*<0.001) for alogliptin vs placebo
- CV outcomes
- Primary: HR 0.96 (upper boundary of the one-sided repeated CI, ≤1.16); *P*=0.32 for superiority; *P*<0.001 for noninferiority
  - Secondary: HR 0.95 (upper boundary of the one-sided repeated CI, ≤1.14*); *P*=0.26 for superiority
- No difference between alogliptin and placebo in incidence of acute and chronic pancreatitis, cancer, renal impairment, angioedema, or severe hypoglycemia
- NS increased risk HHF

EXAMINE: Clinical Outcomes

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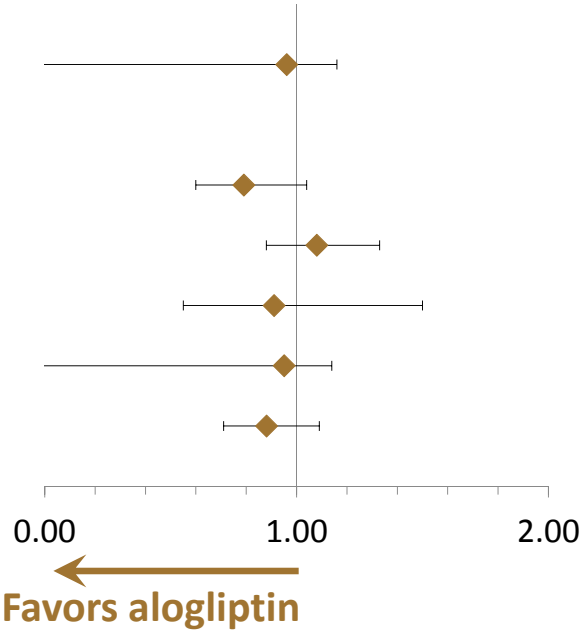
	Hazard ratio (95% CI)	*P* value
Primary composite	0.96 (≤1.16)*	0.32
Primary endpoint components		
CV death	0.79 (0.6-1.04)	0.10
Nonfatal MI	1.08 (0.88-1.33)	0.47
Nonfatal stroke	0.91 (0.55-1.50)	0.71
Primary secondary endpoint†	0.95 (≤1.14)*	0.26
Death from any cause	0.85 (0.66-1.10)	0.21



*Upper boundary of 1-sided repeated CI, alpha level 0.01.
†CV death, nonfatal MI, nonfatal stroke, urgent revascularization for unstable angina.
CI, confidence interval; CV, cardiovascular; EXAMINE, Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care; MI, myocardial infarction.

White W, et al. *N Engl J Med*. 2013;369:1327-1335.

TECOS: Trial Evaluating Cardiovascular Outcomes with Sitagliptin

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Study Design

- **Patients** with T2D and CVD (n=14,671)
- **Randomization**
  - Sitagliptin: n=7,332
  - Placebo: n=7,339
- **Noninferiority study**: 1.3 marginal upper boundary of 2-sided 95% CI. Testing for superiority also performed
- **Primary endpoint**: Composite of CV death, nonfatal MI, nonfatal stroke, or hospitalization for unstable angina
- **Secondary endpoint**: Composite of CV death, nonfatal MI, or nonfatal stroke

Key Results

- Median follow-up: 3.0 years
- Least squares mean difference in A1C: -0.29% (95% CI -0.32 to -0.27) for sitagliptin vs placebo
- Noninferior to placebo for cardiovascular outcomes
  - Primary: HR 0.98 (95% CI 0.88 to 1.09); *P*<0.001 for noninferiority
  - Secondary: HR 0.99 (95% CI 0.89 to 1.11); *P*<0.001 for noninferiority
  - Superiority not demonstrated
- No difference between sitagliptin and placebo in incidence of infections, cancer, renal failure, hypoglycemia, or noncardiovascular death

Green JB, et al. *N Engl J Med*. 2015;373:232-242.

TECOS: Primary and Other Outcomes

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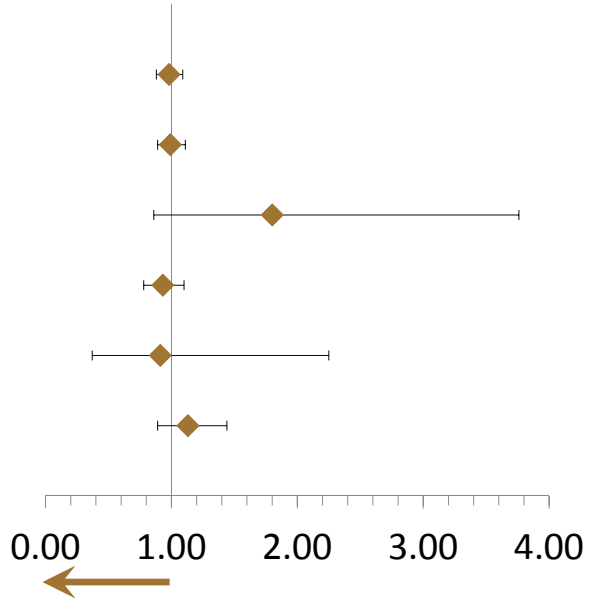

	Hazard ratio (95% CI)	*P* value
Primary composite endpoint*	0.98 (0.88-1.09)	<0.001 (NI)
Secondary composite endpoint†	0.99 (0.89-1.11)	<0.001 (NI)
Acute pancreatitis	1.80 (0.86-3.76)	0.12
Any cancer (except nonmelanoma skin cancer)	0.93 (0.78-1.10)	0.38
Pancreatic cancer	0.91 (0.37-2.25)	0.85
Severe hypoglycemia	1.13 (0.89-1.44)	0.31

*Cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for unstable angina.
†Secondary composite: cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke.
NI=non-inferiority
TECOS, Trial Evaluating Cardiovascular Outcomes with Sitagliptin.

Green JB, et al. *N Engl J Med*. 2015;373:232-242.

TECOS: Individual Secondary Outcomes

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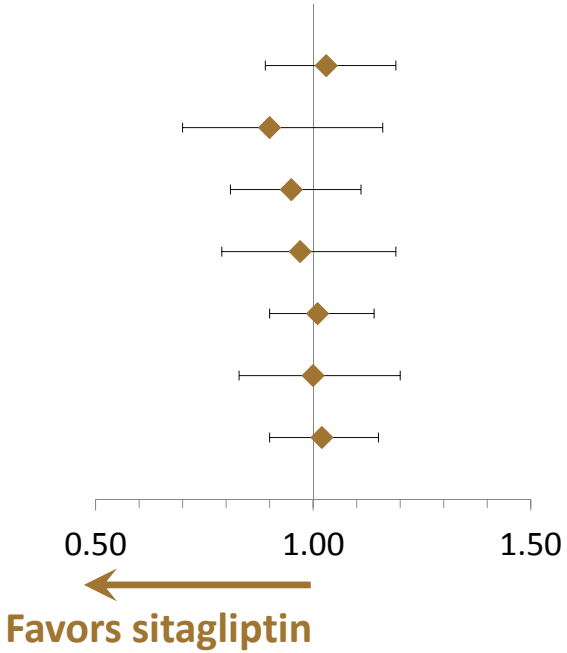
	Hazard ratio (95% CI)	*P* value
CV death	1.03 (0.89-1.19)	0.71
Hospitalization for unstable angina	0.90 (0.70-1.16)	0.42
Fatal or nonfatal MI	0.95 (0.81-1.11)	0.49
Fatal or nonfatal stroke	0.97 (0.79-1.19)	0.76
Death from any cause	1.01 (0.90-1.14)	0.88
Hospitalization for heart failure	1.00 (0.83-1.20)	0.98
Hospitalization for heart failure or CV death	1.02 (0.90-1.15)	0.74



TECOS, Trial Evaluating Cardiovascular Outcomes with Sitagliptin.

Green JB, et al. *N Engl J Med*. 2015;373:232-242.

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CVOTs:
SGLT2 Inhibitors

EMPA-REG: Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients

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Study Design

- **Patients** with T2D and CVD (n=7,020)
- **Randomization**
  - Empagliflozin: n=4,687
  - Placebo: n=2,333
- **Noninferiority study**: prespecified HR margin = 1.3 for primary endpoint
- **Primary endpoint**: composite of CV death, nonfatal MI (excluding silent MI), or nonfatal stroke
- **Secondary endpoint**: composite of CV death, nonfatal MI (excluding silent MI), nonfatal stroke, and hospitalization for unstable angina

Key Results

- Median follow-up: 3.1 years
- Week 206 A1C, difference from placebo
  - Empagliflozin 10 mg: -0.24% (95% CI, -0.40% to -0.08%)
  - Empagliflozin 25 mg: -0.36% (95% CI, -0.51% to -0.20%)
- CV outcomes (pooled empagliflozin 10 mg + 25 mg)
  - Primary: HR 0.86 (95.02% CI 0.74 to 0.99); *P*=0.04 for superiority; *P*<0.001 for noninferiority
  - Secondary: HR 0.89 (95% CI 0.78 to 1.01); *P*=0.08 for superiority; *P*<0.001 for noninferiority
- Significantly lower rates of all-cause death, CV death, and HF hospitalization with empagliflozin
- Increased rates of genital infections in empagliflozin-treated patients

CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; MI, myocardial infarction.

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

EMPA-REG: Clinical Outcomes

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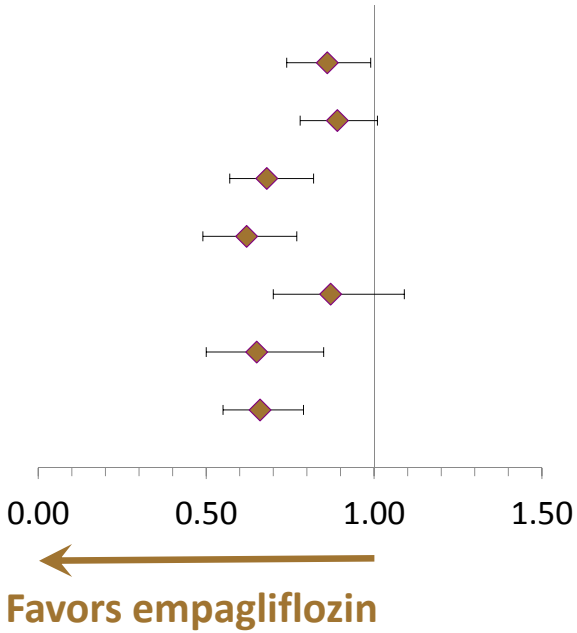
	Hazard ratio (95% CI)	*P* value
Primary composite endpoint*	0.86 (0.74-0.99)	0.04
Secondary composite endpoint†	0.89 (0.78-1.01)	0.08
Death from any cause	0.68 (0.57-0.82)	<0.001
CV death	0.62 (0.49-0.77)	<0.001
Fatal or nonfatal MI	0.87 (0.70-1.09)	0.23
Hospitalization for HF	0.65 (0.50-0.85)	0.002
Hospitalization for HF or CV death	0.66 (0.55-0.79)	<0.001



*CV death, nonfatal MI (excluding silent MI), or nonfatal stroke; †CV death, nonfatal MI (excluding silent MI), nonfatal stroke, and hospitalization for unstable angina.

CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; MI, myocardial infarction.

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

EMPA-REG: Cardiovascular Outcomes and Death From Any Cause

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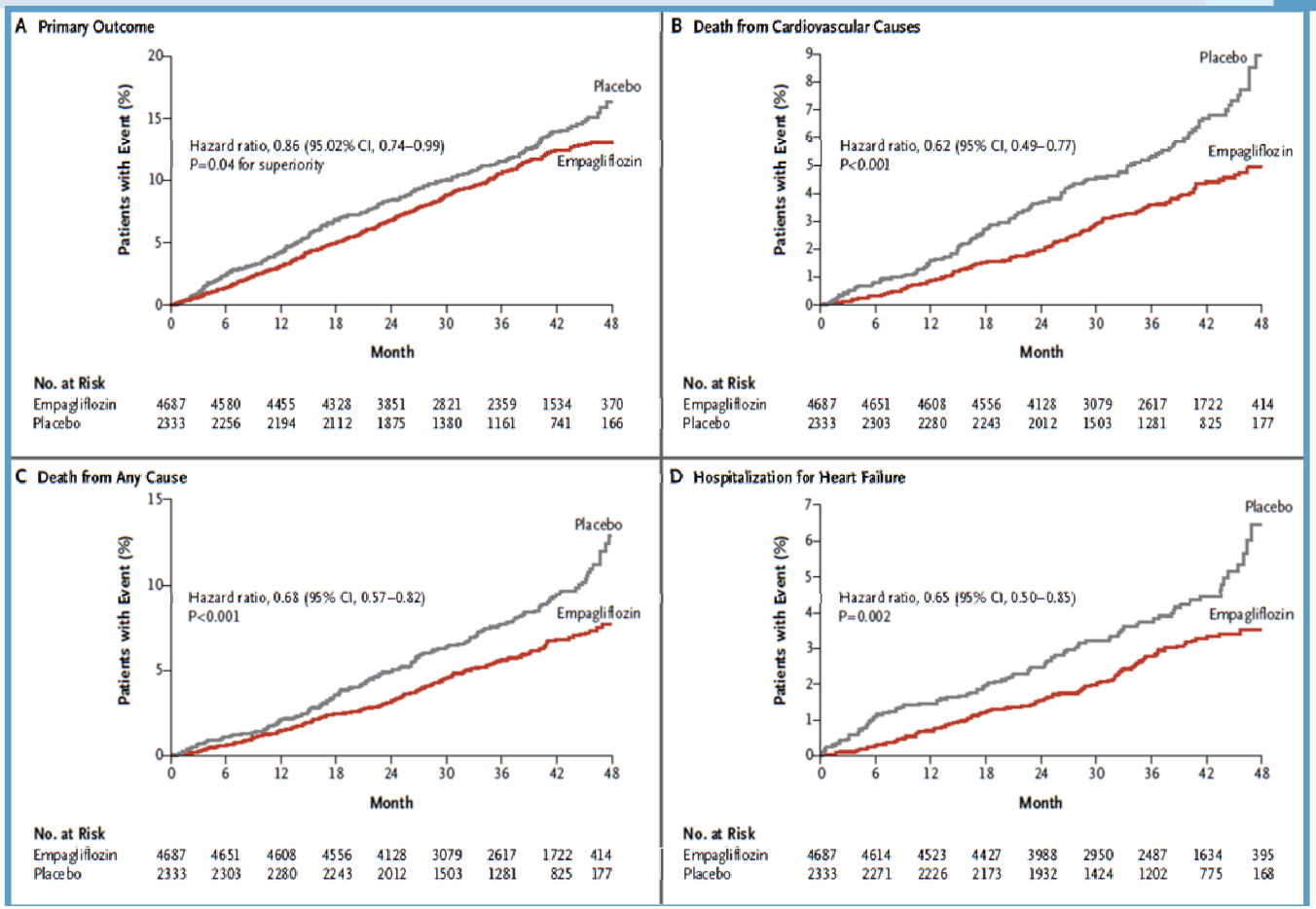

Zinman B, et al. *N Engl J Med*. 2015;373:2117-2128.

EMPA-REG: Renal Outcomes Over 3.2 Years

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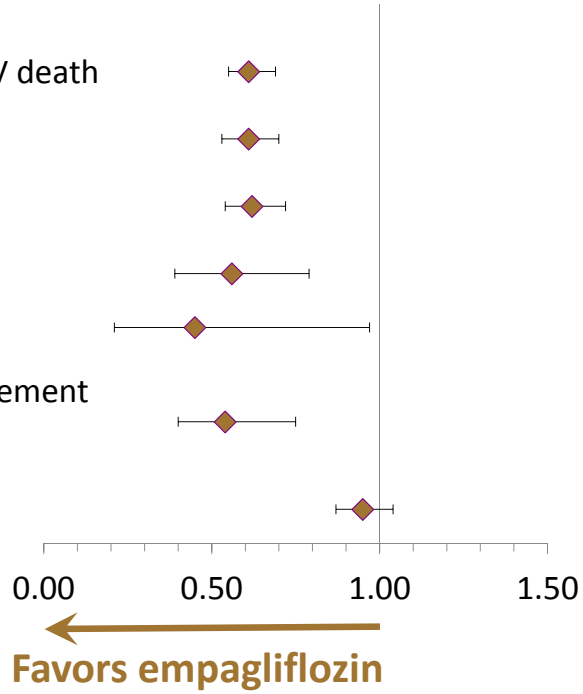
	Hazard ratio (95% CI)	*P* value
Incident or worsening nephropathy or CV death	0.61 (0.55-0.69)	<0.001
Incident or worsening nephropathy	0.61 (0.53-0.70)	<0.001
Progression to macroalbuminuria	0.62 (0.54-0.72)	<0.001
Doubling of SCr + eGFR ≤45	0.56 (0.39-0.79)	<0.001
Initiation of renal replacement therapy	0.45 (0.21-0.97)	0.04
Doubling of SCr + eGFR ≤45, renal replacement therapy, or renal disease death	0.54 (0.40-0.75)	<0.001
Incident albuminuria*	0.95 (0.87-1.04)	0.25



*In patients with normal albuminuria at baseline.

CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate in mL/min/1.73 m^2; HR, hazard ratio; SCr, serum creatinine.

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

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CVOTs:
GLP-1 Receptor Agonists

ELIXA: Evaluation of Lixisenatide in Acute Coronary Syndrome

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Study Design

- **Patients** with T2D and recent ACS event (n=6,068)
- **Randomization**
  - Lixisenatide: n=3,034
  - Placebo: n=3,034
- **Noninferiority study**: prespecified margin = 1.3 for upper bound of 95% CI of the HR for the primary endpoint
- **Primary endpoint:** composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for unstable angina
- **Secondary endpoint**: composite of the primary end point and hospitalization for heart failure, or coronary revascularization procedures

Key Results

- Duration of follow up: 2 years
- CV Outcomes
- Primary: HR 1.02 (95% CI 0.89 to 1.17); *P*<0.001 for noninferiority; *P*=0.81 for superiority
- Secondary: There were no significant differences in the rate of hospitalization for HF (HR 0.96; 95% CI, 0.75 to 1.23) or the rate of death (HR 0.94; 95% CI, 0.78 to 1.13)
- Findings were similar in those with a history of heart failure
- Modest weight gain benefit favoring lixisenatide: -0.6 kg with lixisenatide vs. -0.0 kg for placebo ($p < 0.001$)
- Hospitalization for heart failure: 4.2% vs. 4.0%

Pfeffer MA, et al. *N Engl J Med*. 2015; 373:2247-2257.

LEADER: Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results

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Study Design

- **Patients** with T2D and high CVD risk (n=9,340)
- **Randomization**
  - Liraglutide: n=4,672
  - Placebo: n=4,668
- **Noninferiority study**: prespecified margin = 1.3 for upper bound of 95% CI of the HR for primary endpoint
- **Primary endpoint**: composite of CV death, nonfatal MI (including silent MI), or nonfatal stroke
- **Secondary endpoint**: composite of CV death, nonfatal MI (including silent MI), nonfatal stroke, coronary revascularization, and hospitalization for unstable angina or HF

Key Results

- Median follow-up: 3.5 years
- Difference from placebo at 36 months
  - A1C: −0.40% (95% CI, −0.45% to −0.34%)
  - Weight: 2.3 kg (95% CI, 2.5 to 2.0 kg)
  - SBP: 1.2 mm Hg (95% CI, 1.9 to 0.5 mm Hg)
- CV outcomes
  - Primary: HR 0.87 (95% CI 0.78 to 0.97); *P*=0.01 for superiority
  - Secondary HR: 0.88 (95% CI 0.81 to 0.96); *P*=0.005 for superiority
- Significantly lower rates of all-cause death and CV death with liraglutide
- Increased rates of GI events in liraglutide-treated patients
- Lower numerical incidence of pancreatitis in liraglutide group (not statistically significant)

CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; MI, myocardial infarction.

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

LEADER: Clinical Outcomes

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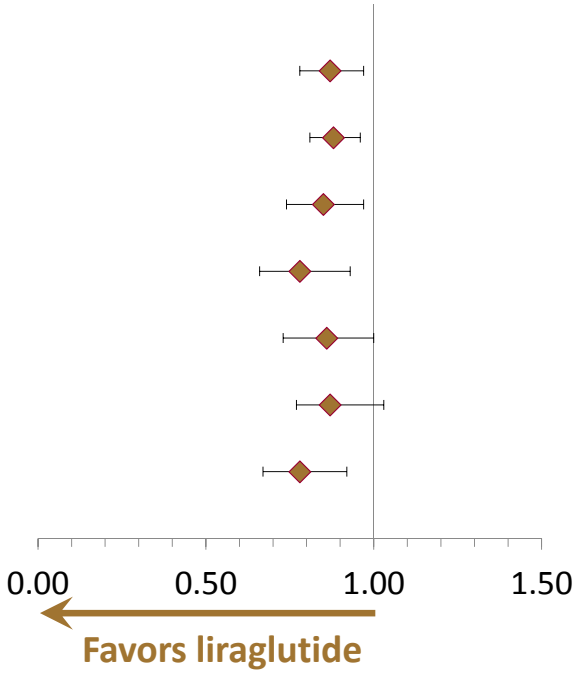
	Hazard ratio (95% CI)	*P* value
Primary composite endpoint*	0.87 (0.78-0.97)	0.01
Expanded composite endpoint†	0.88 (0.81-0.96)	0.005
Death from any cause	0.85 (0.74-0.97)	0.02
CV death	0.78 (0.66-0.93)	0.007
Fatal or nonfatal MI	0.86 (0.73-1.00)	0.046
Hospitalization for HF	0.87 (0.73-1.05)	0.14
Nephropathy‡	0.78 (0.67-0.92)	0.003



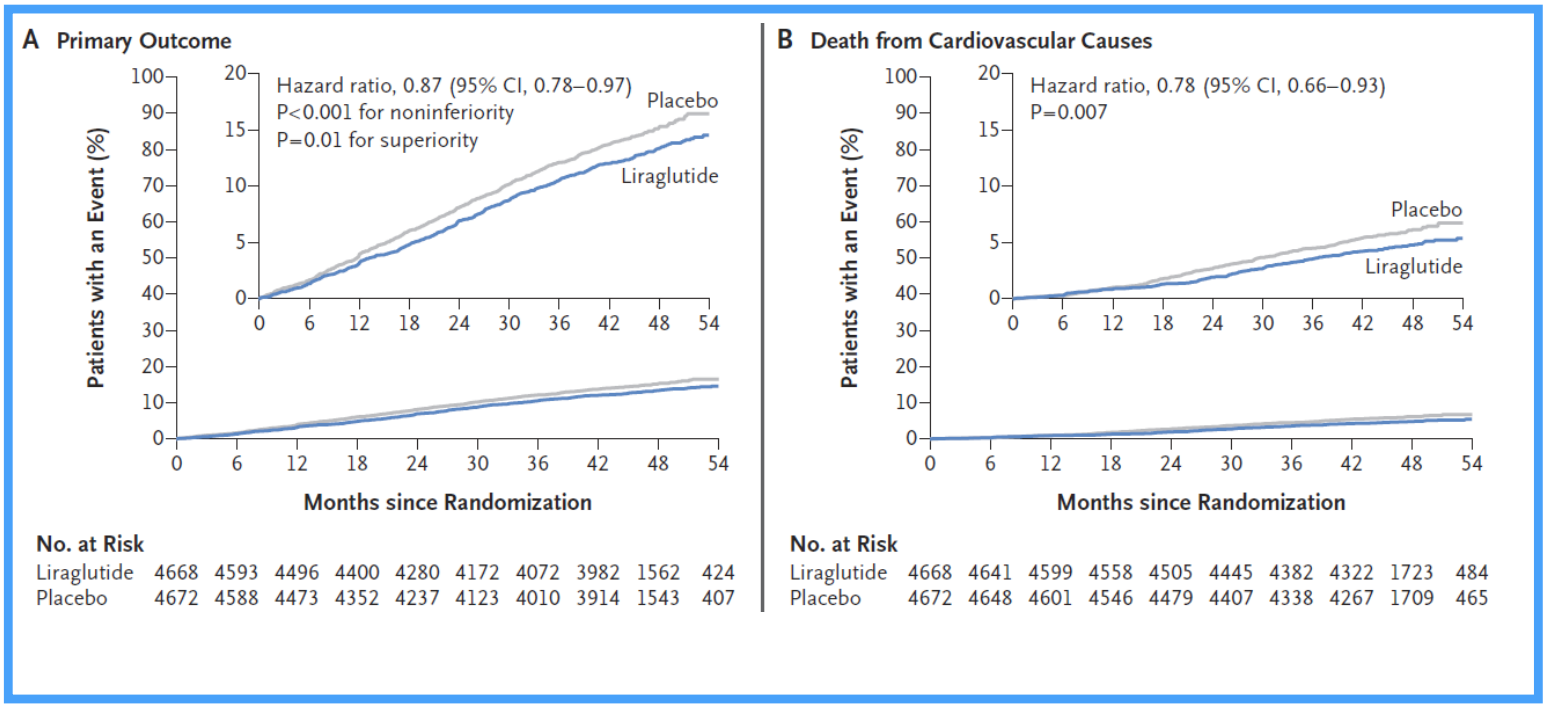
*CV death, nonfatal MI (including silent MI), or nonfatal stroke; †CV death, nonfatal MI (including silent MI), nonfatal stroke, coronary revascularization, and hospitalization for unstable angina or HF; ‡Defined as new onset of macroalbuminuria or a doubling of the serum creatinine level and an eGFR of ≤45 mL/min/1.73 m^2, the need for continuous renal-replacement therapy, or death from renal disease

CI, confidence interval; CV, cardiovascular; MI, myocardial infarction

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

LEADER: Clinical Outcomes

MANAGED CARE REVIEW BOARD®



*CV death, nonfatal MI (including silent MI), or nonfatal stroke.

CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; MI, myocardial infarction.

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

SUSTAIN 6: Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes

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Study Design

- **Patients** with T2D (n=3,297) age ≥50 years with established CVD or stage ≥3 CKD or age ≥60 years with at least one CV risk factor
- **Randomization**
  - Semaglutide: n=3,034
  - Placebo: n=3,034
- **Noninferiority study**: prespecified margin = 1.3 for upper bound of 95% CI of the HR for the primary endpoint
- **Primary endpoint**: first occurrence of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke
- **Secondary endpoints**: first occurrence of an expanded composite CV outcome (death from CV causes, nonfatal MI, nonfatal stroke, revascularization [coronary or peripheral], and hospitalization for UA or HF), an additional composite outcome (death from all causes, nonfatal MI, or nonfatal stroke), the individual components of the composite outcomes, retinopathy complications, and new or worsening nephropathy

Key Results

- Duration of follow up: 2 years
- CV Outcomes
- Primary: HR 0.74 (95% CI 0.58 to 0.95); *P*<0.001 for noninferiority; *P*=0.02 for superiority
- Secondary:
  - Nonfatal MI: HR 0.74 (95% CI, 0.51 to 1.08; *P*=0.12
  - Nonfatal stroke: HR 0.61 (95% CI, 0.38 to 0.99; *P*=0.04)
  - Rates of CV-related death were similar
  - Rates of new/worsening nephropathy were lower in the semaglutide group
  - Rates of retinopathy complications were significantly higher in the semaglutide group; HR 1.76 (95% CI, 1.11 to 2.78); *P*=0.02

Marso SP, et al. *N Engl J Med*. 2016;375:1834-1844.

SUSTAIN-6: Cardiovascular Outcomes

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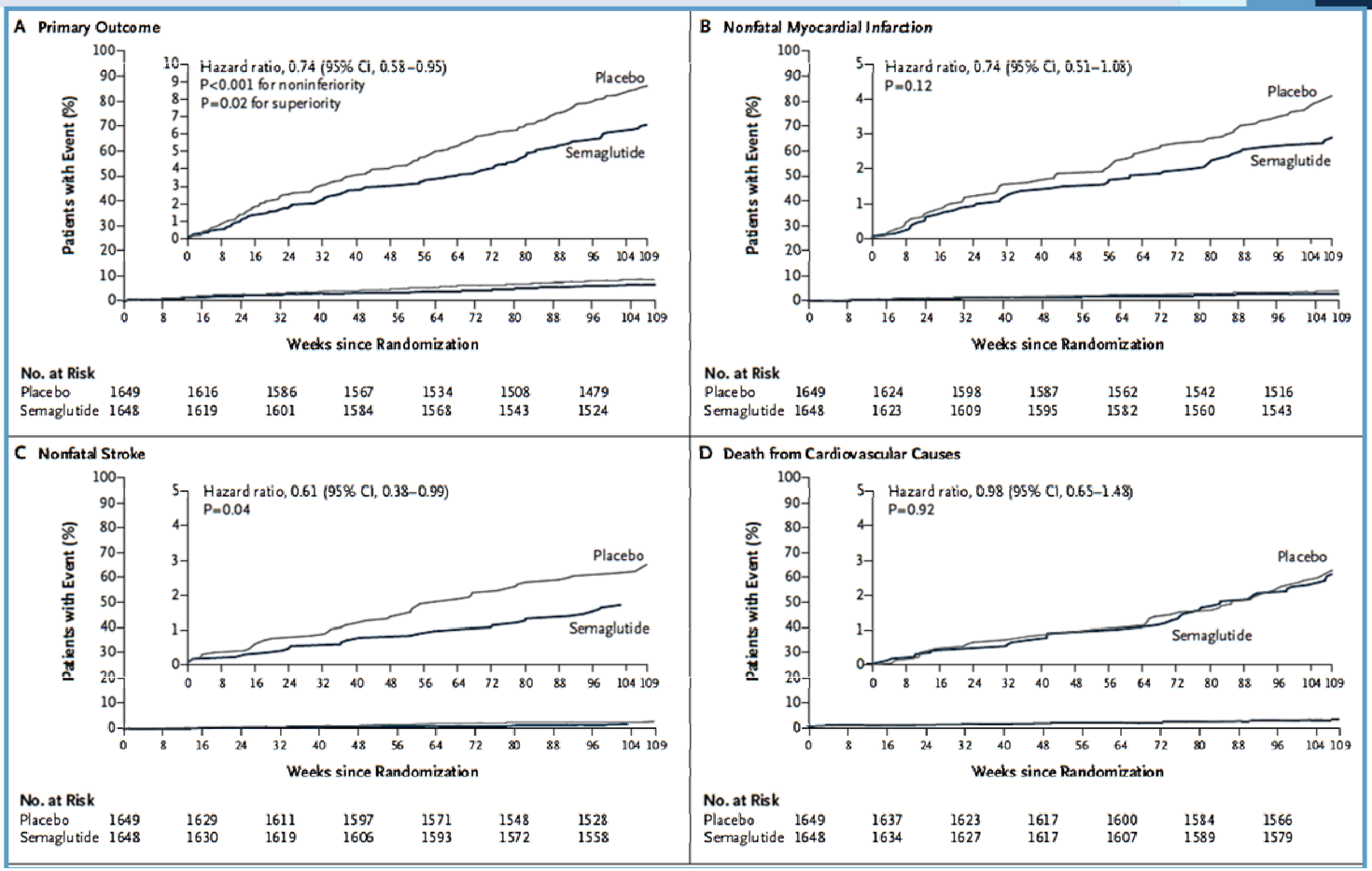

Marso SP, et al. *N Engl J Med*. 2016;375:1834-1844.

Summary of Completed CVOT Trials

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Drug Class	SAVOR TIMI-53	EXAMINE	TECOS
DPP-4 inhibitor	Neutral*	Neutral*	Neutral*
	LEADER	ELIXA	SUSTAIN-6
GLP-1 agonist	Beneficial	Neutral	Beneficial
	EMPA-REG		
SLGT2-Inhibitor	Beneficial		

*Although the DPP-4 inhibitor trials were neutral, there was no increase in the number of patients hospitalized for heart failure with sitagliptin (TECOS trial). Saxagliptin (SAVOR TIMI-53 trial), showed an increase in heart-failure events. Alogliptin (EXAMINE trial) showed a trend toward an increased risk of heart-failure events in T2DM patients.

Summary

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- Diabetes is a significant contributor to cardiovascular disease risk
- In 2008, the FDA mandated that all new therapies for diabetes must be rigorously assessed for CV safety
  - Majority of CVOTs have been designed to compare effects of antihyperglycemic agent to placebo, thus lack head-to-head comparisons
  - Methodological differences between trials and a focus on high risk populations, limits generalization of the results
- Seven CVOTs of have been completed; 3 show a reduction in CV risk (LEADER, SUSTAIN-6 and EMPA-REG) and 4 were neutral (eg, demonstrated noninferiority to placebo)

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Aligning Managed Care Type 2 Diabetes Treatment Algorithms with Recent Cardiovascular Outcomes Trial Data

John Fox, MD, MHA

Vice President, Associate Chief Medical Officer

Medical Affairs

Priority Health

Learning Objective

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- Examine alignment of managed care type 2 diabetes treatment algorithms with recent cardiovascular outcomes trial data

Standards of Medical Care in Diabetes—2017

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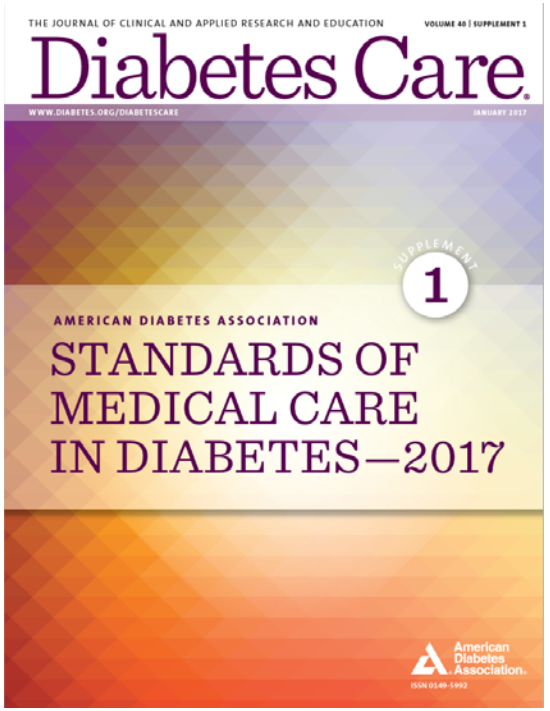
- Annual update from the American Diabetes Association (ADA)
- Includes new guidance multiple topics including
  - Glycemic targets
  - Pharmacologic approaches to achieving glycemic targets
  - Cardiovascular disease risk management
  - Lifestyle management
  - Patient-centered care



American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

Diabetes Care Delivery Challenges

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- Up to 50% of patients fail to meet targets for A1C, blood pressure (BP), or lipids
- Only 14% of patients meet targets for all A1C, BP, lipids, and nonsmoking measures
- CVD risk factor reduction continues to be a public health priority
- Care delivery remains fragmented
- Data on comparative effectiveness of treatment alternatives is limited

American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

Achieving A1C Treatment Goals: 2010-2015

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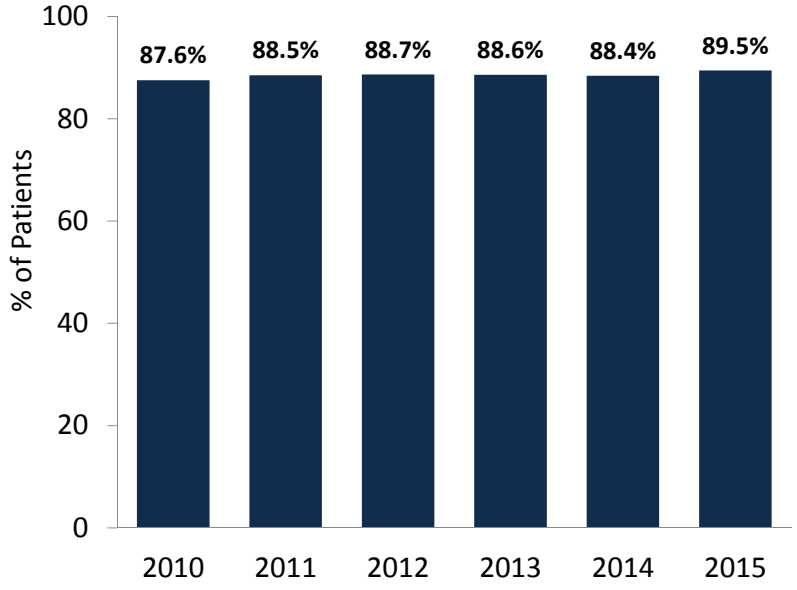
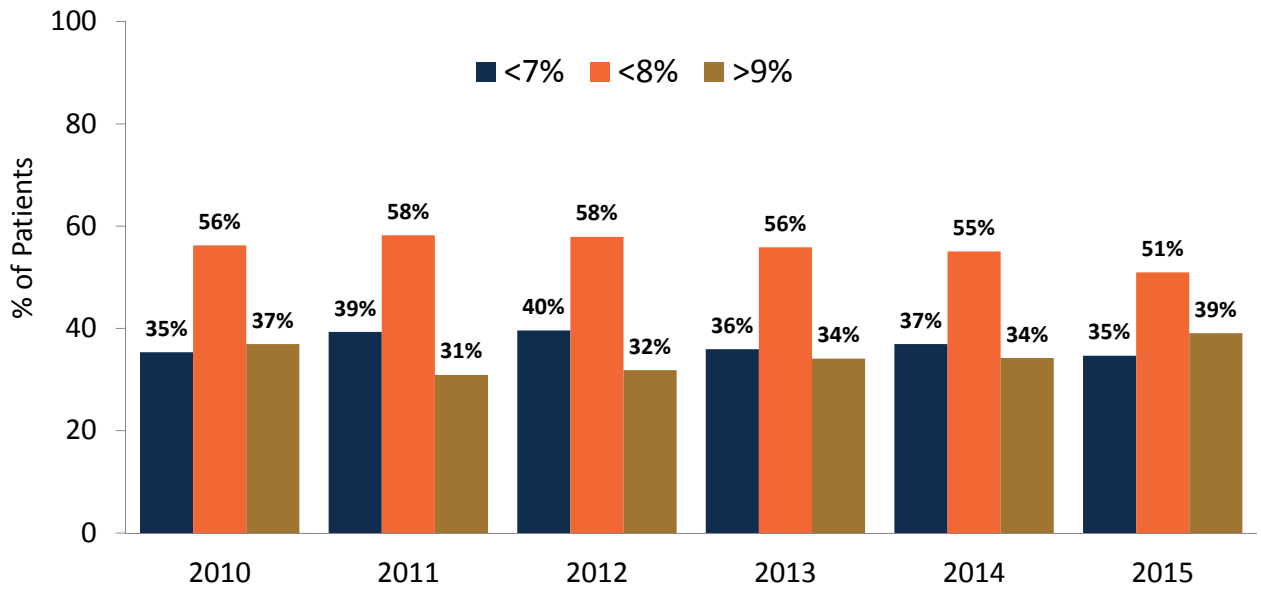
Screening for A1C in Commercial Plans 2010-2015



Achievement of ADA A1C Targets in Commercial Plans 2010-2015



National Committee for Quality Assurance. http://www.ncqa.org/report-cards/health-plans/state-of-health-care-quality/2016-table-of-contents/diabetes-care. Accessed February 2017.

Management Strategies to Improve Diabetes Outcomes

MANAGED CARE REVIEW BOARD®

- Early screening/prompt diagnosis
- Early intervention with agents supported by evidence-based treatment guidelines
- Intensify treatment to achieve and maintain glycemic goals
- Manage relevant comorbidities
- Tailor treatment decisions to patient preferences, prognosis, and goals
- Foster strong therapeutic relationships between the patient and physician

American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.
Inzucchi SE, et al. *Diabetes Care*. 2012;35:1364-1379.

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Achieving Glycemic Goals

Recommended A1C Goals for Adults

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Population	A1C Goal
Nonpregnant adults	**<7%**
Patients with • Short duration of diabetes • Type 2 diabetes treated with lifestyle or metformin only • Long life expectancy • No significant cardiovascular disease	**<6.5%**
Patients with • History of severe hypoglycemia • Limited life expectancy • Advanced microvascular or macrovascular complications • Extensive comorbid conditions • Long-standing diabetes in whom the goal is difficult to achieve	**<8%**

American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

Treatment Intensification to Achieve and Maintain Appropriate Glycemic Levels

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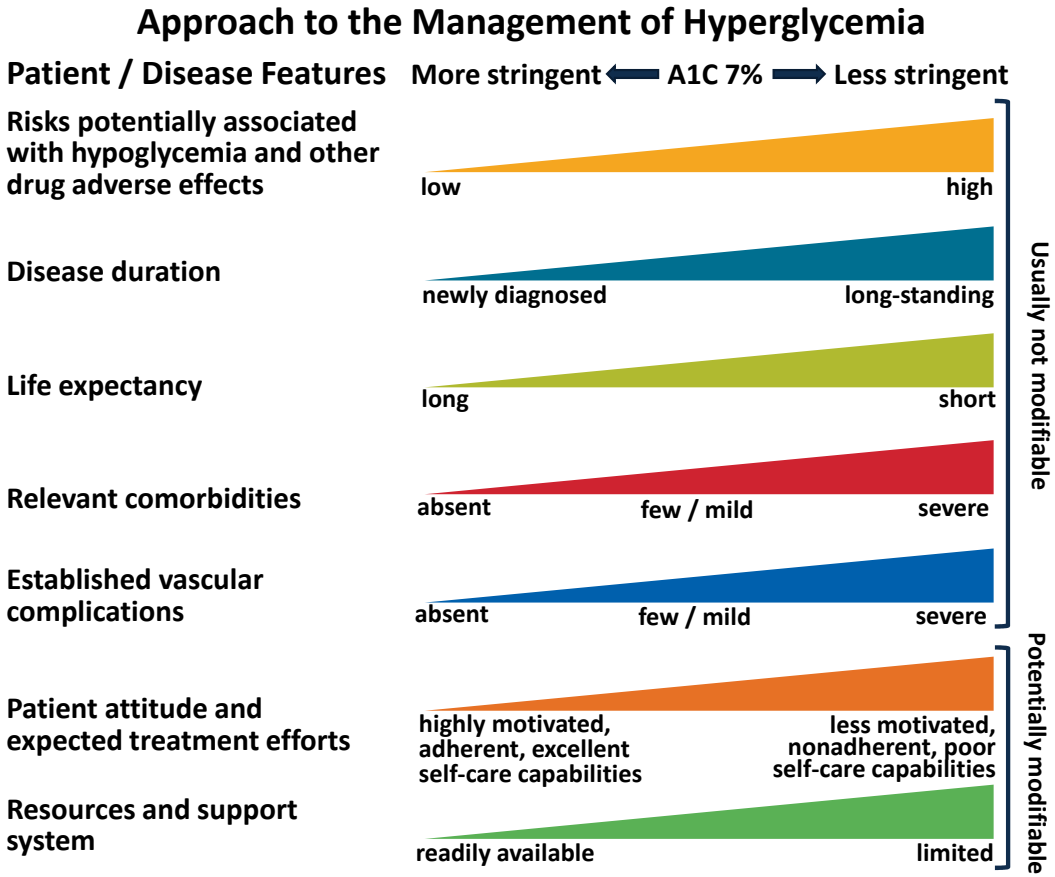
- Intensification approach should be individualized to match the needs of each patient and characteristics of the disease



American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

Improving Glycemic Levels With Lifestyle Interventions

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- Lifestyle modifications form the foundation of anti-glycemic care
- Activities include
  - Diabetes self-management
  - Weight optimization
  - Following a healthy diet
  - Increased physical activity levels
  - Smoking cessation
  - Routine immunization
  - Diagnosis and management of psycho-social conditions

American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

Pharmacologic Therapy for Type 2 Diabetes: General Principles

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- Goal: Reduce blood glucose levels and minimize side effects (especially hypoglycemia)
- Develop a treatment plan and set therapeutic goals
  - Drug choice is based on patient, disease, drug characteristics, and patient preference
- Start aggressively and taper (if necessary)
  - Assume each medication will improve HgA1c by 1%
  - Always add new agent first, titrate to get control, then stop first agent
- Cost-effectiveness models have suggested that some newer agents may be of relatively lower clinical utility based on high cost and moderate glycemic effect

American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

Pharmacologic Options

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Oral Agents

- Metformin
- α-glucosidase inhibitors
- Sulfonylureas
- Meglitinides
- Thiazolidinediones
- Sodium–Glucose Cotransporter 2 Inhibitors
- DPP-4 inhibitors (incretin)

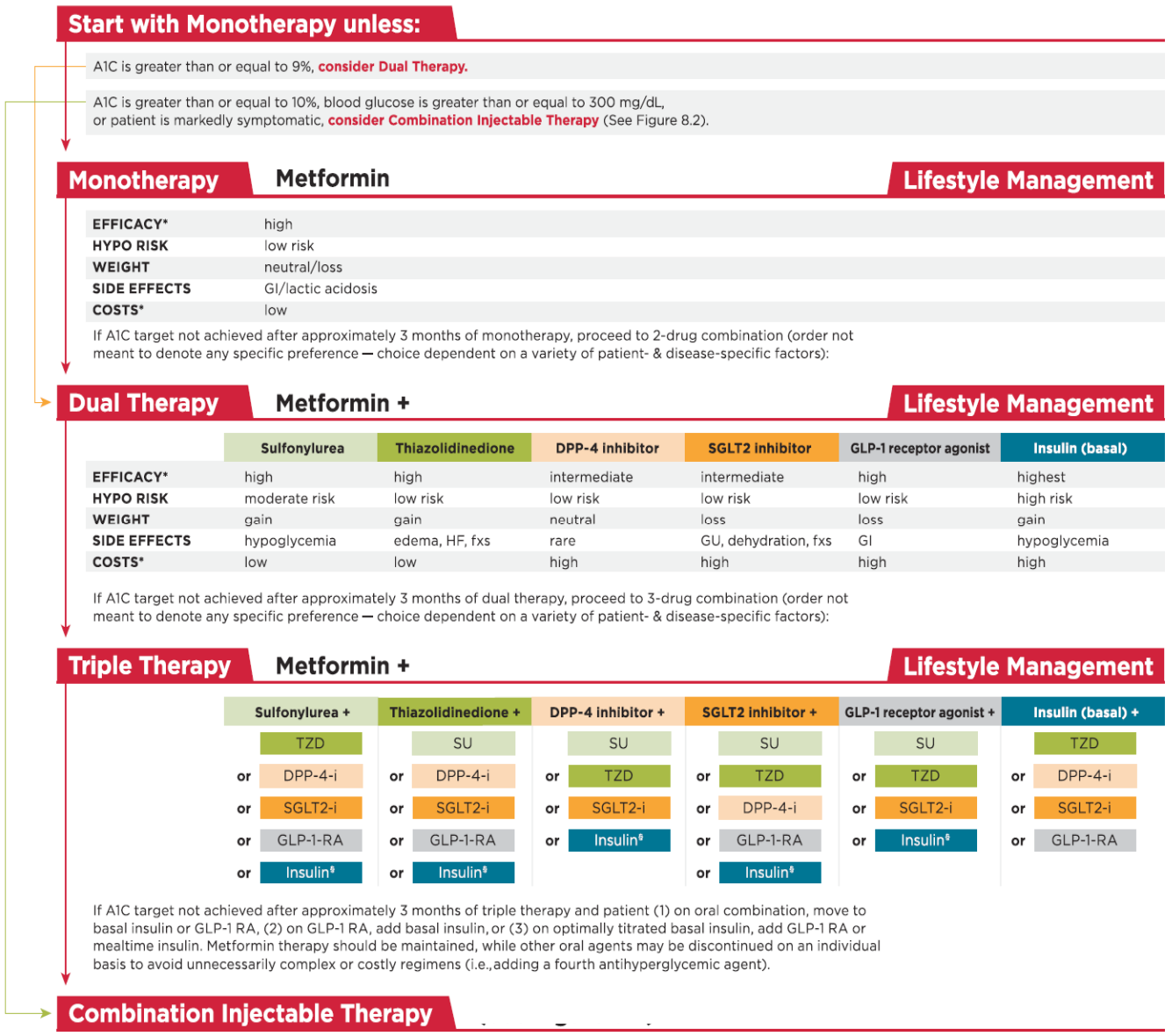
Injectable Agents

- Insulin
- Amylin analogs
- GLP-1 agonists (incretin)

American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

T2DM Treatment Algorithm

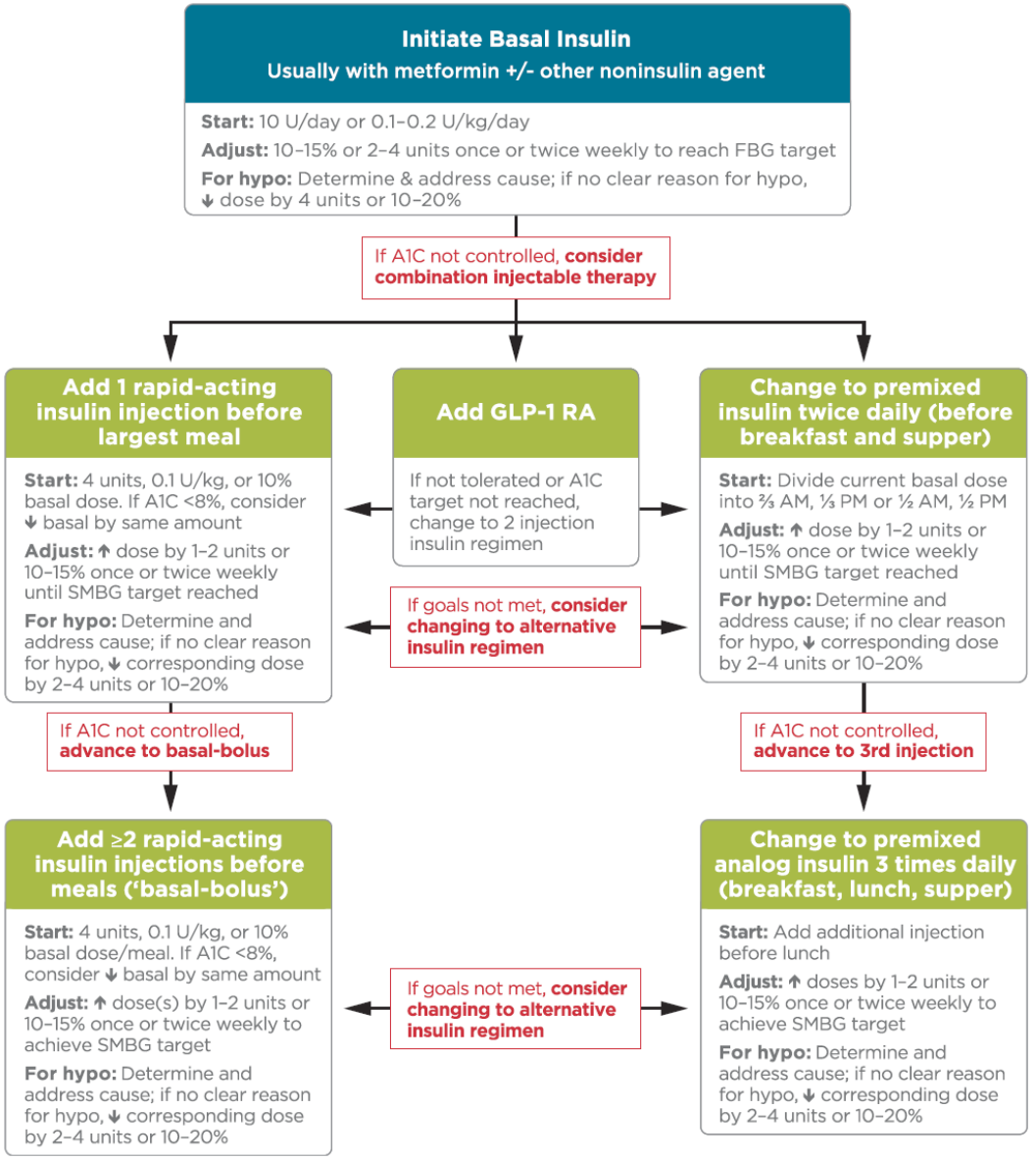
- General ADA recommendations for antihyperglycemic therapy in type 2 diabetes



American Diabetes Association. *Diabetes Care*. 2017;40(suppl 1):S1-S135.

T2DM Treatment Algorithm: Use of Insulin

- General ADA recommendations for use of combinations of injectable therapies
- Consider initiating when blood glucose is ≥300 mg/dL or A1C is ≥10% or if symptoms of hyperglycemia are present
- Regimens may be simplified as glucose targets are approached



American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

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CVOT Results and Diabetes Treatment Guidelines

A1C and Cardiovascular Outcomes

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The relationship between glycemic control and CVD has been examined in several trials completed **prior** to the FDA-mandated initiation of CVOTs

DCCT

- Trend toward lower risk of CVD events with intensive control (type 1)

EDIC

- 57% reduction in risk of nonfatal MI, stroke, or CVD death (type 1)

UKPDS

- Nonsignificant reduction in CVD events (type 2)

ACCORD, ADVANCE, VADT

- Suggested no significant reduction in CVD outcomes with intensive glycemic control (type 2)

American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

Overview of CVOTs with Antihyperglycemic Agents

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Drug Class	Trial	Drug	Primary Endpoint	N	Status
DPP-4 inhibitors	TECOS	Sitagliptan	MACE + UA	14,671	Completed
	SAVOR-TIMI 53	Saxagliptin	MACE	16,492	Completed
	EXAMINE	Alogliptin	MACE	5380	Completed
	CAROLINA	Linagliptan	MACE + UA	6000	2018
	CARMELINA	Linagliptan	CV risk	8300	2018
GLP-1 RA	LEADER	Liraglutide	MACE	9340	Completed
	SUSTAIN-6	Semaglutide	MACE	3297	Completed
	ELIXA	Lixisenatide	MACE	6068	Completed
	EXSCEL	Exenatide	MACE	14,000	2018
	ITCA	Exenatide	MACE	4000	2018
	REWIND	Dulaglutide	MACE	9622	2019
	HARMONY	Albiglutide	MACE	9400	2019
SGLT2 inhibitors	EMPA-REG	Empagliflozin	MACE	7020	Completed
	CANVAS	Canaglifozin	MACE	4407	2017
	DECLARE-TIMI-58	Dapagliflozin	MACE	17,150	2019
Insulin	DEVOTE	Degludec	MACE	7500	2018

MACE = major adverse cardiac events (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke); **UA**= hospitalization for unstable angina

Smith RJ, et al. *Diabetes Care*. 2016; 39:738-742; Jayawardene D, et al. *Heart Lung Circ.* 2014;23:997-1008.

Inclusion of CVOT Data in the 2017 Update of the Treatment Guidelines

MANAGED CARE REVIEW BOARD®

ADA guidelines include a brief review of 2 CVOTs that demonstrated benefits in high-risk patients with type 2 diabetes

Empagliflozin

Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME)

Liraglutide

Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results—A Long-Term Evaluation (LEADER) trial

EMPA-REG Results: Primary Endpoint

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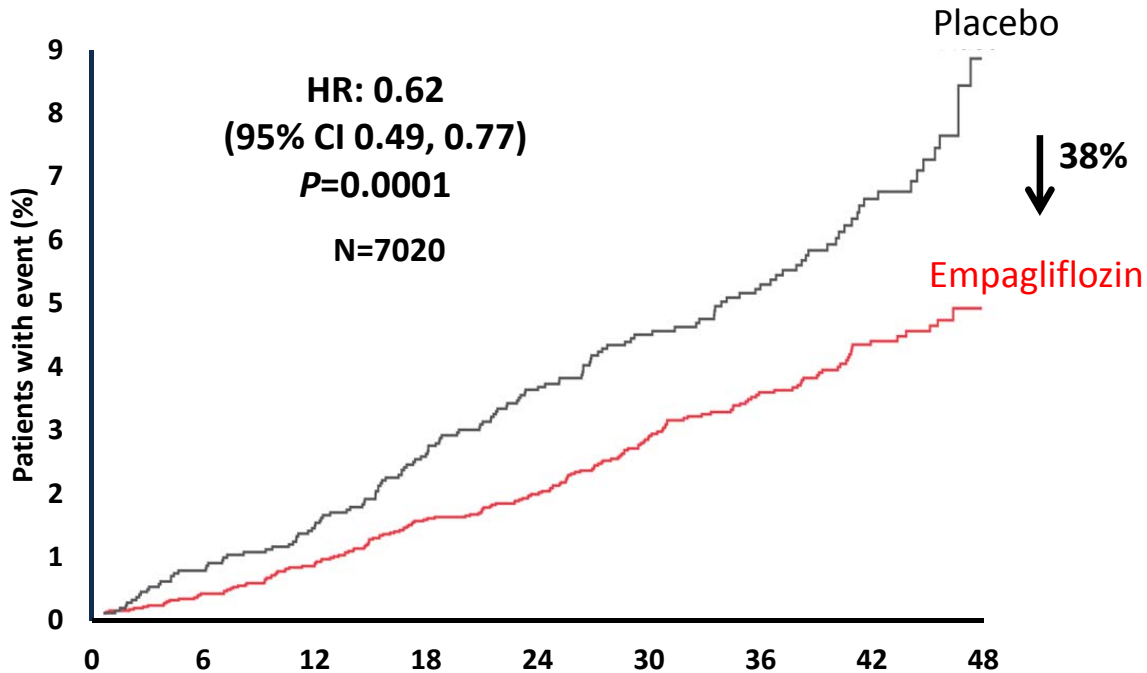
- Primary composite outcome
  - Death from cardiovascular causes
  - Nonfatal myocardial infarction
  - Nonfatal stroke
- Key secondary composite outcome
  - Hospitalization for unstable angina
- Conclusion
  - Type 2 diabetes patients at high risk for CV events treated with standard care empagliflozin had a lower rate of CV outcomes and death from any cause



Number of patients									
Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722	414
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177

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

LEADER Results: Primary Endpoint

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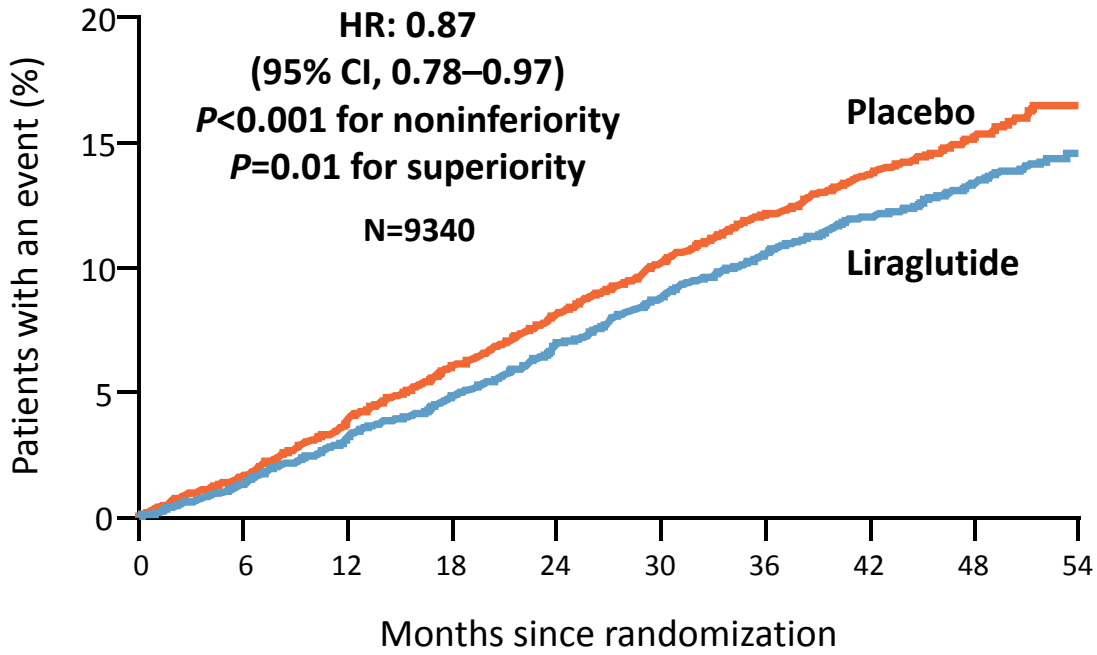
- Primary composite outcome
  - Death from cardiovascular causes
  - Nonfatal myocardial infarction
  - Nonfatal stroke
- Key secondary composite outcome
  - Hospitalization for unstable angina or heart failure
- Conclusion
  - Rate of first occurrence of death from CV causes, nonfatal MI, and nonfatal stroke was lower with liraglutide vs placebo



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

What Effect will CVOT Results Have on Clinical Practice Guidelines?

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- There are now 7 completed CVOTs involving 3 classes of drugs
  - DDP-IV inhibitors (3 trials)
  - GLP-1 receptor antagonists (3 trials)
  - SGLT2 inhibitors (1 trial)
- Results from these trials provide evidence of the overall cardiovascular safety of incretins and SGLT2 inhibitors
  - Results from specific agents may not be applicable to other members of the same class

Abdul-Ghani M, et al. *Diabetes Care.* 2016;39:717-725; American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

Summary

MANAGED CARE REVIEW BOARD®

- The goal of antihyperglycemic treatment is to reduce blood glucose levels and minimize side effects (especially hypoglycemia)
- The 2017 ADA treatment guidelines provide recommendations on diabetes care delivery including updated glycemic targets and antihyperglycemic pharmacotherapy
- Results from 2 of 7 large CVOT trials are included in the revised guidelines
  - Results from these trials provide evidence of the overall cardiovascular safety of the incretins and SGLT2 inhibitors
- Specific treatment recommendations based on the results of these and future CVOTs trials is anticipated in future editions of the guidelines

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CVOT Results and Plan Benefit Designs: Maximizing Value for Emerging Type 2 Diabetes Therapies

Vanita Pindolia, PharmD, BCPS
Vice President, Ambulatory Clinical Pharmacy Programs
Henry Ford Health System/Health
Alliance Plan of Michigan

Learning Objective

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- Discuss the potential impact of CVOT results on benefit design strategies

CVOT in Diabetes: Perspective

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- Seventeen CVOT clinical trials involving >140,000 subjects have been completed or are ongoing in accordance with the FDA guidance issued in 2008[1]
- The 7 completed trials involve three different drug classes (SGLT2 inhibitors, GLP-1 agonists, DPP-4 inhibitors)[1-5]
  - Each has met their primary objective to exclude an unacceptable level of ischemic CV risk (as defined in the FDA guidance)[1-5]
  - One trial found an increased risk of hospitalization for heart failure (SAVOR-TIMI 53[2]) while 3 others demonstrated a reduction in cardiovascular death (EMPA-REG[3], LEADER[4], SUSTAIN-6[5])
- To date, a heightened risk of CV ischemic events has not been demonstrated across several classes of new diabetes drugs

How will these data impact the diabetes pharmacy benefit?

1. Smith RJ, Goldfine AB, Hiatt WR. *Diabetes Care*. 2016;39:738-742; 2. Scirica BM, et al. *N Engl J Med*. 2013;369,1317-1326; 3. Zinman B, et al. *N Engl J Med*. 2015;373:2117-2128; 4. Marso SP, et al. *N Engl J Med*. 2016; 375:311-322; 5. Marso SP, et al. *N Engl J Med*. 2016;375:1834-1844.

Nearly 28 Million Americans Have Type 2 Diabetes*

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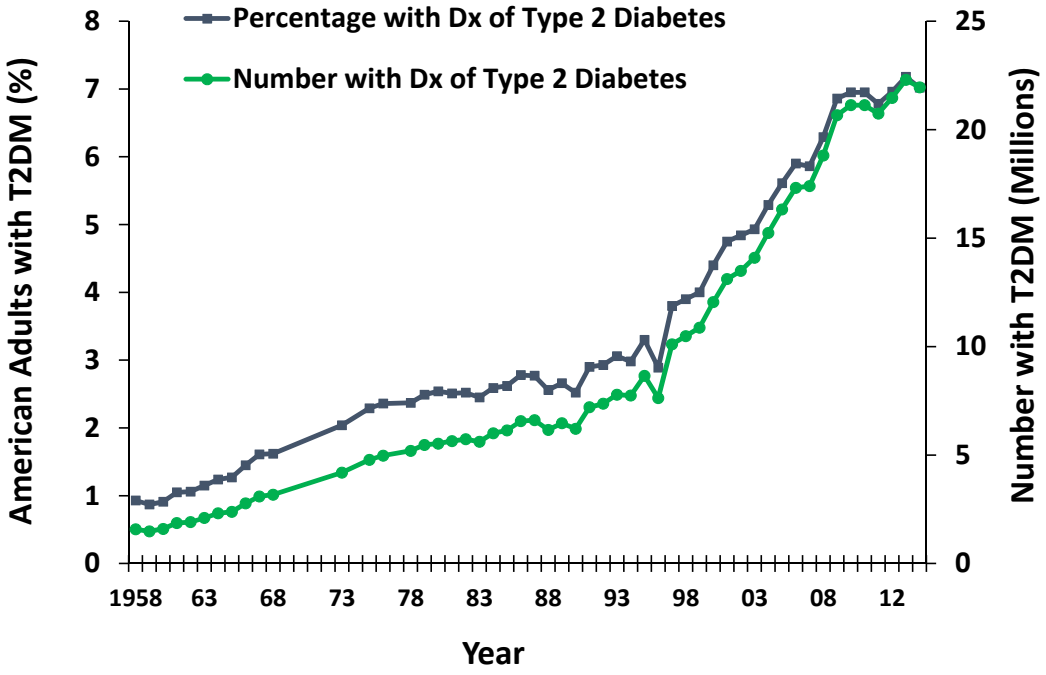

Nearly 1 in every 10 Americans carries a diagnosis of type 2 diabetes

*7.7 Million Americans with type 2 diabetes remain undiagnosed

American Diabetes Association. http://www.diabetes.org/diabetes-basics/statistics/. Accessed March 2017.

Diabetes Increases Risk of CV Morbidity and Mortality

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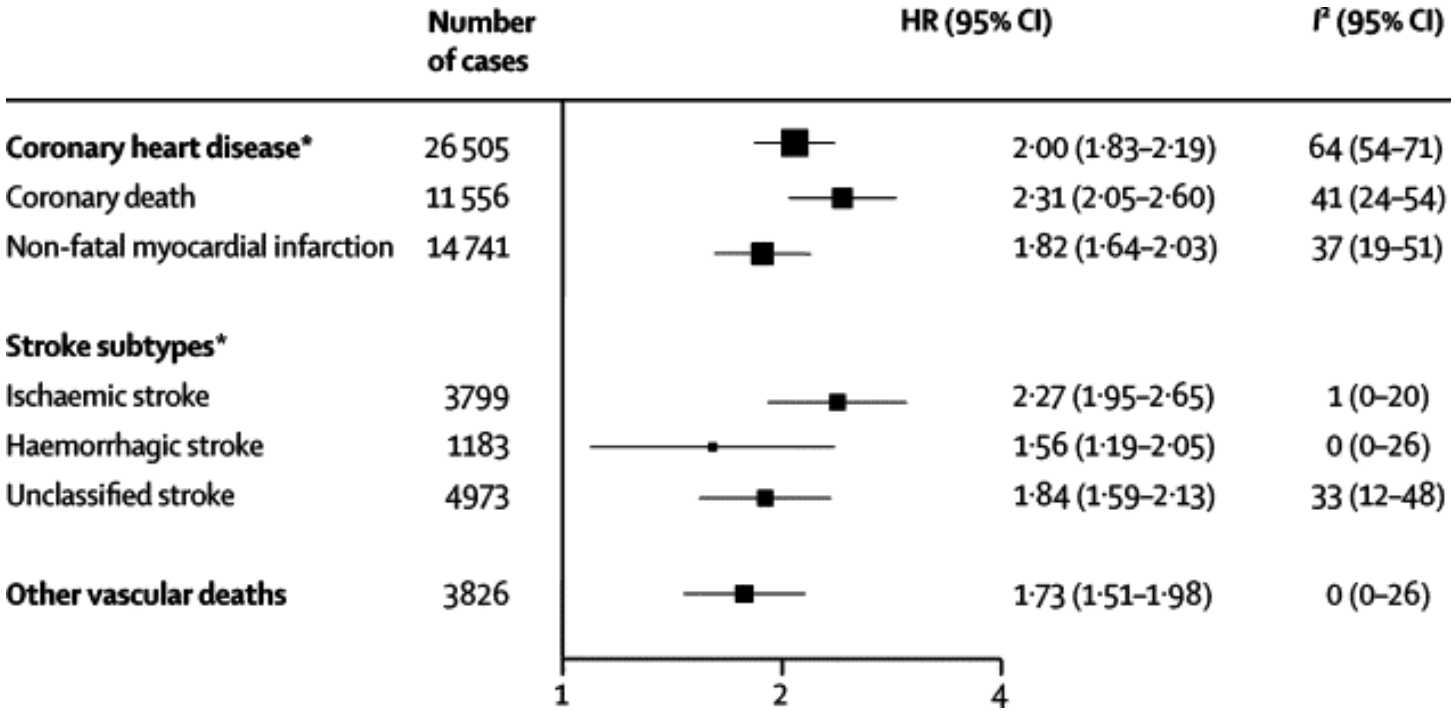
Meta-analysis of 102 clinical trials evaluating the risk of CV events due to T2DM



Diabetes mellitus significantly increases the risk of adverse CV events

Emerging Risk Factors Collaboration. *Lancet* 2010;375:2215-2222.

Diabetes is the Most Expensive Traditional Therapy Class When Ranked by PMPY

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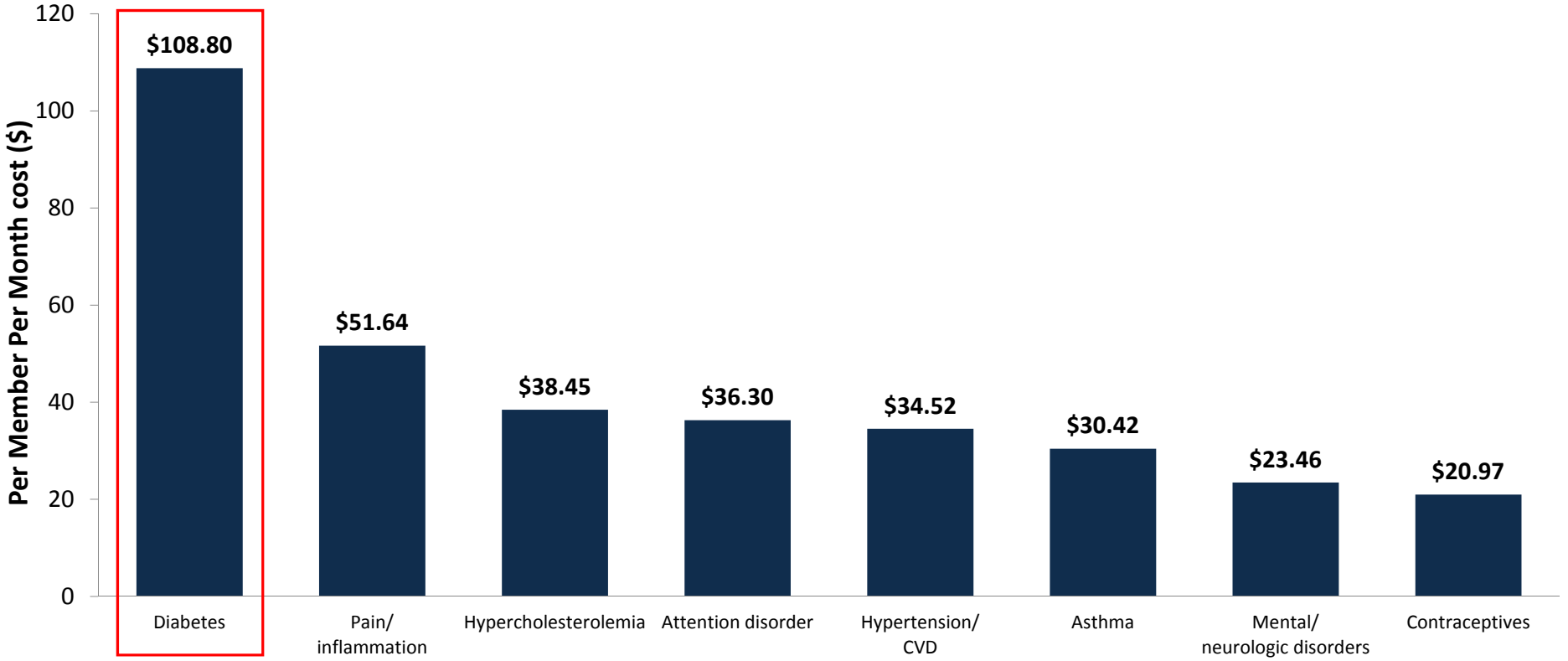

Express Scripts 2016 Drug Trend Report.

Finding a Balance Between Cost Shifting and Patient Adherence is a Challenge

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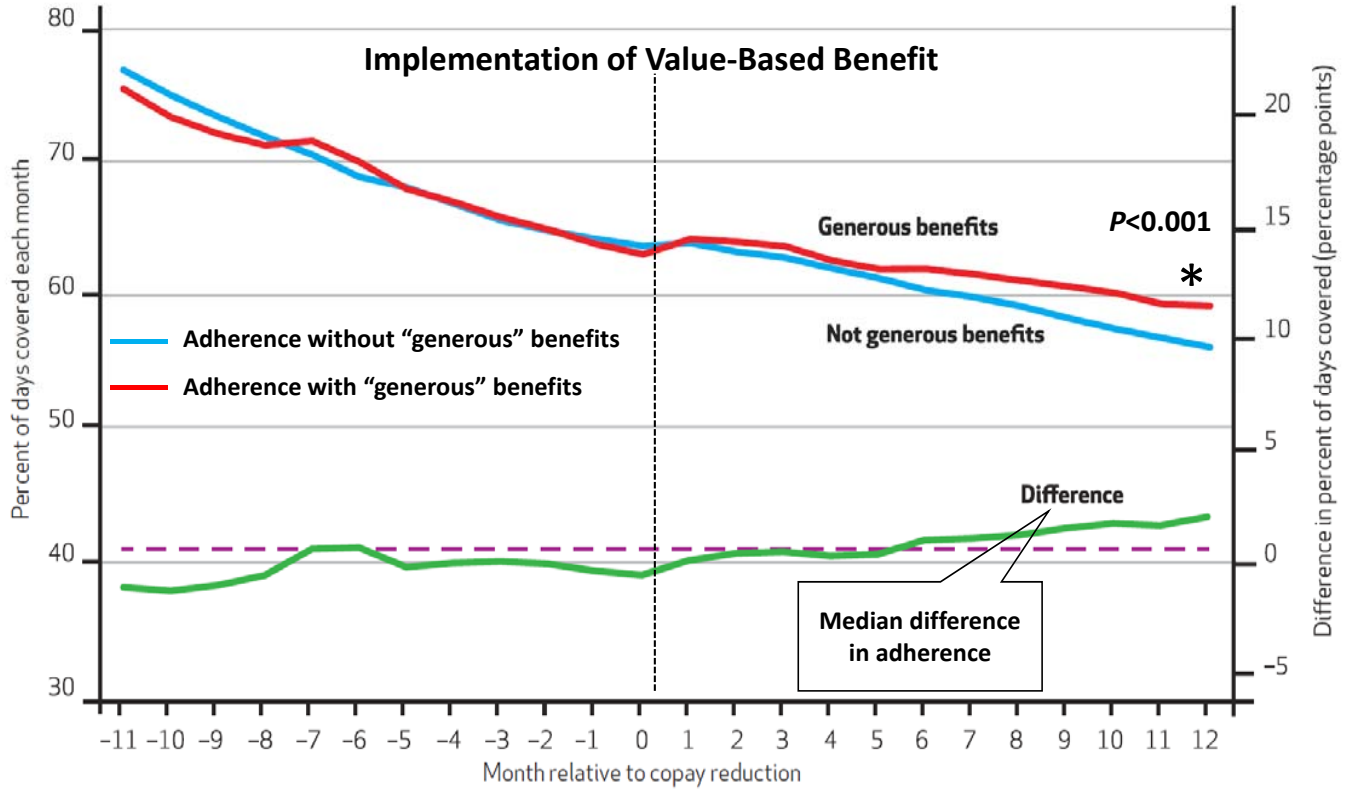
Patients Receiving More Generous Benefits Had Significantly Greater Adherence



Choudhry NK, et al. *Health Aff (Millwood)*. 2014;33:493-501.

Tenets of a Diabetes Benefit Plan Design

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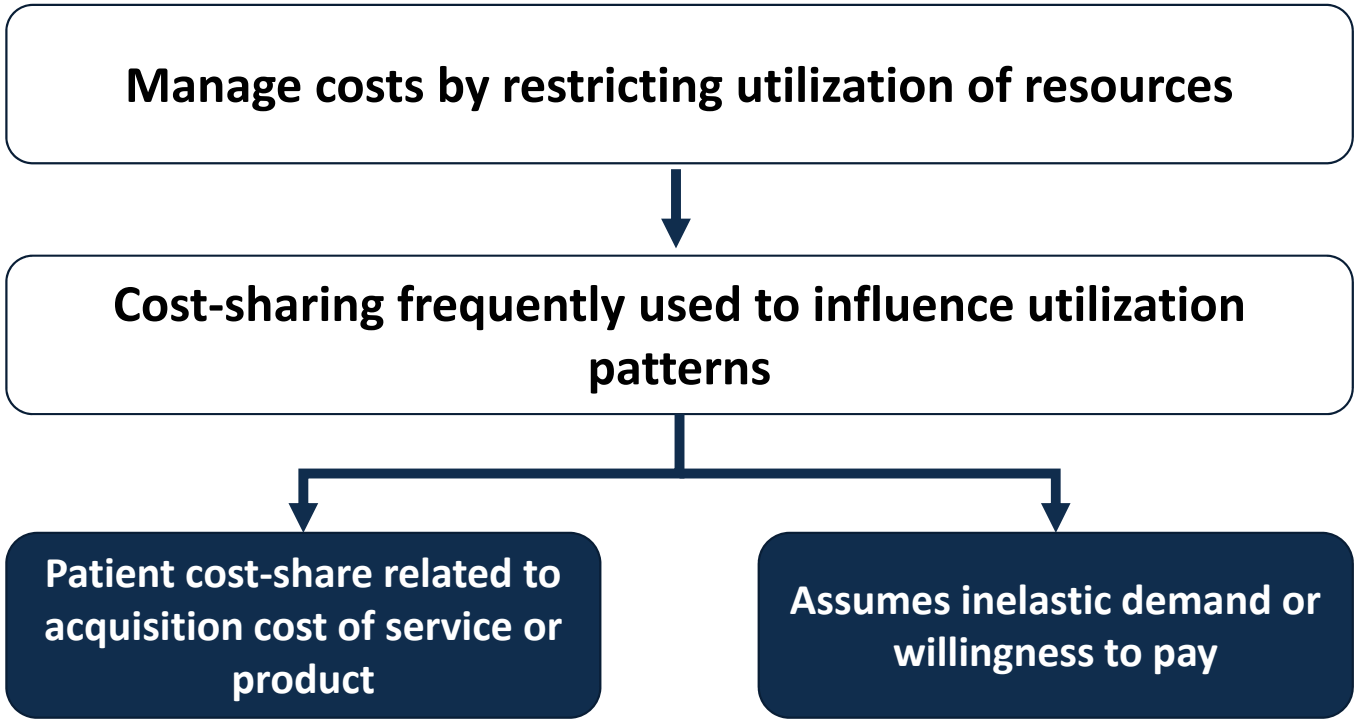

Willey VJ, et al. *Am J Manag Care*. 2008;14:S252-S263.

Common Components of Diabetes Benefit Design

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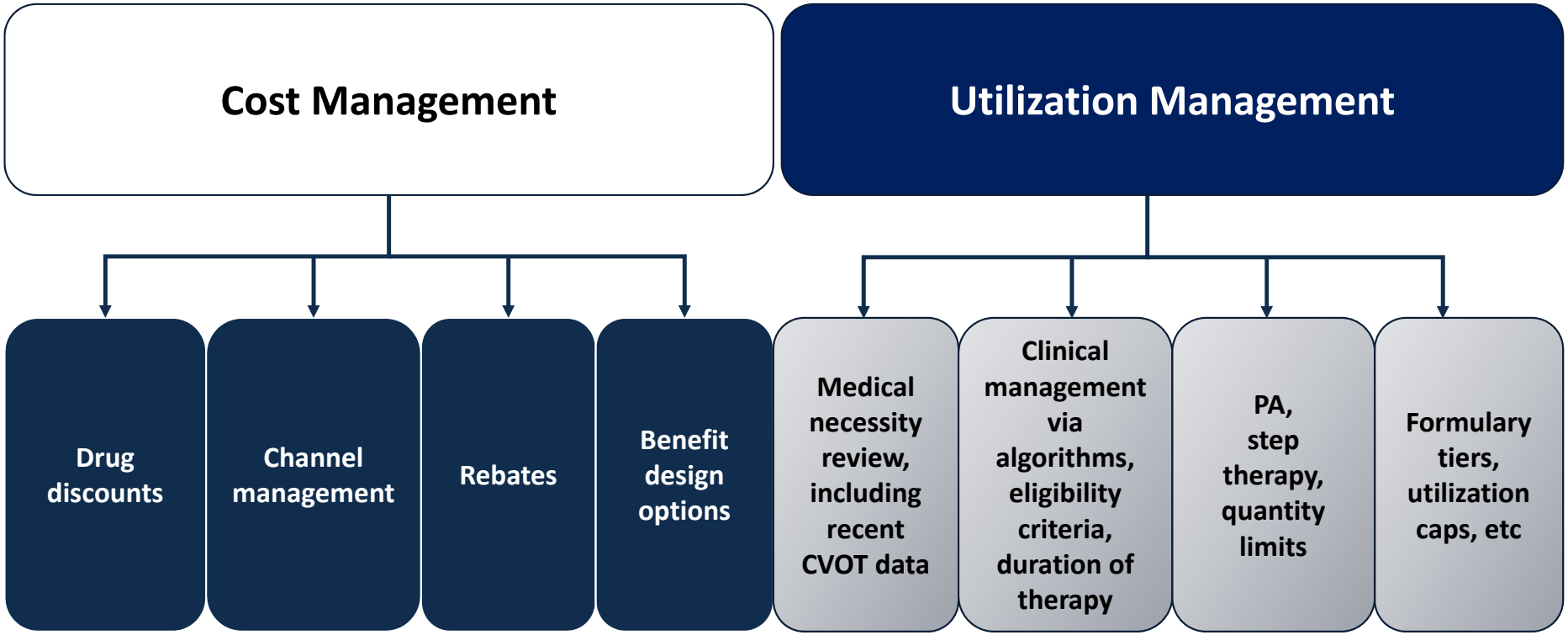

Stern D, et al. *J Manag Care Pharm*. 2008;14(suppl S):S12-S16.

Management Strategies to Consider for Diabetes Pharmacy

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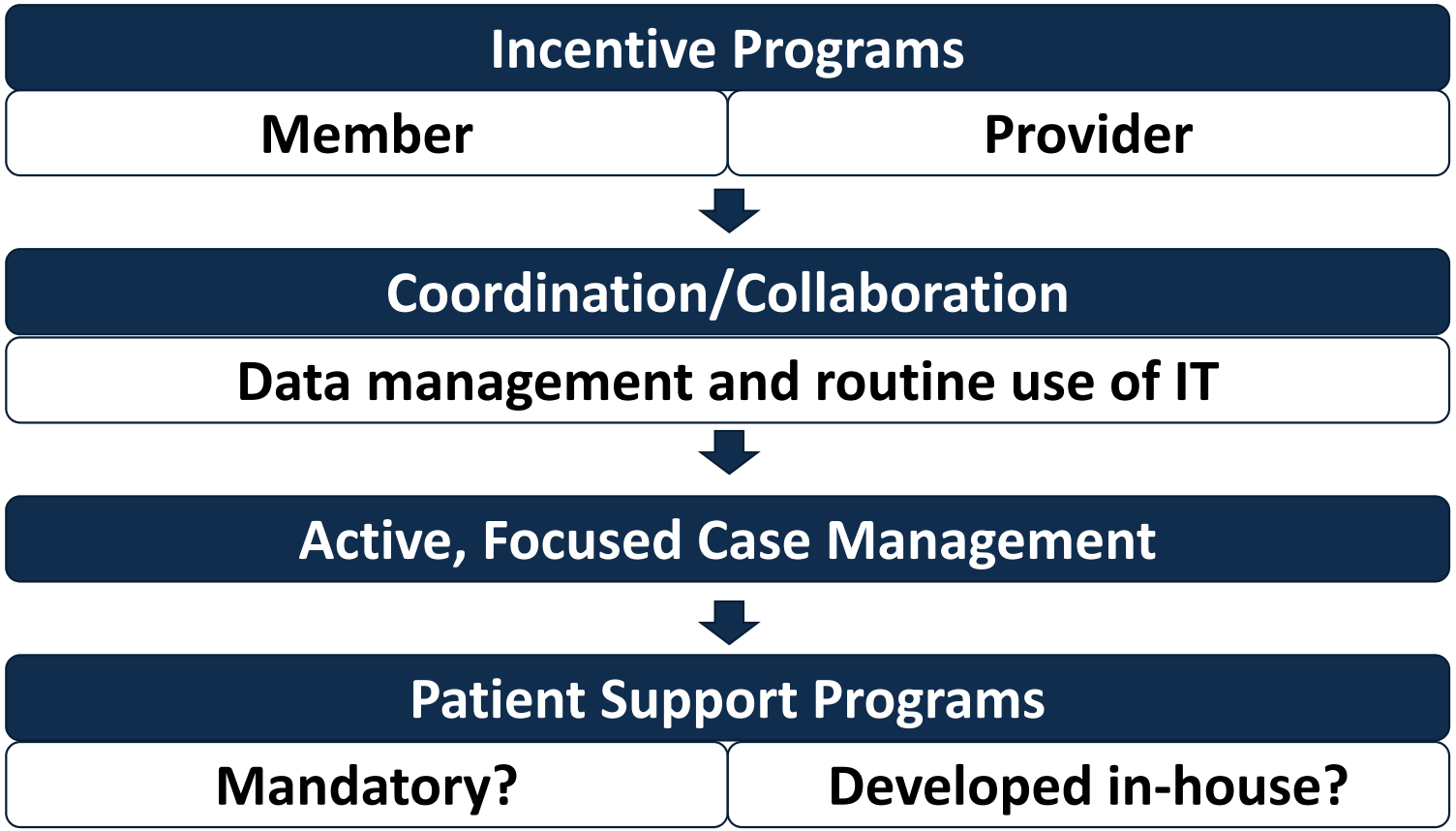

Benefit Design Strategies to Consider for Diabetes Pharmacy

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Benefit Design

Tiers
- **Evaluating out-of-pocket expenses**

Biosimilars
- **First biosimilar insulin (insulin glargine) approved in January 2016**

Application of Guidelines, Algorithms, and Disease Management

Patient Behavior Considerations for Diabetes Pharmacy

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Disease and Treatment Variables	Health Care Delivery Variables

• Complex therapy
• Treatment tolerability
• Multiple comorbidities
  • CV disease
  • Kidney disease
  • Obesity
	• Patient awareness/education
	• Strengthening patient-provider relationships
	• Patient empowerment
	• Integrated communication channels
	• Medication therapy management
	• Medication reminders
	• Telephone/email counseling

Formulary Management Considerations for Diabetes Pharmacy

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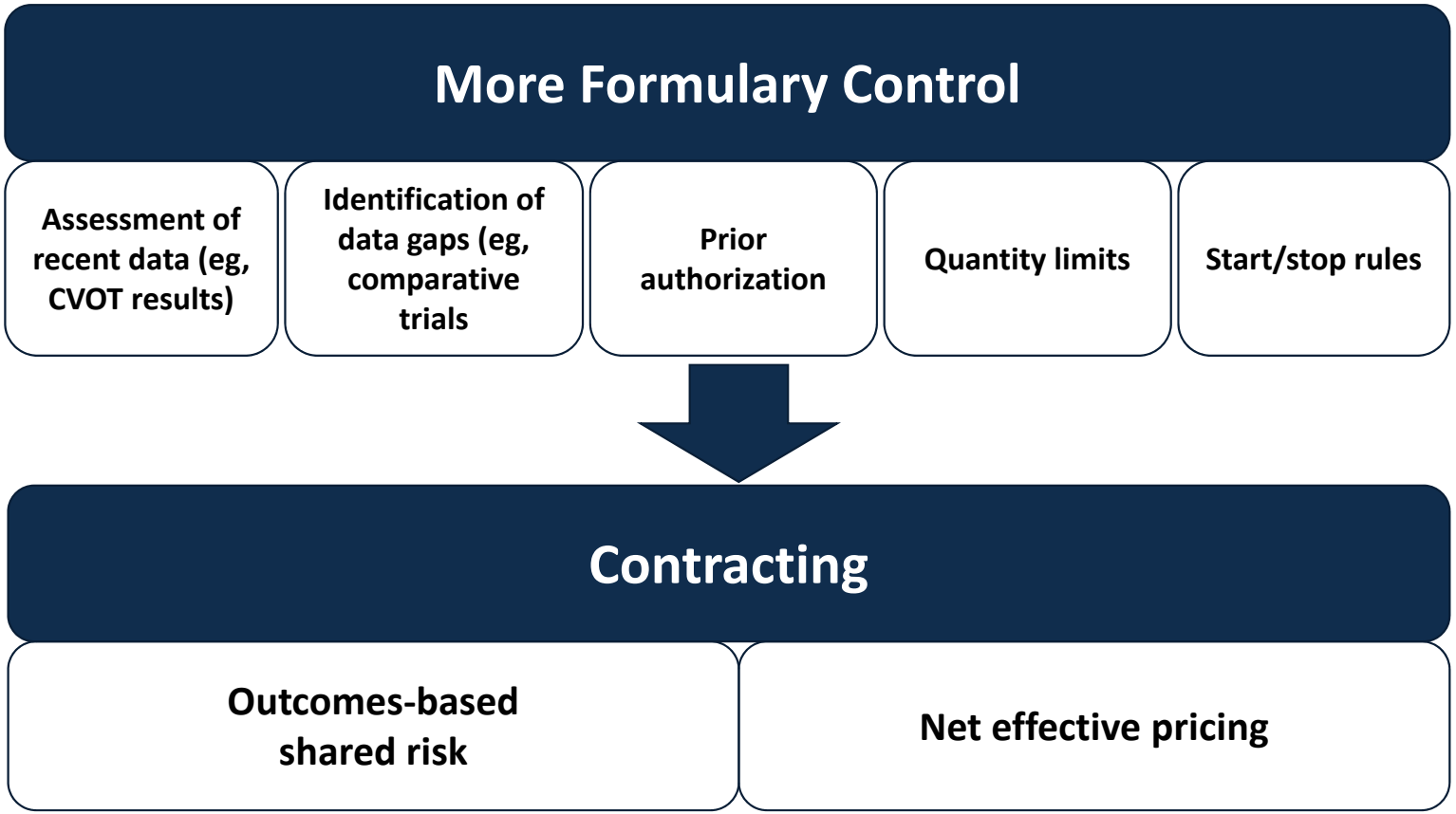

Moving Away From *Volume* and Toward *Value*

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- Payment/delivery paradigm emphasis is on rewarding value instead of volume
  - Value-based benefit design: shared savings, gain-sharing, bundled payments, capitation, etc
- Incentives driven by CMS are being implemented to coordinate care among/across providers
  - CMS Quality Strategy
  - CMS EHR incentive program
- Establishment of organizational infrastructure that promotes actual and virtual integration
  - Accountable care organizations (ACOs), medical homes, home-based chronic care management, community health teams, health care innovation zones

Key Elements of an Value-Based Design

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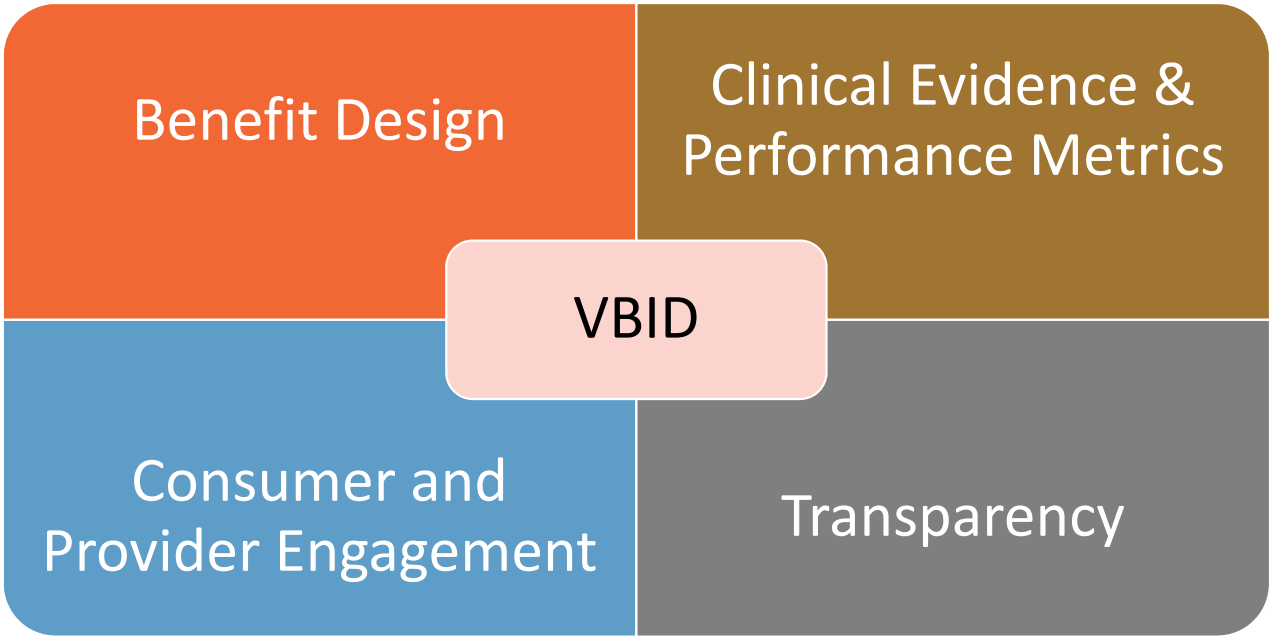

VBID=value-based insurance design

Patient-centered Benefit Plan Designs

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- Development guided by principles of value-based insurance design
  - Set cost shares that consider cost and value while prioritizing primary care and frequently needed care for management of chronic comorbidities including cardiovascular disease
  - Set fixed copays as much as possible; limit coinsurance to less frequently used benefits or services with high variability in cost as necessary to meet required actuarial values
  - Apply a stair-step approach for setting member cost shares for a service across each tier
- Reassess benefits each year based on emergence of new clinical trial data (eg, CVOT results) and patient experience related to access and cost

Summary

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- Managed care will be required to develop novel solutions to meet the continued growth of the diabetes population
- Limited resources challenge patients, providers, and payers
- Diabetes pharmacy is a current and future concern for plan sponsors and patients
- Current plan designs often do not consider recent clinical trial data and thus, may not apply to the ongoing and future needs of diabetes pharmacy
- Benefit design should be reassessed annually and consider new clinical trial data (eg, CVOT results) as well as patient experience related to access and cost
- Newer approaches should be implemented that consider the needs of all stakeholders including patients, physicians, managed care organizations, industry, and payers

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Patient-Centered Strategies to Minimize Cardiovascular Risk in Patients in a Managed Care Setting

Curtis Triplitt, PharmD, CDE

Texas Diabetes Institute, University Health System

Associate Professor of Medicine, Clinical/Division of Diabetes

University of Texas Health Science Center at San Antonio

Learning Objective

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- Implement patient-centered strategies to minimize cardiovascular risk in patients treated in a managed care setting

CVD Risk in T2DM: More Risks = Higher Mortality

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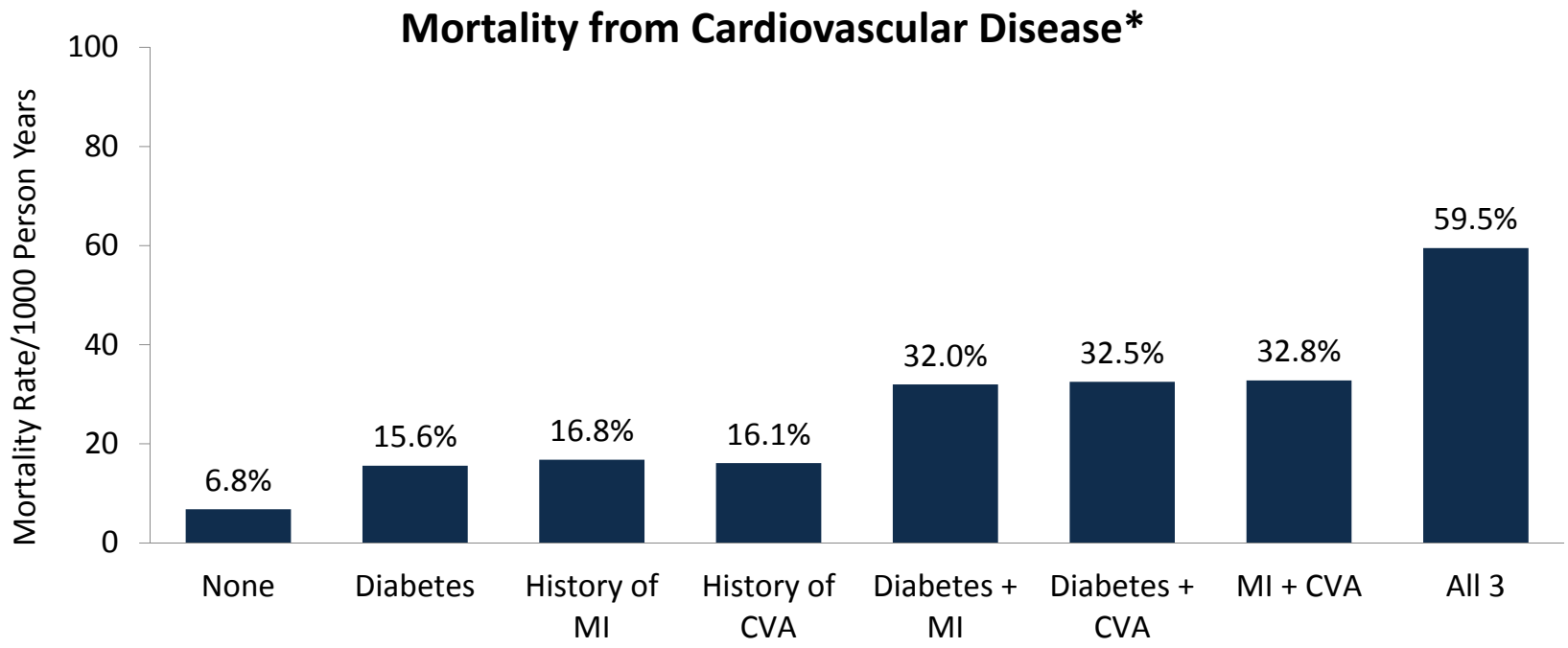

*Morality per 1000 person years adjusted to age 60; N=689,300; Baseline surveys conducted 1960-2007; mortality follow up to 2013; 128,843 deaths
MI=myocardial infarction; CVA=cerebrovascular accident

Emerging Risk Factors Collaboration. *JAMA.* 2015;314:52-60.

More Than Two-Thirds of Adults With T2DM Die From CV Disease

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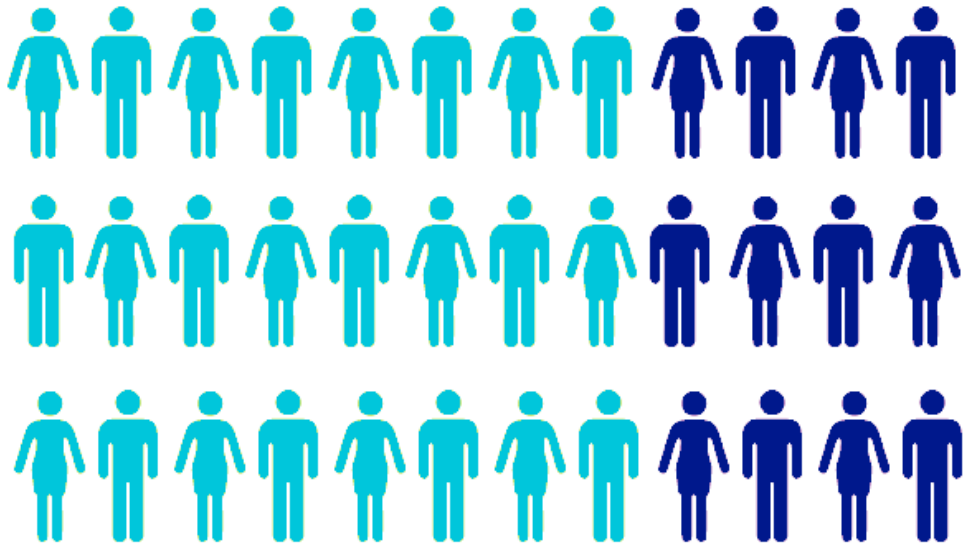
More than two-thirds of patients with T2DM die from cardiovascular disease



American Heart Association. Cardiovascular disease and diabetes. http://www.heart.org/HEARTORG/Conditions/More/Diabetes/WhyDiabetesMatters/Cardiovascular-Disease-Diabetes_UCM_313865_Article.jsp/#.WLm63YWcGbg. Accessed March 2017.

Glycemic Control Reduces Long-Term Risk of Myocardial Infarction

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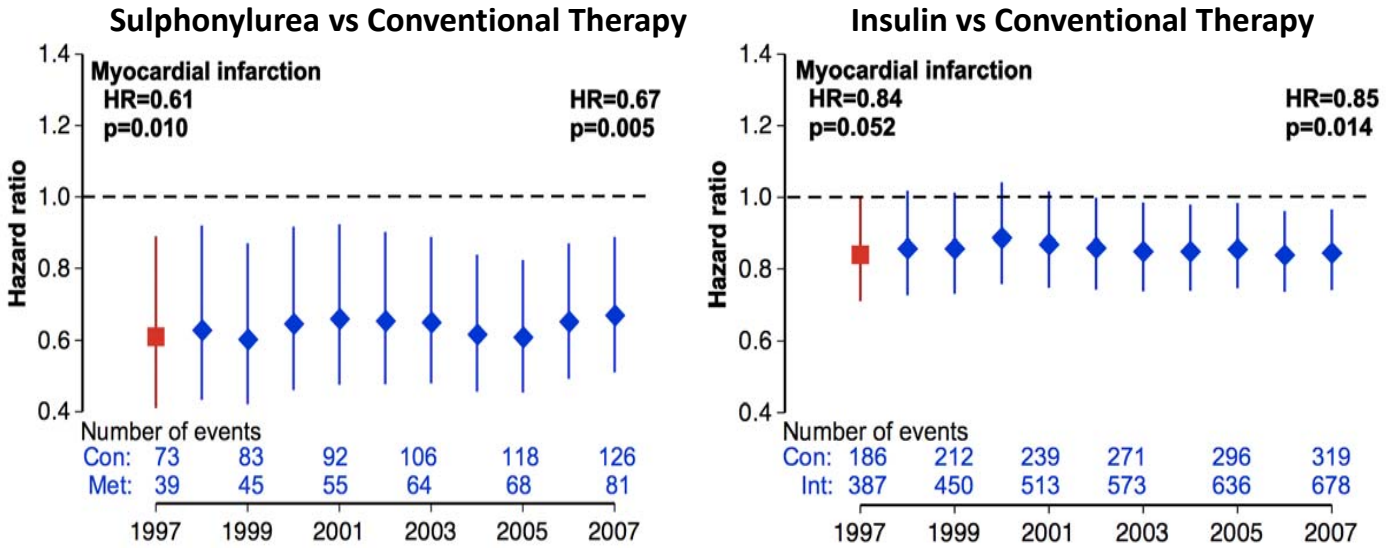
Glycemic control takes a long time for CVD risk reduction; We are often too glucocentric in diabetes



United Kingdom Prospective Diabetes Study (UKPDS)
10-Year Follow-Up

Holman, RR et al. *N Engl J Med.* 2008;359:1577-1589.

Diabetes Becomes More Difficult to Treat Over Time

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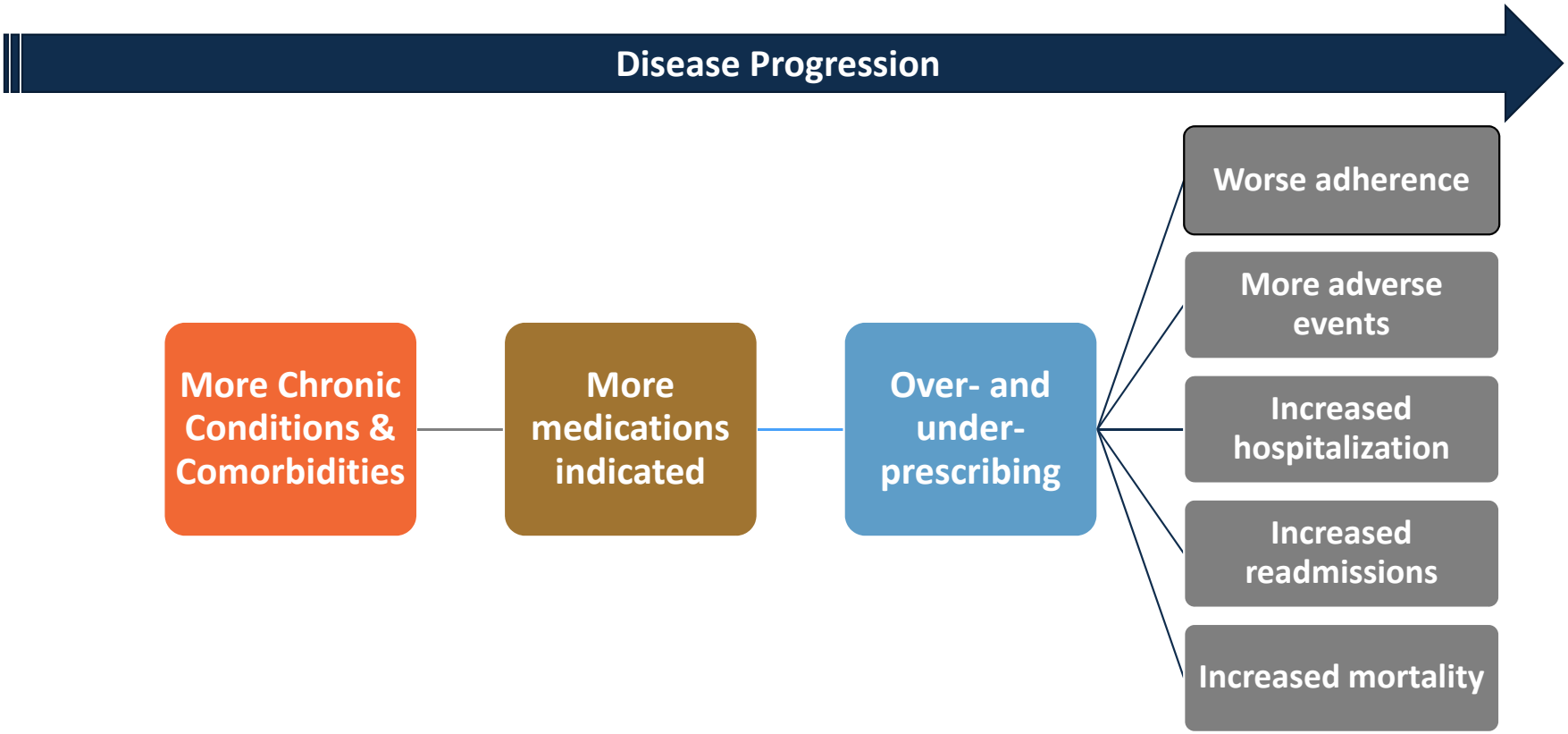

Mansur N, et al. *Am J Geriatr Pharmacother*. 2012;10;223-229.
Wilson MN, et al. *Ann Pharmacother*. 2014;48;26-32.

ADA Recommendations for When Goals Are Not Met: Treatment Intensification

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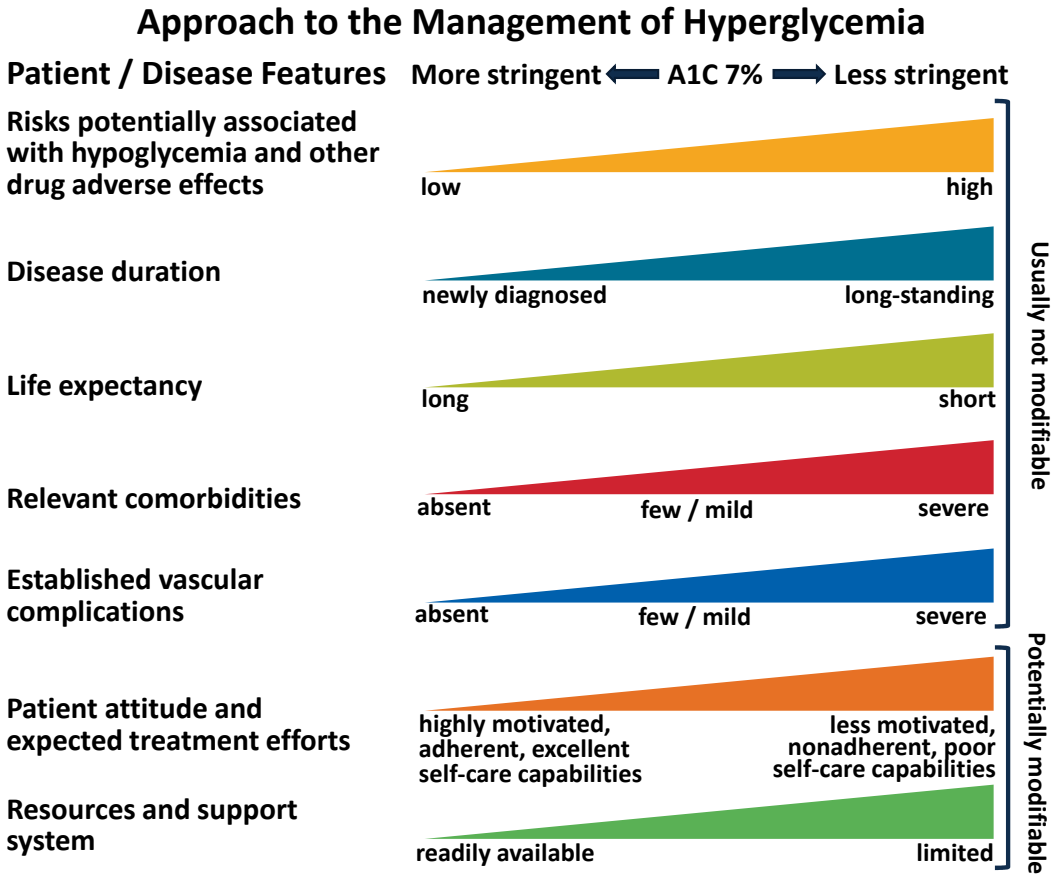
- Patient and disease features dictate the intensity of therapy
- Patients with high baseline A1C or at high risk for complications often require intensive treatment
  - Monotherapy is often insufficient
  - Consider initiating combination therapy



American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

Achieving Cardiovascular Risk Reduction in Diabetes Patients Remains Challenging

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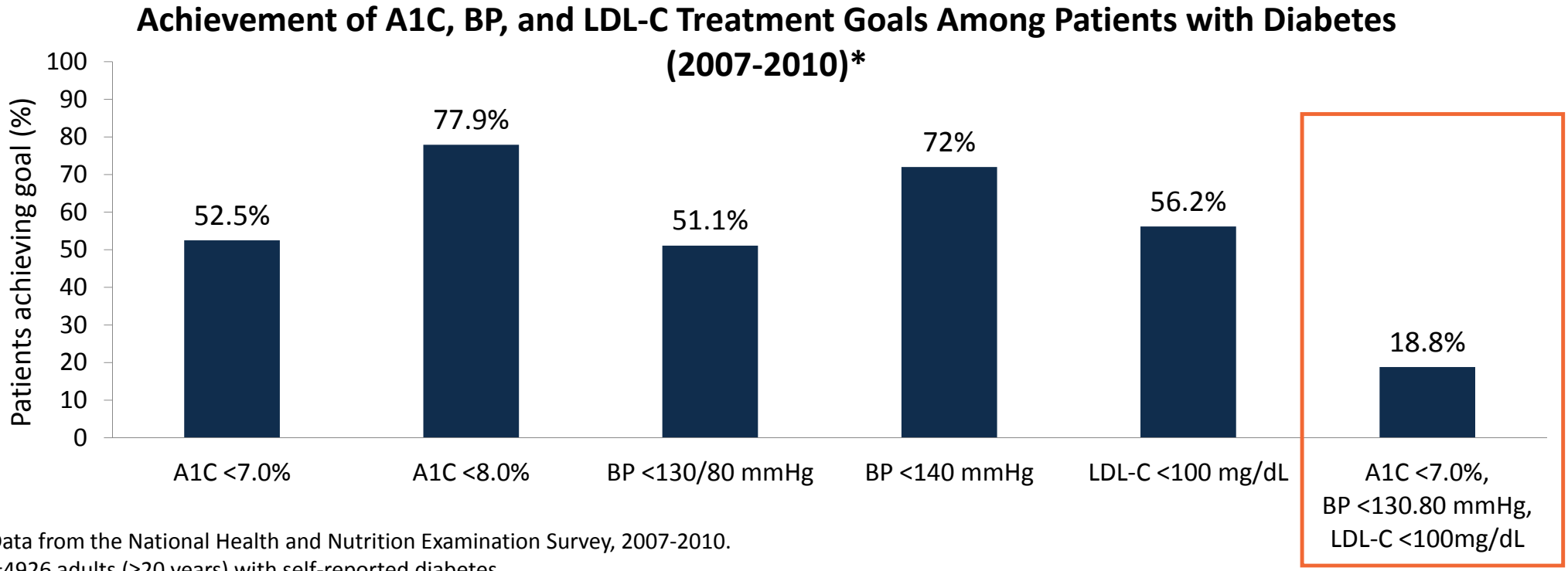

*Data from the National Health and Nutrition Examination Survey, 2007-2010.
N=4926 adults (≥20 years) with self-reported diabetes.
BP=blood pressure; LDL-C=low density lipoprotein cholesterol.

Casagrande SS, et al. *Diabetes Care*. 2013;36;2271-2279.

Organizing Care to Achieve Treatment Goals

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- The ADA recommends prioritizing timely and appropriate treatment intensification of lifestyle and/or drug therapy for patients who have not achieved BP, lipid, or glucose goals
- Strategies include
  - Explicit goal setting with patients
  - Identifying and addressing barriers to care
  - Integrating evidence-based guidelines
  - Incorporating care management teams

American Diabetes Association. *Diabetes Care.* 2017;40(suppl 1):S1-S135.

ADA Recommendations for When Goals Are Not Met: Adherence

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- Address issues related to patient adherence
- Barriers to adherence may include
  - Patient factors (eg, remembering to obtain or take medications, fears, depression, and health beliefs)
  - Medication factors (eg, regimen complexity, multiple daily dosing, cost, side effects)
    - Simplifying a complex treatment regimen may improve adherence
  - System factors (eg, inadequate follow-up and support)

American Diabetes Association. *Diabetes Care.* 2016;39 (Suppl. 1): S1-S2.

Considering the Patient's Perspective

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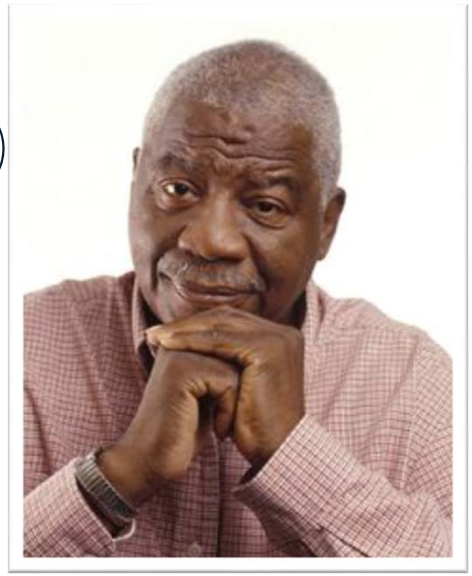

What if my therapy fails?

What happens if I forget to take my medicine?

Why is lowering blood glucose so important?

Do I need to use a needle to get my insulin?

Don't those drugs have bad side effects?

I don't feel bad…why do I have to take any medicine?

How long do I have to take these drugs?

Patient-Centered Care

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- You as provider or managed care expert:
  - You are the expert on diabetes information, treatments, algorithms, etc
  - Large amount of information you know on chronic diseases
- This will not help if the patient doesn't know or won't do it
- Patient
  - I follow the advice of my HCP, but I may trust my neighbor more than my HCP
  - I have a disease that is called "chronic"—I live with it everyday
  - No one knows me better than me
  - I already have most of the answers, but I may not have made the connection
  - Am I being non-adherent? Or is it a choice—something I am missing
- Finding common language, common ground, and partnering with your patients to succeed to "make the connections"

Strategies for Improving Diabetes Care: A Patient-Centered Approach

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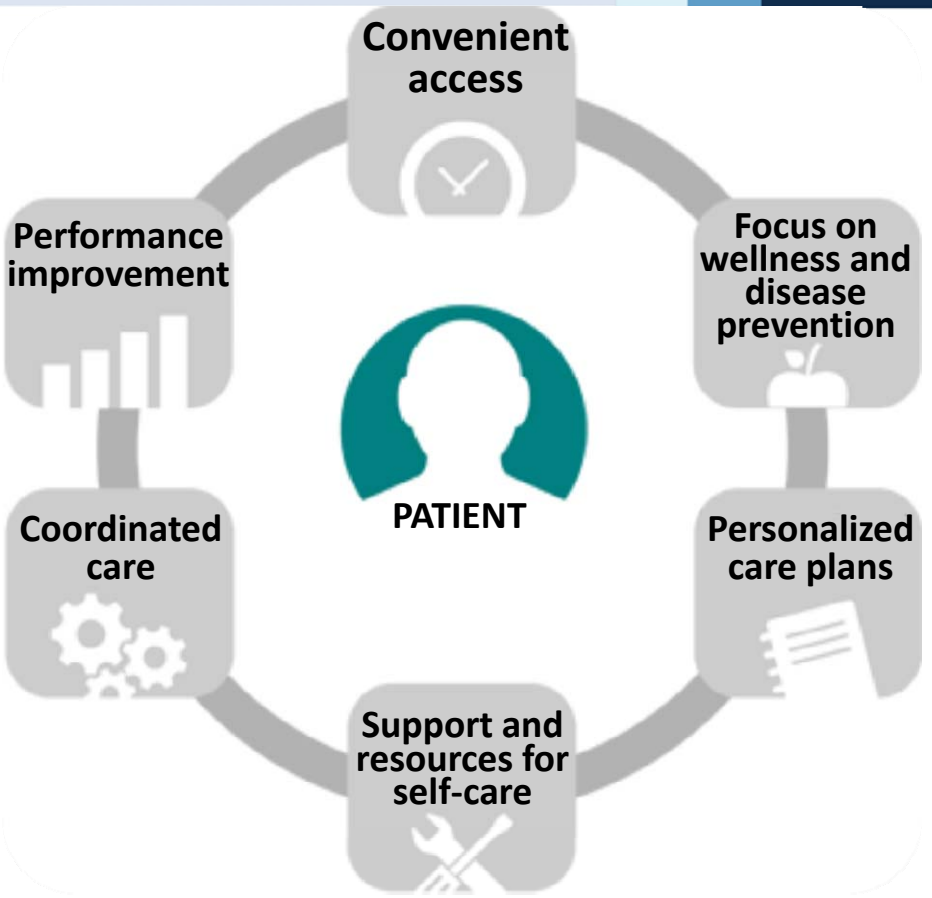
- *"…providing care that is respectful of and responsive to individual patient preferences, needs, and values, ensuring that patient values guide clinical decisions"*
- Underlying principles
  - Evidence-based care individualized based on disease characteristics and patient needs, goals and values
  - Encourages shared decision-making
  - Provides coordinated, multidisciplinary care
  - Continuity of care across the life span



Inzucchi SE, et al. *Diabetes Care*. 2015;38:140–149.

Patient-Provider Interactions are Key to Individualizing Care

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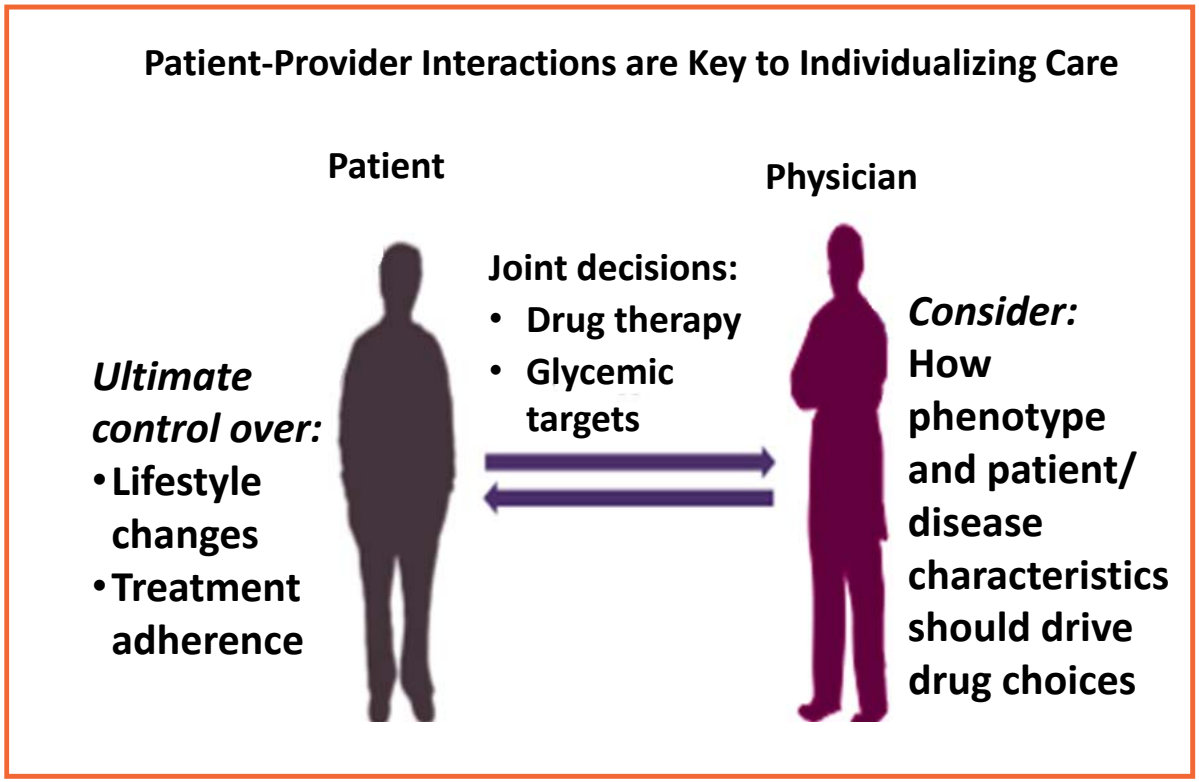
Ideal Patient Behaviors

- Actively engaged
- Provides his/her perspective
- Willing to contribute to the decision-making process



Ideal Provider Behaviors

- Active listening
- Negotiation-motivational interviewing
- Provides information when needed or in response to a question

Delivering Patient-Centered Care Through the Medical Home

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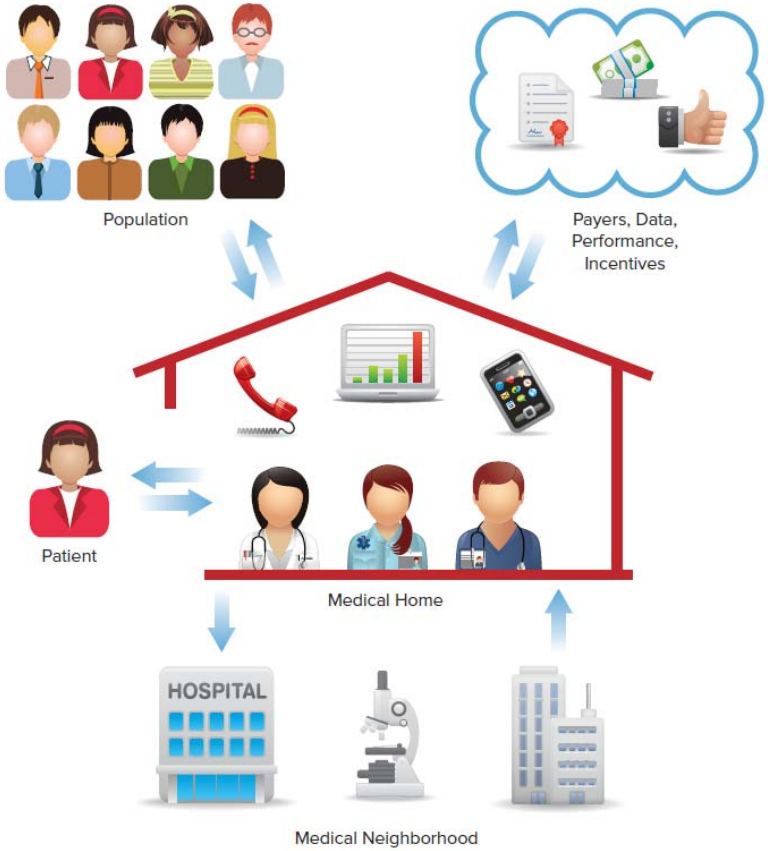
- Features of the patient-centered medical home (PCMH) that support better diabetes outcomes
  - Diabetes self-management education
  - Team-based care
  - Care coordination/case management
  - Specialty providers as members of the care team
  - Electronic record capabilities for tracking outcomes and performance improvement



Ackroyd SA, Wexler DJ. *Curr Diab Rep*. 2014;14:471.

Evidence for the Effectiveness of the PCMH in Diabetes Care is Encouraging

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Ranking of Quality Improvement Strategies for Lowering A1C			
Rank	**Intervention**	**Number of Trials**	**Mean Difference in A1C (95% CI)**
1	Promotion of self-management	60	-0.57 (-0.83 to -0.31)
2	Team changes	47	-0.57 (-0.71 to -0.42)
3	Case management	57	-0.50 (-0.65 to -0.36)
4	Patient education	52	-0.48 (-0.61 to -0.34)
5	Facilitated relay of clinical data	32	-0.46 (-0.60 to -0.33)
6	Electronic patient registry	27	-0.42 (-0.61 to -0.24)
7	Patient reminders	21	-0.39 (-0.65 to -0.12)
8	Audit and feedback	8	-0.26 (-0.44 to -0.08)
9	Clinician education	15	-0.19 (-0.35 to -0.03)
10	Clinician reminders	18	-0.16 (-0.31 to -0.02)
ALL		**120**	**-0.37 (-0.45 to -0.28)**

Ackroyd SA, Wexler DJ. *Curr Diab Rep*. 2014;14:471; Tricco AC, et al. *Lancet*. 2012;379:2252-2261.

Summary

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- Diabetes patients are at increased risk for CV morbidity and mortality
- We are often glucocentric in diabetes, yet 2/3 will die from CVD
- Achieving cardiovascular risk reduction in diabetes patients remains challenging
- Patient-centered care may help to address barriers to CV risk reduction by increasing patient involvement in the care decision-making process
- The PCMH provides a venue for increased patient engagement and improved diabetes care delivery