Cardiovascular Outcomes Trials in Type 2 Diabetes

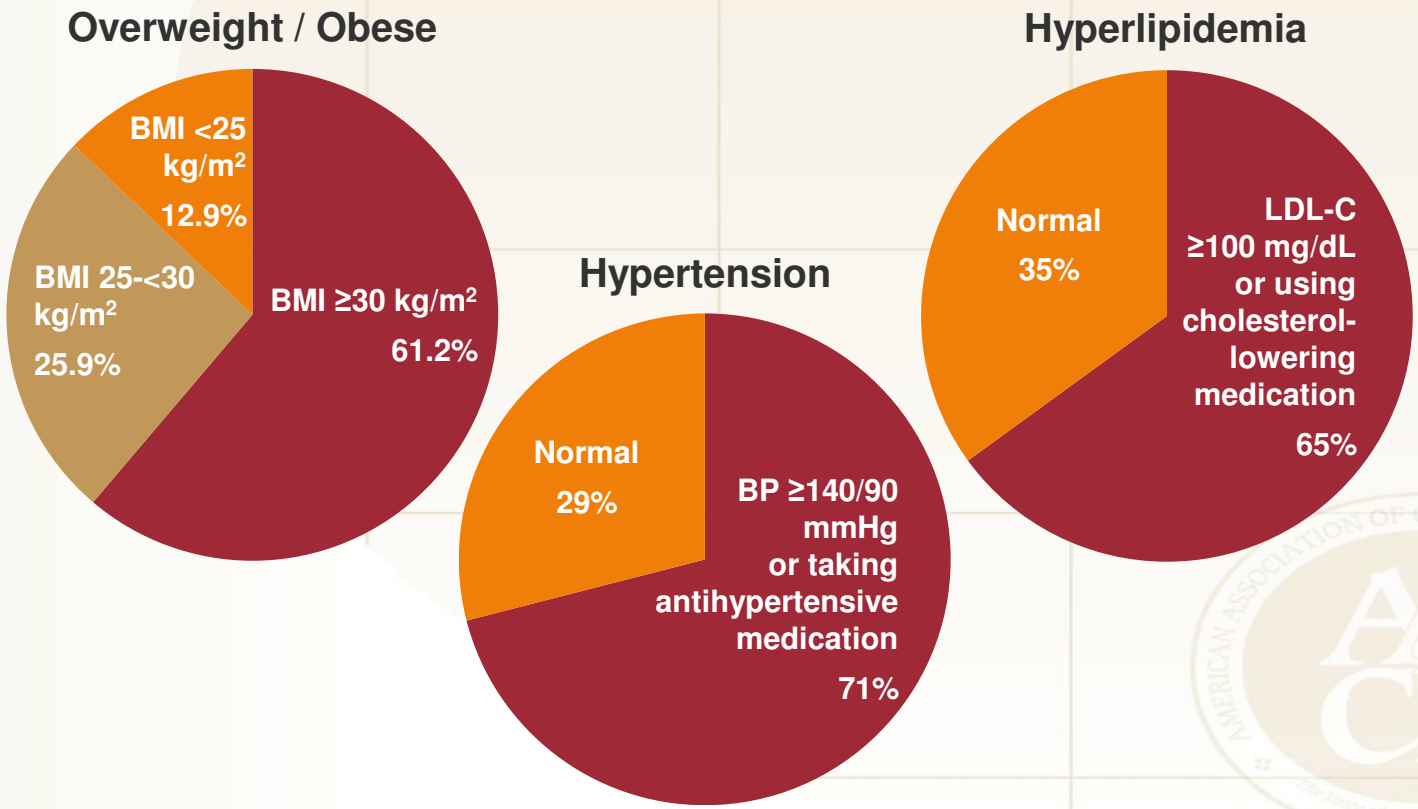
Cristin Bruns, MD
Oklahoma Heart Institute
Department of Endocrinology

Disclosures

- Speaker for:
  - Astra Zeneca
  - Novo Nordisk
  - Boehringer Ingelheim
  - Sanofi

Cardiovascular Disease in Type 2 Diabetes
Why Do We Care?

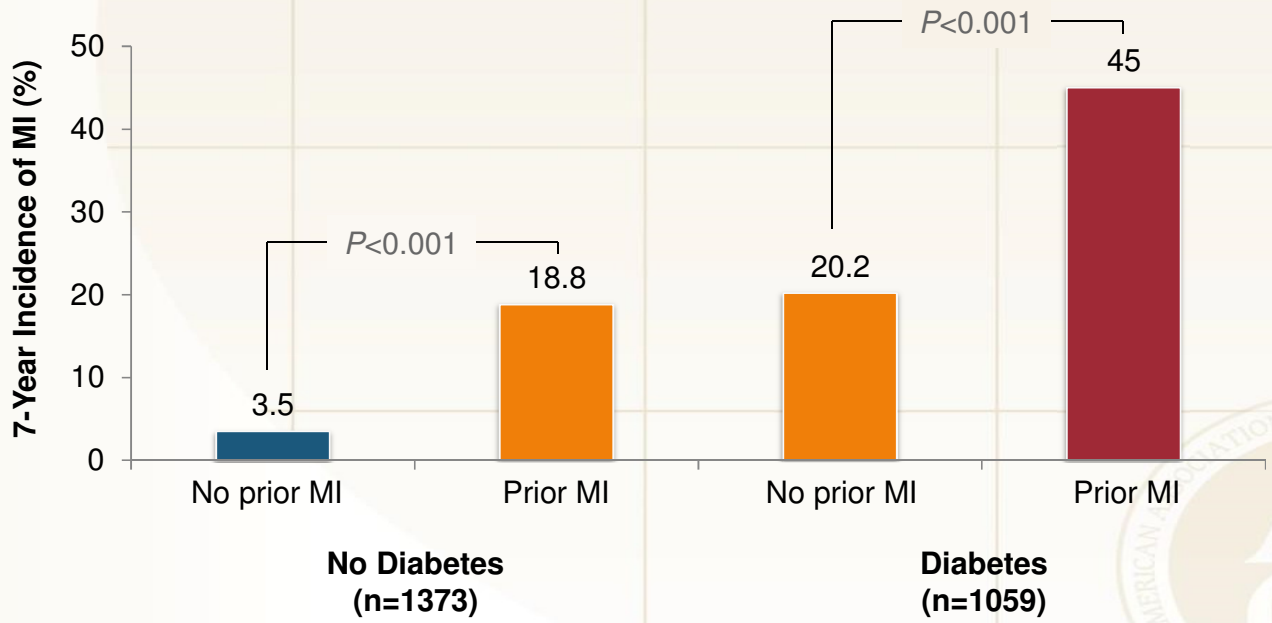
Prevalence of CV Risk Factors in Diabetes



BMI, body mass index.

Selvin S, et al. *Ann Intern Med.* 2014;160:517-525. CDC. National diabetes statistics report, 2014. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, 2014.

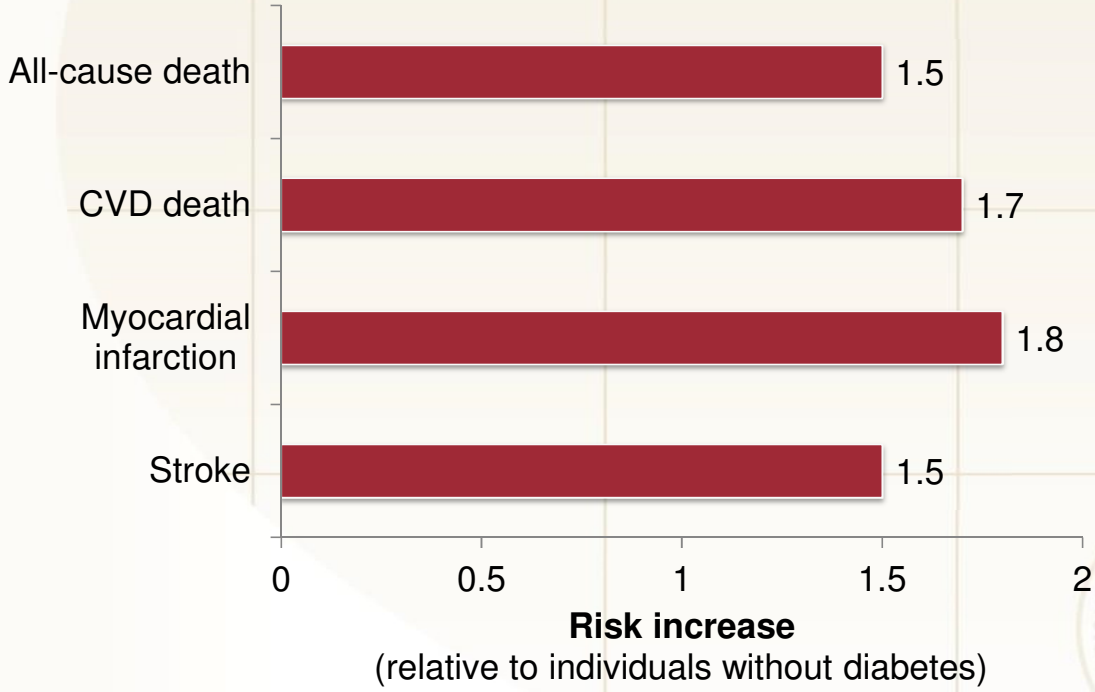
Diabetes Is a Cardiovascular Disease Risk Equivalent



MI, myocardial infarction.

Grundy SM, et al. *Circulation*. 2004;110:227-239.
Haffner SM, et al. *N Engl J Med*. 1998;339:229-234.

Diabetes and Morbidity and Mortality



CDC. National diabetes statistics report, 2014. http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf

Cardiovascular Disease in Type 2 Diabetes
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- ~2/3 die from CV disease

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- T2DM reduces life expectancy by 6 years

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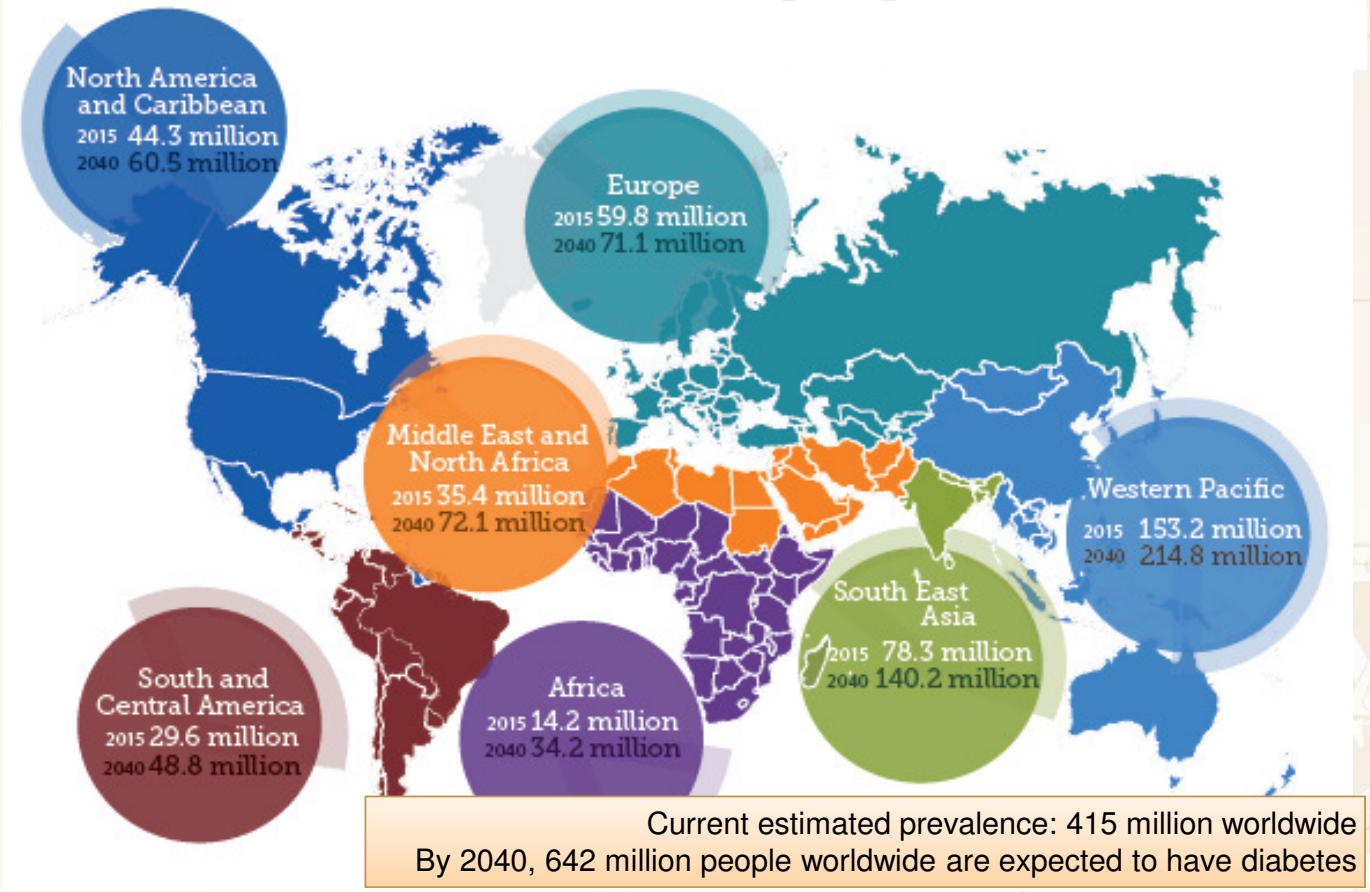
- T2DM with h/o MI ⇩ by 12 years

Cardiovascular Disease in Type 2 Diabetes
Why Do We Care?

- ~2/3 die from CV disease
- T2DM reduces life expectancy by 6 years
- T2DM with h/o MI ⇩ by 12 years
- T2DM with h/o MI and stroke ⇩ by 15 years

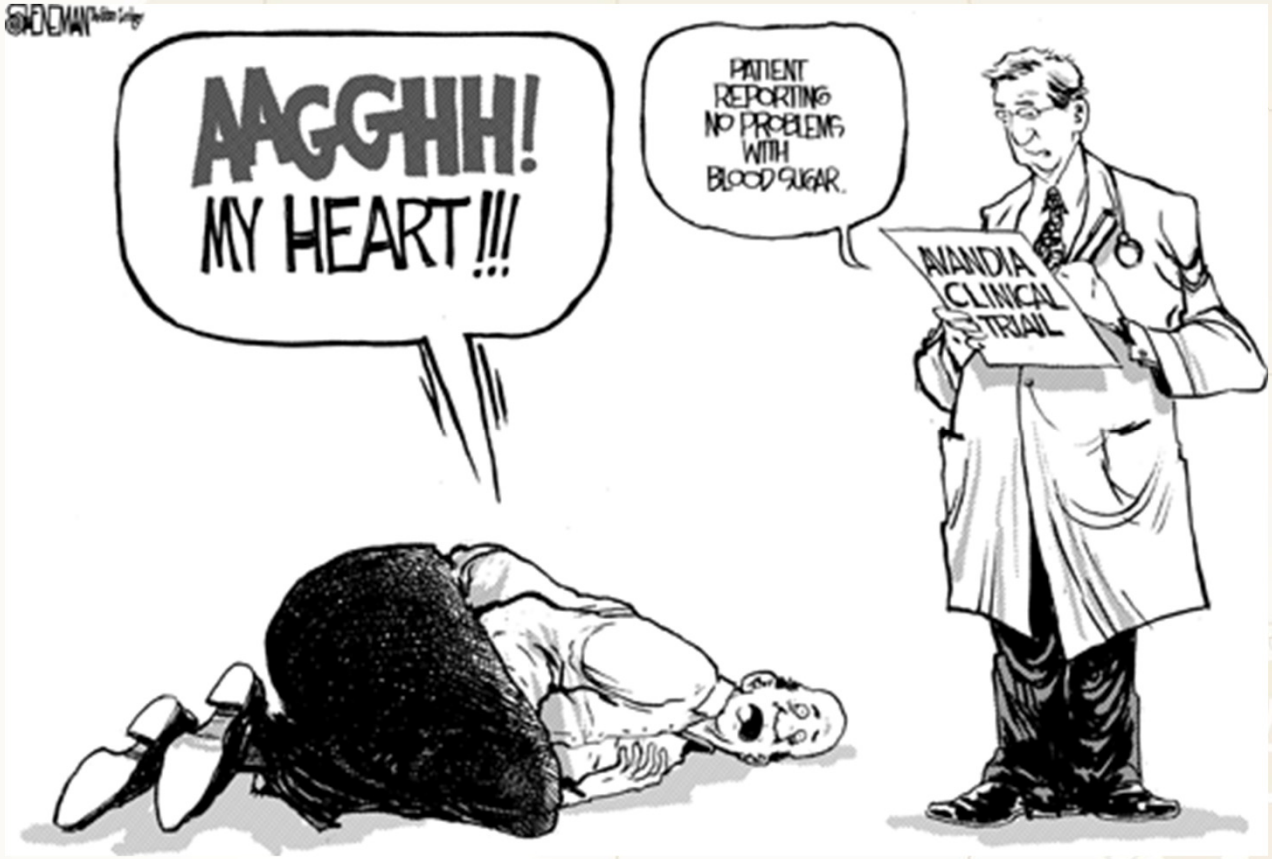
Worldwide Prevalence of Diabetes



Current estimated prevalence: 415 million worldwide
By 2040, 642 million people worldwide are expected to have diabetes

IDF. Diabetes Atlas Update 2015. Available at: http://www.idf.org/sites/default/files/Atlas7e-poster.pdf.

Jump back a decade…


AAGGHH!
MY HEART!!!
PATIENT REPORTING NO PROBLEMS WITH BLOOD SUGAR.
AVANDIA CLINICAL TRIAL

Cardiovascular Outcomes Trials: A Brief History

- 2008 FDA mandates assessment of CV safety of all antihyperglycemic agents in RCTs

MACE = major adverse cardiovascular events; RCTs, randomized controlled trials.

FDA. Guidance for industry: evaluating cardiovascular risk in new antidiabetic therapies to treat type 2 diabetes. http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm071627.pdf.

Cardiovascular Outcomes Trials: A Brief History

- 2008 FDA mandates assessment of CV safety of all antihyperglycemic agents in RCTs
  - Non-inferiority studies to demonstrate study drug was not associated with more MACE than placebo (*ie safe)*
    - Some study designs tested for superiority if noninferiority criteria were met (*ie good for the CV system)*

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Cardiovascular Outcomes Trials: A Brief History

- 2008 FDA mandates assessment of CV safety of all antihyperglycemic agents in RCTs
  - Non-inferiority studies to demonstrate study drug was not associated with more MACE than placebo (*ie safe)*
    - Some study designs tested for superiority if noninferiority criteria were met (*ie good for the CV system)*
  - Primary endpoint: composite of cardiovascular death, nonfatal MI, and nonfatal stroke (3 point MACE)
    - Some primary endpoints included additional components

MACE = major adverse cardiovascular events; RCTs, randomized controlled trials.

FDA. Guidance for industry: evaluating cardiovascular risk in new antidiabetic therapies to treat type 2 diabetes. http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm071627.pdf.

What are Classes of T2DM Medications Since 2008?

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- DPP4 inhibitors

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- GLP1 receptor agonists

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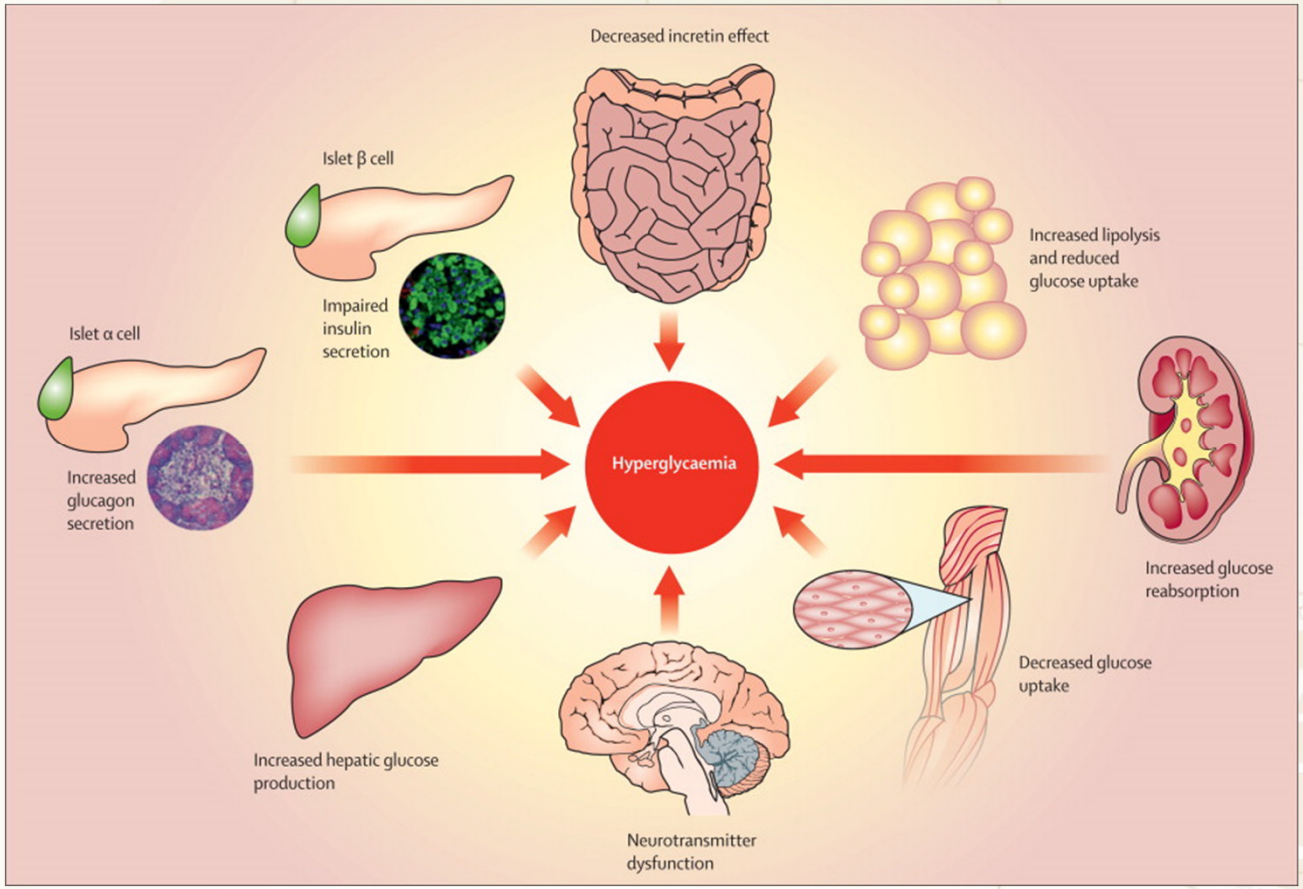
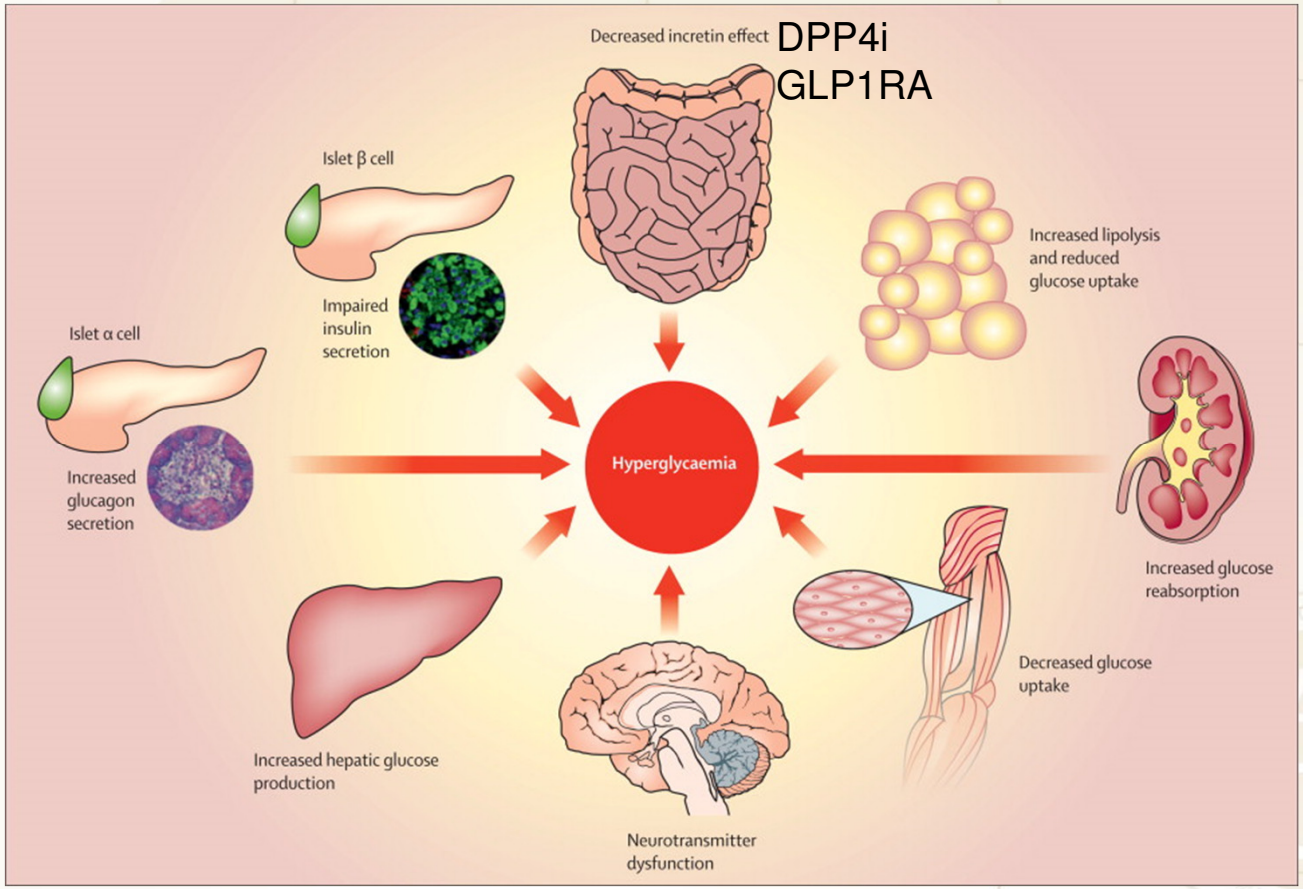
- DPP4 inhibitors
- GLP1 receptor agonists
- SGLT2 inhibitors

The Ominous Octet



The Ominous Octet



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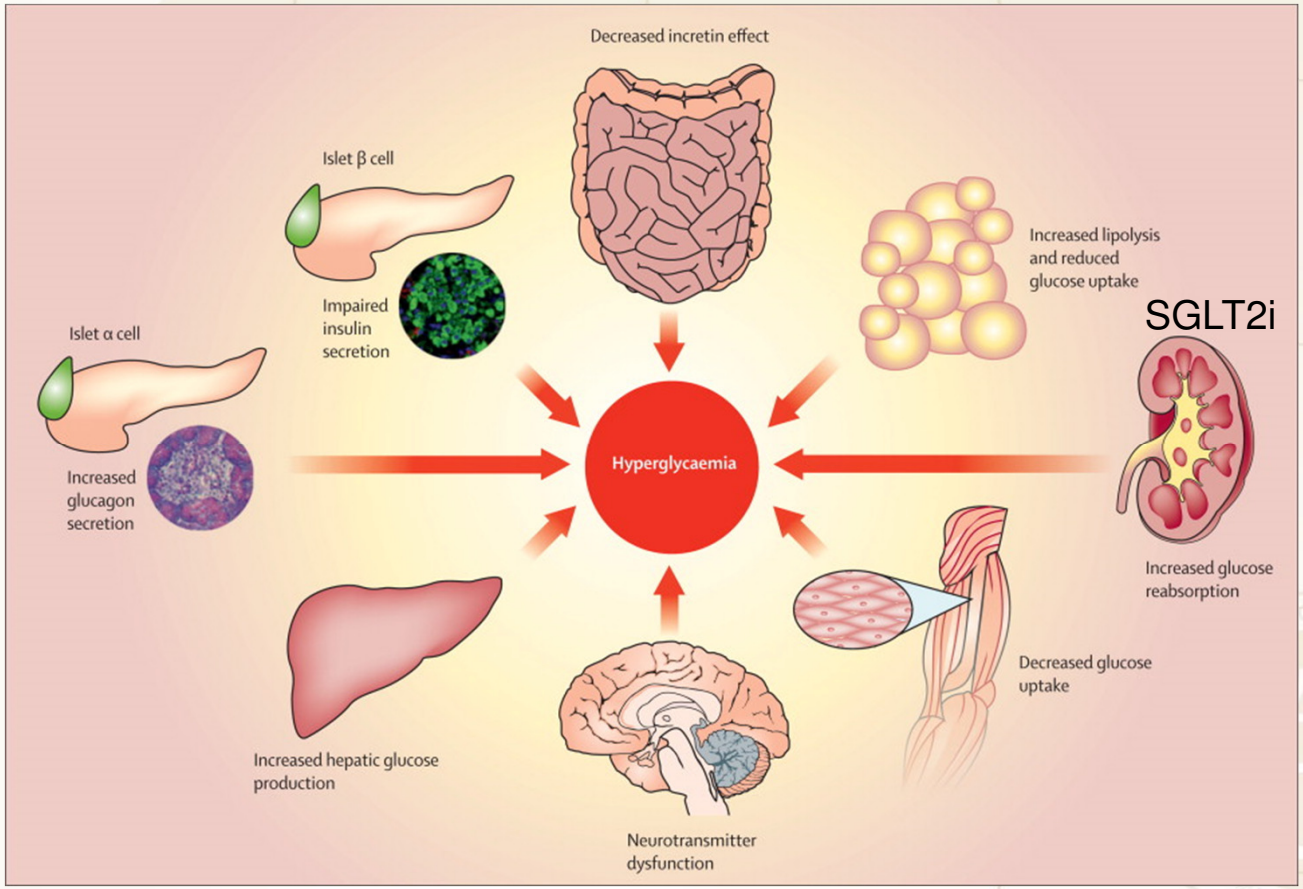
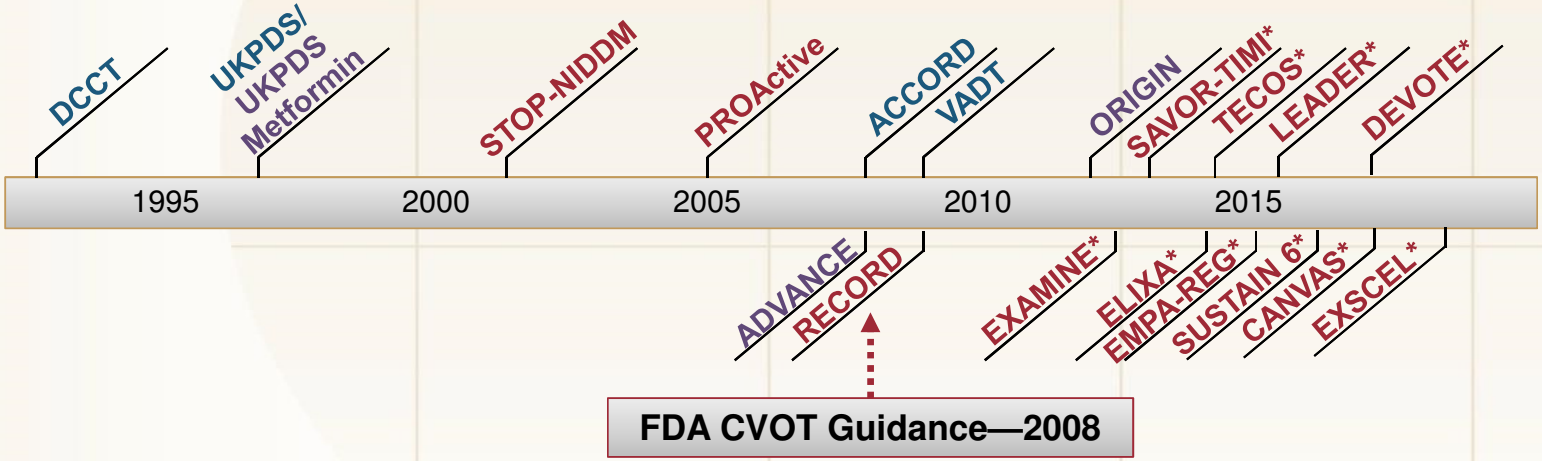


Timeline of Major Diabetes Outcomes Trials



Blue = Intensive vs standard control using same set of glucose-lowering agent(s)
Purple = Intensive control with a specific agent vs standard care
Red = Placebo- or active-controlled study
* = FDA-mandated cardiovascular safety trial

ACCORD, Action to Control Cardiovascular Risk in Diabetes; ADVANCE, Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation; CANVAS, Canagliflozin Cardiovascular Assessment Study; DCCT, Diabetes Control and Complications Trial; DEVOTE, Trial Comparing Cardiovascular Safety of Insulin Degludec versus Insulin Glargine in Patients with Type 2 Diabetes at High Risk of Cardiovascular Events; EXAMINE, Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care; ELIXA, Evaluation of Lixisenatide in Acute Coronary Syndrome; EMPA-REG, EMPA-REG OUTCOME trial; Exenatide Study of Cardiovascular Event Lowering; LEADER, Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results; ORIGIN, Outcome Reduction with an Initial Glargine Intervention; PROActive, Prospective Pioglitazone Clinical Trial in Macrovascular Events; RECORD, Rosiglitazone Evaluated for Cardiovascular Outcomes in Oral Agent Combination Therapy for Type 2 Diabetes; SAVOR-TIMI, Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus–Thrombolysis in Myocardial Infarction; STOP-NIDDM, Study to Prevent Non-Insulin-Dependent Diabetes Mellitus; SUSTAIN, Trial to Evaluate Cardiovascular and Other Long-Term Outcomes with Semaglutide in Subjects with Type 2 Diabetes; TECOS, Trial Evaluating Cardiovascular Outcomes with Sitagliptin; UKPDS, United Kingdom Prospective Diabetes Study; VADT, Veterans Affairs Diabetes Trial.

Agents Shown to have CV Safety

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- All anti-hyperglycemic agents to date

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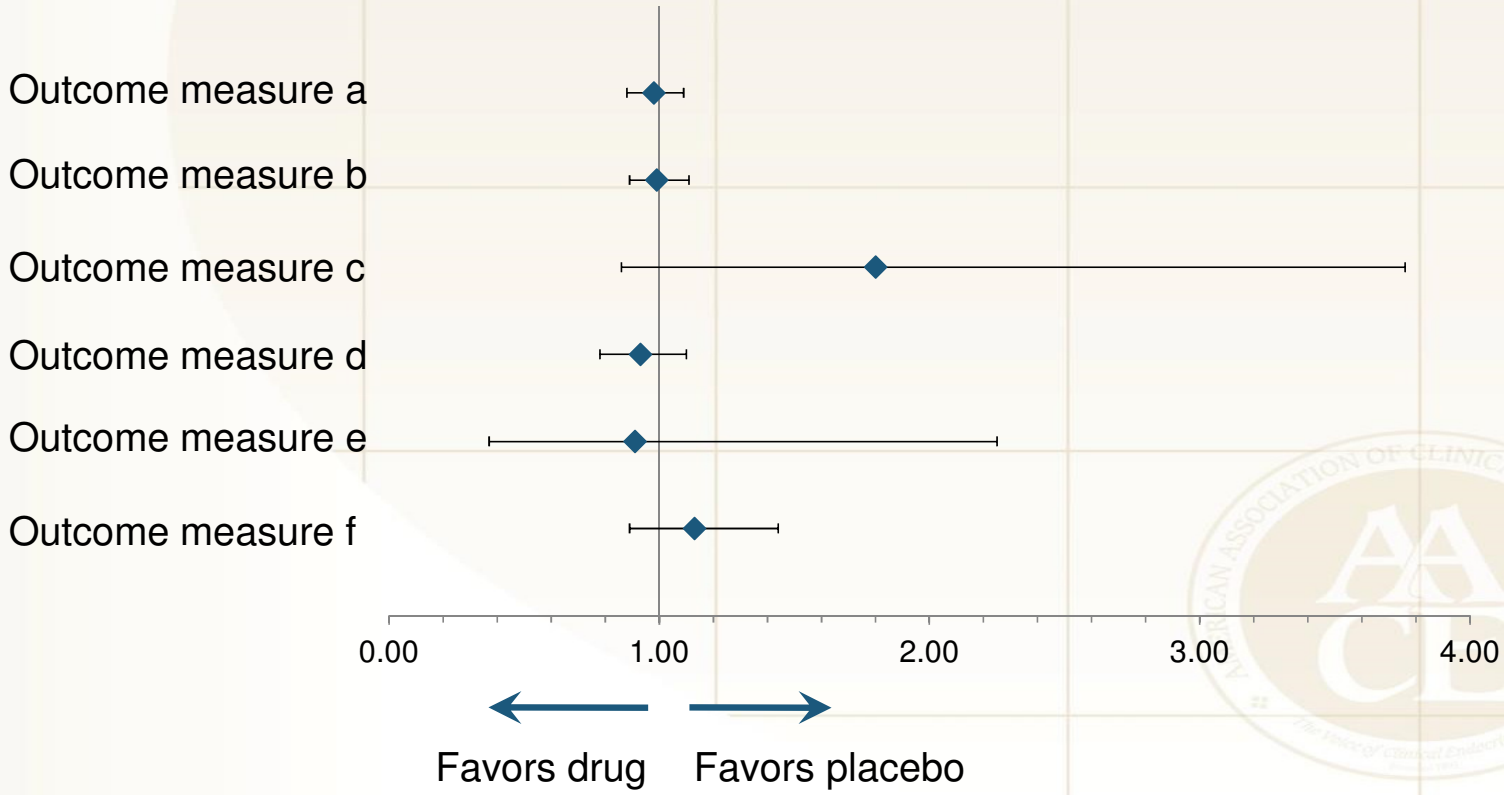
- All anti-hyperglycemic agents to date

Have any agents shown CV benefit?

How to Read a Forest Plot



DPP4 Inhibitors

DPP4 Inhibitors

FDA-Approved Agents

- Sitagliptin (Januvia)
- Saxagliptin (Onglyza)
- Linagliptin (Tradjenta)
- Alogliptin (Nesina)

DPP4, dipeptidyl peptidase 4; GIP, glucose-dependent insulinotropic polypeptide; GLP1, glucagon-like peptide 1.

Garber AJ, et al. *Endocr Pract.* 2016;22:84-113.

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- Linagliptin (Tradjenta)
- Alogliptin (Nesina)

Key Features

- Oral administration
- Increase endogenous GLP1 and GIP levels
- Increase glucose-dependent insulin secretion
- Suppress glucagon production

DPP4, dipeptidyl peptidase 4; GIP, glucose-dependent insulinotropic polypeptide; GLP1, glucagon-like peptide 1.

Garber AJ, et al. *Endocr Pract.* 2016;22:84-113.

DPP4 Inhibitors

- Sitagliptin (Januvia)

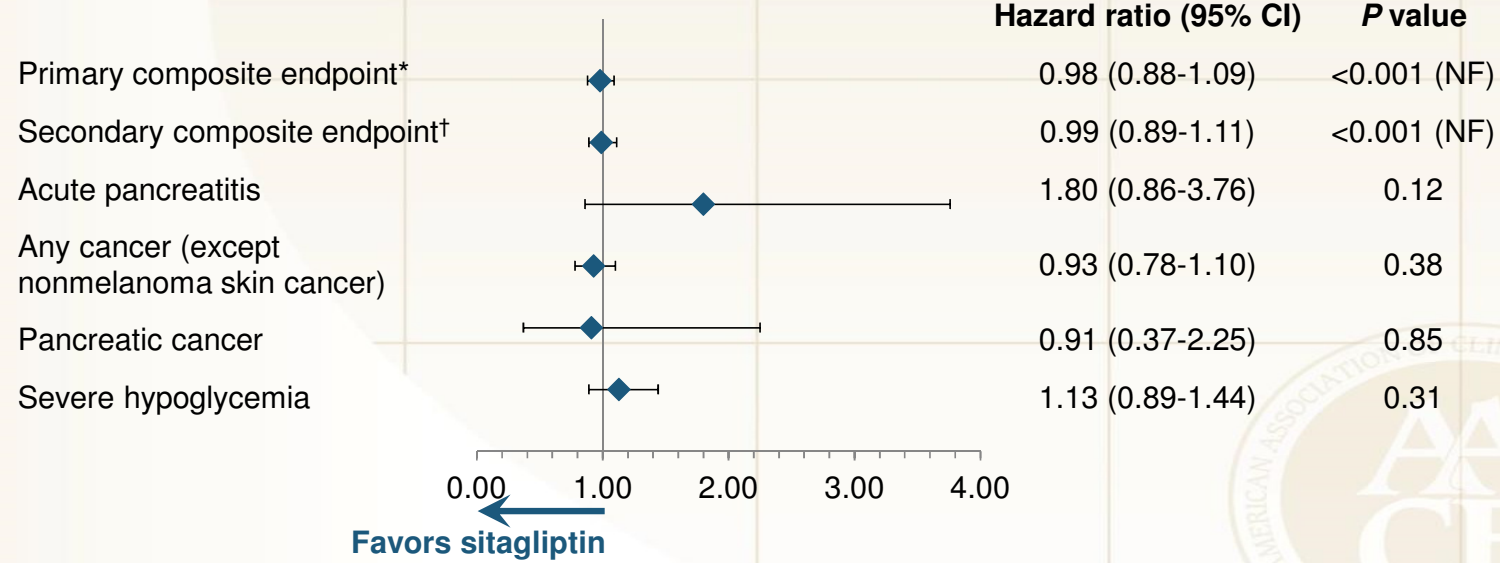
TECOS

(Trial Evaluating Cardiovascular Outcomes with Sitagliptin)

Primary and Secondary Outcomes with Sitagliptin

TECOS Per Protocol Analysis (n=14,523)

Median follow-up: 3.0 years



*Cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for unstable angina.

†Secondary composite: cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke.

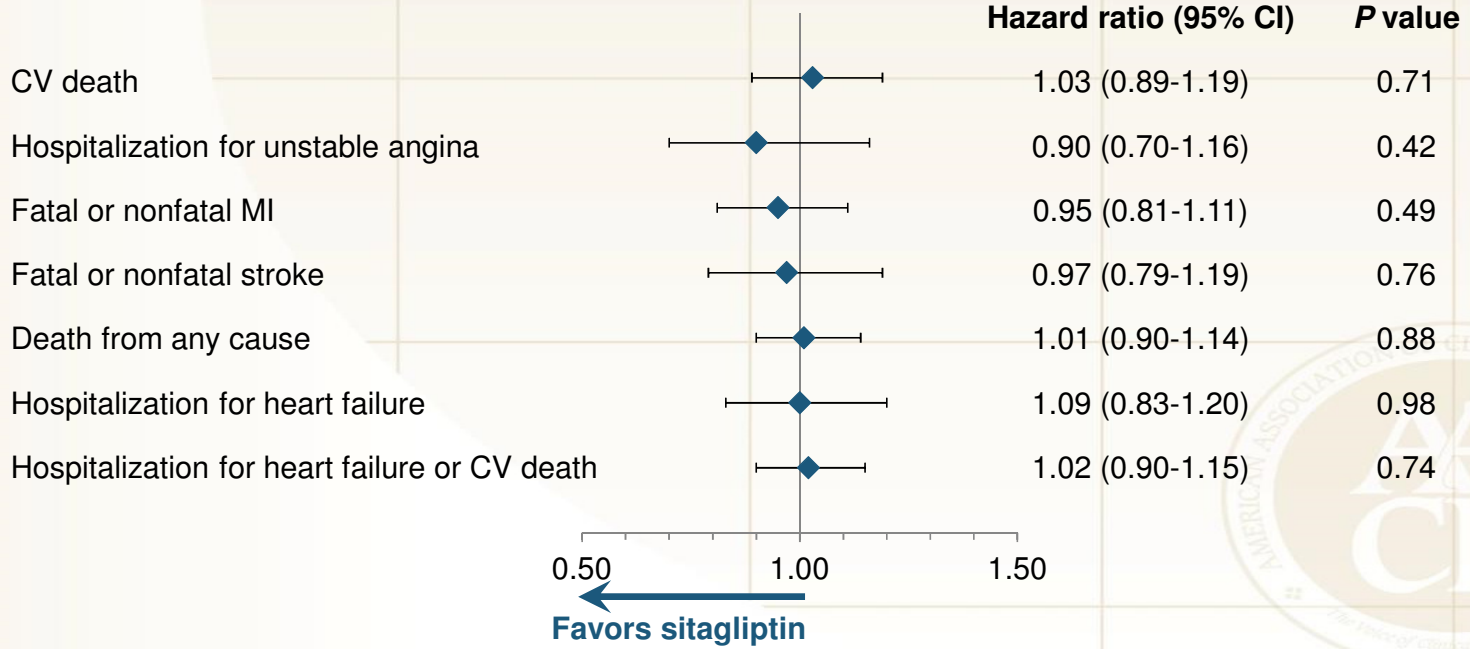
NF, noninferiority; TECOS, Trial Evaluating Cardiovascular Outcomes with Sitagliptin.

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

Individual Secondary Outcomes with Sitagliptin

TECOS Intent to Treat Analysis
n=14,671, T2DM and CVD

Median follow-up: 3.0 years



CV, cardiovascular; MI, myocardial infarction; NF, noninferiority; TECOS, Trial Evaluating Cardiovascular Outcomes with Sitagliptin.

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

DPP4 Inhibitors

- Saxagliptin (Onglyza)

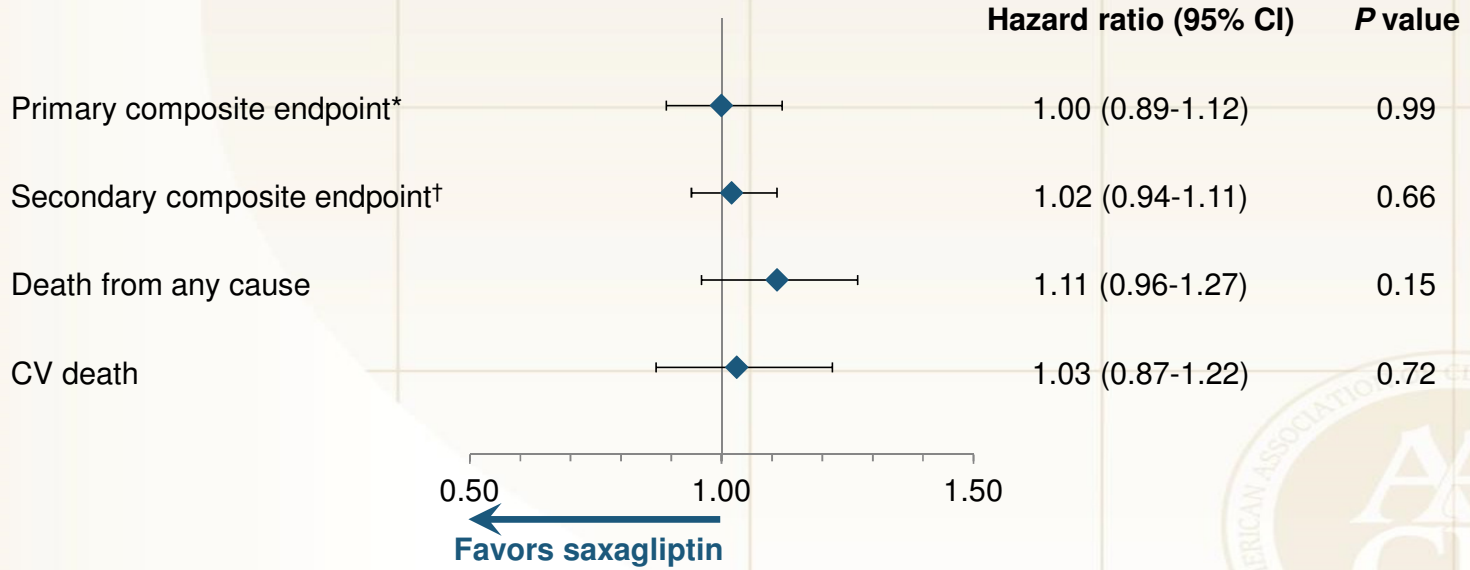
SAVOR-TIMI

(Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus–Thrombolysis in Myocardial Infarction)

Clinical Outcomes with Saxagliptin

SAVOR-TIMI Prespecified Composite Endpoints and Mortality
n=16,492, T2DM and CVD or CVD risk

Median follow-up: 2.1 years



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

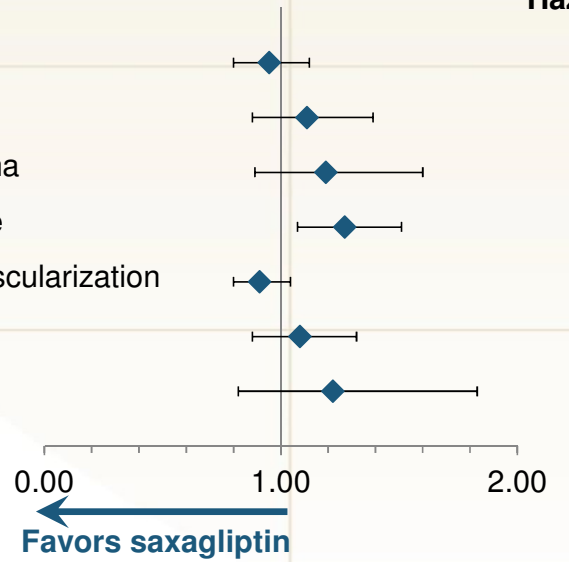
CI, confidence interval; CV, cardiovascular; HF, heart failure; MI, myocardial infarction; SAVOR-TIMI, Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus–Thrombolysis in Myocardial Infarction.

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

Individual Secondary Outcomes with Saxagliptin

SAVOR-TIMI Prespecified Individual Endpoints (n=16,492)

Median follow-up: 2.1 years



	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.

DPP4 Inhibitors

- Linagliptin (Tradjenta)
  - CAROLINA (Cardiovascular Outcome Study of Linagliptin Versus Glimepiride in Patients With Type 2 Diabetes)
    - Not resulted yet
  - CARMELINA (CArdiovascular safety and Renal Microvascular outcomE with LINAgliptin in patients with type 2 diabetes at high vascular risk)
    - Top line results: shows CV safety

DPP4 Inhibitors

- Alogiptin (Nesina)

EXAMINE

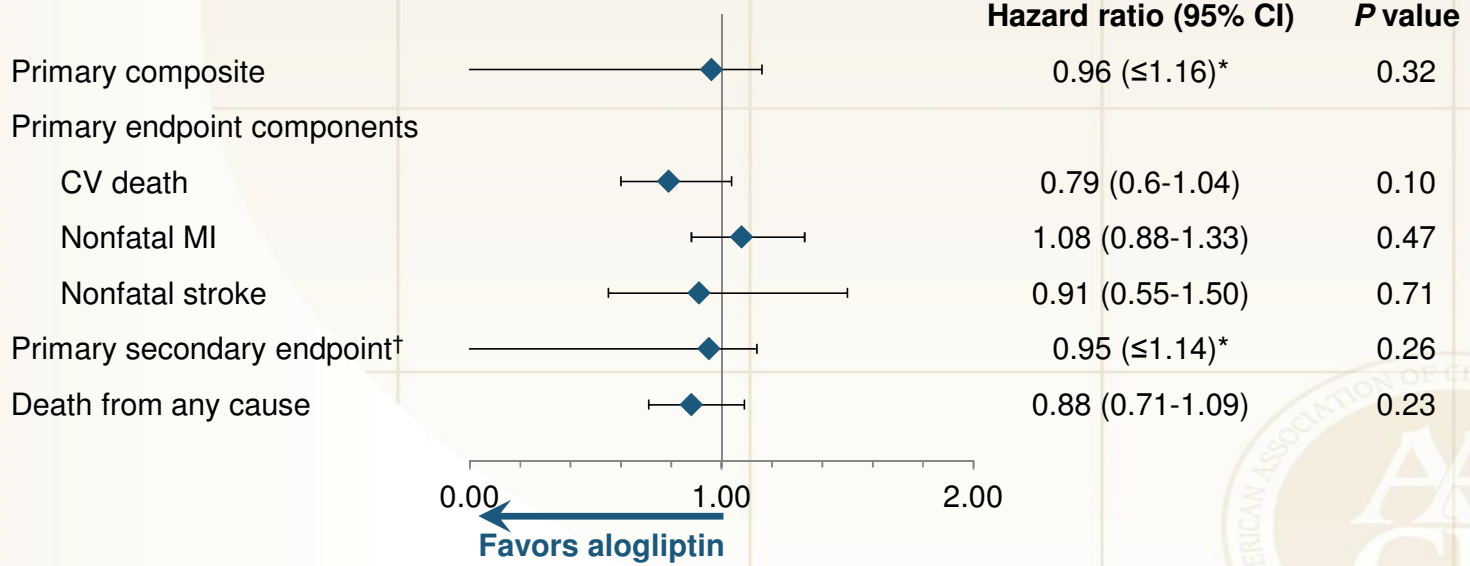
(Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care)

Clinical Outcomes with Alogliptin

3.9% (alogliptin) vs 3.3% (placebo) hospitalization for heart failure

EXAMINE Safety Endpoints
n=5380, T2DM and ACS

Median follow-up: 18 months



*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.

DPP4 Inhibitors

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- All resulted have shown CV safety

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  - possible ↑ risk of HF hospitalization with saxagliptin, alogliptin

DPP4 Inhibitors

- All resulted have shown CV safety
  - possible ↑ risk of HF hospitalization with saxagliptin, alogliptin
- None have shown CV benefit to date

SGLT2 Inhibitors

SGLT2 Inhibitors

FDA-Approved Agents

- Empagliflozin (Jardiance)
- Canagliflozin (Invokana)
- Dapagliflozin (Farxiga)
- Urtogliflozin (Steglatro)

SGLT2, sodium-glucose cotransporter 2.

DeFronzo RA, et al. *Diabetes Obes Metab*. 2012;14:5-14.

SGLT2 Inhibitors

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- Canagliflozin (Invokana)
- Dapagliflozin (Farxiga)
- Urtogliflozin (Steglatro)

Key Features

- Oral administration
- Inhibit reabsorption of glucose into the bloodstream from renal fluid

SGLT2, sodium-glucose cotransporter 2.

DeFronzo RA, et al. *Diabetes Obes Metab*. 2012;14:5-14.

SGLT2 Inhibitors

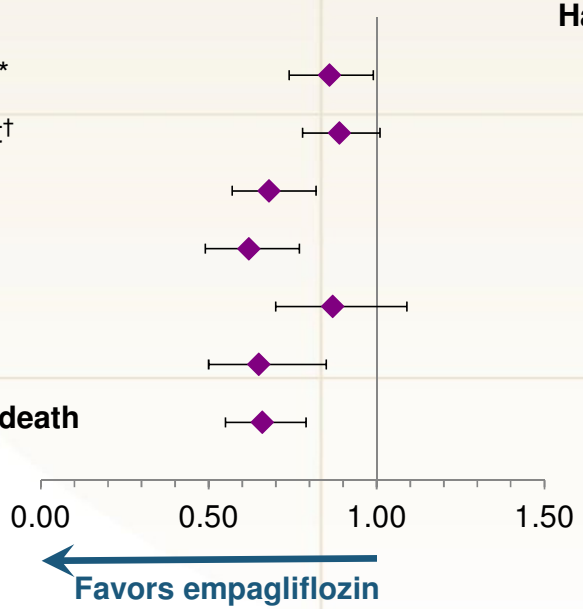
- Empagliflozin (Jardiance)

EMPA-REG OUTCOME (Empagliflozin cardiovascular Outcome event trial in type 2 diabetes mellitus patients)

Clinical Outcomes with Empagliflozin

EMPA-REG OUTCOME Pooled Analysis
N=7020, T2DM and CVD

Median follow-up: 3.1 years



	Hazard ratio (95% CI)	*P* value	RRR
Primary composite endpoint*	0.86 (0.74-0.99)	0.04	**14%**
Secondary composite endpoint†	0.89 (0.78-1.01)	0.08	
Death from any cause	0.68 (0.57-0.82)	<0.001	**32%**
CV death	0.62 (0.49-0.77)	<0.001	**38%**
Fatal or nonfatal MI	0.87 (0.70-1.09)	0.23	
Hospitalization for HF	0.65 (0.50-0.85)	0.002	**35%**
Hospitalization for HF or CV death	0.66 (0.55-0.79)	<0.001	**34%**

*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.

SGLT2 Inhibitors

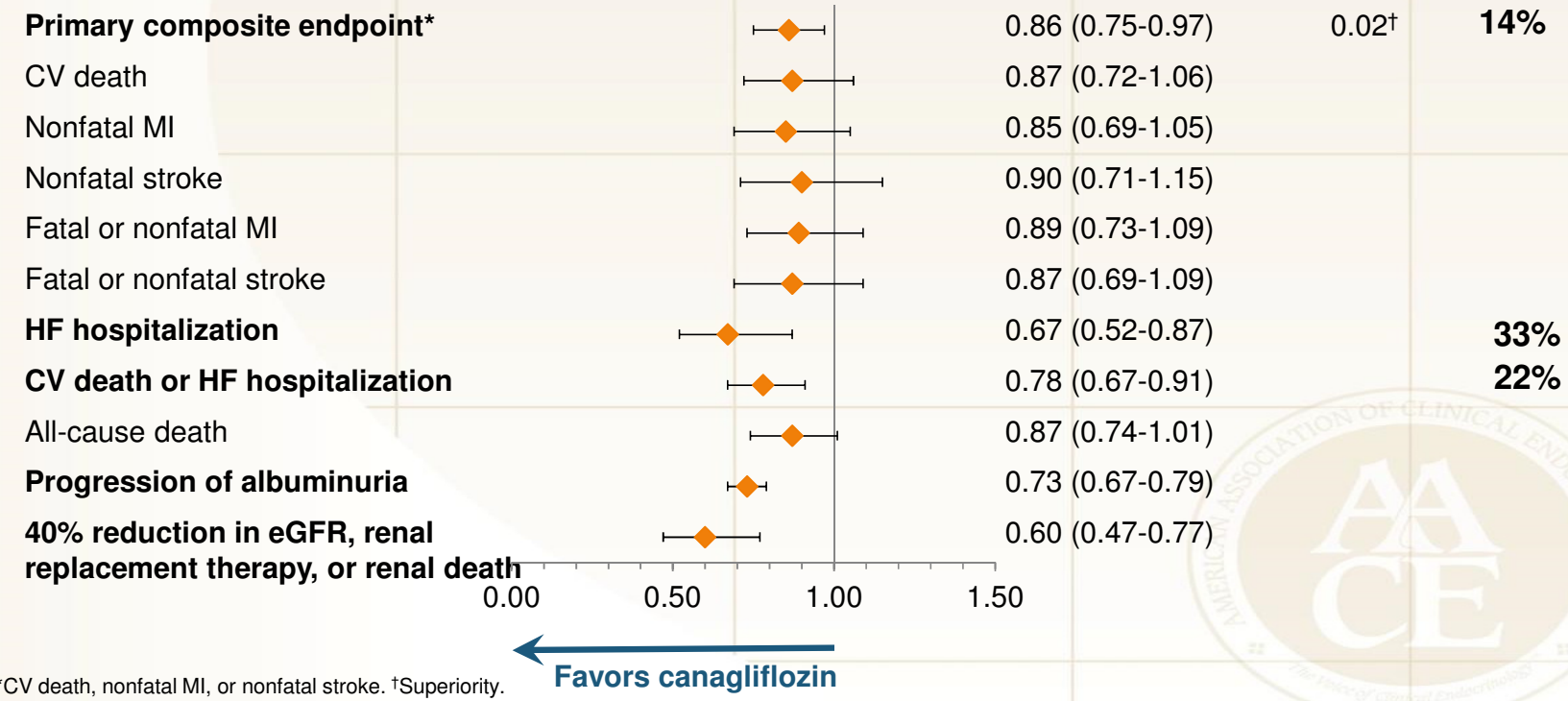
- Canagliflozin (Invokana)

CANVAS
(Canaglflozin Cardiovascular Assessment Study)

Clinical Outcomes with Canagliflozin

CANVAS Program
N=10,142, T2D and high CV risk

Median follow-up: 2.4 years



*CV death, nonfatal MI, or nonfatal stroke. †Superiority.

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

Neal B, et al. *N Engl J Med*. 2017 Jun 12 [epub ahead of print].

Adverse Events with Canagliflozin

CANVAS Program* Safety Results

Event	Canagliflozin	Placebo	P value
	Events per 1000-patient years		
All serious adverse events	104.3	120.0	0.04
Adverse events leading to discontinuation	35.5	32.8	0.07
Diabetic ketoacidosis (adjudicated)	0.6	0.3	0.14
Events of interest occurring in significantly more canagliflozin-treated patients			
Amputation	**6.3**	**3.4**	**<0.001**
Bone fracture (adjudicated)			
All	**15.4**	**11.9**	**0.02**
Low trauma	**11.6**	**9.2**	**0.06**
Infection of male genitalia	34.9	10.8	<0.001
Osmotic diuresis†	34.5	13.3	<0.001
Volume depletion†	26.0	18.5	0.009
Mycotic genital infection in women†	68.8	17.5	<0.001

*Includes patients from CANVAS and CANVAS-R (N=10,142). †CANVAS-only population (n=4330).

Neal B, et al. *N Engl J Med*. 2017 Jun 12 [epub ahead of print].

SGLT2 Inhibitors

- Dapagliflozin (Farxiga)

DECLARE TIMI-58

(Dapagliflozin Effect on Cardiovascular Events)

  - Includes large cohort (~60%) primary prevention
  - Top line results: Reduction in hospitalization for heart failure or CV Death

SGLT2 Inhibitors

- Ertugliflozin (Steglatro)

VERTIS CV

(Cardiovascular Outcomes Following Ertugliflozin Treatment in Type 2 Diabetes Mellitus Participants With Vascular Disease)

-Sept 2019 completion

SGLT2 Inhibitors

CVD-Real

(Comparative effectiveness of cardiovascular outcomes in new users of sodium glucose cotransporter-2 inhibitors)

Clinical Outcomes with SGLT2 Inhibitors

CVD-REAL Study Design

- Retrospective, observational trial
  - Data collected across claims databases, registries, and inpatient and outpatient data sources
  - Follow-up: 190,164 person-years
- N=309,056 propensity-matched patients newly initiated on antihyperglycemic therapy
  - SGLT2 inhibitor: n=154,528
    - 53% Canagliflozin, 42% Dapagliflozin, 5% Empagliflozin
  - Other glucose-lowering agent: n=154,528
- Outcomes
  - Hazard ratios for HHF, death, and composite of HHF or death

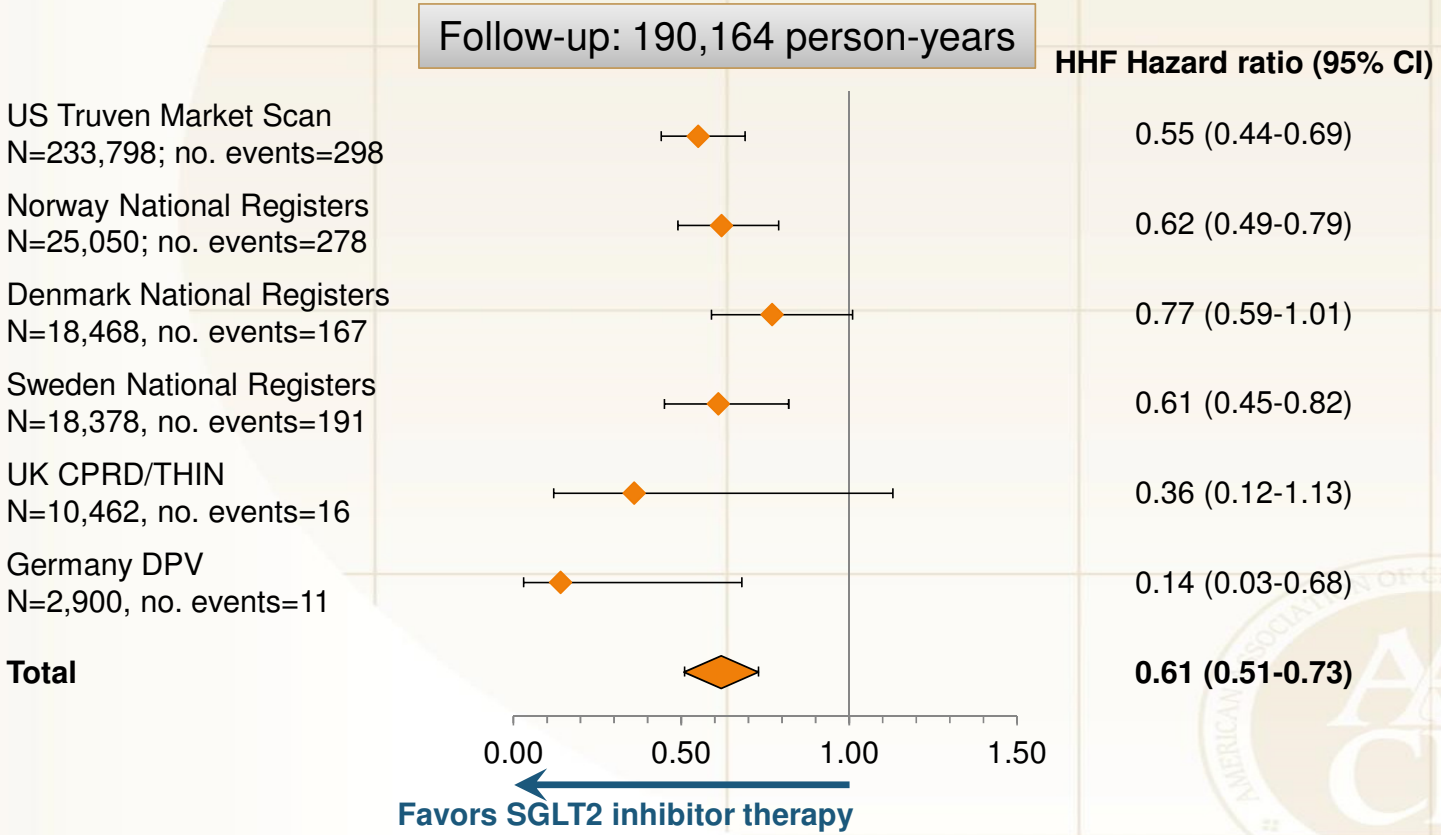
CVD-REAL, Comparative Effectiveness of Cardiovascular Outcomes in New Users of Sodium Glucose Cotransporter-2 Inhibitors; HHF, heart failure hospitalization.

Kosiborod M, et al. *Circulation*. 2017;136:249-259.

Clinical Outcomes with SGLT2 Inhibitors

CVD-REAL Observational Study Results

Follow-up: 190,164 person-years



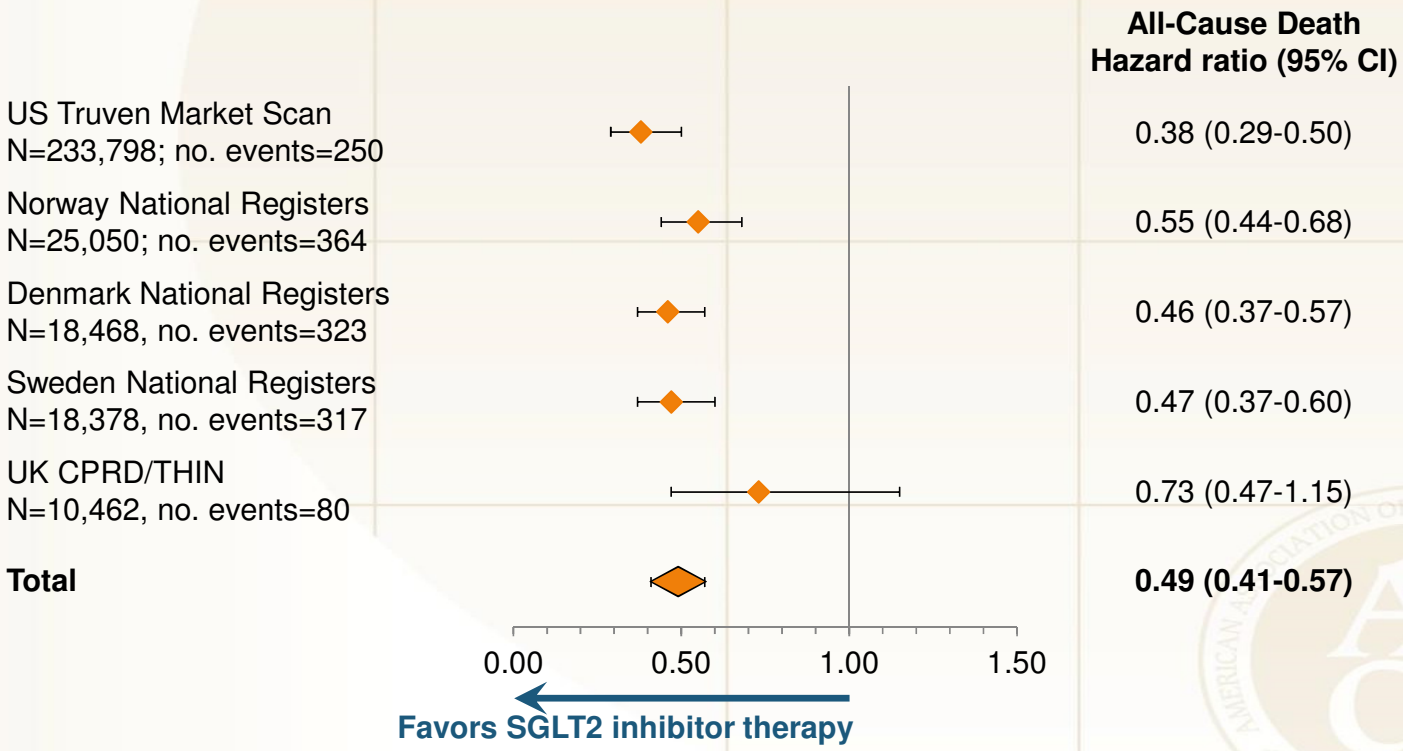
CPRD, Clinical Practice Research Datalink; CVD-REAL, Comparative Effectiveness of Cardiovascular Outcomes in New Users of Sodium Glucose Cotransporter-2 Inhibitors; DPV, Diabetes Patientenverlaufsdokumentation (Diabetes Prospective Follow-up); HHF, heart failure hospitalization; THIN, The Health Improvement Network.

Kosiborod M, et al. *Circulation*. 2017;136:249-259.

Clinical Outcomes with SGLT2 Inhibitors

CVD-REAL Observational Study Results

Follow-up: 190,164 person-years



CPRD, Clinical Practice Research Datalink; CVD-REAL, Comparative Effectiveness of Cardiovascular Outcomes in New Users of Sodium Glucose Cotransporter-2 Inhibitors; DPV, Diabetes Patientenverlaufsdokumentation (Diabetes Prospective Follow-up); HHF, heart failure hospitalization; THIN, The Health Improvement Network.

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SGLT2 Inhibitors

- All resulted have shown CV safety
- All have shown CV benefit to date
- Mechanism?

GLP1 Receptor Agonists

GLP1 Receptor Agonists

FDA-Approved Agents

- Exanatide (Byetta)
- Lixisenatide (Adlyxin)
- Liraglutide (Victoza)
- Exenatide QW (Bydureon, Bcise)
- Dulaglutide (Trulicity)
- Semaglutide (Ozempic)
- Albiglutide (Tanzeum)

ER, extended release; GLP1, glucagon-like peptide 1.

Garber AJ, et al. *Endocr Pract.* 2016;22:84-113.

GLP1 Receptor Agonists

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- Albiglutide (Tanzeum)

Key Features

- Injectable administration
- Mimic action of native GLP1
- Increase glucose-dependent insulin secretion
- Suppress glucagon production
- Slow gastric emptying

ER, extended release; GLP1, glucagon-like peptide 1.

Garber AJ, et al. *Endocr Pract.* 2016;22:84-113.

GLP-1 RA

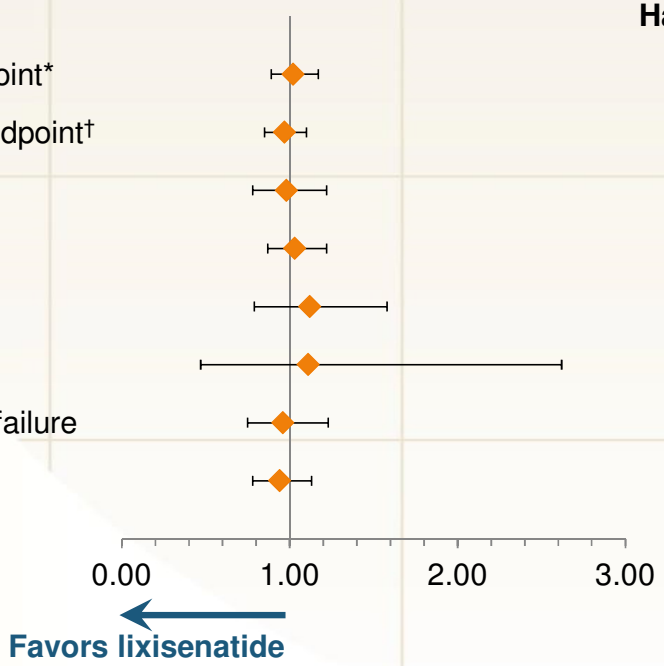
- Lixisenatide (Adlyxin)

ELIXA

(Evaluation of Lixisenatide In Acute coronary syndrome)

Clinical Outcomes with Lixisenatide

ELIXA
N=6068, T2D and ACS within 180 days



	Hazard ratio (95% CI)	*P* value
Primary composite endpoint*	1.02 (0.89-1.17)	0.81
Secondary composite endpoint†	0.97 (0.85-1.10)	0.63
CV death	0.98 (0.78-1.22)	0.85
Fatal or nonfatal MI	1.03 (0.87-1.22)	0.71
Stroke	1.12 (0.79-1.58)	0.54
Unstable angina	1.11 (0.47-2.62)	0.81
Hospitalization for heart failure	0.96 (0.75-1.23)	0.75
Death from any cause	0.94 (0.78-1.13)	0.50

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

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

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

GLP-1 RA

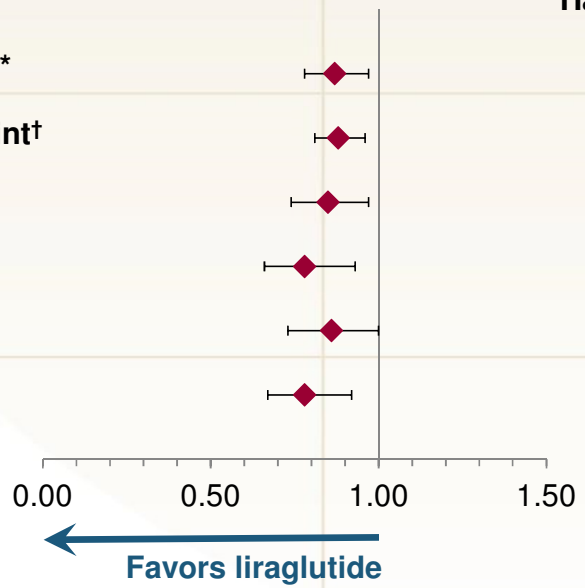
- Liraglutide (Victoza)

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

Clinical Outcomes with Liraglutide

LEADER
N=9340, T2DM and high CV risk

Median follow-up: 3.8 years



	Hazard ratio (95% CI)	*P* value	RRR
Primary composite endpoint*	0.87 (0.78-0.97)	0.01	**13%**
Expanded composite endpoint†	0.88 (0.81-0.96)	0.005	**12%**
Death from any cause	0.85 (0.74-0.97)	0.02	**15%**
CV death	0.78 (0.66-0.93)	0.007	**22%**
Fatal or nonfatal MI	0.86 (0.73-1.00)	0.046	**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.

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

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

GLP-1 RA

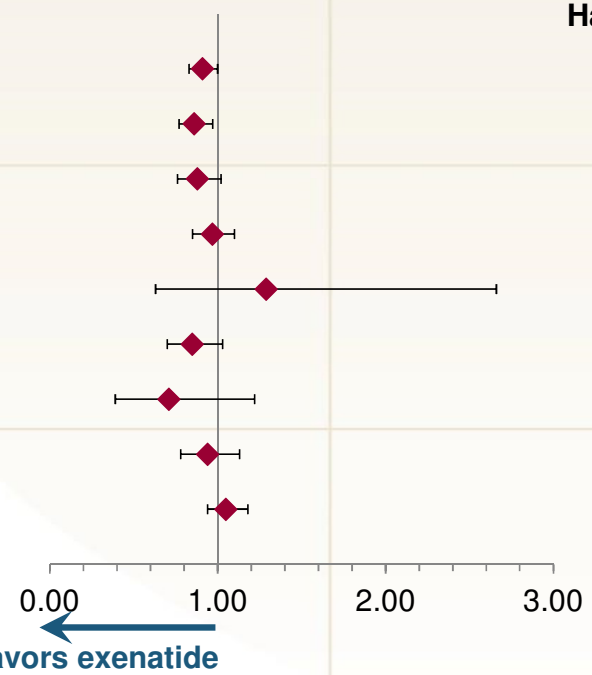
- Exenatide QW (Bydureon)

EXSCEL
(Exenatide study of cardiovascular event lowering)

Clinical Outcomes with Exenatide

EXSCEL: pragmatic design
N=14,752, T2DM with or without CVD

Median follow-up: 3.2 years



	Hazard ratio (95% CI)	*P* value†	RRR
Primary composite endpoint*	0.91 (0.83-1.00)	0.06	**9%**
Death from any cause	0.86 (0.77-0.97)	NS	
CV death	0.88 (0.76-1.02)		
Fatal or nonfatal MI	0.97 (0.85-1.10)		
Fatal MI	1.29 (0.63-2.66)		
Fatal or nonfatal stroke	0.85 (0.70-1.03)		
Fatal stroke	0.71 (0.39-1.30)		
Hospitalization for HF	0.94 (0.78-1.13)		
Hospitalization for ACS	1.05 (0.94-1.18)		

*CV death, nonfatal MI, or nonfatal stroke. †For superiority.

ACS, acute coronary syndrome; CI, confidence interval; CV, cardiovascular; EXSCEL, Exenatide Study of Cardiovascular Event Lowering; HF, heart failure; MI, myocardial infarction; NS, not statistically significant based on hierarchical testing plan.

Holman RR, et al. *N Engl J Med*. 2017 Sept 14 [Epub before print].

GLP-1 RA

- Dulaglutide (Trulicity)

REWIND

(Researching Cardiovascular Events With a Weekly Incretin in Diabetes)

-Completed, no results reported

GLP-1 RA

- Semaglutide (Ozempic)

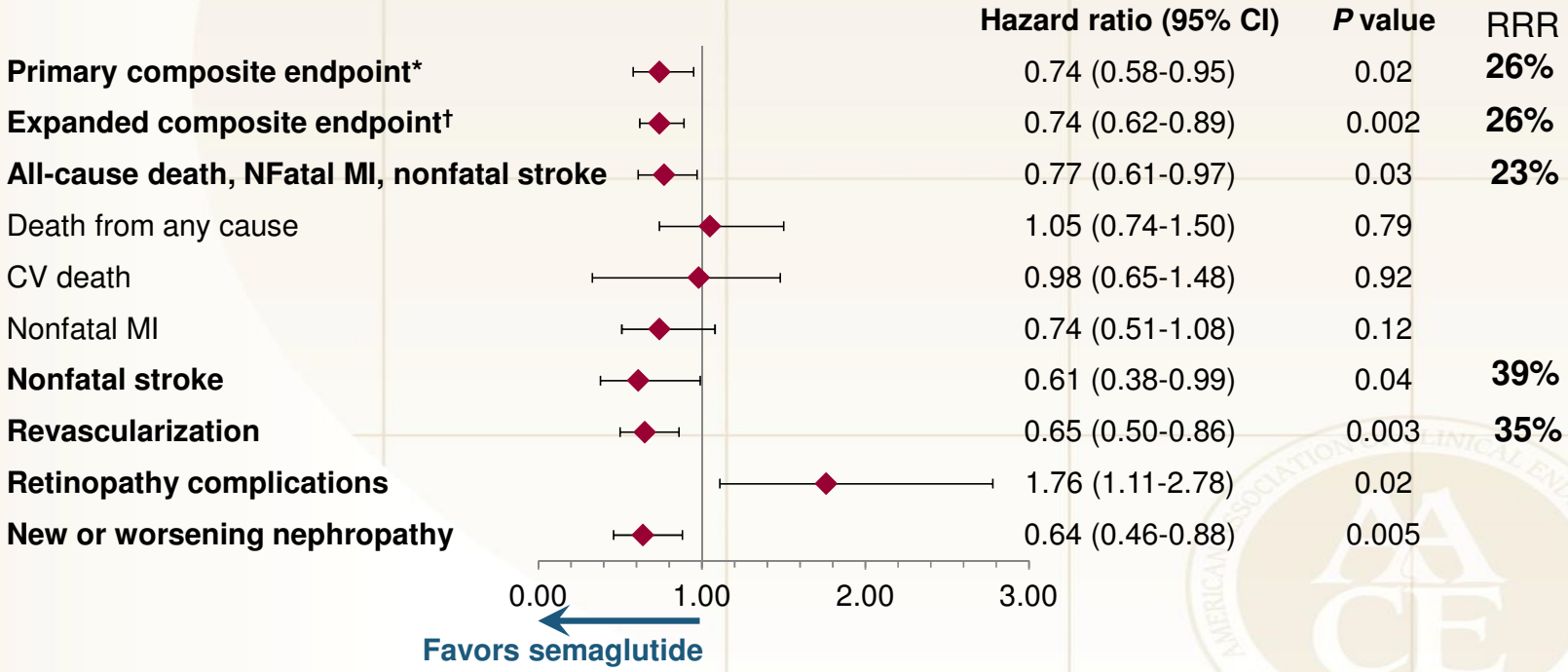
SUSTAIN-6
(Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes)

Clinical Outcomes with Semaglutide

SUSTAIN 6 Results

N=3297, T2DM with CVD, CHF, CKD or age ≥60 with ≥1 CV risk factor

Median follow-up: 2.1 years



*CV death, nonfatal MI (including silent MI), or nonfatal stroke; †CV death, nonfatal MI, nonfatal stroke, coronary or peripheral revascularization, and hospitalization for unstable angina or HF.

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

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

GLP1 Receptor Agonists

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- Mechanism?

Summary

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- Massive undertaking of CVOTs since 2008
- Every single T2DM drug studied since then has shown CV safety

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- 2 classes of medications show clear benefit for CVD
  - SGLT2i
  - GLP1RA

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- 2 classes of medications show clear benefit for CVD
  - SGLT2i
  - GLP1RA
- If no contraindications, these classes preferred particularly in established CVD

What about Avandia?

What about Avandia?

- **Safety Announcement 11-25-2013**
- FDA has determined that recent data for rosiglitazone-containing drugs, such as Avandia, Avandamet, Avandaryl, and generics, **do not show an increased risk of heart attack** compared to the standard type 2 diabetes medicines metformin and sulfonylurea. As a result, we are requiring removal of the prescribing and dispensing restrictions for rosiglitazone medicines that were put in place in 2010. This decision is based on our review of data from a large, long-term clinical trial and is supported by a comprehensive, outside, expert re-evaluation of the data conducted by the Duke Clinical Research Institute (DCRI).


Fortuitous (adj.):
Happening by luck; fortunate


HOW DO WE GET THERE

Questions?