Housekeeping Items

- Welcome to L.A. Care Provider Continuing Education (PCE) Program's Live Webinar!
- Webinar participants are muted upon entry and exit of webinar.
- ***Webinar attendance will be noted via log in and call in. There are 2 Requirements: Please log in through a computer (instead of cell phone) to Join Webinar / Join Event and also call in via telephone by choosing the Call In Option with the event call in number, event access code and assigned unique attendee ID number. If your name does not appear on the WebEx Final Attendance and Activity Report (only as Caller User #) and no submission of online survey, no CME or CE certificate will be provided.***
- Webinar is being recorded.
- Questions will be managed through the Chat feature and will be answered at the end of the presentation. ***Please keep your questions brief and send to All Panelists.*** One of the Learning and Development Team members / Panelist and webinar co-host, will read the questions submitted via Chat when it's time for Q & A session (last 30 minutes of live webinar).
- Please send a message to the Host via Chat if you cannot hear the presenter or see the presentation slides.

L.A. Care PCE Program Friendly Reminders

- ***Partial credits are not allowed at L.A. Care's CME/CE activities for those who log in late (more than 15 minutes late) and/or log off early.***

- PowerPoint Presentation is allotted 60 minutes and last 30 minutes for Q&A session, total of 90-minute live webinar, 1.50 CME credits for Providers / Physicians, 1.50 CE credits for NPs, RNs, LCSWs, LMFTs, LPCCs, LEPs, and other healthcare professionals. A Certificate of Attendance will be provided to webinar attendees without credentials.

- **Friendly Reminder,** a survey will pop up on your web browser after the webinar ends (please do not close your web browser and wait a few seconds) and please complete the survey. ***Please note:*** ***the online survey may appear in another window or tab after the webinar ends.***

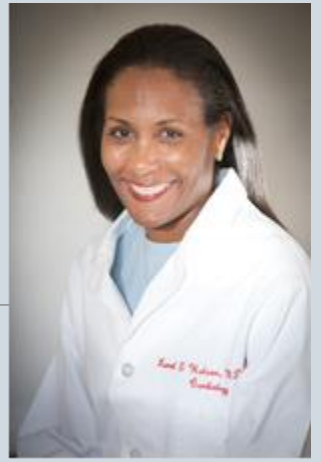
- Within two (2) weeks after webinar and upon completion of the online survey, you will receive the pdf CME or CE certificate based on your credential and after verification of your name and attendance duration time of at least 75 minutes for this 90-minute webinar.

- **The PDF webinar presentation will be available within 3 weeks after webinar date on lacare.org website located at**

  https://www.lacare.org/providers/provider-central/provider-programs/classes-seminars

- Any questions about L.A. Care Health Plan's Provider Continuing Education (PCE) Program and our CME/CE activities, please email Leilanie Mercurio at lmercurio@lacare.org

Presenter's Bio



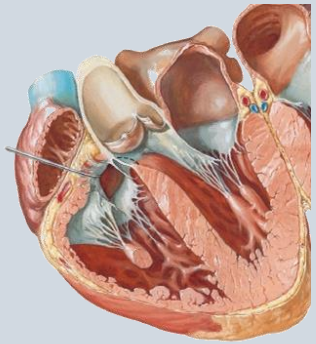
Karol E. Watson, MD, PhD, FACC, is an attending Cardiologist and Professor of Medicine/Cardiology and the John C. Mazziotta Term Chair in Medicine at the David Geffen School of Medicine at UCLA.

Dr. Watson received her undergraduate degree from Stanford University, her Medical Degree from Harvard Medical School, magna cum laude, and her PhD in Physiology from UCLA. She completed a residency in Internal Medicine and a fellowship in Cardiology at UCLA, and continued there as part of the UCLA Specialty Training and Academic Research program and as Chief Fellow in Cardiovascular Diseases at UCLA.

Dr. Watson was honored to be named Cardiologist of the Year, by the California chapter of the American College of Cardiology (ACC) for 2017-18.

Dr. Watson is Director of the UCLA Barbra Streisand Women's Heart Health Program, Co- Director of the UCLA Program in Preventative Cardiology, and Director of the UCLA Cardiology Fellowship. She is a Principal Investigator for several large NIH studies and her research focuses on prevention of heart disease, vascular calcification, hypertension, hypercholesterolemia, and cardiovascular disparities.

The link between Diabetes and CVD – Reducing the risk



KAROL E. WATSON, MD, PHD, FACC

PROFESSOR OF MEDICINE/CARDIOLOGY

DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA

CO-DIRECTOR, UCLA PROGRAM IN PREVENTIVE CARDIOLOGY

November 17, 2022, Live Webinar via WebEx, 12:00 pm – 1:30 pm PST, 1.50 CME/CE Credits
Directly Provided CME/CE Activity by L.A. Care Health Plan

Disclosures

The following CME Planners do not have relevant financial relationships with ineligible companies.

Leilanie Mercurio, L.A. Care PCE Program Manager, CME Planner.
Alex Li, MD, L.A. Care Deputy Chief Medical Officer, CME Planner.

The following ineligible companies have relevant financial relationships with CME Presenter Dr. Karol Watson, Director of the UCLA Barbra Streisand Women's Heart Health Program, Co- Director of the UCLA Program in Preventative Cardiology, and Director of the UCLA Cardiology Fellowship .

Consultant: Amarin, Amgen, Boehringer-Ingelheim, Esperion, Eli Lilly.
Grants: NHLBI, NIDDK, NIH BD2K.

All relevant financial relationships of Dr. Karol Watson, CME Presenter, with ineligible companies have been mitigated.

An ineligible company is any entity whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Commercial support was not received for this CME/CE activity.

Learning Objectives

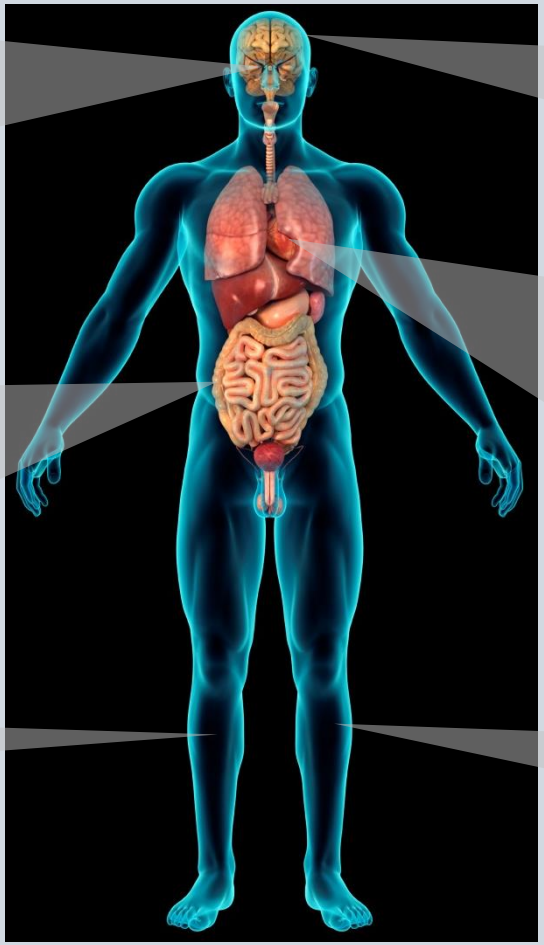
- Identify the link between diabetes and cardiovascular disease (CVD).
- List two (2) therapies proven to prevent CVD in patients with diabetes.
- Specify two (2) new diabetes drugs that fit in with other therapies for cardiovascular risk reduction.
- Specify the role of SGLT2 inhibitors and GLP1-RAs in reducing CV events in diabetics.
- Discuss the role of diabetes therapies in heart failure management

Microvascular Complications

Diabetic Retinopathy
Leading cause of blindness in working-age adults[1]

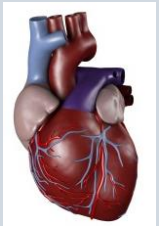
Diabetic Nephropathy
Leading cause of end-stage renal disease[2]

Diabetic Neuropathy
Leading cause of nontraumatic lower extremity amputations[3]



Macrovascular Complications

Stroke
2- to 4-fold increase in cardiovascular mortality and stroke[4,5]



Heart Disease[6]

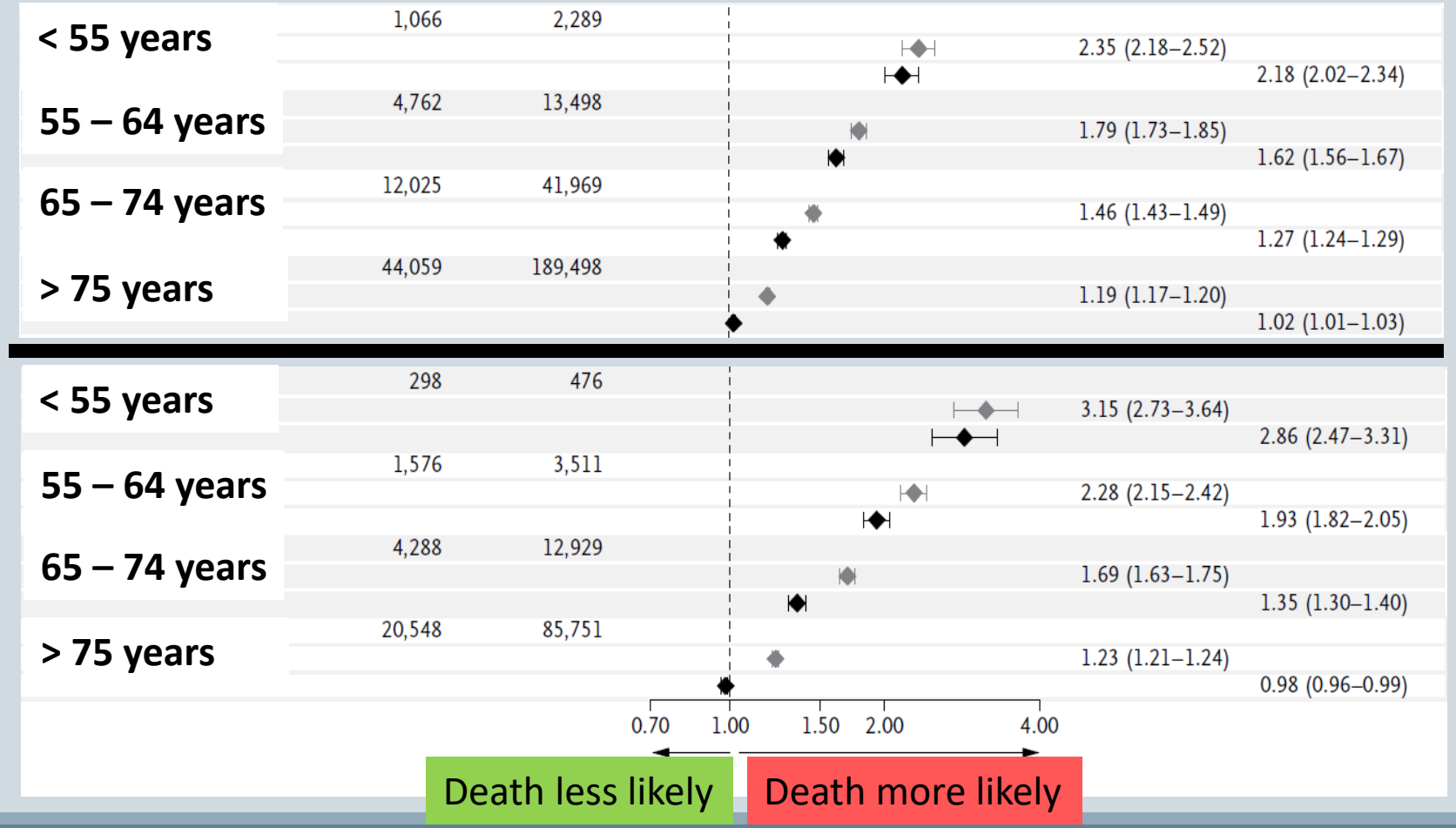
Peripheral Vascular Disease[6]

1. IDF. *Fact Sheet Diabetes and Eye Disease*. Available at: http://www.idf.org/node/1186?unode=C1CCADE9-4A03-4D17-A662-155B3ED59FDB. 2. The Renal Association. *UK Renal Registry*. Twelfth Annual Report. December 2009. Available at http://www.renalreg.com/Reports/2009.html. 3. Dang, CN., Boulton, AJ., *International Journal of Lower Extremity Wounds*. 2003; 2(1):4-12. 4. Jeerakathil, T., *et al*. *Stroke*. 2007;38(6):1739-43. 5. Kaul, S., *et al. Circulation*. 2010;121:1868-77. 6. IDF. *Fact sheet: Diabetes and Cardiovascular Disease (CVD).* Available at: http://www.idf.org/fact-sheets/diabetes-cvd.

Adjusted Hazard Ratios for Total and Cardiovascular Mortality in T2DM

Total Mortality

Cardiovascular Mortality



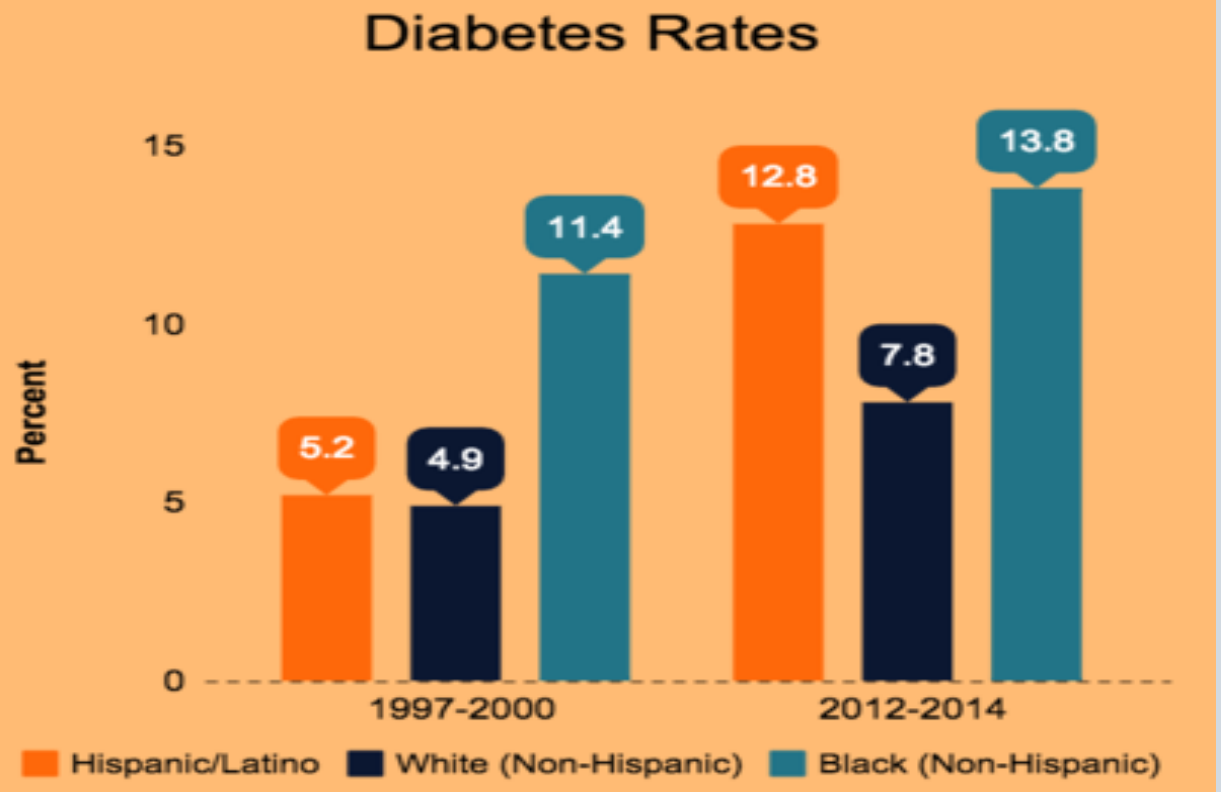
Tancredi M et al. N Engl J Med 2015;373:1720-1732.

Learning Objectives

- Identify the link between diabetes and cardiovascular disease (CVD).
- **List two (2) strategies proven to prevent CVD in patients with diabetes.**
- Specify two (2) new diabetes drugs that fit in with other therapies for cardiovascular risk reduction.
- Specify the role of SGLT2 inhibitors and GLP1-RAs in reducing CV events in diabetics.
- Discuss the role of diabetes therapies in heart failure management

Diabetes Disparities

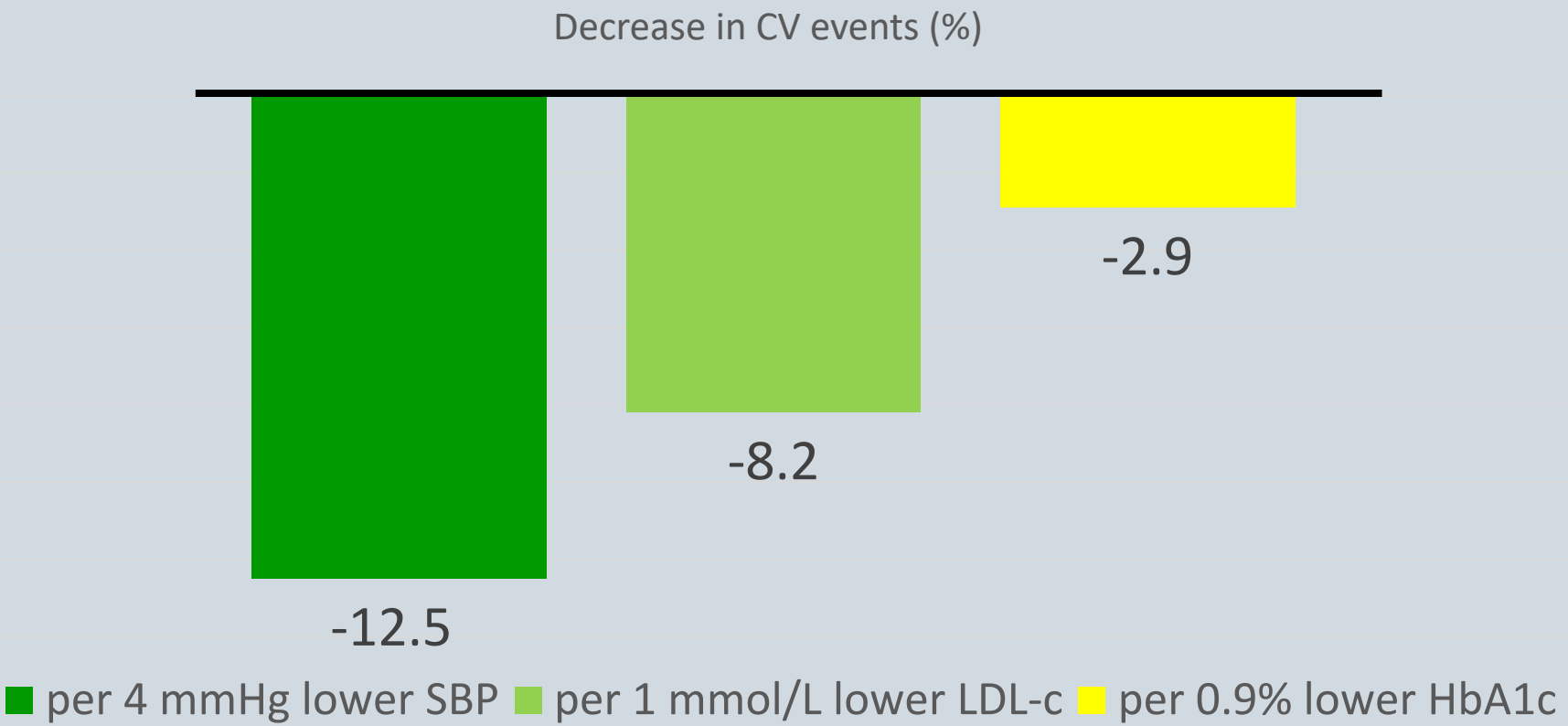
Hispanics have seen the largest increase in age-adjusted diabetes rates, 4.7 points higher than that of whites and 5.2 points higher than that of blacks.



Source: RI Behavioral Risk Factor Surveillance System, RI Department of Health

RI NPR
ARE YOU LISTENING?
88.5FM 91.5FM 102.7FM

Benefit of different interventions for Type 2 diabetes



CV: cardiovascular; SBP: systolic blood pressure; LDL-c: low density lipoprotein cholesterol; HbA1c: glycated hemoglobin;

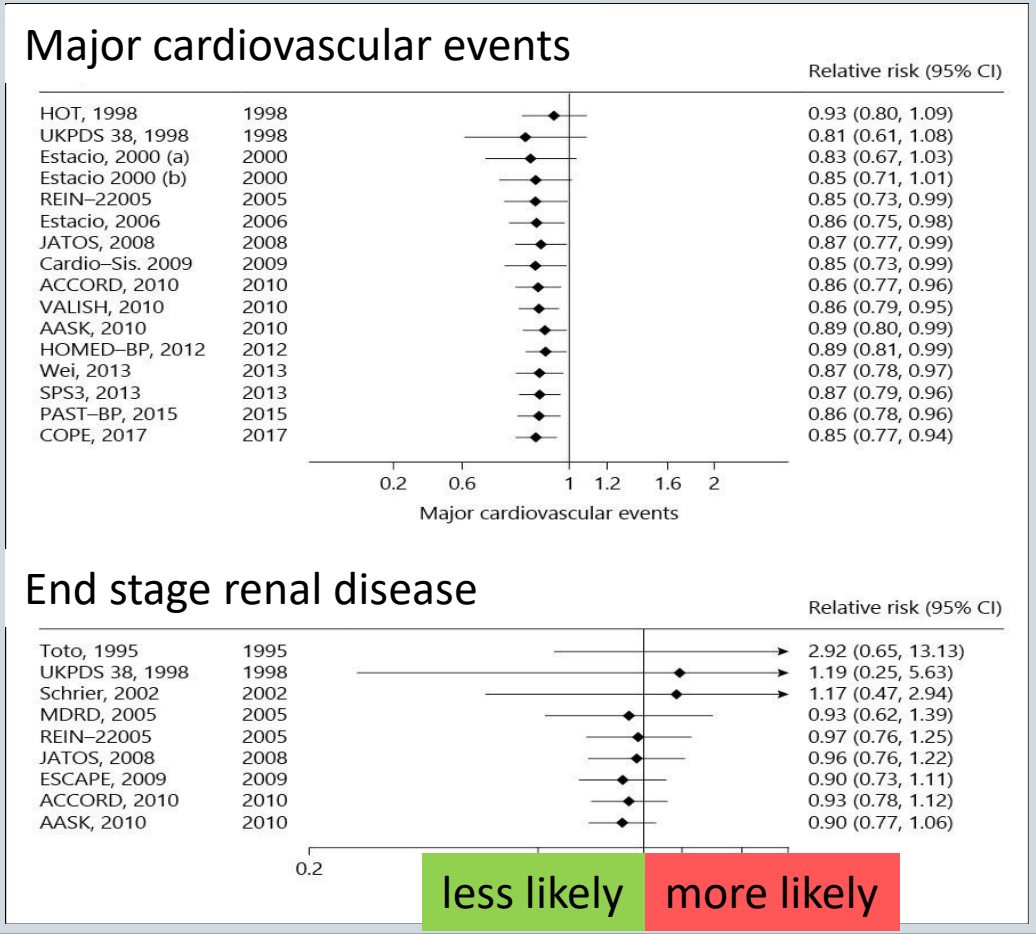
Ray et al. Lancet 2009;373(9677):1765-72

Intensive BP control in Type 2 DM

Meta-analysis of RCTs (56,687 individuals) comparing intensive vs. standard BP control

Intensive BP control significantly reduced:

- major cardiovascular events
  - RR: 0.85; 0.77–0.94; $p = 0.001$
- myocardial infarction
  - RR: 0.87; 95% CI: 0.76–1.00; $p = 0.044$
- stroke
  - RR: 0.77; 95% CI: 0.66–0.89; $p < 0.001$

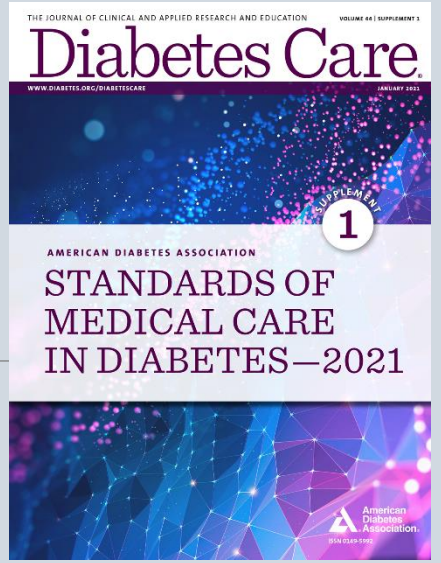


AHA/ACC HTN guidelines: BP Goals

Clinical Condition	BP Goal
Clinical CVD or 10-year ASCVD risk ≥10%	<130/80
No clinical CVD and 10-year ASCVD risk <10%	<130/80
Older persons (≥65; noninstitutionalized, ambulatory)	<130 (SBP)
Diabetes mellitus	<130/80
Chronic kidney disease	<130/80
Chronic kidney disease after renal transplantation	<130/80
Heart failure	<130/80
Stable ischemic heart disease	<130/80
Secondary stroke prevention	<130/80
Secondary stroke prevention (lacunar)	<130/80
Peripheral arterial disease	<130/80

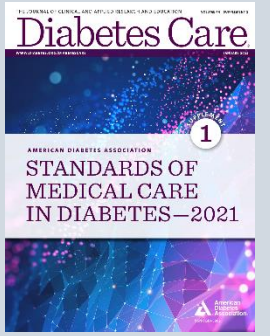
J Am Coll Cardiol. 2017 Nov

2021 ADA Standards of Care



- **A** Clear evidence from well-conducted RCTs
- **B** Supportive evidence from well-conducted cohort studies
- **C** Supportive evidence from poorly controlled or uncontrolled studies
- **E** Expert consensus or clinical experience

2021 ADA Recommendations: Blood Pressure



- For individuals with diabetes and hypertension at lower risk…blood pressure target of <140/90 mmHg. **A**

- For individuals with diabetes and hypertension at higher cardiovascular risk…blood pressure target of <130/80 mmHg **C**

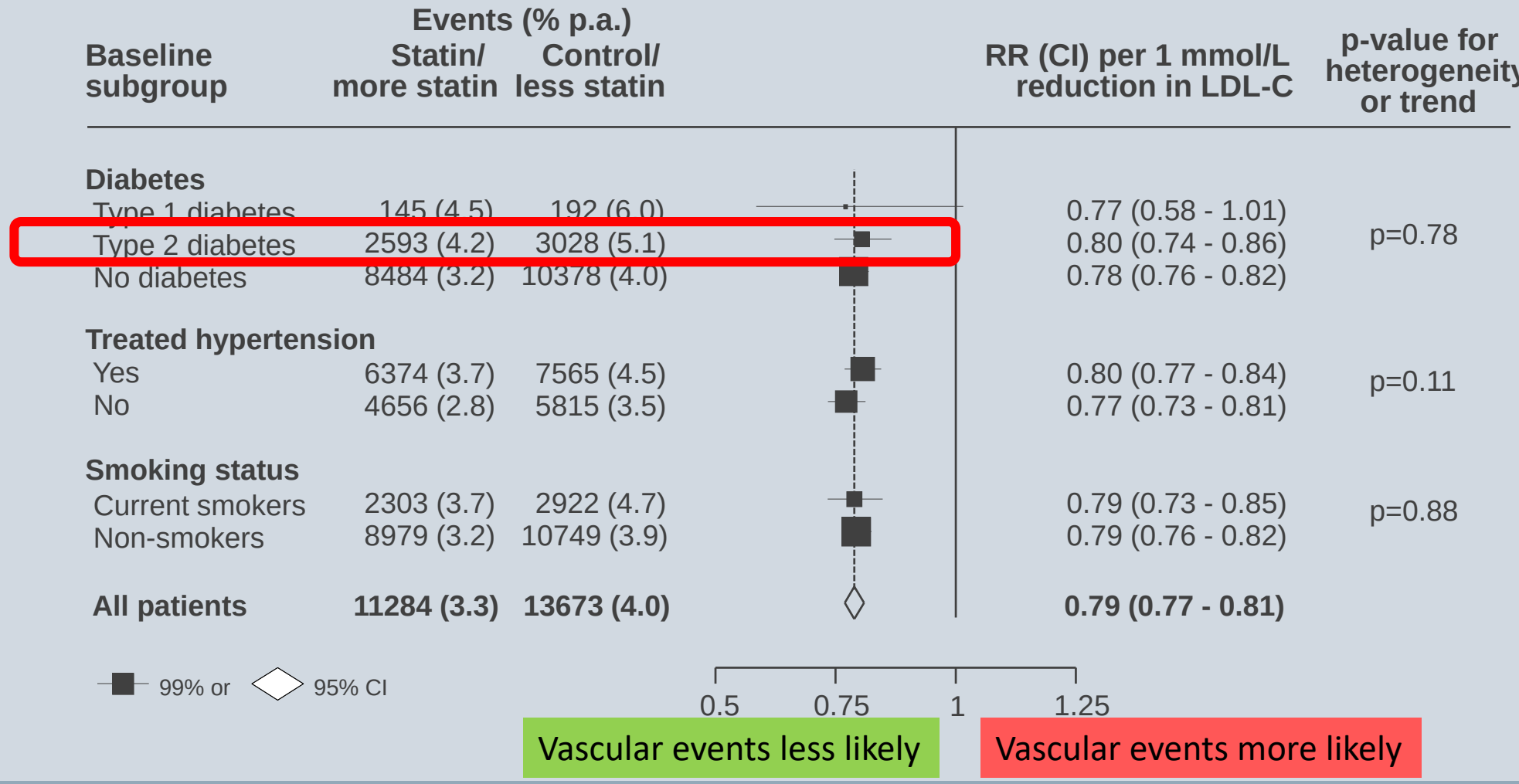
Higher risk = 10-year ASCVD risk >15%),

REDUCING RISK IN PATIENTS WITH T2DM

Blood Pressure Control

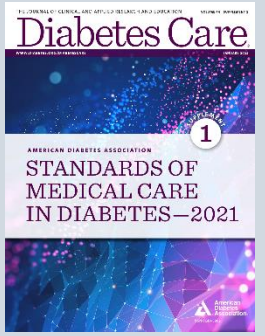
< 130/80 mm Hg

Statin Effects on Major Vascular Events



CTT. Lancet 2008 371: 117-125

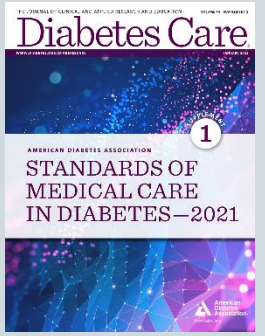
2021 ADA Recommendations: Lipids



- For patients…with diabetes and ASCVD or 10-year ASCVD risk >20%, **high-intensity statin therapy** A

- **if LDL cholesterol is ≥70** mg/dL…consider adding ezetimibe or PCSK9 inhibitor. A

2021 ADA Recommendations: Lipids



- In patients with diabetes who have **multiple ASCVD risk factors**, especially those ages **50-70** it is reasonable to **consider high-intensity statin** therapy. **B**

- For patients **20-39 years** with additional **ASCVD risk factors**…it is reasonable to consider **statin therapy** (no mention of intensity) **C**

- For patients 40-75 years ***without*** additional ASCVD risk factors…it is reasonable to consider **moderate intensity statin therapy** **A**

American Diabetes Association Standards of Medical Care in Diabetes - 2021. Diabetes Care 2021;44(Suppl. 1):S1-S2

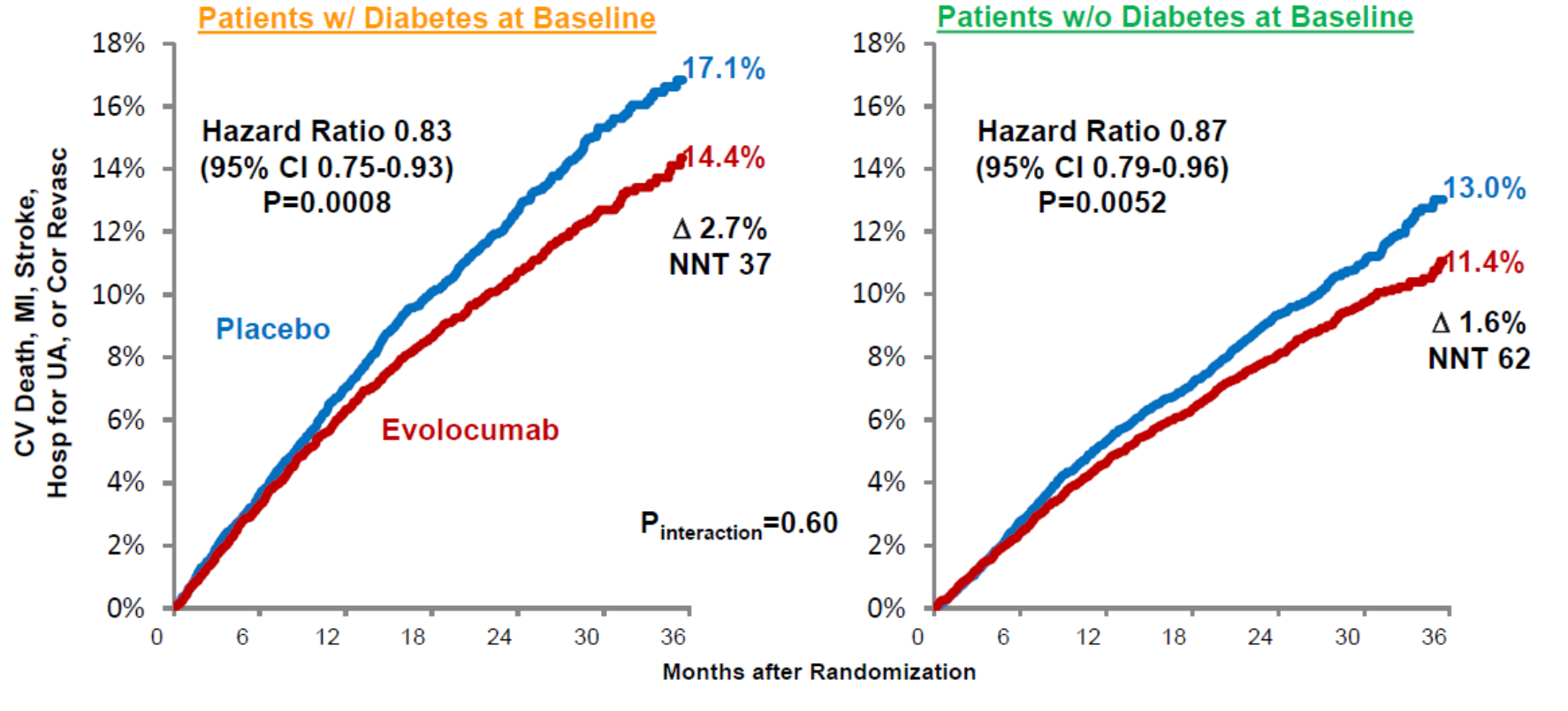
IMPROVE-IT (Ezetimibe) Major Pre-specified Subgroups

In many lipid trials, the diabetes subgroup has greater benefit than the overall trial population

Cannon CP et al. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med June 3, 2015

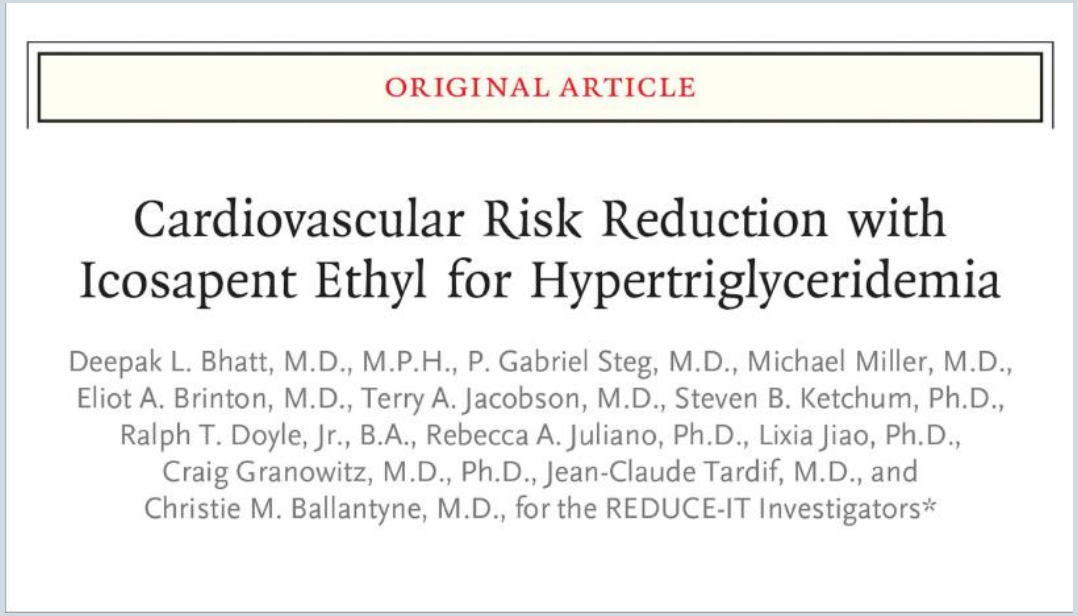
Fourier Trial: Diabetes Subgroup

Post MI patients on statin therapy randomized to receive addition of PCSK9i or placebo



Reduce – It Trial

8,179 patients with elevated triglycerides, on maximum tolerated statin therapy were randomized to EPA only fish oil 4 g daily or mineral oil placebo.



ORIGINAL ARTICLE

Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

Deepak L. Bhatt, M.D., M.P.H., P. Gabriel Steg, M.D., Michael Miller, M.D., Eliot A. Brinton, M.D., Terry A. Jacobson, M.D., Steven B. Ketchum, Ph.D., Ralph T. Doyle, Jr., B.A., Rebecca A. Juliano, Ph.D., Lixia Jiao, Ph.D., Craig Granowitz, M.D., Ph.D., Jean-Claude Tardif, M.D., and Christie M. Ballantyne, M.D., for the REDUCE-IT Investigators*

Bhatt et. al. January 3, 2019 N Engl J Med 2019; 380:11-22

Reduce – It Baseline Characteristics

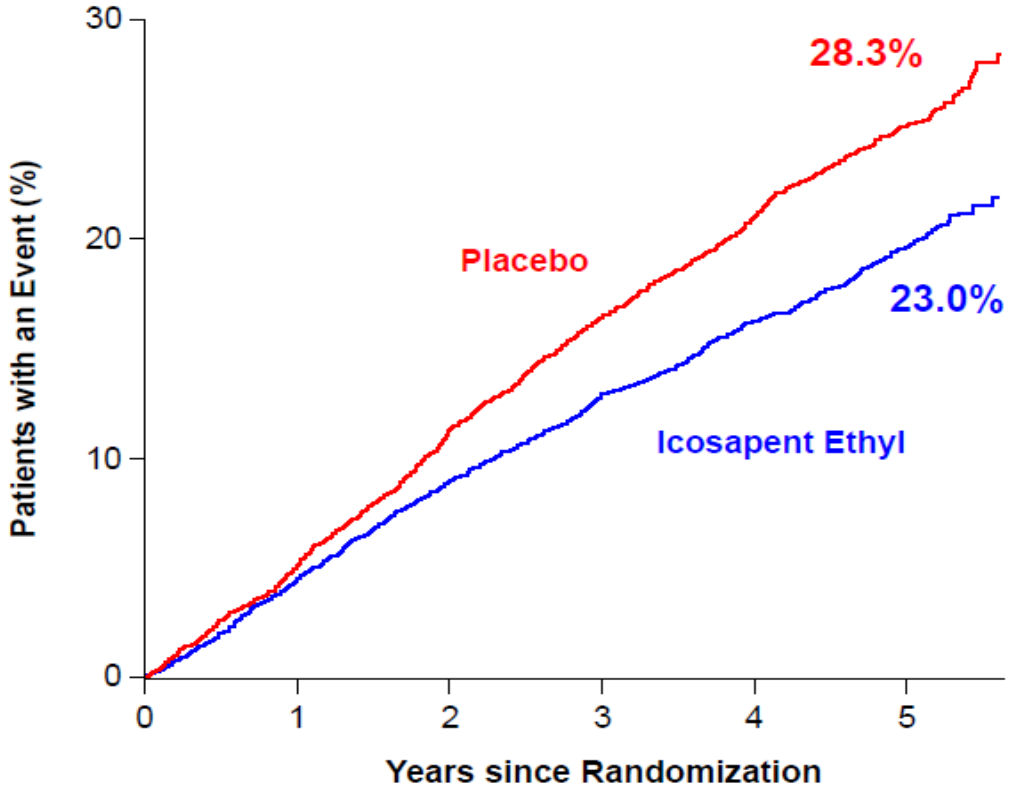
	Icosapent Ethyl (N=4089)	Placebo (N=4090)
Age (years), Median (Q1-Q3)	64.0 (57.0 - 69.0)	64.0 (57.0 - 69.0)
Female, n (%)	1162 (28.4%)	1195 (29.2%)
Non-White, n (%)	398 (9.7%)	401 (9.8%)
Secondary Prevention Cohort	2892 (70.7%)	2893 (70.7%)
Primary Prevention Cohort	1197 (29.3%)	1197 (29.3%)
Low-intensity statin	254 (6.2%)	267 (6.5%)
Moderate-intensity statin	2533 (61.9%)	2575 (63.0%)
High-intensity statin	1290 (31.5%)	1226 (30.0%)
Type 2 Diabetes, n (%)	2367 (57.9%)	2363 (57.8%)
Triglycerides (mg/dL), Median (Q1-Q3)	216.5 (176.5 - 272.0)	216.0 (175.5 - 274.0)
HDL-C (mg/dL), Median (Q1-Q3)	40.0 (34.5 - 46.0)	40.0 (35.0 - 46.0)
LDL-C (mg/dL), Median (Q1-Q3)	74.0 (61.5 - 88.0)	76.0 (63.0 - 89.0)
Triglycerides Category		
<150 mg/dL	412 (10.1%)	429 (10.5%)
150 to <200 mg/dL	1193 (29.2%)	1191 (29.1%)
≥200 mg/dL	2481 (60.7%)	2469 (60.4%)

Bhatt DL, Steg PG, Miller M, et al. *N Engl J Med.* 2018.

REDUCE-It Trial

Primary End Point:

CV Death, MI, Stroke, Coronary Revasc, Unstable Angina



Hazard Ratio, 0.75
(95% CI, 0.68–0.83)

REDUCE-It Controversy

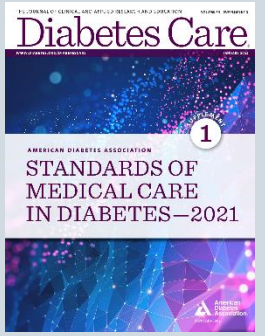
Vascepa decreased triglycerides 22% (falling to 170 mg/dL)

BUT...Patients who received placebo (mineral oil) had a 10% increase in LDL-c, 6% more than in the Vascepa group

ALSO levels of c-reactive protein increased from 2.1 mg/L to 2.8 mg/L in the placebo arm – a 30% increase.

IN ADDITION, median APO-B levels increased in the placebo arm from 83 mg/dL to as high as 89 mg/dL.

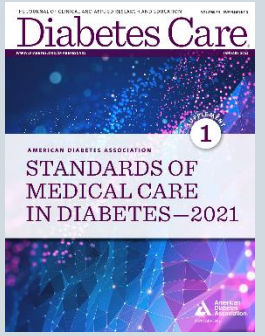
2021 ADA Recommendations: Lipids



In patients with ASCVD or other cardiac risk factors on a statin with controlled LDL-C, but elevated triglycerides (135-499 mg/dL), the addition of icosapent ethyl can be considered to reduce cardiovascular risk·

A

2021 ADA Recommendations: Lipids



- Combination therapy with **statin + fibrate** … **generally not recommended**. A

- Combination therapy with **statin + niacin** … **generally not recommended**. A

DON’T DO IT!!!!!!!!!!

American Diabetes Association Standards of Medical Care in Diabetes - 2021. Diabetes Care 2021;44(Suppl. 1):S1-S2

REDUCING RISK IN PATIENTS WITH T2DM

Statin therapy

+/- Ezetimibe, PCSK9i, EPA

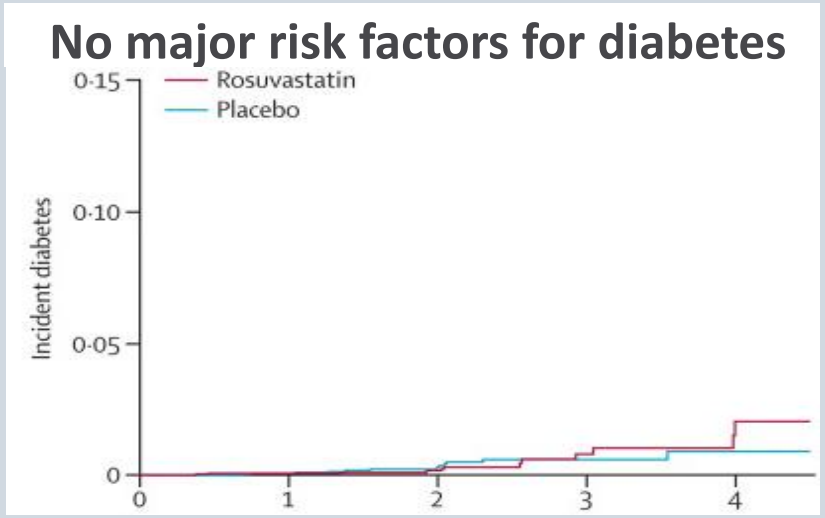
Association between statins and development of diabetes

Statin	Odds ratio (95% CI)
Overall (n=91 140)	1.09 (1.02–1.17)
Atorvastatin only (n=7773)	1.14 (0.89–1.46)
Simvastatin only (n=18 815)	1.11 (0.97–1.26)
Rosuvastatin only (n=24 714)	1.18 (1.04–1.33)
Pravastatin (n=33 627)	1.03 (0.90–1.19)
Lovastatin (n=6211)	0.98 (0.70–1.38)

Sattar N et al. *Lancet* 2010;375:735-42.

Statins, Diabetes, CV Events

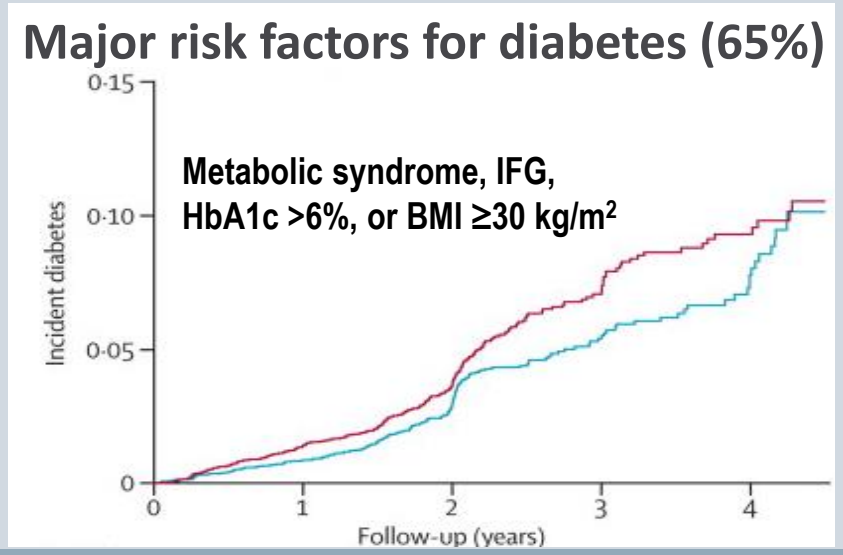
No major risk factors for diabetes



HR 0.99
(0.45-2.21)
p=0.99

86 deaths or vascular events prevented
0 excess cases of diabetes

Major risk factors for diabetes (65%)



HR 1.28
(1.07-1.54)
p=0.01

134 deaths or vascular events prevented
54 excess cases of diabetes

They estimated that it accelerated dx by ~1 year

Ridker PM et al. *Lancet* 2012;380:565

FDA reports on the Risk of Diabetes with statins

February 2012

A small increased risk of elevated blood sugar levels and the development of Type 2 diabetes have been reported with the use of statins.

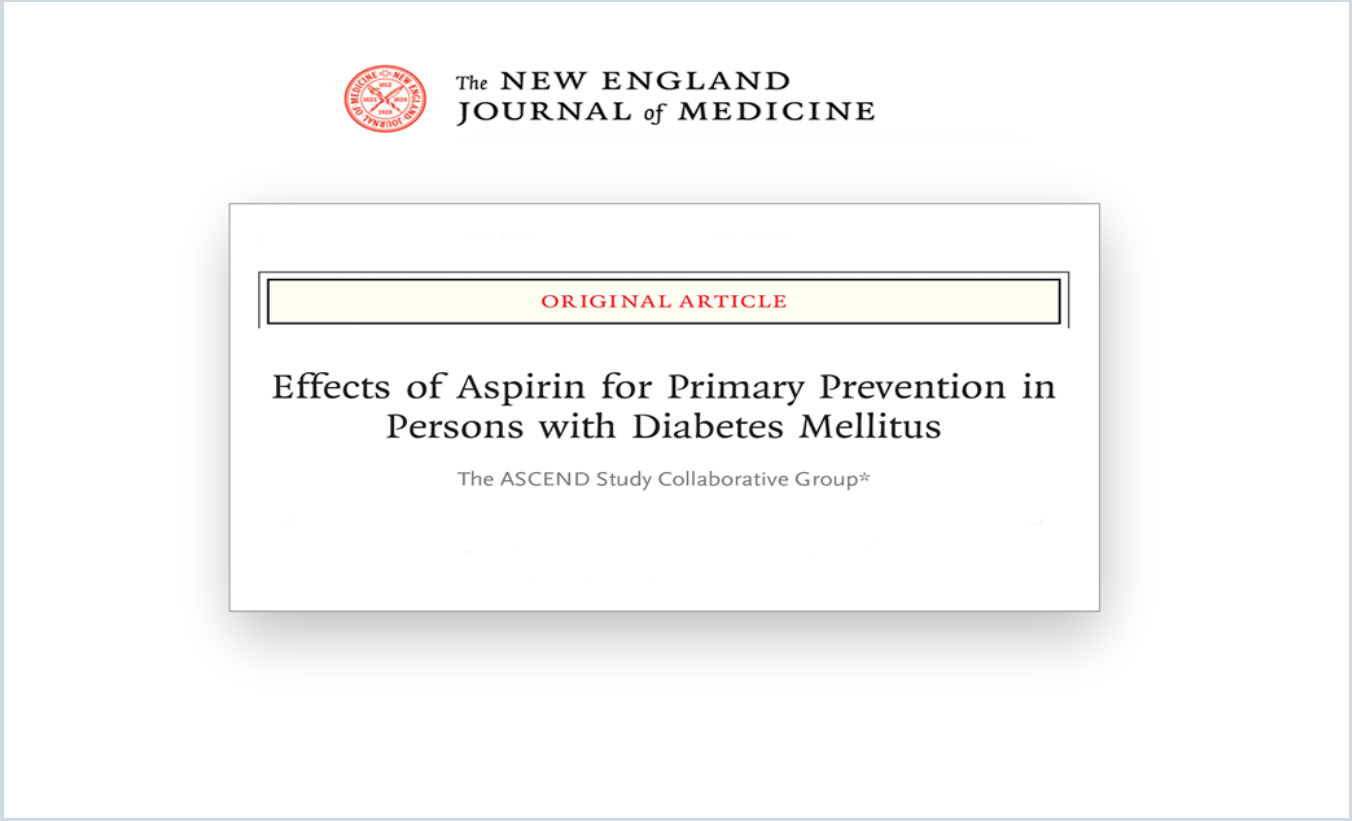
"Clearly we think that the heart benefit of statins outweighs this small increased risk"

But blood-sugar levels may need to be assessed after instituting statin therapy.

Aspirin

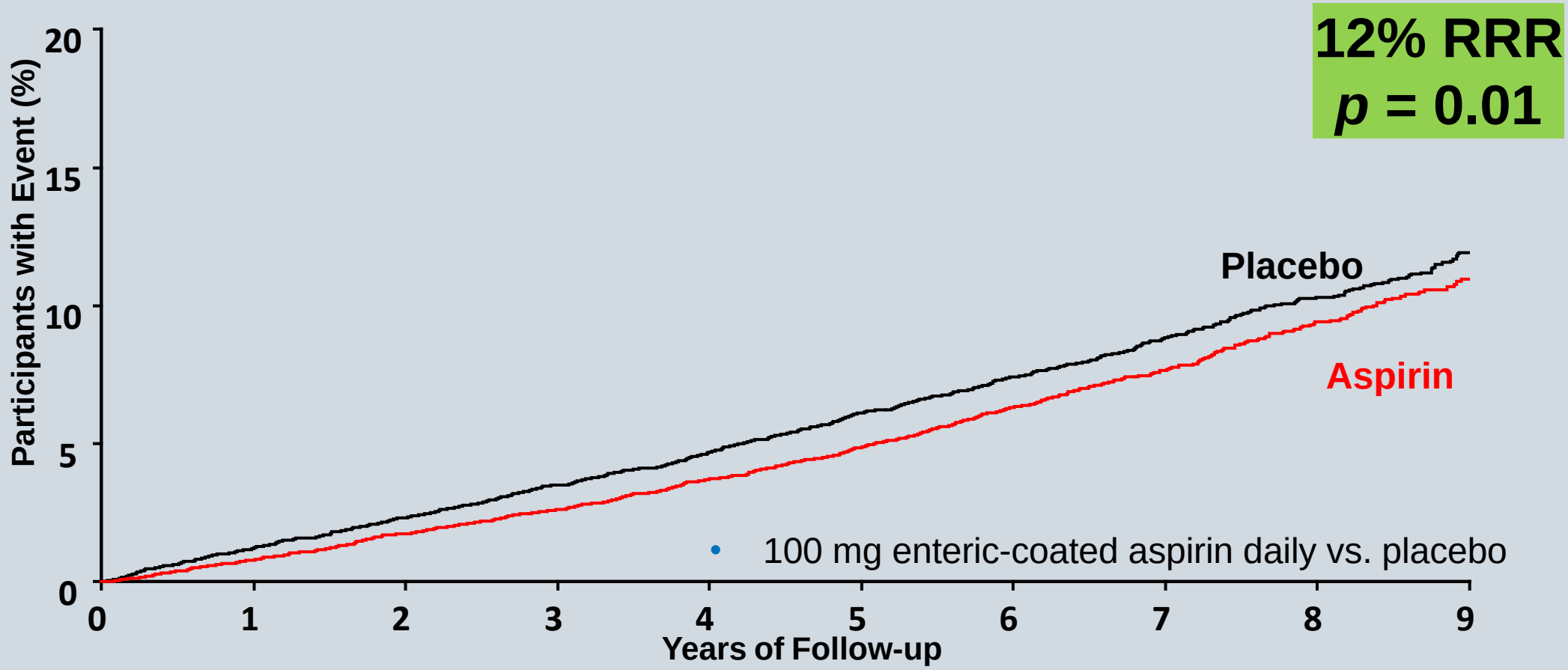
Everyone agrees … every secondary prevention patient (with or without diabetes) should receive aspirin.

But what about patients with diabetes and NO CVD?



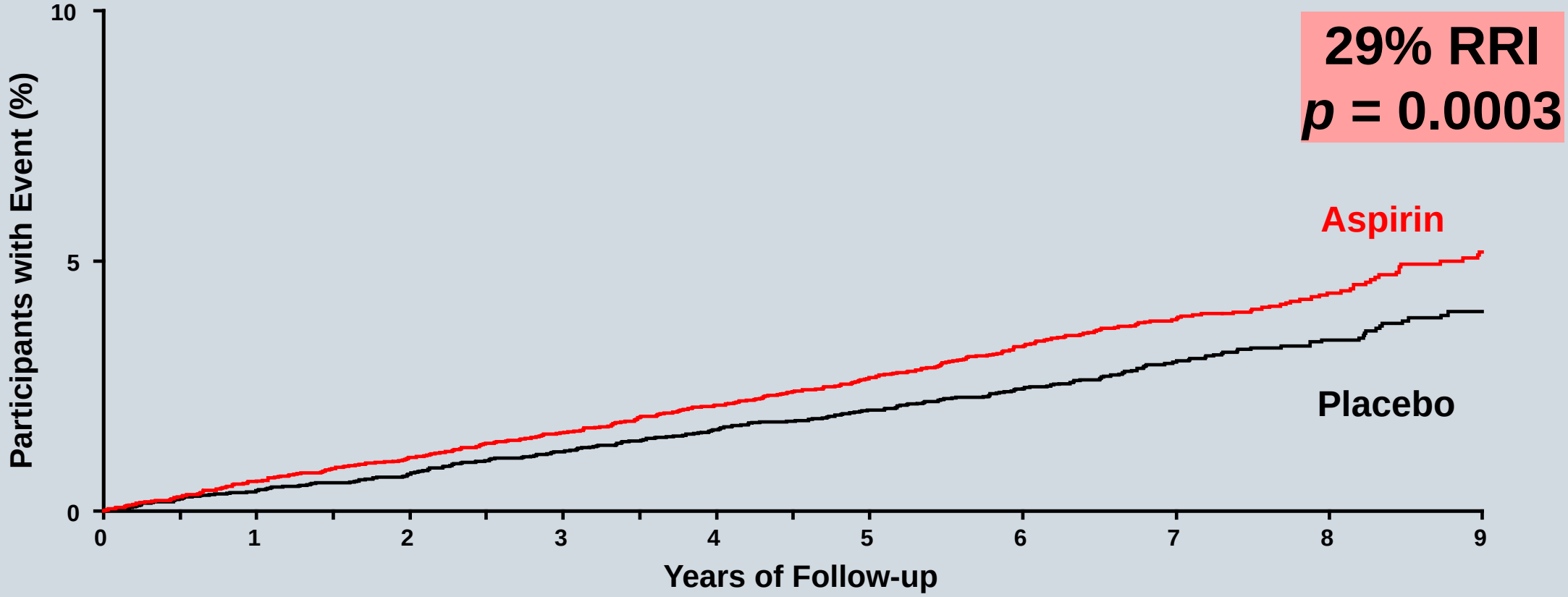
ASCEND: **15,480 patients** Age ≥ 40 years, + DIABETES and no baseline cardiovascular disease; **Randomized to Aspirin 100 mg daily vs. placebo**

ASCEND: Primary Outcome CVD death, MI, UA, Stroke or TIA

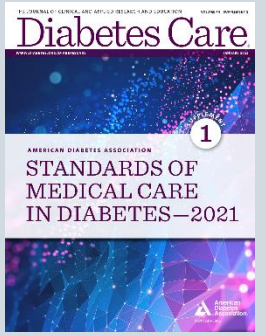


ASCEND Study Collaborative Group. Am Heart J 2018;198:135-144

ASCEND: major bleeding



2021 ADA Recommendations: Aspirin



Recommendations

- Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes and a history of ASCVD. **A**

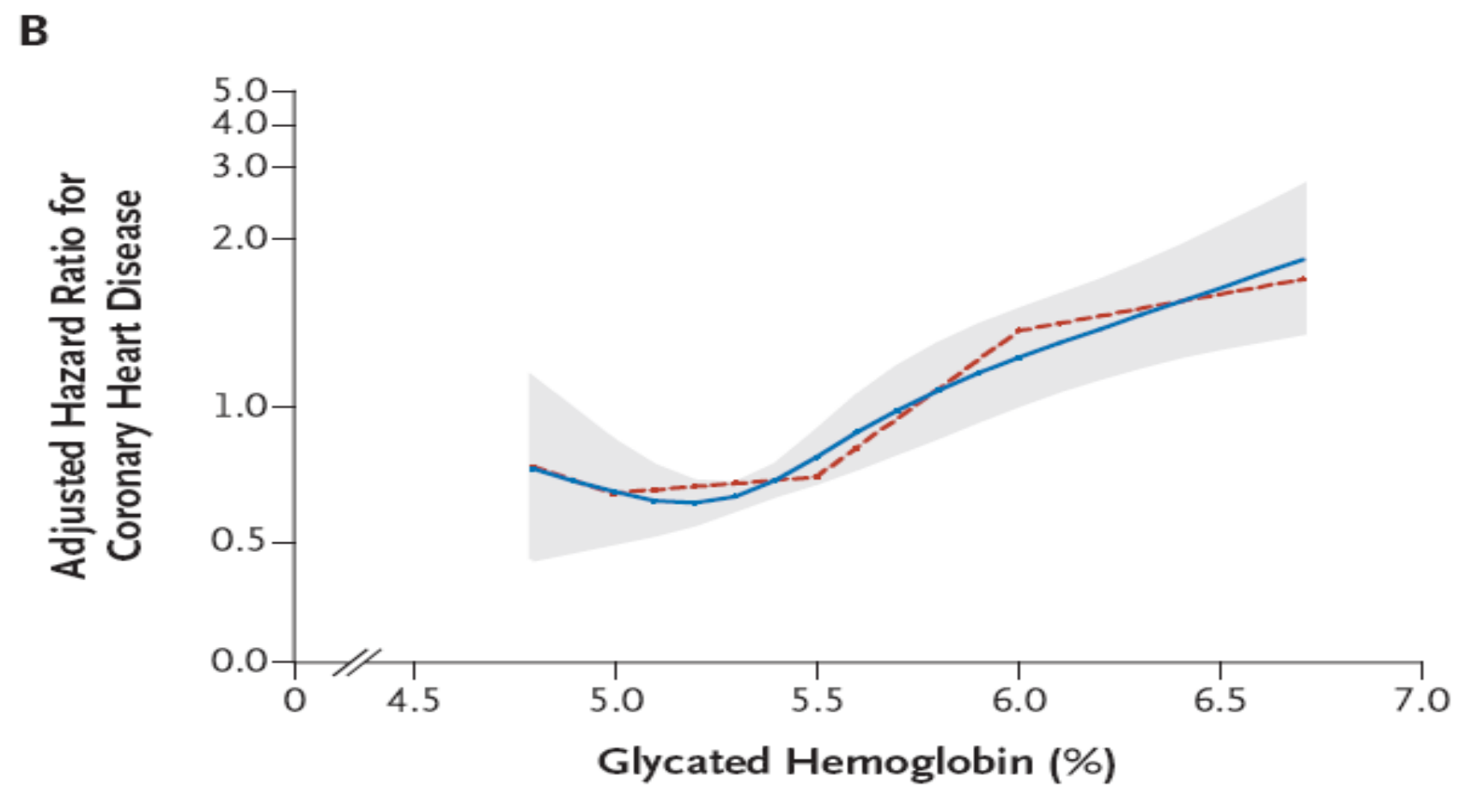
- Aspirin therapy (75–162 mg/day) may be considered as a primary prevention strategy in those with diabetes who are at increased cardiovascular risk, after a comoprehensive discussion with the patient on the benefits versus increased risk of bleeding. **A**

REDUCING RISK IN PATIENTS WITH T2DM

Low dose aspirin in secondary prevention

Use only after a comprehensive risk discussion

Association between HbA1c and CVD

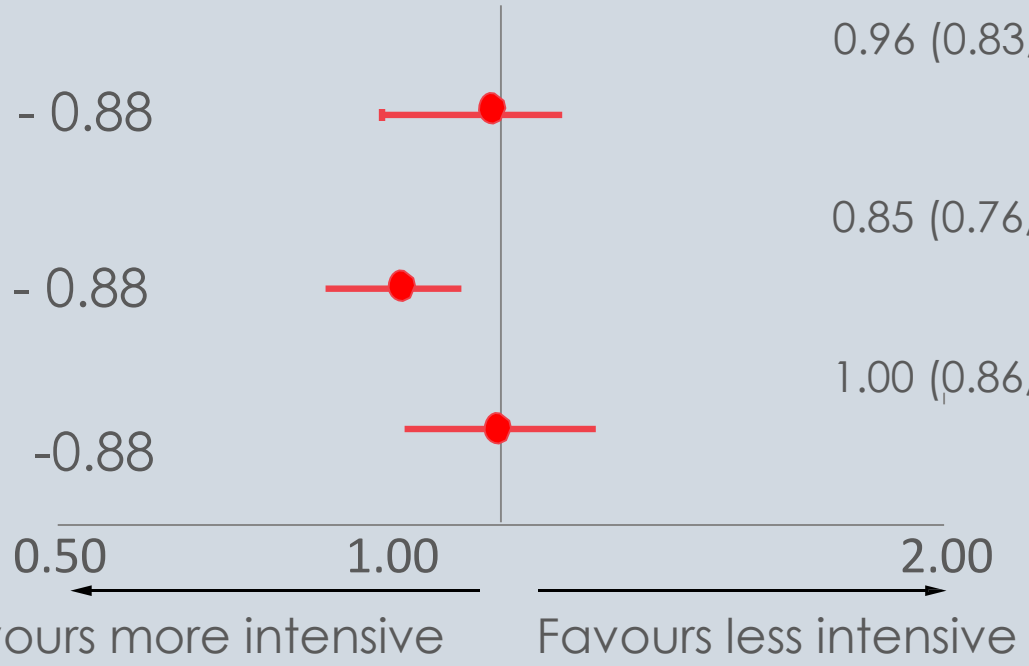


Sabin et al. NEJM March 2010

Intensive glucose control and CV events

27,049 participants, 2370 major vascular events

	More intensive	Less intensive	Difference in HbA1c (%)	HR (95% CI)
Stroke	378	370	- 0.88	0.96 (0.83, 1.10)
Myocardial infarction	730	745	- 0.88	0.85 (0.76, 0.94)
Heart failure hospitalization or death	459	446	-0.88	1.00 (0.86, 1.16)



Turnbull FM et al. Diabetologia 2009;52:2288–2298

ACCORD Glycemia Trial: 10,251 patients with T2DM randomized to HbA1c goal of <6 or 7-7.9

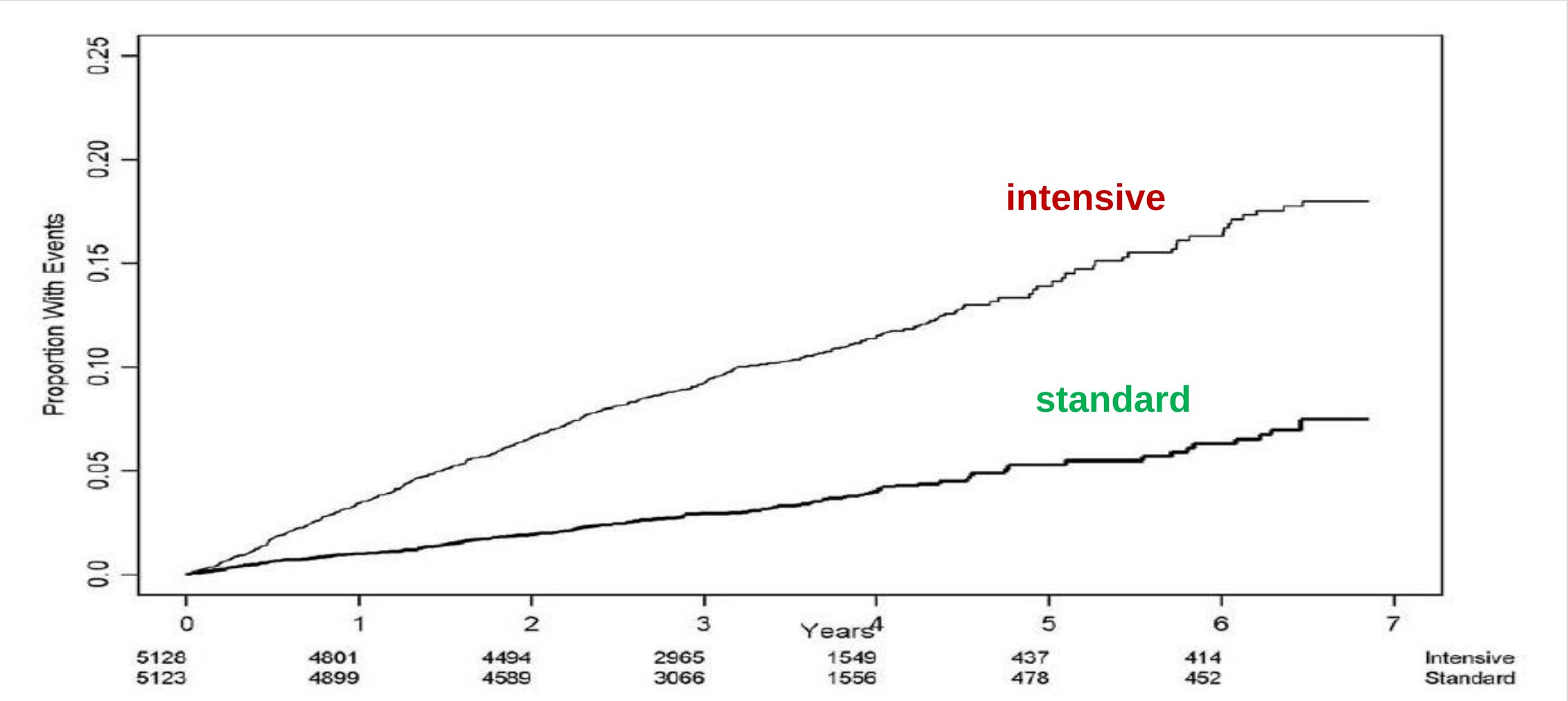
		andard N (%)	HR (95% CI)	P
Primary		1 (7.23)	0.90 (0.78-1.04)	0.16
Secondary				
Mortality	257 (5.01)	203 (3.96)	1.22 (1.01-1.46)	0.04
Nonfatal MI	186 (3.63)	235 (4.59)	0.76 (0.62-0.92)	0.004
Nonfatal Stroke	67 (1.31)	61 (1.19)	1.06 (0.75-1.50)	0.74
CVD Death	135 (2.6			
CHF	152 (2.96)			

22% Increase in mortality with an intensive glucose control strategy

24% decrease in nonfatal myocardial infarctions with an intensive glucose control strategy

ACCORD Study Group, NEJM 2008 358:2545-2549.

Severe Hypoglycemia in ACCORD glycemia Trial



ACCORD Study Group, NEJM 2008 358:2545-2549.

Learning Objectives

- Identify the link between diabetes and cardiovascular disease (CVD).
- List two (2) therapies proven to prevent CVD in patients with diabetes.
- **Specify two (2) new diabetes drugs that fit in with other therapies for cardiovascular risk reduction.**
- Specify the role of SGLT2 inhibitors and GLP1-RAs in reducing CV events in diabetics.
- Discuss the role of diabetes therapies in heart failure management

Risk of All-Cause and CV Mortality With Sulfonylureas vs other diabetes medications

Meta-analysis of 82 RCTs and 26 observational studies among patients with T2DM receiving SUs vs placebo or other antihyperglycemic drugs

	All-Cause Mortality	Cardiovascular Mortality
SU vs. Placebo	1.07 (0.90-1.28)	1.25 (0.98-1.62)
SU vs. Biguanide (Metformin)	1.37 (1.03-1.84)	1.38 (0.90-2.16)
SU vs. Thiazolidinedione	1.54 (1.14-2.10)	3.05 (1.79-5.54)
SU vs. DPP-4 inhibitor	2.03 (1.22-3.58)	4.42 (1.92-13.0)
SU vs. GLP-1 receptor agonist	1.85 (0.80-5.19)	45.4 (2.07-362.8)
SU vs. SGLT2 inhibitor	NA	42.6 (1.71-359.1)
SU vs. Insulin	1.21 (1.01-1.45)	1.30 (1.02-1.66)

Bain S, et al. Diabetes Obes Metab. 2017;19:329-335.

Diabetes medications through the years

INSULIN

METFORMIN

ALPHA GLUCOSIDASE INHIBITORS

THIAZOLIDINEDIONES (TZDs)

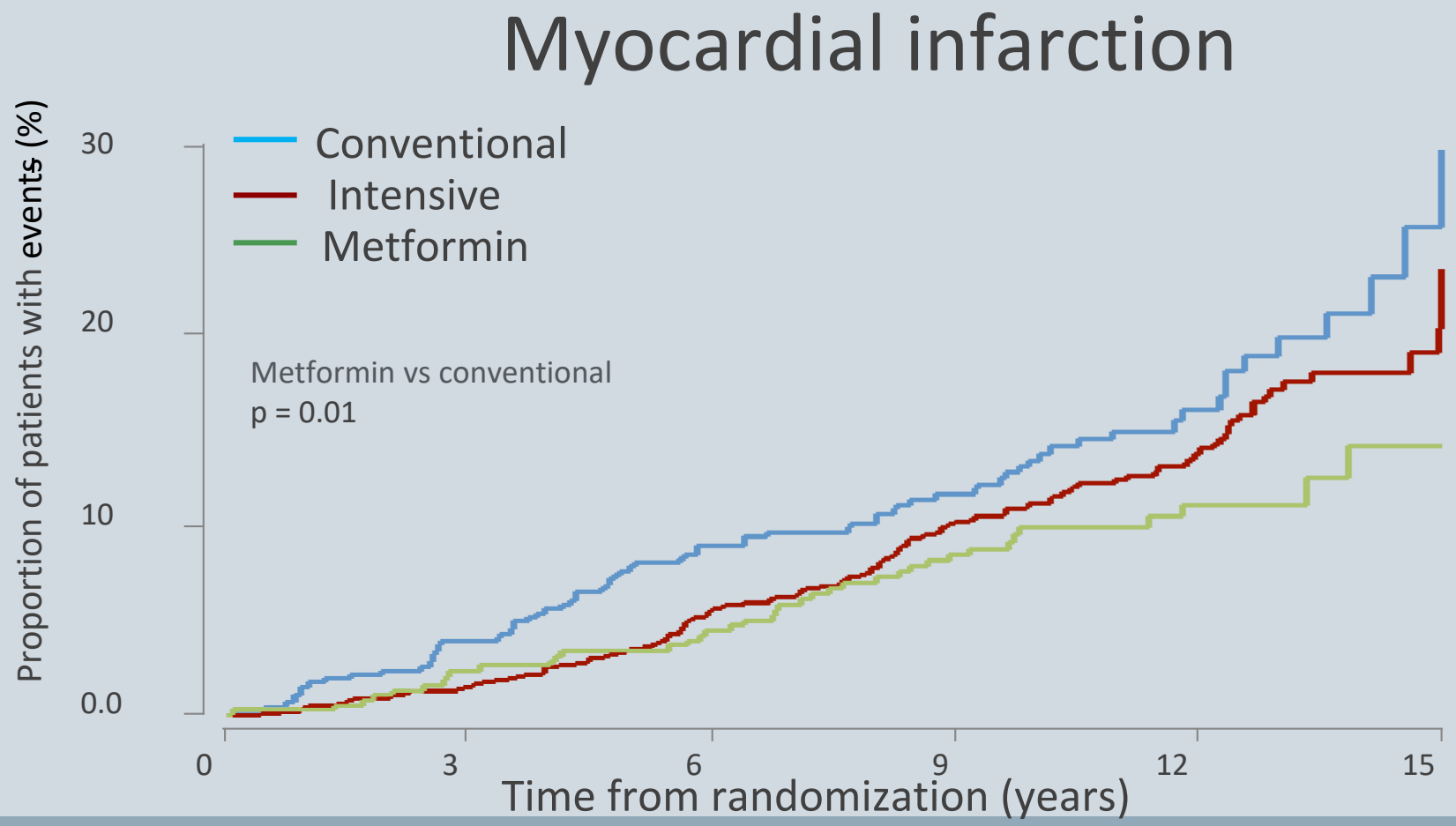
MEGLITINIDES

1921 | 1930’s | 1950’s | 1980’S | 1990’S

INSULIN

SULPHONYLUREAS

UKPDS: Newly-diagnosed obese, type 2 diabetes patients randomized to metformin, intensive glucose control (with SU or insulin), or conventional glucose control (SU or insulin)



Diabetes medications through the years

INSULIN

METFORMIN
ALPHA GLUCOSIDASE INHIBITORS
THIAZOLIDINEDIONES
MEGLITINIDES

DPP4 inhibitors

SGLT2 inhibitors

1921 | 1930's | 1950's | 1980'S | 1990'S | 2000 | 2001-10 | 2010-15

GLP1 receptor agonists

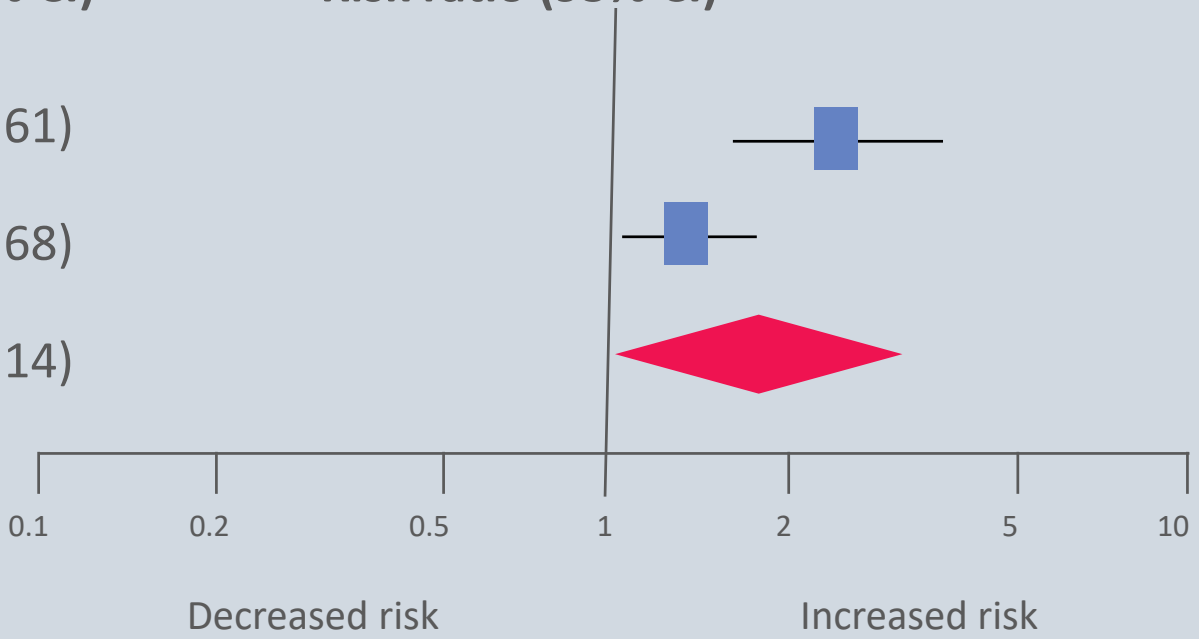
INSULIN

SULPHONYLUREAS

Increased risk of congestive heart failure with both pioglitazone and rosiglitazone

- Meta-analysis of 20,191 patients with pre-diabetes treated with T2D as compared to other glucose lowering agents.

	Weight	Risk ratio (95% CI)
Rosiglitazone trials	46.2%	2.41 (1.61–3.61)
Pioglitazone trials	53.8%	1.32 (1.04–1.68)
Total	100.0%	1.74 (0.97–3.14)

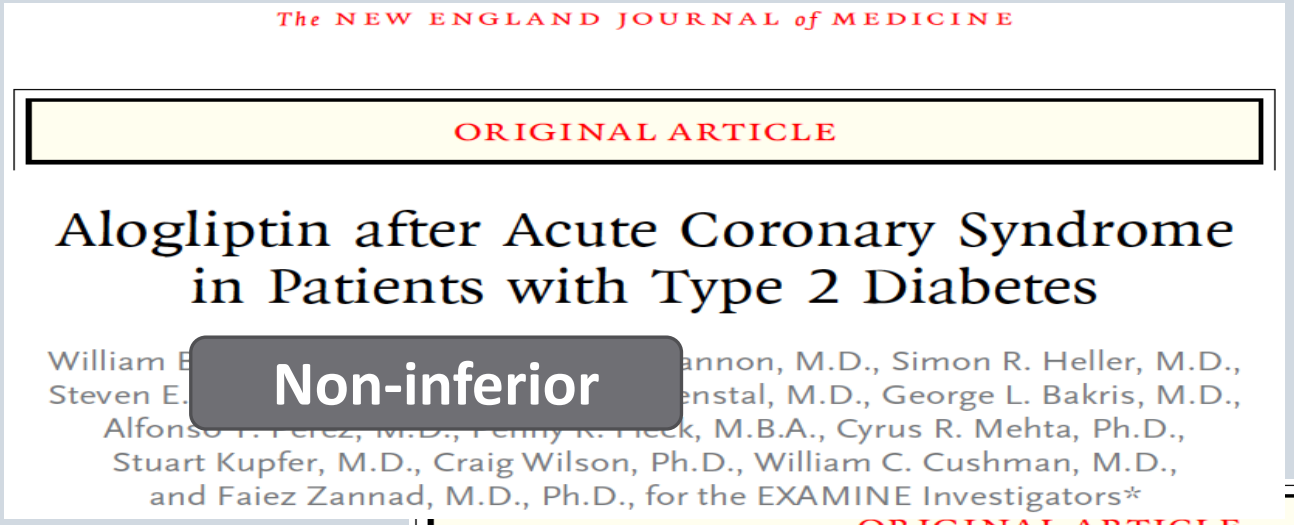


Lago et al. Lancet 2007;370:1129–36.

The FDA approach

- ✓ FDA would continue to approve anti diabetes medications on basis of HbA1c lowering
- ✓ But now FDA mandated post-approval large randomized outcomes trials to verify cardiovascular safety of newly approved anti diabetes medications. They need to prove “noninferiority.” (FDA mandated upper boundary 1.3)

The DPP-4 inhibitor Studies



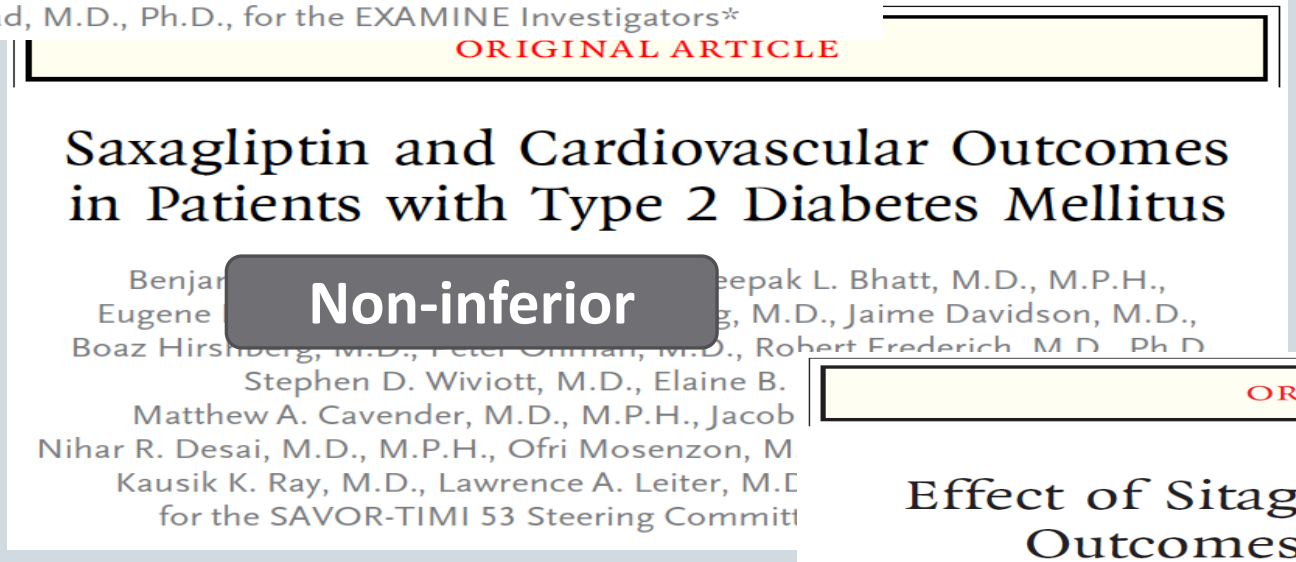
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Alogliptin after Acute Coronary Syndrome in Patients with Type 2 Diabetes

William E… annon, M.D., Simon R. Heller, M.D., Steven E… enstal, M.D., George L. Bakris, M.D., Alfonso … k, M.B.A., Cyrus R. Mehta, Ph.D., Stuart Kupfer, M.D., Craig Wilson, Ph.D., William C. Cushman, M.D., and Faiez Zannad, M.D., Ph.D., for the EXAMINE Investigators*

Non-inferior

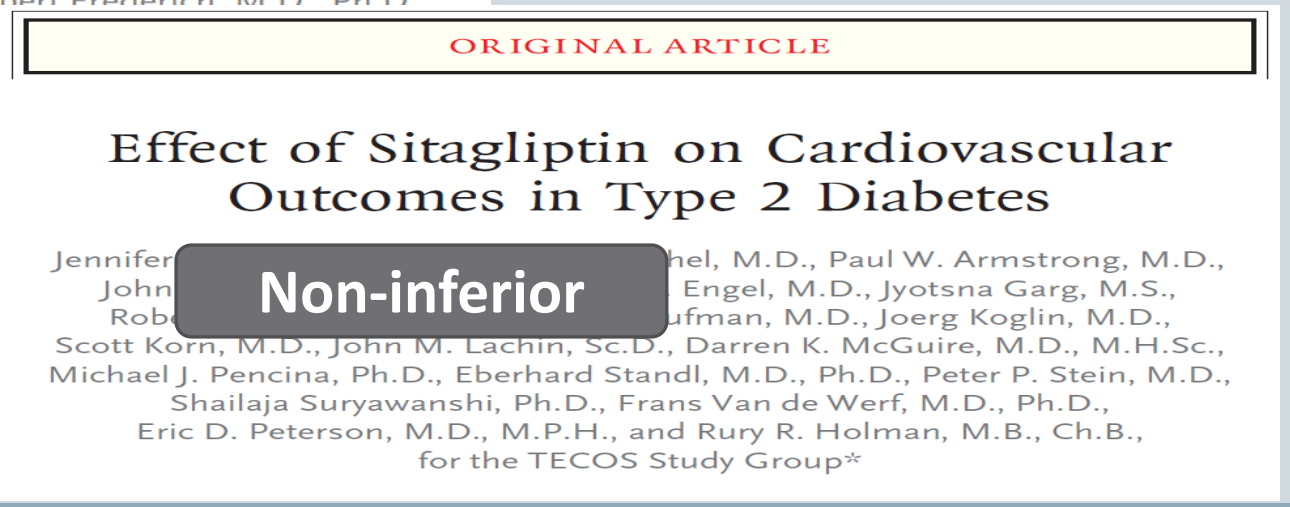


ORIGINAL ARTICLE

Saxagliptin and Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus

Benjar… epak L. Bhatt, M.D., M.P.H., Eugene … g, M.D., Jaime Davidson, M.D., Boaz Hirsh… Robert Frederich, M.D., Ph.D., Stephen D. Wiviott, M.D., Elaine B. … Matthew A. Cavender, M.D., M.P.H., Jacob … Nihar R. Desai, M.D., M.P.H., Ofri Mosenzon, M… Kausik K. Ray, M.D., Lawrence A. Leiter, M.D… for the SAVOR-TIMI 53 Steering Committ…

Non-inferior



ORIGINAL ARTICLE

Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes

Jennifer… hel, M.D., Paul W. Armstrong, M.D., John… Engel, M.D., Jyotsna Garg, M.S., Robe… ufman, M.D., Joerg Koglin, M.D., Scott Korn, M.D., John M. Lachin, Sc.D., Darren K. McGuire, M.D., M.H.Sc., Michael J. Pencina, Ph.D., Eberhard Standl, M.D., Ph.D., Peter P. Stein, M.D., Shailaja Suryawanshi, Ph.D., Frans Van de Werf, M.D., Ph.D., Eric D. Peterson, M.D., M.P.H., and Rury R. Holman, M.B., Ch.B., for the TECOS Study Group*

Non-inferior

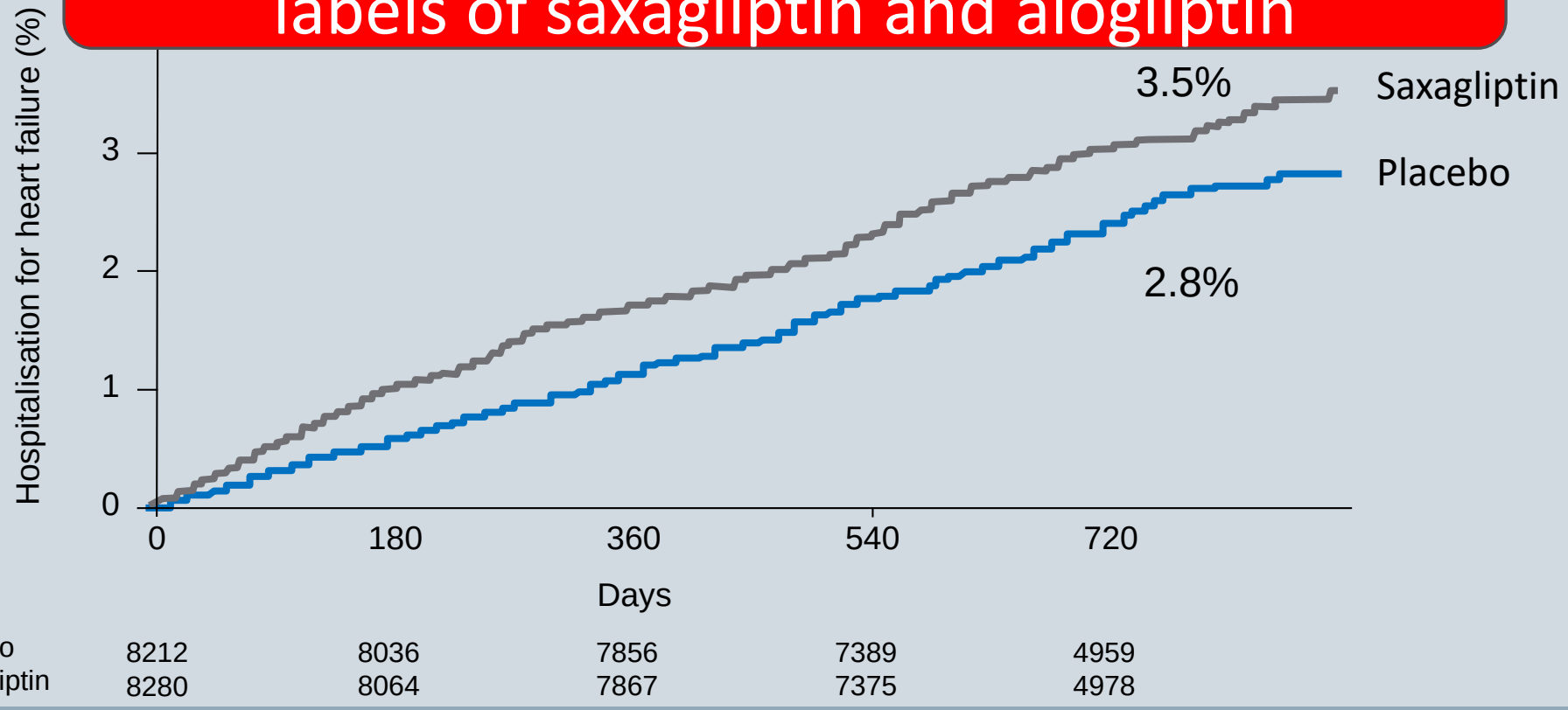
White WB et. al. N Engl J Med 2013; 369:1327-1335

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

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

Increased risk of heart failure hospitalization with saxagliptin

FDA adds warnings about heart failure risk to labels of saxagliptin and alogliptin



Scirica et al. Circulation 2014;130:1579–88.

The GLP1-RA Studies

ORIGINAL ARTICLE

Lixisenatide in Patients with Type 2 Diabetes ...te Coronary Syndrome

Non-inferior

Marc A. Pfeffer, M.D., Ph.D., Brian Claggett, Ph.D., Rafael Diaz, M.D.,
Kenneth Dickstein, M...
Francesca C. ...
Eldrin F. ...
John J.V. Mc...
Matthew C. Riddle, M...

ORIGINAL ARTICLE

Liraglutide and Cardiovascular Outcomes ...e 2 Diabetes

SUPERIOR

Steven ... aniels, M.D., Kirstine Brown-Frandsen, M.D.,
Peter Kristensen, M...
Michael A. Nauck, M.D.
Neil R. Poulter, ...
William M. Steinberg, M.D...
Richard M. Bergenstal, M.D...
Steering Committee ...

ORIGINAL ARTICLE

Semaglutide and Cardiovascular Outcomes ...ts with Type 2 Diabetes

SUPERIOR

Steven P. Marso, M.D., Stephen C. Bain, M.D., Agostino Consoli, M.D.,
Freddy G. Eliaschewitz, M.D., Esteban Jódar, M.D., Lawrence A. Leiter, M.D.,
Ildik...
Jochen S...
Oluf Hansen, ...
and Ti...

Albiglutide and cardiovascular outcomes in patients with type 2 ...ascular disease (Harmony Outcomes): a double-blind, randomised placebo-controlled trial

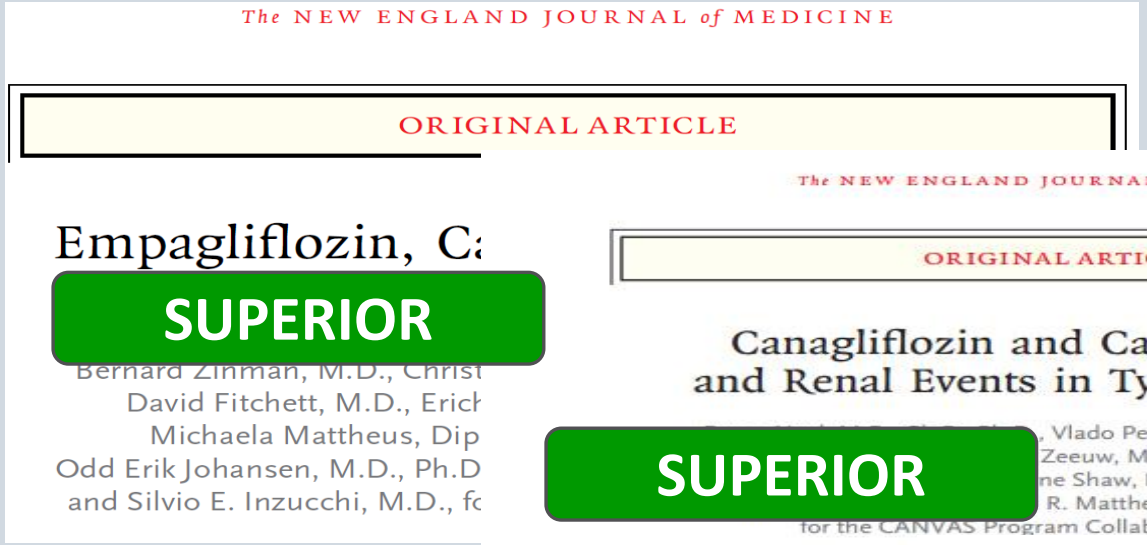
SUPERIOR

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

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

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

The SGLT-2i Studies

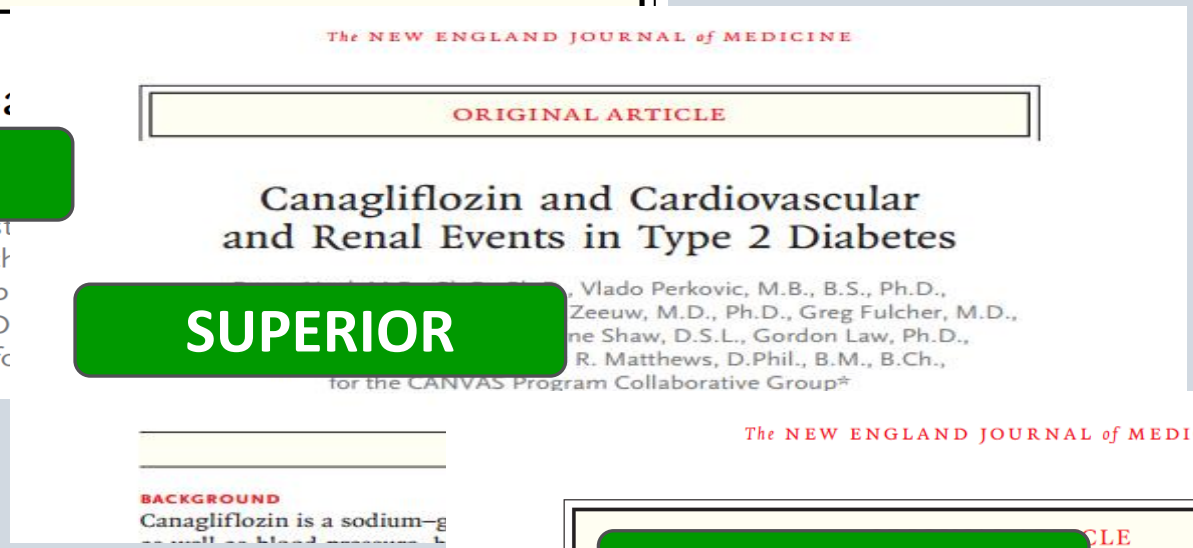

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Empagliflozin, C

SUPERIOR

Bernard Zinman, M.D., Christ
David Fitchett, M.D., Erick
Michaela Mattheus, Dip
Odd Erik Johansen, M.D., Ph.D
and Silvio E. Inzucchi, M.D., fc


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

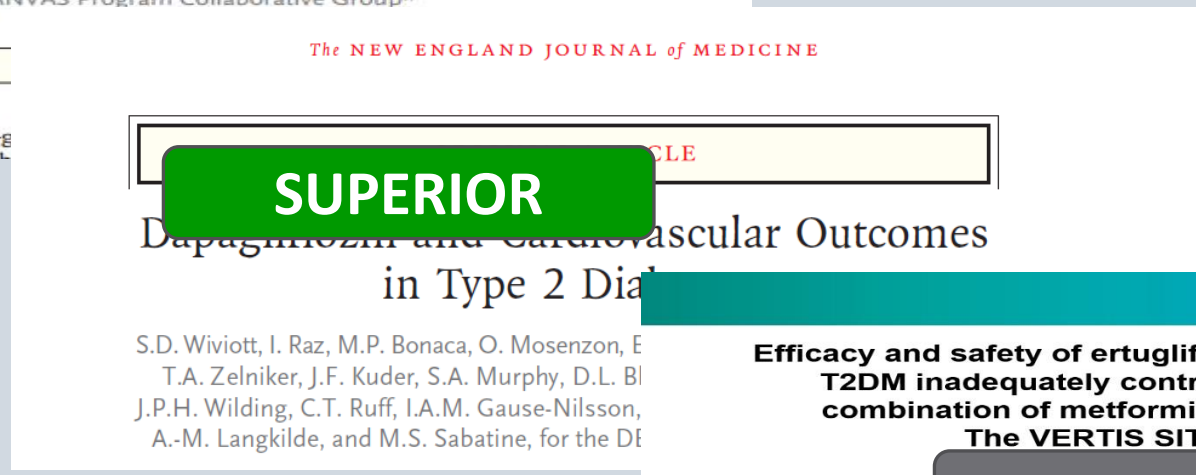
Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes

SUPERIOR

, Vlado Perkovic, M.B., B.S., Ph.D.,
Zeeuw, M.D., Ph.D., Greg Fulcher, M.D.,
ne Shaw, D.S.L., Gordon Law, Ph.D.,
R. Matthews, D.Phil., B.M., B.Ch.,
for the CANVAS Program Collaborative Group*

BACKGROUND

Canagliflozin is a sodium–g

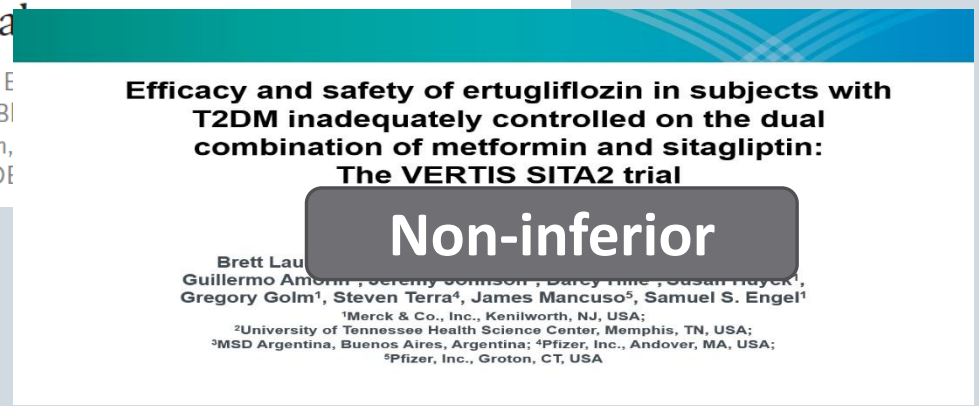

The NEW ENGLAND JOURNAL of MEDICINE

CLE

SUPERIOR

ascular Outcomes in Type 2 Dia

S.D. Wiviott, I. Raz, M.P. Bonaca, O. Mosenzon, E
T.A. Zelniker, J.F. Kuder, S.A. Murphy, D.L. Bl
J.P.H. Wilding, C.T. Ruff, I.A.M. Gause-Nilsson,
A.-M. Langkilde, and M.S. Sabatine, for the DE


Efficacy and safety of ertugliflozin in subjects with T2DM inadequately controlled on the dual combination of metformin and sitagliptin: The VERTIS SITA2 trial

Non-inferior

Brett Lau
Guillermo Amorin, Jeremy Johnson, Darcy Hille, Susan Hayek,
Gregory Golm[1], Steven Terra[4], James Mancuso[5], Samuel S. Engel[1]
[1]Merck & Co., Inc., Kenilworth, NJ, USA;
[2]University of Tennessee Health Science Center, Memphis, TN, USA;
[3]MSD Argentina, Buenos Aires, Argentina; [4]Pfizer, Inc., Andover, MA, USA;
[5]Pfizer, Inc., Groton, CT, USA

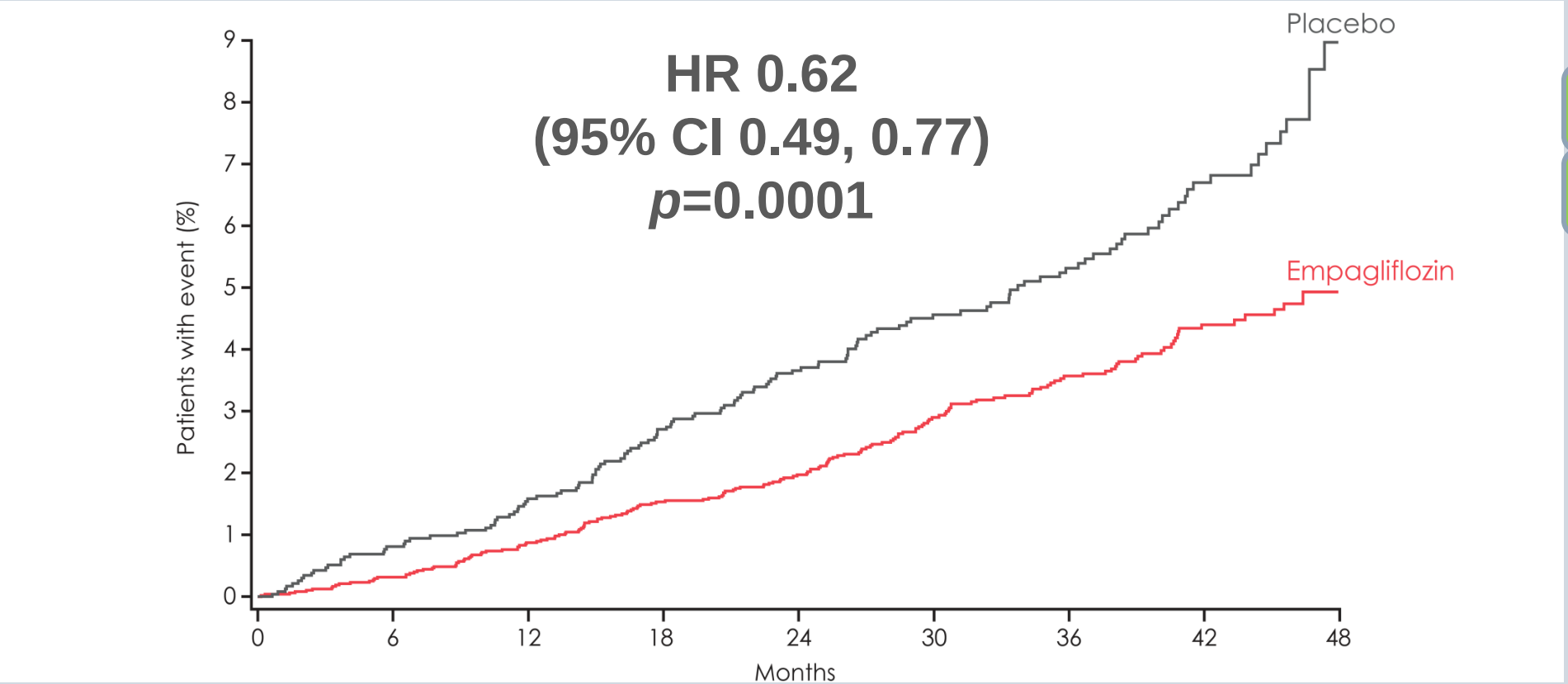
Zinman B et al. N Engl J Med 2015; 373: 2117-28

Neal B et al. N ngl J Med 2017. DOI: 10.1056/NEJMoa1611925

Wiviott SB et al. N ngl J Med 2018.

Presented at ADA 2020

EMPA-REG OUTCOME: Cardiovascular death



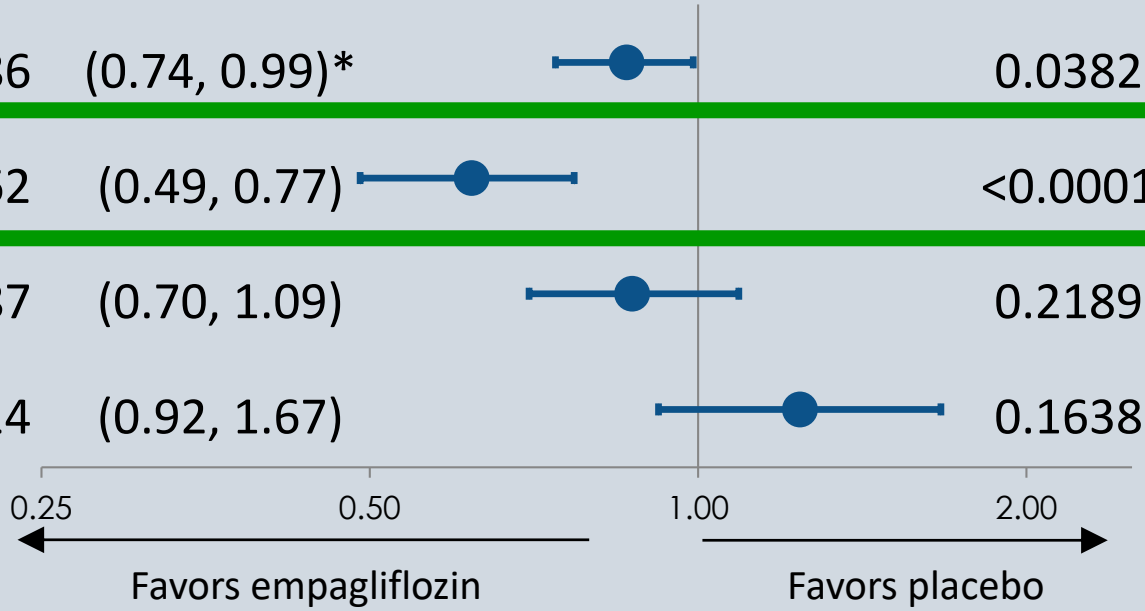
38% RRR

NNT = 45

Zinman B *et al. N Engl J Med* 2015, published on-line, 9-1-15, DOI:10.1056/NEJMoa1504720

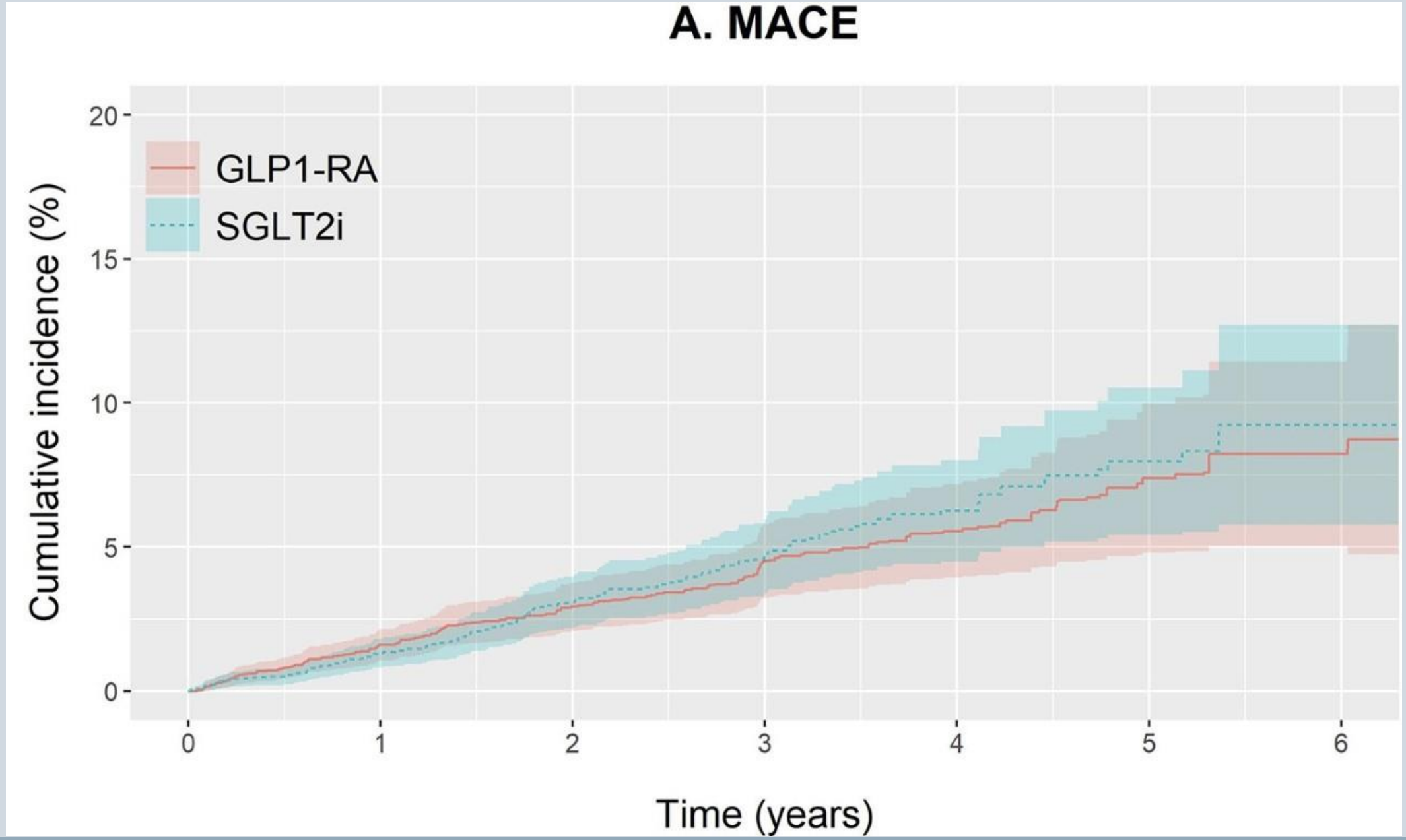
EMPA-REG OUTCOME: 3-point MACE

	Patients with event/analysed				
	Empagliflozin	**Placebo**	**HR**	**(95% CI)**	*p*-value
Primary outcome:					
3-point MACE	490/4687	282/2333	0.86	(0.74, 0.99)*	0.0382
CV death	172/4687	137/2333	0.62	(0.49, 0.77)	<0.0001
Non-fatal MI	213/4687	121/2333	0.87	(0.70, 1.09)	0.2189
Non-fatal stroke	150/4687	60/2333	1.24	(0.92, 1.67)	0.1638

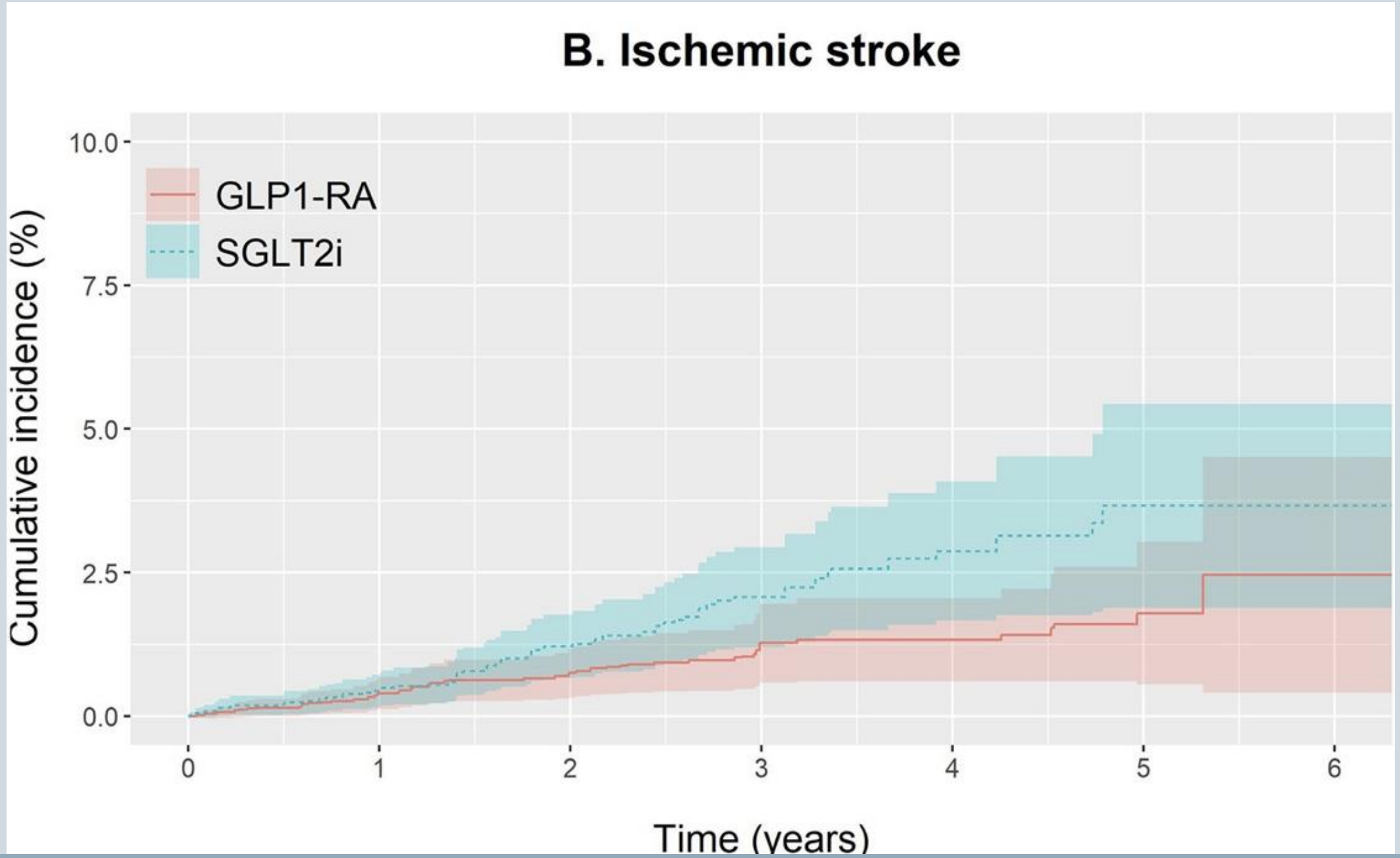


Learning Objectives

- Identify the link between diabetes and cardiovascular disease (CVD).
- List two (2) therapies proven to prevent CVD in patients with diabetes.
- Specify two (2) new diabetes drugs that fit in with other therapies for cardiovascular risk reduction.
- **Specify the role of SGLT2 inhibitors and GLP1-RAs in reducing CV events in diabetics**.
- Discuss the role of diabetes therapies in heart failure management

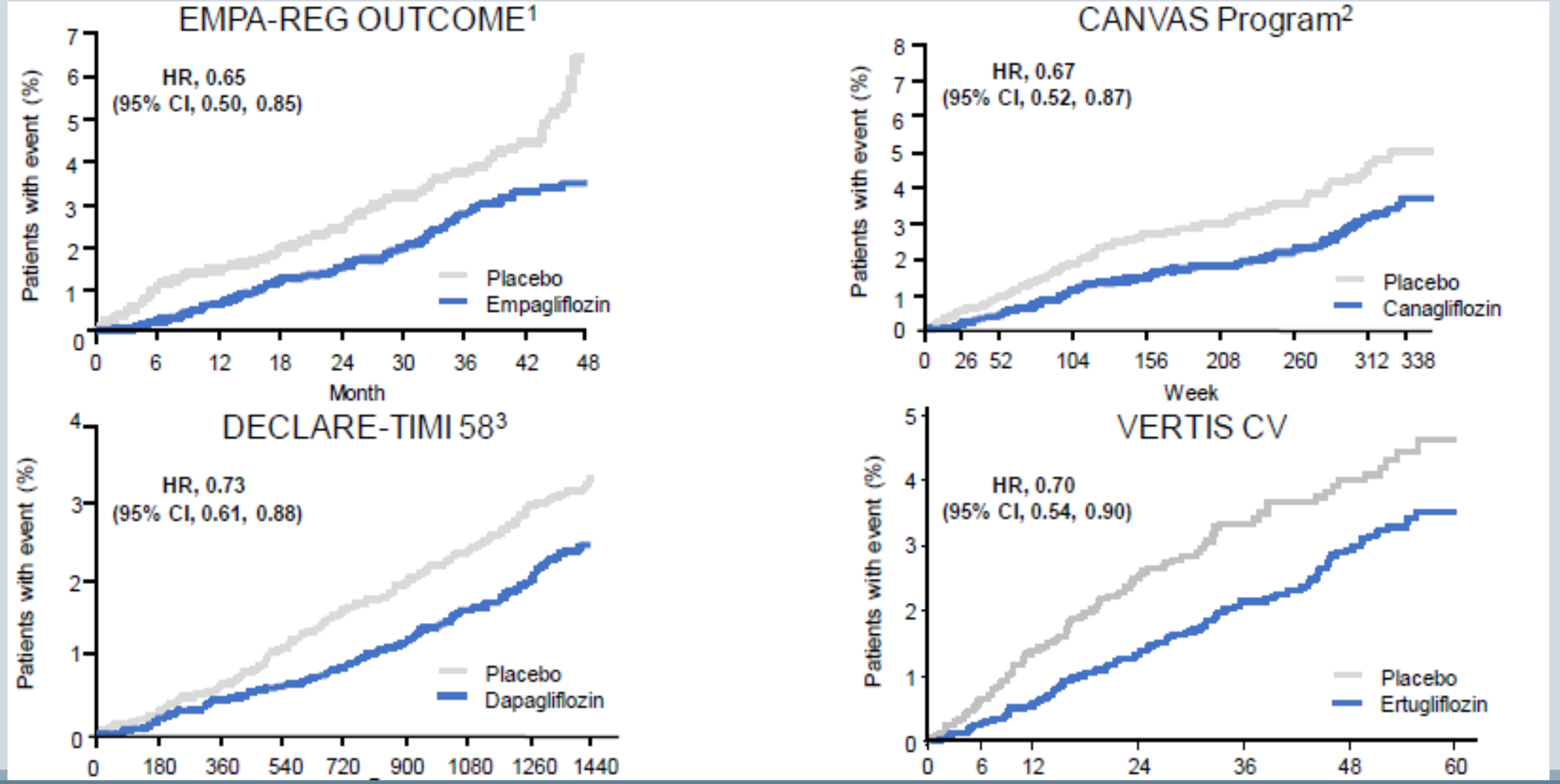


Fu et al. Int J. Cardiol. Vol. 352. Pg 172-179 April 1, 2022



Fu et al. Int J. Cardiol. Vol. 352. Pg 172-179 April 1, 2022

SGLT2i: Consistent benefit on HF Hospitalization



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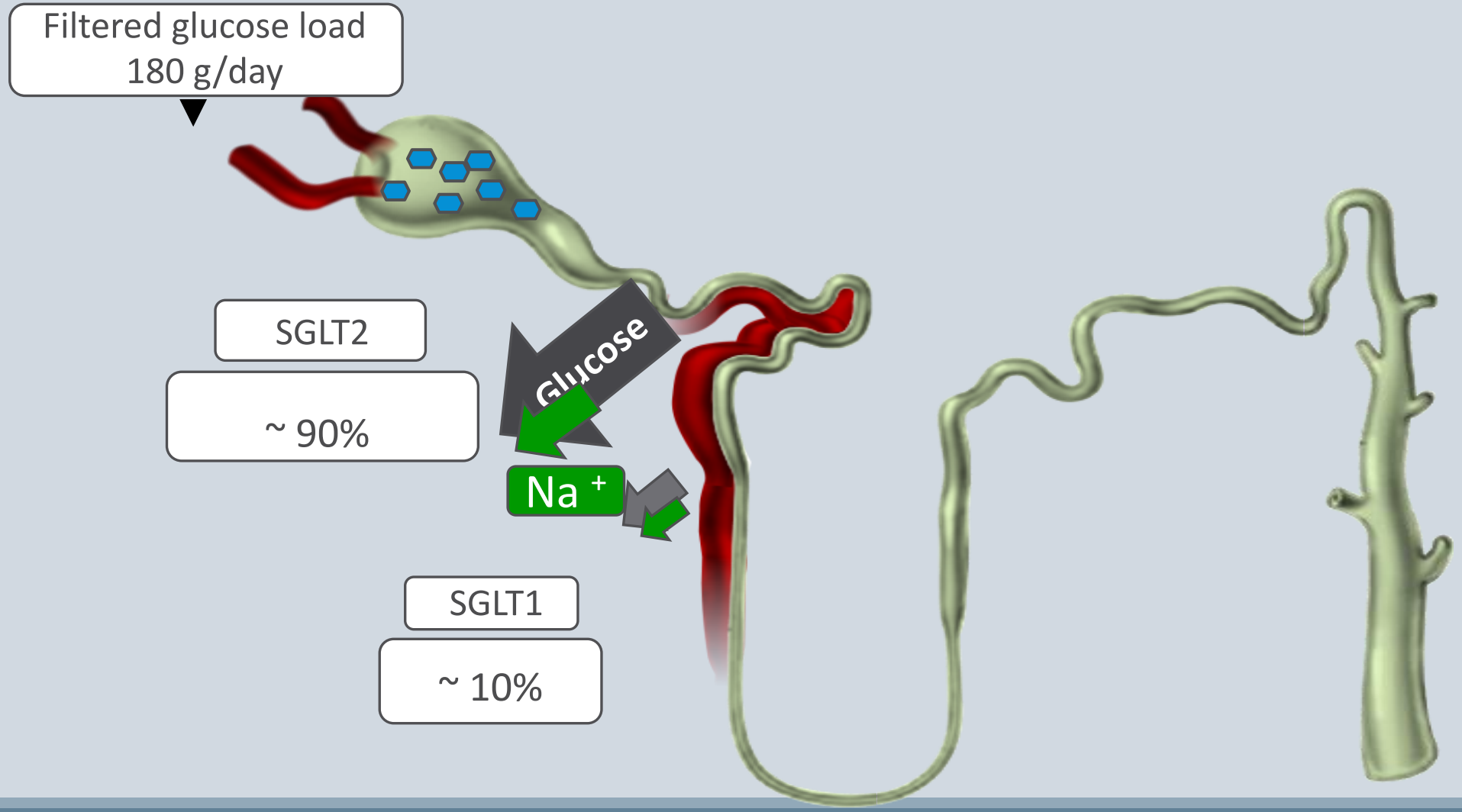
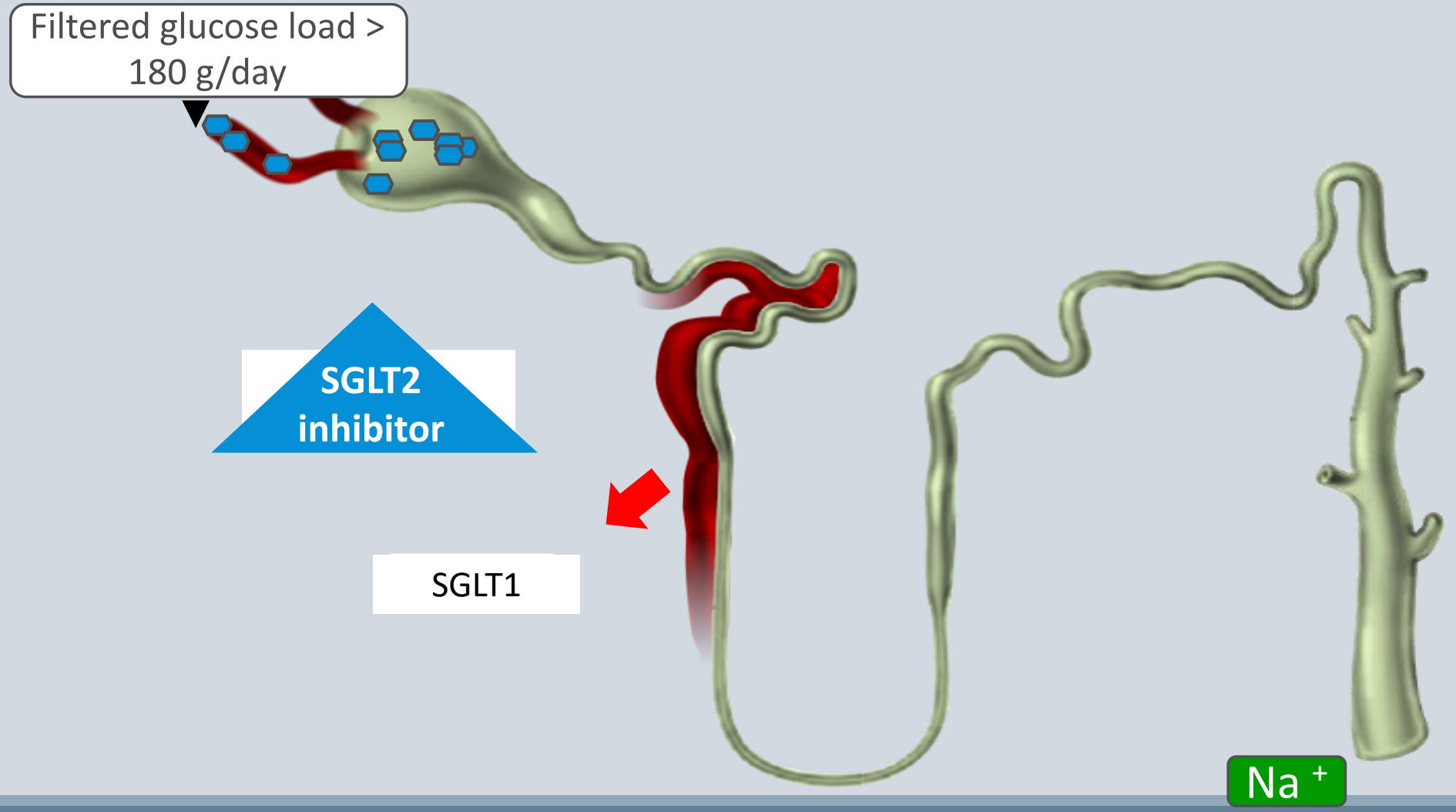
Renal handling of glucose



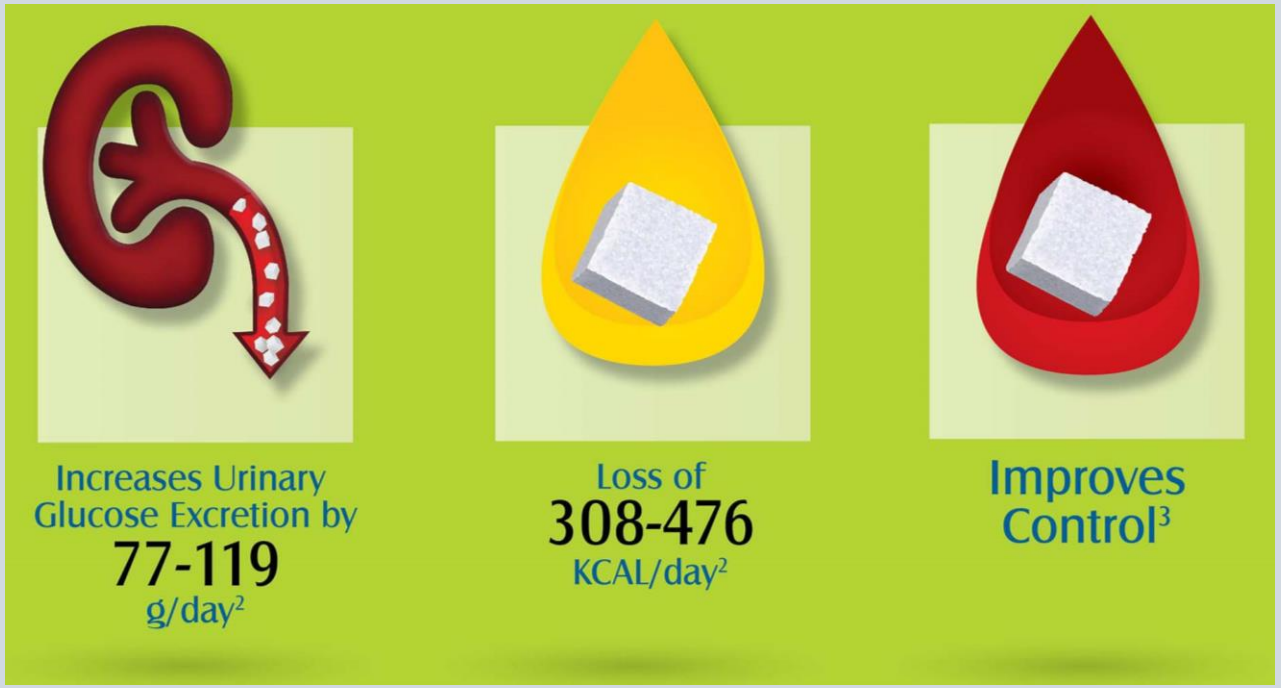
Gerich JE. *Diabet Med*. 2010;27:136–142.

SGLT2 inhibitor mechanism



1Bakris et al. Kidney Int 2009;75;1272–7.

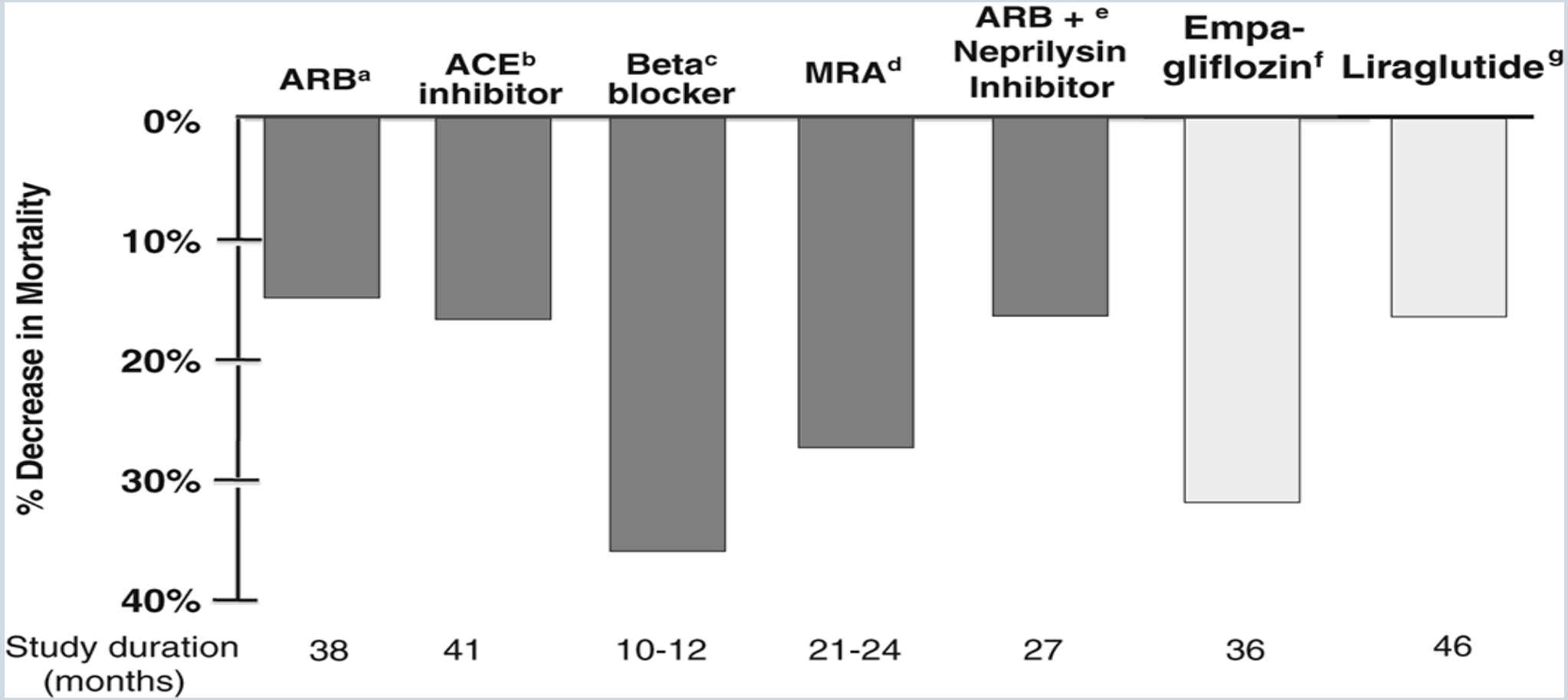
SGLT2 inhibitors: Glucose loss



1 g glucose = 4 kcal

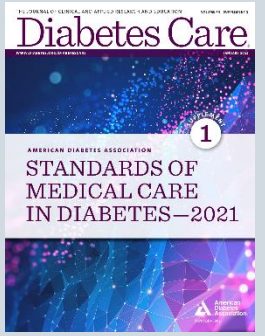
1. Nomura S, et al. J Med Chem. 2010; 53(17):6355-6360. 2. Sha S, et al.; Diabetes Obes Metab. 2011;13(7):669-672. 3. Liang Y, et al. PLoS One. 2012; 7(2):e30555. 4. Devineni D, et al. Diabetes Obes Metab. 2012. 5. Rosenstock J, et al. Diabetes Care. 2012 Abdul-Ghani MA, DeFronzo RA. Endocr Pract. 2008; Nair S, Wilding JP. J Clin Endocrinol Metab. 2010.

Heart failure outcomes in clinical trials



European Journal of Heart Failure. Volume 19, Issue 1, pages 43-53, 21 SEP 2016 DOI: 10.1002/ejhf.633

2021 ADA Recommendations: Glucose



- In patients with type 2 diabetes who have established ASCVD, or **multiple ASCVD risk factors** or ***established kidney disease***, an **SGLT2 inhibitors or GLP-1 receptor agonists** with demonstrated cardiovascular disease benefit…is recommended. **A**

- **SGLT2 inhibitor** to reduce the risk of **MACE and/or HF hospitalization** **A**

- **GLP-1 receptor agonist** to reduce the risk of **MACE** **A**

2018 ACC Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

Endorsed by the American Diabetes Association

Writing Committee

Sandeep R. Das, MD, MPH, FACC, *Co-Chair*
Brendan M. Everett, MD, MPH, FACC, *Co-Chair*

Kim K. Birtcher, PharmD, MS, CDE, AACC
Jenifer M. Brown, MD
William T. Cefalu, MD*
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Rita Rastogi Kalyani, MD*
Mikhail Kosiborod, MD, FACC
Melissa L. Magwire, RN, CDE
Pamela B. Morris, MD, FACC
Laurence S. Sperling, MD, FACC

*American Diabetes Association representative.

Task Force on Expert Consensus Decision Pathways

James L. Januzzi, Jr, MD, FACC, *Chair*

Tariq Ahmad, MD, MPH, FACC
Brendan Everett, MD, FACC
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Pamela B. Morris, MD, FACC
Robert N. Piana, MD, FACC
Sunil V. Rao, MD, FACC
Marielle Scherrer-Crosbie, MD, PhD
Karol E. Watson, MD, FACC
Barbara S. Wiggins, PharmD, AACC

Key Points from ACC Consensus Pathway

- The CV specialist is well-positioned to incorporate…newer antihyperglycemic agents into routine practice.
- Patients and providers can choose medications that have demonstrated benefits in reducing heart attack, stroke, and CV death, rather than just reducing blood glucose.
- Cardiologists should consider these new medications part of their armamentarium in reducing CV morbidity and mortality

Writing Committee et al. JACC 2018;j.jacc.2018.09.020

The link between Diabetes and CVD

- To reduce risk in patients with T2DM focus on blood pressure control, lipid control, and appropriate use of glucose lowering medications
- Many (most) of our patients with CVD have diabetes, pre-diabetes, or IR
- Ask the question of every ASCVD patient “Do they also have T2DM?”
- In patients with ASCVD and T2DM use a glucose lowering agent of proven cardiovascular benefit
- Aim for a HbA1c that the patient can achieve safely **AVOID HYPOGLYCEMIA**

RESOURCES

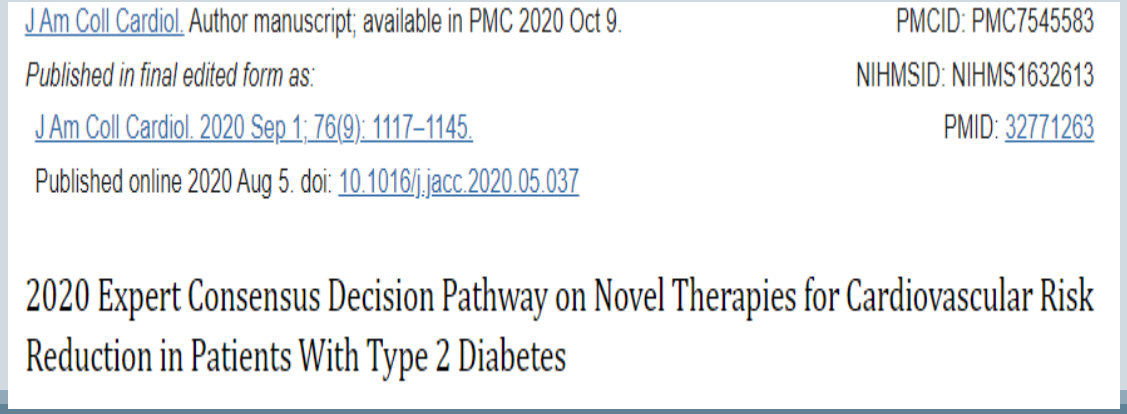
Standards of Medical Care in Diabetes—2022 Abridged for Primary Care Providers | Clinical Diabetes | American Diabetes Association (diabetesjournals.org)


The ADA's 2022 Standards of Medical Care in Diabetes Update

Feb. 23, 2022 0 Comments

Tagged: Practice Transformation

2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes - PMC (nih.gov)


J Am Coll Cardiol. Author manuscript; available in PMC 2020 Oct 9.

PMCID: PMC7545583

Published in final edited form as:

NIHMSID: NIHMS1632613

J Am Coll Cardiol. 2020 Sep 1; 76(9): 1117–1145.

PMID: 32771263

Published online 2020 Aug 5. doi: 10.1016/j.jacc.2020.05.037

2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes

Presenter’s Contact Information

Karol Watson, MD, PhD, FACC
KWatson@mednet.ucla.edu

Frequently Asked Questions (FAQs)

1. Can we prevent diabetes?
Yes. Diabetes can be prevented with lifestyle measures such as diet and exercise.

2. Does tight glycemic control reduce CVD?
Tight glycemic control has been shown to consistently decrease microvascular events such as neuropathy, nephrophathy, and blindness. But tight glycemic control has NOT been consistently shown to decrease MACROvascular events such as CVD events of myocardial infarction and stroke.

3. How do the new diabetes drugs fit in with other therapies for cardiovascular prevention?
New diabetes therapies with documented cardiovascular benefit should be used in conjunction with other preventive therapies in diabetes such as statins.

4. Are the new diabetes drugs useful for preventing CVD in metabolic syndrome patients?
This has never been studied.

Q & A

L.A. Care PCE Program Friendly Reminders

- **Friendly Reminder,** a survey will pop up on your web browser after the webinar ends (please do not close your web browser and wait a few seconds) and please complete the survey.

Please note: ***the online survey may appear in another window or tab after the webinar ends.***

- Upon completion of the online survey, you will receive the pdf CME or CE certificate based on your credential, verification of name and attendance duration time, within two (2) weeks after webinar.

- ***Webinar participants will only have up to two weeks after webinar date to email Leilanie Mercurio at lmercurio@lacare.org to request the evaluation form if the online survey is not completed yet. No name, no survey or completed evaluation and less than 75 minutes attendance duration time via log in means No CME or CE credit, No CME or CE certificate.***

Thank you!