# Optimal Management of Cardiovascular Risk in Diabetes

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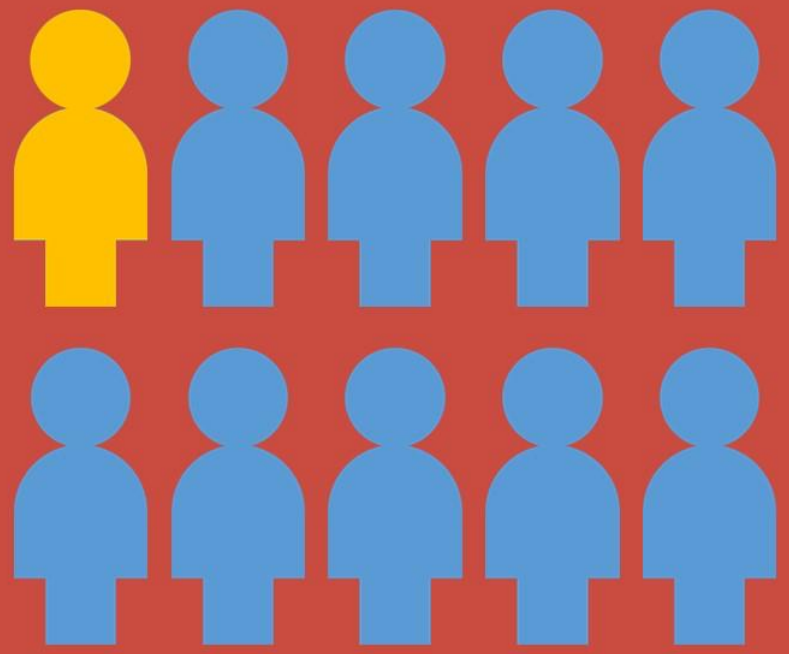
3/23/2019

# Disclosures:

- ✓None for Dr. Mushref
- ✓Dr. Murrow reports the following:  Owner, Infrared Rx.

# Why Should We Care?

30.3 million people have diabetes in the US



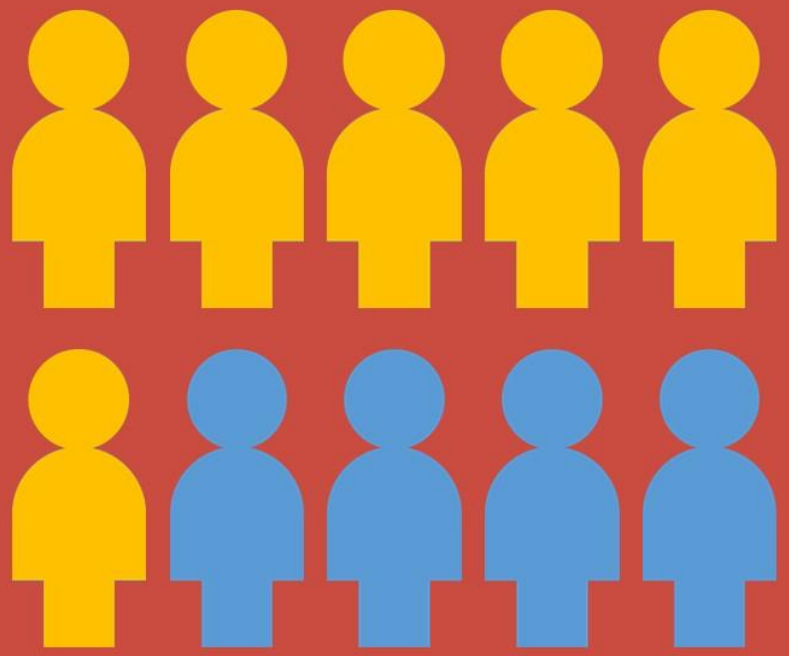
**1/10**
**PEOPLE**

have diabetes

Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2017

# Why Should We Care?

Two thirds of diabetic patients will die of cardiovascular disease (CVD)



**6/10**

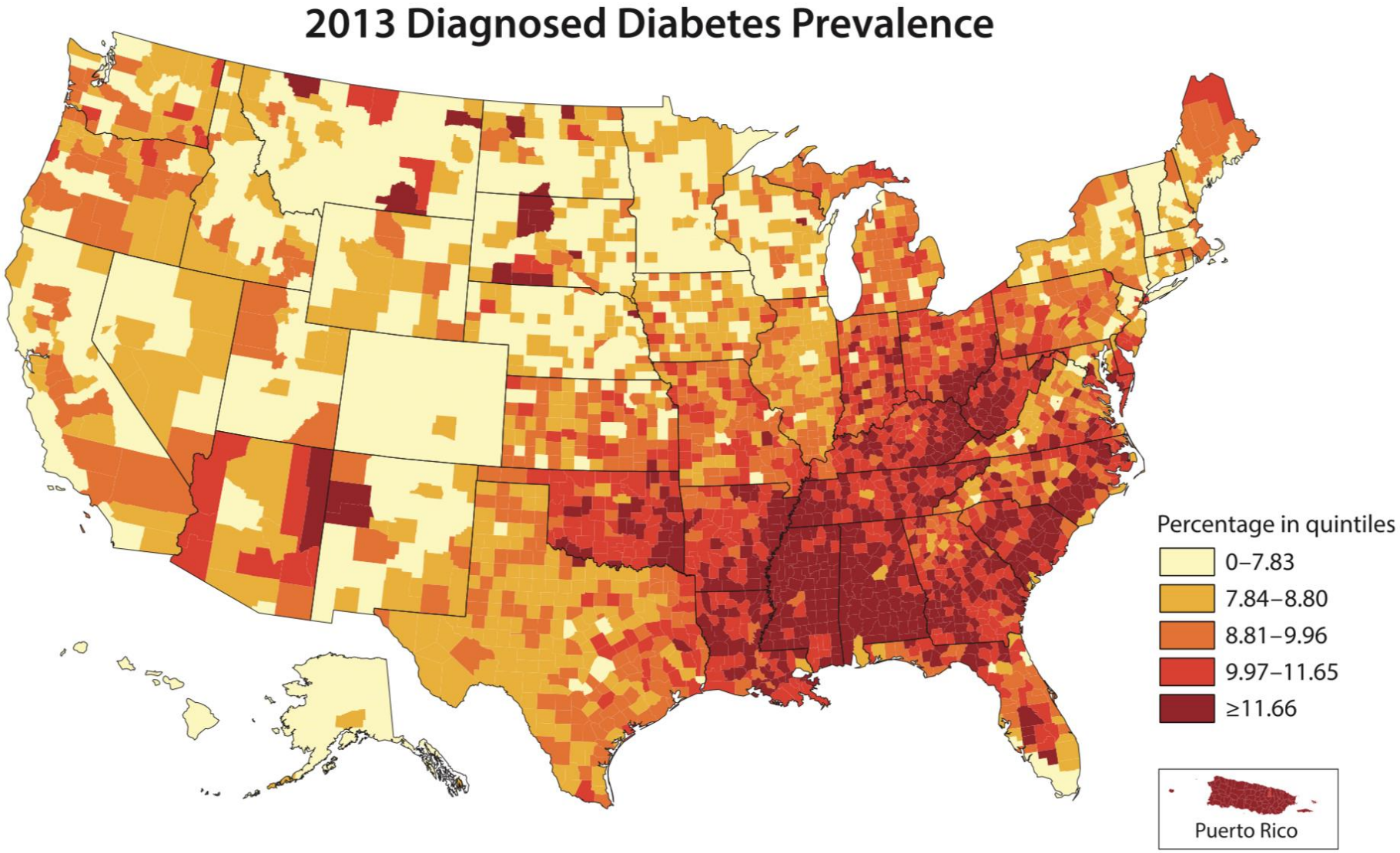
**PEOPLE**

with diabetes will die of CVD

Diabetes Care 2003 Jan; 26(1): 230-237.

# Diabetes Belt

CDC
Centers for Disease Control and Prevention




National Diabetes Statistics Report 2017

# Life's Simple 7

# Objectives:

- ✓Individualize glycemic goal
- ✓Apply new therapies when appropriate
- ✓Importance of smoking cessation
- ✓Encourage Lifestyle intervention

# Patient One

# Patient One:

- 60 year-old male
- Type II diabetes for 15 years
- HTN, CAD, Stroke, Diabetic neuropathy
- HbA1c 8.5%, GFR>60

# Patient One:

What is you HbA1c target to reduce further CVD?

a) Less than 10%

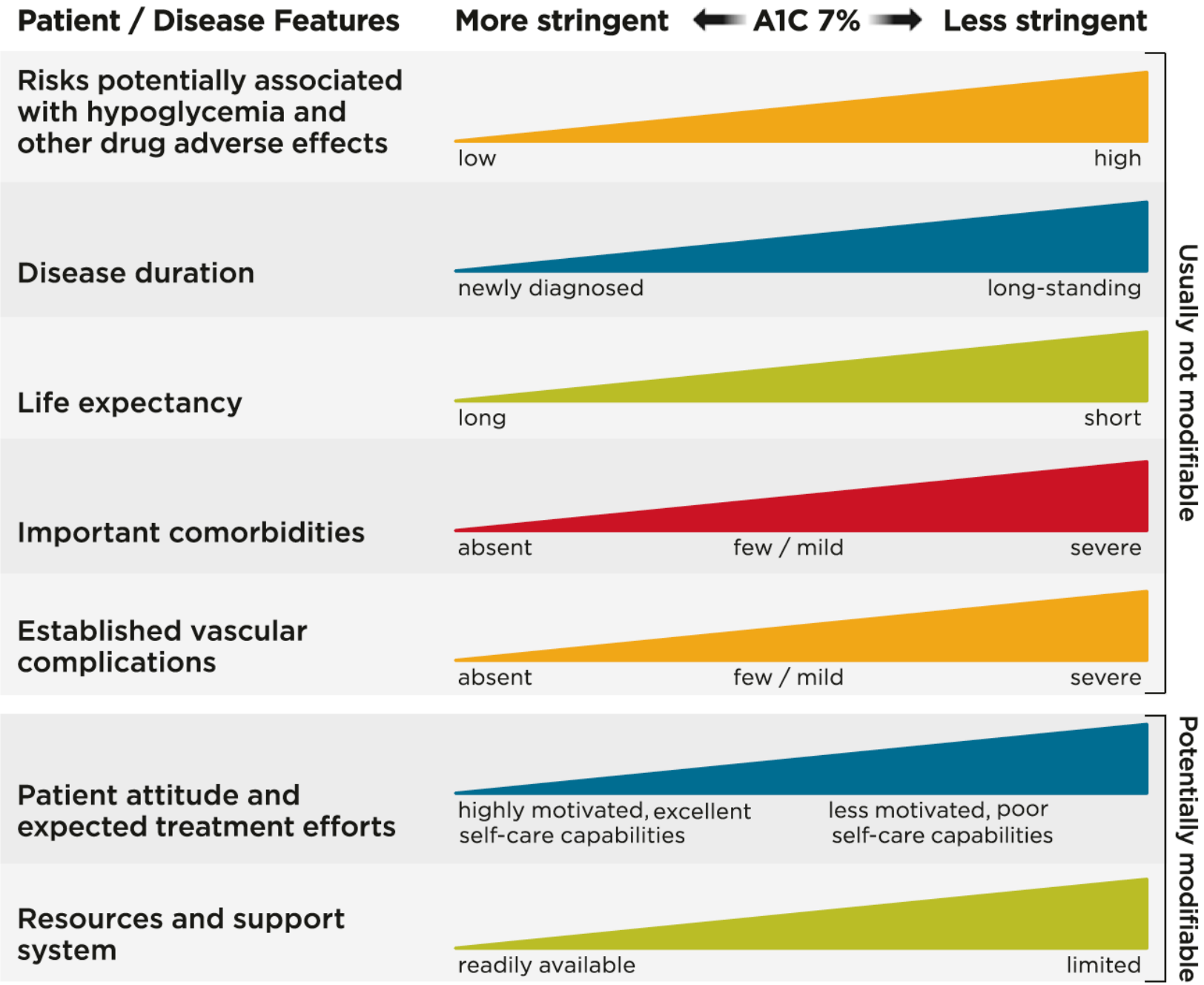
b) Less than 9%

c) Less than 8%

d) Less than 7%

| Clinical Trial | Population | Intensive | Conventional | Outcome |
|---|---|---|---|---|
| UKPDS 1998<br><br>Follow up 2008 | Newly diagnosed T2DM<br><br>Age 25-65 | Achieved HgbA1C 7% | Achieved HgbA1C 7.9% | ✓ 10 years : No effect on mortality.<br><br>✓ 20 year follow up: ↓mortality |
| DCCT 1993 | Young T1DM patients | Achieved HgbA1C= 7.2% | Achieved HgbA1C=9.1% | ✓ No CVD benefit |
| EDIC 2005 | Same as DCCT | Same as DCCT | Same as DCCT | ✓ Reduced CVD by 42% |
| ACCORD 2008 | T2DM with HgbA1C≥ 7.5%<br>Age 40-79 with CAD | Achieved A1C 6.4% | Achieved A1C 7.5% | ✓ No benefit in primary outcome<br><br>✓ Higher CV mortality |
| ADVANCE 2008<br><br>Follow up 2014 | T2DM Age ≥ 55 years | Achieved A1C 6.5% | Achieved A1C 7.3% | ✓ No benefit in macrovascular events<br><br>✓ 10 y follow up no benefit in mortality or CVD events |
| VADT 2009<br><br>Follow up 2015 | T2DM<br>Average age 60<br>DM for 11.5 years | Achieved A1C 6.9% | Achieved A1C 8.4% | ✓ No initial benefit<br><br>✓ 10 y follow-up reduction in CVD events with no mortality benefit |

# Approach to the Management of Hyperglycemia



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a) Add sitagliptin

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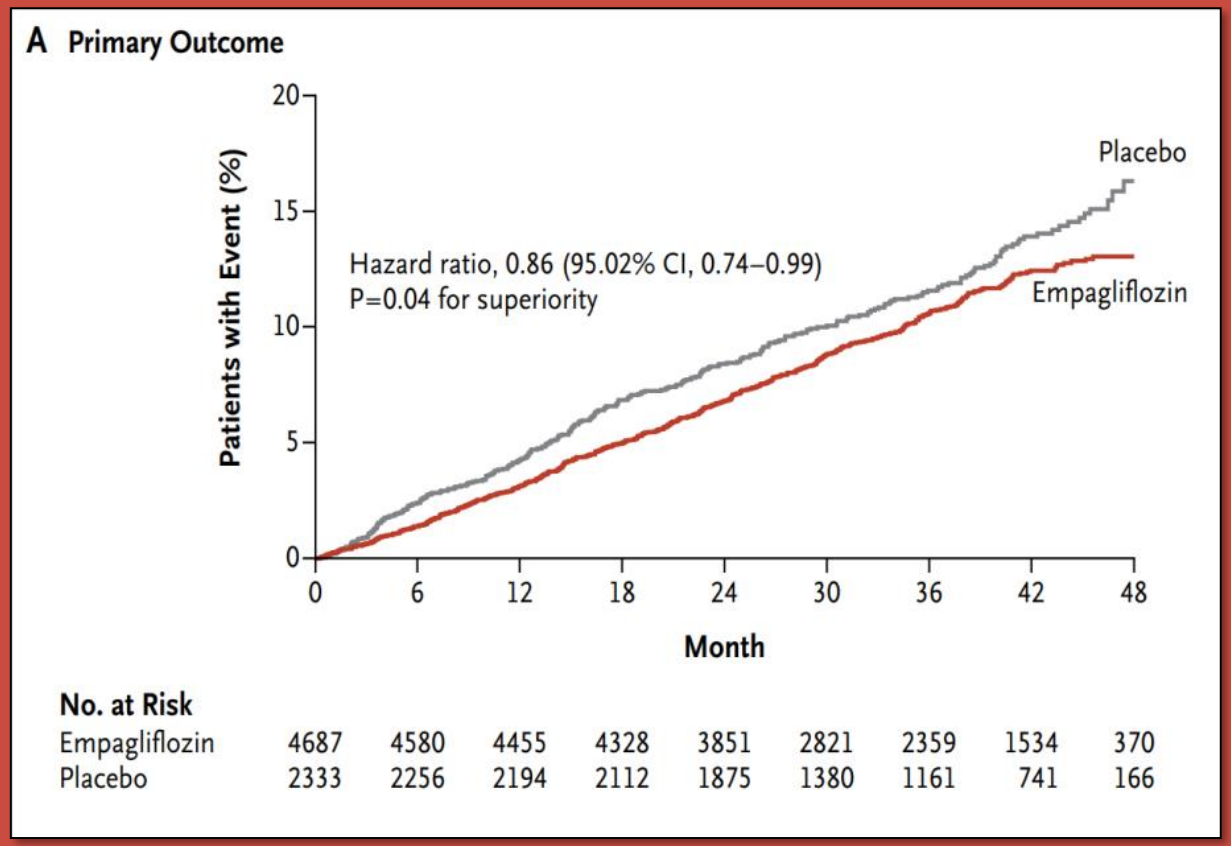
c) Add liraglutide

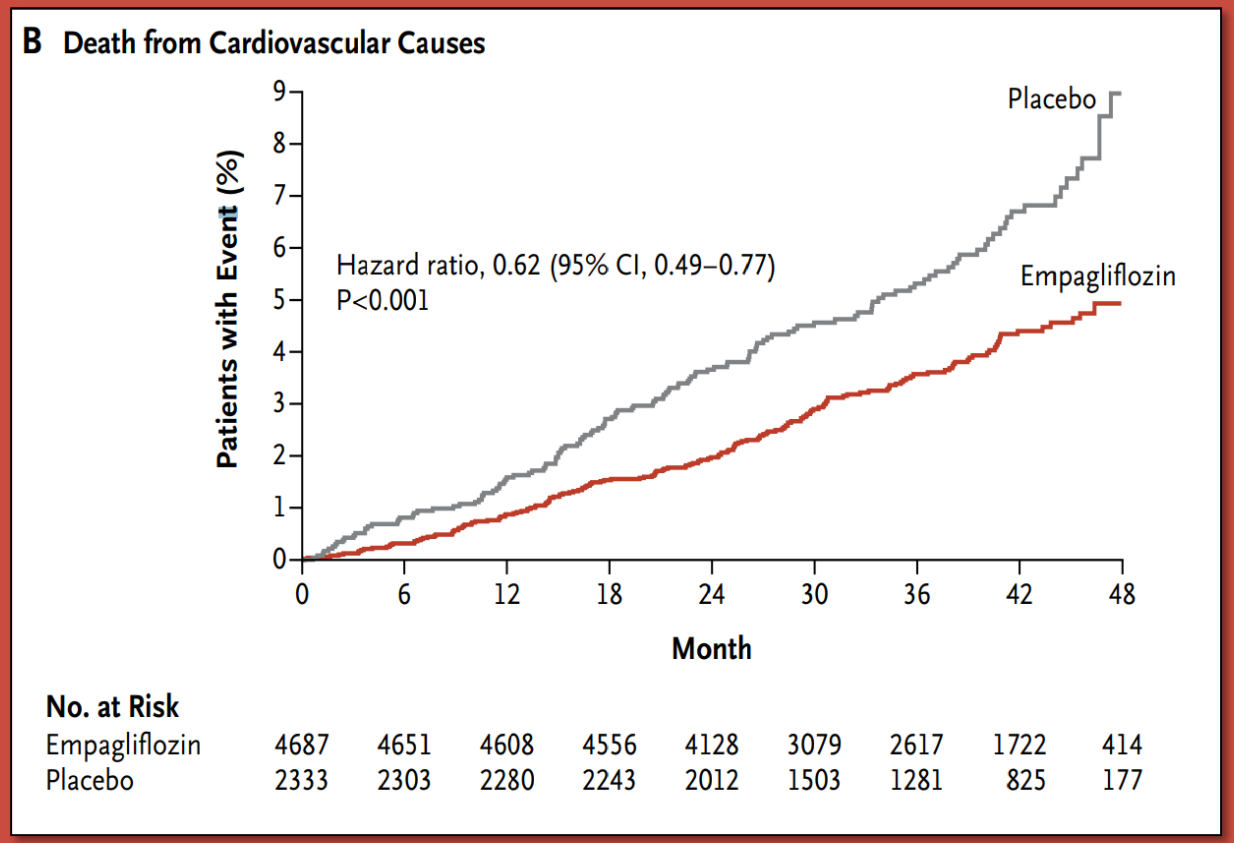
d) Add basal insulin

# New Medications:

- ✓2008, FDA issued a guidance for drug industry
- ✓All new DM therapy has to prove CVD safety
- ✓EMPA-REG and LEADER trials showed benefit!

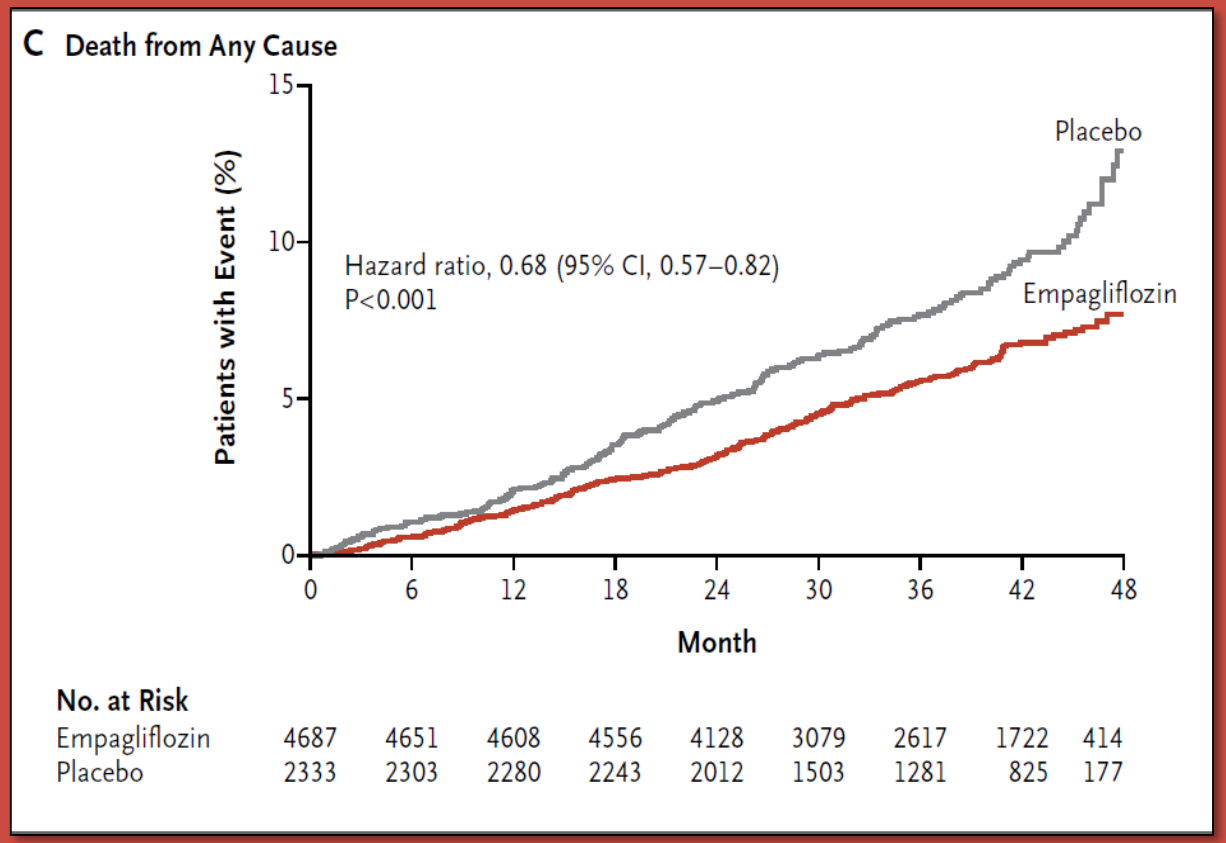
# EMPA-REG: Empagliflozin

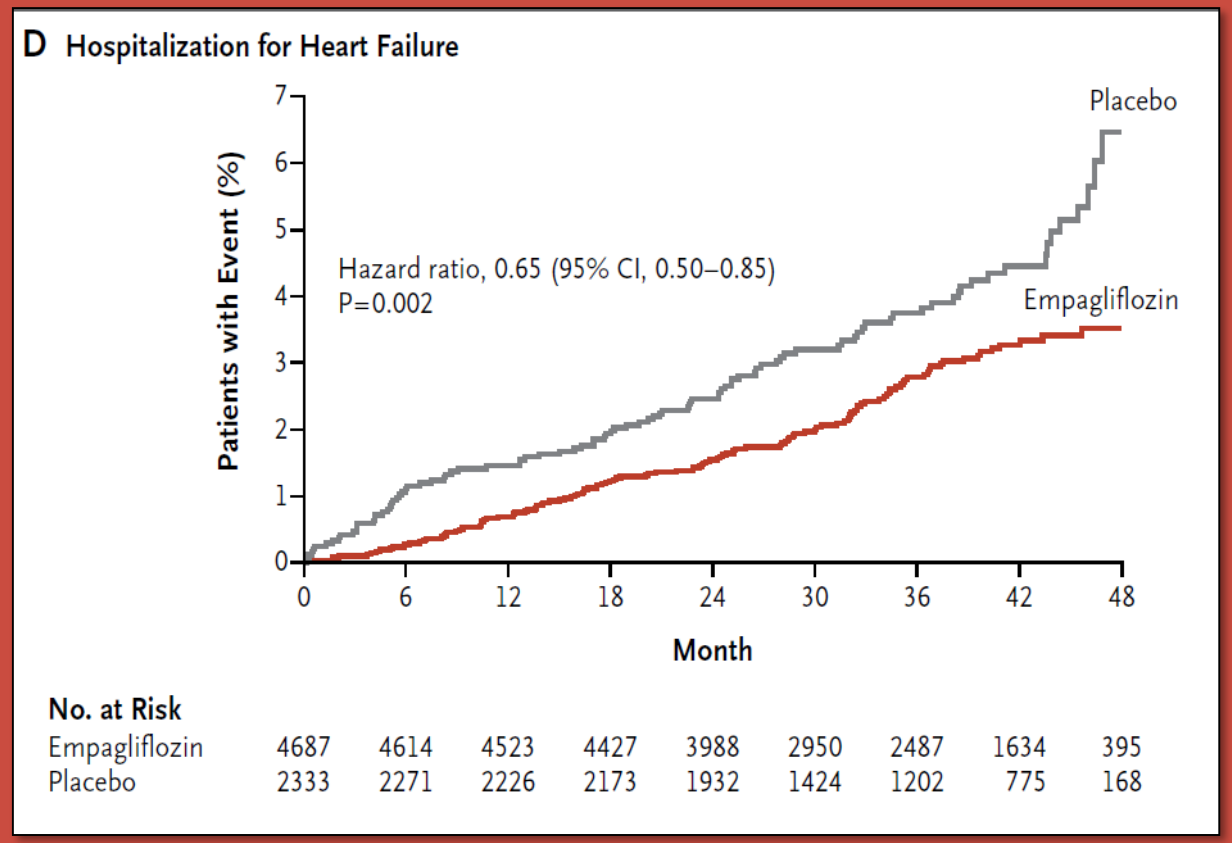



*N. Engl. J. Med. 373, 2117–2128 (2015)*

# EMPA-REG: Empagliflozin

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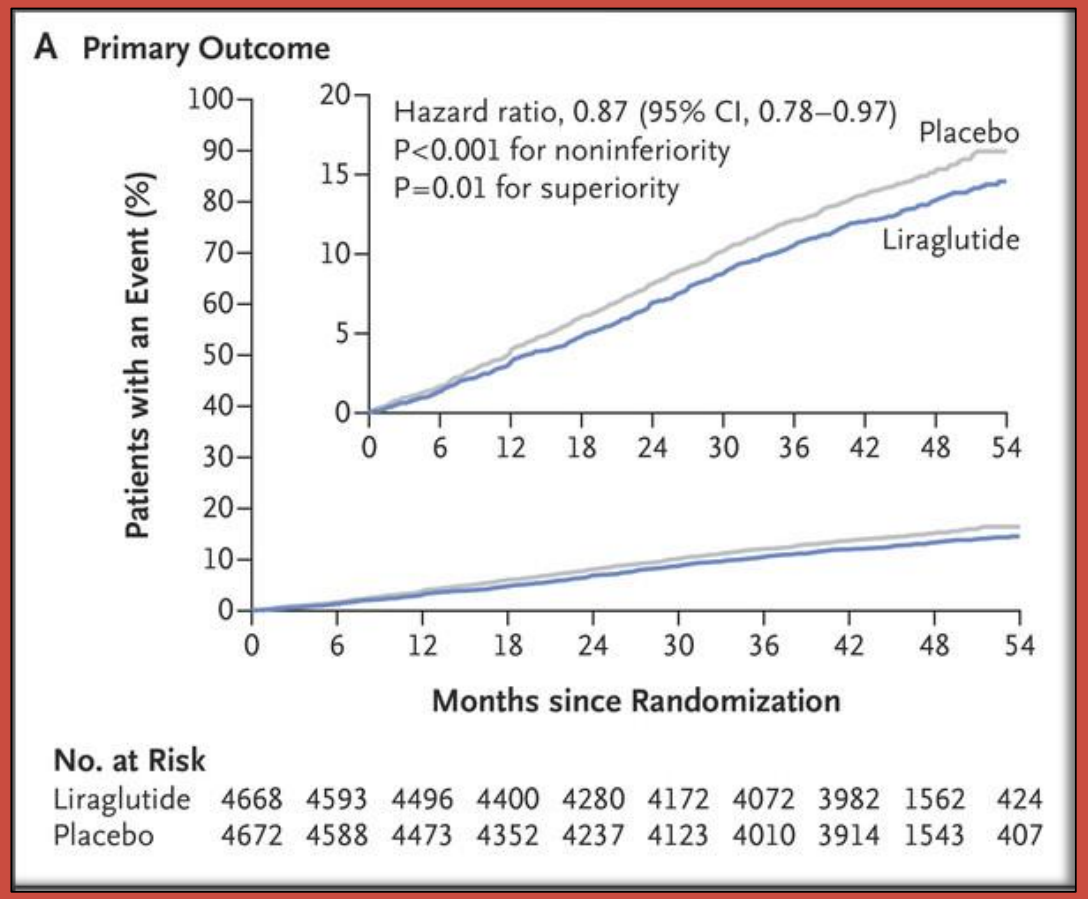
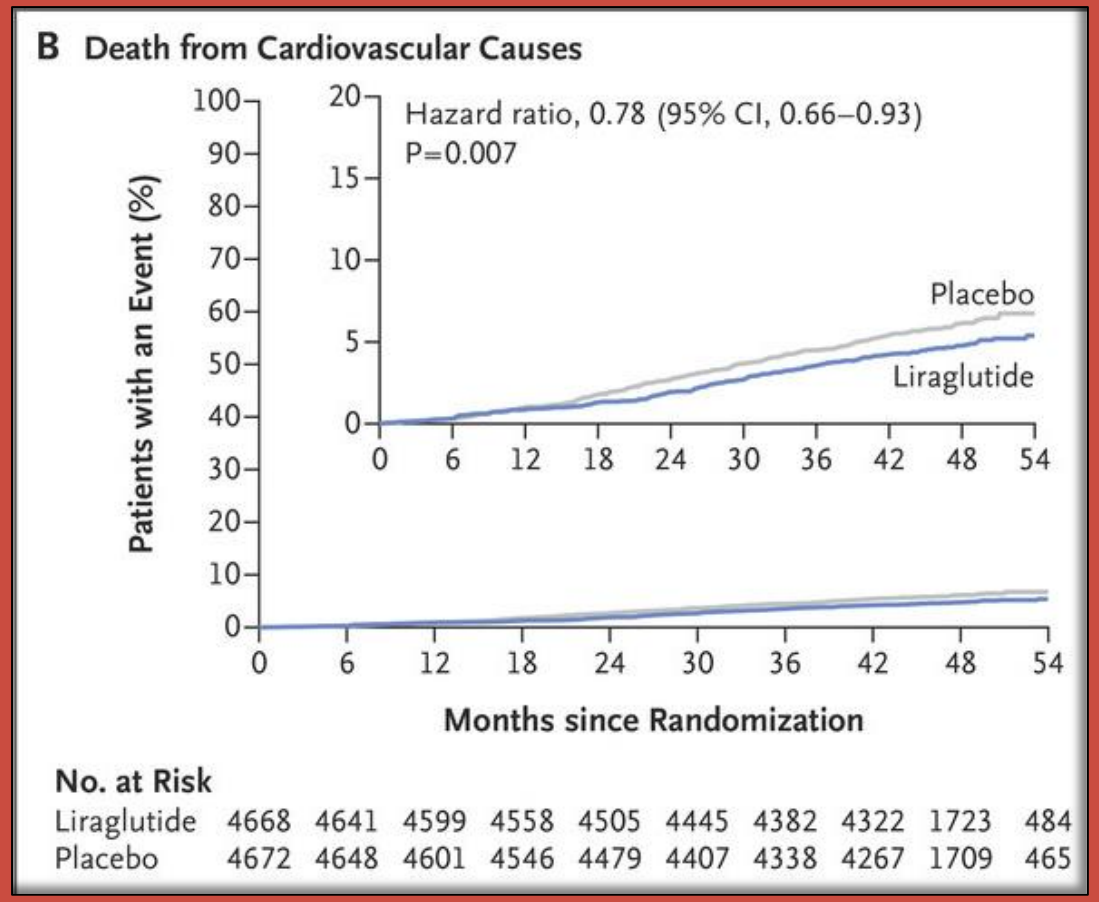
# LEADER: Liraglutide




*N Engl J Med 2016;375:311-322*

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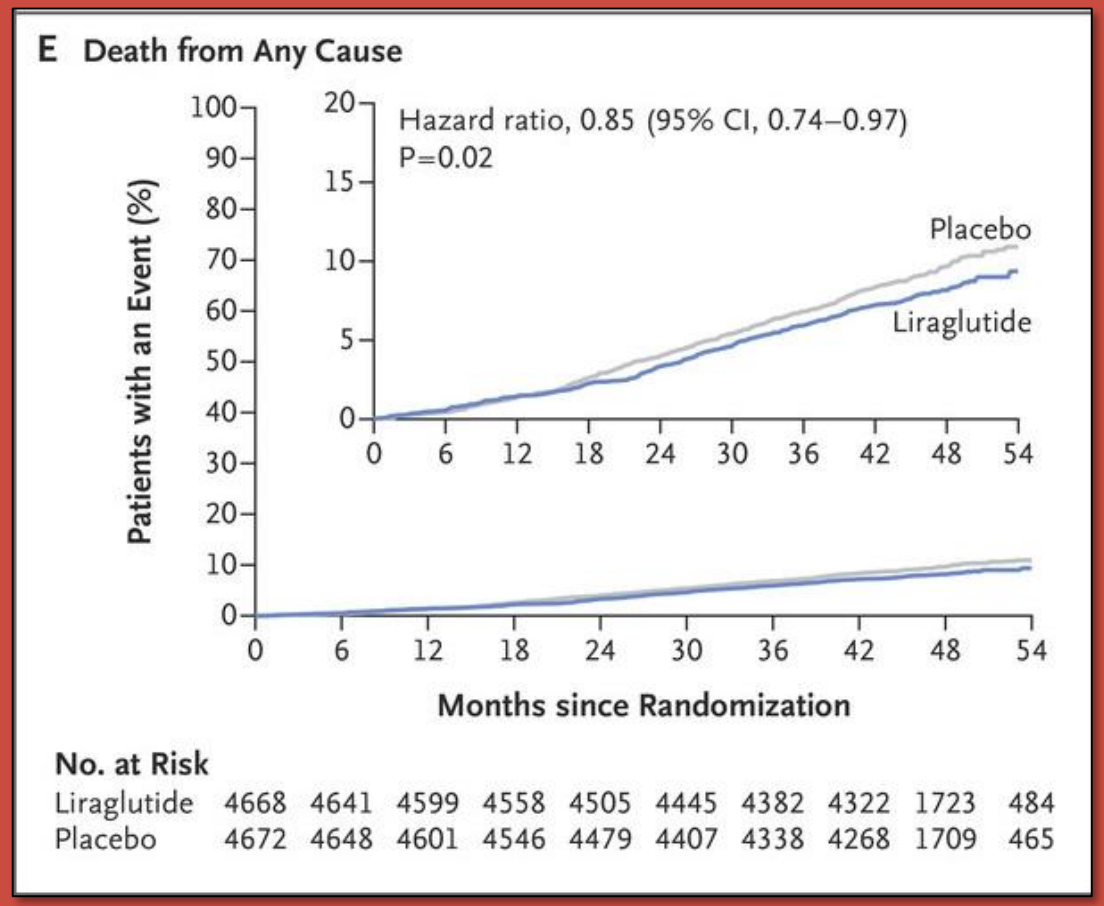


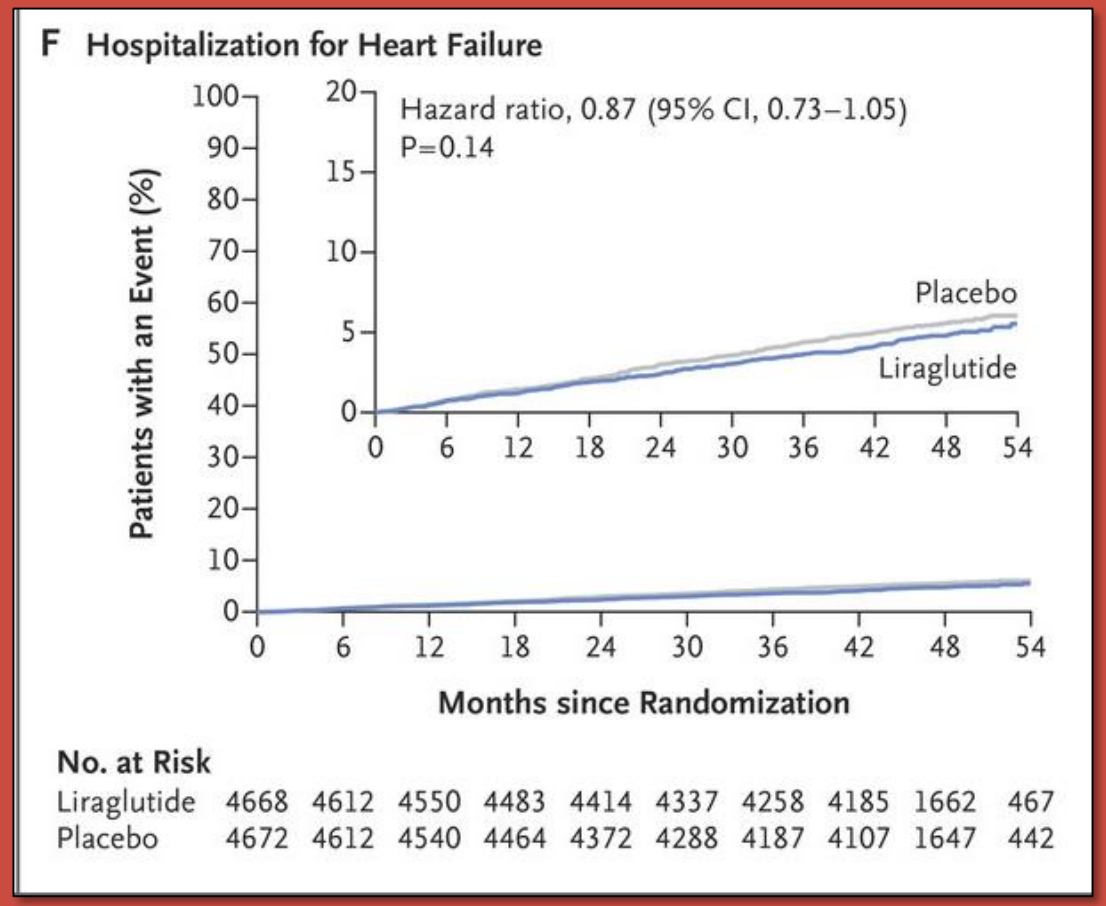


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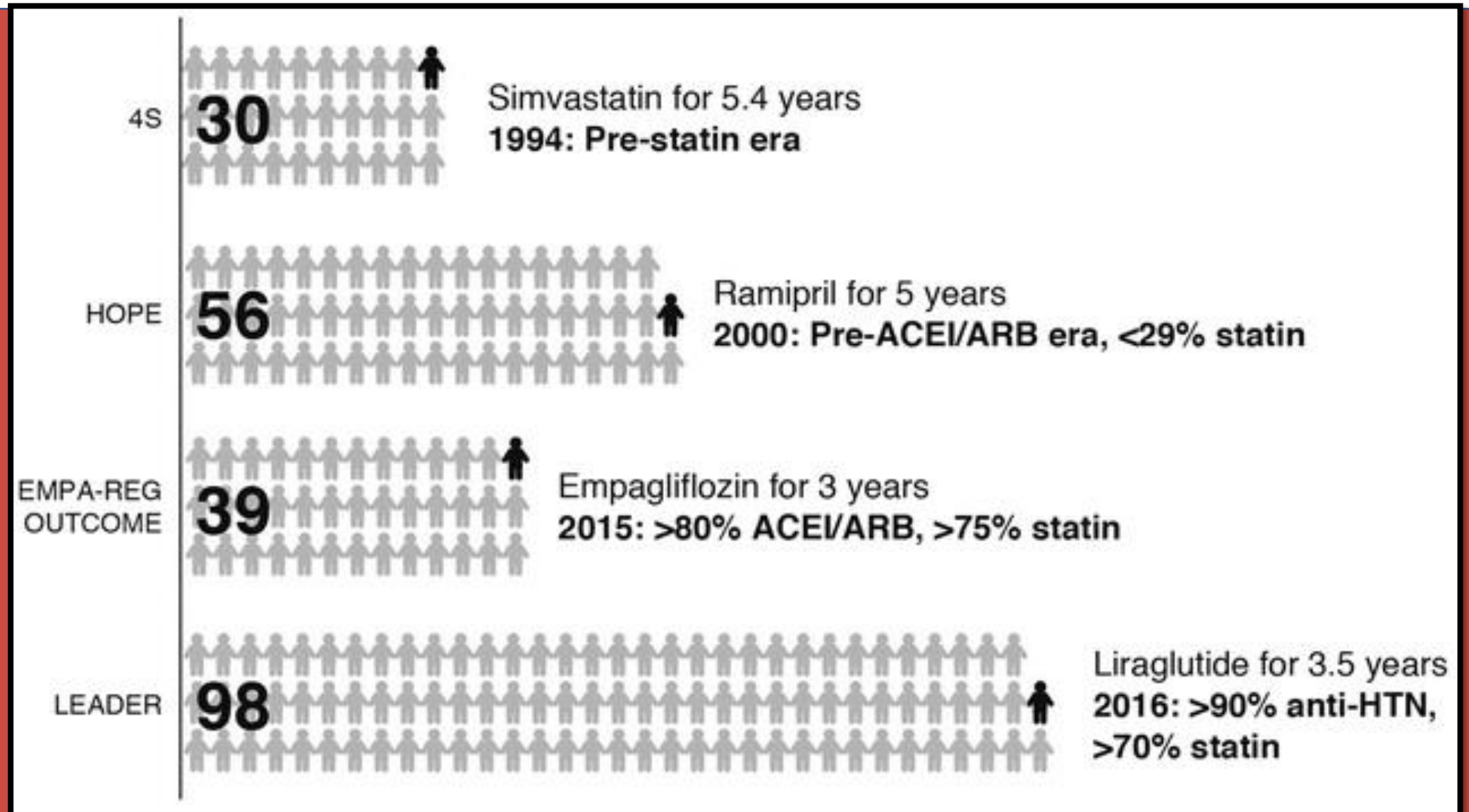
# Number Needed to Treat



# New Therapies:

- Metformin is still the first line
- Both SGLTi and GLP-RA lower BP and decrease weight
- SGLT-i class effect?
- Weekly GLP-1 RA (Semaglutide, Exenatide)

Special considerations: GLP-1 receptor antagonists and SGLT2 inhibitors

| Outcome | GLP-1 receptor antagonists | SGLT2 inhibitors |
|---|---|---|
| A1c reduction (%) | 0.7–1.7 | 0.32–1.17 |
| Target of BG lowering | Shorter acting, mostly postprandial BG; longer acting, target fasting and postprandial BG | Fasting and postprandial BG |
| Hypoglycemia risk | Low | Low |
| Weight loss (kg) | 2–5 | 1.5–3.0 |
| Systolic blood pressure reduction (mmHg) | 2–5 | 3–5 |

*Vasc Health Risk Manag. 2016; 12: 239–249*

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# Patient Two

# Patient Two:

- 45 years old male
- Type II Diabetes for 5 years
- HTN, LDL, Tobacco use
- HgbA1C 9%, LDL 120

# Patient Two:

Which of the following the strongest predictor of death in this patient?

a) Smoking
b) Dyslipidemia
c) Uncontrolled A1c
d) Uncontrolled hypertension

**Figure 1 (facing page).**

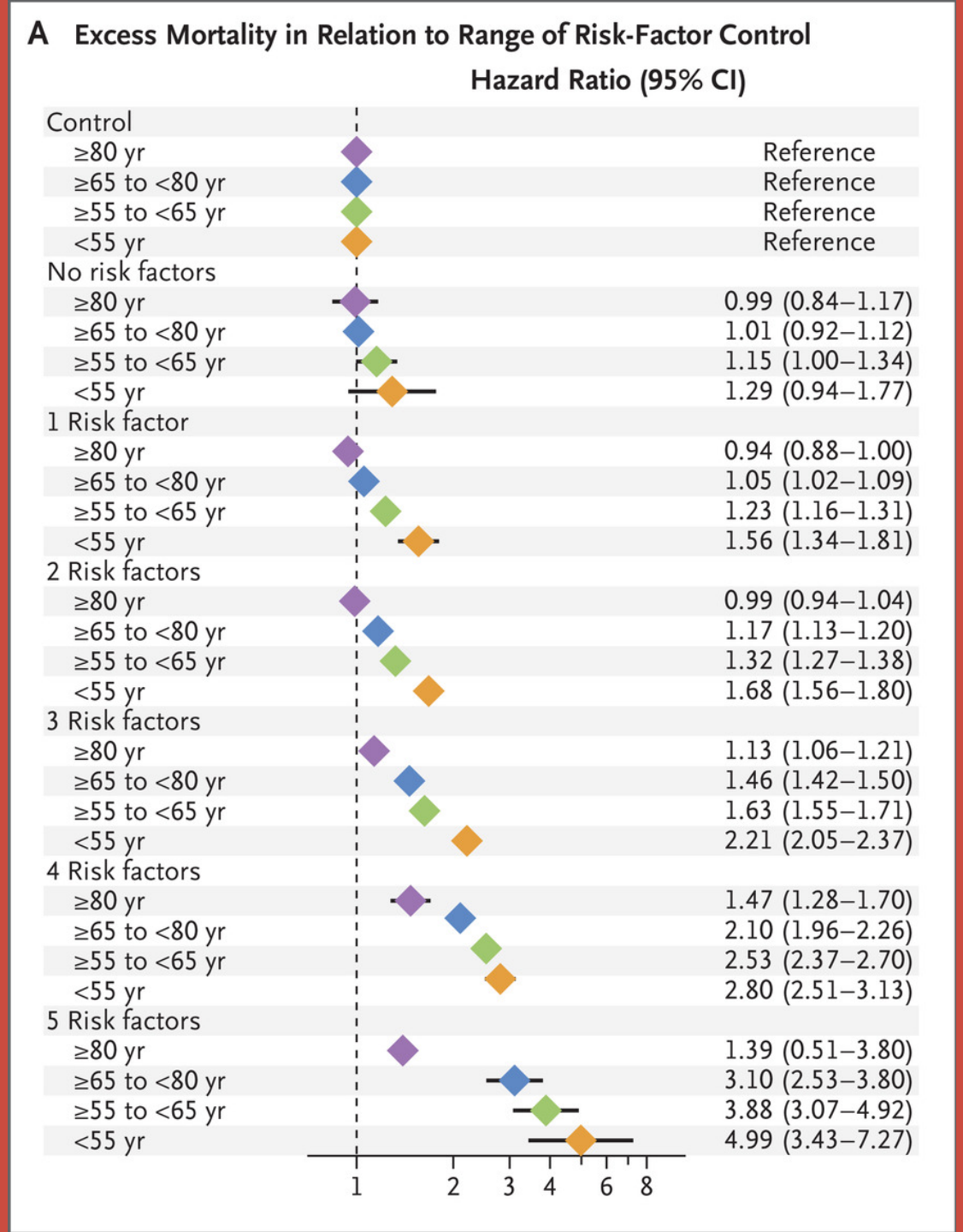
**Adjusted Hazard Ratios for Outcomes, According to Age Category and Number of Risk-Factor Variables outside Target Ranges, among Patients with Type 2 Diabetes, as Compared with Matched Controls.**

## METHODS

Cohort of 271,174 patients with type 2 diabetes in the Swedish National Diabetes Register matched with 1,355,870 controls

Risk factors:

- elevated HbA1c
- LDL
- albuminuria
- smoking
- high blood pressure




N Engl J Med 2018;379:633-44.

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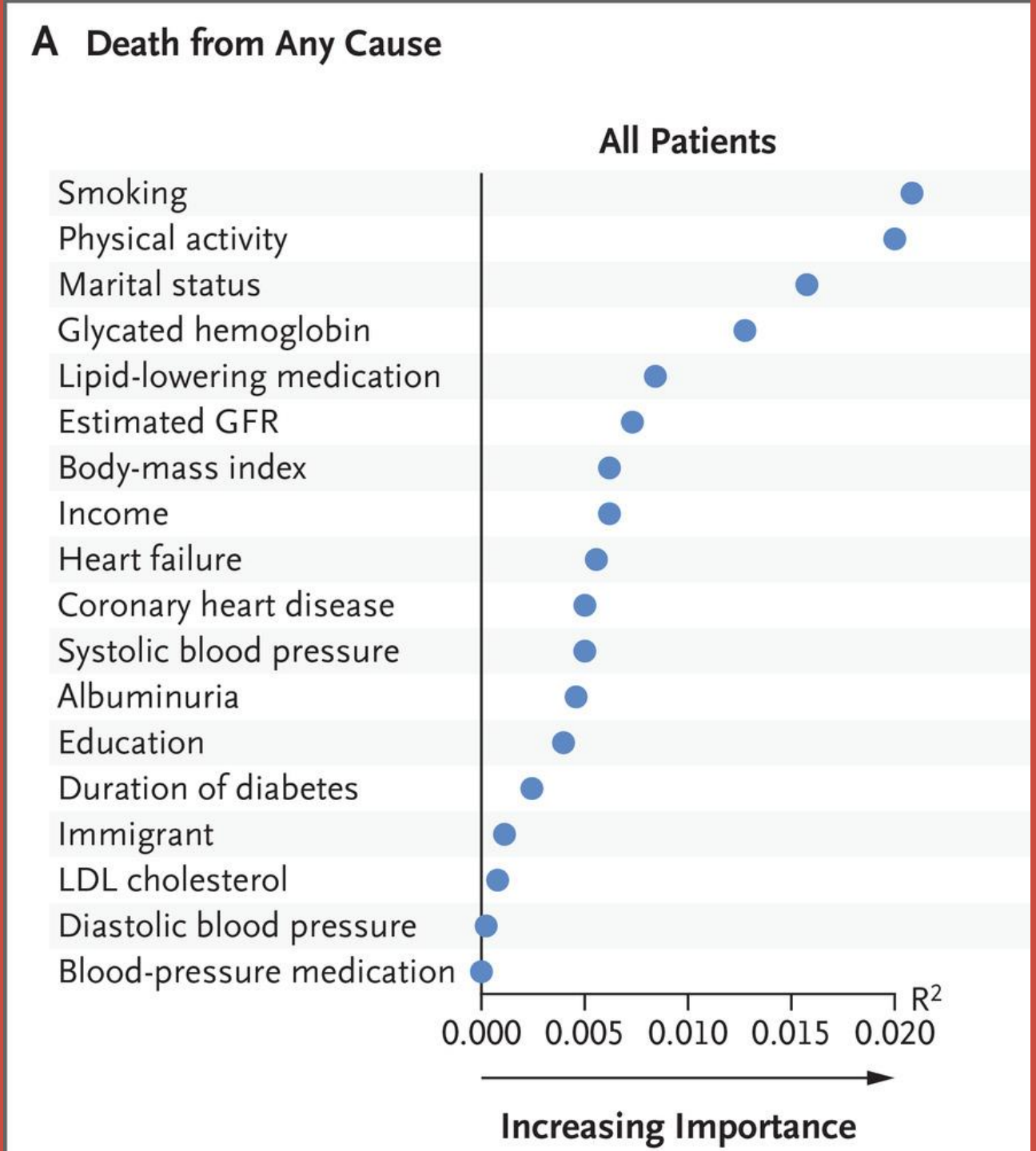


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| Intervention | Annual Event Rate | Risk Reduction | Number Needed to Treat (NNT) | NNT Range | Source |
|---|---|---|---|---|---|
| **ASPIRIN - PRIMARY** | | | Insufficient evidence | | USPTF 2016 |
| **ASPIRIN – SECONDARY**<br>**Fatal and nonfatal CV events** | 2.8% | 0.80 (0.73–0.88) | **201** | **134–302** | *Lancet* 2009;373:1849–60 |
| **STATIN – PRIMARY**<br>**Fatal and nonfatal CV events** | 5.63% | 0.72 (0.65–0.79) | **63** | **51–81** | *Lancet* 2008;371:117–25 |
| **STATIN – SECONDARY**<br>**All coronary events** | 10.5% | 0.78 (0.69–0.87) | **43** | **31–73** | *Ibid* |
| **PCSK9 inhibitor – SECONDARY**<br>**CV events** | 11.3% | 0.85 (0.79–0.92) | **133** | **84–222** | *NEJM* 2017;376:1713-22. (FOURIER) |
| **Statin-associated DM** | 3.5% | 1.13 (1.03–1.23) | **219** | **125–1000** | *Diabetes Care* 2009; 32:1924–1929. |
| **BLOOD PRESSURE CONTROL**<br>**All CV events among diabetics** | 1.3% | 0.89 (0.83–0.95) | **260** | **170–640** | *JAMA.* 2015;313(6):603-615 |
| **TOBACCO CESSATION** | | | **22** | | *Am J Prev Med.* 2010; 39(3): 285–286. |

# Smoking Cessation

- Counselling every visit
- Nicotine replacement
- Medications

# Back To Patient Two:

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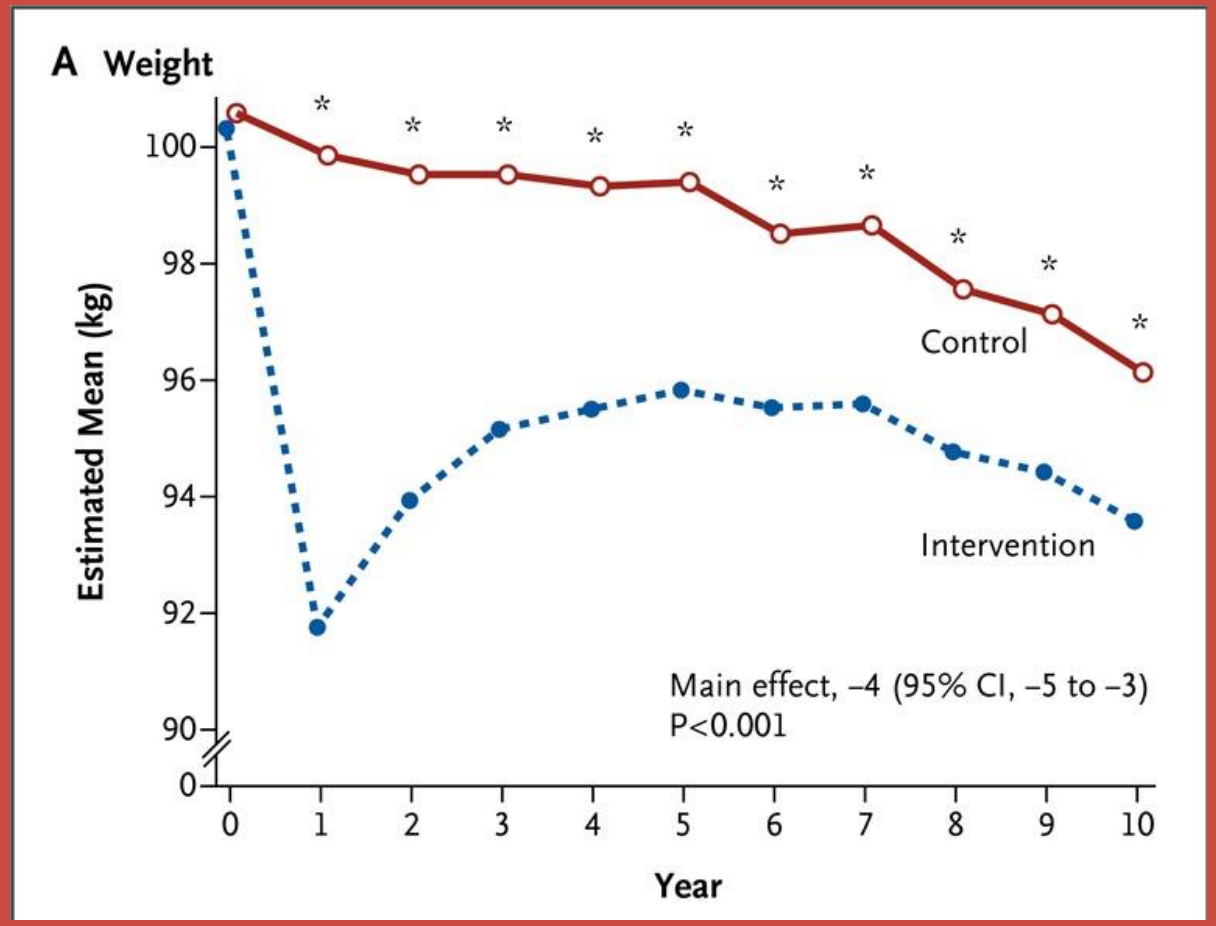
# Back to Patient Two:

He is not interested in smoking cessation but would like to change his diet. Which of the following can decrease cardiovascular events?

a) Ketogenic diet
b) Vegetarian diet
c) Mediterranean diet
d) Calorie restricted diet
e) Any weight loss will reduce CVD risk

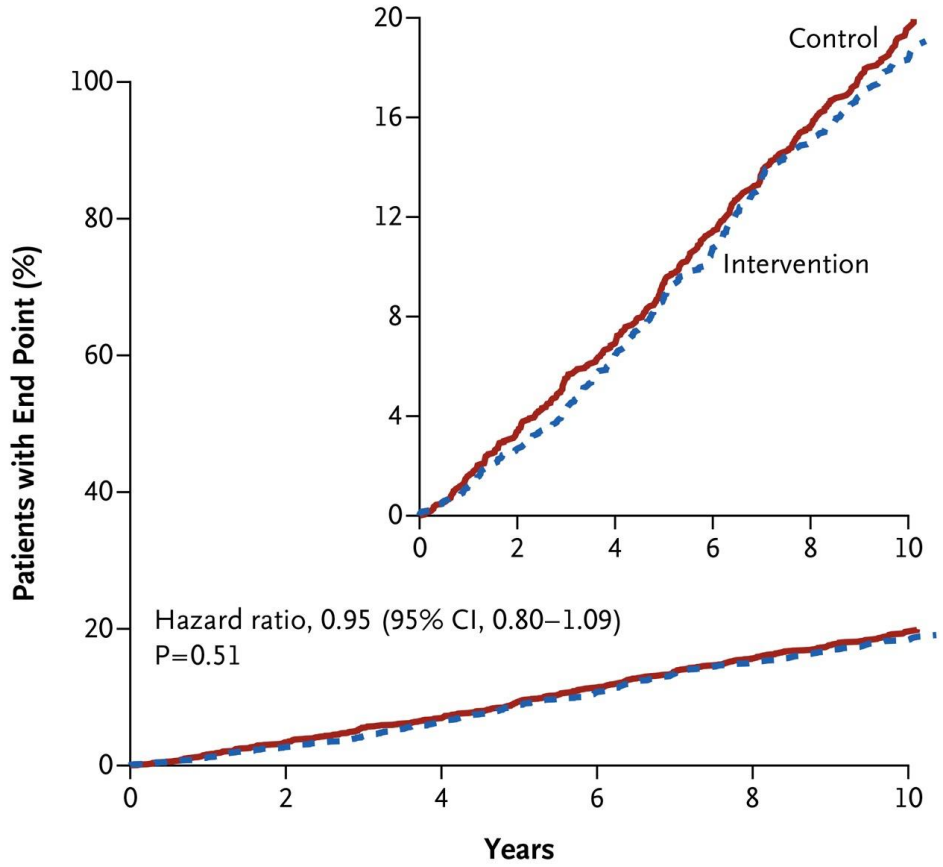
# Lifestyle Intervention: Look AHEAD trial




*N Engl J Med 2013; 369:145-154*

# Lifestyle Intervention: Look AHEAD trial

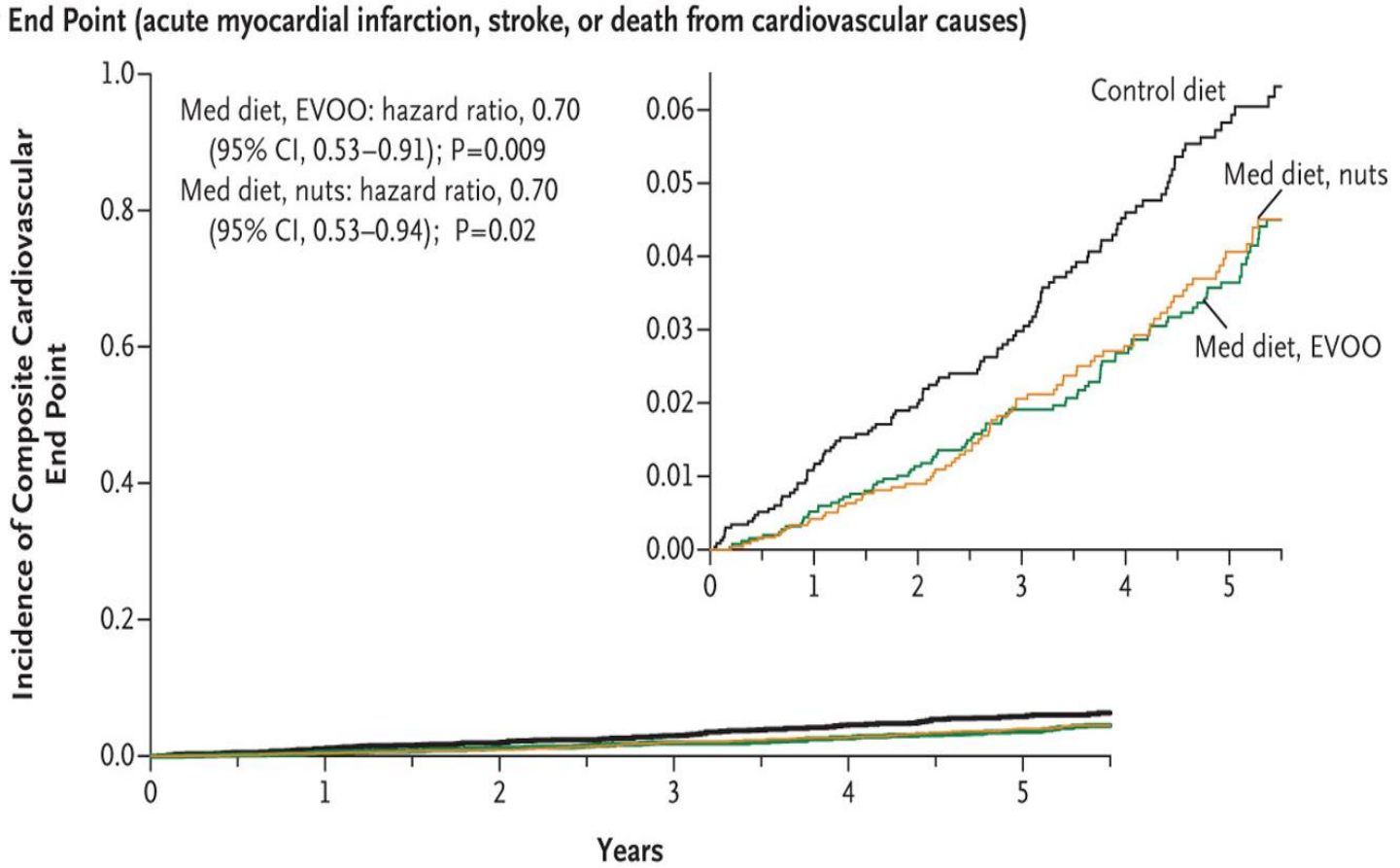
- Improved most CVD risk factors
- Outcome: HR 0.83 to 1.09;P=0.51




| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Control | 2575 | 2425 | 2296 | 2156 | 2019 | 688 |
| Intervention | 2570 | 2447 | 2326 | 2192 | 2049 | 505 |

*N Engl J Med 2013; 369:145-154*

# Lifestyle Intervention: PREDIMED trial




**No. at Risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| Control diet | 2450 | 2268 | 2020 | 1583 | 1268 | 946 |
| Med diet, EVOO | 2543 | 2486 | 2320 | 1987 | 1687 | 1310 |
| Med diet, nuts | 2454 | 2343 | 2093 | 1657 | 1389 | 1031 |

# Lifestyle Intervention:

- ✓5% weight loss should be recommended for overweight and obese DM patients
- ✓Reduced calorie intake is paramount but quality of consumed fat is important

- ✓ Actively help your diabetics to quit smoking every visit

- ✓ Recommend a Mediterranean diet


- ✓ A1C<7% in young and newly diagnosed

- ✓ Add empagliflozin and liraglutide to metformin

# *Thank You For Listening!*

Special Thanks to:
Dr. Jonathan Murrow
Dr. Catherine Apaloo