Management of Diabetes in the Older Adult

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SPED-AACE Annual Meeting

December 15, 2019

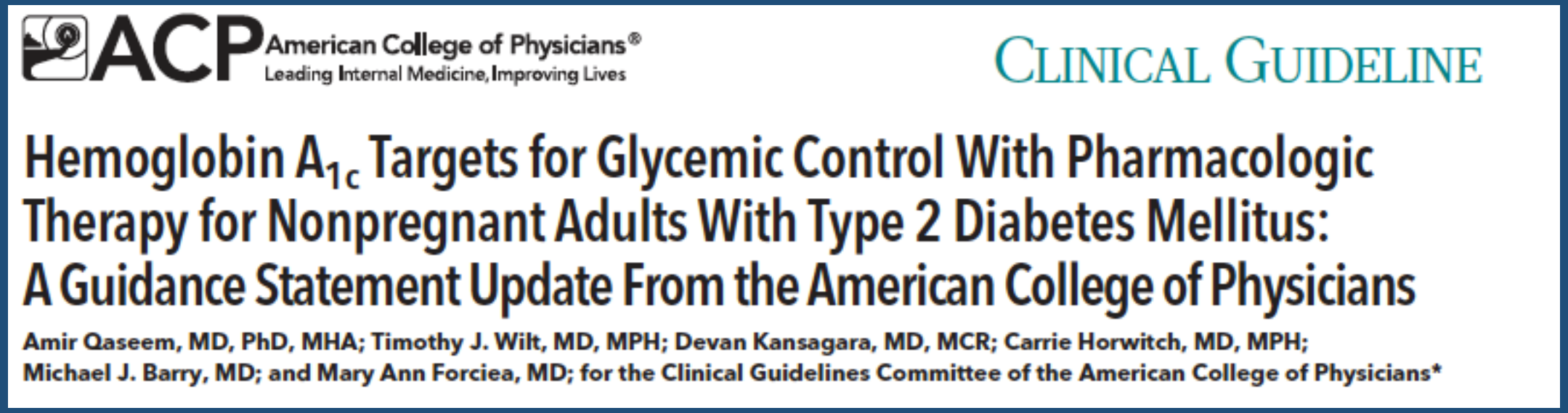
Disclosure

•Dr. Jose M. Garcia Mateo, endocrinologist, declares that he serves as a speaker and consultant for the following pharmaceutical companies: ***Eli Lilly, Astra Zeneca, Sanofi , Amgen, Boehringer Ingelheim, Janseen, Akcea, Abbvie, Medicure and Merck.***

Objectives

- Describe the complexity of managing DM in the elderly patient based on the presence of multiple comorbidities that interfere with therapeutic interventions.
- Discuss clinical practice guidelines for the management of this growing population in our society with emphasis in those recently published by the Endocrine Society.
- Present various clinical scenarios commonly seen in practice for discussion of different therapeutic options that may or may not be applied to this challenging diabetic population.

ACP 2018 A1C Targets for Glycemic Control Practically Starts This Controversy



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CLINICAL GUIDELINE

Hemoglobin A_{1c} Targets for Glycemic Control With Pharmacologic Therapy for Nonpregnant Adults With Type 2 Diabetes Mellitus: A Guidance Statement Update From the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Timothy J. Wilt, MD, MPH; Devan Kansagara, MD, MCR; Carrie Horwitch, MD, MPH; Michael J. Barry, MD; and Mary Ann Forciea, MD; for the Clinical Guidelines Committee of the American College of Physicians*

ACP 2018 A1C Targets for Glycemic Control

- ***Guidance Statement 4: Clinicians should treat patients with type 2 diabetes to minimize symptoms related to hyperglycemia and avoid targeting an HbA1c level in patients with a life expectancy less than 10 years due to advanced age (80 years or older), residence in a nursing home, or chronic conditions (such as dementia, cancer, end-stage kidney disease, or severe chronic obstructive pulmonary disease or congestive heart failure) because the harms outweigh the benefits in this population.***


TYPE 2 DIABETES

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E02. Diabetes in Older Adults Guideline: *An Endocrine Society Clinical Practice Guideline*

Read the guideline and associated resources by navigating to endocrine.org/2019Diabetes

ENDO2019

Guideline Writing Committee

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Key Points

- Prediabetes is highly prevalent in older people, however, interventions to delay progression from prediabetes to diabetes are especially effective in this age group.
- The prevalence of type 2 diabetes increases as individuals age and exaggerates the incidence of both microvascular and macrovascular complications.
- Clinicians should perform regular screening for prediabetes and diabetes in the older population and implement interventions as indicated in this guideline.
- Given the heterogeneity of the health status of older people with diabetes, the guideline emphasizes shared decision-making and provides a framework to assist health care providers to individualize treatment goals.

Key Points (cont.)

- The problems that older individuals with diabetes face, in contrast to younger people with the disease, include sarcopenia, frailty and cognitive dysfunction. Such complications can lead to an increased risk of poor medication adherence, hypoglycemia (from certain medications), falls, and loss of independence in daily living activities.
- The guideline presents evidence for the various effects of diabetes in the older patients and the relevant therapies for glycemic control, hyperlipidemia and hypertension.
- Guideline recommendations also address common co-morbidities such as renal impairment, which affects the pharmacokinetics and pharmacodynamics of specific agents, and concomitant heart disease.

Case Questions

Case 1: Screening

Case 1

- 77 y/o widowed Hispanic lady retired living alone
- Good health and active. Independent living w/o any help
- + Aortic Stenosis + HTN: BP 125/68. BMI 28 kg/m2. SEM III/VI.
- Sisters with history of DM2
- Annual screening: FBS 115 mg/dL
- Lipids: TC: 115; TG 162; HDL-C 43; LDL:48; nonHDL 72.
- She is very concerned about her risk for DM.

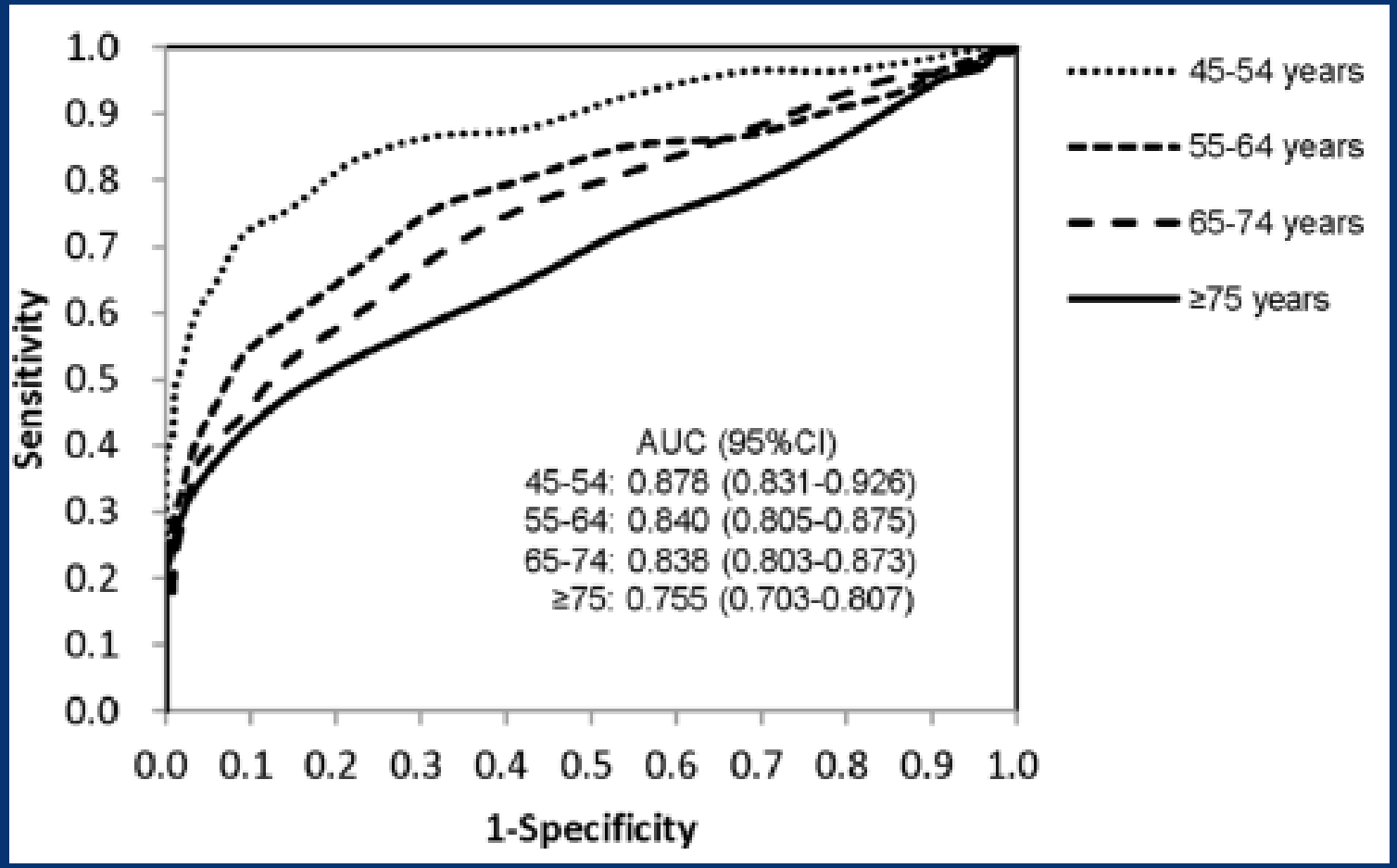
Case #1: Screening (cont.)

Question: What is the next best test, according to the new Endo Society CPG, to establish whether or not she has diabetes? *(Audience Response)*

A. HbA1C level
B. 2 hour post 75 gm OGTT
C. Fructosamine
D. 2 hour postprandial BG

Age and Diagnostic Accuracy of HbA1c

- The diagnostic accuracy of HbA1c decreases with age.



Wu L, et al. PLoS One. 2017;12(9):e0184607

Proportion of U.S. Population with Diagnosed and Undiagnosed Diabetes NHANES 2011-2012

Age Group	A1c/FPG	A1c/FPG/2hrPG
20-44 yrs	4.5%	5.0%
45-64 yrs	16.2%	17.5%
>65 yrs	24.7%	33.0%

Menke et al., AMA 2015;314:1021

Conditions Affecting Hemoglobin A_{1c}

- Hemoglobin A_{1c} values are influenced by red blood cell survival; thus, falsely high values in relation to mean blood glucose values can be obtained when red blood cell turnover is low, resulting in a disproportionate number of older red cells; this problem can occur in patients with iron, vitamin B_{12}, or folate deficiency anemia
- In contrast, rapid red blood cell turnover leads to a greater proportion of younger red cells and falsely low hemoglobin A_{1c} values; examples include patients with hemolysis; patients treated for iron, vitamin B_{12}, or folate deficiency; and patients treated with erythropoietin

These conditions are common in the elderly patient.

Case 2:
Glucose Target – Assess Overall Health

Case 2

- 68 y/o Hispanic male with DM2 for 20 years with inconsistent glycemic control.
- Started initially on SU and then added metformin both at maximal doses.
- A1C increased over time to 9% but reluctant to start insulin due to concern of hypoglycemia as he worked climbing light poles at AEE and still perform high risk physical tasks at home.
- HTN and dyslipidemia and has been inconsistent with health care and prescribed Rx. Costs of therapy was an issue as his insurance was cut short.
- Now retired and on Medicare with better access to healthcare. Wife concerned about he is more forgetful and slightly disoriented. He wants to improve his condition as he understands that poor glycemic control can lead to complications .

Case 2

- Chronic back pain and markedly reduced night vision.
- + nocturia, no SMBG and minimal diabetes education.
- PE: Older for age, oriented to person but not to place or time. Bath, dress and toilet by himself but has issues managing his finances and taking his meds.
- BP = 165/95, BMI = 27.4 kg/m2. Bilateral cataracts and evidence of retinal bleeding on fundoscopic exam. His cardiac, pulmonary and abdominal exams are WNL. He has absent lower extremity reflexes and reduced pedal pulses. On foot exam his nails are thickened, he has callous formation and a loss of proprioception and sensation.

Case #2: Glucose Target – Assess Overall Health (cont.)

His HbA1c = 9.2%. LDL = 136 mg/dl, HDL = 36 mg/dl and TG = 237 mg/dl, eGFR = 36 and 2+ protein in his urine.

Question: What would be your initial target HbA1c for this patient? *(Audience Response)*

A. Less than 9% and 8% or greater
B. Less than 8.5%
C. Less than 8% and 7.5% or greater
D. Less than 7.5%

Key Recommendation for Overall Health Assessment

- In patients aged 65 and older with diabetes, we advise assessing the patient's overall health and personal values prior to the determination of treatment goals and strategies (see Framework). (Ungraded Good Practice Statement)

Overall Health Assessment - Framework

		Good Health	Intermediate Health	Poor Health
Patient characteristics		≤2 chronic conditions* *AND* No ADL impairments and ≤1 IADL impairment	≥3 chronic conditions* *AND/OR* Any of the following: • Mild cognitive impairment / early dementia • ≥2 IADL impairments	Any of the following: • End-stage medical condition • Moderate to severe dementia • ≥2 ADL impairments • Residence in a long-term nursing facility
HbA1c goal		Shared decision making: *individualized* targets may be lower or higher		
Use of drugs that may cause hypoglycemia? (e.g., insulin, SU, glinides)	No	**<7.5%** *FPG: 90-130 md/dL HS: 90-150 mg/dL*	**<8%** *FPG: 90-150 md/dL HS:100-180 mg/dL*	**<8.5%** *FPG: 100-180 md/dL HS: 110-200 mg/dL*
	Yes	**<7.5% *and* ≥7%** *FPG: 90-150 md/dL HS: 100-180 mg/dL*	**<8% *and* ≥7.5%** *FPG: 100-150 md/dL HS: 150-180 mg/dL*	**<8.5% *and* ≥8%** *FPG: 100-180 md/dL HS: 150-250 mg/dL*

Adapted from: Cigolle CT, et al. *J Gerontol A Biol Sci Med Sci. 2012; 67:1313-20 and* Kirkman, et al. *Diabetes Care.* 2012;35:2650-64.

Step 1: Assessing Overall Health

	Good Health	Intermediate Health	Poor Health
Patient characteristics	≤2 chronic conditions* ***AND*** No ADL impairments and ≤1 IADL impairment	≥3 chronic conditions* ***AND/OR*** Any of the following: • Mild cognitive impairment / early dementia • ≥2 IADL impairments	Any of the following: • End-stage medical condition ** • Moderate to severe dementia • ≥2 ADL impairments • Residence in a long-term nursing facility

* Does not include diabetes **e.g. metastatic cancer, oxygen-requiring COPD
ADL: activities of daily living (e.g., eating, bathing, dressing)
IADL: instrumental activities of daily living (e.g., managing money, doing housework)

Step 2: Identify HbA1c and Glucose Targets

		Good Health	Intermediate Health	Poor Health
HbA1c goal				
Is the patient taking drugs that may cause hypoglycemia? (e.g., insulin, SU, glinides)	No	**<7.5%** *FPG: 90-130 md/dL* *HS: 90-150 mg/dL*	**<8%** *FPG: 90-150 md/dL* *HS:100-180 mg/dL*	**<8.5%** *FPG: 100-180 md/dL* *HS: 110-200 mg/dL*
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Inclusion of a floor value to prevent hypoglycemia risk

Case 2: Recommended Antidiabetic Rx

- As he is already on metformin can keep on it but at a max 1 gram daily (GFR 30-45 ml/min) dose.
- Due to cost issues can maintain SU but at lower dose and glipizide is preferred as it's metabolite is inactive if accumulated based on his renal status.
- Add basal insulin with a simple titration algorithm but include family for support.
- GLP1RA is an excellent option for glycemic control and improve compliance (weekly presentations) but costs and GI SE's are barriers.
- SGLT2i attractive for renal protection **(not for glycemic control**) based on CREDENCE but cost and complication of therapeutic regimen has to be considered in this patient.
- A1C too high for a DPP4i.

Case 3:
Medication Selection to Minimize Hypoglycemia

Case 3

- 72 year old Hispanic female with a 20+ year history of type 2 diabetes.
- A1C of 6.8 –7.5%. Eats carefully, takes her meds and goes to an exercise class for seniors 3 x wk.
- For the past 10 years has been on long acting insulin with premeal RAI. She occasionally uses a correction scale before meals.
- Recently she has noted a decrease in her appetite. She fell and fractured her right wrist and this has made management of her diabetes more difficult.
- Lives with her family but she is alone most of the day.
- Episodes of mild hypoglycemia several times per week lately.
- eGFR fallen from 60 to 30 over the past two years. BMI: 24.3 kg/m2.

Overall Health Assessment - Framework

		Good Health	Intermediate Health	Poor Health
Patient characteristics		≤2 chronic conditions* *AND* No ADL impairments and ≤1 IADL impairment	≥3 chronic conditions* *AND/OR* Any of the following: • Mild cognitive impairment / early dementia • ≥2 IADL impairments	Any of the following: • End-stage medical condition • Moderate to severe dementia • ≥2 ADL impairments • Residence in a long-term nursing facility
HbA1c goal		Shared decision making: *individualized* targets may be lower or higher		
Use of drugs that may cause hypoglycemia? (e.g., insulin, SU, glinides)	No	**<7.5%** *FPG: 90-130 md/dL HS: 90-150 mg/dL*	**<8%** *FPG: 90-150 md/dL HS:100-180 mg/dL*	**<8.5%** *FPG: 100-180 md/dL HS: 110-200 mg/dL*
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Adapted from: Cigolle CT, et al. *J Gerontol A Biol Sci Med Sci. 2012; 67:1313-20 and* Kirkman, et al. *Diabetes Care.* 2012;35:2650-64.

Case #3: Medication Selection to Minimize Hypoglycemia

Question: Which approach would most safely and effectively reduce her risk of hypoglycemia? *(Audience Response)*

A. Attempting to taper her off prandial insulin onto a regimen of basal insulin plus a DPPIV-inhibitor

B. Changing her rapid acting insulin to after-eating rather than before meals

C. Attempting to taper her off prandial insulin onto a regimen of basal insulin plus metformin

D. Adding a GLP-1 RA

Key Recommendation for Medication Selection to Minimize Hypoglycemia

- In patients aged 65 years and older with diabetes, we recommend that outpatient diabetes regimens be designed specifically to minimize hypoglycemia. (1⊕⊕⊕O)

  Technical Remark:

  Although evidence for specific targets is lacking, glycemic targets should be tailored to overall health and management strategies (e.g., whether or not a medication that can cause hypoglycemia is used) (see Framework).

Case 3: Recommended Antidiabetic Rx

- Consider a higher A1C target or adding a floor.
- Although the change from RAI to DPP4i can lead to a worsening of glycemic control, she still has room for a higher target and prevent hypoglycemia using a floor. Still basal insulin can be optimized if no nocturnal or fasting hypoglycemia. If cost is not a barrier ultrabasal insulins as glargine U300 or degludec are options with less hypoglycemia. If high risk for HHF avoid saxagliptin.
- Using RAI post meal is another option for this patient at the expense of maintaining a complicated regimen and still hypoglycemia may be an issue.
- A less complicated regimen with premixed insulin BID or QD with an oral agent is an alternative.
- Metformin not a good option to start in this patient with GFR 30-45 ml/min and recent renal deterioration.

Case 3: Recommended Antidiabetic Rx

- GLP1RA not an attractive option based on patient's recent loss of appetite where gastroparesis may be the cause and also promoting weight loss can lead to sarcopenia.
- SGLT2i despite it's cardiorenal benefits is not a good option for this patient that may be at risk for orthostatism and hypotension (ck for AHA's) that can further increase further the risk of fall and fractures (seen in CANVAS). Also at her GFR it's glycemic efficacy is poor.
- TZD has low risk for hypoglycemia but are associated with fractures and HF.
- Professional CGM is an excellent tool to evaluate glycemic variability and timing of hypo and hyperglycemic excursions and can motivate patient to use a personal device. These devices help in therapeutic decisions with antidiabetic regimen efficacy and safety. Also in this population can mitigate the issues with A1C due to alterations in RBC turnover.

Case 4:
Lipid Management

Case 4

- 90 year male with10 year history DM2.
- Rx with metformin and a DPP-IV inhibitor with A1C of 6.6%.
- No family or personal hx of CVD and no cardiac symptoms. No HTN.
- Concerned that LDL-C has gone up from 95 to 126 mg/dl.
- He has read that statin Rx should be started if his LDL > 100 mg/dl and wants your opinion.

Question: You tell him:

A.Gentle diet modification to lower his cholesterol

B. Start on a statin

C. Start on ezetimibe

D. Marker of CV risk (hsCRP, CAC, Lp(a),etc)

E. See a cardiologist for testing

Key Recommendation for Lipid Management

- In patients aged 65 years and older with diabetes, we recommend statin therapy and the use of an annual lipid profile to achieve the recommended levels for reducing absolute CVD events and all-cause mortality. (1⊕⊕⊕⊕)

  Technical Remarks:

  - *Since the Writing Committee did not rigorously evaluate the evidence for specific LDL-C targets in this population, we refrained from endorsing specific LDL-C targets in this guideline.*
  - *For patients aged 80 years old and older or with short life expectancy, we advocate that LDL-C goal levels should not be so strict.*

PROSPER

5,804 high-risk elderly patients

- Age 70–82 years
- Pre-existing vascular disease (coronary, cerebral, or peripheral)
- High-risk for vascular disease (smoking, hypertension, or diabetes)
- Total cholesterol 4.0–9.0 mmol/L
- Triglyceride < 6.0 mmol/L

Pravastatin
40 mg per day
n = 2,891

Placebo
n = 2,913

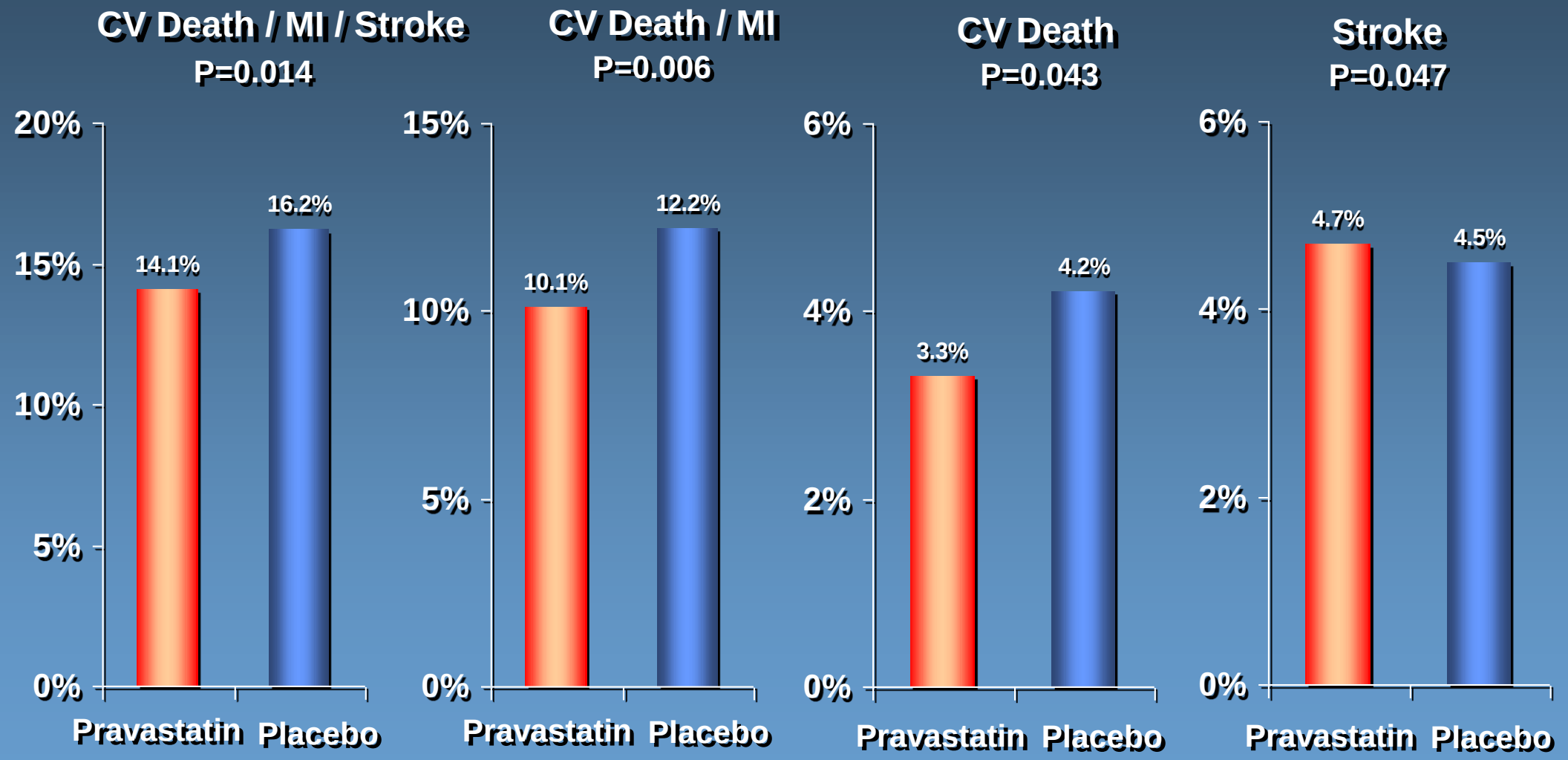
Average follow-up = 3.2 years

Endpoints:

- Primary – composite of coronary death, non-fatal myocardial infarction, and fatal or non-fatal stroke

Lancet 2002; 360: 1623–30

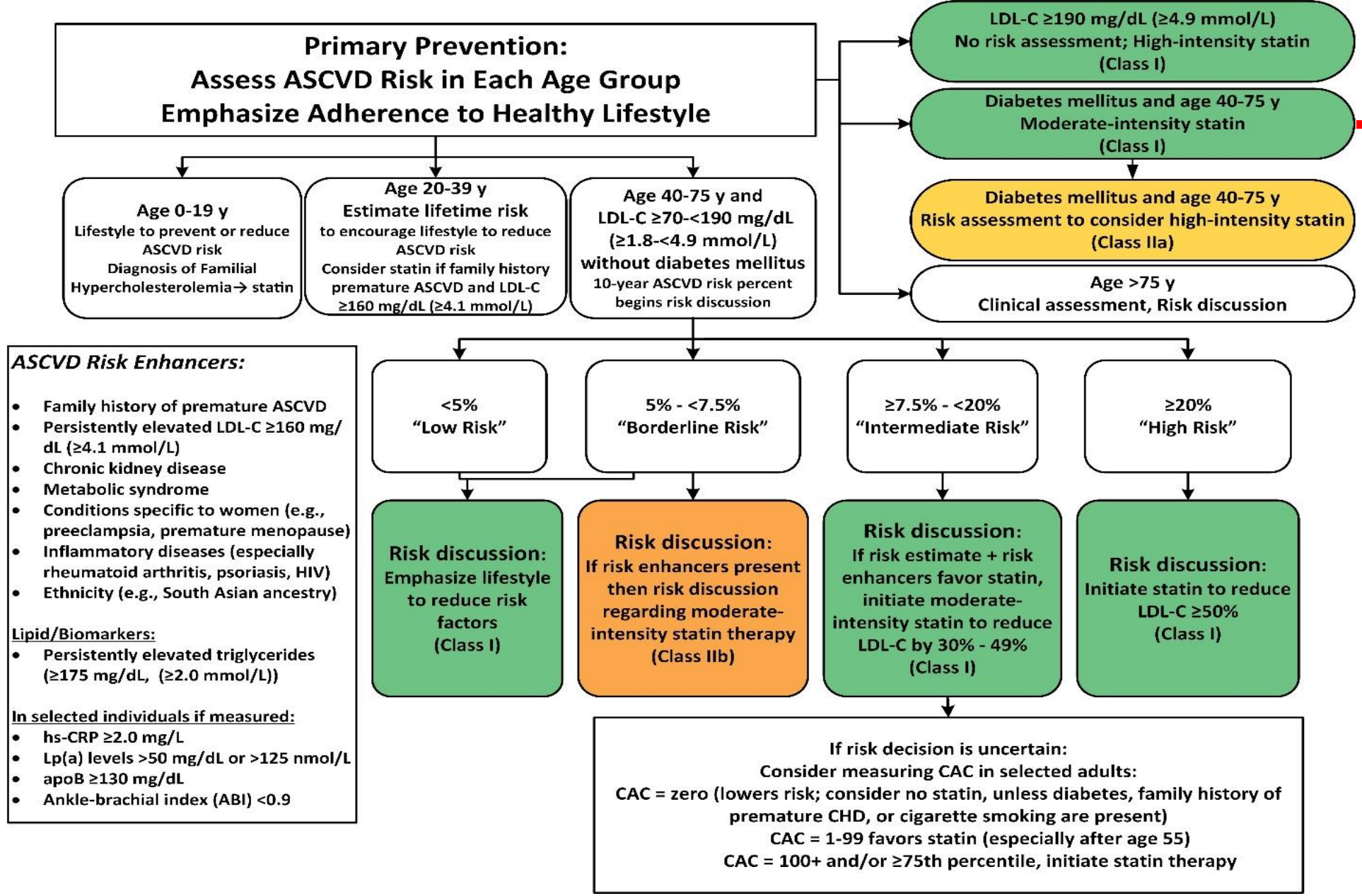
PROSPER: Clinical Events*



www.Clinical trial results.org

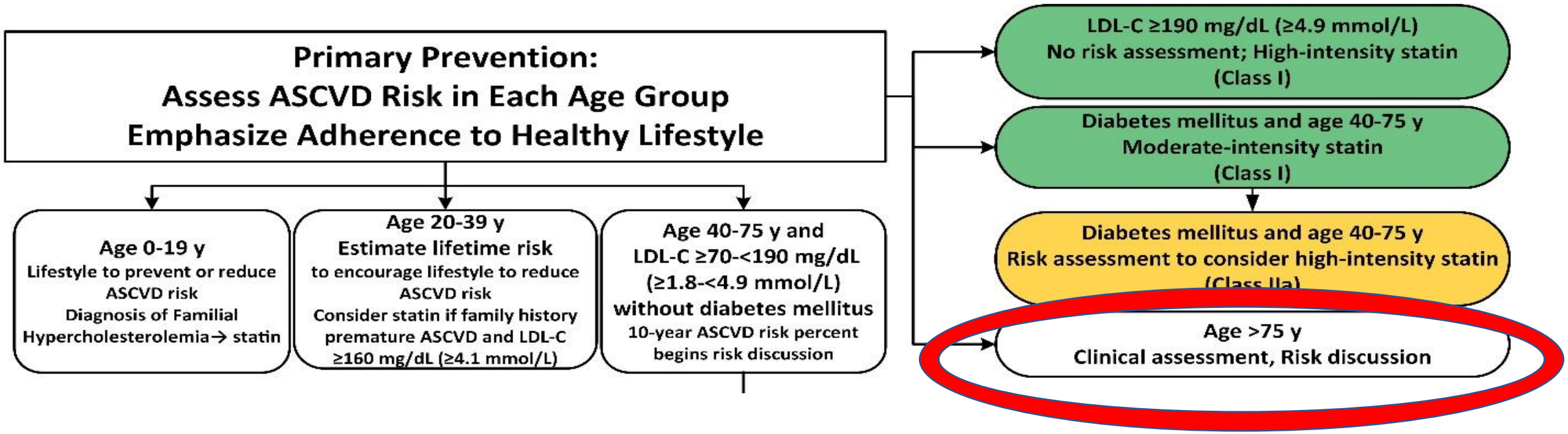
* Mean follow-up = 3.2 years

Lancet 2002; 360: 1623–30



AMERICAN COLLEGE of CARDIOLOGY

American Heart Association.



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American Heart Association.

Primary Prevention in Other Age Groups (Older Adults)

Recommendations for Older Adults		
COR	**LOE**	**Recommendations**
IIb	**B-R**	**In adults 75 years of age or older with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), initiating a moderate-intensity statin may be reasonable.**
IIb	**B-R**	**In adults 75 years of age or older, it may be reasonable to stop statin therapy when functional decline (physical or cognitive), multimorbidity, frailty, or reduced life-expectancy limits the potential benefits of statin therapy.**
IIb	**B-R**	**In adults 76 to 80 years of age with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it may be reasonable to measure CAC to reclassify those with a CAC score of zero to avoid statin therapy.**

Case 4

Question: You tell him:

A.Gentle diet modification to lower his cholesterol

B. Start on a statin

C. Start on ezetimibe

D. Marker of CV risk (hsCRP, CAC, Lp(a),etc)

E. See a cardiologist for testing

Consider use higher CAC risk cutpoint (> 100) as most > 65 y/o patients have coronary calcification due to aging.

Case 5:
Hypertension Management

Case 5

- 66 y/o hispanic F
- T2D x 20 years
- HTN x 25 years
- CAD, s/p CABG, systolic CHF w EF 25%
- Has DKD:
  - Cr up to 2's; UACR: 900 mg/g creat
  - On carvedilol 25 mg bid: HR 65 BP 145/90
  - On max dose irbesartan and amlodipine

    - **BP CONTROL ?? < 130/80 or < 140/90**

ACCORD BP Study: Primary and Secondary Outcomes

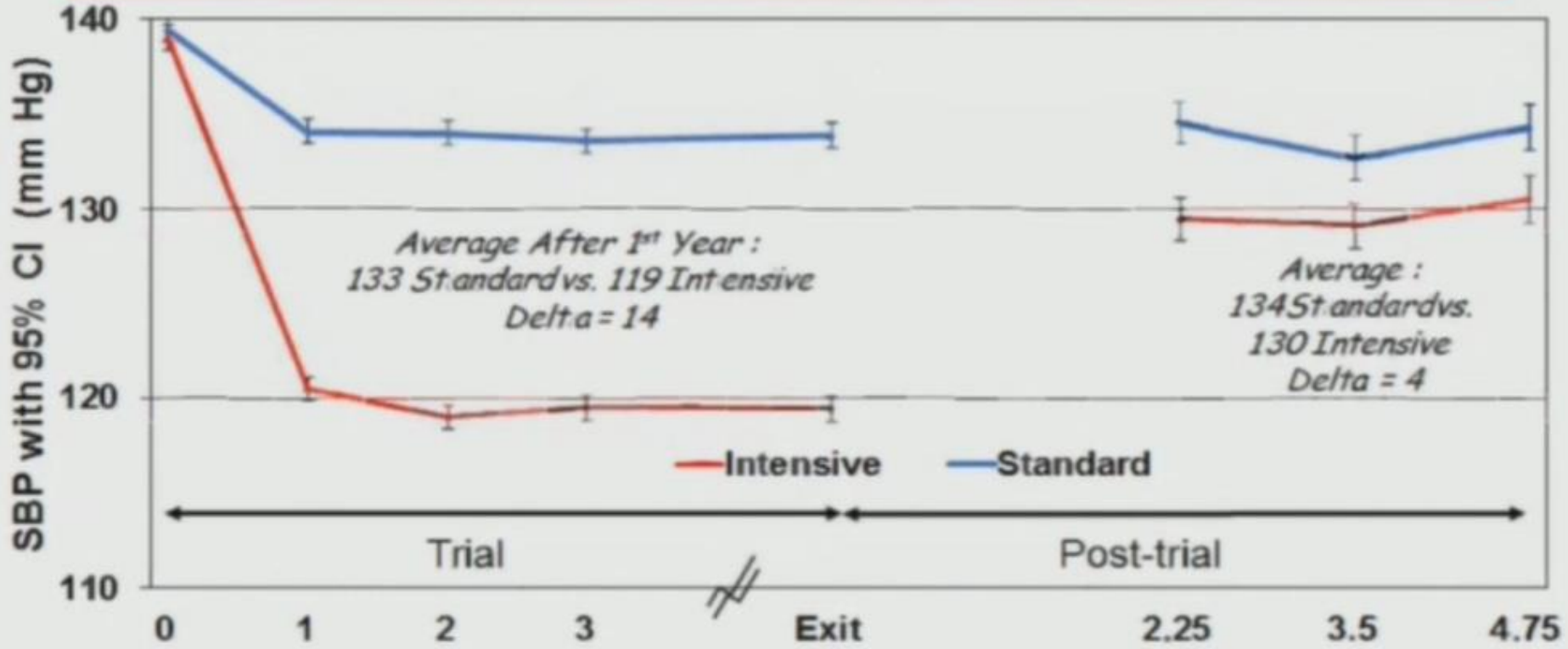
- Patients with T2D and hypertension (N = 4733)
- Random assignment
  - Intensive therapy: target SBP < 120 mm Hg
  - Standard therapy: target SBP < 140 mm Hg
- 1° outcome: nonfatal MI, nonfatal stroke, death from CV causes
- Mean follow-up = 4.7 y

Outcome	Intensive	Standard	HR	*P*-value
SBP after 1 year (mmHg)	119.3	133.5	NR	NR
1° outcome (annual rate)	1.87	2.09	0.88	.20
Death from any cause (annual rate)	1.28	1.19	1.07	.55
Stroke (annual rate)	0.32	0.53	0.59	.01
AEs (rate)	3.3	1.3	NR	<.001

The ACCORD Study Group. *N Engl J Med.* 2010 March 14. [Epub ahead of print].

ACCORDION
ACCORD TRIAL FOLLOW-ON STUDY

SBP Over Time (years)



Mean Number of Medications Prescribed

Intensive	3.2	3.4	3.4	3.4	2.3	2.2	2.1
Standard	1.9	2.1	2.1	2.2	2.0	1.9	1.9
Intensive N =	2174	2071	1973	2019	1132	1223	1147
Standard N =	2208	2136	2077	2062	1218	1279	1196

Cushman WC et.al. AHA presentation 2015

Hypertension: The SPRINT Systolic blood PRessure INtervention Trial

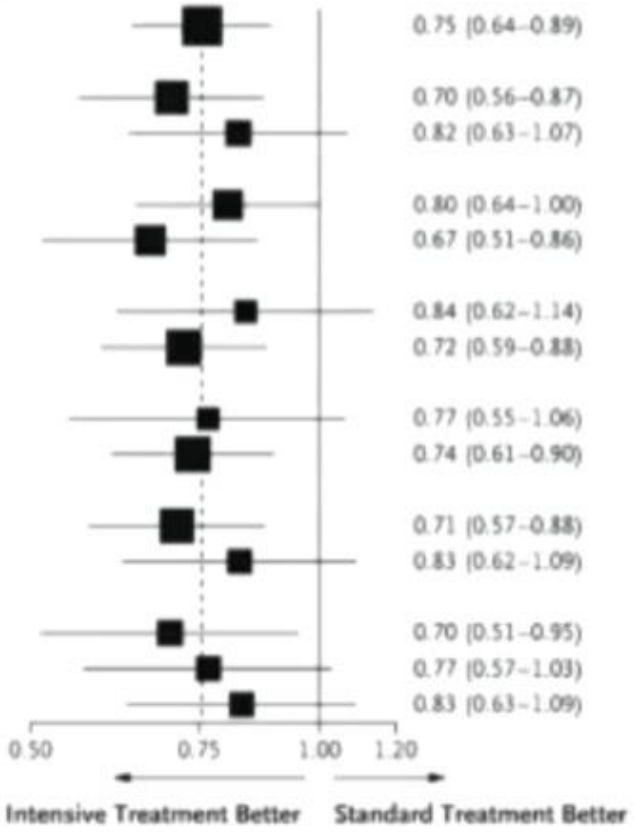
- Randomized Controlled Trial of SBP <140 vs. SBP<120 in non-diabetic people older than 50, who were at higher risk of cardiovascular events
- Primary outcome: Composite of MI, other acute coronary syndromes, stroke, heart failure, cardiovascular death
- Secondary outcomes: many including all-cause death
- 9361 participants, 28% with CKD (GFR<60), 28% were ≥ 75 years old
- Study stopped after a mean f/u of 3.26 years due to lower rate of primary outcome in the intensive arm
- Primary outcome: 1.65% intensive, 2.19% standard
- All-cause mortality: 155 deaths intensive, 210 deaths standard, HR 0.73 (0.6-0.9)

Treatment Arm	Standard	Intensive
SBP achieved, mean	136.2 mm Hg	121.4 mm Hg
Primary outcome	2.2% per year	1.7% per year
All-cause mortality	210 deaths	155 deaths

HR 0.73 (0.6-0.9)!

Hypertension: The SPRINT
Systolic blood PRessure INtervention Trial

Subgroup	Intensive Treatment	Standard Treatment	Hazard Ratio (95% CI)	*P* Value for Interaction
	no. of patients with primary outcome/total no. (%)			
Overall	243/4678 (5.2)	319/4683 (6.8)	0.75 (0.64–0.89)	
Previous CKD				0.36
No	135/3348 (4.0)	193/3367 (5.7)	0.70 (0.56–0.87)	
Yes	108/1330 (8.1)	126/1316 (9.6)	0.82 (0.63–1.07)	
Age				0.32
<75 yr	142/3361 (4.2)	175/3364 (5.2)	0.80 (0.64–1.00)	
≥75 yr	101/1317 (7.7)	144/1319 (10.9)	0.67 (0.51–0.86)	
Sex				0.45
Female	77/1684 (4.6)	89/1648 (5.4)	0.84 (0.62–1.14)	
Male	166/2994 (5.5)	230/3035 (7.6)	0.72 (0.59–0.88)	
Race				0.83
Black	62/1454 (4.3)	85/1493 (5.7)	0.77 (0.55–1.06)	
Nonblack	181/3224 (5.6)	234/3190 (7.3)	0.74 (0.61–0.90)	
Previous cardiovascular disease				0.39
No	149/3738 (4.0)	208/3746 (5.6)	0.71 (0.57–0.88)	
Yes	94/940 (10.0)	111/937 (11.8)	0.83 (0.62–1.09)	
Systolic blood pressure				0.77
≤132 mm Hg	71/1583 (4.5)	98/1553 (6.3)	0.70 (0.51–0.95)	
>132 to <145 mm Hg	77/1489 (5.2)	106/1549 (6.8)	0.77 (0.57–1.03)	
≥145 mm Hg	95/1606 (5.9)	115/1581 (7.3)	0.83 (0.63–1.09)	

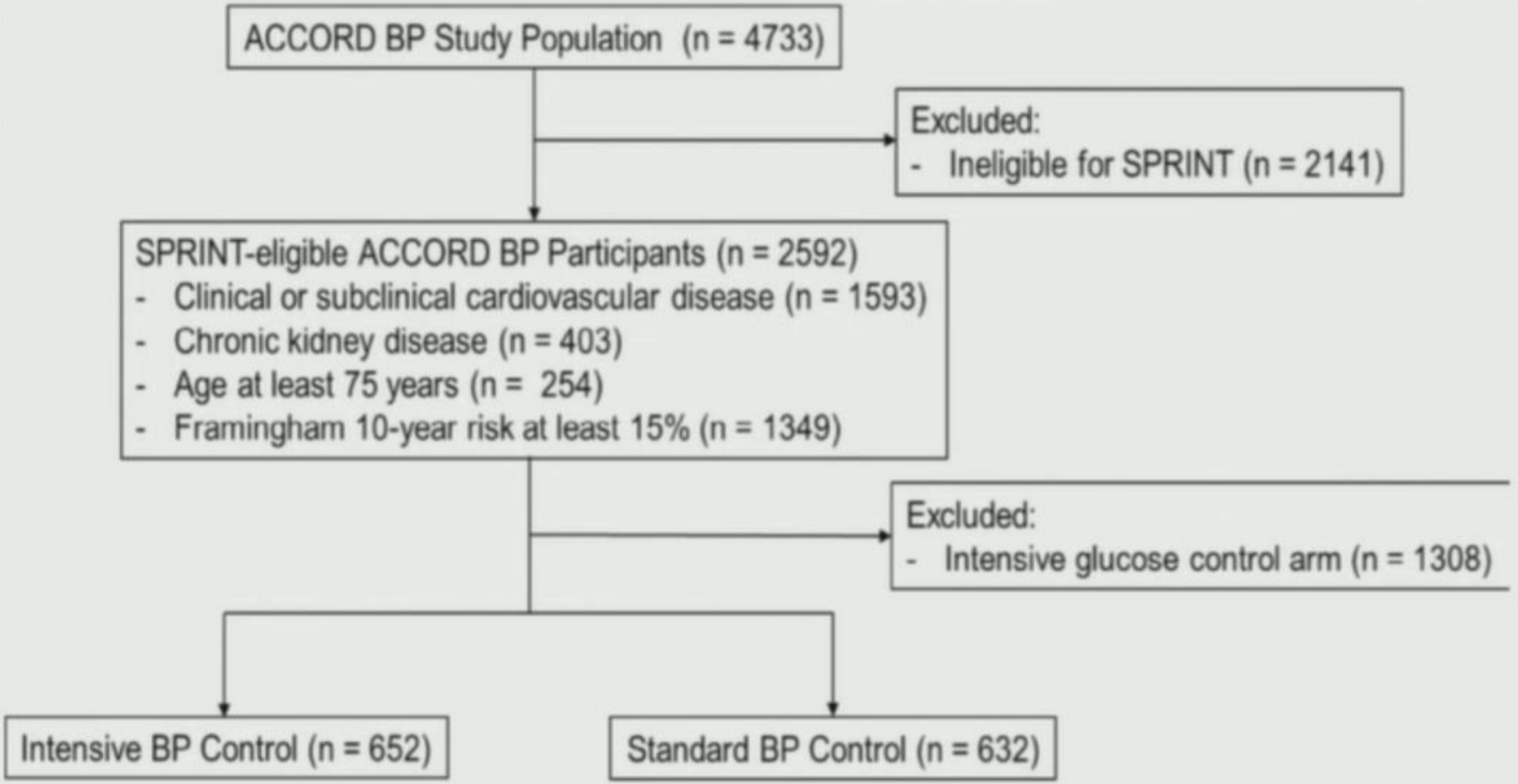


Renal Disease Outcomes

		Intensive		Standard			
		Events	%/yr	Events	%/yr	HR (95% CI)	P
Participants with CKD at Baseline							
	Primary CKD outcome	**14**	**0.33**	**15**	**0.36**	**0.89 (0.42, 1.87)**	**0.76**
	≥50% reduction in eGFR*	10	0.23	11	0.26	0.87 (0.36, 2.07)	0.75
	Dialysis	6	0.14	10	0.24	0.57 (0.19, 1.54)	0.27
	Kidney transplant	0	-	0	-	-	.
	Secondary CKD Outcome						
	Incident albuminuria**	49	3.02	59	3.90	0.72 (0.48, 1.07)	0.11
Participants without CKD at Baseline							
	Secondary CKD outcomes						
	≥30% reduction in eGFR*	127	1.21	37	0.35	**3.48 (2.44, 5.10)**	**<.0001**
	Incident albuminuria**	110	2.00	135	2.41	0.81 (0.63, 1.04)	0.10

*Confirmed on a second occasion ≥90 days apart **Doubling of urinary albumin/creatinine ratio from <10 to >10 mg/g

Consort Diagram of ACCORDIAN Study



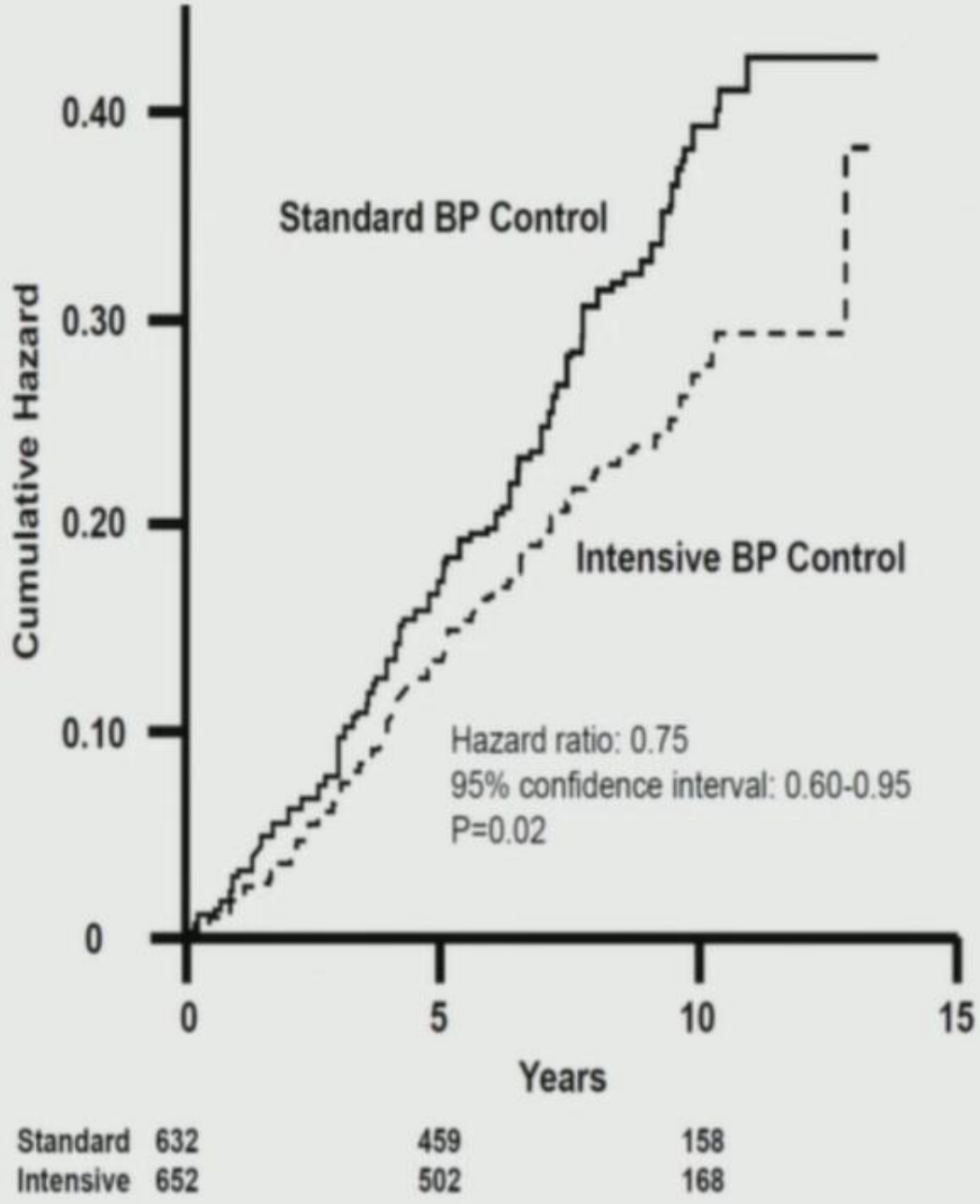
Buckley L et.al. Diab Obes Metab 2018, In press

Intensive Blood Pressure Control in Patients with Type 2 Diabetes Mellitus Over 9 Years of Follow-Up: A Subgroup Analysis of High-Risk ACCORDION Trial Participants

Buckley L et.al Diab Obes Metab, in press

Characteristic	Intensive BP Control (n = 652)	Standard BP Control (n = 632)	P-Value
Age, years	63.9±7.8	63.8±7.9	0.72
Female sex, n (%)	200 (30.7)	190 (30.1)	0.81
Criteria for SPRINT eligibility			
History of cardiovascular disease, n (%)	392 (60.1)	391 (61.9)	0.52
Chronic kidney disease, n (%)	99 (15.2)	84 (13.3)	0.58
Age at least 75 years, n (%)	57 (8.7)	59 (9.3)	0.71
Framingham risk score, n (%)	332 (50.9)	339 (53.6)	0.70
Current smoking, n (%)	106 (16.3)	98 (15.5)	0.71
Heart failure, n (%)	43 (6.6)	44 (7.0)	0.79
Baseline systolic blood pressure, mm Hg	139.8±16.7	140.8±16.4	0.30
Baseline diastolic blood pressure, mm Hg	74.6±10.6	75.4±10.5	0.19
Estimated glomerular filtration rate, mL/min/1.73 m^2	87.9±26.3	87.8±24.4	0.98
Non-high density lipoprotein cholesterol (mg/dL)	150.3±48.0	148.9±48.0	0.59
Statin use, n (%)	457 (69.9)	444 (70.3)	0.49
Aspirin use, n (%)	400 (61.3)	347 (54.9)	0.02
Framingham 10-year coronary heart disease risk score, %	14.5±9.2	14.8±9.2	0.56
Hemoglobin A1c, %	8.3±1.1	8.3±1.1	0.63

Intensive BP control reduced the risk of the main outcome (*composite of CV death, nonfatal MI and nonfatal stroke*) compared to standard BP control over the combined 9-year follow-up period



Buckley L et.al. Diab Obes Metab 2018, In press

2017 BP Guideline Goals-for DM

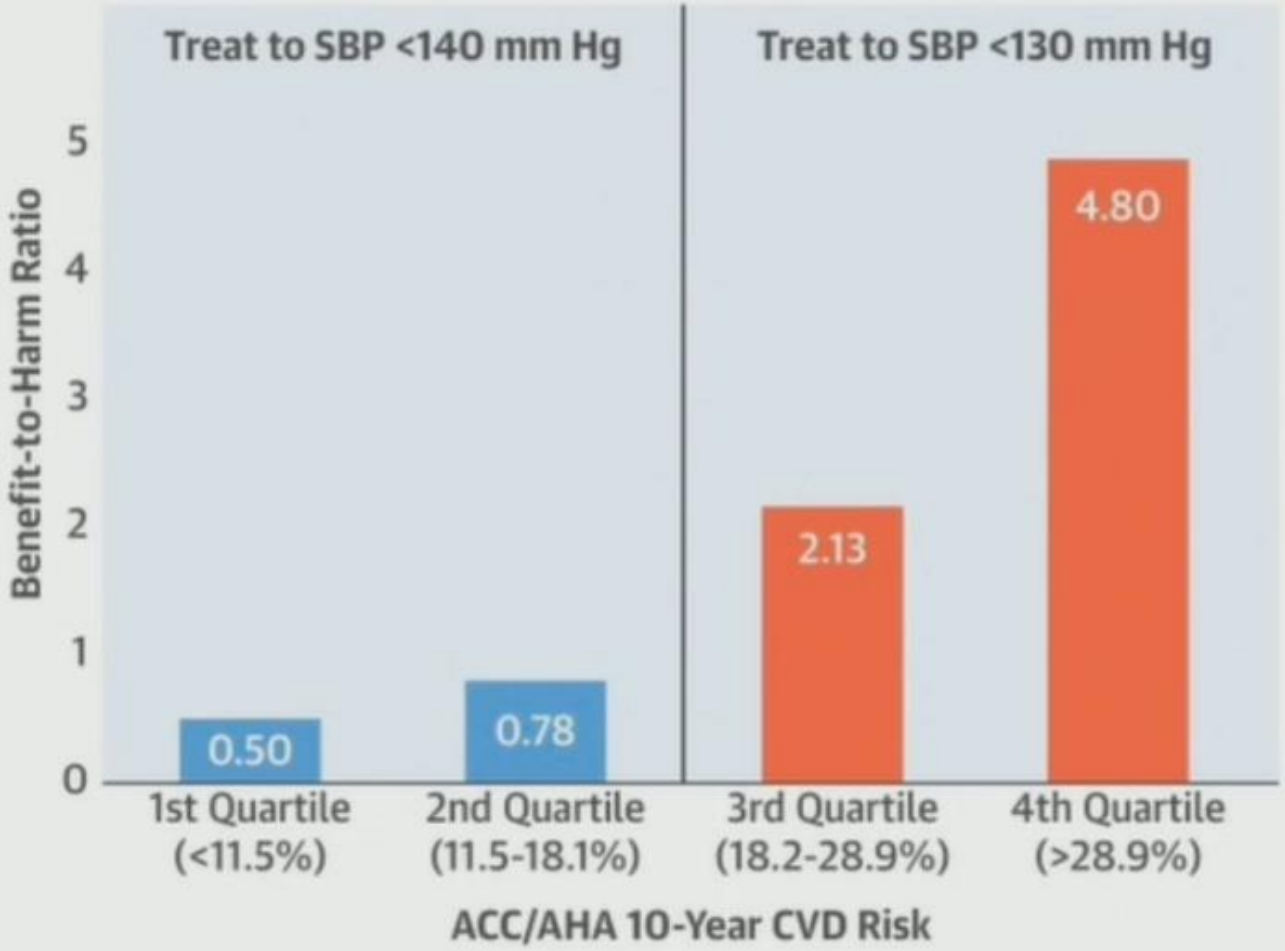
Need to Assess CV Risk of Individual Patient

(Assumption: *all people with Type 2 Diabetes will have a >10% 10 year CV risk*)

- **<140/90 mmHg-for everyone and those a high risk <130 mmHg-**
- **Avoid Diastolic BP ≤ 60**

ADA Clinical Practice Guidelines-Diabetes Care (Suppl.)2017; BP position paper ADA De Boer I, Bakris G et.al. Diabetes Care 2017, Sept. 2017

CENTRAL ILLUSTRATION: Treatment Recommendations Based on Benefit and Harm Experienced in SPRINT by 10-Year CVD Risk



Phillips, R.A. et al. J Am Coll Cardiol. 2018;71(15):1601-10.

Key Recommendations for Hypertension Management

- In patients aged 65 to 85 years with diabetes, we recommend a target BP of 140/90 mmHg to decrease the risk of CVD outcomes, stroke, and progressive CKD. (1|⊕⊕⊕O)

  Technical Remarks:

  - *Patients in certain high-risk groups could be considered for lower BP targets (130/80 mmHg), such as those with previous stroke or progressing CKD (eGFR <60 mL/min/1.73 m^2 and/or albuminuria). If lower BP targets are selected, careful monitoring of such patients is needed to avoid orthostatic hypotension.*
  - *Patients with high disease complexity (Group 3, Poor health, Framework) could be considered for higher BP targets (145–160/90 mmHg).*
  - *Choosing a BP target involves shared decision-making between the clinician and patient, with full discussion of the benefits and risks of each target.*

Key Recommendations for Hypertension Management (cont.)

- In patients aged 65 years and older with diabetes and hypertension, we recommend that an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker should be the first-line therapy. (1|⊕⊕⊕O)

  Technical Remark:

  If one class is not tolerated, the other should be substituted.

There is no unique Indication for ACE Inhibitors or ARBs for Primary Prevention of Kidney Disease in Diabetic Patients.

ACE Inhibitors and ARBs are Definitely Indicated for Treatment inPatients with Albuminuria/Proteinuria

RAAS STUDY DESIGN (TYPE 1 DIABETES)

- Randomized, double-blind, double dummy, placebo controlled study

- **Participants underwent a renal biopsy and fundus photography at entry and at exit, 5 years later**

M. Mauer, et.al. *N.Engl.J.Med. 361 (1):40-51, 2009.*

RANDOMIZATION

- Participants were randomized after their baseline biopsy into one of three treatment groups:

- **ACEI (enalapril) - 20 mg once daily**
- **ARB (losartan) - 100 mg once daily**
- **Placebo - once daily**
- **Stratification by center and gender**

M. Mauer, et.al. *N.Engl.J.Med. 361 (1):40-51, 2009.*

Table 2. Effects of Enalapril and Losartan on Change in the Mesangial Fractional Volume, Albumin Excretion Rate, and Glomerular Filtration Rate, According to Study Group.*

End Point	Enalapril	Losartan	Placebo
Mesangial fractional volume			
Mean at baseline	0.201±0.044	0.189±0.041	0.187±0.045
Mean change at 5 yr	0.005±0.050	0.026±0.054	0.016±0.048
Change vs. placebo			
Mean difference	−0.011	0.010	0 (reference)
P value	0.16	0.17	
Adjusted change vs. placebo			
Mean difference	−0.006	0.008	0 (reference)
P value	0.38	0.26	

M. Mauer, et.al. *N.Engl.J.Med. 361 (1):40-51, 2009.*

Baseline Data of Am. Indians with Early Type 2 Diabetes and Normotension

Characteristic	Normoalbuminuria			Microalbuminuria		
	Placebo (n = 46)	Losartan (n = 45)	P	Placebo (n = 39)	Losartan (n = 39)	P
Male (%)	13 (28.3)	10 (22.2)	0.63	12 (30.8)	11 (28.2)	1.00
Age, years	41.9 ± 11.7	39.5 ± 10.6	0.31	42.3 ± 10.9	41.8 ± 8.9	0.83
Diabetes duration, years	10.4 ± 6.0	8.8 ± 4.7	0.18	14.1 ± 8.4	10.3 ± 5.2	0.02
BMI (kg/m^2)	36.6 ± 8.0	37.4 ± 8.8	0.62	33.8 ± 7.2	34.6 ± 9.1	0.69
Blood pressure, mmHg						
Systolic	118 ± 14	115 ± 11	0.36	123 ± 12	118 ± 15	0.15
Mean	89 ± 9	88 ± 7	0.61	92 ± 8	90 ± 10	0.34
Diastolic	75 ± 7	75 ± 7	0.97	77 ± 7	77 ± 9	0.70
HbA_{1c}, %	8.1 ± 2.2	9.2 ± 2.0	0.01	10.3 ± 2.1	9.5 ± 2.3	0.11
GFR, mL/min*	152 ± 40	171 ± 38	0.02	168 ± 43	166 ± 43	0.85
Urinary albumin-to-creatinine ratio, mg/g	14 (9–26)	15 (10–23)	0.61	80 (46–165)	66 (39–205)	0.47

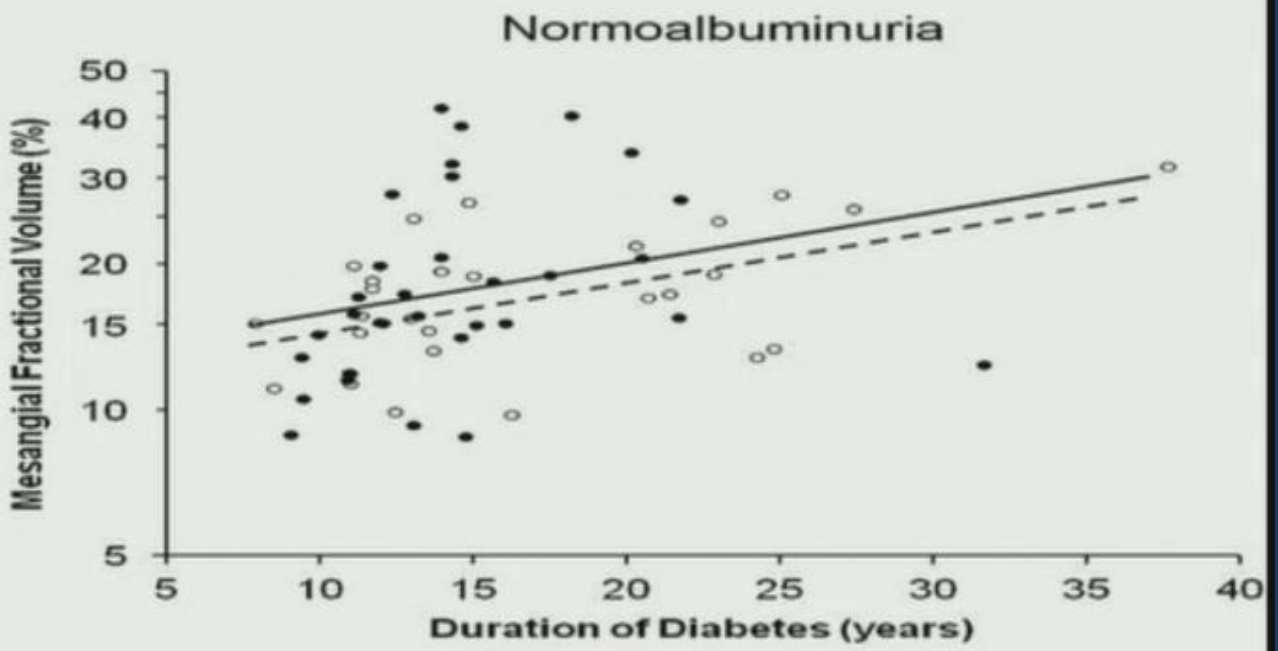
Data are means ± SD, median (25th and 75th percentiles), or n (%). *Baseline GFR was not measured in two normoalbuminuric patients who received losartan.

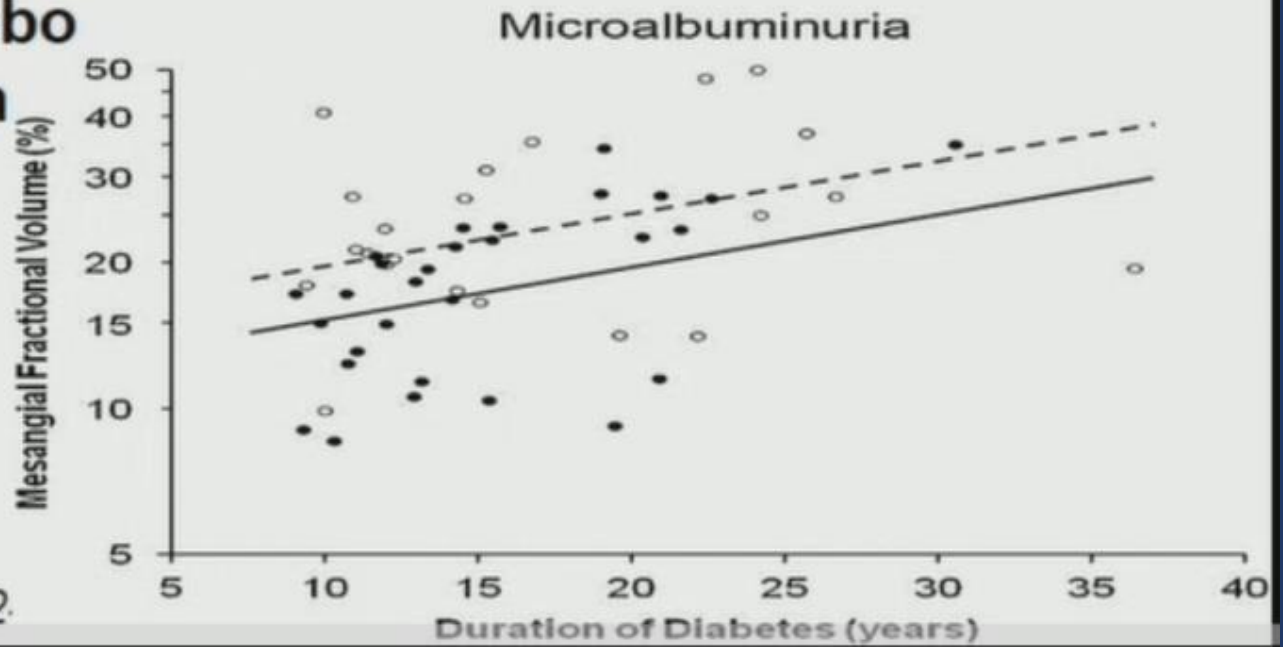
Weill EJ et.al. Diabetes 2013;62:3224-3231

Mesangial Expansion of Am. Indians with Early Type 2 Diabetes

[○] = placebo
[●] = losartan

dashed line = placebo
solid line = losartan





Weill EJ et.al. Diabetes 2013;62:322

What about BB??

- Use it only for indications: HF, post MI, HR.
- Do not use it only for BP control and mostly in the elderly.
- In obesity guidelines metoprolol is practically contraindicated due to weight gain.
- If used in DM try to use the more metabolically benign as carvedilol and nevibolol.

How to use ACEI's correctly, specially in the elderly:

- All ACEI's, *except for trandolapril and fosinopril are dyalizable*, so dose it after dyalisis as 50% will be loss by dyalisis.
- All ACEI's, *except for trandolapril and fosinopril*, are BID drugs if GFR is > 60 ml/min.
- If GFR < 60 ml/min use it QD.

How to use ARB's correctly

- All ARB's *are not dyalizable*.
- If GFR is > 60 ml/min losartan and valsartan are BID drugs, all other are QD.
- If GFR < 60 ml/min use all QD.

How to use diuretics in DM HTN w and w/o DKD, specially in the elderly:

- Increase sugar (thiazides), so increase MONITORING.
- About 2 liters of fluid/day specially if using SGLT2i.
- Older people : HCTZ as it is short acting and safer than chlorthalidone. Indapamide is long acting and safer than chlorthalidone in elderly as it came in lower doses.
- Adjust doses if using SGLT2i, mostly in lower GFR and advanced age.
- Ck K if on MRA, ARB or ACEI and SGLT2i in combination (USED IN HF). *Remember EMPA-REG, CANVAS, DECLARE and DAPA-HF when consider SGLT2i in HF.*
- If GFR < 30 ml/min and for symptomatic reHF and peHF consider loop.
- Remember that MRA is the best 4th drug after r/o 2ry causes of HTN. But careful in CKD (no start GFR < 30 ml/min, K > 5) (GFR < 45 mL/min and K > 4.5 predicts hyperkalemia, if used start spiro 12.5 QD, progress to 25 QD and 25 mg BID if needed)

Case 5

- 66 y/o hispanic F
- T2D x 20 years
- HTN x 25 years
- CAD, s/p CABG, systolic CHF w EF 25%
- Has DKD:
  - Cr 1.5; GFR 36 ml/min. Prot to creat ratio 0.9g/g creat (mostly albumin)
  - On carvedilol 25 mg bid: HR 65 BP 145/90
  - On max dose irbesartan and amlodipine

    - **BP CONTROL ?? < 130/80 if obtained w/o side effects of therapy**
    - **Would you consider SGLT2i??**

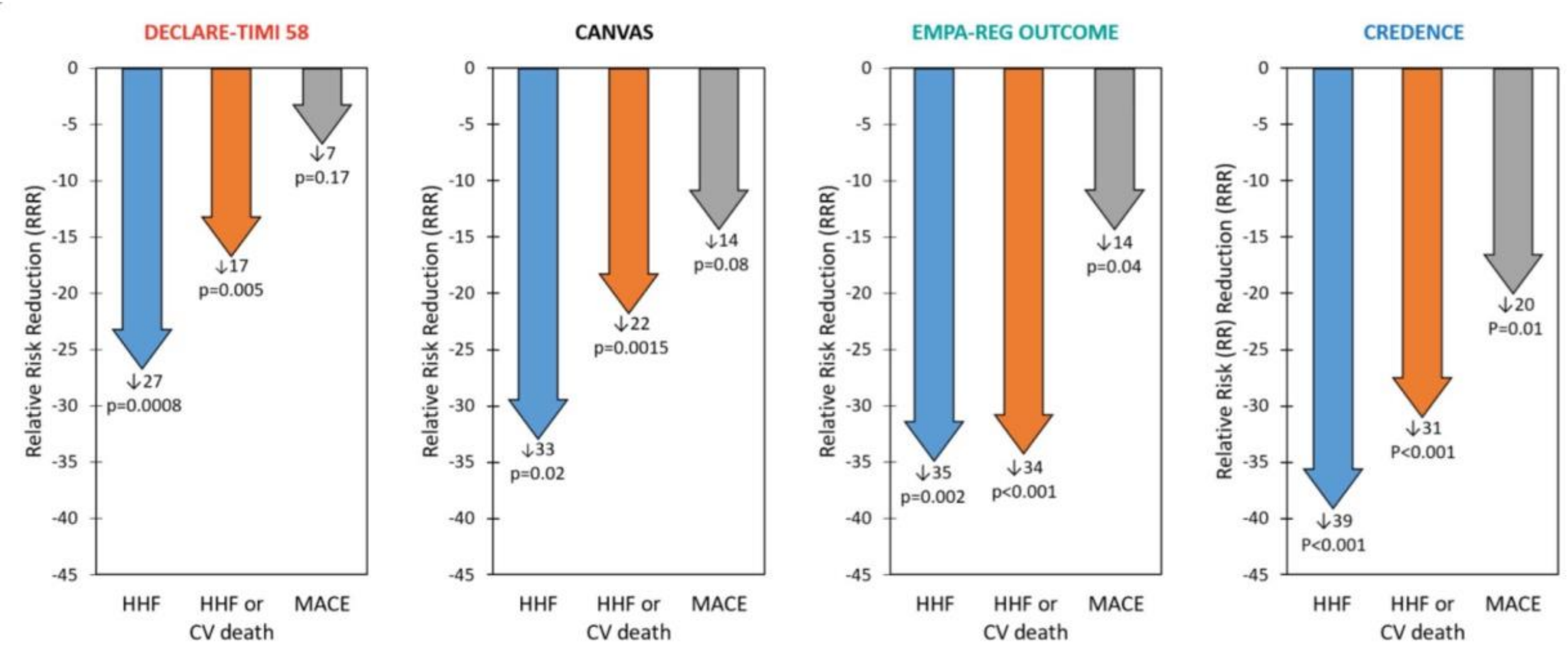
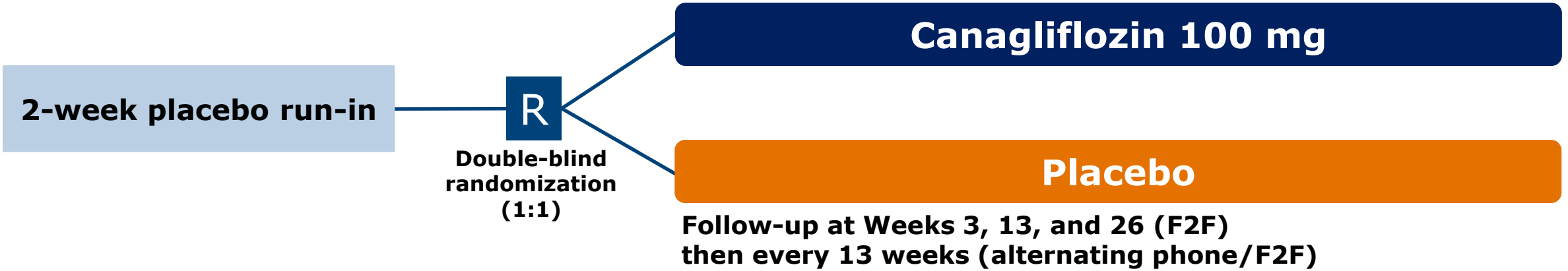


Fig. 4 Heart failure hospitalization (HHF), HHF and cardiovascular (CV) death, and major adverse cardiovascular event (MACE) relative risk reductions (RRRs) in the Dapagliflozin Effect on CardiovascuLAR Events (DECLARE-TIMI 58), CANagliflozin CardioVascular Assessment Study (CANVAS) Program, Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients–Removing Excess Glucose (EMPA–REG OUTCOME), and Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trials. Statistical outcomes displayed as RRR, p-value. RRRs were calculated from hazard ratios

Study Design

Key inclusion criteria
- ≥30 years of age
- T2DM and HbA1c 6.5% to 12.0%
- eGFR 30 to 90 mL/min/1.73 m^2
- UACR 300 to 5000 mg/g
- Stable max tolerated labelled dose of ACEi or ARB for ≥4 weeks

Key exclusion criteria
- Other kidney diseases, dialysis, or kidney transplant
- Dual ACEi and ARB; direct renin inhibitor; MRA
- Serum K^+ >5.5 mmol/L
- CV events within 12 weeks of screening
- NYHA class IV heart failure
- Diabetic ketoacidosis or T1DM

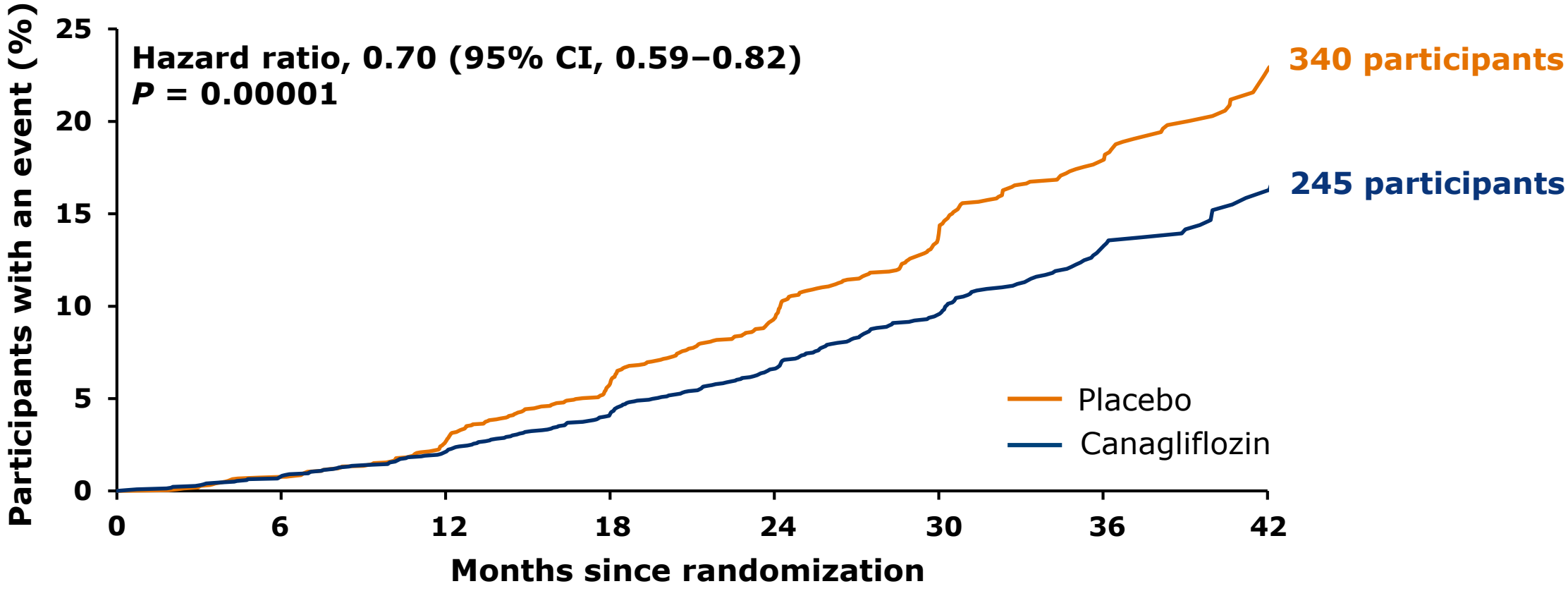


Participants continued treatment if eGFR was <30 mL/min/1.73 m^2 until chronic dialysis was initiated or kidney transplant occurred.

Demographics and Disease History

	Canagliflozin (n = 2202)	Placebo (n = 2199)	Total (N = 4401)
Mean age, years	63	63	**63**
Female, %	35	33	**34**
Mean duration of diabetes, years	16	16	**16**
Hypertension, %	97	97	**97**
Heart failure (NYHA I-III), %	15	15	**15**
CV disease, %	51	50	**50**
Prior amputation, %	5	5	**5**

Primary Outcome:
ESKD, Doubling of Serum Creatinine, or Renal or CV Death

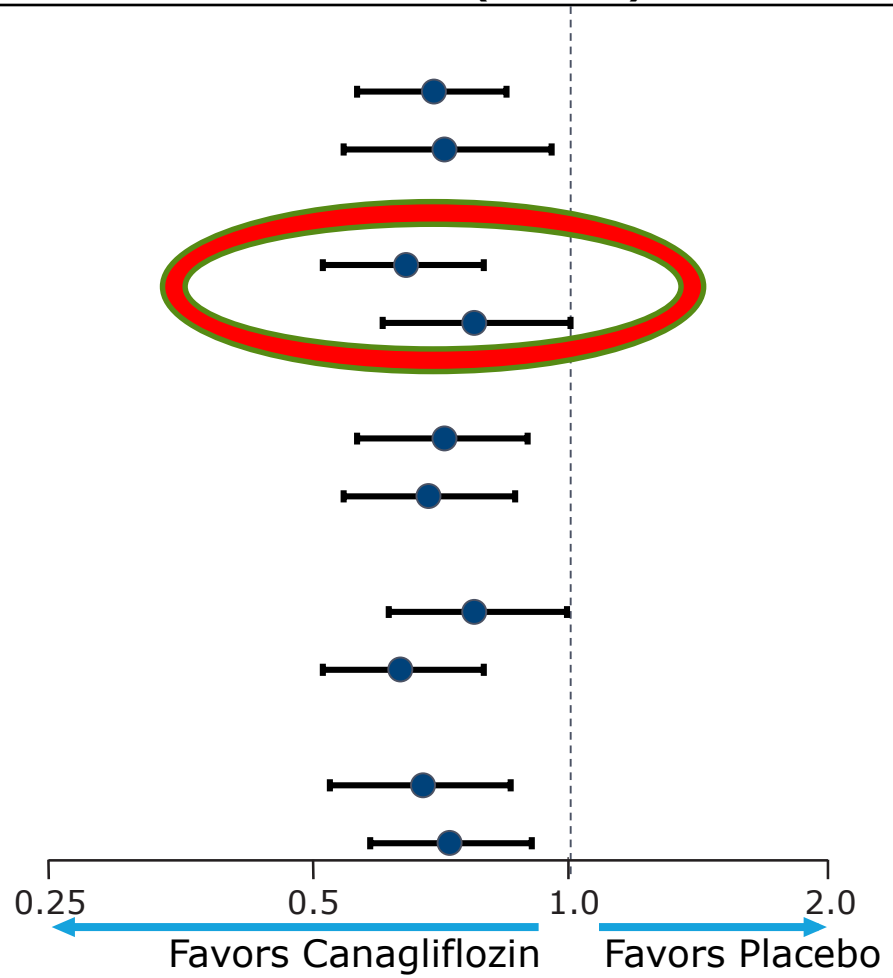


No. at risk								
Placebo	2199	2178	2132	2047	1725	1129	621	170
Canagliflozin	2202	2181	2145	2081	1786	1211	646	196

CREDENCE

Primary Outcome: Demographic and Risk Factor Subgroups

	Hazard ratio (95% CI)	Interaction *P* value
Sex		0.84
Male	0.69 (0.56–0.84)	
Female	0.71 (0.54–0.95)	
Age		0.83
<65 years	0.64 (0.51–0.79)	
≥65 years	0.77 (0.60–1.00)	
Baseline BMI		0.26
<30 kg/m^2	0.71 (0.56–0.89)	
≥30 kg/m^2	0.68 (0.54–0.86)	
Baseline HbA1c		0.22
<8%	0.77 (0.61–0.99)	
≥8%	0.63 (0.51–0.79)	
Systolic BP		0.61
≤Median	0.67 (0.52–0.85)	
>Median	0.72 (0.58–0.90)	



CREDENCE

Case 5

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  - Cr 1.5; GFR 36 ml/min. Prot to creat ratio 0.9g/g creat (mostly albumin)
  - On carvedilol 25 mg bid: HR 65 BP 145/90
  - On max dose irbesartan and amlodipine

Would you consider SGLT2i??

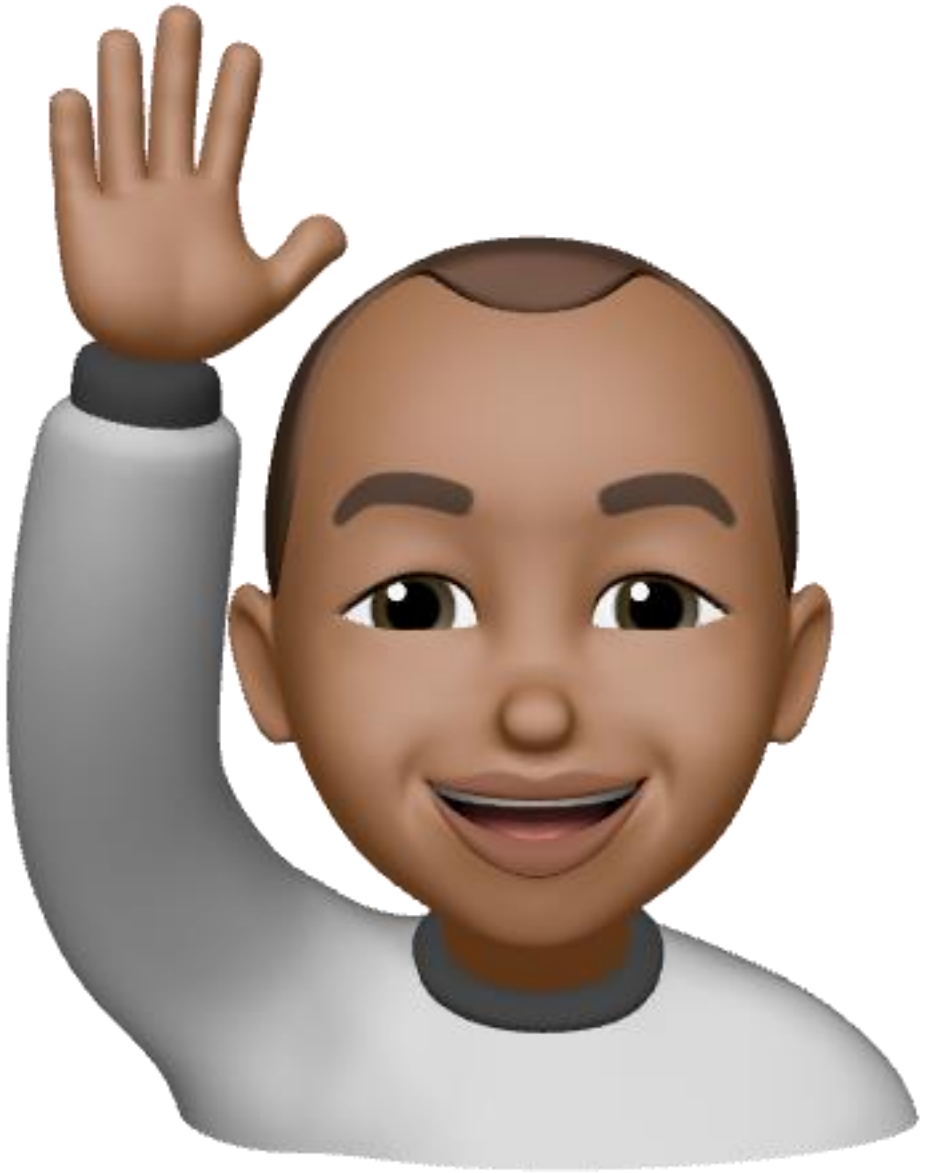
- Can be considered based on proven CV, renal and HHF benefits as patients > 65 y/o were included in these trials.
- Cost and safety in the elderly are barriers.
- If used, close monitoring of BP, GFR, elyte disturbance, weight and concomitant antihypertensive and antidiabetic agents.
- Hypoglycemia not much an issue if no insulin or SU and with GFR < 45 ml/min as glucose lowering efficacy of SGLT2i is compromised with decreased GFR.

Conclusions

- The diabetic elderly population has increased as cardiovascular mortality and other complications has decreased with better management strategies.
- Glycemic control should be individualized with emphasis in lowering A1C to decrease diabetes related complications but avoiding the complications of therapy, specially hypoglycemia. Comorbidities and cognitive status of the older diabetic patient are highly emphasized in current recommendations for classification between good, intermediate and poor health for A1C target recommendations.

Conclusions

- Therapeutic options for the older adult with diabetes occasionally is limited due to comorbidities and complications associated with the aging process: renal insufficiency, liver disease, cognitive dysfunction, visual impairment, economic issues, social and family support, among others.
- Dyslipidemia, hypertension and other commonly associated conditions of diabetes should be managed individually considering the risks and benefits of different therapeutic strategies.
- The application of recently approved cardiorenal benefits of some antidiabetic agents should also be considered cautiously in the older adult with diabetes to get it’s maximum benefit but avoiding risks.



After knowing this information:

- ***I am not worried any more to develop diabetes and get older.***
- ***If those who will take care of me follow these recommendations and individualize my care, I will live longer.***

THANK YOU and MERRY CHRISTMAS