Blood pressure treatment target in diabetes

Should it be <130 mmHg?

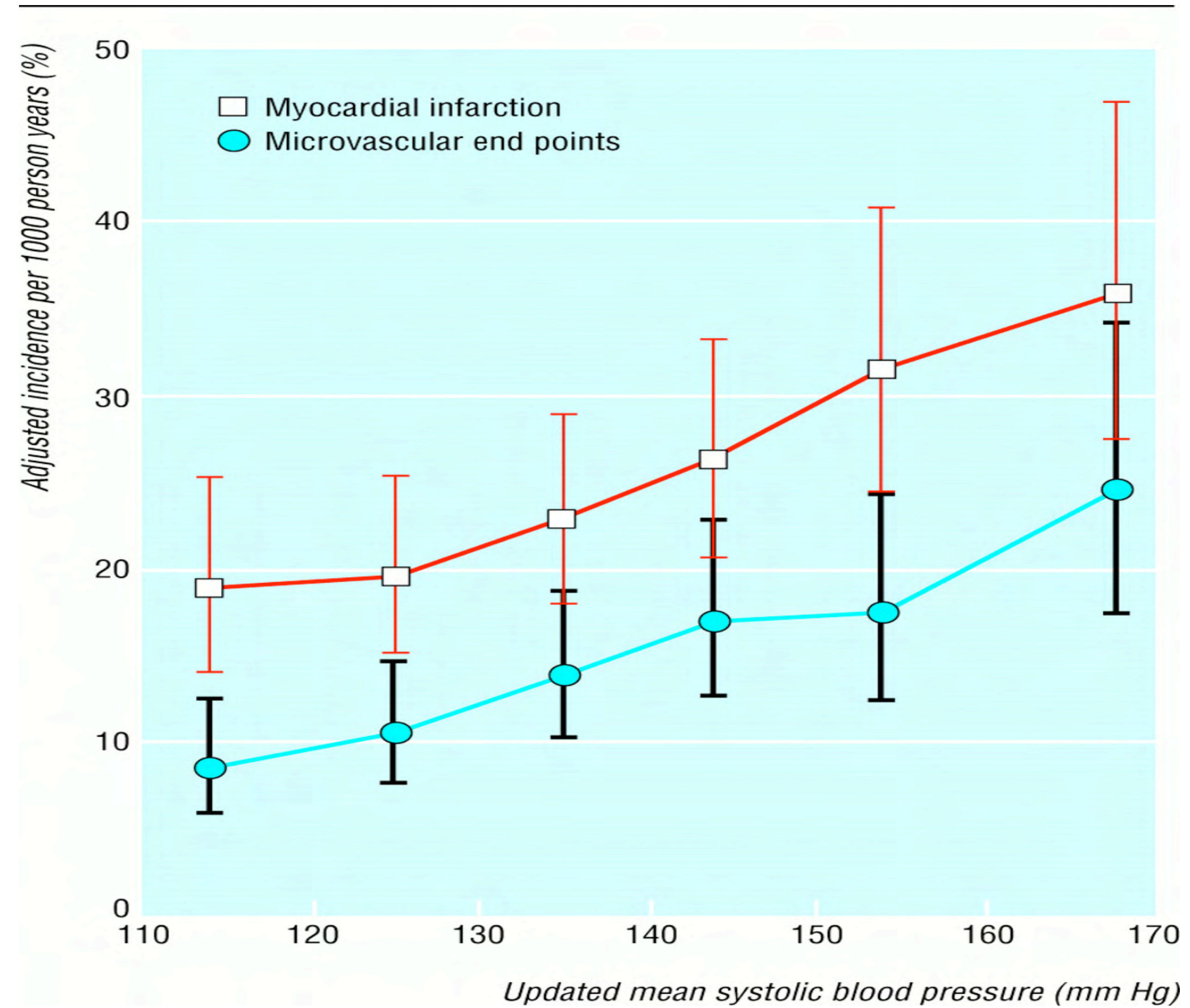
Types of evidence

- Observational cohort (level 3)
- Indirect (level 2)
  - Analysis of outcomes based on achieved BP targets
    - randomized to antihypertensive agents (placebo or active comparator trials)
- Direct (level 1)
  - Prospectively designed to randomize patients to different BP targets (SBP preferred)

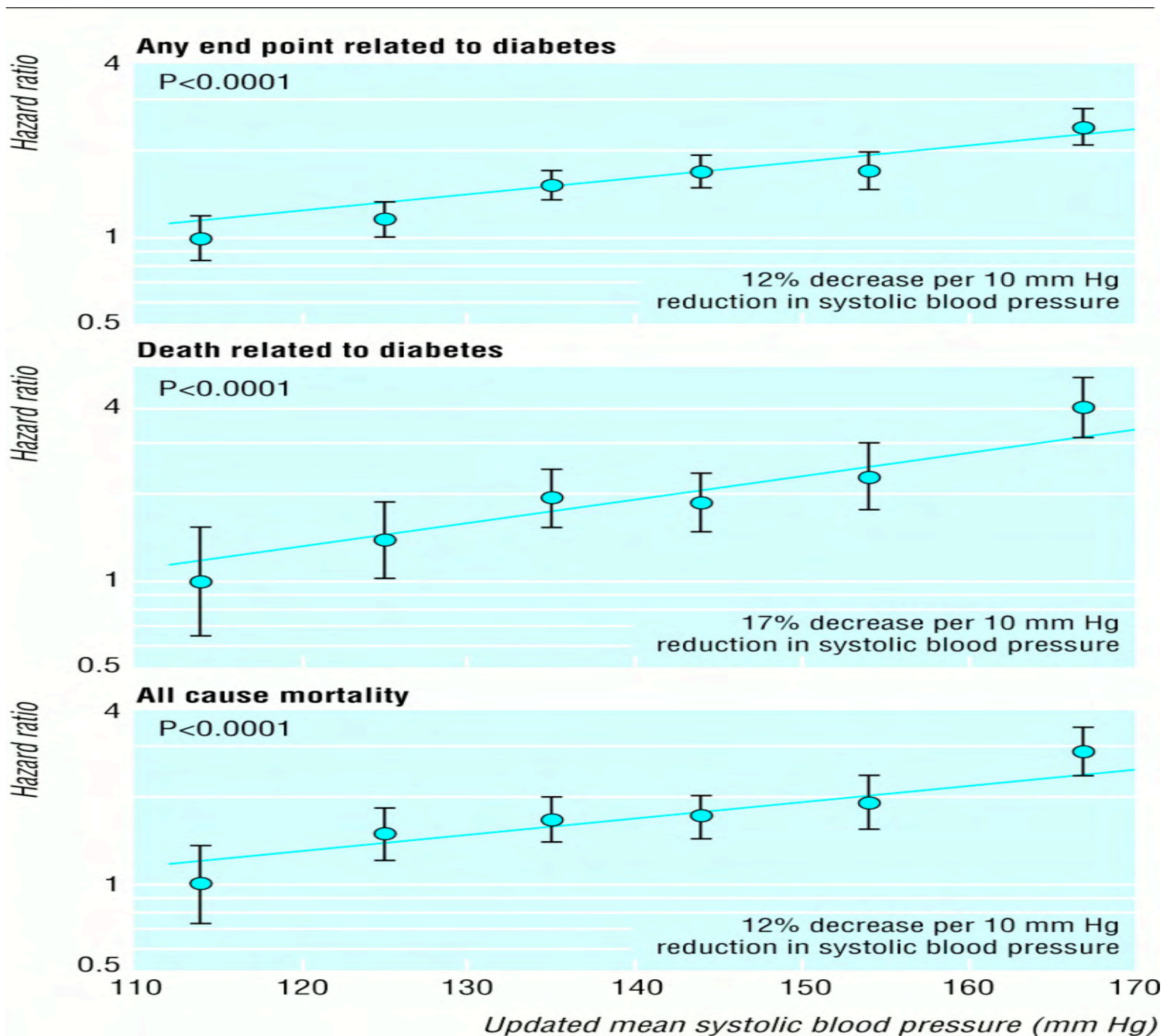
Current CDA recommendations of a SBP target of <130 mmHg are …

- Not based prospectively designed clinical trials where patients were randomized to different systolic treatment targets.

- Based on 2 cohort studies & 1 small RCT
  - Pittsburgh EDC study
    - n =589; 10yrs; type 1; [illegible]CV, death with [illegible] SBP
  - UKPDS 36
    - n = 4,801; 8.4 yrs; type 2



UKPDS 36 Adler A I et al. BMJ 2000;321:412-419



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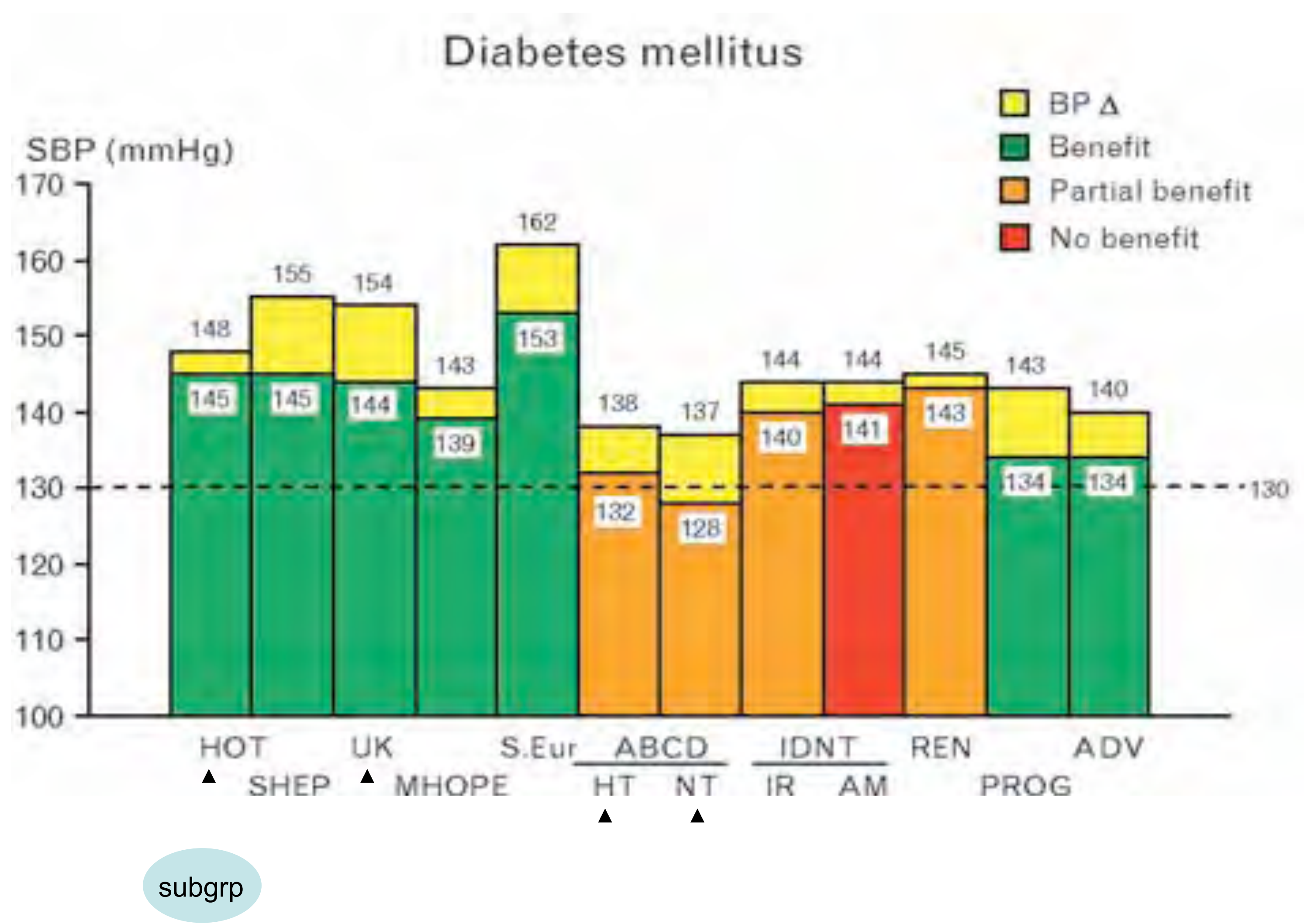


Adapted from Reappraisal of Guidelines on Hypertension Management
Mancia et. Al. J Hypertens 2009;27:2121-58.

ABCD-NT (n=480, duration 5.3yrs)

- Inclusion
  - DBP 80-89 mmHg on no meds
- Goal
  - achieve DBP 10 mmHg below baseline (intensive grp) vs maintaining 80-89 mmHg (moderate grp)
- Achieved BP was
  - 128/75 in intensive group (nisoldipine or enalopril)
  - 137/81 in moderate group (placebo)

ABCD-NT

- Results
  - No significant difference in 1° outcome ([illegible] in CrCl)
  - Benefit in some 2° outcomes
    - Progression of albuminuria
    - Progression of retinopathy
    - Stroke
  - No benefit in all cause mortality, MI or HF

ABCD-NT

- CDA guidelines acknowledge SBP target recommendation based on weaker evidence
- Do not give findings from ABCD-NT level 1 status
  - No stat correction for many 2° outcomes tested
  - Results of some outcomes, i.e stroke, based on small numbers
- State ACCORD BP would provide stronger evidence

ACCORD (published April 2010)

- Randomized 4,733 patients with hypertension & type 2 diabetes at "high risk" for CV events to
  - **Intensive:** target SBP < 120 mmHg, or
  - **Standard:** target SBP <140 mmHg
- Primary composite outcome (MI, stroke or CV)
- Mean follow-up 4.7 years

1.87%/yr vs 2.09%/yr
HR = 0.89
95% CI (0.73-1.07)

Patients with Events (%)

20
15
10
5
0

0 1 2 3 4 5 6 7 8

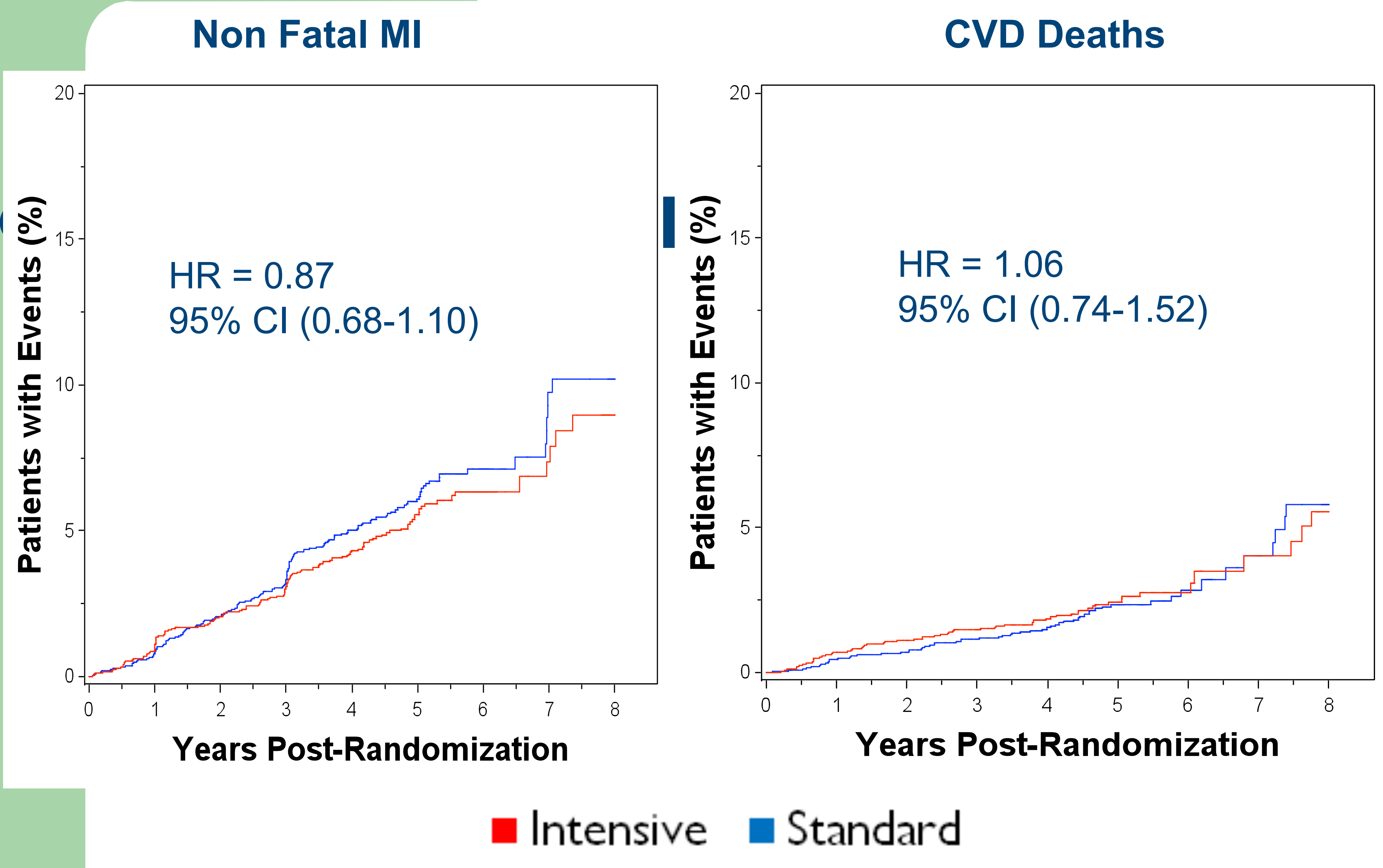
Years Post-Randomization

Intensive — Standard

119 mmHg — 133.5 mmHg

The ACCORD Study Group. *N Engl J Med.* 2008;358(24):2545-2559

PRESPECIFIED SECONDARY OUTCOMES



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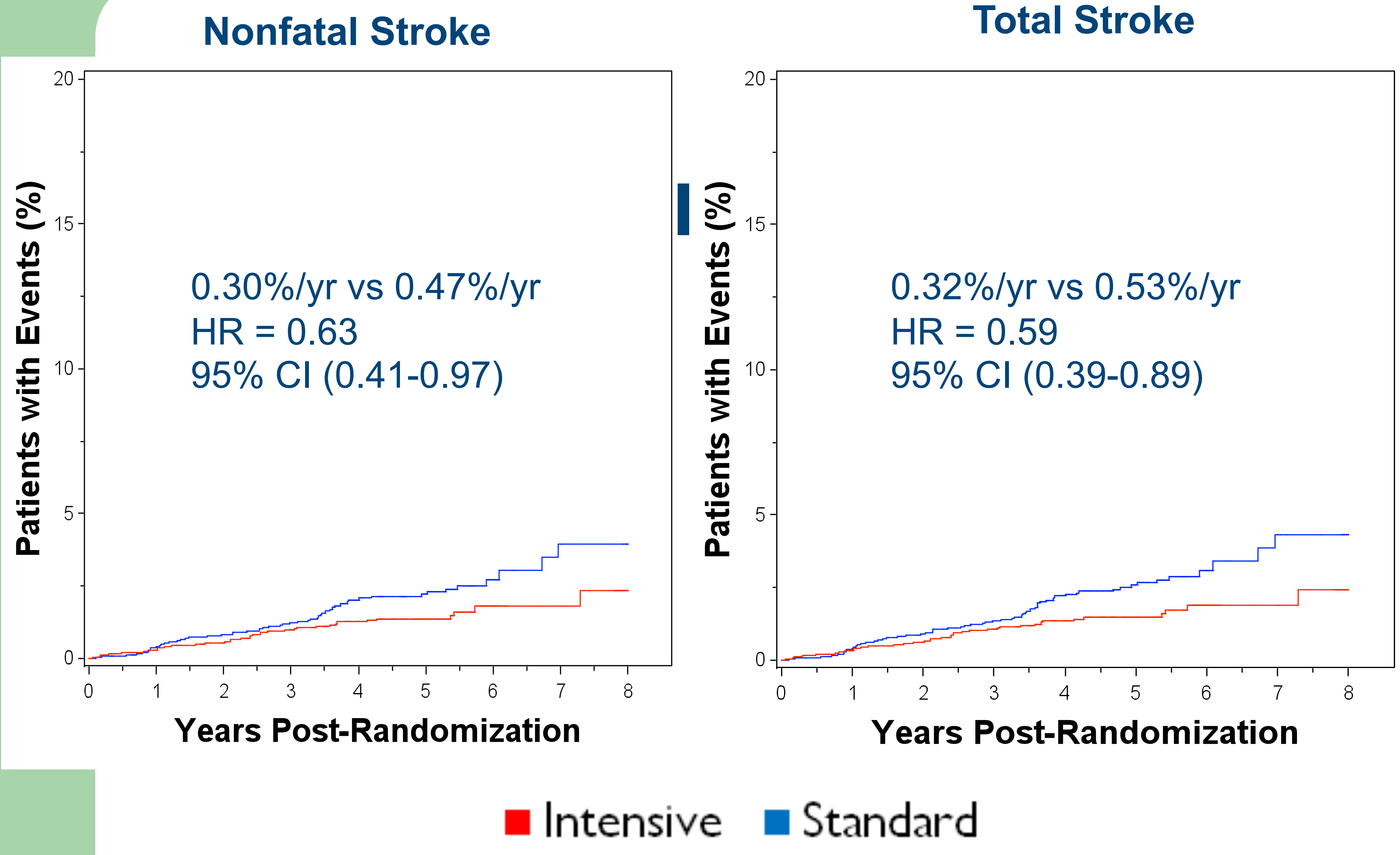

The ACCORD Study Group. *N Engl J Med.* 2008;358(24):2545-2559

Stroke outcome

- 97.4% of patients in the standard group did not have a stroke
- 98.5% of patients in the intensive group did not have a stroke
- The difference : 1.1%

ACCORD Authors Conclusions

- Targeting a SBP <120 mmHg **did not** CV events compared to a SBP <140 mmHg
  - **BUT** there was a significant reduction in stroke (non-fatal and fatal) as a 2° outcome

- # of meds taken by intensive group (3.4 vs 2.3 drugs)

- a.e. in the intensive group (i.e. hypotension, hyper- kalemia)

SECONDARY ANALYSIS OF INVEST

- INVEST
  - N = 22,576 Duration 2.7 years
  - Patients with CHD and hypertension
  - Verapamil + trandolapril vs atenolol + trandolapril
- INVEST – DM subgroup N = 6400

  <130 vs 130-139 vs >139

No sig difference in
-- All cause mortality, stroke and MI – Primary
-- Non-fatal stroke, MI

Cooper-Dehoff JAMA 2010

INVEST Authors Conclusions

- Tight SBP control (<130 mmHg) was not associated with improved CV outcomes compared with usual control (≥130 -<140 mmHg) in patients with diabetes and CAD

Interpretation of Recent Evidence Should SBP target be <130 mmHg?

- Tempting to conclude that a BP target <130 in patients with diabetes offers no additional CV benefit over usual control & maybe even increased harm

BUT

- Can we apply this conclusion to all patients with type 2 diabetes?

What about patients with CKD?

- Observational data tell us
  - diabetes + CKD (esp. proteinuric) = [illegible] CV events & ESRD
  - [illegible] SBP = [illegible] CV events & ESRD
  - Maybe SBP differences in the 120-140 range = sig [illegible] events
- Indirect evidence to suggest <130mmHg [illegible]'s ESRD
  - subgroup of ND-CKD patients with proteinuria
- But no direct, level 1 evidence
  - ACCORD did not include patients with substantive evidence of renal disease

Overall Conclusion

- No compelling evidence that decreasing SBP < 130 mmHg is beneficial in patients with diabetes and normal renal function.

- Thus place emphasis on maintaining BP between 130-139 mmHg while focusing on
  - weight loss
  - healthful eating
  - other signs of CV morbidity

  to further [illegible] long term CV risk.

Adherence to medication

- When prescribing
  - Use once daily dosing regimens, combo products
- Get patient more involved
  - Encourage patients to monitor their BP
  - Educate the patient & family about CV risk etc
- Improve overall management
  - Multidisciplinary team approach
    - Provide patient with regular reminders (office visit, phone or mail contact, compliance aids, pharmacy)

Low salt diet

- Do
  - Eat more fresh foods
  - Check labels on processed foods
  - Use unsalted spices
  - Eat out less; use less sauce on food
  - Eat foods with < 400 mg Na per serving; preferably even < 200 mg
- Don't
  - Add salt; buy or eat heavily salted foods