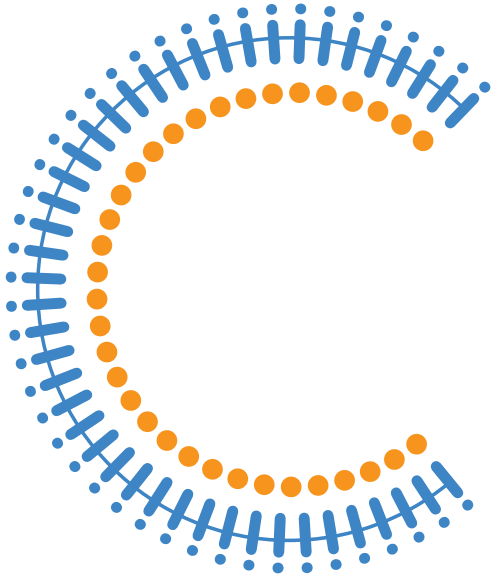

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The Complex Patient:

Hypertension and Stroke Prevention and Management in Patients

Case Development & Disclosures

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  - None

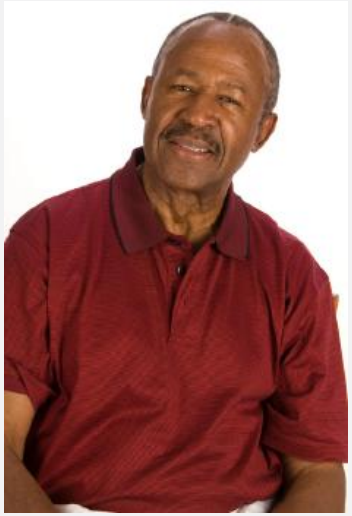
Mitigating Potential Bias

- Altering control over content: information and recommendations given in the program are evidence-based and sourced from multiple clinical practice guidelines/scientific professional associations.
- Program material is peer-reviewed by a committee with members representative of the target audience.

Outline of Today's Activity

- Introduction
- Case Presentation
- Key Learnings & Questions
- Wrap Up

Case 3:
Hypertension and Stroke Prevention in Patients



John

A 60 year old African-Canadian male with severe hypertension. During his visit, his wife discusses her concerns about the risk of stroke.

Learning Objectives

Upon completion of this case study, participants should be able to:

1. Plan to assess and screen patients blood pressure at all appropriate visits.

2. Discuss modifiable cardiovascular risk factors with patients.

3. Discuss blood pressure targets and need for anticoagulation/anti-platelet therapy in people who have just suffered a stroke.

Statement of Need

"My greatest challenge as a health care professional in the management of patients with ***multiple morbidities*** *is _____"*

Question 1

How often should John have his blood pressure screened?

Question 1. How often should John have his BP screened?

a) 1 x/ month
b) Every other month
c) 2 x/ year
d) 1 x/ year
e) At each appropriate visit to his doctor's office

Question 1. How often should John have his BP screened?

e) *At all appropriate visits, at each health care encounter*

Risk Factor Screening

Hypertension

- Health care professionals who have been specifically trained to measure BP accurately should assess BP in all adult patients at all appropriate visits to determine CV risk and monitor antihypertensive treatment

Case Presentation

- John is a 60 year old male with hypertension.
- Sister who is 10 years older died from a hemorrhagic stroke 5 years ago.
- His wife is concerned about his risk of stroke and comes in with him to discuss this with you.

Patient history

- John is a plumber.
- He has a history of hypertension and obesity (BMI 32 kg/m^2).
- He is also an ex-smoker, having smoked 20 cigarettes a day for 40 years, quitting when his sister had the stroke.

Family history

- Father, sister and paternal uncle
  - suffered a stroke in their 60s.

Current Medications

- None
- He had been started on an ACE inhibitor 4 years ago but it had not lowered his blood pressure
- He was then started on atenolol but it also did not lower his BP and made him feel tired, he did not continue with either medication

Physical Examination

- Height: 175 cm
- Weight: 98 kg
- BMI: 32 kg/m^2
- BP (both arms, seated):

mmHg using an automated device

  – 164/102 mmHg

- Funduscopic: arteriolar narrowing, AV nicking
- Neck-Thyroid palpable, no nodule
- Heart: S4 gallop
- Lungs: Normal
- Abdomen: no murmurs
- Arteries: Normal
- Ankle edema: nil
- Neuro: grossly intact

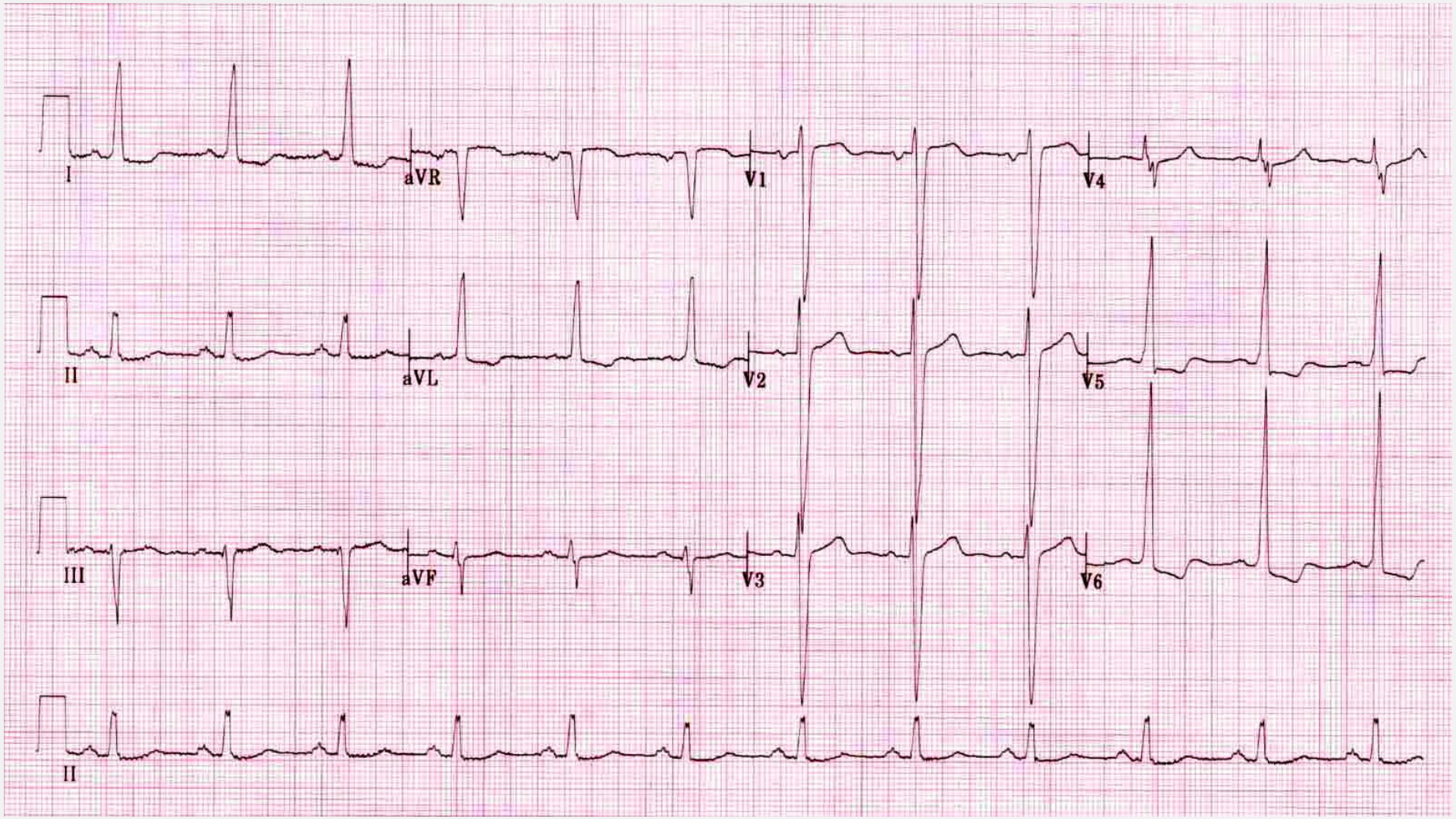
Laboratory Investigations

Test	Results	Normal Values
Glucose	6.0 mmol/L	4.0-8.0 mmol/L
Urea	5.2 mmol/L	3.0-7.0 mmol/L
Creatinine	87 µmol/L eGFR 99 ml/min	44-106 µmol/L
K	3.8 mmol/L	3.5-5.0 mmol/L
Na	138 mmol	135-145 mmol/l

- *Note that labs are done prior to the next visit*

Laboratory Investigations

Test	Results	Normal values
LDL	3.9 mmol/L	<2.0 mmol/L
Total chol	5.8 mmol/L	<5.20 mmol/L
TG	1.6 mmol/L	<1.70 mmol/L
HDL	0.8 mmol/L	>0.99 mmol/L
Non-HDL	5.0 mmol/L	<2.7 mmol/L
TC:HDL	7.25	High risk target: <4.0 Mod risk target: <5.0 Low risk target: <6.0


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

Laboratory Investigations

Test	Results	Normal Values
HbA1c	0.053	0.045 - 0.057 mmol/L
Dipstick Urinalysis	Negative	Negative
Alb/creat	9.2 mg/mmol	< 2.0 mg/mmol
ECG confirms LVH and strain pattern		

- *Note that labs are done prior to the next visit*

Question 2

What risk reduction strategies should be focused on to help John address his vascular risk?

Question 2. What areas should be discussed with John to help address his vascular risk?

a) Blood pressure control
b) Diet and sodium intake
c) Exercise and weight loss
d) Alcohol intake
e) Lipid management
f) All of the above

Question 2. What areas should be discussed with John to help address his vascular risk?

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f) All of the above

Blood pressure control

As of Nov 2015, pt would meet eligibility of being a "SPRINT" patient, and thus new BP target would be **SBP<120 mm Hg**

-What is the SPRINT trial?

-How to achieve BP control in this patient?

Usual Office BP **Threshold Values** for Initiation of Pharmacological Treatment

Population	SBP	DBP
High Risk (SPRINT population)	≥130	NA
Diabetes	≥130	≥80
Moderate-to-high risk (TOD or CV risk factors)*	≥140	≥90
Low risk (no TOD or CV risk factors)	≥160	≥100

TOD = target organ damage

***AOBP threshold ≥135/85**

Hypertension CANADA

Recommended Office BP Treatment Targets

Treatment consists of **health behaviour ± pharmacological management**

Population	SBP	DBP
High Risk #	≤ 120	NA
Diabetes	< 130	< 80
All others*	< 140	< 90

Based on AOBP

* Target BP with AOBP < 135/85

SPRINT Trial:
Systolic blood PRessure INtervention Trial

- Compares < 120 vs < 140 mmHg
- NHLBI RCT
  - Age 50+
  - SBP 130-180
  - High CV risk (other than stroke)
    - CKD (eGFR 20 - <60)
    - 10 Year Framingham risk of 15%+
    - Age 75+
- Excludes: DM, prior stroke, eGFR <20

Would John be a SPRINT Patient?

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Framingham Risk Score - RESULTS [2,3]

Your patient's Framingham Risk Score is > 30%

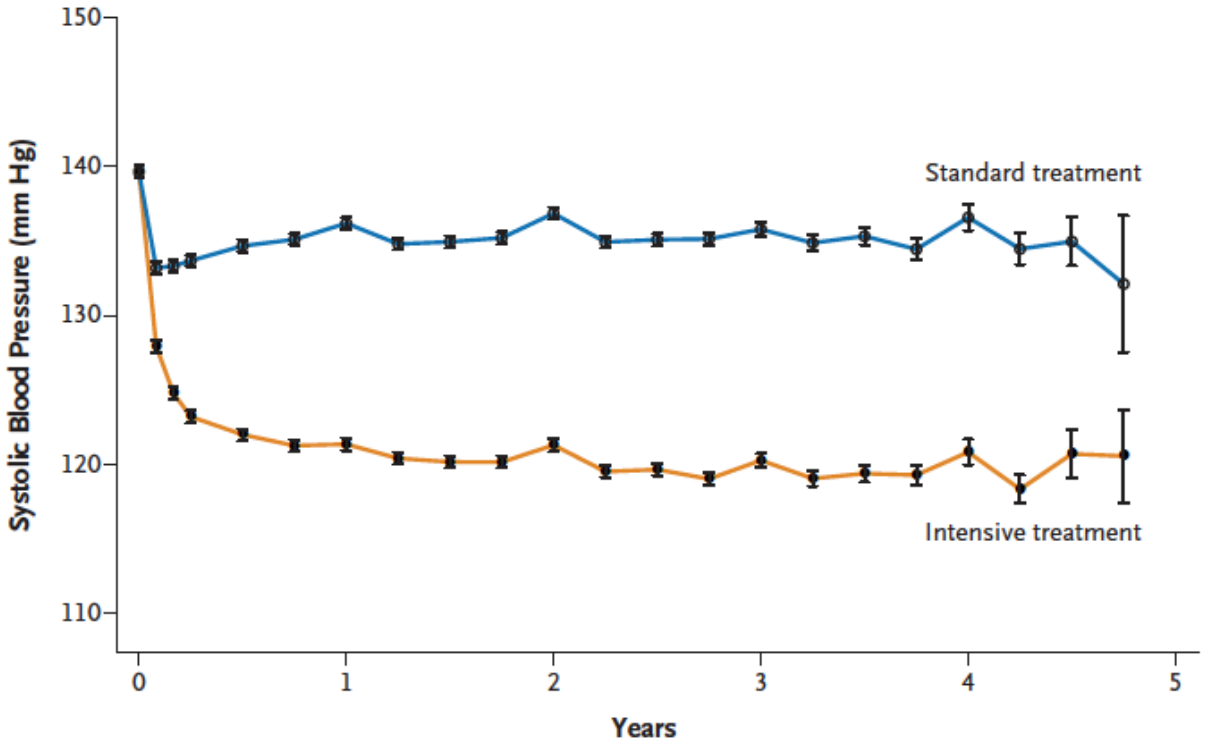
2009 CCS Canadian Cholesterol Guidelines Recommendation [1]

Risk Level	Initiate/consider treatment if any of the following:	Primary LDL-C targets
High* (FRS > 20% RRS > 20%)	Consider treatment in all patients.	**Either:** - 2.0 mmol/L or ≥ 50% reduction

Adapted from Genest et al. Can J Cardiol. 2009. [1]

SPRINT – SBPs Achieved

Average # of meds:
Intensive care: 2.8
Standard care: 1.8

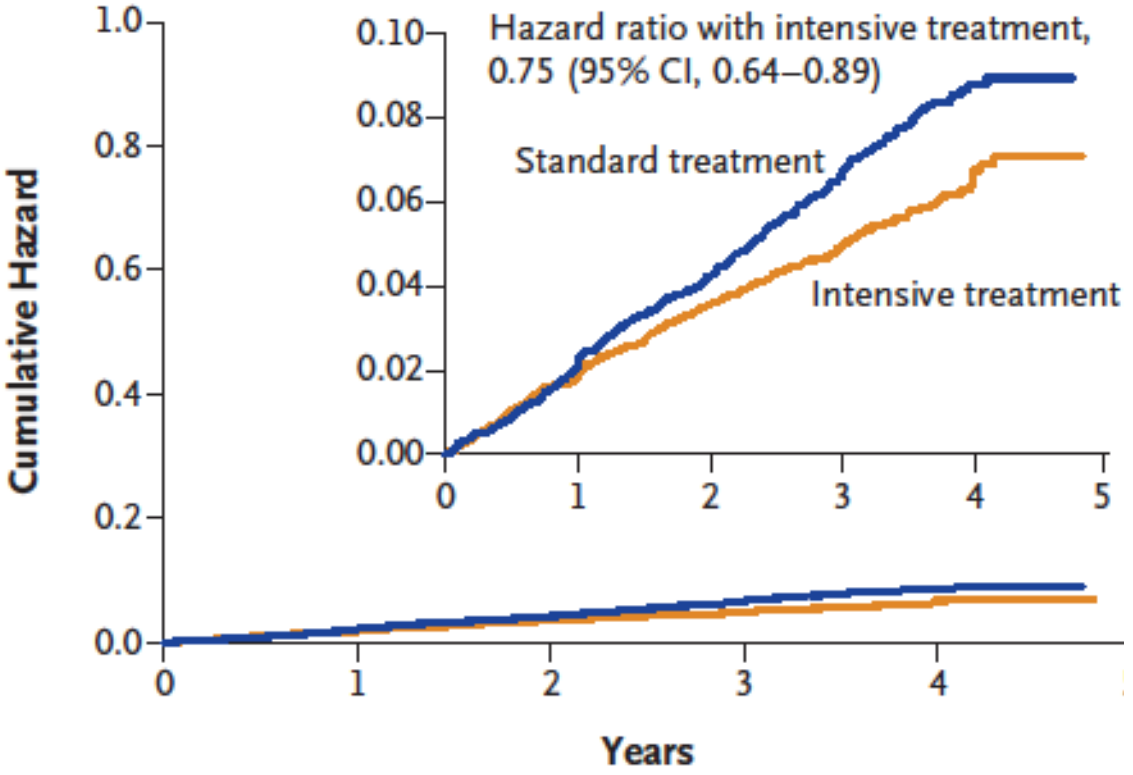


No. with Data										
Standard treatment	4683	4345	4222	4092	3997	3904	3115	1974	1000	274
Intensive treatment	4678	4375	4231	4091	4029	3920	3204	2035	1048	286
Mean No. of Medications										
Standard treatment	1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9
Intensive treatment	2.3	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8	3.0

SPRINT: NEJM Nov 9 2015

SPRINT - Primary Outcome (MI, ACS, Stroke, CHF, CV death)

NNT=61



No. at Risk

Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

SPRINT: NEJM Nov 9 2015

Table 3. Serious Adverse Events, Conditions of Interest, and Monitored Clinical Events.

Variable	Intensive Treatment (N=4678)	Standard Treatment (N=4683)	Hazard Ratio	P Value
	no. of patients (%)			
Serious adverse event*	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest				
Serious adverse event only				
Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall†	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure‡	193 (4.1)	117 (2.5)	1.66	<0.001
Emergency department visit or serious adverse event				
Hypotension	158 (3.4)	93 (2.0)	1.70	<0.001
Syncope	163 (3.5)	113 (2.4)	1.44	0.003
Bradycardia	104 (2.2)	83 (1.8)	1.25	0.13
Electrolyte abnormality	177 (3.8)	129 (2.8)	1.38	0.006
Injurious fall†	334 (7.1)	332 (7.1)	1.00	0.97
Acute kidney injury or acute renal failure‡	204 (4.4)	120 (2.6)	1.71	<0.001
Monitored clinical events				
Adverse laboratory measure§				
Serum sodium <130 mmol/liter	180 (3.8)	100 (2.1)	1.76	<0.001
Serum sodium >150 mmol/liter	6 (0.1)	0		0.02
Serum potassium <3.0 mmol/liter	114 (2.4)	74 (1.6)	1.50	0.006
Serum potassium >5.5 mmol/liter	176 (3.8)	171 (3.7)	1.00	0.97
Orthostatic hypotension¶				
Alone	777 (16.6)	857 (18.3)	0.88	0.01
With dizziness	62 (1.3)	71 (1.5)	0.85	0.35

Impact of SPRINT on this Case

- Benefits of BP lowering to < 120 with NNT of 61 for primary outcome and 90 to prevent one death (3.26 years)
- Equal impact for those > 75 years old
- But:
  - With eGFR 60+ there was more loss of GFR by 30% or more to eGFR< 60 in intense group
  - More hypotension, syncope, AKI, hyponatremia, and hypokalemia

Hypertension CANADA

New Guideline Post-SPRINT

- For high-risk patients, aged ≥ 50 years, with systolic BP levels ≥130 mm Hg, intensive management to target a systolic BP ≤120 mm Hg should be considered
- Intensive management should be guided by automated office BP measurements (AOBP)
- Patient selection for intensive management is recommended and caution should be taken in certain high-risk groups

Question 2. What areas should be discussed with John to help address his vascular risk?

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f) All of the above

Blood pressure control

As of Nov 2015, pt would meet eligibility of being a "SPRINT" patient, and thus new BP target would be **SBP<120 mm Hg**

-What is the SPRINT trial?

-How to achieve BP control in this patient?

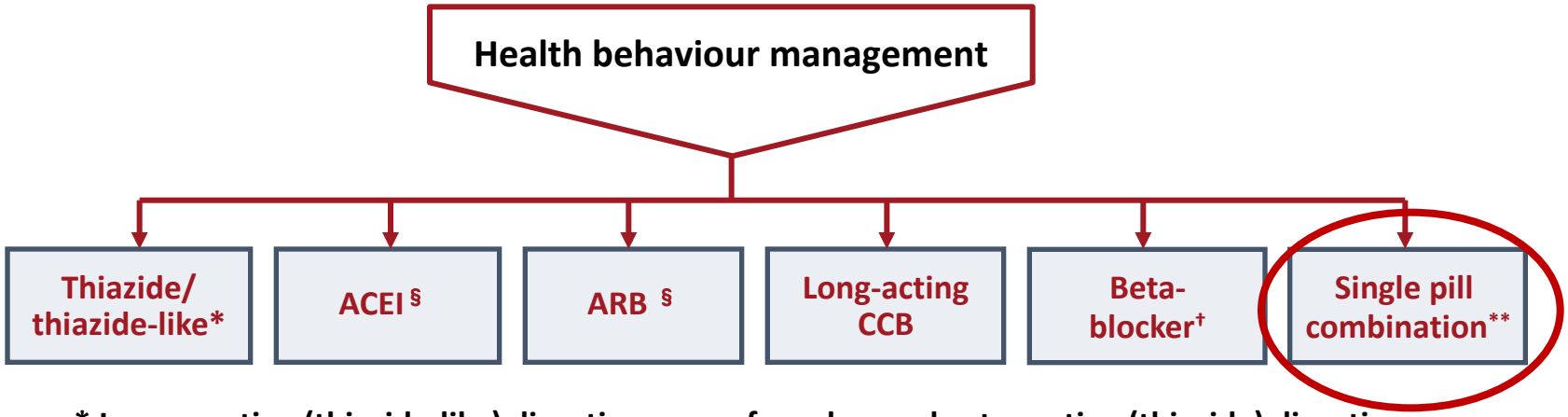
Hypertension CANADA

First Line Treatment of Adults with Systolic/Diastolic Hypertension Without Other Compelling Indications

New 2017

TARGET <135/85 mmHg (automated measurement method)

INITIAL TREATMENT



*** Longer-acting (thiazide-like) diuretics are preferred over shorter-acting (thiazide) diuretics**

† BBs are not indicated as first line therapy for age 60 and above

§ Renin angiotensin system (RAS) inhibitors are contraindicated in pregnancy and caution is required in prescribing to women of child bearing potential

****Recommended SPC choices are those in which an ACE-I is combined with a CCB, an ARB with a CCB, or an ACE-I or ARB with a diuretic**

Considerations Regarding the Choice of First-Line Therapy

- Use caution in initiating therapy with 2 drugs in those whom adverse events are more likely (e.g. frail elderly, those with postural hypotension or who are dehydrated).
- Diuretic-induced hypokalemia should be avoided through the use of potassium sparing agents if required.
- **ACE-inhibitors are not recommended (as monotherapy) for patients of 'black race' without another compelling indication** (Theory: HTN not as angiotensin II – dependent in 'black' population).
  - Pts of 'black race' have smaller reduction in BP in response to ACEi, ARB, and most BB when given as monotherapy
  - However, these drugs are effective when given in combination with thiazide-diuretics or CCB

Common Classes of anti-HTN Meds:

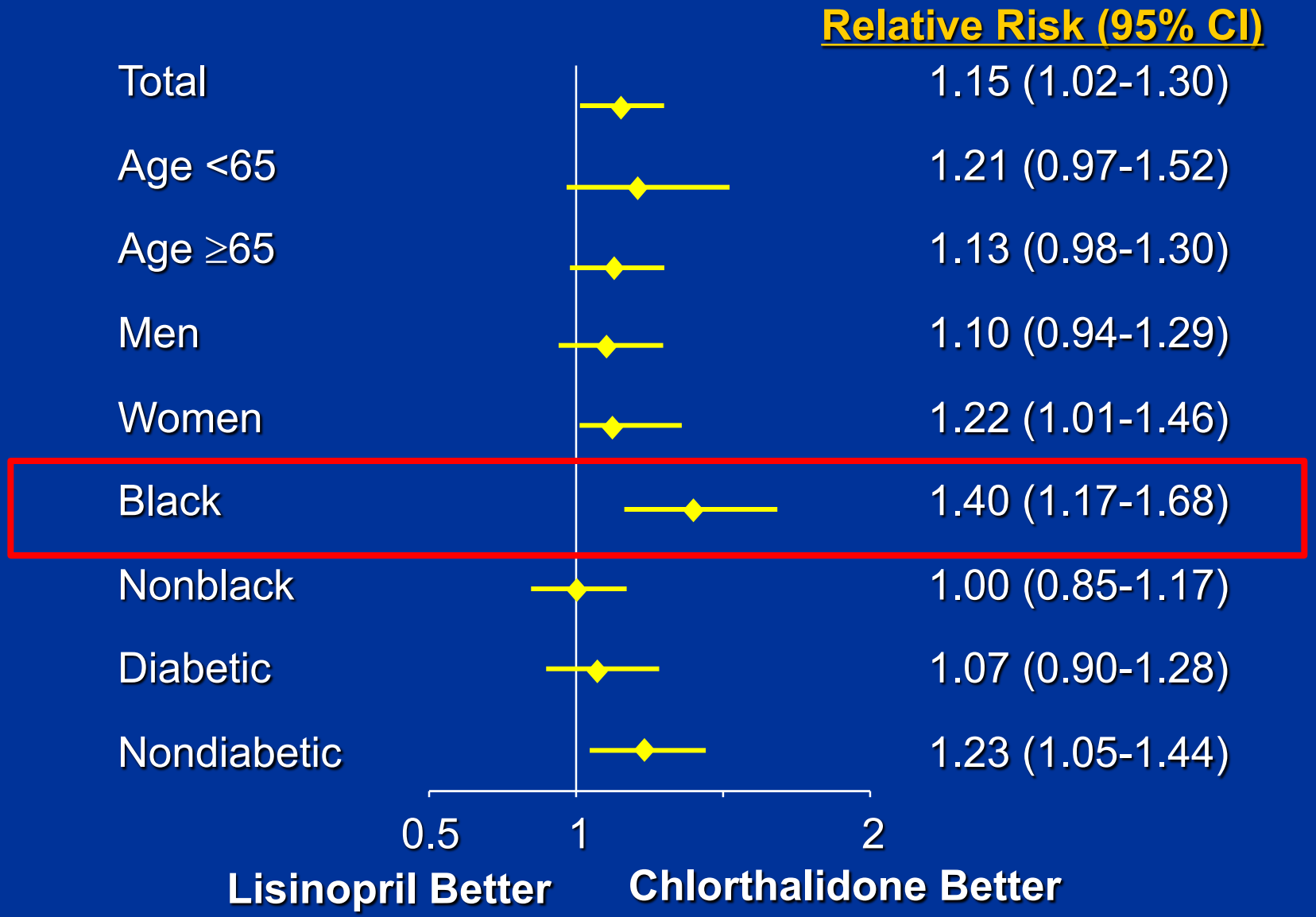
A – ACEi or ARB; Alpha Blocker

B – BB

C – CCB (DHP vs Non-DHP)

D - Diuretic

ALLHAT: Stroke (Lisinopril vs Chlorthalidone) Subgroups



ALLHAT Collaborative Research Group. *JAMA* 2002;288:2981-97.

ALLHAT - Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial

- ALLHAT (n=33,357) randomized to chlorthalidone, amlodipine, or lisinopril.
- Second drug added was usually a beta-blocker: atenolol
- Men and women age 55+ w/ HTN and 1+ other CVD risk (metabolic syndrome)
- Outcomes
  - Despite thiazide-type diuretics less favourable metabolic profile (increases blood sugar), in patients with metabolic syndrome, these drugs are superior to CCB and ACEi for preventing one or more major forms of CVD (ex. stroke, HF), although similar risk of death and non-fatal MI
  - Particularly true for participants of 'black race'.

Question 2. What areas should be discussed with John to help address his vascular risk?

f) All of the above

Weight and Diet: John's BMI is 32 kg/m^2 (Class I obesity). You discuss eating a nutritionally balanced diet to achieve and maintain a healthy body weight

Sodium: To decrease BP, reduce sodium intake towards 2,000 mg (5g or 1 teaspoon salt) per day.

Exercise: To achieve health benefits, adults aged 18-64 should accumulate at least 150 minutes of moderate-vigorous intensity aerobic physical activity per week, in bouts of 10 minutes of more.

Question 2. What areas should be discussed with John to help address his vascular risk?

f) All of the above

Smoking: You review John's smoking status (ex- smoker)

Alcohol: You review John's alcohol consumption and advise that he have two or fewer standard drinks per day (fewer than 14 drinks/week for men).

Lipid Status: You start John on a statin with the goal of reducing his LDL < 2.0 (FRS >20% - high risk)

Case Progression

You start John on Chlorthalidone 25 mg/d and ask him to come back to see you within 2 months to check his BP and further titrate his medication.

Follow-up of BP above targets

- Patients with BP above target are recommended to be followed at least every 2nd month
- Follow-up visits are used to increase the intensity of lifestyle and medication therapy, monitor the response to therapy, and assess adherence

Case Progression

John misses his appointment despite phone calls to remind him.

Three months after John's last visit with you, he develops an ischemic stroke. He comes to see you in your office after the acute phase, to be monitored.

His BP remains uncontrolled. His only anti-hypertensive is chlorthalidone. His statin has been restarted.

Question 3

What is John’s BP target?

Question 3. What is John's BP target?

a) < 140/90 mmHg

b) < 135/85 mmHg

c) < 130/80 mmHg

d) < 120 mmHg

Question 3. What is John's BP target?

a) < 140/90 mmHg

Treatment Targets

Stroke Rehabilitation

- Following the acute phase of a stroke, BP lowering treatment is recommended to a target of consistently <140/90 mmHg

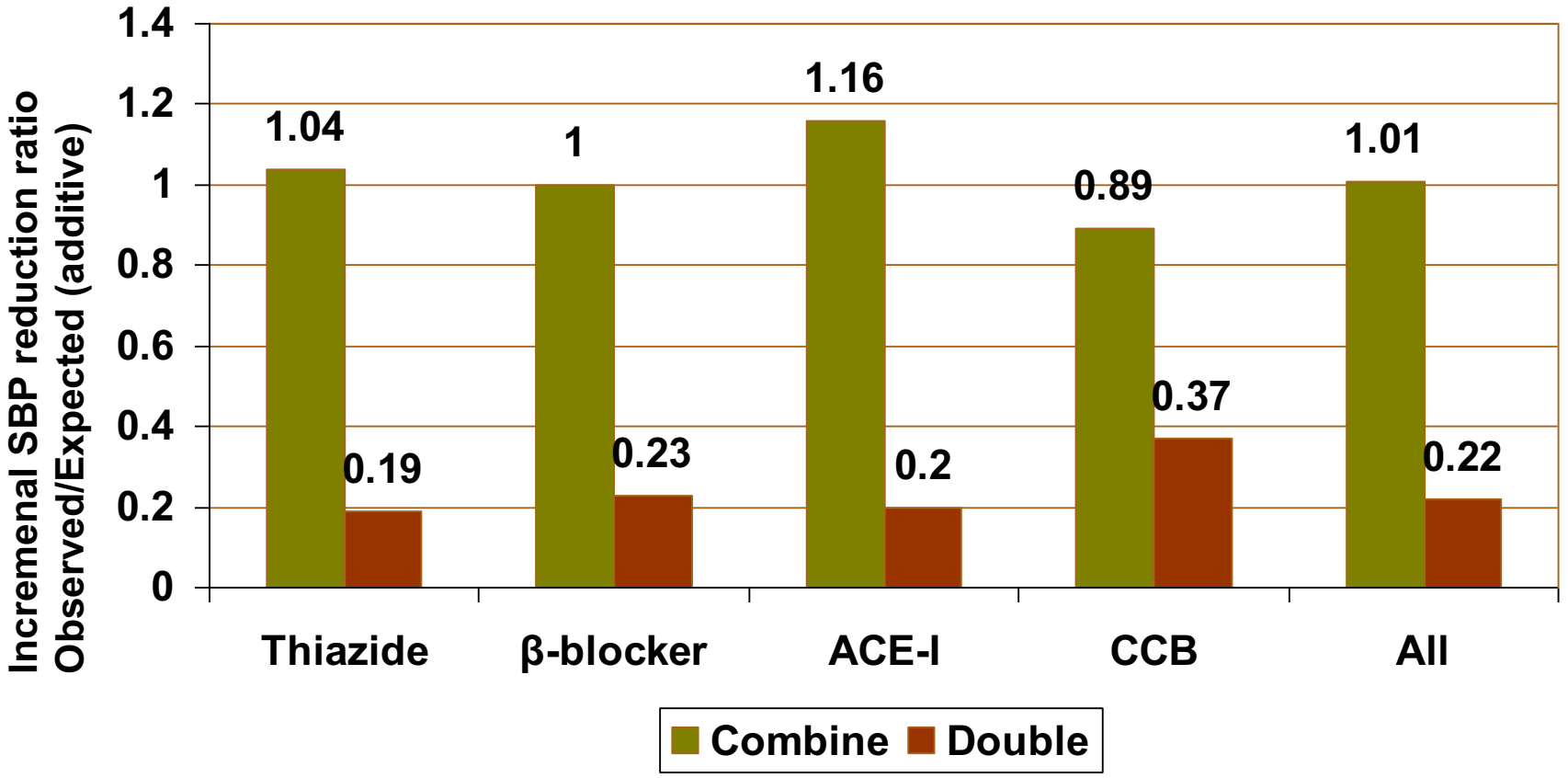
Note: John is no longer a "SPRINT" patient, since patients with stroke were excluded from study – use clinical judgment

BP lowering effects from antihypertensive drugs

- Dose response curves for efficacy are relatively flat
- 80% of the BP lowering efficacy is achieved at half-standard dose
  - rather side effect profile of meds may increase with increased dose
- Combinations of standard doses have additive blood pressure lowering effects
  - supports use of Single Pill Combination (SPC) meds

Law. *BMJ* 2003

Ratio of Incremental SBP lowering effect at "standard dose"– Combine or Double?



Wald et al. Combination Versus Monotherapy for Blood Pressure Reduction, *The American Journal of Medicine*, Vol 122, No 3, March 2009

Case Progression

You add an ACE inhibitor and a calcium channel blocker to chlorthalidone over the next few weeks and achieve BP control < 140/90 mm Hg.

Given his history of non-adherence, you discuss the importance of taking the medication regularly.

His renal function and potassium are unchanged.

Question 4

Upon examining John, you note no evidence of atrial fibrillation (confirmed with ECG and HOLTER) as part of stroke work-up.

What would you prescribe, what options are available?

Question 4. What would you prescribe, what options are available?

a) Dabigatran (150 mg)

b) Warfarin (5 mg)

c) Clopidogrel (75 mg)

d) ASA (81 mg)

e) ASA (25mg)/dipyridamole (200 mg)

Question 4. What would you prescribe, anti-platelet therapy, what options are available?

d) ASA (81 mg)

Pharmacologic and/or procedural therapy

- Antiplatelet therapy: all patients with ischemic stroke or transient ischemic attack should be prescribed antiplatelet therapy for secondary prevention of recurrent stroke unless there is an indication for anticoagulation.
- ASA (81mg), combined ASA (25 mg) and extended-release dipyridamole (200 mg), or clopidogrel (75 mg) are all appropriate options and selection should depend on the clinical circumstances.

Discussion & Reflection

1. Do you need to change your current practice to implement any of these recommendations?
2. How do you engage patients and their families in therapy and manage expectations?
3. What are some other adherence strategies that were discussed or not discussed that could work for your practice?
4. Who are some agents of change who can help you implement the recommendations?

Key Learnings:

- Assess BP in all adult patients at all appropriate visits to determine CV risk and monitor antihypertensive treatment
- Persons at risk of stroke should be assessed for vascular disease risk factors and lifestyle management issues
- Following the acute phase of stroke, patients should have their BP controlled to target of less than 140/90 mm Hg
- Antiplatelet therapy should be prescribed in all patients with ischemic stroke or transient ischemic attack for secondary prevention of recurrent stroke, unless indication for anticoagulation