Module 1:
Heart and Hypertension

Managing Hypertension to Prevent Heart Failure and Atrial Fibrillation

Case Development & Disclosures

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Hypertension CANADA

Northern Ontario School of Medicine

École de médecine du Nord de l'Ontario

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CEPD
continuing education and professional development

Faculty/Presenter Disclosure Slide 1

- **Faculty:**

- **Relationships with commercial interests:**
  - **Grants/Research Support:**
  - **Speakers Bureau/Honoraria:**
  - **Consulting Fees:**

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Disclosure of Commercial Support Slide 2

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- **Potential for conflict(s) of interest:**
  - None to declare

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.

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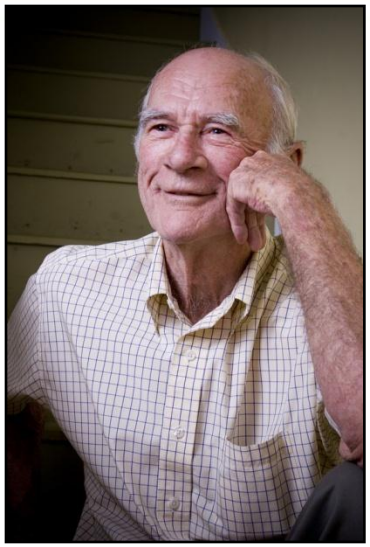
Outline of Today's Activity

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

Module 1: Heart and Hypertension



Cliff

A 76-year-old man presents to your office with a new complaint of shortness of breath and intermittent palpitations at rest.

Learning Objectives

Upon completion of this activity, participants

should be able to:

- Apply the Canadian Hypertension Education Program (CHEP) clinical practice guidelines for the management of hypertension in association with heart failure
- Explain the relationship between hypertension and heart failure, and in relation to a specific case
- Explain the relationship between hypertension and atrial fibrillation, and in relation to a specific case

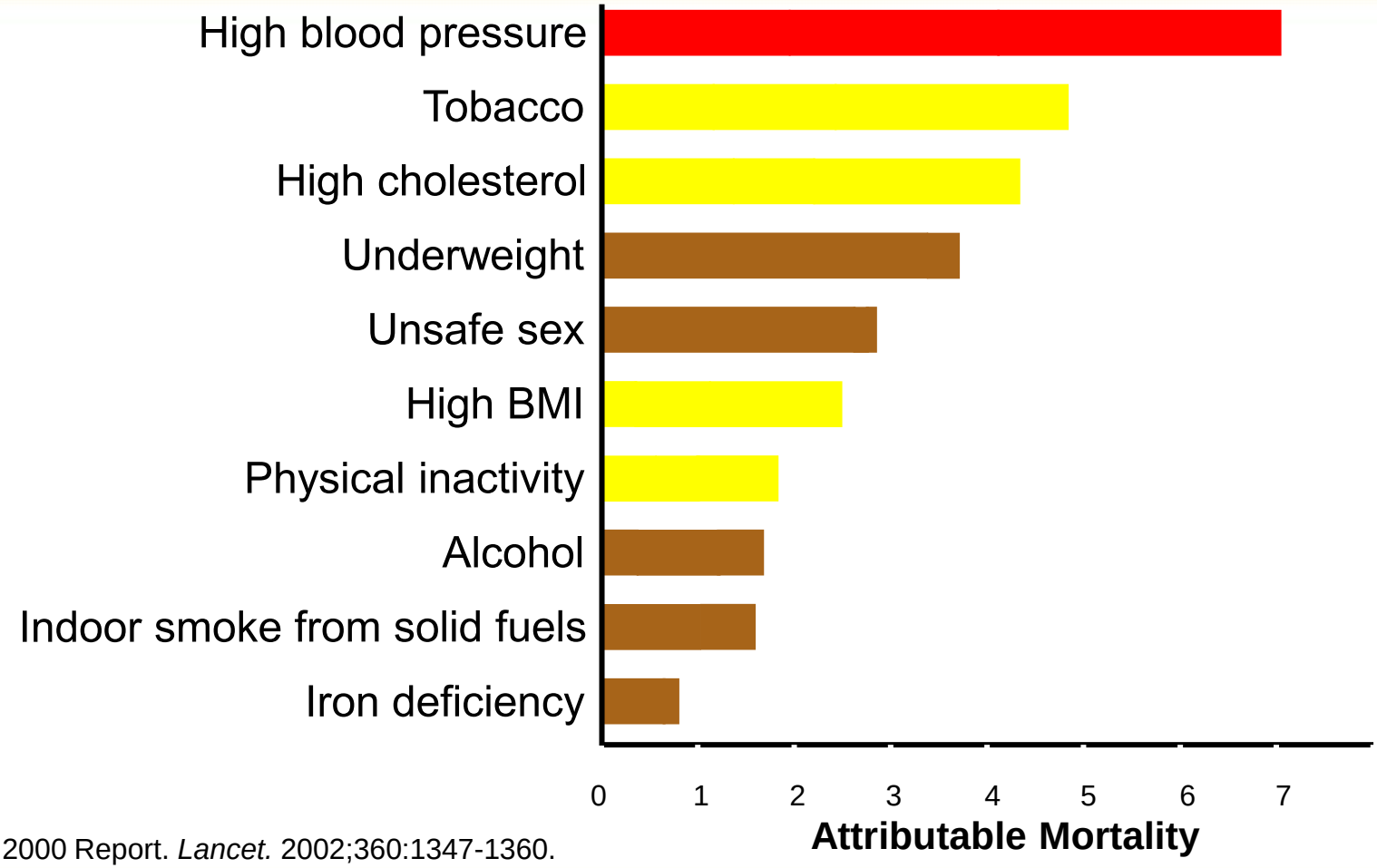
Statement of Need

"My greatest challenge as a health care provider in the management of patients with hypertension is

"

_____

Proportion of Deaths Attributable to Leading Risk Factors Worldwide (2000)



WHO 2000 Report. *Lancet.* 2002;360:1347-1360.

Hypertension as a Risk Factor

Hypertension is a significant risk factor for:

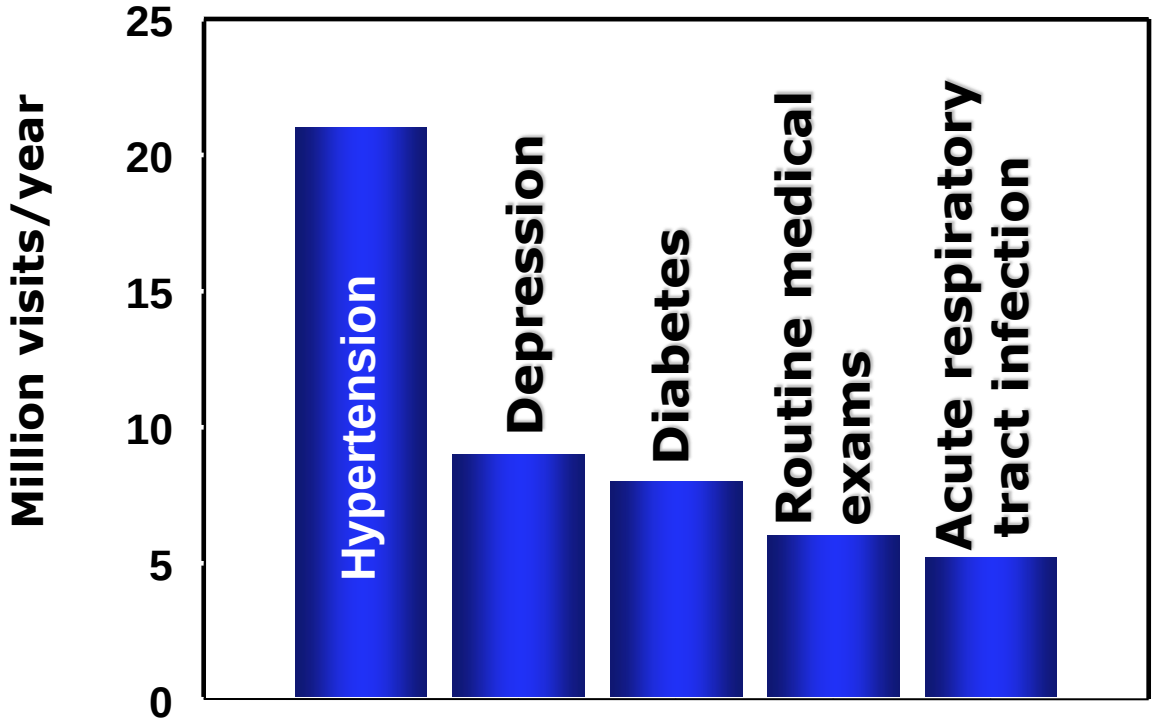
- cerebrovascular disease
- coronary artery disease
- congestive heart failure
- renal failure
- peripheral vascular disease
- dementia
- atrial fibrillation

Blood Pressure and Risk of Stroke and Ischemic Heart Disease Mortality

- Higher blood pressure is associated with an **increased** risk of stroke and ischemic heart disease mortality
- For every **20 mmHg** systolic blood pressure above 120 mmHg, the risk of dying doubles
- For every **10 mmHg** increase in diastolic blood pressure the risk **doubles**

Lancet 2002;360:1903-13

Leading Diagnoses Resulting in Visits to Physician Offices in Canada



Source: IMS HEALTH Canada 2002

History of Present Illness

- Cliff is a 76-year-old man who presents to your office with a new complaint of shortness of breath and intermittent palpitations at rest
- Present lifestyle
  - Non-smoker, averages 2 beers/day
  - Married; 2 children out of town

History of Present Illness

- A week ago
  - he noted dyspnea with exertion while climbing the stairs at the theatre
- 3 nights ago
  - he woke up from sleep with dyspnea and had to sit on the edge of his bed, with palpitations
- He noticed that he is winded after his usual walks with the dog
- No chest pain, no cough, no edema

Past History

- Hypertension
  - diagnosed and treated for 10 years
- Acute myocardial infarction
  - 6 years ago (thrombolysed) preserved LV function immediately after discharge
- Osteoarthritis
  - was an athlete in the past, retired physical education teacher

LV = left ventricular

Family History

- Mother
  - history of hypertension, stroke at age 75
- Father
  - Alzheimer's dementia at age 81
- Sisters
  - 2 sisters, both diagnosed with diabetes
- Brother
  - died at age 60 of colon cancer

Current Medications

- Hydrochlorothiazide 50 mg OD
- Amlodipine 5 mg OD
- ECASA 81 mg OD
- Rosuvastatin 10 mg OD
- Celecoxib 200 mg OD

Physical Examination

- Height: 172 cm
- Weight: 85 kg
- Waist 102 cm
- BMI: 28.7 kg/m^2
- BP (left arm, seated):
  144/84 mmHg using an automated device
- Pulse: 96 regular
- Systolic murmur 2/6 over aortic area with no radiation
- Not dyspneic at rest
- No edema
- Lungs clear on chest exam

You decide to send Cliff for an ECG

Discussion Question 1

What are the benefits of performing an ECG in this patient?

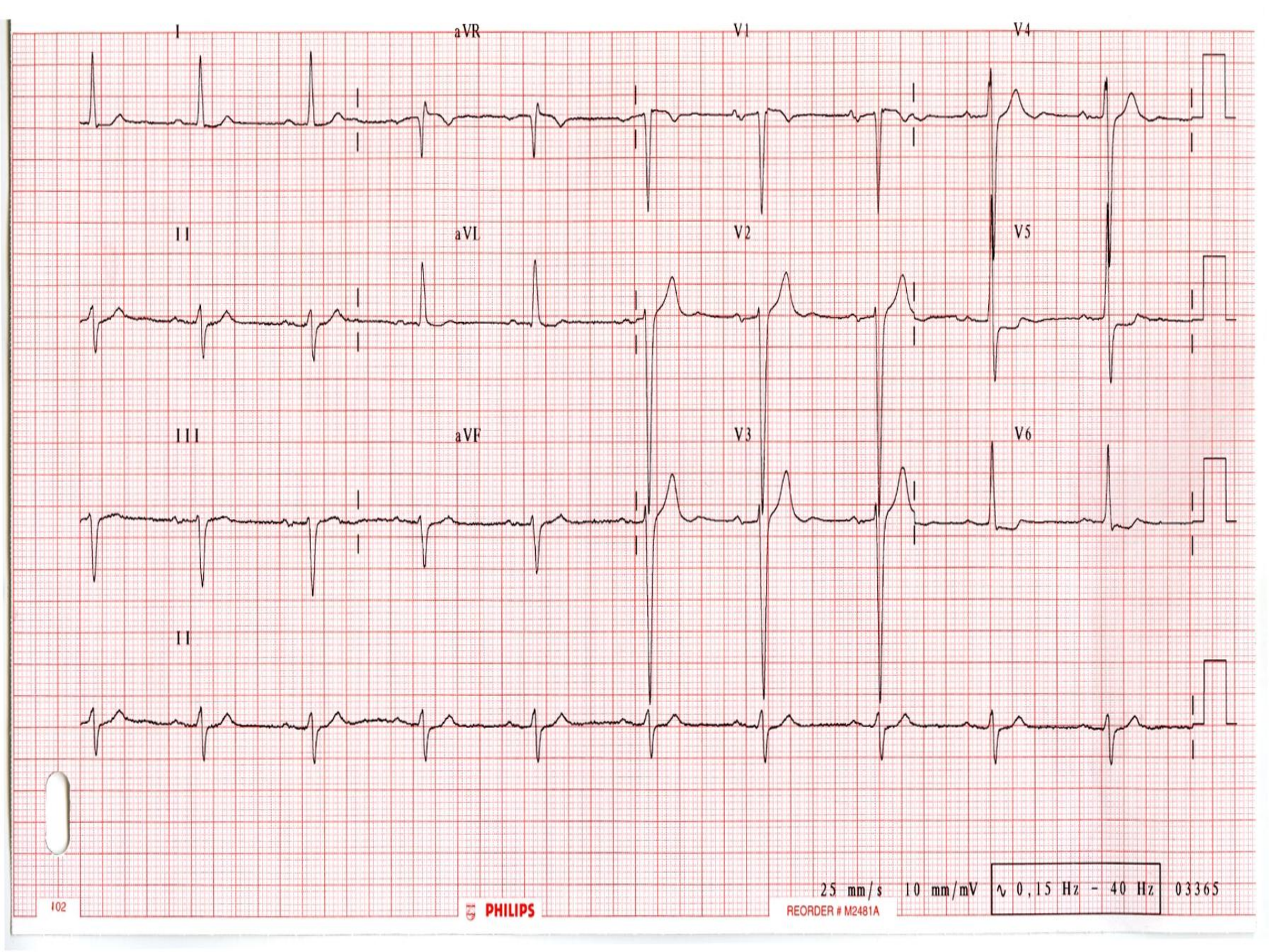
Discussion Question 1) What are the benefits of performing in ECG in this patient?

a) Document the patient's heart rhythm
b) Assessing for LVH or atrial abnormality or previous MI
c) Measure baseline QT interval that may be affected by pharmacologic therapy

Note: Discussion questions do not necessarily have only one correct answer

a, b and c are all correct

- Documenting the patient's heart rhythm
- Assessing for LVH or atrial abnormality or previous MI
- Measuring baseline QT interval that may be affected by pharmacologic therapy


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
25 mm/s
10 mm/mV
0,15 Hz - 40 Hz
03365
102
PHILIPS
REORDER # M2481A

Findings

- The ECG indicates sinus rhythm, left ventricular hypertrophy and strain

Laboratory Investigations

Test	Results	Normal Values
Glucose	6.5 mmol/L	4.0-8.0 mmol/L
Urea	6.8 mmol/L	3.0-7.0 mmol/L
Creatinine	105 µmol/L eGFR 50ml/min	44-106 umol/L
K	3.4 mmol/L	3.5-5.0 mmol/L
Hb	112 g/L	115-165 g/L

•Note that labs are done prior to the next visit. Hb: hemoglobin, K: potassium

Laboratory Investigations

Test	Results	Target Values for High Risk
LDL	2.5 mmol/L	<2.00 mmol/L
Total Chol	3.8 mmol/L	<5.20 mmol/L
TG	2.4 mmol/L	<1.71 mmol/L
HDL	0.8 mmol/L	>1.29 mmol/L
TC:HDL	4.75	

European Society of Hypertension Classification of Blood Pressure

Category	Systolic		Diastolic
Optimal	**<120**	**and / or**	**<80**
Normal	**<130**	**and / or**	**<85**
High-Normal	**130-139**	**and / or**	**85-89**
Grade 1 (mild hypertension)	**140-159**	**and / or**	**90-99**
Grade 2 (moderate hypertension)	**160-179**	**and / or**	**100-109**
Grade 3 (severe hypertension)	**≥ 180**	**and / or**	**≥ 110**
Isolated Systolic Hypertension (ISH)	**≥140**	**and**	**<90**

The category pertains to the highest risk blood pressure

*ISH=Isolated Systolic Hypertension. J Hypertension 2007;25:1105-87,

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**

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

* Target BP with AOBP < 135/85

Management Plan

- What are the nonpharmacological treatment options for this patient?

Management Plan

- Nonpharmacological
  - Sodium restriction, consult dietitian
  - Weight loss
  - Exercise
  - Reduction of alcohol intake

Impact of health behaviours on blood pressure

Intervention	Systolic BP (mmHg)	Diastolic BP (mmHg)
Diet and weight control	-6.0	-4.8
Reduced salt/sodium intake	- 5.4	- 2.8
Reduced alcohol intake (heavy drinkers)	-3.4	-3.4
DASH diet	-11.4	-5.5
Physical activity	-3.1	-1.8
Relaxation therapies	-3.7	-3.5
Multiple interventions	-5.5	-4.5

CHEP

Clinical Guideline : Methods, evidence and recommendations National Institute for Health and Clinical Excellence (NICE) May 2011

Hypertension CANADA

2014

Discussion Question 2

What are the main reasons for dyspnea in Cliff?

Discussion Question 2

What are the main reasons for dyspnea in Cliff?

a) Diastolic Heart failure
b) Angina equivalent
c) Hypertension
d) Anemia
e) Valvular heart disease

Note: Discussion questions do not necessarily have only one correct answer

a) Diastolic heart failure

- He has all the risk factors associated with this condition
- Possible atrial fibrillation, hypertension, ischemic heart disease
- ECG showing LVH

b) Angina equivalent

- Dyspnea can be a result of angina, especially in elderly persons

C) Hypertension

- Patients with uncontrolled hypertension will be asymptomatic until they develop target organ damage so this is unlikely

d) Anemia

- Patients with progressive anemia can manifest with shortness of breath
- Patient may have developed silent GI bleed or renal insufficiency as a cause
- Hb of 112 is unlikely to cause these symptoms even if acute

e) Valvular Heart Disease

- Clinical evaluation of possible aortic and mitral valve disease is more frequently misleading at the extremes of age (young/old)
- He is only 76 and has a murmur
- Consider aortic stenosis

Discussion Question 3

What risk factors does Cliff have for developing atrial fibrillation?

Discussion Question 3) What risk factors does Cliff have for developing atrial fibrillation?

a) Hypertension
b) LVH
c) Age
d) Ischemic heart disease

Note: Discussion questions do not necessarily have only one correct answer

a, b, c and d are all correct

- This patient has high risk of developing atrial fibrillation (hypertension, LVH, age, ischemic heart disease and alcohol* use)

* alcohol: best evidence is for those drinking 5+ per day

Discussion Question 4

If there is concern about underlying atrial fibrillation, what should be performed?

Discussion Question 4) If there is concern about underlying atrial fibrillation, which of the following should be performed?

a) Comprehensive review of symptom patterns
b) Review historical risk factors
c) Careful physical examination
d) CBC, electrolytes, renal function and thyroid function

Note: Discussion questions do not necessarily have only one correct answer

a) Comprehensive review of symptom patterns

- Determine if the pattern is one of paroxysmal or persistent atrial fibrillation
- Determine past history of atrial fibrillation

b) Review historical risk factors

- Consider hypertension and medication use
- Alcohol abuse, thyroid disease, sleep apnea

c) Careful physical examination

- Look for evidence of LVH and risk factors for thromboembolic disease

d) CBC, electrolytes, renal function and thyroid function

- Recommended for the evaluation of patients with atrial fibrillation

Discussion Question 5

The ECG shows that Cliff is in sinus rhythm with LVH and strain. Which tests will you now order?

Discussion Question 5) The ECG shows that Cliff is in sinus rhythm with LVH and strain. Which of the following tests will you now order?

a) Chest Radiograph
b) Diagnostic Holter
c) Echocardiography
d) Treadmill test exercise
e) Trans-esophageal echo

Note: Discussion questions do not necessarily have only one correct answer

a) Chest Radiograph

- A normal part of assessment for patients with shortness of breath
- Should be performed irrespective of ECHO

b) Diagnostic Holter

- Negative test does not rule out atrial fibrillation
- Holter is often insufficient to diagnose paroxysmal atrial fibrillation
- Cardiac loop monitor over 7 days or 2 weeks is better; documents arrhythmia, assesses rate control, assesses episodes of bradycardia

c) Echocardiography

- This is the best test to:
  - Measure size of the LA
  - Assess LV systolic function
  - Assess for ventricular function in including diastolic dysfunction
  - Assess for valvular disease
  - Assess for LVH
  - Also can estimate the PA pressure (right ventricular systolic Pressure)

d) Treadmill exercise test

- Indicated for those with exertional dyspnea, particularly without a cause
- Assesses functional capacity, BP and HR response to exercise
- Helps to guide care

e) Trans-esophageal echo

- Not a routine test
- This test helps to assess left atrial size and rule out an left atrial thrombus
- Invasive

Case Progression

After the ECG and after getting booked for the stress test, the Holter and Echo, Cliff left your office before therapy could be prescribed for his hypertension as he was concerned about the parking meter. He returns 4 weeks later to review the results of his tests. He has had occasional symptoms during that time.

His exercise stress test was normal. The Holter showed premature atrial contractions, and some episodes of supraventricular ectopy. The Echo shows normal EF, mitral annular calcification, mild left atrial dilation, concentric LVH and moderate diastolic dysfunction.

BP 148/78, HR is 85, SAO2 96%, RR is 16

Discussion Question 6

What's Your Treatment Plan?

Discussion Question 6
What's Your Treatment Plan?

a) Reduce afterload with a renin-angiotensin-aldosterone system (RAAS) blocker (ie ARB or ACEi)
b) Add bisoprolol 5 mg/day
c) Reduce HCTZ to 25 mg/day
d) Stop calcium channel blocker (amlodipine)
e) Stop celecoxib

Note: Discussion questions do not necessarily have only one correct answer and some may be incorrect

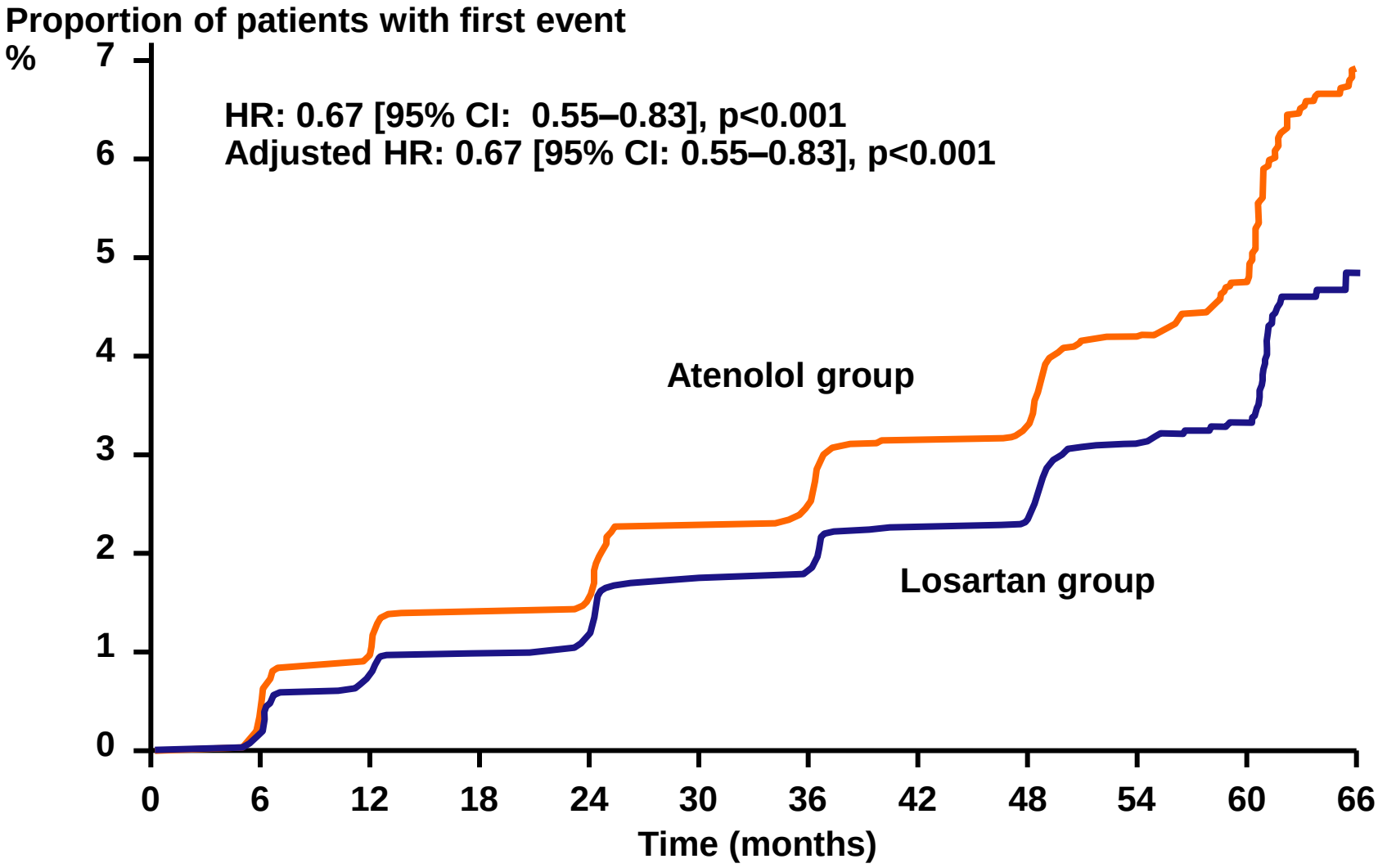
a) Reduce afterload with a RAAS blocker (i.e. ARB or ACEi)

- This helps treat symptoms of diastolic heart failure and achieve better control of blood pressure
- Helps to raise his potassium
- Reduces the chance of first episode of atrial fibrillation

Expected results:

BP 130/78, HR is 85, SAO2 96%, RR is 16

LIFE: New Onset Atrial Fibrillation Prevented



Wachtell et al J Am Coll Cardiol 2005

Atrial Fibrillation in Hypertension Does not Resolve with RAAS Blockade

- LIFE study (2005)
- Studies have attempted to reduce atrial fibrillation and cardiac events in patients with hypertension and AF using ARBs:
    1. GISSI-AF (2009)
    2. ACTIVE-I (2011)
    3. ANTIPAF (2007, 2011)
- Renin angiotensin blockade seemed to be good for AF prevention, studies have not demonstrated this (for those who have had AF)

b) Add bisoprolol 5 mg/day

- Good choice to slow the heart rate and lower blood pressure
- Does not address hypokalemia

Expected results:

BP 136/73, HR is 64, SAO2 96%, RR is 16

c) Reduce HCTZ to 25 mg/day

- Lowering the dose of HTCZ will help to reverse his hypokalemia which, in the setting of heart disease, can predispose to cardiac arrhythmias
- Lowering HTCZ will not address hypertension management
- Lowering HTCZ and adding ACEi or ARB will help to lower his blood pressure and correct his hypokalemia

Expected results:
BP 152/88, HR is 90, SAO2 96%, RR is 18

d) Stop calcium channel blocker (amlodipine)

- CCBs are not to be used routinely in patients with low ejection fraction systolic heart failure.
- If other forms of BP or HR lowering therapy are not available or tolerated, then these can still be used if necessary
- However he has a normal ejection fraction

Expected results:

BP 158/85, HR is 78, SAO2 96%, RR is 16

e) Stop celecoxib

- NSAIDS and coxibs lead to sodium retention and heart failure and increase the risk for hyperkalemia and hyponatremia
- Will also reduce effectiveness of most antihypertensives

Expected results:

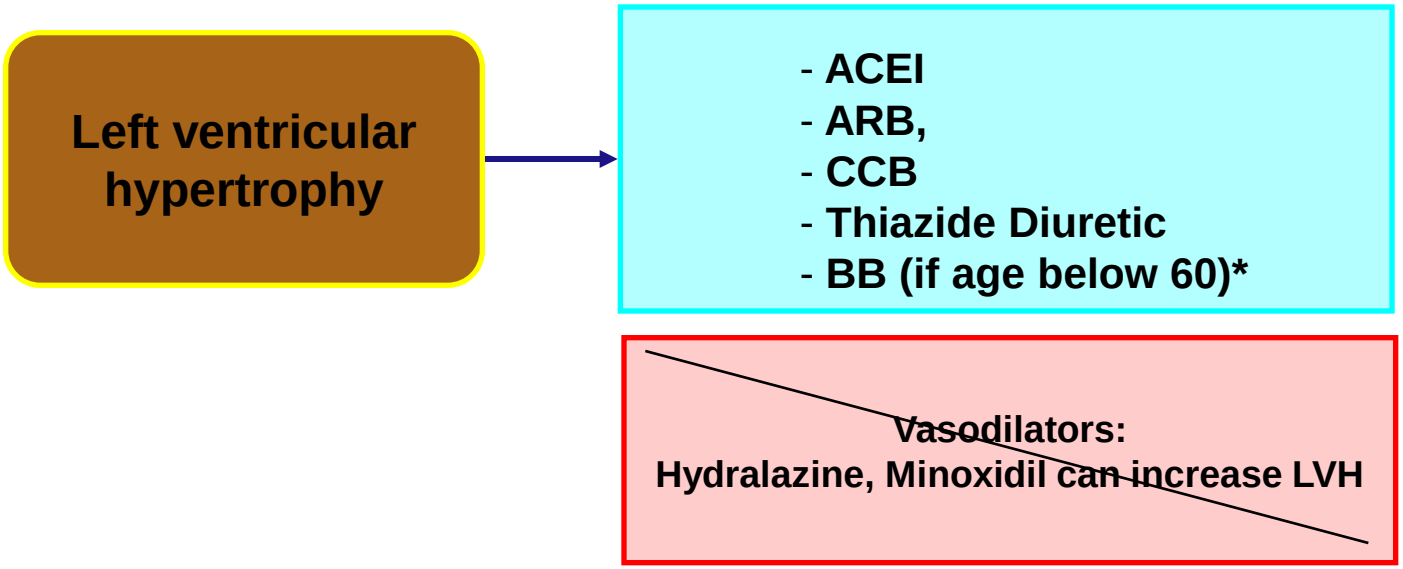
BP 142/72, HR is 84, SAO2 96%, RR is 18

Adjusted Medications

	Previous	Adjusted
Hydrochlorothiazide	**50 mg OD**	**25 mg OD**
Amlodipine	5 mg OD	5 mg OD
ECASA	81 mg OD	81 mg OD
Rosuvastatin	10 mg OD	10 mg OD
Celecoxib (previous) **Perindopril (new)**	**200 mg OD**	 **8 mg OD**

Treatment of Hypertension in Patients with Left Ventricular Hypertrophy

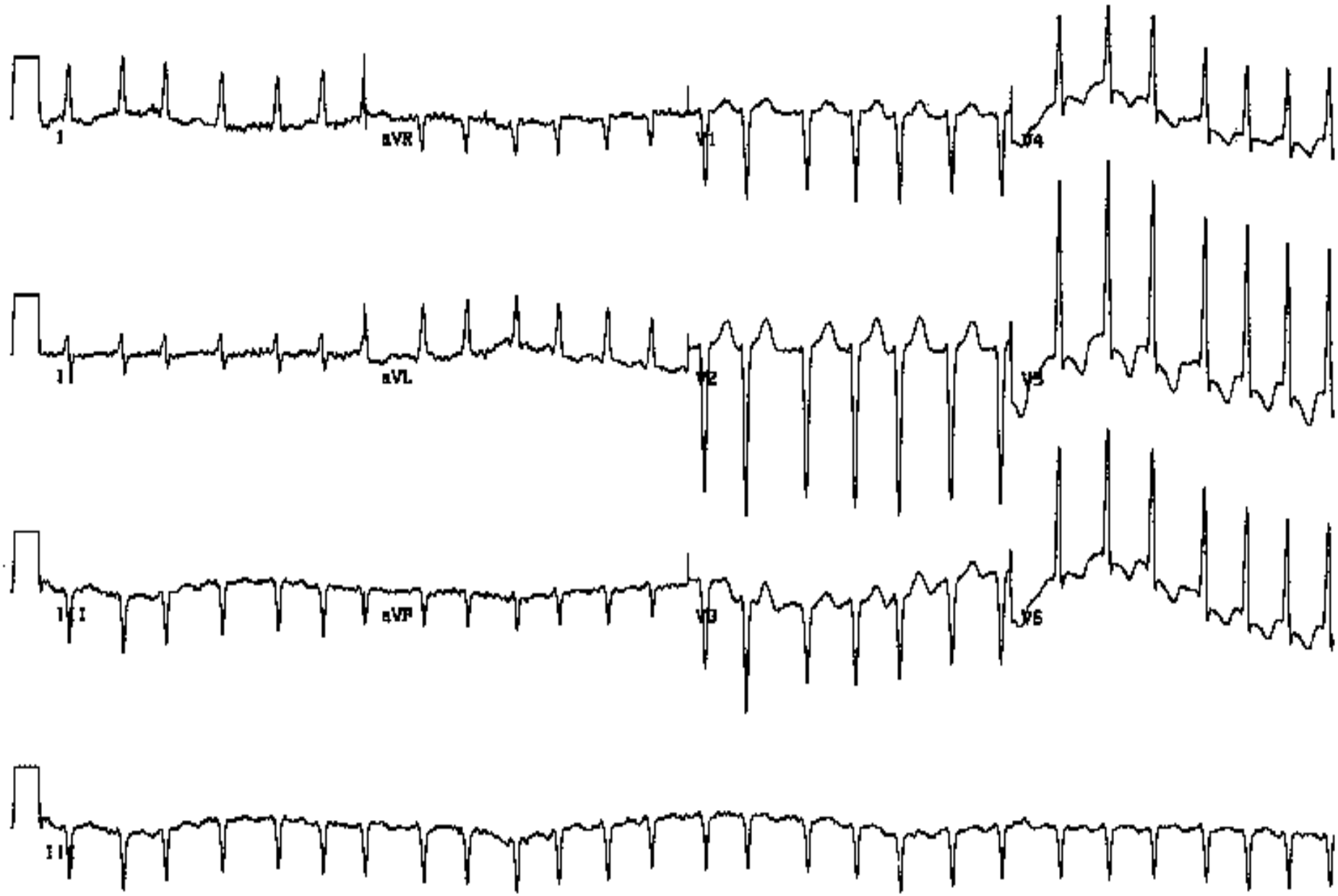
Hypertensive patients with left ventricular hypertrophy should be treated with antihypertensive therapy to lower the rate of subsequent cardiovascular events.



Case Progression

- Cliff tolerated therapy with an ACEi at a maximally recommended dose and a reduction of his HCTZ to 25 mg/day. Celecoxib was stopped as well
- His creatinine is 123 umol/L and potassium is now 4.0 mmol/L
- He continues to get palpitations associated with dypsnea and fatigue and his pulse is irregular during these episodes. He comes to your office and says he is experiencing these symptoms now
- You perform an ECG (slide follows)

BP 138/78, HR is 130, SAO2 96%, RR is 16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V2
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I
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V3
V6
II

Atrial Fibrillation: Uncontrolled Rate

- You start him on bisoprolol 5 mg/day for rate control
- His rate drops to 70-80 bpm but he remains in atrial fibrillation

Discussion Question 7

What's Your Treatment Plan?

Discussion Question 7
What's Your Treatment Plan?

a) Send him to the emergency room

b) Consult a cardiologist or an internist with expertise for atrial fibrillation

c) Start oral anticoagulant (e.g. warfarin 5 mg/day) and monitor INR to achieve a level of 2.0 – 3.0

d) Continue ECASA 81 mg/day

e) Start clopidogrel 75 mg/day

Note: Discussion questions do not necessarily have only one correct answer

a) Send him to the emergency room

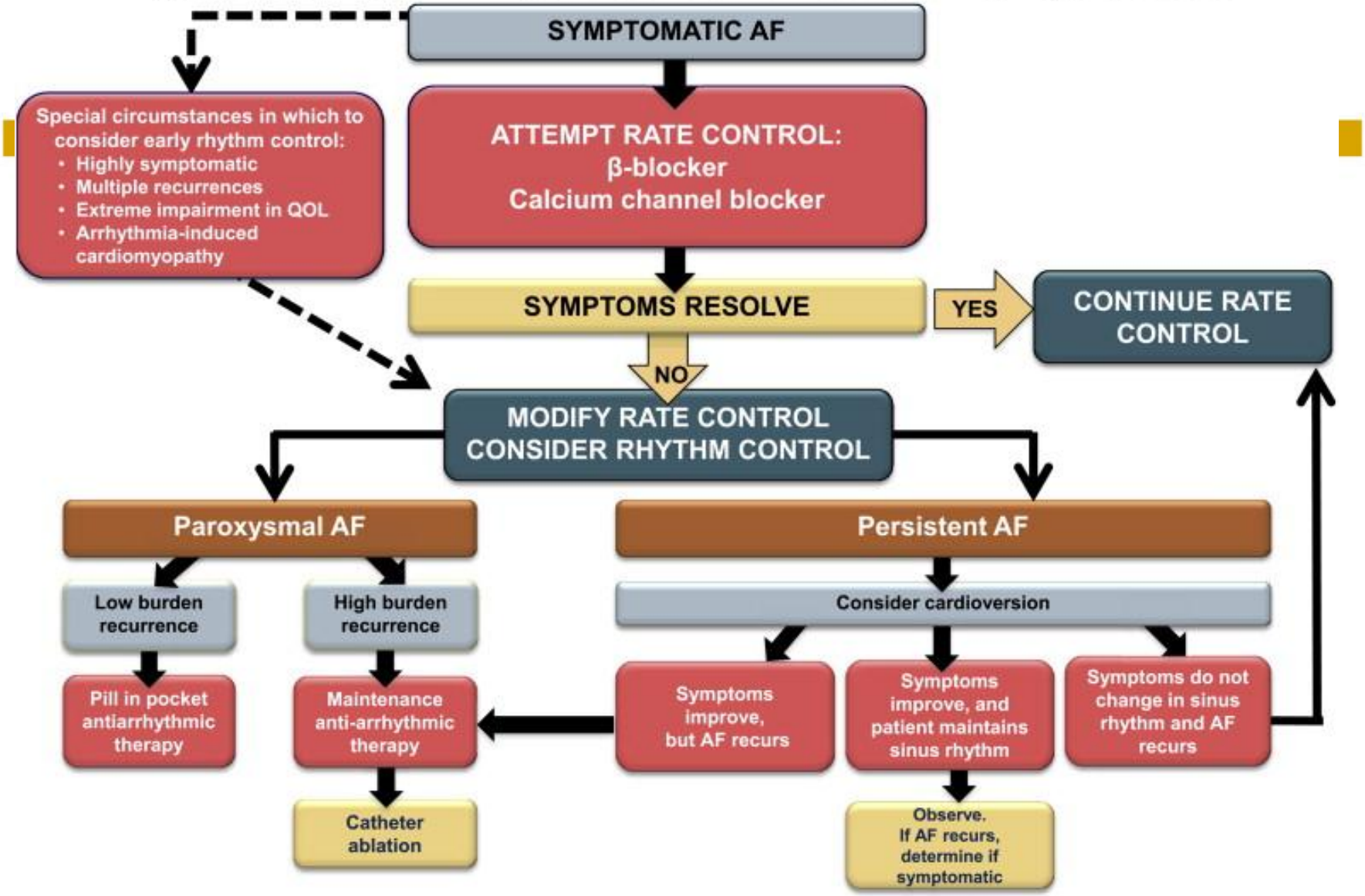
- In the absence of symptoms to suggest an acute event or hemodynamic instability, he can be managed as an outpatient
- If atrial fibrillation is of duration longer than 48 hours, he should have an anticoagulant for 3 weeks prior to cardioversion

b) Consult a cardiologist or an internist with expertise for atrial fibrillation

- No survival advantage from rhythm control over rate control alone (AFFIRM study*) even in severe CHF
- Patient requires management while waiting for appointment

*NEJM 2002;347:1825-33
*NEJM 2008;348:1284-86

Algorithm for Rate vs Rhythm Control for Patients With Symptomatic AF



Canadian Journal of Cardiology 2014 30 1114

c) Start oral anticoagulant (e.g. warfarin 5 mg/day or dabigatran) and monitor INR to achieve a level of 2.0 – 3.0

- His risk of stroke using the CHADS2 method is scored at 2

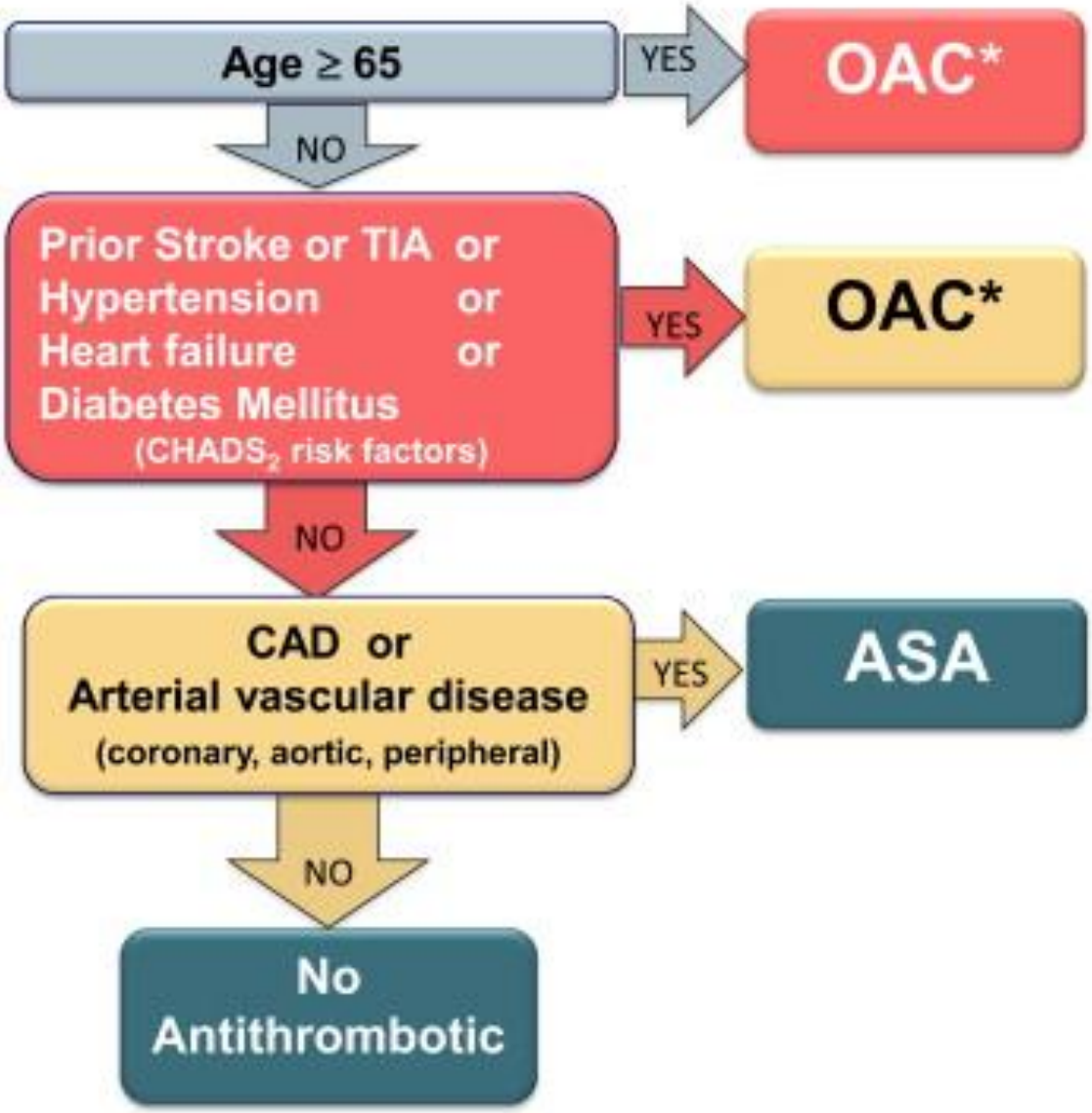
CHADS2	Points
Congestive Heart Failure	1
Hypertension	1
Age over 75 yrs	1
Diabetes Mellitus	1
Stroke or TIA history	2

CHADS2 Score

$CHADS_2$ Score	Risk of Stroke	Appropriate Therapy
0	Low	ASA 81 mg po od
1	Intermediate	Oral anticoagulation or ASA 81 mg po od
≥ 2	High	Oral anticoagulation

Note that other risk factors, such as systolic dysfunction, can also be considered when making a therapy choice with CHADS2 score of 1.

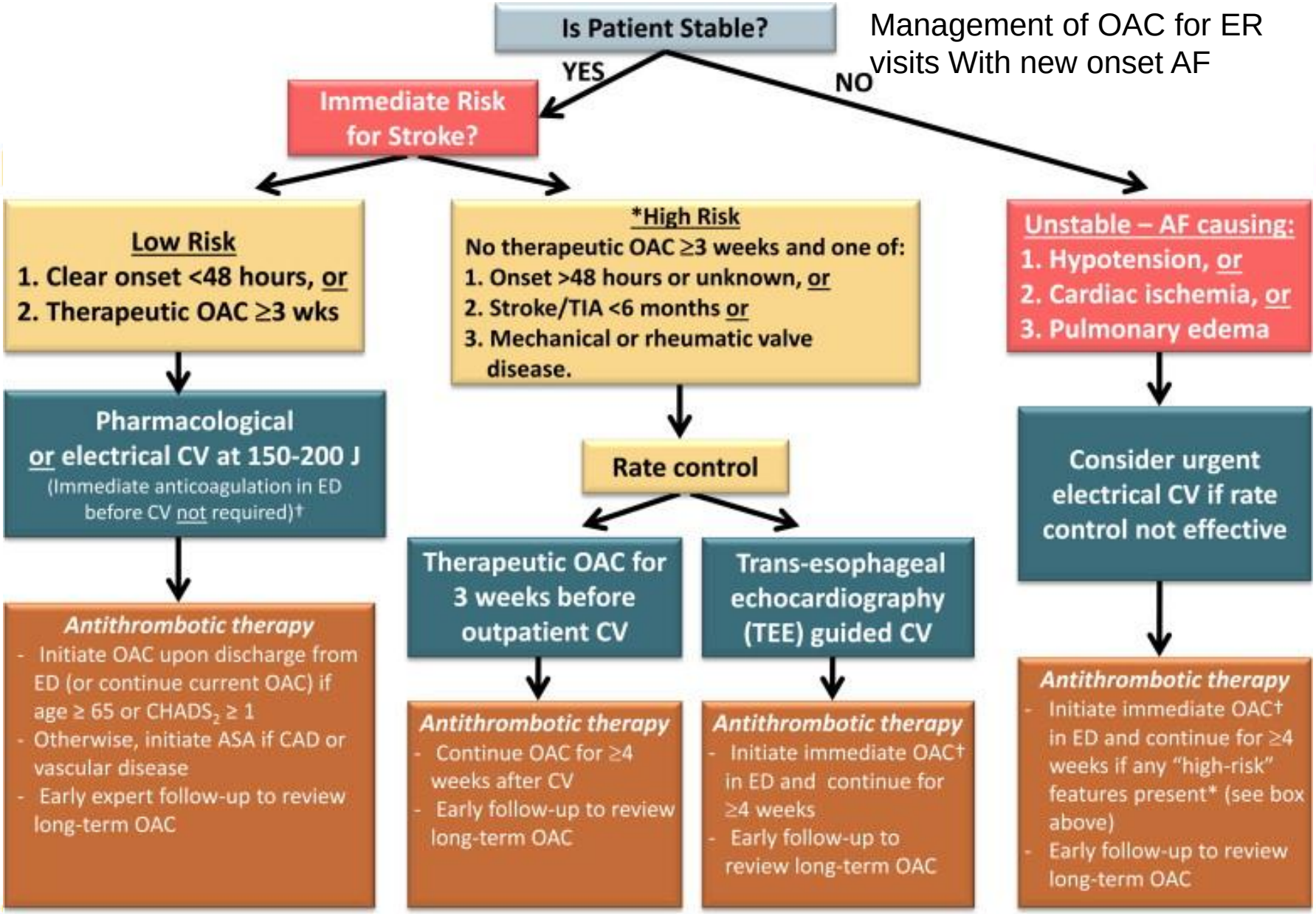
The "CCS Algorithm" for OAC Therapy in AF



Consider and modify (if possible) all factors influencing risk of bleeding during OAC treatment (hypertension, antiplatelet drugs, NSAIDs, excessive alcohol, labile INRs) and specifically bleeding risks for NOACs (low eGFR, age ≥ 75, low body weight).†

Canadian Journal of Cardiology 2014 30, 1114

Management of OAC for ER visits With new onset AF



Canadian Journal of Cardiology 2014 30, 1114

d) Continue ASA 81 mg/day

- Stop ASA*
- His CHADS2 score is 2, indicating moderate-high risk of stroke
- Indicates anticoagulation

*Don’t add ASA for associated stable vascular disease in a patient with atrial fibrillation receiving anticoagulation. Lip GY BMJ 2008;336:614

e) Start clopidogrel 75 mg/day

- His CHADS2 score is 2, indicating moderate-high risk of stroke
- Indicates anticoagulation

Case Progression

Cliff was started on a NOAC and rate control with bisoprolol has been effective. He is now back for a 2 month follow-up visit. He is feeling better. His exercise is back to baseline and is tolerating his medications.

- Perindopril 8 mg/day
- HCTZ 25 mg/day
- Amlodipine 5 mg/day
- Rosuvastatin 10 mg/day
- Bisoprolol 5 mg/day
- NOAC

BP 130/78, HR is 78, SAO2 96%, RR is 16

Discussion Question 8

What is your plan for follow up?

Discussion Question 8
What is your plan for follow up?

a) Review Cliff's blood pressure in clinic 3-4 times a year

b) Monitor global cardiovascular risk factors

c) Refer him for a pacemaker insertion

d) Continue lifestyle modifications

Note: Discussion questions do not necessarily have only one correct answer

a) Review Cliff's blood pressure in clinic

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

b) Monitor global cardiovascular risk factors

- This patient is higher risk so he is on a statin
- Ensure his blood pressure remains controlled
- Target systolic< 120 mmHg as he has chronic kidney disease, if he agrees, otherwise < 140 mmHg, LDL <2.0 and he is on a RAAS blocker

Systolic blood Pressure INtervention Trial SPRINT

- 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 and prior stroke

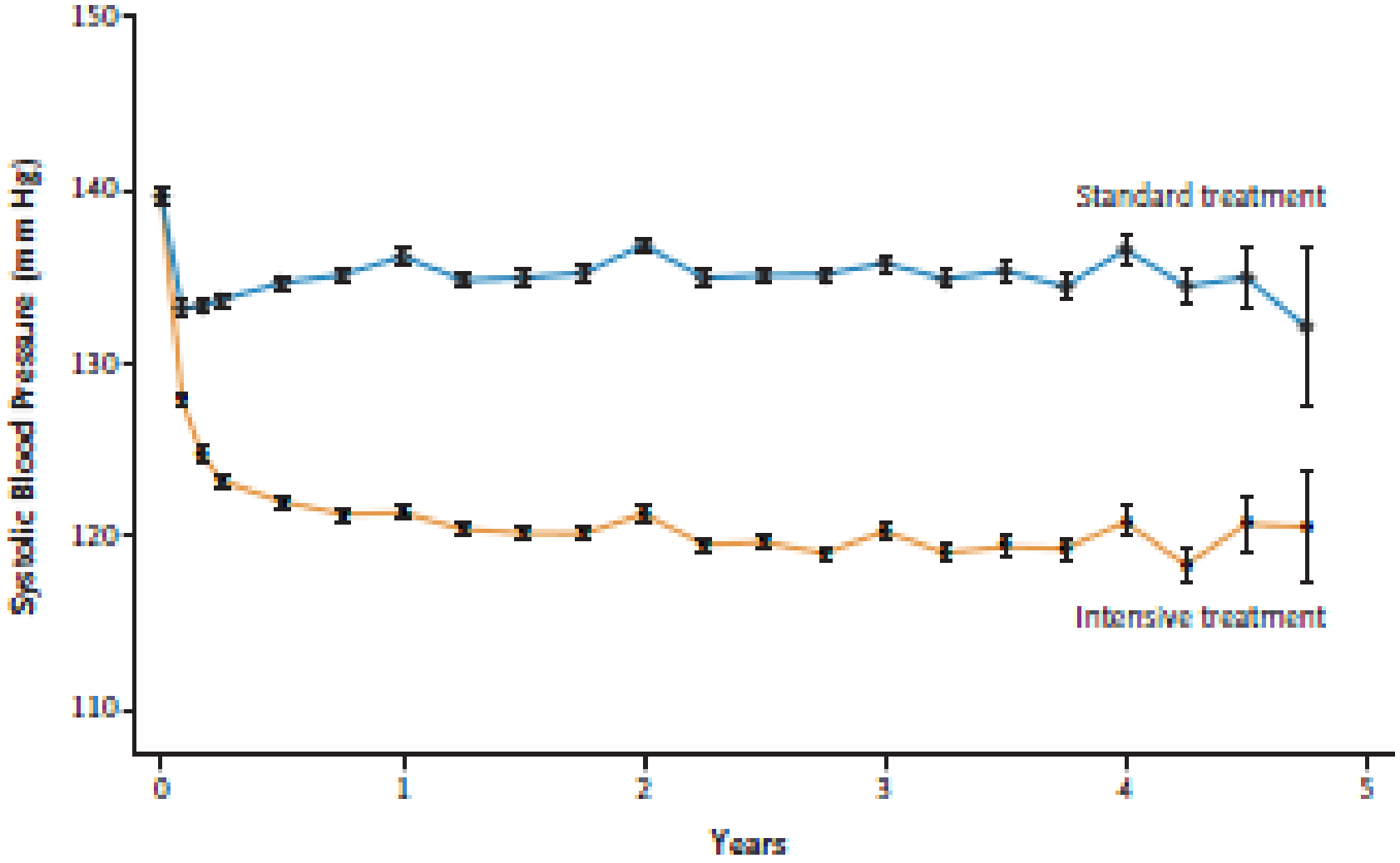
SPRINT: NEJM Nov 9 2015

Would Cliff Initially be a SPRINT Patient?

- Yes as he is 76 years old

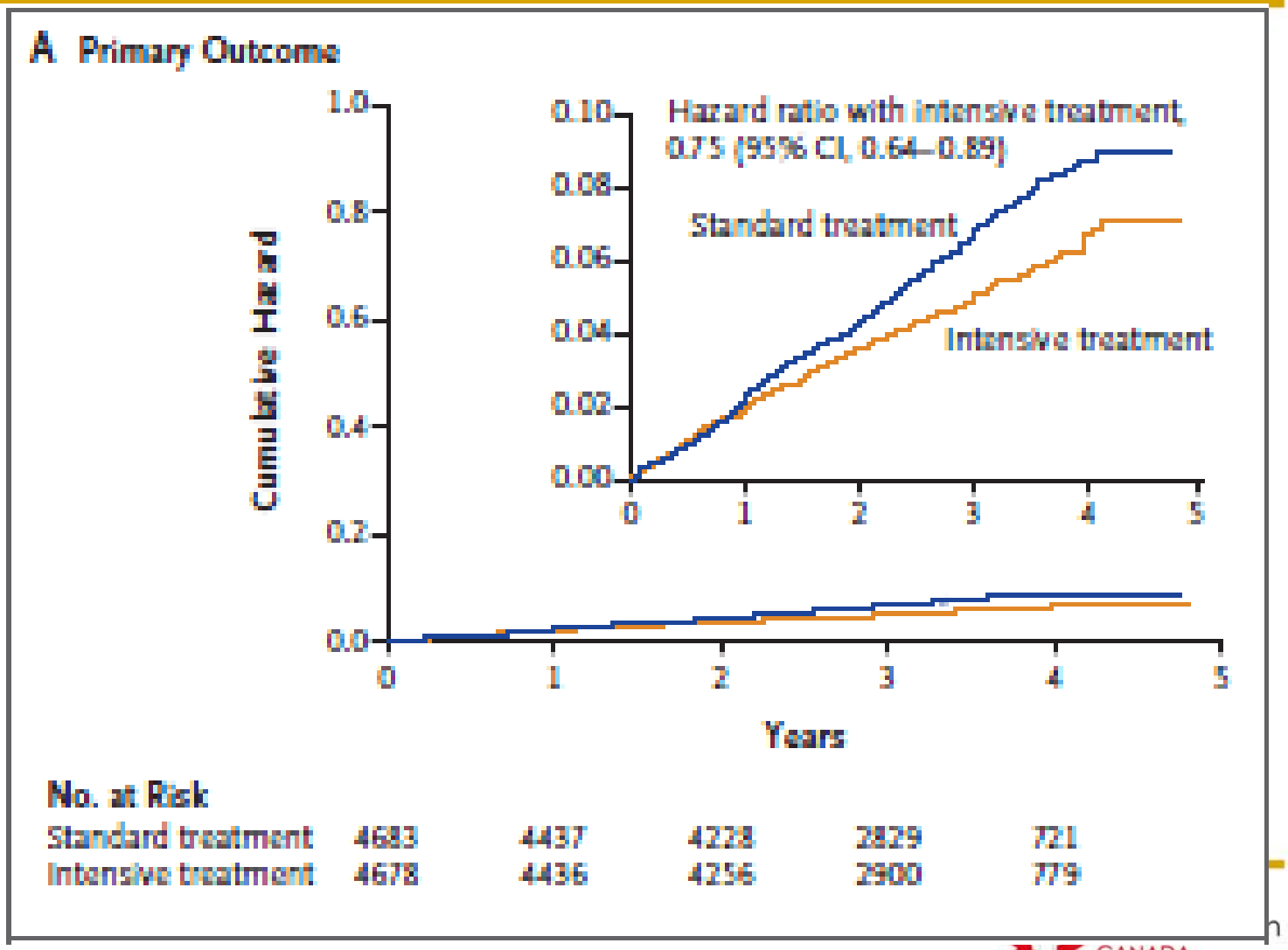
  - **High CV risk (other than stroke)**
    - CKD (eGFR 20 - <60)
    - 10 Year Framingham risk of 15%+
    - Age 75+
- Excludes: DM and prior stroke

SPRINT BP Over Time



SPRINT: NEJM Nov 9 2015

SPRINT Primary Outcome
MI, ACS, Stroke, CHF, CV death



- 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

SPRINT Implications for Cliff

- Should his BP target now be < 120 mmHg?
  - (he would have been a SPRINT candidate)
- How would we achieve the lower BP target and at what risk and benefit?
  - Current antihypertensive meds
    - Perindopril 8 mg/day
    - HCTZ 25 mg/day
    - Amlodipine 5 mg/day
    - Bisoprolol 5 mg/day

c) Refer him for a pacemaker insertion

- Unnecessary

d) Continue lifestyle modifications

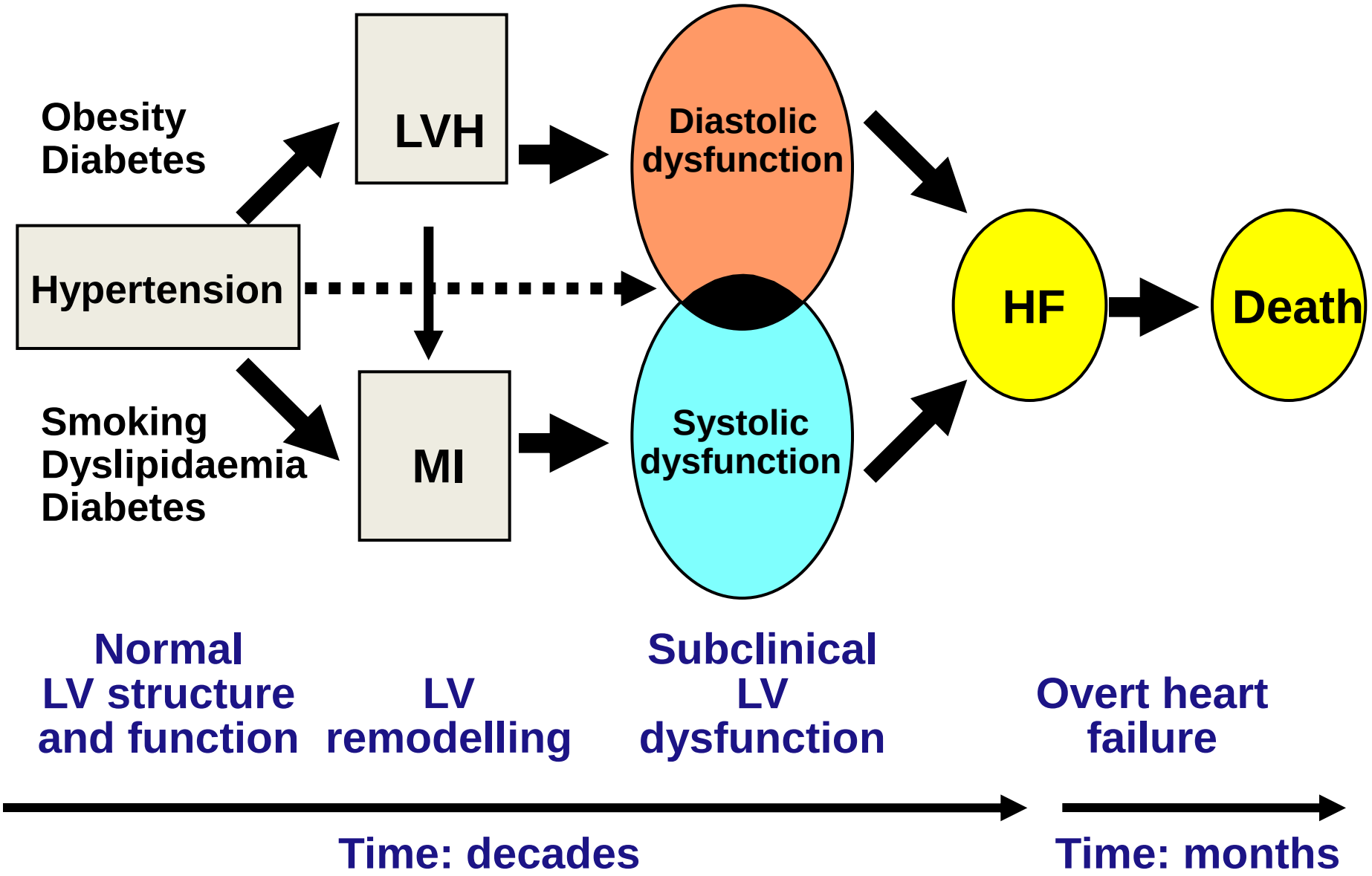
- Frequent brief interventions double the rate of lifestyle changes
- All hypertensives require ongoing support to initiate and maintain lifestyle changes

Cliff's wife who is also hypertensive asks: "What can I do to prevent a similar outcome?"

- Cliff is a 76 year old man with longstanding hypertension presenting with dyspnoea
- Likely a manifestation of CHF and atrial fibrillation
- Treated effectively with BP control and management of his atrial fibrillation

How might this have been prevented?

Progression from Hypertension to Heart Failure



The Major Risk Factors for the Development of Heart Failure

- Hypertension
- Myocardial infarction
- Angina pectoris
- Diabetes
- Left ventricular hypertrophy
- Valvular disease

Key Learnings and Reflection

- ✓ Keeping blood pressure controlled helps to prevent left ventricular hypertrophy and lowers the risk for developing heart failure
- ✓ Hypertension and heart failure are risks for the new onset of atrial fibrillation
- ✓ Controlling hypertension is likely the single most effective means of preventing both heart failure and atrial fibrillation