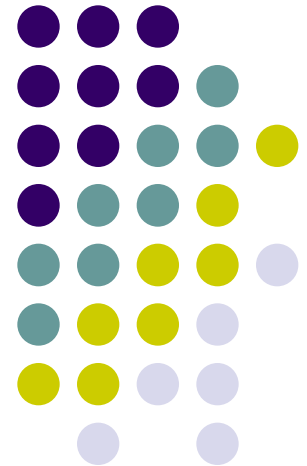


Canadian Hypertension Guidelines: A Focus on Drug Therapy and Adherence

Dr. Douglas Doucette, BSc(Pharm), PharmD, FCSHP
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The Moncton Hospital
Horizon Health Network, New Brunswick



Learning Objectives



- To review 2009 and 2010 Canadian Hypertension Education Program (CHEP) Guidelines and the rationale for these changes using a case-based format



Facilitator's Disclosure

I have received:

- Lecturer honoraria from AstraZeneca, MerckFrosst, NovoNordisk, Pfizer, and
- Research funds from MedBuy Inc.

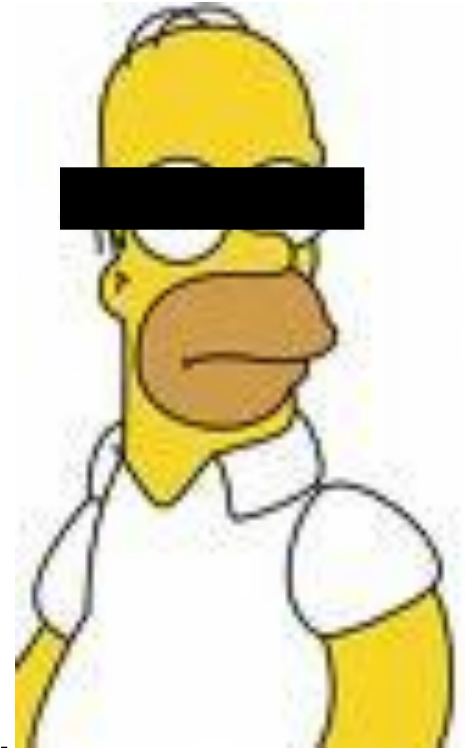
Acknowledgement:

- Ann Thompson, RPh, for her assistance in preparing this workshop presentation



Case 1

- Homer is a 46 y.o. white male who works at a major donut/coffee chain
- Med conditions:
 - Type 2 diabetes (diagnosed 7 years ago),
 - Obesity, ex-smoker x 4 years (20 pk-yr)
 - Hypertension, dx 4 years ago
- Meds: metformin 1000 mg bid, gliclazide 80 mg bid, lisinopril 20 mg od





Case 1

- BP usually 160/90 despite therapy
 - A1C 7.6 (6 months ago, was 7.4)
 - New dx of microalbuminuria
-
- **How common is H's situation in your practice?**

CHEP Annual Update 2009: What's new in the recommendations?



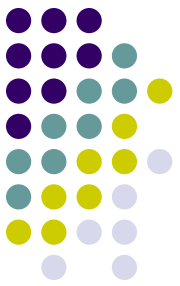
- **CHEP Theme for 2009: Hypertension in the diabetic patient**
- CHEP specifically does not recommend the use of the combination of an ACE inhibitor and angiotensin receptor blocker (ARB) in patients with: 1) uncomplicated hypertension, 2) ischemic heart disease in the absence of heart failure, 3) prior stroke, 4) non proteinuric chronic kidney disease and 5) diabetes without microalbuminuria
- CHEP specifically recommends that age not be used as a factor in prescribing pharmacotherapy for hypertension
- CHEP continues to encourage home measurement of blood pressure as a step towards greater patient self efficacy

Hypertension and Diabetes



- Hypertension is an important risk factor for patients with diabetes
 - 2/3 of Canadians with diabetes and hypertension have uncontrolled BP (above 130/80)
 - Up to 3/4 of diabetes complications can be attributed to hypertension
- More intensive reduction in blood pressure in people with diabetes is one of the few medical interventions that may reduce overall health costs

The Canadian Hypertension Education Program (CHEP)



- CHEP is an innovative knowledge translation program designed to reduce the disease burden of the leading risk for death in Canada.
 - Provides practical, trustworthy, up-to-date knowledge to health care professionals
 - This collaborative organization began in 1999
 - Provides annual updates of its recommendations to inform health care professionals about the newest information on hypertension
- Many slide decks included on public website www.hypertension.ca
 - Some slides are included in this presentation



CHEP

Goal

- To reduce the burden of cardiovascular disease in Canada through optimized hypertension management

Activities

- Regularly updated evidence-based recommendations for the management of hypertension
- Implementation of the recommendations
- Regular evaluation and revision of the program
- Assessment of patient outcomes



In 2010, CHP, BP Canada & CHS will merge to form Hypertension Canada

- See www.htnupdate.ca for resources



Benefits of Treating Hypertension

- Younger than 60 (reducing BP 10/5-6 mmHg)
 - reduces the risk of stroke by **42%**
 - reduces the risk of coronary event by **14%**
- Older than 60 (reducing BP 15/6 mmHg)
 - reduces overall mortality by **15%**
 - reduces cardiovascular mortality by **36%**
 - reduces incidence of stroke by **35%**
 - reduces coronary artery disease by **18%**

Challenges to Hypertension Management: Public Perceptions



- 44% of people could not identify a normal or a high blood pressure
- 80% of people were unaware of the association between hypertension and heart disease
- 63% believed that hypertension was not a serious condition
- 38% of people thought they could control high blood pressure without the help of a health professional

Impact of Lifestyle Therapies on Blood Pressure in Hypertensive Adults



Intervention	Intervention	SBP/DBP
Reduce foods with added sodium	-1800 mg/day sodium Hypertensive	-5.1 / -2.7
Weight loss	-1 kg	-1.1 / -0.9
Alcohol intake	-3.6 drinks/day	-3.9 / -2.4
Aerobic exercise	120-150 min/week	-4.9 / -3.7
Dietary patterns	DASH diet Hypertensive	-11.4 / -5.5
	Normotensive	-3.6 / -1.8

Applying the 2005 Canadian Hypertension Education Program recommendations: 3. Lifestyle modifications to prevent and treat hypertension Padwal R. et al. CMAJ · SEPT. 27, 2005; 173 (7) 749-751

Lifestyle Therapies in Hypertensive Adults: Summary



Intervention	Target	
Reduce foods with added sodium	< 2300 mg /day	
Weight loss	BMI <25 kg/m ²	
Alcohol restriction	≤ 2 drinks/day	
Physical activity	30-60 minutes 4-7 days/week	
Dietary patterns	DASH diet	
Smoking cessation	Smoke free environment	
Waist Circumference	Men	Women
- Europid	<94 cm	<80 cm
- South Asian, Chinese	<90 cm	<80 cm

Treatment of Adults with Systolic/ Diastolic Hypertension without Other Compelling Indications

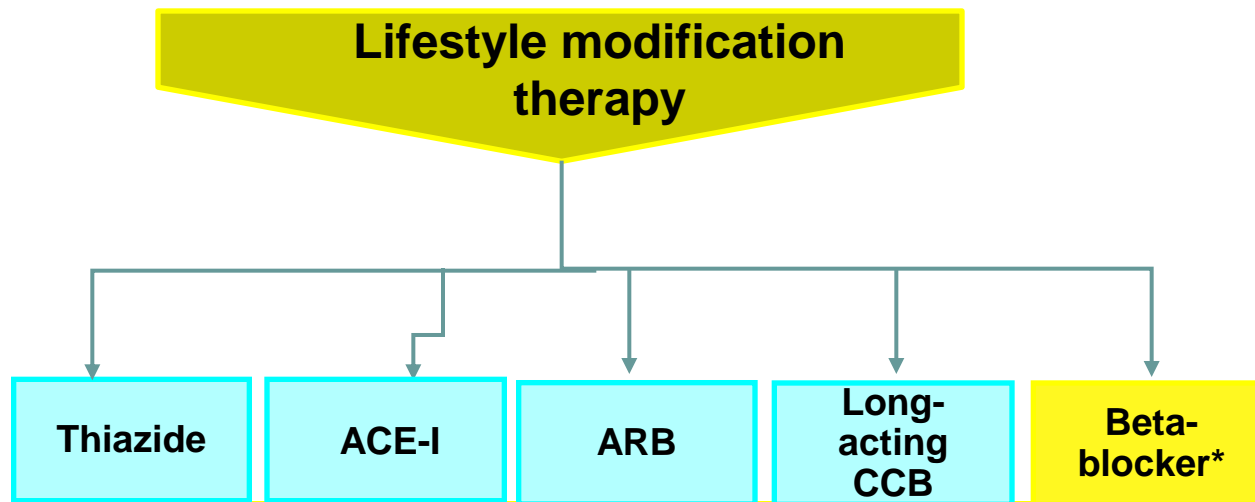


TARGET <140/90 mmHg

INITIAL TREATMENT AND MONOTHERAPY



A combination of first line drugs may be considered as initial therapy if the blood pressure is ≥ 20 mmHg systolic or ≥ 10 mmHg diastolic above target



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

ACEI and ARB are contraindicated in pregnancy and caution is required in prescribing to women of child bearing potential.

Do not prescribe and ACEI and ARB together unless there is a compelling indication

Case 2



- Peter - 56 y.o. white male
 - Works as a fisherman
 - Married with 3 children
 - BMI 31.5, smokes 1 ppd, 20-24 beer/week
- Diagnosed 4 years ago with HTN
- Meds:
 - Hydrochlorothiazide 12.5 mg daily
 - Ramipril 10 mg daily (x 1 year)
 - Candesartan 8 mg daily (x 2 months)





Case 2

- In office today, BP 146/94
 - Peter is still not at goal BP (140/90)
- His attempts at implementing lifestyle changes have not been successful
- **In small groups, discuss therapy options for Peter**

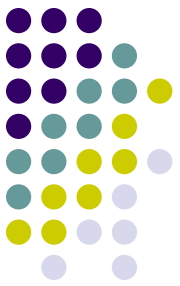
Case 2: Group Discussion



- **Treatment recommendation?**

CHEP Annual Update 2009:

What's new in the recommendations?



- CHEP Theme for 2009: Hypertension in the diabetic patient
- **CHEP specifically does not recommend the use of the combination of an ACE inhibitor and angiotensin receptor blocker (ARB) in patients with: 1) uncomplicated hypertension, 2) ischemic heart disease in the absence of heart failure, 3) prior stroke, 4) non proteinuric chronic kidney disease and 5) diabetes without microalbuminuria**
- CHEP specifically recommends that age not be used as a factor in prescribing pharmacotherapy for hypertension
- CHEP continues to encourage home measurement of blood pressure as a step towards greater patient self efficacy

ONTARGET: Background



- ACEI have been shown to reduce death, MI, and stroke in high-risk patients, but they are not tolerated in 15-20% of patients
- Based on mechanism of action, ARBs are often interchanged in these patients but this is not supported by evidence

The clinical questions asked by ONTARGET:

- In high risk patients, with CV disease or DM but without HF, is telmisartan 80mg daily non-inferior to ramipril 10mg daily in preventing CV death, MI, stroke or hospitalization for HF?
- Is the combination superior to ramipril alone?

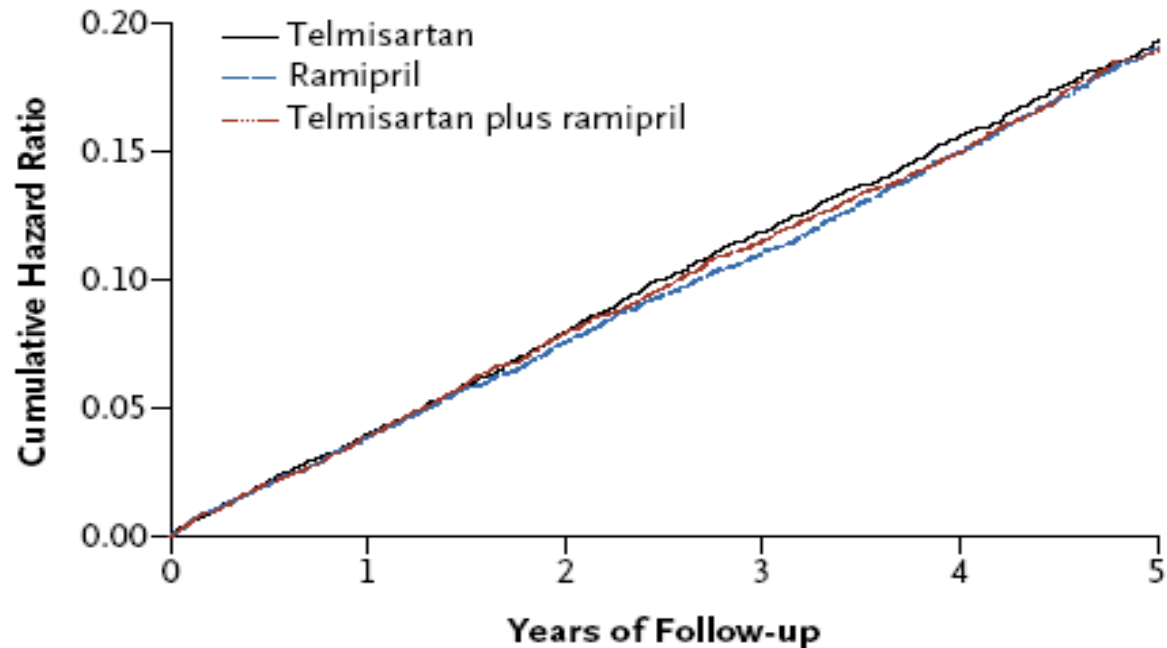
ONTARGET: Methods



- Design: DB, AC, RCT (1:1:1), n = 25 620, f/u 5.5 years
- Inclusion:
 - Patients > 55yo with prior history of: CAD, PVD, stroke/TIA, or DM with evidence of target organ damage
- Randomization:
 - Ramipril 10 mg daily OR Telmisartan 80 mg OR Combo
- Primary Outcomes:
 - CV death, MI, stroke, or hospitalization from HF
 - Non-inferiority: telmisartan vs ramipril
 - Superiority: combo vs ramipril



ONTARGET: Main Results



No. at Risk

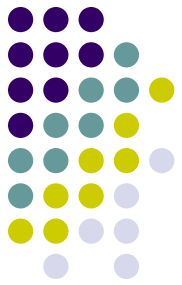
Telmisartan	8542	8177	7778	7420	7051	1687
Ramipril	8576	8214	7832	7472	7093	1703
Telmisartan plus ramipril	8502	8133	7738	7375	7022	1718



ONTARGET: Main Results

Blood Pressure

	Ramipril	Telmisartan	Combo
Systolic	-6.0	-6.9	-8.4
Diastolic	-4.6	-5.2	-6.0



ONTARGET: Tolerability

	Ram n=8576	Ram + Tel n=8502	Ram + Tel vs. Ram	
			RR	P
Hypotension	1.7%	4.8%	2.75	<0.0001
Syncope	0.2%	0.3%	1.95	0.032
Cough	4.2%	4.6%	1.10	0.1885
Diarrhea	0.1%	0.5%	3.28	<0.001
Angioedema	0.3%	0.2%	0.73	0.30
Renal Impairment	0.7%	1.1%	1.58	<0.001
Any Discontinuation	24.5%	29.3%	1.20	<0.001

ONTARGET: Summary




● Bottom line:

- Telmisartan is non-inferior to ramipril
- Combination therapy is not more effective than ramipril monotherapy and is associated with a higher rate of ADRs


What's New in CHEP 2010: Treatment of Hypertension in Patients with Ischemic Heart Disease



-  ACEI or ARB are recommended for most patients with established CAD
 - Although ARB may be non-inferior to ACEI, there is significantly more outcomes evidence favoring ACEI
 - Those at low risk or with well controlled risk factors may not benefit from ACEI therapy

What's New in CHEP 2010: Treatment of Hypertension in Patients with Ischemic Heart Disease (cont.)



-  When combination therapy is indicated for hypertensive control in patients with high CV risks, consider DHP CCB* plus ACEI
 - ACCOMPLISH: Despite having similar BP reductions, there was a 20% RRR in CV events & deaths of amlodipine/benazepril vs diuretic/benazepril

**DHP= dihydropyridine family of CCB, e.g. amlodipine, felodipine (NOT diltiazem or verapamil)*

Case 3



- Monty is 82 y.o. male in your practice
- He is relatively good health but has resisted treatment of hypertension (170-175 / 85-90) for the past 5 years
- A younger friend recently suffered a stroke
 - Monty is having second thoughts about drug therapy for his high BP



Case 3

- Monty has no history of CAD, DM or CKD
- He lives in his own home and is physically active
- **In small groups, discuss therapy options for Monty**

Case 3: Group Discussion



- **Treatment recommendation?**

CHEP Annual Update 2009:

What's new in the recommendations?



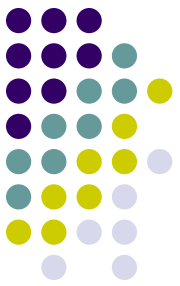
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Treating BP in the Very Elderly Patient



- A meta-analysis of treating HTN in those > 80 years old demonstrated that the reduction in stroke was offset by an increase in any-cause death (*Lancet* 1999;353:793-6)
- What are the benefits and risks of treating hypertension in patients 80 years and older?

HYVET trial



The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

**Treatment of Hypertension in Patients 80 Years
of Age or Older**

Nigel S. Beckett, M.B.,Ch.B., Ruth Peters, Ph.D., Astrid E. Fletcher, Ph.D., Jan A. Staessen, M.D., Ph.D.,
Lisheng Liu, M.D., Dan Dumitrascu, M.D., Vassil Stoyanovsky, M.D., Riitta L. Antikainen, M.D., Ph.D.,
Yuri Nikitin, M.D., Craig Anderson, M.D., Ph.D., Alli Belhani, M.D., Françoise Forette, M.D.,
Chakravarthi Rajkumar, M.D., Ph.D., Lutgarde Thijs, M.Sc., Winston Banya, M.Sc.,
and Christopher J. Bulpitt, M.D., for the HYVET Study Group*

- R, DB, PC trial done at 195 centers in 13 countries in Europe, China, Australasia, and Tunisia
- **Follow-up**: Median 1.8 years (mean 2.1, range 0-6.5)

HYVET Trial: Inclusion/Exclusion



- **Inclusion criteria:**

- 80 y.o. or more with persistent hypertension*

* Sustained sBP 160-199 mm Hg and dBP 90-109 mm Hg over 2 months with 2 office visits 1 month apart, 2 BP readings at each visit

N.B. In 2003, protocol amendment allowed dBP < 110 mm Hg, thereby allowing patients with ISH to be enrolled.

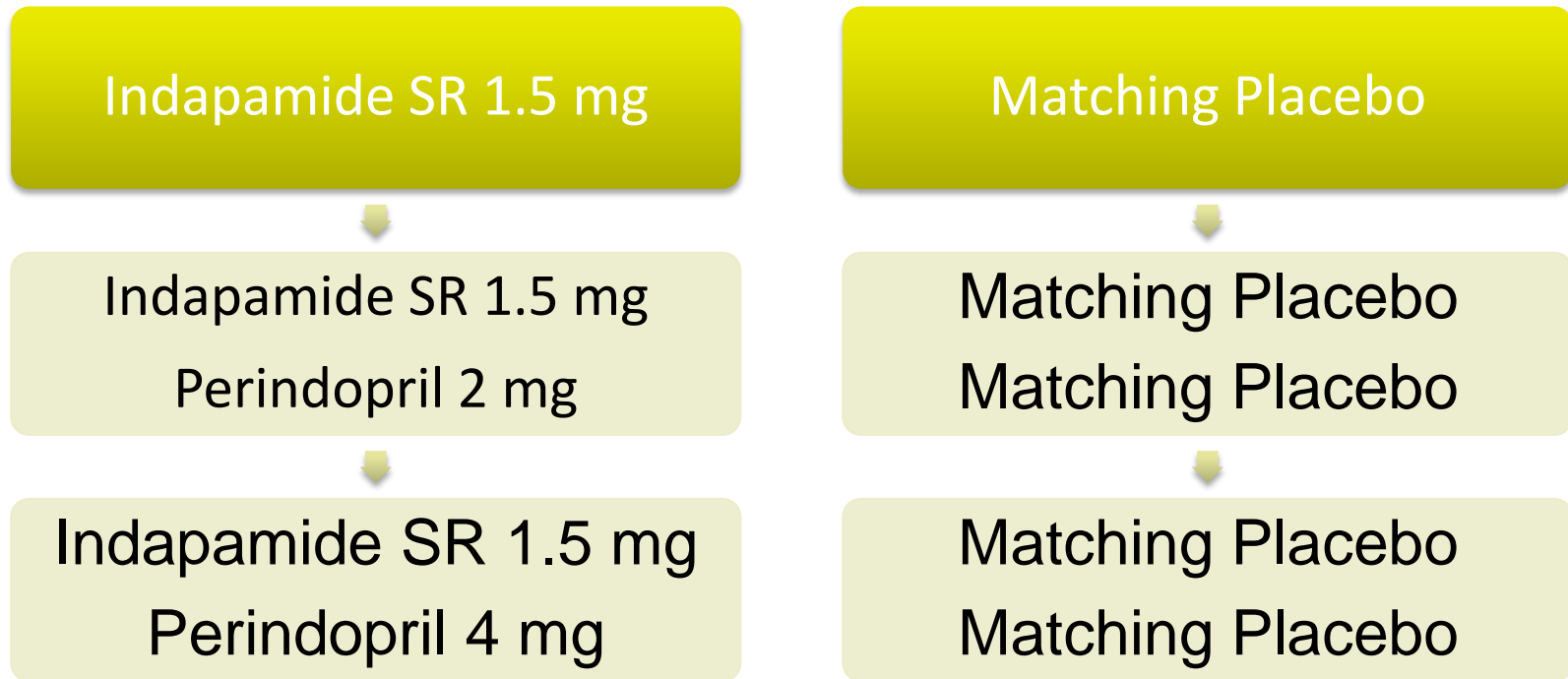
- **Exclusion criteria:**

- Contraindication to study med
- Accelerated or secondary hypertension
- Hemorrhagic stroke in the previous 6 months
- Heart failure requiring treatment with anti-HTN medication
- Serum creatinine level > 150 $\mu\text{mol/L}$
- K^+ < 3.5 mmol/L or > 5.5 mmol/L
- Gout
- Diagnosis of clinical dementia
- Requirement of nursing care

HYVET Trial: Design



Average baseline BP 173/91



Follow up every 3 months x 1 year, then every 6 months



HYVET Trial: Endpoints

- 1° Endpoint: Any stroke (fatal or nonfatal)
- 2° Endpoints:
 - Death from any cause
 - Death from cardiovascular causes
 - Death from cardiac causes (fatal MI, HF, or sudden death)
 - Death from stroke

HYVET: Baseline Characteristics



- 3845 patients randomized
- Average age: 83.6 ± 3.2
- 60% were female
- Average BP 173/91

- 65% of patients were on antihypertensives prior to enrolment
- Only 12% had history of CV disease

HYVET Trial: Results



Table 2. Main Fatal and Nonfatal End Points in the Intention-to-Treat Population.

End Point	Rate per 1000 Patient-Yr (No. of Events)		Unadjusted Hazard Ratio (95% CI)	P Value
	Active <i>no. (%)</i>	Placebo <i>no. (%)</i>		
Stroke				
Fatal or nonfatal	12.4 (51)	17.7 (69)	0.70 (0.49–1.01)	0.06
Death from stroke	6.5 (27)	10.7 (42)	0.61 (0.38–0.99)	0.046
Death				
From any cause	47.2 (196)	59.6 (235)	0.79 (0.65–0.95)	0.02
From noncardiovascular or unknown causes	23.4 (97)	28.9 (114)	0.81 (0.62–1.06)	0.12
From cardiovascular cause	23.9 (99)	30.7 (121)	0.77 (0.60–1.01)	0.06
From cardiac cause*	6.0 (25)	8.4 (33)	0.71 (0.42–1.19)	0.19
From heart failure	1.5 (6)	3.0 (12)	0.48 (0.18–1.28)	0.14
Fatal or nonfatal				
Any myocardial infarction	2.2 (9)	3.1 (12)	0.72 (0.30–1.70)	0.45
Any heart failure	5.3 (22)	14.8 (57)	0.36 (0.22–0.58)	<0.001
Any cardiovascular event†	33.7 (138)	50.6 (193)	0.66 (0.53–0.82)	<0.001

NNT

12

5

45

53

34

* Death from cardiac causes was defined as fatal myocardial infarction, fatal heart failure, and sudden death.

† Any cardiovascular event was defined as death from cardiovascular causes or stroke, myocardial infarction, or heart failure.

HYVET Trial: Treatment Effect on BP



Parameter	Active Treatment Arm	Placebo Arm
Baseline BP Sitting Standing	173/91 168/89	173/91 168/89
BP lowering Achieved (in mm Hg)	-29.5/-12.9	-14.5/-6.8
Mean Change in BP	-15/-6.1	
Final BP Achieved	143/78	159/84
% on indapamide only	25.8%	14.2% (Placebo)
Indap + perind 2mg	23.9%	13.4% (Placebo)
Indap + perind 4mg	49.5%	71.8% (Placebo)
% achieving BP target	48%	19.9%

*Degree of adherence to therapy not stated

HYVET Trial: Adverse Effects



Parameter	Active Treatment Arm	Placebo Arm	P-value
Change in serum K+ (normal = 3.5-5)	-0.02 mmol/L	+0.03 mmol/L	P=0.09
Change in uric acid (normal =220-420)	+11.6 μ mol/L	+3.5 μ mol/L	P=0.07
Change in glucose (normal = 4.0-6.0)	+0.16 mmol/L	+0.11 mmol/L	P=0.56
Change in Scr (normal = 60-110)	+3.4 μ mol/L	+2.3 μ mol/L	P=0.30
Number of reported serious adverse events (no details provided)	358 (18.5%)	448 (23.4%)	P=0.001

HYVET Trial: Summary

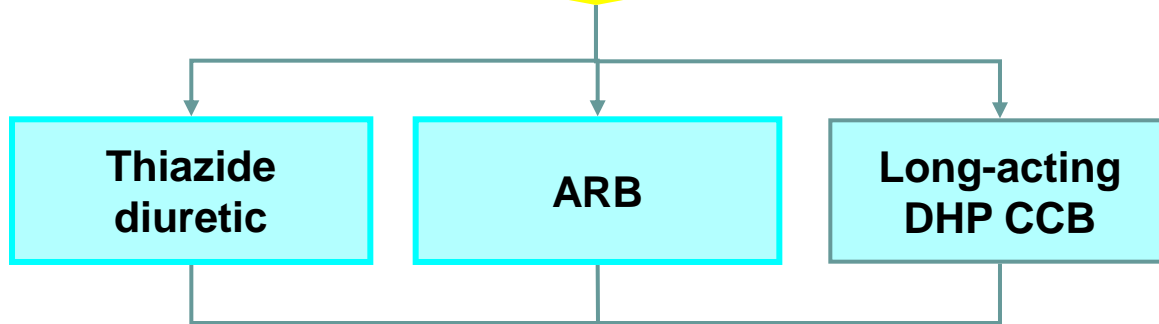


- Lowering BP to 150/80 or lower in octogenarians reduces all-cause mortality as well as fatal stroke and any heart failure.
- The thiazide diuretic indapamide and ACEI perindopril are safe to use in this population.
- “Healthy” patients in this age category can be screened to identify patients at risk, and then institute treatment if appropriate.
 - Caution in the frail elderly where postural hypotension may be more prevalent

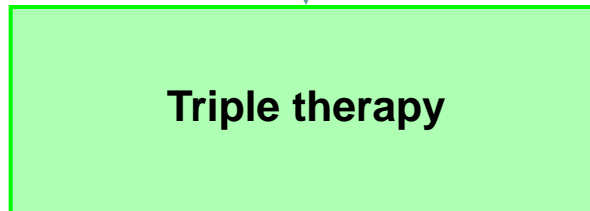
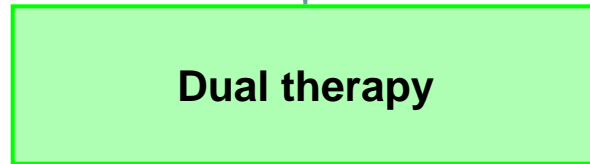
Treatment of Isolated Systolic Hypertension without Other Compelling Indications



TARGET <140 mmHg

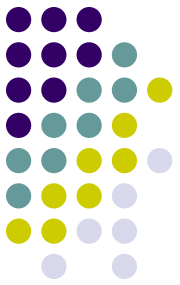


- CONSIDER**
- Nonadherence
 - Secondary HTN
 - Interfering drugs or lifestyle
 - White coat effect



*If blood pressure is still not controlled, or there are adverse effects, other classes of antihypertensive drugs may be combined (such as ACE inhibitors, alpha blockers, centrally acting agents, or nondihydropyridine calcium channel blocker).

Case 4



- Homer was prescribed an ACEI-thiazide diuretic combination 6 months ago
- His BP fell about 15/5 mmHg to 145/85, still short of target 130/80
- The physician suggests adding a third agent which concerns Homer, i.e. so many pills, potential side effects, etc.
- **How would you respond to the patient's concerns?**

Factors associated with high adherence to antihypertensive therapy



Factor	Odds ratio (95% CI)	p
>5 concurrent medications	1.62 (1.43–1.83)	<0.001
Diabetes mellitus	1.40 (1.15–1.71)	<0.001
Dyslipidemia	1.52 (1.24–1.87)	<0.001
Obesity	1.50 (1.26–1.78)	<0.001
Being on multiple drug combinations	1.29 (1.15–1.45)	<0.001

Dose Response for Antihypertensive Agents (on sBP)



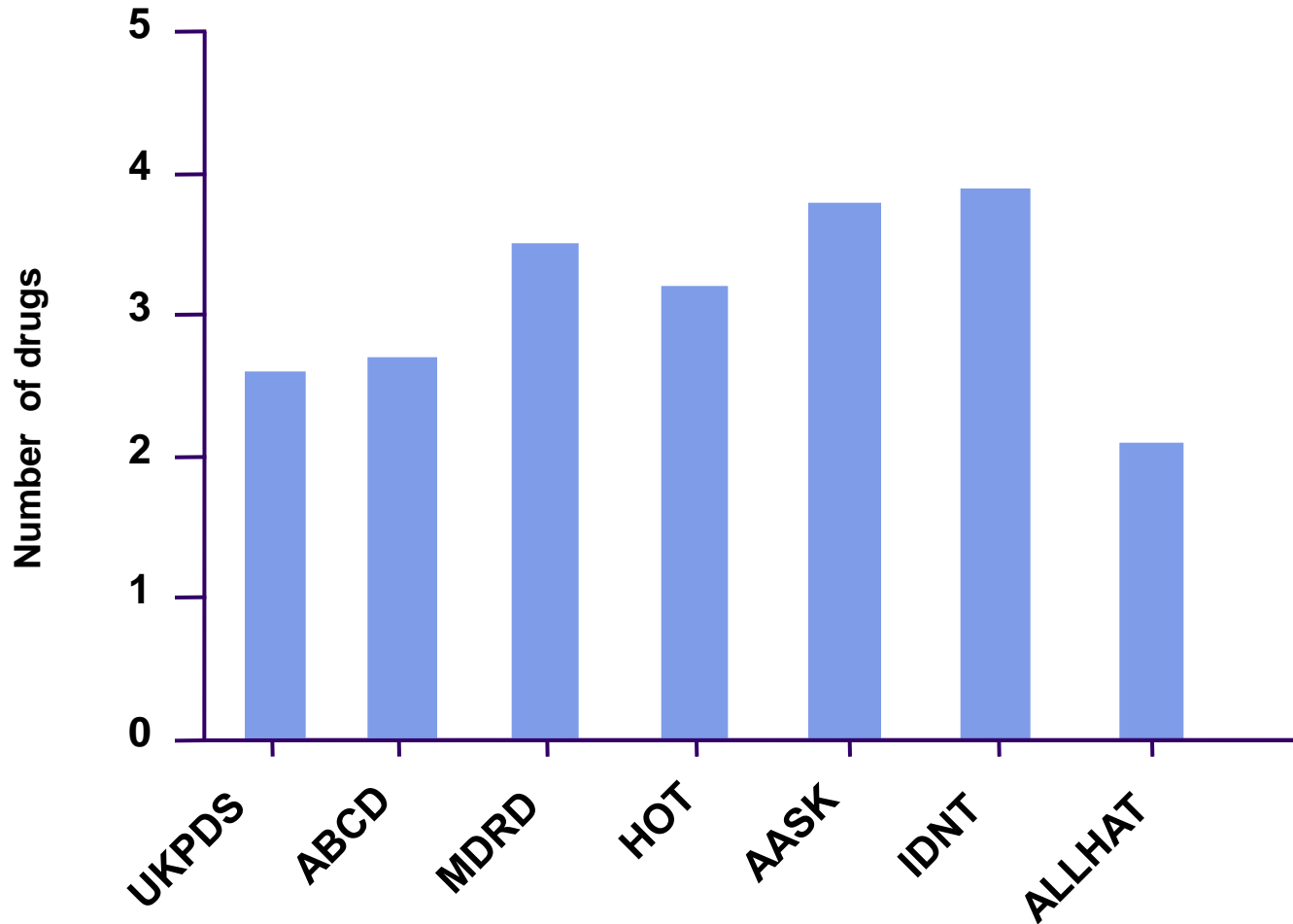
Class	Half SD	Standard Dose	Twice SD
Thiazides	7.4	8.8	10.3
BB	7.4	9.2	11.1
ACEI	6.9	8.5	10.0
ARB	7.8	10.3	12.3
CCB	5.9	8.8	11.7

Dose Response for BP Lowering and Adverse Effects



- Dose response curves for efficacy are relatively flat
- 1/2-standard dose regimen achieves 80% of BP lowering and is associated with significantly fewer adverse events
- Using combination therapy at standard doses has additive BP lowering effects

Most Hypertension Patients Need More Than One Drug



UKPDS = United Kingdom Prospective Diabetes Study; ABCD = Appropriate Blood Pressure Control in Diabetes; MDRD = Modification of Diet in Renal Disease; HOT = Hypertension Optimal Treatment; AASK = African American Study of Kidney Disease and Hypertension; IDNT = Irbesartan in Diabetic Nephropathy Trial; ALLHAT = Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial.

Managing Non-Adherence



- Patient non-adherence may involve gaps in:
 - Knowledge
 - Of disease and/or drug
 - Motivation
 - Patient beliefs based on experience/bias of drugs, disease, lack of confidence, caregivers, etc.
 - Adherence depends on perceived need for the treatment exceeding treatment-related fears
 - Ability
 - Dosing, side effects, compatible with lifestyle, acceptable price, disabilities, etc.

CHEP 2007: Adherence to Antihypertensive Management Can Be Improved By a Multi-Pronged Approach



- Assess adherence to pharmacological and non-pharmacological therapy at every visit
- Teach patients to take their pills on a regular schedule associated with a routine daily activity
- Simplify medication regimens using long-acting once-daily dosing
- Use fixed-dose combination pills
- Use unit-of-use packaging
- Encourage greater patient responsibility/autonomy in regularly monitoring their BP
- Educate patients and patients' families about their disease/treatment regimens verbally and in writing
- **Replace multiple pill antihypertensive combinations with single pill combinations**



CHEP Annual Update 2009:

What's new in the recommendations?



- **CHEP Theme for 2009**: Hypertension in the diabetic patient
- CHEP specifically does not recommend the use of the combination of an ACE inhibitor and angiotensin receptor blocker in patients with 1) uncomplicated hypertension, 2) ischemic heart disease in the absence of heart failure, 3) non proteinuric chronic kidney disease and 4) diabetes without microalbuminuria
- CHEP specifically recommends that age not be used as a factor in prescribing pharmacotherapy for hypertension
- **CHEP continues to encourage home measurement of blood pressure as a step towards greater patient self efficacy**

CHEP 2010: Key messages for the management of hypertension



- ✓ Know the current blood pressure of all your patients.
- ✓ Encourage the use of approved devices and proper technique to measure blood pressure at home.
- ✓ Assess and manage CV risk in hypertensives including: high dietary sodium intake, smoking, dyslipidemia, dysglycemia, abdominal obesity, unhealthy eating, and physical inactivity.



CHEP 2010: Key messages (cont.)

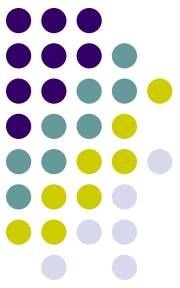
- ✓ Sustained lifestyle modification is the cornerstone for the prevention and control of hypertension and the management of CV disease. Encourage reducing sodium intake according to Health Canada's recommendations.
- ✓ Treat blood pressure to $<140/90$ mmHg. In people with diabetes or chronic kidney disease target to $<130/80$ mmHg and more than one drug is usually required including diuretics to achieve BP targets.
- ✓ Keep up to date with evidence and resources for hypertension management, go to: www.htnupdate.ca
 - Download the latest tools at: www.hypertension.ca/tools
 - Have your patients sign up at www.myBPsite.ca to access the latest hypertension resources for patients.



What's New for 2010

- CHEP recognizes that automated office blood pressure monitors are more frequently being used and provides early guidance on their use
- Sodium intake recommendations now in line with Health Canada: lower targets recommended with advancing age
- ARBs = ACEIs for most indications
- Combination therapy using first line agents:
 - Replace multiple pill antihypertensive combinations with single pill combinations
 - In high risk patients the combination of an ACEI and a DHP CCB is preferred

Questions?



- Thank you for your attention!
- Douglas.Doucette@HorizonNB.ca



Supplemental slides



Hypertension Care Pearls



- Multidisciplinary Team Care
 - Involvement of a multidisciplinary team improves adherence
- Combination Therapy of ACE inhibitor with ARB
 - Reassess all patients on this combination
 - Consider other combinations
 - Should only be considered in selected and closely monitored patients with advanced heart failure, or severe proteinuric nephropathy

Hypertension Care Pearls (cont.)



- Lifestyle changes are important to make.
 - Frequent brief interventions double the rate of lifestyle changes
 - All patients with hypertension require lifestyle assessment and ongoing support to initiate and maintain lifestyle changes
- 50% of hypertensives < 45 years old are not treated with antihypertensives even if they have multiple cardiovascular risks.
 - Start pharmacotherapy for hypertensive patients with multiple cardiovascular risks factors immediately, in addition to lifestyle changes
 - In particular, reduce risk factors in smokers who cannot quit



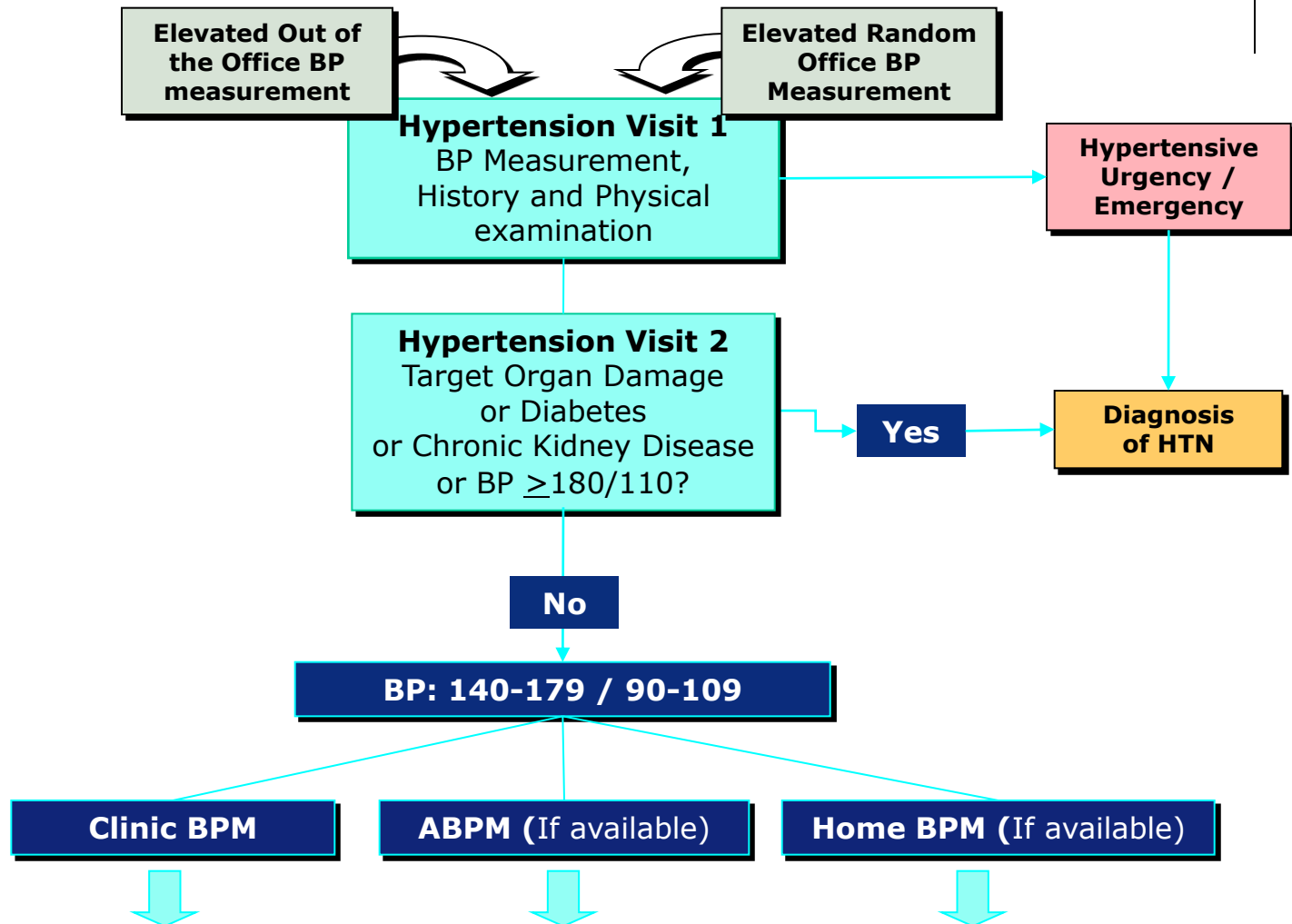
Home measurement of blood pressure

Home BP measurement should be encouraged to increase patient involvement in care

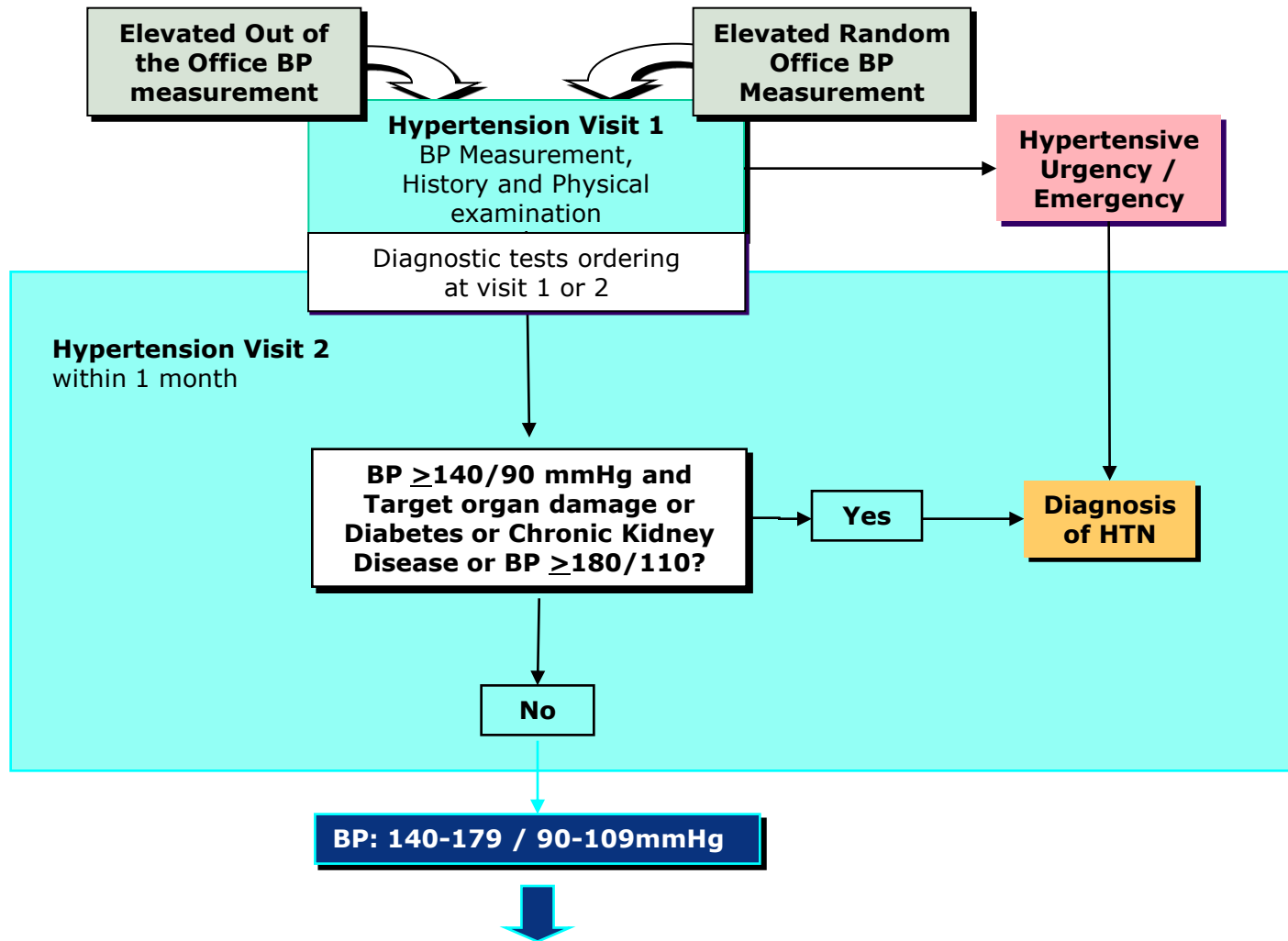
- **Uncomplicated hypertension**
- **Diabetes mellitus**
- **Chronic kidney disease**
- **Suspected non adherence**
- **Office-induced blood pressure elevation (white coat effect)**
- **Masked hypertension**

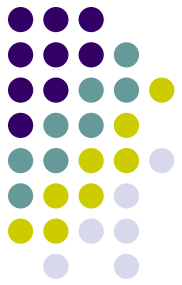
Average BP equal to or over 135/85 mm Hg should be considered elevated

II. Criteria for the diagnosis of hypertension and recommendations for follow-up

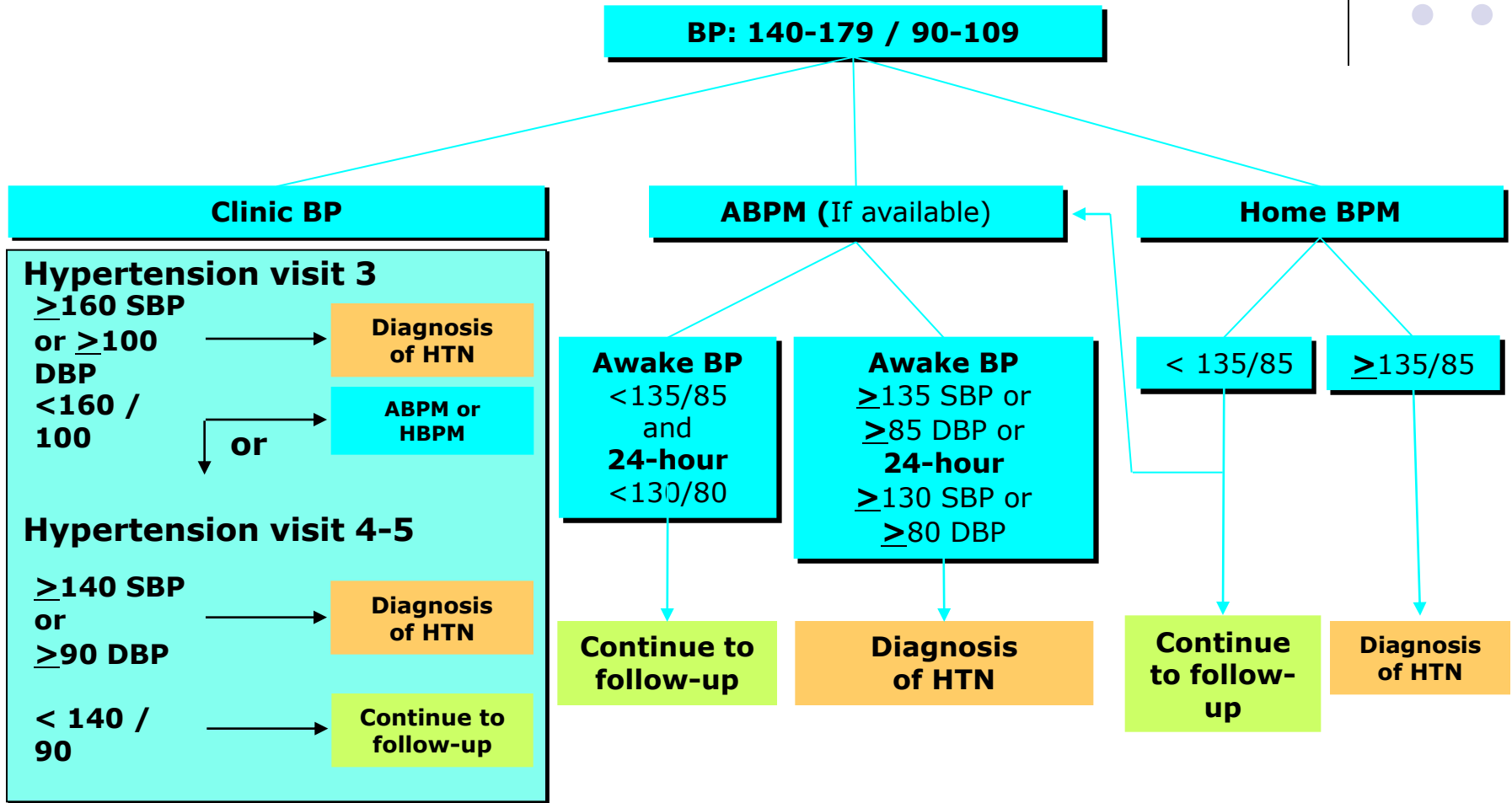


II. Criteria for the diagnosis of hypertension and recommendations for follow-up





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Patients with high normal blood pressure (clinic SBP 130-139 and/or DBP 85-89) should be followed annually.