

Hypertension

NICE, in conjunction with the British Hypertension Society, have just published new guidelines on the management of hypertension (NICE CG 127, August 2011). This Update Update focuses on the key changes, and answers some of the questions the guidelines raise.

The key changes are:

- **Ambulatory blood pressure is suggested as the investigation of choice for all with suspected hypertension.** Home readings are an alternative, if ambulatory cannot be used. Clinic BP readings are no longer recommended for the diagnosis of hypertension, however they can (and should) be used to monitor responses to treatment.
- **Hypertension is now defined as stage 1 and 2.** This affects who we treat. More on this later.
- **The threshold blood pressure for offering drug therapy has changed,** partly reflecting the move to ambulatory BP monitoring.
- **Diuretics have moved to third line drugs** after ACE inhibitors and calcium channel blockers
- **The thiazide-like diuretic of choice is now indapamide or chlortalidone rather than bendroflumethiazide** or hydrochlorothiazide. The reasons for this are discussed in the FAQs section. However NICE say that those already established on bendroflumethiazide or hydrochlorothiazide need not be changed to chlortalidone or indapamide.

These guidelines do not apply to those with diabetes – this is covered in the NICE guidelines relating to diabetes, which is discussed in the diabetes chapter of The GP Update Handbook.

IMPORTANT NOTE:

The text and flow charts in the NICE guidance contradict themselves when it comes to the 10year CVD risk at which treatment should be offered. The text says treatment should be offered if the 10y CVD risk is 20% or greater. The flow chart says initiate treatment if the 10y CVD risk is greater than 20% (i.e. 21% and above). Given that 20% and above is the usual cut off in all other guidance, we have worked on the assumption that the text is correct, and reflected this throughout our summary. There are also some other places in document where we wonder if NICE may have got in a bit of muddle with their <, >, ≤ and ≥ signs! We have drawn your attention to these where they occur!

PRAGMATIC PAUSE

So often when you read national guidance there appears to be a gap between what in reality can be done on the ground and how the guideline writers would like things to be done! These guidelines are no exception – NICE recommend that everyone who has a raised blood pressure reading in a single consultation should be fitted with an ambulatory monitor. The evidence for ambulatory machines is that they are better than home/clinic BP readings (25% lower over diagnosis rate, better CV outcomes, as discussed later. But fitting it after having elevated readings during a single consultation? How realistic is that?

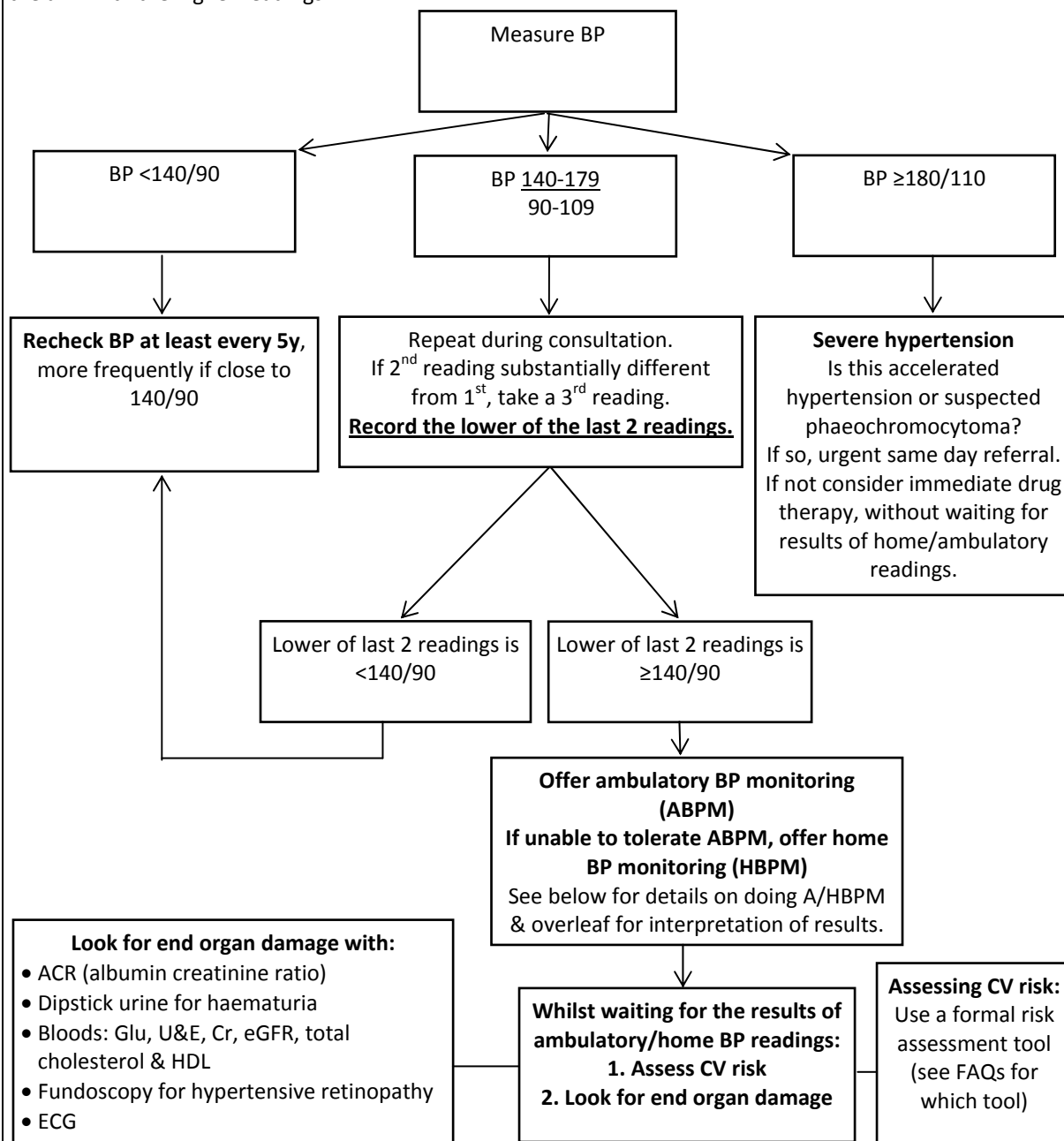
As you read on you will also see that NICE gives us multiple different BP targets to remember – clinic readings, diagnostic thresholds, treatment thresholds, all of which are different and also vary according to age. I accept that this may be the very 'best' way to do things according to the evidence, but I am struggling to remember all the different numbers, and maybe choosing targets that were not quite so perfect but might be memorable, might have achieved better outcomes overall as we might actually have had a hope of remembering, and therefore achieving them!

*So, to help you out I have included our practice protocol at the end of this Update Update. It's a single sheet of paper that takes a pragmatic approach, based on the NICE guidance with a few pragmatic tweaks: we do extra BP readings before fitting an ambulatory machine, we allow patients to choose between ambulatory and home monitoring, as long as they know ambulatory is a bit better, we code those not on medication differently to avoid unnecessary recalls. It also summarises all the different numbers in a single place. **Use it if it is helpful, ignore it if not! (Best viewed in colour!)***

NICE on Hypertension

NICE CG 127, 2011

- Measure BP using a validated device, with the patient sitting with the arm supported, using an appropriately sized cuff.
- If using an automated device check the pulse first: automated devices may not measure BP accurately if the pulse is irregular.
- NICE suggest measuring blood pressure in both arms initially. If the difference between the 2 arms is >20mmHg, repeat the readings. If this difference persists, all subsequent BP readings should be measured in the arm with the higher readings.

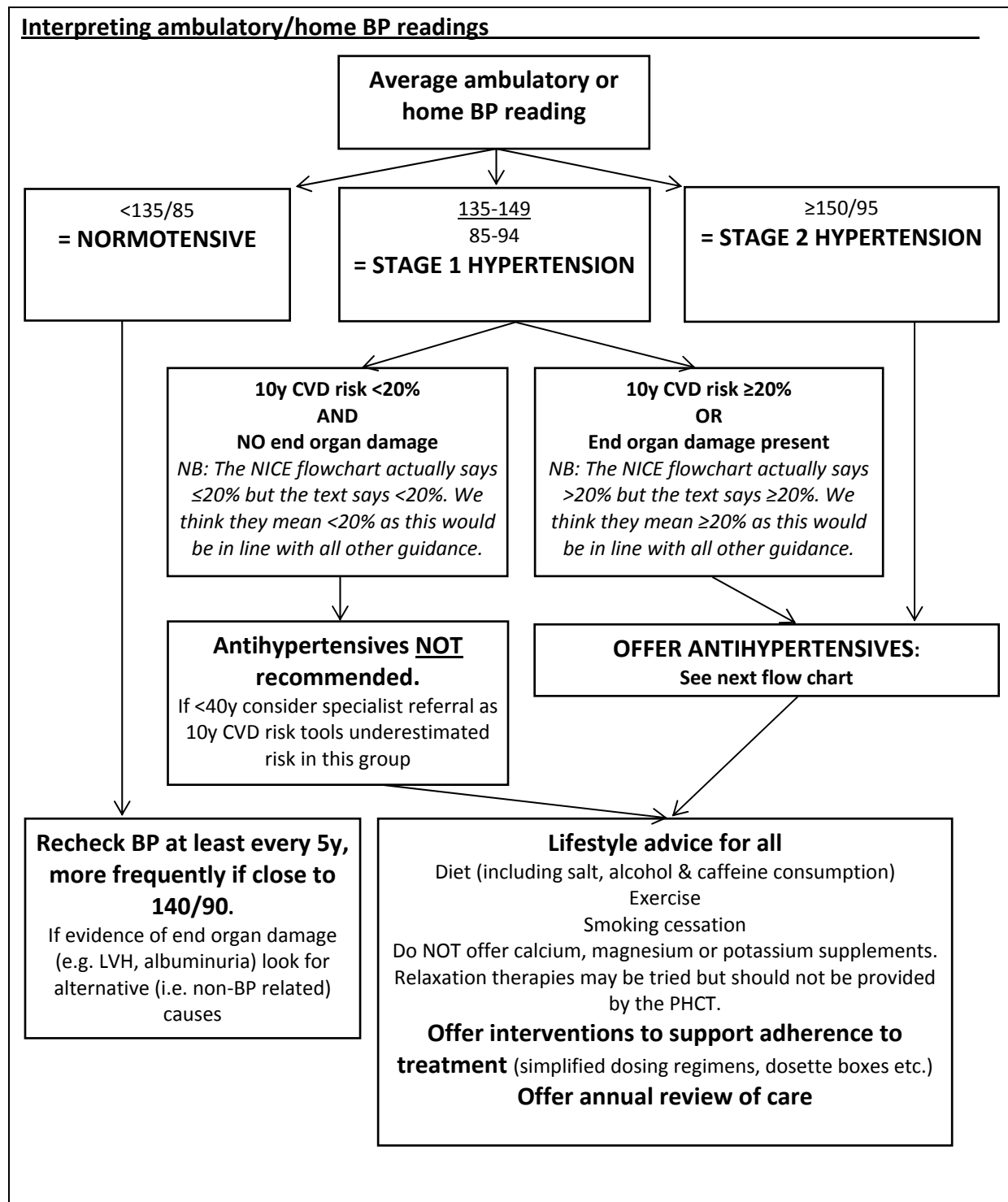


Ambulatory BP readings (ABPM)

- Use a device that measures at least 2 measurements/hour during waking hours.
- **You need to have at least 14 readings to average.**
- In the past we added 10/5 to ABPM before making decisions – there is no need to do this now, since the decision flow charts are based on ABPM not clinic readings.

Home BP monitoring (HBPM)

- Take readings morning & evening for at least 4d, preferably 7d.
- On each occasion take 2 readings ≥1min apart, whilst seated.
- **Discard the first day's readings, and average the remaining readings.**



Drug therapy

- Aim for drugs to be taken only once daily.
- Do NOT use ACE inhibitors and angiotensin receptor antagonists together (no evidence of additional benefit, increased risk of side effects).
- Treat women of child bearing age in line with the NICE guidelines on hypertension in pregnancy (NICE CG 107, 2010), summarised in the Pregnancy Chapter of this Handbook.
- Treat isolated systolic BP (SBP ≥ 160) in the same way as when both the diastolic and systolic BPs are raised.
- NICE say 'Treat people over 80y in the same way as those aged <80y' but in reality they then actually don't suggest we do this (see flow chart below and BP targets)!
- Do note that NICE now prefer chlortalidone (12.5-25mg daily) or indapamide (1.5mg modified release once daily or 2.5mg normal release once daily). The reasons for this are discussed in the FAQs section.

OFFER ANTIHYPERTENSIVES IF:

Stage 1 hypertension if <80y old
(average ambulatory/home BP $\geq 135/85$ -149/94)

AND EITHER

10y CVD risk $\geq 20\%$

OR

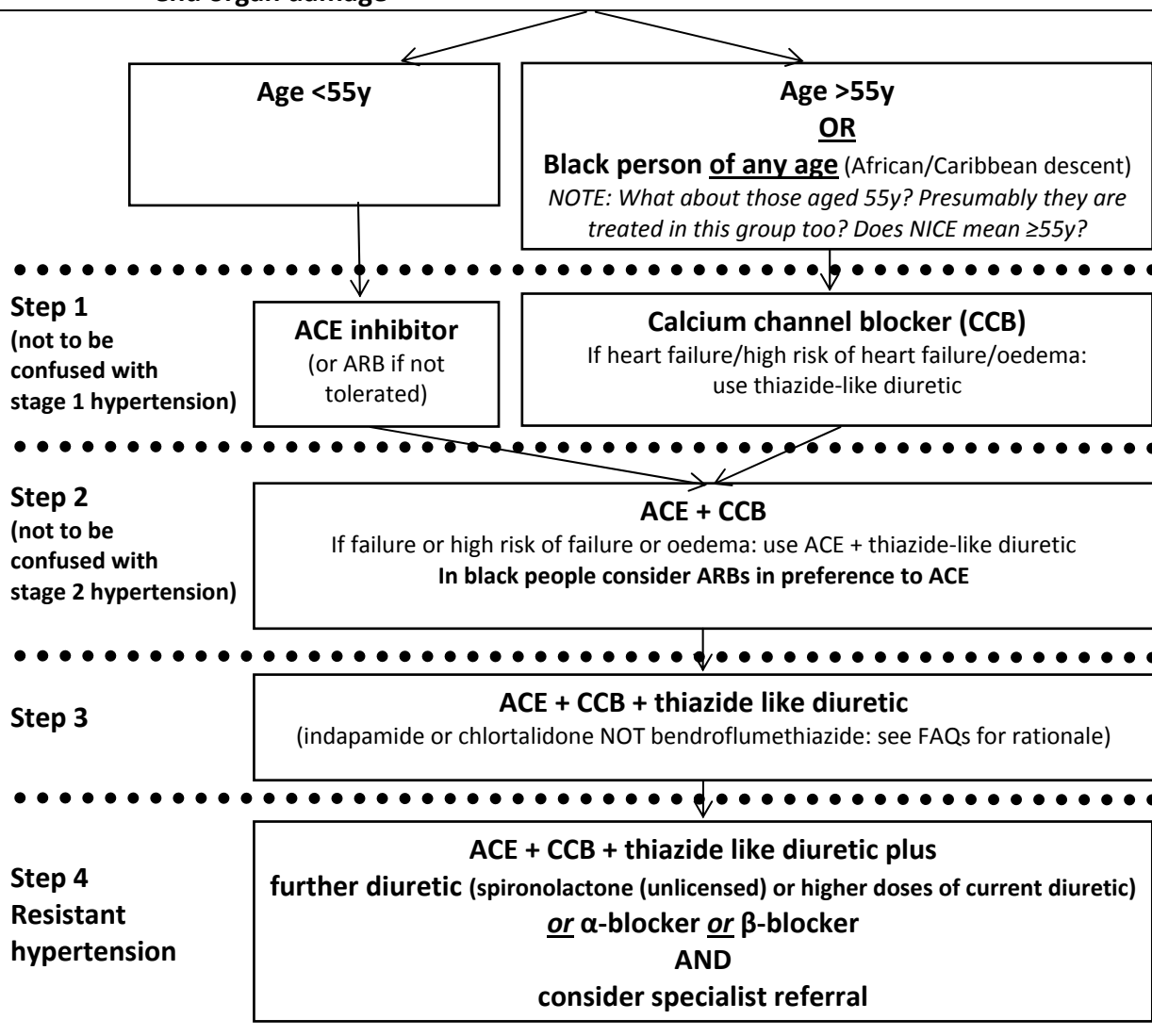
established CVD/diabetes/renal disease

OR

end organ damage

OR

Stage 2 hypertension at any age
(average ambulatory/home BP $\geq 150/95$)



BP targets/when to step up therapy

- Use clinic BP readings to monitor response to treatment.
- Ambulatory/home readings can be used in those with known ‘white coat’ hypertension (defined as a discrepancy of >20/10 between clinic and average ambulatory or home readings at time of diagnosis).
- Increase drug therapy if these targets are not achieved.

Aim for:

Clinic BP readings of:

<80y <140/90
>80y <150/90

Ambulatory/home average readings of:

<80y <135/85
>80y <145/85

(NICE seem to forget some people are actually aged 80y!)

Specialist referral

Refer same day if:

- **Accelerated hypertension** (BP usually >180/110 with signs of papilloedema and /or retinal haemorrhages).
- **Suspected pheochromocytoma** (labile blood pressure with hypertension and postural hypotension, headache, palpitations, pallor and diaphoresis (excessive sweating)).

Routine referral

- **Consider if secondary hypertension suspected**
- **Consider in those aged under 40 with hypertension** as they need a more detailed assessment for end organ damage and because 10y CVD risk estimations tend to underestimate risk in these younger individuals.

Postural hypotension

In those with falls or dizziness on standing, NICE suggest checking lying and standing BP. NICE suggest this can be done by checking the BP whilst sitting and repeating after the patient has been standing for at least 1 minute. NICE suggest a fall in systolic BP of 20mmHg or more should prompt us to:

- Review medication
- Measure subsequent BPs with the person standing.
- Consider referral if symptoms persist.

Frequently asked questions from the NICE guidance

Here I will cover:

- Why shift to ambulatory BP for diagnosis?
- Why differentiate initial treatment based on age?
- Why differentiate initial therapy on race?
- Which CVD risk assessment tool should we use?
- Why the change in first line diuretics?
- What do we do with people on bendroflumethiazide?
- Why are diuretics now only third line?
- Step 4 therapy/resistant hypertension: what next?

Why shift to ambulatory BP for diagnosis?

NICE looked at the evidence on clinic v home v ambulatory BP monitoring to determine which reflected the ‘best’ outcomes (greatest clinical benefit in terms of lowest CV endpoints, cost etc) (for details on individual trials please see the NICE ‘Methods, evidence, and recommendations’ document produced alongside the quick reference guide and full guidance documents). This showed that:

- **Ambulatory BP monitoring is better than home BP monitoring, which is better than clinic BP readings, both in terms of clinical outcomes (CV endpoints) and in terms of costs (QALYs)**

Also note that...

Evidence for ABPM was more robust than for home readings (partly because there is more of it, partly because higher quality).

Home readings have a significant 'over diagnosis rate' when compared with ABPM. Clinic readings have the greatest 'over diagnosis rate'. Home readings result in an over diagnosis rate of 14%, clinic readings result in an over diagnosis rate of 25%.

And just in case you were thinking you'd ignore this NICE recommendation and carry on using home BP monitoring for most... here is a quote you may want to read first!

'The Guideline Development Group noted that based on current data, home BP monitoring could not be considered equivalent to ABPM with regard to accuracy of diagnosis and emphasised that that ABPM is the preferred means of confirming or refuting the diagnosis of hypertension.' (NICE CG 127: Methods, evidence, and recommendations, 2011).

Why differentiate initial treatment based on age?

NICE argue that clinical trials have shown that younger people respond better to ACE inhibitors and ARBs than older people, when used as first line therapy. However, it has been noted that ACE/ARBs do seem to be effective as second or third line drugs, suggesting that some event (possibly some reduction in blood pressure) occurs with other therapies that allows the ACE inhibitors to become more effective. This was disputed by the DTB in 2008 who felt that there was no justification for stratifying by age, although agreed with the stratification by race (DTB 2008;46:65-69).

Why differentiate initial therapy on race?

This is mainly based on sub group analysis of the ALLHAT trial (1/3rd of the study population of over 40 000 were black (of African/Caribbean descent)) which showed that, calcium channel blockers were significantly better than ACE inhibitors at reducing the risk of:

- CV events overall
- Stroke

But that CCB and ACE inhibitors were similar in black people at reducing the risk of CHD and heart failure.

Do note that ACE/ARBs are associated with an increased risk of angioedema in black people compared with non-blacks, although the overall risk is small – there were just 53 cases of angioedema in 42 000 study participants.

Which CVD risk assessment tool should we use?

This NICE guideline doesn't specify whether QRISK2 or Framingham should be used. However, in the section on CVD risk and lipids later in this Handbook, we will discuss why the QRISK2 tool may be most accurate for the UK population.

Why the change in first line diuretics?

NICE now recommend that the thiazide-like diuretic of choice is now indapamide or chlortalidone rather than bendroflumethiazide or hydrochlorothiazide. Why?

Firstly, what's the difference?

Thiazides and thiazide-like diuretics both lower blood pressure by inhibiting the sodium chloride co-transporter in the distal nephrons of the kidney. However the thiazide-like diuretics have other properties, not shared with the thiazides themselves. For example, thiazide-like diuretics affect carbonic anhydrase in the kidney 10 000 fold more, and also have a different effect on platelet

aggregation and angiogenesis. However the clinical significance of these differences is not fully known.

Much of the data on the benefits of bendroflumethiazide came from old trials where doses of 10mg were used – 4x the usual dose used nowadays. In addition, bendroflumethiazide is rarely used outside the UK. **There is no evidence for the use of bendroflumethiazide at 2.5mg showing improved clinical outcomes, although there are some trials showing it reduces blood pressure! Of course this doesn't mean it doesn't work, but why use a drug for which we haven't the evidence, when there are other drugs that have shown evidence of benefit?** There is also limited evidence for the use of hydrochlorothiazide at current dosages.

There is better data for the thiazide-like diuretics (indapamide and chlortalidone) than the thiazides at currently used doses. Importantly this data looks not just at whether they lower blood pressure, but shows reduced CV outcomes too.

What dose?

Indapamide comes as 2.5mg ordinary release tablet (dose: 2.5mg/daily), or a 1.5mg slow release preparation (dose: 1 tablet daily).

Chlortalidone dose is 12.5-25mg daily, but you can currently only get a 50mg tablet so forget it!

What are the cost differences?

Based on drug tariff price (Dec 2010) monthly costs are:

Bendroflumethiazide (2.5mg)	£0.79	for 28	
Chlortalidone (50mg)	£1.77	for 28	
Indapamide ordinary release 2.5mg	£1.27	for 28	
	£2.01	for 56	Making these the cheapest.
Indapamide slow release 1.5mg	£3.40	for 30	

What do we do with people on bendroflumethiazide?

For those with established hypertension, do we need to change from bendroflumethiazide or hydrochlorothiazide to chlortalidone or indapamide?

- NO! NICE clearly state that there is no need to change for those established on bendroflumethiazide or hydrochlorothiazide.
- Indapamide or chlortalidone should be used for those with newly diagnosed hypertension or in those with established hypertension in whom we are changing the diuretic for some other reason.

Why are diuretics now only third line?

The previous hypertension guidance offered us a choice of CCB or diuretic for those aged 55 or over or black people of any age. This has now changed and CCB are the first choice here, with ACE inhibitors being the second agent to add, and diuretics being third line for all patients.

Diuretics have been relegated to third line agent because of the ACCOMPLISH trial. This was a large RCT (over 11 000 people) randomised to an ACE inhibitor and CCB or an ACE inhibitor and thiazide diuretic (NEJM 2008;359:2417). The ACCOMPLISH trial showed:

- ACE+CCB was significantly more effective at preventing MI compared with ACE + diuretic (the trial was stopped early because of this).
- There were also fewer withdrawals from the study on the ACE + CCB combination compared with ACE+diuretic, suggesting better tolerability

This contradicts the ALLHAT trial which showed that thiazides (in this case the thiazide-like diuretic chlortalidone) was as effective as ACE inhibitors and calcium channel blockers in preventing fatal and non-fatal cardiovascular endpoints (Circulation 2006;113:2201). However in the ALLHAT trial drugs

were being used predominately as single agents, not in combination, as in the ACCOMPLISH trial. The ACCOMPLISH trial therefore probably better reflects real life situations where combination therapies are used.

However NICE do acknowledge that their recommendations to move diuretics to third line therapy is based on a single trial (the ACCOMPLISH trial), and the difference between CCB and diuretics may be small.

The relegation of diuretics to third line therapy is interesting as there is some evidence around their role in preventing the development of heart failure (and remember, hypertension is a major contributory factor in the development of heart failure). A meta-analysis of almost a quarter of a million patients with hypertension (in 26 trials), looked at which treatment of hypertension was most effective at reducing the development of heart failure (Arch Intern Med 2010, doi:10.1001/archinternmed.2010.427).

- **Diuretics were the most effective drug at reducing the risk of developing heart failure. (odds ratio 0.59, CI 0.47–0.73).**
- **ACE inhibitors/ARBs were the next most effective (OR 0.71 and 0.76 respectively).**
- **Calcium channel blockers, beta-blockers and alpha blockers were the least effective at preventing the onset of chronic heart failure (CHF).**

Step 4 therapy/resistant hypertension: what next?

So your patient is on an ACE, calcium channel blocker and a thiazide like diuretic but their clinic blood pressure is still >140/90. What do you do?

NICE calls this **resistant hypertension** and recommend the following:

- **Adding additional diuretic**

If serum potassium is ≤ 4.5 mmol/l: add low dose spironolactone (25mg once daily). This is an unlicensed indication. Be particularly careful in those with reduced eGFR because they are at increased risk of hyperkalaemia.

If serum potassium is >4.5 mmol/l: increase whichever thiazide-like diuretic you are using.

When adding additional diuretic (regardless of type), monitor electrolytes and renal function after 1m (and again as clinically indicated).

- **Add an alpha or beta-blocker if additional diuretics are not tolerated or contraindicated.**
- **If BP not controlled on four drugs, seek specialist advice.**



Hypertension

- Ambulatory blood pressure is now the diagnostic investigation of choice for hypertension.
- Clinic BP readings are no longer recommended for the diagnosis of hypertension, however they can (and should) be used to monitor responses to treatment.
- Hypertension is now defined as stage 1 and stage 2. All those with stage 2 disease should be offered anti-hypertensives, but only some of those with stage 1 should be offered anti-hypertensives.
- The threshold BP for offering drug therapy has changed, partly reflecting the move to ambulatory BP monitoring.
- Diuretics have moved to third line drugs after ACE inhibitors and calcium channel blockers
- The thiazide-like diuretic of choice is now indapamide rather than bendroflumethiazide or hydrochlorothiazide. However those already established on bendroflumethiazide or hydrochlorothiazide need not be changed to indapamide.



Is it time to update your practice protocol?

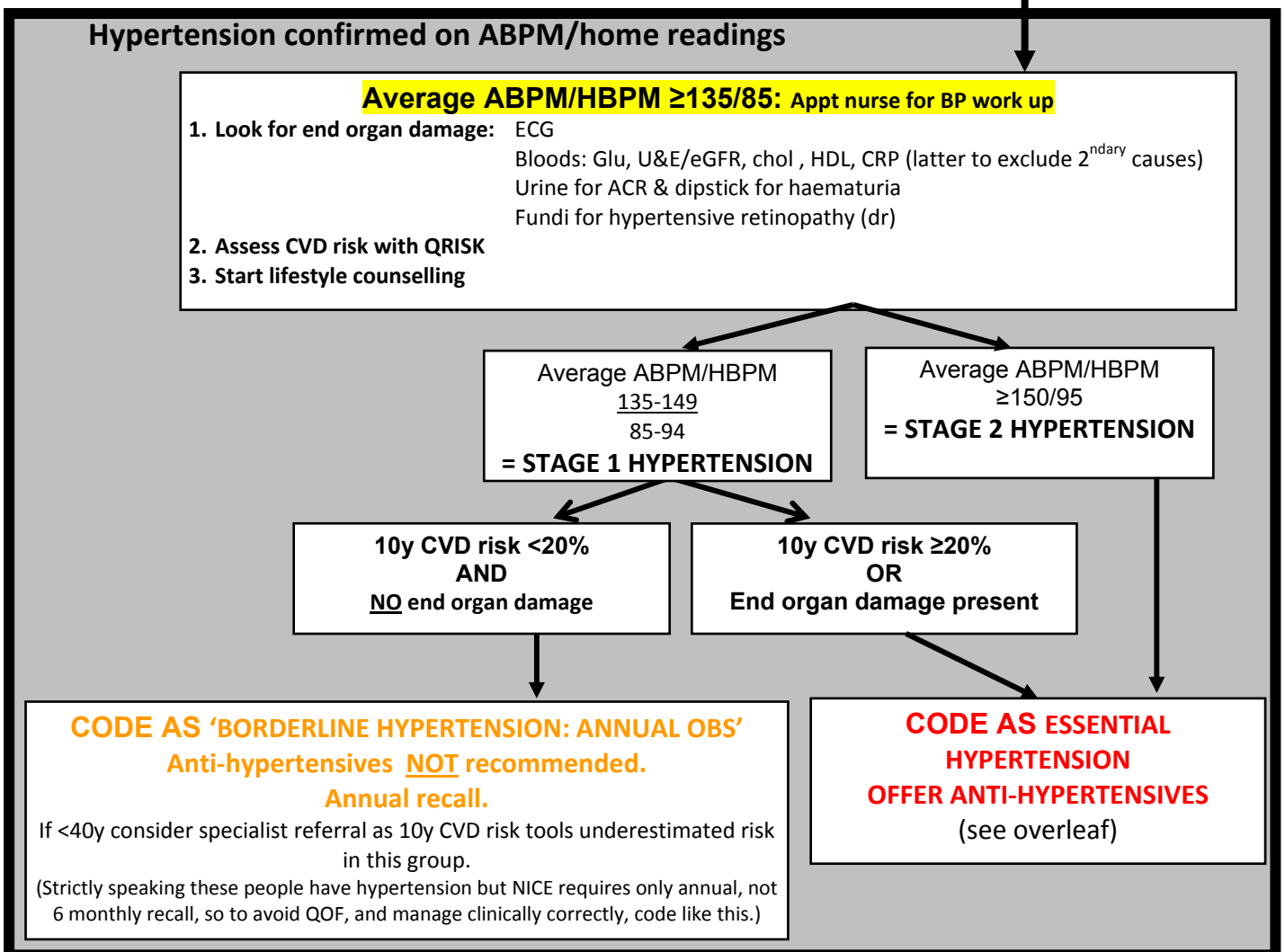
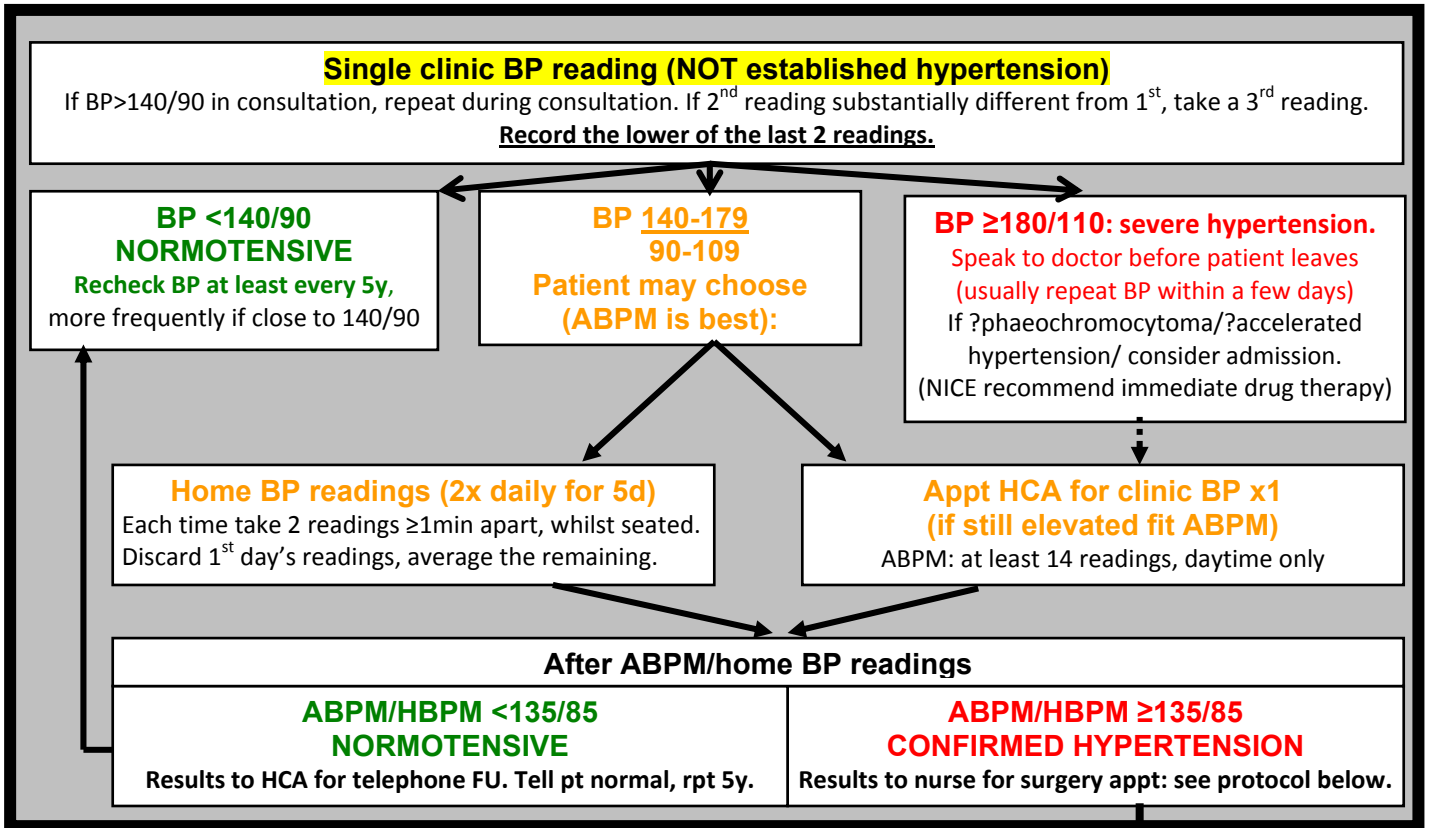


For professionals:

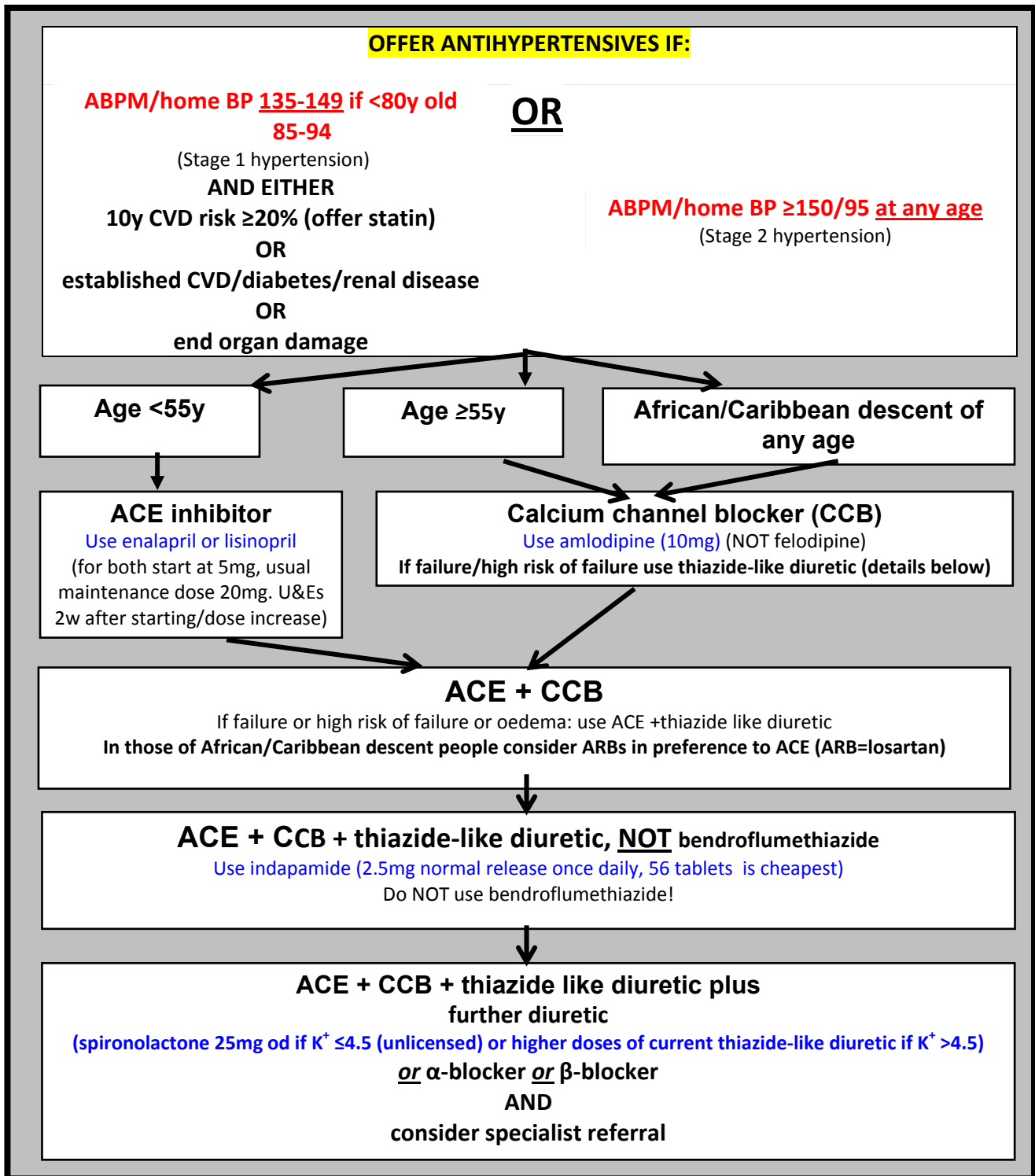
The British Hypertension Society website lists machines that have been validated for ambulatory & home readings, which is regularly updated: www.bhsoc.org

Mill Stream Surgery Raised BP/hypertension protocol, 2011

(based on NICE 127, 2011 & lots of pragmatism!)



Mill Stream hypertension protocol, 2011:
DRUG THERAPY for established hypertension (based on NICE CG 127, 2011)



BP targets

Use clinic BP to assess response to therapy. Add additional drug if these are not met:

<80y	<140/90
≥80y	<150/90

Use ABPM/home BP to assess response to treatment only if marked white coat hypertension (>20/10 difference between home & clinic readings at diagnosis). In this case aim for:

<80y ABPM/home BP <135/85	≥80y ABPM/home BP <145/85
---------------------------	---------------------------

The GP Update Course – A one day course for GPs and GP Registrars, by GPs.

We trawl through all the journals and do all the legwork to bring you up to speed on the latest issues, research and guidelines in General Practice. **We set all this in the context of the consulting room and the requirements of revalidation.** We focus on actions - getting the literature into practice and ensuring it counts towards revalidation. We make it entertaining too, without compromising the content!

Course delegates receive a copy of **The GP Update Handbook**, a 400 page book outlining the results of the most important research relevant to primary care over the last 5 years, access to **GP Update Handbook Online** from the date of booking to a year after the course. We will also give you a copy of the **GP Update Revalidation Action Pack** which contains step by step guidance on audits, reflective practice and service developments related to the course, so that you have documented evidence of improved care for your next appraisal and for revalidation. We've included lots of material for locums too.

The GP Update Course is completely free from pharmaceutical company sponsorship. This means that you can be totally reassured that there will be no biasing of the information presented to you and that there will be no reps there on the day!

Spring 2012 dates:

London - Friday March 9
London - Saturday March 10
Leeds - Thursday March 15
Oxford - Friday March 16
Birmingham - Saturday March 17

Summer 2012 dates:

Exeter - Wednesday May 16
Bristol - Thursday May 17
London - Friday May 18
London - Saturday May 19
Newcastle - Wednesday May 23
Sheffield - Thursday May 24
Manchester - Friday May 25
Birmingham - Saturday May 26
Norwich - Tuesday May 29
London - Wednesday May 30

GPs £185 (if booked before 31/12/11 - £195 thereafter), ST1, 2 & 3 and Nurses £150.

For more details see www.gp-update.co.uk

We make every effort to ensure the information in these pages is accurate and correct at the date of publication, but it is of necessity of a brief and general nature, and this should not replace your own good clinical judgement, or be regarded as a substitute for taking professional advice in appropriate circumstances. In particular check drug doses, side effects and interactions with the British National Formulary. Save insofar as any such liability cannot be excluded at law, we do not accept any liability for loss of any type caused by reliance on the information in these pages.

*GP Update Limited and Primary Care Education LLP
December 2011*