

# New NICE Guideline on the Treatment of Hypertension

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**CHEUNG AND CHEUNG: New NICE guideline on the treatment of Hypertension.** *The British guidelines on the management of primary hypertension, developed by the National Institute for Clinical Excellence (NICE), have just been published in August 2011. There are several significant changes in the diagnosis and the treatment for primary hypertension in adults. Ambulatory blood pressure measurement should be regarded as the new gold standard in the diagnosis. Home blood pressure monitoring is also useful for the diagnosis and monitoring of hypertension. Because of the results of the Anglo-Scandinavian Cardiac Outcomes Trial study, calcium channel blockers (CCB) and blockers of the renin-angiotensin system have surpassed diuretics and beta-blockers as first line options. Patients younger than 55 should receive an ACE inhibitor, or an angiotensin receptor blocker if the former is not tolerated. Older patients should be started on a CCB. A thiazide diuretic can be used as an adjunct to the first line treatment. Chorthalidone and indapamide are preferred as they showed favorable outcomes in large clinical trials. Treatment with these three drug classes should be sufficient in the majority of patients, but if triple therapy is still insufficient, referral to a hypertension specialist is recommended. Further diuretic therapy with spironolactone can be used as the fourth line treatment. Some aspects of the new guideline are controversial, such as the practical difficulties of using ambulatory blood pressure monitoring in family practice, and the arbitrary blood pressure cutoff levels. Many doctors also believe that control of blood pressure is best achieved using a wider range of drugs to suit the individual patient. (J HK Coll Cardiol 2012;20:15-20)*

*Guideline, hypertension, NICE*

## 摘要

由英國國家衛生與臨床優化研究所對治療原發性高血壓的新指南已於2011年8月出版，新指南對成人原發性高血壓的診斷和治療作出了重要的更新。在高血壓的診斷中，動態血壓監測被視為新的診斷標準，而家庭自測血壓對於高血壓的診斷和監測也是非常有用的。從ASCOT研究結果所得，鈣離子通道阻滯劑和血管收縮素系統抑制劑已成為第一線藥物，效果比利尿劑和 $\beta$ -受體阻滯劑更為優勝。年齡小於55歲的患者應該首選血管收縮素轉化酶抑制劑，如果患者對這種藥物產生不良反應，可以選用血管收縮素受體阻滯劑。而老年患者應該首選鈣離子通道阻滯劑治療高血壓，如果使用一線藥物後血壓控制仍然未如理想，可以考慮使用二線藥物噻嗪類利尿劑。氯噻酮和吲達帕胺更在大型臨床試驗中有優越的結果。聯用這三類藥物應該足以治療大部份的病人，但如果血壓仍未能受到控制，就需要將病人轉介到治療高血壓的專家跟進。螺旋內酯利尿劑可作為第四線的藥物。新指南在某些方面是具爭議性的，例如在家庭中進行動態血壓監測的可行性以及界定高血壓的標準。現時許多醫生都認為需要使用多種降壓藥物才能有效地控制高血壓。

關鍵詞：指南，高血壓，英國國家衛生與臨床優化研究所

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## Introduction

In Hong Kong, the prevalence of hypertension has been increasing among young and middle-aged men, and is approaching 50% among the elderly. Hypertension has been shown to increase the risk of stroke and myocardial infarction, and increase the incidence of heart failure and the progression of chronic kidney disease. The key to reducing cardiovascular complications in patients with hypertension is early detection and effective treatment leading to good blood pressure control. Therefore, guidelines on the management of hypertension are developed. The British guidelines developed by the National Institute for Clinical Excellence (NICE) have just been published in August 2011.<sup>1</sup> The guidelines cover the new methods of blood pressure measurement for the diagnosis of hypertension; blood pressure thresholds for intervention with drug therapy and blood pressure targets for treatment. Most importantly, there are significant changes in the recommendations for the treatment of hypertension.

## NICE Methodology

The NICE guidelines on hypertension is highly evidence based and it incorporates cost-effectiveness considerations. Compared to many other consensus guidelines, it is less dependent on expert opinion, but it also includes a diverse range of opinions, including non-specialists, non-clinicians, and the pharmaceutical industry. These stakeholders were engaged in the guideline development process.

## Blood Pressure Measurement for the Diagnosis of Hypertension

Ambulatory blood pressure is now the new gold standard in the diagnosis of hypertension. If the clinic blood pressure is 140/90 mmHg or higher, it is recommended to offer patients ambulatory blood pressure monitoring to confirm the diagnosis, unless at

presentation, the patient already has severe hypertension. It is measured twice every hour during the usual waking hours of the individual. This is valuable not only in people with white coat hypertension, but also in people whose ambulatory blood pressures are higher than blood pressure readings in the clinic. This entity is called reverse white coat hypertension or masked hypertension.<sup>2</sup> In this scenario, traditional blood pressure measurements fail to identify patients at risk. As a result, patients with masked hypertension have a higher cardiovascular risk due to under-treatment. Due to the need to diagnose white coat and masked hypertension, the new guidelines recommend ambulatory or home blood pressure monitoring.

However, ambulatory blood pressure monitoring is not always available and its repeated use for monitoring purposes is inconvenient. Home blood pressure monitoring is now also recognized to be useful in the diagnosis of hypertension and the monitoring of blood pressure.<sup>3</sup> Patients are recommended to measure the blood pressure twice daily, each recording with two consecutive measurements of at least 1 minute apart, for at least four days a week. Home blood pressure monitoring is widely promoted as the machines are inexpensive and readily available. Therefore, it encourages patients to be involved in their own care and they can provide more comprehensive readings spreading over a long period of time. However, they cannot be calibrated as easily as the machines used in clinics, and the accuracy of home readings depends on adequate resting before measurement, proper application of cuff and correct operation of the machine. Significant measurement errors may occur in patients with arrhythmias such as atrial fibrillation. There is also a potential concern that patients may adjust their medications according to the home blood pressure readings, which should be discouraged in most circumstances.

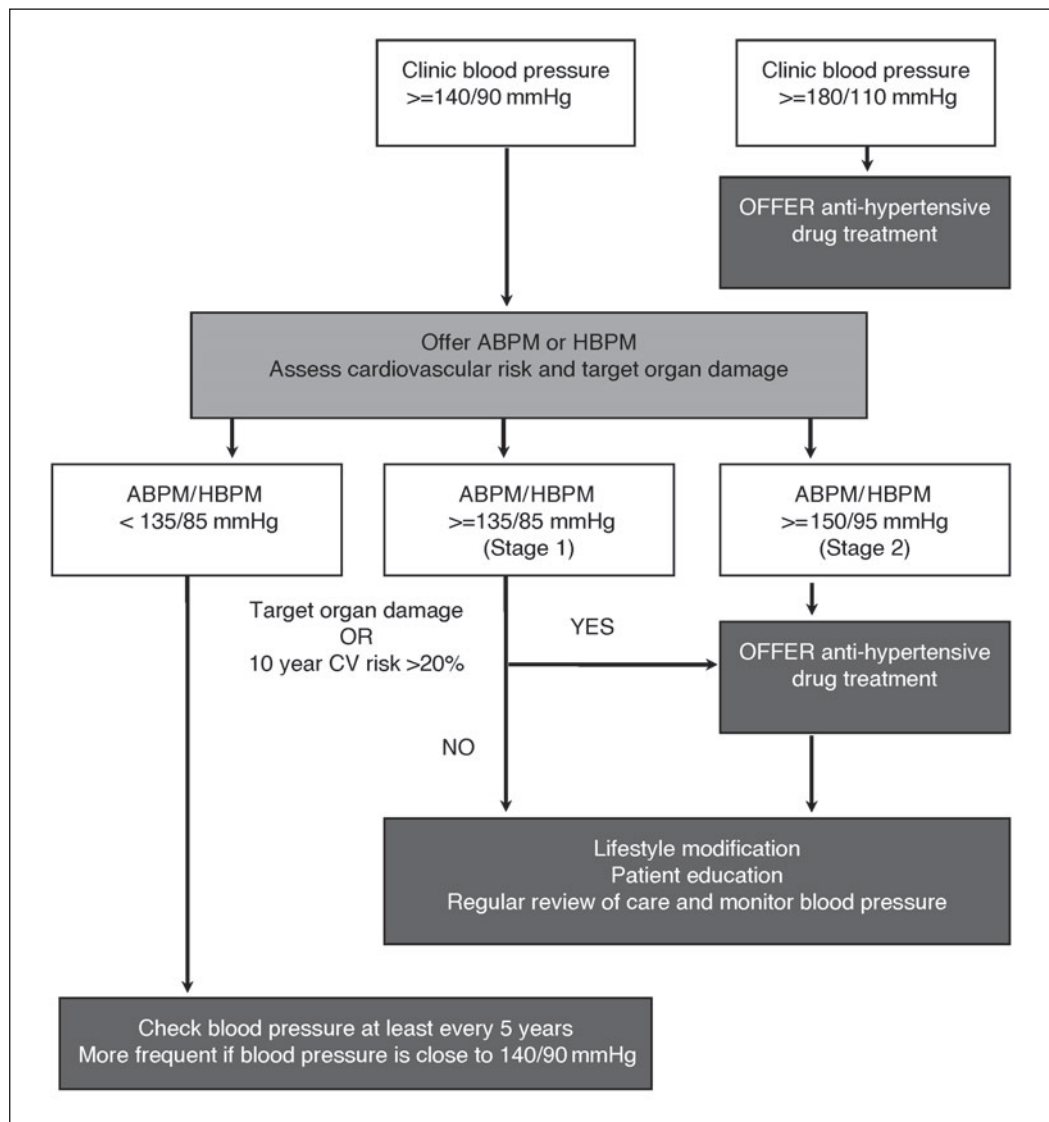
Ambulatory blood pressure monitoring and home blood pressure monitoring pose an enormous challenge to family practices where there are large numbers of patients with hypertension. The new NICE guideline has not set out recommendations on what to do if neither is available. A practical compromise is to carry out

multiple measurements of blood pressure, preferably on separate occasions, in well-rested patients by a trained staff such as the practice nurse.

### Blood Pressure Threshold for Intervention

In the new guidelines, patients who present with more severe hypertension, e.g. stage 2 hypertension (clinic blood pressure  $\geq 160/100$  mmHg or ambulatory/home blood pressure  $\geq 150/95$  mmHg) should be treated promptly with anti-hypertensive medications to achieve

satisfactory blood pressure control. Patients aged under 80 years with stage 1 hypertension and evidence of target organ damage such as left ventricular hypertrophy, albuminuria, hypertensive retinopathy; established cardiovascular disease, renal disease, diabetes or those whose 10-year cardiovascular risk exceeds 20% should also receive drug treatment early. If the risk is not over 20%, then stage 1 hypertension can be treated less aggressively with lifestyle changes, patient education and periodic follow-up and monitoring. The recommended care pathway is set out in Figure 1. It should be noted that ambulatory blood pressure plays a



**Figure 1.** Care pathway for hypertension.

key role in this algorithm. It is believed that ambulatory blood pressures are more accurate and reflect prognosis better, so that there should be less overtreatment (white coat hypertension) and undertreatment (masked hypertension).

## Target Blood Pressure for Treatment

Clinic blood pressure measurements remain as the most useful measurement for monitoring the response to treatment. The target blood pressure for those younger than 80 years old is defined as lower than 140/90 mmHg. If the 'white coat effect' is present, home blood pressure monitoring can be used with a target average blood pressure of 135/85 mmHg.

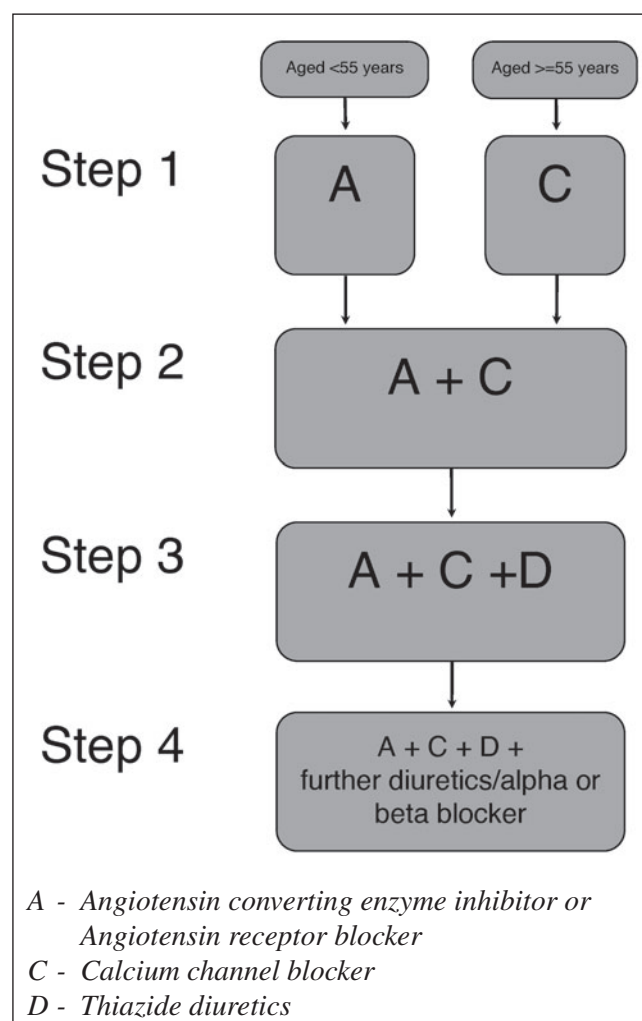
The new guidelines set a lower clinic blood pressure target for people aged 80 and over i.e. 150/90 mmHg based on the HYpertension in the Very Elderly Trial (HYVET).<sup>4</sup> For ambulatory and home blood pressure monitoring, the target of below 145/85 mmHg is recommended. Setting a higher target is based on the rationale that elderly often have a wide pulse pressure, such that if the systolic blood pressure is brought below 140 mmHg, the diastolic blood pressure can be considerably lower than 90 mmHg. Moreover, elderly patients often take multiple drugs, which would lead to considerable side effects and potential non-compliance to the drug treatments.

## Treatment Strategy for Hypertension

In the new guidelines, there are important changes to the recommended first line treatment. Patients under the age of 55 are recommended to receive an angiotensin-converting enzyme inhibitor or a 'low-cost' angiotensin receptor blocker first. The combination of an angiotensin converting enzyme inhibitor with an angiotensin receptor blocker is generally not recommended for the indication of treatment of hypertension. For patients aged 55 or older, a calcium channel blocker is the first drug to be used. Patient aged 80 and over should be offered the same anti-hypertensive treatment taken into account of any co-morbidities

(Figure 2). Diuretics are now a second line agent and they could offer an alternative for patients who cannot tolerate calcium channel blockers.

Calcium channel blockers (CCB) and blockers of the renin-angiotensin system have surpassed diuretics and beta-blockers as first line drugs because of the results of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) study,<sup>5</sup> which showed that those newer agents were better than the older agents in terms of cardiovascular outcomes. Moreover, in ASCOT and in the relevant meta-analyses, ARB and ACEI were associated with a decrease in incidence of new onset diabetes whereas diuretics and beta-blockers were associated with an increase in the incidence.<sup>6</sup>



**Figure 2.** Summary of anti-hypertensive drug treatment.

If the blood pressure is not controlled by calcium channel blocker or blocker of the renin-angiotensin system alone, combination of both drugs is recommended. For those who cannot tolerate calcium channel blockers or with evidence of heart failure, thiazide diuretics are the appropriate alternative. Interestingly, chlorthalidone and indapamide are the recommended thiazide diuretic as they showed favorable outcomes in large clinical trials, such as Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)<sup>7</sup> and HYVET. Patients can continue the use of bendroflumethiazide or hydrochlorothiazide if they are already taking them with satisfactory control of blood pressure.

Treatment with these three drug classes should be sufficient in the majority of patients, but if triple therapy is still insufficient, the patient is deemed to have resistant hypertension and referral to a hypertension specialist is recommended. Alpha-blockers were found to be inferior in ALLHAT, in which treatment with an alpha-blocker was associated with an increased risk of heart failure. Beta-blockers were already relegated to fourth line treatment in the previous NICE guidelines, because they control blood pressure poorly in the elderly and tend to cause type 2 diabetes.

Although spironolactone is useful for resistant hypertension, it may increase the risk of hyperkalaemia, especially in patients with reduced glomerular filtration rate. In those high risk patients, higher dose of a thiazide diuretic should be considered. If further diuretic therapy for resistant hypertension is not tolerated, or is contraindicated or ineffective, alpha or beta blocker can be used as the ultimate options. Spironolactone has been found to cause cancer in rodents. The uncertain carcinogenic risk may pose a dilemma for patients with hypertension who usually have a good life expectancy.

### Limitation of the New NICE Guidelines

The new UK guidelines, based on the best available current evidence, may be criticized for the heavy reliance on large scale randomized controlled trials. Therefore, newer drugs tend to be recommended while older drugs may be disadvantaged due to the

lack of new evidence. Similarly, lifestyle measure and population measures have not been emphasized because of the paucity of randomized controlled trials showing improvements in hard endpoints. A set of guidelines based on clinical trial evidence is therefore limited by the availability of evidence. Brown et al have set out the gaps in evidence-based treatment of hypertension.<sup>8</sup>

The European guidelines on hypertension management take the view that the differences among classes of antihypertensive drugs in terms of cardiovascular outcome are minimal, and so control of blood pressure should be of paramount importance, using the whole range of drug classes if necessary.<sup>9</sup> Indeed, there are hypertension experts who think that beta-blockers are under-valued in the NICE guidelines.<sup>10</sup>

In the new guidelines, special groups such as secondary hypertension, diabetic, pregnant or paediatric patients are not covered. Other than those patients, the levels of office, ambulatory or home blood pressures chosen for the diagnosis of hypertension and target blood pressures are arbitrary, because the relationship between blood pressure and cardiovascular risk is continuous. Treatment decisions should therefore not be based on blood pressure levels alone, a comprehensive assessment of risks and benefits should also be included.

### Conclusions

Hypertension is more prevalent in the elderly and because of aging of the Hong Kong population, the prevalence of hypertension will continue to rise. Therefore, improvements in diagnosing, treating and controlling hypertension are badly needed. Lifestyle modifications and promotion of healthy diet should be started early in life. For those who have already developed hypertension, early diagnosis and treatment are crucial. No single anti-hypertensive drug is ideal for the treatment of hypertension; the majority of patients require combination therapy. The new NICE guidelines help us optimize treatment strategy based on the best available evidence.

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