

Management of Arterial Hypertension

2007 Guidelines for the Management of Arterial Hypertension compiled by the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

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THE latest joint guidelines on the management of arterial hypertension from the European Society of Hypertension and the European Society of Cardiology¹ follow on from the recently published guidelines of the UK National Institute for Health and Clinical Excellence (NICE), the Joint British Societies and the American JNC 7 guidelines², and the just-published American Heart Association Scientific Statement for the Treatment of Hypertension in the Prevention and Management of Ischaemic Heart Disease.³

“Hypertension is being misdiagnosed in as many as a third of all patients attending for routine blood pressure measurement”

In empathy with our colleagues in general practice who have to wrestle with this bevy of recommendations (as well as many other guidelines), Jan Staessen and I pleaded for the harmonization of guidelines on hypertension in an editorial in *Heart*.² We concluded: “The international opinion leaders know each other and should be able to come together to produce an international consensus guideline on hypertension, which would relieve practitioners from the burden of identifying the differences in policies between the guidelines. Realistically, we know that international consensus is unlikely, but surely European agreement should be possible, which begs the question as to why there have to be British guidelines within the context of the European Union?”²

The decision as to which guideline to follow is, therefore, particularly relevant for us in Ireland. Though there are many similarities and

areas of agreement between the European, the British and the American guidelines, there are significant differences. Whereas the recent European guidelines are by no means perfect, they provide, in my opinion, the most reliable recommendations (83 pages) based on evidence-based publications (825 peer-reviewed papers).

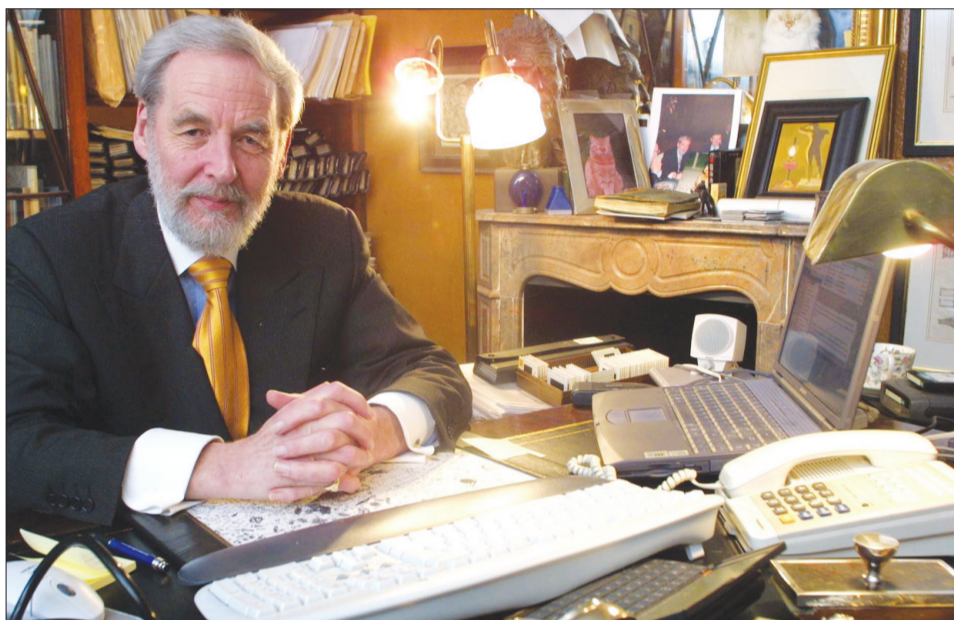
This guideline, compiled by more than 50 experts (of which I was one) from many European countries, while undoubtedly based on evidence, also reflects the complex relationship between the influence of respective authors in the process and the bias of their individual interests, which ultimately influences the final interpretation of data. This failing applies to all multi-authored guidelines, and the European guidelines are no better, or worse, than others in this regard. The fact simply needs to be stated and doctors who follow guidelines “should realize that recommendations can never replace sound clinical judgment or take precedence upon the personal interaction between patient and doctor”.²

In the following brief review of the European guideline, I have of necessity confined myself to areas where I believe guidance that was lacking previously is now provided, but I will also highlight aspects of hypertension management that, in my opinion, have not been addressed adequately.

Definition of hypertension

Systolic and diastolic blood pressures are independently and similarly predictive of stroke and coronary mortality, and both must be taken into account in defining hypertension. The contribution of pulse pressure to outcome is small, particularly in individuals aged less than 55 years; whereas, in middle aged and elderly hypertensive patients with cardiovascular risk factors or associated clinical conditions, pulse pressure shows a strong predictive value for cardiovascular events.

Blood pressure has a unimodal distribution in the population and the relationship with cardiovascular risk is continuous down to systolic and diastolic levels of 115-110mmHg and 75-70mmHg, respectively. For various well-founded reasons, the European guidelines do not adopt



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the American JNC 7 guideline approach to unifying the normal and high normal blood pressure categories into a single entity termed ‘prehypertension’. The European classification is shown in Table 1.

Blood pressure measurement

Now comes my major difficulty — one that I have been expressing for years.⁴ When a definition or classification is dependent on a measurement, then surely it follows that if that measurement is inaccurate, all the recommendations relating to diagnosis, management and treatment must be flawed at best, and misleading to clinical practice at worst.

The management of hypertension is damned by a technique introduced in 1896 that

has repeatedly been shown to be grossly inaccurate but which still forms the basis of definitions and classifications as listed in Table 1. Is there any other test in use in medicine with such a provenance?

There might be some excuse for persisting to use an inaccurate technique if we had no other methodology. But the European guideline states that cross-sectional and longitudinal studies have shown that office blood pressure has a limited relationship with 24-h ambulatory blood pressure measurement (ABPM) which: “(i) correlates with hypertension-related organ damage and its changes by treatment more closely than does office blood pressure; (ii) has a relationship with cardiovascular events that is

steeper than that observed for clinic blood pressure, with a prediction of cardiovascular risk greater than, and additional to the prediction provided by office blood pressure values in populations as well as untreated and treated hypertensives; and (iii) measures more accurately than clinic blood pressure the extent of blood pressure reduction induced by treatment, because of a higher reproducibility over time and an absent or negligible ‘white coat’ and placebo effect.”

One would have thought that these advantages should lead to the logical recommendation of the automated technique as the preferred method of measurement. But no — the guideline, ignoring the above, goes on to recommend “multiple blood pres-

sure measurements, taken on separate occasions over a period of time” to overcome the “large spontaneous variations both during the day and between days, months and seasons”.

The guideline further acknowledges that white-coat hypertension (individuals with elevated office blood pressures and normal daytime ABPM) and masked hypertension (individuals with normal office blood pressures and elevated daytime ABPM), each of which has no distinguishing clinical characteristics, may each occur in some 15 per cent of the population. This leads to the salutary conclusion that hypertension is being misdiagnosed in as many as a third of all patients attending for routine blood pressure measurement.

If we are going to base guideline recommendations on evidence, surely the time has come when the recommendation from experts must be that doctors who are prepared to diagnose and treat hypertension without the benefit of ABPM are in breach of best clinical practice.

Hypertension within the total risk profile

Though hypertension is listed by the WHO as the first cause of death worldwide, elevated blood pressure should never be managed in isolation from concomitant risk factors, such as dyslipidaemia, smoking, diabetes, etc. Evidence is now available that in high-risk individuals thresholds and goals for antihypertensive treatment, as well as other treatment strategies, should be different from those recommended in lower risk individuals. The European categorization of total risk as low, moderate, high and very high added risk has the merit of simplicity; the term ‘added risk’ refers to the risk additional to the average one (see Figure 1).

Target organ damage

A full section of the European guideline is devoted to searching for subclinical organ damage where evidence for the additional risk of each subclinical alteration is discussed and the proposed cut-off values are justified. These include estimates of creatinine clearance by the Cockcroft-Gault formula, or of glomerular filtration rate by the MDRD formula, microal-

Category	Systolic		Diastolic
Optimal	< 120	and	< 80
Normal	120-129	and/or	80-84
High normal	130-139	and/or	85-89
Grade 1 hypertension	140-159	and/or	90-99
Grade 2 hypertension	160-179	and/or	100-109
Grade 3 hypertension	≥ 180	and/or	≥ 110
Isolated systolic hypertension	≥ 140	and	< 90

Table 1: Definitions and classification of blood pressure (BP) levels (mmHG)

Isolated systolic hypertension should be graded (1,2,3) according to systolic blood pressure values in the ranges indicated, provided that diastolic values are <90mmHg. Grades 1, 2 and 3 correspond to classification in mild, moderate and severe hypertension, respectively. These terms have been now omitted to avoid confusion with quantification of total cardiovascular risk.

buminuria, concentric left ventricular hypertrophy on echocardiography, increased pulse wave velocity, and a low ankle to brachial blood pressure ratio, all of which is fine where these investigations are readily to hand, but I come back to the empirical priority of measurement being more in need of radical change than the search for subclinical target organ change.

When to treat

The decision to start antihypertensive treatment should be based on two criteria, i.e.:

1. The level of systolic and diastolic blood pressure as classified in Table 1; and
2. The level of total cardiovascular risk as illustrated in Figure 2.

Choice of drug

Comparative randomized trials show that for similar blood pressure reductions, differences in the incidence of cardiovascular morbidity and mortality between different drug classes are small, thus strengthening the conclusion that their benefit largely depends on blood pressure lowering per se. However, the European guideline does clarify certain issues in relation to treatment.

Beta-blockers: Beta-blockers (in combination with thiazide diuretics) fared badly compared to amlodipine in combination with perindopril in the ASCOT study, and the British recommendations are that beta-blockers should not be used as first-line therapy.

However, in the European guideline, the proven benefit of beta-blockers in patients with angina pectoris, heart failure and a recent myocardial infarction and the potential advantages of the newer beta-blockers, restore the beta-blockers as an option for initial and subsequent antihypertensive treatment strategies.

Interestingly, beta-blockers also stage a comeback in the American Heart Association Scientific Statement, which recommends beta-blockers as the first-line therapy in hypertensive patients with ischaemic heart disease.³ However, because beta-blockers tend to favour an increase in weight, have adverse effects on lipid metabolism and increase (com-

pared with other drugs) the incidence of new onset diabetes, they should not be the drugs of choice in hypertensives with multiple metabolic risk factors including the metabolic syndrome. This applies also to thiazide diuretics, which have dyslipidaemic and diabetogenic effects when used at high doses.

These disadvantages may not apply, however, to vasodilator beta-blockers, such as carvedilol and nebivolol, which have less or no dysmetabolic action, as well as a reduced incidence of new onset diabetes compared with classical beta-blockers.

Poor blood pressure control is one of the singular failures of 20th Century medicine, which shows little sign of abating as we move into this century

ARB v ACEI: The European guideline considers the recent claim that angiotensin receptor antagonists might provide less protection against myocardial infarction than other antihypertensive agents, such as ACE inhibitors. However, this has not been confirmed by a comprehensive meta-analysis published recently, which shows the incidence of myocardial infarction to be similar to that occurring with other drugs.

Direct comparisons between the overall and cause-specific beneficial effects of angiotensin receptor antagonists and ACE inhibitors are, therefore, awaited with interest.

Lifestyle modification

There is an interesting admission of failure in the European guideline, which acknowl-

edges the failure of lifestyle modification in preventing cardiovascular complications in hypertensive patients, and the notoriously poor long-term compliance with their implementation. This view is also stated in the recently published American guideline, which goes a little further by stating: "Although hypertension, hypercholesterolemia, cigarette smoking, obesity, and sedentary lifestyles are potentially modifiable risk factors for IHD (ischaemic heart disease), it has never been proven that lifestyle modifications can reduce clinical events in individual patients."³ We need to be clear as to how these views should be interpreted. Neither guideline is advocating that lifestyle modification should be abandoned. In fact, the European guideline states: "The lifestyle measures that are widely agreed to lower blood pressure or cardiovascular risk, and that should be considered in all patients, are: 1) smoking cessation; 2) weight reduction in the overweight; 3) moderation of alcohol consumption; 4) physical activity; 5) reduction of salt intake; and 6) increase in fruit and vegetable intake and decrease in saturated and total fat intake."

However, both the European and the American guidelines are placing the imperative for drug treatment in context by emphasizing the importance of initiating efficacious antihypertensive drug treatment as soon as possible; gone should be the day when prescribing antihypertensive medication had to await the response to lifestyle modification — to do so, especially in high-risk patients, is only facilitating the onset of stroke and heart attack. The message is clear: in patients with elevated blood pressure, the sooner optimal blood pressure levels are achieved the greater the reduction in future stroke and heart attack.

Therapeutic approach in special conditions

The European guideline provides useful information on the intricacies of drug treatment in the elderly (who are prone to the effects of excessive treatment); patients with diabetes mellitus (who require optimal

Figure 1: Blood pressure (mmHg)

Other risk factors OD or disease	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 HT SBP 140-159 or DBP 90-99	Grade 2 HT SBP 160-179 or DBP 100-109	Grade 3 HT SBP ≥180 or DBP ≥110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1-2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors MS, OD or diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Established CV or renal disease	Very high added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

Stratification of CV risk in four categories. SBP: systolic blood pressure; DBP: diastolic blood pressure; CV: cardiovascular; HT: hypertension. Low, moderate, high and very high risk refer to 10-year risk of a CV fatal or non-fatal event. The term 'added' indicates that in all categories, risk is greater than average. OD: subclinical organ damage; MS: Metabolic syndrome. The dashed line indicates how definition of hypertension may be variable, depending on the level of total CV risk.

blood pressure control to prevent premature renovascular disease in particular); patients with cerebrovascular disease (in whom the PROGRESS trial using the ACE inhibitor perindopril in association with indapamide showed a 30 per cent reduction in recurrent stroke (both haemorrhagic and ischaemic) in actively treated patients); patients with coronary artery disease (in whom there is clear evidence favouring administration of antihypertensive agents such as beta-blockers, ACE inhibitors and angiotensin receptor antagonists); in patients with a recent myocardial infarction (particularly if complicated by systolic dysfunction); patients with atrial fibrillation (for which hypertension is the most important risk factor and which increases the risk of cardiovascular morbidity and mortality by approximately two- to fivefold with a marked increase in the risk of embolic stroke); patients with non-diabetic renal disease (in whom blood pressure should be lowered to at least 120/80mmHg); women (in whom isolated systolic hypertension is common and whose hypertension is influenced by oral contraceptives, hormone replacement therapy and pregnancy); patients with the metabolic syndrome (in whom careful selection of medication is required to avoid worsening the metabolic abnormalities); and patients with resistant hypertension (usually defined as hypertension unresponsive to treatment with at least three drugs and in whom spironolactone may be an effective additional drug).

Treatment of associated risk factors — especially the use of statins

The European guideline recommends concomitant use of a statin in patients up to the age of at least 80 years who have established cardiovascular disease such as coronary heart disease, peripheral artery disease, previous stroke or long-term diabetes. This recommendation is based largely on the evidence of the ASCOT study in which administration of 10mg/day of atorvastatin in more than 10,000 hypertensive patients reduced total car-

diovascular events by 36 per cent and stroke by 27 per cent.

Poor blood pressure control

Poor blood pressure control is one of the singular failures of 20th Century medicine, which shows little sign of abating as we move into this century. The European guideline reminds us that in most clinical trials (conducted under ideal conditions as opposed to clinical practice) the achieved average systolic blood pressure remained above 140mmHg, and even in trials achieving average blood pressure values <140mmHg, the control rate included at most 60 to 70 per cent of recruited patients. The situation in practice is, of course, worse and the 'rule of halves' operates across Europe: half of the population over the age of 50 years has elevated blood pressure; half of these people are unaware that their blood pressure is high; half of those who have been diagnosed with hypertension are untreated; of those receiving drug treatment only half are achieving normal blood pressure and all of this despite the fact that we know if normal blood pressure was achieved in Ireland we would prevent at least 5,000 of the 10,000 strokes occurring every year, as well as significantly reducing heart attack.

Whose responsibility is blood pressure control?

It is always easy to blame the doctor for failing to achieve blood pressure control, but as the European guideline points out, the responsibility for control reaches further. Patients with elevated blood pressure have to become involved in complying with treatment and management advice, but they must also be prepared to question (if blood pressure is not optimal) why this is so and they must also ask why they are so often being denied ABPM that will provide information on their blood pressure status that cannot be provided by any other methodology. But is it reasonable to expect general practitioners to provide a facility that the Government will not reimburse?

As the guideline states: "Health providers sometimes wrongly consider the management of hypertension as the matter of few-minute visits, and reimburse doctors accordingly. They often see guidelines as an instrument to reduce cost and limit reimbursement to high-risk conditions defined by arbitrary cut-offs. Therefore, policy makers and all those responsible for the organization of the system should be involved in the development of a comprehensive preventive program."

Which is where Minister for Health Ms Mary Harney and HSE CEO Prof Brendan Drum should take the stage, and might I suggest that they could begin to tackle the problem of uncontrolled hypertension and thereby dramatically reduce the occurrence of stroke (and other cardiovascular sequelae of hypertension) by firstly providing all general practitioners with the facilities to perform and interpret ABPM on all hypertensive patients. ■

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Figure 2: Blood pressure (mmHg)

Other risk factors OD or disease	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 HT SBP 140-159 or DBP 90-99	Grade 2 HT SBP 160-179 or DBP 100-109	Grade 3 HT SBP ≥180 or DBP ≥110
No other risk factors	No BP intervention	No BP intervention	Lifestyle changes for several months then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + Immediate drug treatment
1-2 risk factors	Lifestyle changes	Lifestyle changes	Lifestyle changes for several months then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + Immediate drug treatment
≥3 risk factors MS or OD	Lifestyle changes	Lifestyle changes and consider drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Immediate drug treatment
Diabetes	Lifestyle changes	Lifestyle changes + Drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Immediate drug treatment
Established CV or renal disease	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment

Initiation of antihypertensive treatment