

The Evolving Definition of Systemic Hypertension

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In the 21 years since the third report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC), the first to recommend goals for systolic and diastolic blood pressure (BP), goal BP levels recommended by JNC expert panels have been decreasing steadily.¹ With the publication of the most recent JNC report (JNC 7), the panel has for the first time suggested an emphasis on the disease process in patients with BP <140/90 mm Hg cut-off point for the diagnosis of uncomplicated hypertension. The JNC 7 experts have coined the term “prehypertension” to denote these subjects, specifically those with BP of 120/80 to 139/89 mm Hg, who should be viewed as being at higher than average risk for cardiovascular events compared with subjects at lower levels of BP (Table 1).² The well-intentioned term “prehypertension” has alerted patients and physicians to the possibility of increased risk for cardiovascular events in this group, but the panel did not suggest practical steps beyond lifestyle modifications to mitigate this risk, a fact that has led to confusion and even alarm regarding the clinical and possible medicolegal implications of the term.

It is beyond doubt that aggressive steps to lower BP are necessary in patients with clearly defined hypertension (i.e., BP >140/90 mm Hg or >130/80 mm Hg in those with diabetes mellitus or renal disease). It is also clear that substantial clinical benefits follow from BP control (i.e., reduced risk for cardiovascular events and premature mortality).³ Epidemiologic data suggest a direct relation between a 2 mm Hg difference in systolic BP and reduced cardiovascular risk.⁴ What is not clear is when to start to intervene aggressively in patients with lower BP levels (e.g., those who now fall within the JNC 7 prehypertension category). For clinicians, the questions relate to ascertaining which “prehypertensive” subjects require therapy more aggressive than lifestyle modification counseling and how aggressive that intervention should be. In the absence of clinical data based on BP numbers alone, it remains unclear when pharmacologic intervention is justified in this group of subjects.

Into this uncertainty comes a new definition from the Hypertension Writing Group⁵: “Hypertension is a progressive cardiovascular syndrome arising from complex and interrelated etiologies. Early markers of the syndrome are often present before BP elevation is observed; therefore, hypertension cannot be classified solely by discrete BP thresholds. Progression is strongly associated with functional and structural cardiac and vascular abnormalities that damage the heart, kidneys, brain, vasculature and other organs and lead to premature morbidity and death.” The

goal of this expanded definition of hypertension is twofold, according to the writing group⁵: to offer a more risk-based approach to identifying subjects at any BP level who “have a reasonable likelihood” of developing future cardiovascular events and to encourage further research aimed at detecting and treating disease at an earlier phase.

Recent data from clinical trials strongly support treating patients with elevated BP as early as possible, at an early age, and at an earlier stage in the disease process. For example, BP-related cognitive decrease has been documented in hypertensive patients aged 18 to 46 years, to an extent similar to that seen in older patients.⁶ Also, new data suggest that treating patients with lower levels of BP may result in clinical benefit. Adults with systolic BP of 120 to 139 mm Hg and diastolic BP of 80 to 89 mm Hg (i.e., those who qualify for the JNC 7 prehypertension group) have a 3.5 times greater relative risk for myocardial infarction and a 1.7 times greater relative risk for symptomatic myocardial ischemia than subjects with lower BP levels.⁷ A recent analysis of data collected in the 1999 to 2000 National Health and Nutrition Examination Survey showed that subjects who fall into the prehypertension group are 1.65 times more likely to have ≥ 1 other adverse cardiovascular risk factor than subjects with lower BP.⁸ Further evidence that cardiovascular risk factors tend to cluster in subjects comes from the ATTICA study, conducted in the Attica region of Greece, which found that compared with subjects with lower BP, those with JNC 7–defined prehypertensive levels of BP had statistically significantly higher blood levels of inflammatory markers, such as C-reactive protein, tumor necrosis factor- α , and amyloid-A, linked to the atherosclerotic process.⁹

These findings support the clinical relevance of the writing group’s most important position, namely, that BP be considered 1 component of a subject’s global cardiovascular risk rather than an isolated risk factor. The writing group’s contribution may be most significant if it results in the elevation of other cardiovascular risk factors to the status previously afforded to elevated BP alone.

The writing group’s⁵ definition of hypertension, based on overall cardiovascular risk, eliminates the term “prehypertension,” instead grading risk as follows: normal (rare or no BP elevations; no identifiable cardiovascular disease; and no cardiovascular risk factors, early disease markers, or evidence of target organ disease), stage 1 hypertension (occasional or intermittent BP elevations or risk factors or markers suggesting early cardiovascular disease, ≥ 1 cardiovascular risk factor, 0 or 1 marker of early disease, and no evidence of target organ disease), stage 2 hypertension (sustained elevation of BP or evidence of progressive cardiovascular disease, multiple cardiovascular risk factors, ≥ 2 markers of early disease, early signs of target organ disease), and stage 3 hypertension (marked and sustained elevations of BP or evidence of advanced cardiovascular disease, presence of multiple cardiovascular risk factors, presence of ≥ 2 early disease markers, and overtly present

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Table 1
Hypertension Writing Group definition and classification of hypertension*

| Classification | Normal BP | Hypertension | | |
|---|--|---|---|---|
| | | Stage 1 | Stage 2 | Stage 3 |
| Descriptive category (BP pattern and cardiovascular disease status) | Normal BP or rare BP elevations and no identifiable cardiovascular disease | Occasional or intermittent BP elevations or risk factors or markers suggesting early cardiovascular disease | Sustained BP elevations or evidence of progressive cardiovascular disease | Marked and sustained BP elevations or evidence of advanced cardiovascular disease |
| Cardiovascular risk factors | 0 | ≥1 | >1 | >1 |
| Early disease markers | 0 | 0–1 | ≥2 | ≥2 present plus cardiovascular disease |
| Target-organ disease | 0 | 0 | Early signs present | Overtly present with or without cardiovascular disease events |

* This paradigm expands on the JNC 7 definition and classification of hypertension by classifying individuals by BP. From Giles et al,⁵ with permission.

Table 2
Blood pressure classification

| BP (mm Hg) | Systolic BP (mm Hg) | Diastolic BP (mm Hg) |
|-----------------|---------------------|----------------------|
| Normal | <120 and | <80 |
| Stage 1 | 140–159 or | 90–99 |
| Prehypertension | 120–139 or | 80–89 |
| Stage 2 | ≥160 or | ≥100 |

target organ disease with or without a history of cardiovascular events) (Table 2 and Figure 1). Although the benefit of the writing group’s definition of hypertension in the clinical setting remains to be seen, available and emerging clinical trial data support taking steps necessary to reduce a patient’s global cardiovascular risk. The new definition suggests that subjects with elevated BP on some but not all measurements—the classic “white coat” hypertensives—may be diagnosed with hypertension to their benefit using additional criteria. It also suggests that subjects with BP levels that fall into the JNC 7 prehypertension category but who do not have other cardiovascular risk factors may escape being

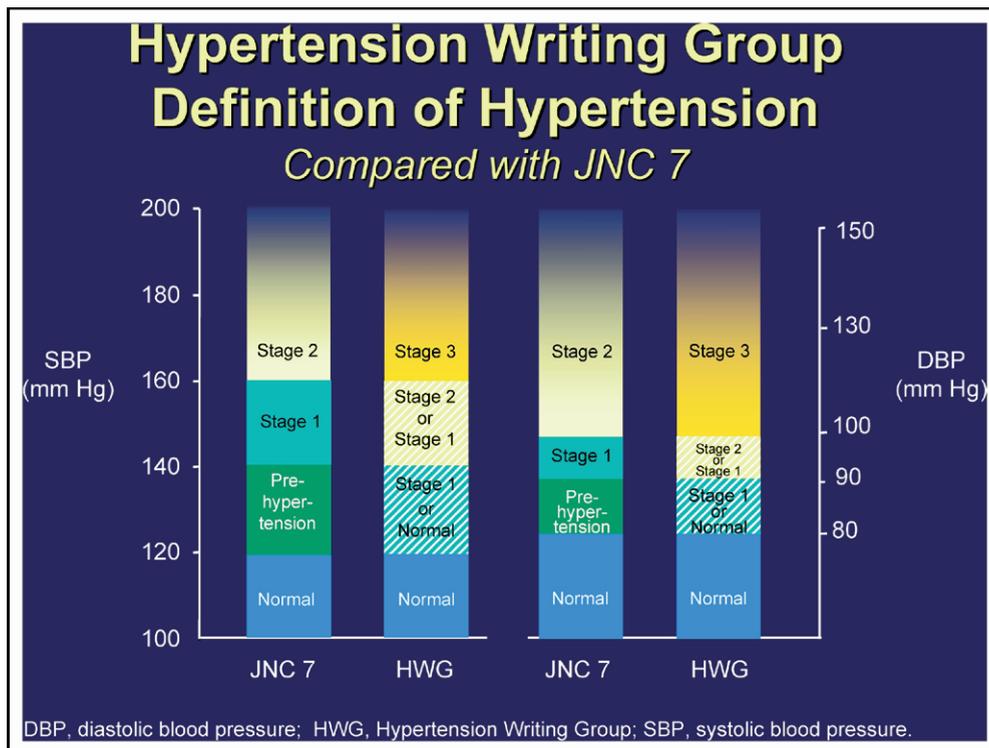


Figure 1. Evolution of BP categories from those proposed in JNC 7² to those proposed by the Hypertension Writing Group (HWG).⁵ Blood pressure levels are considered as only 1 criteria used to classify patients with hypertension; classification also considers cardiovascular status (as listed in Table 2). DBP = diastolic blood pressure; SBP = systolic blood pressure. (From Giles et al,⁵ with permission.)

unnecessarily labeled as being at higher than average risk for cardiovascular events, a reassuring result for patients, physicians, and third parties such as health insurance payers. In an editorial accompanying the writing group's report, Kostis et al¹⁰ noted that BP of 125/85 mm Hg has a different significance in a 70-year-old man who smokes, with low-density lipoprotein and blood glucose of 190 mg/dl, than in a 26-year-old woman who does not smoke, with low-density lipoprotein and blood glucose of 80 mg/dl. The 2 subjects fall into the JNC 7 prehypertension group, but the clinical response is likely to be different on the basis of the other risk factors present in the individual cases.

The writing group's expanded definition of hypertension is a welcome transition point, a move away from looking at BP numbers alone to looking at a cardiovascular risk "report card" similar to the Framingham risk profile.¹¹ This cardiovascular risk assessment would include factors such as BP, age, body mass index, waist circumference, lipids, fasting blood, lifestyle recommendations, endothelial function measurements, and renal parameters, such as microalbuminuria.⁵ In the future, it can be surmised that genetic factors will also become a part of this risk assessment. The clinical view of hypertension is evolving from a situation in which diagnosis and management are based solely on numbers to a future in which management decisions are based on a structured profile of overall cardiovascular risk, and it is recognized that every subject at every stage of life has a cardiovascular risk that falls on this gradient.

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