Rates of progression to hypertension among non-hypertensive subjects: implications for blood pressure screening

It is widely acknowledged that adults in western societies experience an increase in blood pressure with age[1]. Regular screening of blood pressure of non-hypertensive adults has been recommended to detect the onset of hypertension promptly, so that appropriate non-pharmacological and pharmacological measures can be initiated in order to prevent the morbidity and the mortality due to elevated blood pressure[2,3].

Current recommendations for screening non-hypertensive individuals

Non-hypertensive individuals are divided into three categories in the sixth report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure in the United States (JNC VI)[2] and the recent World Health Organization-International Society of Hypertension (WHO-ISH) report[3]: optimal (<120/80 mmHg), normal (120–129/80–84 mmHg) and high normal blood pressure (130–139/85–89 mmHg), staging being based on the higher of systolic or diastolic blood pressure readings. There is a broad consensus among experts that the interval for periodic blood pressure screening should be related to the initial blood pressure level because the higher the baseline blood pressure, the greater the age-associated increase[4]. Yet, expert panels have proposed varying blood pressure screening intervals for the three non-hypertensive blood pressure categories. The JNC VI recommends that individuals with high normal blood pressure should undergo annual blood pressure measurements, while those with normal or optimal blood pressure should be screened every 2 years[2]. The British Hypertension Society advises that subjects with a systolic blood pressure between 135–139 mmHg or a diastolic blood pressure of 85–89 mmHg should be monitored annually, while those with lower levels of blood pressure (i.e. <135/85 mmHg) should be evaluated at 5-year intervals[5]. The European Task Force on Prevention of Coronary Disease advocates that all non-hypertensive individuals should be examined at least once every 5 years[6]. A principal reason for the variation in these recommendations is the lack of information regarding the short-term rates of progression to hypertension for the three non-hypertensive blood pressure categories.

Short-term rates of progression to hypertension in the Framingham Heart Study

In a recent investigation[7], we evaluated repeated blood pressure measures in 9845 Framingham Heart Study participants (57% women; mean age 52 years) who were non-hypertensive (blood pressure<140/90 mmHg) and who attended more than one examination during the time period 1978–1994. We classified individuals into one of the three non-hypertensive blood pressure categories, i.e. optimal, normal or high normal blood pressure at the baseline examination (as defined by the JNC VI and the WHO-ISH reports). We evaluated the incidence of hypertension among participants at the next Framingham clinic examination 4 years later according to their initial blood pressure category[7].

Over a follow-up period of 4 years, 1907 participants (19%) developed hypertension including 6% of subjects with optimal blood pressure, 20% of those with normal blood pressure, and 37% of people with high normal blood pressure[7]. Hypertension incidence among participants in each of the three non-hypertensive categories increased with age. Accordingly, we evaluated two major age groups: 35–64 years, and 65 years or more. Among participants between ages 35 and 64 years, 5% (95% CI 4–6%) of those with optimal blood pressure, 18% (95% CI 15–20%) of those with normal blood pressure and 37% (95% CI 33–42%) of people with high normal blood pressure progressed to hypertension over a 4-year period. Corresponding 4-year rates of
progression for individuals 65 years and older were 16% (95% CI 12–21), 26% (95% CI 20–31), and 50% (95% CI 43–56), respectively for the three non-hypertensive blood pressure categories. It is noteworthy that about 15% of subjects with high normal blood pressure had progressed to Stage II or greater degrees of hypertension over 4 years. Annual incidence rates of hypertension are displayed in Table 1 and increased in stepwise fashion across the three blood pressure categories[7]. Annual rates were highest for older individuals with high normal blood pressure (16%) and lowest in young individuals with optimal blood pressure (below 2%).

Other factors influencing hypertension incidence: impact of weight gain, obesity, and gender

Compared with optimal blood pressure, high normal blood pressure was associated with a 5- (age 35–64 years) to 12-fold (age 65 years or over) elevated odds of hypertension on follow-up[7]. A 5% increase in weight over the 4-year interval (equivalent to a gain of 4 kg in an average man, or 3 kg in an average woman) was associated with a 21 to 30% increased odds of developing hypertension on follow-up. An increase in body mass index at baseline also emerged as an important correlate of future hypertension in this group[7]. These findings are consistent with previous reports linking obesity to the risk of developing hypertension[8]. Gender was not an important determinant of risk of hypertension in our sample; incidence rates of hypertension were similar in men and women, at any age and for each of the baseline blood pressure categories. This observation, while consistent with findings from the NHANES Study[9], is distinctive from other reports that have noted both lower[10] and higher[11] incidence rates in women compared with men.

Hypertension incidence rates: comparison with published literature

While several epidemiological investigations have evaluated the incidence rates of hypertension in the community[8–11], only one prior study has provided information on short-term rates of progression to hypertension according to JNC VI/WHO-ISH blood pressure categories[12]. In that investigation, the annual incidence rates of hypertension among people with high normal blood pressure varied from 9.6% (ages 35–54) to 15.3% (ages 55–75 years), observations that are remarkably similar to findings from Framingham. The placebo arms of clinical trials of non-pharmacological interventions in individuals with high normal blood pressure are an alternative source of information regarding the rates of progression to hypertension[13–15]. While comparing clinical trial data with our results it is important to emphasize that these trials predominantly enrolled younger subjects who were required to be overweight (entry criteria), and who had a diastolic blood pressure level encompassing the entire normal and high normal diastolic blood pressure range (80–89 mmHg). Furthermore, the entry-level systolic blood pressure varied in these trials, and the incidence of hypertension was determined by multiple screening and follow-up examinations. Despite these differences in selection criteria and in study methods, the rates of progression in our younger subjects (age group 35–64 years) were similar to those reported in these hypertension prevention trials at about 10% per year[13–15].

Why rates of progression to hypertension among three non-hypertensive blood pressure categories differ

There are several possible reasons for the stepwise increase in hypertension incidence rates across the three non-hypertensive blood pressure categories[7]. First, there is a gradient of increasing prevalence of risk factors for hypertension across the three categories (such as increasing age and BMI from optimal to normal to high normal blood pressure). Second, smaller increments of blood pressure on follow-up (by definition) are needed for individuals with high normal blood pressure and normal blood pressure in order to progress to hypertension compared to people with optimal blood pressure. Third, it has been well documented that change in systolic blood pressure during follow-up varies directly with the initial levels; this has been termed the ‘horse-racing’ effect, where there is a close correlation between the speeds of horses and their positions in the race[16]. Thus, subjects with high normal blood pressure have higher baseline blood pressure levels indicating that they are ‘faster runners’. These individuals would be expected to track and maintain their blood pressure ranking on follow-up relative to the two other groups. Fourth, it is possible that some subjects with hypertension were misclassified as having high normal blood pressure at baseline, and these individuals were most likely to have hypertension on follow up[17].
**Importance of multiple blood pressure readings**

Incidence rates of hypertension among non-hypertensive individuals in the community are likely to vary depending on the initial blood pressure value, the variance of blood pressure measurements, the duration of follow up, and the presence of factors predisposing to hypertension\(^4,17,18\). It is important to emphasize that the inherent variability of blood pressure measurements can contribute to inaccuracies in the classification of blood pressure categories. Accordingly, multiple measurements obtained on one or more occasions have been recommended for assessment of blood pressure status\(^2,3\).

**Clinical implications: defining optimal blood pressure screening intervals**

The desirable frequency of screening non-hypertensive individuals for the early detection of hypertension depends on several factors such as the rates of progression to hypertension, the accuracy of clinical assessment, the costs of screening, and the risks associated with undetected and untreated hypertension relative to the health benefits of blood pressure lowering\(^7\). Observations from Framingham indicate that rates of hypertension incidence vary with age and according to the baseline blood pressure category\(^7\). A considerable proportion of persons with high normal blood pressure develop hypertension over a 1-year period (11–16%, depending on age group, Table 1), suggesting that annual screening may be desirable for this group regardless of age. Conversely, blood pressure screening at 5-year intervals, as recommended by the European Task Force on Prevention of Coronary Disease\(^6\), would seem unjustifiable for this blood pressure category since between a third to one half of these individuals develop hypertension after only 4 years. Individuals with normal or optimal blood pressure need not undergo annual blood pressure screening but could be re-examined at longer intervals\(^7\). Overall, our prospective investigation of blood pressure progression in the community-based Framingham cohort supports the blood pressure screening intervals recommended by the current JNC VI guidelines.

**References**