

**Question: Why isn't smoking listed with the lifestyle modifications in the HTN module key message 1?
What is the average drop in BP with smoking cessation?**

The table of lifestyle modifications that is included in Key Message 1 of the hypertension module specifically summarizes recommendations for preventing and managing hypertension. These recommendations were taken from the Science Advisory from the American Heart Association (AHA), American College of Cardiology (ACC) and Centers for Disease Control and Prevention, on effective control of high blood pressure.[1] Smoking was not mentioned in this advisory.

In addition, the *2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report from the Panel Members Appointed by the Eighth Joint National Committee (JNC8 Report)* states that the authors did not conduct an evidence review of lifestyle treatments for managing hypertension.[2] The authors of the JNC8 Report did, however, state their support for the recommendations of the 2013 Lifestyle Work Group. The recommendations of this Work Group were published in the 2013 AHA/ACC *Guideline on Lifestyle Management to Reduce Cardiovascular Risk*, but the authors state that smoking, among other interventions, was not included in the report due to time and resource limitations.[3]

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC7 Report), published in 2003, does mention as a footnote in the table of lifestyle modifications that smoking should be stopped as an overall cardiovascular risk reduction measure, however no references are provided for this recommendation.[4]

It is widely known and well established that smoking contributes to cardiovascular disease and increases the risk of cardiovascular events through multiple mechanisms, including effects on endothelial function, inflammatory processes, lipid modifications, coagulation and thrombosis.[5] While the overlapping pathogenesis of smoking and hypertension can further increase risk of cardiovascular events, a causal relationship between smoking and hypertension has not been demonstrated. It is known that cigarette smoking is associated with acute increases in blood pressure and heart rate via stimulation of the peripheral sympathetic nervous system. However, the chronic effect of smoking on blood pressure appears to be the opposite, with several epidemiological studies showing that smokers have lower blood pressure compared to non-smokers and that smoking cessation is associated with either no change or increases in brachial blood pressure, even when results are adjusted for possible confounding factors. Conversely, smoking has been associated with both acute and chronic increases in central blood pressure and arterial stiffness, with reductions shown after smoking cessation. A sampling of observational data and results of 1 controlled trial evaluating impact of smoking cessation on blood pressure are described below.

Changes associated with quitting cigarette smoking during the Framingham Study, a benchmark observational cohort study on the epidemiology of cardiovascular disease, were published in 1975.[6] Investigators evaluated both short-term (2 year) and long-term (12 year) changes in several cardiovascular characteristics in cohorts of men and women that quit smoking compared to those that continued smoking during these intervals. Overall, there was a 24% decrease in the number of male smokers and a 9% decrease in the number of female smokers during the 18-year study period. Due to

the small number of women that quit smoking during the study, data on changes over time were only analyzed for men. Authors noted there were no blood pressure exclusions in the Framingham Study. A total of 803 non-smokers and 1,498 smokers under the age of 65 were evaluated at entry, with no significant differences in baseline age-adjusted mean systolic blood pressure (SBP), 138.1 mmHg vs. 136.1 mmHg, respectively, or diastolic blood pressure (DBP), 87.8 mmHg vs. 85.4 mmHg, respectively. Cardiovascular characteristics were compared among non-smokers and smokers, which were further stratified by number of cigarettes per day (1-10 vs. 20 at entry) and quit status at each 2-year interval. There were no significant differences in average change in SBP or DBP whether subjects continued smoking, quit smoking, continued not smoking or started smoking between visits. Similarly, there were no significant differences in long-term (12 year) changes in SBP or DBP among those who quit smoking compared to those who continued smoking, regardless of number of cigarettes per day. The authors concluded that no significant changes in blood pressure were associated with quitting cigarette smoking.

Another large cross-sectional study evaluated observed changes in cardiorespiratory symptoms and laboratory findings after quitting smoking in patients that received repeated multiphasic health check-ups in Kaiser Permanente Medical Centers in Oakland and San Francisco, CA between 1964 and 1973.[7] These changes were analyzed for persistent smokers and those who quit smoking in an average 1 ½ year period between 2 check-ups. A questionnaire was utilized to determine smoking status. A total of 9392 persistent smokers and 3825 patients that quit smoking were analyzed. Changes in SBP were reported for white men and white women. Changes in age-adjusted mean SBP were not significantly different between white women that persisted smoking and those that quit, -0.5 mmHg vs. 0.3 mmHg, respectively. In white men, there was a significantly greater increase in age-adjusted mean SBP in those that quit vs. those that persisted smoking, 3.8 mmHg vs. 2.2 mmHg, respectively ($p < 0.05$). The authors noted that in black women, the decrease in SBP was significantly greater in quitters vs. persistent smokers ($p < 0.05$) but actual results were not reported. They concluded that short-term changes in blood pressure were small and inconsistent across the race-sex groups comparing smokers vs. quitters.

A small randomized controlled trial testing the effects of cigarette smoking on cardiovascular risk factors, utilized serum thiocyanate concentrations to confirm tobacco exposure.[8] Subjects were recruited through the media for smoking cessation and randomized to a control group and 3 different smoking cessation intervention groups. Questionnaires were administered and relevant measurements and blood draws performed prior to randomization. A total of 140 subjects were enrolled, 33 in the control group and a total of 107 among the intervention groups. The authors noted that no significant differences in outcomes among the intervention groups occurred so data for all 3 groups was pooled for comparison to the control group. Mean age at entry was 40 years, mean cigarettes smoked was 30 per day. There were no significant differences between the groups for any baseline measures. After the completion of smoking cessation interventions, serum thiocyanate concentrations were significantly reduced ($p < 0.05$) in the subjects that quit or reduced smoking compared to the control group and the results correlated with their reported cigarette consumption. There were no differences in changes in average SBP or DBP post intervention compared to the control group (SBP -2.6 ± 1.4 mmHg vs. -3.3 ± 2.3 mmHg, respectively; DBP -1.6 ± 1.1 vs. -2.5 ± 1.8 , respectively). Likewise, there were no differences in changes in average SBP or DBP between those that quit and those that continued to smoke in the intervention group (SBP -1.4 ± 2.2 mmHg vs. -3.1 ± 1.8 mmHg, respectively; DBP 0.7 ± 2.0 mmHg vs. -2.7

± 1.4 mmHg, respectively). The authors concluded that cigarette smoking cessation did not change blood pressure in this population.

An observational study of healthy male employees in a Korean manufacturing company was conducted to determine the effects of smoking cessation on changes in blood pressure and incidence of hypertension [9]. All workers received annual health check-ups consisting of clinical and laboratory measurement and information on lifestyle factors obtained as self-reported on questionnaires. Male workers between 25 and 50 years old, considered to be without hypertension if SBP was not ≥ 160 mmHg and DBP was not ≥ 95 mmHg and not receiving any antihypertensive medications, were eligible for follow-up 4 years later. Subsequently, those with baseline SBP between 140 and < 160 mmHg or DBP between 90 and < 95 mmHg were excluded, as well as those with diabetes mellitus, hypercholesterolemia, other known cardiovascular diseases or diseases requiring medication. A total of 8170 men were included in the analysis. At baseline SBP and DBP were lower for current smokers compared to non-smokers (SBP 114.7 ± 10.1 vs. 115.5 ± 9.9 mmHg, respectively; DBP 72.4 ± 6.7 vs. 73.3 ± 6.6 mmHg, respectively). At follow-up both non-smokers and quitters for 1 to 3 years had significantly larger increases in both crude and adjusted blood pressure measurements compared to smokers (adjusted SBP 4.9 (4.4-5.3), 5.2 (4.3-6.2) and 3.8 (3.5-4.0) mmHg, respectively; adjusted DBP 3.8 (3.5-4.2), 4.1 (3.4-4.8) and 2.9 (2.7-3.1) mmHg, respectively [$p < 0.000$]). The crude and adjusted relative risk of developing hypertension during the follow-up period was significantly greater in those that had quit smoking for ≥ 3 years compared to current smokers, 4.8 (95% CI 2.4 to 9.5) and 3.5 (95% CI 1.7 to 7.4), respectively. Authors concluded that smoking cessation may result in increasing blood pressure and even hypertension in some men.

More recently, an observational study in an internal medicine clinic in Japan was conducted to determine whether smoking cessation with varenicline improved central blood pressure (CBP) and arterial stiffness.[10] Patients included in the study received smoking cessation treatment with varenicline for 12 weeks. The observational study was conducted for 1 year after completion of treatment. Brachial blood pressure and CBP were measured along with multiple measures of arterial stiffness before and 60 weeks after the completion of smoking cessation treatment. Results indicated that of the 70 patients that participated, 37 quit smoking until 1 year after treatment (smoking cessation group) and 33 resumed smoking either during treatment or before the end of the 1-year period (smoking group). Baseline characteristics were similar between the 2 groups. The authors noted that overall 30% of patients had hypertension but only those not receiving antihypertensives were included in the study. Neither brachial SBP nor DBP were significantly reduced in either of the 2 groups after smoking cessation (SBP 138.3 ± 6.4 mmHg vs. 136.7 ± 6.4 mmHg in the smoking cessation group and 135.9 ± 7.3 mmHg vs. 134.8 ± 6.3 mmHg in the smoking group; DBP at baseline was 85.4 ± 3.1 mmHg in the smoking cessation group and 84.2 ± 4.6 in the smoking group, with measures at the end of the 1-year period not reported). In the smoking cessation group, CBP significantly decreased from 109.4 ± 2.1 mmHg before initiation of treatment to 102.3 ± 1.7 mmHg after smoking cessation. Whereas CBP remained unchanged in the smoking group (110.1 ± 2.9 mmHg vs. 111.3 ± 2.8 mmHg before and after smoking cessation, respectively). Similarly, arterial stiffness decreased significantly in the smoking cessation group whereas it remained unchanged in the smoking group. The authors concluded that based on the decreases observed in CBP and arterial stiffness in patients that quit smoking compared to

those that did not, their results supported smoking cessation as a primary approach to preventing cardiovascular events.

In summary, while the evidence does not provide support for smoking cessation as a means of reducing brachial blood pressure in the treatment of hypertension, the overlapping pathogenesis and independent risks of cardiovascular events associated with each do warrant smoking cessation as an obvious lifestyle modification in patients with hypertension.

References:

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