

Is White-Coat Hypertension Associated With Risk of Cardiovascular Diseases?



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REFERENCES

- Franklin SS, Thijs L, Asayama K, et al. The cardiovascular risk of white-coat hypertension. *J Am Coll Cardiol* 2016;68:2033-43.
- Huang Y, Huang W, Mai W, et al. White-coat hypertension is a risk factor for cardiovascular diseases and total mortality. *J Hypertens* 2017;35:677-88.
- Mancia G, Grassi G. The heterogeneous nature of white-coat hypertension. *J Am Coll Cardiol* 2016;68:2044-6.
- Cuspidi C, Sala C, Grassi G, et al. White coat hypertension: to treat or not to treat? *Curr Hypertens Rep* 2016;18:80.
- Mancia G. Clinical significance of white-coat hypertension. *J Hypertens* 2016;34:623-66.

REPLY: Is White-Coat Hypertension Associated With Risk of Cardiovascular Diseases?



The interesting study by Franklin et al. (1) showed that the risk of cardiovascular disease (CVD) in most individuals with white-coat hypertension (WCH) is comparable to age- and risk-adjusted normotensive subjects and only increased in older high-risk WCH subjects. The authors postulated that this association may be caused by undetected isolated systolic hypertension (ISH) in some older patients. We wish to discuss some of our views.

First, in contrast to the analysis by Franklin et al. (1), our recently meta-analysis (2) showed that WCH, either detected by ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring, is associated with long-term risk of CVD and total mortality. The risk of CVD is similar in participants with average age <55 years compared with those age \geq 55 years. We concluded that WCH is not a "benign phenomenon" and is associated with long-term health risks. The underlying mechanisms may include neurogenic abnormality, anxiety personality, and a higher possibility of progressing to hypertension. The Franklin et al. study (1) may be underpowered to detect the risk in the younger population due to the small number of patients with WCH (3).

Second, ABPM has an intrinsic variability between recording sessions, which may affect the consistency of WCH classification (4), so we agree with Franklin et al.'s postulation that the association of WCH and CVD risk may be partially caused by undetected ISH (1). However, it does not seem practical to reduplicate ABPM within a few days or weeks in all people with WCH. The important implication for medical practice from Franklin et al.'s study (1) was it highlighted the importance of risk stratification in WCH. In addition to stratifying the risk factors detected in Franklin et al.'s study, other useful methods including performing multiple office visits or collecting both ABPM and home blood pressure monitoring values (5).

In conclusion, WCH might be associated with increased risk of CVD. Future studies are needed to develop systematic risk evaluation in WCH and selected high-risk subpopulations for pharmacological treatment trials.

The meta-analysis by Dr. Huang and colleagues (1) critiquing our study (2) failed to note the importance of using age-matching rather than age-adjusting in persons with white-coat hypertension (WCH) versus their normotensive comparators. Indeed, we noted in the *JACC* study that the white-coat effect increased dramatically with age, so that there was about a 3.9 mm Hg increase in the white-coat effect per decade of age from about 30 to 80 years of age (see [Figure 1](#)). Because there was a 12-year greater age in the patients with WCH than in their normotensive comparators in the *JACC* WCH study, this alone would falsely increase cardiovascular disease (CVD) risk considerably in this IDACO (International Database of Ambulatory blood pressure in relation to Cardiovascular Outcome) study of persons with WCH (2). The Huang and colleagues' (1) meta-analysis was based on age-adjusted summary statistics, an approach that is less effective than age matching in removing the confounding effect of age.

Secondly, Huang and colleagues (1) concluded from their aggregate data meta-analysis that WCH is associated with increased cardiovascular risk both in participants aged <55 years and in those \geq 55 years.

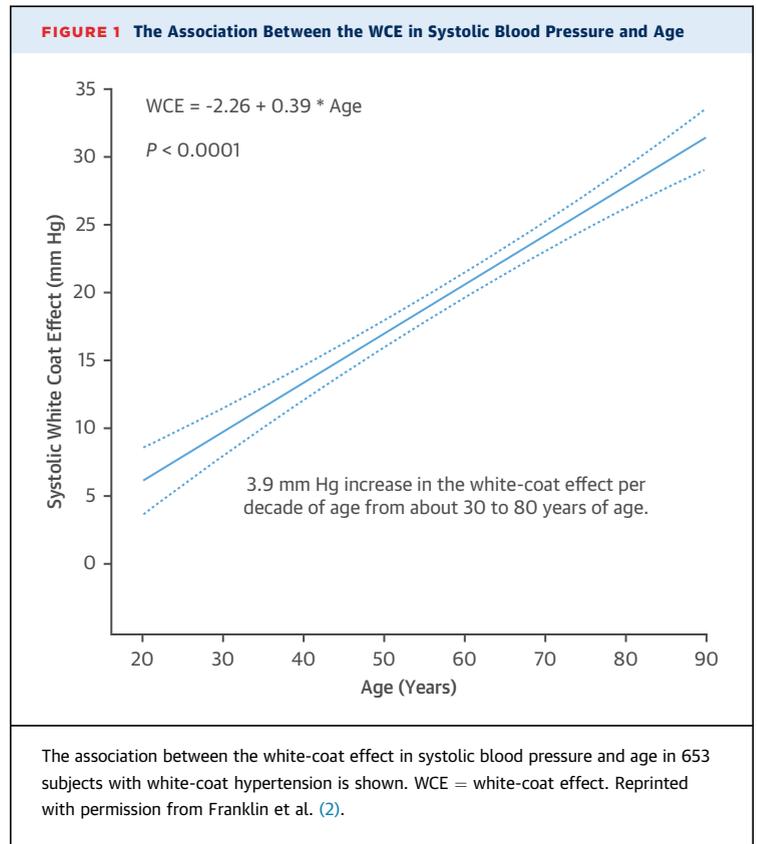
Our subject-level meta-analysis is obviously the preferred method to assess the differential effect of age on the risk associated with WCH. Indeed, the Huang and colleagues' (1) statement on subjects <55 years was based on 5 studies with an average age <55 years. Their results are probably partly driven by the inclusion of subjects age ≥55 years with multiple cardiovascular risk factors.

Thirdly, Huang and colleagues (1) suggested that the IDACO JACC study was underpowered to detect risk in individuals age <60 years. This IDACO study consisted of 653 subjects with WCH from 11 countries and with a 10.6-year follow-up for new cardiovascular events. This consisted of 494 persons with WCH <60 years of age (75.7% consisted of younger subjects) and 159 persons with WCH age ≥60 years (24.3% consisted of older subjects). To our knowledge, this is the largest group of subjects with untreated WCH in the published reports and with the longest follow-up for new cardiovascular events.

In summary, we did not find any credible evidence from the Huang and colleagues' (1) meta-analysis that in any way challenges the findings of our JACC publication (2).

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REFERENCES

1. Huang Y, Huang W, Mai W, et al. White-coat hypertension is a risk factor for cardiovascular diseases and total mortality. *J Hypertension* 2017;35:677-88.
2. Franklin SS, Thijs L, Asayama K, et al. The cardiovascular risk of white-coat hypertension. *J Am Coll Cardiol* 2016;68:2033-43.