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EDITORIAL COMMENT

# Lowering the Thresholds of Diseases

## Is Anyone Still Healthy?*

Franz H. Messerli, MD,[a,b,c] Sripal Bangalore, MD, MHA[d]

Lowering the threshold of markers that indicate "disease" has become a fashionable trend in contemporary cardiovascular medicine. The intent is to identify diseases at the earliest stage possible, so treatment can be initiated before harm has been done. Currently, it has become an ubiquitous phenomenon: levels deemed no longer acceptable of blood pressure (BP), lipids, blood sugar, body mass index, and estimated glomerular filtration rate have all been set lower (1,2). However, such reclassification can be considered like replacing the fishing rod by a fishing trawler, thereby "capturing many more innocent subjects than it should."

Indeed, in the new 2017 American College of Cardiology (ACC)/American Heart Association (AHA) Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure the new magic number is now 130/80 mm Hg, replacing the decades old 140/90 mm Hg (3). Anyone with an office BP of >130/80 mm Hg will said to be hypertensive and on-treatment BP target also should be <130/80 mm Hg. Of note, these BP targets are identical for younger and older patients, with and without diabetes or chronic kidney disease. As is outlined in this issue of the *Journal* in the article by Muntner et al. (4), using data from the 2011 through 2014 National Health and Nutrition Examination Survey (N = 9,623), according to this definition, the prevalence of hypertension will increase from 31.9% (Joint National Committee 7 or 8) to 45.6% or to 103.3

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million people. Just a few months ago, the ACP/AAFP guidelines arrived at the conclusion that clinicians initiate treatment in adults aged ≥60 years with systolic BP persistently at or >150 mm Hg to achieve a target of <150 mm Hg (5). Although these guidelines were not exactly endowed with expertise (6), we still have to come to grips with the fact that within a few months the number of U.S. adults meeting the definition for hypertension has become inflated to an alarming >100 million people (**Figure 1**). Muntner et al. (4) attempt to reassure us by stating that, despite the increase in the number of hypertensives, there only was a small increase in the number of U.S. adults recommended for treatment with antihypertensive medication (and, what they did not state, that the guidelines, therefore, were not disease mongering or pandering to Big Pharma). One may appropriately ask the simple question as to why the 31 million increase in the number of hypertensive patients in the United States led to only a 4.2 million increase in the number recommended for treatment. The reason for this discrepancy is 2-fold.

1. As can be seen in Table 3 (4), the Joint National Committee 7 guidelines consistently recommend treatment in many more patients than those meeting the definition for hypertension. This recommendation was based on the thought that antihypertensive therapy could be beneficial in normotensive subjects at high risk (such as for those with diabetes or chronic kidney disease). However, as shown in the HOPE-3 trial (Heart Outcomes Prevention Evaluation-3), antihypertensive therapy in normotensive subjects conferred no outcome benefits (7). Combination therapy with candesartan

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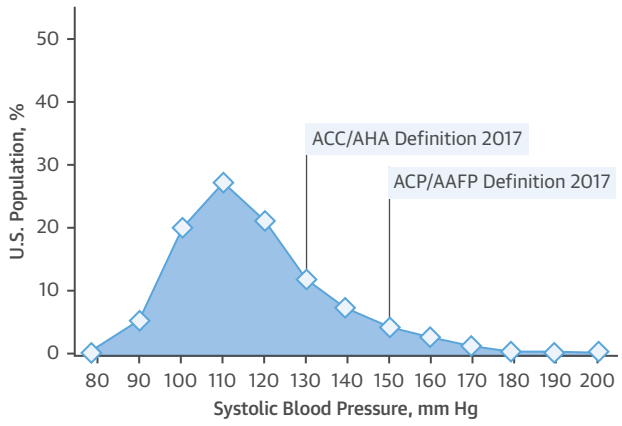
From the [a]Department of Cardiology and Clinical Research, University Hospital, Bern, Switzerland; [b]Division of Cardiology, Mount Sinai Medical Center, Icahn School of Medicine, New York, New York; [c]Jagiellonian University Krakow, Poland; and [d]The Leon H. Charney Division of Cardiology, New York University School of Medicine, New York, New York. Dr. Messerli is a consultant or advisor for the American College of Cardiology, Daiichi-Sankyo, Pfizer, Abbott, Servier, Medtronic, WebMD, Menarini, Ipca, and Hikma. Dr. Bangalore is a consultant or advisor for Daiichi-Sankyo, Pfizer, Abbott, Merck, Boerhinger-Ingelheim, Gilead, and Abbott Vascular.

**FIGURE 1 Percentage of the U.S. Population Defined as Being Hypertensive**




Percentage of the U.S. population defined as being hypertensive, based on American College of Cardiology (ACC)/American Heart Association (AHA) and American College of Physicians (ACP)/American Academy of Family Physicians (AAFFP) guideline definitions.

plus hydrochlorothiazide decreased BP by 6/3 mm Hg from a mean of 138/82 mm Hg, but this did not lower the incidence of the primary outcome compared with placebo (4.1% vs. 4.4%); however, it did lower the incidence of stroke in a subgroup only with highest baseline systolic BP (>143 mm Hg) (7). Other studies have attested to the futility of antihypertensive therapy in normotensive subjects (8). The exception to the rule seems to be the SPRINT (Systolic Blood Pressure Intervention Trial) (9), which has stirred up the placid leaves in the hypertension teapot, mostly because of the unique way BP was monitored in this study (10,11).

2. As Muntner et al. (4) document, in 11.0% of U.S. adults meeting the definition of hypertension as per ACC/AHA guideline, nonpharmacological intervention is advised and antihypertensive medication not recommended. This means that in the vast majority (>80%) of U.S. adults with a BP of 130/80 to 139/89 mm Hg, nonpharmacological therapy on its own is the only recommended therapy. Muntner et al. (4) are optimistic that "lower BP levels used to define hypertension in the 2017 ACC/AHA guideline may lead to the earlier adoption of lifestyle modification and prevent the need for antihypertensive medication for some individuals."

We are somewhat less optimistic in this regard for 2 reasons.

1. Although there is no doubt that an on-treatment BP of just below 130/80 mm Hg provides an optimal balance between efficacy and safety, as we have shown in our recent network meta-analysis of seventeen trials enrolling 55,163 patients with 204,103 patient-years of follow-up (12), labeling a healthy person with a disease comes at a cost. The act of labeling someone as hypertensive not only triggers absenteeism (an increase by as much as 80% in the year after labeling) (13), neuroticism, anxiety, and perception of poor health, but also may cause a subsequent increase in BP, most probably mediated by increased sympathetic activity (14,15). Thus, becoming aware that one has hypertension may beget more hypertension.
2. Adherence to so-called nonpharmacological intervention or lifestyle modifications is notoriously poor in most patients in general and in the elderly specifically. A notable exception to this was the approach by Kempner (16), who was exceedingly successful to keep his patients on a very low salt, hypocaloric diet but had to resort to use a whip to endorse compliance (17). Thus, among the 11.0% of U.S. adults of Muntner et al. (4) who meet the definition of hypertension as per the ACC/AHA guideline but in whom nonpharmacological intervention only is advised, most will never reach the target of consistently having a BP of <130/80 mm Hg. Any attempt to postpone antihypertensive therapy will merely accelerate target organ disease.

However, regardless of how exactly we define hypertension we should remember a simple but inescapable truth in medicine (18): "patients are genetically, physiologically, metabolically, pathologically, psychologically, and culturally different. Accordingly, there never will be only one way to diagnose and treat many medical disorders, including hypertension." As clinicians, we personally consider it ill-advised and not in the best interest of all patients to uniformly lower BP to <130/80 mm Hg, regardless of the ACC/AHA guidelines. As can be seen from the figure in Muntner et al. (4), very few U.S. citizens older than 75 years of age remain "healthy." However, it would be equally ill-advised to maintain BP levels of <150/90 mm Hg in all patients >60 years of age as the ACP/AAFP guidelines are telling us. We can only hope that, despite the recent plethora of guidelines, physicians will continue to treat patients and not mm of Hg only.

Otherwise, we run the risk that the dictum of Molière's Malade Imaginaire will become true, that "Presque tous les hommes meurent de leur remèdes, et non pas de leur maladies" (Nearly all people die of their remedies, and not of their illnesses) (19).

**ADDRESS FOR CORRESPONDENCE:** Dr. Franz H. Messerli, Department of Cardiology and Clinical Research, University Hospital, Freiburgstrasse, 3010 Bern, Switzerland. E-mail: messerli.f@gmail.com.

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