HYPE201607818R

Is it time to reappraise blood pressure thresholds and targets?

A Statement from the International Society of Hypertension – A Global Perspective.

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Short title: Blood pressure targets and global relevance

Key words: hypertension, international guidelines, SPRINT

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The SPRINT findings (1), together with the publication of other major studies within the last year addressing how low blood pressure should be targeted to prevent cardiovascular events in patients with hypertension (2-4), supports what we have known for a long time that: 1) blood pressure >115/75 mmHg is associated with increased risk of cardiovascular disease and stroke, 2) blood pressure lowering is associated with reduced morbidity and mortality, 3) antihypertensive drugs reduce the incidence of hypertension-associated events, and 4) prevention of cardiovascular morbidity is largely related to blood pressure lowering per se, although other effects of the drugs used contribute to this benefit.

The questions that are now posed, particularly in response to an editorial commentary by the Editors of this Journal (5), are: What is the threshold at which anti-hypertensive treatment should be initiated and what target blood pressure should we strive for to achieve maximum benefit in patients with hypertension? SPRINT and other recent meta-analyses and trials provide new data that allow us to sharpen and refine recommendations for blood pressure targets in people with hypertension (1-4). Here we will briefly address the questions in the worldwide context of hypertension.

In hypertensive patients without diabetes, prior stroke or polycystic kidney disease, SPRINT has provided strong evidence that targeting systolic blood pressure of <120 mmHg (as measured by an automated measurement protocol in the office) (1) provides significantly stronger protection from cardiovascular events and death than the traditionally accepted target of <140 mmHg. This study was conducted in a hypertensive patient cohort of intermediate-to-high cardiovascular risk. It should be highlighted that the target of 120 mmHg in SPRINT was based on blood pressure readings using a defined protocol with an office automated device, where blood pressure was measured three times in the absence of clinical personnel (1). Based on

the known differences between readings obtained by automated devices and conventional measurements (6), this average would translate to higher readings (130 mmHg) in clinical practice. Hence, if the goal were to reduce blood pressure to <120 mmHg using conventional methods, there is a risk that blood pressures would in fact be lower than SPRINT's 120 mmHg, with unknown consequences, as highlighted in a recent editorial (7). Accordingly, it is critical that the SPRINT findings are interpreted in the context of the protocol that was used to measure blood pressure.

Moreover, while SPRINT aimed for <120 mmHg it should be emphasized that the study did not actually achieve its target below 120 mmHg, with the intensively treated group having an overall systolic blood pressure of ≈ 122 mmHg as recorded by the defined measurement protocol (1). Hence, considering the method used to measure the blood pressure, it may be more appropriate to conclude that SPRINT's benefits were evident at conventional levels closer to 130 mmHg, in line with other recent reports from individual trials and meta-analyses, which support a target of <130 mmHg (2-4,8).

Importantly, the SPRINT findings do not exclude any particular patient subgroups, except diabetes and prior stroke. Indeed, black patients benefited equally as well as white, and the results in older patients (75 and above) were at least as good as in the younger group. However, for patients aged over 80 years, in whom safety data at this low blood pressure are still limited, it would be prudent to follow a cautious path in approaching the <130 mmHg target (9). Regarding safety concerns, mainly reductions in renal function, electrolyte abnormalities and hypotensive symptoms, SPRINT suggests that the benefits of intensive management outweigh adverse outcomes for patients at heightened risk of events.

It should be acknowledged, based on HOPE 3 (10), that there is some uncertainty about whether there is sufficient evidence to support the initiation of antihypertensive treatment in patients with systolic blood pressures below 140 mmHg, particularly if other major cardiovascular risk factors are not present. It should be noted, however, that HOPE 3 did not test differing blood pressure targets.

Since SPRINT excluded hypertensive patients with a history of diabetes or stroke, considerations for blood pressure targets in patients with diabetes need to be considered from data in other trials. For diabetic patients, the ACCORD trial (11), supported by some but not all studies and meta-analyses, appears to suggest a systolic treatment target of <140 mmHg is sufficient. The one caveat is stroke: in ACCORD and at least one other trial, stroke appeared to be best prevented at <120 mmHg. But to further complicate decision-making, meta-analysis as well as individual trials suggest the possibility of increasing some fatal and non-fatal cardiovascular outcomes as well as adverse renal effects if the pressure is reduced to <130 mmHg or <120 mmHg in patients with diabetes (12-14). Even so, given the serious and justifiably feared consequences of stroke and the inconsistency of the currently available evidence, clinicians should consider discussing the selection of treatment targets with their patients. Meanwhile reaching a target of 130 mmHg seems an acceptable compromise.

A Global Perspective by the International Society of Hypertension

The International Society of Hypertension has a strong commitment to and interest in the work of preventing, identifying and treating hypertensive patients throughout the world. We recognize that recommendations made for more prosperous nations cannot fully apply to all communities or to low and middle income countries. Indeed,

hypertension diagnosis and management are often hampered by such fundamental problems as the lack of blood pressure measuring devices, shortage of personnel trained to measure blood pressures or to advise patients and initiate therapy.. Basic laboratory procedures to check for concomitant conditions such as diabetes or lipid disorders may not be available. Moreover, even though most modern antihypertensive agents are now produced in inexpensive generic formulations, their cost and availability still limit treatment in many parts of the world.

In 2014, in collaboration with the America Society of Hypertension, ISH published Guidelines on the Treatment of Hypertension in the Community (15). Even though those guidelines recommended a systolic blood pressure of 140 mmHg as the usual hypertension threshold, they recognized that in several parts of the world this could put an excessive burden on limited budgets. So, it was suggested for patients without other risk factors, and with systolic blood pressures below 160 mmHg, that initial treatment could be based on lifestyle modifications alone. But even this suggestion, although well intended, could not address the reality that resources to identify additional risk factors in hypertensive patients are often lacking in low income areas and that, in any case, lifestyle modifications that require dietary adjustments, other than moderation of salt intake, are often unavailable or unaffordable. These challenges may be further compounded by insufficient or ineffective education of health care providers, policy makers and the population.

The findings from SPRINT and the other new reports of the benefits of aggressive therapy emphasize that many underserved hypertensive patients are now even more remote from optimal care. This could be a compelling concern in Africa given the strong benefits achieved by the black patients in SPRINT. In African and many other developing countries overcrowded clinics are dealing mostly with infectious diseases.

We therefore anticipate that the wide publicity given SPRINT and other new high-impact reports will help bring a sense of urgency to resolving this major public health issue – which has more wide-ranging environmental challenges beyond aggressive antihypertensive therapy alone.

Taking into consideration the global target population of interest to the International Society of Hypertension, together with evidence derived from SPRINT and other recent meta-analyses and clinical trials, the practical message from the International Society of Hypertension is to strive for a systolic blood pressure target of 130 mmHg in most patients with hypertension. This is especially important considering that blood pressure measurements in the community are not likely to be performed using the SPRINT protocol. So, advocating a target of <120 mmHg is not justified in clinical practice and in any case would incur the costs of increased clinic visits, more intensive health care and more medications. In regions of low resources this added financial and logistical burden is not tenable. Accordingly, while we recognize that there might be benefits in targeting treatment to below our recommended level of 130 mmHg in non-diabetic hypertensive patients at high cardiovascular risk (as in the SPRINT population), the International Society of Hypertension believes it is premature to advocate such low targets at a global level.

Funding: Dr Touyz is supported through a Chair from the British Heart Foundation (CH/12/4/29762). Dr Schiffrin is supported by a Canada Research Chair (CRC) on Hypertension and Vascular Research by the CRC Government of Canada/CIHR Program.

Disclosures:

There are no disclosures to declare by any of the authors.

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