LETTERS

Letters to the Editor

When should treatment be started for hypertension?

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The article by Emily Atkins and Vlado Perkovic[1] provides a welcome review of contemporary issues regarding blood pressure and vascular risk. Understanding blood pressure and its relationship to premature morbidity and mortality, and the use of effective interventions, has been a major success of the last 100 years. Yet, areas of uncertainty remain.

In contrast to previous definitions, the new, lower definition of hypertension adopted in recent US guidelines[2] is based on the level of blood pressure where there is increased cardiovascular risk (observational data), rather than where treatment (interventional data) has demonstrated a net benefit. The recent article[1] suggests that antihypertensive treatment may be worthwhile at a systolic blood pressure of less than 140 mmHg. However, there is little direct evidence to support this in patients without established vascular disease. The SPRINT trial[3] is not informative for treatment thresholds, as 90% of the patients were established on therapy before enrolment. In contrast, the HOPE 3 trial[4] demonstrated that baseline blood pressure was a significant determinant of risk reduction in intermediate-risk individuals. Those with higher blood pressure (systolic >143.5 mmHg) benefited from therapy, while those with lower blood pressure did not. A well-designed meta-analysis (incorporating the PICO elements of patient population, intervention, comparator and outcome) also suggests a treatment benefit with a threshold of 140 mmHg systolic.[5]

A careful approach is also needed in people with elevated blood pressure, who could, by virtue of age and sex, be considered low risk. Early clinical trials,[6] where blood pressures were markedly elevated, had very high event rates, and very low numbers needed to treat (NNT=2) to prevent one event over 12 months. It is important to understand, particularly for younger doctors who may have limited personal experience with managing accelerated or malignant hypertension,[7,8] that hypertension can be a disease, as well as a risk factor.

Rather than the unnecessarily polarising view that a cardiovascular risk-based approach is best for determining when to start antihypertensive therapy, a more nuanced approach is helpful. Decisions on initiating antihypertensives should be based on both blood pressure and risk, as has been advocated in Australian blood pressure guidelines for some years.[9,10]

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The recent article[1] predominantly discusses blood pressure treatment targets, not thresholds. The recommendations are based largely on the SPRINT study[2] and the recent US guidelines.[3] The authors suggest, quoting one reference, that blood pressure measurement in SPRINT (automated office blood pressure) equates to usual clinic blood pressure

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measurement. However, the majority opinion is that systolic blood pressure measured by automated office blood pressure is 10–20 mmHg lower than usual clinic blood pressure,[4,5] which has been used in all the clinical trials that provide the evidence base for the treatment of hypertension. In SPRINT, achieving systolic blood pressure less than 120 mmHg was also associated with serious treatment-related adverse events. SPRINT is therefore not a suitable study on which to base major treatment recommendations.

In contrast, the recent European hypertension guidelines[5] have provided a well-argued case that treatment to lower blood pressure with both lifestyle change and drug therapy is of benefit if the 'clinic' systolic blood pressure is more than 140 mmHg, across the range of blood pressures, cardiovascular risk, comorbidity, sex, ethnicity and age up to 80 years. This was based on available evidence including the SPRINT trial. The European guidelines also demonstrate the lack of evidence for initiating treatment if systolic blood pressure is 130–140 mmHg, except possibly for those at very high cardiovascular risk and with established cardiovascular disease.

Target systolic blood pressure should initially be less than 140 mmHg and, if tolerated, less than 130 mmHg but not less than 120 mmHg. In my opinion the European recommendations are more broadly applicable to the management of hypertension in Australia than the recommendations given in the article.

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Emily Atkins and Vlado Perkovic, the authors of the article, comment:

We thank the letter writers for their responses and welcome the discussion.

A key issue is their suggested separation of treatment thresholds from treatment targets. We disagree with this distinction, and believe that blood pressure targets and thresholds should be considered consistently, once a decision to intervene is reached. We agree that blood pressure treatment is worthwhile in hypertensive urgencies or emergencies, and blood pressure should be considered separately in this specific context.

We strongly believe SPRINT should guide blood pressure treatment approaches. The small increase in adverse events was clearly outweighed by a substantive reduction in cardiovascular events *and* all-cause mortality. It is criticised for the rigorous approach to blood pressure measurement, but we believe this careful measurement is a strength and would advocate for its recommendation and incorporation in guidelines, as has happened in US and Canadian guidelines.[1,2] We believe this is a small ask given patients are committed to potentially lifelong therapy.

Genevieve Gabb and Leonard Arnolda highlighted a meta-analysis. However, this did not exclude trials of dual inhibition of the renin–angiotensin–aldosterone system, which has minimal effects on blood pressure, substantial toxicity, and is contraindicated in guidelines. They highlight the HOPE 3 heterogeneity by baseline blood pressure, but we note the blood pressure reduction achieved in this trial was only 3 mmHg, limiting power. The 95% confidence intervals for the treatment estimate are still consistent with a 19% risk reduction even for participants in the lowest blood pressure tertile. We agree additional data would be helpful.

We believe targeting systolic blood pressure less than 120 mmHg in high-risk people will ensure maximal cardiovascular protection if it is tolerated and appropriate for the individual patient.

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