

Blood pressure-lowering treatment should be based on the level of cardiovascular risk, not on the level of blood pressure

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Malcolm R Law

Queen Mary University of London, Wolfson Institute of Preventive Medicine, London, UK

Correspondence to: Dr Malcolm R Law, Queen Mary University of London, Wolfson Institute of Preventive Medicine, Charterhouse Square, London EC1M 6BQ, UK; m.r.law@qmul.ac.uk

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Context

The 2008 report of the Health Survey for England included a chapter on 'cholesterol' (with no mention of 'hypercholesterolemia') and another on 'hypertension' (with no mention of 'blood pressure').¹ This dichotomy echoed a prevalent view. Treatment guidelines advocated blood pressure-lowering drugs for everybody with blood pressure above a certain threshold (somewhat arbitrarily defined) but not for people with blood pressure below the threshold. There was a view (unsupported by evidence) that below the threshold reducing blood pressure did not reduce risk. However, cholesterol-lowering drugs were advocated for everyone at higher risk, irrespective of pretreatment cholesterol; the relationship with cardiovascular disease was correctly judged to be continuous.

There is strong evidence that blood pressure-lowering drugs should also be used in this way.^{2,3} Proportional risk reduction was shown to be independent of baseline blood pressure in analyses of data on 1 million adults in 61 cohort (prospective observational) studies² and on 460 000 participants in 147 randomised trials of blood pressure-lowering drugs.³

There has since been some progress. The Health Survey for England modified its chapter heading to 'Blood pressure and hypertension' and the 2014 guidelines from the Joint British Societies acknowledged that the relationship between blood pressure and cardiovascular disease was continuous,⁴ but there has been little change in practice. This systematic review and meta-analysis may help change practice.

Methods

In a meta-analysis of individual data from 11 randomised placebo-controlled trials of blood pressure-lowering drugs, the trial participants (treated and placebo) were separated into four groups according to increasing baseline risk of major cardiovascular disease events (on average 6%, 12%, 18% and 27% respectively), using a risk prediction equation.

Findings

The proportional risk reduction from blood pressure-lowering drugs in treated, compared to placebo participants was similar in all four risk groups (18%, 15%, 13% and 15% respectively), irrespective of pretreatment blood pressure. Absolute risk reduction increased with increasing baseline risk (–1.4% in the lowest risk group to –3.48% in the highest risk group).

This meta-analysis also reinforces existing evidence that the major determinant of a person's risk of a cardiovascular disease event is age. In the four groups defined by increasing cardiovascular disease risk, there was large variation in mean age (59, 68, 72 and 75 years).

These data will underestimate the effect of age on risk because trials generally impose an upper age limit for participants, so the proportion of elderly people will be smaller among the trial participants than in the general population. By contrast, there was no difference in mean blood pressure across the four risk groups (125, 125, 126 and 126 mm Hg). Serum low-density lipoprotein cholesterol was not measured, but using non-high-density lipoprotein cholesterol as a surrogate, values were actually directionally higher in the lowest risk group (4.3, 4.2, 4.1 and 3.9 mmol/L, respectively). Age is by far the strongest determinant of risk.

Commentary

It may appear counterintuitive that lowering blood pressure and cholesterol has a great effect in reducing cardiovascular risk yet their pretreatment values make little contribution to estimates of individual risk. A likely explanation is that pretreatment blood pressure and cholesterol are important determinants of risk, but that risk depends more on duration of exposure than intensity of exposure. The effect of duration of exposure would be measured as age. This pattern of causation has long been recognised in relation to smoking and lung cancer: risk is proportional to the first power of intensity of exposure (number of cigarettes smoked per day) but the fourth power of duration of smoking.⁵ In other words, risk is proportional to number smoked per unit time×years exposed×years exposed×years exposed×years exposed. A further explanation of the paradox lies in the observation that single measurements of a person's blood cholesterol and blood pressure poorly reflect a person's average values because there is a substantial within-person fluctuation over time in both.

The observation that risk increases so steeply with increasing age means that almost everybody in the population will cross the risk threshold, some a little younger than others. We have previously argued that it may be better to offer people blood pressure-lowering and cholesterol-lowering drugs above a fixed age threshold (say 55) rather than a fixed risk threshold, an approach judged valid by the Joint British Societies.⁴ This would reduce cost by eliminating frequent measurements and consultations and avoid anxiety through people being told that they are at increased cardiovascular risk.

Implications for practice

Doctors should instigate treatment with blood pressure-lowering drugs according to the overall level of cardiovascular risk, not the level of blood pressure.

Competing interests MRL is a co-holder of patents on the formulation of a combined pill to reduce cardiovascular risk factors.

Provenance and peer review Commissioned; internally peer reviewed.



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