Cochrane report on lowering blood pressure

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Routine blood pressure measurement is widely performed as a method of screening for future cardiovascular events, notably myocardial infarction and stroke. It is perhaps one of the most widely used methods of screening, even though it is rarely part of a systematic screening programme. The intervention that follows identification of a person with a blood pressure above a specified level is usually the prescription of blood pressure lowering medication. There has been a longstanding debate over what blood pressure cut-off level should be used before treatment is offered, or whether instead of a cut-off level people should be offered medication on the basis of their overall risk of a heart attack or stroke, possibly doing this using a person's age, even if their blood pressure is not regarded as raised.

The debate was unfortunately confused by a 2012 report from the Cochrane Collaboration. The report concluded that lowering blood pressure was of unproven benefit in the primary prevention of cardiovascular disease in most people.[1] The report stated that blood pressure lowering drugs used in primary prevention in people with blood pressure in the range 140-159 mmHg systolic and/or 90-99 mmHg diastolic "have not been shown to reduce mortality or morbidity in randomised controlled trials" and added that "more trials are needed".[1] This would mean that blood pressure lowering drugs should only be used by the small proportion of the adult population with blood pressure above 160 mmHg systolic/100 mmHg diastolic.

A meta-analysis based on 21 published randomised controlled trials of people with blood pressure in this range showed a highly statistically significant reduction in risk of stroke (by about 30%) and coronary heart disease events (by about 15%) from treatment with one blood pressure lowering drug. The Cochrane group, however, based their conclusions on the results of two trials only. [2] They did this because they stipulated that, to be informative, every single participant in a trial should have a pre-treatment blood pressure within the specified ranges they selected, 140-159 mmHg systolic and/or 90-99 mmHg diastolic.[1] Accordingly, they sought individual patient data from the trialists, with the intention of conducting an analysis limited to people with a pre-treatment blood pressure within their ranges. Only three trial investigators provided individual data and in one of these trials there were no events in the blood pressure subset, so their analysis was limited to just two trials,[1] with 10 v 20 strokes (treatment v no treatment) and 71 v 64 coronary heart disease events in total – too few data to allow any conclusion.

Blood pressure in the placebo group fell over the course of the two trials by about 10–12 mmHg systolic and 5–6 mmHg diastolic.[3,4] Such a fall is expected due to regression to the mean; the participants were selected as having high blood pressure at a single point in time but in most of them this was not their usual blood pressures so their blood pressure subsequently fell to their usual value. Therefore most of the participants in the subset from the two trials had usual blood pressures below the range specified by the authors of this review.

To determine efficacy within a specified blood pressure range trials should be selected in which blood pressure in the placebo group over the course of the trial was within the range;[2] not every individual in the trials will have usual blood pressure within the range, and the minority above and the minority below the range will roughly cancel out. This analysis yields the unbiased estimate of the fall in blood pressure referred to above.[2]

There is no need for "more trials". Conducting further large trials similar to those already published, but with minor protocol variations, would be a poor use of resources, and, given knowledge of the effect, unethical.

The results from the trials are best considered together with cohort study evidence. In this regard the Prospective Studies Collaboration database provides strong evidence of a continuous dose-response relationship down to values of 110 mmHg systolic/70 mmHg diastolic or lower,[5] with no evidence of a threshold.[5,6]

A non-significant result in an underpowered analysis is not evidence against a valid positive result in an adequately powered meta-analysis particularly when the evidence from trials and cohort studies both show that lowering blood pressure across the adult population is worthwhile.

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Declaration of Interest: Nicholas Wald and Malcolm Law jointly hold an interest in European, Canadian and US patents for a combination pill for the prevention of cardiovascular disease