Mild hypertension in people at low risk

Evidence suggests no net benefit from drug treatment of mild hypertension in people without the higher risks of diabetes or chronic kidney disease, says Stephen A Martin and colleagues

Measurement of blood pressure is an iconic part of modern medicine. Over the past century, life insurers, public health organisations, and prospective studies, including the Framingham Heart Study, have established the relation between increased blood pressure and long term morbidity and mortality.[1]

About 40% of adults have hypertension globally; the prevalence is highest in the African region.[2] In the United States, hypertension is the most common diagnosis at a medical visit.[3 4] Complications of hypertension may account for nearly half of global deaths from cardiovascular disease, though this proportion is the subject of debate.[5 6] The scale of the problem has resulted in large scale interventions[7] and national and international plans for action, such as the 2013 World Health Day.[5 8 9]

Antihypertensive drugs have an important role in the treatment of malignant hypertension, secondary prevention of cardiovascular disease, and primary prevention for people at high risk: those with moderate to severe hypertension (≥160/100 mm Hg), diabetes, or chronic kidney disease. Debate continues, however, about the level at which treatment should begin and the appropriate targets for treatment (see supplementary box on bmj.com). The greatest uncertainty surrounds mild hypertension (140-159/90-99 mm Hg), which accounts for over 60% of those with hypertension[2] or 22% of the global adult population. Evidence suggests no net benefit from drug treatment of mild hypertension in people without the higher risks of diabetes or chronic kidney disease.[10] Nevertheless, most people with mild hypertension are treated with drugs. In this article, we examine the overdiagnosis and overtreatment of mild hypertension.

Changing definitions and treatment thresholds

Over time, hypertension has been diagnosed at progressively lower blood pressures (table 1). In 2003, the seventh US Joint National Committee (JNC) guidelines introduced the category of "pre-hypertension."[11] This term was removed in 2013 by JNC 8[12]; both reports define mild hypertension as 140-159/90-99 mm Hg. The JNC 8 authors explain that for the first time their guidelines were derived from evidence rather than expert consensus.

Treatment thresholds have similarly decreased, though JNC 8 raised the systolic blood pressure treatment threshold to 150 mm Hg for those aged 60 and older and from 130 mm Hg to 140 mm Hg for people with diabetes and kidney disease.

The new JNC guidance has been controversial because contemporaneous guidelines from the American Heart Association, the American College of Cardiology, the Centers for Disease Control and Prevention, and guidelines by the American and International Societies of Hypertension[13 14] essentially endorse the status quo. Five members of JNC 8 issued a separate report advocating that the threshold of 140 mm Hg be maintained for people aged 60 years or older.[15] Differences also exist between US and Canadian, European, and UK guidance.[16-18] Patients and clinicians have been left confused.[19 20]

Rationale for change

Changes in a surrogate marker, such as blood pressure, may correlate with or even cause a decline in health (see animation on bmj.com). However, treatment to modify a surrogate marker does not necessarily result in health improvements and can lead to overly aggressive intervention.[21 22] Although raised blood pressure is correlated with cardiovascular disease in observational studies, we cannot assume the logical reverse—that antihypertensives should prevent disease at an individual or population level.

The harm from bloodletting shows that not all techniques or agents that reduce blood pressure also reduce cardiovascular risk

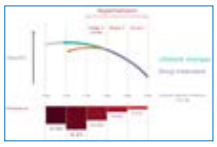
If lowering blood pressure is beneficial, for example, then partial exsanguination should be worthwhile.[23] However, the harm from bloodletting shows that not all techniques or agents that reduce blood pressure also reduce cardiovascular risk. Similarly, α blockers,[24] immediate release calcium channel blockers,[25] guanethidine,[26] and renal denervation and its sham[27] all reduce blood pressure but are inferior choices for long term treatment of hypertension.

These findings reinforce the need for randomised controlled trials to show whether each antihypertensive drug reduces morbidity and mortality.[28] A recent example shows that we have ignored this lesson. The US Food and Drug Administration approved aliskiren, a new type of antihypertensive (renin inhibitor) in 2007; it was prescribed to nearly half a million US patients within four years.[29] However, the drug has not been shown to reduce cardiovascular disease, only to reduce blood pressure.[30] It had this effect in a recent trial, but the study was stopped early as the drug caused harm without benefit.[31]

Further debate surrounds how much drug should be given and whether blood pressure should be treated to a target. Evidence is lack-

Table 2 | Blood pressure ranges and supported interventions in low risk individuals

Blood pressure (mm Hg)	Global prevalence (%)[2]	Risk of cardiovascular disease	Individual risk assessment helpful?	Drug treatment (unselected risk)	Supported interventions37 38
120/80-139/89	36.8	Uncertain[39] or increases[40]	Uncertain	No evidence of benefit[41]	Public health › lifestyle
Stage 1: 140/90- 159/99	22	Uncertain[39] or increases[40]	Yes16 17 42	Uncertain benefit[10]	Lifestyle + public health
Stage 2/3: ≥160/100	13.5	Increases	Yes16 17	Evidence of benefit	Lifestyle + medication + public health



Access this article online to see a video-based animation about mild hypertension in people at low risk

PATIENT COMMENTARY: MOVING GOALPOSTS

I believe that I have had hypertension for about 10 years, but I have lost track. It may be longer. Although the length of time is a haze, one point is very clear in my mind: throughout the years the medical goalposts seem to have changed, and they keep on changing. For a patient, this is extremely confusing.

I am now 59 years old, my family is riddled with high blood pressure problems, and I have a continuous battle with my weight, although I am not obese. I work part time and am very bad at sitting still for long periods. I go through stressful periods, and I am sure this does not help my blood pressure.

When I was first diagnosed with hypertension I was very unwilling to take tablets. The general practitioner's response was to look serious and imply that I might drop dead at any moment. He probably did not use these exact words, but I certainly got the impression that I had a big problem. Yet a few years later a different GP recommended a meditation course to lower my blood pressure. This seemed to work, and I came off the tablets. Unfortunately, the figures went up again and I had a stint with a 24 hour monitoring machine. I went back on the tablets, but a couple of years ago I was told not to worry because my case was very mild, although it would be a good idea to remain on medication. I cannot be specific about my exact figures because I tend to rely more on GP reaction and advice rather than the specifics. I am currently aiming for 140/80 but am usually higher on both figures. My prescription has not changed for years, and I have no side effects from the medication. I always remember to take it because it is part of my routine.

I do not understand why the official figures for hypertension seem to have changed

Currently, I do not visit my GP for any blood pressure checks. I take my own blood pressure at home for a couple of days before visiting the doctor when I have an appointment for something else. I have found that a blood pressure check in the surgery is a complete waste of time because I suffer from white coat syndrome and the readings shoot up when I am faced by a doctor or nurse pumping up my arm. However, I have no idea whether my readings at home with my monitor are correct.

I live with the optimistic assumption that I am a borderline case with nothing to worry about. But I'm not really sure, and I'm probably burying my head in the proverbial sand. I was given a handout at some point detailing acceptable thresholds but it was very generalised. I do not understand why the official figures for hypertension seem to have changed and what was once a cause for concern has become almost normal. I am sure my GP will tell me if there's a real problem but am realistic enough to suspect that he may be influenced by official guidelines, budgets, and people pressure on surgeries.

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ing that the benefits outweigh the harms of such targets.[32 33] US guidelines for patients 65 years and older acknowledge the 140/90 mm Hg target is based only on expert opinion.[34] Nonetheless, the push to lower blood pressure to a "normal level" continues.[35] This language of hypertension has become broadly influential in medicine, with terms such as "good control," "poorly controlled," and "at goal" now readily associated with other conditions. These terms have powerful effects on physicians, payers, employers, governments, and patients. For many patients, such control of hypertension is challenging; indeed, targets were not achieved in up to 40% of participants in closely monitored trials.[36] Table 2 summarises the most effective interventions for each range of blood pressure.

Rise in treatment

The trend has been to expand the indications for drug treatment alongside the definitions of hypertension. In the US, for example, when a definition of stage 1 (mild) hypertension was introduced in1977 drug treatment was not indicated; a conditional indication for treatment was added in 1984 and full indication in 1993 (table 1). Now having hypertension is virtually synonymous with taking a medication for it. While over 60% of Americans with hypertension have stage 1,[43] surveys find from 62.6% to more than 90% of Americans with hypertension report being prescribed a medication for the condition.[44 45] Among people aged 65 years or older with hypertension, 94% take an antihypertensive.[45] This conflation has turned the diagnosis of mild hypertension into a proxy for its overtreatment with drugs.

In addition, use of a sharp, uniform blood pressure threshold to define risk from hypertension ignores evidence to the contrary. Reassessment of Framingham data has found, for example, that the levels at which systolic blood pressure is related to increases in all cause and cardiovascular disease mortality vary with age and sex.[39] A substantial proportion of the population with a systolic pressure ≥140 mm Hg are therefore at no increased risk.

Uncertainty of evidence

Even if mild hypertension is accurately diagnosed, evidence of epidemiological risk is not supported by corresponding data that drug treatment reduces that risk. A 2012 Cochrane review used individual patient meta-analysis to identify all patients with mild hypertension studied in randomised trials and suitable for primary prevention. This review found that compared with a placebo, treatment with an antihypertensive drug did not reduce any outcome, including total mortality (relative risk 0.85, 95% confidence interval 0.63 to 1.15), total cardiovascular events (0.97, 0.72 to 1.32), coronary heart disease (1.12, 0.80 to 1.57), or stroke (0.51, 0.24 to 1.08).[10] It therefore remains uncertain whether treatment is beneficial, neutral, or harmful for this population.

The Cochrane review exposed how studies of more severe hypertension are used to buttress more diffuse treatment. When guidelines claim support for drug treatment for mild hypertension, they tend to do so by citing studies that focused almost exclusively on either moderate to severe hypertension or secondary prevention. JNC 8, for example, opens with "abundant evidence" of benefit for drug treatment and cites three studies, each of which studied moderate to severe hypertension.[12]

Guidelines for the UK, Canada, and Europe recognise the insufficient evidence for drug treatment of mild hypertension in people at low risk.[16-18 46] The 2013 European guidelines conclude that drug treatment of mild hypertension is "still open to question."[18] The 2011 UK National Institute for Health and Care Excellence (NICE) and 2013 Canadian Hypertension Education Program (CHEP) recommendations encourage drug treatment only if there is a significant comorbidity such as diabetes.

How blood pressure is measured is important

A further concern is that the way blood pressure is measured can lead to overdiagnosis of hypertension (table 3, see bmj.com).[47-49] Traditional, office based measurements by doctors may be incorrect. Switching to automated office blood pressure cuff measurements, being wary of recent patient nicotine or caffeine use, allowing five restful minutes before the first check, repeating the measurement at least once, and excluding physician measurements all improve accuracy.[49 50] Perhaps routine office measurement of blood pressure should be abandoned altogether. Home blood pressure is prognostically superior to office based blood pressure readings[51 52 53] and identifies the roughly 20% of the hypertensive population who have white coat hypertension. NICE and CHEP guidelines both advise diagnostic confirmation with ambulatory or home blood pressures,[16 17] and home monitoring has been recommended as the new standard of care.[54]

Costs to patients and systems

The cost of drug treatment of mild hypertension in the US has been estimated at $32.1bn (£19bn; €24bn) a year. This corresponds to more than 1% of annual healthcare costs and more than one third of US total national expenditures on public health.[55 56]

Analyses of absolute cardiovascular risk show that drug treatment based on blood pressure alone is likely to have little individual effect in low risk patients with mild hypertension.[57 58] In addition, nearly half of cardiovascular events in a primary care population occur in a small subset of those with previous cardiovascular events.[59 60] Rather than focusing substantial healthcare efforts on low risk individuals with unclear benefits, targeting efforts at high risk patients —with severe hypertension, diabetes, chronic kidney disease, and previous cardiovascular events—would be less costly and yield patient centred outcomes such as reduced cardiac events or improved quality of life.[60-62] For patients with mild hypertension, the focus on drug treatment reduces emphasis on lifestyle changes. Unlike drug treatment, lifestyle changes are free of side effects and provide benefits beyond reduced blood pressure.[63-65] The health benefits of lifestyle interventions have been known for decades,[37] yet the medical system does not adequately support these approaches. Comments are often made about lack of adherence to advice about behaviour change, but 50-80% of patients are non-adherent with antihypertensive drugs.[66]

Proved harms from antihypertensive drugs include hip fracture, drug related hospital admissions, and poorer self rated physical and mental health.[67 68 69] Even in high risk groups, stricter systolic pressure targets have been associated with increased mortality.[70 71] In general, harms have not been sufficiently measured in clinical trials of antihypertensive medication.[72]

How to do better

Blood pressure must be measured more accurately to ensure patients are correctly identified. Consideration should be strongly given to home measurement as the default.[54] For patients with mild hypertension doctors should be open about the lack of known benefit for drug treatment[10] and the benefits of lifestyle improvements (box). Payers, quality organisations, and healthcare organisations will need to promote and reward lifestyle care in meaningful ways. This is likely to require transfer of resources from medical care to public health.

Use of global outcome scores[73] rather than blood pressure thresholds could also improve the approach for individual patients. Pay for performance metrics that increasingly compel patients, at all ages and levels of risk, to lower their blood pressure must also be revised. These metrics may incentivise medication of patients with mild hypertension while those with severe hypertension are relatively ignored.[74 75]

Better management

- Accurate measurement of blood pressure— resting for at least five minutes, at least two measurements, preferably at home—is crucial
- Encourage lifestyle changes to treat hypertension including weight loss, smoking cessation, decreased alcohol consumption, and increased exercise
- Ensure patients are aware that drug treatment of mild hypertension in low risk people has not been proved to reduce cardiovascular disease
- Abandon unproved and unrealistic blood pressure targets

The optimal blood pressure target for an individual patient with hypertension remains unclear.[32] Systematic reviews show benefit from average blood pressure decreases of 10 mm Hg systolic and 5 mm Hg diastolic.[76 77] Targets are a crude method to reach a "sweet spot" on the harm-benefit gradient,[71 78] and risk iatrogenic harm such as falls, decreased quality of life, and increased mortality. For those aged 90 or older a target of 160/90 mm Hg has recently been suggested in light of available data.[79] The innumerable hours of patient, clinician, and administrative time to reach current targets add up to a substantial opportunity cost.

Conclusion

Fifteen years ago, Jeremiah Stamler advised tackling hypertension at the population level rather than pursuing catch-up in the medical system. He cautioned that, "The high-risk strategy of the last 25 years—involving detection, evaluation, and treatment (usually including drug therapy) of tens of millions of people with already established high BP [blood pressure]—useful as it has been, has serious limitations: It is late, defensive, mainly reactive, time-consuming, associated with adverse effects (inevitable with drugs, however favourable the mix of benefit and risk), costly, only partially successful, and endless. It offers no possibility of ending the high BP epidemic."[37]

Nonetheless, this medicalised strategy remains the default policy of most healthcare systems. In its dilution of effort, it fails people at high risk, who need more clinical attention. In diverting resources, it fails the many more that would benefit from a population based public health approach that tackles the structural drivers of hypertension such as cheap and empty calories, excess sodium and sugars, tobacco and heavy alcohol use, and inadequate physical activity.[38] As healthcare systems grow and adopt a "big data" approach, the idea that medical care can substitute for population based strategy has become an irresistible temptation.

Disagreements among experts reveal cracks in the guideline enterprise. In the US, the American College of Cardiology and American Heart Association plan to publish a new guideline in 2015 for clinicians to follow as "the national standard."[80] The idea that heated controversies in 2014 can be turned into a national standard in 2015 seems impossible, unless, as others advise, our decisions about treatment acknowledge uncertainty and defer to the preferences of patients.[81 82] Only with this acknowledgment can we best use the past century's understandings to inform the right care for the individual and public alike.

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This article is part of a series on overdiagnosis looking at the risks and harms to patients of expanding definitions of disease and increasing use of new diagnostic technologies.

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