BMJ 2016;352:i813 doi: 10.1136/bmj.i813 (Published 25 February 2016)

EDITORIALS

Blood pressure targets in primary care

A balancing act between the certainty of evidence and the messier reality of everyday practice

Christiane Muth *senior researcher in general practice*[1], Marjan van den Akker *epidemiologist and associate professor*[2 3], Paul P Glasziou *general practitioner and professor of evidence based medicine*[4]

[1]Institute of General Practice, Johann Wolfgang Goethe University, D-60590 Frankfurt, Germany; [2]Department of Family Medicine, School CAPHRI, Maastricht University, Maastricht, Netherlands; [3]Academic Center for General Practice/Department of Public Health and Primary Care, KU Leuven, Leuven, Belgium; [4]Centre for Research in Evidence-Based Practice (CREBP), Bond University, Gold Coast, Robina, QLD 4226, Australia

Management of high blood pressure is crucial, to forestall end organ damage, disability, and death and to reduce societal costs from cardiovascular disease. Good management is particularly important in general practice, where most patient care occurs.[1] Recent clinical practice guidelines recommend treatment to systolic blood pressure (SBP) targets of <140 mm Hg,[2-5] but for patients at high risk, such as those with previous stroke, many guidelines recommend lower targets.[2-5]

Is a lower SBP target feasible in general practice? The linked randomised controlled trial by Mant and colleagues (doi:10.1136/bmj.i708)[6] investigated the effects of an SBP target of below 130 mm Hg or a reduction in SBP of at least 10 mm Hg to reduce the recurrence of cerebrovascular events among adults with a history of previous stroke or transient ischaemic attack.[7] Control participants had an SBP target of below 140 mm Hg. Participants in both groups had their blood pressure checked quarterly by a practice nurse (or monthly if SBP was above target) and were treated at their general practitioner's discretion, supported by a guideline based computerised algorithm. Use of the more intensive target led to a statistically significant but modest difference of about 3 mm Hg in SBP between groups (16.1 mm Hg reduction for intervention versus 12.8 for control), at the expense of more changes of antihypertensive drugs in the intervention group, a higher dropout rate (20% v 12%), and an increase in the workload of general practitioners and nurses.[6] These results raise several questions about the application, feasibility, and desirability in practice of lower blood pressure targets recommended by evidence based guidelines.

What does a "target" of 130 mm Hg mean? The trial's intervention group had a mean systolic blood pressure of 143 (SD 14) mm Hg at baseline and 127 (15) mm Hg at 12 months.[6] From these figures, we might assume that most of the intervention group participants would achieve their target blood pressure—below 130 mm Hg—but that is not so. For 95% of these participants to reach a target below 130 mm Hg, their mean systolic blood pressure would need to be 102 mm Hg (assuming a normal distribution and a standard deviation of 14 mm Hg), leaving half of all patients with a blood pressure below that level. Particularly for older patients, morbidity, such as falls and cognitive decline, could increase dramatically.[8]

Is titration to target feasible with unreliable measurements? Another problem occurs because blood pressure readings vary greatly within individuals, with an estimated SD of 10-15 mm Hg.[9 10] Taking an average of multiple measures (for example, 28 home blood pressure readings) could narrow this within person SD to 4.0 mm Hg or less.[11] Then, to achieve 95% of these averaged SBP measurements below 130 mm Hg would require a true systolic blood pressure of 122 mm Hg (again, about 2 SD below the target). Taking an average of multiple blood pressure readings would reduce both false positive readings that seem above target (and lead to an inappropriate up-titration of drugs) and false negative readings below target.[12]

Polypharmacy and unnecessary changes to treatment resulting from unreliable blood pressure measurements may further diminish adherence, which is already poor among adults taking antihypertensives.[13-16] In Mant and colleagues' trial,[6] a lower target blood pressure led to increased losses to follow-up, more patients declining treatment intensification, worse adherence, and symptoms attributed to treatment including postural hypotension (intervention group 110/266 (41%) patients; controls 57/263 (22%)).

Does one target suit everyone? In another linked paper (doi:10.1136/bmj.i717), Brunström and Carlberg considered the appropriateness of blood pressure targets in patients with hypertension and diabetes mellitus.[17] Their meta-analyses of 49 trials found an overall benefit of treating hypertension but some evidence of harm associated with further treatment of patients with a systolic blood pressure below 140 mm Hg.[17] These findings contrast with a previous meta-analysis suggesting significant benefits from lowering blood pressure to below 130 mm Hg in the subgroup with diabetes.[18] This discrepancy may be due to chance or to confounding by differences in the

Correspondence to: C Muth muth@allgemeinmedizin.uni-frankfurt.de

included trials such as population age, morbidity, and treatment. This is a limitation shared by many meta-analyses based on aggregated data, and cautious interpretation of results is preferable to immediate calls for action.[18 19]

Moreover, most patients in the mega-trials that dominated both meta-analyses were younger and had less comorbidity,[18 20] compared with patients with hypertension in primary care who are often older and multimorbid.[21] Applying targets achieved from highly selected populations to real world patients in primary care may result in overzealous treatment decisions.[22] Unless doctors and patients share realistic treatment goals that work across all their comorbidities, we risk perpetuating a disease specific perspective on treatment that often results in an unbearable treatment burden for patients and even in harms.[23-25] If preventing stroke recurrence is the top priority for a patient, their individualised management will include diligent treatment of hypertension. As knowing a patient's true blood pressure is difficult, to achieve maximal benefit and avoid harms we may need to prescribe antihypertensives in accordance with known trial based blood pressure reductions (in mm Hg reduction per drug), use home monitoring wisely, and follow up carefully for clinical symptoms of hypotension and adverse effects.[9]

Competing interests: We have read and understood the BMJ policy on declaration of interests and declare the following interests: none.

Provenance and peer review: Commissioned; not peer reviewed.

1 Forouzanfar MH, Alexander L, Anderson HR, et al. GBD 2013 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;386:2287-323.26364544.

2 National Institute for Health and Care Excellence. *Hypertension in adults: diagnosis and management*. NICE, 2011 (available at http://guidance.nice.org.uk/CG127).

3 Kernan WN, Ovbiagele B, Black HR, et al. American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014;45:2160-236. doi:10.1161/STR.0000000000000024. 24788967.

4 Mancia G, Fagard R, Narkiewicz K, et al. Task Force Members. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2013;31:1281-357. doi:10.1097/01.hjh.0000431740.32696.cc. 23817082.

5 Rosendorff C, Lackland DT, Allison M, et al. American Heart Association, American College of Cardiology, and American Society of Hypertension. Treatment of hypertension in patients with coronary artery disease: a scientific statement from the American Heart Association, American College of Cardiology, and American Society of Hypertension. *Circulation* 2015;131:e435-70. doi:10.1161/CIR.0000000000000207. 25829340.

6 Mant J, McManus RJ, Roalfe A, et al. Different systolic blood pressure targets for people with history of stroke or transient ischaemic attack: PAST-BP (Prevention After Stroke—Blood Pressure) randomised controlled trial. *BMJ* 2016;352:i708.

7 Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. *Lancet* 2015;S0140-6736(15)00805-3.26559744.

8 Farrell B, Monahan A, Dore N, Walsh K. Blood pressure targets in the very old: development of a tool in a geriatric day hospital. *Can Fam Physician* 2014;60:e350-5.25022653.

9 Bell KJ, Hayen A, Macaskill P, et al. Monitoring initial response to Angiotensin-converting enzyme inhibitor-based regimens: an individual patient data meta-analysis from randomized, placebo-controlled trials. *Hypertension* 2010;56:533-9. doi:10.1161/HYPERTENSIONAHA.110.152421. 20625081.

10 Warren RE, Marshall T, Padfield PL, Chrubasik S. Variability of office, 24-hour ambulatory, and self-monitored blood pressure measurements. *Br J Gen Pract* 2010;60:675-80. doi:10.3399/bjgp10X515403. 20849695.

11 McManus RJ, Glasziou P, Hayen A, et al. Blood pressure self monitoring: questions and answers from a national conference. *BMJ* 2008;337:a2732. doi:10.1136/bmj.a2732. 19103628.

12 Mohammed MA, Marshall T, Gill P. The effect of chance variability in blood pressure readings on the decision making of general practitioners: an internet-based case vignette study. *PLoS One* 2012;7:e46556. doi:10.1371/journal.pone.0046556. 23133591.

13 Calderón-Larrañaga A, Diaz E, Poblador-Plou B, Gimeno-Feliu LA, Abad-Díez JM, Prados-Torres A. Non-adherence to antihypertensive medication: The role of mental and physical comorbidity. *Int J Cardiol* 2016;207:310-6. doi:10.1016/j.ijcard.2016.01.069. 26814635.

14 Horne R, Weinman J, Barber N, et al. Concordance, adherence and compliance in medicine taking: report for the National Co-ordinating Centre for NHS Service Delivery and Organisation R & D (NCCSDO). 2005. http://www.netscc.ac.uk/hsdr/files/project/SDO_FR_08-1412-076_V01.pdf.

15 Krueger KP, Berger BA, Felkey B. Medication adherence and persistence: a comprehensive review. *Adv Ther* 2005;22:313-56. doi:10.1007/BF02850081. 16418141.

16 Vrijens B, Vincze G, Kristanto P, Urquhart J, Burnier M. Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories. *BMJ* 2008;336:1114-7. doi:10.1136/bmj.39553.670231.25. 18480115.

17 Brunström M, Carlberg B. Effect of antihypertensive treatment at different blood pressure levels in patients with diabetes mellitus: systematic review and meta-analyses. *BMJ* 2016;352:i717.

18 Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet* 2015;S0140-6736(15)01225-8.26724178.

19 Laurent S, Boutouyrie P. Blood pressure lowering trials: wrapping up the topic?*Lancet* 2015;S0140-6736(15)01344-6.26724177.

20 Van Spall HG, Toren A, Kiss A, Fowler RA. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. *JAMA* 2007;297:1233-40. doi:10.1001/jama.297.11.1233. 17374817.

21 Sarki AM, Nduka CU, Stranges S, Kandala NB, Uthman OA. Prevalence of Hypertension in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. *Medicine (Baltimore)* 2015;94:e1959. doi:10.1097/MD.0000000000001959. 26683910.

22 Greenhalgh T, Howick J, Maskrey N. Evidence Based Medicine Renaissance Group. Evidence based medicine: a movement in crisis?*BMJ* 2014;348:g3725. doi:10.1136/bmj.g3725. 24927763.

23 May C, Montori VM, Mair FS. We need minimally disruptive medicine. *BMJ* 2009;339:b2803. doi:10.1136/bmj.b2803. 19671932.

24 Muth C, van den Akker M, Blom JW, et al. The Ariadne principles: how to handle multimorbidity in primary care consultations. *BMC Med* 2014;12:223. doi:10.1186/s12916-014-0223-1. 25484244.

25 Tinetti ME, Bogardus ST Jr, , Agostini JV. Potential pitfalls of disease-specific guidelines for patients with multiple conditions. *N Engl J Med* 2004;351:2870-4. doi:10.1056/NEJMsb042458. 15625341.