



## CLINICAL TRIAL HIGHLIGHTS

of Blood Pressure in Stroke and Other At-Risk Groups trial [TASMIN-SR; ISRCTN87171227] was to determine if self-management, consisting of self-monitoring with self-titration of antihypertensives, effectively lowers BP in patients with high-risk conditions such as stroke and diabetes [O'Brien C et al. *BMC Cardiovasc Disord* 2013]. Richard J. McManus MA, PhD, University of Oxford, Oxford, United Kingdom, presented key results from this study.

Eligible patients were aged >35 years with hypertension plus stroke, diabetes mellitus, coronary heart disease or chronic kidney disease, with a BP >130/80 mm Hg, not currently taking >3 antihypertensives, and willing to self-monitor and self-titrate their medication. Pregnant women and patients with dementia or terminal disease were excluded.

Participants were randomized to self-management or standard care as determined by their physician. BP targets were 130/80 mm Hg in office and 120/75 mm Hg for home. A color-coded system instructed patients on what actions to take based on their BP readings (Table 1). Patients returned for follow-up at 6 and 12 months. The primary outcome measure was systolic BP, with secondary outcomes of diastolic BP, costs, anxiety, health behaviors, and patient preferences. The study was powered to detect a 5 mm Hg difference between treatment groups.

Table 1. Traffic Light System to Adjust Medication

Color	Level	Blood Pressure	Action
Red	HIGH	SBP ≥181 mm Hg OR DBP ≥101 mm Hg	Your BP is too high.  Records a <b>RED</b> reading.  Make an appointment within 48 hours to see the study GP or nurse.
Amber	RAISED you may need to alter your medication	SBP 121 to 180 mm Hg OR DBP 76 to 100 mm Hg	Your BP is raised.  Record an <b>AMBER</b> reading.  If you have FOUR or more <b>AMBER</b> readings in 1 week or 2 consecutive months then look at your medication change instructions.
Green	NORMAL	SBP 101 to 120 mm Hg AND DBP ≤75 mm Hg	Your BP is normal.  Record a <b>GREEN</b> reading.  This is fine provided you have no side effects.
Blue	LOW	SBP ≤100 mm Hg	Your BP is too low.  Record a <b>BLUE</b> reading.  Make an appointment within 48 hours to see the study GP or nurse.

BP=blood pressure; DBP=diastolic BP; GP=general physician; SBP=systolic BP.

A total of 552 patients were enrolled; 276 per treatment group. At the 12-month follow-up, data from 220 (78%) from the self-management group and 230 patients (83%) in the standard care group were available for analysis. Forty-five percent had diabetes, 32% had chronic kidney disease, 31% had coronary heart disease, and 17% had cerebrovascular disease. The mean number of antihypertensive drugs at baseline was 1.6.

In the primary analysis, the self-management group had lower unadjusted mean systolic BP (128.2 mm Hg; 95% CI, 125.9 to 130.4) compared with the standard care group (137.8; 95% CI, 135.4 to 140.3) at 12 months. At the 12-month time point, the self-management group was taking more antihypertensive medications (mean, 2.24; 95% CI, 2.09 to 2.39) than the standard-care group (1.75, 95% CI, 1.62 to 1.88). There were no significant differences between the two groups in the occurrence of side effects. "We have data on health behaviors and resource costs. Both of these will be important in understanding our trial fully," Prof. McManus noted.

In this study, self-monitoring with self-titration of antihypertensive medication resulted in lower systolic BP compared with standard care. It is expected that this reduction in BP would significantly lower stroke and coronary heart disease risk. While there was evidence of greater use of antihypertensive medications in the self-management group, this was not accompanied by increased side effects. Prof. McManus concluded that self-management may not be suitable for every patient but should be offered to those willing to try.

## Meta-Analysis of Hypertension Trials Confirms Benefits of Blood Pressure Lowering

Written by Muriel Cunningham

Costas Thomopoulos, MD, San Luca Hospital, IRCCS Istituto Auxologico, Milan, Italy, presented the results of a meta-analysis of blood pressure (BP)-lowering trials that have been published over the past 47 years. Dr. Thomopoulos and colleagues conducted this meta-analysis of hypertension randomized trials to determine the effect of differential BP lowering on hard clinical outcomes.

BP-lowering randomized controlled trials can utilize an intentional or nonintentional design. Intentional design trials can be further subdivided into the following classifications: active treatment versus placebo or no treatment; more intensive versus less intensive active treatment; or a more intensive lowering strategy versus a less intensive lowering strategy, including predefined



systolic and diastolic BP. For the present meta-analysis, both intentional and nonintentional design trials were included. However, the following types of trials were excluded: nonrandomized trials; those with a mean follow-up <6 months; trials with <5 events reported; trials with different additional interventions among the two study arms; heart failure trials; studies of acute myocardial infarction (MI) and acute stroke; studies where the baseline hypertension prevalence was <40%; and comparison trials between active treatments of similar intensity.

MEDLINE was the primary source used to identify appropriate trials. Secondary sources included the Cochrane Database, the Scopus Database, and reference lists of previous meta-analyses.

Clinical outcomes included MI (fatal and nonfatal), stroke (fatal and nonfatal), heart failure, cardiovascular death, all-cause death, a composite of MI and stroke, and a composite of MI, stroke, and heart failure. The key findings of active treatment versus placebo or no treatment from intentional trials are presented in Table 1.

**Table 1. Effects of Active Treatment Versus Placebo/No Treatment\* in Intentional Trials**

Outcome	Number of Trials	Risk Ratio (95% CI)	Risk Reduction With Active Treatment** (%)
MI	29	0.88 (0.83 to 0.94)	12
Stroke	29	0.68 (0.62 to 0.75)	32
Heart failure	18	0.63 (0.52 to 0.77)	37
CV mortality	30	0.84 (0.79 to 0.90)	16
All-cause death	30	0.90 (0.86 to 0.94)	10
MI and stroke	30	0.79 (0.74 to 0.85)	21
MI, stroke, and heart failure	20	0.75 (0.69 to 0.82)	25

CV=cardiovascular mortality; MI=myocardial infarction. \*p<0.001 for all outcomes; \*\*vs placebo/no treatment.

The findings from meta-analysis conducted after pooling all types of intentional and nonintentional trials (Table 2) were consistent with the results from intentional trials of active treatment versus placebo or no treatment.

A metaregression analysis indicated that the difference in achieved BP was negatively correlated with all outcomes (all p≤0.005) except MI (p=0.09 for systolic BP change and p=0.26 for diastolic BP change).

Prof. Thomopoulos concluded that lowering BP per se, regardless of whether an intentional or nonintentional design was employed, led to a reduction in all hard clinical endpoints. In addition, achieved systolic and diastolic BP changes were correlated with a reduction in all events except MI.

**Table 2. All Intentional and Nonintentional Blood Pressure-Lowering Trials**

Outcome	No. of Trials	Heterogeneity	ΔBP	Ratio of Events	RR (95% CI)	Standardized RR (95%CI) for 10/5 mm Hg BP Reduction
MI	64	I <sup>2</sup> =11.5%, Q=83.6, p=0.21	8.2/4.7	5113/151,956 vs 5937/161,408	0.91 (0.88–0.94)	0.90 (0.86–0.93)
Strokes	59	I <sup>2</sup> =57.2%, Q=161.1, p<0.001	8.6/4.7	5325/153,090 vs 6626/163,133	0.77 (0.72–0.83)	0.75 (0.69–0.81)
HF	44	I <sup>2</sup> =42.1%, Q=82.9, p=0.001	7.9/4.2	3641/101,831 vs 4280/101,159	0.83 (0.77–0.89)	0.79 (0.72–0.87)
Composite MI and stroke	59	I <sup>2</sup> =48%, Q=140, p<0.001	8.1/4.6	10,177/150,652 vs 12,113/160,731	0.85 (0.81–0.88)	0.83 (0.78–0.86)
Composite MI, stroke, and HF	44	I <sup>2</sup> =66.1%, Q=147.1, p<0.001	8.5/4.6	12,148/112,205 vs 14,402/122,376	0.84 (0.80–0.88)	0.82 (0.77–0.86)
CV mortality	63	I <sup>2</sup> =39%, Q=121, p<0.001	8.2/4.7	6064/148,802 vs 6658/158,833	0.93 (0.88–0.98)	0.92 (0.86–0.97)
All-cause mortality	71	I <sup>2</sup> =31.7%, Q=117, p=0.004	8.0/4.5	113,382/155,280 vs 12,164/161,126	0.96 (0.92–0.99)	0.95 (0.90–0.99)

BP=blood pressure; CV=cardiovascular; HF=heart failure; MI=myocardial infarction.

The editors would like to thank the many members of the European Society of Hypertension and presenting faculty who generously gave their time to ensure the accuracy and quality of the articles in this publication.

