Optimal systolic blood pressure target, time to intensification, and time to follow-up in treatment of hypertension: population based retrospective cohort study

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ABSTRACT

OBJECTIVES

To investigate the optimal systolic blood pressure goal above which new antihypertensive medications should be added or doses of existing medications increased ("systolic intensification threshold") and to determine the relation between delays in medication intensification and follow-up and the risk of cardiovascular events or death.

DESIGN

Retrospective cohort study.

SETTING

Primary care practices in the United Kingdom, 1986–2010.

PARTICIPANTS

83 756 adults with hypertension from The Health Improvement Network nationwide primary care research database.

MAIN OUTCOME MEASURES

Rates of acute cardiovascular events or death from any cause for patients with different hypertension treatment strategies (defined by systolic intensification threshold, time to intensification, and time to follow-up over the course of a 10 year treatment strategy assessment period) after adjustment for age, sex, smoking status, socioeconomic deprivation, history of diabetes, cardiovascular disease or chronic kidney disease, Charlson comorbidity index, body mass index, medication possession ratio, and baseline blood pressure.

RESULTS

During a median follow-up of 37.4 months after the treatment strategy assessment period, 9985 (11.3%) participants had an acute cardiovascular event or died. No difference in risk of the outcome was seen between systolic intensification thresholds of 130–150 mm Hg, whereas systolic intensification thresholds greater than 150 mm Hg were associated with progressively greater risk (hazard ratio 1.21, 95% confidence interval 1.13 to 1.30; P < 0.001 for intensification threshold of 160 mm Hg). Outcome risk increased progressively from the lowest (0–1.4 months) to the highest fifth of time to medication intensification (hazard ratio 1.12, 1.05 to 1.20; P = 0.009 for intensification between 1.4 and 4.7 months after detection of elevated blood pressure). The highest fifth of time to follow-up (> 2.7 months) was also associated with increased outcome risk (hazard ratio 1.18, 1.11 to 1.25; P < 0.001).

CONCLUSIONS

Systolic intensification thresholds higher than 150 mm Hg, delays of greater than 1.4 months before medication intensification after systolic blood pressure elevation, and delays of greater than 2.7 months before blood pressure follow-up after antihypertensive medication intensification were associated with increased risk of an acute cardiovascular event or death. These findings support the importance of timely medical management and follow-up in the treatment of patients with hypertension.

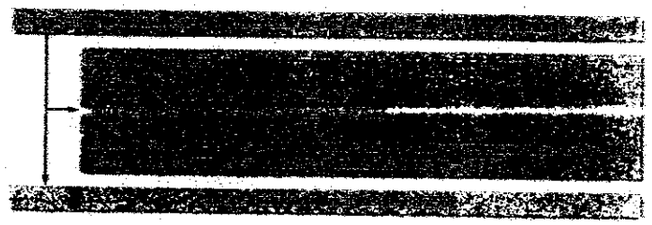

Fig 1 | Study patients and exclusion criteria. THIN = The Health Improvement Network

Table 1 | Baseline characteristics of study patients. Values are numbers (percentages) unless stated otherwise

No of participants	88 756
Mean (SD) age, years	58.5 (11.9)
Male sex	36 800 (41.5)
Mean (SD) body mass index	27.6 (5.0)
Past/current smoker	50 176 (56.5)
History of any cardiovascular disease	9907 (11.2)
History of coronary artery disease	6827 (7.7)
History of congestive heart disease	601 (0.7)
History of stroke	2450 (2.8)
History of peripheral vascular disease	981 (1.1)
History of diabetes	5863 (6.6)
Chronic kidney disease	2420 (2.7)
Mean (SD) modified Charlson index	0.27 (0.6)
Mean (SD) Townsend deprivation score	2.66 (1.3)

Table 2 | Effects of patients' baseline characteristics on risk of cardiovascular event or death

Female sex	0.74 (0.71 to 0.77)	< 0.001
Age (years):*		
< 60	1.00	—
60–74	2.37 (2.19 to 2.57)	< 0.001
≥ 75	5.99 (2.54 to 6.49)	< 0.001
Townsend deprivation score†	1.09 (1.08 to 1.11)	< 0.001
Past or current smoker	1.21 (1.16 to 1.27)	< 0.001
Modified Charlson comorbidity index‡	1.14 (1.11 to 1.17)	< 0.001
Body mass index:		
< 20	1.95 (1.66 to 2.29)	< 0.001
20–24.9	1.00	—
25–29.9	0.97 (0.93 to 1.02)	0.27
≥ 30	1.08 (1.02 to 1.14)	0.006
Pre-existing medical conditions:		
Diabetes	1.62 (1.51 to 1.73)	< 0.001
Coronary artery disease	1.48 (1.40 to 1.57)	< 0.001
Chronic heart failure	1.61 (1.38 to 1.87)	< 0.001
Cerebrovascular disease	1.45 (1.32 to 1.77)	< 0.001
Peripheral vascular disease	1.60 (1.44 to 1.73)	< 0.001
Chronic kidney disease	1.15 (1.02 to 1.30)	0.021

Results of multivariable Cox proportional hazards regression model of time to death from any cause or cardiovascular event that included variables in tables 2 and 3.
*Age categories were calculated at beginning of outcome assessment period.
†Hazard ratio for Townsend deprivation score is per fifth increase in socioeconomic deprivation.
‡History of cardiovascular disease and diabetes were omitted from calculation of modified Charlson index; hazard ratio is per 1 point increase in Charlson score.

Table 3 | Effects of characteristics of treatment strategy assessment period on risk of cardiovascular event or death

Minimum systolic intensification threshold (mm Hg):			
130	12 229 (13.8)	0.98 (0.91 to 1.07)	0.69
140	20 458 (23.0)	1.00	—
150	21 329 (24.0)	1.03 (0.97 to 1.10)	0.34
160	17 513 (19.7)	1.21 (1.13 to 1.30)	< 0.001
170	8978 (10.1)	1.42 (1.31 to 1.55)	< 0.001
≥ 80	8249 (9.3)	1.69 (1.55 to 1.84)	< 0.001
Fifths of mean time to intensification (months):			
0–1.439	17 752 (20.0)	1.00	—
1.440–4.681	17 751 (20.0)	1.12 (1.05 to 1.20)	0.009
4.682–8.689	17 749 (20.0)	1.23 (1.15 to 1.32)	< 0.001
8.690–15.320	17 753 (20.0)	1.19 (1.11 to 1.28)	< 0.001
≥ 15.321	17 751 (20.0)	1.25 (1.17 to 1.35)	< 0.001
Fifths of mean time to follow-up after intensification (months)			
0–0.723	18 283 (20.6)	1.06 (0.99 to 1.13)	0.085
0.724–1.018	17 524 (19.7)	1.00	—
1.019–1.544	17 887 (20.2)	1.01 (0.95 to 1.08)	0.71
1.545–2.727	17 537 (19.8)	1.07 (1.00 to 1.14)	0.050
≥ 2.727	17 525 (19.7)	1.18 (1.11 to 1.25)	< 0.001
Mean systolic blood pressure (mm Hg) elevation over intensification threshold (%):*			
1–9	47 173 (53.1)	1.00	—
10–19	31 376 (35.4)	1.13 (1.07 to 1.19)	< 0.001
20–29	8514 (9.6)	1.38 (1.27 to 1.49)	< 0.001
30–39	1508 (1.7)	1.51 (1.31 to 1.73)	< 0.001
40–49	185 (0.2)	1.78 (1.26 to 2.50)	0.001
Medication possession ratio	0.859 (0.19)	0.80 (0.73 to 0.88)	< 0.001

Results of multivariable Cox proportional hazards regression model of time to death from any cause or cardiovascular event that included all variables in tables 2 and 3.
*Mean difference between actual blood pressure and systolic intensification threshold at beginning of each hypertensive period.

Table 4 | Effects of characteristics of treatment strategy assessment period on overall mortality risk

Minimum systolic intensification threshold (mm Hg):			
130–139	10 853 (13.4)	0.99 (0.90 to 1.09)	0.80
140–149	18 646 (23.0)	1.00	—
150–159	19 724 (24.3)	1.05 (0.97 to 1.14)	0.22
160–169	16 177 (19.9)	1.26 (1.15 to 1.37)	< 0.001
170–179	8253 (10.2)	1.42 (1.28 to 1.58)	< 0.001
≥ 180	7525 (9.3)	1.69 (1.53 to 1.87)	< 0.001
Fifths of mean time to intensification (months):			
0–1.406	16 233 (20.0)	1.00	—
1.407–4.646	16 238 (20.0)	1.11 (1.03 to 1.20)	0.009
4.647–8.684	16 236 (20.0)	1.24 (1.14 to 1.34)	< 0.001
8.685–15.350	16 238 (20.0)	1.20 (1.10 to 1.30)	< 0.001
≥ 15.351	16 233 (20.0)	1.30 (1.19 to 1.42)	< 0.001
Fifths of mean time to follow-up after intensification (months):			
0–0.723	16 652 (20.5)	1.02 (0.95 to 1.10)	0.55
0.724–1.018	14 747 (18.2)	1.00	—
1.019–1.544	17 110 (21.1)	1.01 (0.93 to 1.09)	0.90
1.545–2.694	16 577 (20.4)	1.05 (0.98 to 1.15)	0.18
≥ 2.695	16 092 (19.8)	1.21 (1.13 to 1.30)	< 0.001
Mean systolic blood pressure (mm Hg) elevation over intensification threshold (%):*			
1–9	43 576 (53.7)	1.00	—
10–19	28 627 (35.3)	1.12 (1.05 to 1.20)	< 0.001
20–29	7521 (9.3)	1.31 (1.19 to 1.44)	< 0.001
30–39	1301 (1.6)	1.58 (1.34 to 1.85)	< 0.001
40–49	153 (0.2)	1.98 (1.34 to 2.92)	< 0.001
Medication possession ratio	0.861 (0.192)	0.92 (0.82 to 1.03)	0.14

Results of multivariable Cox proportional hazards regression model of time to death from any cause that included all variables in tables 2 and 4.

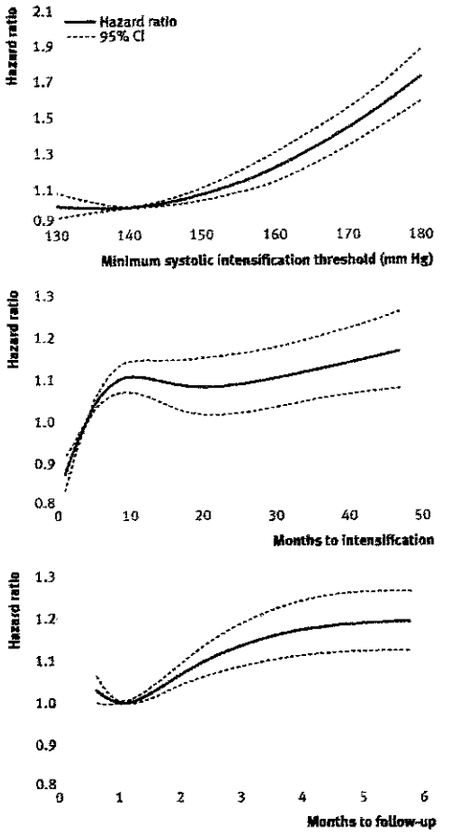

Fig 2 | Effects of systolic blood pressure intensification threshold, time to antihypertensive intensification, and time to follow-up after intensification on risk of acute cardiovascular event or death. Top panel: hazard ratio for acute cardiovascular event or death in relation to systolic blood pressure intensification threshold. Middle panel: hazard ratio for acute cardiovascular event or death in relation to mean months elapsed between systolic blood pressure elevation above minimum intensification threshold and either antihypertensive medication intensification or censoring of unintensified period (via spontaneous normalization of blood pressure). Bottom panel: hazard ratio for acute cardiovascular event or death in relation to mean months elapsed between each antihypertensive medication intensification and next blood pressure measurement. Solid lines indicate hazard ratios; dashed lines indicate 95% confidence intervals calculated using natural cubic spline regression. Reference points are placed at means of respective distributions for time to intensification and time to follow-up. Knots are placed at 5th, 25th, 75th, and 95th centiles of each variable. Multivariable model was adjusted for age, sex, body mass index, smoking status, socioeconomic deprivation, history of cardiovascular disease or diabetes, other chronic medical conditions as represented by Charlson comorbidity index, minimum systolic intensification threshold, mean initial blood pressure elevation above intensification threshold, and medication possession ratio