# Outcomes of blood pressure targets in clinical trial versus primary care setting

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## Background

Results of the Systolic Blood Pressure Intervention Trial (SPRINT) in the US showed considerable survival benefits of treatment of systolic blood pressure (SBP) to a target of less than 120 mmHg compared to a target of less than 140 mmHg. The main adverse effect of the intensive treatment was adverse renal outcome, with the hazard raised threefold in patients without chronic kidney disease (CKD) at baseline.

## Objective

Compare survival and adverse renal outcomes in patients without CKD in SPRINT with similar patients managed in routine primary care in the UK, for SBP reduction to below 140 mmHg compared to below 120 mmHg.

## Methods

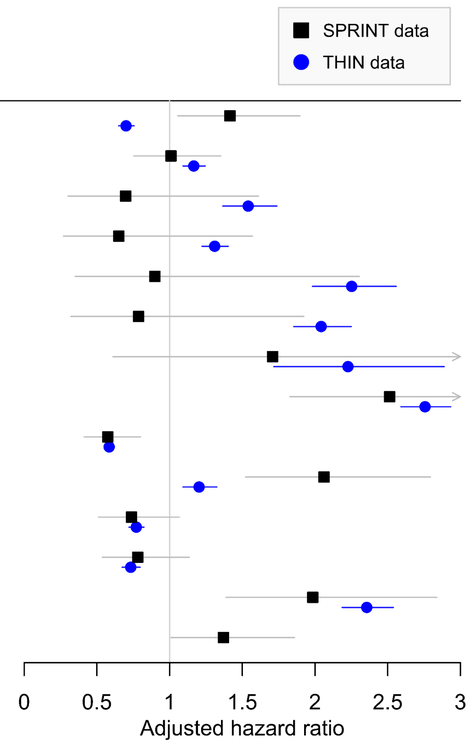
- SPRINT design was replicated in the UK primary care setting using data of The Health Improvement Network (THIN) database.
- SPRINT participants were enrolled between Nov 2010 – Mar 2013 and followed up to Aug 2015. THIN patients with at least four SBP readings were selected between Jan 1995 – Jan 2005 and followed up to Jan 2011.

| Target SBP | SPRINT | THIN |
|---|---|---|
| <120 mmHg | 3,348 | 4,780 |
| <140 mmHg | 3,367 | 10,184 |

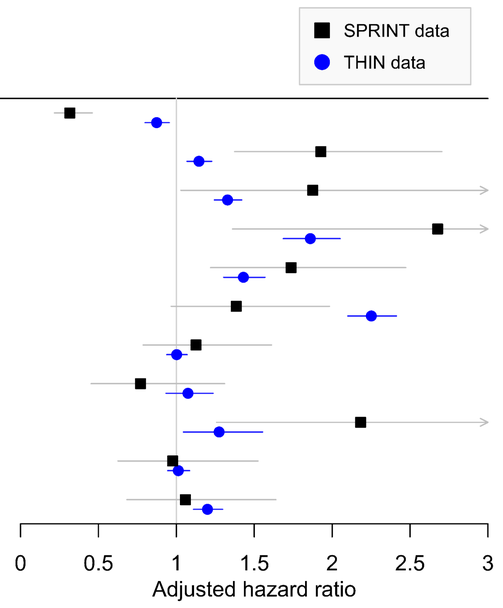
- The hazards of all-cause mortality or adverse renal outcome (defined as eGFR reduction ≥30% in SPRINT and as CKD stage ≥3 in THIN) associated with SBP targets were estimated by a Cox's proportional hazards regression, adjusted for confounders and multilevel on clinical site.
- Final models were obtained through backward elimination.

## Results

| All−cause mortality | SPRINT HR (95%CI) | THIN HR (95%CI) |
|---|---|---|
| Treatment SBP<140 | 1.42 (1.06−1.90) | 0.70 (0.65−0.76) |
| Baseline SBP>=140 | 1.01 (0.75−1.35) | 1.17 (1.09−1.24) |
| 1−2 agents | 0.70 (0.30−1.61) | 1.54 (1.37−1.74) |
| 3+ agents | 0.65 (0.27−1.57) | 1.31 (1.22−1.40) |
| 0 agents & additional | 0.90 (0.35−2.30) | 2.25 (1.98−2.56) |
| 1−2 agents & additional | 0.79 (0.32−1.92) | 2.04 (1.85−2.25) |
| 3+ agents & additional | 1.71 (0.61−4.78) | 2.23 (1.72−2.89) |
| Age>=75 | 2.51 (1.83−3.46) | 2.76 (2.59−2.93) |
| Female | 0.57 (0.41−0.80) | 0.58 (0.55−0.62) |
| CVD | 2.06 (1.52−2.79) | 1.20 (1.09−1.33) |
| Overweight | 0.74 (0.51−1.07) | 0.77 (0.72−0.82) |
| Obese | 0.78 (0.54−1.14) | 0.73 (0.67−0.80) |
| Smoker | 1.98 (1.39−2.84) | 2.36 (2.19−2.54) |
| Black race | 1.37 (1.01−1.86) | |




| Adverse renal outcome | SPRINT HR (95%CI) | THIN HR (95%CI) |
|---|---|---|
| Treatment SBP<140 | 0.32 (0.22−0.46) | 0.87 (0.80−0.95) |
| Baseline SBP>=140 | 1.93 (1.37−2.70) | 1.15 (1.07−1.23) |
| 1−2 agents | 1.88 (1.03−3.42) | 1.33 (1.24−1.42) |
| 3+ agents | 2.68 (1.36−5.27) | 1.86 (1.69−2.05) |
| Additional agents | 1.74 (1.22−2.47) | 1.43 (1.30−1.57) |
| Age>=75 | 1.38 (0.97−1.98) | 2.25 (2.10−2.41) |
| Female no CVD | 1.13 (0.79−1.61) | 1.00 (0.94−1.07) |
| Male CVD | 0.77 (0.45−1.31) | 1.07 (0.93−1.24) |
| Female CVD | 2.18 (1.26−3.79) | 1.27 (1.05−1.55) |
| Overweight | 0.98 (0.63−1.52) | 1.01 (0.94−1.09) |
| Obese | 1.06 (0.68−1.64) | 1.20 (1.11−1.30) |




Baseline levels: treatment target SBP<120 mmHg, baseline SBP<140 mmHg, no antihypertensive agents at baseline, no additional antihypertensive agents at trial entry, age<75, male, no cardiovascular disease, normal weight (BMI<25), non-current smoker, and non-black race.

## Discussion and conclusion

- Treatment target of SBP<120 mmHg was associated with survival benefits in SPRINT, but with an increased hazard of all-cause mortality in THIN.
- Treatment target of SBP<120 mmHg was associated with an increased hazard of adverse renal outcome in both SPRINT and THIN.
- Patients with polypharmacy tended to have worse survival and adverse renal outcomes in both SPRINT and THIN.
- The differences in results may be due to the earlier time-span of THIN data, that prescription changes in THIN could signify sicker patients, and that lower SBP readings in THIN could signify unwell patients. Additionally, the way of measuring SBP in SPRINT may have resulted in lower readings compared to those recorded in primary care.
- Intensive treatment of SBP may benefit a selected subgroup of patients, but it appears harmful for the broader population.

## References

SPRINT Research Group. (2015). A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*, *2015*(373), 2103-2116.