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RESEARCH PAPER

The optimal blood pressure target in old and very old patients with hypertension

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Abstract

Background: With the rise in older population globally, the optimal blood pressure (BP) target for antihypertensive therapy in those aged 60 and above remains to be evaluated in the real-world practice. This study evaluated the effectiveness and safety of standard versus lower BP targets in old (aged 60–79) and very old (aged ≥80) patients with hypertension in real-world clinical settings.
Methods: We emulated a target trial using electronic medical records from the Hong Kong Hospital Authority, including patients aged 60 years or above with a diagnosis of hypertension, uncontrolled BP and records of antihypertensives adjustments from 2008 to 2013. Patients were first categorized into 3 age groups (60–69, 70–79, ≥ 80) and then assigned to BP targets of either 130–140/80–90 mmHg or below 130/80 mmHg. Outcomes included major cardiovascular disease (CVD), end-stage renal disease, all-cause mortality and major adverse events related to antihypertensive treatment.
Results: Of 132 430 eligible patients identified, 52 553, 28 661 and 7106 patients aged 60–69, 70–79 and ≥ 80 years had BP targets of 130–140/80–90 mmHg, respectively; 11 148, 5636 and 1203 of patients in the same age groups had targets below 130/80 mmHg. Lower BP target was associated with reduced overall CVD and all-cause mortality: aged 60–69 years (CVD HR: 0.91 [95% CI, 0.85–0.96]; all-cause mortality: 0.89 [0.81–0.98]), aged 70–79 years (CVD: 0.87 [0.82–0.93]; all-cause mortality: 0.84 [0.78–0.91]), and aged≥80 years (CVD: 0.77 [0.69–0.86]; all-cause mortality: 0.80 [0.72–0.89]). No significant increase in major adverse events was observed in any age group. Results were consistent across all subgroups.
Conclusion: Lowering BP of below 130/80 mmHg in old and very old patients was associated with better cardiovascular and mortality outcomes without increased adverse events. These findings suggest that a lower BP target may be beneficial and safe for older patients with hypertension.

Keywords: hypertension; blood pressure; antihypertension management; older patients

Key points

- A blood pressure target below 130/80 mmHg is beneficial to prevent the hypertension-related complications for old and very old patients with hypertension.
- A blood pressure target below 130/80 mmHg is safe for old and very old patients with hypertension.
- The lower blood pressure target can be considered among very old patients (≥80 years) in the future treatment guideline.

Introduction

Hypertension is a leading risk factor for mortality and cardiovascular diseases (CVDs) in the older adults [1]. Given the ageing population, the optimal blood pressure (BP) for antihypertensive management among this population remains to be evaluated. The current guidelines on the BP target for the older patients remain inconsistent. For instance, the American College of Cardiology / American Heart Association (ACC/AHA) guideline recommended the BP target of less than 130/80 mm Hg [2], while the other guideline such as European Society of Hypertension (ESH)/European Society of Cardiology (ESC) [3] and World Health Organization (WHO) [4] recommended a BP target of less than 140/90 mmHg and The Eighth Joint National Committee (JNC 8) [5] or National Institute for Health and Care Excellence (NICE) [6] recommended an even higher BP target of less than 150/90 mm Hg for the old or very old patients with hypertension.

The uncertainty of the lower BP target for old and very old patients is partially due to the underrepresentation of the randomised controlled trial (RCT) among the old adults align with the absent of the RCTs among the very old patients with the lower BP target. The findings of the Hypertension in the Very Elderly Trial (HYVET) provided the evidence for the antihypertensive treatment among very old patients with hypertension to achieve the target BP of 150/80 mmHg [7]. However, the participants in HYVET achieved the SBP of 143.5 mmHg after 2 years of treatment, providing limited evidence on the effects on SBP lower than 140 mmHg. Later evidence from the Systolic Blood Pressure Intervention Trial (SPRINT) comparing the standard BP control (systolic BP less than 140 mmHg) and the intensive BP target (less than 120 mmHg) have reported a lower risk of major CVD events and all-cause mortality in adults aged over 75 years receiving intensive management [8]. Nevertheless, the conclusions of this study may not be fully reflected in the real-world because this study only recruited patients with higher cardiovascular risks, included relatively small number of very old patients (most participants were between 75 and 80 years old) and excluded those older patients with some common chronic diseases. A subsequent RCT conducted in older patients among Chinese population (STEP) have observed similar benefits from the lower SBP target of 110 to less than 130 mm Hg compared to the higher SBP target of 130 to less than 150 mmHg among patients with aged between 60 to 80 years [9]. However, whether the benefits of the lower BP target could be observed across the wider population of older

patients remained unknown. Therefore, high-quality real-world evidence is much needed to inform the optimal BP target in clinical practice considering the substantial cost and ethical issues associated with large-scale RCT among older patients.

This study aimed to investigate the optimal BP target in clinical settings through emulating the risk and benefits of hypertension-related complications and adverse events in old (aged 60–79) and very old (aged 80 years and over) patients based on data from real-world electronic health records (EHRs).

Method

Study design and data sources

To evaluate the effects of the optimal BP target among old and very old patients, a target trial was emulated by clone-censor-weight approach [10] using the electronic health records from the clinical management system provided by the Hong Kong Hospital Authority (HKHA). The HKHA manages all the public healthcare services in Hong Kong, covering more than 80% of healthcare managements.

Participants

All patients aged 60 years or above with a documented diagnosis of hypertension on or before December 2013 with BP ≥130/80 mmHg and adjusted prescription record of antihypertensives in the electronic health system were eligible in our study. The date of the first antihypertensive prescription change during January 2008 to December 2013 was defined as the baseline. Patients with any history of cardiovascular diseases or with eGFR less than 15 ml/min/1.73 m^2 on or before the baseline were excluded from this study. The included patients were categorized into 3 age groups (60 to 69, 70 to 79 and ≥ 80 years) for analysis. The details of the emulation and the study design were summarised in Appendix, Table S1 and Appendix, Figure S1, respectively.

Treatment strategies

Two treatment strategies were considered for the comparison in this study: (i) continued being treated to the target of SBP 130–140 mmHg and DBP 80–90 mmHg or (ii) lower BP target of SBP <130 mmHg and DBP <80 mmHg.

Outcome measures and follow-up period

This study examined several outcomes, including the overall incidence of major CVDs [a composite of heart failure and stroke, coronary heart disease (CHD) and stroke], and the specific subtypes of major CVDs. Additionally, the study assessed the incidence of end-stage renal disease (ESRD), all-cause mortality and seven serious adverse events associated with intensive treatment: hypotension, syncope, bradycardia, electrolyte abnormalities, falls, acute kidney injury and dizziness. Disease diagnoses were based on the International Classification of Primary Care, 2nd edition (ICPC-2), International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), or relevant clinical parameters (Appendix, Table S2). The adverse events of BP treatment were defined as the diagnosis that required hospital admission. All patients were followed from the baseline until the outcome events, or the end of the study (31 December 2022), whichever occurred first.

Statistical analysis

We estimated the per-protocol effect of the BP targets. The details of the clone-censor-weight were summarised in the Appendix, Supplementary Methodology and the details of the construction of weighting were shown in the Appendix, Table S3. A pooled logistic model was fitted to estimate the hazard ratio (HR) for the effect of the lower blood pressure target on the incidence of outcome events. The indicators for the assigned treatment strategy, month of follow-up (linear and quadratic term) and baseline covariates were included in the models with time-varying weights.

The aforementioned pooled logistic regression model with interaction terms between treatment and follow-up time after standardising the outcomes using the joint distribution of the covariates in the entire study population was used to estimate the 5-year absolute risk differences and the corresponding number needed to treat. The 95% CIs for the absolute risk differences were obtained from a nonparametric bootstrap with 500 replicates.

Multiple imputation using the chained equation method was applied to handle the missing data. Based on all baseline covariates and the primary outcome, missing values were imputed five times to produce five individual datasets that were applied to the statistical analysis. Rubin's rule was then utilised to pool the results together [11].

Subgroup analysis and sensitivity analysis

Seven subgroup analyses were predefined. Patients were stratified by (i) gender; (ii) frailty status [defined as Charlson comorbidity index (CCI) <6, CCI ≥6]; (iii) smoking status; (iv) CVD risk using Framingham risk score formula (<10, 10–20 ≥ 20); (v) obesity status; (vi) history of DM; and (vii) history of CKD. Interaction between treatment and each subgroup were also evaluated. Five sensitivity analyses were performed. Firstly, to estimate the intention to treat effect, we applied the same RCT emulation without the adjustment of time-varying confounders to estimate the results [12]. This captured the effect of being assigned to lower treatment compared with the standard treatment at baseline on the risk of outcomes. Secondly, to explore the influence of the last SBP carried forward for missing data at follow-up, patients with missing BP (defined as the interval from the last BP records till the next BP records was over 1 year) at follow-up were censored. Thirdly, the compete case analysis was conducted using the same study design. Fourthly, the interaction effect by age group was investigated. Fifthly, the adverse events reported

from the outpatient clinics were included to investigate the safety of the lower BP target.

All analyses were performed in Stata/MP 17.0. Statistical significance was defined as a 2-tailed P value less than 0.05.

Ethical approval

Ethical approval for this study was granted by the Institutional Review Board of the University of HK/HA HK West Cluster (UW19-361) and was conducted according to the Declaration of Helsinki, with an exemption for informed consent from participants as patients' confidentiality was maintained in this retrospective cohort study.

Results

A total of 132 430 eligible older patients with hypertension were identified in this study (Figure 1). Of those individuals with a BP target of 130–140/80–90 mmHg, 52 553 (67.5%), 28 661(65.6%) and 7106 (65.0%) were aged 60–69 years, 70–79 years and ≥80 years, respectively. Among the patients with a BP target of less than 130/80 mmHg, 11 148 (14.3%), 5636 (12.9%) and 1203 (11.0%) patients were aged 60–69 years, 70–79 years and ≥80 years, respectively. Other patients who did not achieve the traditional treatment target after grace period, or patients without follow-up after baseline, were censored from the study during the grace period. The baseline characteristics are shown in Table 1. The crude incidence rates for each outcome are summarised in Table 2. Over 50% of the patients adhered to their assigned treatment strategy (Appendix, Figure S1) at the end of the study period. With an average follow-up of 7 years, patients with lower BP target were observed to incur a lower risk of HT-related complications (Figure 2 and Table 2) in all age groups. The cumulative incidence curves are shown in Figure 3. Specifically, patients aged 60–69 years with lower BP target showed reduced risk of developing major CVDs [HR (95% CI): 0.91 (0.85–0.96)], CHD [0.86 (0.78–0.94)], stroke [0.92 (0.84–1.00)], ESRD [0.66 (0.54–0.81)] and all-cause mortality [0.89 (0.81–0.98)]. The absolute risk reduction was observed for major CVDs [−0.67% (95% CI, −0.98 to −0.40%)] and all-cause mortality [−0.43% (95% CI, −0.60 to −0.26%)]. In patients aged 70–79 years, similar benefits were observed: major CVDs [HR (95% CI): 0.87 0.82–0.93)], CHD [0.82 (0.73–0.91)], heart failure [0.83 (0.73–0.94)], ESRD [0.74 (0.62–0.89)] and all-cause mortality [0.84 (0.78–0.91)]. The risk reduction was observed for major CVDs [absolute risk difference, −1.52% (95% CI, −1.90 to −1.14%)] and all-cause mortality [absolute risk difference −1.95% (95% CI, −2.20%, −1.62%)]. The very old patients with lower BP target were observed having benefits on preventing CVDs and all-cause mortality: major CVDs [HR (95% CI): 0.77 (0.69–0.86)], CHD [0.73 (0.59–0.91)], heart failure [0.77 (0.65–0.91)], stroke [0.78 (0.66–0.91)] and all-cause mortality [0.80 (0.72–0.89)]. The risk reduction was observed for major CVDs [absolute risk difference, −3.71% (95% CI, −4.94 to −2.48%)] and all-cause mortality [absolute risk difference, −3.99% (95% CI, −4.90%, −2.89%)]. The number needed to treat based on these findings suggests that a strategy of lower BP target for 5 years would be expected to prevent 1 death from any cause for every 250 persons, 27 persons, 25 persons treated in older patients aged 60–69 years, 70–79 years and ≥80 years, respectively.

There was no significant increased risk for the adverse events (Table 2 and Figure 2) in the lower BP group compared to the traditional treatment target were observed in all age groups, including falls [HR (aged 60–69): 1.01 (95% CI: 0.92–1.11); aged 70–79: 0.95 (95% CI: 0.87–1.03); aged ≥80: 0.95 (95% CI: 0.83–1.08)] and dizziness [HR (aged 60–69): 1.06 (95% CI: 0.96–1.16); aged 70–79: 1.06 (95% CI: 0.96–1.16); aged ≥80: 1.02 (95% CI: 0.86–1.22)]. Sensitivity and subgroup analyses reported largely consistent findings (Appendix, Tables S4–S16). Notably, a similar reduction in CVD risk was observed across patients with different baseline CVD risks and CCI scores.

Discussion

Our study demonstrated that the lower BP monitoring target (<130/80 mmHg) in old and very old patients is associated with a significantly lower risk of cardiovascular events and all-cause mortality compared to conventional targets (130–140/80–90 mmHg). The observed clinical benefits conferred by the lower BP target were consistent across subgroups of patients with different comorbidity statuses and risk factors for disease outcomes evaluated. Importantly, patients treated with lower BP target did not incur a greater risk of adverse effects. These findings emphasise the feasibility and safety of the lower BP monitoring target of BP less than 130/80 mmHg in real-world older populations, particularly in patients with existing comorbidities posing as risk factors for adverse cardiovascular events. Given the rapidly growing population aged 80 years and older worldwide, the clinical benefits from lower BP management provided timely and critical clinical evidence to support the optimal care for these patients.

The study reported consistent findings in the benchmark age group (aged 60–79 years) with previous large-scale trials, such as SPRINT [8] and STEP [9], supporting the adoption of a lower BP management target in the updated guidelines for older patients. Our findings also suggest that benefits and safety of the lower BP target extend to patients older than 80 years. Very old patients have been underrepresented in previous RCTs examining the clinical benefits of lower BP targets, leaving recommendations in the current guidelines for this group ambiguous. A secondary analysis from the SPRINT trial on participants aged ≥80 indicated reduced CVD and all-cause mortality but an increased risk of changes to the kidney function in the adults with lower BP control [13]. However, that analysis may have limited generalisability in real-world very old population because of limited sample size, exclusion of common chronic diseases and short follow-up of study population. With the vastly extended follow-up period of this study of up to 11 years

Table 1. Baseline characteristics.

Demographic	Age 60–69 years		Age 70–79 years		Age ≥ 80 years	
	SBP 130–140 mmHg and DBP 80–90 mmHg (*N* = 52 553)	SBP < 130 mmHg and DBP < 80 mmHg (*N* = 11 148)	SBP 130–140 mmHg and DBP 80–90 mmHg (*N* = 28 611)	SBP < 130 mmHg and DBP < 80 mmHg (*N* = 5636)	SBP 130–140 mmHg and DBP 80–90 mmHg (*N* = 7106)	SBP < 130 mmHg and DBP < 80 mmHg (*N* = 1203)
Sex (male)	28 481 (54.2%)	5491 (49.3%)	14 481 (50.6%)	2844 (50.5%)	2763 (38.9%)	477 (39.7%)
Age	63.9 (2.8)	63.9 (2.8)	74.3 (3.0)	74.2 (3.1)	84.6 (3.5)	84.5 (3.4)
Smoking status	3504 (6.7%)	804.0 (7.2%)	2129 (6.7%)	432.0 (7.7%)	526 (7.4%)	105.0 (8.7%)
Systolic blood pressure	157.3 (16.3)	154.9 (15.5)	161.5 (17.0)	158.4 (16.2)	165.2 (18.3)	162.7 (18.2)
Diastolic blood pressure	89.9 (7.9)	88.9 (7.2)	88.1 (7.2)	87.9 (7.0)	87.5 (7.1)	87.4 (6.9)
Fasting glucose	6.2 (1.8)	6.2 (1.9)	6.1 (1.7)	6.1 (1.7)	5.9 (1.5)	5.9 (1.6)
Low-density lipoprotein cholesterol	3.3 (0.9)	3.3 (0.9)	3.2 (0.9)	3.2 (0.9)	3.2 (0.9)	3.1 (0.9)
Total cholesterol	5.3 (1.0)	5.3 (1.0)	5.3 (1.0)	5.3 (1.0)	5.2 (1.0)	5.2 (1.0)
High-density lipoprotein cholesterol	1.3 (0.4)	1.3 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)
Triglyceride level	1.6 (1.1)	1.6 (1.1)	1.5 (0.9)	1.5 (0.9)	1.4 (0.7)	1.4 (0.7)
Body mass index	25.8 (3.7)	25.4 (3.6)	25.1 (3.7)	25.0 (3.6)	24.2 (3.8)	24.1 (3.6)
Estimated glomerular filtration rate	94.8 (41.4)	94.8 (20.4)	83.9 (21.9)	84.0 (21.3)	73.7 (23.5)	73.6 (23.4)
Charlson comorbidity index	2.8 (1.5)	2.9 (1.6)	3.9 (1.5)	4.0 (1.6)	5.0 (1.5)	5.1 (1.5)
Use of ACEI/ARB	14 005 (26.6%)	2934 (26.3%)	7430 (26.0%)	1362 (24.2%)	1640 (23.1%)	255 (21.2%)
Use of β-blocker	15 030 (28.6%)	3118 (28.0%)	8675 (30.3%)	1531 (27.2%)	2034 (28.6%)	292 (24.3%)
Use of calcium channel blockers	35 702 (67.9%)	7854 (70.5%)	19,587 (68.5%)	4048 (71.8%)	5108 (71.9%)	920 (76.5%)
Use of diuretic	6463 (12.3%)	1217 (10.9%)	4593 (16.1%)	907 (16.1%)	1177 (16.6%)	201 (16.7%)
Use of other antihypertensive drugs	3270 (6.2%)	603 (5.4%)	3159 (11.0%)	614 (10.9%)	978 (13.8%)	182 (15.1%)
Use of lipid-lowering agents	14 044 (26.7%)	3134 (28.1%)	6487 (22.7%)	1347 (23.9%)	953 (13.4%)	188 (15.6%)
Dementia	26 (0.0%)	10 (0.1%)	148 (0.5%)	31 (0.6%)	158 (2.2%)	29 (2.4%)
Diabetes mellitus	13 240 (25.2%)	2959 (26.5%)	7143 (25.0%)	1443 (25.6%)	1488 (20.9%)	267 (22.2%)
Doctor consultations in general outpatient clinics[a]	4.3 (3.1)	4.6 (3.4)	4.9 (3.1)	5.1 (3.3)	5.0 (3.1)	5.4 (3.5)
Doctor consultations in specialist outpatient clinics[a]	0.3 (0.9)	0.3 (1.0)	0.3 (1.0)	0.3 (1.0)	0.3 (1.1)	0.3 (1.0)
Accident and emergency services[a]	0.2 (0.7)	0.3 (1.0)	0.3 (0.8)	0.3 (0.9)	0.4 (0.9)	0.4 (1.0)
Inpatient visit[a]	0.1 (0.5)	0.1 (0.5)	0.2 (0.7)	0.2 (0.7)	0.4 (0.9)	0.4 (0.8)

[a]Number of specialist, general outpatient clinics attendance, accident and emergency and hospitalisation were counted within 1 year before baseline.

Table 2. Risk of outcomes for different blood pressure treatment targets. .

Outcome	SBP 130–140 mmHg and DBP 80–90 mmHg		SBP < 130 mmHg and DBP < 80 mmHg			
	Events/follow-up time	Crude incidence rate (95% CI)	Events/follow-up time	Crude incidence rate (95% CI)	Adjusted hazard ratio (95% CI)	Absolute risk difference (95%)
Age 60–69 years						
Major CVD	3750/6.3	16.31 (15.80–16.84)	770/6.3	15.13 (14.10–16.24)	0.91 (0.85–0.96)	−0.67% (−0.98%, −0.40%)
CHD	1876/6.5	7.94 (7.58–8.30)	378/6.4	7.25 (6.56–8.02)	0.86 (0.78–0.94)	−0.50% (−0.75%, −0.26%)
Heart failure	528/6.7	2.19 (2.01–2.38)	98/6.5	1.84 (1.51–2.25)	0.94 (0.80–1.10)	−0.03% (−0.19%, 0.01%)
Stroke	1792/6.5	7.57 (7.22–7.93)	375/6.4	7.17 (6.48–7.94)	0.92 (0.84–1.00)	−0.32% (−0.45%, −0.20%)
ESRD	515/6.7	2.13 (1.96–2.32)	69/6.6	1.29 (1.02–1.64)	0.66 (0.54–0.81)	−0.23% (−0.40%, −0.08%)
Mortality	1871/6.7	7.71 (7.37–8.06)	391/6.6	7.32 (6.63–8.08)	0.89 (0.81–0.98)	−0.43% (−0.60%, −0.26%)
Serious adverse event						
Hypotension	235/6.7	0.97 (0.85–1.10)	46/6.6	0.86 (0.65–1.15)	0.95 (0.75–1.20)	0.03% (−0.03%, 0.08%)
Syncope	551/6.6	2.29 (2.11–2.49)	127/6.5	2.40 (2.01–2.85)	1.02 (0.87–1.18)	0.33% (0.06%, 0.14%)
Bradycardia	39/6.7	0.16 (0.12–0.22)	8/6.6	0.15 (0.07–0.30)	0.67 (0.34–1.34)	NA
Electrolyte abnormality	6/6.7	0.02 (0.01–0.06)	2/6.6	0.04 (0.01–0.15)	1.55 (0.48–5.01)	NA
Falls	1393/6.6	5.85 (5.55–6.16)	301/6.5	5.73 (5.12–6.42)	1.01 (0.92–1.11)	0.05% (−0.08%, 0.15%)
Acute kidney disease	400/6.7	1.65 (1.50–1.82)	75/6.6	1.41 (1.12–1.76)	0.82 (0.69–0.97)	0.02% (−0.05%, 0.06%)
Dizziness	1306/6.6	5.48 (5.19–5.79)	280/6.5	5.33 (4.74–5.99)	1.06 (0.96–1.16)	−0.00% (−0.01%, 0.01%)
Age 70–79 years						
Major CVD	3170/5.9	31.05 (29.99–32.15)	641/5.8	30.92 (28.62–33.41)	0.87 (0.82–0.93)	−1.52% (−1.90%, −1.14%)
CHD	1132/6.3	10.40 (9.81–11.02)	220/6.1	9.97 (8.74–11.38)	0.82 (0.73–0.91)	−0.86% (−1.11%, −0.61%)
Heart failure	836/6.4	7.59 (7.09–8.12)	144/6.2	6.42 (5.45–7.56)	0.83 (0.73–0.94)	−0.57% (0.81%, −0.33%)
Stroke	1759/6.2	16.46 (15.71–17.25)	361/6.0	16.66 (15.03–18.47)	0.92 (0.84–1.00)	−0.55% (−0.82%, −0.27%)
ESRD	490/6.5	4.38 (4.01–4.79)	70/6.3	3.08 (2.44–3.89)	0.74 (0.62–0.89)	−0.51% (−0.65%, −0.36%)
Mortality	2441/6.5	21.69 (20.84–22.56)	458/6.3	20.07 (18.31–22.00)	0.84 (0.78–0.91)	−1.95% (−2.20%, −1.62%)
Serious adverse event						
Hypotension	248/6.5	2.22 (1.96–2.51)	56/6.3	2.47 (1.90–3.21)	1.09 (0.89–1.35)	0.02% (−0.09%, 0.12%)
Syncope	524/6.4	4.74 (4.35–5.16)	97/6.2	4.31 (3.54–5.26)	0.90 (0.77–1.05)	−0.07% (−0.23%, 0.10%)
Bradycardia	64/6.5	0.57 (0.45–0.73)	11/6.3	0.48 (0.27–0.87)	0.66 (0.40–1.11)	NA
Electrolyte abnormality	8/6.5	0.07 (0.04–0.14)	0/6.3	NA	NA	NA
Falls	1655/6.2	15.40 (14.67–16.16)	337/6.1	15.43 (13.87–17.17)	0.95 (0.87–1.03)	−0.32% (−0.56%, 0.03%)
Acute kidney disease	465/6.4	4.17 (3.80–4.56)	71/6.3	3.13 (2.48–3.95)	0.82 (0.02–0.69)	−0.36% (−0.49%, −0.18%)
Dizziness	1156/7.1	10.67 (10.07–11.30)	251/6.2	11.43 (10.10–12.94)	1.06 (0.96–1.16)	0.44% (0.19%, 0.68%)
Age ≥ 80 years						
Major CVD	933/5.1	53.54 (50.22–57.09)	153/5.1	46.61 (39.78–54.61)	0.77 (0.69–0.86)	−3.71% (−4.94%, −2.48%)
CHD	282/5.6	14.64 (13.03–16.45)	48/5.5	13.35 (10.06–17.71)	0.73 (0.59–0.91)	−1.76% (−3.05%, −1.45%)
Heart failure	386/5.5	20.29 (18.36–22.42)	61/5.5	17.11 (13.31–21.99)	0.77 (0.65–0.91)	−1.67% (−2.41%, −0.92%)
Stroke	491/5.4	26.36 (24.13–28.80)	74/5.4	21.28 (16.94–26.72)	0.78 (0.66–0.91)	−1.71% (−2.68, −0.75%)
ESRD	161/5.8	8.15 (6.98–9.51)	32/5.7	8.71 (6.16–12.31)	0.95 (0.72–1.25)	0.11% (−0.13%, 0.15%)
Mortality	1114/5.8	55.83 (52.64–59.20)	193/5.7	52.19 (45.32–60.10)	0.80 (0.72–0.89)	−3.99% (−4.90, −2.89%)
Serious adverse event						
Hypotension	82/5.8	4.15 (3.34–5.15)	14/5.6	3.83 (2.27–6.46)	1.03 (0.72–1.47)	0.15% (−0.21%, 0.50%)
Syncope	122/5.7	6.24 (5.23–7.45)	23/5.6	6.34 (4.21–9.54)	1.11 (0.86–1.43)	0.33% (−0.02%, 0.86%)
Bradycardia	18/5.8	0.90 (0.57–1.44)	4/5.7	1.09 (0.41–2.89)	0.82 (0.34–1.97)	NA
Electrolyte abnormality	1/5.8	0.05 (0.01–0.36)	0/5.7	NA	NA	NA
Falls	613/5.3	33.76 (31.19–36.54)	107/5.2	31.53 (26.09–38.11)	0.95 (0.83–1.08)	−0.46% (−1.33%, 0.41%)
Acute kidney disease	156/5.7	7.91 (6.76–9.25)	20/5.7	5.43 (3.50–8.41)	0.58 (0.42–0.79)	−1.50% (−1.92%, −1.09%)
Dizziness	290/5.5	15.34 (13.67–17.21)	59/5.4	16.81 (13.02–21.69)	1.02 (0.86–1.22)	0.13% (−0.61%, 0.87%)

Note: Major CVD: composite outcomes of heart failure, chronic heart disease and stroke; CHD, chronic heart disease; ESRD, end-stage renal disease; analyses adjusted for sex, age, smoking status, history of chronic kidney disease, history of diabetes, fasting glucose, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, total cholesterol, eGFR, Charlson comorbidities index, usage of ACEI/ARB, β-blocker, calcium channel blockers, diuretic; history of fall, syncope and electrolyte abnormality, specialist, general outpatient clinics attendance, accident and emergency and hospitalisation (within 1 year before baseline).

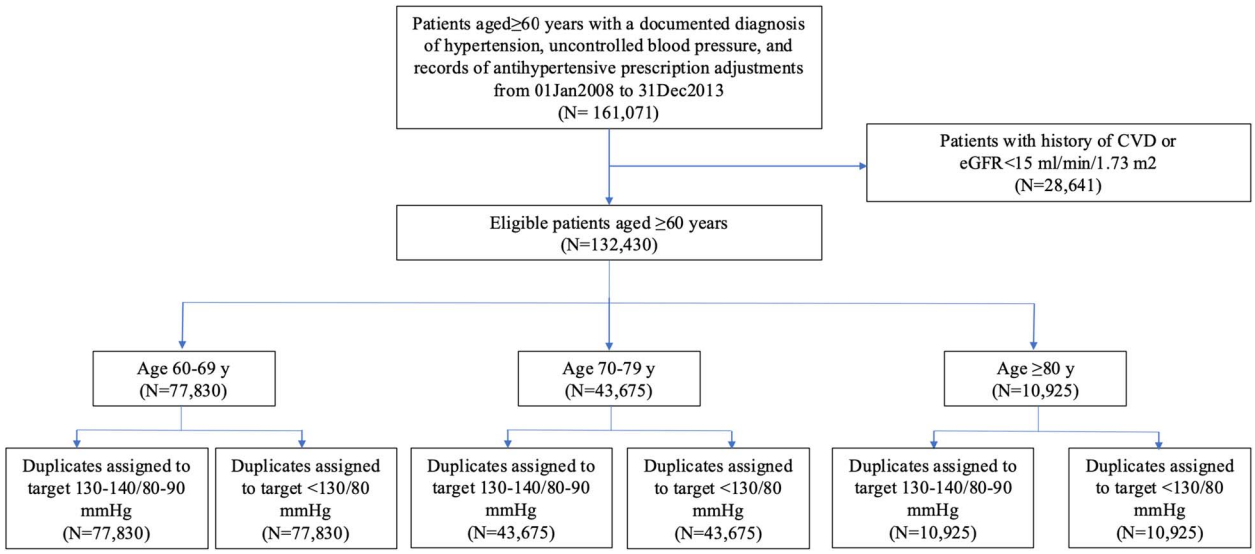

Figure 1. Flowchart of patient selection.

compared to the relatively shorter follow-up in the SPRINT [8] and STEP [9] trials, the findings from this study provided a more representative illustration on the long-term clinical benefits from lower BP target management. In addition, findings from this study enriched the evidence on the effectiveness and safety of lower BP target in older patients with hypertension and diabetes which were not represented in the SPRINT trial [8].

Several meta-analyses and systematic reviews have examined the BP target in the older patients. Although many reported reduced risk of adverse CVD events with lower BP targets, those analyses generally evaluated targets of 130–140/80–90 mmHg, the benefits and safety of a target <130/80 mmHg therefore remain uncertain. Furthermore, debates on optimal targets in patients with frailty or multimorbidity [13–16]. In our study, the results from the subgroup analysis on the CCI status enriched the evidence on the benefits on the decreased risk of adverse CVD events and all-cause mortality and safety of the lower BP target on patients with multimorbidity and frailty (defined as those CCI higher than 6). With considerations on the limitation from the existing RCTs, our current findings reinforced and provided more extensive assessment on the benefits and safety of lower BP target in older populations.

Beyond the cardiovascular benefits, our analysis revealed that lower BP monitoring targets conferred a significant renal-protective effect in reducing the risk of end-stage renal disease by up to 35% compared the standard treatment targets. This aligns with pathophysiological evidence that sustained hypertension exacerbates glomerular hyperfiltration and accelerates nephron loss, particularly in older patients with comorbid diabetes or chronic kidney disease (CKD). A lowered BP level achieved through intensive monitoring target may help lessen intraglomerular pressure, a critical factor in the progression of CKD, while maintaining microvascular health in the renal cortex [17, 18].

From a clinical perspective, the optimal BP targets should prioritise a patient's health status and frailty over chronological age, ensuring sustainable management that balances cardiovascular benefits with risks such as falls or kidney dysfunction. Nevertheless, evidence on the clinical benefits and safety of lower BP controls remains limited. Future research examining the clinical benefits of lower BP targets in older patients with varying degree of frailty, functional status and risk factors for adverse cardiovascular events should be conducted to support the determination of the optimal BP target and therapeutic strategies for individual patients in clinical settings [19, 20].

Through a comprehensive electronic healthcare record, this study provides robust and generalisable clinical evidence supporting a lower BP treatment target associated with a lower risk of cardiovascular events and mortality. The extensive time of follow-up in this study also demonstrated the clinical benefits of a lower treatment target for the long-term management of this chronic disease. However, there are several limitations in this study. Firstly, the information on the exact BP target for patients are not available to be accessed in our dataset. Although the specific BP targets are not defined, our criteria for treatment assignment and censoring are based on the assumption that escalating treatment in individuals who have already achieved a normal BP level may indicate that an even lower BP target is intended in the absence of other comorbidities. However, the missing BP targets may introduce the misclassification since the patients with lower BP target were probably assigned to the traditional treatment target group and vice versa, which may lead to the results being underestimated or overestimated. Secondly, the number of patients aged over 80 years is relatively smaller compared to the other age groups. This may be attributed to the limited evidence regarding the benefits and safety of targeting lower BP levels in the very old population. Besides, some potential confounders such as lifestyle factors

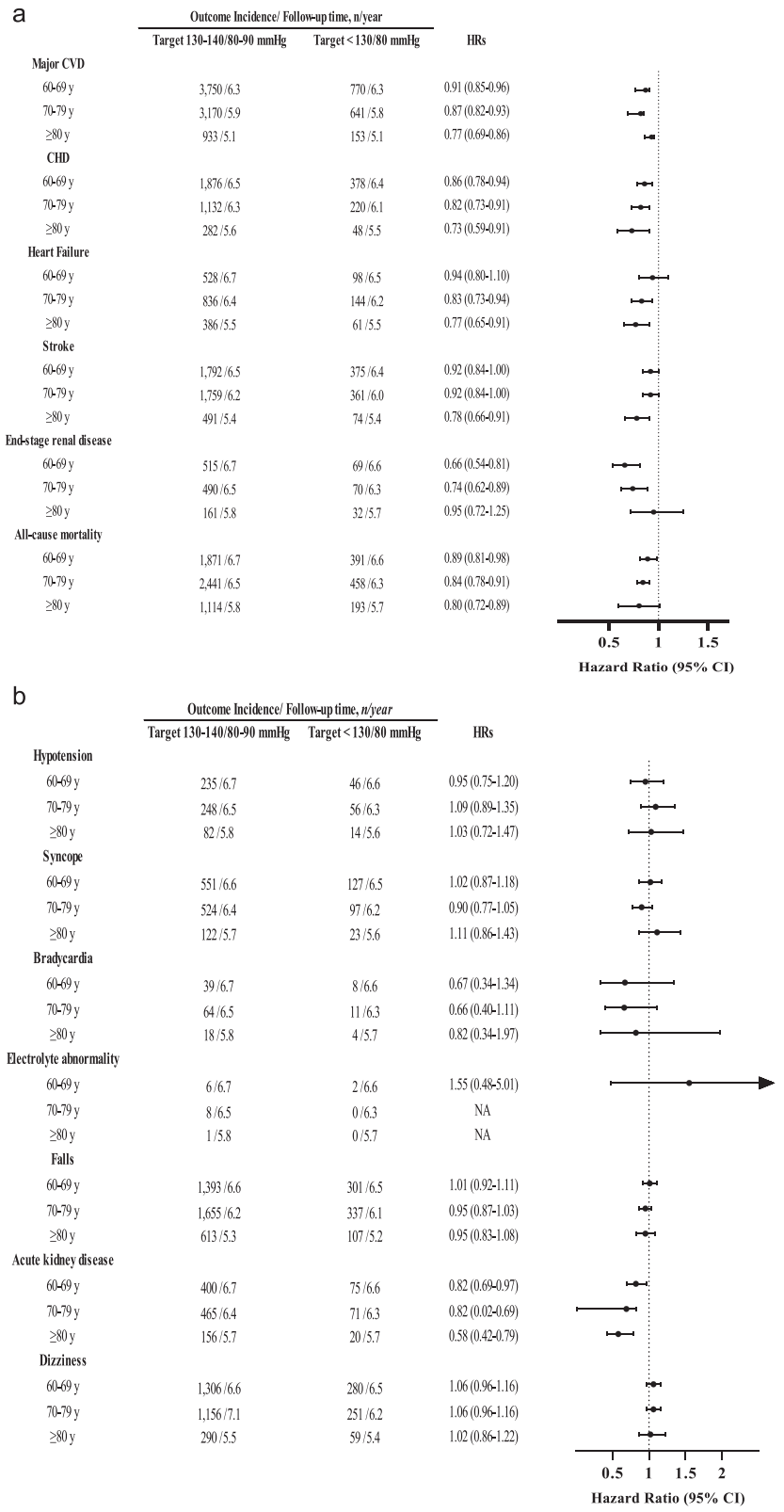

Figure 2. (a) Estimate of hazard ratios between traditional treatment target and lower treatment target (hypertension related complications) in 3 age groups. (b) Estimate of hazard ratios between traditional treatment target and lower treatment target (serious adverse events) in 3 age groups.

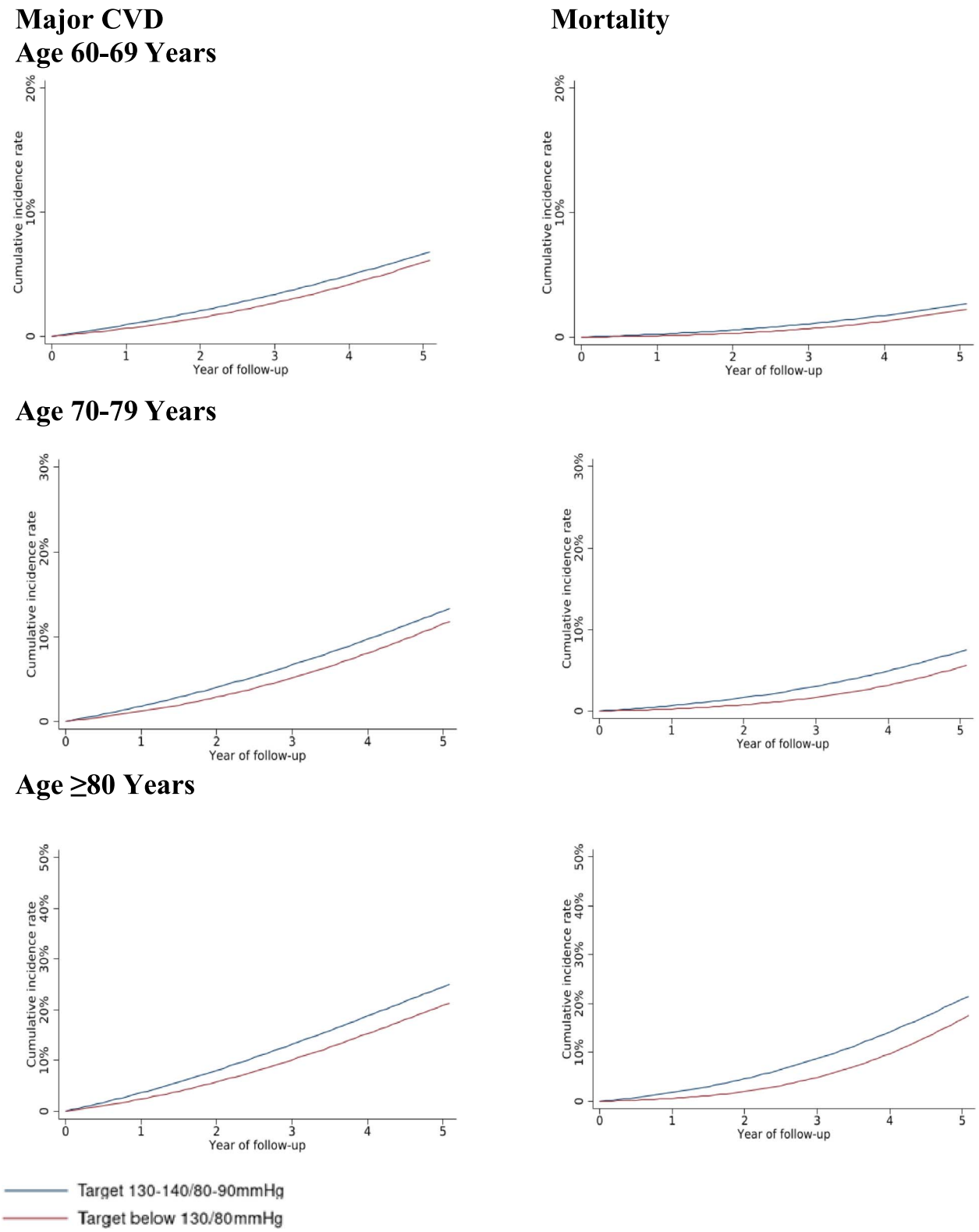

Figure 3. Cumulative incidence curves for major cardiovascular diseases and all-cause mortality.

including diet and physical activity socioeconomic status and educational level are unavailable in our study, which may have introduced bias to our results. In addition, the analyses among some subgroups were restricted by small sample-size of patients, which may lead to the inadequacy of statistical power for finding significant differences in risks. Moreover, our dataset only covered patients' health records since January 2008. It was possible that we had missed patients who

were treated to a lower BP target but had de-escalation of treatment due to adverse events before 2008. This could result in potential misclassification of patients with initial lower treatment BP target to the traditional treatment BP target group and underestimated the risks of the adverse events among patients with lower treatment BP target. However, the database used in our study still provides a long data visibility of 15 years, so this should not significantly change the conclusion. Lastly, ICPC-2 and ICD-9-CM were used to identify the diagnosis in the CMS database and might lead to the misclassification. However, as demonstrated in the previous studies using this database, the history of chronic diseases in the HKHA has been recorded with a high coding accuracy [21, 22].

Conclusion

This study reported the risk reduction benefits in cardiovascular events and all-cause mortality in older patients with hypertension from a lower blood pressure management target of less than 130/80 mmHg based on real-world electronic medical records. Such findings supported clinical decision in determining the optimal management targets for individual patients.

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Supplementary Data: Supplementary data is available at *Age and Ageing* online.

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