Cost-effectiveness of treatment in adults with blood pressure of 130–139/80–89 mmHg and high cardiovascular risk in China: a modelling study

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Summary

Background The most recent updated hypertension guidelines recommend individuals with systolic blood pressure (SBP)/diastolic blood pressure (DBP) of 130–139/80–89 mmHg and high cardiovascular risk should receive antihypertensive drug treatment. This study aimed to assess the benefits and cost-effectiveness of medication for people aged ≥35 years with this blood pressure stratum and high cardiovascular risk in China.

Methods The benefits of drug treatment in adults aged ≥35 years with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk were evaluated in decision-analytic simulation models. Decreasing numbers of cardiovascular disease (CVD) events and premature deaths from all causes and increasing quality-adjusted life-years (QALYs) from drug treatment were estimated in 10-year and lifetime horizons. The incremental cost-effectiveness ratios (ICER) for drug treatment were calculated.

Findings Among approximately 106.60 million Chinese adults aged ≥35 years with this blood pressure stratum and high cardiovascular risk, drug treatment was estimated to prevent 2,060,000 strokes and 660,000 myocardial infarctions over a 10-year time horizon. Adults prescribed antihypertensive drugs could gain 0.034 incremental QALYs. Over a lifetime horizon, adults who start treatment earlier could benefit more in preventing CVD and gaining incremental QALYs. The medication treatment is cost-effective either over a 10-year time horizon with an ICER of Int$13321.29 per QALY gained or over the remaining lifetime.

Interpretation Antihypertensive treatment of adults with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk would gain substantial benefits with cost-effectiveness. The young and middle-aged population would derive the most benefit.

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Keywords: Benefit; Incremental cost-effectiveness ratios; Cost-effectiveness; Hypertension; Cardiovascular disease

Introduction

Elevated blood pressure (BP) is the leading modifiable risk factor for cardiovascular disease (CVD) globally and in China.[1] Observational studies have found that systolic blood pressure (SBP)/diastolic blood pressure (DBP) of 130–139/80–89 mmHg is associated with an increased long-term risk of CVD and target organ damage.[2–6] Evidence from the latest meta-analyses of randomized clinical trials suggests that antihypertensive drug treatment could reduce the risk of CVD among people with this BP stratum.[7] In China, where the lifetime risk of stroke is the highest in the world,[8] 76% of individuals

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Research in context

Evidence before this study

We searched PubMed for articles on the cost-effectiveness of antihypertensive drug treatment in Chinese adults with systolic blood pressure (SBP)/diastolic blood pressure (DBP) of 130–139/80–89 mmHg and published between 2017 and 2023 using the following search terms: "hyperten*" or "blood pressure" (for population), "value", "monetary", "money", "budget*", "fee", "financ*", "price*", "pricing", "resourc*", "effective*", "utilit*", "benefit*", "cost*", "economic*", "cost-benefit analysis", "costs and cost analysis", "economics", "fees and charges", "resource allocation", and "value of life" (for cost-effectiveness), and "China", "Chinese", "Taiwan", "Hongkong", and "Macao" (for setting). We identified only two relevant studies, both of which used 2017 prices of the antihypertensive drug for the cost estimations, and which obtained conflicting conclusions. One study explored the cost-effectiveness of drug treatment versus placebo in individuals aged 30–80 years and the other study limited the estimation of the cost-effectiveness of drug treatment versus nondrug treatment to individuals aged ≥65 years. However, China implemented a new centralized medicine procurement policy in 2019 to substantially lower antihypertensive drug prices. There is no information on the cost-effectiveness of drug treatment for SBP/DBP of 130–139/80–89 mmHg based on contemporary healthcare costs.

Added value of this study

More than 10 of the latest hypertension guidelines issued by different professional organizations, including 2021 World Health Organization guidelines, recommend that individuals with high cardiovascular risk and SBP/DBP of 130–139/80–89 mmHg should receive pharmacological antihypertensive treatment. This recommendation will support earlier intervention for hypertension or elevated blood pressure, and lower the risk of stroke, especially in the young and middle-aged population. However, scientific evaluation and evidence for the health benefits and cost-effectiveness of this expansion of antihypertensive drug treatment must be urgently provided because of the large numbers of patients and limited medical resources. This information will affect the development of health policies, especially medical insurance policies and the allocation of medical resources. In this modelling study, we estimated the health benefits and cost-effectiveness of antihypertensive drug treatment for Chinese adults aged ≥35 years with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk based on the latest antihypertensive drug prices. We found that this strategy would be cost-effective and could prevent a large number of cardiovascular disease cases. The young and middle-aged population would derive the most benefit.

Implications of all the available evidence

In China, after nearly 50 years of efforts to control hypertension, the blood pressure of most patients with hypertension is still not well controlled. Many patients experience target organ damage because they start treatment too late. Stroke therefore remains the top cause of death in China, and China faces the greatest burden from stroke in the world. Approximately one-third of stroke deaths worldwide occur in China. The mortality from stroke in the young and middle-aged population in China was four to five times higher than in Japan, Korea and the USA. Our findings imply that antihypertensive drug treatment in adults with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk is cost-effective with considerable health benefits. The cost-effectiveness was particularly sensitive to antihypertensive drug costs and relative reduction in stroke. More effort is therefore needed to improve awareness of the health impact of elevated blood pressure and enhance the full implementation of essential prescription medication and insurance policies to reap the benefits of improved hypertension control and reduced burden of cardiovascular disease.

with an SBP/DBP of 130–139/80–89 mmHg are young or middle-aged adults, and 65% of these will progress to BP ≥ 140/90 mmHg if not treated.[6,9] More than 12% of strokes and 26.5% of CVD-related deaths in young or middle-aged adults in China could be attributable to having BP at this level stratum.[6]

The most recently updated hypertension guidelines recommend that individuals with an SBP/DBP of 130–139/80–89 mmHg and a high cardiovascular risk should receive antihypertensive medication treatment.[10–13] However, there is a high prevalence of SBP/DBP of 130–139/80–89 mmHg in China's large population, and approximately one-third of people with this BP stratum are at high cardiovascular risk.[9] The short-term and long-term benefits and cost-effectiveness of this strategy need to be assessed to guide the development of relevant evidence-based policies, particularly prescription and insurance policies. The cost-effectiveness of antihypertensive medication has been assessed in Chinese adults aged 30–80 years with SBP/DBP of 130–139/85–89 mmHg in one study and in those aged ≥65 years with SBP/DBP of 130–139/80–89 mmHg in another study.[14,15] However, the prices used for the antihypertensive agents in these studies were not in line with contemporary costs.

The aim of this study was to estimate the 10-year and lifetime benefits of antihypertensive drug treatment in adults aged ≥35 years with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk in China, and the corresponding cost-effectiveness using the latest antihypertensive medication costs and data from multiple sources.

Methods

Study design and model structure

A decision-analytic model was constructed using the Markov method to estimate healthcare costs and quality-adjusted life-years (QALYs) in antihypertensive drug-naïve Chinese adults aged ≥35 years with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk.[16] This simulation study focused on adults ≥35 years, due to the evidence on the treatment effect of antihypertensive drug mainly from adults aged ≥35 years,[7] and the National Basic Public Health Service Standards of China issued in 2009 recommended that adults aged ≥35 years should measure BP at their first visit to any clinic.[17] Two models were simulated: one that adults under the status of SBP/DBP of 130–139/80–89 mmHg initiated antihypertensive drug treatment, and the other that adults under this status did not receive antihypertensive drug. The model estimated the incremental cost-effectiveness ratio (ICER) for antihypertensive drug treatment compared to not using antihypertensive drugs for adults with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk (Fig. 1). We also used a Monte Carlo microsimulation to estimate the numbers of various outcomes that could be prevented by antihypertensive medication treatment in individuals aged ≥35 years with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk in China.[9] Using the seventh nationwide population census, we estimated that there were approximately 106.60 million adults with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk (Supplementary Table S1).

All adults aged ≥35 years with SBP/DBP of 130–139/80–89 mmHg were entered into the model as the baseline population (Supplementary Fig. S1). The outcomes with predefined probabilities included: (1) maintenance of baseline health status with SBP/DBP of 130–139/80–89 mmHg; (2) occurrence of fatal or non-fatal acute stroke/myocardial infarction (MI); and (3) death from other causes. For survivors of stroke or MI, the possible outcomes in the following year were as follows: (1) recurrence of fatal or non-fatal stroke or MI events; (2) occurrence of fatal or non-fatal MI after stroke or stroke after MI; and (3) death from other causes. In the first year after stroke or MI, if survivors did not experience these events, they were assumed to have entered a chronic post-stroke or post-MI state, and their outcomes included: (1) maintenance of the chronic state; (2) recurrence of fatal or non-fatal stroke or MI events; (3) occurrence of fatal or non-fatal MI after post-stroke or stroke after post-MI; and (4) death from other causes.

The model cycle length was 1 year, and half-cycle corrections were applied.[18] We evaluated the cost-effectiveness of antihypertensive drug treatment in 10-year and lifetime horizons. The mean life expectancy is 77.93 years in China,[19] and thus we set the end of the lifespan at 80 years.

The model development and analyses were performed using TreeAge Pro Healthcare 2023 (TreeAge Software, Inc., Williamstown, MA, USA). The study was designed and reported according to the Consolidated Health Economic Evaluation Reporting Standards Statement.[20]

Main assumptions

The following probabilities of events or death were assigned to the model: (1) incidence of acute MI or

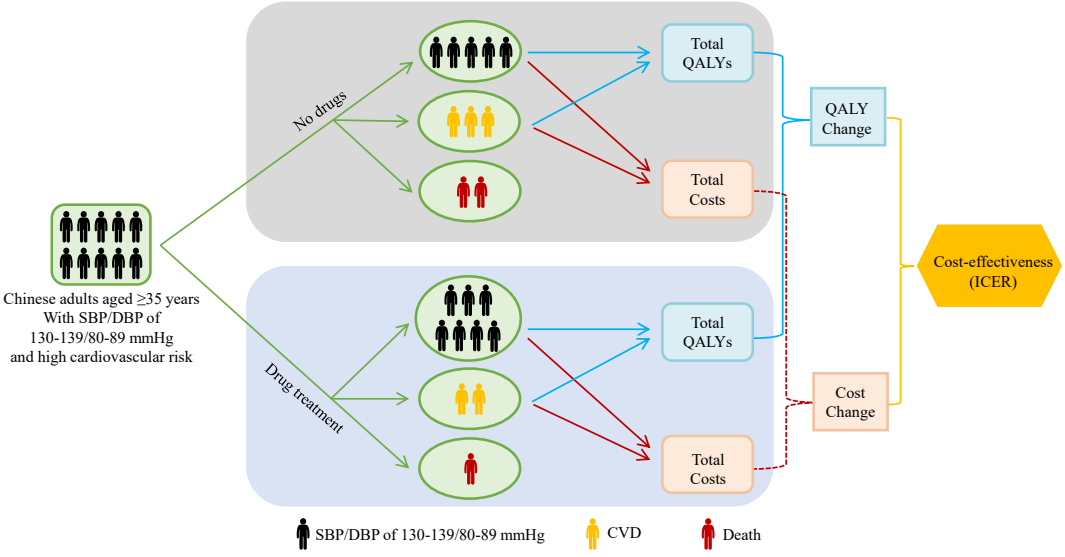

***Fig. 1:* Conceptual diagram of the simulation model.** CVD = cardiovascular disease; DBP = diastolic blood pressure; ICER = incremental cost-effectiveness ratio; QALYs = quality-adjusted life-years; SBP = systolic blood pressure.

stroke and all-cause mortality among the population with SBP/DBP of 130–139/80–89 mmHg and (2) incidence and recurrence of acute MI/stroke and all-cause mortality in the population with stroke or MI. The probabilities of events among the population with SBP/DBP of 130–139/80–89 mmHg, under the strategy of antihypertensive medication treatment were estimated by the relative risk of incident events standardized for a 10-mmHg reduction in SBP.

The probabilities in the population with SBP/DBP of 130–139/80–89 mmHg were derived from the Kailuan study, the design of which has been described in detail elsewhere.[21] Briefly, 126,050 participants were recruited for examinations in 2006 and 2008. After the exclusion of 4757 participants with established CVD and 6918 with incomplete data, the 10-year CVD risk was evaluated in 114,375 participants, 45,136 of whom had a high risk of CVD (Supplementary Table S2).[22] In total, 10,509 of the 45,136 participants with SBP/DBP of 130–139/80–89 mmHg were included to calculate the rate/person-year of stroke incidence, MI incidence, and all-cause mortality (Supplementary Fig. S2). We calculated the rate/person-year of stroke incidence, MI incidence, and all-cause mortality in various age groups (35–44, 45–54, 55–64, 65–74, and ≥75 years) in the first 10 years of follow-up (Supplementary Table S3). The rate/person-year of participants aged ≥35 years was weighted by age, which was used for the 10-year time horizon (Table 1). The weights of each age group among the population with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk were calculated using the seventh nationwide population census of China in 2020, the China Hypertension Survey, and the Kailuan study (Supplementary Table S1).[9,19] For the lifetime horizon, the lifetime risks of acute MI, stroke, and all-cause death up to the age of 80 years were calculated at the index ages of 35, 45, 55, and 65 years using a modified Kaplan–Meier method[5,23,24] (Supplementary Fig. S3 and Tables S4–S7). Probabilities of other outcomes among the population with stroke (including all-cause mortality, incidence of MI, and recurrence of stroke) or MI (including all-cause mortality, incidence of stroke, and recurrence of MI) were derived from previous studies[14,25–33] (Table 2).

Each health state was assigned a utility value that was used to estimate the health benefits and harms of antihypertensive drug treatment in the model. This included utilities for SBP/DBP of 130–139/80–89 mmHg, acute MI, stroke, post-MI, and post-stroke. The QALYs were calculated by multiplying the duration of time in a specific health state by the utility value associated with that state. The utility values were derived from published cost-effectiveness studies.[14,15,34] The QALYs were discounted at 3% annually in the future for the primary projections.[35]

For adults who did not receive antihypertensive agents, direct medical costs over the remaining lifetime were calculated for each individual, including costs of BP screening, hospitalization costs for acute stroke/MI, and annual outpatient management costs for post-stroke/post-MI. For adults who received antihypertensive drugs, the costs of antihypertensive agents and health management for BP were added. Direct medical costs to both the health care system and patients were calculated. Patients' indirect costs were not included.

The average antihypertensive drug costs for the standard (recommended) dose per year were calculated using the annual costs of five first-line antihypertensive medications and the prescription frequency for each medication,[36] including angiotensin-converting-enzyme inhibitors, angiotensin-receptor blockers, calcium-channel blockers, beta-blockers, and diuretics. Prices for antihypertensive agents after implementation of the new centralized medicine procurement policy in China were derived from the national centralized procurement policy announcement file of the winning bid[37] and included prices for angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and calcium channel blockers. Prices for beta-blockers and diuretics were taken from a nationwide cross-sectional survey.[36] In view of a meta-analysis showing that all five drug categories produced similar BP reductions and that the average reduction in SBP was 9.1 mmHg with treatment at a 1.0 standard dose,[38] we assumed a 10% increase in antihypertensive drug costs to achieve a 10-mmHg

Observed year	Age-weighted rate/person-year		
	Stroke	MI	All-cause death
From 0 to 1	0.0021	0.0021	0.0025
From 1 to 2	0.0033	0.0006	0.0046
From 2 to 3	0.0041	0.0017	0.0067
From 3 to 4	0.0064	0.0020	0.0146
From 4 to 5	0.0040	0.0011	0.0165
From 5 to 6	0.0042	0.0020	0.0189
From 6 to 7	0.0041	0.0017	0.0186
From 7 to 8	0.0068	0.0016	0.0195
From 8 to 9	0.0053	0.0017	0.0227
From 9 to 10	0.0067	0.0017	0.0220

The age-weighted rate/person-year of stroke, MI, and death are weighted average of the age-specific rates of stroke incidence, MI incidence, and all-cause mortality among participants with SBP/DBP of 130–139/80–89 mmHg, respectively, which were calculated in various age groups (35–44, 45–54, 55–64, 65–74, and ≥75 years) in the first 10 years of follow-up of Kailuan Study. The weights are the proportions of persons in the corresponding age groups according to the seventh nationwide population census of China in 2020 and the China Hypertension Survey. Weights of age 35–44, 45–54, 55–64, 65–74, and ≥75 years were 13.08%, 28.49%, 25.42%, 21.39%, and 11.62%, respectively. These probabilities were used to estimate the health benefit, cost, and cost-effectiveness of antihypertensive drug treatment among adults aged ≥35 years with systolic/diastolic blood pressure 130–139/80–89 mmHg and a high risk of cardiovascular disease in the 10-year time horizon. DBP = diastolic blood pressure; MI = myocardial infarction; SBP, systolic blood pressure.

Table 1: **Age-weighted rate/person-year of stroke, MI, and all-cause death in every year of the first decade during follow-up among adults with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk.**

Variable	Estimate	Distribution	Sources
Transition probability			
MI incidence after stroke	0.065 (0.055, 0.075)	Beta	Wong 2003[24]
Stroke recurrence after stroke	0.177 (0.170, 0.184)	Beta	China National Stroke Registry[25]
Stroke recurrence after post-stroke	0.071 (0.069, 0.073)	Beta	China Kadoorie Biobank Study[26]
All-cause mortality after stroke or post-stroke	0.047 (0.039, 0.055)	Beta	Wong 2003[24]
Stroke incidence after MI	0.012 (0.009, 0.015)	Beta	China-OASIS Registry[27]
MI recurrence after MI	0.032 (0.027, 0.037)	Beta	China PEACE Prospective AMI study[28]
MI recurrence after post-MI	0.009 (0.004, 0.014)	Beta	China Coronary Secondary Prevention Study[29]
All-cause mortality after MI or post-MI	0.029 (0.020, 0.040)	Beta	Zhou 2020[14]
Effect of drug treatment (RR of events)			
Stroke	0.53 (0.36, 0.79)	Triangular	Meta-analysis of RCT[7]
MI	0.94 (0.74, 1.19)	–	Meta-analysis of RCT[7]
Death	0.96 (0.77, 1.21)	–	Meta-analysis of RCT[7]
Quality-of-life weights (health utility)			
SBP/DBP of 130–139/80–89 mmHg	0.98 (0.95, 1.00)	Beta	Kawalec 2015[33]
Stroke	0.63 (0.26, 0.89)	Beta	Zhou 2020[14]
Post-stroke	0.65 (0.46, 0.82)	Beta	Zhou 2020[14]
MI	0.76 (0.50, 0.89)	Beta	Chen 2017[15]
Post-MI	0.88 (0.67, 0.94)	Beta	Chen 2017[15]
Death	0	–	
Costs (Int$)[a]			
Screening or monitoring visit costs	16.58 (14.58, 17.30)	Triangular	WHO CHOICE (China)[39]
Average antihypertensive drug costs of 1.0 standard dose per year	30.49 (11.58, 69.20)	–	Beijing medicine sunshine purchase[36] China PEACE MPP primary health-care survey[35]
Annual cost for health management	39.05 (32.59, 45.52)	Triangular	The National basic public health service project[38]
Hospitalization cost for stroke	4207.29 (1257.39, 7157.19)	Gamma	China Health Statistics Yearbook 2022[18]
Hospitalization cost for MI	7044.51 (3133.93, 10955.08)	Gamma	China Health Statistics Yearbook 2022[18]
Annual cost for post-stroke	1289.75 (590.48, 1989.02)	Gamma	China Health and Retirement Longitudinal Survey[41]
Annual cost for post-MI	1693.23 (1472.08, 1914.39)	Gamma	The Fifth National Health Services Survey[40]

DBP = diastolic blood pressure; MPP, Million Persons Project; MI, myocardial infarction; OASIS, Organization to Assess Strategies for Ischemic Syndrome; PEACE, China Patient-Centered Evaluative Assessment of Cardiac Events Prospective Study of Acute Myocardial Infarction; PROGRESS, The Perindopril Protection Against Recurrent Stroke Study; RCT, randomized controlled trial; RR, relative risk; BP = systolic blood pressure; WHO CHOICE, World Health Organization's Choosing Interventions That Are Cost Effective. [a]All cost inputs were inflated to the 2022 price level in China and converted into international dollars (Int$) according to the purchasing power parity exchange rate published by the Organization for Economic Co-operation and Development (1 Int$ = 4.02 Chinese yuan [RMB] in 2022).

Table 2: **Main assumptions for the cost-effectiveness analysis model.**

reduction in SBP among participants with an SBP/DBP of 130–139/80–89 mmHg. Other hypertension-related costs were obtained from the published literature, including screening or monitoring visit costs and health management costs.[39,40] Hospitalization costs for stroke were calculated using the hospitalization costs for cerebral hemorrhage and cerebral infarction from the China Health Statistics Yearbook 2022,[19] considering the proportion of each subtype in total stroke based on the China Kadoorie Biobank Study.[27] Hospitalization costs for MI were extracted from the China Health Statistics Yearbook 2023.[19] Annual costs for post-stroke and post-MI were derived from the Fifth National Health Services Survey[41] and China Health and Retirement Longitudinal Survey.[42] All cost inputs were inflated to the 2022 price level in China and converted into international dollars (Int$) using the purchasing power parity exchange rate published by the Organization for Economic Co-operation and Development (1 Int$ equalled 4.02 Chinese yuan [RMB] in 2022).[43,44] Future costs were discounted at 3% annually.[35]

Cost-effectiveness

Cost-effectiveness was measured by the ICER, which was calculated using the differences in projected incremental costs and QALYs between adults with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk who received antihypertensive drugs and those who did not. This enabled us to estimate the incremental cost required to gain one additional QALY over the 10-year and lifetime horizons. We used the willingness-to-pay thresholds recommended by the World Health Organization's Choosing Interventions That Are Cost Effective (WHO-CHOICE) initiative to determine the cost-effectiveness of antihypertensive medication treatment in China. The WHO-CHOICE defines an ICER less than the gross domestic product (GDP) per capita as highly cost-effective, an ICER of one to three times the

GDP per capita as moderately cost-effective, and an ICER of more than three times the GDP per capita as not cost-effective. In 2022, the GDP per capita in China was Int$ 21,318 (85,698 RMB).[45] Analyses were interpreted from both payer's and health system perspectives.

Exploratory and sensitivity analyses

Monte Carlo probabilistic sensitivity analyses were conducted to evaluate the sensitivity of the results to variations in simultaneous changes in several variables and to calculate the proportion of ICERs falling under our predetermined willingness-to-pay threshold. In the probabilistic sensitivity analyses, the model was run 10,000 times, each taking random draws from the respective distribution of each parameter (Supplementary Table S8). We explored the impact of uncertainty among individual values on cost-effectiveness estimates, including transition probabilities, effects of antihypertensive drug treatment, costs, health utilities, and discount rates, using one-way sensitivity analyses. We also compared the cost-effectiveness of the various classes of antihypertensive agents, assuming that all five categories produced similar reductions in BP.[38] Finally, several scenarios were simulated: (1) the treatment rate was 40.3%; (2) the control rate was 40.1% among treated participants; (3) the adherence rate was 100% for the first year, and 50% for every year after the first year; (4) the adherence rate was 100% for the first 5 years, and then 50% for every year after the first 5 years; and (5) the relative risk of incident events standardized for a 5.0 mmHg reduction in SBP at a 1.0 standard dose. Due to a lack of relevant data, the reported treatment rate,[9] control rate,[9] and treatment adherence rate[46] in hypertensive patients aged 45–54 years were used to represent the corresponding rates of SBP/DBP of 130–139/80–89 mmHg.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Health benefits of antihypertensive drug treatment

Among 106.60 million adults aged ≥35 years with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk in China, the strategy of antihypertensive medications treatment was projected to avert 2,060,000 stroke cases and 660,000 acute MI cases over a 10-year time horizon (Table 3). Over a lifetime horizon, adults who start treatment earlier could benefit more in terms of avoiding stroke and MI (Fig. 2). Adults prescribed antihypertensive agents could gain 0.034 incremental QALYs. In the remaining lifetime horizon, the incremental gain in QALYs was 0.22 for treatment starting at age 35 years, 0.21 for 45, 0.18 for 55, and 0.11 for 65 years (Fig. 3A).

Costs and cost-effectiveness of antihypertensive drug treatment

The antihypertensive drug treatment strategy for adults with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk was projected to cost on average an additional Int$454.48 per person over a 10-year horizon (Table 3). The incremental costs were mainly attributable to additional antihypertensive drug treatment costs for adults with SBP/DBP of 130–139/80–89 mmHg but with fewer costs for stroke or MI than nondrug treatment (Table 3). Adults starting antihypertensive drug treatment at the age of 35 years would incur the highest incremental costs over a lifetime horizon (Fig. 3B).

The strategy of antihypertensive drug treatment was highly cost-effective with an ICER of Int$13321.29 per QALY gained over a 10-year time horizon, which was below a threshold of 1 time the GDP per capita (Int$21318) (Table 3). Furthermore, antihypertensive drug treatment for adults with this BP stratum was highly cost-effective over a lifetime horizon regardless of the age when treatment was started (Fig. 3C).

Exploratory and sensitivity analyses

At a willingness-to-pay threshold of 1 time the GDP per capita, the antihypertensive drug treatment strategy was highly cost-effective in 98% of probabilistic simulations (Supplementary Fig. S4). The top 10 parameters to which the model was sensitive in one-way sensitivity analyses are shown in Supplementary Fig. S5. The ICER was most sensitive to changes in the costs of antihypertensive drugs, the relative risk of stroke, and utility of post-stroke. Assuming the use of the most expensive drug, drug treatment for adults aged ≥35 years with an SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk was projected to be moderately cost-effective (Supplementary Fig. S6). After accounting for treatment rate, control rate, treatment adherence rate and even the average reduction in SBP of 5.0 mmHg with treatment at a 1.0 standard dose, the antihypertensive drug treatment strategy remained cost-effective (Supplementary Table S9).

Discussion

Stroke remains the leading cause of death in the Chinese population, and approximately one-third of stroke deaths worldwide occur in China.[47] There has also been a significant increase in mortality from stroke and its subtypes in young Chinese adults, and the mortality rate in China is now double that in the United States and China's neighbours, Japan and Korea.[48] The leading risk factor for stroke is high BP (SBP ≥115 mmHg), which accounts for 62% of disability-adjusted life-years from stroke in China.[47] Starting antihypertensive treatment at

	Drug treatment	No drugs	Differences (95% UI)
Number of events			
Occurrence of Stroke	3,510,000	5,570,000	2,060,000 (1,480,000, 2, 640,000)
Occurrence of MI	2,260,000	2,920,000	660,000 (210,000, 1,110,000)
Premature deaths from all causes	12,750,000	13,220,000	470,000 (−470,000, 1,420,000)
Mean QALYs	8.13	8.10	0.034 (0.030, 0.038)
Mean costs per person by status (Int$)			
SBP/DBP 130–139/80–89 mmHg	727.89	131.85	596.67 (580.68, 612.18)
Occurrence of Stroke	140.37	248.23	−104.44 (−130.27, −82.85)
Occurrence of MI	196.30	232.25	−35.20 (−41.43, −29.93)
Total costs per person (Int$)	1068.67	614.86	454.48 (423.56, 482.92)
ICER (Int$/ QALY)	13321.29 (11352.22, 15789.64)		

DBP = diastolic blood pressure; CVD = cardiovascular disease; ICER = incremental cost-effectiveness ratio; MI = myocardial infarction; QALY = quality-adjusted life-years; UI = uncertainty interval; SBP = systolic blood pressure.

Table 3: **Results of drug treatment and no drugs for SBP/DBP of 130–139/80–89 mmHg with high risk of CVD in 10-year time horizon.**

an earlier stage is therefore crucial to reduce the burden of stroke in China. Most recent national and international guidelines recommend that individuals with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk should receive antihypertensive medication. However, the economic burden and high number of people who need treatment mean that the benefit and cost-effectiveness are based on the premise that this strategy can be effectively implemented in China and other countries in the same situation.

Using contemporary incidence events and cost data, this modelling study found that antihypertensive medications could avert cases of stroke and MI, and gain more QALYs in Chinese adults aged ≥35 years with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk. We estimated that there would be 557,000 new stroke cases annually in adults with this BP stratum and high cardiovascular risk under assumptions of no antihypertensive medication. Of these, 37.0% (206,000) could be prevented by antihypertensive drug treatment. Antihypertensive drug treatment was projected to prevent a larger number of cases of CVD and gain more incremental QALYs if treatment started earlier. In the China Hypertension Survey, 76% of adults with this BP stratum were under 55 years old,[9] and therefore mainly the working-age population. From a public health perspective, our findings highlight the importance of earlier treatment in people with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk to prevent continuously elevated BP and the subsequent CVD burden among younger people.

We also found that antihypertensive drug treatment for SBP/DBP of 130–139/80–89 mmHg among Chinese adults aged ≥35 years with high cardiovascular risk was cost-effective. To date, only two studies have evaluated the cost-effectiveness of antihypertensive drug treatment in Chinese adults with this BP stratum.[14,15] Chen et al. estimated that the ICERs would be more favorable for antihypertensive drug treatment over a lifetime horizon in Chinese adults aged 30–80 years with SBP/DBP of 130–139/85–89 mmHg and without CVD.[15] However, they calculated transition probabilities in prediction models using data from a cross-sectional study and only simulated the effect of antihypertensive drug treatment on the risk of hypertension. Zhou et al. found that antihypertensive drug treatment resulted in fewer QALYs despite cost savings in adults aged ≥65 years with SBP/DBP of 130–139/80–89 mmHg and without CVD.[14] They estimated the probability of events in antihypertensive drug-treated adults with SBP/DBP of 130–139/80–89 mmHg based on adults whose BP in this stratum was controlled by antihypertensive drugs. However, those adults may have had long-term cumulative exposure to elevated BP before receiving antihypertensive drug treatment and a more substantial burden of subclinical CVD than their untreated counterparts.[49] This might therefore have led to a lower number of QALYs in adults who received antihypertensive medication treatment than in those who did not. China's new centralized medicine procurement policy has successfully reduced drug costs and lowered out-of-pocket costs for patients.[50] After the full implementation of this policy in 2019, the average price of medicines is estimated to have decreased by 52%,[50] and the annual cost of antihypertensive medication is now approximately 120 RMB per person in China.[37]

To our knowledge, this modelling study is the first to evaluate the cost-effectiveness of antihypertensive drug treatment for people with BP of 130–139/80–89 mmHg based on contemporary cost data and has demonstrated its cost-effectiveness across 10-year and lifetime horizons. It is also the first of which we are aware to assess the cost-effectiveness of antihypertensive drug treatment for this BP stratum across a wide range of ages. We found that implementation of treatment among Chinese adults with a high cardiovascular risk was cost-

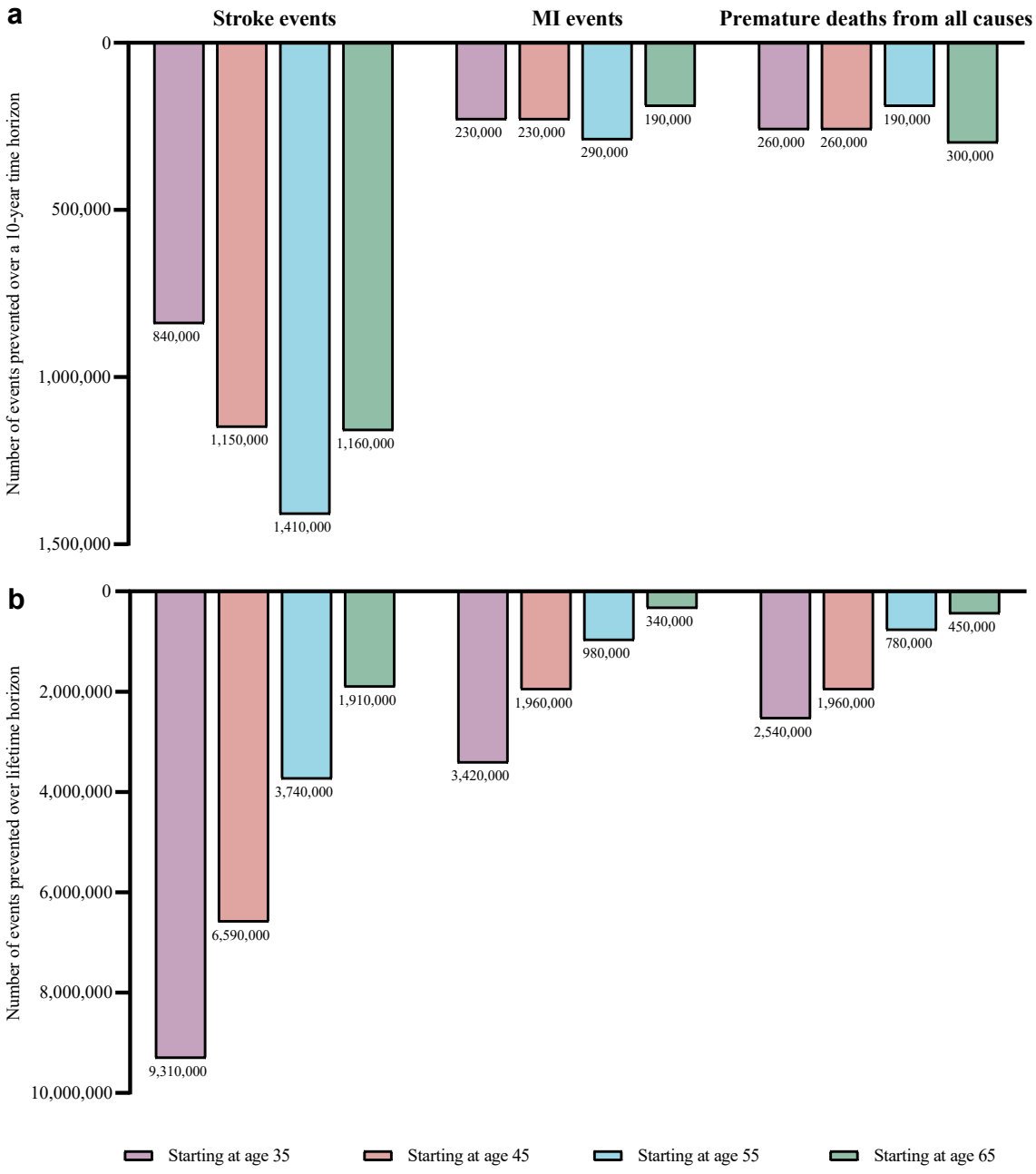

Fig. 2: **Numbers of acute stroke events, MI, and premature deaths from all causes prevented.** MI = myocardial infarction.

effective across their remaining lifetime regardless of when antihypertensive medication treatment was started. From both a societal and a healthcare sector perspective, antihypertensive drug treatment for SBP/DBP of 130–139/80–89 mmHg among individuals with high cardiovascular risk is a cost-effective strategy, despite the enormous healthcare costs in China, which has a large population and a high prevalence of this BP stratum.

This study had several limitations. First, it did not account for the risks of adverse events and their corresponding costs. The main adverse event associated with antihypertensive treatment is symptomatic hypotension.[51] However, symptoms of hypotension occurring as a result of antihypertensive treatment are uncommon and usually not life-threatening.[31] They are also reversible after drug withdrawal, and the economic burden related to hypotension would therefore be limited. More

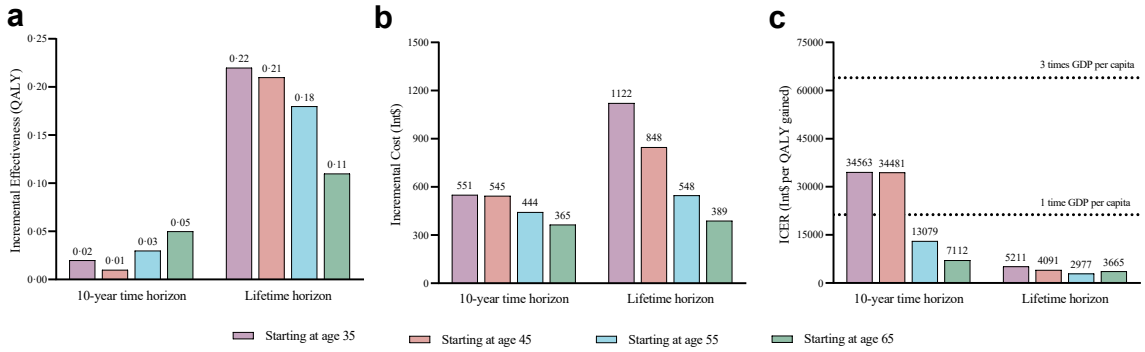

Fig. 3: **Age-stratified results of antihypertensive drug treatment over 10-year and lifetime horizon.** GDP = gross domestic product; ICER = incremental cost-effectiveness ratio; QALYs = quality-adjusted life-years.

randomized controlled trials are needed to explore the incidence of adverse events associated with antihypertensive drug treatment among Chinese adults with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk. Second, this study assumed that the relative risks for various outcomes of antihypertensive drug treatment among adults with SBP/DBP of 130–139/80–89 mmHg were the same for different age groups, due to no evidence of relative risk reductions for prevention of major cardiovascular events varied by age group in these population. However, the hazard ratios associated with antihypertensive drug treatment for risk of major cardiovascular events were lower among those aged <55 years than among those aged ≥55 years, as reported by the Blood Pressure Lowering Treatment Trialists' Collaboration.[52] Therefore, our results may underestimate the health benefit but overestimate the ICER among the young and middle-aged adults. Finally, the probabilities of CVD incidence and death among adults with SBP/DBP of 130–139/80–89 mmHg were calculated using data from a large community-based cohort study in northern China. Although these probabilities were weighted by age using the seventh nationwide population census of China in 2020 to represent the whole country, more studies are needed to confirm our results.

In conclusion, this simulation study has demonstrated that antihypertensive drug treatment can avert CVD events and improve the quality of life, particularly in the young and middle-aged population. Furthermore, this strategy is cost-effective in adults with SBP/DBP of 130–139/80–89 mmHg and high cardiovascular risk. Antihypertensive drug treatment in this population should be considered an effective and cost-saving strategy and will be important for obtaining the benefits of improved control of elevated BP and a reduction in the subsequent CVD burden across a wide range of ages.

Contributors

DZ and YQ contributed to initial concepts and study design. JL and YQ analyzed data and drafted the manuscript. DZ, JC, SC, and SW revised the manuscript critically. All authors contributed to manuscript's final version approval. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data sharing statement

The datasets of the Kailuan study are not publicly available due to ethical constraints in consideration of participants' privacy and intellectual property protection but are available from the corresponding author on reasonable request. Other relevant data are contained within the manuscript text.

Declaration of interests

All other authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2023.100962.

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