

Cost-Effectiveness of Salt Substitution and Antihypertensive Drug Treatment in Chinese Prehypertensive Adults

Zhijia Sun, Haijun Zhang, Yinqi Ding, Canqing Yu, Dianjianyi Sun, Yuanjie Pang, Pei Pei, Ling Yang, Yiping Chen, Huaidong Du, Weijie Hu, Daniel Avery, Junshi Chen, Zhengming Chen, Liming Li, Jun Lv*, on behalf of the China Kadoorie Biobank Collaborative Group

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Members of the China Kadoorie Biobank collaborative group

International Steering Committee: Junshi Chen, Zhengming Chen (PI), Robert Clarke, Rory Collins, Liming Li (PI), Jun Lv, Richard Peto, Robin Walters.

International Co-ordinating Centre, Oxford: Daniel Avery, Maxim Barnard, Derrick Bennett, Lazaros Belbasis, Ruth Boxall, Ka Hung Chan, Yiping Chen, Zhengming Chen, Charlotte Clarke, Johnathan Clarke; Robert Clarke, Huaidong Du, Ahmed Edris Mohamed, Hannah Fry, Simon Gilbert, Pek Kei Im, Andri Iona, Maria Kakkoura, Christiana Kartsonaki, Hubert Lam, Kuang Lin, James Liu, Mohsen Mazidi, Iona Millwood, Sam Morris, Qunhua Nie, Alfred Pozarickij, Maryanm Rahmati, Paul Ryder, Saredo Said, Dan Schmidt, Becky Stevens, Iain Turnbull, Robin Walters, Baihan Wang, Lin Wang, Neil Wright, Ling Yang, Xiaoming Yang, Pang Yao.

National Co-ordinating Centre, Beijing: Xiao Han, Can Hou, Qingmei Xia, Chao Liu, Jun Lv, Pei Pei, Dianjianyi Sun, Canqing Yu, Lang Pan.

10 Regional Co-ordinating Centres:

Qingdao CDC: Zengchang Pang, Ruqin Gao, Shanpeng Li, Haiping Duan, Shaojie Wang, Yongmei Liu, Ranran Du, Yajing Zang, Liang Cheng, Xiaocao Tian, Hua Zhang, Yaoming Zhai, Feng Ning, Xiaohui Sun, Feifei Li. **Licang CDC:** Silu Lv, Junzheng Wang, Wei Hou. **Heilongjiang Provincial CDC:** Wei Sun, Shichun Yan, Xiaoming Cui. **Nangang CDC:** Chi Wang, Zhenyuan Wu, Yanjie Li, Quan Kang. **Hainan Provincial CDC:** Huiming Luo, Tingting Ou. **Meilan CDC:** Xiangyang Zheng, Zhendong Guo, Shukuan Wu, Yilei Li, Huimei Li. **Jiangsu Provincial CDC:** Ming Wu, Yonglin Zhou, Jinyi Zhou, Ran Tao, Jie Yang, Jian Su. **Suzhou CDC:** Fang Liu, Jun Zhang, Yihe Hu, Yan Lu, Liangcai Ma, Aiyu Tang, Shuo Zhang, Jianrong Jin, Jingchao Liu. **Guangxi Provincial CDC:** Mei Lin, Zhenzhen Lu. **Liuzhou CDC:** Lifang Zhou, Changping Xie, Jian Lan, Tingping Zhu, Yun Liu, Liuping Wei, Liyuan Zhou, Ningyu Chen, Yulu Qin, Sisi Wang. **Sichuan Provincial CDC:** Xianping Wu, Ningmei Zhang, Xiaofang Chen, Xiaoyu Chang. **Pengzhou CDC:** Mingqiang Yuan, Xia Wu, Xiaofang Chen, Wei Jiang, Jiaqiu Liu, Qiang Sun. **Gansu Provincial CDC:** Faqing Chen, Xiaolan Ren, Caixia Dong. **Maiji CDC:** Hui Zhang, Enke Mao, Xiaoping Wang, Tao Wang, Xi zhang. **Henan Provincial CDC:** Kai Kang, Shixian Feng, Huizi Tian, Lei Fan. **Huixian CDC:** XiaoLin Li, Huarong Sun, Pan He, Xukui Zhang. **Zhejiang Provincial CDC:** Min Yu, Ruying Hu, Hao Wang. **Tongxiang CDC:** Xiaoyi Zhang, Yuan Cao, Kaixu Xie, Lingli Chen, Dun Shen. **Hunan Provincial CDC:** Xiaojun Li, Donghui Jin, Li Yin, Huilin Liu, Zhongxi Fu. **Liuyang CDC:** Xin Xu, Hao Zhang, Jianwei Chen, Yuan Peng, Libo Zhang, Chan Qu.

Supplemental Methods

We excluded participants who had a self-reported history of cardiovascular diseases (CVD, including myocardial infarction, stroke, or transient ischemic attack), hypertension, or were taking blood-pressure-lowering medication at baseline of the China Kadoorie Biobank (CKB) study. The remaining participants (N=151,788) in the analysis ranged in age from 35 to 75 years old and had blood pressure levels of 130-139/80-89 mmHg.

We used the Cox proportional hazards model to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations between a 10 mmHg reduction in systolic blood pressure (SBP) and the first occurrence of non-fatal ischemic heart disease (IHD), non-fatal ischemic stroke (IS), non-fatal hemorrhagic stroke (HS), and fatal CVD events. Models were stratified by study area and adjusted for sex, education, area, smoking, alcohol intake, and body mass index (BMI). We calculated the HRs for four age groups separately (35-44, 45-54, 55-64, and 65-75 years).

To adjust for regression dilution bias, we generated regression dilution ratios (RDR) using repeated SBP measurements taken at baseline and the first resurvey of the CKB study. We used Rosner's regression method to calculate RDR¹, which is the slope of the regression line between baseline and resurvey SBP values, and further calculated the corrected HRs. Since SBP was positively and log-linearly associated with CVD events, we further transferred the HRs for a 10 mmHg SBP reduction to 5.6 mmHg and 2 mmHg reduction separately.

References

1. Rosner B, Willett WC, Spiegelman D. Correction of logistic regression relative risk estimates and confidence intervals for systematic within-person measurement error. *Stat Med.* 1989;8:1051-1069; discussion 1071-1053. doi: 10.1002/sim.4780080905
2. Blood Pressure Lowering Treatment Trialists Collaboration. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. *Lancet.* 2021;397:1625-1636. doi: 10.1016/S0140-6736(21)00590-0

Table S1. Disease progression inputs for prehypertensive individuals

Transition	35-44y	45-54y	55-64y	65-75y
All individuals				
From prehypertension to				
IS	0.0158	0.0445	0.0794	0.1372
HS	0.0030	0.0058	0.0102	0.0169
Acute MI	0.0012	0.0029	0.0048	0.0087
Other IHD	0.0188	0.0459	0.0718	0.1166
CVD death	0.0028	0.0082	0.0209	0.0814
Death from other causes	0.0146	0.0319	0.0673	0.1713
Individuals at high risk for CVD				
From prehypertension to				
IS	0.0940	0.1039	0.1113	0.1407
HS	0.0121	0.0104	0.0135	0.0174
Acute MI	0.0054	0.0060	0.0063	0.0091
Other IHD	0.1020	0.0945	0.0913	0.1204
CVD death	0.0128	0.0175	0.0304	0.0841
Death from other causes	0.0262	0.0418	0.0754	0.1735

IS: ischemic stroke; HS: hemorrhagic stroke; MI: myocardial infarction; IHD: ischemic heart disease; CVD: cardiovascular disease.

Table S2. Disease progression inputs in CVD individuals

Transition	35-75y	45-75y	55-75y	65-75y
From IS to				
HS	0.0047	0.0048	0.0049	0.0054
Acute MI	0.0022	0.0023	0.0026	0.0032
Other IHD	0.0283	0.0295	0.0322	0.0362
CVD death	0.0172	0.0184	0.0233	0.0331
Death from other causes	0.0228	0.0245	0.0312	0.0443
From HS to				
IS	0.0542	0.0581	0.0620	0.0616
Acute MI	0.0010	0.0011	0.0010	0.0010
Other IHD	0.0129	0.0145	0.0179	0.0203
CVD death	0.0666	0.0724	0.0923	0.1206
Death from other causes	0.0370	0.0411	0.0550	0.0777
From Acute MI to				
IS	0.0286	0.0305	0.0351	0.0505
HS	0.0015	0.0017	0.0017	0.0016
Other IHD	0.1436	0.1486	0.1560	0.1788
CVD death	0.0353	0.0380	0.0465	0.0655
Death from other causes	0.0211	0.0229	0.0279	0.0406
From other IHD to				
IS	0.0318	0.0344	0.0382	0.0438
HS	0.0023	0.0024	0.0027	0.0032
Acute MI	0.0044	0.0047	0.0054	0.0062
CVD death	0.0149	0.0164	0.0218	0.0321
Death from other causes	0.0189	0.0208	0.0275	0.0406

IS: ischemic stroke; HS: hemorrhagic stroke; MI: myocardial infarction; IHD: ischemic heart disease; CVD: cardiovascular disease.

Table S3. Sensitivity analysis of the cost-effectiveness of intervention strategies in prehypertensive individuals (120mmHg≤SBP<140mmHg)

	All individuals			High CVD risk individuals		
	Costs (\$)	QALYs	ICER (\$/QALY)	Costs (\$)	QALYs	ICER (\$/QALY)
From age 40 years						
No intervention	3088.30	16.39	Ref	8798.27	15.11	Ref
Salt substitution	3256.88	16.42	6849.26	8920.25	15.19	Extended dominance ^a
Drug treatment	4471.84	16.45	Extended	9403.03	15.32	Dominated ^b
Salt substitution and drug	4504.45	16.47	24799.47	9222.26	15.38	1673.53
From age 50 years						
No intervention	1655.47	14.04	Ref	2730.42	13.42	Ref
Salt substitution	1947.19	14.07	11636.60	3082.49	13.46	7992.71
Drug treatment	2950.11	14.10	Extended	3910.67	13.53	Extended dominance ^a
Salt substitution and drug	3050.62	14.12	21004.83	3967.81	13.57	8567.84
From age 60 years						
No intervention	733.51	10.69	Ref	902.89	10.49	Ref
Salt substitution	1001.91	10.71	15768.74	1200.39	10.51	13411.36
Drug treatment	1776.51	10.73	Extended	1931.14	10.55	Extended dominance ^a
Salt substitution and drug	1846.76	10.75	23066.36	1994.94	10.57	15574.57
From age 70 years						
No intervention	394.89	5.57	Ref	409.04	5.56	Ref
Salt substitution	556.54	5.58	24650.17	575.57	5.56	24503.87
Drug treatment	934.84	5.58	Extended	951.28	5.57	Extended dominance ^a
Salt substitution and drug	963.98	5.59	32748.16	980.20	5.58	30882.11

SBP: systolic blood pressure; CVD: cardiovascular disease; \$: Chinese Yuan; QALYs: quality-adjusted life year; ICER: incremental cost-effectiveness ratio.

^a Extended dominance indicates larger ICER than a more effective strategy. ^b Dominated indicates higher cost and lower QALYs than the comparator.

Table S4. Sensitivity analysis of the cost-effectiveness of intervention strategies in individuals with a 10-year CVD risk of more than 20%

	Costs (\$)	QALYs	ICER (\$/QALY)
From age 40 years			
No intervention	12486.56	14.27	Ref
Salt substitution	12646.49	14.36	Dominated ^a
Drug treatment	12916.10	14.49	Dominated ^a
Salt substitution and drug treatment	12639.95	14.56	519.24
From age 50 years			
No intervention	4113.63	12.66	Ref
Salt substitution	4562.30	12.72	Extended dominance ^b
Drug treatment	5197.33	12.81	Extended dominance ^b
Salt substitution and drug treatment	5201.71	12.87	5332.43
From age 60 years			
No intervention	1246.88	10.11	Ref
Salt substitution	1604.02	10.14	Extended dominance ^b
Drug treatment	2258.13	10.19	Extended dominance ^b
Salt substitution and drug treatment	2309.39	10.22	10282.76
From age 70 years			
No intervention	479.63	5.48	Ref
Salt substitution	660.30	5.49	20173.10
Drug treatment	1027.61	5.50	Extended dominance ^b
Salt substitution and drug treatment	1055.16	5.51	24448.68

CVD: cardiovascular disease; QALYs: quality-adjusted life year; ICER: incremental cost-effectiveness ratio.

^a Dominated indicates higher cost and lower QALYs than the comparator.

^b Extended dominance indicates larger ICER than a more effective strategy.

Table S5. Sensitivity analysis of the cost-effectiveness of intervention strategies based on drug treatment effectiveness from RCT studies

	All individuals			High CVD risk individuals		
	Costs (\$)	QALYs	ICER (\$/QALY)	Costs (\$)	QALYs	ICER (\$/QALY)
From age 40 years						
No intervention	3276.66	16.33	Ref	8751.02	15.12	Ref
Salt substitution	3445.75	16.36	6413.62	8889.45	15.19	2009.11
Drug treatment	4669.82	16.38	Extended dominance ^a	9631.89	15.27	Dominated ^b
Salt substitution and drug treatment	4690.65	16.40	26979.82	9443.49	15.33	4019.44
From age 50 years						
No intervention	1742.56	13.98	Ref	2746.19	13.40	Ref
Salt substitution	2036.70	14.01	11069.04	3096.16	13.44	8027.92
Drug treatment	2993.32	14.04	Extended dominance ^a	3888.95	13.50	Extended dominance ^a
Salt substitution and drug treatment	3089.95	14.07	18628.24	3944.46	13.54	8567.84
From age 60 years						
No intervention	763.12	10.65	Ref	925.84	10.45	Ref
Salt substitution	1032.28	10.67	14601.21	1222.26	10.47	Extended dominance ^a
Drug treatment	1750.52	10.70	Extended dominance ^a	1891.46	10.51	Extended dominance ^a
Salt substitution and drug treatment	1820.10	10.72	16893.40	1954.82	10.53	12226.35
From age 70 years						

No intervention	406.90	5.55	Ref	418.44	5.54	Ref
Salt substitution	568.15	5.56	Extended dominance ^a	583.47	5.55	Extended dominance ^a
Drug treatment	904.06	5.57	Extended dominance ^a	916.14	5.56	Extended dominance ^a
Salt substitution and drug treatment	933.21	5.57	20156.89	945.12	5.57	19496.39

SBP: systolic blood pressure; CVD: cardiovascular disease; \$: Chinese Yuan; QALYs: quality-adjusted life year; ICER: incremental cost-effectiveness ratio.

The association between SBP reduction and major cardiovascular events by drug treatment used in this analysis was from a meta-analysis of individual participant-level data from 48 randomized trials².

^a Extended dominance indicates larger ICER than a more effective strategy.

^b Dominated indicates higher cost and lower QALYs than the comparator.

Table S6. Sensitivity analysis of the cost-effectiveness of intervention strategies based on low compliance rate

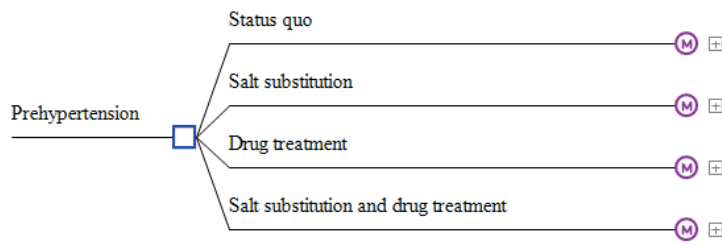
	All individuals			High CVD risk individuals		
	Costs (\$)	QALYs	ICER (\$/QALY)	Costs (\$)	QALYs	ICER (\$/QALY)
From age 40 years						
No intervention	3276.66	16.33	Ref	8757.99	15.12	Ref
Salt substitution	3445.75	16.36	6413.62	8896.00	15.19	2001.79
Drug treatment	4740.71	16.35	Extended	9791.99	15.22	Dominated ^b
Salt substitution and drug	4760.91	16.38	63085.33	9605.38	15.28	7843.77
From age 50 years						
No intervention	1742.56	13.98	Ref	2746.06	13.40	Ref
Salt substitution	2036.70	14.01	11069.04	3096.06	13.44	8029.53
Drug treatment	3069.03	14.01	Extended	3993.94	13.46	Extended dominance ^a
Salt substitution and drug	3163.61	14.04	43061.10	4047.02	13.50	17344.27
From age 60 years						
No intervention	763.12	10.65	Ref	926.18	10.45	Ref
Salt substitution	1032.28	10.67	14601.21	1222.62	10.47	12609.49
Drug treatment	1817.38	10.67	Extended	1968.27	10.48	Extended dominance ^a
Salt substitution and drug	1885.53	10.69	41361.82	2030.01	10.50	26825.23
From age 70 years						
No intervention	406.90	5.55	Ref	418.72	5.54	Ref
Salt substitution	568.15	5.56	22335.16	583.77	5.55	22208.13
Drug treatment	951.17	5.56	Extended	964.81	5.55	Extended dominance ^a
Salt substitution and drug	979.84	5.56	54922.78	993.30	5.55	51904.13

SBP: systolic blood pressure; CVD: cardiovascular disease; \$: Chinese Yuan; QALYs: quality-adjusted life year; ICER: incremental cost-effectiveness ratio.

^a Extended dominance indicates larger ICER than a more effective strategy.

^b Dominated indicates higher cost and lower QALYs than the comparator.

S1A. Markov decision tree for interventions



S1B. Markov decision tree for health states of each intervention



Figure S1. Structure of the Markov model

IS: ischemic stroke; HS: hemorrhagic stroke; MI: myocardial infarction; IHD: ischemic heart disease; CVD: cardiovascular disease.