高血壓防治預防腦中風

心臟內科 陳璟毓醫師
陳煌奇耳鼻喉科診所
2020/04/12

學經歷

- 台大醫學系畢業
- 台大醫院內科住院醫師
- 台大醫院心臟科醫師
- 台灣內科醫學會專科醫師
- 中華民國心臟學會專科醫師
- 中華民國心律學會會員
- 台灣高血壓學會會員
- 台大醫學院生理學研究所博士

現任

- 陳煌奇診所內科心臟科主治醫師
- 台大醫院心臟科兼任主治醫師

大 綱

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

大 綱

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

為什麼要控制血壓？

- 血壓沒控制會怎樣？
- 控制血壓有什麼好處？

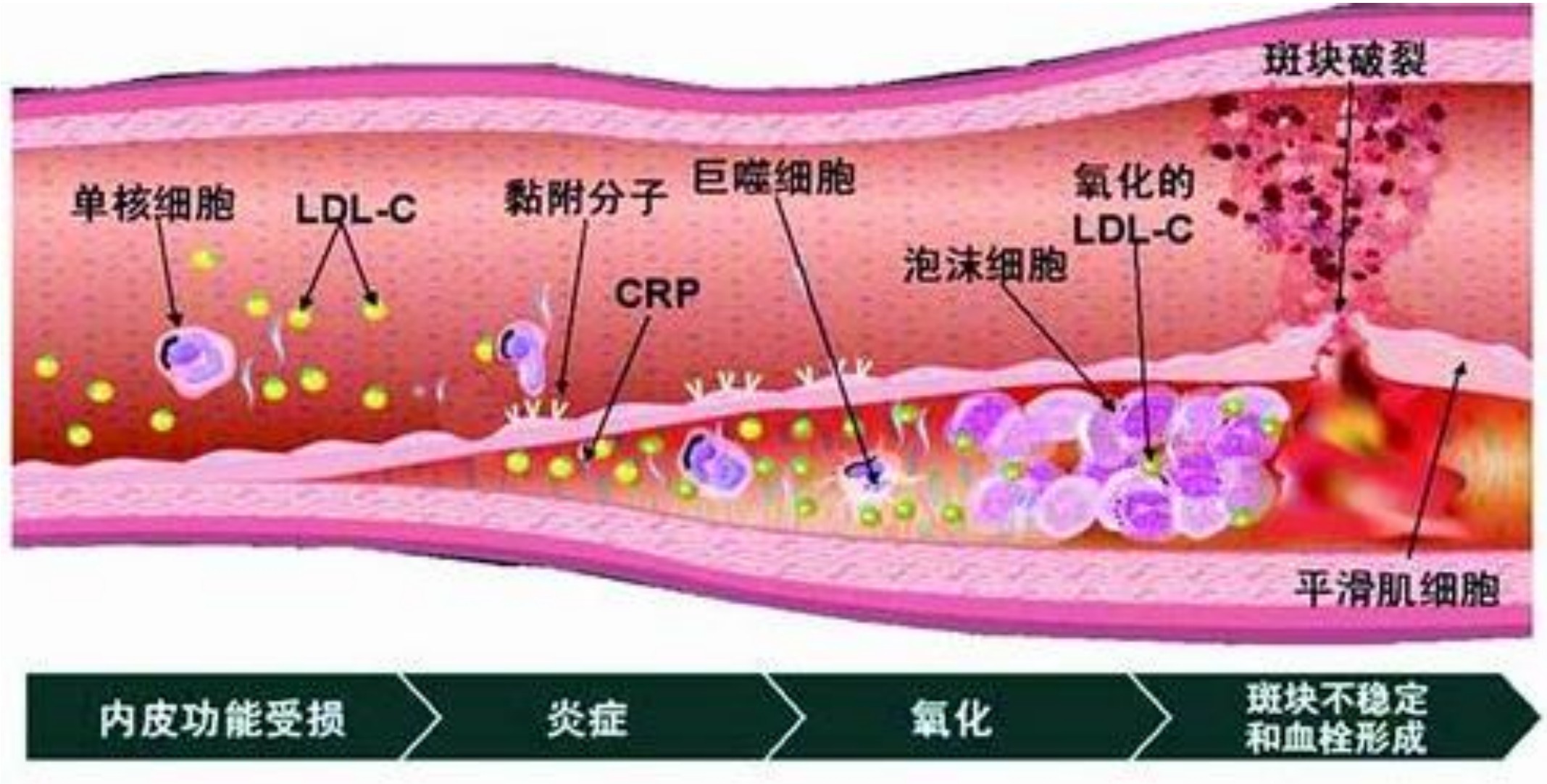
為什麼要控制血壓？

- 血壓沒控制會怎樣？
- 控制血壓有什麼好處？

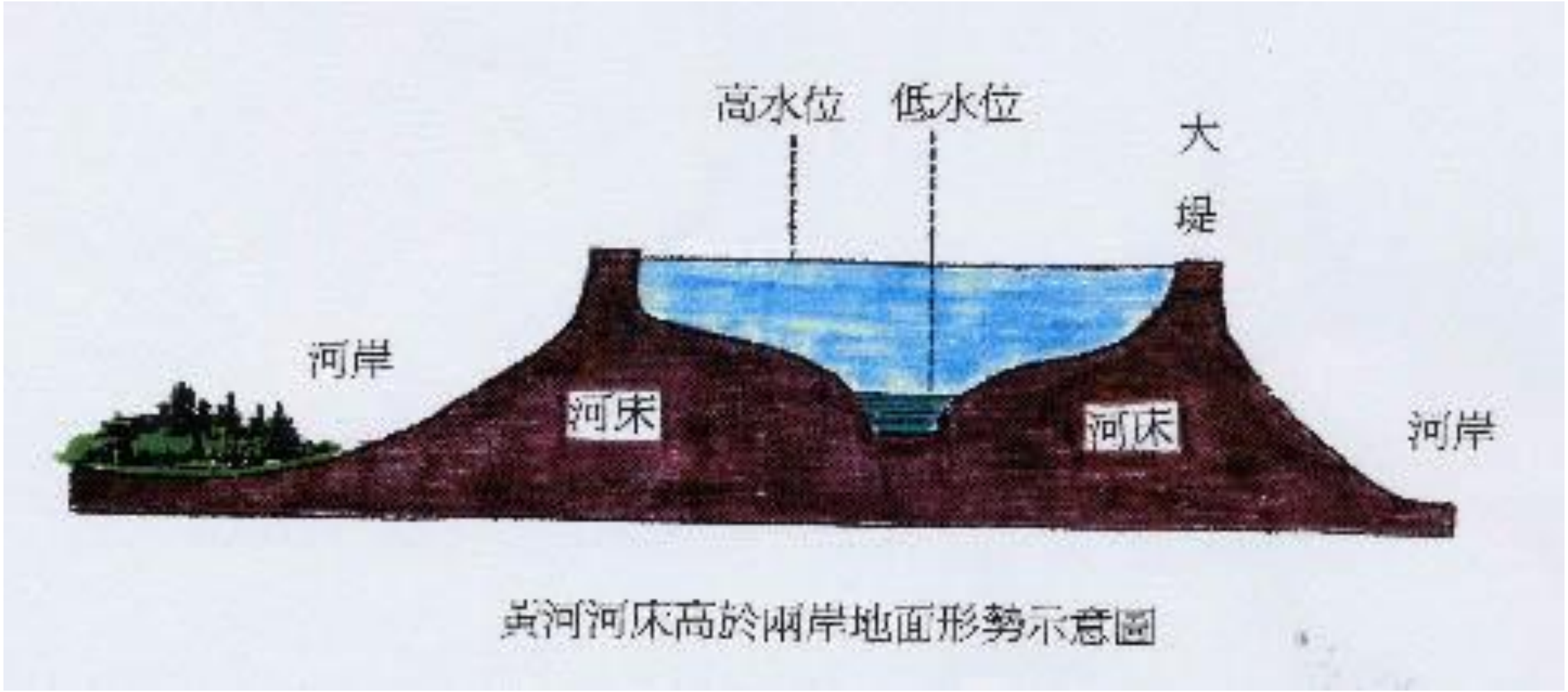
高血壓會傷害血管


大不了顯示過重就好了
VIA 9GAG.COM
翻譯:好色龍 http://hornydragon.blogspot.com
有必要這樣嗎,體重計?

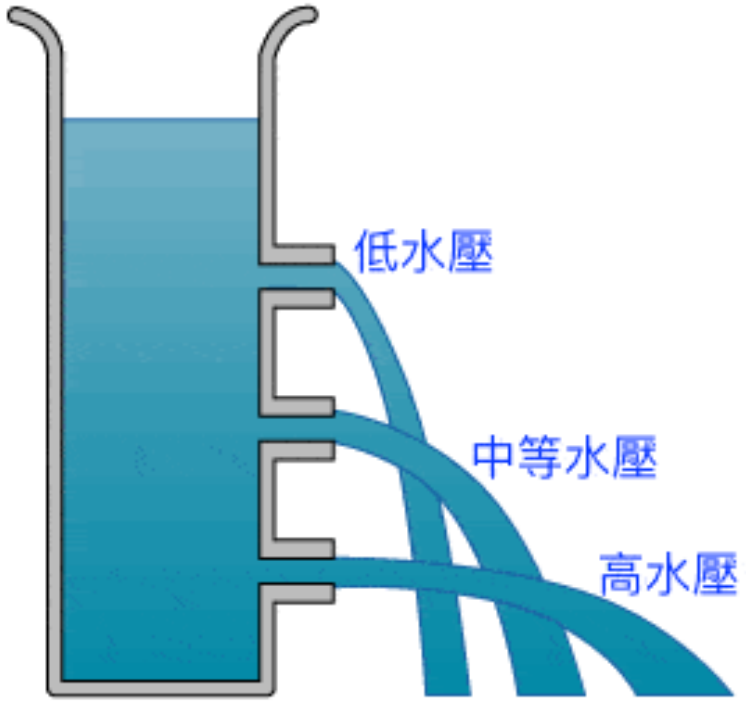
血管受損 → 動脈硬化 → 血管阻塞



黃河之水天上來 – 惡性循環



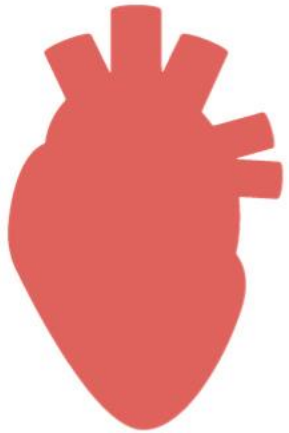
水壓愈高，愈容易破裂！



高血壓有哪些併發症?

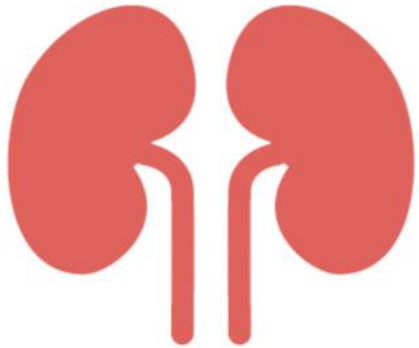
腦血管病變

腦溢血
腦中風



心血管病變

心絞痛, 心衰竭
冠狀動脈肥大



腎臟病變

腎功能病變
腎衰竭

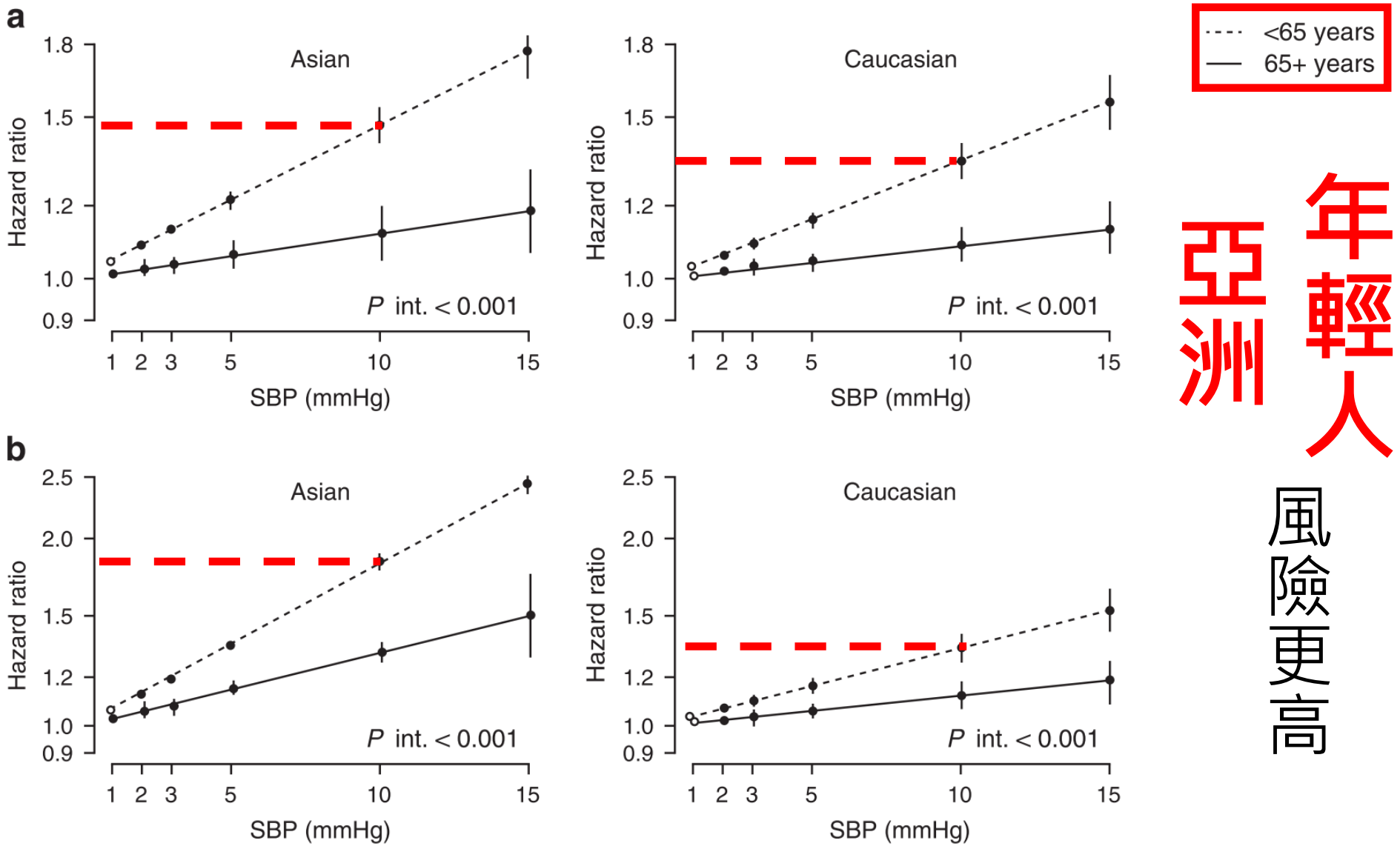
視網膜病變

視力障礙
視網膜出血

血壓愈高，風險愈大，尤其是中風

冠心病

中風

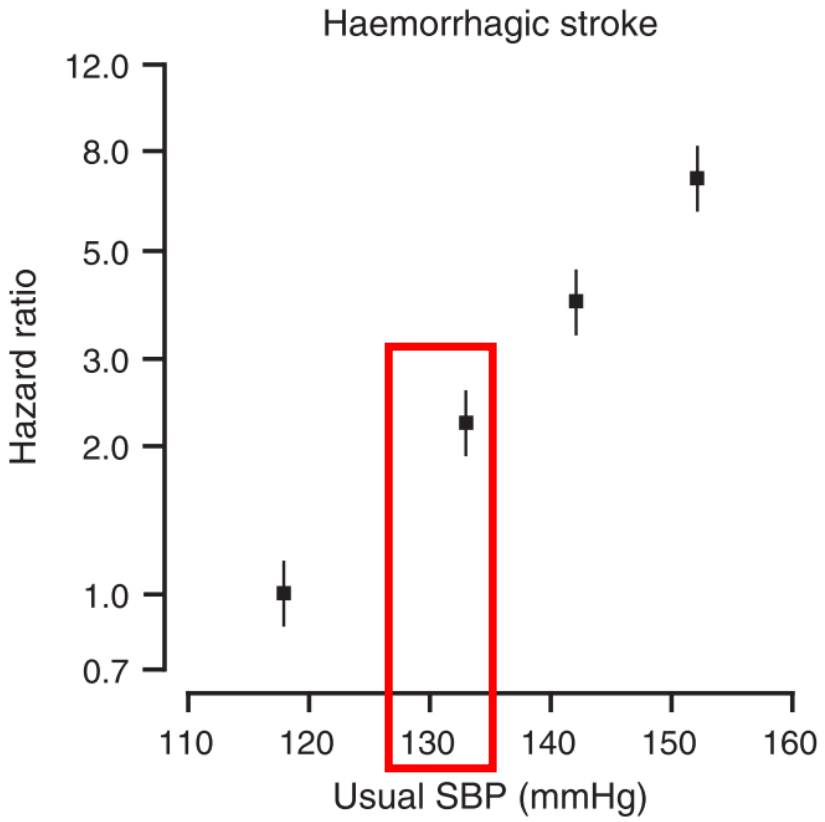


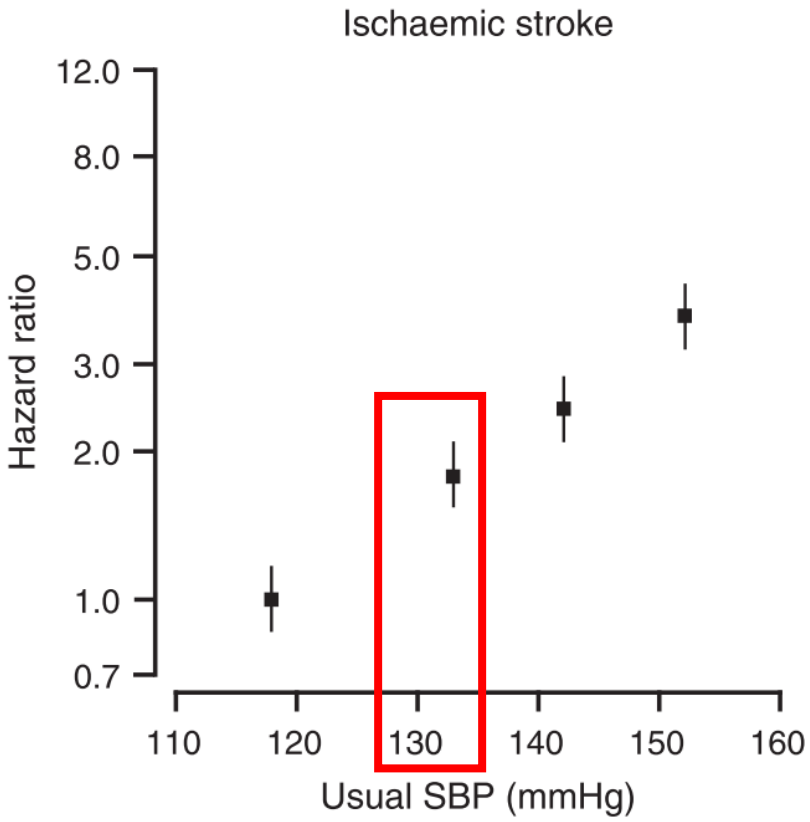
亞洲年輕人

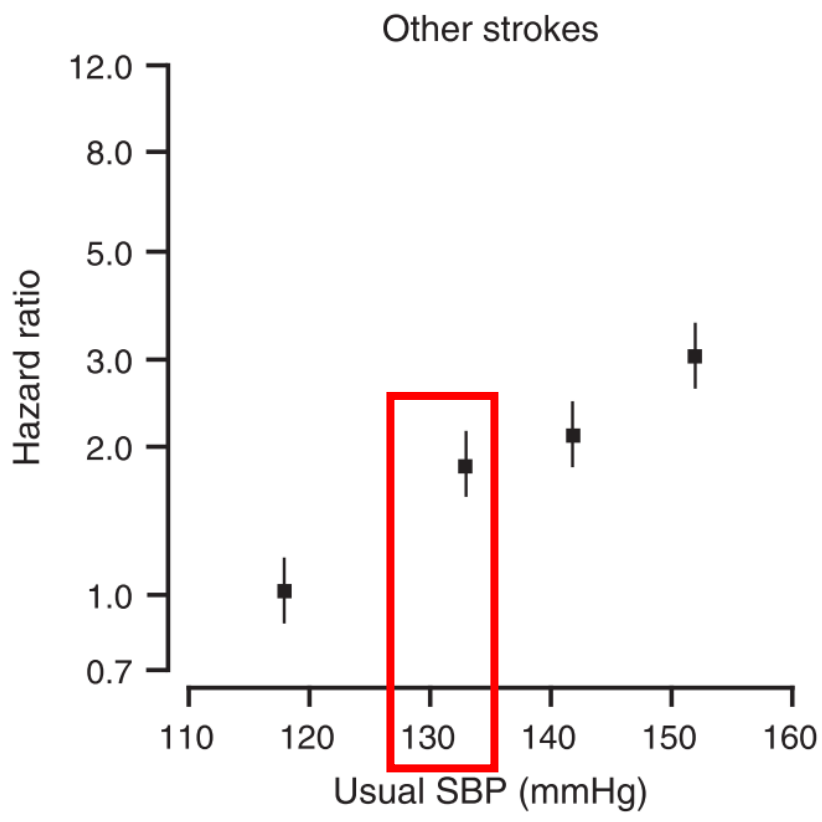
風險更高

Park et al. Hypertens Res. 2015;38:227-36.

亞洲人收縮壓超過130就有中風風險





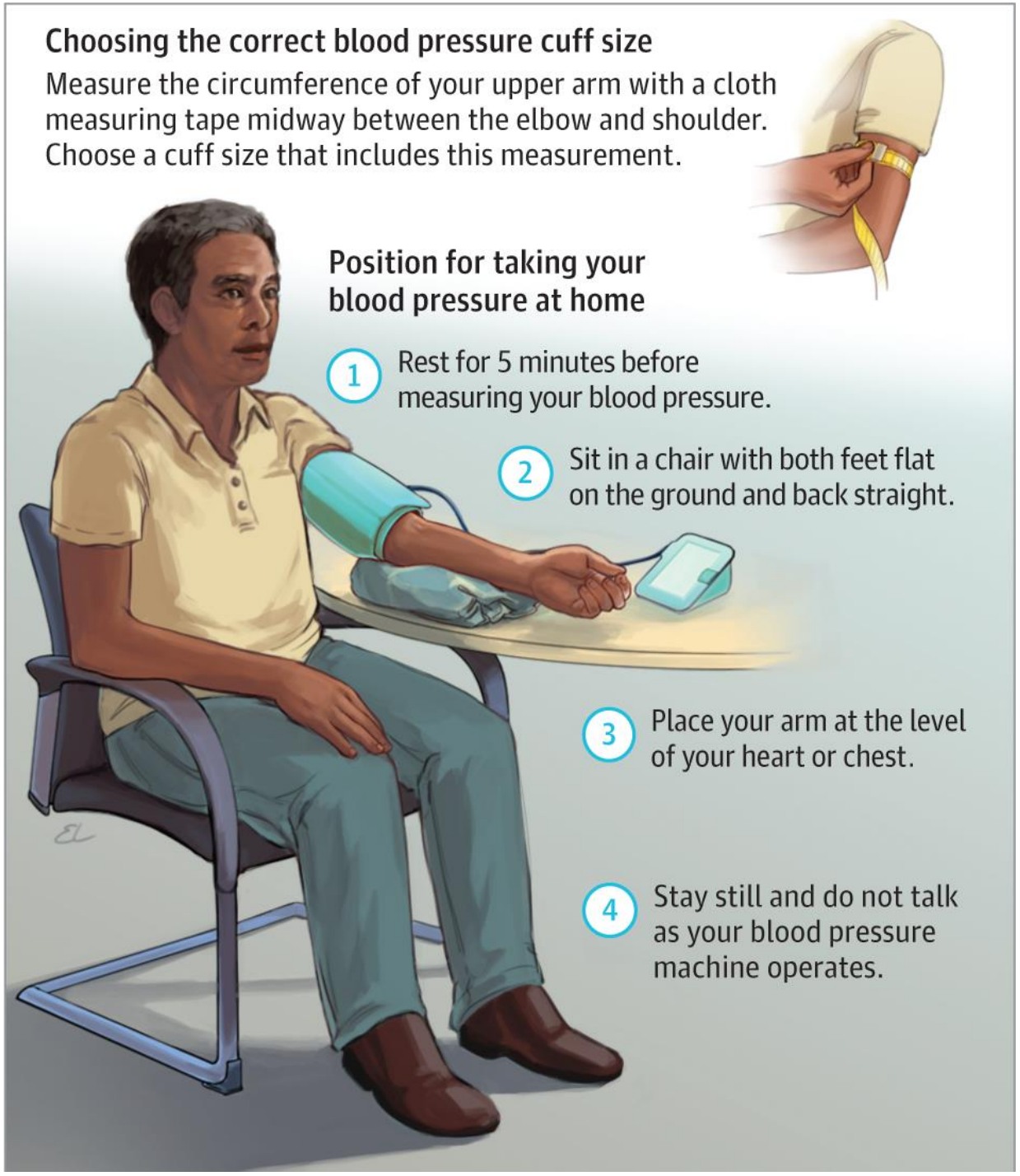


Park et al. Hypertens Res. 2015;38:227-36.

高血壓的定義與分級

Staging	Systolic BP (mmHg)		Diastolic BP (mmHg)
Normal	<120	and	<80
Prehypertension	120-139	or	80-89
Stage 1 hypertension	140-159	or	90-99
Stage 2 hypertension	160-179	or	100-109
Stage 3 hypertension	≥180	or	≥110
Isolated systolic hypertension	≥140	and	<90

Chiang et al. J Chinese Medical Association 2015;78:1-47



如何正確量血壓？

- ✓ 早晚各量一次
- ✓ 量血壓前
  - 一小時不吃飯、喝咖啡、抽菸
  - 半小時不運動
- ✓ 量之前休息五分鐘
- ✓ 每個時段量2-3次取平均，間隔1-2分鐘

Chiang et al. J Chinese Medical Association 2015;78:1-47
Lin et al. JAMA. 2017;318(3):310. doi:10.1001/jama.2017.6670

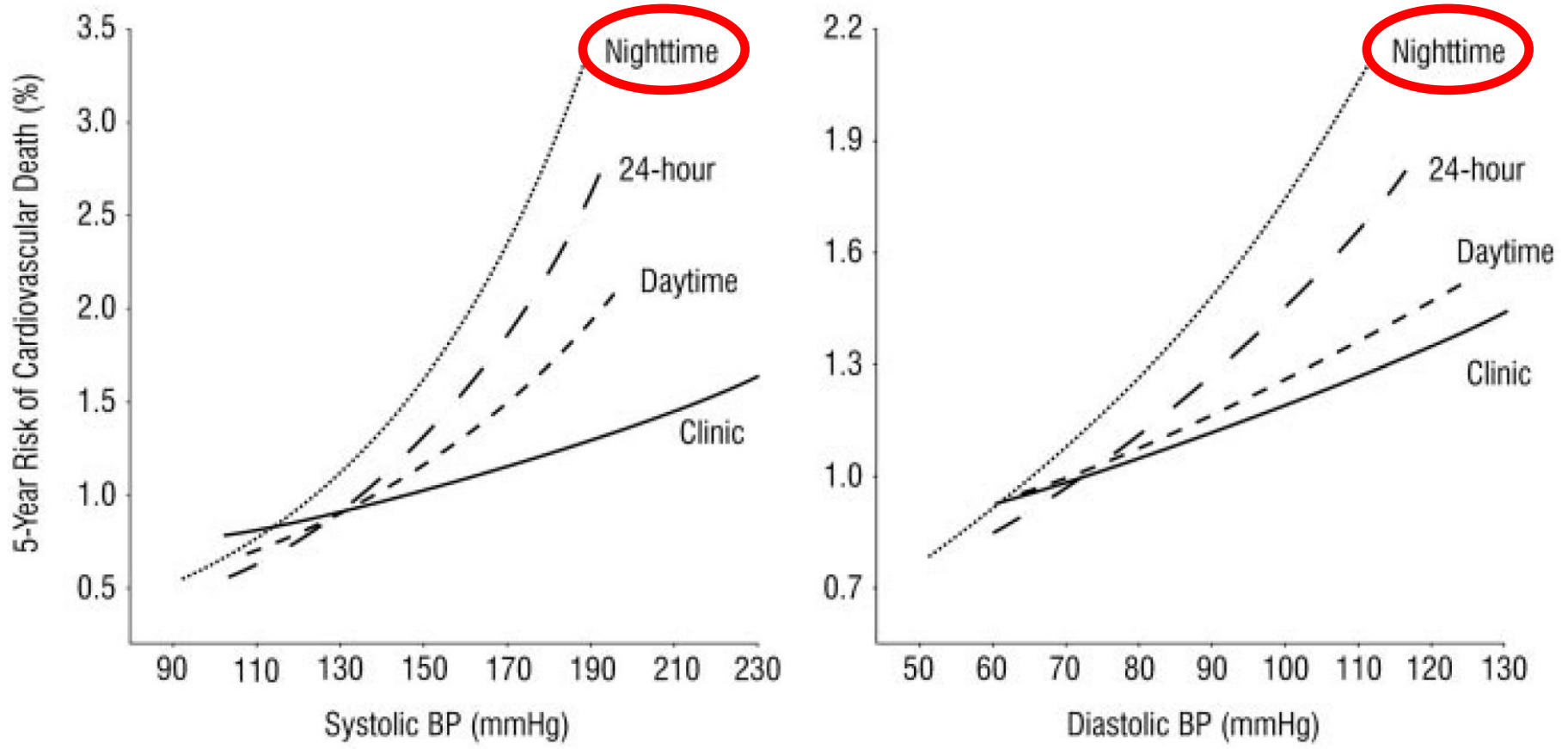
其他高血壓的定義

Category	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)
HBPM 家裡量的	≥135	or	≥85
ABPM 24小時平均	≥130	or	≥80
Daytime	≥135	or	≥85
Nighttime	≥120	or	≥70

HBPM = home blood pressure monitoring
ABPM = ambulatory blood pressure monitoring

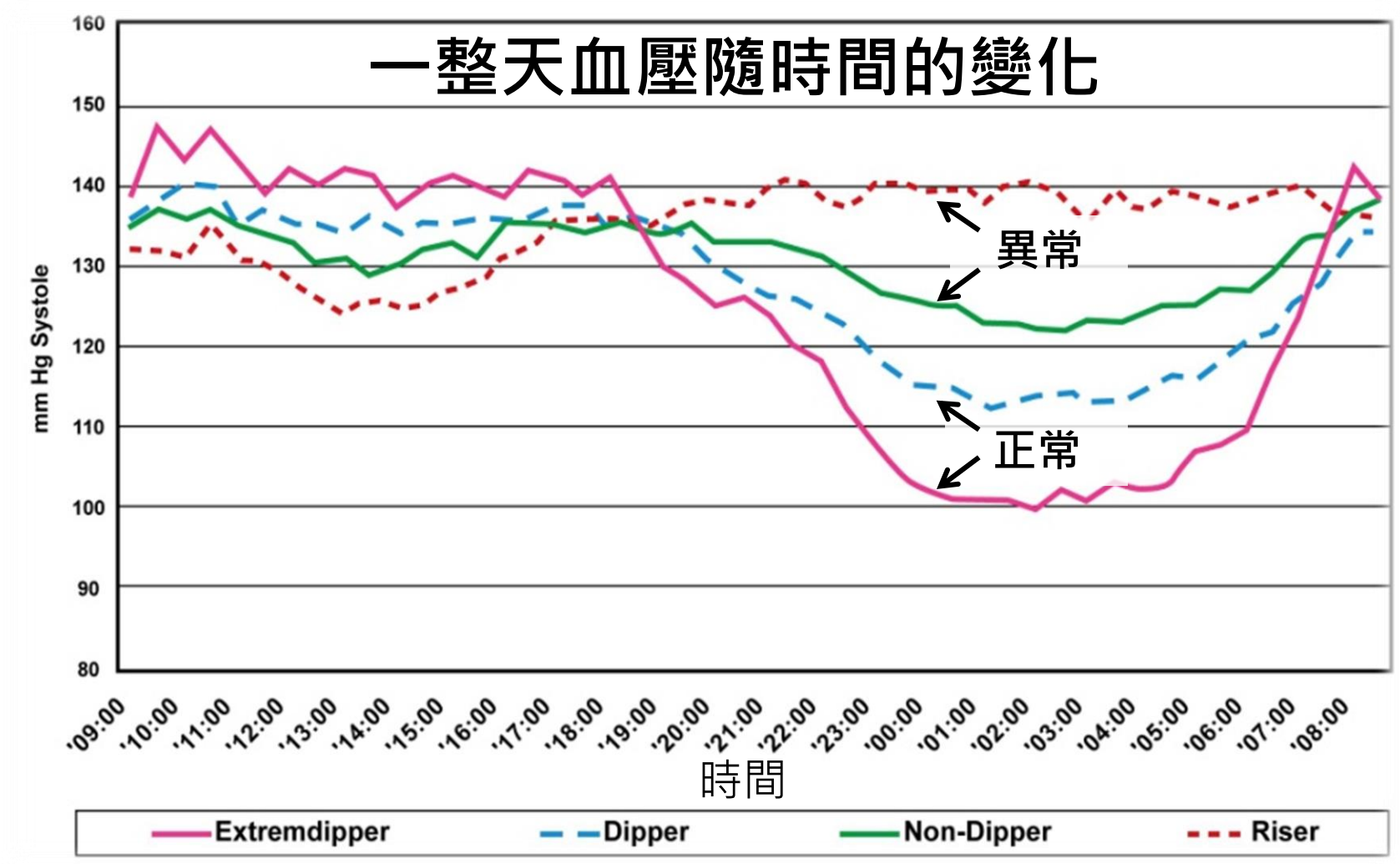
Chiang et al. J Chinese Medical Association 2015;78:1-47

夜間血壓最重要！



Dolan et al. Hypertension 2005;46:156-161

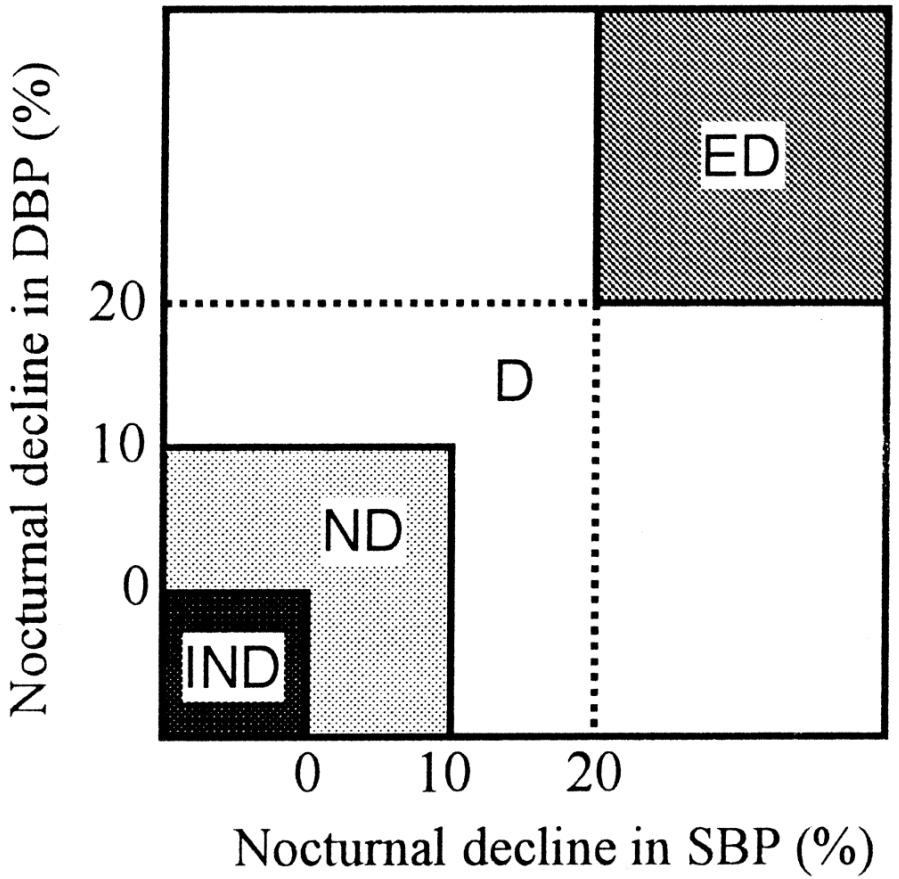
正常睡覺時血壓會下降 (dipping)



>20%　　10-20%　　<10%

Slany J Journal Fur Hypertonie 2008;12(2):34

正常睡覺時血壓會下降 (dipping)

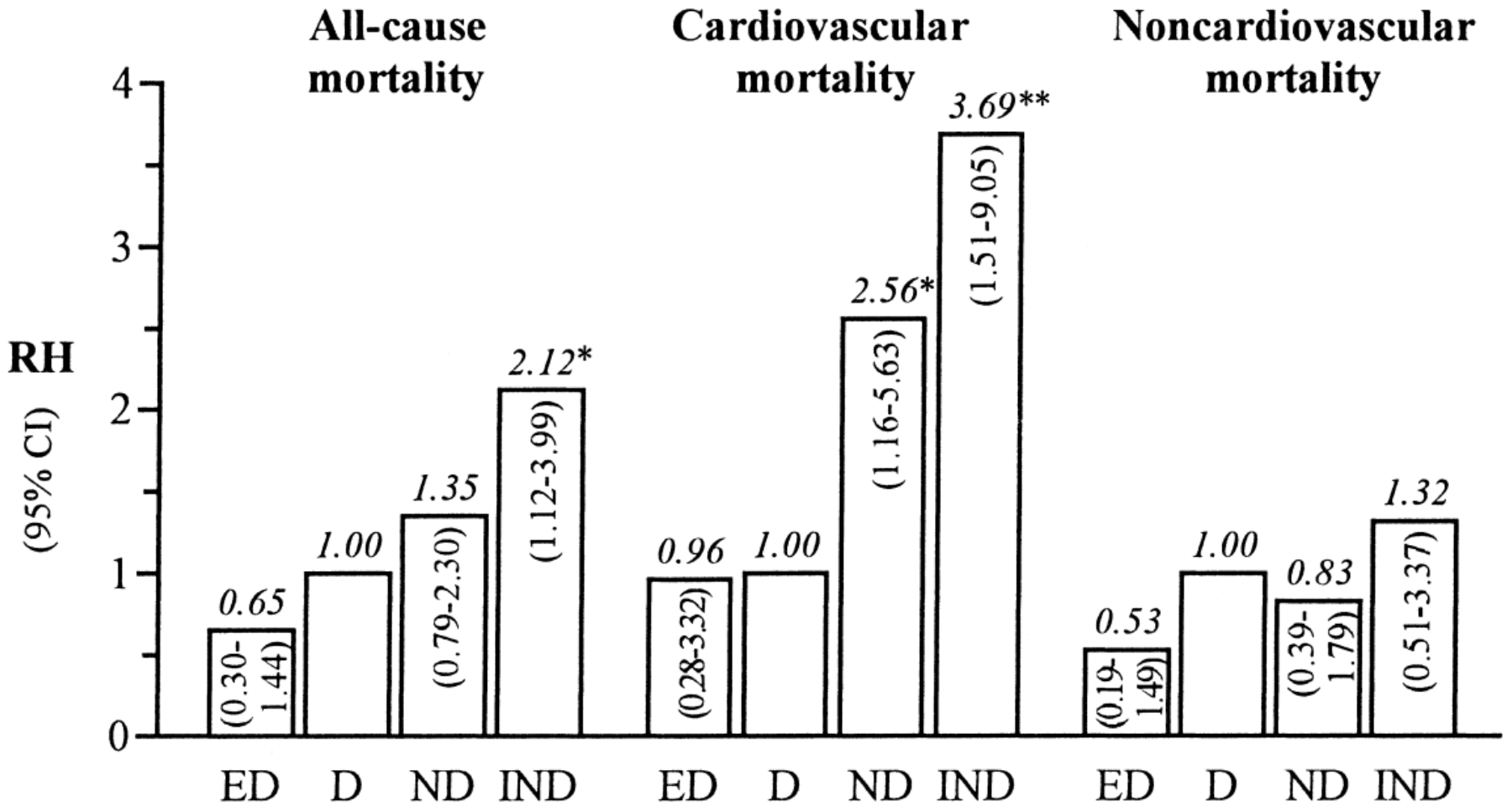


ED = extreme dippers; **D** = dippers; **ND** = non-dippers; **IND** = inverted dippers

16.5% 67.5% 13.0% 3.0%

Ohkubo et al. Am J Hypertens 1997;10:1201-1207

夜間血壓不降反升較危險！



ED = extreme dippers; D = dippers; ND = non-dippers; IND = inverted dippers

Ohkubo et al. Am J Hypertens 1997;10:1201-1207

為什麼要控制血壓？

- 血壓沒控制會怎樣？
- 控制血壓有什麼好處？

降血壓可減少**冠心病**和**中風**的發生率

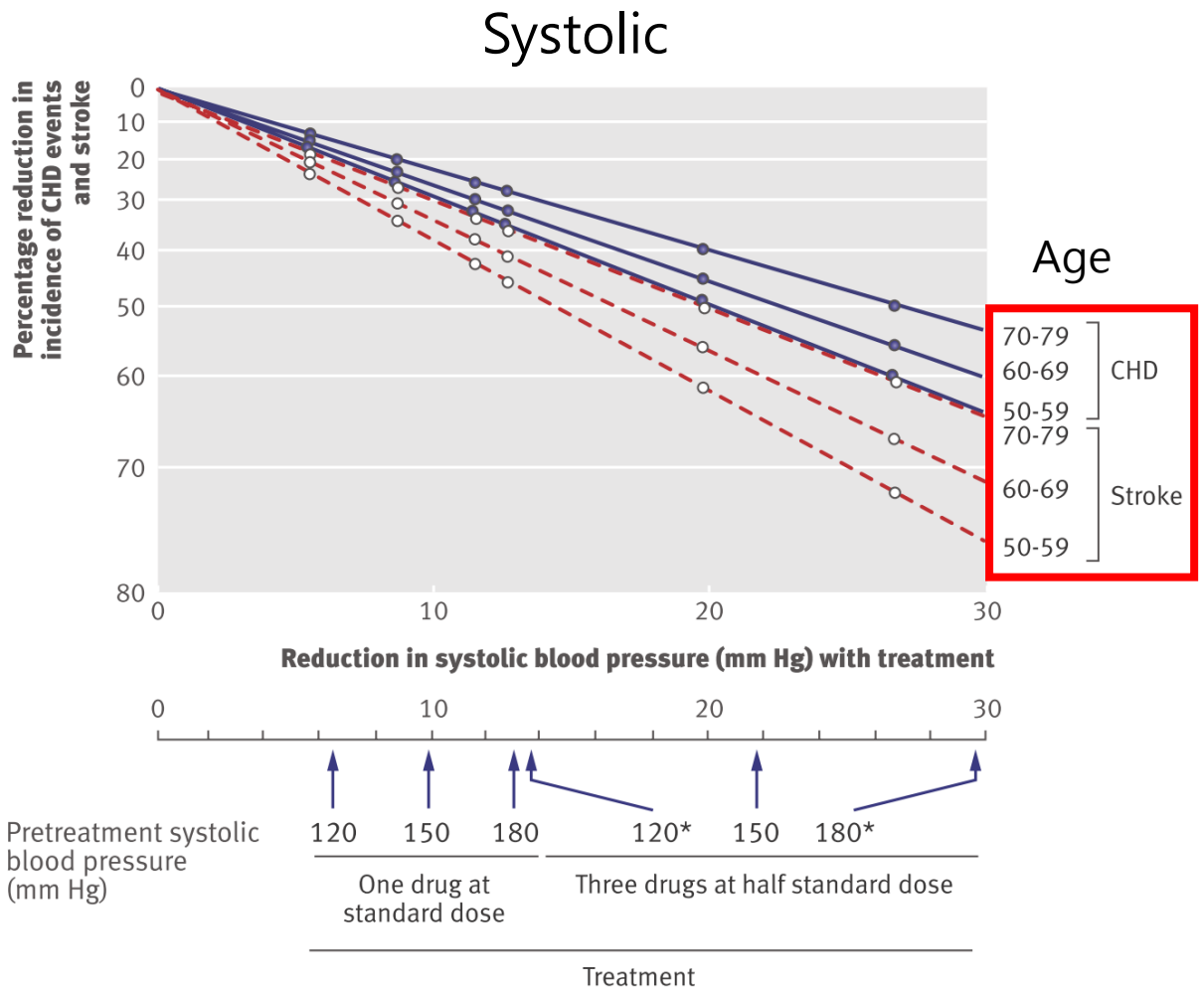
-21%　　-46%

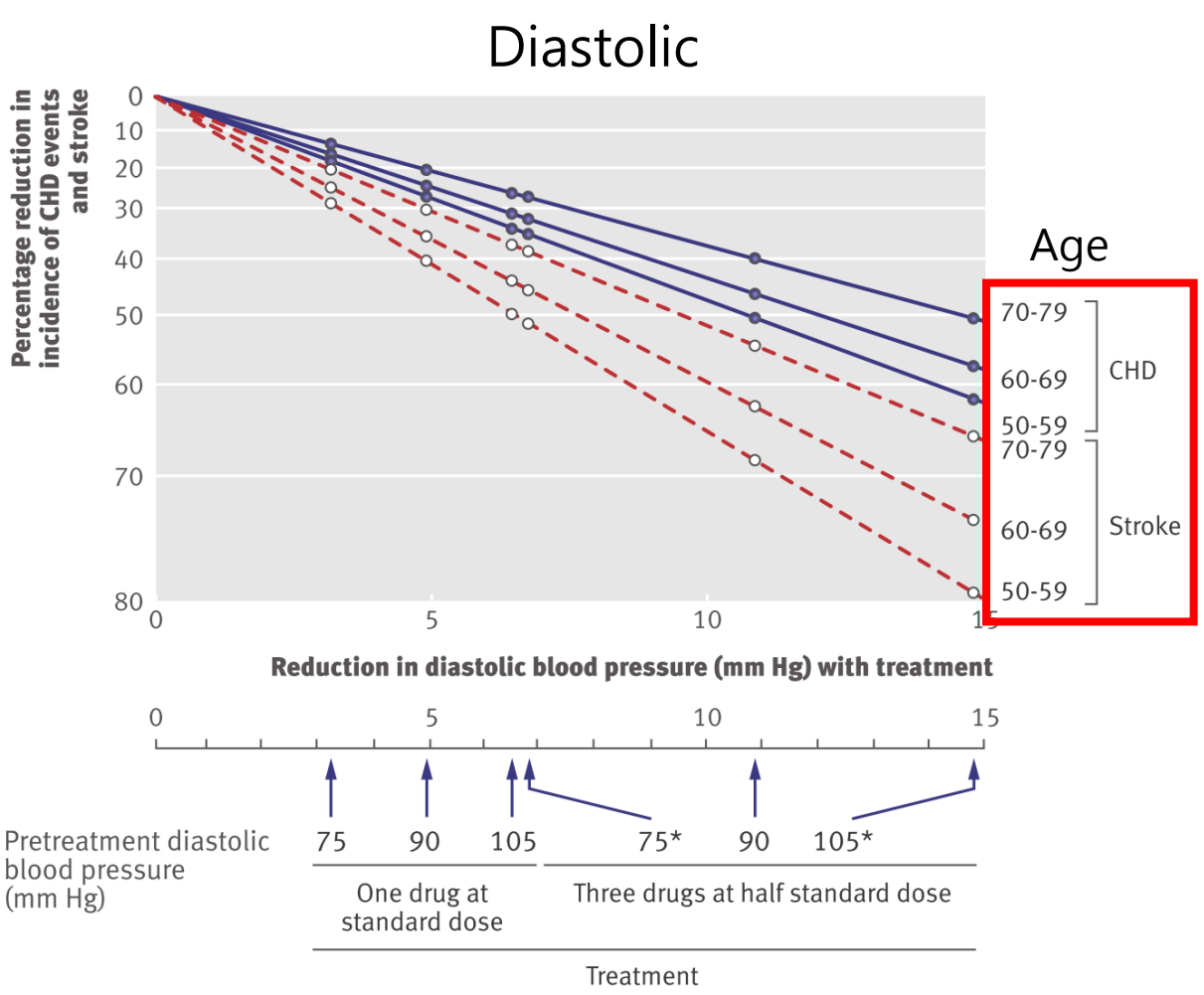
Clinical history of participants on entry	No of trials	Standardised for blood pressure reduction	
		CHD events	Stroke
No vascular disease	27	0.79 (0.72 to 0.86)	0.54 (0.45 to 0.65)
CHD*	37	0.76 (0.68 to 0.86)	0.65 (0.53 to 0.80)
Stroke	13†	0.79 (0.62 to 1.00)	0.66 (0.56 to 0.79)
All trials*	72	0.78 (0.73 to 0.83)	0.59 (0.52 to 0.67)

血壓每下降10/5mmHg

Law et al. BMJ 2009;338:b1665

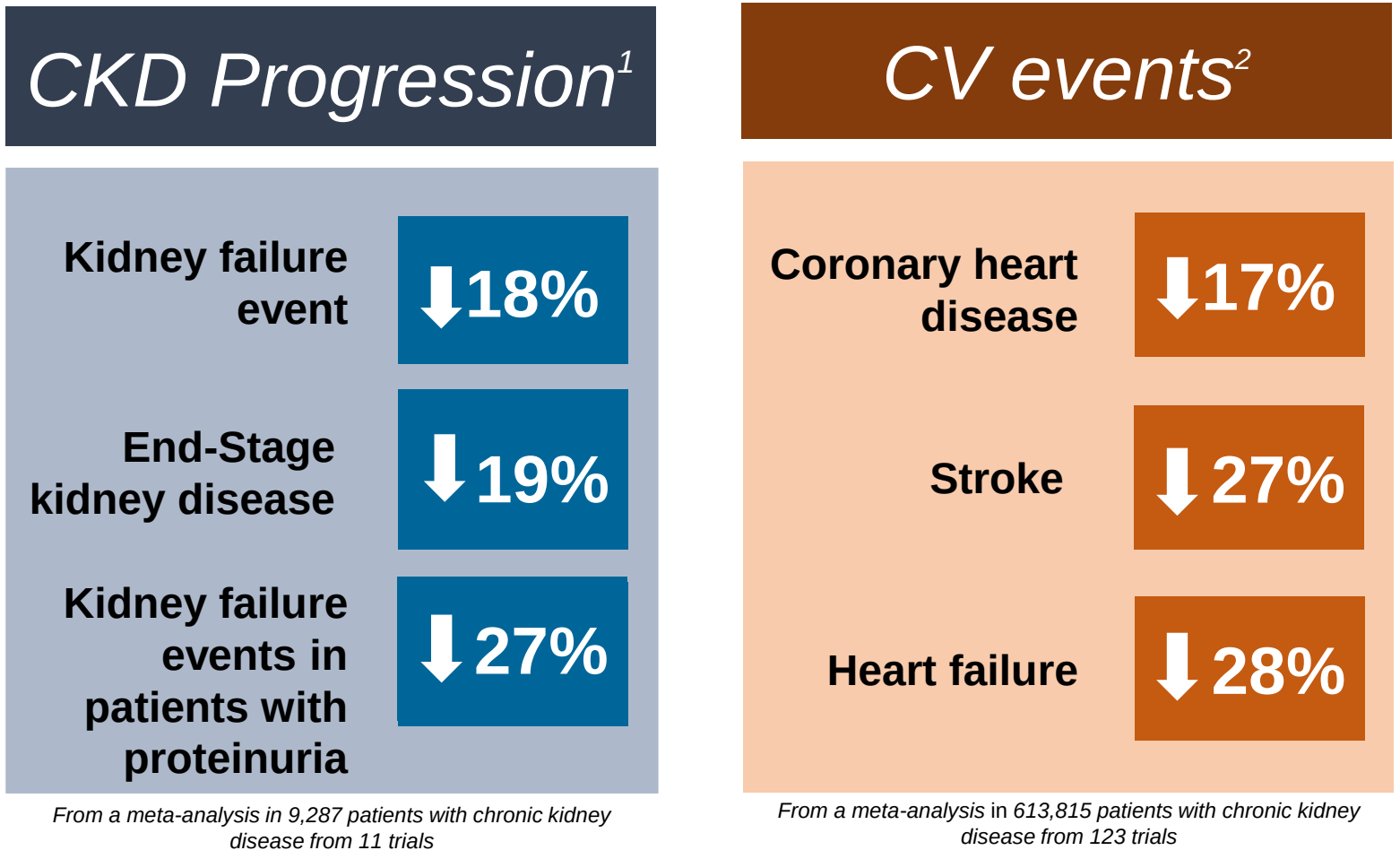
年紀愈輕，好處愈大





Law et al. BMJ 2009;338:b1665

積極的血壓控制顯著降低風險

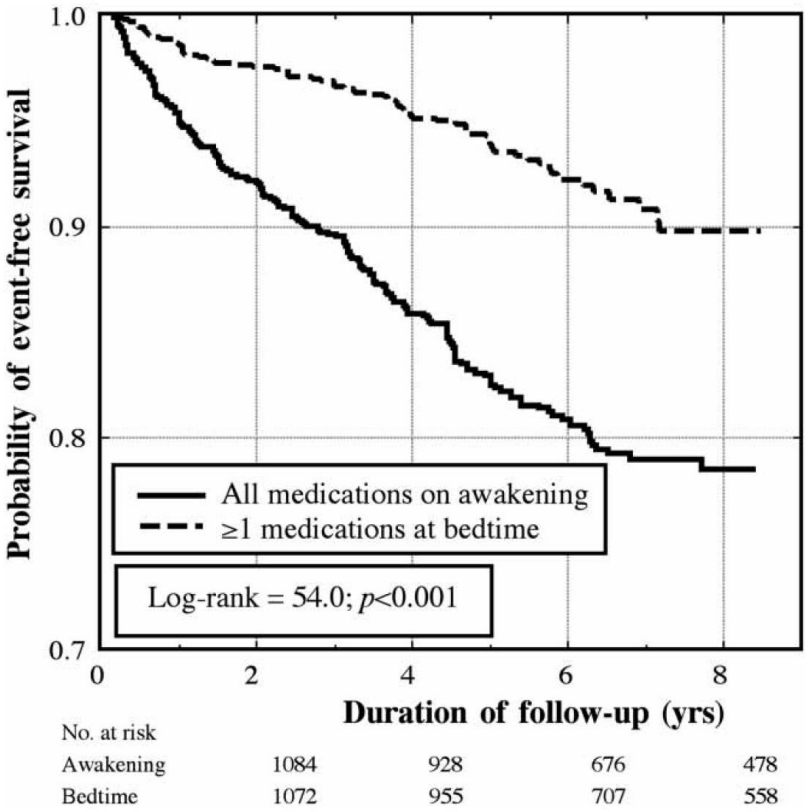


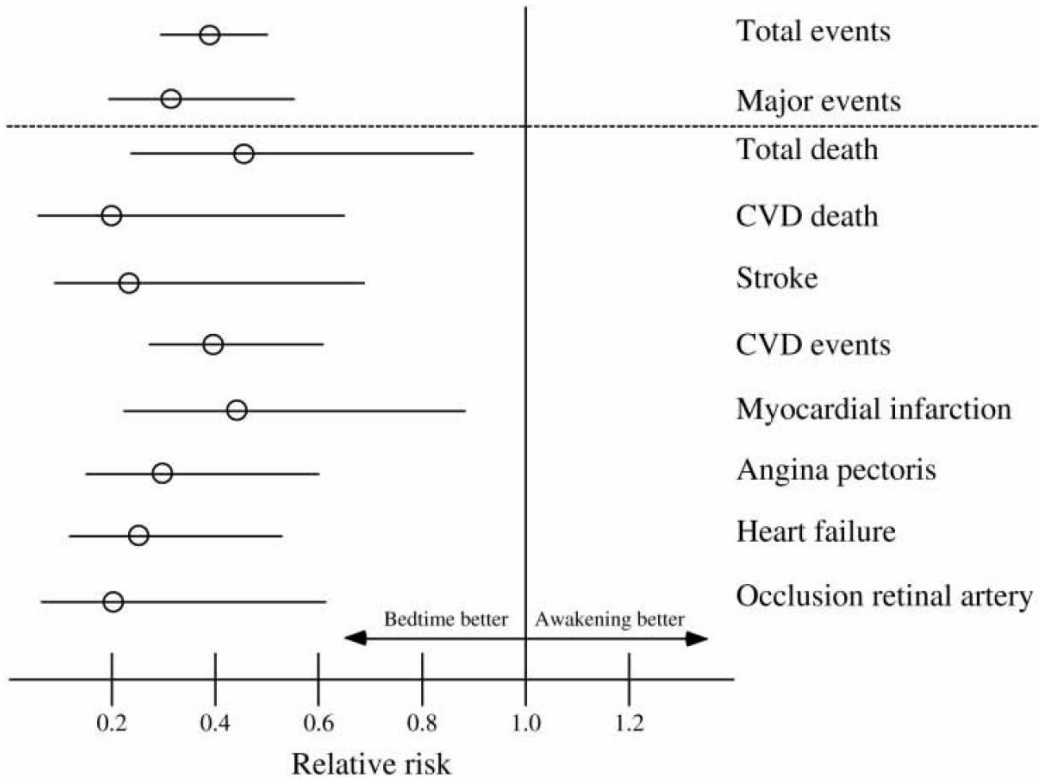
From a meta-analysis in 9,287 patients with chronic kidney disease from 11 trials

From a meta-analysis in *613,815 patients with chronic kidney disease from 123 trials*

1. Lv et al. CMAJ. 2013;185:949-957.
2. Lancet 2015; DOI:10.1016/S0140-6736(15)01225-8

至少一種血壓藥**睡前吃**
預後好





Hermida et al. Chronobiology International 2010;27:1629-1651

至少一種血壓藥**睡前吃**
血壓控制更好，尤其是睡覺時

Variable*	Awakening	Bedtime	*p* between groups
Patients, n	1084	1072	
Changes in clinic and ambulatory BP from baseline			
Clinic SBP, mm Hg	−10.0 ± 17.7	−13.1 ± 19.7	<.001
Clinic DBP, mm Hg	−6.0 ± 10.7	−7.4 ± 10.8	.004
Clinic PP, mm Hg	−4.0 ± 11.2	−5.7 ± 12.2	.001
Clinic HR, beats/min	−1.6 ± 10.6	−1.9 ± 11.1	.410
Awake SBP mean, mm Hg	−9.4 ± 13.3	−8.9 ± 13.4	.401
Asleep SBP mean, mm Hg	−6.6 ± 12.5	−11.8 ± 13.2	<.001
48-h SBP mean, mm Hg	−8.6 ± 12.3	−9.7 ± 12.5	.028
Sleep-time relative SBP decline, %	−1.5 ± 6.7	2.9 ± 7.4	<.001
Awake DBP mean, mm Hg	−7.2 ± 8.5	−6.5 ± 8.9	.035
Asleep DBP mean, mm Hg	−5.2 ± 8.3	−7.9 ± 8.5	<.001
48-h DBP mean, mm Hg	−6.6 ± 7.9	−6.8 ± 8.1	.534
Sleep-time relative DBP decline, %	−1.4 ± 7.8	3.1 ± 8.3	<.001

Sleep-time relative BP decline (%) = [(awake BP mean – asleep BP mean)/awake BP mean] x 100
看BP dipping

Hermida et al. Chronobiology International 2010;27:1629-1651

大 綱

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

SPRINT Trial

有心血管疾病風險者，收縮壓<120 vs 140mmHg (排除糖尿病和中風)

- 50歲以上，有以下一個條件
  - ➢ 已知有心血管疾病 (中風除外)
  - ➢慢性腎病 (eGFR 20-60mL/min/1.73m^2 BSA)
  - ➢10年CV risk ≧ 15%
- 75歲以上

✓ **AOBP**

SPRINT. NEJM 2015;373:2103-16

AOBP
Automated Office Blood Pressure

Table 1. Four essential elements of AOBP (EMAU)

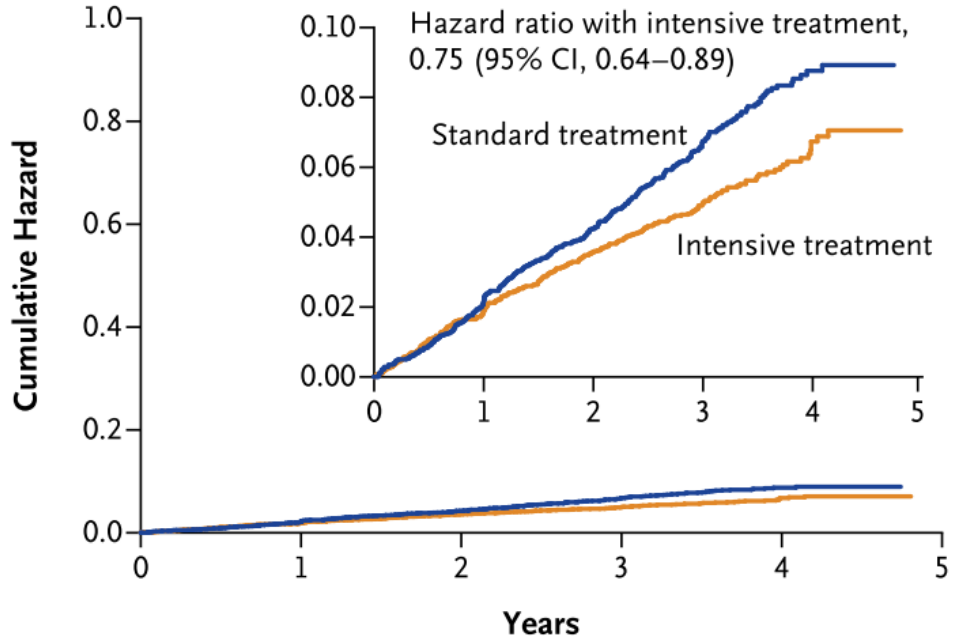
E	**E**lectronic and automated device
M	**M**ultiple readings (三次，間隔一分鐘)
A	**A**veraged mean
U	**U**nattended and **u**ndisturbed spaces

AOBP和家裡量的差不多，比診間低16/7mmHg

Chiang et al. J Chinese Medical Association 2017;33:213-225

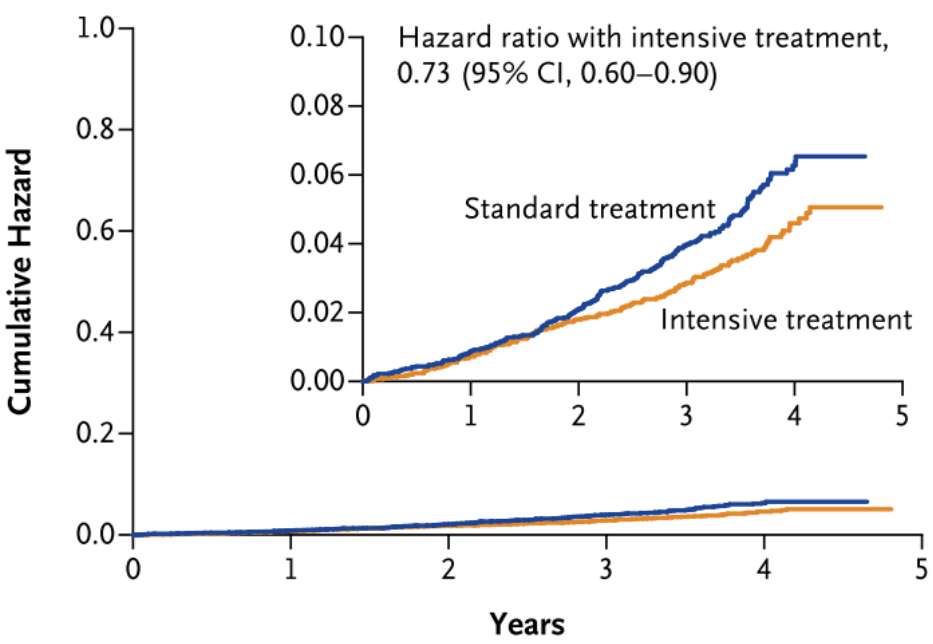
高危險群者，就減少**心血管事件**而言
收縮壓<120優於140mmHg (AOBP)

A Primary Outcome



No. at Risk					
Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

B Death from Any Cause



No. at Risk					
Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

Primary outcome:
ACS, ADHF, stroke, CV death (composite)

SPRINT. NEJM 2015;373:2103-16

減少心衰竭風險，但要注意腎功能

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	*% per year*	*no. of patients (%)*	*% per year*		
All participants	**(N=4678)**		**(N=4683)**			
Primary outcome†	243 (5.2)	1.65	319 (6.8)	2.19	0.75 (0.64–0.89)	<0.001
Secondary outcomes						
Myocardial infarction	97 (2.1)	0.65	116 (2.5)	0.78	0.83 (0.64–1.09)	0.19
Acute coronary syndrome	40 (0.9)	0.27	40 (0.9)	0.27	1.00 (0.64–1.55)	0.99
Stroke	62 (1.3)	0.41	70 (1.5)	0.47	0.89 (0.63–1.25)	0.50
Heart failure	62 (1.3)	0.41	100 (2.1)	0.67	0.62 (0.45–0.84)	0.002
Death from cardiovascular causes	37 (0.8)	0.25	65 (1.4)	0.43	0.57 (0.38–0.85)	0.005
Death from any cause	155 (3.3)	1.03	210 (4.5)	1.40	0.73 (0.60–0.90)	0.003
Primary outcome or death	332 (7.1)	2.25	423 (9.0)	2.90	0.78 (0.67–0.90)	<0.001
Participants with CKD at baseline	**(N=1330)**		**(N=1316)**			
Composite renal outcome‡	14 (1.1)	0.33	15 (1.1)	0.36	0.89 (0.42–1.87)	0.76
≥50% reduction in estimated GFR§	10 (0.8)	0.23	11 (0.8)	0.26	0.87 (0.36–2.07)	0.75
Long-term dialysis	6 (0.5)	0.14	10 (0.8)	0.24	0.57 (0.19–1.54)	0.27
Kidney transplantation	0		0			
Incident albuminuria¶	49/526 (9.3)	3.02	59/500 (11.8)	3.90	0.72 (0.48–1.07)	0.11
Participants without CKD at baseline‖	**(N=3332)**		**(N=3345)**			
≥30% reduction in estimated GFR to <60 ml/min/1.73 m^2§	127 (3.8)	1.21	37 (1.1)	0.35	3.49 (2.44–5.10)	<0.001
Incident albuminuria¶	110/1769 (6.2)	2.00	135/1831 (7.4)	2.41	0.81 (0.63–1.04)	0.10

SPRINT. NEJM 2015;373:2103-16

低血壓、暈倒、急性腎衰竭、低血鈉的機會增加

Variable	Intensive Treatment (N=4678)	Standard Treatment (N=4683)	Hazard Ratio	P Value
	no. of patients (%)			
Serious adverse event*	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest				
Serious adverse event only				
Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall†	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure‡	193 (4.1)	117 (2.5)	1.66	<0.001
Emergency department visit or serious adverse event				
Hypotension	158 (3.4)	93 (2.0)	1.70	<0.001
Syncope	163 (3.5)	113 (2.4)	1.44	0.003
Bradycardia	104 (2.2)	83 (1.8)	1.25	0.13
Electrolyte abnormality	177 (3.8)	129 (2.8)	1.38	0.006
Injurious fall†	334 (7.1)	332 (7.1)	1.00	0.97
Acute kidney injury or acute renal failure‡	204 (4.4)	120 (2.6)	1.71	<0.001
Monitored clinical events				
Adverse laboratory measure§				
Serum sodium <130 mmol/liter	180 (3.8)	100 (2.1)	1.76	<0.001
Serum sodium >150 mmol/liter	6 (0.1)	0		0.02
Serum potassium <3.0 mmol/liter	114 (2.4)	74 (1.6)	1.50	0.006
Serum potassium >5.5 mmol/liter	176 (3.8)	171 (3.7)	1.00	0.97
Orthostatic hypotension¶				
Alone	777 (16.6)	857 (18.3)	0.88	0.01
With dizziness	62 (1.3)	71 (1.5)	0.85	0.35

SPRINT. NEJM 2015;373:2103-16

病人如果問：

聽說美國現在血壓的標準有放寬？

他可能是看了網路文章...

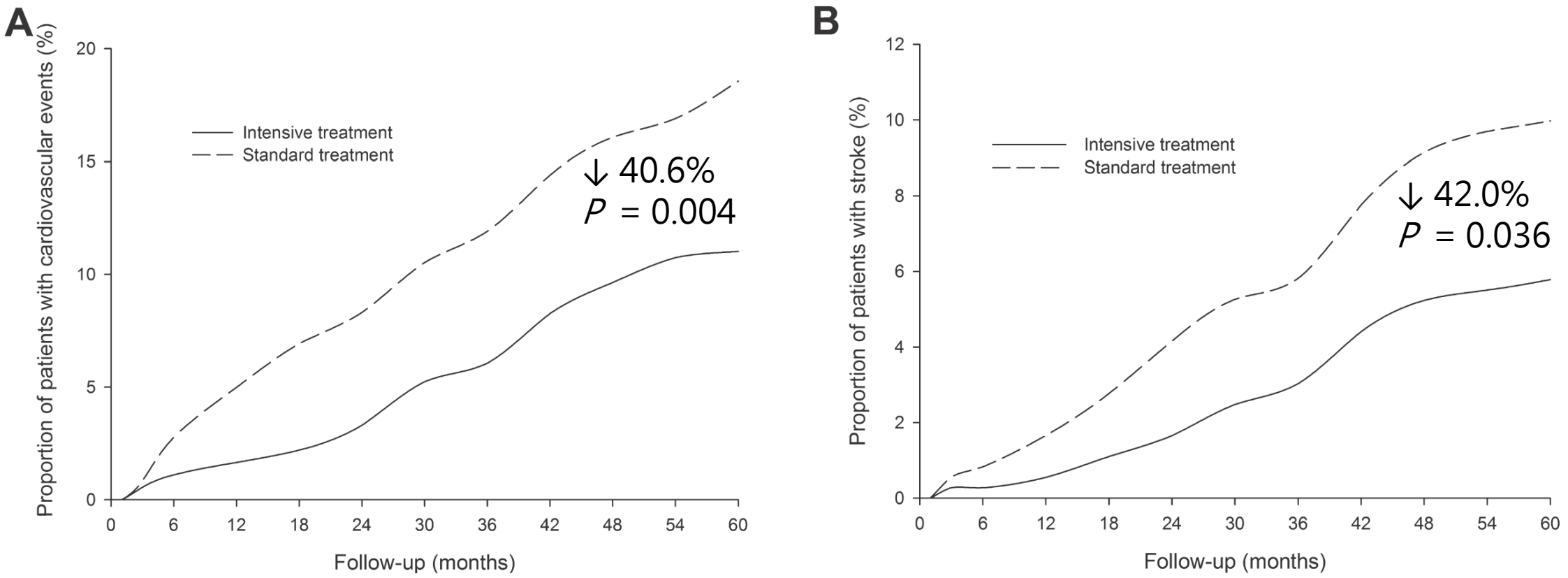
真相與闢謠
真相說明
保健闢謠

老人家血壓太高沒關係？

1.近日網路謠傳以吳氏計算血壓公式，即正常血壓收縮壓為年齡加上82 mmHg (男性)-80 mmHg(女性)，認為收縮壓超過140 mmHg無需就醫。另網站也表示美國醫學會雜誌，血壓指標委員會經過五年研究後認為，美國民眾60歲以上人士的高血壓指標擬改為高於150/90mmHg，收縮壓在140至150mmHg無需服藥治療等訊息。

2. 經詢台大教授表示該資料係2004年網路資料，引用之吳氏計算法查無研究實証基礎，考量其推展性有限，故不建議民眾採行。

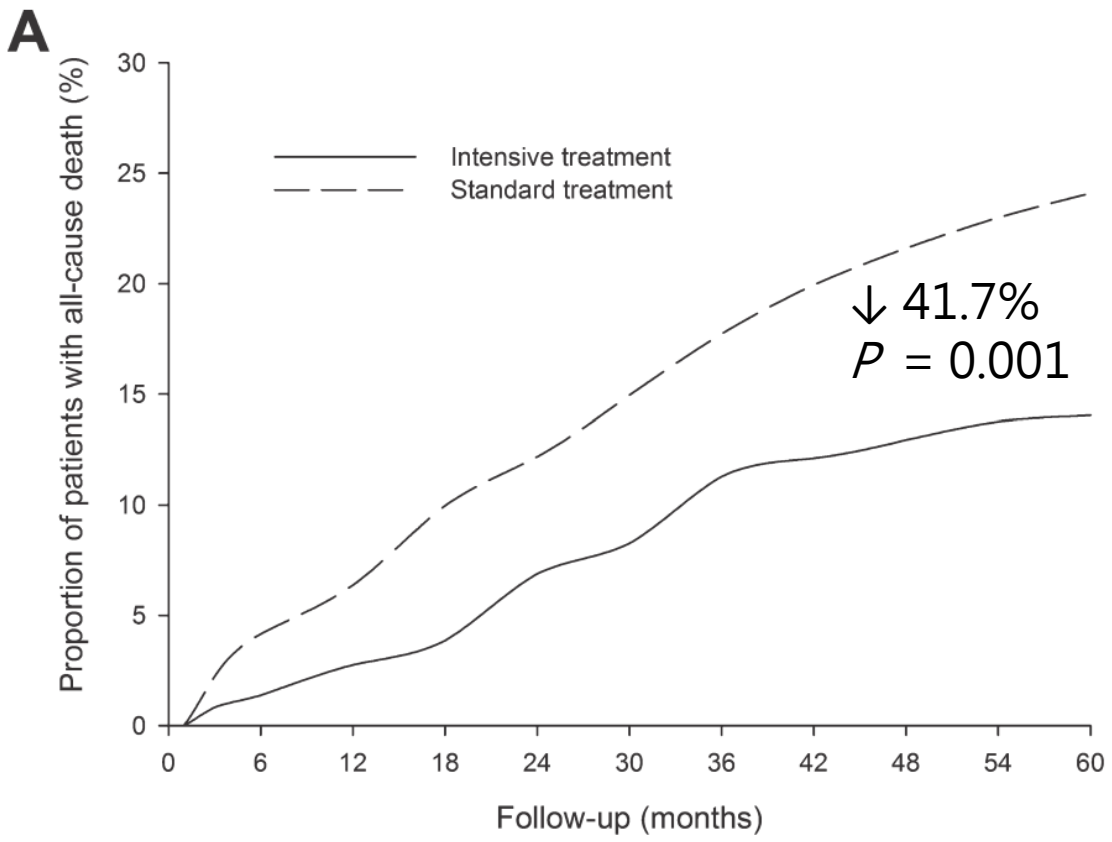
70歲以上，將收縮壓控制在140mmHg以內可減少心血管事件和**中風**機會 (中國研究)

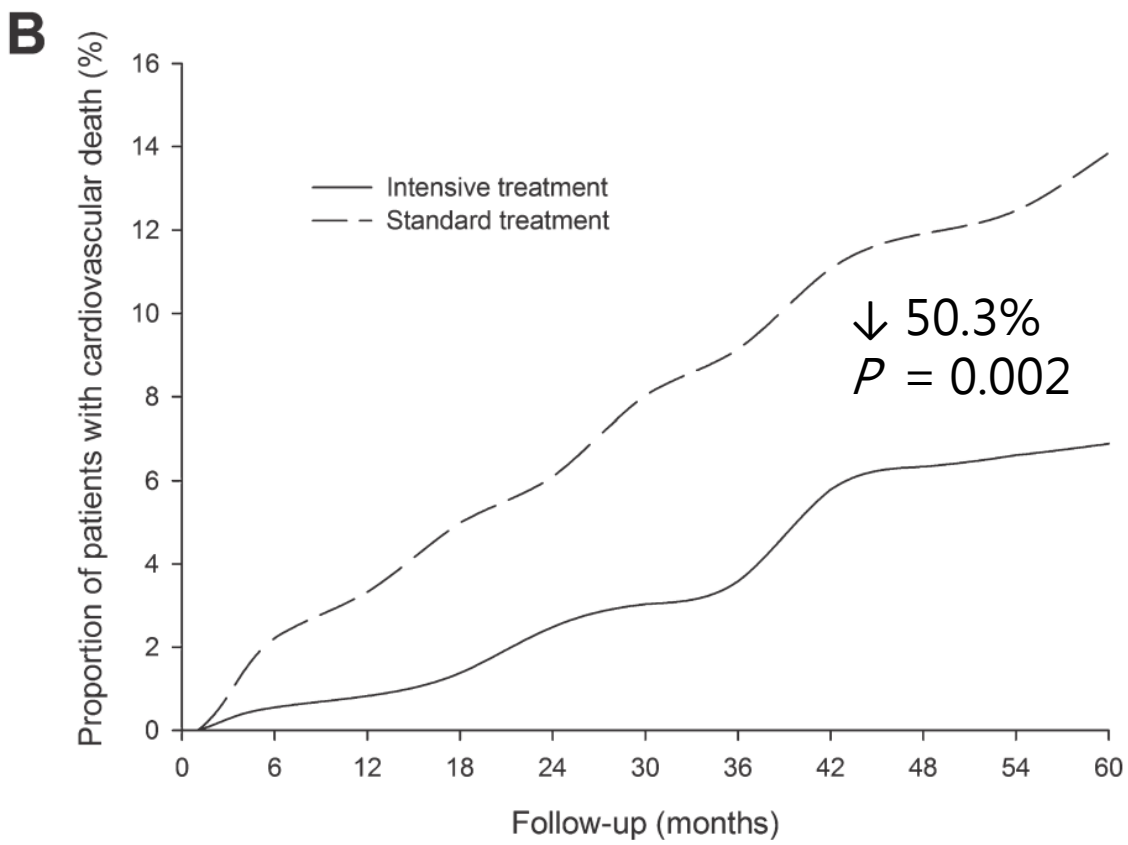


724 ≧ 70 y/o patients, randomly assigned, 4 yrs

J Clin Hypertens 2013;15:420-7

70歲以上，將收縮壓控制在140mmHg以內可減少心血管和**總體死亡率** (中國研究)





724 ≧ 70 y/o patients, randomly assigned, 4 yrs

J Clin Hypertens 2013;15:420-7

65歲以上，將收縮壓控制在140mmHg以內可減少心血管事件、心血管死亡率、心衰竭機會

Clinical Outcomes	Intensive BP Lowering	Standard BP lowering	Pooled RR (95% CI)	p Value	I^2
Efficacy					
MACE	200/5,437 (3.7)	280/5,420 (5.2)	0.71 (0.60-0.84)	0.0001	0
Cardiovascular mortality	60/5,437 (1.1)	94/5,420 (1.7)	0.67 (0.45-0.98)	0.04	25%
Myocardial infarction	57/5,437 (1.0)	72/5,420 (1.3)	0.79 (0.56-1.12)	0.18	0
Stroke	116/5,437 (2.1)	142/5,420 (2.6)	0.80 (0.61-1.05)	0.11	19%
Heart failure	49/3,892 (1.3)	79/3,886 (2.0)	0.63 (0.40-0.99)	0.04	21%
Safety					
Serious adverse events	1,274/5,074 (25.1)	1,252/5,059 (24.7)	1.02 (0.94-1.09)	0.69	19%
Renal failure	57/5,067 (1.1%)	28/5,049 (0.6)	1.81 (0.86-3.80)	0.12	46%

Meta-analysis of SPRINT-SENIORS, JATOS, VALISH, Wei et al. (J Clin Hypertens 2013;15:420-7)
10,857 ≧ 65 y/o patients, follow-up 3.1 yrs

JACC 2017;69:486-93

血壓目標

Categories	Targets (mmHg)	COR	LOE
Primary prevention	< 140/90	I	B
Secondary prevention			
Diabetes	< 130/80	I	B
CHD	< 120/NA[AOBP]	I	B
Stroke	< 140/90	I	A
CKD	< 120/NA[AOBP]	I	B
Elderly (age ≥ 75 years)	< 120/NA[AOBP]	I	B
Patients receiving antithrombotics for stroke prevention	< 130/80	I	B

AOBP, unattended automated office blood pressure measurement; BP, blood pressure; CHD, coronary heart disease; CKD, chronic kidney disease; COR, class of recommendation; LOE, level of evidence; NA, not available.

AOBP和家裡量的差不多，比診間低16/7mmHg

Chiang et al. J Chinese Medical Association 2017;33:213-225

診間血壓目標

Categories	Targets (mmHg)	COR	LOE
Primary prevention	< 140/90	I	B
Secondary prevention			
Diabetes	< 130/80	I	B
CHD	< 130/80	I	B
Stroke	< 140/90	I	A
CKD	< 140/90	I	A
CKD with proteinuria	< 130/80	IIb	C
Elderly (age ≥ 75 years)	< 140/90	I	B
Patients receiving antithrombotics for stroke prevention	< 130/80	I	B

Chiang et al. J Chinese Medical Association 2017;33:213-225

高血壓病患生活型態的調整

	全名	要點	血壓下降
S	**S**odium (鈉)	2-4g/天	2.5mmHg/1g
A	**A**lcohol (酒精)	男<30g/天；女<20g/天	2-4mmHg
B	**B**MI (身體質量指數)	22.5-25kg/m^2	1mmHg/1kg
C	**C**igarette (菸)	戒菸!!	(本來就要戒)
D	**D**iet (飲食)	DASH diet (得舒飲食)：少油多蔬果	10-12mmHg
E	**E**xercise (運動)	一週3-4次；一次40分鐘	3-7mmHg

Chiang et al. J Chinese Medical Association 2015;78:1-47

大 綱

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

相關 / 危險因子

Risk factors
Family and personal history of hypertension, CVD, stroke, or renal disease
Family and personal history of associated risk factors (e.g. familial hypercholesterolaemia)
Smoking history
Dietary history and salt intake
Alcohol consumption
Lack of physical exercise/sedentary lifestyle
History of erectile dysfunction
Sleep history, snoring, sleep apnoea (information also from partner)
Previous hypertension in pregnancy/pre-eclampsia

European Heart Journal (2018) 39, 3021–3104

會影響血壓的因素

Characteristics of patients with resistant hypertension	Causes of secondary resistant hypertension	Drugs and substances that may cause raised BP
Demographics ● Older age (especially >75 years) ● Obesity ● More common in black people ● Excess dietary sodium intake ● High baseline BP and chronicity of uncontrolled hypertension	**More common causes** ● Primary hyperaldosteronism ● Atherosclerotic renovascular disease ● Sleep apnoea ● CKD	**Prescribed drugs** ● Oral contraceptives ● Sympathomimetic agents (e.g. decongestants in proprietary cold remedies) ● Non-steroidal anti-inflammatory drugs ● Cyclosporin ● Erythropoietin ● Steroids (e.g. prednisolone and hydrocortisone) ● Some cancer therapies
Concomitant disease ● HMOD: LVH and/or CKD ● Diabetes ● Atherosclerotic vascular disease ● Aortic stiffening and isolated systolic hypertension	**Uncommon causes** ● Phaeochromocytoma ● Fibromuscular dysplasia ● Aortic coarctation ● Cushing's disease ● Hyperparathyroidism	**Non-prescription drugs** ● Recreational drugs (e.g. cocaine, amphetamines, and anabolic steroids) ● Excessive liquorice ingestion ● Herbal remedies (e.g. ephedra and ma huang)

European Heart Journal (2018) 39, 3021–3104

隨時注意**次發性**高血壓的可能性

Characteristic
Younger patients (<40 years) with grade 2 hypertension or onset of any grade of hypertension in childhood
Acute worsening hypertension in patients with previously documented chronically stable normotension
Resistant hypertension (see section 8.1)
Severe (grade 3) hypertension or a hypertension emergency (see section 8.3)
Presence of extensive HMOD
Clinical or biochemical features suggestive of endocrine causes of hypertension or CKD
Clinical features suggestive of obstructive sleep apnoea
Symptoms suggestive of phaeochromocytoma or family history of phaeochromocytoma

European Heart Journal (2018) 39, 3021–3104

次發性高血壓的表現與必要檢查

Cause	Prevalence in hypertensive patients	Suggestive symptoms and signs	Screening Investigations
Obstructive sleep apnoea	5–10%	Snoring; obesity (can be present in non-obese); morning headache; daytime somnolence	Epworth score and ambulatory polygraphy
Renal parenchymal disease	2–10%	Mostly asymptomatic; diabetes; haematuria, proteinuria, nocturia; anaemia, renal mass in adult polycystic CKD	Plasma creatinine and electrolytes, eGFR; urine dipstick for blood and protein, urinary albumin:creatinine ratio; renal ultrasound
Renovascular disease			
Atherosclerotic renovascular disease	1–10%	Older; widespread atherosclerosis (especially PAD); diabetes; smoking; recurrent flash pulmonary oedema; abdominal bruit	Duplex renal artery Doppler or CT angiography or MR angiography
Fibromuscular dysplasia		Younger; more common in women; abdominal bruit	

European Heart Journal (2018) 39, 3021–3104

Cause	Prevalence in hypertensive patients	Suggestive symptoms and signs	Screening Investigations
Primary Aldosteronism	5 - 15%	Mostly asymptomatic; muscle weakness (rare)	Plasma aldosterone and renin, and aldosterone:renin ratio; hypokalaemia (in a minority): note hypokalaemia can depress aldosterone levels
Phaeochromocytoma	<1%	Episodic symptoms (the 5 'Ps'): paroxysmal hypertension, pounding headache, perspiration, palpitations, and pallor; labile BP; BP surges precipitated by drugs (e.g. beta-blockers, metoclopramide, sympathomimetics, opioids, and tricyclic antidepressants)	Plasma or 24 h urinary fractionated metanephrines
Cushing's syndrome	<1%	Moon face, central obesity, skin atrophy, striae and bruising; diabetes; chronic steroid use	24 h urinary-free cortisol
Thyroid disease (hyper- or hypothyroidism)	1 - 2%	Signs and symptom of hyper- or hypothyroidism	Thyroid function tests
Hyperparathyroidism	<1%	Hypercalcaemia, hypophosphataemia	Parathyroid hormone, Ca^{2+}

European Heart Journal (2018) 39, 3021–3104

次發性高血壓的表現與必要檢查

Cause	Prevalence in hypertensive patients	Suggestive symptoms and signs	Screening Investigations
Coarctation of the aorta	<1%	Usually detected in children or adolescence; different BP (≥20/10 mmHg) between upper–lower extremities and/or between right–left arm and delayed radial-femoral femoral pulsation; low ABI interscapular ejection murmur; rib notching on chest X-ray	Echocardiogram

European Heart Journal (2018) 39, 3021–3104

檢查有無**器官損傷**

Recommendations	Class[a]	Level[b]
Heart		
12-lead ECG is recommended for all hypertensive patients.[120]	I	B
Echocardiography: • Is recommended in hypertensive patients when there are ECG abnormalities or signs or symptoms of LV dysfunction.[42,134]	I	B
• May be considered when the detection of LVH may influence treatment decisions.[42,134]	IIb	B
Blood vessels		
Ultrasound examination of the carotid arteries:	I	B
• May be considered for the detection of asymptomatic atherosclerotic plaques or carotid stenosis in patients with documented vascular disease elsewhere.[42]	IIb	B
Measurement of PWV may be considered for measuring arterial stiffness.[109,189]	IIb	B
Measurement of ABI may be considered for the detection of advanced LEAD.[153,190]	IIb	B

European Heart Journal (2018) 39, 3021–3104

檢查有無**器官損傷**

Recommendations	Class[a]	Level[b]
Kidney		
Measurement of serum creatinine and eGFR is recommended in all hypertensive patients.[180]	I	B
Measurement of urine albumin:creatinine ratio is recommended in all hypertensive patients.[43,180]	I	B
Renal ultrasound and Doppler examination should be considered in patients with impaired renal function, albuminuria, or for suspected secondary hypertension.	IIa	C
Fundoscopy		
Is recommended in patients with grades 2 or 3 hypertension and all hypertensive patients with diabetes.	I	C
May be considered in other hypertensive patients.	IIb	C
Brain		
In hypertensive patients with neurological symptoms and/or cognitive decline, brain MRI or CT should be considered for detecting brain infarctions, microbleeds, and white matter lesions.[168,169]	IIa	B

European Heart Journal (2018) 39, 3021–3104

建議該做的檢查

Routine tests

- Hemoglobin and hematocrit
- Serum creatinine with estimated creatinine clearance (Cockroft-Gault formula) or glomerular filtration rate (Modification of Diet in Renal Disease formula)
- Serum sodium, potassium and calcium
- Fasting glucose
- Total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides
- Serum uric acid
- Urinalysis
- Electrocardiogram
- Chest X-ray

Recommended tests

- Oral glucose tolerance test or HbA1C (if fasting plasma glucose $\geq$100 mg/dL)
- High sensitivity C reactive protein
- Quantitative microalbuminuria/proteinuria
- Fundoscopy
- Echocardiography
- Carotid ultrasound
- Home and ambulatory blood pressure monitoring
- Ankle-brachial index
- Pulse wave velocity

Chiang et al. J Chinese Medical Association 2015;78:1-47

大 綱

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

血壓藥如何選擇？

- 病患的共病：器官保護/副作用
- 離目標多遠：降壓強度/複方藥

血壓藥如何選擇？

- 病患的共病：器官保護/副作用
- 離目標多遠：降壓強度/複方藥

器官保護

Clinical conditions	Drugs
Target organ damage	
Left ventricular hypertrophy	ARB
Microalbuminuria	ACEI, ARB
Asymptomatic atherosclerosis	CCB
Clinical events	
History of myocardial infarction	BB, ACEI, ARB
Coronary Heart Disease	BB, ACEI, ARB, CCB (long-acting)
Heart failure	Thiazide diuretic, loop diuretic, BB, ACEI, ARB, MRA
Stroke	ACEI, ARB, Thiazide diuretic, CCB,
Chronic kidney disease	ACEI, ARB, loop diuretic
Peripheral artery disease	CCB
Diabetes mellitus	ACEI, ARB, DRI
Associated conditions	
Isolated systolic hypertension	Thiazide diuretic, CCB, ARB
Metabolic syndrome	ACEI,ARB
Benign prostate hypertrophy	Alpha-blocker

ACEI/ARB：心、腎

CCB：動脈硬化

J Chinese Medical Association 2015;78:1-47

不適合用特定降血壓藥的情形

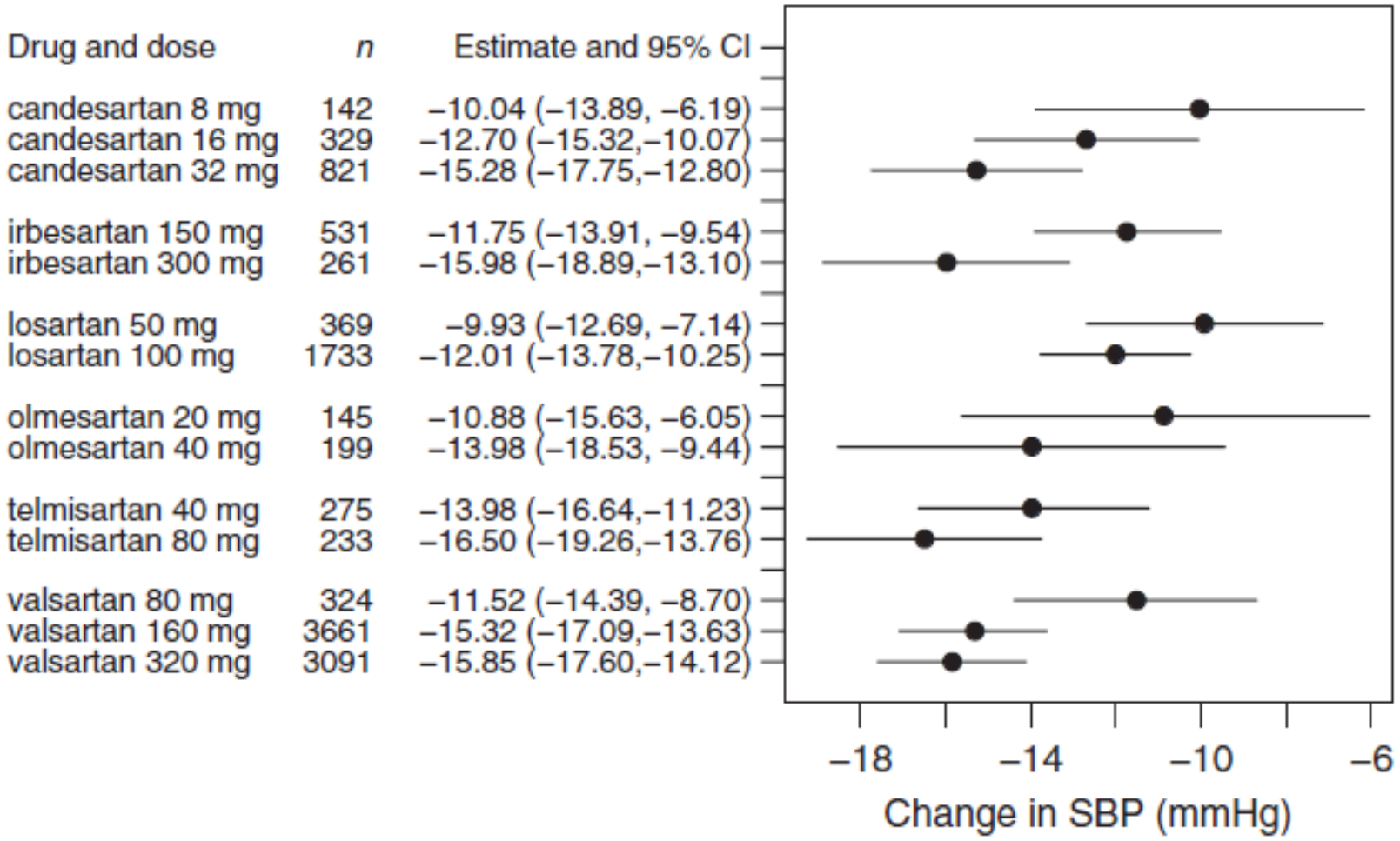
	Contraindications	Unfavorable conditions
Thiazide diuretics		Gout, hypokalemia, hyponatremia, metabolic syndrome, pregnancy
BB	Bronchial asthma, sick sinus syndrome, 2nd and 3rd degree AV block	Peripheral artery disease, Metabolic syndrome
CCB (non-DHP)	Sick sinus syndrome, 2nd and 3rd degree AV block	Systolic heart failure
ACEI	Bilateral renal artery stenosis, pregnancy, angioedema	Hyperkalemia
ARB	Bilateral renal artery stenosis, pregnancy	Hyperkalemia
DRI	Bilateral renal artery stenosis, pregnancy	Hyperkalemia
MRA	Hyperkalemia	
Alpha-blocker		Systolic heart failure

J Chinese Medical Association 2015;78:1-47

血壓藥如何選擇？

- 病患的共病：器官保護/副作用
- 離目標多遠：降壓強度/複方藥

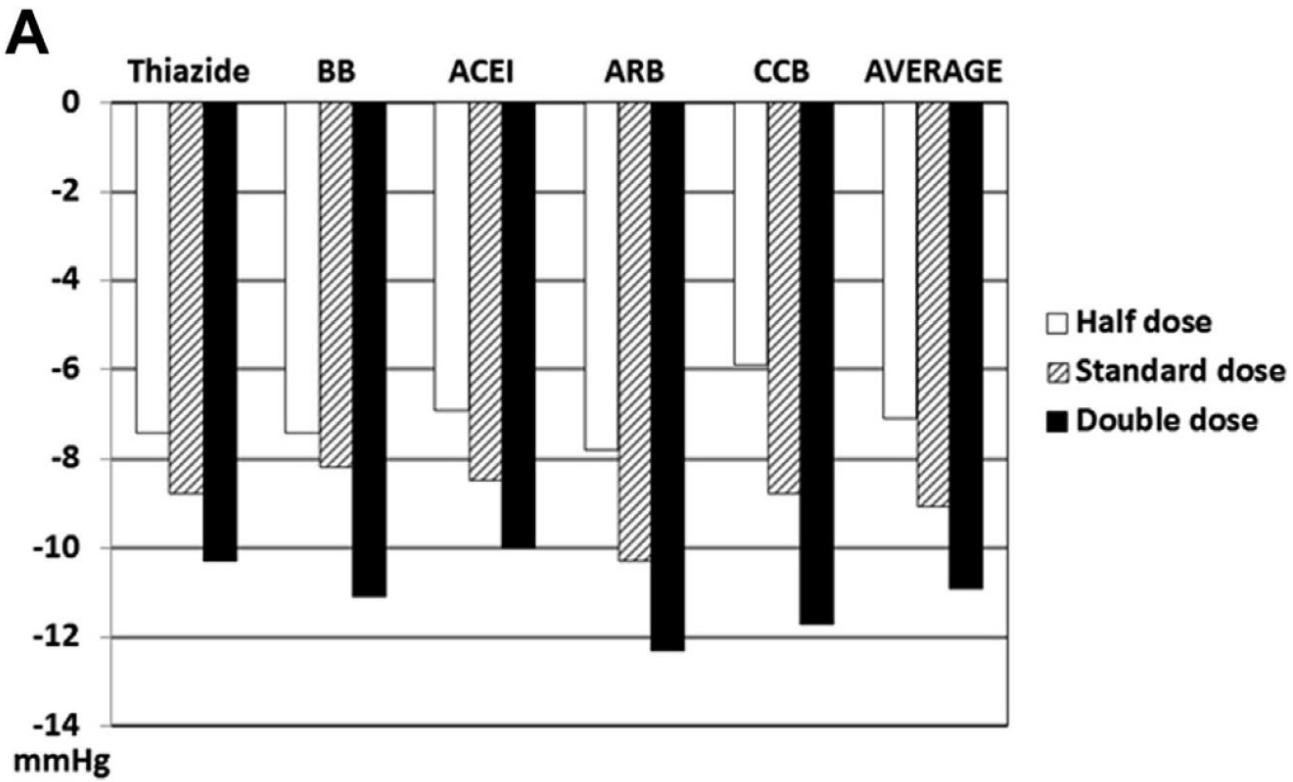
不同ARB的降壓效果

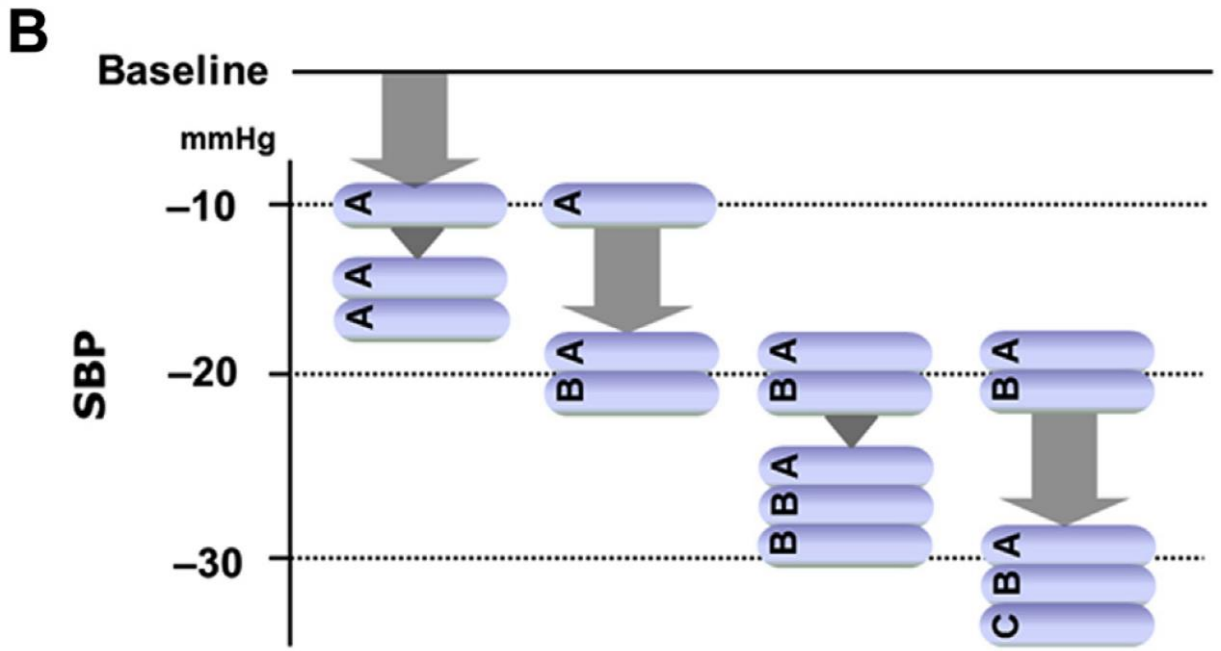


Data extracted from 31 RCTs (n=13,110)

Int J Clin Pract. 2009 May;63(5):766-75

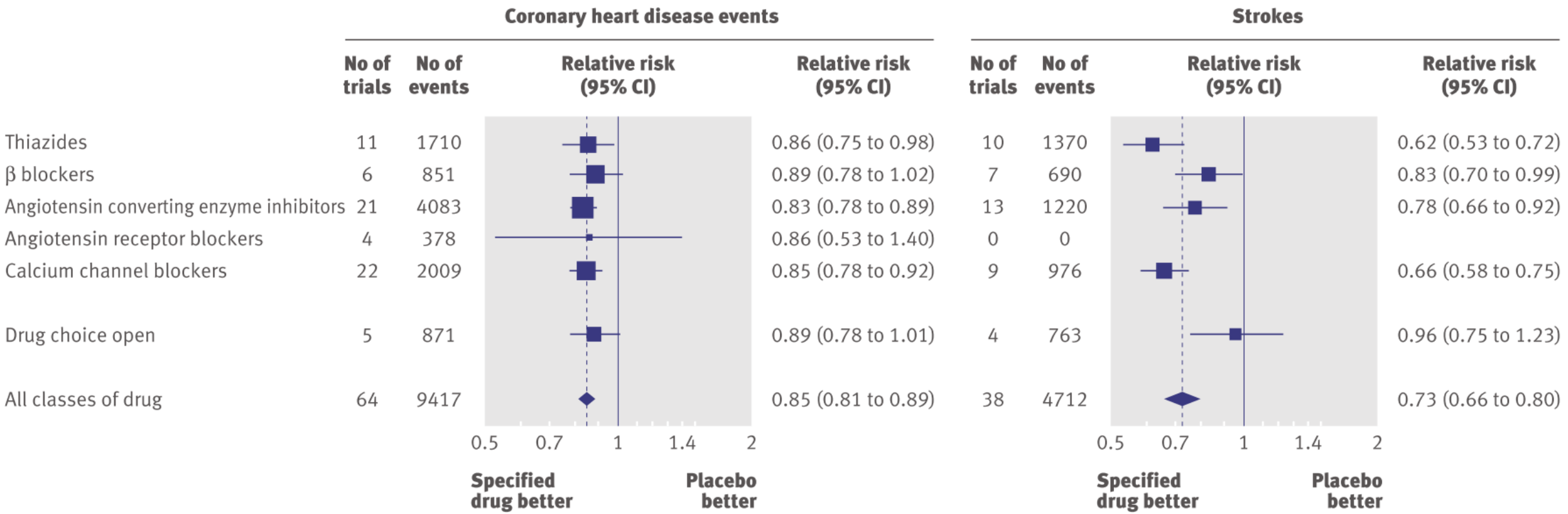
多種用藥搭配使用效果較佳
Rule of 10





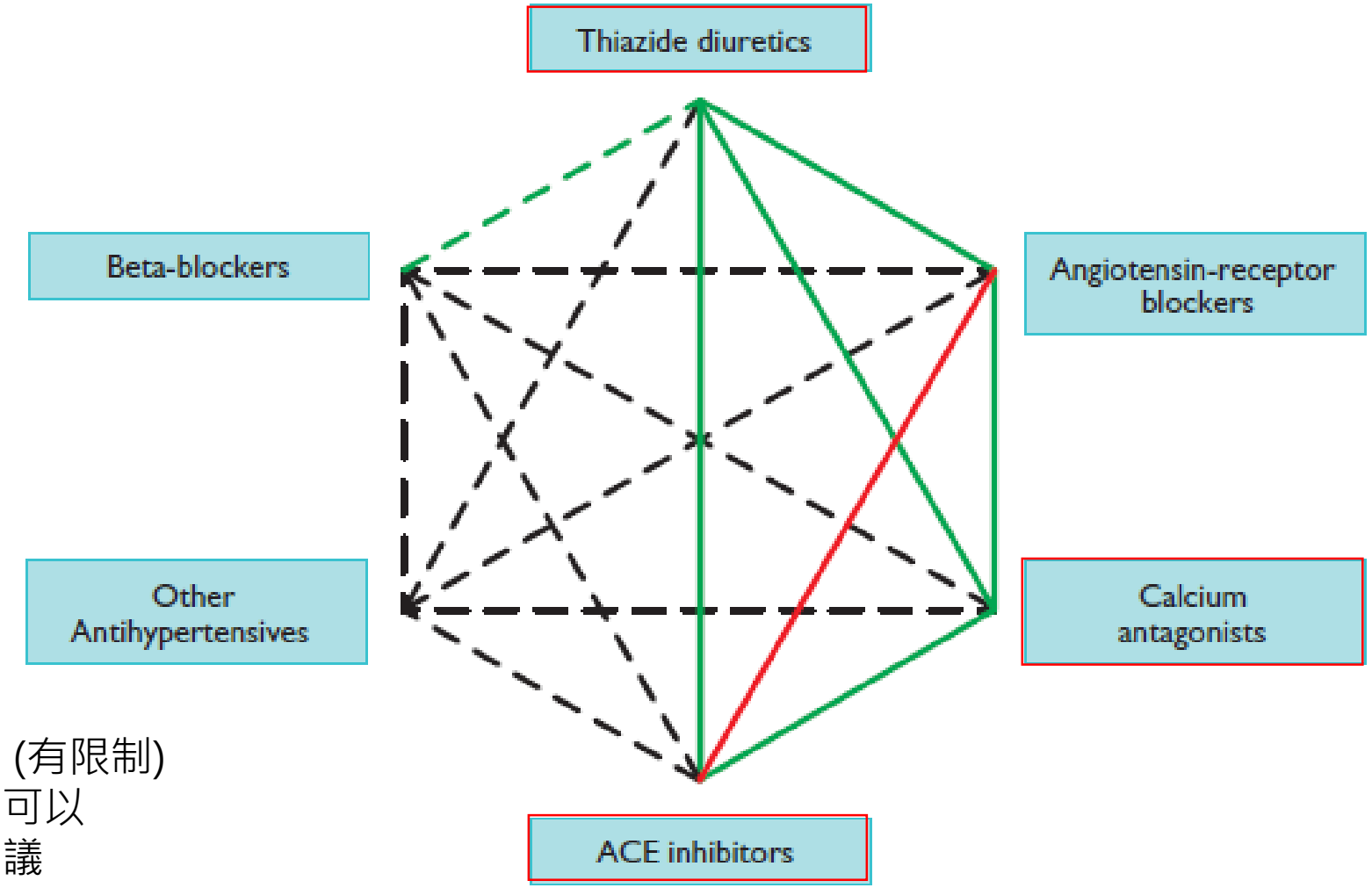
J Chinese Medical Association 2015;78:1-47

各種降壓藥**初級預防**的效果



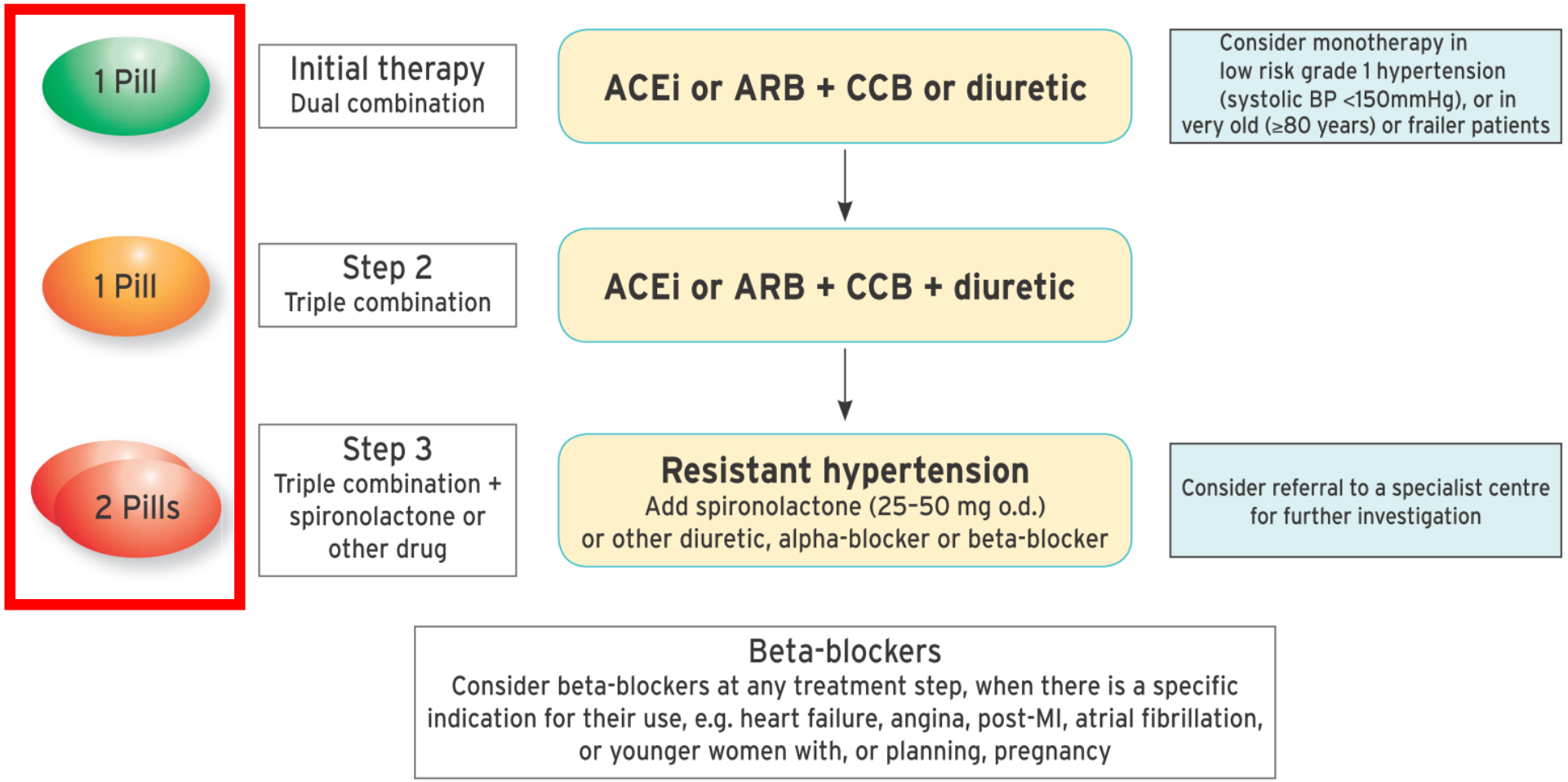
BMJ 2009;338:b1665

降血壓藥的搭配



2013 ESH/ESC guideline for the management of arterial hypertension

一般從 A+C 或 A+D 開始
(除非有其他考量)



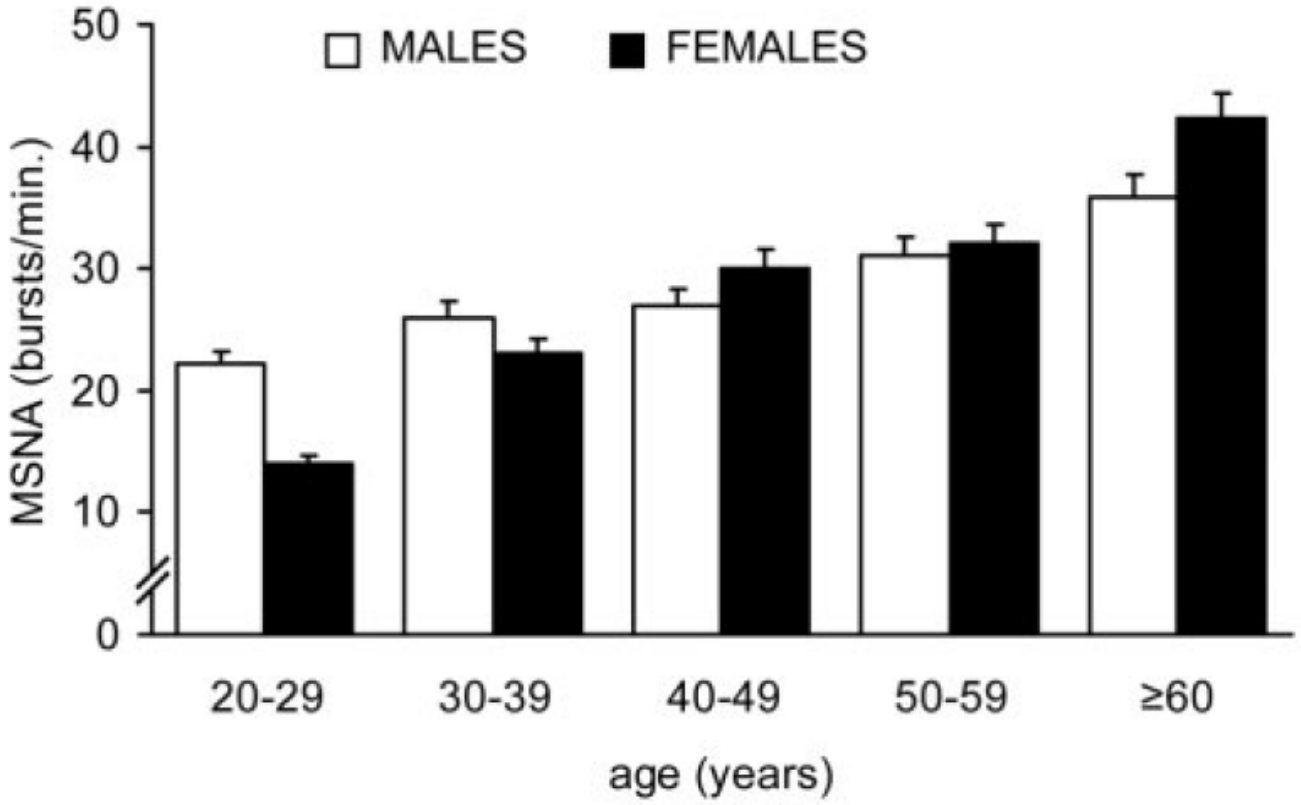
2018 ESH/ESC guideline for the management of arterial hypertension

何時會想用beta-blockers**降血壓**？

合併

- 心肌梗塞
- 心衰竭
- 心跳快
- 心律不整

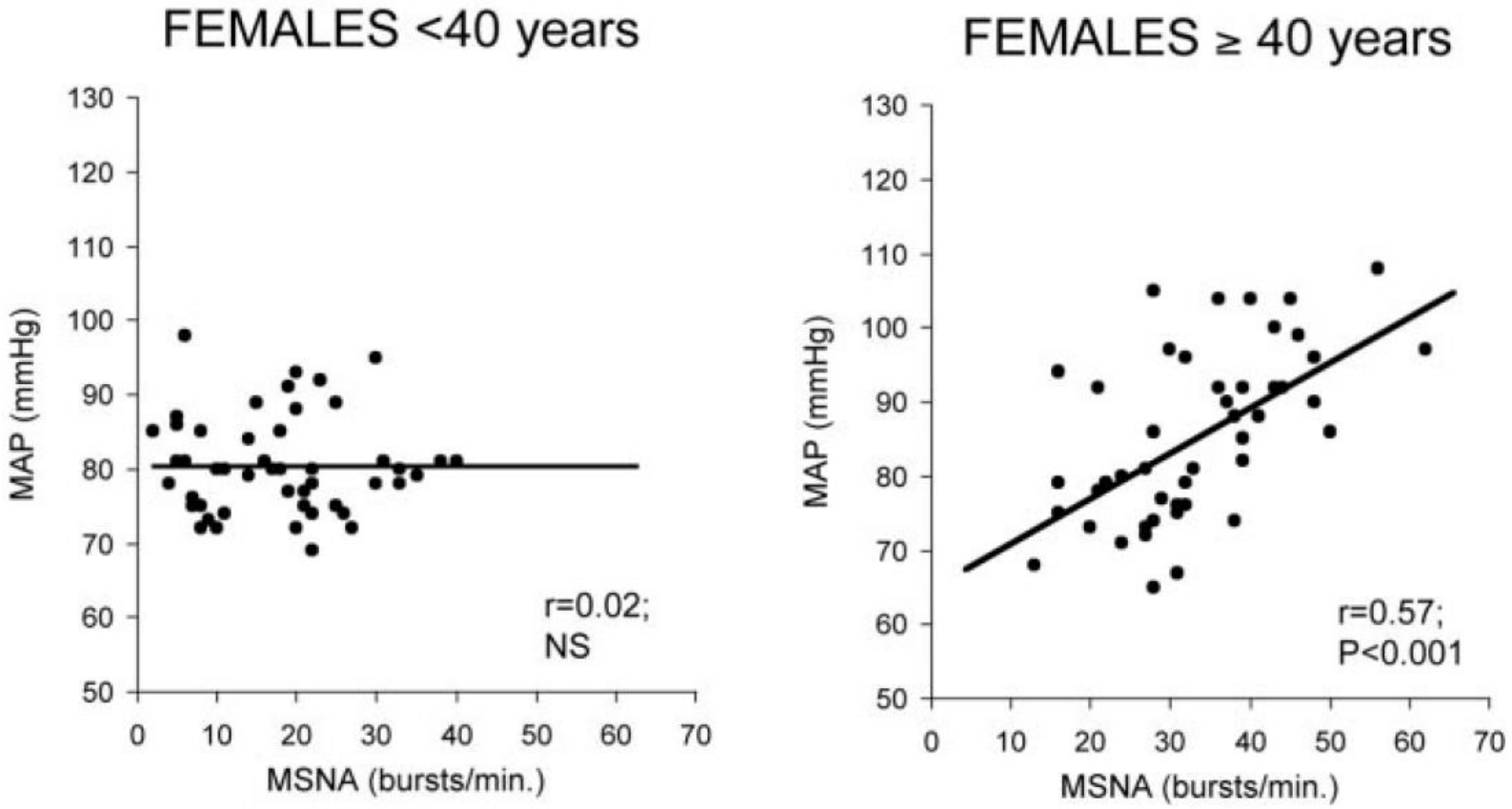
年長女性**交感神經**普遍較興奮



96 females, 120 males
MSNA: muscle sympathetic nervous activity

Narkiewicz et al. Hypertension 2005;45:522-525

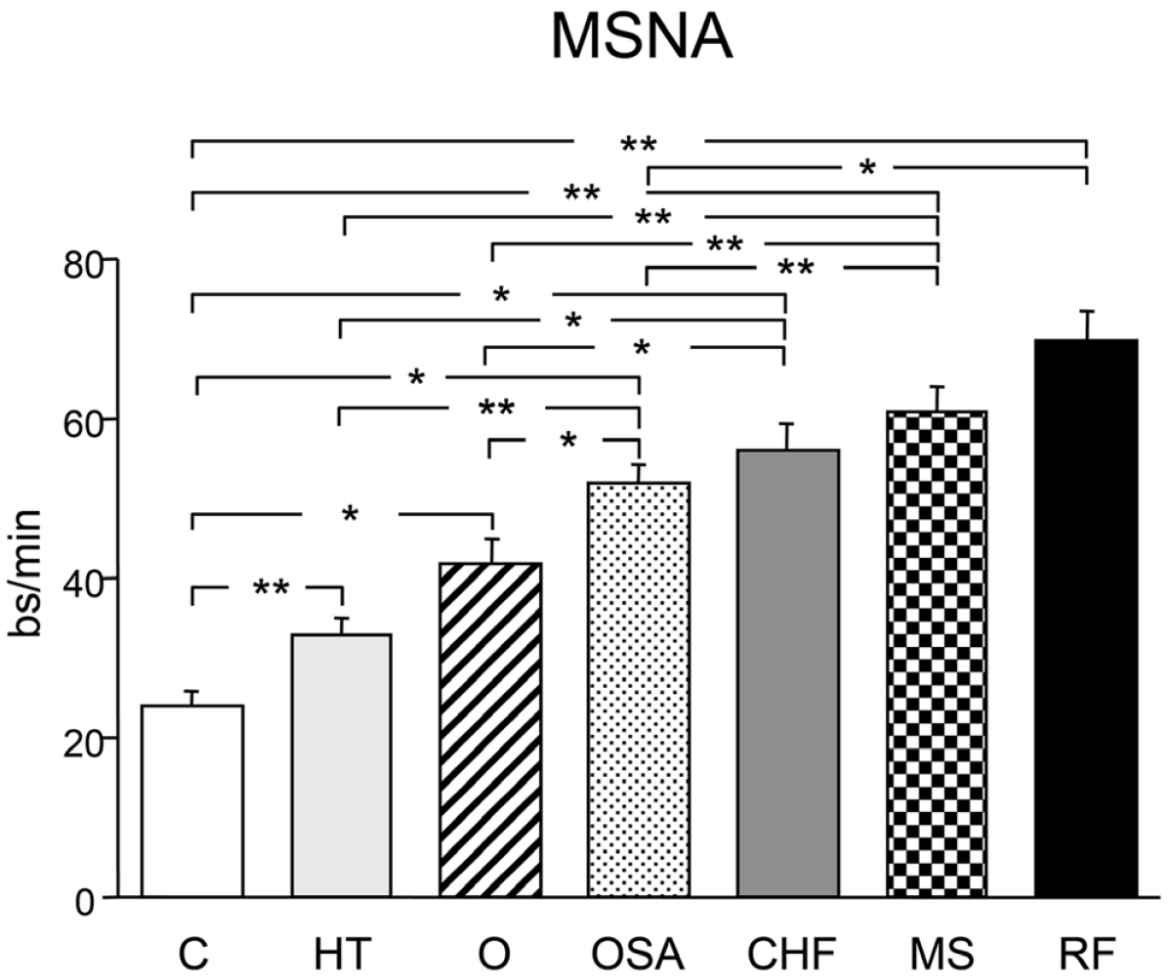
年長女性**交感神經**興奮程度和血壓呈正相關



96 females
MSNA: muscle sympathetic nervous activity

Narkiewicz et al. Hypertension 2005;45:522-525

許多情形都會伴隨**交感神經**興奮

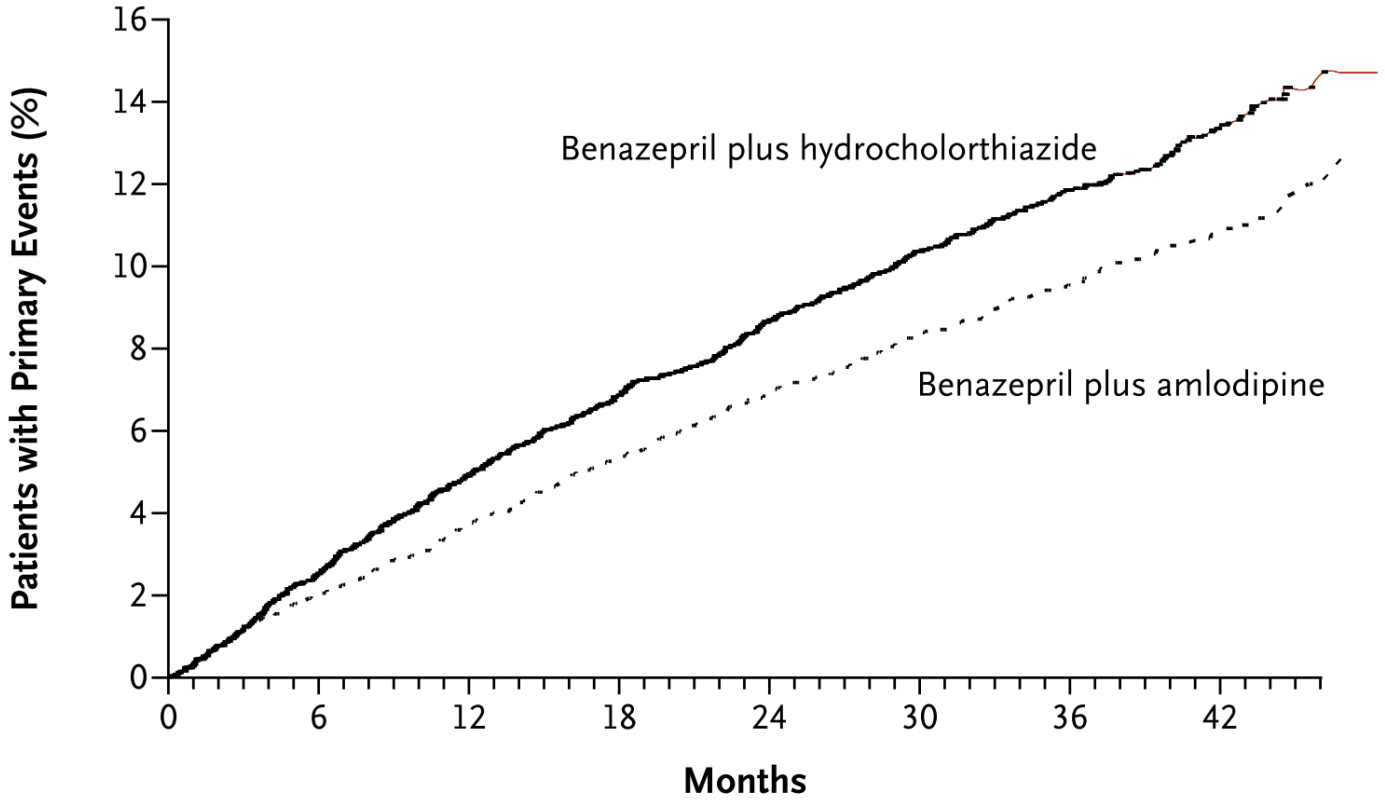


MSNA: muscle sympathetic nervous activity
C: healthy controls
HT: hypertension
O: obesity
OSA: obstructive sleep apnea
CHF: congestive heart failure
MS: metabolic syndrome
RF: renal failure

Mancia et al. Circ Res. 2014;114:1004-1021

心血管高危險群 A+C > A+D

Myocardial infarction
Revascularization
Stroke
Chronic kidney disease
Peripheral arterial disease
Left ventricular hypertrophy
Diabetes mellitus

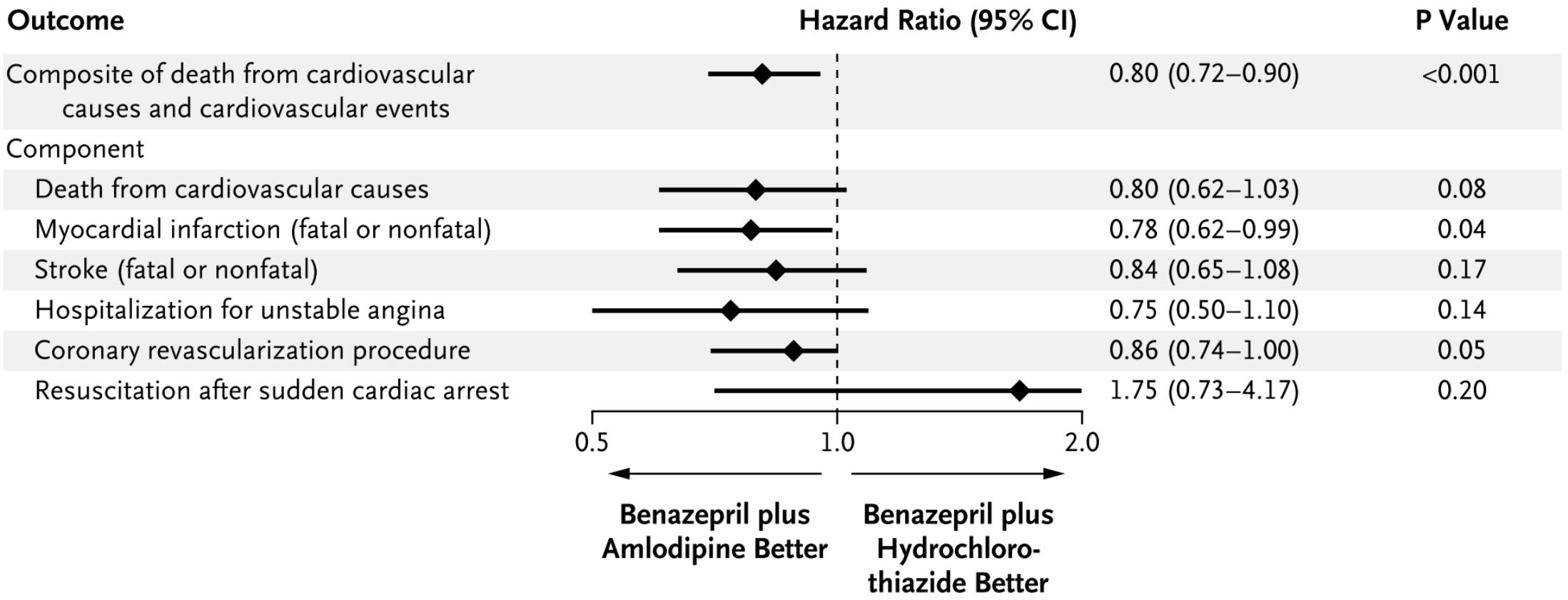


No. at Risk							
Benazepril plus amlodipine	5512	5317	5141	4959	4739	2826	1447
Benazepril plus hydrochlorothiazide	5483	5274	5082	4892	4655	2749	1390

Primary events: CV death and CV events

ACCOMPLISH. NEJM 2008;359:2417-28

對於心血管高危險群
A+C 比 A+D 更能預防心肌梗塞



ACCOMPLISH. NEJM 2008;359:2417-28

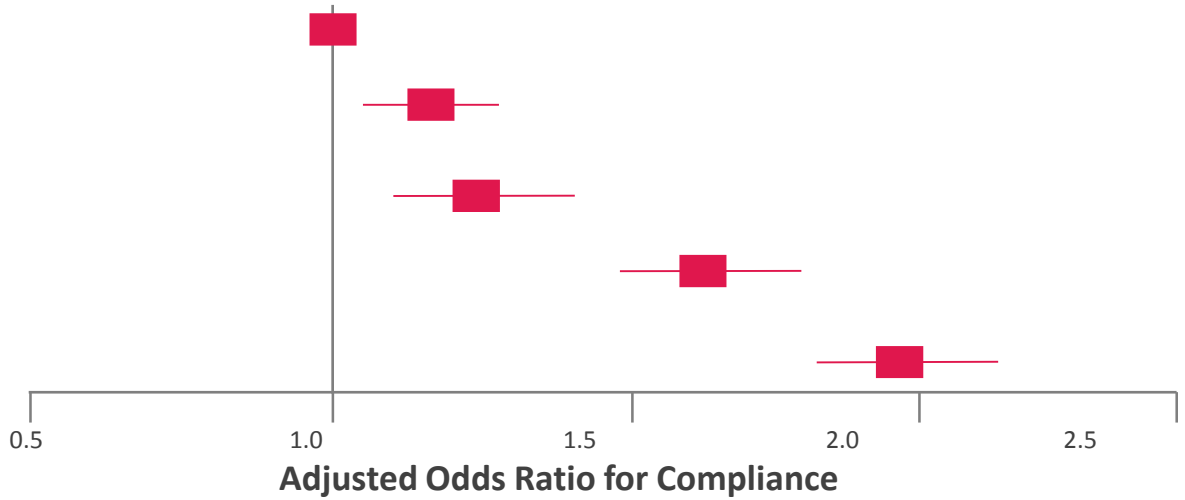
藥愈少顆，順從性愈高

No. of Additional Prescription Medications

Less Pills

6+
3-5
2
1
0

Relative likelihood of compliance based on No. of Additional Medications

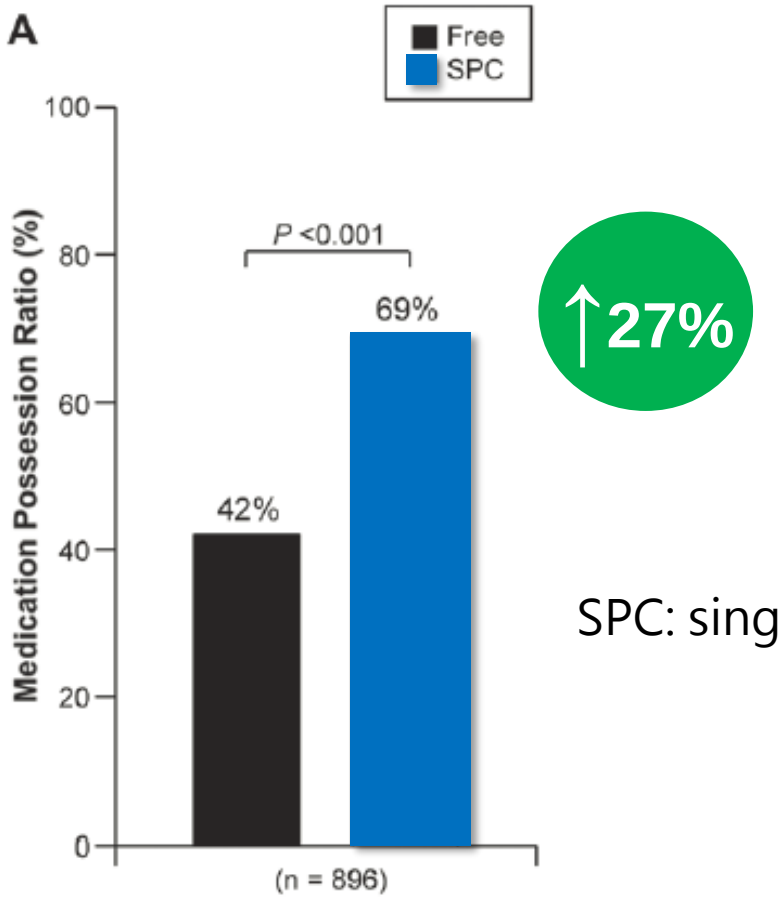


Baseline medication: concomitant antihypertensive and lipid lowering therapy

Increasing Levels of Compliance

Chapman RH, et al. Arch Intern Med 2005;165:1147-52.

單錠複方可以增加服藥順從性



SPC: single-pill combination

Wang et al. Hypertension. 2014;63:958-967

順從性佳有較低的心血管風險和死亡率

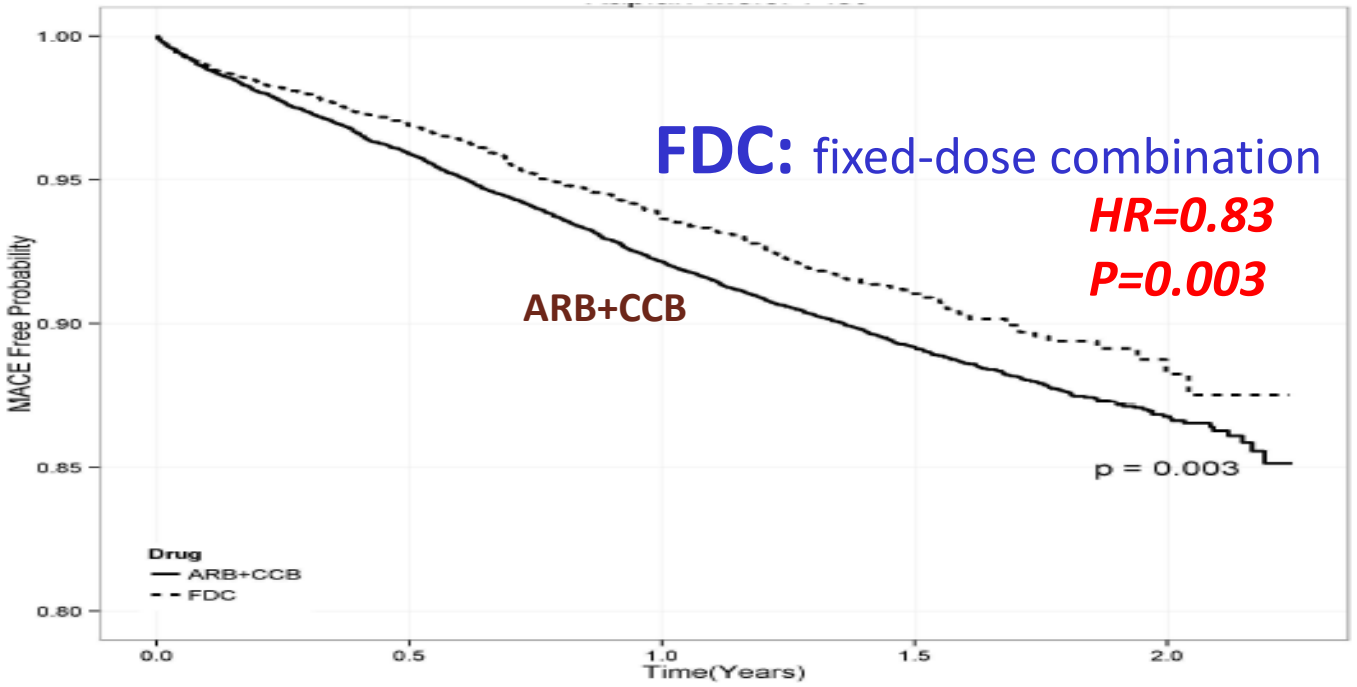
Meta-analysis of prospective epidemiological studies, including 44 prospective studies comprising 1978,919 participants

	No. of studies	No. of participants	No. of events	RR (95% CI)
(2) Method to assess adherence to antihypertensives:				
Medication possession ratio	7	138,012	11,723*	0.73 (0.63, 0.83)
	3	5118	644	0.48 (0.31, 0.73)
Proportion of days covered	3	307,387	19,201	0.84 (0.71, 1.00)
	3	50,411	8,677*	0.69 (0.53, 0.90)
Other indirect**	3	106,744	5262	0.87 (0.82, 0.92)
	5	150,069	2,967*	0.81 (0.70, 0.93)

*Groups in which not all studies reported the number of events. No study was available for these analyses that used a direct method to assess adherence.
**Includes the following methods: medication refill adherence (MRA), fill frequency, purchase or not or 3 month supply, persistence or not for >90 days, length of continuous use in first 2 years of treatment, proportion of study visits when pills taken >80% since last visit, amount taken/amount received, returned pill count, self report, the MORISKY instrument.

European Heart Journal (2013) 34, 2940–2948

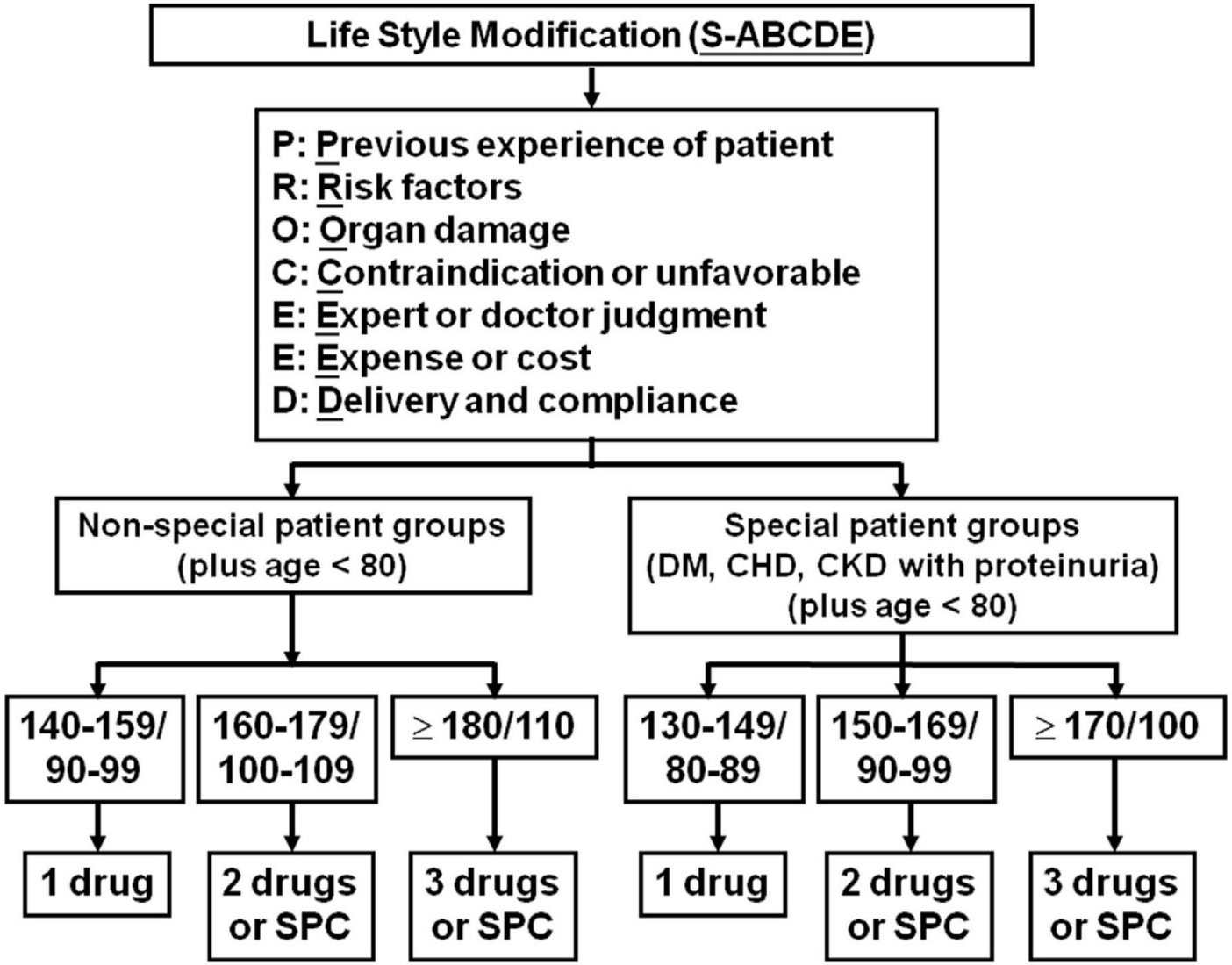
使用 A+C 的複方比分開使用更能降低心血管風險



	FDC	ARB+CCB	p-value
Myocardial Infarction	19 (0.58%)	122 (0.92%)	0.052
Percutaneous cardiac intervention	25 (0.76%)	167 (1.26%)	0.015
Coronary artery bypass grafting	3 (0.09%)	11 (0.08%)	1.000
Heart failure	70 (2.12%)	431 (3.26%)	<0.001
Stroke	197 (5.97%)	864 (6.54%)	0.228
Malignant dysrhythmia	6 (0.18%)	55 (0.42%)	0.047
Thrombolysis	29 (0.88%)	183 (1.39%)	0.021
Cardiac shock	4 (0.12%)	16 (0.12%)	1.000
Pulmonary embolism	1 (0.03%)	10 (0.08%)	0.705
Deep vein thrombosis	8 (0.24%)	32 (0.24%)	1.000

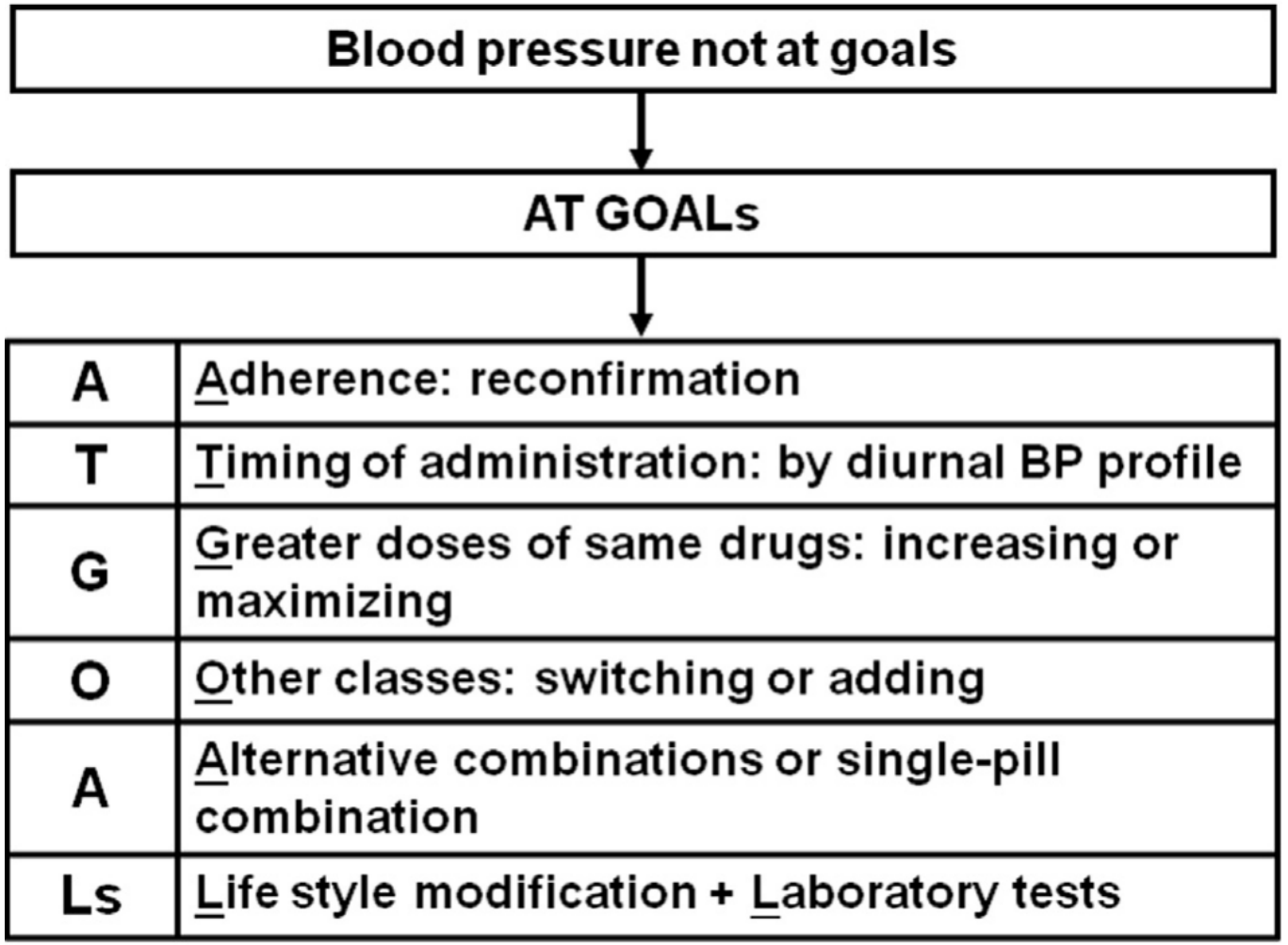
J Clin Hypertens (Greenwich) 2014;17(1):51-8.

依照病患的屬性選擇藥物



J Chinese Medical Association 2015;78:1-47

如果血壓控制不好

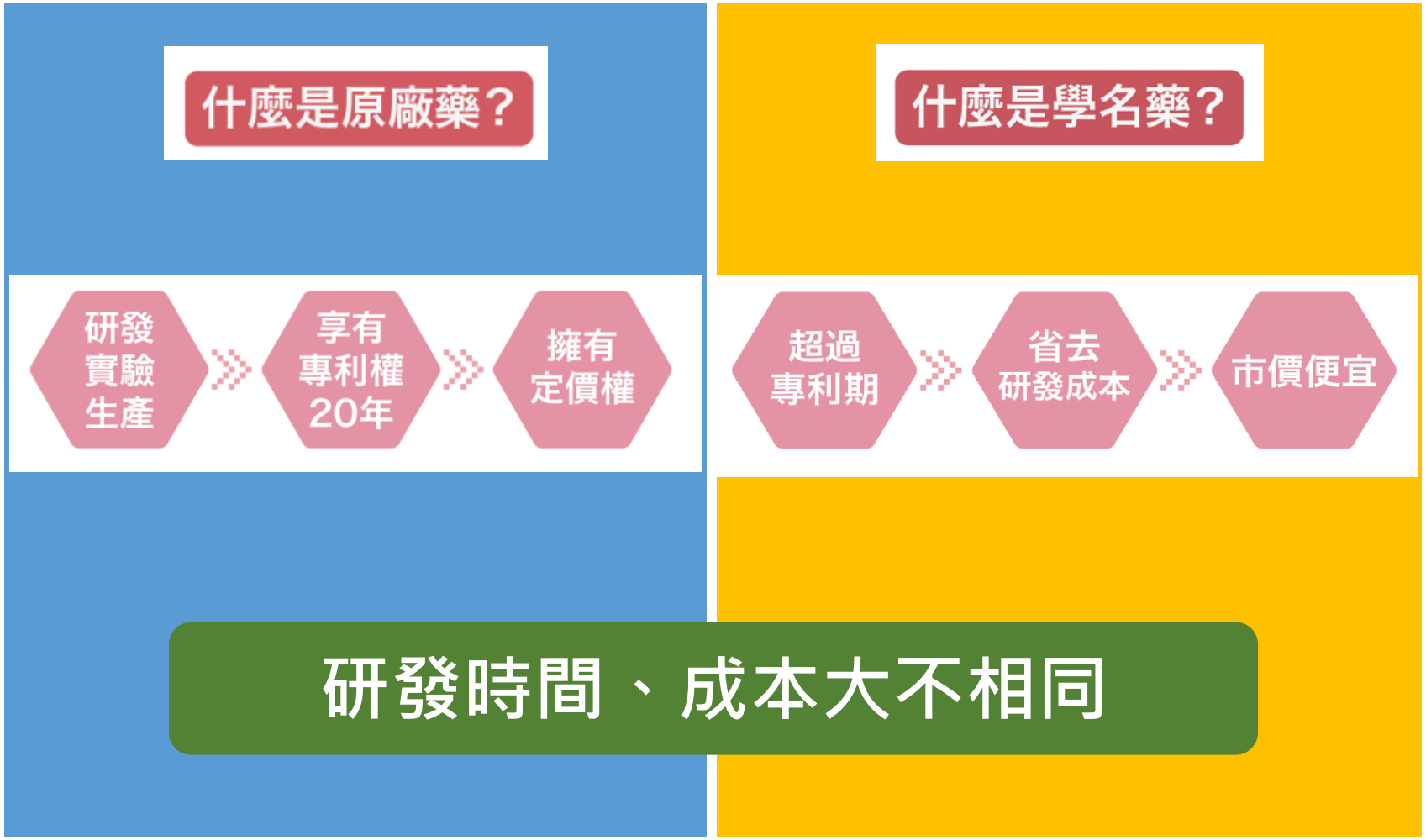


Chiang et al. J Chinese Medical Association 2015;78:1-47

大 綱

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

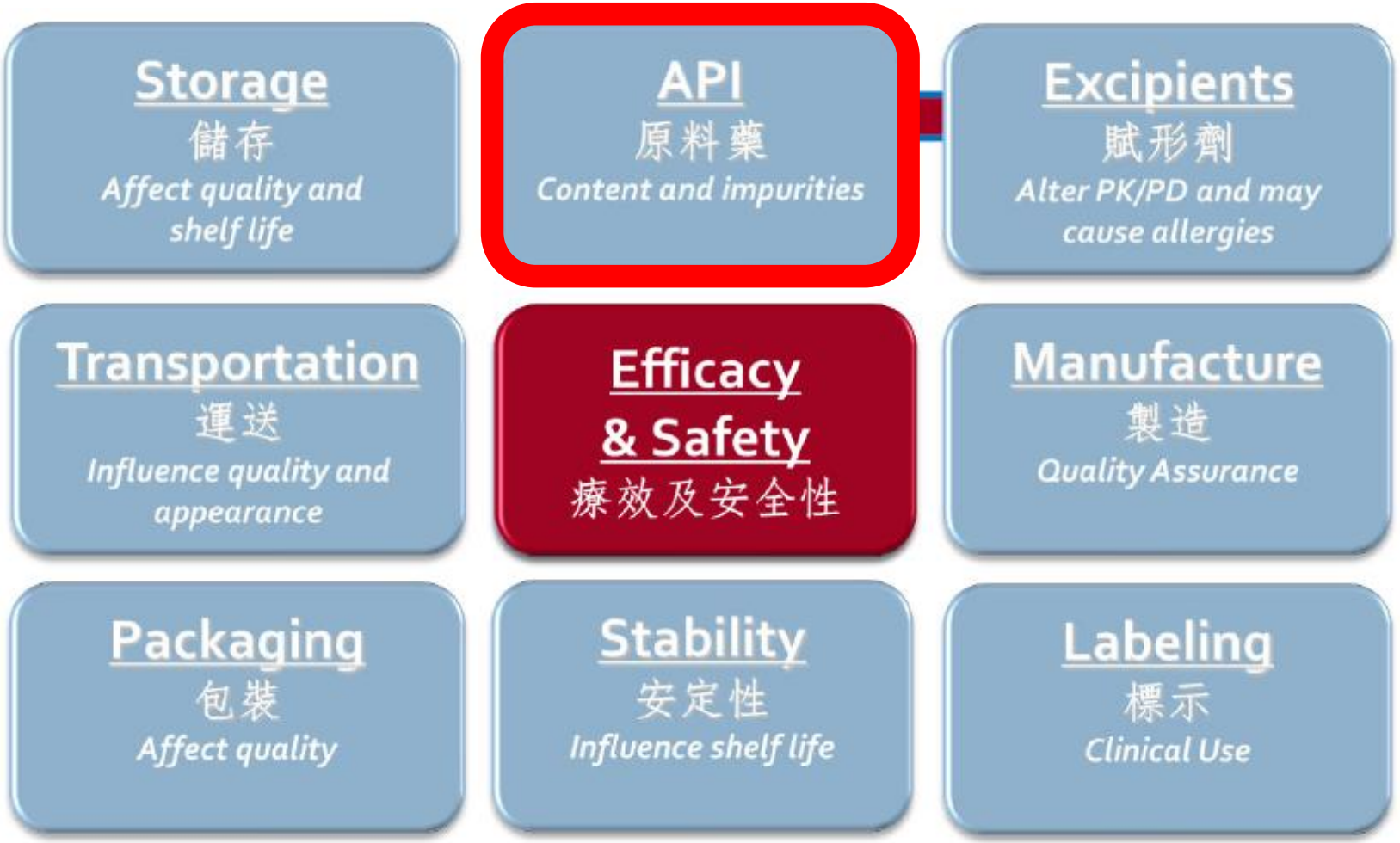
原廠藥與學名藥的差別



Ref: 醫師勞動改革小組

除了原料藥，還有其他的關鍵

- 任何藥品的組成成分及製造的過程都可能會影響到藥品品質



新藥與學名藥上市審查項目的差異
學名藥其療效與安全性只須通過BA/BE

Review Items 審查項目	New Chemical Entities (NCE) 新藥	Generics 學名藥
Efficacy & Safety 療效與安全性	● Pharmacology ● Toxicology ● PK, Pharmacokinetics ● PD, Pharmacodynamics ● Pre-clinical Data ● Clinical Trials Results	● BA, Bioavailability ● BE, Bioequivalence 
Quality 品質	● CMC, Chemistry, Manufacturing and Control ● GLP, Good Laboratory Practice ● GCP, Good Clinical Practice ● cGMP, Current Good Manufacturing Practice	
Package Insert 仿單	Labeling (Direction of Use)	

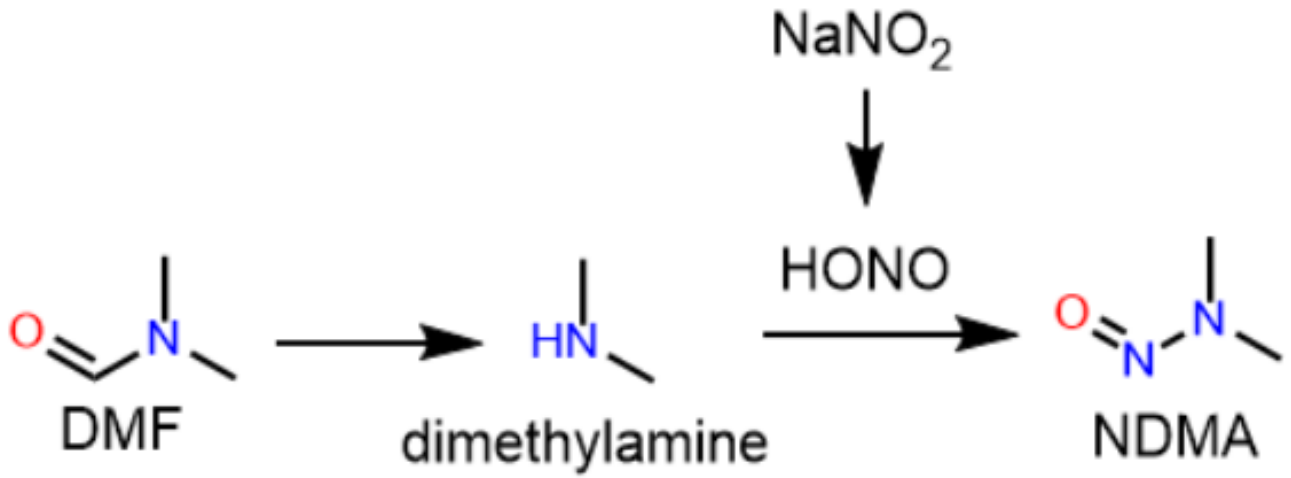
相同的**食譜**，做出來的菜也可能不同

食材	製作過程	安全性
種類	廚具	衛生
等級	熟度	品管
新鮮度	手藝	檢驗

≠

原料藥製程中添加之特定溶劑及反應物有關

製程



使用**DMF溶劑**在酸性環境
與亞硝酸鹽反應會產生NDMA

食藥署於3月12日公告5種Sartan類不純物檢驗結果：
諾華含Valsartan全產品均不含NDMA或NDEA

衛生福利部食品藥物管理署
Taiwan Food and Drug Administration

食藥署公布目前市售效期內5種沙坦類（Sartan）藥品中「N-亞硝基二甲胺（NDMA）」與「N-亞硝基二乙胺（NDEA）」不純物之檢驗結果 【發布日期：2019-03-12】

二、 強化業者自我管理責任，確保原料藥品質: 要求藥廠應自主逐批檢驗原料藥，未檢出NDMA或NDEA始得供製造使用，並將其列入GMP稽查重點，以確保業者落實執行。

三、 輔導業者主動評估及檢測製程，確保民眾用藥安全:食藥署已要求各藥品許可證持有商應主動評估及檢測製程所可能產生亞硝胺類(Nitrosamine)不純物之風險，並且應以經確效的分析方法檢測。若發現存在nitrosamine者，應主動調查發生原因或變更製程，並且通報食藥署，如對於製程有任何疑問，可檢附相關資料向食藥署申請諮詢。

TFDA公告資訊
https://www.fda.gov.tw/TC/newsContent.aspx?cid=4&id=t448587

大 綱

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

Is it a stroke?

Act F.A.S.T.

FACE
droops
微笑

ARM
weakness
殭屍

SPEECH
difficulty
會說話

TIME
is critical.

總結

- 為什麼要控制血壓？

→ 避免血管受到傷害

- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

總結

- 為什麼要控制血壓？
- 應將血壓控制在多少？

→ 高危險群應積極控制

- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

總結

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？

→ 排除影響血壓的因素

- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

總結

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？

→ 複方藥可改善服藥順從性

- 血壓藥致癌風波
- 辛辛那提中風指標

總結

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波

→ 並非所有血壓藥都有問題

- 辛辛那提中風指標

總結

- 為什麼要控制血壓？
- 應將血壓控制在多少？
- 該注意哪些細節？
- 血壓藥如何選擇？
- 血壓藥致癌風波
- 辛辛那提中風指標

→ 微笑、殭屍、會說話

謝謝大家的聆聽！