

## 고혈압 최신지견

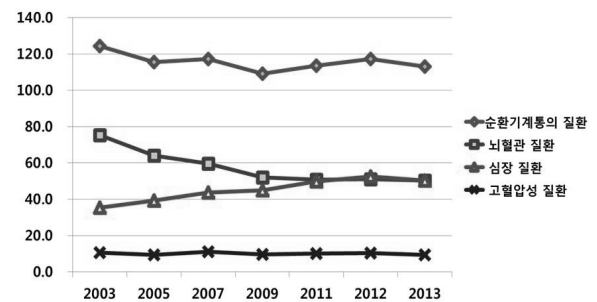
김 영 식

울산의대 서울아산병원 가정의학과

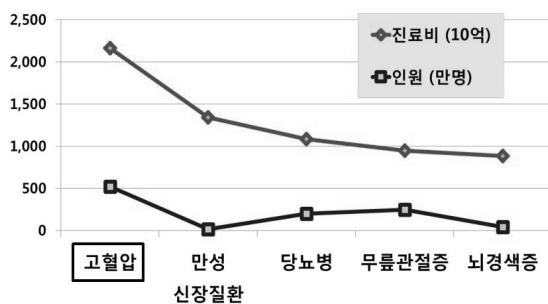
### 발표 내용

- ㄴ 고혈압 관련 역학
- ㄴ 고혈압 치료 근거
- ㄴ 고혈압 진단
- ㄴ 고혈압 약물요법
  - 장기 보호효과
  - 항고혈압제 진료지침
- ㄴ 항고혈압제 순응도
- ㄴ 항고혈압제 병합요법

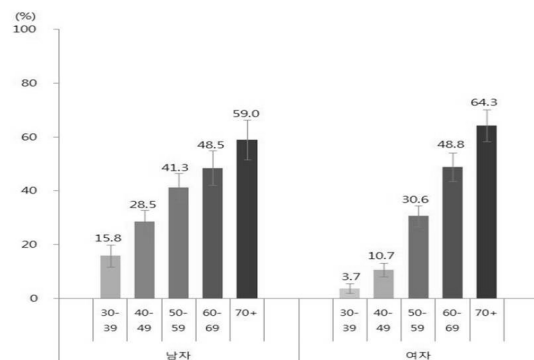
### 순환기 질환 사망률 추이



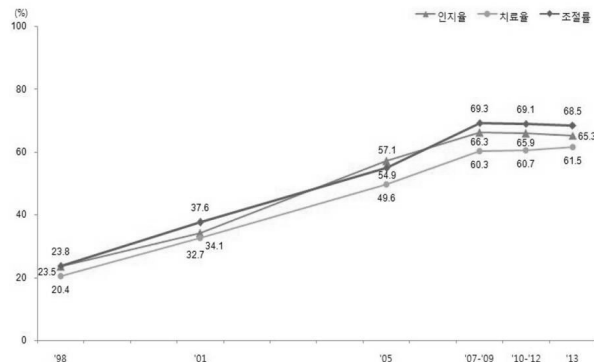
### 만성질환 진료비 2013



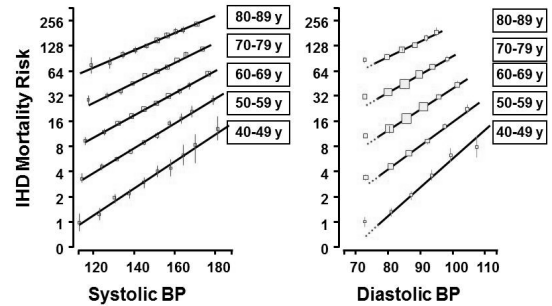
### 연령별 고혈압 유병률 2013



## 고혈압 인지율, 치료율, 조절률 ≥30세



## CAD Mortality & Usual BP by Age



## 혈압의 측정과 고혈압의 진단

- 진료실에서 혈압을 측정할 때는 측정의 원리를 적용하여 정확하게 측정해야 한다.
- 문제점
  - 백의고혈압(white coat hypertension)
  - 가면고혈압(masked hypertension)
- 대책
  - 가정자기혈압 측정(home BP monitoring)
  - 24시간 활동혈압(24h ambulatory BP monitoring)

## 혈압 분류 및 고혈압 진단 KAMS 2014

혈압분류	수축기혈압 (mmHg)	이완기혈압 (mmHg)
정상혈압*	< 120	그리고 < 80
고혈압 전단계	1기 120 - 129	또는 80 - 84
	2기 130 - 139	또는 85 - 89
고혈압	1기 140 - 159	또는 90 - 99
	2기 ≥ 160	또는 ≥ 100
수축기 단독고혈압	≥ 140	그리고 < 90

## 측정방법에 따른 고혈압 기준

혈압 측정법	수축기혈압 (mmHg)	이완기혈압 (mmHg)
진료실 혈압	≥ 140	≥ 90
24시간 활동혈압		
일일 평균 혈압	≥ 130	≥ 80
주간 평균 혈압	≥ 135	≥ 85
야간 평균 혈압	≥ 120	≥ 70
가정혈압	≥ 135	≥ 85

## 생활습관개선에 따른 혈압감소 효과

생활요법	혈압감소 수축기/확장기혈압(mmHg)	권고 사항
소금섭취 제한	-5.1/-2.7	하루 소금 6g 이하
체중감량	-1.1/-0.9	매 체중 1kg 감소
절주	-3.9/-2.4	하루 2잔 이하(남자 20-30 gm, 여자 10-20 gm의 알코올)
운동	-4.9/-3.7	하루 30~50분, 일주일에 5일 이상
식사조절	-11.4/-5.5	채식 위주의 건강한 식습관

## 2013 ESH/ESC, 2014 KAMS/JNC8

※ 심혈관 위험에 상관없이 목표혈압 < 140/90mmHg

● DM, CKD, Stroke, CHD

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
A SBP goal <140 mmHg:		
a) is recommended in patients at low-moderate CV risk;	I	B
b) is recommended in patients with diabetes;	I	A
c) should be considered in patients with previous stroke or TIA;	Ila	B
d) should be considered in patients with CHD;	Ila	B
e) should be considered in patients with diabetic or non-diabetic CKD.	Ila	B

## 2013 ESH/ESC, 2014 KAMS 지침

※ 고령환자 수축기 고혈압

치료기준 ≥ 160mmHg,

치료목표: <140 (<80세)

<150 (≥80세)

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In elderly hypertensives less than 80 years old with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	Ilb	C
In individuals older than 80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg provided they are in good physical and mental conditions.	I	B

## 2014 JNC8 지침

※ 고령환자 수축기 고혈압

치료목표: < 150mmHg (≥60세)

< 140mmHg (<60세, DM, CKD)

Guideline	Population	Goal BP, mm Hg	Initial Drug Treatment Options
2014 Hypertension guideline	General ≥60 y	<150/90	Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB
	General <60 y	<140/90	Black: thiazide-type diuretic or CCB
	Diabetes	<140/90	Thiazide-type diuretic, ACEI, ARB, or CCB
	CKD	<140/90	ACEI or ARB

## 2013 ESH/ESC, 2014 KAMS 지침

※ 2, 3단계 고혈압은 신속히 약물치료 시작 권고

● 생활습관개선과 동시 또는 몇 주후

※ 고위험군 1단계 고혈압: 약물치료 권고

● OD, DM, CVD, CKD

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Prompt initiation of drug treatment is recommended in individuals with grade 2 and 3 hypertension with any level of CV risk, a few weeks after or simultaneously with initiation of lifestyle changes.	I	A
Lowering BP with drugs is also recommended when total CV risk is high because of OD, diabetes, CVD or CKD, even when hypertension is in the grade 1 range.	I	B

## 2013 ESH/ESC, 2014 KAMS 요약

※ 1차 선택약 :

●이뇨제:

※티아자이드, 클로르탈리돈, 인다파마이드

●CCB

●ACEI, ARB

●BB

## 2014 JNC8 요약

※ 1차 선택약 :

●이뇨제(티아자이드),CCB, ACEI, ARB

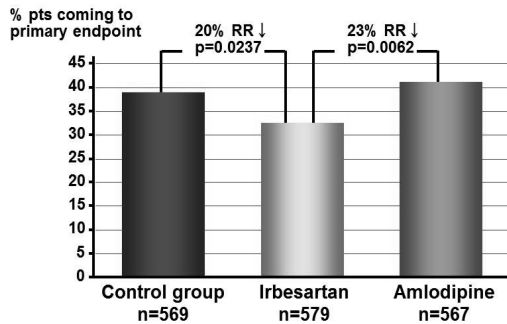
※ 2차 선택약 :

●Aldosterone antagonist: Spironolactone

●베타차단제

●알파차단제

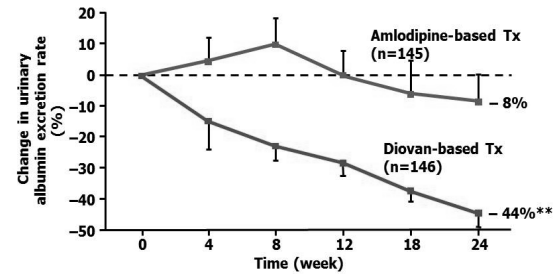
### IDNT: 신부전 진행률 비교: ARB vs CCB



Primary endpoint = Doubling of serum creatinine, ESRD, total mortality  
RR = Relative Risk

Lewis et al. *N Engl J* 2001

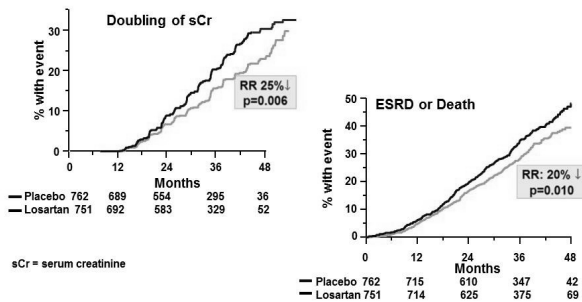
### MARVAL: 당뇨병에서 미세알부민뇨 개선효과: ARB vs CCB



\*\*p<0.001 vs amlodipine

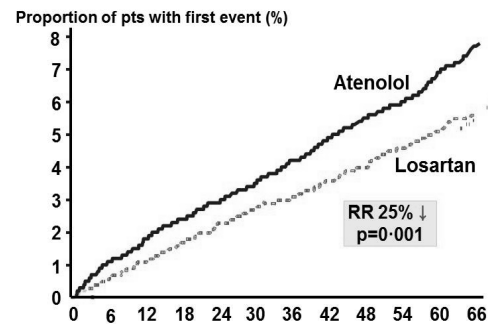
Viberti G et al. *Circulation* 2002;106:672-8

### RENAAL: HT에서 ARB 신장보호 효과



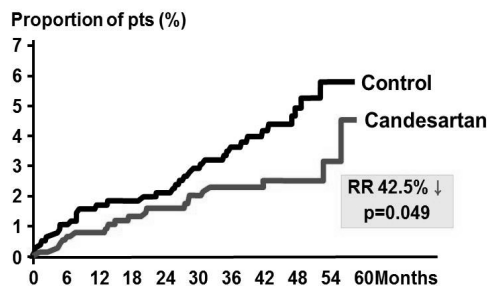
Brenner BM et al. *N Engl J Med* 2001;345:861-9

### LIFE: 뇌졸중 발생률: ARB vs BB



Dahlof et al. *Lancet* 2002;359:995

### SCOPE: 고혈압에서 뇌졸중 발생률



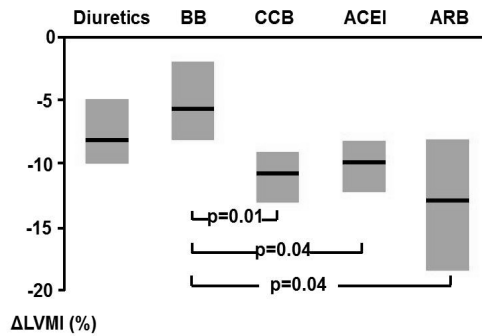
Papademetriou et al

### 인지저하/치매발생과 항고혈압제

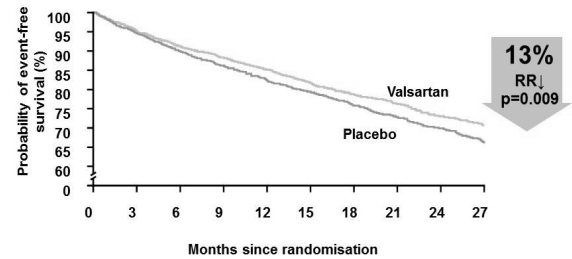
Treatment	Comparison group	Placebo	CCBs	ACE inhibitors	β-blockers	Diuretics
ARBs		0.60 ± 0.18 (P = 0.02)	0.57 ± 0.24 (P = 0.06)	0.47 ± 0.17 (P = 0.04)	0.67 ± 0.18 (P = 0.01)	0.54 ± 0.19 (P = 0.04)
CCBs		0.02 ± 0.19 (P = 0.91)	-	-0.11 ± 0.22 (P = 0.65)	0.10 ± 0.17 (P = 0.58)	-0.03 ± 0.24 (P = 0.89)
ACE inhibitors		0.13 ± 0.17 (P = 0.49)		-	0.21 ± 0.15 (P = 0.23)	0.07 ± 0.17 (P = 0.70)
β-blockers		-0.08 ± 0.13 (P = 0.59)			-	-0.13 ± 0.19 (P = 0.50)
Diuretics		0.06 ± 0.17 (P = 0.76)				-

Levi Marpillat N, *J Hypertens*. 2013

## 항고혈압제간 LVH 위험도 변화

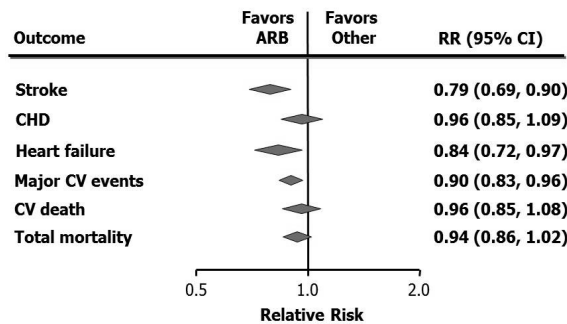
Klingbeil A. et al, *Am J Med* 2003;115:4-46

## Val-HeFT: 심부전에서 ARB 효과

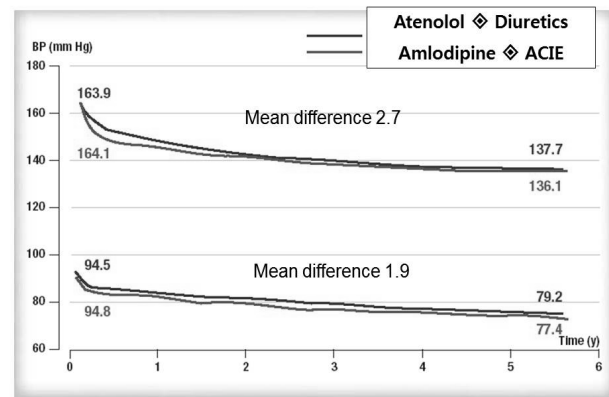


Mortality and morbidity rates: placebo 32%; valsartan 29%

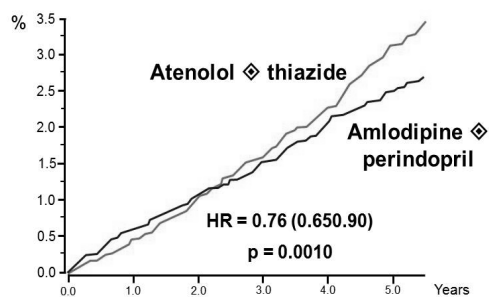
## BP-lowering treatment trialists: ARB vs other

Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet*. 2003;362:1527-35

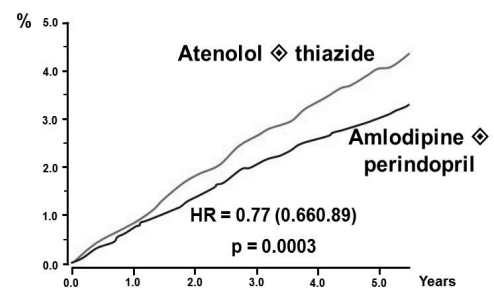
## ASCOT: Blood Pressure



## ASCOT: CV mortality

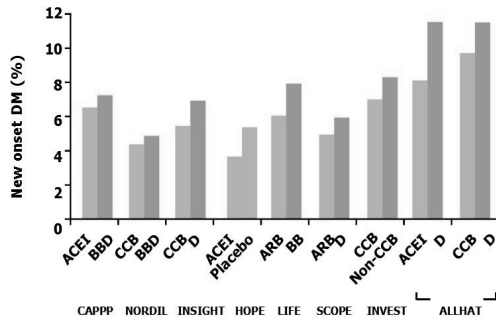


## ASCOT: Stroke



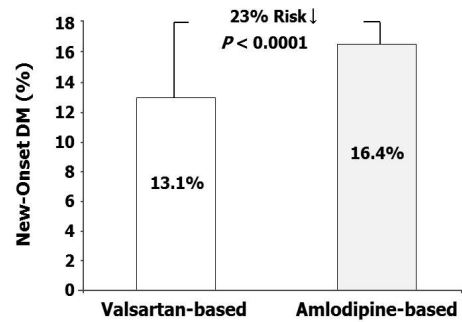
## Incidence of new cases of DM

Comparison of CCB, ACEI & ARB vs BB & Diuretics



Mancia G et al. *J Hypertension* 2005

## VALUE: Incidence of new-onset DM



Julius S et al. *Lancet*. 2004;363.

## 항고혈압제 적응증 2013 ESH/ESC

Condition	Drug
Asymptomatic organ damage	
LVH	ACE inhibitor, calcium antagonist, ARB
Asymptomatic atherosclerosis	Calcium antagonist, ACE inhibitor
Microalbuminuria	ACE inhibitor, ARB
Renal dysfunction	ACE inhibitor, ARB
Clinical CV event	
Previous stroke	Any agent effectively lowering BP
Previous myocardial infarction	BB, ACE inhibitor, ARB
Angina pectoris	BB, calcium antagonist
Heart failure	Diuretic, BB, ACE inhibitor, ARB, mineralocorticoid receptor antagonists
Aortic aneurysm	BB
Atrial fibrillation, prevention	Consider ARB, ACE inhibitor, BB or mineralocorticoid receptor antagonist
Atrial fibrillation, ventricular rate control	BB, non-dihydropyridine calcium antagonist

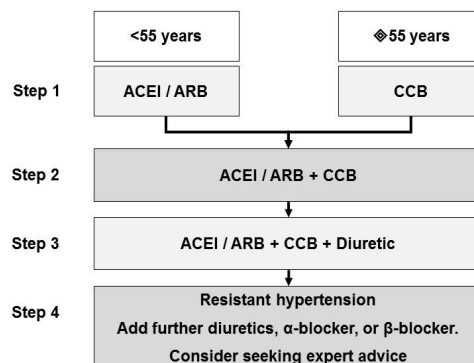
## 항고혈압제 적응증 2013 ESH/ESC

ESRD/proteinuria	ACE inhibitor, ARB
Peripheral artery disease	ACE inhibitor, calcium antagonist
Other	
ISH (elderly)	Diuretic, calcium antagonist
Metabolic syndrome	ACE inhibitor, ARB, calcium antagonist
Diabetes mellitus	ACE inhibitor, ARB
Pregnancy	Methyldopa, BB, calcium antagonist
Blacks	Diuretic, calcium antagonist

## 항고혈압제의 금기증 2013 ESH/ESC

Drug	Compelling	Possible
Diuretics (thiazides)	Gout	Metabolic syndrome Glucose intolerance Pregnancy Hypercalcaemia Hypokalaemia
Beta-blockers	Asthma A-V block (grade 2 or 3)	Metabolic syndrome Glucose intolerance Athletes and physically active patients Chronic obstructive pulmonary disease (except for vasodilator beta-blockers)
Calcium antagonists (dihydropyridines)		Tachyarrhythmia Heart failure
Calcium antagonists (verapamil, diltiazem)	A-V block (grade 2 or 3, trifascicular block) Severe LV dysfunction Heart failure	
ACE inhibitors	Pregnancy Angioneurotic oedema Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Angiotensin receptor blockers	Pregnancy Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Mineralocorticoid receptor antagonists Spironolactone	Acute or severe renal failure (eGFR <30 mL/min) Hyperkalaemia	

## 영국 NICE guidelines 2015



## 영국 NICE guidelines 2015

### Step 1:

- 55세 미만
  - ▮ ACEI 또는 ARB
- 55세 이상
  - ▮ CCB 우선

## 영국 NICE guidelines 2015

### Step 1:

- 베타차단제: 젊은 환자
  - ▮ ARB/ACEI 부작용 또는 금기
  - ▮ 임신 가능 여성: Labetalol
    - (nifedipine, hydralazine, methyldopa)
  - ▮ 교감신경 활성화가 확인된 경우
- BB에 2차 약물 추가하는 경우
  - ▮ CCB >> 이뇨제
  - ▮ 이유: 당뇨병 발생 위험 ↓

## 영국 NICE guidelines 2015

### Step 2:

- ARB/ACEI + CCB

## 영국 NICE guidelines 2015

### Step 3:

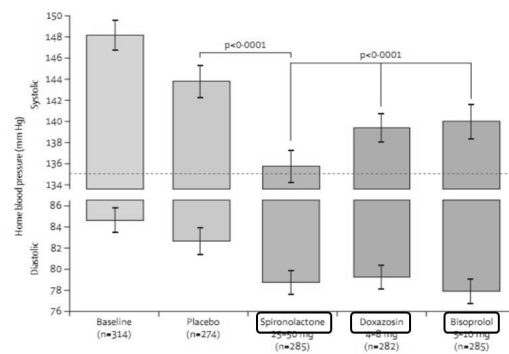
- ARB/ACEI + CCB + Diuretics
- Thiazide-like Diuretics:
  - ▮ 적응증: CCB에 의한 부작용(부종, 심부전증)
  - ▮ Chlortalidone 12.5-25mg, Indapamide 1.5 MR/2.5mg >
  - ▮ Thiazide 12.5-25mg

## 영국 NICE guidelines 2015

### Step 4: Resistant HTN

- A + C + D +
- 이뇨제 추가
  - ▮  $K \leq 4.5$ : Spironolactone 25mg
  - ▮  $K > 4.5$ : high dose Thiazide-like D
  - ▮ Na, K, Cr monitor
- 다른 약제 추가
  - ▮ 알파차단제
  - ▮ 베타차단제

## 3제 요법에 추가한 항고혈압제 효과 비교

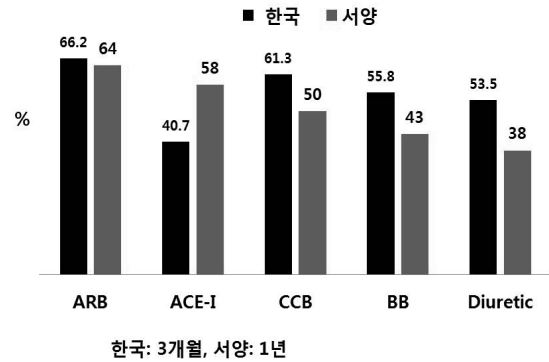


Williams B. et al, *Lancet* 2015

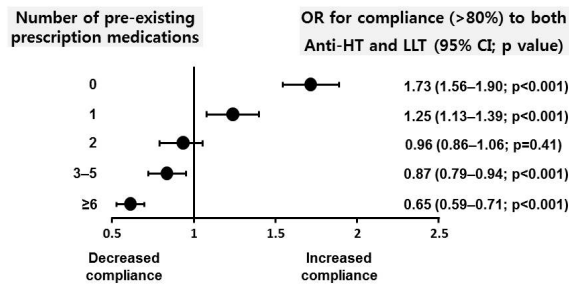
## 투약 불순응의 주요 요인

약물	<ul style="list-style-type: none"> <li>1일 복용횟수 증가/동시에 복용하지 않는 약물 종류 증가</li> <li>부작용 경험, 인식/장기간의 치료</li> </ul>
환자	<ul style="list-style-type: none"> <li>정신질환/약물남용/경제문제/사회지지 부족/불안정한 환경</li> <li>바쁜 스케줄/신체적 기동력이 떨어지거나 활동 불능</li> <li>의료인 언어에 무지/질병에 대한 부정</li> <li>질병이나 합병증에 대한 민감성 낮음/질병 위중도 낮음</li> <li>복약순응 중요하지 않게 여김/복약순응에 대한 자신감 부족</li> </ul>
의료 서비스 제공자	<ul style="list-style-type: none"> <li>의사소통 기술 부족</li> <li>환자와 건강신념 불일치</li> <li>긍정적 강화를 제공하지 않음</li> </ul>
보건의료 체계	<ul style="list-style-type: none"> <li>비싼 약값</li> <li>외래이용 또는 약품비 본인부담율이 높음</li> <li>의료기관이나 약국에 접근성 낮음</li> </ul>

## 항고혈압제 계열별 투약 지속률

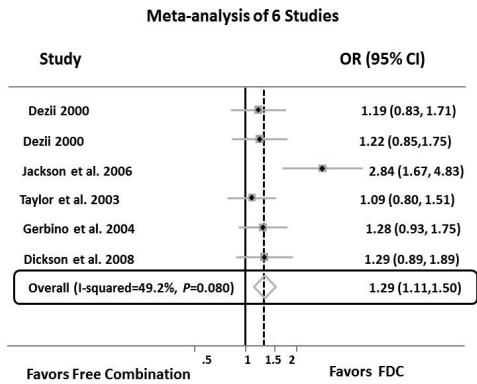


## 기존 약제 갯수와 복약순응도



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

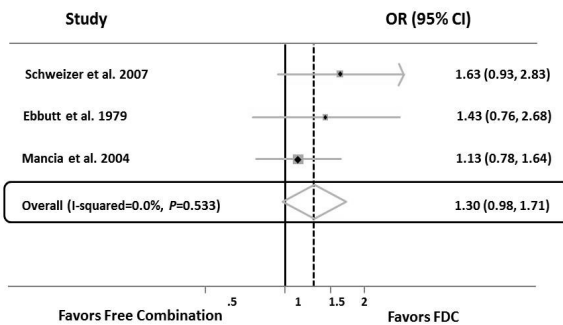
## FDC increase persistence and compliance



Gupta AK, et al. Hypertension. 2010

## FDC increase normalization of BP

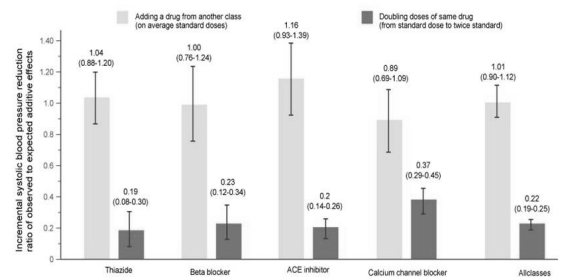
Meta-analysis of 3 Studies



Gupta AK, et al. Hypertension. 2010

## Adding is More Effective Than Titrating

Combining 2 different classes: 5X > doubling 1 drug'



Wald et al. Am J Med 2009;122:290-300



## 병합요법의 장점

- ㉪ 부작용이 적다: 저용량 병합 > 고용량 단독
  - 작용 기전이 상호 보완적
  - CCB-related edema, diuretic-related hypokalemia ↓
- ㉪ 단독요법의 실패나 목표장기 손상을 방지할 수 있다.
- ㉪ 고정용량 복합제는 순응도가 높다.
  - 사용이 간편하고, 비용이 저렴.
- ㉪ 병합요법으로 시작하는 경우 목표도달이 빠르다.
- ㉪ 최근의 진료지침

## 요약

- ㉪ 고혈압진단에 가정혈압이나 24시간 활동혈압 활용
- ㉪ 단독요법으로 조절이 안되거나 2단계 고혈압부터 병용요법 권장
- ㉪ ARB와 CCB를 우선적으로 병용, CCB 부작용시 ARB와 Thiazide계 이뇨제 병용
- ㉪ 3제 병용은 ARB, CCB, Thiazide계 이뇨제를 권장
- ㉪ 3제로 조절이 안되는 경우는 이뇨제를 추가/증량, 알파차단제 또는 베타차단제를 추가한다.
- ㉪ 계열별 부작용을 파악하여 적절한 약물로 대체한다.

## 2014 JNC8 요약

- ㉪ 1차 선택약 : 이뇨제(티아자이드), CCB, ACEI, ARB
- ㉪ 심혈관 위험에 상관없이 혈압목표 < 140/90 mmHg
- ㉪ 고령환자 (≥60세) 치료목표 < 150/90 mmHg