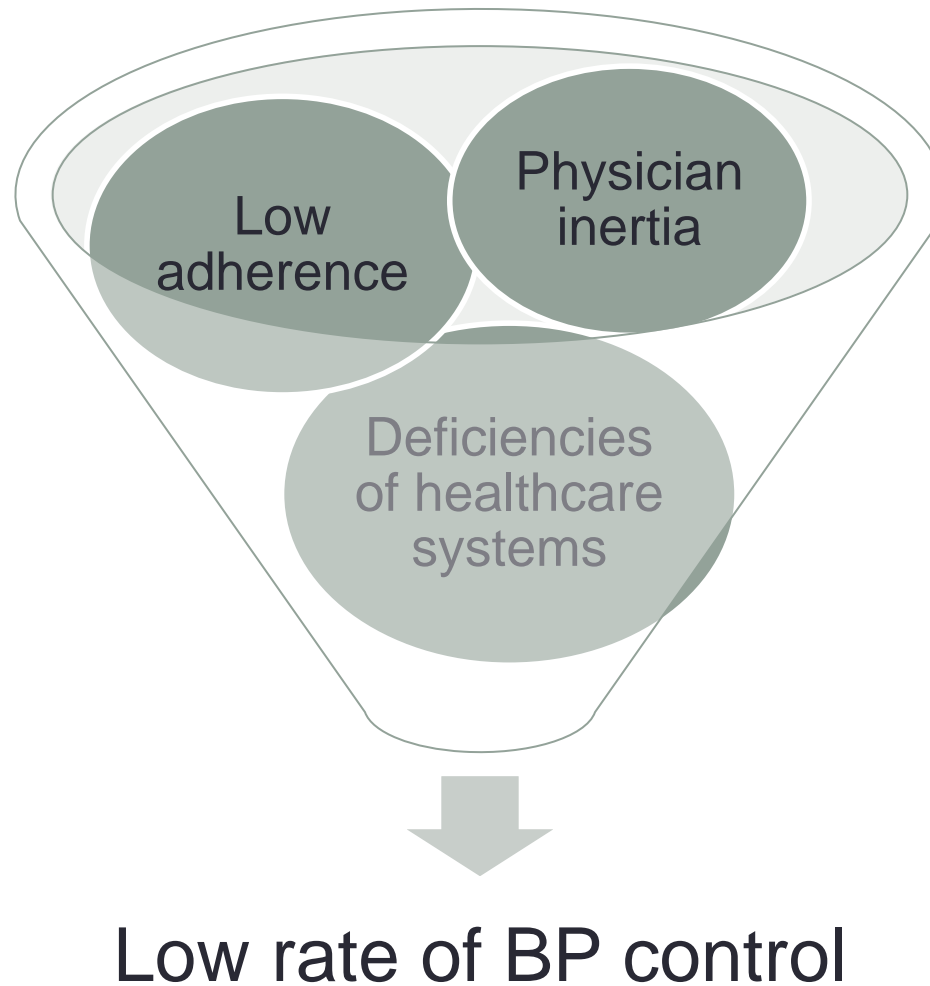


Improving Adherence in Hypertension Management

Jidong Sung
Division of Cardiology
Sungkyunkwan University School of Medicine

Three Main Causes of The Low Rate of BP Control

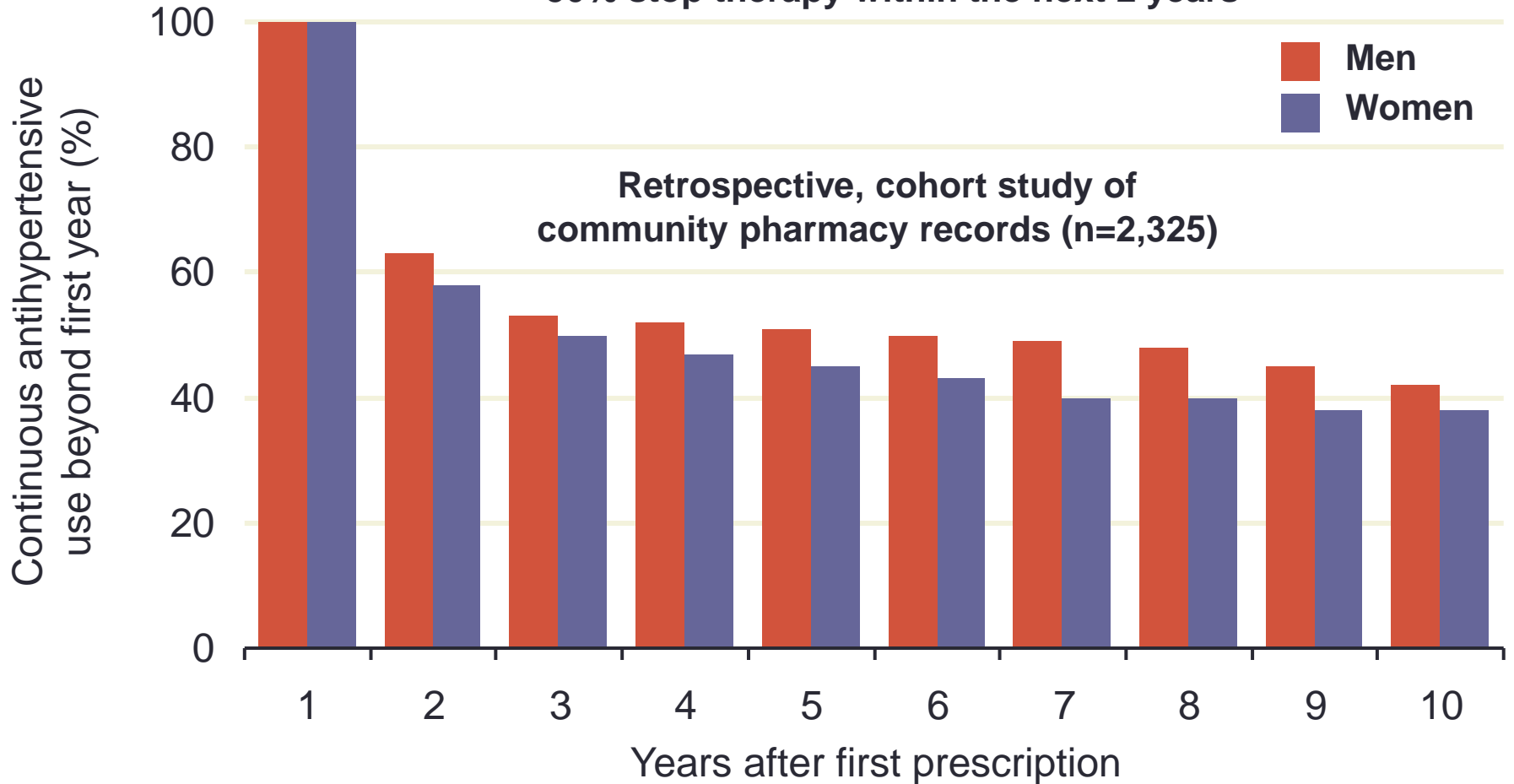


Patients' adherence in various therapeutic area

Therapeutic Area	No. of Reports	Mean Compliance Rate (%)	Range (%)
Cancer ¹⁴⁻¹⁸	5	80	35-97
Cardiovascular—all ¹⁹⁻⁴³	26	71	39-93
<u>Hypertension only</u>	17	73	39-93
Other cardiovascular	9	71	64-93
Epilepsy ^{4,44,45}	3	70	46-88
Fertility ⁴⁶⁻⁵⁰	5	71	34-97
Glaucoma ^{9,10}	2	78	76-80
Infectious disease ^{13,51-57}	8	74	40-92
Medical, general—all ⁶⁶⁻⁷⁸	14	75	51-85
Diabetes only	3	73	66-85
Thalassemia only	3	79	72-85
Other medical only	8	74	51-84
Medical education ⁸³	1	47	-
Psychiatry ⁷⁹⁻⁸²	4	78	75-83
Respiratory—all ⁵⁸⁻⁶⁵	10	54	37-92
Asthma only	7	55	37-92
Chronic obstructive pulmonary disease only	3	51	50-52

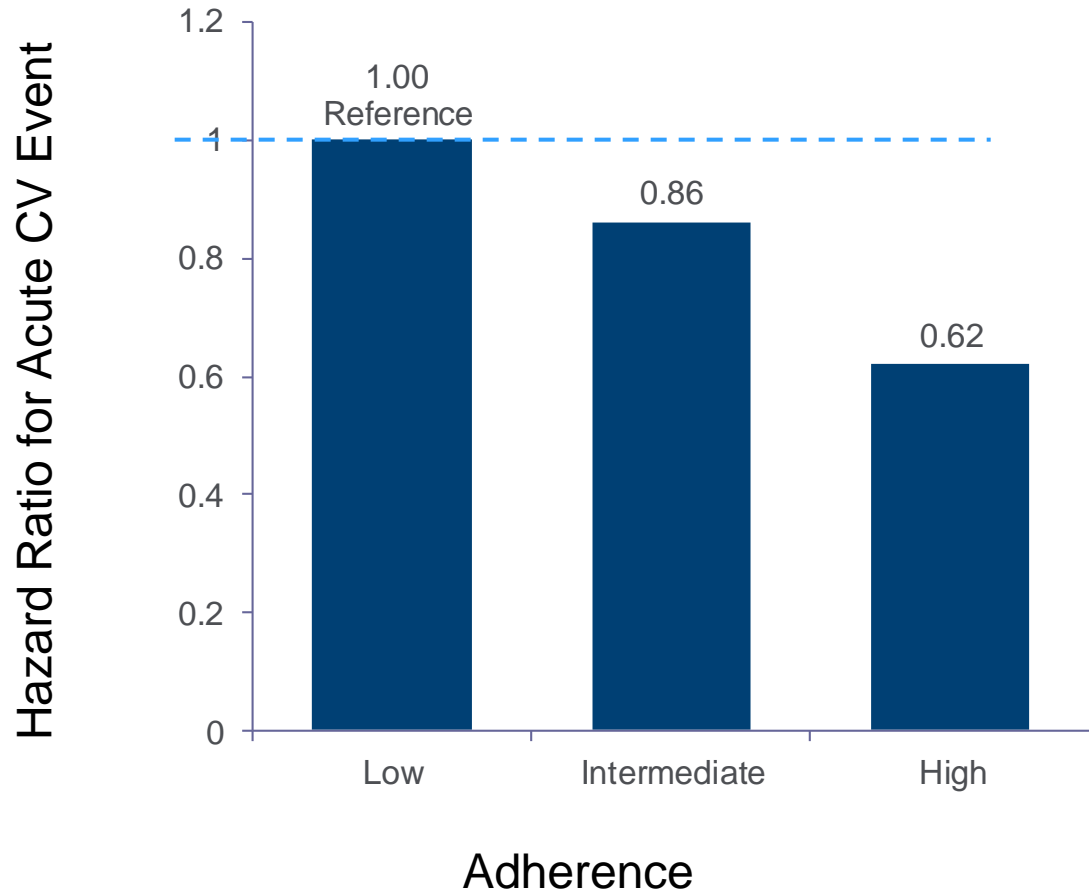
Poor Adherence and Persistence with Antihypertensive Treatment

Among patients receiving therapy after the first year, ~50% stop therapy within the next 2 years

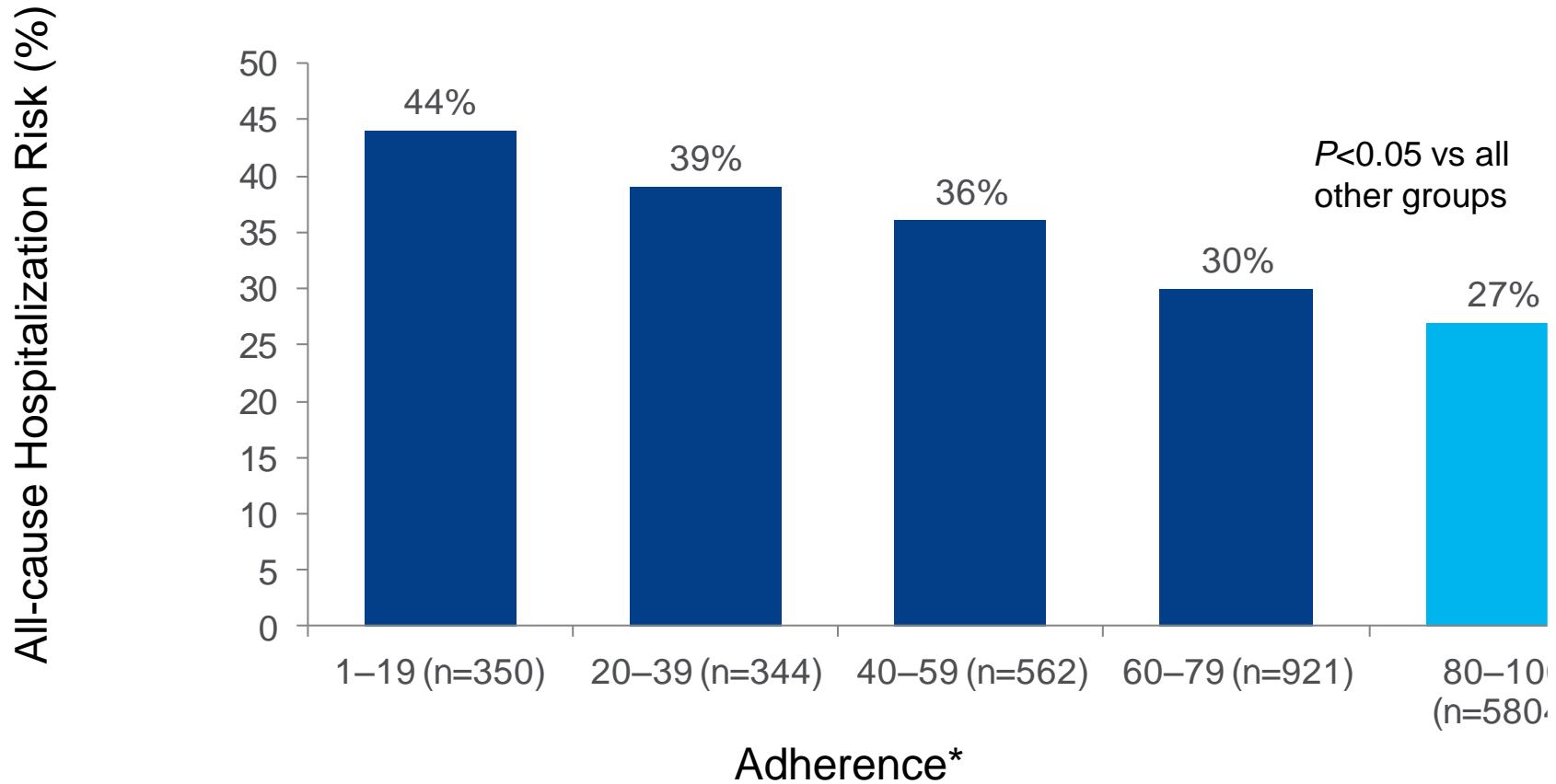


Adherence to Antihypertensive Treatment Has Been Found to Decrease Risk of Acute CV Events

- 18,806 newly diagnosed hypertensive patients aged ≥ 35 years (mean age at entry, 62 years)
- Newly treated for HTN and initially CVD free
- Adherence:
 - High: $\geq 80\%$ of days covered
 - Intermediate: 40–79% of days covered
 - Low: $\leq 40\%$ of days covered
- Mean follow-up: 4.6 years



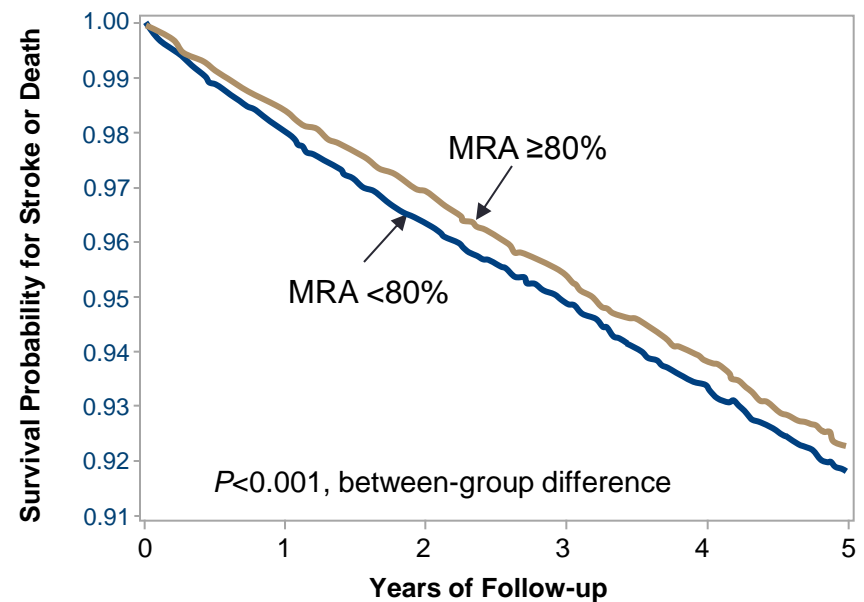
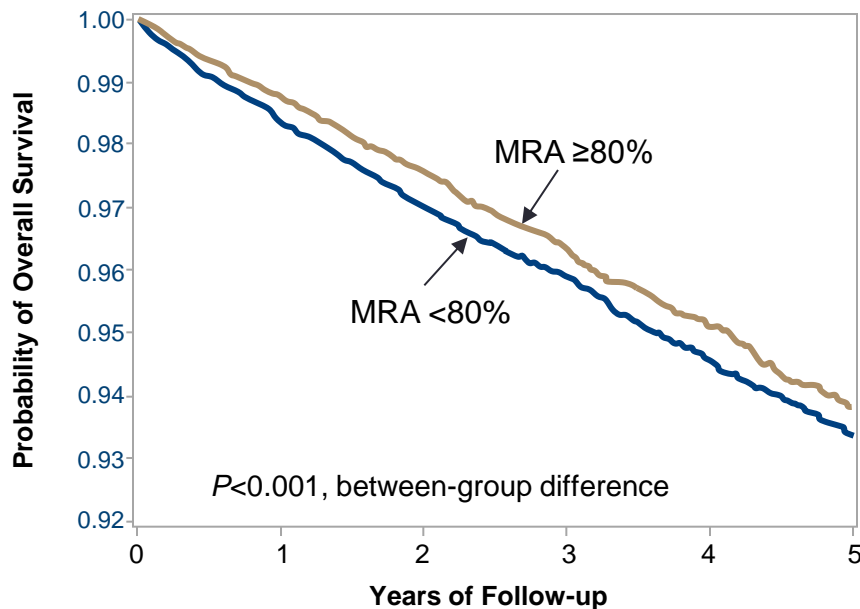
Adherence Has Been Found to Decrease Risk of Hospitalization



*Adherence was defined as the percentage of days during the analysis period that patients had a supply of ≥ 1 maintenance medications for the condition.

Adherence to Antihypertensive Treatment Has Been Found to Decrease Mortality Risk

- Retrospective cohort study included all chronic medication-treated patients with HTN enrolled in Tennessee's Medicaid program (TennCare) for an average of 4.7 years during the period 1994–2000 (N=49,479)



Adjusted Kaplan-Meier survival curves demonstrate that $\geq 80\%$ baseline refill adherence was associated with better 5-year estimated survival than $< 80\%$ refill adherence for a combined outcome of stroke or death ($P < 0.001$)

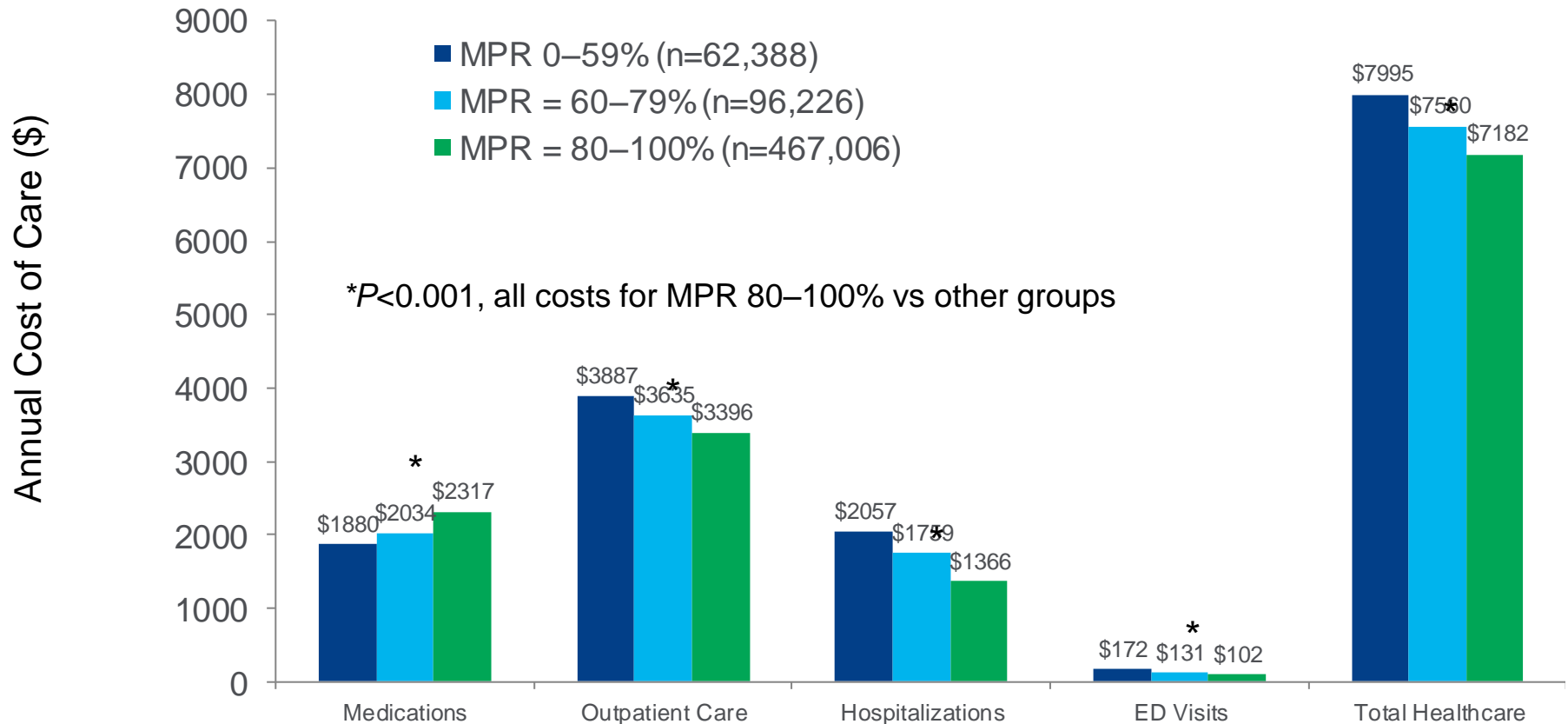
Medication Refill Adherence (MRA) was calculated as the percentage of eligible prescription days filled (total days' supply for all qualifying drug classes/ total number of days from the first to the last fill in the interval $\times 100$, capped at 100%) for all antihypertensive medications taken in the time period.

HTN=hypertension; MRA=medication refill adherence.

Bailey JE, et al. *J Gen Intern Med.* 2010;25:495-503.

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Poor Adherence Has Been Found to Increase Cost of Care



ED=emergency department; MPR=medication possession ratio.

STUDY OF COMPLIANCE TO ANTIHYPERTENSIVE MEDICATION IN KOREAN HYPERTENSIVE PATIENTS USING MEDICATION EVENT MONITORING SYSTEM

Division of Cardiology, Cardiac and Vascular Center, Samsung Medical Center
Department of Internal Medicine, Sungkyunkwan University School of Medicine

Jidong Sung, MD, MPH, Jin-Ho Choi, MD, Sang-Chol Lee, MD, Young Keun On, MD, Hyeon Cheol Gwon, MD, Seung Woo Park, MD, June Soo Kim, MD, Eun-Seok Jeon, MD, Duk-Kyung Kim, MD, Sang Hun Lee, MD, Kyung Pyo Hong, MD, Jeong Euy Park, MD, Jung-Don Seo, MD



Methods of measuring adherence

- In practice
 - Attendance at appointments
 - Clinical response to medications
 - Patient self-report
- In research
 - Pill count at home visits
 - Monitoring prescription refills
 - Drug Assays in body fluids
 - Tracers
 - “Memory” pill containers

Medication Event Monitoring System (MEMS)



Considered to be gold standard in measuring adherence

MEMS-HTN study

– Inclusion and exclusion

- Inclusion

- Diagnosed HTN
- Both drug-naïve and in ongoing treatment
- In or about to start monotherapy

- Exclusion

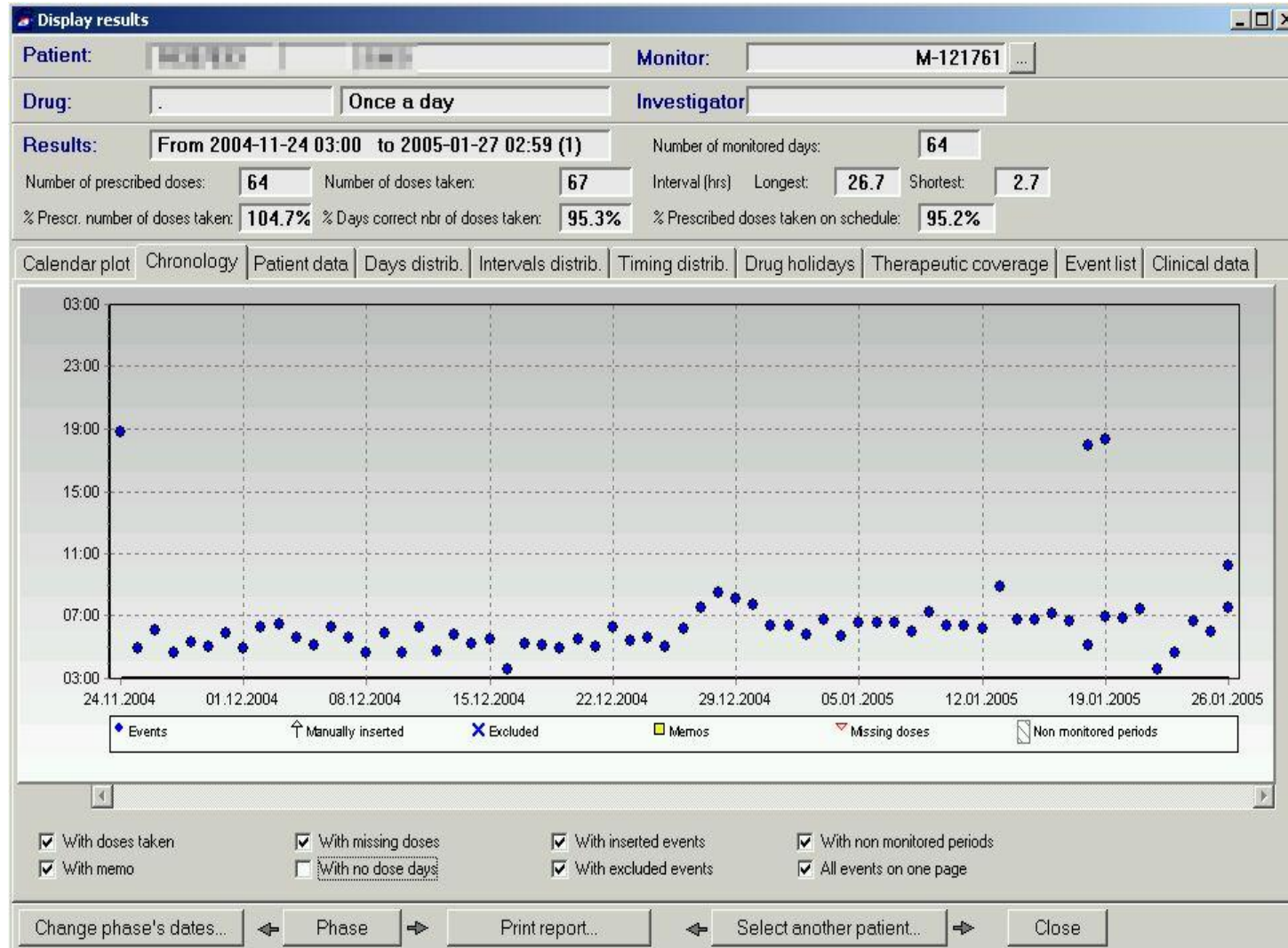
- Who needs more than two drugs to control BP
- \geq Twice a day medication
- Hypertensive emergency or urgency
- Comorbidity is not a limiting factor unless it necessitate co-administration of other drugs
- Patient's refusal

MEMS-HTN study

– Subjects

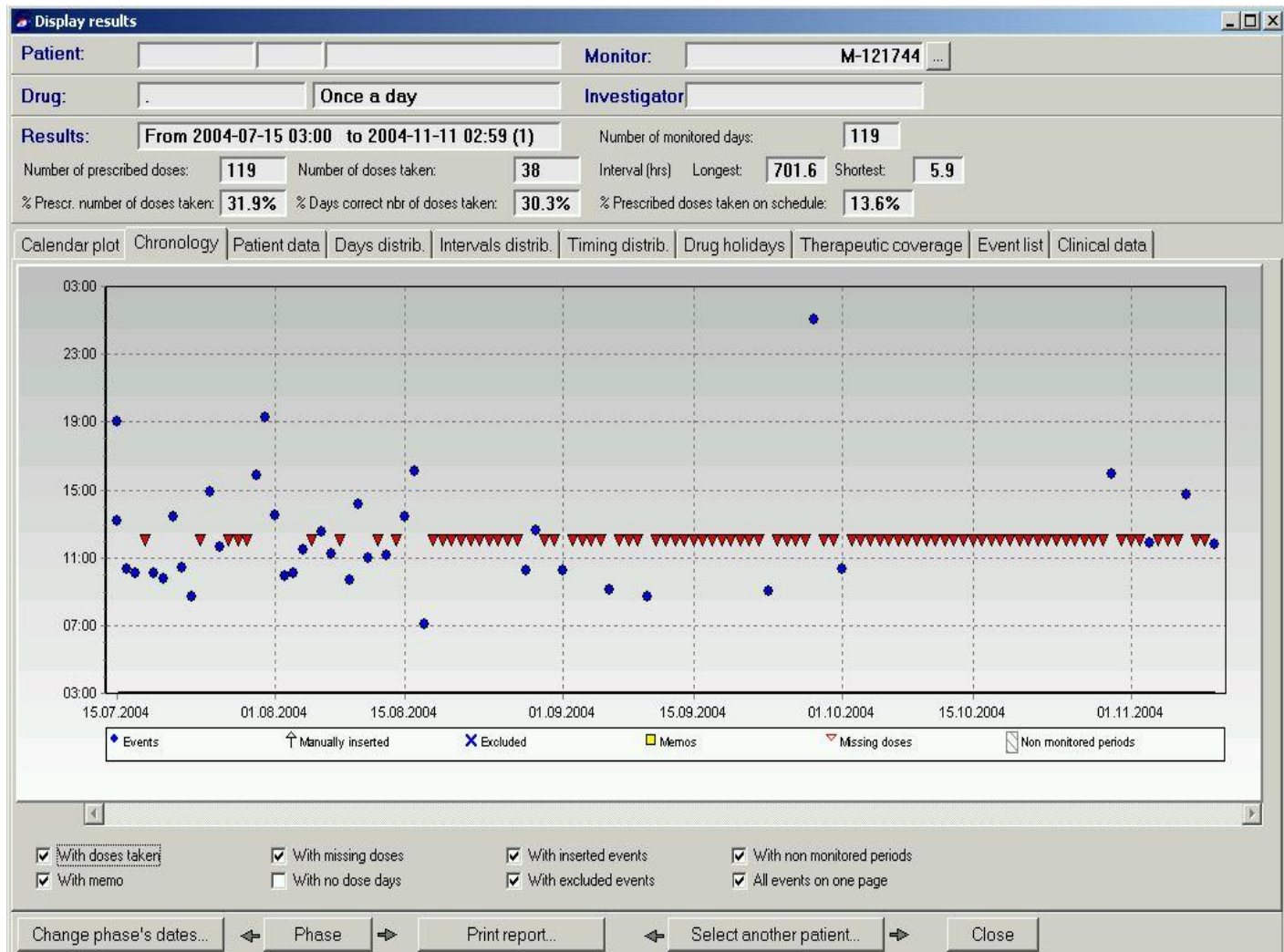
- N=80 (M:F=52:38%), Age: 53 ± 10 yrs
- \leq Stage I HTN: 77%
- Total duration of hypertensive medication: median 11 months (range: 0-204 months)
- Drug-naïve: 15%
- No medication in recent 1 month: 30%
- History of self discontinuation of medication within 1 year: 5%
- Education level: \geq college-graduated 63%

Near-perfect adherence

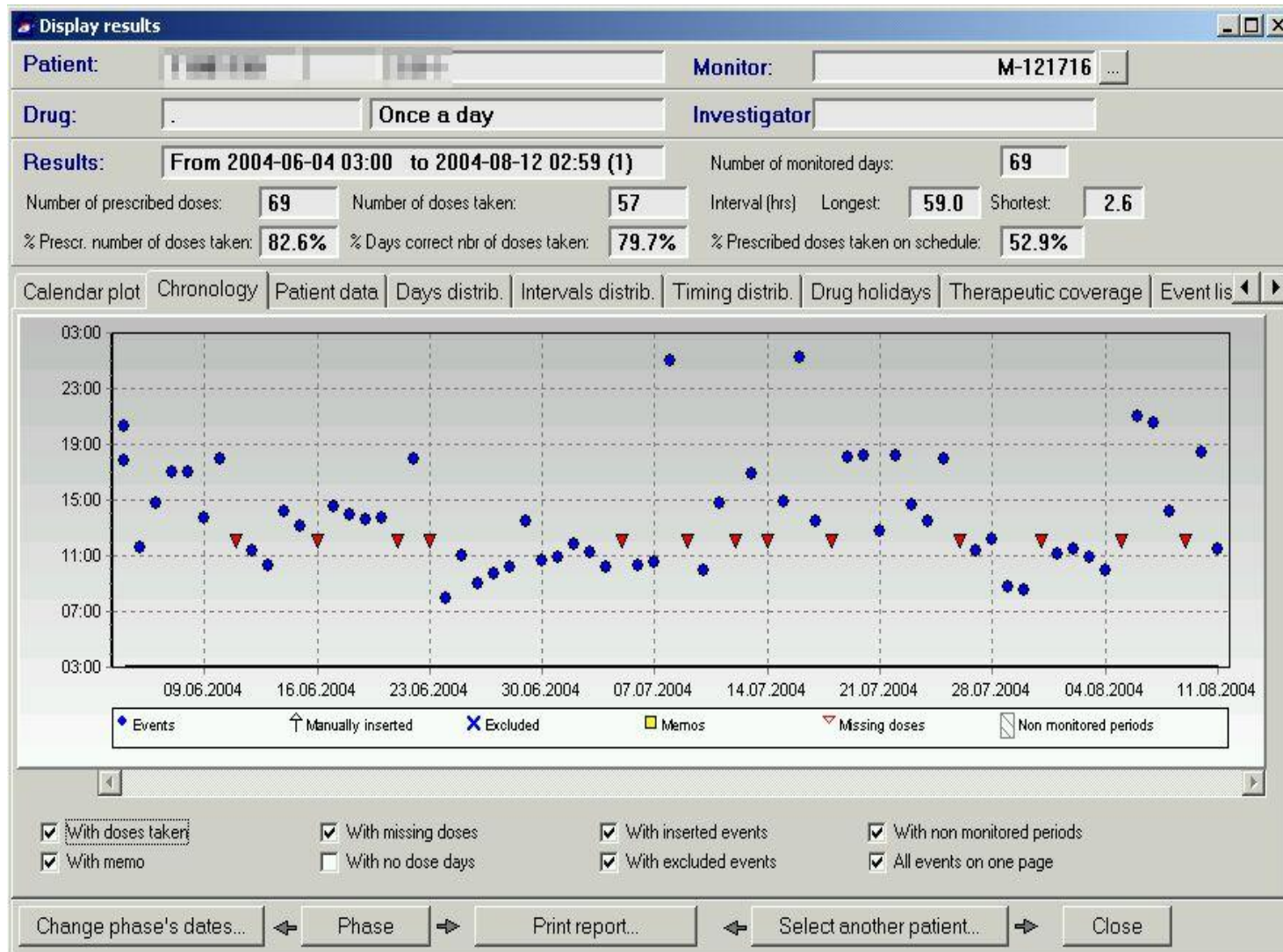


Poor adherence

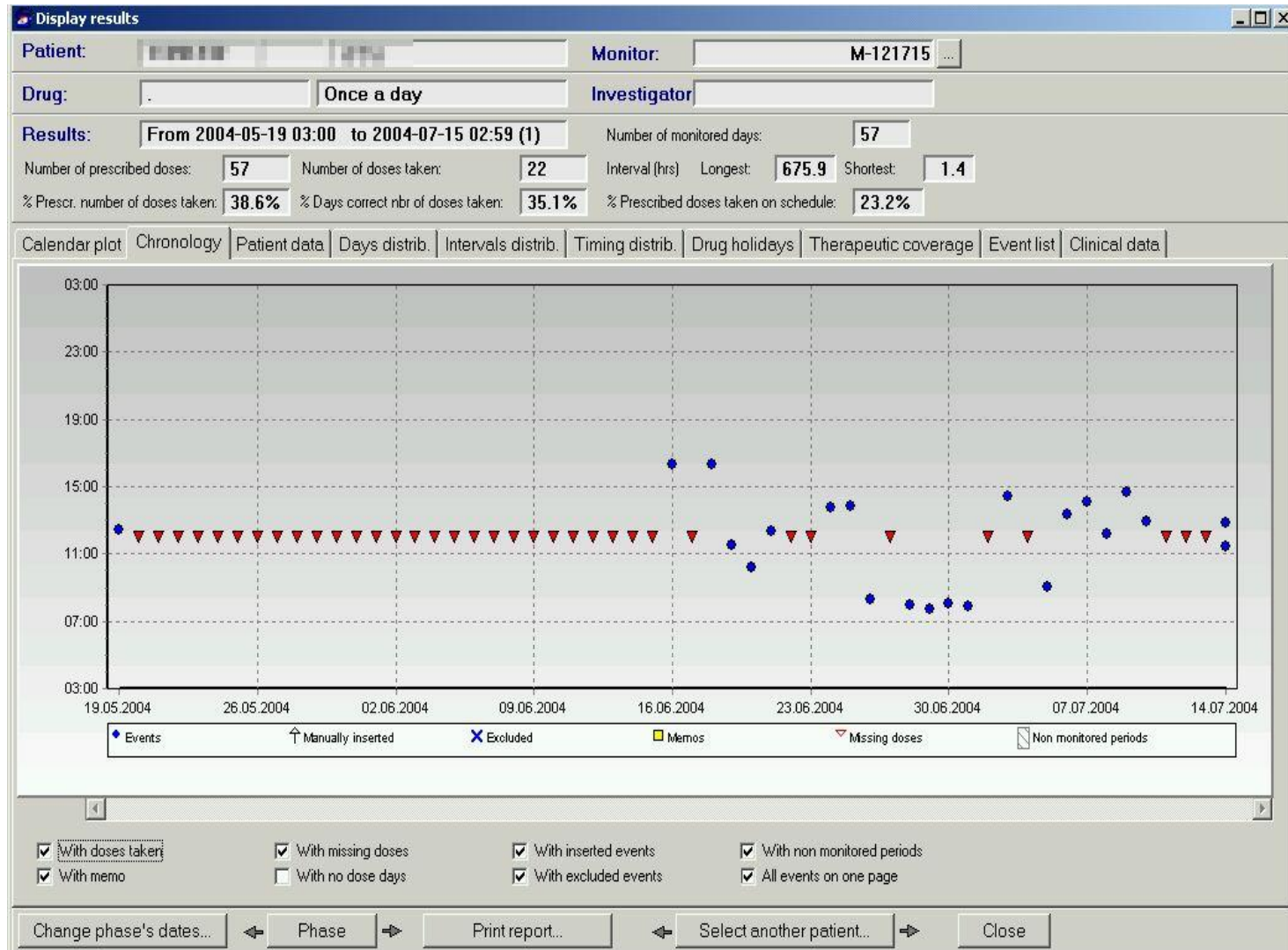
- due to psychological resistance



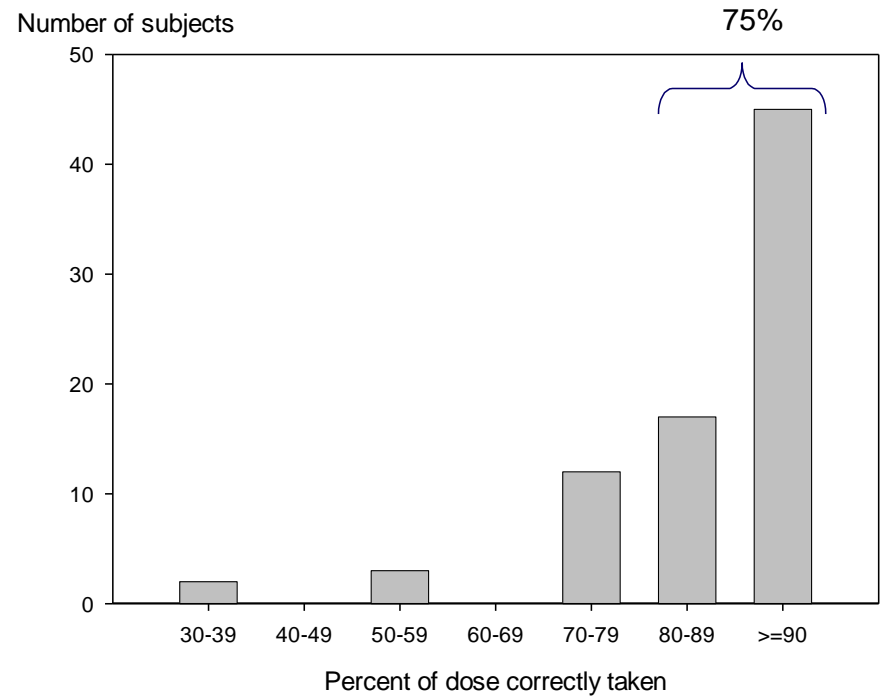
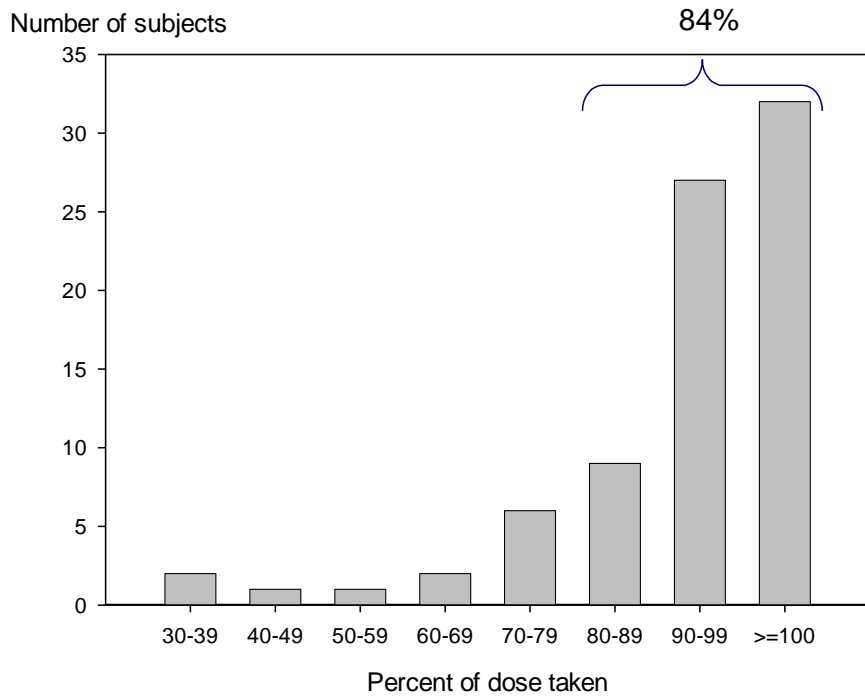
'Random' non-adherence



'White coat adherence'



Overall compliance parameters

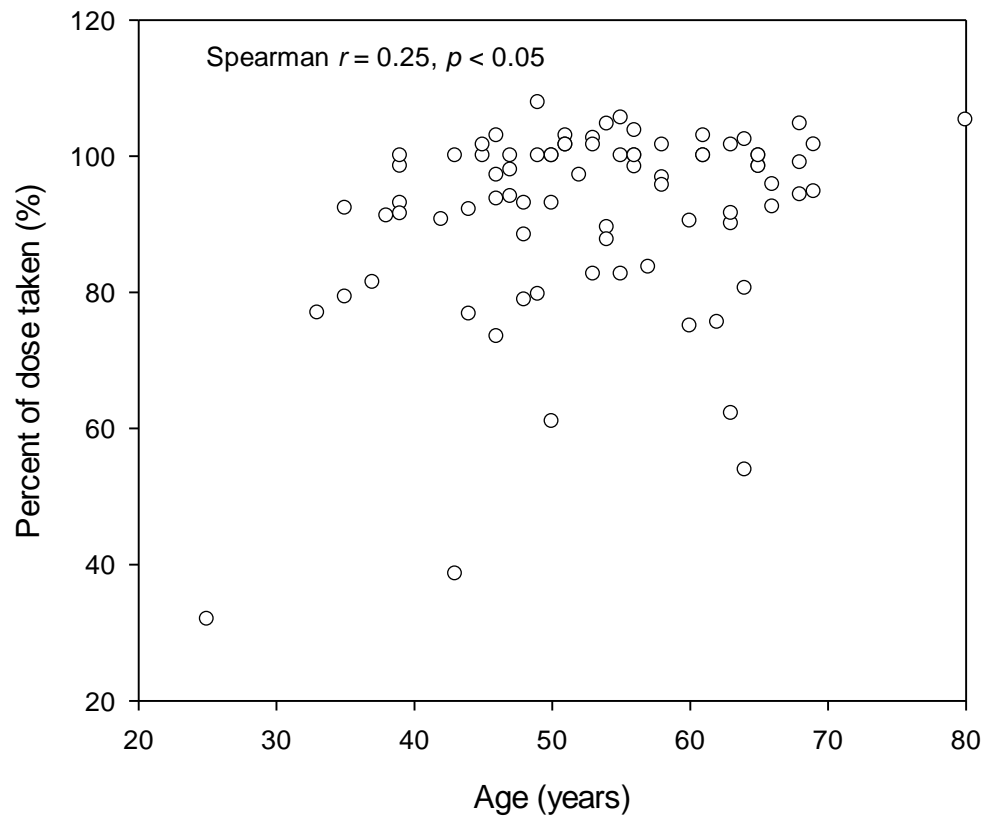


Predictors of poor compliance (1)

Percent of dose taken	<80%	80-99%	>=90%	p for trend
Previous history of medication discontinuation	15%(2/13)	13% (1/8)	3% (2/59)	0.04
Currently not in drug treatment	46% (6/13)	38% (3/8)	25% (15/59)	0.06

Percent of dose taken correctly	<80%	80-99%	>=90%	p for trend
Previous history of medication discontinuation	15% (2/13)	9% (2/22)	2% (1/45)	0.03
Currently not in drug treatment	46% (6/13)	35% (8/22)	22% (10/45)	0.04

Predictors of poor compliance (2)



Methods to Improve Adherence

Patient level

Information combined with motivational strategies (see Section 5.1.6 on smoking cessation).

Group sessions.

Self-monitoring of blood pressure

Self-management with simple patient-guided system.

Complex interventions.

Drug treatment level

Simplification of the drug regimen

Reminder packaging

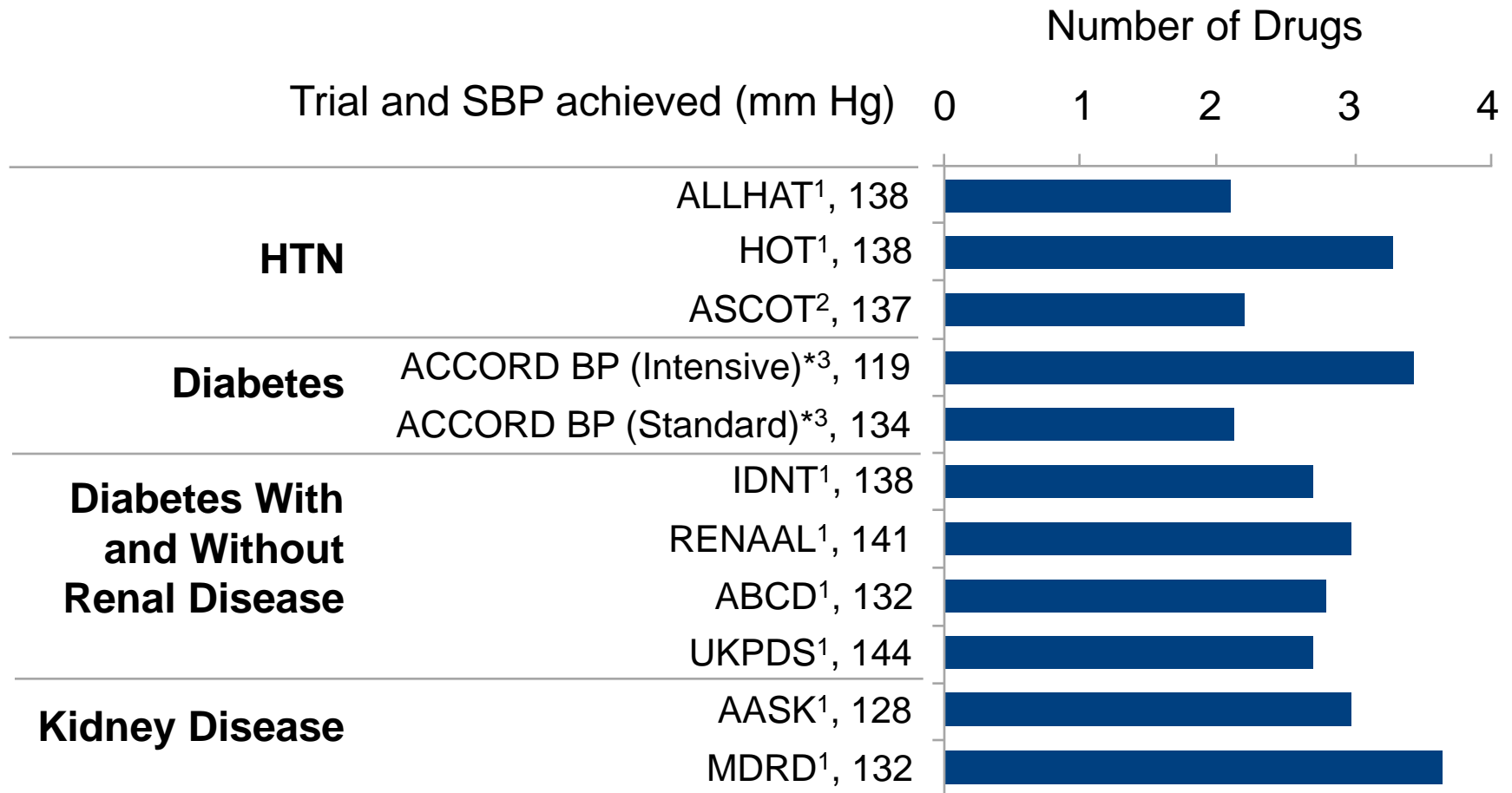
Health system level

Intensified care (monitoring, telephone follow-up, reminders, home visits, telemonitoring of home blood pressure, social support, computer-aided counseling and packaging).

Interventions directly involving pharmacists.

Reimbursement strategies to improve general practitioners' involvement in evaluation and treatment of hypertension

Trials in Which Multiple Antihypertensive Medications Were Required



*Target BP control groups in ACCORD defined as <120 mm Hg (intensive) and <140 mm Hg (standard).

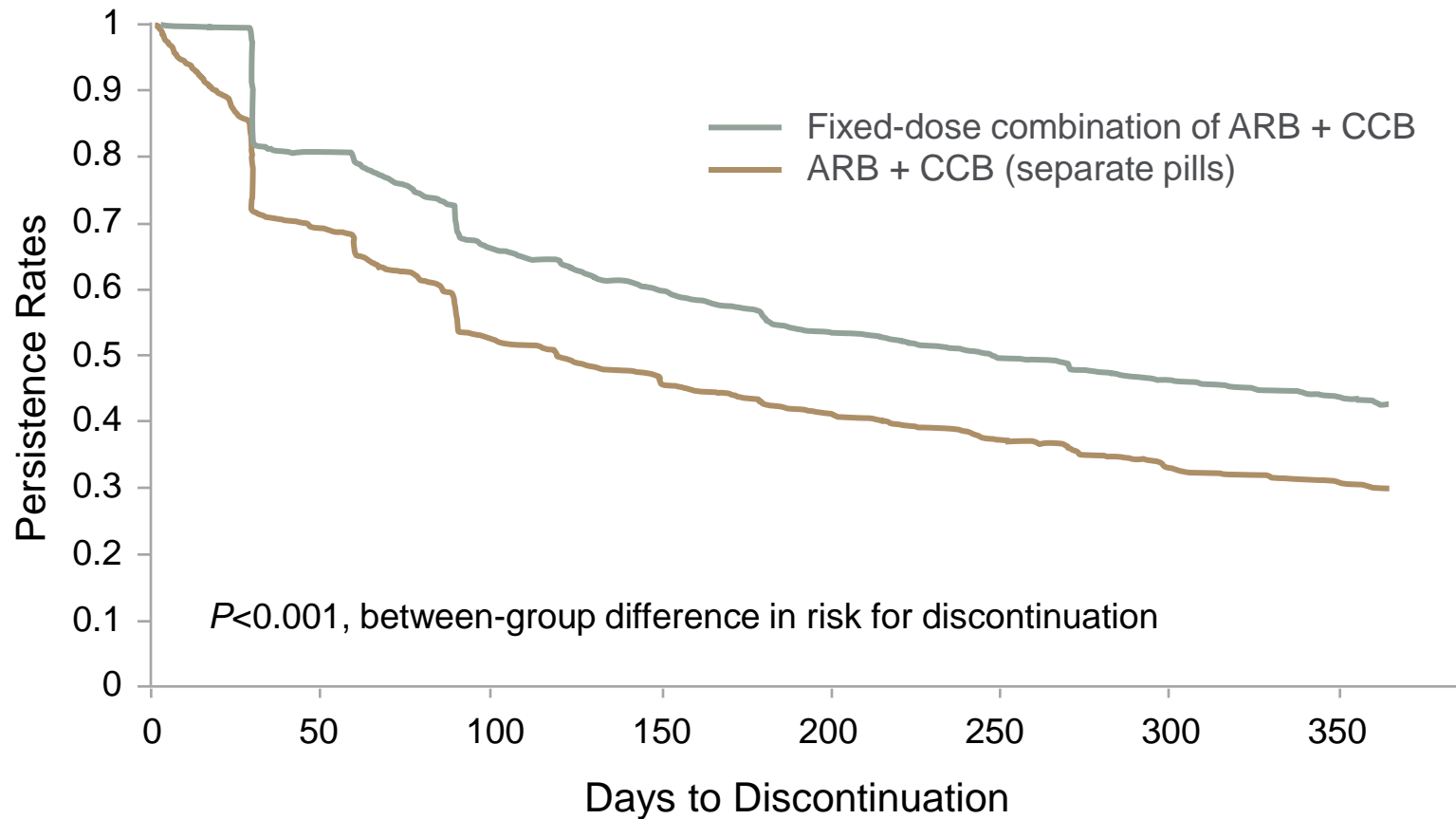
1. Bakris GL. *Am J Med.* 2004;116:30S-38S. 2. Dahlof B, et al. *Lancet.* 366:895-906. 3. Cushman WC, et al. *N Engl J Med.* 2010;362:1575-1585.

Advantages of combination therapy

- esp. single-pill combination (SPC)

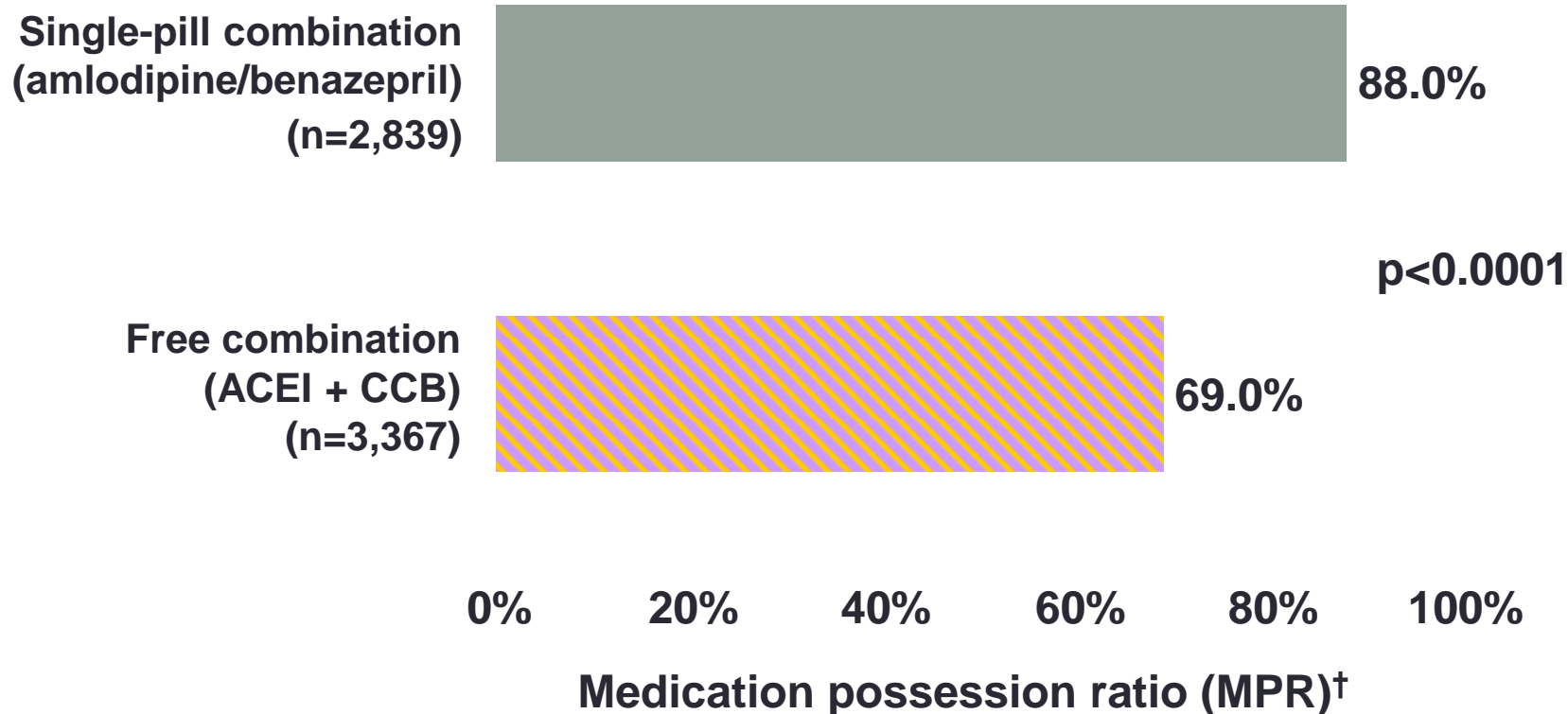
- Additive antihypertensive efficacy
 - complementary mechanisms of action
- Higher patient response rates
- Simple titration and dosing schedules
- Maintained or improved tolerability
- Improved patient adherence
- Attenuation of adverse effects / metabolic effects
- Cost effective

Improved Persistence Found With Fixed-Dose Combination vs Free-Dose Components



ARB=angiotensin receptor blocker; CCB=calcium channel blocker.

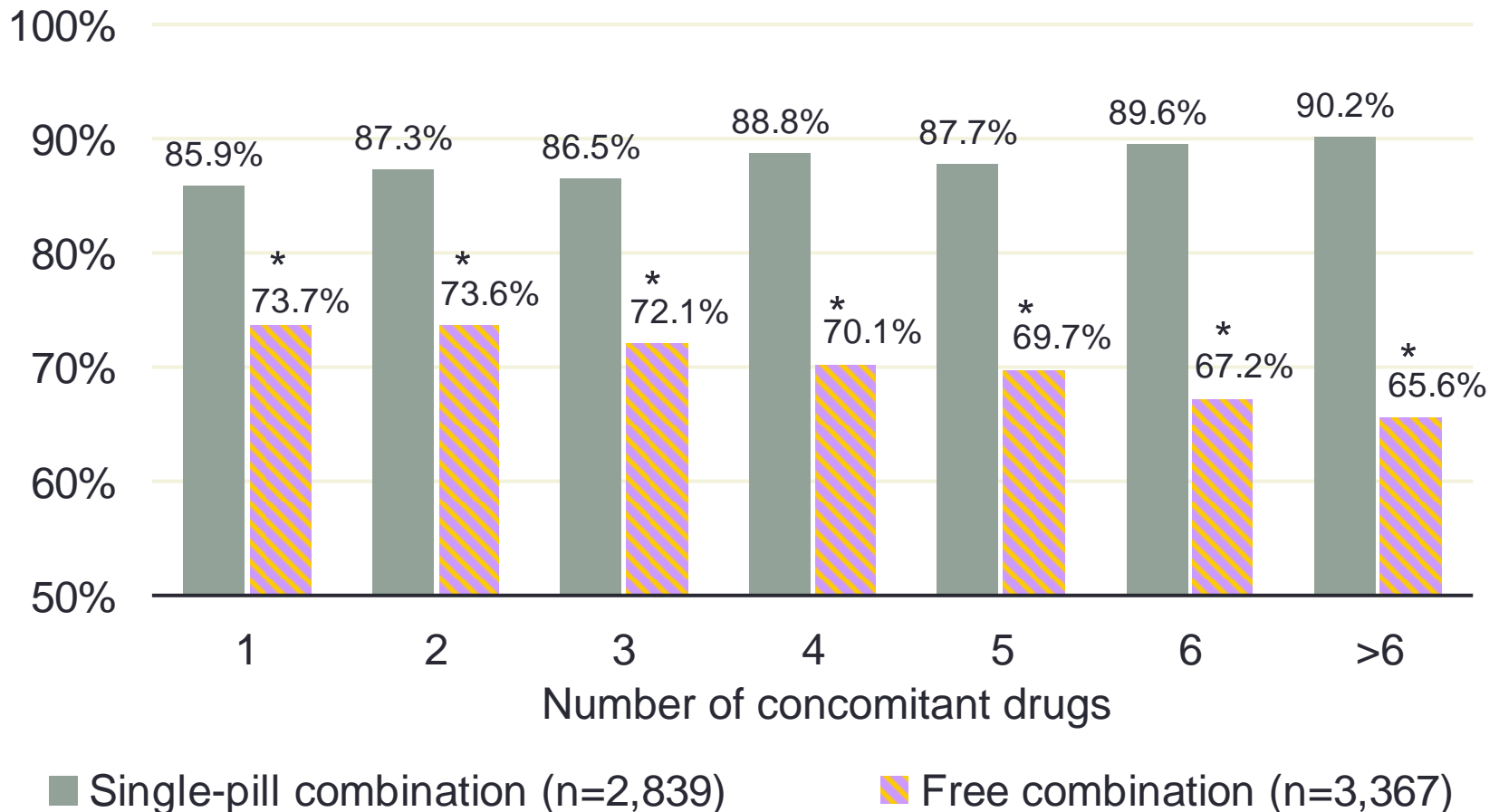
Improved Compliance with Single-pill Combination Therapy Compared with Free-combination Therapy



†Defined as the total number of days of therapy for medication dispensed/365 days of study follow-up

Single-pill Combinations Improve Compliance Regardless of Concomitant Medications

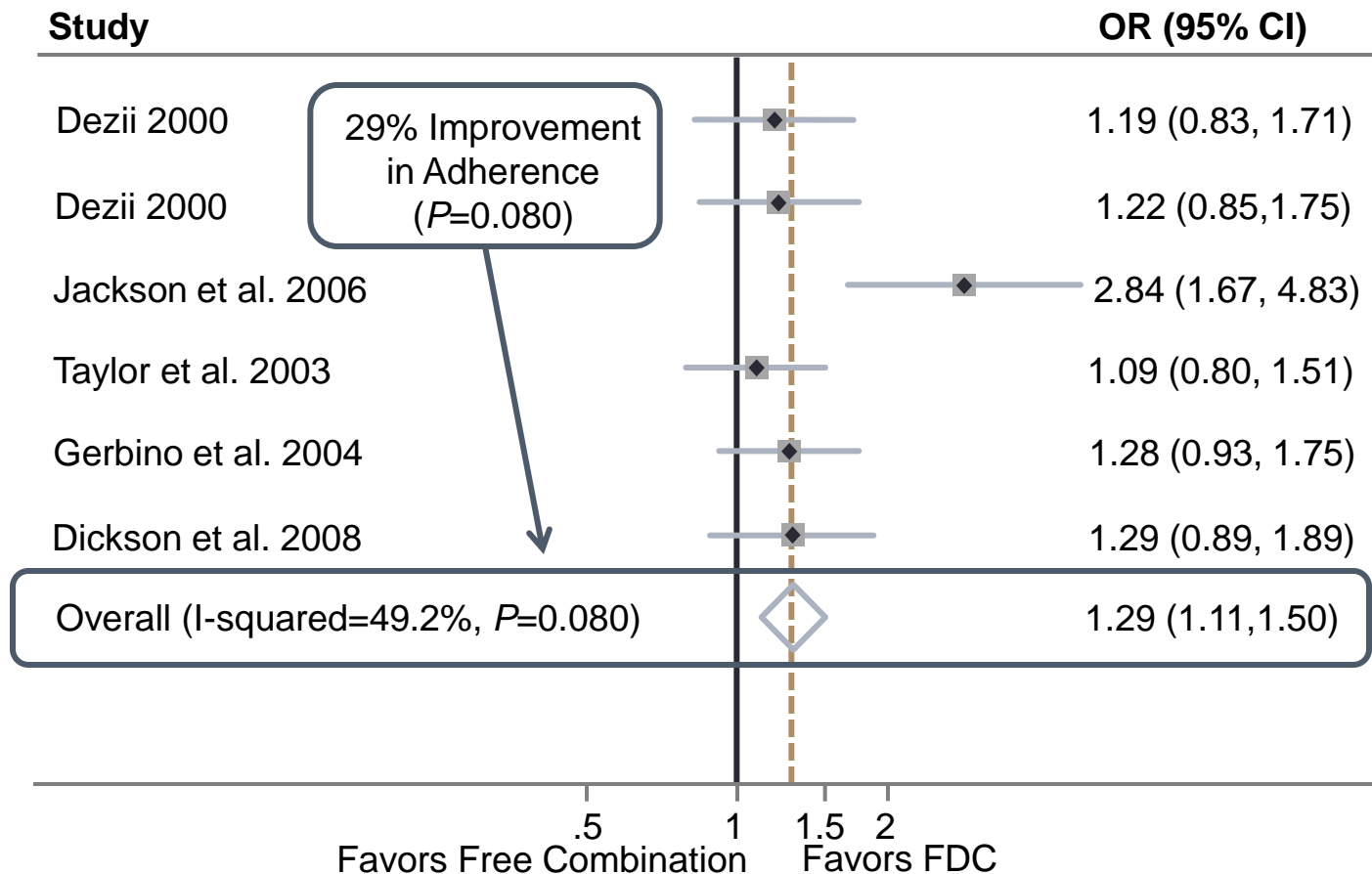
Medication-possession ratio



*p<0.0001

Fixed-Dose Combinations Resulted in Increased Persistence and Compliance

Meta-analysis of 6 Studies

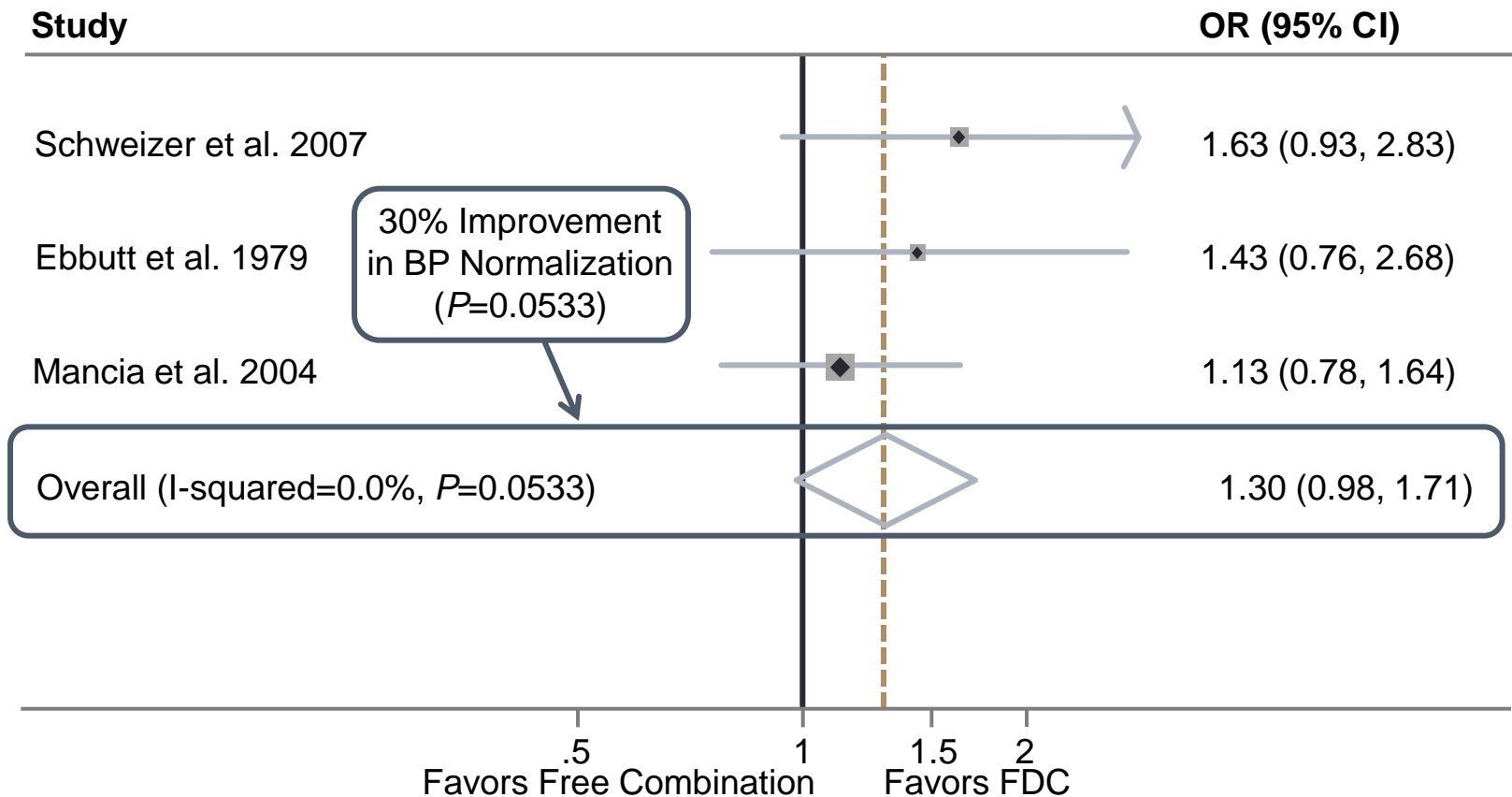


CI=confidence interval; FDC=fixed-dose combination; OR=odds ratio.

Gupta AK, et al. *Hypertension*. 2010;55:399-407.

Fixed-Dose Combinations Resulted in Increased Normalization of BP

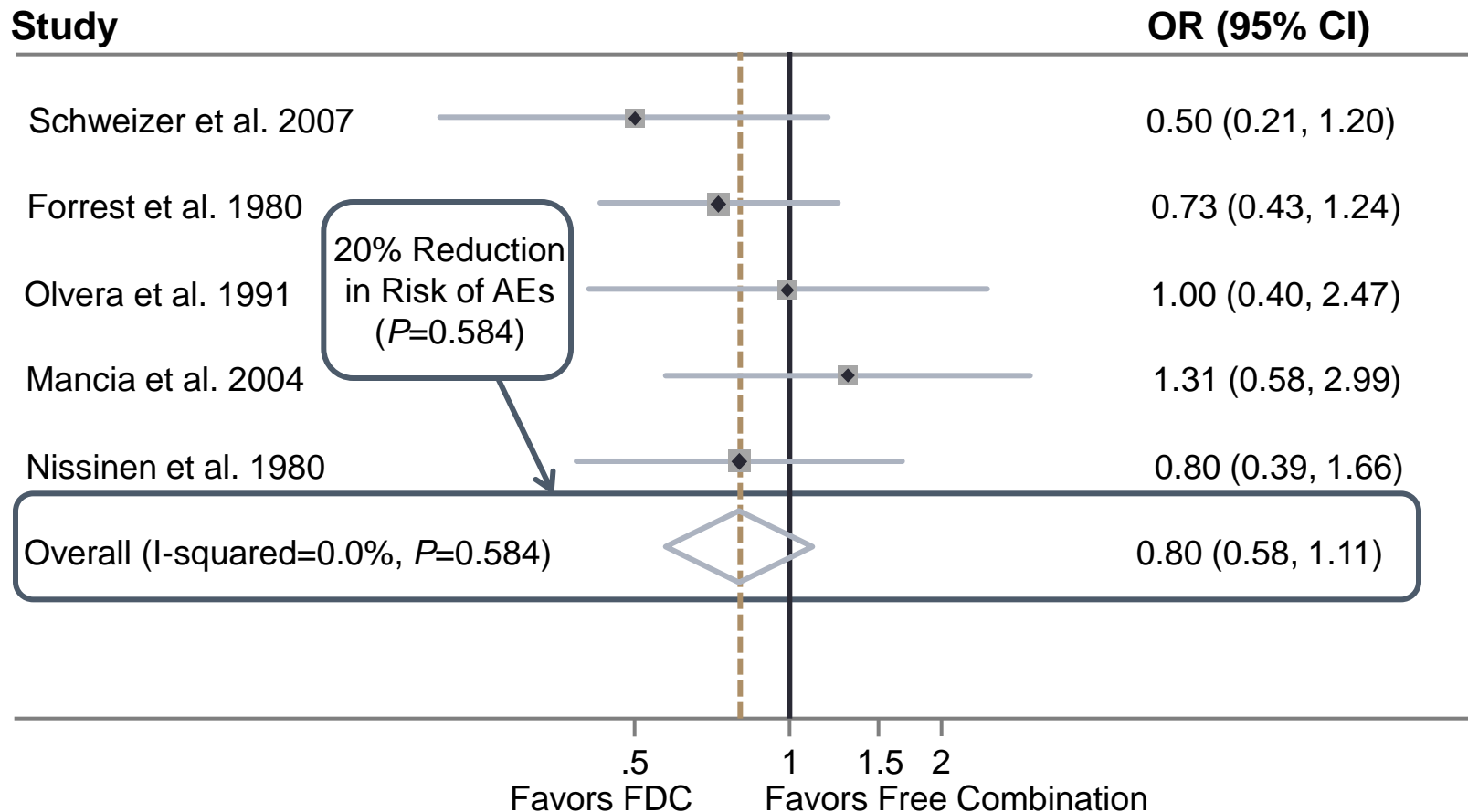
Meta-analysis of 3 Studies



BP=blood pressure; CI=confidence interval; FDC=fixed-dose combination; OR=odds ratio.

Fixed-Dose Combinations Decreased Risk of AEs

Meta-analysis of 5 Studies



20% Reduction
in Risk of AEs
(P=0.584)

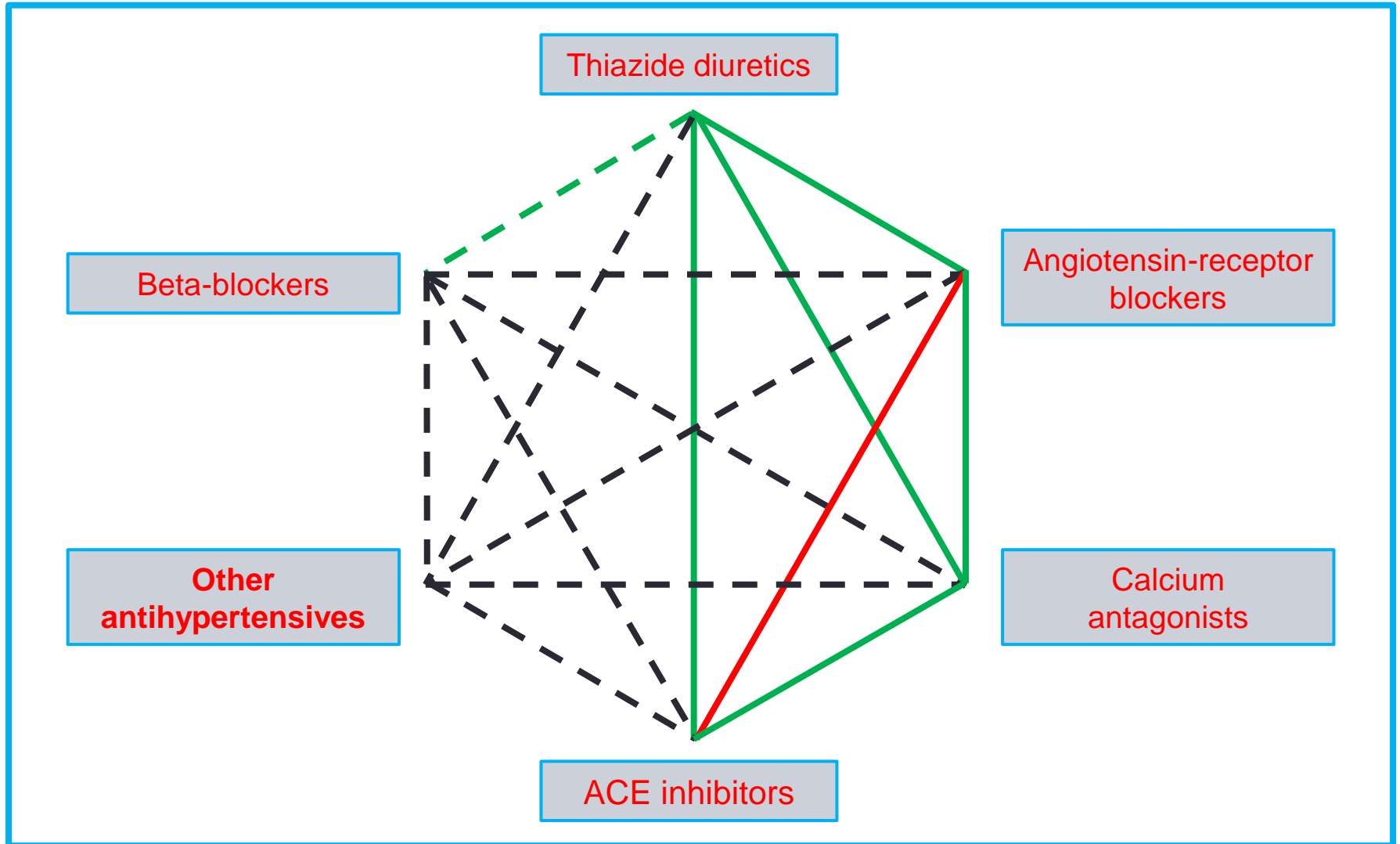
Overall (I-squared=0.0%, P=0.584)

AEs=adverse events; CI=confidence interval; FDC=fixed-dose combination; OR=odds ratio.

Guideline for Fixed-Dose Combination

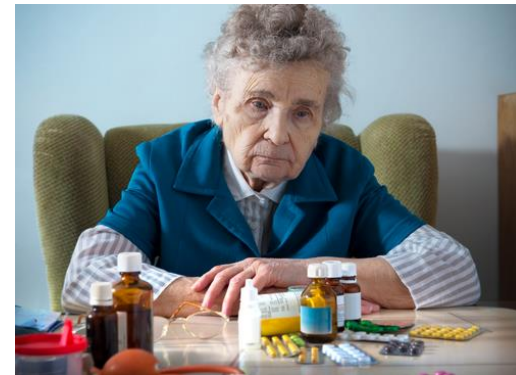
Recommendations	Class ^a	Level ^b
<p>Combinations of two antihypertensive drugs at fixed doses in a single tablet may be recommended and favoured, because reducing the number of daily pills improves adherence, which is low in patients with hypertension.</p>	IIb	B

Recommended Combination Therapy on Guidelines



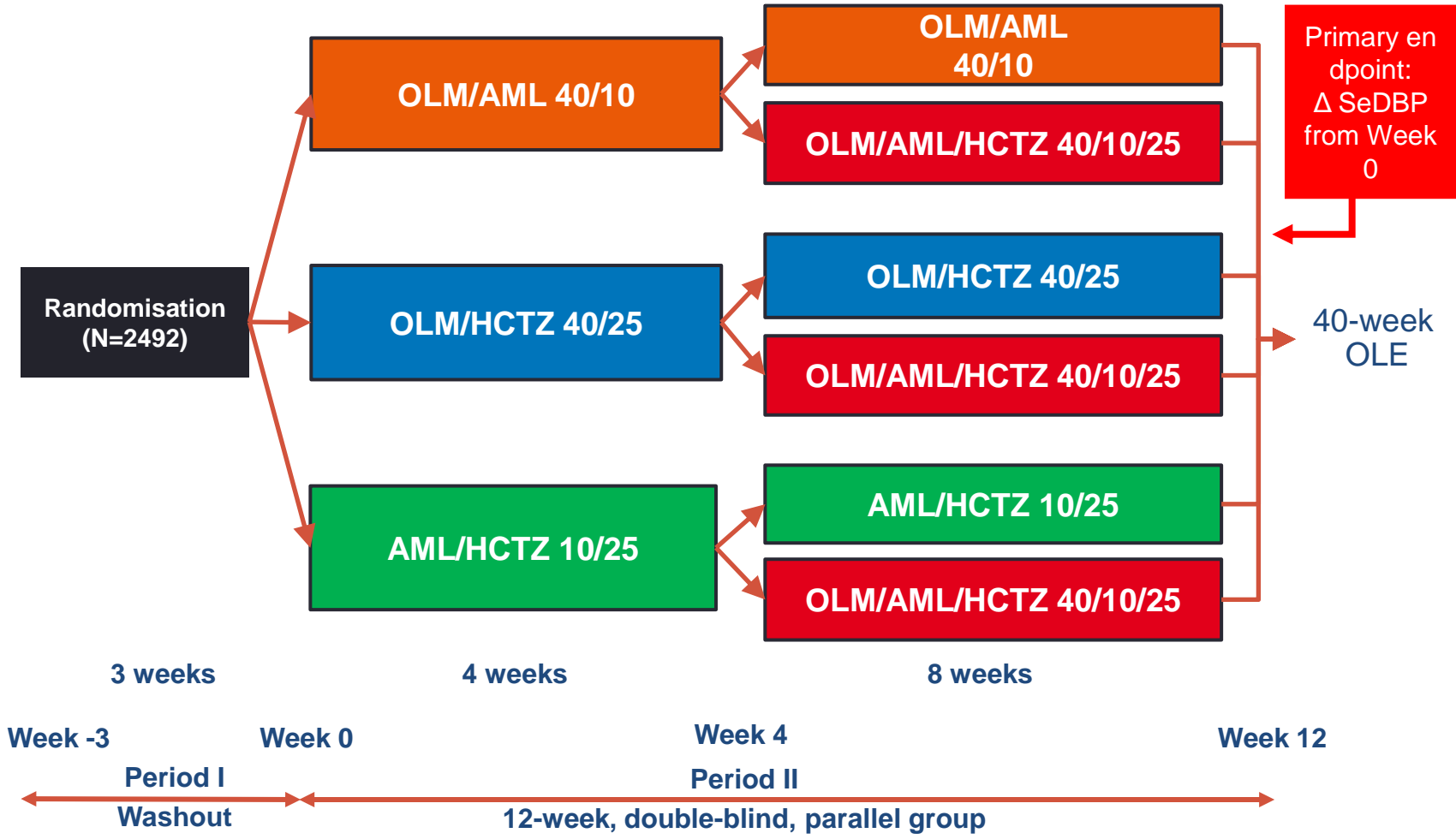
We need to understand the feelings generated by hypertension

- Our patients
 - reaction to being diagnosed with hypertension and facing a lifetime of treatment
 - worries about side effects of drugs and interactions
 - difficulties with complex regimens



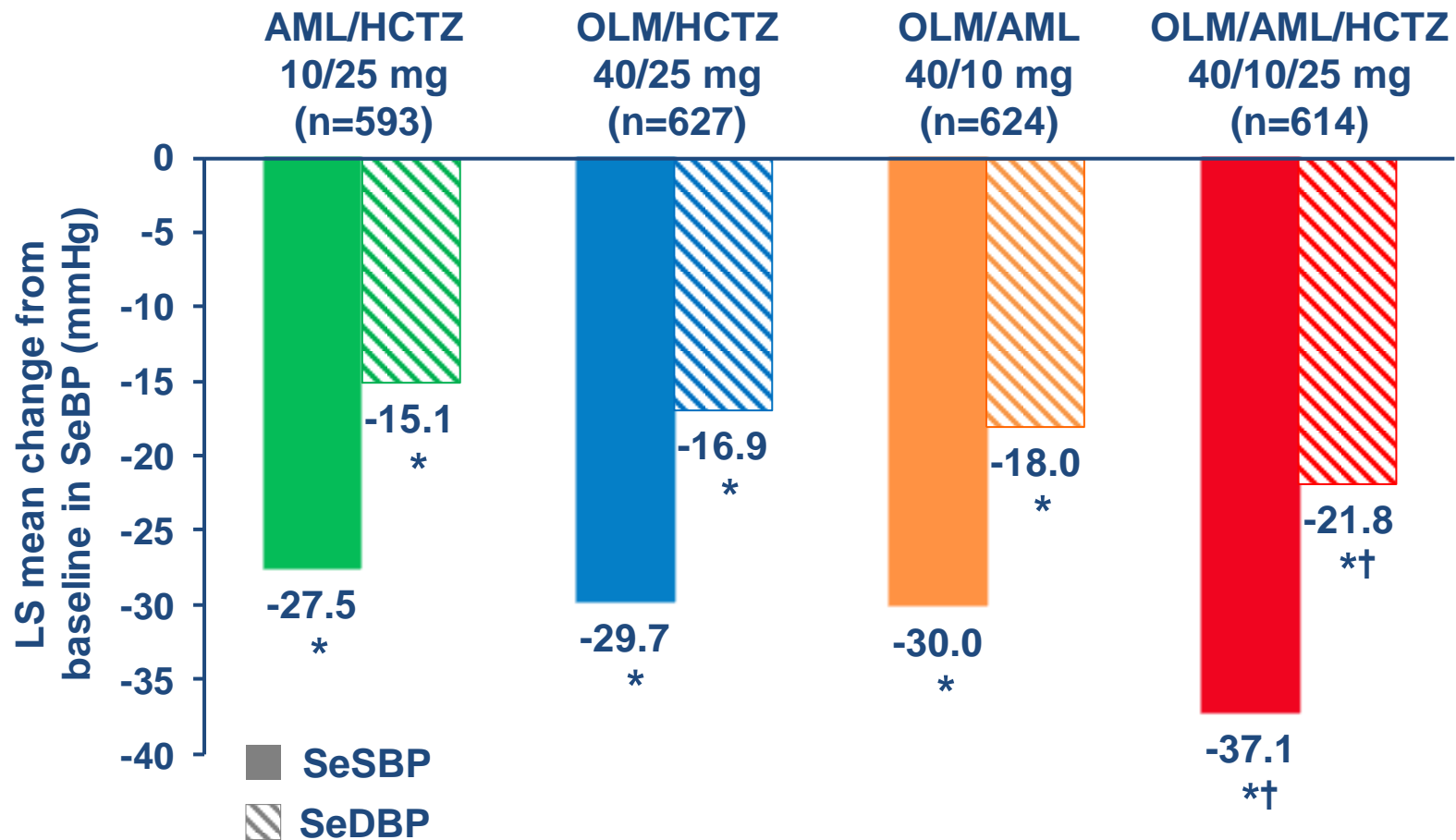
- Ourselves, as physicians
 - frustrations over poor BP control
 - concerns about poor adherence
 - personal and patient motivation

Triple Therapy with High Dose Olmesartan/AML/HCTZ in the TRINITY Study



Oparil et al. Clin Ther 2010;32:1252-69

High Dose OLM/AML/HCTZ Triple Combination Therapy is Superior to Dual Combination at Lowering BP (TRINITY study)



*p<0.001 vs. baseline
 †p<0.001 for triple vs. each dual combination

In patients with baseline mean SeBP 168.5/100.9 mmHg, at ter 12 weeks of treatment

Oparil et al. Clin Ther 2010;32:1252-69

Take-home Messages

- Barriers to good BP control
 - Physicians' side: clinical inertia
 - Patients' side:
poor persistence and/or adherence
- Poor persistence/adherence is not uncommon and has significant influence on prognosis.
- There is no short answer in improving persistence/adherence.
 - Patient's health belief

However,

Simplifying regimen using single-pill combination is the easiest and the most feasible way to improve patient's adherence.