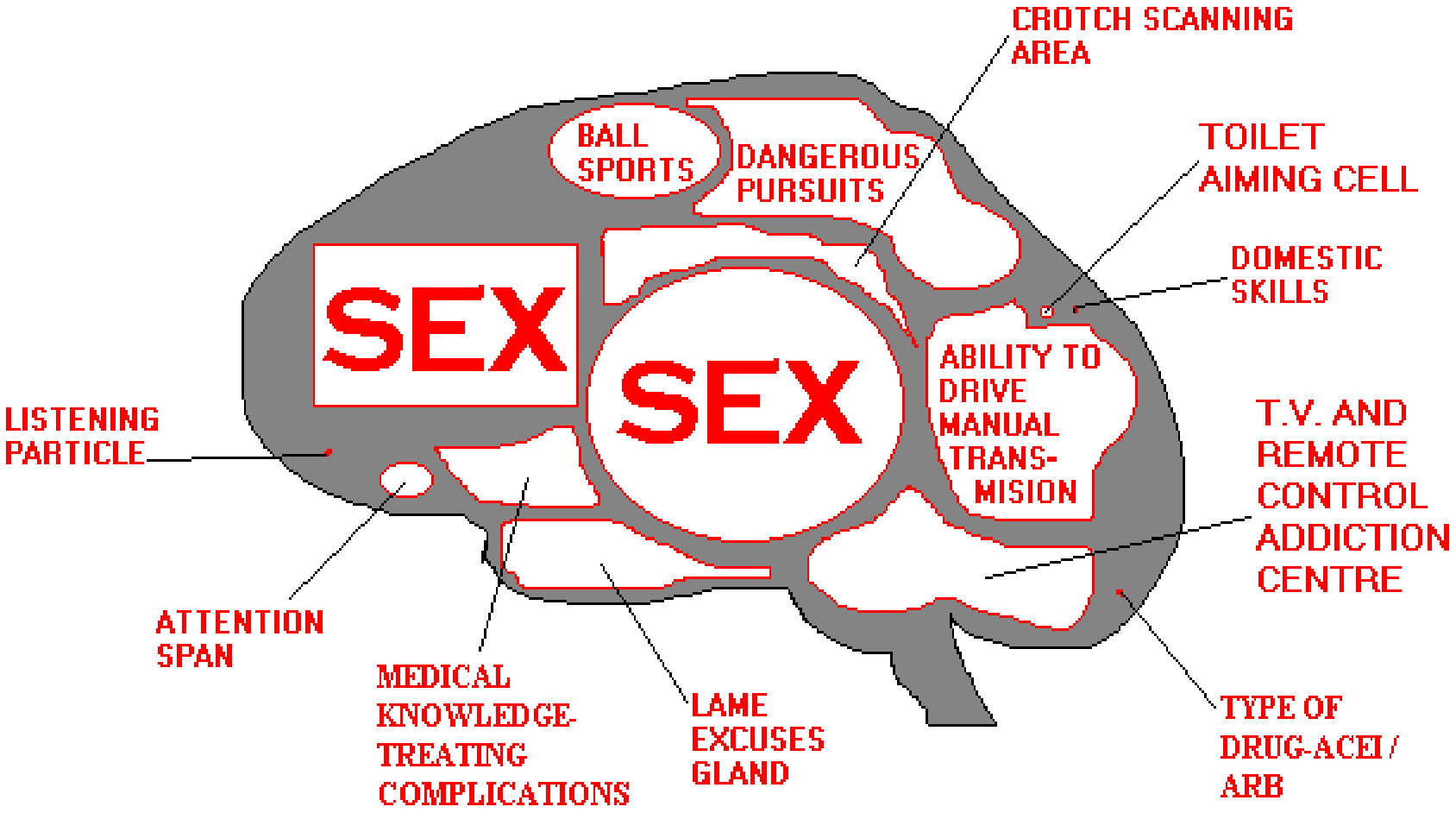
I will use ARB for my hypertensive patients!

Dr Goh Heong Keong

HK Goh vs Goh HK

THE MALE BRAIN



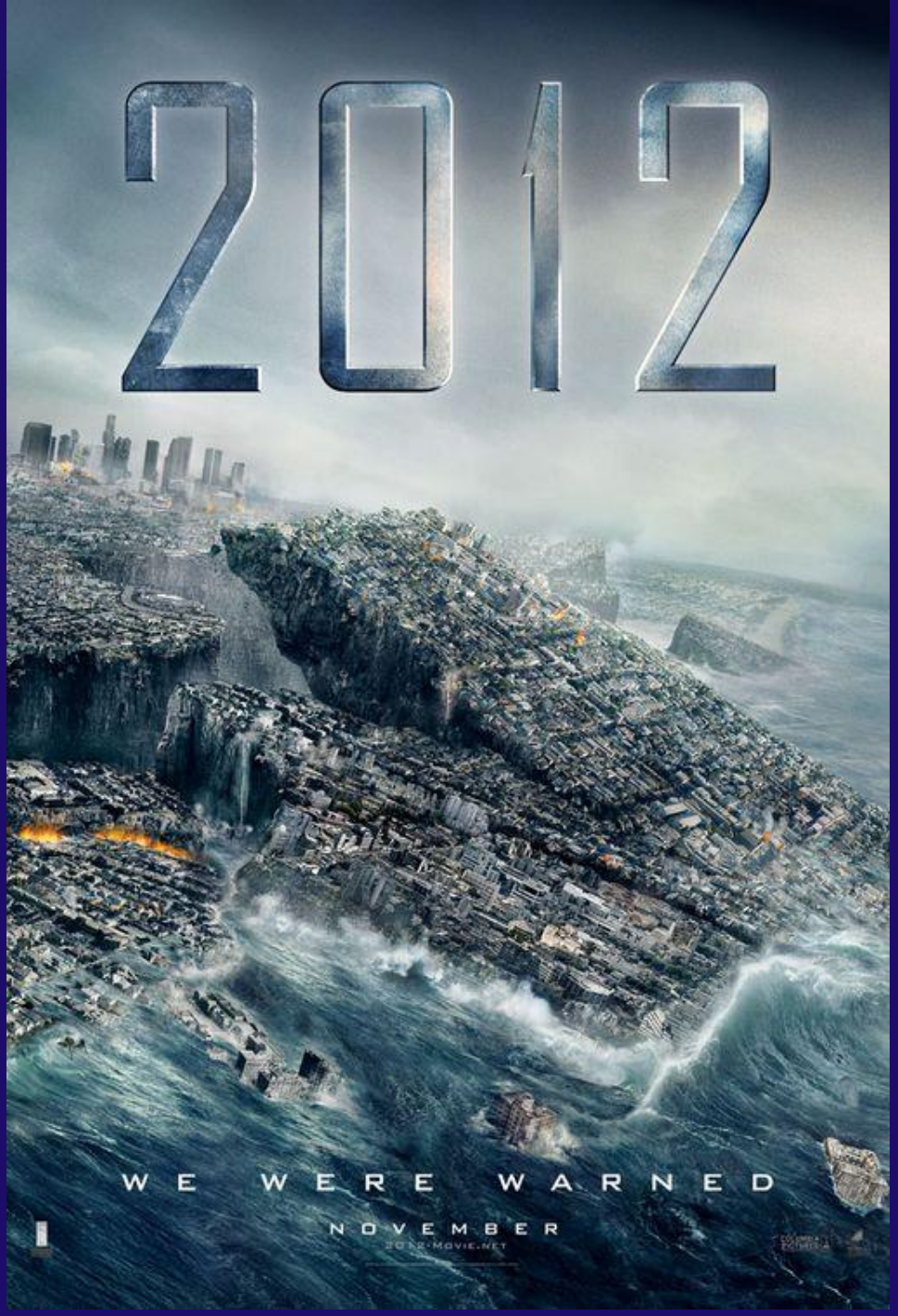
FOOTNOTE: the "Listening to children cry in the middle of the night" gland is not shown due to it's small and underdeveloped nature. Best viewed under a microscope.

Conclusion

MY STAND:

Yes, evidence shows that ARB is certainly more superior choice than ACEI for treating hypertension!

You Should Do the same as well!!


2012
WE WERE WARNED
NOVEMBER
2012-MOVIE.NET

The World Health Organization describes hypertension as the number one risk factor for mortality, as worldwide annually 7.5 million deaths (13% of all deaths) are attributable to high blood pressure (BP)-related diseases, particularly cardiovascular diseases (CVD)

Introduction

In the United States, about 76.4 million people age 20 and older have high blood pressure.

One in three adults in the United States has high blood pressure.

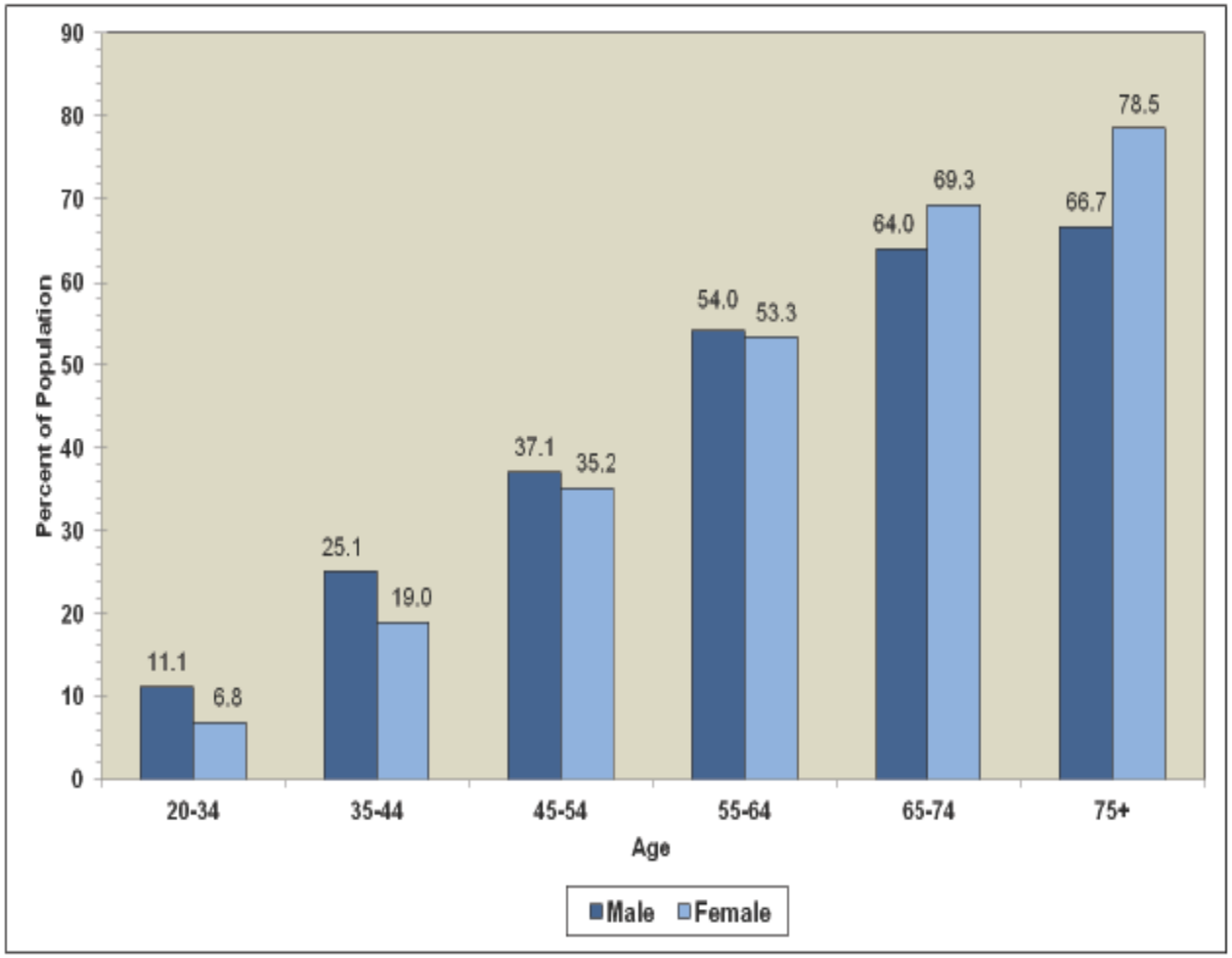
About 69% of people who have a first heart attack, 77% who have a first stroke, and 74% who have congestive heart failure have blood pressure higher than 140/90 mm Hg.

American Heart Association | American Stroke Association

High blood pressure was listed on death certificates as the primary cause of death of 61,005 Americans in 2008.

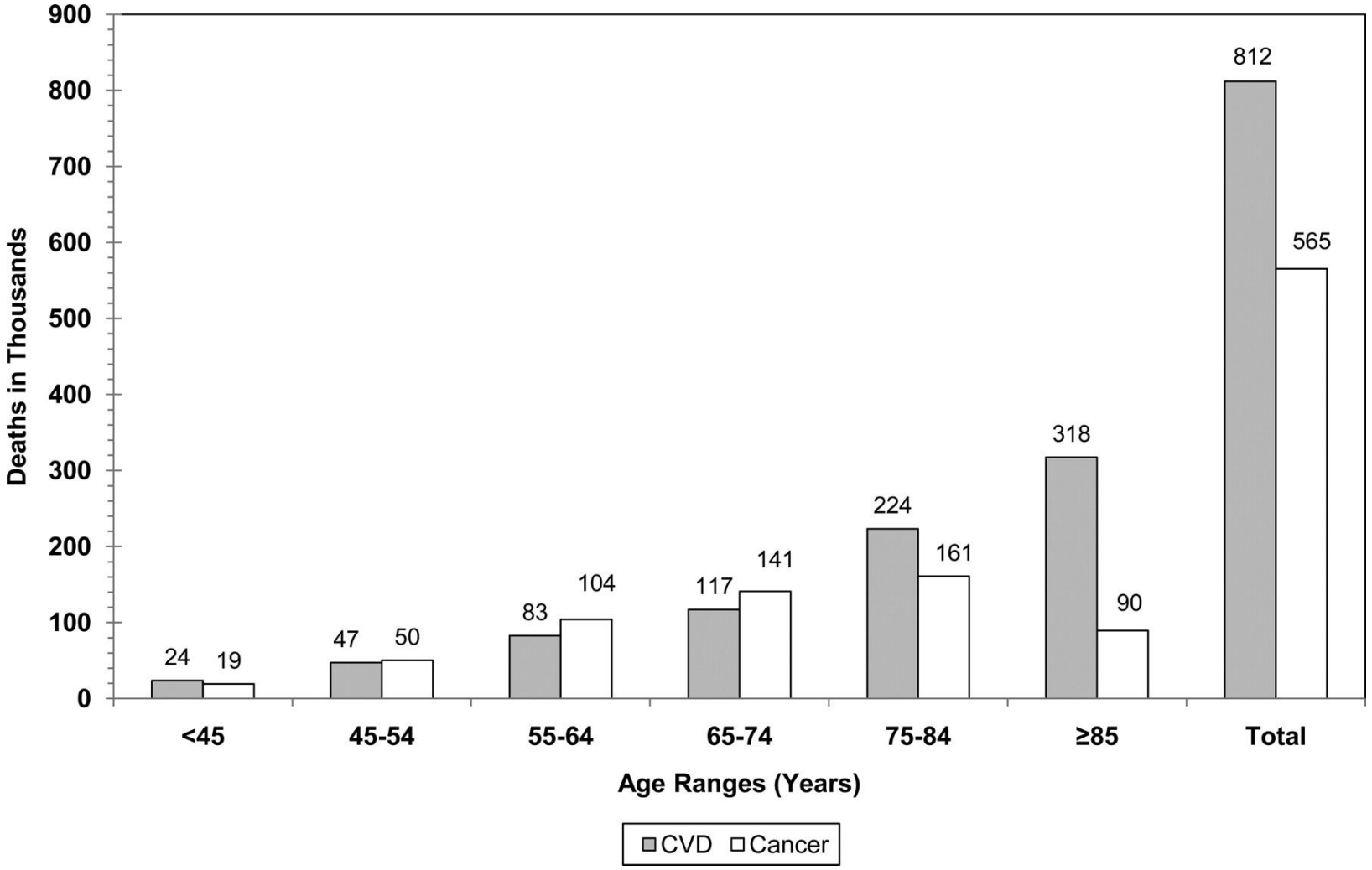
The estimated direct and indirect cost of high blood pressure in 2008 is $50.6 billion.

Prevalence of High Blood Pressure in Adults Age 20 and Older by Age and Sex. NHANES: 2005–08



Source: NCHS and NHLBI. Hypertension is defined as SBP 140 mm Hg or DBP 90 mmHg, taking antihypertensive medication, or being told twice by a physician or other professional that one has hypertension.

Cardiovascular disease (CVD) deaths vs cancer deaths by age (United States: 2008).

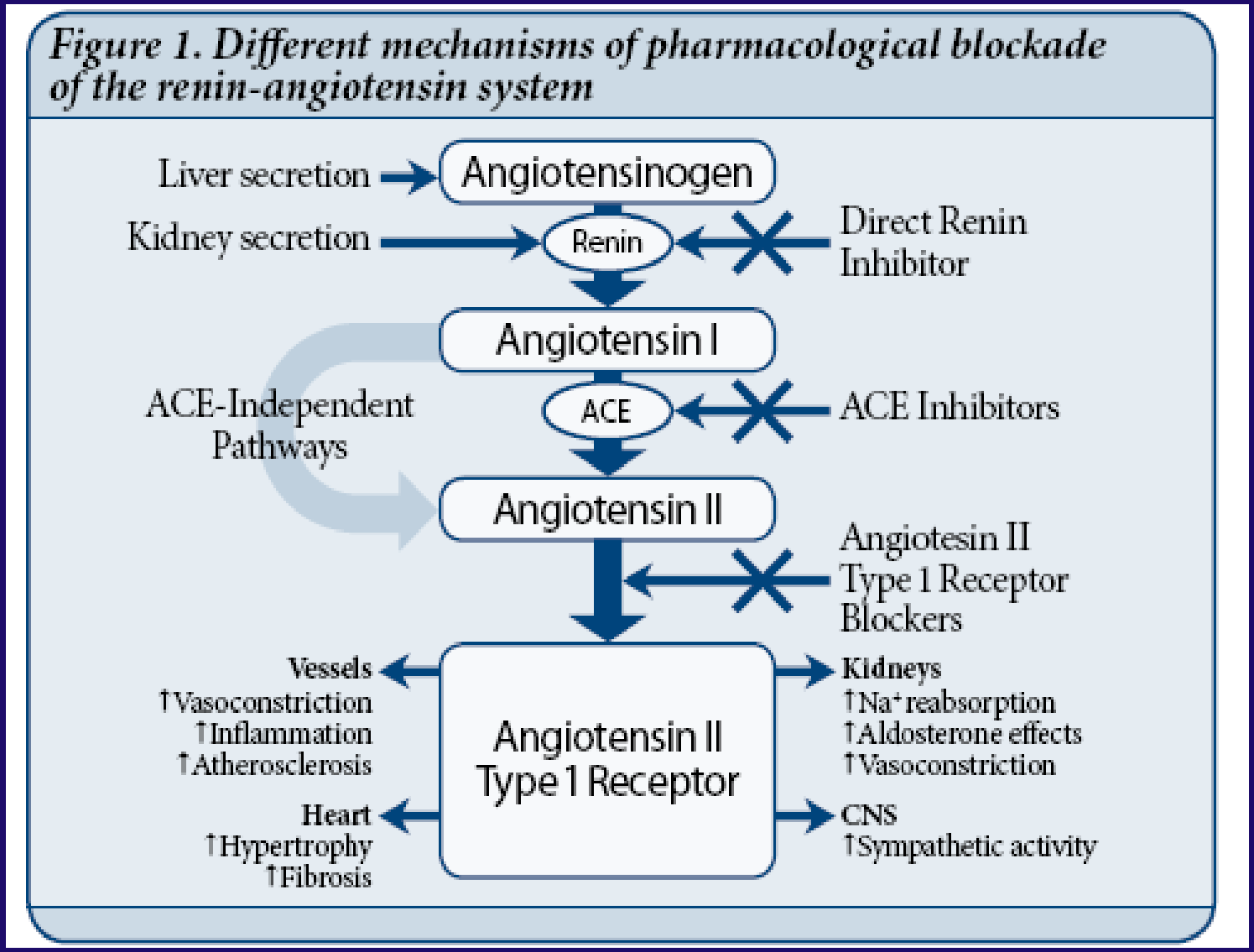


Writing Group Members et al. Circulation 2012;125:e2-e220

Data from NHANES 2005–08 showed that of those with high blood pressure,

- 79.6% are aware they have it
- 47.8% have it controlled
- 70.9% are under current treatment
- 52.2% do not have it controlled

Mechanism of Action



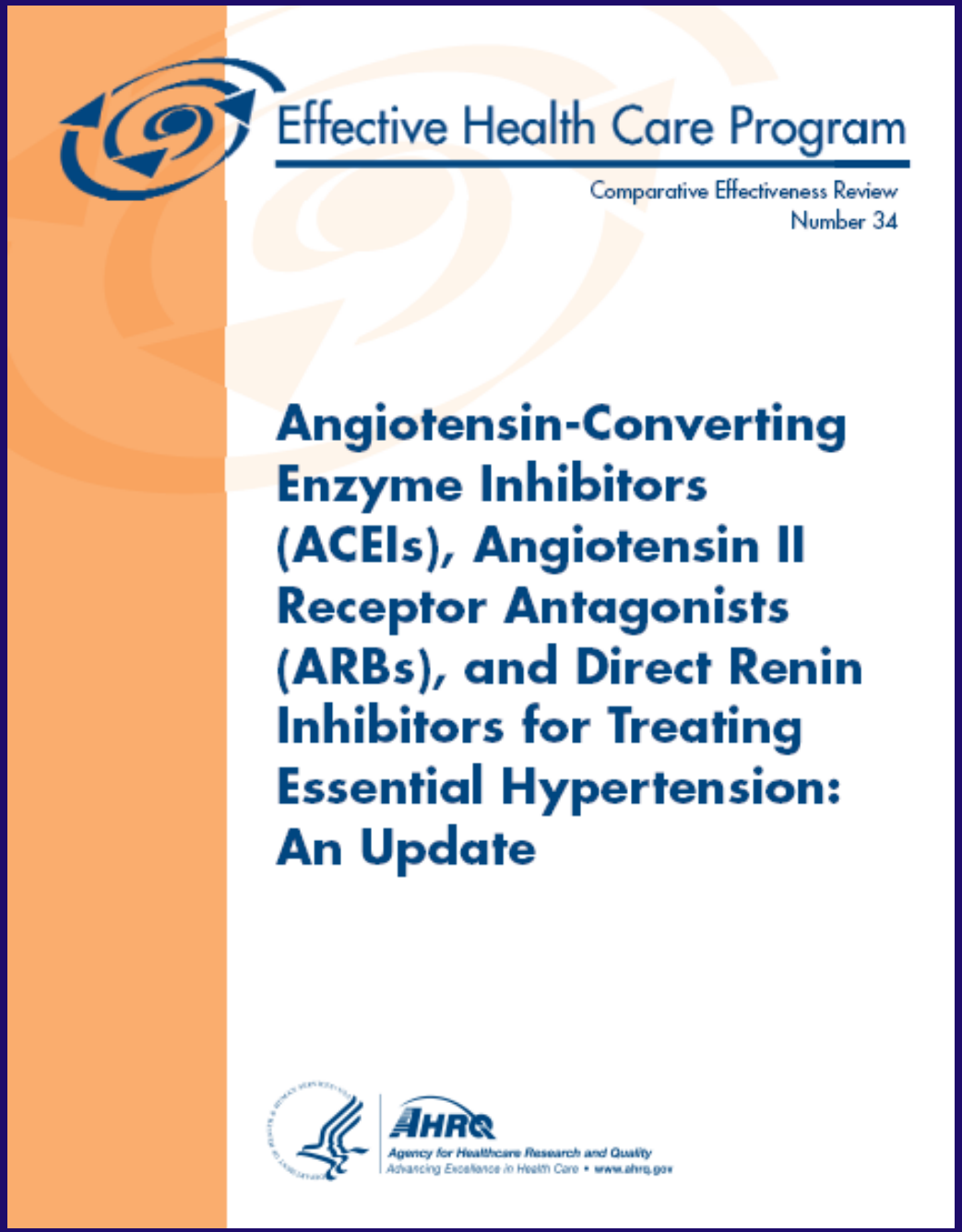
Good Drug??

blood pressure control

cardiovascular risk reduction

quality of life, and other outcomes

safety, adverse events,tolerability, persistence with drug therapy, and treatment adherence

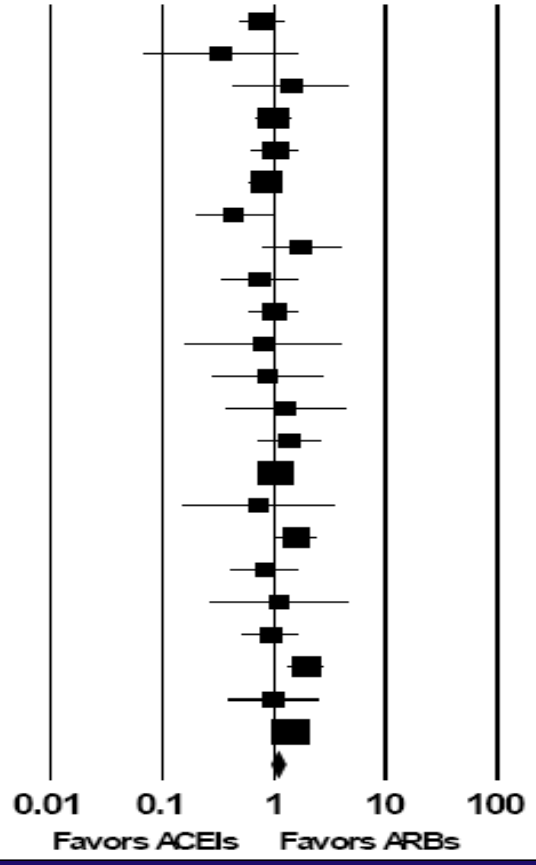


The Agency for Healthcare Research and Quality's (AHRQ) mission is to improve the quality, safety, efficiency, and effectiveness of health care for all Americans. As 1 of 12 agencies within the Department of Health and Human Services, AHRQ supports research that helps people make more informed decisions and improves the quality of health care services.

Blood Pressure Control??

Figure 3. Random-effects analysis of RCTs for successful blood pressure control on monotherapy (ARBs vs. ACEIs)

Study name	Odds ratio	Lower limit	Upper limit
Townsend et al., 1995	0.787	0.487	1.272
Ruff et al., 1996	0.335	0.069	1.632
Larochelle et al., 1997	1.425	0.434	4.676
Argenziano et al., 1999	1.000	0.692	1.446
Karlberg et al., 1999	1.032	0.633	1.682
Neutel et al., 1999	0.841	0.595	1.190
Lacourciere et al., 2000	0.438	0.199	0.963
Mogensen et al., 2000	1.761	0.768	4.036
Ruilope et al., 2001	0.738	0.328	1.659
Cuspidi et al., 2002	1.005	0.604	1.672
Kavgaci et al., 2002	0.796	0.155	4.083
Eguchi et al., 2003	0.875	0.281	2.729
Ghiadoni et al., 2003	1.278	0.370	4.418
Fogari et al., 2004	1.385	0.725	2.644
Malacco et al., 2004	1.040	0.789	1.371
Robles et al., 2004	0.727	0.151	3.493
Saito et al., 2004	1.574	1.023	2.422
Rosei et al., 2005	0.831	0.408	1.689
Uchiyama-Tanaka et al., 2005	1.105	0.262	4.671
Tedesco et al., 2006	0.924	0.510	1.675
Hosohata et al., 2007	1.936	1.329	2.820
Menne et al., 2008	0.997	0.386	2.574
Malacco et al, 2010	1.407	1.109	1.785
	1.083	0.937	1.252



Effect on Mortality and Major Cardiovascular Events

The literature review identified 26 publications[25,26,28,30,32,36,37,39,43,48,52,53,55,74,88,98,101,103-105,107,108,110-113] describing 21 separate studies that reported patient mortality, myocardial infarction (MI), or clinical stroke as outcomes. Seventeen studies (22 publications) were RCTs.[25,26,28,30,32,36,37,39,43,48,52,53,55,74,88,98,101,103-105,107,108] The 21 studies reported on 40,749 patients (38,589 of whom received an ACEI, an ARB, or a DRI) and ranged in duration from 12 weeks to 5 years; most reported blood pressure measurements as primary endpoints. The treatment comparisons evaluated were (one study per comparison, unless otherwise noted):

- "ACEIs" versus "ARBs" (3 studies);[110,112,113]
- Candesartan versus lisinopril;[32]
- Eprosartan versus enalapril (2 studies, 6 publications);[30,36,39,43,48,55]
- Losartan versus enalapril (2 studies);[53,74]
- Losartan versus fosinopril;[88]
- Losartan versus ramipril;[98]
- Losartan versus quinapiril;[52]
- Telmisartan versus ramipril;[108]
- Telmisartan versus enalapril (2 studies);[37,101]
- Valsartan versus lisinopril (3 studies);[26,28,111]
- Valsartan versus enalapril;[25]

The studies were of good (n = 8), fair (n = 9), and poor (n = 4) quality. Notably, the majority of studies in this review—including those reporting mortality and major cardiovascular events—excluded patients with significant cardiovascular disease and often other comorbid conditions.

The studies evaluated shed little light on the issue of relative rates of mortality, MI, or stroke with ACEIs versus ARBs versus direct renin inhibitors. In 21 studies involving 40,749 patients,

Table 9. Characteristics of studies reporting LV mass/function outcomes

Study	Agents studied	Population	Design and size*	Duration	Quality	Outcome	Result
Cuspidi et al., 2002[109]	Candesartan vs. enalapril	LVH (Pts 33%)	RCT N = 196 (145)	48 wk	Fair	LVMI & LVEF	↓LVMI both, no difference between agents, no change in LVEF
Spoelstra-de Man et al., 2006[33]	Candesartan vs. lisinopril	DM and HTN (? %LVH)	RCT N = 46	12 mo	Good	LVMI	↓LVMI both, but ARB not compared to ACEI
Schieffer et al., 2004[93]	Irbesartan vs. enalapril	CAD (? %LVH)	RCT N = 60 (48)	3 mo	Poor	LVEF	No difference No detailed data by treatment group
Gunteki[illegible] et al., 2006[87]	Irbesartan vs. quinapril	New HTN (? %LVH)	RCT N = 65 (38)	12 mo	Poor	LV posterior wall thickness	↓LV posterior wall thickness both, no difference reported between agents
Awanza et al., 2000[80]	Losartan vs. enalapril	LVH (100%)	Non-rand controlled clinical trial N = 30	10 mo	Poor	LVMI	↓LVMI both, no difference between agents, combo ACEI/ARB best
De Rosa et al., 2002[41]	Losartan vs. enalapril	LVH (44–53%)	RCT N = 50 (42)	3 yr	Fair	LVMI	Non-statistical ↓LVMI both, no difference between agents
Shibasaki et al., 2002[74]	Losartan vs. enalapril	ESRD with LVH (100%)	RCT N = 20	6 mo	Fair	LVMI & LVEF	↓LVMI both, ARB better than ACEI, no change in LVEF
Tedesco et al., 2006[34]	Losartan vs. enalapril	HTN (30–33% LVH)	RCT N = 259 (185)	2 yr	Good	LVMI	↓LVMI both, ARB more than ACEI, but ARB higher baseline
Verdecchia et al., 2000[99]	Losartan vs. enalapril	LVH (23–24%)	Case-control N = 88	3.3 yr	Poor	LVMI	↓LVMI both, no difference between agents
Rajzer et al., 2003[92]	Losartan vs. quinapril	HTN (? %LVH)	RCT N = 118	6 mo	Poor	LVMI & LVEF	No change in LVMI or LVEF in either group No detailed data by treatment group
Scaglione et al., 2007[31]	Losartan vs. ramipril	HTN (53% LVH)	RCT N = 57	24 wks	Good	LVMI	↓LVMI both, no difference between agents
Celik et al., 2005[81]	Telmisartan vs. ramipril	HTN (? %LVH)	RCT N = 100	6 mo	Poor	LVEF	No change in LVEF in either group
Solomon et al., 2009[107]	Aliskiren vs. losartan	HTN (100% LVH)	RCT N = 465 (400)	34 wks	Good	LVMI	↓LVMI both, no difference between groups (aliskiren, ARB, combination)

LV Mass and Function

NO DIFFERENCE!!

LIPID PROFILES

Table 8. Studies reporting significant changes in lipid profiles with ACEIs and/or ARBs

Study	N	Population	Quality	Comparators	ΔTC	ΔLDL	ΔHDL	ΔTG
Lacourcière et al., 2000[53]	103	- Mean age 58 - 96% white - Canada - Diabetes	Fair	Losartan vs. enalapril	-2.1%* vs. -4.2%*	-6.5%* vs. NR	NR	NR vs. -11.3%*
Derosa et al., 2003[23]	96	- Mean age 54 - Europe - Diabetes	Good	Candesartan vs. perindopril	-1 mg/dL vs. -12 mg/dL*†	-4 mg/dL vs. -14 mg/dL†	+2 mg/dL vs. -2 mg/DL	+2 mg/dL vs. -22 mg/dL
Kavgaci et al., 2002[88]	33	- Mean age 53 - 100% white - Turkey - Diabetes	Poor	Losartan vs. fosinopril	+0.01% vs. -0.1%*	NR	NR	-0.23%* vs. -0.21%*
Tedesco et al., 2006[34]	520	- Mean age 54 - 100% white - Italy - No diabetes	Good	Losartan vs. enalapril	-10 mg/dL* vs. +1 mg/dL	NR	NR	NR
Yilmaz et al., 2007[102]	96	- Mean age 48 - Turkey - Metabolic syndrome	Poor	Ramipril vs. valsartan	14.3 to 12.0 mmol/L* vs. 14.9 to 12.6 mmol/L*	7.3 to 5.5 mmol/L* vs. 7.7 to 6.1 mmol/L*	2.0 to 2.4 mmol/L* vs. 1.9 to 2.3 mmol/L*	8.8 to 7.6 mmol/L* vs. 11.0 to 8.9 mmol/L*
Xu et al., 2007[101]	96	- Mean age 51 - China - Abnormal serum lipids	Poor	Telmisartan vs. enalapril	6.1 to 5.8 mmol/L vs. 6.1 to 5.9 mmol/L	3.1 to 2.3 mmol/L vs. 3.1 to 3.0 mmol/L	1.5 to 1.7 mmol/L† vs. 1.4 to 1.4 mmol/L	2.8 to 2.0 mmol/L† vs. 2.8 to 2.6 mmol/L

NO DIFFERENCE!!

*Statistically significant within-treatment change (baseline to follow-up)
†Statistically significant comparison between treatments
HDL = low-density lipoprotein; LDL = low-density lipoprotein; N = number of subjects; NR=not reported; TC = total cholesterol; TG = triglyceride

No difference!!

How about side effects??

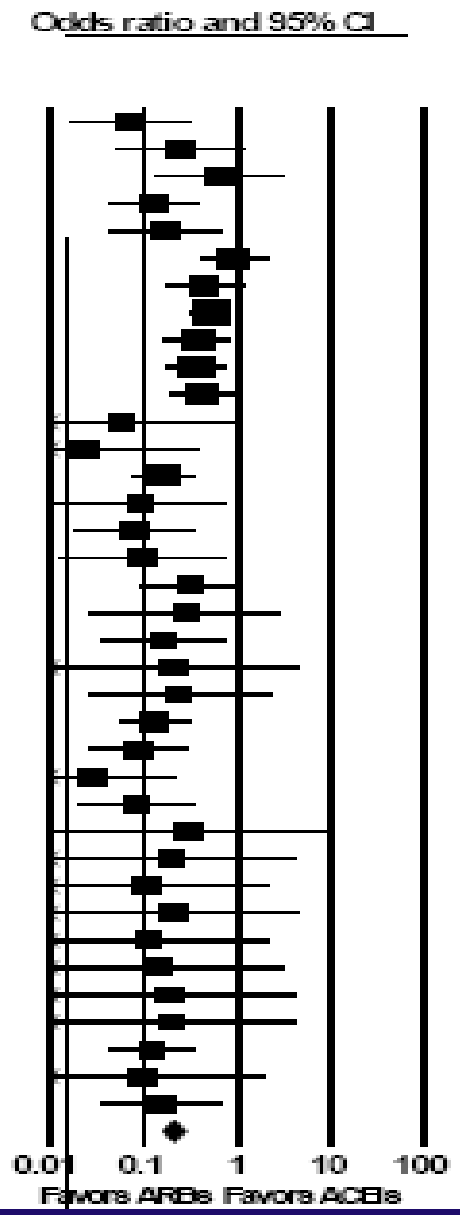
Lin chi-ling

zhang zhi yi

Cough! Cough!

Figure [illegible] Random-effects analysis of RCTs for cough (ARBs vs. ACEIs)

Study name	Odds ratio	Lower limit	Upper limit
Tikkanen et al., 1995	0.072	0.017	0.308
Townsend et al., 1995	0.248	0.051	1.182
Ruff et al., 1996	0.638	0.131	3.098
Black et al., 1997	0.127	0.042	0.390
Larochelle et al., 1997	0.168	0.043	0.660
Roca-Cusachs et al., 1997	0.905	0.408	2.009
Mimran et al., 1998	0.446	0.174	1.147
Elliott, 1999	0.514	0.324	0.815
Karlberg et al., 1999	0.368	0.163	0.832
Naidoo et al., 1999	0.363	0.179	0.738
Neutel et al., 1999	0.411	0.186	0.908
Lacourciere et al., 2000	0.057	0.003	1.017
Malmqvist et al., 2000	0.023	0.001	0.389
McInnes et al., 2000	0.160	0.076	0.337
Ruilope et al., 2001	0.092	0.012	0.724
Amerena et al., 2002	0.078	0.018	0.334
Coca et al., 2002	0.095	0.012	0.759
Cuspidi et al., 2002	0.313	0.091	1.076
Derosa et al., 2002	0.280	0.027	2.898
Ragot et al., 2002	0.160	0.035	0.723
Derosa et al., 2003	0.200	0.009	4.279
Fogari et al., 2004	0.240	0.026	2.198
Malacoo et al., 2004	0.129	0.054	0.305
Koylan et al., 2005	0.087	0.026	0.288
Lacourciere et al., 2006	0.028	0.004	0.206
Williams et al., 2006	0.084	0.020	0.358
Deyneli et al, 2006	0.307	0.011	8.309
Fogari et al, 2006	0.195	0.009	4.127
Tedesoo et al, 2006	0.108	0.006	2.024
Xu et al, 2007	0.209	0.010	4.462
Fogari et al, 2008	0.109	0.006	2.052
Kloner et al, 2008	0.150	0.008	2.937
Zhu et al, 2008	0.187	0.009	4.062
Nakamura et al, 2009	0.192	0.009	4.207
Spinar et al, 2009	0.122	0.043	0.345
Akat et al, 2010	0.099	0.005	1.904
Malacoo et al, 2010	0.152	0.034	0.678
	0.211	0.159	0.281



Evidence of Adverse Effects

Cough is more prevalent in patients on ACEIs than those on ARBs (About 9% of patients treated with an ACEI and about 2% of patients treated with an ARB report a cough).

Systematic review and meta-analysis of ethnic differences in risks of adverse reactions to drugs used in cardiovascular medicine

Sarah E McDowell, Jamie J Coleman, R E Ferner

Cite this article as: BMJ, doi:10.1136/bmj.38803.528113.55 (published 5 May 2006)

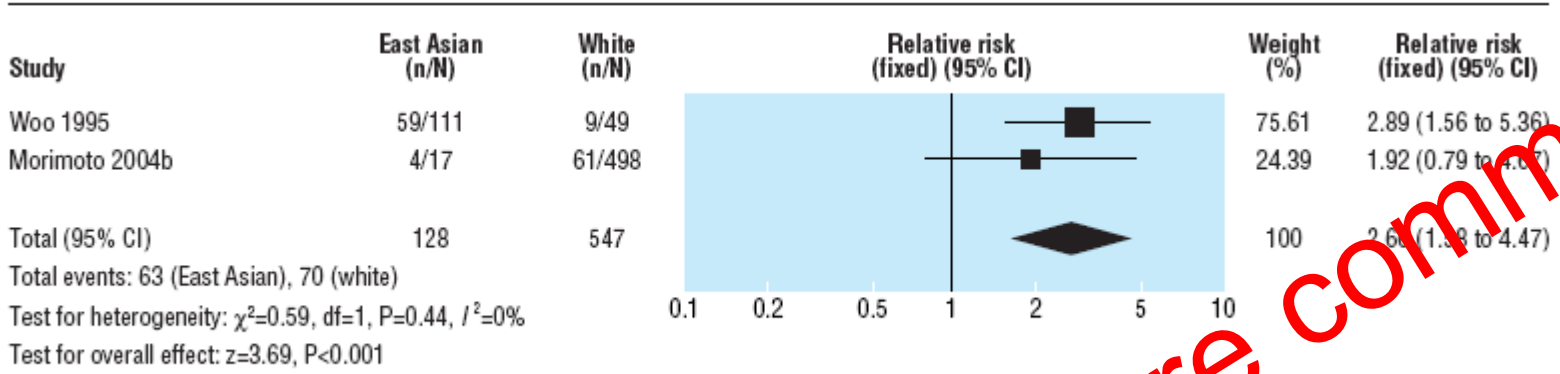
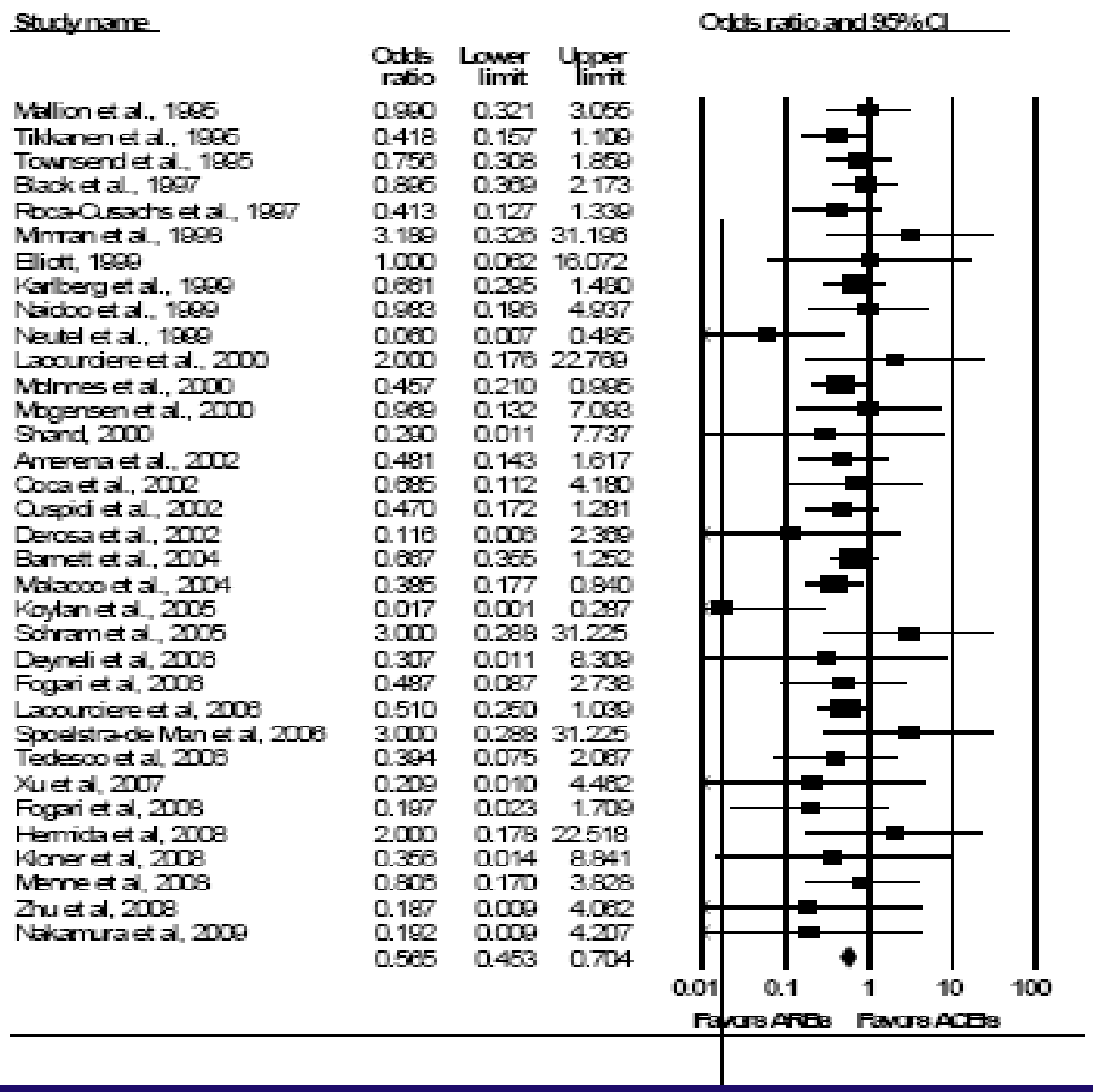


Fig 3 Pooled analysis of proportion of East Asian and white patients with cough associated with use of ACE inhibitors

2.7 X more common

Figure 9. Random-effects analysis of RCTs for withdrawals due to adverse events (ARBs vs. ACEIs)



ACEIs were associated with lower rates of persistence and higher rates of withdrawals due to adverse events when compared with ARBs

European Heart Journal Advance Access published April 17, 2012

European Heart Journal
doi:10.1093/eurheartj/ehs075

CLINICAL RESEARCH

Angiotensin-converting enzyme inhibitors reduce mortality in hypertension: a meta-analysis of randomized clinical trials of renin–angiotensin–aldosterone system inhibitors involving 158 998 patients

Laura C. van Vark[1]*, Michel Bertrand[2], K. Martijn Akkerhuis[1], Jasper J. Brugts[1], Kim Fox[3], Jean-Jacques Mourad[4], and Eric Boersma[1]

[1]Department of Cardiology, Thoraxcenter, Erasmus MC, 's Gravendijkwal 230, 3015 GE Rotterdam, The Netherlands; [2]Lille Heart Institute, Lille, France; [3]Royal Brompton and National Heart Hospital, London, UK; and [4]Avicenne University Hospital, Bobigny and Paris 13 University, Paris, France

Received 24 August 2011; revised 15 February 2012; accepted 5 March 2012

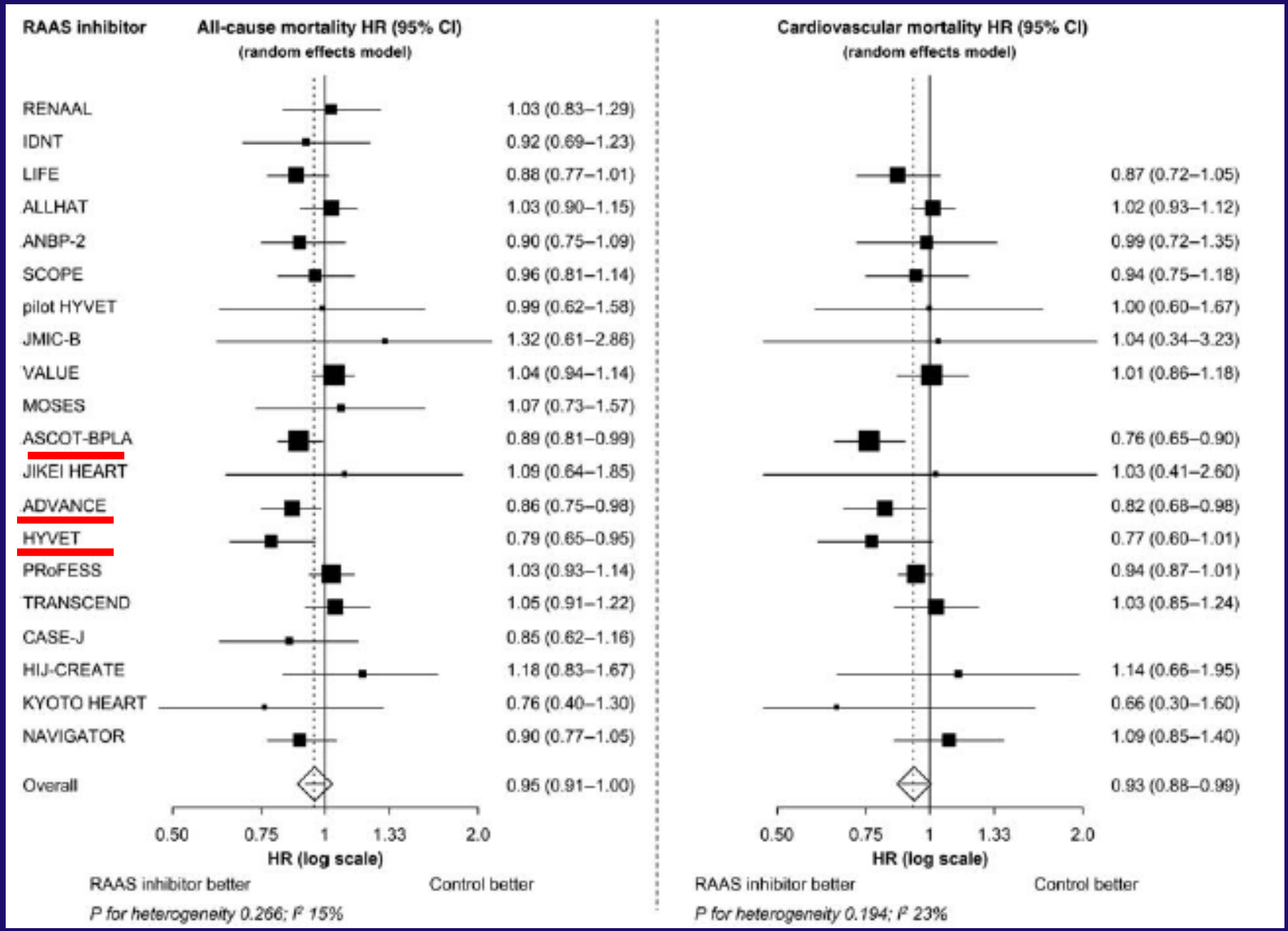
Conclusion

In patients with hypertension, treatment with an ACE inhibitor results in a significant further reduction in all-cause mortality. Because of the high prevalence of hypertension, the widespread use of ACE inhibitors may result in an important gain in lives saved.

Table 1 Baseline characteristics of study population in 20 trials ($n = 158\,998$)

Trial acronym	Year	n	Active drug	Control	Mean follow-up, years	Hypertension, %
RENAAL[9]	2001	1513	Losartan	Placebo	3.09	96.5
IDNT[28]	2001	1715	Irbesartan	Amlodipine or placebo	2.86	100
LIFE[25]	2002	9193	Losartan with and without HCTZ	Atenolol with and without HCTZ	4.82	100
ALLHAT[30]	2002	33 357	Lisinopril	Chlorthalidone or amlodipine	5.01	100
ANBP-2[33]	2003	6083	ACE inhibitor (enalapril)	Diuretic (HCTZ)	4.06	100
SCOPE[29]	2003	4937	Candesartan	Placebo	3.74	100
pilot HYVET[24]	2003	1283	Lisinopril	Diuretic or no treatment	1.12	100
JMIC-B[34]	2004	1650	ACE inhibitor	Nifedipine	2.25	100
VALUE[27]	2004	15 245	Valsartan	Amlodipine	4.32	100
MOSES[32]	2005	1352	Eprosartan	Nitrendipine	2.50	100
ASCOT-BPLA[26]	2005	19 257	Amlodipine with and without perindopril	Atenolol with and without bendroflumethiazide	5.50	100
JIKEI HEART[11]	2007	3081	Valsartan	Non-ARB	2.81	87.6
ADVANCE[31]	2007	11 140	Perindopril with indapamide	Placebo	4.30	68.7
HYVET[23]	2008	3845	Indapamide with and without perindopril	Placebo	2.11	89.9
PRoFESS[22]	2008	20 332	Telmisartan	Placebo	2.50	74.0
TRANSCEND[35]	2008	5926	Telmisartan	Placebo	4.67	76.4
CASE-J[20]	2008	4703	Candesartan	Amlodipine	3.30	100
HIJ-CREATE[19]	2009	2049	Candesartan	Non-ARB	4.03	100
KYOTO HEART[21]	2009	3031	Valsartan	Non-ARB	2.92	100
NAVIGATOR[10]	2010	9306	Valsartan	Placebo	6.10	77.5

HCTZ, hydrochlorothiazide; ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; SBP, systolic blood pressure; IR, incidence rate per 1000 patient-years.


RAAS inhibitor
All-cause mortality HR (95% CI)
(random effects model)
RENAAL 1.03 (0.83–1.29)
IDNT 0.92 (0.69–1.23)
LIFE 0.88 (0.77–1.01)
ALLHAT 1.03 (0.90–1.15)
ANBP-2 0.90 (0.75–1.09)
SCOPE 0.96 (0.81–1.14)
pilot HYVET 0.99 (0.62–1.58)
JMIC-B 1.32 (0.61–2.86)
VALUE 1.04 (0.94–1.14)
MOSES 1.07 (0.73–1.57)
ASCOT-BPLA 0.89 (0.81–0.99)
JIKEI HEART 1.09 (0.64–1.85)
ADVANCE 0.86 (0.75–0.98)
HYVET 0.79 (0.65–0.95)
PRoFESS 1.03 (0.93–1.14)
TRANSCEND 1.05 (0.91–1.22)
CASE-J 0.85 (0.62–1.16)
HIJ-CREATE 1.18 (0.83–1.67)
KYOTO HEART 0.76 (0.40–1.30)
NAVIGATOR 0.90 (0.77–1.05)
Overall 0.95 (0.91–1.00)
0.50 0.75 1 1.33 2.0
HR (log scale)
RAAS inhibitor better
Control better
P for heterogeneity 0.266; I² 15%
Cardiovascular mortality HR (95% CI)
(random effects model)
0.87 (0.72–1.05)
1.02 (0.93–1.12)
0.99 (0.72–1.35)
0.94 (0.75–1.18)
1.00 (0.60–1.67)
1.04 (0.34–3.23)
1.01 (0.86–1.18)
0.76 (0.65–0.90)
1.03 (0.41–2.60)
0.82 (0.68–0.98)
0.77 (0.60–1.01)
0.94 (0.87–1.01)
1.03 (0.85–1.24)
1.14 (0.66–1.95)
0.66 (0.30–1.60)
1.09 (0.85–1.40)
0.93 (0.88–0.99)
0.50 0.75 1 1.33 2.0
HR (log scale)
RAAS inhibitor better
Control better
P for heterogeneity 0.194; I² 23%

In ASCOT-BPLA an amlodipine-based regimen was compared to a atenolol- based regimen; perindopril 4-8 mg was only added to amlodipine "as required", as step 3 (like an underdosed bendroflumethiazide added to atenolol) and so only 58,5% of participants in all study received perindopril

In HYVET the comparison was between placebo and an indapamide-based regimen, with perindopril 2-4 mg added only as step 2 and 3, as required to reach the blood pressure target; at two years in the active group only 73% of patients received some amount of perindopril.

in ADVANCE the comparison was not between perindopril and other drugs, but between the thiazide-like diuretic indapamide and no diuretic: it was indapamide, indeed, that made the difference

1) Dahl?f B, Sever PS, Poulter NR, et al. Lancet 2005; 366: 895-906.
2) Beckett NS, Peters R, Fletcher AE, et al. N Engl J Med 2008;358:1887-98.
3) ADVANCE Collaborative Group. : a randomised controlled trial. Lancet 2007; 370: 829-40

Conclusion

Yes, evidence shows that ARB is as good as ACEI if not superior with less side effect!!

AND

You are more likely to have a compliant patient if ARB is used instead of ACEI!!

Sometimes it's best just to jump in !

Potts M et al, *BMJ* 2006; 333:701-703

Thank you

for your attention !

"I hear, I know.

I see, I remember.

I do, I understand."

(Confucius, 551BC - 479)