











1 REVIEW ARTICLE

2 Comparative efficacy of angiotensin-converting
3 enzyme inhibitors versus angiotensin receptor
4 blockers for blood pressure lowering in adults
5 with essential hypertension: a systematic
6 review and meta-analysis

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10 ABSTRACT

11 **Background:** Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) serve
12 as primary treatments for essential hypertension. Nonetheless, research is scarce directly comparing the effi-
13 cacy of these medications in controlling blood pressure. This systematic review and meta-analysis sought to
14 assess and compare the safety and efficacy of these drugs in adults diagnosed with essential hypertension.

15 **Methods:** A comprehensive review of randomized controlled trials (RCTs) published from 2015 to 2025 was
16 carried out using PubMed, Medline, and Scopus. The studies selected for inclusion compared ACEIs and ARBs
17 in adult patients with essential hypertension, specifically focusing on alterations in systolic blood pressure
18 (SBP), and/or diastolic blood pressure (DBP).

19 **Results:** A total of five RCTs involving 852 participants were included. The meta-analysis showed no significant differ-
20 ence between ACEIs and ARBs in reducing SBP standardized mean differences [SMD = 0.01; 95% confidence intervals
21 (CI): -0.16 to 0.18; $p = 0.91$; $I^2 = 0\%$]. For DBP, the pooled analysis suggested a slight advantage for ACEIs
22 (SMD = -1.52; 95% CI: -2.86 to -0.19; $p = 0.03$), but this finding was driven by a single outlier study ($I^2 = 97\%$). After
23 sensitivity analysis, the difference was no longer significant (SMD = -0.31; 95% CI: -0.90 to 0.28; $p = 0.30$). Blood pres-
24 sure normalization rates (<140/90 mmHg) did not differ significantly between groups (OR = 0.95; 95% CI: 0.66-1.37;
25 $p = 0.79$; $I^2 = 13\%$). The safety profiles were similar, but ACEIs were associated with a higher incidence of cough.

26 **Conclusion:** ACEIs and ARBs are equally effective in lowering SBP and managing blood pressure control in
27 adults with essential hypertension. The decision to choose between these medications should be based on
28 tolerability, individual patient factors, and considerations regarding vascular health, rather than differences in
29 their ability to reduce blood pressure.

30 **Keywords:** Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, essential hypertension,
31 blood pressure lowering, antihypertensive therapy.

32 Introduction

33 Hypertension is a major risk factor for cardiovascular
34 diseases, accounting for over 10 million deaths
35 worldwide. It also contributes significantly to various
36 health issues, leading to a considerable economic burden
37 on healthcare systems [1,2]. Hypertension is commonly
38 treated with angiotensin receptor blockers (ARBs) and
39 angiotensin-converting enzyme inhibitors (ACEIs). It

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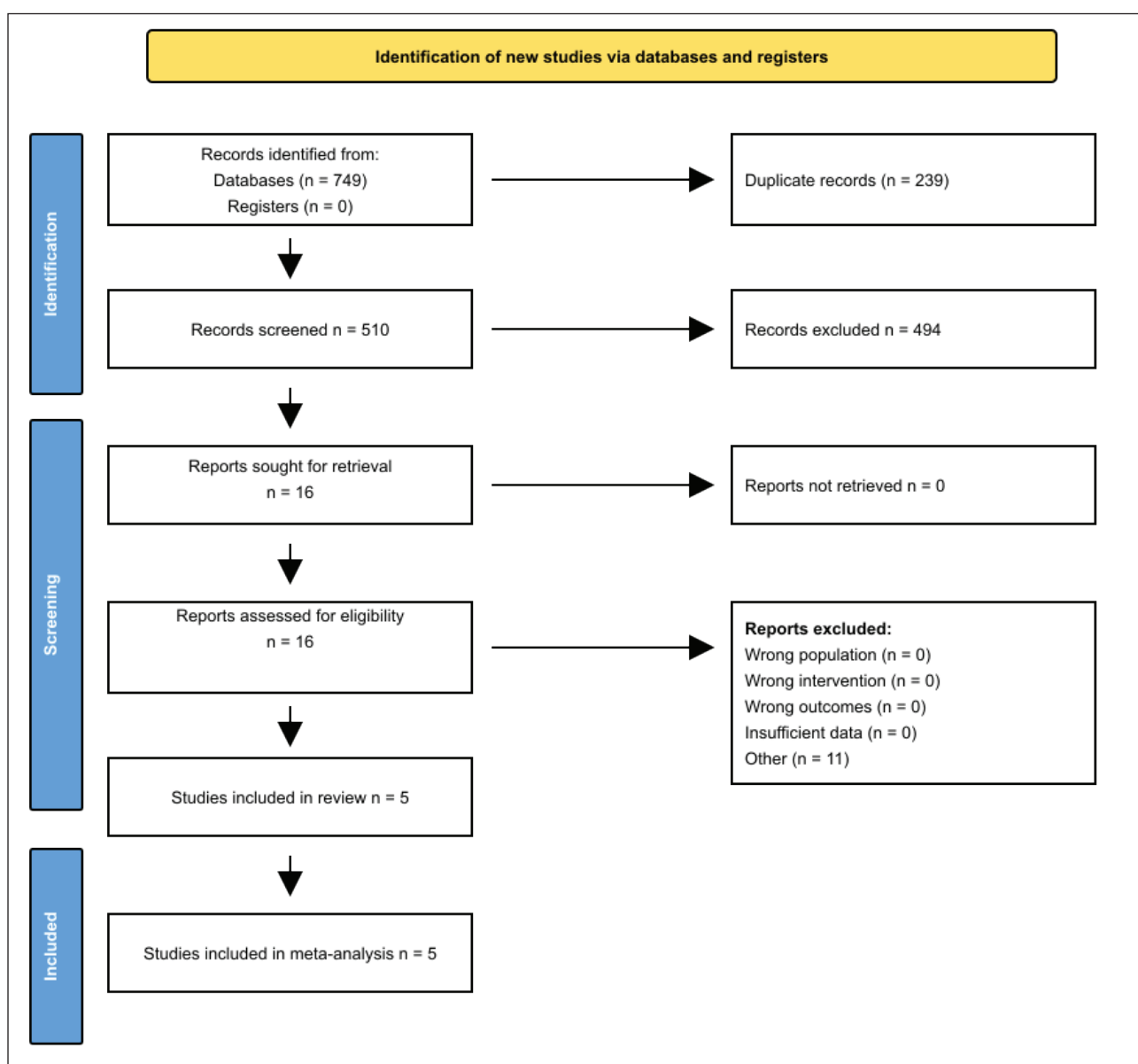
44	was shown that ACEIs can reduce both mortality and	100
45	morbidity, while ARBs do not demonstrate the same	101
46	effectiveness [3].	
47	A comprehensive review indicated that ACEIs and	102
48	ARBs are comparable in their effectiveness in managing	103
49	blood pressure. However, ACEIs tend to cause more	104
50	coughing than ARBs. Additionally, information is scarce	105
51	regarding other effects associated with these medications	106
52	[4]. Furthermore, another study found that both ACEIs	107
53	and ARBs can effectively lower blood pressure. ACEIs	108
54	have been linked to a decrease in both total mortality	109
55	and fatalities associated with cardiovascular problems,	110
56	whereas ARBs have not shown similar advantages as	111
57	ACEIs [5].	112
58	Studies indicate that ARBs are comparable in effectiveness	113
59	and tolerability to ACEIs but have fewer adverse effects.	114
60	Many studies had fewer than 500 participants and less	115
61	than 10 events per group, making it difficult to accurately	116
62	assess the comparative efficacy and drawbacks of ACEIs	117
63	and ARBs. Furthermore, the presence of additional health	118
64	conditions, such as blood disorders or musculoskeletal	
65	issues, as well as the inclusion of high-risk patient groups,	
66	can significantly affect the outcomes of these evaluations	
67	[3,6-10]. The Reduction of Atherothrombosis for	
68	Continued Health study discovered that individuals who	
69	took ARBs experienced a 10% decrease in cardiovascular	
70	events [11]. Conversely, another study suggested that	
71	there might be an increased risk of myocardial infarction	
72	linked to the use of ARBs [12].	
73	Both classes of medications are still recommended as	
74	initial treatment options, despite their limitations. ACEIs	
75	tend to be prescribed more frequently for hypertension	
76	compared to ARBs [13,14]. However, there are	
77	significant knowledge gaps, particularly a lack of direct	
78	comparisons, as most studies do not evaluate ACEIs and	
79	ARBs head-to-head. Therefore, our study aims to assess	
80	the efficacy of ACEIs compared to ARBs in lowering	
81	blood pressure.	
82	Methodology	
83	This review and meta-analysis were conducted in	
84	accordance with the PRISMA 2020 guidelines [15].	
85	Search strategy	
86	A comprehensive search was performed in PubMed,	
87	MEDLINE, and Scopus for articles published between	
88	2015 and 2025. The search utilized a combination of	
89	Medical Subject Headings and free-text terms. The	
90	complete PubMed search string was:	
91	("ACE Inhibitors" OR "Angiotensin Converting Enzyme	
92	Inhibitors" OR "ACEI" OR "Lisinopril" OR "Captopril"	
93	OR "Enalapril" OR "Ramipril" OR "Perindopril" OR	
94	"Benazepril" OR "Fosinopril" OR "Quinapril" OR	
95	"Moexipril" OR "Trandolapril")	
96	AND ("Angiotensin Receptor Blockers" OR "ARBs"	
97	OR "Angiotensin II Receptor Antagonists" OR "AT1	
98	Receptor Blockers" OR "AT2 Receptor Blockers"	
99	OR "Losartan" OR "Valsartan" OR "Irbesartan" OR	
	"Candesartan" OR "Olmesartan" OR "Telmisartan" OR	100
	"Eprosartan" OR "Azilsartan")	101
	AND ("Blood Pressure" OR "Blood Pressure Reduction"	102
	OR "BP Lowering" OR "Hypertension Control" OR	103
	"Systolic Blood Pressure (SBP)" OR "Diastolic Blood	104
	Pressure (DBP)" OR "Mean Arterial Pressure" OR	105
	"Antihypertensive Effect")	106
	AND ("Essential Hypertension" OR "Primary	107
	Hypertension" OR "High Blood Pressure" OR	108
	"Idiopathic Hypertension" OR "Chronic Hypertension"	109
	OR "Hypertensive Patients")	110
	The same keywords and filters were used on PubMed,	111
	MEDLINE, and Scopus. The filters applied included	112
	studies involving humans, adults aged 18 years and	113
	older, randomized controlled trials (RCTs), English	114
	language publications, and a date range from 2015 to	115
	2025. Additionally, the reference lists of relevant reviews	116
	and included trials were manually screened to ensure	117
	completeness.	118
	Inclusion and exclusion criteria	119
	The inclusion criteria for this study are adults aged 18	120
	and over with essential hypertension, specifically RCTs	121
	comparing ACEIs and ARBs. Eligible studies must report	122
	changes in SBP and/or DBP with a minimum follow-	123
	up of 4 weeks and be published in English between	124
	2015 and 2025. Exclusion criteria include pediatric	125
	populations, secondary hypertension, patients with	126
	significant comorbidities like chronic kidney disease	127
	or heart failure, and non-randomized studies lacking	128
	extractable outcomes.	129
	Study selection	130
	The selection of studies was conducted by two reviewers	131
	who examined titles and abstracts to determine their	132
	relevance. Full texts of studies that appeared to meet	133
	eligibility criteria were obtained and evaluated for final	134
	inclusion. Any disagreements that arose were addressed	135
	through discussion or by involving a third reviewer for	136
	consensus.	137
	Data extraction	138
	Data extraction was conducted independently by two	139
	reviewers utilizing a standardized form that captured	140
	essential study characteristics, including the author, year	141
	of publication, and country of the research. Additionally,	142
	participants' demographic data, including age, sex,	143
	and baseline blood pressure, were documented. The	144
	details of the interventions were meticulously recorded,	145
	encompassing the type of drug used, its dosage, and the	146
	duration of the treatment. Finally, the outcomes were	147
	thoroughly assessed, focusing on changes in SBP and	148
	DBP, mean arterial pressure, and any adverse effects	149
	associated with the intervention.	150
	Statistical analysis	151
	Quality assessment of the included RCTs was performed	152
	using the RoB2 tool [16]. Statistical analyses were	153
	performed using Review Manager (version 5.4.1;	154

155 The Cochrane Collaboration, London, UK) [17].
 156 Dichotomous variables were assessed as proportions,
 157 and continuous variables were analyzed by calculating
 158 standardized mean differences (SMD) with 95%
 159 confidence intervals (CI), using random-effects models.
 160 To evaluate statistical heterogeneity across studies,
 161 I^2 -squared (I^2) and chi-squared tests were used; I^2 values
 162 exceeding 50% indicated significant heterogeneity. A
 163 leave-one-out sensitivity analysis was performed for
 164 high heterogeneity.

165 Results

166 A comprehensive search yielded 749 articles from three
 167 databases: PubMed, Medline, and Scopus. Of these, 239
 168 were removed due to duplication, and 494 were excluded
 169 based on their titles and abstracts. Following a full-text
 170 screening, 11 studies were excluded. Ultimately, only
 171 five studies were included in our review (Figure 1).

172 Table 1 summarizes five randomized clinical trials that
 173 compare ACEIs and ARBs in patients with hypertension.
 174 The studies varied in their design, sample size, and
 175 geographic locations, but all evaluated the efficacy
 176 and/or safety of these antihypertensive agents over
 177 treatment periods ranging from 8 weeks to 6 months.
 178 Many of the studies focused on patients suffering from
 179 essential hypertension [18-22], with some also including
 180 individuals who had additional health conditions like
 181 diabetes [18,19], dyslipidemia [20,21], and metabolic
 182 syndrome [21]. Two larger multicenter trials utilized
 183 combination treatment involving Hydrochlorothiazide
 184 (HCTZ) and targeted populations at high risk for
 185 cardiovascular issues [20,21]. It is worth noting that the
 186 sample sizes in these studies were typically moderate,
 187 and information on other medications participants
 188 took was not consistently detailed. The results present
 189 a comparative review of ACEIs, including ramipril,
 190 enalapril, and zofenopril, and angiotensin II receptor



191 **Figure 1.** Schematic representation of the criteria for selecting studies in the systematic review.

Table 1. Summary of randomized clinical trials comparing ACEIs and ARBs in patients with hypertension.

First author (Year)	Study design, country	Sample size (Total,subgroups)	Age (mean/median \pm SD or range)	Gender (M/F)	Intervention (drug, dose, duration)	Comorbidities	Concomitant Medications
Ki et al. 2017 [18]	Single-center, randomized, open-label trial; South Korea	Total: 20 Ramipril: 10 Teimisartan: 10	57.9 \pm 11.3 years	12/8	Ramipril: 5 mg daily, possible up-titration at week 4, duration 8 weeks. Teimisartan: 40 mg daily, possible up-titration at week 4, duration 8 weeks	All patients had essential hypertension. Diabetes mellitus: Ramipril 2/10 (20%), Teimisartan 3/10 (30%)	All prior antihypertensive medications were discontinued for a 2-week washout period before randomization. After washout, no concomitant antihypertensive or other medications were listed
Hadi et al. 2017 [19]	Randomized, single-center, single-blinded, parallel-group clinical trial conducted in Iraq	Total: 120 Hypertensive Patients: 80 (randomized into two groups of 40). Analyzed Patients: 60 (30 per group after attrition) Normotensive Controls: 40	Hypertensive Patients: 58 \pm 15 years. Normotensive Controls: 57 \pm 14 years	Teimisartan Group: 22/8 Enalapril Group: 20 / 10	Group 1 (Teimisartan): 80 mg once daily. Group 2 (Enalapril): 20 mg once daily. Duration: 6 months	All patients had essential hypertension; patients with diabetes, cardiovascular disease, renal impairment, arrhythmias, pregnancy, or secondary HTN were excluded (No other comorbidities reported)	No concomitant medications were reported
Modesti et al. 2016 [20]	Randomized, double-blind, parallel-group multicenter trial conducted in Italy, Romania, and Russia	Total randomized: 230 participants. Full analysis set (efficacy population): 216 (Z = 107; I = 109)	Zofenopril group: 72.6 \pm 6.0 years Irbesartan group: 72.3 \pm 5.8 years	Zofenopril: 55.1% male, 44.9% female Irbesartan: 56.0% male, 44.0% female	Zofenopril + HCTZ: Zofenopril 30 mg + HCTZ 12.5 mg once daily, up-titrated to 60 mg if needed, duration 18 weeks Irbesartan + HCTZ: Irbesartan 150 mg + HCTZ 12.5 mg once daily, up-titrated to 300 mg if needed, duration 18 weeks	All patients had essential hypertension (by inclusion criteria) Cardiac disease: Zofenopril 39/107 Irbesartan 35/109 Dyslipidemia: Zofenopril 68/107 Irbesartan 60/109 Diabetes: Zofenopril 39/107 Irbesartan 37/109 Metabolic syndrome: Zofenopril 86/107 Irbesartan 72/109	Previous antihypertensive therapy allowed (\leq 2 agents); agents acting on RAS, β -blockers, α -blockers, CCBs, diuretics
Napoli et al. 2016 [21]	Multicenter, randomized, double-blind, parallel group, phase III study in Italy and Romania	Total: 482 essential hypertensive patients Subgroups: ACE: 231 (Zofenopril plus Hydrochlorothiazide) ARB: 235 (Irbesartan plus hydrochlorothiazide)	59 \pm 10 years	247/219	Group 1: Zofenopril 30 mg + HCTZ 12.5 mg once daily. Dose doubled to Zofenopril 60 mg at Week 8 if not normalized. Group 2: Irbesartan 150 mg + HCTZ 12.5 mg once daily. Dose doubled to Irbesartan 300 mg at Week 8 if not normalized. Duration: 24-week double-masked treatment period	All patients had - Essential Hypertension - Metabolic Syndrome (ATP-III criteria) Specific Comorbidities: - Diabetes: 75.1% Dyslipidemia: 70% - Cardiac Disease: 31%	-Oral hypoglycemic drugs: 71.0% (Zofenopril) vs. 60.9% (Irbesartan) -Lipid-Lowering Drugs: 67.1% (Zofenopril) vs. 54.9% (Irbesartan)
Raja et al. 2016 [22]	Prospective, randomized, comparative, observational study in India	Total: 100 Teimisartan: 50 Ramipril: 50	More than 25 years of age	NR	Tablet teimisartan 40 mg orally once a day in the morning for 24 weeks. Tablet ramipril 5 mg orally once a day in the morning for 24 weeks	Mild to moderate hypertension	No concomitant medications were reported

ACE: Angiotensin-Converting Enzyme, ACEI: Angiotensin-Converting Enzyme Inhibitor, ARB: Angiotensin II Receptor Blocker, CCB: Calcium Channel Blocker, HCTZ: Hydrochlorothiazide, HTN: Hypertension, M/F: Male/Female, NR: Not Reported, RAS: Renin-Angiotensin System, SD: Standard Deviation.

193 antagonists, including telmisartan and irbesartan. This
194 analysis considers both single and combination therapies
195 among various groups of patients with hypertension.

196 Table 2 demonstrates that both ACEIs (ramipril, enalapril,
197 zofenopril) and ARBs (telmisartan, irbesartan) are
198 effective in lowering blood pressure. Most studies reported
199 high rates of blood pressure control, achieving levels
200 below 140/90 mmHg. Notably, Ki et al. [18] suggested
201 that ramipril may have a superior effect on vascular
202 health, potentially preserving endothelial function better
203 than telmisartan. In combination therapy studies [20,21],
204 the pairing of zofenopril and hydrochlorothiazide
205 showed consistent non-inferiority compared to irbesartan
206 plus hydrochlorothiazide. Adverse events were generally
207 mild and typical for these drug classes. This included
208 dizziness, headache, fatigue, and the characteristic cough
209 associated with ACEIs, resulting in a low but significant
210 discontinuation rate. Overall, the evidence supports both
211 drug classes as effective and well-tolerated options for
212 managing hypertension. Specific patient factors and
213 considerations regarding vascular health may influence
214 the choice between these medications.

215 Three studies showed a low risk across all evaluated
216 domains, indicating a strong design and implementation.
217 However, two studies were assessed as having a high
218 overall risk, primarily due to concerns in key areas,
219 including the randomization process, handling of protocol
220 deviations, and management of missing data (Figure 2).

221 Figure 3 compares ACEIs and ARBs on SBP across five
222 randomized trials. The overall pooled SMD was 0.01
223 (95% confidence intervals (CI): -0.16 to 0.18; $p = 0.91$),
224 showing no significant difference in efficacy. Subgroup
225 analyses also revealed no significant differences among
226 drug pairs. These findings indicate that ACEIs and ARBs
227 are equally effective in lowering SBP in hypertensive
228 patients.

229 Figure 4 reveals significant statistical heterogeneity ($I^2 =$
230 97%) in the comparative effect of ACEIs and ARBs on
231 DBP reduction. The overall pooled effect slightly favors
232 ACEIs (SMD = -1.52, 95% CI: -2.86 to -0.19, $p = 0.03$).

233 This sensitivity analysis removed the Hadi et al. [19]
234 study due to its extreme effect size to test the robustness
235 of the original DBP findings. After its removal, the overall
236 pooled effect was no longer statistically significant (SMD
237 = -0.31, 95% CI: -0.90 to 0.28; $p = 0.30$), indicating that
238 the earlier advantage of ACEIs over ARBs in reducing
239 DBP was primarily driven by this outlier study, as shown
240 in Figure 5.

241 Figure 6 shows that the blood pressure normalization
242 rates (<140/90 mmHg) do not differ significantly between
243 ACEIs and ARBs. The pooled odds ratio was 0.95 (95%
244 CI: 0.66-1.37; $p = 0.79$), with minimal heterogeneity
245 observed ($I^2 = 13%$). These results suggest that both drug
246 classes are equally effective in achieving standard blood
247 pressure control targets in patients with hypertension.

248 Figure 7 compares the safety of an ACEI (zofenopril) and
249 an ARB (irbesartan), both with hydrochlorothiazide. The
250 analysis found no significant difference in adverse events
251 between the treatments, with a pooled odds ratio of 0.82

(95% CI: 0.43-1.57; $p = 0.55$), suggesting similar safety
252 profiles. 253

254 Discussion

255 Our review found no significant differences between
256 ACEIs and ARBs in reducing SBP or achieving
257 normalized blood pressure (defined as less than 140/90
258 mmHg). While ACEIs appeared to show a slight
259 advantage in reducing DBP, this finding was driven
260 primarily by a single outlier study and was not consistent
261 across sensitivity analyses. The safety profiles of the two
262 drug classes were largely similar; however, ACEIs were
263 consistently associated with a higher incidence of cough.

264 Our meta-analysis found no significant difference in
265 SBP reduction between ACEIs and ARBs. This finding
266 was consistent across all included RCTs. Hadi et al. [19]
267 reported comparable SBP reductions with telmisartan
268 and enalapril, while Modesti et al. [20] and Napoli
269 et al. [21] found zofenopril plus hydrochlorothiazide
270 non-inferior to irbesartan plus hydrochlorothiazide in
271 elderly and metabolic syndrome populations. Raja et al.
272 [22] observed a slightly greater reduction in SBP with
273 telmisartan than with ramipril. These results align with a
274 previous review, which concluded that ACEIs and ARBs
275 achieve similar reductions in SBP [3]. A recent review
276 indicates that ARB offers greater benefits than ACEI for
277 managing blood pressure. Compared with ACEI, ARB
278 has shown greater reductions in both SBP and DBP.

279 Regarding DBP, our pooled analysis suggested a slight
280 advantage of ACEIs in reducing DBP. Hadi et al. [19]
281 reported greater DBP reduction with enalapril than with
282 telmisartan, whereas Raja et al. [22] found that telmisartan
283 produced earlier and more pronounced reductions in
284 DBP than ramipril. Ki et al. [18] observed comparable
285 reductions in DBP with ramipril and telmisartan, though
286 ramipril was associated with improved endothelial
287 function. Moreover, our analysis found no significant
288 difference in normalization rates between ACEIs and
289 ARBs. This was consistent with the majority of included
290 RCTs. Modesti et al. [20] reported similar normalization
291 rates between zofenopril + HCTZ and irbesartan +
292 HCTZ, while Napoli et al. [21] found nearly identical
293 normalization rates (65.8% vs. 67.7%). Ki et al. [18]
294 observed slightly higher normalization with ramipril
295 compared to telmisartan, but the small sample size limits
296 interpretation. These results are consistent with the 2017
297 ACC/AHA guideline evidence review, which concluded
298 that both ACEIs and ARBs are effective for achieving
299 blood pressure (BP) control [6].

300 The safety profiles identified in the studies displayed
301 comparable trends, with both groups experiencing
302 symptoms such as dizziness, headaches, and fatigue.
303 Notably, ACEIs were repeatedly associated with cough,
304 prompting some patients to discontinue their treatment,
305 as reported by Ki et al. [18]. Additionally, Napoli et al.
306 [21] pointed out a slightly higher rate of drug-related
307 side effects with zofenopril plus HCTZ compared to
308 irbesartan with HCTZ, although both medications were
309 generally well-tolerated. These results align with earlier
310 reviews that have shown ARBs to be better accepted,
311 primarily because they are less likely to cause cough

Table 2. Efficacy and safety outcomes of ACEI and ARB therapy in patients with hypertension.

First author (Year)	Change in blood pressure	Achieving BP control	Adverse event	Conclusion
Ki et al. 2017 [18]	Ramipril group: SBP: from baseline: 151 ± 7.49 After 8 weeks: 130 ± 7.12 mmHg DBP: ↓ from 90.6 ± 9 to 79.2 ± 5.25 mmHg Telmisartan group: SBP: ↓ from 159 ± 3.83 to 131 ± 14.4 mmHg DBP: ↓ from 83.7 ± 14 to 73.1 ± 8.61 mmHg	Achieving Target BP (<140/90 mmHg): Ramipril: 9/10 Telmisartan: 6/10	Ramipril Group (n = 10): 1 case of transient global amnesia; 1 patient switched medication due to cough. Withdrawals/Loss to Follow-up: 4	Both drugs effectively lowered blood pressure, but their effects differed. Telmisartan reduced pulse pressure significantly but did not improve endothelial function. In contrast, ramipril showed a positive association between decreased pulse pressure and improved RHI. The authors noted that telmisartan might impair endothelial vasodilation, whereas ramipril preserves the bradykinin-NO pathway, supporting better vascular health.
Hadi et al. 2017 [19]	Telmisartan: SBP: 156.5 ± 2.09 to 135.33 ± 1.07 mmHg DBP: 94.5 ± 0.73 to 82.67 ± 0.79 mmHg Enalapril: SBP: 157.50 ± 1.43 to 135.50 ± 0.77 mmHg DBP: 97.17 ± 0.57 to 80.50 ± 0.65 mmHg	BP control (<140/90): Achieved in both groups Enalapril showed slightly greater DBP improvement	Telmisartan (10/30): dizziness 4 (13.3%), headache 3 (10%), fatigue 2 (6.7%), impotence 1 (3.3%) Enalapril (8/30): dizziness 2 (6.7%), headache 2 (6.7%), fatigue 3 (10%), impotence 1 (3.3%)	After 6 months, both telmisartan and enalapril effectively reduced blood pressure. Enalapril showed slightly greater DBP improvement.
Modesti et al. 2016 [20]	Office SBP reduction at 18 weeks Z+H: -20.2 mmHg (95% CI: -23.0 to -17.4) I+H: -19.9 mmHg (95% CI: -22.6 to -17.2)	Office BP Normalization (<140/90 mmHg) at 18 Weeks Z+H: (76/114) I+H: (80/116)	Overall Adverse Events Z+H group: 31/114 I+H group: 43/116 Serious Adverse Events 2 patients in each group. One death in I+H group (not drug-related). Study Discontinuation due to AE Z+H: 8/114 I+H: 9/116 Drug-Related Adverse Events Z+H: 5/114 (4.4%) I+H: 7/116	Zofenopril+HCTZ was non-inferior to Irbesartan+HCTZ in reducing BP. Both effective and well tolerated. Zofenopril showed higher BP-control rates at 18 weeks.
Napoli et al. 2016 [21]	At Week 24 Office BP reduction (Mean, 95% CI): SBP: Zofenopril+HCTZ: -17.0 (-19.2, -14.8) mmHg Ibesartan+HCTZ: -18.8 (-21.0, -16.6) mmHg DBP: Zofenopril+HCTZ: -9.8 (-11.1, -8.4) mmHg Ibesartan+HCTZ: -10.4 (-11.8, -9.0) mmHg	Normalization Rate (BP <140/90 mmHg): Zofenopril+HCTZ: 152/231 (65.8%) Ibesartan+HCTZ: 159/235 (67.7%) Responder Rate (Normalized or SBP ₁ ≥ 20/DBP ₁ ≥ 10 mmHg): Zofenopril+HCTZ: 179/231 (77.5%) Ibesartan+HCTZ: 192/235 (81.5%)	- Overall: 28.4% of patients reported an adverse event. Drug-Related: Zofenopril + HCTZ: 36 / 241 (14.9%) Ibesartan + HCTZ: 22 / 241 (9.1%) Patients with Serious AEs (SAEs): Zofenopril + HCTZ: 5 / 241 patients Ibesartan + HCTZ: 7 / 241 patients Deaths: 0 / 482 Patients Withdrawn due to AEs: Zofenopril + HCTZ: 12 / 241 patients Ibesartan + HCTZ: 12 / 241 patients	Zofenopril and hydrochlorothiazide are as effective as irbesartan plus hydrochlorothiazide in lowering blood pressure in hypertensive patients with metabolic syndrome. Both options offer effective 24-hour blood pressure control, especially in the morning, and are well-tolerated with a low incidence of side effects. This study provides clinicians with a safe and effective treatment option for managing hypertension in high cardiovascular risk patients.
Raja et al. 2016 [22]	At 24 weeks Ramipril group: SBP: from 163.4 ± 7.3 to 127.3 ± 5.6 DBP: from 97.1 ± 5.0 to 82.6 ± 3.5 Telmisartan group: SBP: from 165.0 ± 8.3 to 129.6 ± 9.6 DBP: from 98.5 ± 4.3 to 84.1 ± 4.6	NR	NR	Telmisartan and ramipril are both effective medications for managing mild to moderate hypertension. However, telmisartan reduces DBP beginning in the fourth week. Additionally, between the fourth and twelfth weeks, telmisartan results in a greater decrease in SBP and MBP than ramipril.

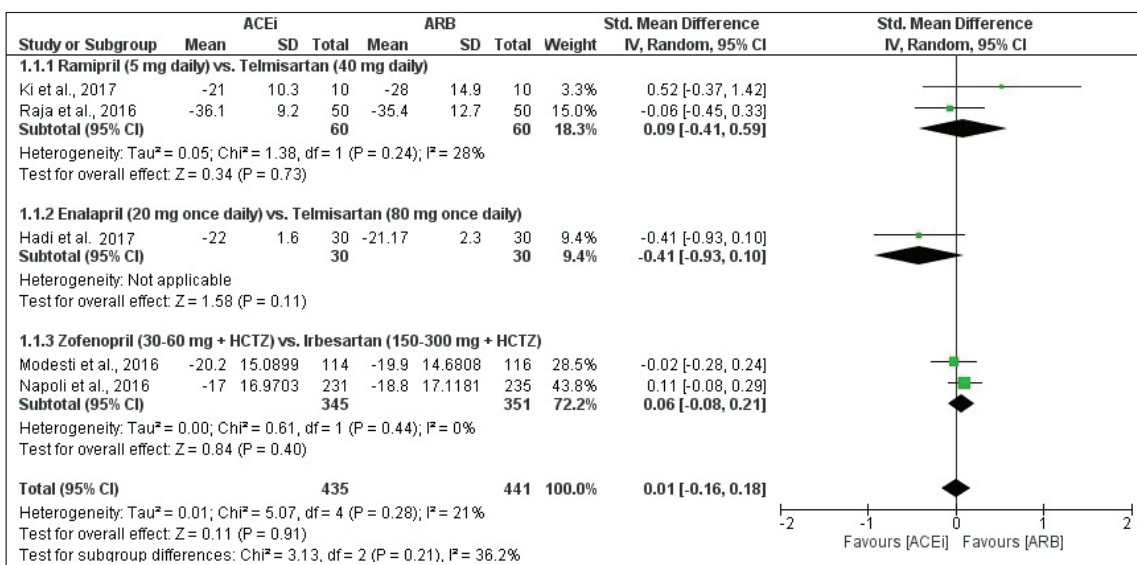
AE: Adverse Event, ARB: Angiotensin II Receptor Blocker, BP: Blood Pressure, CI: Confidence Interval, DBP: Diastolic Blood Pressure, HCTZ: Hydrochlorothiazide, NR: Not Reported, RHI: Reactive Hyperemia Index, SBP: Systolic Blood Pressure, SAE: Serious Adverse Event.

		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Ki et al. 2017	⊗	⊗	⊗	⊖	⊖	⊗
	Hadi et al. 2017	⊖	⊕	⊖	⊕	⊖	⊖
	Modesti et al. 2016	⊕	⊕	⊕	⊕	⊕	⊕
	Napoli et al., 2016	⊕	⊕	⊕	⊕	⊕	⊕
	Raja et al. 2016	⊖	⊗	⊕	⊗	⊖	⊗

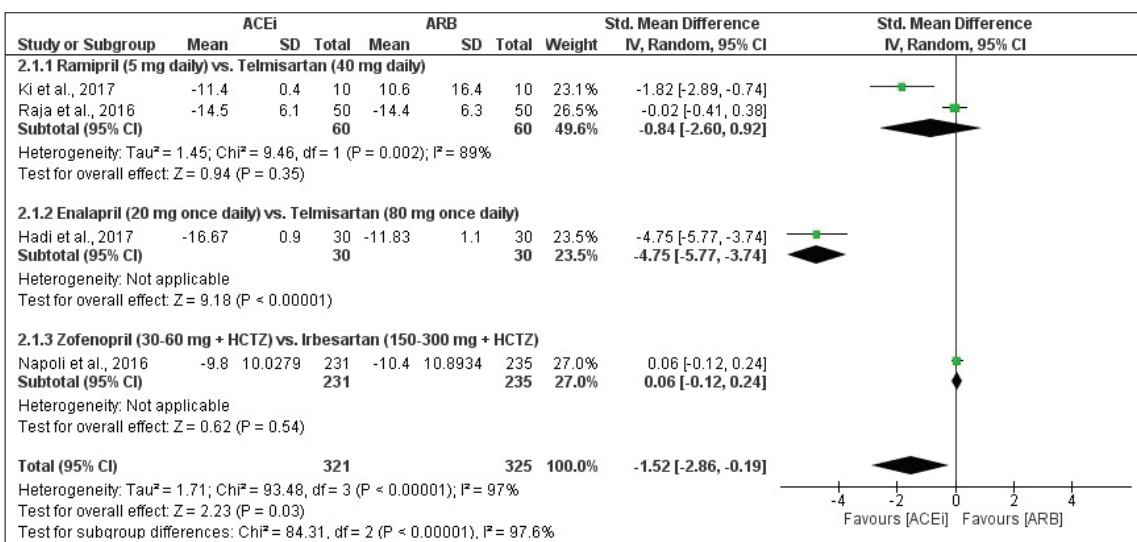
Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
⊗ High
⊖ Some concerns
⊕ Low

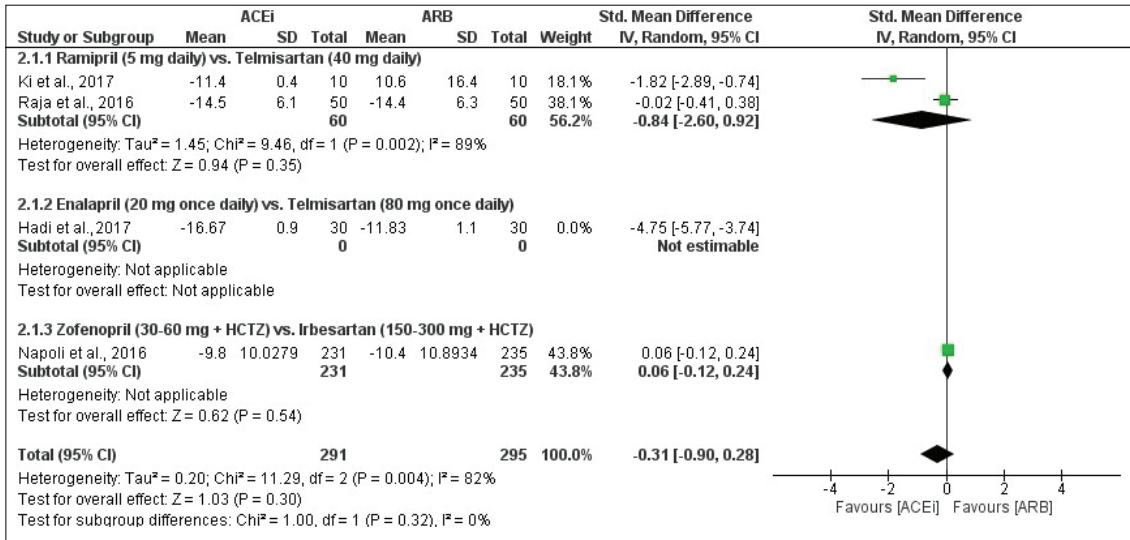
313 **Figure 2.** Risk of bias assessment for included studies.



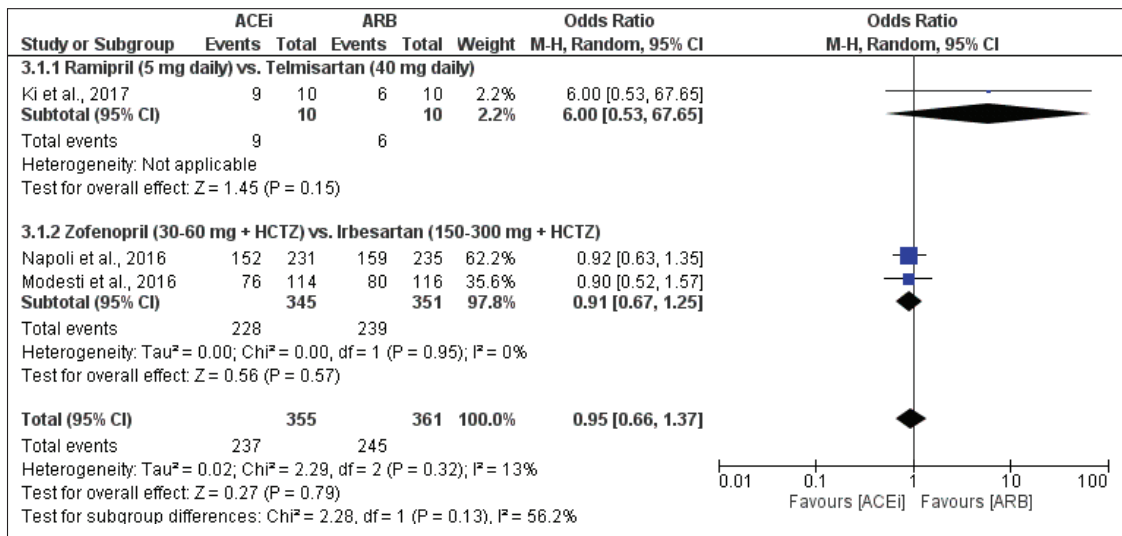
314 **Figure 3.** Forest plot of SMD in SBP reduction: ACEIs versus ARBs.



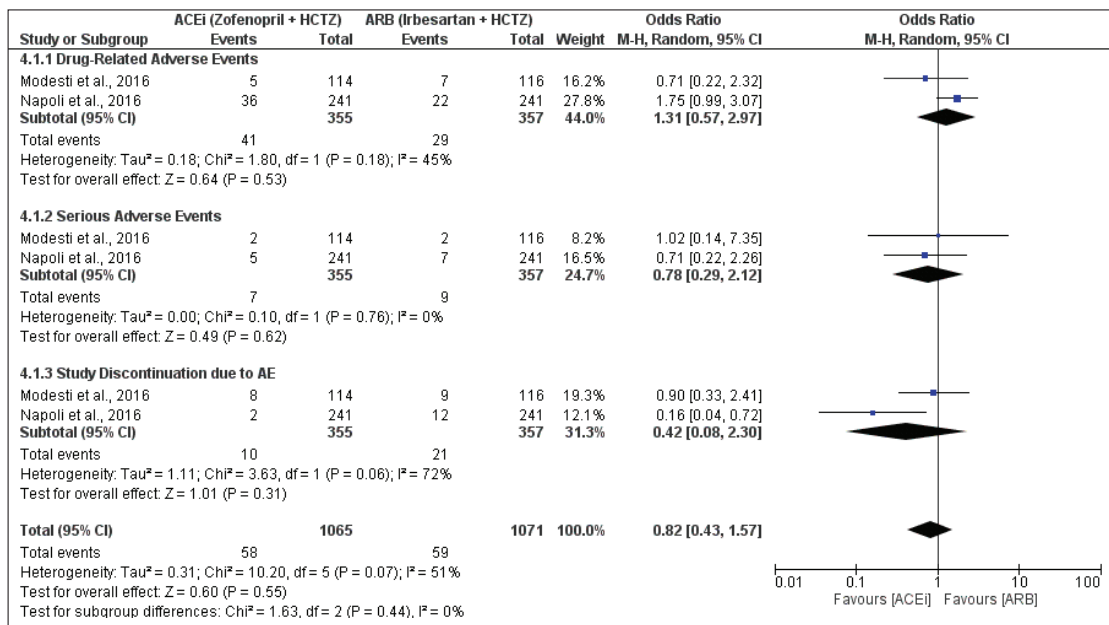
315 **Figure 4.** Forest plot of SMD in DBP reduction: ACEIs versus ARBs.



316 Figure 5. Forest plot of sensitivity analysis: SMD in DBP reduction.



317 Figure 6. Forest plot of odds ratios for blood pressure normalization (<140/90 mmHg) with ACEIs versus ARBs.



318 Figure 7. Forest plot of adverse events: ACEIs versus ARBs

319 and angioedema than ACEIs [3]. Research suggests
 320 that both ACEIs and ARBs are similarly effective in
 321 reducing blood pressure. Nonetheless, ACEIs might
 322 offer additional cardiovascular benefits, particularly by
 323 reducing overall and heart-related mortality. Conversely,
 324 ARBs typically have a better side effect profile, making
 325 them a more suitable choice for patients prone to cough
 326 or angioedema linked to ACEIs.

327 **Limitations**

328 This review highlights several significant limitations,
 329 including the limited number of studies meeting the
 330 inclusion criteria, inconsistent results, variations in
 331 research methodologies, and differences in study
 332 populations. To address these challenges, future
 333 investigations should aim for thorough, well-organized
 334 RCTs that adhere to standardized protocols and include
 335 longer follow-up periods.

336 **Conclusion**

337 Our review indicates that both ACEIs and ARBs are
 338 equally effective at reducing SBP and managing essential
 339 hypertension. ACEIs offer a marginal benefit in reducing
 340 DBP. Both classes of medications have similar safety
 341 profiles; however, ACEIs are more likely to cause cough
 342 as a side effect. Adapting treatment approaches to cater to
 343 the unique needs of each patient is crucial. These results
 344 support current recommendations that suggest ACEIs and
 345 ARBs as effective first-line treatments, emphasizing the
 346 importance of further investigation into their prolonged
 347 impact on cardiovascular health.

348 **List of Abbreviations**

349	ACE	Angiotensin-Converting Enzyme
350	ACEI	Angiotensin-Converting Enzyme Inhibitor
351	AE	Adverse event
352	ARB	Angiotensin II Receptor Blocker
353	BP	Blood pressure
354	CCB	Calcium Channel Blocker
355	CI	Confidence interval
356	DBP	Diastolic blood pressure
357	HCTZ	Hydrochlorothiazide
358	HTN	Hypertension
359	M/F	Male / Female
360	NR	Not reported
361	RAS	Renin-Angiotensin System
362	RCT	Randomized controlled trial
363	RHI	Reactive Hyperemia Index
364	SAE	Serious adverse event
365	SBP	Systolic blood pressure
366	SD	Standard deviation
367	SMD	Standardized mean difference

368 **Conflict of interests**

369 The authors declare that there is no conflict of interest
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