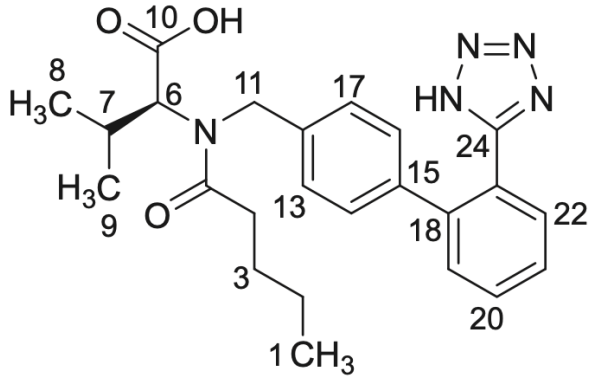
Təzyiq nəzarəti üçün ən ideal kombinasiya axtarışında

Dr. Üzeyir Rəhimov

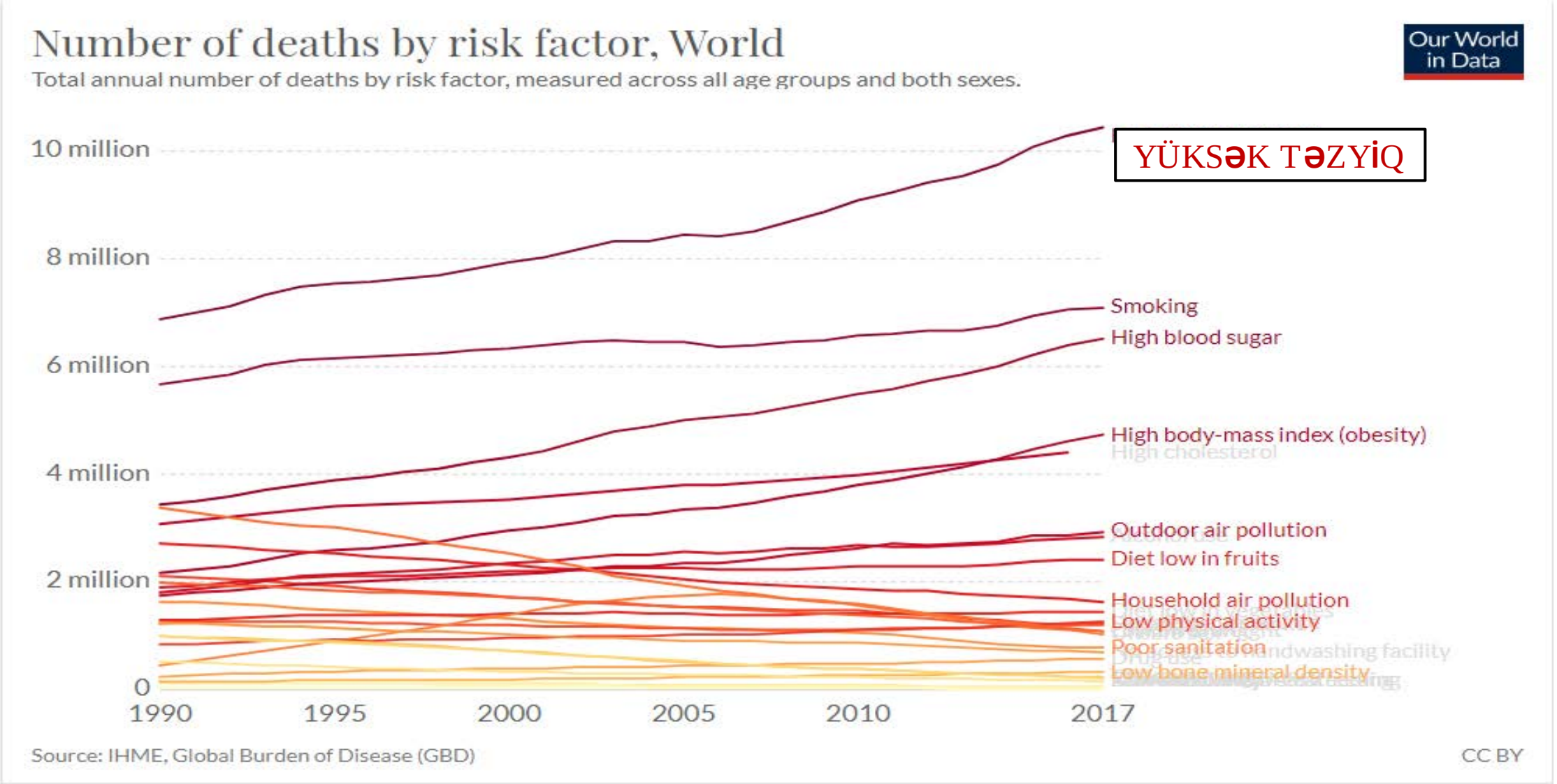


Dünyada ölümün birinci səbəbi nədir?

Ko-Vamloset

KRKA

30 ilə yaxındır ki, hipertenziya ölümün ən əsas səbəbidir.



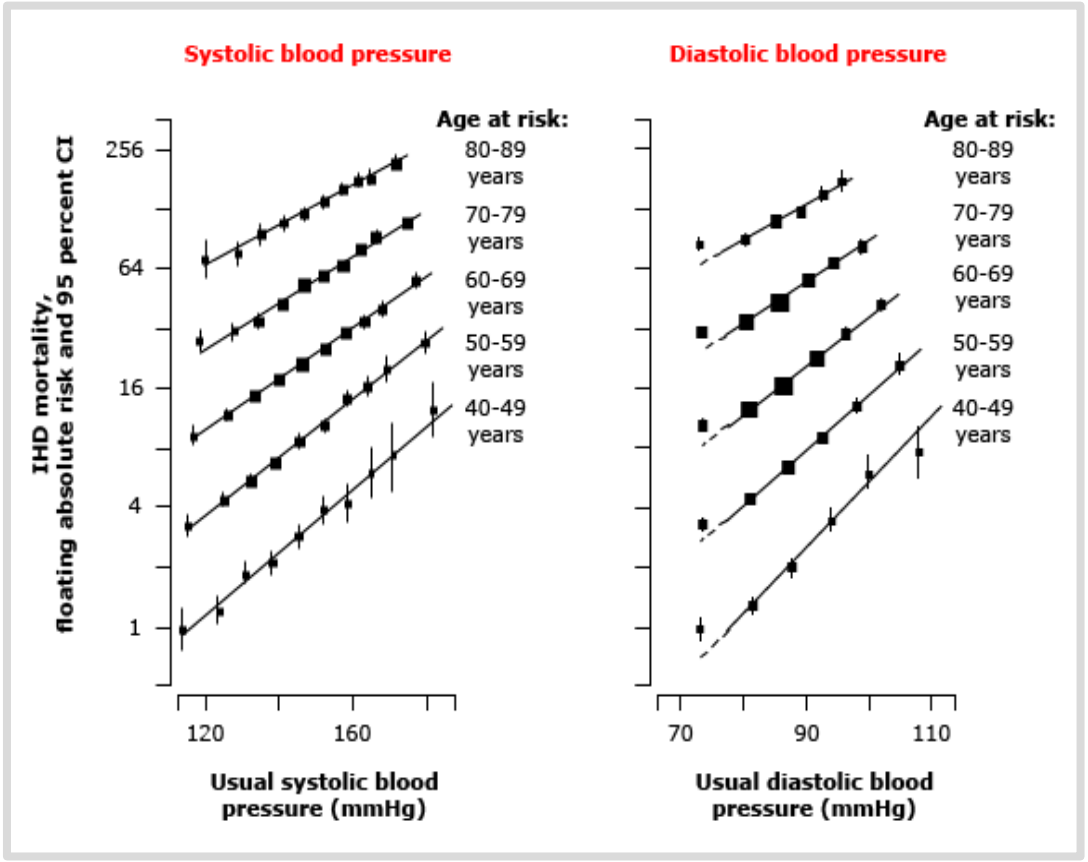
Bəs nə üçün hipertenziya ölümün birinci səbəbidir?

Ko-Vamloset

KRKA

Bəs nə üçün hipertenziya ölümün birinci səbəbidir?

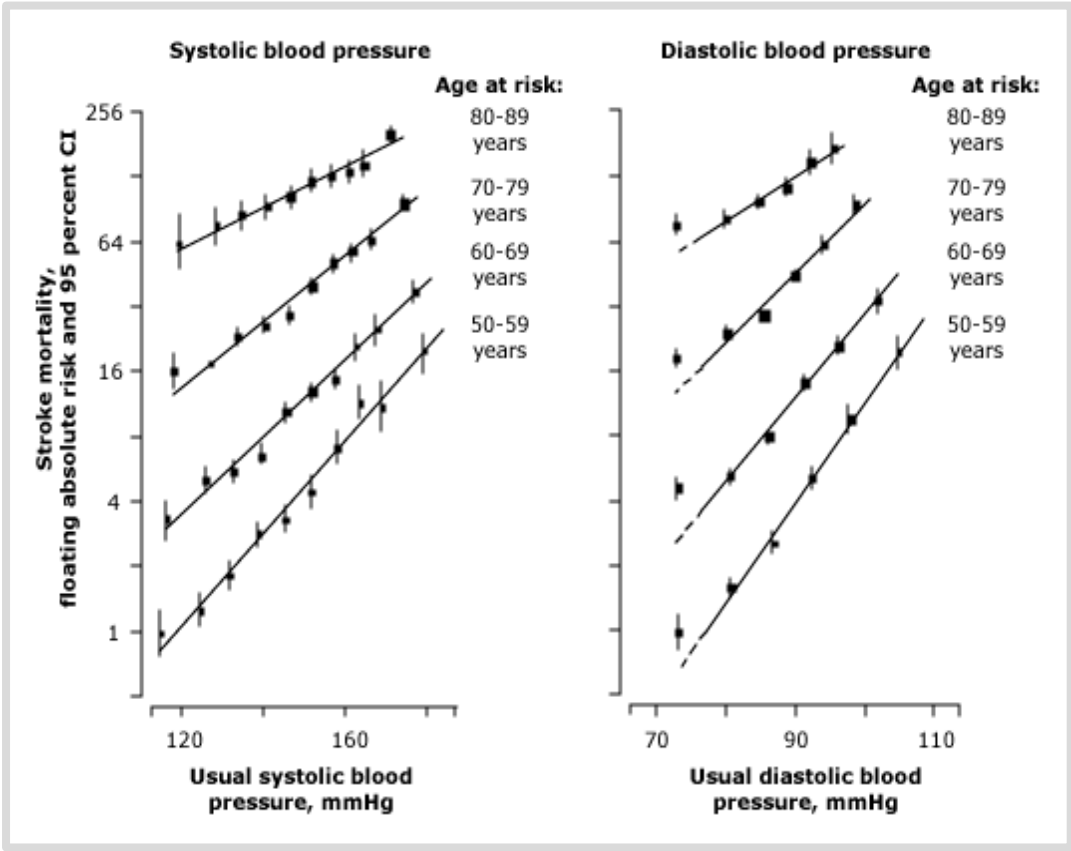
- Yaş artdıqca arterial hipertenziyalı xəstələrdə koronar arteriya xəstəliyindən ölüm ehtimalı artır



Roberto Pastor-Barriuso, Jose´ R. Banegas et al. Lancet 2002; 360:1903

Bəs nə üçün hipertenziya ölümün birinci səbəbidir?

- Yaş artdıqca arterial hipertenziyalı xəstələrdə insult səbəbindən ölüm ehtimalı artır



Roberto Pastor-Barriuso, Jose´ R. Banegas et al. Lancet 2002; 360:1903

Nəzarətsiz hipertenziyanın və dirəncli hipertenziyanın əsas səbəbi nədir?

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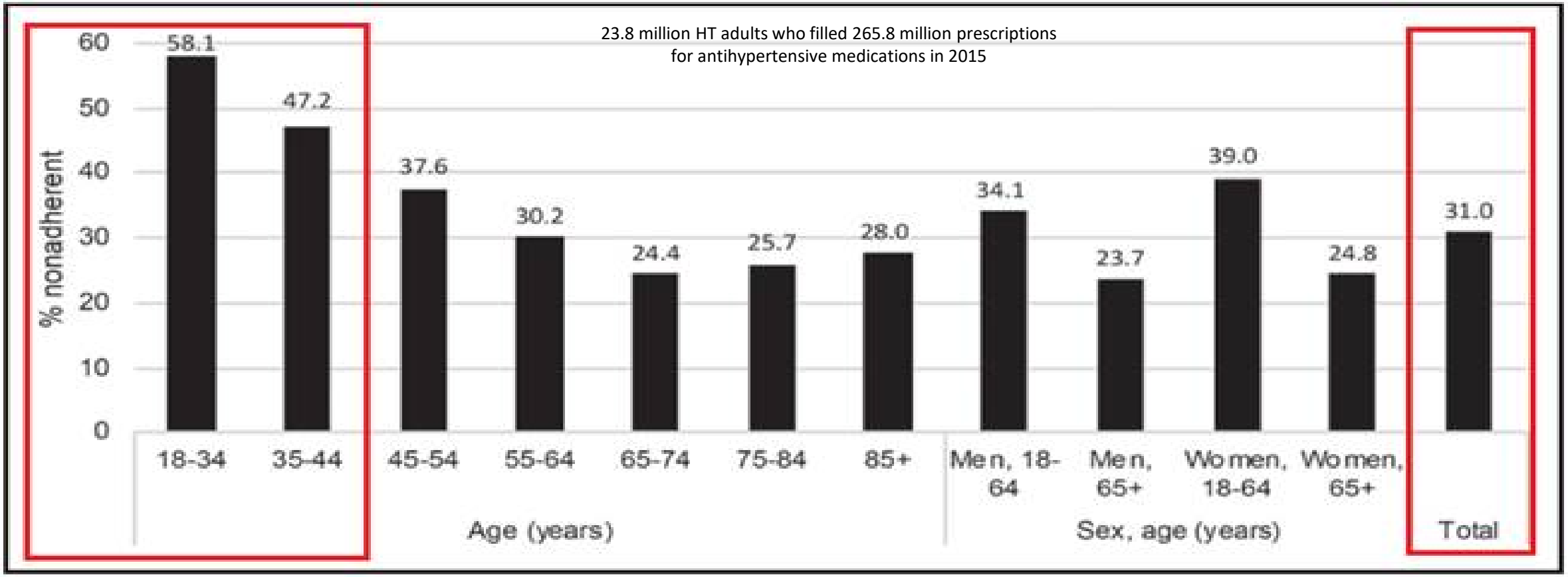
Gənc xəstələr dərman qəbuluna daha az riayət edirlər

1/3 (≈16.3 million) of insured US adults with diagnosed HT were nonadherent to their antihypertensive medication regimen



Chang T et al . Hypertension. 2019;74;1324-1332

ESC European Society of Cardiology
European Heart Journal (2018) 00, 1–98
doi:10.1093/eurheartj/ehy339
ESC/ESH GUIDELINES

2018 ESC/ESH Guidelines for the management of arterial hypertension

10.4 Improvement in blood pressure control in hypertension: drug adherence

There is growing evidence that poor adherence to treatment—in addition to physician inertia (i.e. lack of therapeutic action when the patient's BP is uncontrolled)—is the most important cause of poor BP control.[293,619–621] Non-adherence to antihypertensive therapy correlates with higher risk of CV events.[312,622]

Early discontinuation of treatment and suboptimal daily use of the prescribed regimens are the most common facets of poor adherence. After 6 months, more than one-third, and after 1 year, about one-half of patients may stop their initial treatment.[623] Studies based on the detection of antihypertensive medications in blood or urine have shown that low adherence to the prescribed medications can affect ≤ 50% of patients with apparently resistant hypertension,[352,624] and that poor adherence is strongly and inversely correlated with the number of pills prescribed. Early recognition of a lack of adherence might reduce the number of costly investigations and procedures (including interventional treatment), and avoid the prescription of unnecessary drugs.[625]

Dərman qəbuluna riayət etməmək– nəzarətsiz hipertenziyanın ən önəmli səbəbidir!

A major emphasis of these Guidelines has been to simplify the treatment strategy to try and improve adherence to treatment and BP control, by prescribing a single pill to most patients with hypertension. This is a response to the fact that despite the clear-cut benefits

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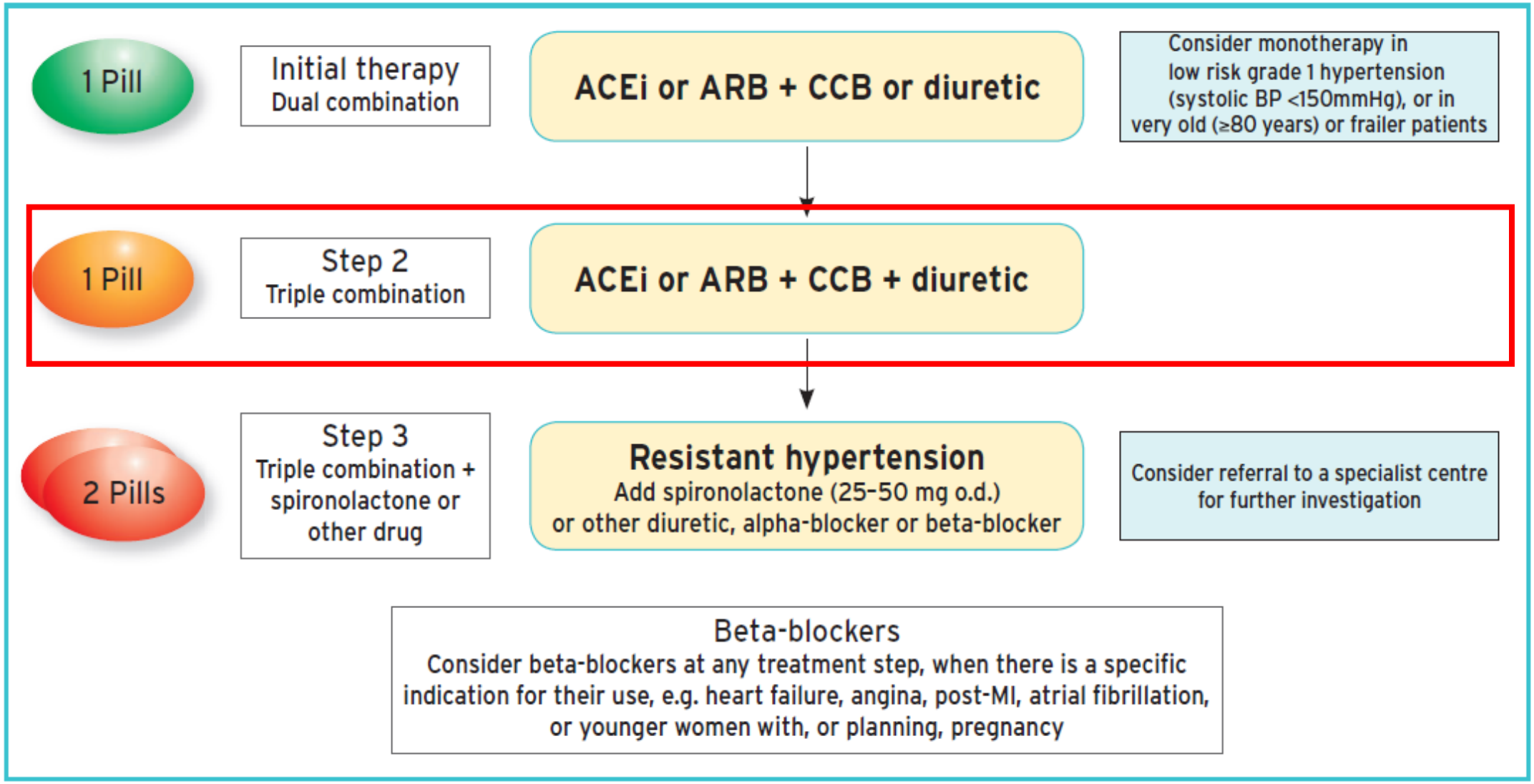
ESC European Society of Cardiology
European Heart Journal (2018) 00, 1–98
doi:10.1093/eurheartj/ehy339
ESC/ESH GUIDELINES

2018 ESC/ESH Guidelines for the management of arterial hypertension

Fəsadlaşmamış HT da dərman müalicəsi



Angiotenzin reseptor blokatorları və ya Angiotenzin çevirici ferment inhibitorları?

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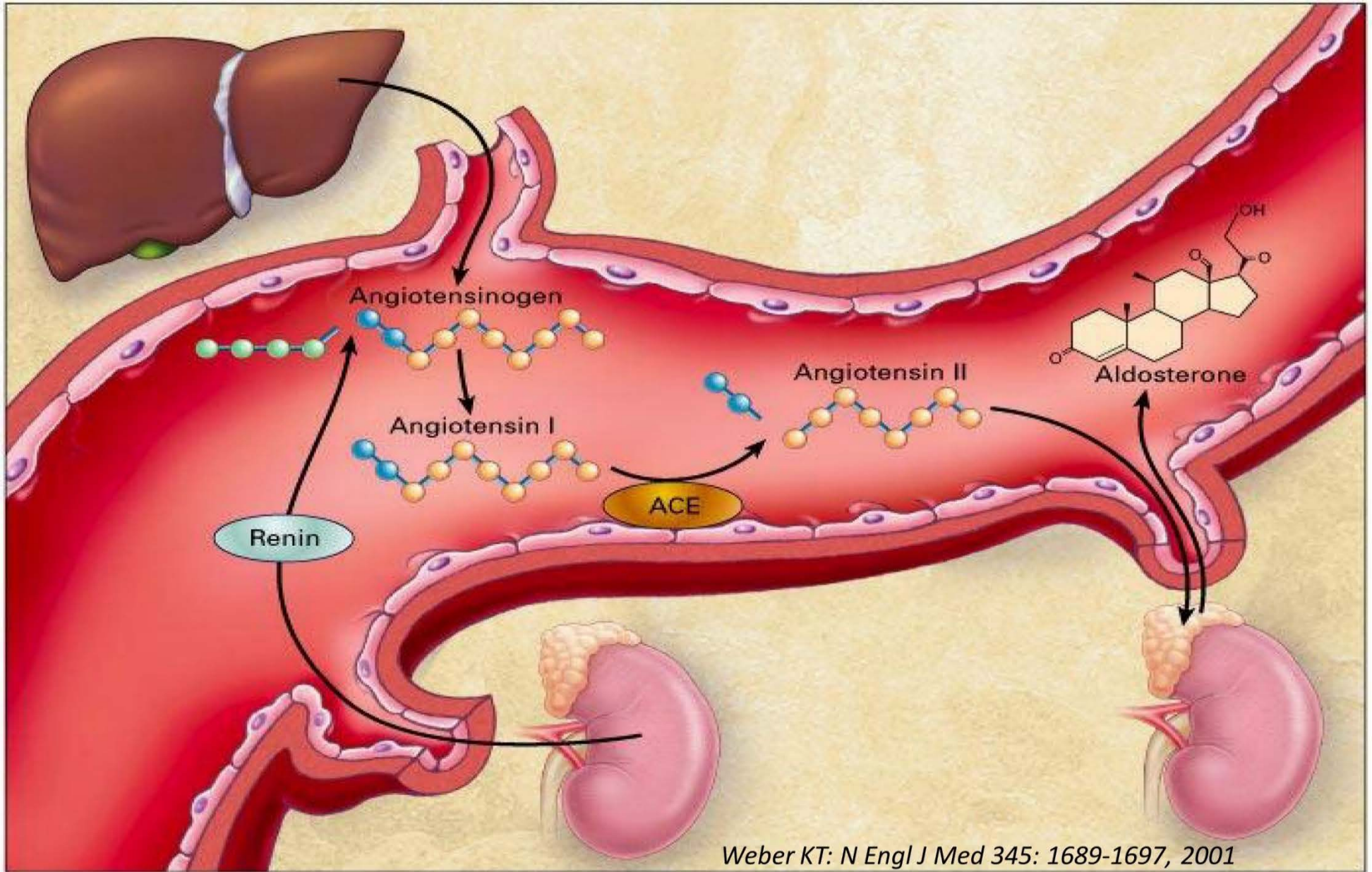
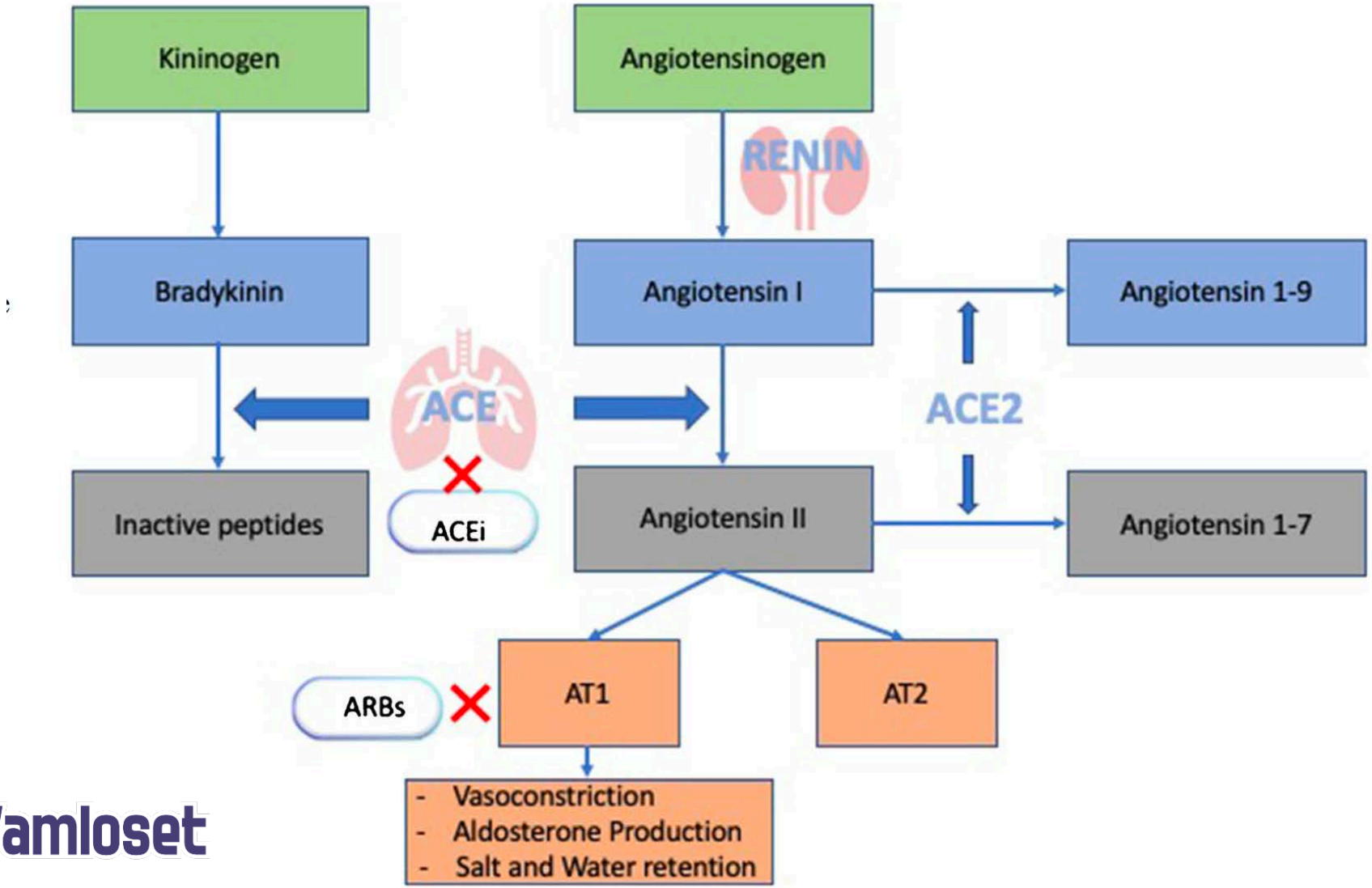
Renin angiotensin aldosteron sistemi



Ən başda ARB yaradılmasında məqsəd AÇFi –nın təsirini tamamlamaq və öskürək, angioödem kimi əlavə təsirləri aradan qaldırmaq olmuşdur.

ARB və AÇFi təsir mexanizmi arasında fərq



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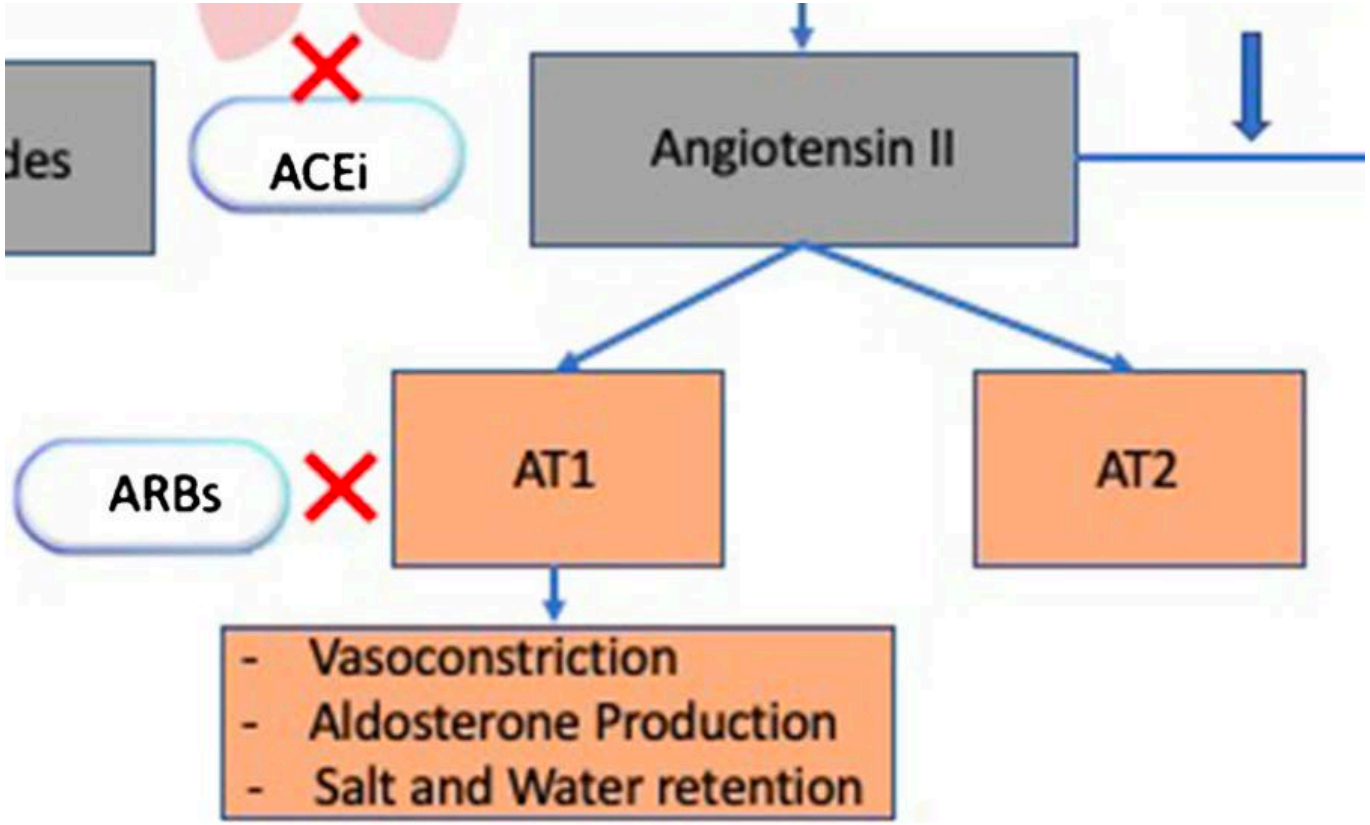
ARB və AÇFi təsir mexanizmi arasında fərq



ACE inhibisiyası nəticəsində həm AT1 həm AT2 reseptorlarına təsir azalır.

ARB lər isə əksinə AT1 reseptorları blok etməklə AT2 üzərinə təsiri artırır

AT_1 stimulə edilməsinin effekti AT_2 stimulə edilməsindən tamamilə fərqlənir, əksdirlər

AT_1 stimulyasiyası

- Vazokonstriksiya
- Maye, duz ləngiməsi
- Yumaqcıq daxili hipertenziya
- Apaptozun aktivləşməsi
- Proiltihab effekt
- Hüceyrə differensasiya və proliferasiyası
- Prokoaqulyant effekt
- Trombositlərin aqreqasiyasının artması
- SAS fəallığının artması

AT_2 stimulyasiyası

- Vazodilatasiya
- Natriurez/diurez artımı
- Antiproteinurik effekt
- Antiapaptoz effekt
- İltihab əleyhinə effekt
- Antipoliferativ effekt
- Antikoaqulyant effekt
- Antiaqreqant effekt
- SAS fəallığının azalması

İlk dəfə ACEi FDA tərəfindən nə vaxt istifadəsi təstiqlənib?

- 1966
- 1971
- 1976
- 1981 Kaptopril
- 1986

İlk dəfə ARB FDA tərəfindən nə vaxt istifadəsi təstiqlənib?

- 1980
- 1985
- 1990
- 1995 Lozartan
- 2000

Hansı təzyiqi daha yaxşı endirir?

REVIEW | Annals of Internal Medicine

Systematic Review: Comparative Effectiveness of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers for Treating Essential Hypertension

David B. Matchar, MD; Douglas C. McCrory, MD, MHS; Lori A. Orlando, MD, MHS; Manesh R. Patel, MD; Uptal D. Patel, MD; Meenal B. Patwardhan, MD, MHSA; Benjamin Powers, MD; Gregory P. Samsa, PhD; and Rebecca N. Gray, DPhil

ARB ilə ACEi hipotenziv təsirlərini müqayisə edən 61 çalışmanın metaanalizidir.

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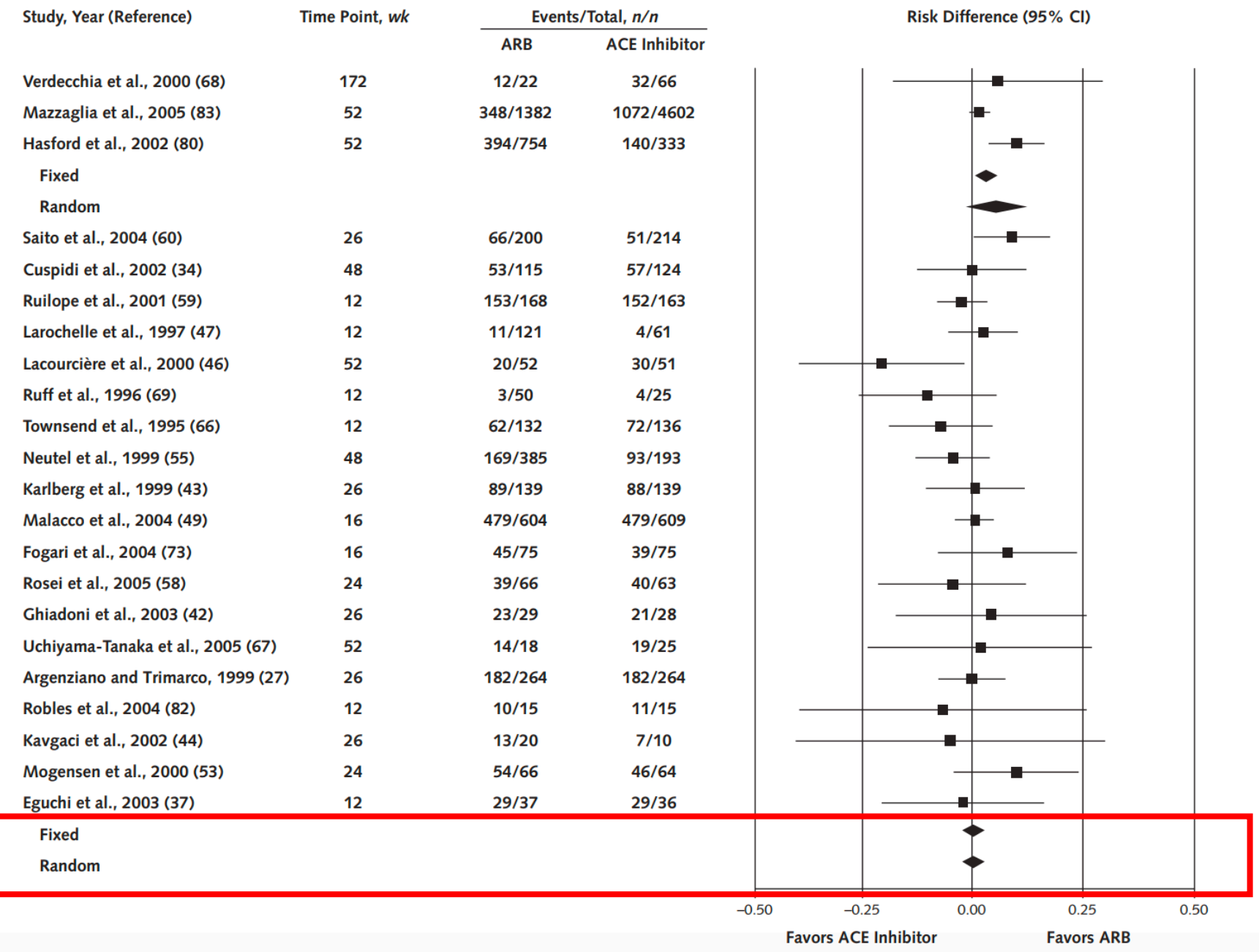
Hipotenziv təsirlərinin müqayisəsi

Figure 2. **Successful monotherapy: angiotensin-converting enzyme (*ACE*) inhibitors versus angiotensin II receptor blockers (*ARBs*).**

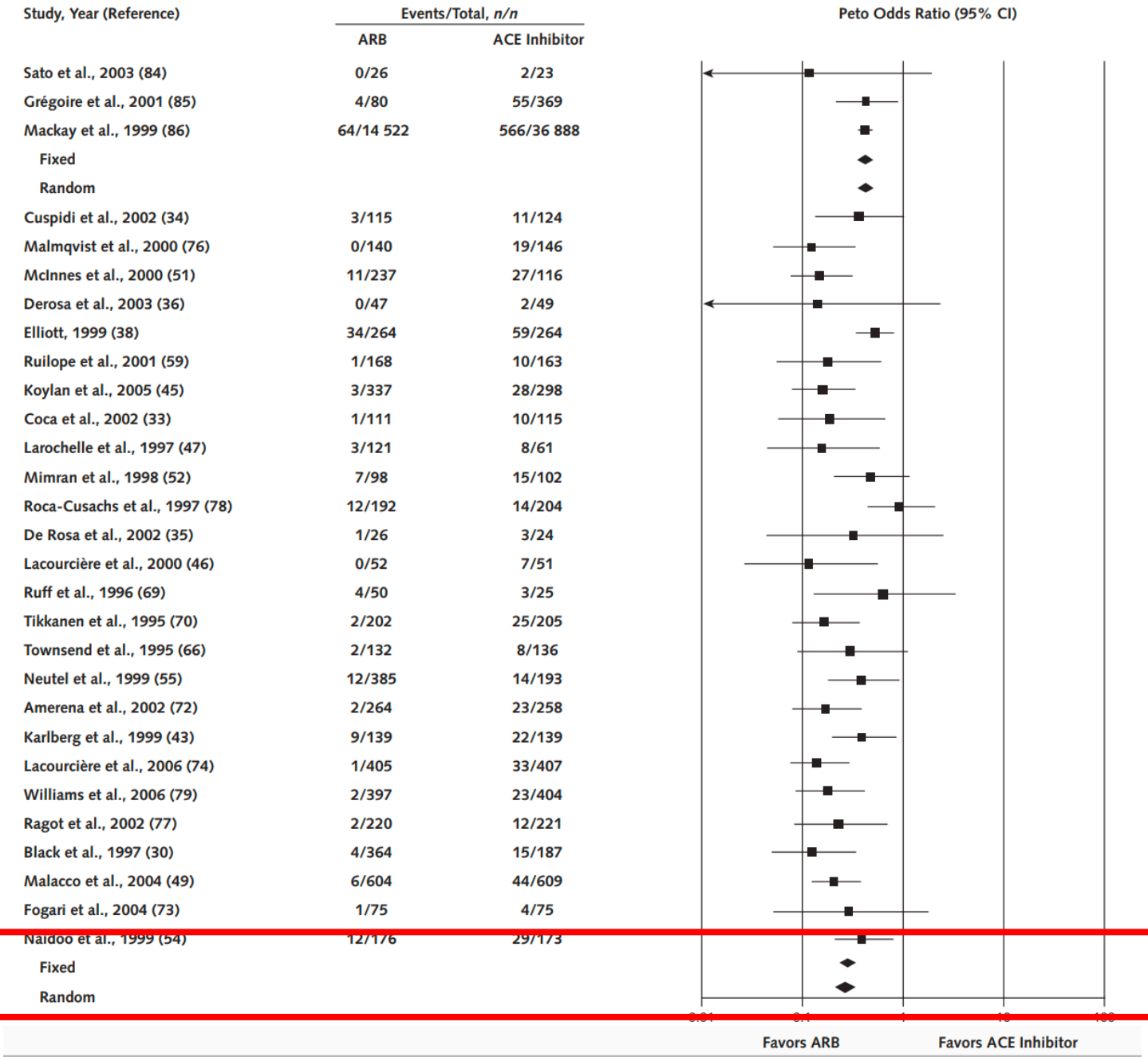


Statistik fərq yoxdur

Əlavə təsir olaraq öskürək

ARB daha üstündür

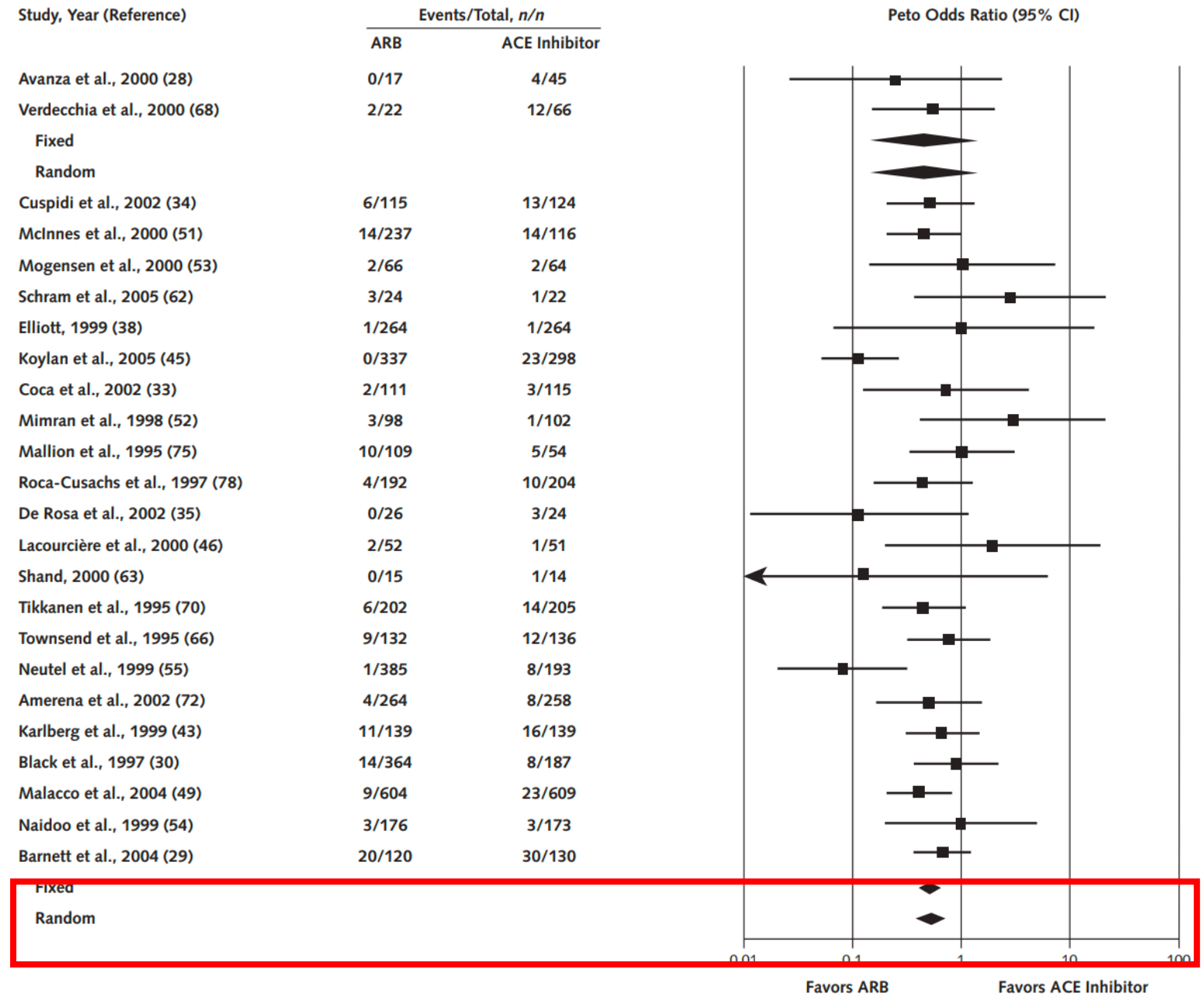
Figure 3. **Cough as an adverse event: angiotensin-converting enzyme (*ACE*) inhibitors versus angiotensin II receptor blockers (*ARBs*).**



Əlavə təsir səbəbi ilə dərmandan imtina

ARB daha üstündür

Figure 4. **Withdrawals due to adverse events: angiotensin-converting enzyme (*ACE*) inhibitors versus angiotensin II receptor blockers (*ARBs*).**



Nəticə: ARB və ACEi hipotenziv təsirləri statistik fərqlənmir. Lakin əlavə təsirlər ACEi qrupunda daha yüksəkdir.

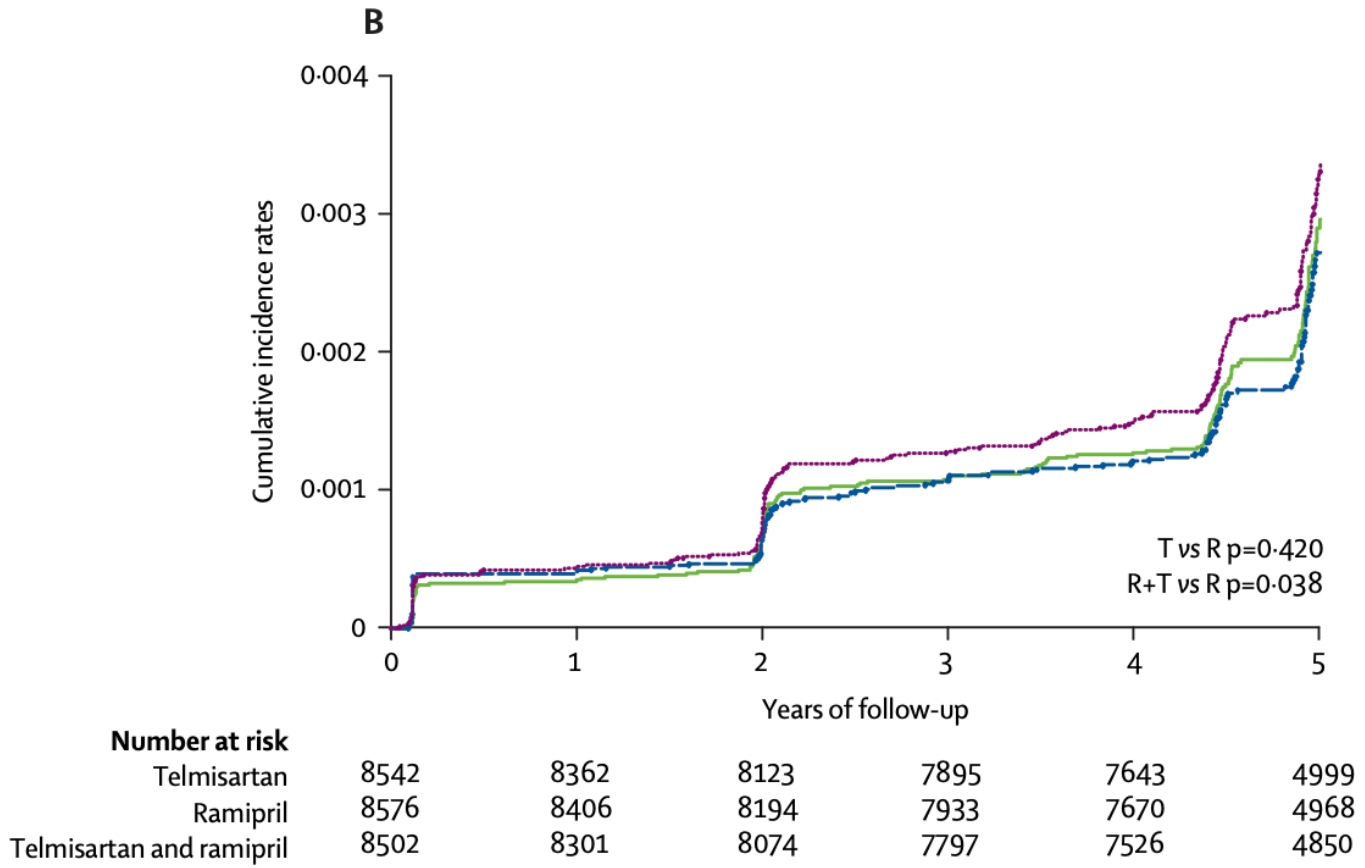
XBÇ zamanı ARB və ya ACEi?

Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial

Johannes F E Mann, Roland E Schmieder, Matthew McQueen, Leanne Dyal, Helmut Schumacher, Janice Pogue, Xingyu Wang, Aldo Maggioni, Andrzej Budaj, Suphachai Chaithiraphan, Kenneth Dickstein, Matyas Keltai, Kaj Metsärinne, Ali Oto, Alexander Parkhomenko, Leopoldo S Piegas, Tage L Svendsen, Koon K Teo, Salim Yusuf, on behalf of the ONTARGET investigators

Dializ və ya Kreatin dəyərinin iki dəfə yüksəlməsi

ARB ilə ACEi arasında statistik önəmli fərq görülmədi.



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https://doi.org/10.1016/S0140-6736(08)61236-2

International Journal of Cardiology 155 (2012) 236–242

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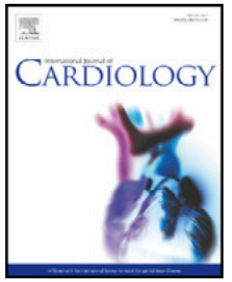
International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard



Angiotensin receptor blockers for prevention of new-onset type 2 diabetes: A meta-analysis of 59,862 patients

Deng-feng Geng [a,1], Dong-mei Jin [b,1], Wei Wu [a], Yun Xu [c], Jing-feng Wang [a,*]

[a] *Department of Cardiology, Sun Yat-sen memorial hospital, Zhongshan University, 510120 Guangzhou, China*
[b] *Department of Rehabilitation Medicine, Sun Yat-sen memorial hospital, Zhongshan University, 510120 Guangzhou, China*
[c] *Department of Endocrinology, 1st affiliated hospital, Zhongshan University, 510080 Guangzhou, China*

ARB və yeni yaranmış diabet

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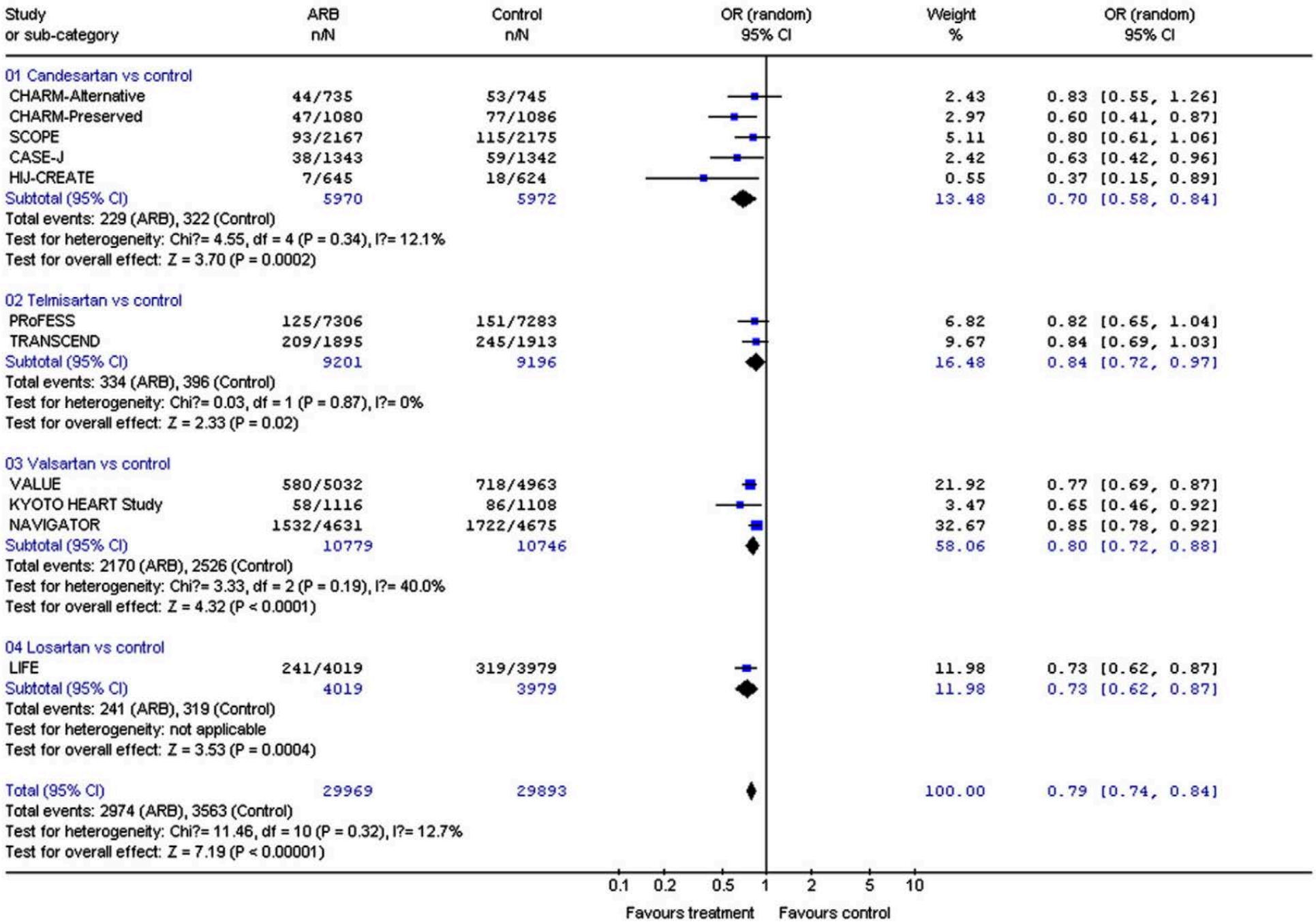
Study or sub-category
ARB n/N
Control n/N
OR (random) 95% CI
Weight %
OR (random) 95% CI
01 Candesartan vs control
CHARM-Alternative 44/735 53/745 2.43 0.83 [0.55, 1.26]
CHARM-Preserved 47/1080 77/1086 2.97 0.60 [0.41, 0.87]
SCOPE 93/2167 115/2175 5.11 0.80 [0.61, 1.06]
CASE-J 38/1343 59/1342 2.42 0.63 [0.42, 0.96]
HIJ-CREATE 7/645 18/624 0.55 0.37 [0.15, 0.89]
Subtotal (95% CI) 5970 5972 13.48 0.70 [0.58, 0.84]
Total events: 229 (ARB), 322 (Control)
Test for heterogeneity: Chi?= 4.55, df = 4 (P = 0.34), I?= 12.1%
Test for overall effect: Z = 3.70 (P = 0.0002)
02 Telmisartan vs control
PRoFESS 125/7306 151/7283 6.82 0.82 [0.65, 1.04]
TRANSCEND 209/1895 245/1913 9.67 0.84 [0.69, 1.03]
Subtotal (95% CI) 9201 9196 16.48 0.84 [0.72, 0.97]
Total events: 334 (ARB), 396 (Control)
Test for heterogeneity: Chi?= 0.03, df = 1 (P = 0.87), I?= 0%
Test for overall effect: Z = 2.33 (P = 0.02)
03 Valsartan vs control
VALUE 580/5032 718/4963 21.92 0.77 [0.69, 0.87]
KYOTO HEART Study 58/1116 86/1108 3.47 0.65 [0.46, 0.92]
NAVIGATOR 1532/4631 1722/4675 32.67 0.85 [0.78, 0.92]
Subtotal (95% CI) 10779 10746 58.06 0.80 [0.72, 0.88]
Total events: 2170 (ARB), 2526 (Control)
Test for heterogeneity: Chi?= 3.33, df = 2 (P = 0.19), I?= 40.0%
Test for overall effect: Z = 4.32 (P < 0.0001)
04 Losartan vs control
LIFE 241/4019 319/3979 11.98 0.73 [0.62, 0.87]
Subtotal (95% CI) 4019 3979 11.98 0.73 [0.62, 0.87]
Total events: 241 (ARB), 319 (Control)
Test for heterogeneity: not applicable
Test for overall effect: Z = 3.53 (P = 0.0004)
Total (95% CI) 29969 29893 100.00 0.79 [0.74, 0.84]
Total events: 2974 (ARB), 3563 (Control)
Test for heterogeneity: Chi?= 11.46, df = 10 (P = 0.32), I?= 12.7%
Test for overall effect: Z = 7.19 (P < 0.00001)
0.1 0.2 0.5 1 2 5 10
Favours treatment
Favours control

Bəzi ARB lər həmçinin adrenokortikal AT1 reseptorlarını blokə etməklə aldosteron sintezini azaldır. Bu xüsusiyyət ən güclü kandesardan və valsartandadır. AÇFi də bu xüsusiyyət yoxdur.

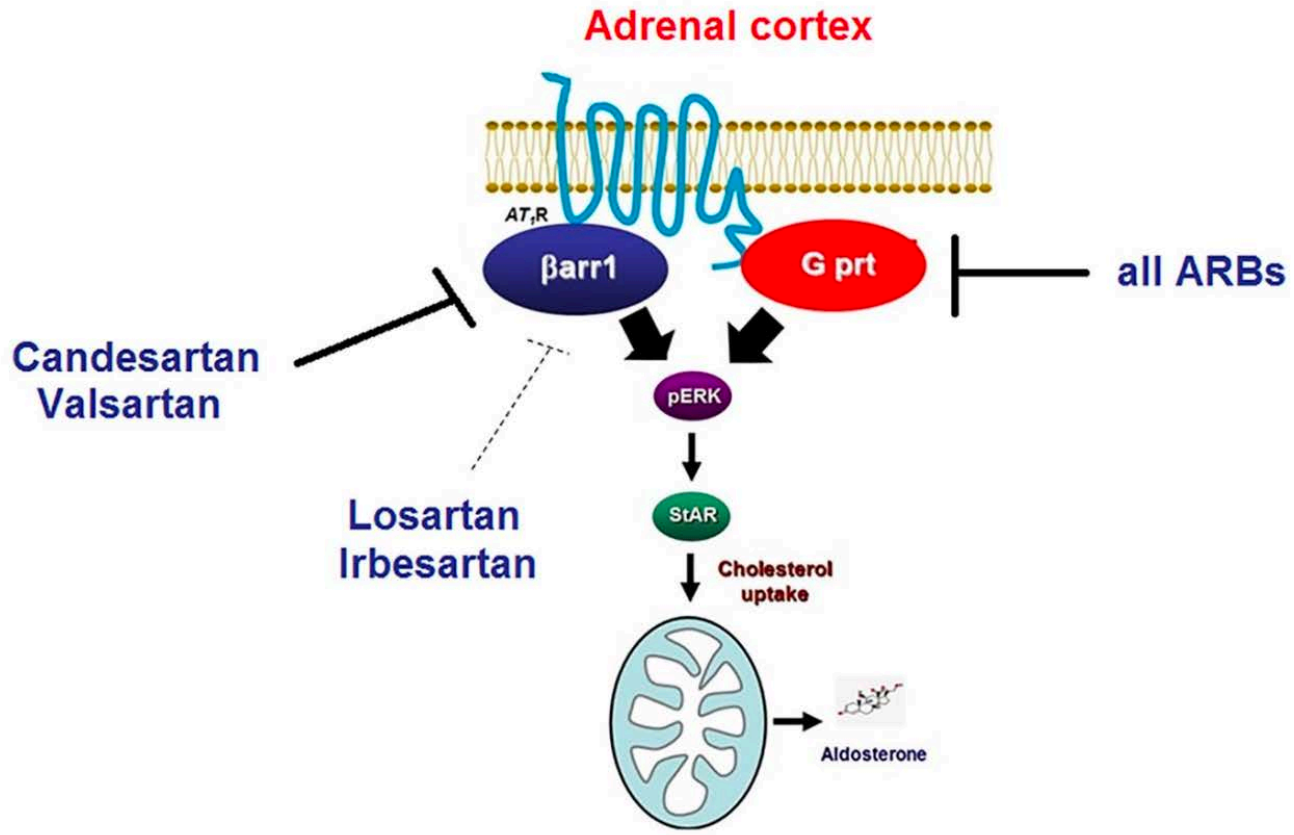

Figure 2. The two components of adrenocortical aldosterone production and the degree of their inhibition by ARBs.
AT_1R, Angiotensin II type 1 receptor; βarr1, β-arrestin-1; G prt, G protein; pERK, phospho-extracellular signal-regulated kinase; StAR, Steroidogenic Acute Regulatory protein. The solid black inhibition sign denotes potent inhibition. The dashed black inhibition sign denotes weak inhibition.

Ther Adv Cardiovasc Dis
2019, Vol. 13: 1–7
https://doi.org/10.1177/1753944719868134

Sartanların pleotropik təsirləri

- Anti inflamatuar
- Koaqulyasiya prosseslərini tənzimləyir
- Gen requlyasiyası

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Sartanların pleotropik təsirləri

- Anti inflamatuar

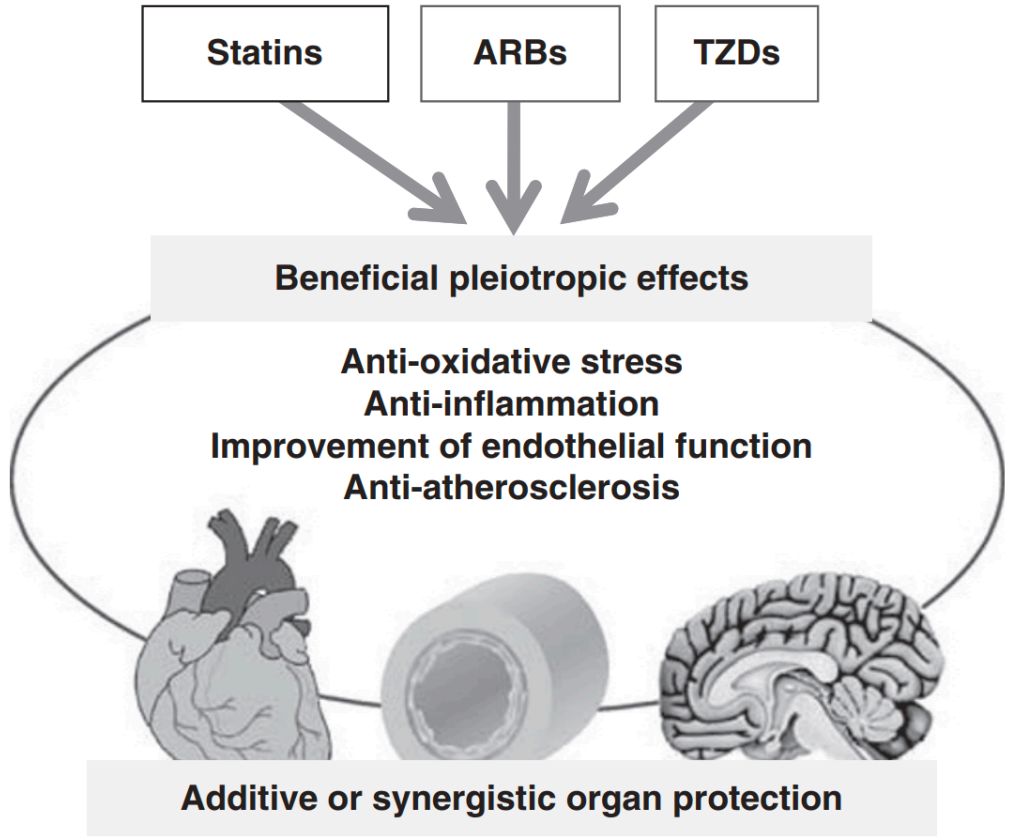

Figure 1 Beneficial pleiotropic effects of statins, angiotensin receptor blockers (ARBs) and thiazolidinediones (TZDs). These different classes of drugs, by different mechanisms, attenuate tissue oxidative stress and inflammation, leading to the amelioration of vascular endothelial dysfunction, atherosclerosis and cardiovascular remodeling.

Hypertension Research (2009) 32, 639–640; doi:10.1038/hr.2009.90; published online 19 June 2009

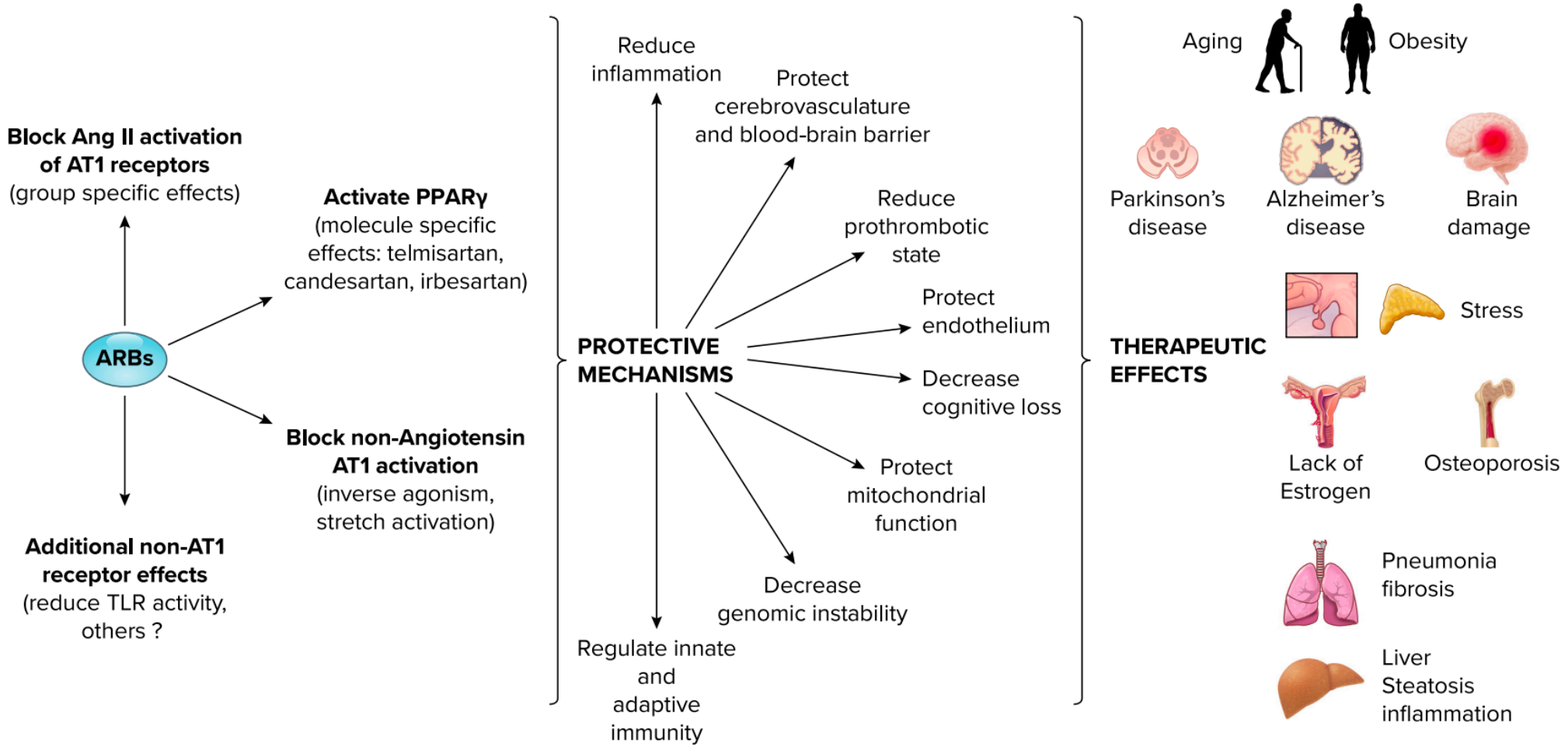

FIGURE 1. **Mechanisms of action, principal protective effects, and influence of angiotensin receptor blocker (ARB) treatment beyond cardiovascular, renal, and metabolic disorders**

ARB effects are group specific, molecule specific, not related to ANG II, or by modulation of non-AT_1 receptors. Principal mechanisms of action include reduction of inflammation, prothrombotic state, and genomic instability, regulation of innate and adaptive immunity, and protection of endothelium, mitochondrial function, cerebral vasculature and blood-brain barrier, and cognition. ARB therapeutic effects are noted in aging, obesity, Alzheimer's and Parkinson's disease, brain damage, stress, lack of estrogens and osteoporosis, pneumonia and lung fibrosis, and liver steatosis and inflammation. PPARγ, peroxisome proliferator-activated receptor-γ; TLR, Toll-like receptor.

PHYSIOLOGY 36: 160–173, 2021. Published April 21, 2021; doi:10.1152/physiol.00036.2020

Sartanların Alzheymer və Parkinson xəstəliklərində rolu

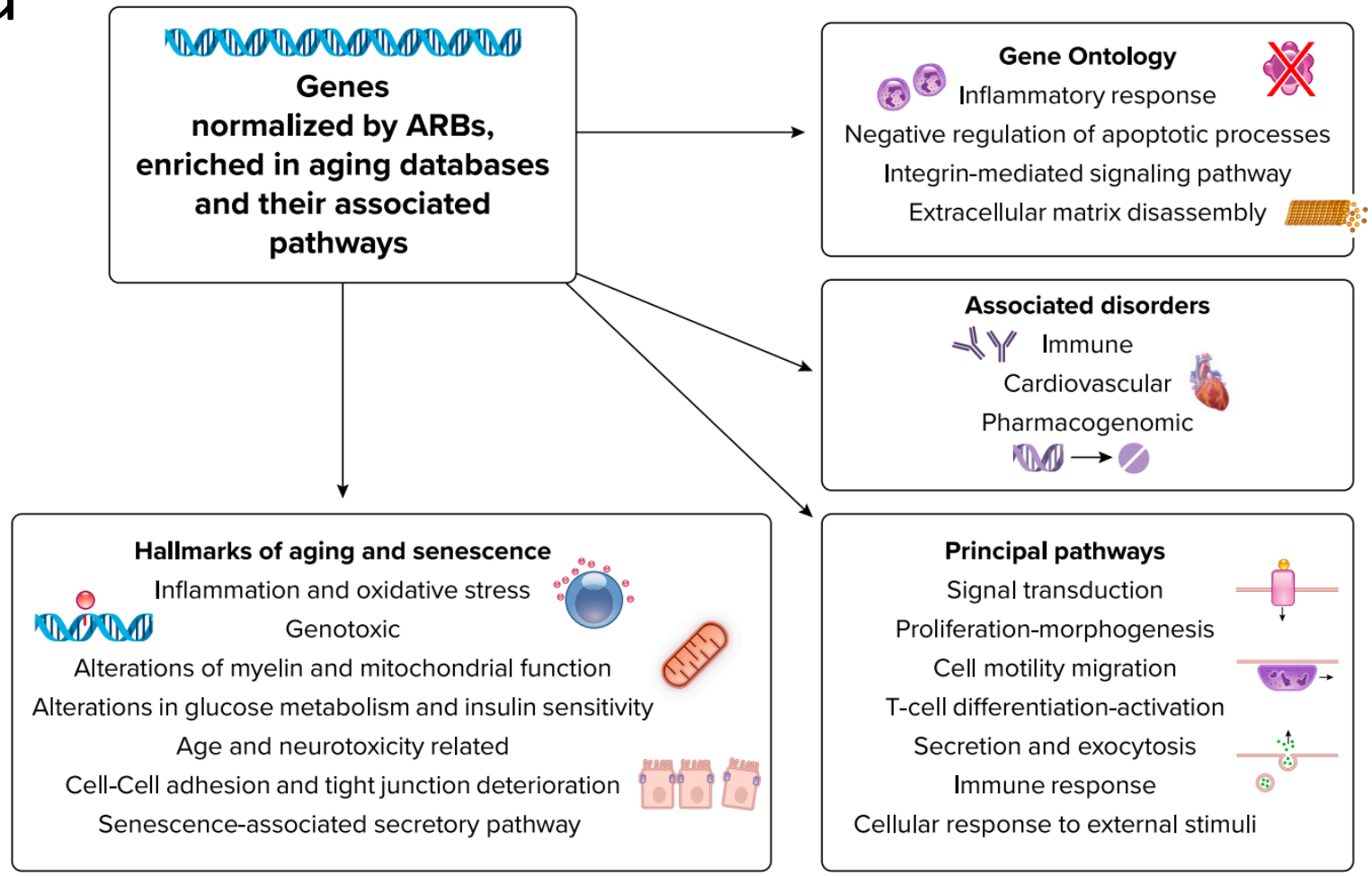

FIGURE 2. **Angiotensin receptor blocker (ARB) treatment normalized the expression of multiple genes enriched in all aging and senescence databases studied**
These genes participate in all hallmarks of aging and senescence; associated disorders; Gene Ontology categories such as inflammation, apoptosis, integrin signaling and extracellular matrix, and immune, cardiovascular, and pharmacogenomic associated disorders; and pathways including signal transduction, T-cell differentiation and immune response, proliferation, cell motility, and secretion and exocytosis.

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Ovarioektomiya və erkən menopauza zamanı sartanların rolu

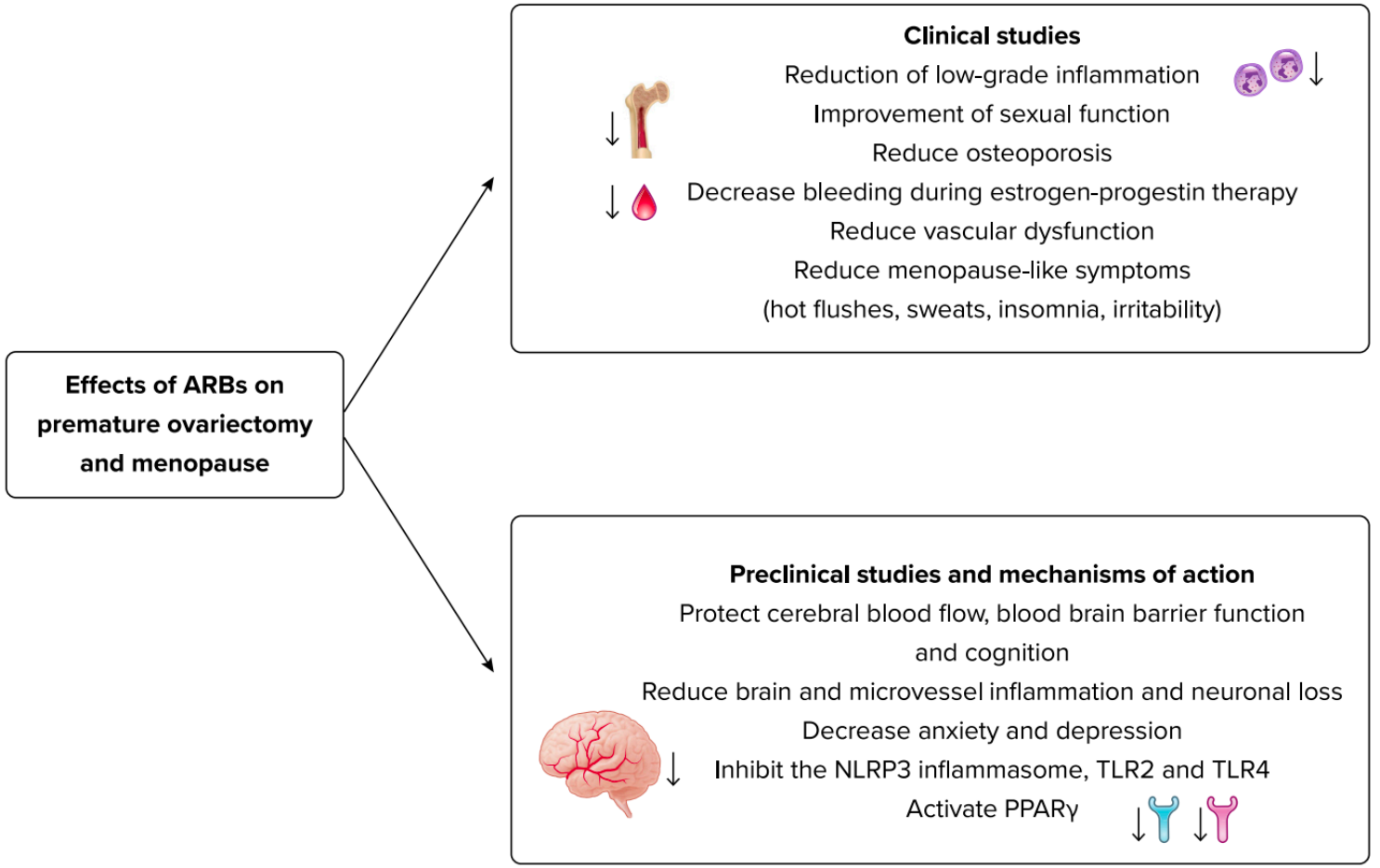

FIGURE 4. **Reciprocal effects of estrogen reduction and angiotensin receptor blocker (ARB) treatment**
ARBs counteract the effects of premature ovariectomy and menopause; protect cerebral blood flow and the blood-brain barrier; reduce brain and microvessel inflammation and neuronal loss; inhibit the NOD-like receptor family, pyrin domain containing 3 (NLRP3) inflammasome and the activity of Toll-like receptors (TLRs); activate peroxisome proliferator-activated receptor-γ (PPARγ); and protect cognition. After menopause, ARBs reduce low-grade inflammation, menopause-like symptoms, vascular dysfunction, and osteoporosis, decrease bleeding during estrogen-progestin therapy, and improve sexual function.

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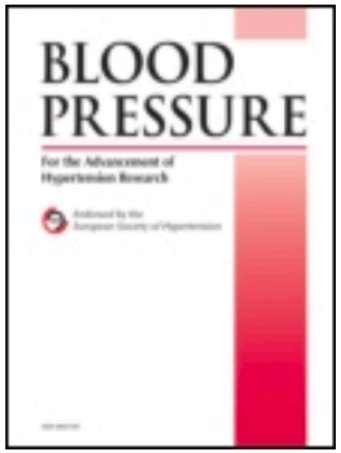

Taylor & Francis
Taylor & Francis Group

Blood Pressure

ISSN: 0803-7051 (Print) 1651-1999 (Online) Journal homepage: https://www.tandfonline.com/loi/iblo20

Effect of the angiotensin II antagonist valsartan on sexual function in hypertensive men

R. Düsing

To cite this article: R. Düsing (2003) Effect of the angiotensin II antagonist valsartan on sexual function in hypertensive men, Blood Pressure, 12:sup2, 29-34, DOI: 10.1080/08038020310021967

To link to this article: https://doi.org/10.1080/08038020310021967

BLOOD PRESSURE
Blood Pressure
ISSN: 0803-7051 (Print) 1651-1999 (Online) Journal homepage: https://www.tandfonline.com/loi/iblo20

Effect of the angiotensin II antagonist valsartan on sexual function in hypertensive men

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To link to this article: https://doi.org/10.1080/08038020310021967

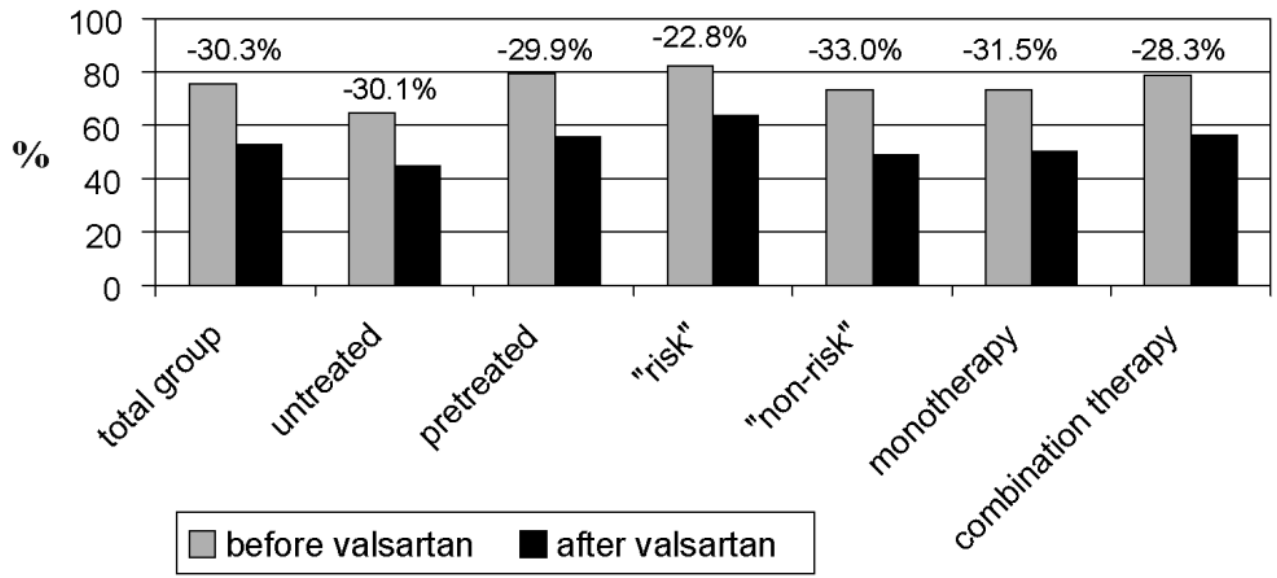

Fig. 1. Percentage of patients with erectile dysfunction according to the International Index of Erectile Function (IIEF) [34] in the total group and in the pre-specified subgroups without and with antihypertensive pre-treatment, with ("risk") and without ("non-risk") pre-existing arteriosclerotic disease and/or diabetes and in patients receiving valsartan as monotherapy or as part of a combination regimen. Given are the data before and after 6 months of therapy with valsartan. Note that the differences in all groups are significant at $p < 0.0001$.

Pediatrik hipertenziyalı xəstələrdə ARB istifadə edə bilərikmi?

Patient Preference and Adherence

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REVIEW

Clinical utility of valsartan in the treatment of hypertension in children and adolescents

Table 1 Angiotensin receptor blockers

Generic name	Trade name	Half life[a] (metabolite)	Pediatric FDA approval	Dosing	Generic form
Valsartan	Diovan	6 hours	Yes	80–160 mg	No
Losartan	Cozaar	2 (6–9) hours	Yes	50 mg	Yes
Irbesartan[b]	Avapro	11–15 hours	No	150–300 mg	No
Telmisartan	Micardis	24 hours	No	40–80 mg	No
Candesartan cilexetil	Atacand	9 hours	Yes	4–32 mg	No
Eprosartan	Teveten	5–9 hours	No	400–800 mg	No
Olmesartan	Benicar	13 hours	Yes	10–40 mg	No

Notes: [a]From www.medscape.com; [b]Irbesartan in a study at a dose of up to 4.5 mg/kg/day once daily did not appear to lower blood pressure effectively in pediatric patients aged 6 to 16 years. Avapro has not been studied in pediatric patients less than 6 years old.

Bütün ARB lərin hipotenziv təsiri eynidirmi?

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META-ANALYSIS

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

Online Extra

Valsartan vs. other angiotensin II receptor blockers in the treatment of hypertension: a meta-analytical approach

R. M. Nixon,[1] E. Müller,[2] A. Lowy,[1] H. Falvey[1]

Toplam 13110 xəstəni əhatə etmiş 31 RKÇ metaanalizi

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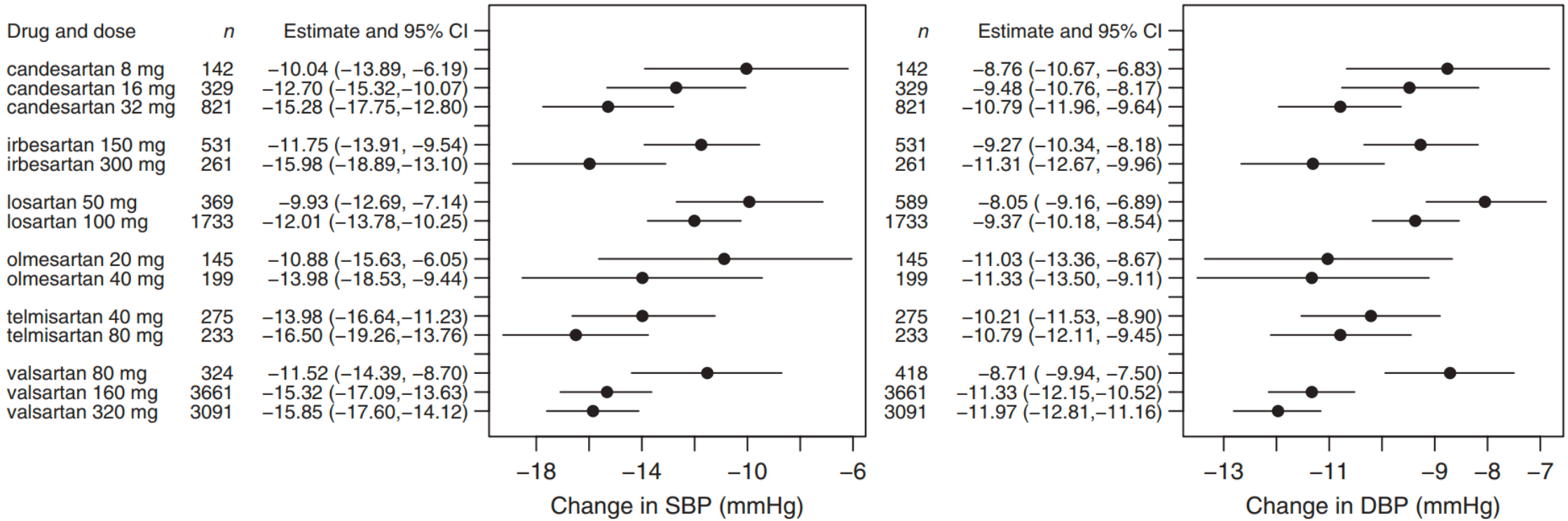

Figure 3 Plot of mean change from baseline SBP and DBP by drug and dose. The number of individuals randomised (*n*) is shown, along with the estimates and 95% CI of the mean change in BP

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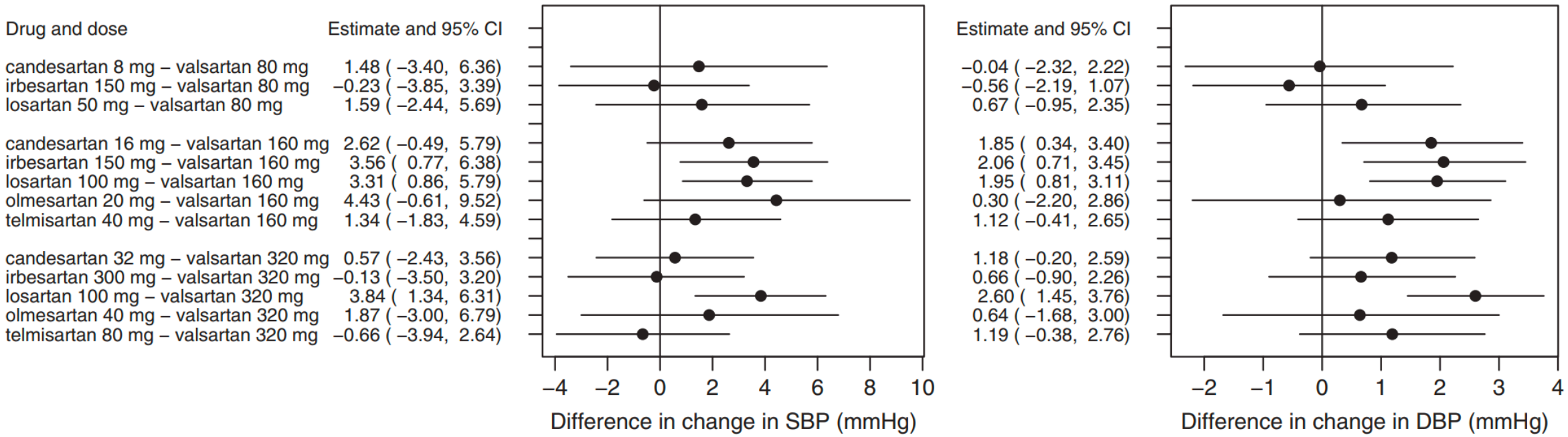

Figure 4 Plot of indirect comparisons of mean change from baseline, and 95% CI, of SBP and DBP by drug and dose. Positive numbers indicate that valsartan is superior to the comparator, negative numbers that valsartan is inferior

Valsartan kanserogendirmi?

Journal of the American Heart Association

ORIGINAL RESEARCH

N-nitrosodimethylamine-Contaminated Valsartan and Risk of Cancer: A Nationwide Study of 1.4 Million Valsartan Users

Imène Mansouri, PhD; Jeremie Botton, PharmD, PhD; Laura Semenzato, Msc; Nadia Haddy, PhD; Mahmoud Zureik, MD, PhD

CONCLUSIONS: Our study was the largest to date to examine cancer risks associated with exposure to NDMA-contaminated valsartan. Our findings suggest a slight increased risk of liver cancer and melanoma in patients exposed to NDMA in regularly taken medications.

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Lakin…

- Kanserogenliyə səbəb Valsartan özü deyil, preporatın tərkibində olan N-Nitrozodimetilamin-dir
- Bütün dərmanların generiklərinin tərkibində N-Nitrozodimetilamin yoxdur

TABLE S1. Manufactures of NDMA contaminated and uncontaminated Valsartan

Contaminated Valsartan	*Uncontaminated Valsartan*
Arrow Generiques	Accord Healthcare
Biogran	ALTER
Cristers	IPSEN Pharma
Evolupharm	KRKA
Mylan	Novartis
Ranbaxy pharmacie generiques	PHR LAB
Sandoz	
Zentiva	
Zydus	

Contaminated Valsartan was fabricated by manufactures who recalled all unexpired valsartan from the market between 06/07/2018 and 20/12/2018 and uncontaminated valsartan was manufactured by those unaffected by the recalls. The official lists of suppliers was obtained from the French National Agency for Medicines and Health Products [2, 21].

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Nəticədə...

- ARB-lər hipotenziv təsir effektinə görə AÇEi-dan geri qalmır
- Daha rahat tolerə edilir.
- Əlavə təsirləri azdır.
- AT2 reseptoruna təsir etməklə əlavə pleotropik təsirləri var.

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HIPERTENZİYADA VALSARTANIN GÜCÜ

Ko-Vamloset

amlodipin/valsartan/hidroxlorotiazid

Valsakor® H HD

valsartan/hidroxlorotiazid

Vamloset®

amlodipin/valsartan

Valsakor®

valsartan

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2023 AKC təlimatlarında HİPERTENZİYA müalicəsinin alqoritmi

1-ci addım

ARB/ AÇFi + KKB/diuretik

məs. Vamloset®
amlodipin/valsartan

Valsakor® H HD
valsartan/hidroxlorotiazid

2-ci addım

ARB / AÇFi + KKB + diuretik

məs. Ko-Vamloset
amlodipin/valsartan/hidroxlorotiazid

Aşağı riskli 1-ci dərəcəli hipertenziya (SBP <150 mmHg) və ya çox yaşlı (>80 yaş) və ya daha zəif pasiyentlərdə monoterapiya.

AÇFi – angiotenzin-çevirən fermentin inhibitoru, ARB – angiotenzin II reseptorların blokatoru, KKB – kalsium kanal blokatoru

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1. Unger T, Borghi C, Charchar F, et al. 2020 International Society of Hypertension global hypertension practice guidelines. J Hypertens. 2020 Jun;38(6): 982-1004.

Amlo/val/HXTZ AT **azaldılmasında** hər **hansı** ikili kombinasiyadan daha **yaxşıdır**[1]

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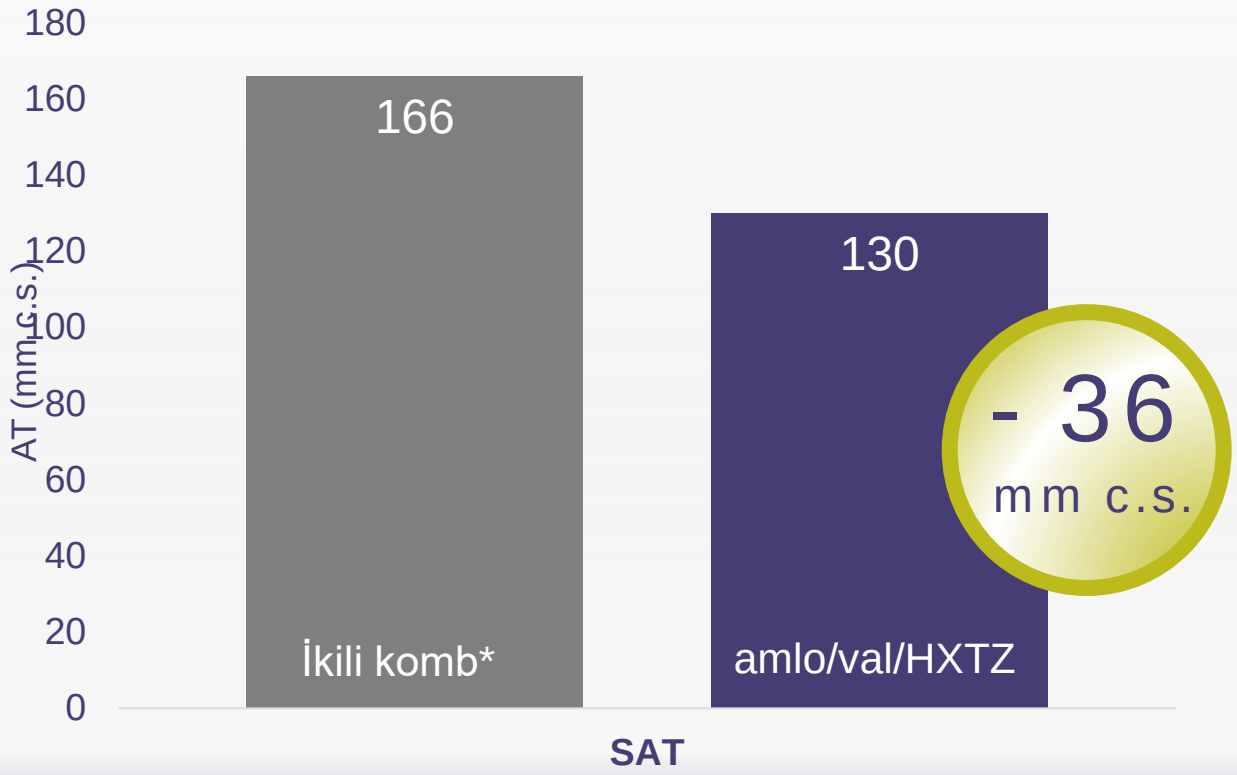
amlodipin/valsartan/hidroxlorotiazid



3 **GÜCÜN BİRLİYİ**

*ARB+ diur, AÇFi+diur, Beta blokator+diur, KKB+diur, AÇFi+KKB, ARB+CCB.
Amlo – amlodipin, val – valsartan, HXTZ – hidroxlorotiaizid, SAT – sistolik arterial təzyiq

1. El-Etriby AMK, Rakha S. Efficacy and safety of amlodipine/valsartan/hydrochlorothiazide single pill combination in Egyptian patients with hypertension uncontrolled on any dual therapy: an observational study. Curr Med Res Opin. 2020; 36(4): 537–544

Təşəkkürlər!