



Would Anti-Hypertensive Treatment be a Risk Factor for National Health Budget of Turkey in 2023?

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Abstract

This study aims to predict the prevalence of hypertension and the cost of anti-hypertensive treatment in future by analyzing the adults diagnosed with hypertension and the drugs prescribed for their treatment in Turkey during a period of five years. This study reviews data related to the patients diagnosed with hypertension amongst the individuals registered within the Medula database of the Turkish Social Insurance Institution from 2009 to 2013. A significant and gradual increase was specified in the prevalence of hypertension during the study period. The number of female patients was significantly higher than the number of male patients over the passing years. The number of anti-hypertensive drug boxes consumed was significantly increased during the study period. Surprisingly, the number of anti-hypertensive boxes annually consumed by the hypertensive patients remained statistically similar between 2009 and 2013. A significant increase was noted in the prescription of angiotensin II receptor blockers, beta blockers, and angiotensin converting enzyme inhibitors during the study period. The cost of anti-hypertensive treatment was found to decrease by 36.7% during the study period. The economical measures currently adopted for drug pricing are successful but health policies developed for the prevention of hypertension are inadequate.

Keywords: Anti-hypertensive drugs; hypertension; pharmacoeconomy; prevalence

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Introduction

Cardiovascular diseases are addressed as the most common cause of morbidity and mortality in adults worldwide [1]. Hypertension is a particular cardiovascular disease which is diagnosed if systolic blood pressure is ≥ 140 mmHg and diastolic blood pressure is ≥ 90 mmHg [2]. Hypertension is responsible for 45% of the cardiovascular disease related deaths worldwide [3]. It is well known that the prevalence of hypertension changes with respect to age, gender, genetic factors and geographical location. According to the World Health Organization, the prevalence of hypertension in developed countries is less than that of the developing countries [4].

As for Turkey, cardiovascular diseases and particularly hypertension also stand for the most frequently encountered reason of morbidity and mortality in adults [5]. Epidemiological research in Turkey shows that the ratio of hypertensive patients was around 31.8% in early 2000s. When age dependent differences were analyzed, 36.1% of the hypertensive patients were woman and 27.5% of them were men [6].

The alterations in the treatment regimens cause the global shares of antihypertensive drugs to vary in drug marketing. Thus, the drug producers try to keep their shares in the antihypertensive drug market by developing new molecules or by promoting the already available ones. Whatever the case, the treatment of hypertension poses a serious risk for the budget integrity of the social insurance institutions.

According to a Turkish study published in 2007, angiotensin receptor blockers-diuretic combination (ARB-D), calcium channel blockers (CCB), angiotensin converting enzyme inhibitors (ACE), beta blockers (BB), ACE-diuretic combination and ARB pills were prescribed in 16.7%, 16.1%, 13.7%, 12.5%, 10.5% and 8.9% of the patients respectively [7]. Since 2007, all data related with health has been recorded within the Medula database in accordance with the initiation of health transformation program in Turkey [8]. However, up to date, no studies have been conducted to clarify the financial burden of anti-hypertensive drugs.

The present study aims to predict the prevalence of hypertension and the cost of anti-hypertensive treatment in future by analyzing the adults diagnosed with hypertension and the

drugs prescribed for the treatment of hypertension in Turkey between 2009 and 2013 within the scope of data obtained from the Medula database of the Turkish Social Insurance Institution.

Materials and Methods

This study was approved by the Ethical Committee of Afyon Kocatepe University Medical Faculty Hospital (grant no: 2014-182). The present study reviews data related to the patients diagnosed with hypertension (ICD code I10) amongst the individuals registered within the Medula database of Turkish Social Insurance Institution from 2009 to 2013. The aforementioned data were obtained from the Board of Data Sharing at the Turkish Social Insurance Institution (grant no: 2014-3919127).

Statistical Analysis

Collected data were analyzed by the Statistical Package for Social Sciences programme version 21.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean $\pm$ standard deviation (range: minimum-maximum) and categorical variables were denoted as numbers or percentages where appropriate. Pearson correlation test was used to identify the relationships between the variables whereas Mann Kendall trend tests were used to calculate the parameters separately for each year.

Results

Table 1 shows the significant and gradual increase in the prevalence of hypertension during the study period. The number of female patients was significantly higher than the number of male patients over the passing years (Table 1).

Despite the significant increase in the number of hypertensive patients, antihypertensive drugs had significantly less share in the total drug expense of the Turkish Social Insurance Foundation (Figure 1). The number of anti-hypertensive drug boxes consumed was significantly increased during the study period. Surprisingly, the number of anti-hypertensive boxes annually consumed by the hypertensive patients remained statistically similar between 2009 and 2013 (Figure 2).

Table 1. The number of hypertensive individuals in Turkey according to years and gender.

Year-Gender		HTP	POP	TP	TPOP
2009	Male	1.400.109	25.572.873	3.823.242	50.890.717
	Female	2.423.133	25.317.844		
2010	Male	1.856.164	27.825.918	4.955.049	55.378.876
	Female	3.098.885	27.552.958		
2011	Male	1.908.781	30.157.199	5.059.744	60.039.895
	Female	3.150.963	29.882.696		
2012	Male	2.073.560	32.147.243	5.537.312	64.053.144
	Female	3.463.752	31.905.901		
2013	Male	2.131.670	30.568.165	5.649.052	60.914.771
	Female	3.517.382	30.346.606		

HTP refers the number of hypertensive individuals, POP; population, TP; the total number of hypertensive individuals, TPOP; total population.

Table 2. The codes and explanations of Anatomical Therapeutic Chemical Classifications (ATC) confirmed by World Health Organization.

ATC CODE	Explanation
C02C	Antiadrenergic agents, peripherally acting
C02CA	Alpha-adrenoceptor blocking agents
C03BA	Sulphonamides
C03DA	Aldosterone antagonists
C03EA	Low-ceiling diuretics and potassium-sparing agents
C07AB	Beta blocking agents, selective
C07AG	Alpha and beta blocking agents
C07BB	Beta blocking agents, selective, and thiazides
C08CA	Dihydropyridine derivatives
C08DA	Phenylalkylamine derivatives
C08DB	Benzothiazepine derivatives
C09AA	ACE inhibitors, plain
C09BA	ACE inhibitors and diuretics
C09BB	ACE inhibitors and calcium channel blockers
C09CA	Angiotensin II antagonists, plain
C09DA	Angiotensin II antagonists and diuretics
C09DB	Angiotensin II antagonists and calcium channel blockers
C10BX	HMG CoA reductase inhibitors, other combinations

Table 3. The amount of consumed antihypertensive drugs in Turkey, the amount of the money paid by Social Security Institution for antihypertensive drugs, and the total amount of drug expense of Turkey according to years.

Years	ATD	ADS (\$)	TPS (\$)
2009	80.317.353	766.311.342,59	6.133.909.347,89
2010	95.543.024	742.153.908,90	6.170.609.510,13
2011	106.338.198	717.881.937,80	6.259.224.802,64
2012	112.985.043	629.619.272,69	6.320.454.466,37
2013	122.529.653	663.182.696,09	6.789.881.615,58

ATD; the amount of consumed antihypertensive drugs (number of boxes), **ADS;** the expense of Antihypertensive drugs by Social Security Institution (dollar) **TPS;** the total expense done by Social Security Institution (dollar).

Table 4a. The number of hypertensive patients according to the group of drug, the gender, and years in Turkey.

Years	Gender	C02C	C02CA	C03BA	C03DA	C03EA	C07AB	C07AG	C07BB
2009	Male	5.441	215.394	250.794	117.884	161.165	1.081.796	217.484	37.959
	Female	23.377	103.556	353.851	135.754	170.104	1.158.500	229.468	50.809
	Total	28.817	318.950	604.645	253.637	331.268	2.240.295	446.952	88.768
2010	Male	2.727	281.887	355.927	116.328	157.369	1.225.567	316.624	36.125
	Female	25.281	108.000	613.100	153.099	207.987	1.530.656	388.142	62.281
	Total	28.007	389.887	969.026	269.427	365.356	2.756.222	704.765	98.406
2011	Male	1.760	290.121	638.661	105.476	146.255	1.212.481	298.405	27.577
	Female	26.821	96.411	1.125.451	144.572	208.487	1.640.224	390.843	58.874
	Total	28.581	386.532	1.764.111	250.048	354.742	2.852.705	689.248	86.451
2012	Male	1.581	253.821	135.744	194.699	145.573	1.290.310	296.105	26.204
	Female	28.493	565.598	316.225	301.764	208.886	1.729.817	381.305	57.153
	Total	30.074	819.418	451.969	496.462	354.459	3.020.127	677.410	83.357
2013	Male	1.461	453.212	366.891	307.312	143.505	1.319.501	289.112	23.855
	Female	28.546	1.958.293	494.629	1.328.657	208.290	1.747.976	367.850	54.350
	Total	30.007	2.411.505	861.520	1.635.969	351.795	3.067.477	656.962	78.205

Table 4b. The number of hypertensive patients according to the group of drug, the gender, and years in Turkey.

Years	Gender	C08CA	C08DA	C08DB	C09AA	C09BA	C09BB	C09CA	C09DA	C09DB	C10BX
2009	Male	802.120	60.896	164.232	697.997	583.850	114.134	424.688	1.015.519	86.089	13.663
	Female	979.933	84.217	158.361	685.710	703.875	150.676	512.410	1.395.144	111.268	18.244
	Total	1.782.053	145.112	322.592	1.383.706	1.287.725	264.810	937.097	2.410.663	197.356	31.906
2010	Male	867.184	51.675	168.217	730.210	566.420	126.267	428.358	1.145.872	106.432	12.907
	Female	1.321.668	90.518	193.002	794.876	801.258	208.192	615.359	2.069.864	166.852	21.562
	Total	2.188.852	142.192	361.219	1.525.085	1.367.677	334.459	1.043.716	3.215.736	273.284	34.468
2011	Male	802.388	39.975	154.965	688.992	546.587	167.062	299.383	901.238	90.556	10.552
	Female	1.403.783	82.394	196.617	786.593	878.054	292.975	474.863	1.969.859	162.014	18.781
	Total	2.206.171	122.369	351.582	1.475.585	1.424.641	460.037	774.246	2.871.097	252.570	29.333
2012	Male	821.345	36.319	157.531	679.273	533.898	194.091	262.043	864.121	93.371	7.054
	Female	1.442.556	74.526	205.103	750.497	840.211	321.908	412.801	1.955.791	168.435	11.144
	Total	2.263.901	110.845	362.634	1.429.770	1.374.109	515.999	674.844	2.819.912	261.806	18.198
2013	Male	800.115	32.840	155.635	657.364	510.403	211.563	257.182	873.367	106.105	4.968
	Female	1.406.651	67.903	207.826	709.033	795.038	340.682	399.365	1.990.437	190.250	7.141
	Total	2.206.766	100.743	363.461	1.366.397	1.305.441	552.245	656.547	2.863.804	296.355	12.109

Table 5a. The range of rate of antihypertensive drug use according to years and gender (%).

Years	Gender	C02C	C02CA	C03BA	C03DA	C03EA	C07AB	C07AG	C07BB
2009	Male	0,39	15,38	17,91	8,42	11,51	77,27	15,53	2,71
	Female	0,96	4,27	14,60	5,60	7,02	47,81	9,47	2,10
	Total	0,75	8,34	15,81	6,63	8,66	58,60	11,69	2,32
2010	Male	0,15	15,19	19,18	6,27	8,48	66,03	17,06	1,95
	Female	0,82	3,49	19,78	4,94	6,71	49,39	12,53	2,01
	Total	0,57	7,87	19,56	5,44	7,37	55,62	14,22	1,99
2011	Male	0,09	15,20	33,46	5,53	7,66	63,52	15,63	1,44
	Female	0,85	3,06	35,72	4,59	6,62	52,05	12,40	1,87
	Total	0,56	7,64	34,87	4,94	7,01	56,38	13,62	1,71
2012	Male	0,08	12,24	6,55	9,39	7,02	62,23	14,28	1,26
	Female	0,82	16,33	9,13	8,71	6,03	49,94	11,01	1,65
	Total	0,54	14,80	8,16	8,97	6,40	54,54	12,23	1,51
2013	Male	0,07	21,26	17,21	14,42	6,73	61,90	13,56	1,12
	Female	0,81	55,67	14,06	37,77	5,92	49,70	10,46	1,55
	Total	0,53	42,69	15,25	28,96	6,23	54,30	11,63	1,38

Table 5b. The range of rate of antihypertensive drug use according to years and gender (%).

Years	Gender	C08CA	C08DA	C08DB	C09AA	C09BA	C09BB	C09CA	C09DA	C09DB	C10BX
2009	Male	57,29	4,35	11,73	49,85	41,70	8,15	30,33	72,53	6,15	0,98
	Female	40,44	3,48	6,54	28,30	29,05	6,22	21,15	57,58	4,59	0,75
	Total	46,61	3,80	8,44	36,19	33,68	6,93	24,51	63,05	5,16	0,83
2010	Male	46,72	2,78	9,06	39,34	30,52	6,80	23,08	61,73	5,73	0,70
	Female	42,65	2,92	6,23	25,65	25,86	6,72	19,86	66,79	5,38	0,70
	Total	44,17	2,87	7,29	30,78	27,60	6,75	21,06	64,90	5,52	0,70
2011	Male	42,04	2,09	8,12	36,10	28,64	8,75	15,68	47,22	4,74	0,55
	Female	44,55	2,61	6,24	24,96	27,87	9,30	15,07	62,52	5,14	0,60
	Total	43,60	2,42	6,95	29,16	28,16	9,09	15,30	56,74	4,99	0,58
2012	Male	39,61	1,75	7,60	32,76	25,75	9,36	12,64	41,67	4,50	0,34
	Female	41,65	2,15	5,92	21,67	24,26	9,29	11,92	56,46	4,86	0,32
	Total	40,88	2,00	6,55	25,82	24,82	9,32	12,19	50,93	4,73	0,33
2013	Male	37,53	1,54	7,30	30,84	23,94	9,92	12,06	40,97	4,98	0,23
	Female	39,99	1,93	5,91	20,16	22,60	9,69	11,35	56,59	5,41	0,20
	Total	39,06	1,78	6,43	24,19	23,11	9,78	11,62	50,70	5,25	0,21

Table 6. The prices of some antihypertensive drugs (\$) and the price change (%).

Tradename	Content	ATC Code	2009	2013	Change %
Co-Diovan 160/12.5/28 Tb	Valsartan + Hydrochlorothiazide	C09DA	16,93	6,26	63,02
Atacand Plus 16/12,5 28 Tb	Candesartan + Hydrochlorothiazide	C09DA	16,25	8,52	47,55
Micardis Plus 80/12,5 28 Tb	Telmisartan + Hydrochlorothiazide	C09DA	15,48	6,53	57,84
Karvezide 330/12,5 28 Tb	Irbesartan + Hydrochlorothiazide	C09DA	17,22	5,80	66,29
Delix plus 5/25 28 Tb	Ramipril + Hydrochlorothiazide	C09BA	4,31	3,84	10,96
Beloc 50/20 Tb	Metoprolol	C07AB	2,78	2,09	24,88
Accuzide Fort 20/25 30 Tb	Quinapril + Hydrochlorothiazide	C09BA	10,47	6,94	33,70
Adalat Crono 30 30 Tb	Nifedipine	C08CA	5,95	4,15	30,18
Aldactazide 50/50 30 Tb	Spirinolactone + Hydrochlorothiazide	C03EA	4,41	4,03	8,56
Norvasc 5 30 TB	Amlodipine	C08CA	5,50	3,24	41,07
Diltizem SR 120 48 Tb	Diltiazem	C08DB	6,62	5,35	19,09

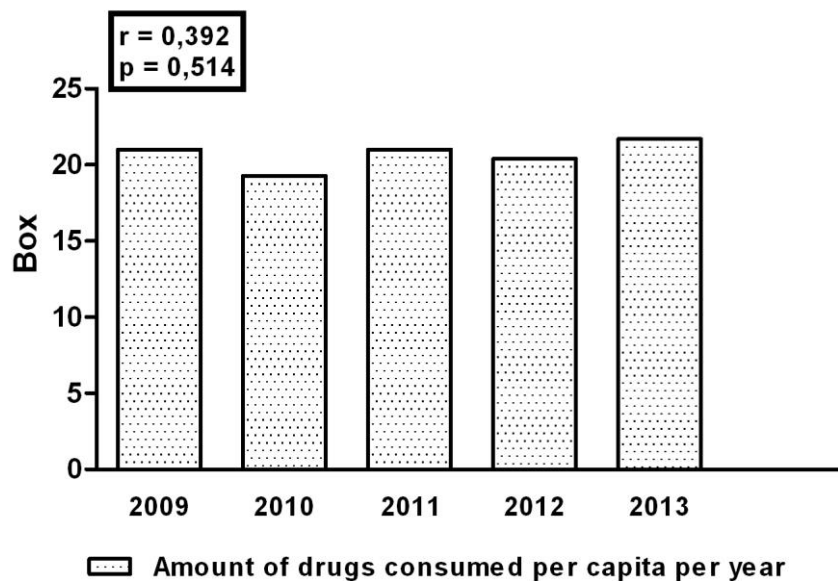


Figure 1. The mainstay of hypertensive individuals in relation to population and the share of antihypertensive drugs in the total drug costs. Statistical results belong to correlations between hypertensive individuals in relation to population and share of antihypertensive drugs in the total drug costs.

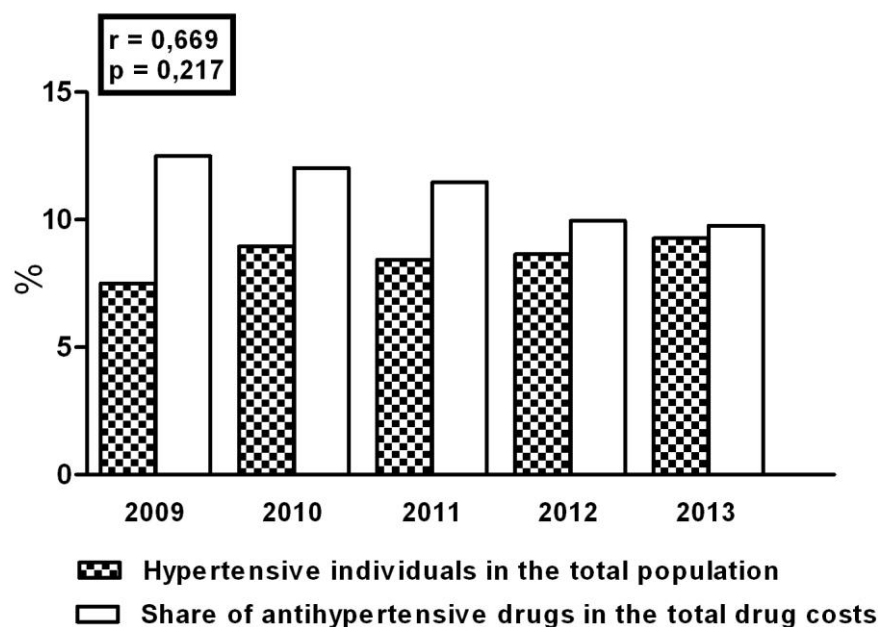


Figure 2. The amount of drugs consumed per capita in Turkey per year. Statistical results belong to correlations between amount of drugs consumed per capita per year and share of antihypertensive drugs in the total drug costs.

The Anatomical Therapeutic Chemical Classification System (ATC) codes published by World Health Organization are enlisted in the Table 2. A significant increase has been noted in the group C02C, C03BA, C03EA, C07AB, C07AG, C07BB, C08CA, C08DA, C08DB, C09DB and C10BX drugs during the study period. While a significant increase occurred in the group C02CA and C09BB drugs, a significant decrease was detected in the group C09AA, C09BA and C09CA drugs. When these results were analyzed with respect to gender-related-differences, the number of women using group C02C drugs was significantly more than the number of men using group C02C drugs. As for 2012 and 2013, the increase in the population of female patients using the group C02CA and C09DA drugs was significantly higher than the increase in the population of male patients using the same drugs. Moreover, the number of male patients using the group C07AB and C09AA drugs was significantly higher than the number of female patients using the same drug groups (Table 4, 5). The cost of anti-hypertensive treatment was found to decrease by 36.7% during the study period (Table 6).

Discussion

Previously conducted local studies in Turkey have pointed out that the prevalence of hypertension is nearly 30%. In contrast, this study yields the prevalence of hypertension as 9.3% for Turkey [5,6]. Such a dramatic difference can be attributed to the size and demographics of the study cohort. Although previous studies have focused on small populations of relatively old individuals, this study reviews all of the adults registered within the database of Turkish Social Insurance Institution. The recruited cohort corresponds to a population of approximately 60 million people which mostly consists of young individuals [8]. Although the large cohort size may provide an advantage, the power of the present study is limited by its retrospective design and the lack of a specially designed and detailed database for hypertension.

Related clinical studies emphasize that hypertension is significantly more prevalent in men than in women worldwide [9]. This result contrasts with the represented findings which imply the significantly higher prevalence of hypertension in Turkish women. This contradiction may be due to the relatively low number of working women and relatively high prevalence of sedentary lifestyle in Turkey. A body of evidence supporting this hypothesis is the

significantly higher frequency of obesity and metabolic syndrome among Turkish women [10,11].

As shown by these results, the prevalence of hypertension in Turkey tends to increase from 2009 to 2013. It can be expected that this increase would end up with a rise in the cost of anti-hypertensive drugs per year. However, the findings demonstrate that the total expense of anti-hypertensive drugs decreases. Such discrepancy may be explained by the government policies for drug pricing in Turkey. Since the initiation of health transformation program in 2007, the drug prices have changed continuously and these changes have caused a significant reduction (nearly 36.7%) in the cost of anti-hypertensive drugs [12,13]. Thus, the decrease in the cost of anti-hypertensive drugs might have exceeded the increase in the prevalence of hypertension.

Despite the increase in the prevalence of hypertension and the number of anti-hypertensive drug boxes prescribed annually, the number of anti-hypertensive drug boxes consumed per person annually remains the same. This may be due to the new products developed by the drug manufacturers against the government policies for drug pricing.

In fact, the pricing of anti-hypertensive drugs depends on many variables including the patent expiration of the drug and the existence of generic drugs [14]. Because of these variables, the prices of group C09CA, C09DA and C09DB drugs are higher than those of group C09AA, C09BA and C09BB drugs. While group C09AA, C09BA and C09BB drugs are preferred more frequently for the treatment of hypertension, group C09CA, C09DA and C09DB groups are prescribed less frequently [15]. The increase in the consumption of group C09BA, C09BB, C09DA, C09DB drugs during the study period implies that the production of combined anti-hypertensive drugs as well as their preparation and prescription in three-month-long packages has become more favorable in Turkey after 2005.

A Turkish study published in 2003 stated that around 9% to 17% of the hypertensive patients were using group C09CA, C09DA and C09DB drugs. On the other hand, 17% to 57% of the hypertensive patients groups used the same drug groups between 2009 and 2013 in Turkey. This evident increase can be attributed to the fact that group C09AA, C09BA and C09BB drugs are more preferable. The reason is that these drugs have more potency, provide symptomatic relief more efficiently, cause less side effects and end up with less severe

resistance [16]. The increase in the consumption of group C07AB drugs may be related with the fact that these drugs cost lower and they can be prescribed for variable indications.

Hypertension can be regarded as an important public health problem for Turkey unless prophylactic measures are put forward in near future. The major reason is that relatively higher prevalence of sedentary lifestyle and obesity persists for all Turkish adults and particularly for women. Although the prices of anti-hypertensive drugs are kept as low as possible, the increase in the prevalence of hypertension may overcome the benefit of this policy for drug pricing. Therefore, it can be concluded that economical measures currently adopted for drug pricing are successful but health policies developed for the prevention of hypertension are inadequate. Further research is warranted to determine the prevalence of hypertension, to clarify the financial burden of anti-hypertensive treatment on national health budget and, thus, to develop more effective and lucrative health policies in near future.

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Conflict of interest

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References

1. Tamosiunas A, Luksiene D, Baceviciene M, Bernotiene G, Radisauskas R, Malinauskiene V, Kranciukaite-Butylkiniene D, Virviciute D, Peasey A, Bobak M. Health Factors and Risk of All-Cause, Cardiovascular, and Coronary Heart Disease Mortality: Findings from the MONICA and HAPIEE Studies in Lithuania. *PLoS One*. 2014;9(12):e114283.

2. De Miguel C, Rudemiller NP, Abais JM, Mattson DL. Inflammation and hypertension: new understandings and potential therapeutic targets. *Curr Hypertens Rep* 2015;17(1):507.
3. Malyszko J, Bachorzewska-Gajewska H, Dobrzycki S. Renalase, kidney and cardiovascular disease: Are they related or just coincidentally associated? *Adv Med Sci.* 2014;60(1):41-9.
4. Hamano T, Kimura Y, Takeda M, Yamasaki M, Isomura M, Nabika T, Shiwaku K. Effect of environmental and lifestyle factors on hypertension: Shimane COHRE study. *PLoS One.* 2012;7(11): e49122.
5. Sengul S, Erdem Y, Akpolat T, Derici U, Sindel S, Karatan O, Turgan C, Hasanoglu E, Caglar S, Erturk S. Controlling hypertension in Turkey: not a hopeless dream. *Kidney Int Suppl.* 2013;3(4):326-31.
6. Altun B, Süleymanlar G, Utaş C, Arınsoy T, Ateş K, Ecder T, Camsarı T, Serdengeçti K. Prevalence, awareness, treatment and control of hypertension in adults with chronic kidney disease in Turkey: results from the CREDIT study. *Kidney Blood Press Res.* 2012;36(1):36-46.
7. Akici A, Kalaça S, Uğurlu U, Toklu HZ, Oktay S. Antihypertensive drug utilization at health centres in a district of Istanbul. *Pharm World Sci.* 2007;29(3):116-21.
8. Tatar M, Mollahaliloğlu S, Sahin B, Aydin S, Maresso A, Hernández-Quevedo C. Turkey. Health system review. *Health Syst Transit.* 2011;13(6):1-186, xiii-xiv.
9. Abramson BL, Melvin RG. Cardiovascular risk in women: focus on hypertension. *Can J Cardiol.* 2014;30(5):553-9.
10. Cengel A. Cardiovascular risk factors in women. *Turk Kardiyol Dern Ars.* 2010;38Suppl 1:17-24.
11. Kitiş Y, Bilgili N, Hisar F, Ayaz S. Frequency and affecting factors of metabolic syndrome in women older than 20 years of age. *Anadolu Kardiyol Derg.* 2010;10(2):111-9.
12. Gür Ali O, Topaler B. How removing prescription drugs from reimbursement lists increases the pharmaceutical expenditures for alternatives. *Eur J Health Econ.* 2011;12(6):553-62.
13. Ide H, Mollahaliloglu S. How firms set prices for medical materials: a multi-country study. *Health Policy.* 2009;92(1):73-8.
14. Kent ST, Shimbo D, Huang L, Diaz KM, Kilgore ML, Oparil S, Muntner P. Antihypertensive medication classes used among medicare beneficiaries initiating treatment in 2007-2010. *PLoS One.* 2014;9(8):e105888.
15. Christe V, Waeber G, Vollenweider P, Marques-Vidal P. Antihypertensive drug treatment changes in the general population: the CoLaus study. *BMC Pharmacol Toxicol.* 2014;15(1):20.
16. Abaci A, Kozan O, Oguz A, Sahin M, Deger N, Senocak H, Toprak N, Sur H, Erol C. Prescribing pattern of antihypertensive drugs in primary care units in Turkey: results from the TURKSAHA study. *Eur J Clin Pharmacol.* 2007;63(4):397-402.