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Received: 18 October 2020 | Accepted: 26 April 2021

DOI: 10.1111/ijcp.14284

ORIGINAL PAPER

Primary Care

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE WILEY

Generic drug prescribing in primary care: A nationwide analysis

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Abstract

Introduction: Dissemination of generic drug (GD) use could provide significant savings on drug expenditures and contribute to the long-term sustainability of healthcare. We aimed to exhibit the nationwide trend of GD use in primary care and investigate potentially relevant drug and patient factors.

Methods: Prescriptions written by primary care physicians in Turkey between 2013 and 2016 were analysed using the National Prescribing Information System. We determined the ratio of GD prescriptions with all prescriptions in terms of quantity and cost. In addition, we analysed the use of GD in terms of demographic characteristics of the patients, the most frequently prescribed preparations and frequent indications.

Results: In the 4-year period, we identified 518,335,821 prescriptions, those with at least one GD constituted 54.0% (n = 786,972,813) with a total cost-share of 36.9%-37.8%. GD use was the highest in 2016 (54.4%) and lowest in 2014 (53.6%). GD prescribing was higher in women than men every year ($P < .001$ for each), with the highest difference in 2016 as 54.7% vs 54.0%. GD utilisation decreased as the age group increased, which was 64.0%-64.5% in <18-year-old group and 46.0%-47.1% in ≥75-year-old group. Among the top ten encountered indications, the highest and lowest GD prescribing was detected in acute tonsillitis (68.1%) and hypertension (33.9%). Metformin had the highest percentage of GD prescribing (96.1%-97.7%), whereas esomeprazole showed the lowest GD prescribing (4.5%-14.8%) among the most frequently used preparations in primary care.

Conclusion: This study shows a modest upward trend of GD utilisation in primary care, though its share appears to be lower than expected. GD use revealed a consistent reduction towards older age groups. GDs were more likely to be prescribed for acute conditions, particularly infectious diseases.

1 | INTRODUCTION

The generic drug (GD) contains the active substance(s) with the same qualitative and quantitative composition as the reference drug and has the same/similar pharmaceutical form. For market approval, a candidate GD only requires demonstration of bioequivalence to the reference drug after patent expiration. No repetition of preclinical and clinical phase trials usually allows for cheaper pricing with the same therapeutic effect.[1] In fact, the price of GDs is reported as 20%-90% less than that of the reference drugs before the patent expires.[2] Therefore, disseminating GD use has been accepted as an effective approach to control increasing drug expenditures.[3] Furthermore, this provides significant savings on healthcare costs and contributes to the long-term sustainability of healthcare.[1,4]

It has been consistently shown that the effectiveness and safety of drugs do not differ between generic and reference preparations.[5-8] Despite a huge evidence base, physicians, other healthcare professionals and patients were often reported to have various

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concerns regarding the quality, efficacy and safety of GDs as well as negative attitudes towards their use.[9-12] In fact, GD use is affected by many further factors, including demographic and clinical features of patients, variety of alternative options of drugs available for a given indication, prescribing with brand/generic name and pharmacological properties of the drug, etc.[13-21]

Primary care prescriptions provide important insights about pharmacotherapy-focused subjects such as the drug utilisation pattern of the majority of the population, overall clinical features and preferences of patients and the prescribing behaviours of physicians. Primary care physicians exercise a fairly large volume of prescribing practice by initiating both the treatments of newly diagnosed patients and maintaining of those with chronic diseases. Therefore, the generic or reference status of the drugs prescribed in primary care can provide important information about GD utilisation patterns across the country. Apart from revealing the physician's behaviour in primary care, such findings will also lay the ground for the possible development areas in pharmacotherapy to make GD use more rational. In this study, we aimed to exhibit the nationwide trend of GD use in primary care and investigate potentially relevant drug and patient factors.

What's known

- Generic drugs have generally lower costs than reference drugs and provide significant savings on healthcare costs.
- Generic drug utilisation varies widely between countries and which is affected by many factors, including demographic and clinical features of patients.

What's new

- In Turkey, generic drugs had a share of 54% in quantity and 37% in cost.
- Generic drug prescribing was decreased as the age group increased, which was lowest in the ≥75-year-old group.
- Generic drugs seem to be more pronounced in acute conditions, particularly infectious diseases.

Clinical significance

- The findings in our study emphasise that one of the prioritised addresses of activities to promote generic drug use is primary care physicians.

2 | MATERIALS AND METHODS

In this cross-sectional study, all electronic prescriptions written by primary care physicians in Turkey between 1 January 2013 and 31 December 2016 were analysed retrospectively. These prescription records were anonymised and obtained via Prescription Information System (PIS) managed by Turkish Medicines and Medical Devices Agency. This study was approved by the Ethics Committee for Non-interventional Studies of Dokuz Eylul University (Approval No: 2019/05-32) and carried out in accordance with the principles in the Helsinki Declaration.

Drug-related data collected from prescriptions included Anatomical Therapeutic Classification (ATC) code, generic/reference drug status, route of administration (injectable/non-injectable), origin (domestic manufactured/imported), number of generic/reference drugs. Patient-related data included gender, age groups ("<18 years," "18-44 years," "45-64 years," "65-74 years" and "≥75 years"), and ICD-10 (International Classification of Diseases-10) diagnostic codes. The percentage of GDs relative to all drugs in these prescriptions was calculated for all patients and also for these subgroups. In addition, the mean number of drugs per prescription (NDPP) for generic and reference drugs was determined.

The most frequently prescribed 20 active ingredients by year were listed and the number/percentages of the GDs were calculated. In addition, the number of references and generic preparations for each of them commercially available in the market for the corresponding year was determined. As the number of generic brands may influence GD prescribing behaviours of the physicians, we tested if any correlation existed between the generic/total brand ratio and GD prescribing for the year 2013-2016.

GD use was also determined in active ingredient groups with varying frequency of prescription: the most frequently prescribed preparations ranked as "1-10," "51-60," "101-110," "251-260" and "501-510" were identified for the total study period and the number and rate of GDs prescribed specifically for each of these groups were examined.

The most frequently used drugs for specific indications were also identified to determine particular GD prescribing rates. This analysis was performed with single-diagnosis prescriptions (282,398,506), which constituted 54.5% of prescriptions, to make possible association of the drug(s) with the particular indications. The top 10 frequent diagnoses in these single-diagnosis prescriptions were determined according to ICD-10 codes and GD use in these diagnoses was examined. In addition, prescriptions with certain other remarkable diagnoses [acute nasopharyngitis (J00), acute sinusitis (J01), depression (F32-F33), low back pain (M54.5), asthma (J45-J46), dyspepsia (K30), acute cystitis (N30.0), osteoarthritis (M15-M19) and type 2 diabetes (E11-E14)] were further analysed to determine GD number/percentages of 30 most commonly prescribed active ingredients for each indication.

In cost-related analyses, the prices of generic and reference drugs were converted into Euro (€) currency. The PIS from which we acquired drug prices and made calculations was initialized to operate in 2010. The prices of drugs introduced to the market until this year were standardised at the currency of 2010. For the drugs that were

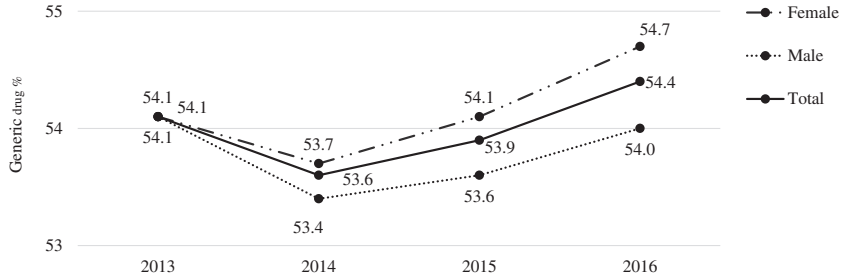


FIGURE 1 Generic drug use by gender in prescriptions written between 2013 and 2016

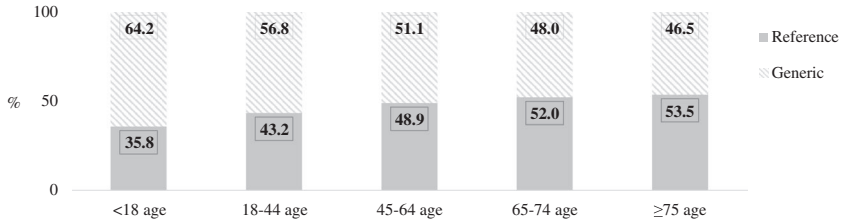


FIGURE 2 Generic drug use by age groups in the total of 4 years covering 2013-2016

licenced within the study period, standardisation was made at the retail prices when they were first released. The mean cost of GDs in the prescriptions containing at least one GD was examined.

2.1 | Statistical analysis

Statistical analyses were performed with GraphPad Prism 5.0 programme. In this descriptive study, the data were expressed as numbers and percentages for categorical variables and as mean and standard deviation for continuous variables. Chi-square test and *t* test were used to compare categorical and continuous variables of the groups, respectively. Correlation analyses were performed with SPSS 25.0 software. An overall type 1 error level of 5% was used to infer statistical significance.

3 | RESULTS

During the 4-year period (covering 2013-2016), we identified 518.3 million prescriptions, those with at least one GD constituted 54.0% (n = 786,972,813). The frequency of GD prescriptions has been found to increase each year, from 53.6% in 2014 to 54.4% in 2016. The annual mean "NDPP" for GDs ranged from 1.51 ± 1.17 to 1.53 ± 1.16 (Supplement S1).

In total, GDs constituted 54.2% and 53.8% of all drugs in the prescriptions generated for women and men, respectively. GD prescribing was significantly higher in women than men every year, with the highest difference in 2016 as 54.7% vs. 54.0% ($P < .001$), (Figure 1). The frequency of GD prescribing declined as the age group increased, from 64.2% in <18-year-old population to 46.5% in ≥75-year-old population ($P < .001$, Figure 2; see Supplement S1 for each year).

The frequency of GD prescribing was also more than half for injectable drugs (53.1%-56.2%) (Supplement S2). During the study period, 97.7%-97.9% of GDs were found to be domestically manufactured.

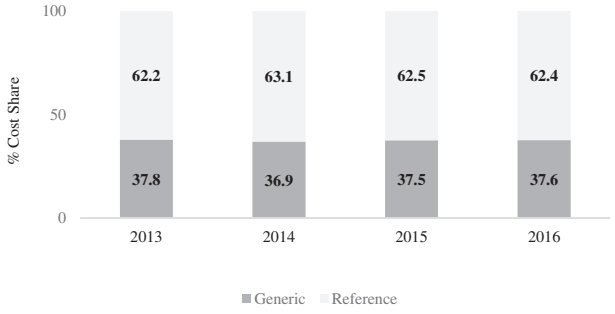


FIGURE 3 The distribution of the cost shares of generic and reference drugs in prescriptions written between 2013 and 2016

The total cost of the drugs prescribed in primary care for 4 years was €24.08 billion. GDs accounted for 37.4% of the total cost (Figure 3). The mean annual cost of all drugs was €6.02 billion (range: €4.81-€6.71 billion), and GDs costed an average of €2.25 billion (range: €1.82-€2.53 billion). Prescriptions containing at least one GD constituted 80.0% of all prescriptions (Supplement S3).

Among the most frequently prescribed preparations with at least one generic and reference brand commercially available in the market, metformin had the highest (96.1%-97.7%) and esomeprazole had the lowest (4.5%-14.8%) GD prescription rate (Table 1). For these top 20 preparations, we detected no significant correlation between generic/total brand ratio and GD prescribing for any of the years (*r*: .448, 0.507, .458, .490 between 2013 and 2016, respectively; $P > .05$). The share of GDs was 71.0% for the group of top 10 frequently prescribed active ingredients and it showed a consistent decline as long as the frequency of prescription decreases (Figure 4).

In the top 10 most frequently encountered diagnoses, GD prescribing was higher in all indications (highest in acute tonsillitis as 68.1%) except "essential hypertension" (33.9%) and "general medical examination" (48.1%) (Table 2). For specific indications, GD

TABLE 1 The reference and generic status parameters of the top 20 prescribed preparations by years

	Years															
	2013				2014				2015				2016			
		Drug Product				Drug Product				Drug Product				Drug Product		
Drug (ATC)	Rank	R	G	Generic Drug n (%)	Rank	R	G	Generic Drug n (%)	Rank	R	G	Generic Drug n (%)	Rank	R	G	Generic Drug n (%)
Other cold preparations (R05X)	1	15	83	15.565.669 (67.2)	1	13	57	19.526.820 (70.5)	1	13	60	18.760.031 (71.2)	1	13	61	19.849.375 (73.5)
Amoxicillin and enzyme inhibitor (J01CR02)	2	11	58	7.517.282 (61.5)	2	11	48	8.112.548 (59.2)	2	11	49	8.110.196 (61.6)	2	10	47	8.163.799 (59.9)
Diclofenac (M01AB05)	3	11	32	7.509.905 (77.6)	3	11	18	9.086.150 (78.1)	3	11	20	8.632.458 (79.4)	4	11	19	8.927.577 (80.8)
Paracetamol (N02BE01)	4	4	60	6.841.644 (71.6)	4	4	32	8.059.438 (72.1)	4	4	28	7.621.211 (71.6)	3	5	23	7.982.833 (69.6)
Lansoprazole (A02BC03)	5	0	34	5.897.327 (100.0)	5	0	35	6.395.227 (100.0)	7	0	33	5.469.175 (100.0)	9	0	30	5.227.879 (100.0)
Acetylcysteine (R05CB01)	6	1	68	5.603.983 (99.7)	7	1	46	5.836.349 (99.8)		1	48	5.241.551 (100.0)	13	0	49	4.897.917 (100.0)
Dexketoprofen (M01AE17)	7	10	28	1.486.414 (27.6)	6	3	21	1.655.758 (27.2)	8	3	27	1.485.790 (27.3)	7	3	24	1.630.743 (29.1)
Ibuprofen (M01AE01)	8	7	31	4.215.142 (81.0)	9	6	12	4.559.475 (82.2)	6	7	12	4.581.494 (83.2)	6	5	16	4.657.838 (81.3)
Thiocolchicoside (M03BX05)	9	5	36	3.605.828 (71.9)	12	5	36	3.781.007 (72.6)	14	5	41	2.922.471 (72.0)	22	5	47	2.310.514 (75.2)
Acetylsalicylic acid (B01AC06)	10	3	10	1.548.558 (33.2)	8	3	6	1.900.931 (32.6)	5	3	6	1.971.689 (33.0)	5	3	5	2.208.209 (33.9)
Various (A01AD11)	11	2	22	4.477.986 (96.3)	10	2	27	5.292.063 (96.6)	11	2	26	4.878.681 (96.6)	8	2	31	5.158.869 (96.9)
Pantoprazole (A02BC02)	12	4	39	3.852.831 (86.6)	11	3	33	4.684.323 (85.7)	10	3	35	4.317.311 (85.4)	10	3	36	4.409.309 (84.4)
Paracetamol comb.[a] (N02BE51)	13	6	32	2.293.341 (54.8)	17	6	18	2.448.175 (55.8)	16	6	20	2.177.287 (57.0)	18	7	22	2.181.316 (60.0)
Flurbiprofen (M01AE09)	14	1	25	4.140.981 (99.9)	14	0	16	4.516.491 (100.0)	20	0	16	3.519.696 (100.0)	21	0	16	3.003.166 (100.0)
Etodolac (M01AB08)	15	1	30	3.492.369 (89.2)	18	1	19	3.835.216 (89.4)	19	1	19	3.147.357 (89.3)	20	1	20	2.684.207 (88.3)
Vitamin B1 comb.[b] (A11DB)	16	4	27	1.424.961 (36.7)	16	4	13	1.598.301 (35.9)	15	4	12	1.464.248 (36.3)	14	3	10	1.460.020 (35.6)
Butamirate (R05DB13)	17	4	12	2.557.566 (69.7)	15	4	10	3.216.081 (71.7)	13	4	16	3.453.846 (75.6)	12	5	16	4.062.028 (82.8)
Cefuroxime (J01DC02)	18	12	78	2.763.598 (80.2)	22	9	43	2.833.598 (78.2)	25	9	44	2.298.625 (80.2)	32	9	44	1.985.362 (81,8)
Metformin (A10BA02)	19	3	23	3.264.065 (97.7)	13	2	17	4.432.090 (96.8)	12	2	20	4.502.473 (96.8)	11	2	21	4.904.285 (96.1)
Naproxen (M01AE02)	20	8	39	455.258 (14.4)	23	8	21	457.006 (12.9)	23	8	19	380.144 (12.6)	26	8	16	325.969 (11.9)
Metoprolol (C07AB02)	23	7	9	428.243 (14.9)	19	7	8	674.663 (18.1)	17	7	7	826.223 (21.8)	15	7	12	993.684 (24.4)
Imidazoles/triazoles in comb. with corticosteroids (D01AC20)	22	1	5	2.179.289 (73.1)	20	2	6	2.726.081 (75.4)	21	1	7	2.663.450 (77.1)	17	1	9	2.920.864 (79.6)
Esomeprazole (A02BC05)	24	6	8	128.148 (4.5)	21	5	4	350.735 (9.7)	18	5	9	526.662 (14.7)	16	5	11	542.654 (14.8)

(Continues)

TABLE 1 (Continued)

Drug (ATC)	2013 Rank	2013 Drug Product R	2013 Drug Product G	2013 Generic Drug n (%)	2014 Rank	2014 Drug Product R	2014 Drug Product G	2014 Generic Drug n (%)	2015 Rank	2015 Drug Product R	2015 Drug Product G	2015 Generic Drug n (%)	2016 Rank	2016 Drug Product R	2016 Drug Product G	2016 Generic Drug n (%)
Oxymetazoline (R01AA05)	27	3	5	907.817 (38.0)	26	3	2	1.073.447 (36.9)	24	3	2	961.685 (33.1)	19	3	3	1.048.967 (32.6)
First 20 Drug Generic Subtotal				88.514.708 (70.7)				102.337.187 (71.0)				93.609.850 (69.8)				93.912.373 (68.5)
Other Generic Drugs				89.795.204 (43.9)				105.706.142 (43.3)				103.423.349 (44.7)				109.674.000 (46.3)
Total Generic Drug				178.309.912 (54.1)				208.043.329 (53.6)				197.033.199 (53.9)				203.586.373 (54.4)

Abbreviations: comb, combination; G, generic drug; R, reference drug.

[a]Except psycholeptics.

[b]Combinations with vitamins B6 and B12.

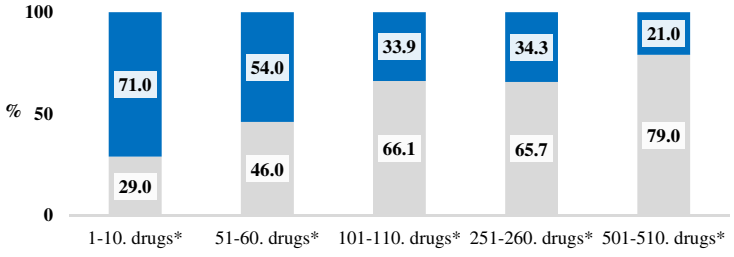
prescribing was higher in infectious (63.8%-65.3%) and several non-infectious diseases (low back pain, osteoarthritis and type 2 diabetes) but lower in depression (41.4%), asthma (42.2%) and dyspepsia (44.7%) (Figure 5).

4 | DISCUSSION

We examined >500 million primary care prescriptions, where GDs had a share of 54% in quantity and 37% in cost. Although this could be lower than expected, it is notable that GD prescribing exhibits a modest upward trend. Another remarkable finding of the study was the higher predominance of GD prescriptions in commonly encountered acute conditions particularly infectious diseases. Nevertheless, the frequency of GD prescribing decreased with age, which might be related to the higher rate of chronic diseases in advanced age groups and observed preference of reference drugs in chronic diseases, including hypertension, asthma and depression.

GD utilisation varies among countries, especially with the effect of different government policies. The share of GDs ranges from 17% to 83% across Europe, 84% in the USA, 68.6% in Canada and 56.2% in Japan.[22,23] This sales volume was reported to vary between 53.6% and 56.6% in Turkey with an increasing trend but still behind that of many OECD countries.[24,25] This increasing trend across the country seems to be compatible with GD use in primary care in our study. However, the fact that 20% of the prescriptions in our study did not contain GDs indicates the need for investigating underlying causes as this modest increase appears to be not sufficient and should be improved. Spreading GD use is an important strategic step in reducing health expenditures. In Europe, policies were developed between 2008 and 2015 where increasing GD use was aimed to decrease drug expenditures by making it compulsory to prescribe drugs with active substance names in many countries such as Belgium, Greece and Spain.[22,26] In a circular issued by the Turkish Ministry of Health in 2009 and re-addressed afterwards if required, it was emphasised that it is not scientifically and legally valid for physicians to write on prescriptions that pharmacists should not substitute reference drugs with GDs.[27] This situation indicates somehow an unsatisfactory level of physicians' adoption for GD prescribing and may have contributed to the limited increase we observed in the study period. On the other hand, the dissemination and promotion of GD use has been incorporated in the year 2018-2022 Action Plan of the health authority regarding rational use of medicines.[28] In this context, our findings might serve as a baseline for further studies that would examine the impact of this intervention.

Among potential patient factors effective on GD use, we did not observe a profound impact of gender—although mildly higher in women—whereas age appears as an important parameter affecting GD use. Although GDs constituted near two-thirds of all drugs in children in our study, we observed that this trend decreased as the age got older and reference drugs became predominant over the age of 65 years. Higher use of GDs in younger patients might be



	1-10. drugs*	51-60. drugs*	101-110. drugs*	251-260. drugs*	501-510. drugs*
Generic Drug n	266.545.984	28.669.459	10.810.196	3.672.965	370.265
Reference Drug n	109.032.856	24.403.473	21.113.139	7.028.692	1.394.839

FIGURE 4 The distribution of the drugs encountered in certain frequent-prescribing ranks by their reference and generic drug status during the study period. *The most frequently prescribed preparations in Turkey between 2013 and 2016

partially associated with their clinical conditions for which the drugs are indicated, for example relative dominance of infectious diseases in younger individuals.[29] In fact, the GD prescribing (63%-68%) detected in acute diagnoses in our study was in parallel with the higher rate of generics of antibiotics prescribed in infectious diseases. It was reported that 66.5% of prescribed antibiotics for acute infections in primary care in Turkey were GDs and its use was highest (66%) in acute pharyngitis.[30] Similarly, in our study, GDs formed 66% of all drugs in this indication. On the other hand, it has been shown in several studies that there is a prejudgement towards GDs in the elderly patient group, for whom we found low use of GDs.[20,31,32] This may have affected the prescribing behaviour of physicians.[33] In addition, the difference in GD prescribing behaviour in chronic diseases that increase with age in our study may partially explain the consistent decreasing trend related to age. It was reported that the use of GDs in patients with multiple chronic diseases was lower than those without, and patients with chronic diseases may have a negative attitude towards GDs.[34-36] Furthermore, such unfavourable attitudes were reported to affect physicians' prescribing with a tendency to reference drugs increased with comorbidity and older age.[37] Consistently, up to 79% of physicians were reported to prefer reference drugs for their patients with some medical conditions including cardiovascular diseases.[38] This was further supported by the lower GD use in chronic conditions in our study, including hypertension (34%), depression (41%) and asthma (42%). In particular, GD use was reported to vary 35%-45% in hypertension, making the performance of our physicians lower than expected.[39,40] This might be partly explained by the fact that about 80% of metoprolol, the only antihypertensive agent among the top used agents, was prescribed as generic in our study. Given the increase in chronic care expenditures, it seems crucial GD use be encouraged in chronic diseases that increase with age in reducing drug-related costs.[41,42] In fact, using GDs in the treatment of CVDs and diabetes has been reported to reduce healthcare expenditures.[42,43] Considering the raising share of chronic disease management in primary care, the findings in our study emphasise that one of the prioritised addresses of activities to promote GD use is primary care physicians.

GDs have generally lower costs than reference drugs. The average price of a reference drug in Turkey was reported to be >3-fold of that for GDs.[44] In our study, GDs constituting 54% of the drugs had a 37% share in the cost. In 2017, the average GD sales volume of 26 OECD member countries was reported to be 52% and its share was 25%.[25] On the other hand, this rate is higher in the USA, and it is reported that generics, which make up 89% of the drugs prescribed in 2016, constitute 26% of the total prescription cost.[45] In this context, our findings on GD use might be suggested as partially satisfactory in primary care. Efforts to encourage and increase GD use reported that drug expenditures were reduced by 61% in the European Union countries with a saving of approximately €100 billion in 2014.[4] This tends to justify enhancement of GD-focused interventions in primary care for a sustainable healthcare service.

Generic market competition is an expected phenomenon in frequently used drug groups. In fact, we observed about 70% share of GDs for the top 20 most frequently prescribed preparations. This value fell below the country average after the first 60 drugs that were most often prescribed, leaving the reference drugs as predominant afterwards. On the other hand, we detected no association between drug's generic brand availability and GD prescribing percentage for the commonly used preparations. This does not seem to confound our findings regarding the impact of age and clinical indication on GD use.

GD use by pharmaceutical forms showed a similar pattern as overall findings in our study, with a very modestly higher use for injectable drugs although with a fluctuating course. While we may suggest that pharmaceutical form does not appear to affect GD use, this needs to be further investigated by qualitative and/or quantitative studies focused on the various forms of the drugs. On the other hand, we observed 98% of GDs to be domestic manufactured in primary care. This was consistent with the previous reports of the overall domestic share of GDs in the country, which may be attributed to the accredited authorised role of the health authority in monitoring and auditing Good Manufacturing Practices internationally.[46]

The percentage of prescribing drugs with their generic name in prescriptions is one of the indicators of rational drug use and increase use of GDs.[47] This practice is exercised in many countries with different strategies. A USA study reported that prioritisation of generic brands during browsing of physicians for drugs in electronic prescribing increased GD share in prescriptions.[48] In addition, this was reported to be further contributed by prescribing with generic names rather than brands.[49]

In this study, GD prescribing patterns of physicians were evaluated. Therefore, the main limitation of this study could be its

TABLE 2 Generic drug use for the top 10 diagnoses encountered in the single-diagnosis prescriptions of the primary care by years

	Year									
	2013		2014		2015		2016		2013-2016	
Diagnosis (ICD-10)	Diagnosis rank	Generic Drug&&&n (%)	Diagnosis rank	Generic Drug&&&n (%)	Diagnosis rank	Generic Drug&&&n (%)	Diagnosis rank	Generic Drug&&&n (%)	Diagnosis rank	Generic Drug&&&n (%)
Acute upper respiratory infection, unspecified (J06.9)	1	6.337.676 (66.3)	2	8.252.215 (66.3)	2	8.051.440 (66.5)	2	8.984.725 (66.9)	2	31.626.056 (66.5)
Acute pharyngitis, unspecified (J02.9)	2	6.208.331 (66.1)	3	7.168.137 (66.5)	3	6.196.689 (66.6)	3	6.031.152 (67.3)	3	25.604.309 (66.6)
Essential hypertension (I10)	3	1.641.225 (29.7)	1	4.073.153 (34.5)	1	3.410.942 (34.0)	1	3.982.946 (35.4)	1	13.108.266 (33.9)
Acute pharyngitis (J02)	4	5.050.367 (66.7)	4	6.331.463 (66.0)	4	5.681.361 (66.3)	5	5.578.262 (66.6)	4	22.641.453 (66.4)
Acute nasopharyngitis [common cold],(J00)	5	3.349.883 (62.4)	5	4.870.798 (62.6)	5	4.390.208 (62.9)	4	4.796.548 (63.9)	5	17.407.437 (63.0)
Acute tonsillitis, unspecified (J03.9)	6	3.725.542 (68.2)	7	4.104.348 (67.9)	7	3.463.976 (68.2)	7	3.534.191 (68.1)	6	14.828.057 (68.1)
Acute tonsillitis (J03)	7	3.469.839 (68.5)	6	4.205.965 (67.4)	6	3.560.292 (68.2)	6	3.590.625 (67.8)	7	14.826.721 (67.9)
Other general examination (Z00.8)	8	1.318.849 (58.8)	(30)	—	(57)	—	(42)	—	(23)	—
Gastroesophageal reflux disease (K21)	9	967.947 (52.0)	9	2.250.306 (52.1)	9	1.744.080 (53.2)	9	1.917.917 (53.6)	9	6.880.250 (52.8)
Gastroesophageal reflux disease without esophagitis (K21.9)	10	820.473 (53.6)	(11)	—	(12)	—	(13)	—	(11)	—
Myalgia (M79.1)	(11)	—	8	2.728.833 (55.7)	8	2.183.127 (56.5)	8	2.421.565 (57.1)	8	8.594.638 (56.9)
General medical examination (Z00.0)	(15)	—	10	2.207.764 (47.5)	10	1.679.682 (47.9)	10	1.901.511 (48.6)	10	6.742.985 (48.1)
First 10 Diagnosis Total[a]		32.890.132 (61.4)		46.192.982 (58.8)		40.361.797 (59.4)		42.739.442 (59.6)		162.260.172 (59.6)

Abbreviation: ICD, International Classification of Diseases.

[a]Drugs related to the diagnoses that are not included in the top 10 diagnoses in the diagnosis order, though given in the table, were not included in the total.

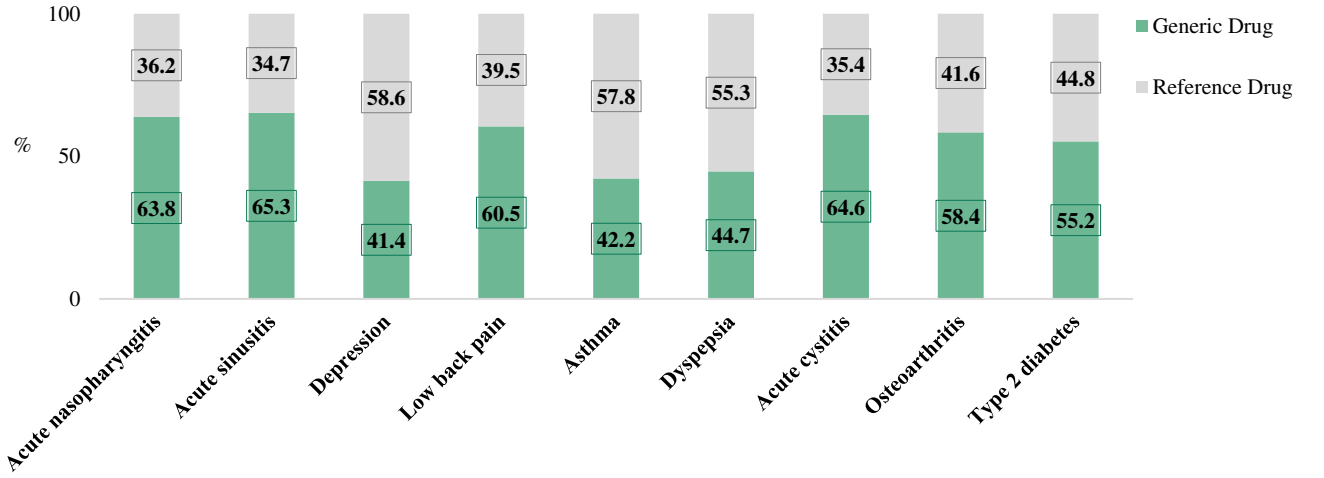


FIGURE 5 The reference and generic status of the top 30 frequently prescribed preparations for selected indications

retrospective design because we could not assess the actual utilisation of the generic or reference drug by patients, including the conditions and changes during its dispending at the pharmacy or reimbursement level. In this descriptive study, the relationship between diagnosis and treatment was not established and drug/diagnosis details were not evaluated by their demographic groups. In addition, for minimising confounding indications, prescriptions with multiple diagnoses were not assessed for indication-oriented GD use, which can be considered as another limitation of this study. Finally, the cost analyses of the study should be interpreted considering that the currency conversion of Turkish Lira to Euro was not performed on actual time, rather on a standardised year.

In conclusion, the extent of GD utilisation in primary care facilities in Turkey has been presented for the first time with a holistic perspective and with the trend of change over the years. This study shows a modest upward trend of GD utilisation in primary care, though its share appears as lower than expected. GDs were less likely to be prescribed in older age groups. This may be related to the fact that chronic conditions increase with age and physicians tend to prefer to prescribe reference drugs in chronic diseases. Primary care physicians are typically more likely to provide health care for patients of all ages, a larger population and diversity than other physicians in a given time period. Therefore, the contribution of primary care physicians to the efforts that aim to increase GD use will be considerably significant. This will also help to enhance drug-based cost savings in a major component of the healthcare system. The striking points obtained from this research not only introduce a perspective on GD use in primary care but also give important clues in critical aspects for the dissemination of GD use.

ACKNOWLEDGEMENTS

The authors thank Dr. Fatma Isli, Esma Kadi and other related staff of the Turkish Medicines and Medical Devices Agency for their contribution to the provision of data and to the study. Link to preprinted version on Authorea: https://doi.org/10.22541/au.160133555.55250410.

DISCLOSURE

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the Supporting Information section.

How to cite this article: Bayram D, Aydin V, Gelal A, Aksoy M, Akici A. Generic drug prescribing in primary care: A nationwide analysis. *Int J Clin Pract*. 2021;75:e14284. https://doi.org/10.1111/ijcp.14284