Drug utilization studies in Turkiye: A systematic review

Ahmet Akici,[1] Dieudonné Havyarimana,[1] Ertan Direnc,[2] Volkan Aydin[3]

[1]Department of Medical Pharmacology, Marmara University Faculty of Medicine, Istanbul, Turkiye

[2]Marmara University Faculty of Medicine, Istanbul, Turkiye

[3]Department of Medical Pharmacology, Istanbul Medipol University International Faculty of Medicine, Istanbul, Turkiye

ABSTRACT

OBJECTIVE: Drug utilization studies (DUS) provide a framework for drug utilization at the national or targeted population level and important information on unmet medical needs, particularly in assessing the rationality of drug use. We aimed to systematically review DUS conducted in Turkiye.

METHODS: We examined 162 DUS with an accessible full-text, published as "research articles" and conducted in Turkiye between 2000 and 2021 using medical records and prescription data. We included English or Turkish papers with English abstracts. We examined the scientific characteristics of the publications, source of the data, place/time of collection, research designs, and studied drug groups.

RESULTS: We found that 79.6% of articles were in English, 45.1% were listed in SCI/SCIE, and 63.0% were on the WOS platform with 3.5 (interquartile range: 1–15) citations. The mean study period and publication time were 2.9±3.1 and 2.9±2.1 years, respectively. The highest number of studies (17.9%) were published in 2021 and (26.5%) were conducted nationwide. We identified that 93.8% of the studies had retrospective design, 67.8% were conducted in secondary/tertiary health-care institutions, and 54.9% used direct hospital data. We detected that 68.5% of the studies were conducted on the general population, 19.1% on adults, 12.4% on children, and 44.4% were antibiotic oriented.

CONCLUSION: Our study showed that a significant portion of the DUS, the trend of which has gained momentum in recent years, was antibiotic focused and conducted with a retrospective design from hospital-based data collected on the general patient population. This situation points to the necessity of expanding the existing DUS range by effectively using the new advantages provided by medical record databases and conducting more DUS that can provide critical clues for specific patients and drug groups.

Keywords: Drug utilization studies; pharmacoepidemiology; research; systematic review.

Drug utilization research is defined as "an eclectic scientific discipline, integrating descriptive and analytical methods for the quantification, understanding, and evaluation of the processes of prescribing, dispensing, and consumption of medicines and for the testing of interventions to enhance the quality of these processes" began in the 1960s throughout the world [1]. Previously, drug utilization studies (DUS) were conducted to assess pharmaceutical companies' targets and investigate differences in drug usage between countries and regions. In time, DUS have started to focus on physicians' prescribing habits and factors influencing them besides evaluating the rationality of their prescriptions [1, 2]. Medicines, despite being a vital tool in modern medicine for disease prevention and treatment, can be harmful to human and public health if not used correctly. DUS can provide important infor-

mation about its cost and effects from an economic and pharmacological perspective, respectively. Such studies have been shown to, directly and indirectly, contribute to the acquisition of information about morbidity, the relationship between treatment and cost, drug effectiveness, therapeutic compliance, the incidence of adverse reactions, and so on [3]. DUS helped to discover differences in the effects and morbidity of drug use between or within countries. The results of these studies have expanded the DUS framework to include social and economic parameters from a public health standpoint. Therefore, it is believed that improving DUS by analyzing them at national and international levels is a high priority today [4].

As DUS have increased, it has been shown that researchers and decision-makers need to collaborate to establish national data collection systems to accurately identify and manage drug consumption in the country [5]. The excessive and irrational use of antibiotics has garnered attention in recent years, and antibiotics have been the focus of many pharmacoepidemiological studies in Turkiye to improve their rational use [6–9]. There has been no systematic review examining the current state of DUS, a subgroup whose spectrum is broad in terms of method and scope, in pharmacoepidemiological studies, the history of which is largely based on the last 20 years in our country [10]. In this study, we aimed to systematically examine DUS published in Turkiye.

MATERIALS AND METHODS

We examined 162 available DUS conducted with medical records and prescriptions in Turkiye between 2000 and 2021 and published as a "research publication" in this systematic review. The data were collected following the approval of the Ethics Committee of Marmara University Institute of Health Sciences, numbered 21.02.2022-25. We analyzed parameters related to age groups, special patient groups, basic drug groups, study designs, place and time of data collection, and quality of the journals, in which the articles were published. During data collection, we followed the current PRISMA checklist and flowchart [11].

Studies published between January 2000 and December 2021 were found by keyword searches on Internet between March 01, 2022, and April 01, 2022, in line with the objective of the study. The keywords were chosen by prioritizing terms that are often used universally for DUS and words related to the most commonly taken medications in Turkiye [12, 13]. These words are listed below in detail, and they were searched through PubMed,

Highlight key points

- Near half of the Turkish drug utilization studies focused on antibiotics.
- The vast majority (93.8%) of the studies were conducted via a retrospective design.
- The mean time to publish was almost 3 years.
- The target group was general population in about two-thirds of the studies.

ScienceDirect, Google Scholar, and National Academic Network and Information Center search engines in both Turkish and English languages. We included all full-text English papers or Turkish papers with an abstract written in English language. "Address-Based Population Registration System 2021 Data" was used in the sections that required population information [14].

We performed the search with the following keywords: Prescription, prescribing, pharmacoepidemiology, rational use of drugs, irrational use of drugs, rational use of medicines, irrational use of medicines, drug utilization, pharmacotherapy, inappropriate use of drugs, inappropriate use of medicines, medication, appropriate medication, inappropriate medication, appropriate prescribing, inappropriate prescribing, drug therapy, drug use, drug usage, antibiotic consumption, antibiotic utilization, antibiotic usage, analgesics, antibiotics, anti-inflammatories, antithrombotics, antihypertensives, vitamins, proton pump inhibitors, thyroid hormones, antiallergics, bronchodilators, antidiabetics, antifungals, mucolytics, antidepressants, corticosteroids, cold preparations, antiemetics, diuretics, iron preparations, muscle relaxants, antiepileptics, alpha-blockers, and statins. Based on the drug studied, we analyzed and compared articles divided into two categories: "Antibiotic-oriented studies" (AOS) and "other non-antibiotic-oriented studies" (NOS).

Statistical Analysis

Quantitative data were analyzed using Microsoft Excel 2021 for Windows (Microsoft Corp., Redmond, WA, USA) and IBM SPSS Statistics for Windows 22.0 (IBM Corp., Armonk, NY, USA) software programs. The data were expressed as numbers and percentages for categorical variables, and mean±standard deviation or median and interquartile range (IQR) for continuous variables. In comparisons, we used the Chi-square test for categorical variables and the t-test for continuous variables. An overall Type-1 error level of 5% was used to infer statistical significance.

Characteristics	All studies (n=162)	AOS (n=72)	NOS (n=90)
Publications in English, n (%)	129 (79.6)	55 (76.4)	74 (82.2)
Number of authors, median (IQR)	6 (4–7)	6 (4–7)	5 (4–7)
Pharmacology affiliation, n (%)	52 (32.1)	14 (19.4)	38 (42.2)[δ]
Open access, n (%)	125 (77.2)	61 (84.7)	64 (71.1)*
Presence of sponsorship, n (%)	11 (6.8)	3 (4.2)	8 (8.9)
Scanning on SCI/SCIE, n (%)	73 (45.1)	34 (47.2)	39 (43.3)
WOS citation, n (%)	81 (50.0)	39 (54.1)	42 (46.7)
WOS number of citations, median (IQR)	3.5 (1–15.0)	5 (1–17.3)	3 (0.3–11.0)

AOS: Antibiotic-oriented studies; NOS: Other non-antibiotic-oriented studies; IQR: Interquartile range; SCI/SCIE: Science Citation Index(/Expanded); WOS: Web of Science database catalog; δ: p=0.002; *: p=0.04.

RESULTS

Out of 162 articles analyzed, we found that 79.6% were written in English, 77.2% had open-access, 45.1% were published in journals indexed in SCI/SCIE, 63.0% were registered on the WOS platform and received a median of 3.5 (IQR: 1–15) citations. A median of six (IQR: 4–7) authors contributed to the articles, 32.1% of which were affiliated with pharmacology. There was no sponsorship in 32.7% of the studies whereas no disclosure was made about whether or not there was a fund in 60.5%. We determined that 44.4% of all studies were in the AOS group. In the remaining NOS group, 34.4% covered all drugs in general, 12.2% focused on analgesics, and 6.6% on antipsychotics. AOS and NOS were found to be similar (p>0.05) in terms of being indexed in SCI/SCIE, median numbers of citations and authors. We found significantly higher rates of the presence of pharmacology affiliation in NOS (42.2% vs. 19.4% of AOS; p=0.002) and open-access publication in AOS (84.7–71.1% of NOS; p=0.04) (Table 1).

We determined that 26.5% (n=43) of the studies were conducted on a nationwide basis in Turkiye. Istanbul (22.8%) and Ankara (17.9%) were the most frequently studied provinces. In the ranking adjusted according to population density, DUS were performed most frequently in Denizli (11.4 per million inhabitants), followed by Samsun and Mugla provinces equally (5.8 per million inhabitants, Fig. 1).

The year covered the most by the studies in terms of data collection period was 2016, with 24.7%. The mean study period was 2.9±3.1 years in total, with 2.2±1.8
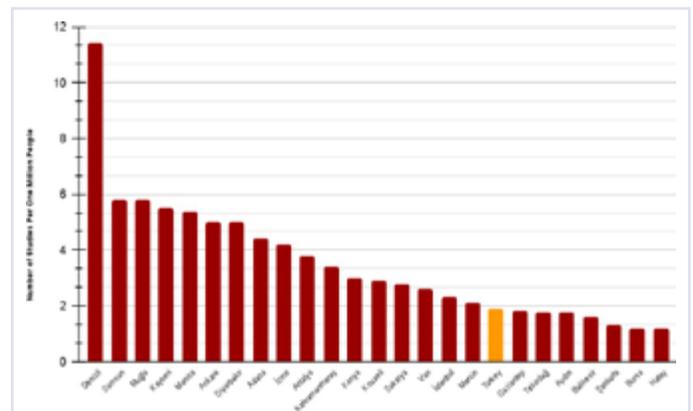

Figure 1. Numerical distribution of studies per 1.000.000 people in provinces with a population over 1 million.

years in AOS and 3.5±3.7 years in NOS. We found that the studies were published within an average of 2.9±2.1 years after the end of data collection. When we examined the highest frequency of the study publication years, we detected that 17.9% (n=29) of the studies were published in 2021, with 13.8% (n=10) published as AOS in 2020, and 24.4% (n=22) in the NOS in 2021 (Fig. 2).

Design-related parameters showed that 93.8% of the studies were performed retrospectively. The most preferred design was cross-sectional studies in 67.3% of all studies, being 73.6% in AOS and 62.2% in NOS. The centers where studies were conducted in both groups were mostly secondary/tertiary health-care institutions, which were more prominent in AOS compared to NOS (78.0% and 60.5%, respectively; p=0.04). We found that AOS data were mostly collected directly from hospitals (73.6%) whereas NOS data were mostly collected

TABLE 2. Methodological characteristics of the analyzed articles in the AOS and NOS groups

Study designs[a]	All studies		AOS		NOS		p
	n	%	n	%	n	%	
Analytical							0.02
Sectional	109	67.3	53	73.6	56	62.2	
Retrospective cohort	6	3.7	2	2.8	4	4.4	
Prospective cohort	4	2.5	3	4.2	1	1.1	
Case-control	2	1.2	1	1.4	1	1.1	
Descriptive							
Descriptive	22	13.6	11	15.3	11	12.2	
Case series	3	1.9	–		3	3.3	
Other[b]*							
Retrospective	10	6.2	–		10	11.1	
Prospective	6	3.7	2	2.8	4	4.4	
Study centers[c]							0.04
Primary health institutions[d]*	38	19.4	11	13.4	27	23.7	
Secondary/tertiary health institutions*	133	67.8	64	78.0	69	60.5	
Other medical institutions[e]	25	12.8	7	8.6	18	15.8	
Data source[c]							<0.001
Direct/local hospital data	89	54.9	53	73.6	36	40.0	
Indirect/general medical record data	73	45.1	19	26.4	54	60.0	
Family health center	9	12.2	3	15.8	6	10.9	
prescription information system	22	29.7	8	42.1	14	25.5	
The Ministry of Health	8	10.8	3	15.8	5	9.1	
IQVIA	4	5.4	1	5.3	3	5.5	
Provincial health directorate	3	4.1	0	0.0.	3	5.5	
Social security institution	3	4.1	0	0.0	3	5.5	
Other	25	33.8	4	21.1	21	38.2	
Study population							<0.001
General population[f]	111	68.5	59	81.9	52	57.8	
Only children	20	12.4	11	15.3	9	10.0	
Only adults*	31	19.1	2	2.8	29	32.2	
Total	**162**	**100.0**	**72**	**100.0**	**90**	**100.0**	

AOS: Antibiotic-oriented studies; NOS: Other non-antibiotic-oriented studies; a: The study design statements declared in the method section of the articles have been preserved exactly and have not been subjected to any new classification; b: Retrospective or prospective studies in which the method is not clearly specified; c: Since a study may have been conducted in more than one health institution or contains data collected from more than one source, the total number is higher than the number of studies; d: Family health and/or community mental health centers; e: Medical center, dental clinic, pharmacy, and/or Turkish Medicines and Medical Devices Authority; f: The age of the population is not specifically specified; *: The subgroup(s) from which the significant difference arises in multiple comparisons.

from non-hospital sources (60.0%, p<0.001). In terms of the target study population, we detected that 68.5% of the studies were conducted on the general population, whereas 19.1% were performed in adults and 12.4% in children. When compared to AOS (2.8%), NOS had a significantly higher rate of only adult-oriented population (32.2%, p<0.001; Table 2). We further observed that 9.1% (n=13) of the studies in adults focused on the elderly and 2.1% (n=3) on pregnant women.

The average number of keywords in the studies was 4.1±1.5, whereas no keywords were detected in seven studies (4.3%). In a total of 657 keywords, 5.2% and 10.3% of the keywords were written directly in the form of a drug active ingredient and drug group, respectively; whereas
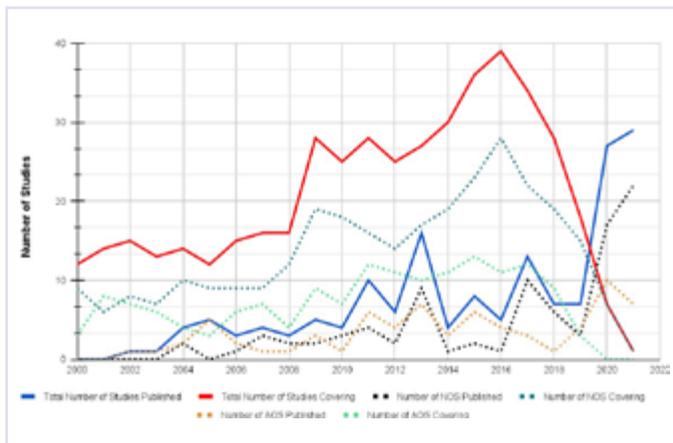
FIGURE 2. Distribution of the years in which the studies covered and were published in the AOS and NOS groups. AOS, antibiotic-oriented studies; NOS, other non-antibiotic-oriented studies. *Number of studies covered denotes the total number of studies containing the data of the relevant year. **Number of published studies denotes the total number of studies published in the relevant year.

84.5% of the keywords were found to be devoid of any drug active ingredient or drug group. The most common keywords in the NOS and AOS groups were polypharmacy (2.1%) and antibiotic (8.0%), respectively (Table 3).

DISCUSSION

Turkiye is a country that has a fairly widespread general health insurance practice and whose medical records have been rapidly digitalized in recent years [15]. In addition, the demographics of its population receiving direct health services and approaching 85 million are gradually changing. With this study, we have systematically reviewed the DUS that possessed certain standards and conducted on medicines available in our country. Accordingly, we observed that about half of the studies focused on antibiotics. The overwhelming majority of studies had a retrospective design and mostly used data from hospitals. Particularly, in the recent 5 years, the number of publications has steadily expanded.

TABLE 3. Distribution of the most frequently used 20 keywords in AOS and NOS publications

Rank no	AOS			NOS		
	Keywords	n	%	Keywords	n	%
1	Antibiotic	22	8.0	Polypharmacy	8	2.1
2	Antibiotic usage	12	4.4	Prescription	7	1.8
3	Cost	6	2.2	Drug utilization	5	1.3
4	Rational antibiotic use	6	2.2	Off-label drug use	5	1.3
5	Antibacterial agents	5	1.8	Older adults	5	1.3
6	Hospital	5	1.8	Analgesic	4	1.0
7	Point prevalence	5	1.8	Asthma	4	1.0
8	Prophylaxis	5	1.8	Methylphenidate	4	1.0
9	Appropriateness	4	1.4	Paracetamol	4	1.0
10	Point prevalence study	4	1.4	Turkey	4	1.0
11	Turkey	4	1.4	Antidepressant	4	1.0
12	Antimicrobial use	3	1.1	Atrial fibrillation	3	0.8
13	Mortality	3	1.1	Generic	3	0.8
14	Pediatric	3	1.1	Physician	3	0.8
15	Prescribing	3	1.1	Pregnancy	3	0.8
16	Restriction policy	3	1.1	Prescribing	3	0.8
17	Surgical prophylaxis	3	1.1	Rational drug use	3	0.8
18	Surveillance	3	1.1	Schizophrenia	3	0.8
19	Antibiotic restriction policy	2	0.7	Antipsychotics	2	0.5
20	Antimicrobial resistance surveillance	2	0.7	Beers criteria	2	0.5

The total keywords number was 657 and nos had a share of 58.3%. AOS: Antibiotic-oriented studies; NOS: Other non-antibiotic-oriented studies.

It is noteworthy that a significant part of the analyzed studies in terms of drug content was antibiotic oriented. It can be assumed that the increasing use of antibiotics in Turkiye [16, 17] and the similarity in the world trend have an impact on the prominence of this drug group [18]. Approximately, 70% of all studies examined in both the AOS and NOS groups were conducted on the general population. Similar findings were reported in a World Health Organization study examining DUS in the Southeast Asia region [19]. Studies focusing on children and the elderly made up around one in five studies, which indicate that additional research is needed in this field to better understand rationality and economic resources in these groups, which make up roughly one-third of the population [14]. Furthermore, a very low share of studies on pregnant women suggests that there is a serious shortage of studies in this field in our country, consistent with those reported from different regions of the world [18]. Due to the challenges and limitations associated with performing clinical drug research on pregnant women, DUS are the primary source of medication information specific to this population [20]. Therefore, the depth of the necessity for such research is made more clear in the current scenario.

More than a quarter of the studies were conducted throughout Turkiye, followed by metropolitan cities such as Istanbul and Ankara. An explanation for this could be related to the density of universities in these areas as research remains an important component of these institutions [21]. On the other hand, when the number of studies proportional to the population was examined, it was noteworthy that most of the studies were conducted in Denizli. We did not come across the circumstance or data that would provide an explanation for this positive performance that is unique to the province of Denizli in our analysis or in the literature.

It is worth noting that the temporal element of the study was disclosed as retrospective or prospective in 16 (9.9%) of the articles analyzed, with no further data about the design revealed. This situation points to serious flaws in the study methodology that should not be overlooked. We also observed a very high percentage of retrospective studies in both AOS and NOS (93.1% and 94.1%, respectively), which was inconsistent with the share prospective studies as 90% reported in a systematic review in India [22]. Although various regulations have been added to the legislation governing observational drug studies in Turkiye since 2008, there are still certain provisions that make conducting prospective studies challenging. This situation can be considered among the major reasons for the absence of the prospective design that we have determined. The failure of these studies to be carried out to the expected extent highlights the importance of developing legislation that will lay the groundwork for prospective designs to be undertaken more easily in our country.

While it is possible to foresee the average duration for each of the phase trials of the drug development process, estimating this period for observational drug research is more challenging. Depending on the study's design, there may be periods of study in DUS that range from a brief period of observation to long periods lasting several decades [23]. In our analysis, we observed that the average study period of all publications was about 3 years, with that of the NOS being longer. The fact that antibiotics are mostly used to treat acute diseases may help to explain the difference between AOS and NOS in this regard. Furthermore, the fact that NOS is a heterogeneous group that covers a wider range of treatment areas may have played a role in this difference.

Every year, the performance of scientific publications in Turkiye, as in many other countries, improves quantitatively [24]. It is foreseeable that this trend will also apply to DUS. According to our analysis, the percentage of studies published in the last 5 years corresponded to roughly half of the studies published between 2000 and 2021, and this percentage was 75% within the last 10 years. Furthermore, this shows a trend toward occurring DUS since 2010. The increased number of scientific publications by about 40% in 2015 versus 2010 also seems consistent with this trend [25].

The absence of NOS publication between 2000 and 2003 indicates that DUS started with antibiotic studies. In fact, AOS is one of the priority and important topics in DUS around the world [25]. On the other hand, because Turkiye has been reported to overconsume antibiotics in recent years, the widespread use of drugs has gotten more attention. Therefore, the frequent discussion of antibiotic irrationality may have been effective in prioritizing AOS [7–9].

Widespread use of electronic health records also has positively impacted the conduction of DUS. Databases offer researchers a wide range of working opportunities and options [26]. Although a few of them have been put into use in recent years in Turkiye, the database that can be used for drug-oriented research is

quite limited in terms of established pharmacoepidemiological studies. Other than the database, conditions that can be used as a source for such research typically consist of local clinical patient records. In our analysis, it was also noticeable that the DUS conducted in the last 20 years in Turkiye mostly benefited from the medical records kept by hospitals and primary health-care institutions in both groups, being more prominent in the AOS. This can be cited as an important reason that restricts researchers, especially pharmacologists who have less access to these records, from working in this field and lowers their expectations. As a matter of fact, the contribution of the pharmacology branch in only about one-third of all studies can be characterized as less than expected. Furthermore, the fact that NOS has a greater pharmacology contribution than AOS may indicate that this branch provides DUS with a perspective that is not limited to a specific therapeutic area.

Being more prevalent in NOS, a high percentage of studies were published in English, about two-thirds of all studies registered on the WOS platform, and about half of them were published in SCIE journals. About half of the articles from Turkiye are published in medical sciences, half of which received citations [25]. Although the publication rates of DUS in well-known indices seem comparably high in our study, it appears that their target audience's interest rates fall short of expectations. In fact, about half of all studies did not receive any citations through WOS. This finding implies that existing studies have issues with quality, interest, or content criteria at the international level.

Any sponsorship of the research must be declared in the articles [27]. The lack of a declaration by the authors about whether or not the studies were sponsored in about two-thirds of cases suggests that they were not. However, as an original finding of our study, the fact that <7% of all studies have a sponsor suggests that DUS have a resource problem in part because no similar findings have been found in the literature. In fact, no significant records exist of the direct transfer of resources to pharmacoepidemiology research from public and private sector sources that have sponsored clinical trials in Turkiye for many years. This may have accounted for the detection of such a low rate of sponsorship in our study. On the other hand, it is foreseeable that research conducted without a sponsor might face qualification issues as a result of various deficiencies, particularly resource constraints. In addition, the relatively low number of DUS published in SCIE journals and receiving WOS-based citations may have contributed to the impossibilities created by the lack of sponsors. Before the countries' DUS legislative arrangements, there were debates that some of these studies could be conducted for marketing/seeding purposes and that various waves of abuse were encountered on the subject [28]. The legal regulation covering this issue in Turkiye has been in force since 2008 and includes various measures to prevent these inconveniences [29]. Given the increased prominence of DUS in Turkiye over the last decade, we may assume that the existing sponsorships in studies offer positive qualities that will increase working opportunities beyond the negative ones in the past. Although it is encouraged due to its positive contribution to the study, the relatively low rates of sponsors observed in our study may be partly attributed to the unfavorable debates voiced in the past [30].

The findings of our study should be interpreted in light of its limitations. The databases we chose were scanned within the predetermined time frame and keywords in accordance with the study's inclusion criteria. The study excluded all other studies with no English abstracts, including with Turkish full-texts, which may partly overlook a few publications if any. While out of our scope, we did not evaluate outcomes of specific clusters of DUS, which could provide clinically relevant insights about specific drug use such as antibiotics or analgesics.

Conclusion

Our study demonstrates that DUS have been steadily increasing in Turkiye over the past few years. About two-thirds of DUS were registered on the WOS and nearly half were published in SCIE journals albeit with comparably low citation rates, suggesting issues with quality, interest, or content. Moreover, methodological analysis indicates a substantial share of antibiotic-oriented research and a vast predominance of retrospective design mainly using hospital-collected data on the general patient population. The establishment of databases containing medical records can be helpful on a national and international level in terms of enhancing the simplicity of carrying out these studies. We may suggest that addressing these needs will lead to more effective use of health service resources and serve as a guide for stakeholders on the individual and professional levels to manage human health more accurately. A noticeably low share of prospective studies may be regarded as another area of development to improve DUS in the country.

REFERENCES

1. Wettermark B, Elseviers M, Almarsdóttir AB, Andersen M, Benko R, Bennie M, at al. Introduction to drug utilization research. In: Elseviers M, Wettermark B, Almarsdóttir AB, Andersen M, Benko R, Bennie M, et al, editors. Drug Utilization Research: Methods and Applications. 1st ed. England: Wiley; 2016. p.3–14. [CrossRef]

2. Shalini S, Ravichandran V, Saraswathi R, Mohanty BK, Dhanaraj SK. Drug utilization studies–an overview. Int J Pharm Sci Nanotech 2010;3:803–10. [CrossRef]

3. Sacristén JA, Soto J. Drug utilization studies as tools in health economics. Pharmacoeconomics 1994;5:299–312. [CrossRef]

4. Bergman U. The history of the Drug Utilization Research Group in Europe. Pharmacoepidemiol Drug Saf 2006;15:95–8. [CrossRef]

5. Duran CE, Christiaens T, Acosta A, Vander Stichele R. Systematic review of cross-national drug utilization studies in Latin America: methods and comparability. Pharmacoepidemiol Drug Saf 2016;25:16–25. [CrossRef]

6. Malhan S, Tekin RN, Oksuz E. Irrational use of antibiotics in Turkey. Value Health 2016;19:A405. [CrossRef]

7. Versporten A, Bolokhovets G, Ghazaryan L, Abilova V, Pyshnik G, Spasojevic T, et al; WHO/Europe-ESAC Project Group. Antibiotic use in eastern Europe: a cross-national database study in coordination with the WHO Regional Office for Europe. Lancet Infect Dis 2014;14:381–7. [CrossRef]

8. Sahin A, Akici A, Aydin V, Melik B, Aksoy M, Alkan A. Variation of antibiotic consumption and its correlated factors in Turkey. Eur J Clin Pharmacol 2017;73:867–73. [CrossRef]

9. Aksoy M, Isli F, Kadi E, Varimli D, Gursoz H, Tolunay T, et al. Evaluation of more than one billion outpatient prescriptions and eight-year trend showing a remarkable reduction in antibiotic prescription in Turkey: a success model of governmental interventions at national level. Pharmacoepidemiol Drug Saf 2021;30:1242–9. [CrossRef]

10. Gulmez SE, Aydin V, Akici A. Footprints of clinical pharmacology in Turkey: past, present, and future. Clin Ther 2020;42:351–62. [CrossRef]

11. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Reprint--preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Phys Ther 2009;89:873–80. [CrossRef]

12. World Health Organization (WHO). World Health Organization Model List of Essential Medicines – 22nd List. (WHO/MHP/HPS/EML/2021.02). Geneva: World Health Organization; 2021. [CrossRef]

13. Karakan T, editor. Türkiye İlaç Pazarı Gözlem Raporu-8. Satış Hacmi ve Değeri Açısından 2020 Yılı Pazar Durumu. Available at: https://titck.gov.tr/storage/Archive/2021/contentFile/T%C3%9CRK%C4%B0YE%20%C4%B0LA%C3%87%20PAZARI%20G%C3%96ZLEM%20RAPORU%20-8_f1f0941c-8119-46ab-915e-0a47a65e2073.pdf. Accessed Jan 12, 2024.

14. Turkish Statistical Institute. The Results of Address Based Population Registration System. Available at: https://data.tuik.gov.tr/Bulten/Index?p=The-Results-of-Address-Based-Population-Registration-System-2021-45500&dil=2#:~:text=According%20to%20the%20results%20of,of%20this%20population%20were%20females. Accessed Jun 04, 2022.

15. Limon S. Transformation of medical documents in hospitals from traditional to electronic. [Article in Turkish]. Isparta University J Appl Soc Sci Fine Arts 2019;1:30–9.

16. Wirtz VJ, Dreser A, Gonzales R. Trends in antibiotic utilization in eight Latin American countries, 1997-2007. Rev Panam Salud Publica 2010;27:219–25. [CrossRef]

17. Karabay O, Hosoglu S. Increased antimicrobial consumption following reimbursement reform in Turkey. J Antimicrob Chemother 2008;61:1169–71. [CrossRef]

18. Bachhav SS, Kshirsagar NA. Systematic review of drug utilization studies & the use of the drug classification system in the WHO-SEARO region. Indian J Med Res 2015;142:120–9. [CrossRef]

19. Allegaert K, Simons S, Van Den Anker J. Research on medication use in the neonatal intensive care unit. Expert Rev Clin Pharmacol 2019;12:343–53. [CrossRef]

20. Chan M, Wong ICK, Sutcliffe AG. Prescription drug use in pregnancy: more evidence of safety is needed. Obstet Gynaecol 2012;14:87–92.

21. Mammadov R, Aypay A. Efficiency analysis of research universities in Turkey. Int J Educ Dev 2020;75:102176. [CrossRef]

22. Gujar A, Gulecha V, Zalte A. Drug utilization studies using WHO prescribing indicators from India: a systematic review. Health Pol Tech 2021;10:100547. [CrossRef]

23. Al-Turkait A, Szatkowski L, Choonara I, Ojha S. Review of drug utilization studies in neonatal units: a global perspective. Int J Environ Res Public Health 2020;17:5669. [CrossRef]

24. TÜBİTAK ULAKBİM Cahit Arf Bilgi Merkezi. Bilim Dallarında Dünya, Ülkeler ve Gruplara Ait Veriler: Tıbbi Bilimler (2010-2015). Available at: https://cabim.ulakbim.gov.tr/bibliyometrik-analiz/turkiye-bilimsel-yayin-performans-raporlari/bilim-dallarinda-dunya-ulkeler-ve-gruplara-ait-veriler-tibbi-bilimler-2010-2015-raporu/. Accessed Jun 04, 2022.

25. Atif M, Scahill S, Azeem M, Sarwar MR, Babar ZUD. Drug utilization patterns in the global context: a systematic review. Health Pol Tech 2017;6:457–70. [CrossRef]

26. Ankrah D, Hallas J, Odei J, Asenso-Boadi F, Dsane-Selby L, Donneyong M. A review of the Ghana National Health Insurance Scheme claims database: possibilities and limits for drug utilization research. Basic Clin Pharmacol Toxicol 2019;124:18–27. [CrossRef]

27. Kansu E, Ruacan Ş. Bilimsel araştırma ve yayın etiğinin temel ilkeleri. [Article in Turkish]. Turk Plast Rekonstr Est Cer Derg 2006;14:82–6.

28. Linden M. Phase IV research and drug utilization observation studies. Pharmacopsychiatry 1997;30:1–3. [CrossRef]

29. Türkiye İlaç ve Tıbbi Cihaz Kurumu. Gözlemsel İlaç Çalışmaları Kılavuzu. Available at: https://titck.gov.tr/storage/Archive/2018/legislation/a232d324-6ae5-4df9-a88e-e1fabba4d9a8.pdf. Accessed Jun 04, 2022.

30. Terzi C. Physicians can no longer rely on the medical literature for valid and reliable information. [Article in Turkish]. Toplum ve Hekim 2010;25:346–79.