

Definition and prevalence over the years of polypharmacy in Turkey: A systematic review

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ABSTRACT: Identification of the trend of polypharmacy over the years is as valuable as determining the common definitions for taking precautions. The aim of this systematic review is to reveal the frequency, commonly used definitions and its change over the years of polypharmacy in Turkey. The reporting of this systematic review follows to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA 2020) checklist. The MEDLINE and ULAKBIM TR Dizin databases were searched for relevant studies published until April, 2021. The studies conducted with patients >18 years in Turkey were included. A total of 361 articles were identified and 52 articles met the inclusion criteria. The most common definition of polypharmacy was ‘combination of 5 or more drugs’, followed by the definitions of ‘two or more drugs’ to ‘10 or more drugs’; and its prevalence ranged between 9% and 95% in the studies. It was determined that the most commonly used definition of polypharmacy was ‘the use of 5 or more drugs’. The prevalence of polypharmacy in Turkey was appeared in a wide range and found higher than the studies in the literature. The prevalence and trends of polypharmacy over the years should be carefully observed, inappropriate use of medicines should be examined and necessary precautions should be taken accordingly.

KEYWORDS: Polypharmacy; Inappropriate prescribing; Definition; Prevalence; Systematic review

1. INTRODUCTION

The prevalence of polypharmacy increases with the aging of the population worldwide. The World Health Organisation (WHO) encourages healthcare professionals to take precautionary actions on preventing inappropriate use of medicines and consequently the rate of polypharmacy by provision of updated information gathered from epidemiological reports. Moreover, WHO has initiated a challenge to reduce preventable drug-related problems by 50% within five years by 2022, but the results of this challenge have not been published yet [1]. In order to increase the awareness among healthcare professionals on polypharmacy, it is necessary to observe the change in the rate of polypharmacy and related interventions over the years.

Various definitions have been used for polypharmacy; such as ‘the number of drugs taken together in a day’, ‘the average number of drugs prescribed in a year’ and ‘the average of the number of drugs prescribed at two-week intervals’ [2, 3]. However, these definitions are not widely used in the literature. Concomitant use of five or more drugs has been reported to increase adverse effects and drug-drug interactions, therefore this has been accepted as the most common definition of polypharmacy in many studies [4]. It can be argued that it is more important to emphasize the necessity and appropriateness of polypharmacy rather than the numerical definitions.

Although polypharmacy can be seen in all age groups, it is more common in older patients due to numbers of comorbidities. Aging has been associated with metabolic changes, decreased drug clearance, increased numbers of drug-drug interactions and prescribing cascades, and potentially inappropriate drug use [5, 6]. It is known that polypharmacy is an independent risk factor for inappropriate drug use and increases the risk of drug interactions, adverse effects, hospitalization, frailty and cognitive deterioration and negatively affects the adherence [7-9]. The studies demonstrated that adverse drug reactions are responsible for 6.5% of hospitalizations where polypharmacy is the leading cause [10, 11].

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The rate of polypharmacy has been reported between 8-67%, which varies according to the definition used and clinical settings of the study (15-17). In a multicenter study conducted in Turkey with 1430 patients, the rate of using five or more drugs was reported as 17.2% [12]. In another study performed at outpatient settings, the rate of chronic use of ≥ 4 drugs was 55%, and ≥ 10 drugs was 8% in male patients [13]. A study investigated the prevalence of polypharmacy (≥ 5 drugs) during hospitalization and at discharge found as 52% and 67%, respectively [14]. In the United States, prescribing ≥ 5 drugs in adults has increased from 8.2% in 1999-2000 to 15% in 2011-2012 [15]. Despite heterogeneity among studies in terms of definitions, methodologies, population characteristics or settings, polypharmacy is acknowledged as a global healthcare problem. It is shown that polypharmacy increased the healthcare related cost 2-3 fold [16]. Therefore, identification of the trend over the years in Turkey will reveal the burden of polypharmacy on economic and clinical outcomes which will further help to take precautionary interventions. In the view of previous studies, this systematic review aims to determine the prevalence of polypharmacy and to reveal the trend in polypharmacy over the years in Turkey.

2. RESULTS

A total of 361 articles were found through the literature search, of those 55 met the inclusion criteria. After performing the quality assessment, 3 studies were excluded because of high risk of bias (Appendix). Finally, 52 studies included in the qualitative assessment and evaluated in detail. Figure 1 shows the selection process of the articles in the study. Among included studies, 5 were interventional and 47 were observational in design. Five studies were designed as descriptive, 38 were analytic (cross-sectional), 5 was interventional, 1 was a validation study, while 3 were not specified in terms of study design. The publication years of the studies included in this systematic review ranged from 2006 to 2020 (Table 1).

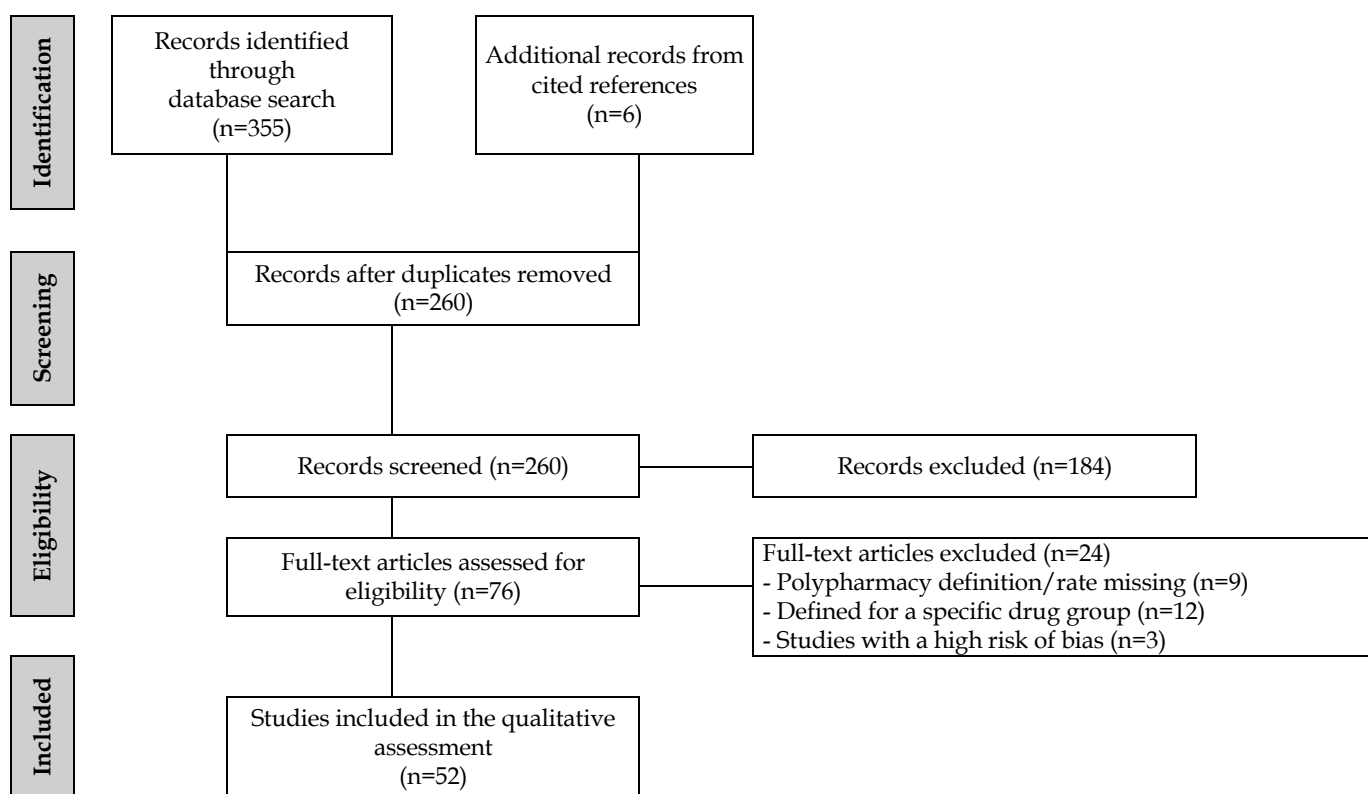


Figure 1. Flowchart of study selection according to the PRISMA checklist.

A total of 6125649 patients were included for the final analysis, of those 56.97% were female. The majority (90%) of the studies included geriatric patients. Thirty-eight studies (73.1%) were conducted in outpatient clinics, 5 (9.6%) in nursing homes, 5 (9.6%) in hospital wards, and 4 (7.7%) in pharmacies and home visits (Table). Common comorbidities indicated in the studies were hypertension, diabetes, muscle-joint diseases, cardiovascular diseases, gastrointestinal diseases, cancer, psychiatric disorders, kidney diseases,

fracture, dementia, hyperlipidemia, osteoporosis, thyroid-related diseases, cerebrovascular accident, chronic obstructive lung disease/asthma, and Parkinson's disease.

Table 1. Characteristics of studies included and the rates of polypharmacy indicated (n=52 studies).

Authors	Year of publication	Study design	Study period	Sample size	Population	Age	Gender (Female)	Definition of polypharmacy	The mean number of medications	Prevalance of polypharmacy
Outpatient clinics										
Discigil G et al. [17]	2006	N/A	N/A	127	≥65 years	77.2 ± 7.9	57	≥4 drug usage	4.5 ± 2.8	60.6%
Kutsal YG et al. [12]	2009	Cross sectional	January 2007 - January 2008	1430	≥65 years	N/A	962	≥5 drug usage	2.5 ± 2.0	17.2%
Bahat G et al. [13]	2013	Cross sectional	N/A	274	≥60 years male	74.4 ± 7.1	N/A	≥4 chronic drug usage ≥5 chronic drug usage	4.5 ± 3.2	55.3% 40.2%
Cakmur H et al. [18]	2014	Cross sectional	October 2012 - December 2012	187	≥65 years	N/A	101	≥5 drug usage	N/A	5.0% (at age of 65-69 years) 1.0% (at age of 70-74 years)
Sonmez Y et al. [19]	2014	Cross sectional	October 2013	687	≥65 years	74.9 ± 7.0	340	≥5 drug usage	3.1 ± 1.9	14.2%
Bahat G et al. [20]	2014	Cross sectional	8 years	515	≥60 years female	73.4 ± 6.9	515	≥4 chronic drug usage ≥5 chronic drug usage	4.8 ± 2.0	63.2% 47.6%
Taskin Sayir C et al. [21]	2014	Descriptive	September 2012 - October 2012	100	≥65 years	73.4 ± 6.8	73	≥4 drug usage	N/A	69.0%
Yuruyen M et al. [22]	2016	Cross sectional	2003 - 2012	1205	≥65 years	75.0 ± 6.9	854	PP: ≥5 drug usage Excessive PP: ≥9 drug usage	4.4 ± 2.8	PP: 45.0% Excessive PP: 8.0%
Kara O et al. [23]	2016	N/A	July 2013 - March 2014	374	≥65 years	74 (69-79)	234	≥5 drug usage daily	5 (3-8)	63.0%
Kayhan Tetik B et al. [24]	2017	Cross sectional	June 2017	333	Outpatients	52.4	154	≥5 drug usage	N/A	43.8%
Ozturk Z et al. [25]	2017	Cross sectional	January 2013 - December 2013	218	≥65 years	75.1 ± 5.5	122	≥5 drug usage	N/A	38.0%
Ozturk GZ et al. [26]	2017	Interventional	July 2017 - September 2017	300	≥65 years	76.3 ± 8.6	170	PP: ≥5 drug usage Hyper-PP: ≥10 drug usage	5.5 ± 2.8	PP: 62.3% Hyper-PP: 9.7%
Gencer MZ et al. [27]	2017	Cross sectional	February 2015 - May 2015	350	≥65 years	N/A	160	≥4 drug usage	N/A	56.6%
Varli M et al. [28]	2017	Cross sectional	February 2017 - June 2017	388	≥60 years	73.0 ± 7.4	241	≥5 drug usage	N/A	47.7%
Ates Bulut E et al. [29]	2018	Cross sectional	January 2013 - January 2017	2816	≥60 years	76 (60-105)	1830	≥5 drug usage	N/A	54.5%
Yilmazel G et al. [30]	2018	Descriptive	June 2014	260	≥65 years female	N/A	260	≥5 drug usage	4.4 ± 2.4	53.8%
Ozturk Z et al. [31]	2018	Cross sectional	November 2013 - December 2013	293	≥65 years	72.0 ± 4.2	152	≥5 drug usage	2.9	8.8%
Unutmaz GD et al. [32]	2018	Cross sectional	January 2014 - February 2016	1579	older patients	75.8 ± 8.8	1024	PP: ≥5 drug usage Hyper-PP: ≥ 10 drug use	5.3 ± 3.4	PP: 56.7% Hyper-PP: 12.0%

Dutoglu E et al. [33]	2019	Cross sectional	December 2016 - April 2018	858	≥65 years female	74.1 ± 8.2	858	≥5 drug usage	N/A	42.1%
Kizmaz M, et al. [34]	2019	Cross sectional	May 2019 - August 2019	358	≥65 years	71.2 ± 6.6	198	≥5 drug usage	3.7 ± 3.0	38.8%
Ertuna E et al. [35]	2019	Cross sectional	December 2017 - July 2018	91	≥65 years	80.3 ± 0.5	131	≥5 drug usage	8.2 ± 0.2	87.5%
Kara E et al. [36]	2019	Interventional	September 2015 - July 2016	181	people with HIV/AIDS	40.4 ± 13.1	37	≥5 drug usage	4.4	29.9%
Kurt M et al. [37]	2019	Descriptive	January 2016 - June 2016	240	≥65 years	71.0 ± 5.4	140	≥5 drug usage	4.3 ± 2.8	42.0%
Paksoy C et al. [38]	2019	Interventional	December 2014 - March 2015	114	≥65 years with cancer	71.8 ± 5.5	51	≥5 drug usage	N/A	94.7%
Tasci I et al. [39]	2019	Cross sectional	N/A	546	≥65 years	74.9 ± 6.3	388	≥5 different classes of medications	4.8 ± 2.8	50.5%
Ozsurekci C et al. [40]	2019	Cross sectional	1 year	76	geriatric patients with alzheimer	78.9 ± 6.4	43	≥5 drug usage	5.0 ± 3.7	65.4% (CDR 1) 74.2% (CDR 2)
Aydos TR et al. [41]	2020	Cross sectional	January 2018 - December 2018	6104798	≥65 years	N/A	3476943	Chronic PP: prescribed ≥5 drugs ≥4 times during a year. Cumulative PP: prescribed ≥5 drugs in 1 month or quarter of year	6.4	Chronic PP: 14.3% Cumulative PP: 16.4% and 20.7%
Arslan M et al. [42]	2020	N/A	N/A	271	≥65 years	71 (65-90)	134	≥5 drug usage	4.6 ± 2.7	49.1%
Kucukdagli P et al. [43]	2020	Cross sectional	June 2000 - June 2014	667	≥60 years	77.6 ± 6.3	421	≥5 drug usage	6.1 ± 3.4	5-10 drug 41.7%
Kocuyigit SE et al. [44]	2020	Cross sectional	January 2017 - July 2019	311	≥60 years	75.4 ± 7.6	222	≥5 drug usage	5.6 ± 3.3	59.5%
Topaloglu US et al. [45]	2020	Cross sectional	January 2016 - September 2019	704	≥18 years	57.1 ± 14.7	352	≥5 different drug usage	5.0 ± 2.9	56.8%
Eyigor S et al. [46]	2021	Cross sectional	N/A	692	≥65 years	N/A	439	≥5 drug usage daily	3.6 ± 2.6	30.1%
Inpatient clinics										
Selcuk A et al. [47]	2015	Interventional	April 2014 - July 2014	133	≥65 years	76.6 ± 8.1	70	≥5 drug usage	9 (6-11)	91.0%
Asci H et al. [48]	2016	Cross sectional	January 2013 - June 2013	111	Hospitalized patients in the ICU	65.8 ± 18.4	44	≥5 drug usage	17.0 ± 8.2	93.6%
Senel G et al. [49]	2017	Cross sectional	October 2012 - March 2013	213	≥18 years patients with cancer	60.3 ± 14.8	87	≥3 drug usage	N/A	Delirium group: 85.8% Not delirium group: 15.7%
Bahsi R et al. [50]	2019	Cross sectional	2014 - 2018	112	≥60 years	79 (63-99)	58	≥10 drug usage	8 (1-16)	31.3%
Demir I et al. [51]	2020	Cross sectional	September 2018 - August 2019	235	≥65 years	N/A	131	≥4 drug usage	N/A	50.2%
Outpatient clinics and inpatients clinics										
Alkan A et al. [52]	2017	Cross sectional	January 2013 - December 2015	445	≥65 years with cancer	70 (65-89)	152	≥5 drug usage	3 (0-14)	30.8%

Abunahlah N et al. [53]	2018	Cross sectional	January 2017	100	Inpatients	62.8 ± 18.3	51	≥5 drug usage	8.1 ± 3.8	64.0%
Umit EG et al. [54]	2020	Cross sectional	2015 - 2018	80	≥65 years with multiple myeloma	69.5 (IQR: 65-86)	46	≥4 drug usage ≥5 drug usage	6 (IQR: 3-10)	≥4 drugs: 81.3% ≥5 drugs: 86.3%
Emergency department										
Duman Atilla O et al. [55]	2012	Cross sectional	January 2012 - April 2012	406	≥65 years	75.6 ± 7.0	268	≥5 drug usage	N/A	14.9%
Atmaca-Temrel T et al. [56]	2019	Cross sectional	January 2018 - March 2018	144	≥65 years	77.2 ± 7.9	88	≥5 drug usage	5.2 ± 2.6	55.6%
Kaplan C et al. [57]	2019	Cross sectional	March 2016 - May 2016	835	≥65 years	74.2 ± 6.6	406	PP: ≥5 drug usage Excessive PP: >10 drug usage	6.8 ± 3.2	PP: 35.0% Excessive PP: 2.0%
Nursing homes										
Sancar M et al. [58]	2011	Descriptive	N/A	146	≥65 years	78.1 ± 8.7	98	≥5 drug usage	5.9 ± 3.6	44.0%
Silay K et al. [59]	2017	Cross sectional	January 2016 - January 2017	105	≥65 years	82.3 ± 6.2	66	≥4 drug usage	5.9 ± 2.8	81.0%
Gocer S et al. [60]	2017	Descriptive	2016	99	N/A	76.0 ± 9.5	41	≥4 drug usage	3.8 ± 2.0	59.6%
Savran M et al. [61]	2018	Cross sectional	August 2017	61	≥65 years	79.2 ± 7.6	24	≥5 drug usage	3.1 ± 3.0	39.3%
Oguzoncul AF et al. [62]	2018	Cross sectional	April 2010 - June 2010	255	≥60 years	72.7 ± 8.3	90	≥5 drug usage	N/A	26.2%
Home visits										
Cakmur H. [63]	2015	Cross sectional	April 2014 - September 2014	168	≥65 years	72.7 ± 7.7	90	using a drug for more than 1 indication at the same time	N/A	19.0%
Onal O et al. [64]	2018	Cross sectional	May 2016 - June 2016	400	≥65 years	74.5 ± 6.8	228	≥5 drug usage	6.0 ± 4.3	36.5%
Pharmacy visits										
Okuyan B et al. [65]	2016	Validation	December 2014	100	≥65 years	74.9 ± 7.6	53	≥5 drug usage	4.8 ± 2.3	46.0%
Sayin Z et al. [66]	2020	Interventional	December 2018 - April 2019	158	≥65 years	73.0 ± 6.0	64	≥5 drug usage	6 (4-8)	69.0%

PP: Polypharmacy, N/A: Not available, CDR: Clinical dementia rating, ICU: Intensive care unit

2.1. Definitions of polypharmacy

Various definitions have been used for polypharmacy in the studies reviewed. The most common definition of polypharmacy was 'combination of 5 or more drugs' used in 43 studies, whereas definition of '4 or more drug use' in 9 studies and 'using a drug for more than one indication at the same time' in 1 study. The definition of '10 or more drug use' for excessive or hyper-polypharmacy was used only in 3 studies. A term of cumulative polypharmacy was defined as 'patients who have prescribed ≥5 drugs in one month or a quarter of year' in 1 study.

2.2. Prevalence of polypharmacy

In order to assess the prevalence, the studies accepted the definition of 'using 5 or more drugs' were included and found that the prevalence has ranged between 8.8% and 94.7%. On the other hand, the prevalence of hyper-polypharmacy (use of 10 or more drugs) varies between 2% and 31.3%. Therefore, the studies that defined polypharmacy as 'using 5 or more drugs' (n=39) were assessed in order to maintain homogeneity in evaluation of change over the years in this systematic review. As a result, the rate of

polypharmacy (using more than 5 drugs) was varied between 14% and 91% and the change of polypharmacy rate over the years was shown in the Figure 2.

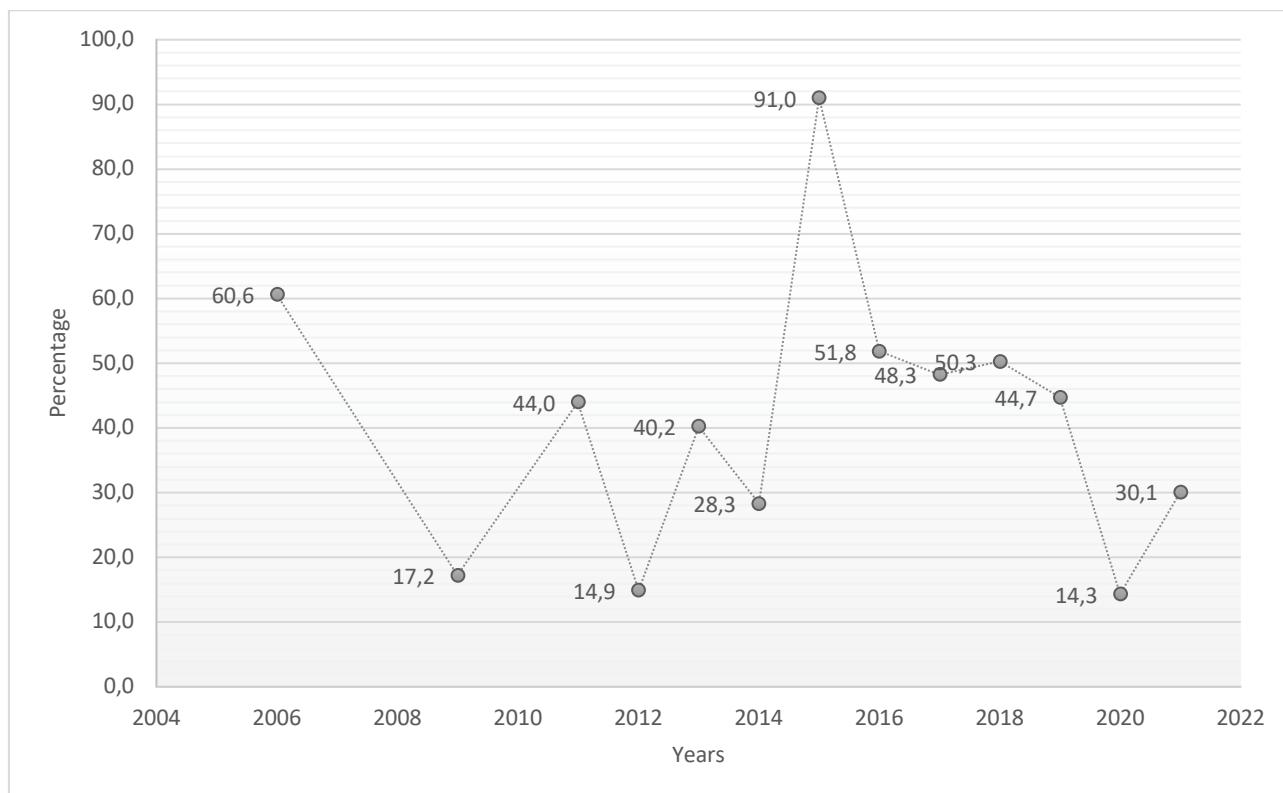


Figure 2. Change in polypharmacy rate in Turkey over the years.

3. DISCUSSION

This systematic review is the first study to evaluate the rate of polypharmacy in Turkey. Although the first published study on polypharmacy in Turkey included data from 2006, a majority of the studies (n=49) were conducted in the last 10 years.

This systematic review has demonstrated that various definitions are used for polypharmacy. Although the most preferred definition of polypharmacy is 'use of 5 or more drugs' [67], there is still a lack of consensus on the definition which makes difficult to compare existing results of the studies and eventually to manage polypharmacy related issues in clinical practice. Therefore, definition for polypharmacy may be accepted as 'use of 5 or more drugs' in future studies in order to capture the trend in multiple drug usage. But, this definition may be modified according to the patient population.

It is shown in the present study that the prevalence of polypharmacy in Turkey has ranged between 8.8% and 94.7% in general, but in studies where polypharmacy is considered as '5 or more drug use', this rate varies between 14% and 91%. In a study conducted among adult patients in the United States, the rate of polypharmacy has increased from 8% to 15% between the years of 1999 and 2012 [15]. In Scotland, it was determined that the rate of polypharmacy doubled between the years of 1995 and 2010 [68]. According to the studies conducted in different regions of the world, 11% of the population in Sweden [69] and 6% of the rural population in China are used five or more drugs per day [70]. Another study conducted in Scotland, which evaluated the number of drug use in community during 3 months in 1995, has shown that the prevalence of drug use in adults using 5-9, 10-14, and 15 or more drugs are 9.7%, 1.5%, and 0.2%, respectively; and these rates increased to 16.3%, 4.7% and 1.1% in 2010 [68].

Unnecessary drug use, especially in older patients, is an important factor leading to polypharmacy. In a study conducted in Canada, unnecessary drug use is determined as the second common reason following inadequate adherence amongst drug related problems [71]. Along with unawareness among healthcare professionals on prescribing practices of others, increased rate of polypharmacy in geriatric patients becomes threatening issue during chronic disease management due to emergence of polypharmacy-related problems

and adverse effects. Therefore, clinicians should be aware of increase in the trend of polypharmacy over the years, and be vigilant on unnecessary drug use.

The rate of polypharmacy is affected by patient-related and health system-related factors. The factors, such as advanced age, high number of comorbidities, involvement of more than one physician in disease management, use of over-the-counter drugs, having mental disorders, and living in nursing home are considered 'patient-related' and lack of prescription review and inadequate duration for patient assessment are considered 'health system-related' factors that increase the rate of polypharmacy [72]. Therefore, reasons and stimulating factors for polypharmacy should be investigated in depth at patient-level and system-level, which could help to identify pattern for inappropriate drug use.

Only five studies included adult patients in the present systematic review, and polypharmacy rates has been reported between 30% and 85%, in which the highest prevalence is refers to a study conducted in patients with cancer. The risk of polypharmacy increases with the numbers of chronic diseases. Given the fact that numbers of people experiencing chronic diseases, such as hypertension, diabetes, and heart disease has been increased in Turkey, this finding becomes a significant health issue due to its burden on health system [73].

In the study of Garfinkel which explored the effect of poly-deprescribing to treat polypharmacy, a significant improvement was observed in overall satisfaction, functional, mental and cognitive status, sleep quality, appetite, sphincter control in the 'deprescribing' group. The number of major complications was significantly reduced in the 'deprescribing' group, while no difference was found in the rates of hospitalization and death. An improvement in health status occurred within 3 months in 83% of patients in 'deprescribing' group and continued for ≥ 2 years in 68% [74]. Deprescribing is one of the intervention to reduce drug-related problems occurred by polypharmacy, therefore should be considered by healthcare professionals in terms of economic and clinical benefits.

It is known that polypharmacy has been associated with undesired clinical outcomes such as adverse drug reactions, drug-drug interactions, functional decline, increased risk of falls and impaired cognitive function in the older patients, medication non-adherence, deterioration of nutritional status, and increased healthcare costs [75]. The prescribing cascade, defined as the addition of new drugs by considering an adverse drug event as a new disease or symptom, can be both a cause and a consequence of polypharmacy [76].

Considering the increase both in the number of older population and in the prevalence of age-related chronic diseases in Turkey, it is inevitable for a developing country to perform necessary actions to prevent polypharmacy or unnecessary drug use, which has a significant burden on the health system. From a clinical perspective, determination of risk factors for polypharmacy can contribute to establishment of health policies to prevent polypharmacy-related problems.

A substantial proportion of studies in this systematic review have not evaluated polypharmacy as a primary outcome, therefore, not provided a comprehensive assessment on polypharmacy. Only the definition and rates of polypharmacy were specified, but information about drugs used was not provided. Furthermore, no data on polypharmacy outcomes were presented or evaluated. Majority of studies were conducted in the geriatric population, which makes difficult to generalize the findings and interpret the outcomes for general population in Turkey. From this perspective, it is clear that more detailed and comprehensive studies on polypharmacy are required.

4. CONCLUSION

In this systematic review, it is demonstrated that the rate of polypharmacy in Turkey is higher than other studies in the literature. In order to have comparable studies, comprehensive and robust definition for polypharmacy is needed. Given the fact that the definition of 'use of 5 or more drugs' is the most commonly used one among the studies included in this systematic review, we do suggest for future studies to evaluate not only the number of drugs used and also the severity of polypharmacy in clinical practice. Evaluation of the impact and consequences of polypharmacy may also make an important contribution to the literature. There is a need for comprehensive studies that demonstrate the risk factors associated with polypharmacy and economic and clinical burden of polypharmacy in different age groups.

5. MATERIALS AND METHODS

5.1. Data source and search strategy

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA 2020) standards were used to generate this systematic review [77]. The search was constructed to address the questions of "What is the prevalence of polypharmacy in Turkey", and "How has it changed over the years?". The MEDLINE and

ULAKBIM TR Dizin databases were searched for relevant studies published until April, 2021. The search was undertaken by using keywords of polypharmacy, polymedication, polytherapy, polyprescription, multi prescriptions, multiple drug treatment and Turkey. The detailed search strategy in PubMed is (((((Turkey AND polypharmacy) OR (Turkey AND polymedication)) OR (Turkey AND polytherapy)) OR ("Turkey"[MeSH Terms] OR "Turkey"[All Fields] OR "Turkey s"[All Fields] OR "Turkeys"[MeSH Terms] OR "Turkeys"[All Fields]) AND "polyprescription"[All Fields])) OR (Turkey AND multi prescriptions)) OR (Turkey AND multiple drug treatment). The protocol for this systematic review was registered on International prospective register of systematic reviews (PROSPERO) (CRD42021241528) [78].

5.2. Inclusion and exclusion criteria

The search strategy was limited by the study design (research articles only) and the publication language (articles in English), any additional articles meet the eligibility criteria were retrieved through cited references from the included articles. Research articles were selected by using filters as clinical studies, observational studies, validation studies, randomized controlled studies and research.

A total of 260 articles were reviewed and 184 were eliminated because they were not relevant with the subject. When evaluating the relevance of the studies to the subject of the systematic review, it was taken into account that the issue of the study is related to polypharmacy, the polypharmacy rate is provided, carried out in Turkey, and that it does not represent a single drug group. Out of the remaining 76 articles, 9 were excluded because there was a the lack of definition and rate of polypharmacy, 12 were excluded due to inclusion of only a specific group of drug, and 3 articles were excluded due to high risk of bias. No exclusion criteria were considered for the study settings (hospital, nursing home, community) or time period.

The studies conducted in Turkey or studies included data related with Turkey were included. Analytic, descriptive and methodology studies that provide data on the prevalence of polypharmacy and definition on polypharmacy were included according to the search strategy. Studies conducted with patients aged <18 years and is not published as a research article (reviews, case reports, editorials, letters to the editor, short reports, comments and congress abstract) were excluded. No limitation was considered for the date of acceptance or publication. As for publication status, published articles or articles in press were considered eligible.

5.3. Study selection and data extraction

Three researchers reviewed the abstracts and full-text of the articles independently, and articles were retained if they met inclusion criteria. The agreement on inclusion or exclusion assignment was unanimous. The articles that all of the three researchers considered appropriate were included directly. On the articles which have opposing views of the researchers, a collaborative discussion was made for the final decision. A flow chart was created for eligible articles (Figure 1). The eligible articles were examined in depth by three researchers for this systematic review. The tool used for evaluating the risk of bias classification is given in the appendix.

5.4. Quality assessment

Three independent researchers assessed the risk of bias for each article by using The Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data [79]. The purpose of this checklist is to assess the methodological quality of a study and also to determine the possibility of bias in design, conduct and analysis of study.

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Conflict of interest statement: The authors declared no conflict of interest.

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Appendix

	Article	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall appraisal
1	Abunahlah N et al., 2018	Y	U	U	Y	Y	Y	Y	Y	U	I
2	Alkan A et al., 2016	Y	Y	U	Y	Y	Y	U	Y	Y	I
3	Bahat G et al., 2013	Y	Y	U	Y	N	Y	U	Y	Y	I
4	Bahat G et al., 2014	Y	Y	Y	Y	Y	Y	U	Y	Y	I
5	Ates Bulut E et al., 2018	Y	Y	U	Y	Y	U	U	Y	Y	I
6	Cakmur H., 2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	I
7	Dutoglu E et al., 2019	Y	Y	U	Y	Y	N	U	Y	Y	I
8	Kayhan Tetik B et al., 2017	Y	Y	U	Y	Y	Y	U	Y	U	I
9	Yilmazel G et al., 2018	Y	Y	U	Y	Y	Y	U	Y	U	I
10	Kizmaz M et al., 2019	Y	Y	Y	Y	Y	Y	U	Y	Y	I
11	Discigil G et al., 2006	Y	Y	U	Y	Y	N	U	Y	Y	I
12	Onal O et al., 2018	Y	Y	Y	Y	Y	Y	Y	Y	Y	I
13	Aydos TR et al., 2020	Y	Y	Y	Y	Y	Y	Y	Y	Y	I
14	Bahsi R et al., 2019	Y	Y	U	Y	Y	Y	U	Y	U	I
15	Yuruyen M et al., 2016	Y	Y	U	Y	Y	U	U	Y	U	I
16	Taskin Sayir C et al., 2014	Y	Y	U	Y	Y	Y	U	Y	U	I
17	Savran M et al., 2018	Y	Y	U	Y	Y	Y	U	Y	U	I
18	Arslan M et al., 2020	Y	Y	Y	Y	Y	Y	Y	Y	Y	I
19	Ozturk Z et al., 2017	Y	Y	U	Y	Y	U	U	Y	Y	I
20	Ozturk GZ et al., 2017	Y	Y	Y	Y	Y	Y	U	Y	Y	I
21	Demir I et al., 2020	Y	U	U	Y	Y	N	U	Y	U	I
22	Kara O et al., 2016	Y	Y	U	Y	Y	U	U	Y	N	I
23	Ertuna E et al., 2019	Y	Y	U	Y	Y	Y	Y	Y	Y	I
24	Eyigor S et al., 2020	Y	Y	Y	Y	Y	Y	U	Y	U	I
25	Gencer MZ et al., 2017	Y	Y	Y	Y	Y	Y	U	Y	Y	I

26	Kara E et al., 2019	Y	Y	U	Y	Y	Y	Y	Y	U	I
27	Kucukdagli P et al., 2020	Y	Y	U	Y	Y	Y	U	Y	Y	I
28	Kurt M et al., 2019	Y	U	Y	Y	Y	N	U	Y	Y	I
29	Kutsal YG et al., 2009	Y	U	Y	Y	Y	Y	Y	Y	Y	I
30	Oguzoncul F et al, 2018	Y	Y	U	Y	Y	Y	Y	U	U	I
31	Okuyan B et al., 2016	Y	Y	U	N	Y	Y	U	Y	Y	I
32	Selcuk A et al., 2015	Y	Y	U	Y	Y	Y	Y	Y	U	I
33	Akdogan N et al., 2019	N	Y	U	Y	Y	U	U	Y	U	E
34	Duman Atilla O et al., 2012	Y	U	U	Y	Y	N	Y	Y	U	I
35	Ozturk Z et al., 2018	Y	Y	U	Y	Y	N	U	Y	Y	I
36	Kaya CA et al., 2009	Y	Y	N	Y	U	U	U	Y	U	E
37	Karahan YA et al., 2014	N	U	U	Y	Y	N	U	N	U	E
38	Paksoy C et al., 2019	Y	Y	U	Y	Y	Y	Y	Y	Y	I
39	Sayin Z et al., 2020	Y	U	U	Y	Y	Y	Y	Y	U	I
40	Senel G et al., 2017	Y	Y	U	Y	Y	Y	U	Y	U	I
41	Silay K et al., 2017	Y	Y	U	Y	Y	Y	U	Y	U	I
42	Tasci I et al., 2019	Y	Y	Y	Y	Y	Y	U	Y	U	I
43	Topaloglu U S et al., 2020	Y	Y	U	Y	Y	U	U	Y	Y	I
44	Umit EG et al., 2020	Y	Y	U	Y	Y	Y	U	Y	Y	I
45	Unutmaz GD et al., 2018	Y	Y	Y	Y	Y	Y	U	Y	Y	I
46	Ozsurekci C et al., 2019	Y	U	U	Y	U	Y	U	Y	U	I
47	Sancar M et al., 2011	Y	Y	U	Y	U	Y	Y	Y	Y	I
48	Asci H et al., 2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	I
49	Gocer S et al., 2017	Y	Y	U	Y	Y	Y	U	Y	Y	I
50	Atmaca-Temrel T et al., 2019	Y	U	Y	Y	Y	Y	Y	Y	U	I
51	Kaplan C et al., 2019	Y	U	U	Y	Y	Y	U	N	U	I
52	Sonmez Y et al., 2014	Y	Y	U	Y	Y	Y	U	Y	Y	I
53	Varli M et al., 2017	Y	Y	U	Y	Y	Y	U	Y	U	I
54	Kocyigit SE et al., 2020	Y	Y	U	Y	Y	Y	U	Y	Y	I
55	Cakmur H et al., 2013	Y	Y	Y	Y	Y	Y	U	Y	Y	I

Y: Yes, N: No, U: Unclear, I: Include, E: Exclude