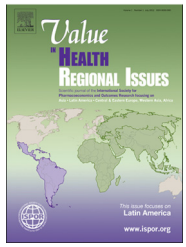
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Cost Evaluation of Inhaler Therapies Used in Respiratory Diseases: 1998–2015 Period in Turkey

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ABSTRACT

Background: With the rise in life expectancy, the burden of chronic diseases, including obstructive pulmonary diseases, has increased throughout the world. **Objectives:** To evaluate the sales trends of inhaler pharmaceuticals. **Methods:** The changes in box sales and sales amounts (in Turkish lira) of inhaler pharmaceuticals during the period 1998 to 2015 were examined and sales were projected for the next 3 years. Pharmaceuticals were classified according to form and pharmacological groups. **Results:** The sales of inhaler pharmaceuticals have increased rapidly since 2008. The fastest increase in consumption has occurred in short-acting β2 agonist preparations and nebulizer pharmaceuticals. Inhaled corticosteroid and long-acting β2 agonist combination sales have been the highest since 2002, when these products entered the Turkish market. **Conclusions:** The inhaler pharmaceutical market has grown over the years, and this growth will continue in the future. The increased use of short-acting preparations, which should be used as symptom relievers, indicates that treatment management continues to be inadequate.

Keywords: inhaler pharmaceuticals, obstructive pulmonary diseases, pharmaceutical economics.

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Introduction

Life expectancy at birth in Turkey increased from 71 years in 2000 to 77.1 years in 2015 [1]. Because increasing life spans represent a global trend, the disease burden of many countries has shifted from acute to chronic diseases. For this reason, chronic diseases, such as hypertension, diabetes, coronary heart diseases, chronic obstructive pulmonary disease (COPD), and asthma, have become a significant economic burden [2].

COPD is one of the major causes of morbidity and mortality worldwide [3]. According to the World Health Organization (WHO), COPD, which causes more than 3 million deaths per year and 5% of all deaths [4], is the fourth most common cause of death in the world and the third most common cause of death in Turkey. In a study conducted by the Ministry of Health using the Global Burden of Disease study method, COPD was found to be the eighth leading cause of disease burden [5].

Pharmaceuticals used in the treatment of COPD are divided into the following four groups: bronchodilators (i.e., β2 agonists, anticholinergics, and metilxanthines), systemic and inhaled corticosteroids, phosphodiesterase-4 inhibitors, and others (e.g., mucolytics, antitussives, immunoregulators, and vasodilators). It has been observed that when different bronchodilator pharmaceuticals are used together, the effect mechanisms can provide more bronchodilatation without increasing side effects. There are also groups of patients for whom regular treatment with intractable corticosteroids with a long-acting bronchodilator is recommended. Some global findings indicate that in most cases of stable COPD treatment, current clinical guidelines are not followed, leading to cases of overtreatment as well as incomplete cure [6,7].

Asthma is thought to affect about 300 million of the world's population. Prevalence rates range from 1% to 18%, varying among different regions of the world. On the basis of age group, the prevalence rates are 2% to 15% in children and 2% to 5% in

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adults. Despite all the developments in diagnosis and treatment, it is estimated that approximately 250,000 people die annually from asthma worldwide [8,9], and the disease is a major cause of school absences and workforce loss worldwide. Therefore, along with treatment and hospital costs, early death and workforce losses due to asthma should be considered when calculating the costs associated with the disease [9,10]. It is important to note that, similar to COPD, emergency admission and hospital admission have greatly increased costs associated with asthma [9].

The aim of treatment in asthma is to control inflammation of the airways. When a patient's current condition is controlled, future risks of asthma attacks will be prevented. If anti-inflammatory treatment is discontinued, recurrences of the problem result. In asthma treatment, two groups of pharmaceuticals are used: controller medications and rescue medications. Controller medications are daily and long-term medications used to keep asthma under control and to prevent future risks. Rescue medications are used to provide comfort as needed [8,9].

The desire to increase life expectancies in Turkey and throughout the world, combined with the need to reduce the growing burden of chronic illness, has increased the amount of research conducted in these areas. This study aimed to evaluate the sales trends of the pharmaceuticals in the Anatomical Therapeutic Chemical (ATC) Classification System R03 inhaler group (pharmaceuticals used in obstructive respiratory disease) and to examine the groups of active agents that constitute these pharmaceuticals in terms of value-based sales (in Turkish lira [TL]) and box sales. Our study is a retrospective study of the sales trends and factors that influenced these pharmaceuticals.

Methods

This article is based on the health technology assessment report of the same name (Evaluation of the Costs of Inhaler Therapy Used in the Treatment of Respiratory Diseases in Turkey: 1998–2015), prepared by the Turkish Medicines and Medical Devices Agency (TMMDA).

Sales values of inhaler pharmaceuticals in the ATC R03 group (obstructive respiratory disease drugs) during years 1998 to 2015 were examined, and the Pharmaceutical Price List published regularly by the TMMDA was used as the basic database of the pharmaceuticals evaluated in this study. The medicines selected were those listed in the R group (respiratory system) at the ATC I level included in this list. The Health Code Coding Reference Server 3 list published by the TMMDA was used to determine the pharmaceuticals' market availability on the basis of their active or passive status. The Pharmaceutical Price List and the Health Code Coding Reference Server 3 list dated December 29, 2015, were used. Since 1998, sales data on the basis of value (in TL) and box number have been obtained from the Information Medical Statistics-Health-Turkey (IMS-Health Retail; Turkey Pharmaceutical National plus Molecule Data view) database. The total number of boxes and sales values in these groups were calculated using Microsoft Excel 2010, and the lines were created via this software. Box and sales values of the inhaler pharmaceuticals in the R03 group were obtained monthly during years 1998 to 2015 from the IMS-Health database. A statistical analysis of the data was performed with IBM SPSS version 20.0 (IBM Corp., Armonk, NY). Inhaler pharmaceuticals included in the Pharmaceutical Price List dated December 29, 2015, were classified according to their descriptive characteristics and ATC groups. The sales trends of inhaler medicines in the R03 group that were licensed at any time before the end of 2015 were examined in detail. Pharmaceuticals in the R03 group were categorized into the following subgroups: metered-dose inhalers (MDIs), nebulizer solutions, and dry-powder inhalers (DPIs). In addition, inhaler medications were also subgrouped according to their pharmacological activity as follows: inhaled corticosteroid (ICS), combination of ICS and long-acting β2 agonist (ICS + LABA), LABA, long-acting antimuscarinic agonist (LAMA), short-acting β2 agonist (SABA), combination of SABA and short-acting antimuscarinic agonist (SABA + SAMA), SAMA, and others. The inhaler products external to the R03 group were not included in the study. Pharmaceuticals investigated in the study were also subgrouped according to whether they were manufactured or imported.

Assuming that the market has not changed, estimated box sales values and pharmaceutical market expenditures during 2016 to 2018 were calculated using the sales values of 2010 to 2015, for which we have the actual data. The Health Transformation Program was initiated in 2003, and the Social Security Reform was implemented in 2006. For this reason, sales figures for the year 2010 and after were used in forecasts, in which the conversion effects are fully occupied (health services and increased access to leisure). In the forecasts, models were developed with time series methods, such as the autoregressive integrated moving average, seasonal autoregressive integrated moving average, and exponential smoothing methods. The model most appropriate for use in this study was determined by testing with mean absolute error, the mean absolute percentage error, and the root mean square error.

Data in our study consist of retail sales. Hospital data were excluded in our study. The Social Security Institution covers 97% of the population and so this majority gives us a chance to understand these trends in almost all populations from each care level.

Results

General Characteristics of Inhaler Pharmaceuticals Used in Obstructive Respiratory Disease

There are a total of 457 active pharmaceuticals in the respiratory system group (ATC-1 R) on the agency's Pharmaceutical Price List dated December 29, 2015. There are 161 active pharmaceuticals listed in the R03 (drugs used in obstructive respiratory disease) group, of which 103 are inhaled.

The number of inhaler pharmaceuticals in the R03 group has shown a rapid increase since 2009 in terms of both product and brand, whereas the number of molecules has not changed considerably. From 1998 to 2015, the number of inhaler pharmaceuticals in the R03 group increased from 45 to 103 (Fig. 1).

Sales Trends of Inhaler Pharmaceuticals Used in Obstructive Respiratory Disease

The total annual sales volume of inhaler pharmaceuticals according to number of boxes and sales amounts (in TL). In the R03 group, 2.6 million boxes of inhaler medicines were sold in 1998, whereas sales in 2015 reached 40 million boxes. Over the years, the share of inhaler sales in total pharmaceutical sales has increased on a box basis. The share, which was 0.4% in 1998, increased to 1.45% in 2010 and to 2.10% in 2015. Similarly, the total amount of sales of these medicines was 6.6 million TL in 2010 and reached 625 million TL in 2015. The highest annual amount, of the years examined in the survey, was realized in 2010, which was 645 million TL. The share of inhaler pharmaceuticals investigated in the study was 1.3% in 1998 and 3.5% to 4.5% in 2006 (both in TL).

The rates of inhaler pharmaceuticals used in the treatment of obstructive respiratory diseases according to their manufacturing and import status are shown in Figure 2A,B. A review of

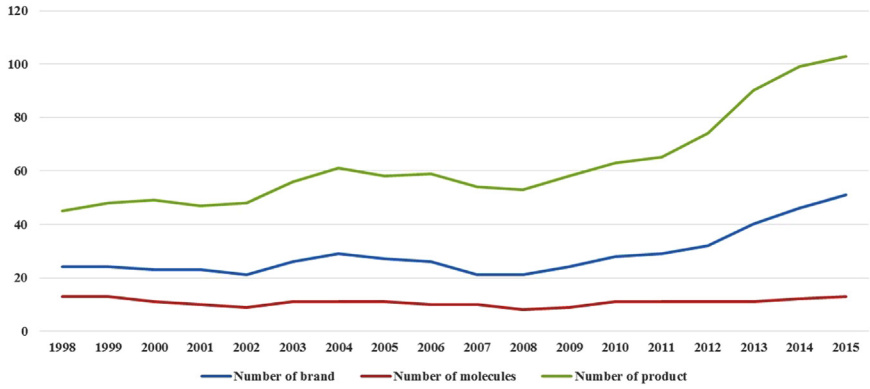


Fig. 1 – The cumulative number of molecules, products, and brands of inhaler medicines in the R03 group that were licensed at any time before the end of 2015, annually.

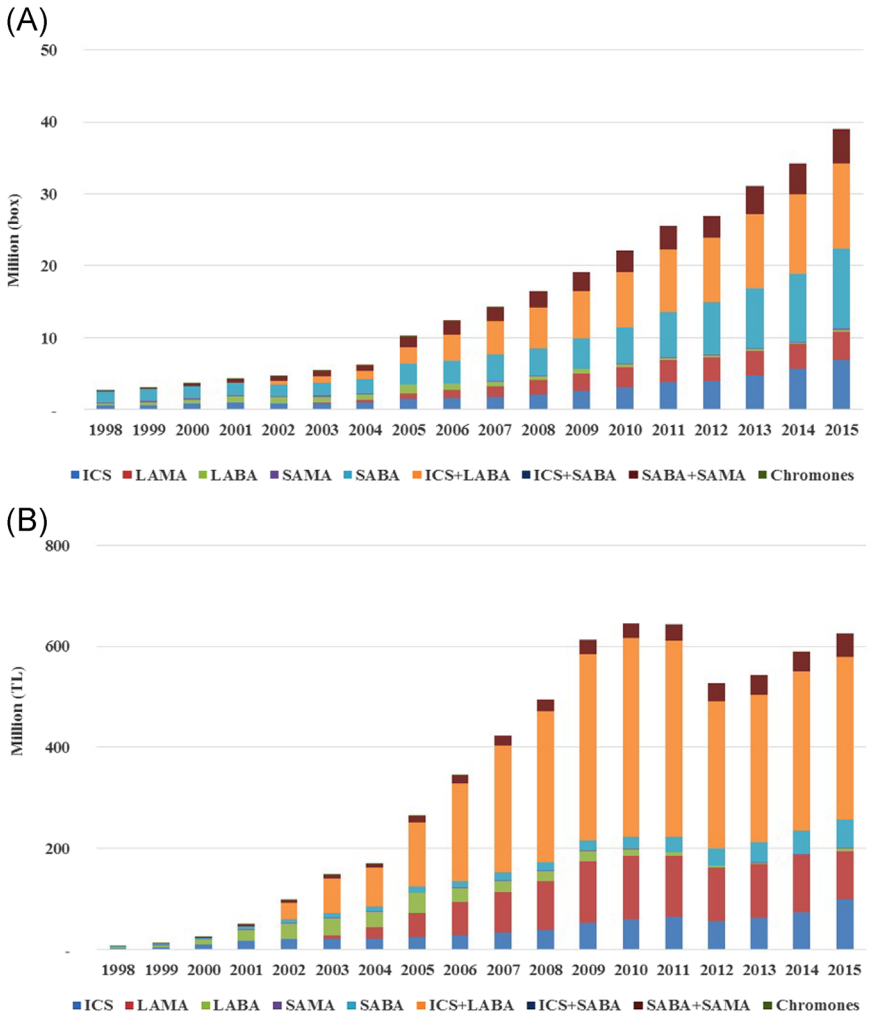


Fig. 2 – (A) Annual box sales. (B) Sales amounts (in TL) of the subgroups of inhaler pharmaceuticals used in the treatment of obstructive respiratory diseases according to their pharmacological activity in the Turkish market between the years 1998 and 2015. ICS, inhaled corticosteroid; ICS + LABA, combination of inhaled corticosteroid and long-acting β2 agonist; LABA, long-acting β2 agonist; LAMA, long-acting antimuscarinic agonist; SABA, short-acting β2 agonist; SABA + SAMA, combination of short-acting β2 agonist and short-acting antimuscarinic agonist; SAMA, short-acting antimuscarinic agonist; TL, Turkish lira.

box-based sales indicated that the production rate, which was 7% in 1998, declined to 1% in 2010. In 2012, this rate started to increase rapidly and reached 20% in 2015. An examination of value-based sales revealed that the production rate, which was 4% in 1998, fell lower than 1% in 2005 and remained at this level until 2012. In line with box sales, this rate started to increase at a rapid pace by 2012 and exceeded 20% by 2015.

Sales Trends of Pharmacological Subgroups of Inhaler Pharmaceuticals Used in Obstructive Respiratory Disease

The annual sales of the subgroups of inhaler pharmaceuticals are presented according to their pharmacological activity in Figure 2A,B; subgroups based on box sales and sales amounts are shown in Figure 2A,B.

The fastest increase in recent years is in combination preparations of SABA and ICS + LABA, followed by ICS preparations. The sales of chromone-group pharmaceuticals decreased until 2005, after which they were pulled out from the market. Since 2002, with the introduction of ICS + LABA combination products in the Turkish pharmaceutical market, their use has increased and has become the most commonly used treatment. As a result, the sales of LABA alone have gradually decreased. Another noteworthy finding is that box sales of both ICS and SABA pharmaceuticals have increased in recent years (Fig. 2A). Total box sales by subgroups in 2015 were 11.8 million boxes for ICS + LABA combinations, 11.1 million boxes for SABA preparations, and 6.8 million boxes for ICS preparations. Prices per box of ICS, SABA, and LAMA increased regularly till 2004. Prices then decreased by 10% on average in all subgroups. In these subgroups prices per box increased by 28% on average from 2005 to 2010. These prices decreased from 2011 to 2015 (Table 1).

A subgroup analysis of the increase in the sales amounts of the inhaler pharmaceuticals in the R03 group revealed that the sales of ICS + LABA combinations are currently the highest since their introduction into the market in 2002. Nevertheless, as of 2012, there has been a slight decrease in the sales of ICS + LABA combinations. Although the LAMA preparations that entered the market in 2003 represent the second highest total sales amount between 2005 and 2014, the total sales amount of ICS preparations in 2015 exceeded this group's sales amount (Fig. 2B). In terms of the subgroups, total sales amounts in the year 2015 were 322.5 million TL for ICS + LABA combinations, 98.9 million TL for ICS preparations, and 94.9 million TL for LAMA preparations.

Sales Trends of Inhaler Pharmaceuticals Used in Obstructive Respiratory Disease According to Their Forms

The annual sales of the subgroups of inhaler pharmaceuticals according to their forms are shown in Figure 3A,B; subgroups are presented based on box sales and sales amounts in Figure 3A,B.

The inhaler pharmaceuticals in the R03 group that are present in the market are metered dose inhalers (MDIs), DPIs (inhaler capsules, Diskus, Turbuhaler, Easyhaler, Handyhaler, and Twisthaler), and nebulizers. In recent years, the use of nebulizers has increased more than that of other inhaler pharmaceuticals. At the end of the 1990s, the ratio of MDI pharmaceuticals was about 70%; nevertheless, it has currently fallen to lower than 30%.

In terms of form types, total box sales were 14.5 million boxes for DPIs, 13.5 million boxes for nebulizers, and 10.9 million boxes for MDIs in 2015. The maximum sales amount is for DPIs, but the number of nebulizers has been maintained regularly during the last 3 years and the number of MDI forms has increased regularly since 2009. The total cost of DPIs has decreased proportionally since 2010 (Fig. 3B). On the basis of form types, total sales amounts were realized as 369.9 million TL for DPIs, 143.5 million TL for nebulizers, and 111.4 million TL for MDIs in 2015.

Table 1 – Price per box of inhaler pharmaceuticals by years 1998–2015.

Year	Price (TL)									
	ICS	LABA	LAMA	SAMA	SABA	ICS + LABA	ICS + SABA	SABA + SAMA	Chromones	Total
1998	4.53		6.57	1.83	1.01		2.28	1.74	3.40	2.49
1999	7.32		10.06	2.91	1.47		3.32	2.47	5.77	4.02
2000	10.84		14.90	3.95	2.15		5.00	3.30	6.85	6.42
2001	16.94		26.01	5.22	3.11		7.35	5.38	8.32	11.37
2002	22.37		37.60	7.87	4.64	69.01	11.32	8.29	14.08	21.16
2003	23.93	70.81	43.22	8.97	5.13	80.14	12.57	9.62	15.36	27.67
2004	20.79	64.36	38.09	9.17	4.81	71.13	11.90	9.14	14.48	27.38
2005	16.88	58.62	33.03	8.67	4.16	55.51	11.57	8.82	13.00	26.06
2006	17.53	56.36	32.77	8.49	4.22	53.23		9.13	13.80	28.11
2007	18.17	53.66	33.77	9.12	4.45	53.87		10.19	19.60	29.72
2008	17.81	50.26	33.11	9.16	4.32	52.51		10.43		30.03
2009	19.90	51.22	36.68	9.93	4.83	56.06		10.77		31.98
2010	19.10	45.14	34.31	9.04	4.71	51.73		9.05		29.08
2011	16.84	39.08	26.00	7.74	4.73	44.45		9.34		25.13
2012	14.19	31.73	18.75	6.74	4.68	32.59		11.27		19.53
2013	12.98	31.12	14.13	7.30	4.80	27.96		10.32		17.46
2014	13.32	31.16	18.42	7.42	4.97	28.21		9.48		17.23
2015	14.41	24.14	22.02	7.40	5.04	27.33		9.45		16.01

ICS, inhaled corticosteroid; ICS + LABA, combination of inhaled corticosteroid and long-acting β2 agonist; ICS + SABA, combination of inhaled corticosteroid and short-acting β2 agonist; LABA, long-acting β2 agonist; LAMA, long-acting antimuscarinic agonist; SABA, short-acting β2 agonist; SABA + SAMA, combination of short-acting β2 agonist and short-acting antimuscarinic agonist; SAMA, short-acting antimuscarinic agonist; TL, Turkish lira.

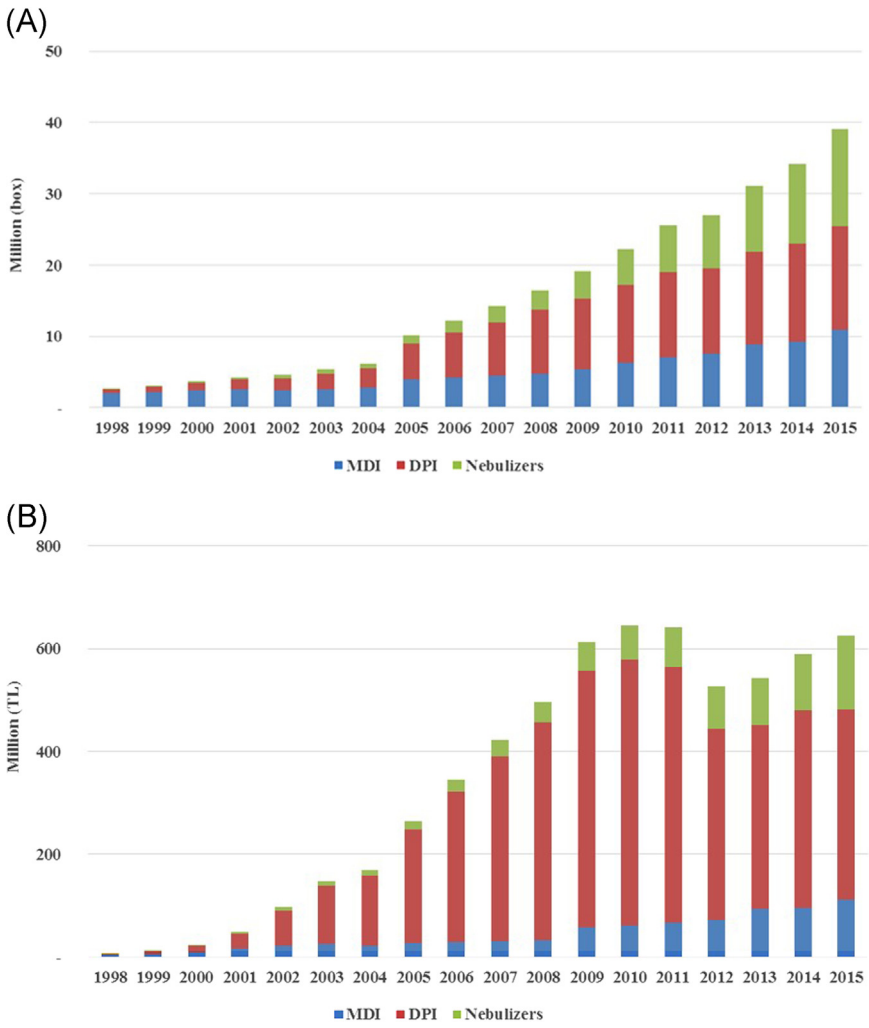


Fig. 3 – (A) Annual box sales. (B) Sales amounts (in TL) of the subgroups of inhaler pharmaceuticals used in the treatment of obstructive respiratory diseases according to their forms in the Turkish market between the years 1998 and 2015. DPI, dry-powder inhalers; MDI, metered-dose inhalers; TL, Turkish lira.

Monthly Sales Projection of Inhaler Pharmaceuticals Used in Obstructive Respiratory Diseases

Data were analyzed to project box sales and sales amounts between the years 2016 and 2018 using the data for 2010 to 2015 of inhaler pharmaceuticals used in the treatment of obstructive respiratory diseases. It was determined that the data are in a nonstationary structure showing seasonality. It has been estimated that the sales of medicines investigated during the surveyed years will increase in terms of both box sales and sales amounts. According to the models implemented in 2015, the annual box sales market is expected to grow by 26% and the market cost by 12% in 2018 (Fig. 4A,B).

Discussion

Consistent with the global trend, the average life span in Turkey has increased [1,2]. The Turkish Statistical Institute has reported that the total population, as well as the population older than 65 years, will continue to increase in the coming years [11]. As a result, the disease burden of many countries is shifting from acute diseases to chronic diseases, such as hypertension, diabetes, coronary heart disease, and COPD [2]. On the basis of the Burden of Obstructive Lung Disease trial conducted in 12 countries, the prevalence of COPD in the population older than 40 years reached 25% when a fixed ratio criterion was used; when the Global Initiative for Chronic Obstructive Lung Disease stage II criterion was used with this ratio, the prevalence was determined to be 10.1% (11.8% in males and 8.5% in females). A part of this study was conducted in Adana, Turkey, in the year 2004, and the prevalence of COPD was determined to be 19.1%, with a fixed ratio of adults older than 40 years [12]. In a study conducted by the Ministry of Health using the Global Burden of Disease study method, COPD was ranked eighth among the leading causes of disease burden. Moreover, the secondary direct (diagnostic and treatment expenditure) and indirect (economic consequences of disability, lost work, premature death, and family income due to illness) costs of COPD are quite high [5]. In the European Union, the direct cost of respiratory disease accounts for 6% of the total health budget, and COPD accounts for 56% of the direct cost of respiratory diseases [6]. A significant portion of the total cost of COPD constitutes treatments and hospital costs for acute exacerbations [13–15]. In addition, hospital and emergency admission costs account for nearly 72.8% of all COPD-related costs [16]. The frequency of asthma is 4.5% in Turkey. The age-standardized

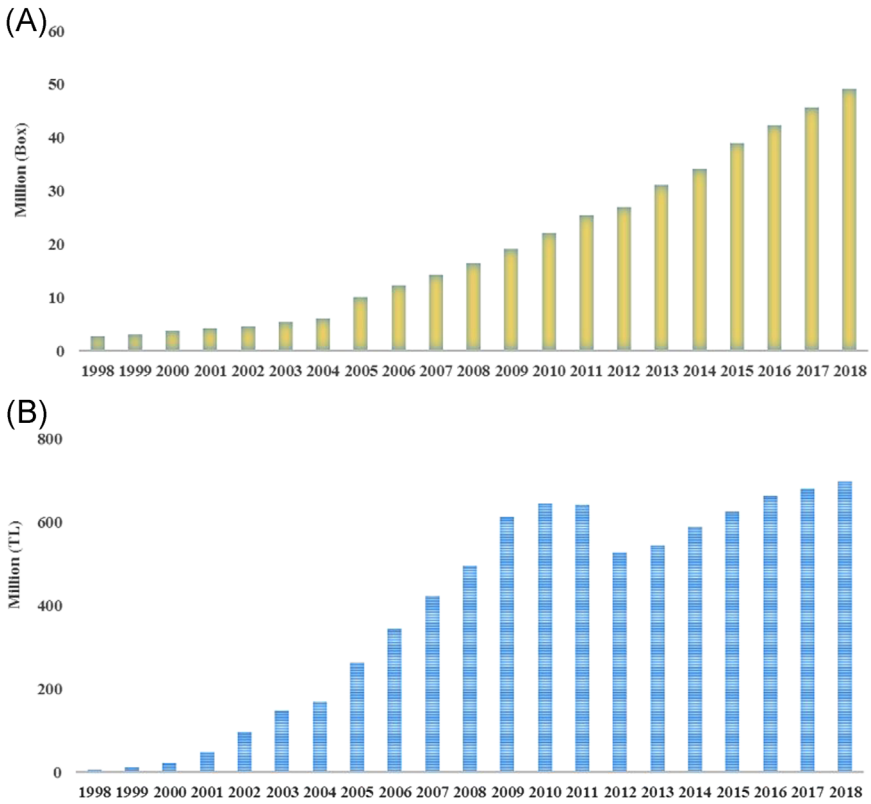


Fig. 4 – (A) Projected box sales. (B) Sales amounts (in TL) between the years 1998 and 2018 using the data for 2010–2015 of inhaler pharmaceuticals used in the treatment of obstructive respiratory diseases in the Turkish market.

asthma frequency is 2% for males and 6.2% for females. Out of the patients with asthma diagnosed by the physician, 62.2% have compliance with medication [17]. Asthma is also a major cause of school absences and workforce loss throughout the world. The WHO reported that, globally, the annual loss of life (15 million injuries per year) is equal to 1% of the total losses due to all diseases [8,9]. In a study of adults with asthma in Turkey, the total annual cost associated with COPD was US $1.467 ± $111.8 [10]. It should be noted that the cost of disease is closely related to asthma severity and control; nevertheless, admission to the emergency room or to the hospital greatly increases the cost [9].

Stable COPD treatment comprises both pharmaceutical and nonpharmaceutical approaches. Patient education, reduction or elimination of exposure to environmental risk factors, smoking cessation, lung rehabilitation, and daily regular physical activity, some of the nonpharmaceutical approaches used, have an important place in treatment management [6,7]. Similarly, asthma treatment consists of both pharmaceutical and nonpharmaceutical treatments (e.g., smoking cessation, prevention of exposure to environmental risk factors, physical activity, prevention of occupational exposures, disruption of disease control, withdrawal of allergens, weight loss, vaccination, and prevention of indoor and outdoor air pollution). Additional treatments include pharmaceutical compliance and control of the inhaler technique, removal of triggers, treatment of altered risk factors, and components of asthma therapy [9].

Turkey became a signatory of the WHO Framework Convention for Tobacco Control in 2004. In 2007, Turkey introduced a comprehensive tobacco control law that included a complete ban on smoking in public places in 2008. The tax on tobacco products was increased to 78% of cigarette costs, which met with WHO recommendations. These interventions have helped to reduce daily smoking prevalence in the Turkish adult population (those aged 15 years or older) from 32.1% in 2003 to 23.8% in 2012 [18]. Nevertheless, the Turkish Pharmacists' Association launched a project titled "Smart Pharmacy" for community pharmacies with the aim to provide better services to patients. First pilot results were obtained for inhaler pharmaceuticals. Results show that the use of salbutamol decreased by about 30% in pilot retail pharmacies [19].

The number of inhaler pharmaceuticals used in respiratory system diseases has shown a rapid increase since 2008 in terms of both product and brand. Nevertheless, consistent with the world market, the number of molecules has not changed substantially. A review of the sales of free pharmaceuticals reveals that sales of inhaler pharmaceuticals used in respiratory system diseases seem to have increased rapidly over the years. In addition, the share of box sales of inhaler pharmaceuticals in total pharmaceutical box sales has appeared to increase. In 1998, these pharmaceuticals constituted 0.4% of total pharmaceutical sales, whereas this share increased to 1.45% in 2010 and to 2.1% in 2015. One of the major reasons for the increase in total pharmaceutical box sales is the ease of access to health care services and the provision of health care services following the Health Transformation Program. As awareness campaigns to recognize the illness have led to the ability for patients to consult with, and undergo diagnosis by, doctors, postgraduation training for physicians has also extended the treatment approaches consistent with the guidelines of the diseases. There are other reasons for the increase in total pharmaceutical box sales, such as population growth, an increase in the proportion of the elderly population in the total population, and individual prolonged life expectancy. Smoking cessation and reduced exposure to environmental and occupational risk factors are major measures that can be taken in the long run to reduce the consumption of this

group of pharmaceuticals. As projected in this study, it is predicted that the market formed by inhaler pharmaceuticals will continue to grow over the years. It has also been acknowledged that the elderly population (5.7 million in 2012) will reach 8.6 million in 2023 [11]. The expected result is the future prevalence of chronic diseases such as COPD and the sales of medicines used in the treatment of these diseases. Similarly, this study indicates that inhaler pharmaceutical box sales are expected to increase by 26% in 2018 (year-on-year from 2015), whereas market costs are expected to increase by 12% on the assumption that current pharmaceutical reimbursement policies will continue and there will be no unusual fluctuations in exchange rates. This study also revealed that consumption of inhaler medications showed seasonal ups and downs and that these periods overlapped with exacerbation periods of asthma and COPD diseases. With respect to COPD and asthma, it is important to note that the cost of major diseases worldwide is closely related to disease control attacks, urgent applications, and hospitalizations [9,10,13–15].

In the treatment of obstructive airway diseases such as asthma and COPD, the medicines recommended in the various treatment guidelines are generally similar, although there have been some changes over the years. Appropriate pharmaceutical therapy is indicated to reduce symptoms and exacerbations associated with these diseases and to improve quality of life, health status, and exercise tolerance [6,7,9]. For this reason, the management of asthma and COPD should be planned in accordance with current guidelines. On the basis of current literature, Spencer et al. [20], in the TRial of Inhaled. STeroids ANd long-acting β2 agonists (TRISTAN) study, showed with the model they developed that the quality of life and the cost benefit were higher in the group using ICS and LABA for patients with COPD. In an extended study conducted by Chandra et al. [21], quality of life and cost-effectiveness were measured by setting up a treatment model involving smoking cessation programs, multidisciplinary care teams, pulmonary rehabilitation, long-term healing therapy, and ventilation strategies in the Ontario study. As observed in this study, the use of ICS + LABA combinations had been increasingly common in the treatment of obstructive pulmonary diseases until 2002, when treatment with short-acting bronchodilators was started in 2002 with the introduction of ICS + LABA combination products to the Turkish pharmaceutical market and clinical treatment guidelines. As a result, LABA and ICS box sales have decreased; in particular, the proportion of LABA sales alone fell to lower than 1%. The recent introduction of SABA and ICS + LABA represents the fastest increase in pharmaceuticals for the treatment of COPD in Turkey. Moreover, one of the fastest increases in consumption in recent years appears to be in SABA preparations. The increase in the use of short-acting preparations, which should be used as symptom relievers, is an indicator that the treatment management of these diseases remains inadequate, which increases the frequency of uncontrolled episodes of patients with asthma, resulting in more expensive hospital treatment. In addition, the consumption of inhaled medicines in nebulizer form, which should be used more often in medical institution settings and to treat hospitalized patients, young children, and patients with poor inhaler compliance, has been increasing regularly in recent years. This suggests that the excess consumption of nebulized pharmaceuticals leads to increased consumption of the β2 agonist preparations.

The total annual costs of inhaler pharmaceuticals during the period 1998 to 2009 increased significantly, as noted in our research. The total annual costs of these pharmaceuticals remained at their current levels between 2009 and 2011, and experienced a sharp decline in 2012. Beginning in 2013, the annual cost has increased to reach the 2009 level again in 2015. Although the political interventions implemented between 2009 and 2011 through Turkey's pharmaceutical pricing and reimbursement policies (i.e., the change in the reference price application and additional public discounts introduced in 2009 and 2011 and the global budget implementation during 2010–2012) were effective in terms of this group of pharmaceuticals, this effect has begun to disappear after the year 2013. This study indicated that the sales amount of ICS + LABA combinations has been the highest since 2002, when the subgroup analysis of the increase in sales amounts of medicines used by the R03 inhalation group was performed. Nevertheless, as of 2012, there has been a slight decrease in ICS + LABA sales figures. As a result, the market shares of each of the ICS + LABA combinations have increased. The LAMA preparations that entered the market in 2003 had the second highest total sales amount between 2005 and 2014, whereas the total sales amount of ICS preparations in 2015 exceeded this group's sales amount. The generics of the LAMA preparations entered the market at the end of 2014.

Many developments that will affect the medicine market and facilitate access to the medicine occurred in line with the Health Transformation Program started in 2003 and the Social Security Reform implemented in 2006. These developments particularly include transferring to reference price implementation in 2004; transferring to Family Medicine System first in pilot provinces in 2005 and then in all provinces in 2010; establishing the Social Security Institution in 2006; establishing the Reimbursement Commission within the Social Security Institution in 2007; bringing about compulsion of reimbursement application file in 2008, retail sales price cuts, and additional reimbursement discounts at the end of 2009; and issuing a global budget between 2010 and 2012, with further retail sales price cuts and additional reimbursement discounts at the end of 2011. In this study, we demonstrated that on transferring to reference price implementation in 2004, retail sales price cuts and additional reimbursement discounts at the end of 2009 and 2011 affected the prices of boxes of all the subgroups. It can be predicted that the total annual costs of inhaler pharmaceuticals could be higher than those occurring without these regulatory interventions during this period [18].

An examination of box-based sales revealed that the manufacturing rate in Turkey had declined from 7% to 1% between 1998 and 2010. As of 2012, this rate started to increase rapidly and reached 20% in 2015. An examination of value-based sales showed that the production rate, which was 4% in 1998, fell to lower than 1% in 2005 and remained at this level until 2012. In line with box sales, this rate started to increase at a rapid pace in 2012 and exceeded 20% by 2015. Despite the increase in the value-based ratios of manufactured inhaler medicines in recent years, the weight of imported medicines in this market continues. For this reason, there is a need to increase the current production capacity and to create a structure that produces higher value-added pharmaceuticals.

Study Limitations

The IMS-Health Retail database shows pharmaceutical sales in the pharmacies from wholesalers. In this form of the database, hospital use of pharmaceutical data is not available. For this reason, our study includes retail sales from public pharmacies. Cost-effectiveness analysis has not been the aim in our study.

Conclusions

Chronic diseases such as COPD and asthma have resulted in a significant economic burden throughout the world. Our study is a retrospective study of the sales trends and factors that influenced these pharmaceuticals. The budget of inhaler pharmaceuticals

has increased over the years. Regulatory interventions such as reference pricing and price cuts have had an impact on the pricing of these products since 2004.

In our study, the increase in the use of short-acting preparations, which should be used as symptom relievers, indicates that the management and treatment of these diseases continue to be inadequate. The necessity of planning the management of asthma and COPD according to current guidelines has once again been confirmed.

Health systems should try to provide better and more cost-effective solutions for delivering health care to an increasing number of patients with chronic illnesses. To analyze other aspects in this scope, further studies such as cost-effectiveness studies need to be carried out in the future.

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