Research Article

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The Investigation of the Relationship Between Pharmaceutical Consumption and Health Status

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ABSTRACT

It is thought that it is important to reveal the contribution of pharmaceutical consumption to health outcomes because the share of pharmaceutical expenditures in health expenditures is quite high and the debate about controlling healthcare costs. The study aims to examine the relationship between pharmaceutical consumption and the health status of EFPIA member countries with canonical correlation analysis. It was found that the health status of the EFPIA member countries and their pharmaceutical consumption were strongly correlated (r_c=75.9). According to canonical cross loadings, the variable of life expectancy at birth (0.846), which has the strongest relationship with its own set, also establishes the strongest relationship with pharmaceutical consumption (0.642). The pharmaceutical consumption dataset remarkably correlates with antidepressant use and lipid use, respectively. According to canonical cross loadings, antidepressant use, which had the strongest association with its own set, had the strongest association with the health status dataset (0.592). This research provides evidence that pharmaceutical consumption and the health status of EFPIA member countries are positive associated. It is thought that the potential of pharmaceutical-related interventions can be exploited as a way to improve the health status.

Keywords: Canonical Correlation Analysis, EFPIA, Health Outcomes, Pharmaceutical Expenditure, Pharmaceutical Industries

1. Introduction

Medicines are critical in the management of diseases at every stage of healthcare, including prevention, diagnosis, treatment, palliative care and rehabilitation. Medicines, play a part in preserving life for health systems. When viewed from a broader perspective, medicines are tools that protect public health. This makes medicines a critical product for the entire society [1, 2]. Medicines, which have a place in the provision of healthcare, constitute a critical part of health expenditures. It is stated that even when medicines used during hospital treatment are not included, spending on pharmaceuticals constitutes approximately one-sixth of health expenditure in Europe [3]. Access to healthcare, treatment and medicine may differ among income groups, ethnicities, cities and countries [4]. It is stated that governments should provide financial support to meet this need. Even pharmaceutical companies are considered to have a human rights responsibility to ensure that medicines, which are seen as the fruits of science, are accessible to all who need them [5].

Pharmaceutical consumption is increasing due to an aging population, the growing need for medicine to treat chronic diseases, and changes in clinical practice. The Organization for Economic Cooperation and Development (OECD) provides data by classifying data on pharmaceutical consumption according to Anatomic Therapeutic Chemical Classification (ATC) codes. However, four main medicine groups have come into prominence, which are used to treat diseases whose prevalence has increased significantly in OECD countries recently. These are antihypertensives, lipid-modifyings (cholesterol-lowering), anti-diabetic and anti-depressants [6]. Chronic diseases are health issues that must be followed throughout life and need long-term medicine use. These diseases include cancer, chronic respiratory diseases, heart diseases, stroke and diabetes [7, 8]. Since the treatment of chronic diseases requires the use of medicines to a large extent, the pharmaceutical industry has positive effects on achieving the desired health outcomes for these patients [9].

Medicines, which are main of medical treatment, constitute a significant burden of health expenditures [10]. The variation in pharmaceutical expenditures and pharmaceutical consumption across countries raises an obvious question. Is there a measurable health benefit from high pharmaceutical consumption? [11]. It is widely accepted to assess each country's health status indicators ~~in~~ to measure health benefits. Measuring the health status of countries has been interesting for years [12]. Generally, indicators such as life expectancy at birth, life expectancy over 65 years, infant mortality rate, mortality rate are preferred to measure the health status of a country [13].

Since many researchers wonder about the evaluation of the health outcomes obtained in return for the resources allocated to health, many researches related to this issue have been carried out in the past [14, 15, 16]. Especially, research on health outcomes obtained through health expenditures draws attention. In research on the pharmaceutical sector, the attention has generally been on the relationship between pharmaceutical expenditures and health status. Many studies have found that the increase in pharmaceutical expenditures is associated with an increase in life expectancy at birth [11, 17, 18, 19, 20]. In a study conducted in European Union countries, in addition to the relationship between health status, health and pharmaceutical expenditures, antibacterial pharmaceutical consumption daily dose per 1000 people was also included in the analysis. In this study, it was concluded that pharmaceutical consumption has a positive effect on life expectancy at birth [17].

It is generally accepted that medicines can provide significant health promotion and, increase life expectancy and decrease infant mortality eventually [18]. The results of the research show that there are strong positive relationships between health outcomes and pharmaceutical expenditures. In fact, there are results that better health outcomes are observed in regions with higher pharmaceutical expenditures [19]. Additionally, it has been stated that innovation in the pharmaceutical industry also leads to promotions in health outcomes [21]. There are results that increased pharmaceutical expenditures result in a reduction in the mortality rate and an increase in quality of life, especially for middle-aged and older people [11, 22, 23].

In the studies associating the pharmaceutical industry with health outcomes, mostly pharmaceutical expenditures were used [11, 17, 18, 19, 20]. Additionally, the pharmaceutical expenditures under the name of pharmaceutical consumption were used in most of the studies expressed as pharmaceutical consumption [11, 22]. It is thought that it is important to reveal the contribution of pharmaceutical consumption to health outcomes because the share of pharmaceutical expenditures in health expenditures is quite high and the debate about controlling healthcare costs. This research aims to examine the relationship between pharmaceutical consumption indicators and health status with canonical correlation analysis in the member countries of the European Federation of Pharmaceutical Industries and Associations (EFPIA), including Turkey.

2. Materials and Methods

EFPIA, represents the pharmaceutical industry operating in Europe [24]. In the research, the relationship between indicators of pharmaceutical consumption and indicators of health status was examined with canonical correlation analysis in 23 EFPIA member countries, including Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Portugal, Slovakia, Slovenia, Spain, Sweden, Turkey, England.

2.1. Variables of The Research

The dependent variables of the research are the variables in the health status category. Variables such as life expectancy, cause-specific and total mortality rates, and infant mortality rate are widely used to assess the health status of the population. Based on the literature, life expectancy at birth, probability of dying from chronic diseases, non-communicable disease mortality rate, adult mortality rate and self-rated health variables were chosen as health status variables [25]. Since the independent variables constituting the second data set as a health status variable are specific to chronic diseases, the probability of dying from chronic diseases and the non-communicable disease mortality rate variables were preferred for the purpose of the research over the maternal and child mortality rate. The source of life expectancy at birth, probability of dying from chronic diseases (%), adult mortality rate (per 1000 population), and percentage of deaths from non-communicable diseases (NCD) is the World Health Organization (WHO). The source of the self-rated health (bad or very bad) variable is the OECD.

The independent variables of the study are the pharmaceutical consumption data of the countries examined. The source of these variables is the OECD. These include the use of hypertension medicine at (defined daily dose per 1000 people), the use of lipid-modifying agents, the use of anti-diabetics, and the use of anti-depressants.

2.2. Analysis of Data

Canonical correlation is a multivariate analysis technique that determines the correlation between two sets of variables. This can be shown as [26]:

$(X_1+X_2+X_3+...+X_n)\leftrightarrow(Y_1+Y_2+Y_3+...+Y_n)$

The canonical correlation coefficient is the correlation coefficient used ~~is~~ to determine the degree of relationship between two sets of quantitative variables ($p\geq2$ and $q\geq2$), one of which contains p and the other q variables. It is not necessary for the number of variables in the clusters to be equal in order to perform this analysis. One of these two sets of variables can be the dependent variable and the other the independent variable [27].

A separate linear component is generated from each of the two sets of variables so that the correlation between the two linear components is maximum. It is obtained from two component pairs as the number of variables in the smallest set. The first component accounts for most of the total variance. Two pairs of derived components, one dependent and the other independent, are called canonical components. Inter-set components are interpreted according to coefficients called inter-set loading. These coefficients reflect the importance of the original variables in the derivation of the components between sets. Additionally, it is also determined which inter-set variable a variable plays an important role in [26].

Significance tests are of great importance as only statistically significant canonical correlations have to be interpreted [28]. There are different approaches to testing significance in canonical correlations. For example, the Barlett test is one of them. It tests whether a canonical correlation or a set of canonical correlation coefficients is nonzero. The Barlett test is a test based on the chi-square distribution. Additionally, the F test is also widely used in testing significance [27].

The hypotheses in the Wilks Lambda test statistic, which is used to test the significance of the canonical correlation coefficients, are as follows [26]:

$H_0= C_1= C_2= \ldots =C_n= 0$

Canonical correlation coefficients are equal to zero. This means that the correlation coefficients are statistically nonsignificant.

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$H_1 \neq C_1 \neq C_2 \neq \ldots \neq C_n \neq 0$

Canonical correlation coefficients are nonzero. This means that the correlation coefficients are statistically significant.

Rejecting the null hypothesis indicates that at least the first canonical correlation coefficient is statistically significant [27]. The Wilks Lambda (Λ) statistic, which can be used to determine the significance level, is obtained as follows. “k” is the number of calculated canonical correlations [27]:

$$\prod_{i=1}^{k}(1-r_{ci}^{2}\,A=\pi r^{2}$$

The chi-square test statistic is obtained as follows:

$$X^2 = -\left[n-1-\frac{p+q+1}{2}\right]\ln(\Lambda)$$

n = Number of observations

p and q = Variable numbers in sets

Canonical loadings are used to interpret the canonical correlation coefficients. Canonical loadings show which variable affects which canonical variates and to what extent. Statistically significant ones among the canonical variates need to be interpreted [26].

Additionally, the variance explained is a value obtained by dividing the sum of the squares of the canonical factor loadings in the relevant cluster by the number of related variables. This value provides information about the average extent to which the variability in the dataset regarding the related canonical loads is explained. Measures that determine the extent to which any variable set explains the variance of the other are called redundancy measures [26, 27].

2.2.1. Assumptions of Canonical Correlation Analysis

Canonical correlation analysis has assumptions of linearity, multivariate normality, homoscedasticity and multicollinearity [29]. The assumption of normality of variables was tested with the Shapiro-Wilk test in this research. Multicollinearity which is another assumption, was tested with multi-correlation analysis among dependent and independent variables. It was observed that there was a significant negative relationship between life expectancy at birth and probability of dying from chronic disease (r_s=-0.971, $p<0.05$); life expectancy at birth and adult mortality rate (r_s=-0.969, $p<0.05$); life expectancy at birth and variables of self-rated health (r_s=-765, $p<0.05$). Additionally, it was observed that there was a significant positive correlation between probability of dying from chronic disease and adult mortality rate (r_s=0.942, $p<0.05$); the probability of dying from chronic disease and the variables of self-rated health (r_s=0.750, $p<0.05$). There was also a significant positive correlation between adult mortality rate and variables of self-rated health (r_s=0.824, $p<0.05$). Because of the analysis assumptions, the probability of dying from chronic disease, self-rated health, and adult mortality rate variables from the health status set were excluded from the scope of the research.

2.2.2. Model of The Research

This research aims to determine whether there is a correlation between the pharmaceutical consumption data set (X_1, X_2, X_3, X_4) and the health status data set (Y_1, Y_2) and to determine the variables that contribute to this correlation at the highest level. The model of the research is given in Figure 1.

2.3. Limitations

Since the research was conducted in European countries, countries that were economically developed or developing countries and whose data could be accessed were included in the study. In studies using secondary data, it is important to include data from the same years in the analysis so that the data can be compared. Although the most recent data obtained in this research is used, it uses data from years close to each other. Additionally, cross-country differences in pharmaceutical consumption may reflect differences both in disease prevalence across countries and variations in clinical practice.

3. Results and Discussion

Descriptive findings of variables used in the study are presented in Table 1. Accordingly, the lowest life expectancy at birth was 75.3, while the highest was 83.2 in the countries studied. The average probability of dying from a chronic disease is 12.4%. However, this probability varies between 8.38% and 22.13%. In the countries studied, an average of 9.3% of the population over the age of 15 rated their health status as bad or very bad. It was found that the antihypertensive drug consumption per 1000 population, averaged of 347. It has been determined that the average consumption of lipid-modifying agents per 1000

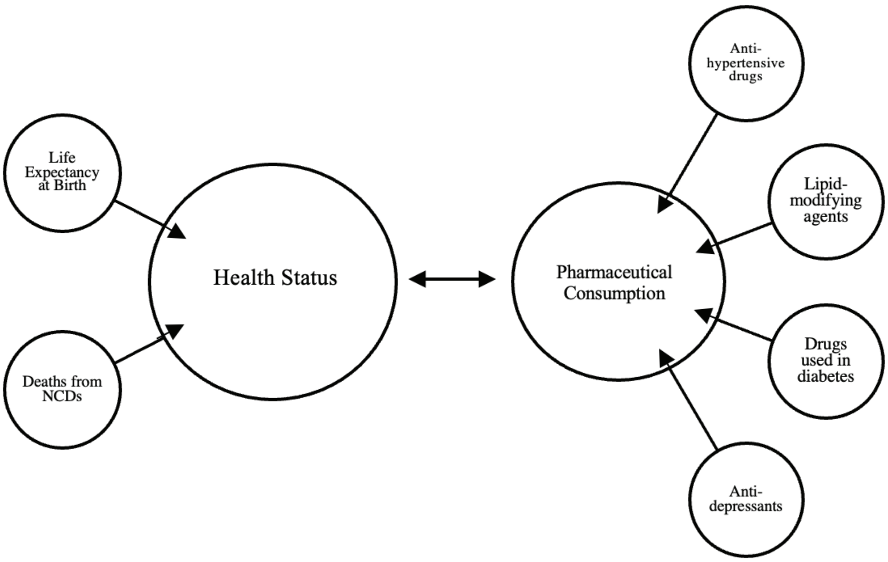

Figure 1. Model of the research.

people is 113.9, the consumption of diabetes is 72 per 1000 people, and the amount of anti-depressant drug consumption is 66 per 1000 people on average.

Table 2 shows the results of the multiple correlation analysis for the health status and pharmaceutical consumption variables examined within the scope of the research. The results of the correlation analysis between dependent and independent variables show that there is a significant positive correlation (r_s=0.477, p<0.05) between life expectancy at birth and anti-depressant consumption. A significant negative correlation was found between the probability of dying from chronic diseases and lipid drug consumption (r_s=-0.459, p<0.05) and the probability of dying from chronic disease and anti-depressant drug consumption (r_s=-0.604, p<0.05). A significant ~~a~~ negative correlation was found between adult mortality rate and lipid drug consumption (r_s=-0.556, p<0.05), and a negative correlation was found between adult mortality rate and consumption of anti-depressants (r_s=-0.590, p<0.05).

Table 3 shows the results of the canonical correlation analysis. It was determined that there is a strong relationship (r_c=75.9) between the dependent variable set and the independent variable set. It is understood that there is a strong relationship between health status and pharmaceutical consumption in EFPIA member countries

When the significance test results of the canonical correlation analysis are examined in Table 4, it was found that the 1st canonical correlation analysis was significant (p<0.05). The first canonical variates is significant and worthy of interpretation.

Table 5 and Table 6 show the standardized coefficients for the health status and pharmaceutical consumption datasets. These coefficients show the relative contributions of the original variables to the data set to which its belong. Since the first function was significant, the first function was interpreted.

$V_1=0.655X_1-0.567X_2$

When the relationship of the variables in the first set with the canonical variates is examined in Table 5, the equation for the first canonical variates is set up as follows:

The largest value belongs to the Y_1 variable of the dependent variables. Therefore, it is the variable with the most weight (significance). Accordingly, the highest contribution to the health status dataset comes from life expectancy at birth.

It is seen that the biggest value is X_1 variable. This is the variable with the most weight (influential) among the independent variables. Accordingly, the highest contribution to the drug consumption data set comes from the variable X_1 (Table 6). When the relationship of the variables in the second set with the canonical

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Table 1. Descriptive findings of the variables examined in the study

Name of variables	Mean±Sd	Median (IQR)	Min.	Max.	n
Life Expectancy at Birth	80.5±2.2	81.4 (82.3-78.8)	75.3	83.2	23
Probability of dying from chronic diseases	12.44±4	10.77 (14.9-9.6)	8.38	22.13	23
Adult mortality rate (per 1000 population)	80.2±31.1	68.6 (104-55.7)	52.5	154.5	23
Self-rated health (bad or very bad)	9.3±3.1	8.6 (11.8-7)	5.1	15.4	23
Percentage of deaths from NCDs	89.7±2.2	90 (91-88)	86	94	23
Anti-hypertensive drugs (per 1000 people)	347.1±115	334.8 (393.1-271.7)	154.4	636.7	23
Lipid-modifying agents (per 1000 people)	113.9±32	121 (146-97)	26	149	23
Drugs used in diabetes (per 1000 people)	72±14	76 (84-59)	48	96	23
Anti-depressants (per 1000 people)	66±31	61 (82-44)	18	146	23

IQR: InterQuartile range; Sd: Standard deviation

Table 2. Multiple correlation analysis results showing relationships between variables

	Life Expectancy at Birth	Probability of dying from chronic diseases	Adult mortality rate	Self-rated health (bad or very bad)	Deaths from NCDs	Consumption of anti-hypertensive	Consumption of lipid-modifying agents	Consumption of drugs used in diabetes	Consumption of anti-depressants
Life Expectancy at Birth	1	-.971**	-.969**	-.765**	-.336	-.092	.477*	.085	.595**
Probability of dying from chronic diseases		1	.942**	.750**	.365	.146	-.459*	-.051	-.640**
Adult mortality rate			1	.824**	.344	.051	-.556**	-.147	-.590**
Self-rated health (bad or very bad)				1	.018	-.065	-.407	-.170	-.398
Deaths from NCDs					1	.345	-.335	-.116	-.357
Consumption of anti-hypertensive						1	.256	.509*	-.075
Consumption of lipid-modifying agents							1	.284	.383
Consumption of drugs used in diabetes								1	.033
Consumption of anti-depressants									1

.**Table 3.** Results of correlation analysis

Canonical function	r_c
1st	0.759
2st	0.360

Table 4. Significance tests for canonical correlation analysis

Root No.	Correlation coefficient	Eigenvalues	F	p-value	Lambda value (λ)
1	0.759	0.369	2.745	0.019	0.360
2	0.360	0.871	0.892	0.464	0.871

Table 5. Standardized canonical coefficients for the health status data set

Health Status	V_1
Y_1	0.655
Y_2	-0.567

Y_1= Life expectancy at birth; Y_2= Percentage of deaths from NCDs

variates is examined in table 6, the equation is set up as follows:

$W_1=-0.579X_1+0.528X_2+0.288X_3+0.528X_4$

Tables 7 and 8 show the canonical loadings of the original variables with their canonical variates. The loadings for health status concluded that, Y_1 dependent variable is the most influential variable in forming V_1 (Table 7). When examining cross loadings, it was found that the variable Y_1 (0.846), which has the most influence with its own set for V_1, also most contribution to the canonical variates (0.642) (W_1; Table 7).

According to the canonical loadings belonging to the pharmaceutical consumption data set in Table 8, the independent variable Y_4 establishes the most influential in forming V_1. The pharmaceutical consumption dataset has a remarkable correlation with X_4 and X_2, respectively. According to cross loadings, the variable X_4 (0.780), which established the strongest relationship with its own set, also most contribution to the canonical variates (0.592) (V_1; Table 8).

Table 9 shows to what extent the variable set explains the variance in itself or in the other. Selected health status indicators explain 66.7% of the variability in health status data set. The rate of explaining the variance of the health status data set by the pharmaceutical consumption data set is 38.4%. Selected pharmaceutical consumption indicators explain 29.6% of the variability in the pharmaceutical consumption data set. 17.1% of the variance of pharmaceutical consumption is explained by the health status data set.

In this study, it was found that there is a positive and strong (r_c=75.9) relationship between pharmaceutical consumption and the health status of EFPIA member countries. There is evidence that pharmaceutical consumption is positively associated with life expectancy at birth, which agrees with the results of this study [17]. It is known that pharmaceutical consumption in a country may be related to many different concepts, such as the country's burden of disease and prescribing policies. Additionally, pharmaceutical consumption data has started to be accepted as a basic indicator showing access to medicines [6].

It is stated in the literature that there are many reasons for not consuming pharmaceuticals. Medication incompatibility in patients is among these reasons. It is stated that this situation causes significant worsening

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Table 6. Standardized canonical coefficients for pharmaceutical consumption data set

Pharmaceutical Consumption	W_1
X_1	-0.579
X_2	0.528
X_3	0.288
X_4	0.528

X_1= Consumption of anti-hypertensive; X_2= Consumption of lipid-modifying agents; X_3= Consumption of drugs used in diabetes; X_4= Consumption of anti-depressants

Table 7. Canonical loadings and cross loadings for health status data set

Health Status	Canonical Loadings	Cross Loadings
Y_1	0.846	0.642
Y_2	-0.787	-0.597

Table 8. Canonical and cross loadings for pharmaceutical consumption data set

Pharmaceutical Consumption	Canonical Loadings	Cross Loadings
X_1	-0.337	-0.256
X_2	0.662	0.503
X_3	0.161	0.122
X_4	0.780	0.592

Table 9. The summary table of variance explained

Variables sets	Number of variables	The variance explained (%)	The variance explained by the other set (%)
Health Status	2	66.7	38.4
Pharmaceutical Consumption	4	29.6	17.1

of the disease, death, and increased healthcare costs. Obstacles to medication compliance are addressed as patient, provider, and health system factors with interactions between them. Identifying specific barriers for each patient and adopting appropriate techniques to overcome them is necessary to improve medication compliance. It is stated that health professionals such as doctors, pharmacists, and nurses have an important role in their daily practices to increase medicine compliance of patients [30].

Additionally, socio-economic factors such as gender, age, income, education, region of residence (urban-rural), unemployment, education, social class; health-related factors such as health insurance, health-related risk factors, chronic diseases, previous experience of using medications; and, other factors such as pharmaceutical prices, prescribing practices, the number of doses to be taken daily also affect pharmaceutical consumption [31]. It is stated that different pharmaceutical consumption data among countries reflect differences in sociocultural, education, healthcare organization, pharmaceutical market and regulatory practices [32].

In the preliminary analysis of the 2020 data, which has not yet been published in the pharmaceutical consumption data, it is stated that the pharmaceutical consumption in the four categories based on the research has remained stable or increased compared to 2019. This means that access to medicine for chronic diseases is maintained during the pandemic [6]. In Europe, with the effect of the COVID-19 pandemic, prescriptions have been written online or over the phone at an increasing rate ~~in~~ recently. It is stated that the pharmaceutical consumption of the countries that are more prominent in online and telephone prescriptions is also increasing [6, 33]. This means that drug consumption can be increased with similar interventions.

4. Conclusion

This research provides evidence that pharmaceutical consumption and the health status of EFPIA member countries are positively associated. Particularly in the medicine groups examined within the scope of this research, the patient is diagnosed with the related disease as a result of the health service and is included in the treatment process in line with the doctor's prescription. Therefore, access to curative care and access to medicine in health care should be viewed as two interconnected parts. Additionally, it may be the case that patients do not consume the medicine even if it is prescribed by a physician. Therefore, it will be beneficial, especially for healthcare providers, to promote patient engagement.

It may be recommended to reduce financial barriers by considering the frequency of diseases for the medicines used for treating of chronic diseases. Performance-based payments may be used, such as the use of financial incentives for prescribers. The burden of chronic disease increases over time in the countries examined within the scope of this study. Therefore, it is thought that the potential of interventions for accessing needed medicines can be benefited from ~~with~~ medicine selection decisions made considering appropriate pharmacoeconomic evaluations as a way to improve health status.

Author Contributions

GO and IA are conceived and designed the analysis, performed the analysis, and wrote the paper. All the authors have read and approved the final manuscript.

Conflict of interest

The authors certify that no conflict of interest.

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