

# ΔΙΑΤΜΗΜΑΤΙΚΟ ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ ΣΤΗ ΔΙΟΙΚΗΣΗ ΕΠΙΧΕΙΡΗΣΕΩΝ

# ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

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Υποβλήθηκε ως απαιτούμενο για την απόκτηση του μεταπτυχιακού διπλώματος στη Διοίκηση Επιχειρήσεων

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# ΕΥΧΑΡΙΣΤΙΕΣ

Θα ήθελα να ευχαριστήσω τον επιβλέποντα καθηγητή Ελευθεριάδη Ιορδάνη για την βοήθειά του στην εκπόνηση της παρούσας διπλωματικής εργασίας καθώς και όλους τους καθηγητές του μεταπτυχιακού προγράμματος οι οποίοι παρά τους περιορισμούς λόγω πανδημίας έκαναν το παν για την ομαλή διεξαγωγή του προγράμματος. Επίσης θα ήθελα να ευχαριστήσω τους γονείς μου για την στήριξή τους στις σπουδές μου.

## **SUMMARY**

During the past several decades, global health expenditures have increased. Population aging and the associated increase in chronic illnesses, advancements in medicine and technology, shifting competitive patterns in the healthcare market, changes in healthcare laws, and a shifting healthcare workforce structure have all contributed to rising health costs. These costs burden governments, patients, and their caregivers and even the pharmaceutical industry with the imposition of measures such as clawback and rebate in some countries. The study and application of health economics is now more than ever compelling.

In the context of this MBA thesis, the fundamental concepts of health economics and pharmacoeconomics are introduced. In the first section, the discipline of health economics is defined, QALYs are presented as a tool for quantifying the condition of human health in utility units, and the factors affecting global health expenditures are examined. In the second section, an introduction is made to the discipline of pharmacoeconomics and the tools that it offers. It is also discussed how these tools can assist to optimize the economic efficiency of healthcare systems and lower pharmaceutical and, by extension, total health expenditures.

# **TABLE OF CONTENTS**

ΕΥΧΑΡΙΣΤΙΕΣ	2
SUMMARY	3
TABLE OF CONTENTS	4
LIST OF FIGURES	. 5
LIST OF TABLES	. 6
CHAPTER 1: INTRODUCTION	7
CHAPTER 2: QUALITY ADJUSTED LIFE YEARS	. 8
CHAPTER 3: HEALTH EXPENDITURE	11
<b>3.1 Health expenditure in relation to GDP before and after the COVID-19 pandemic in OECD nations</b>	12
3.2 Health expenditure and chronic non-communicative diseases	15
3.3 Health expenditure and unsafe care	22
CHAPTER 4: PHARMACOECONOMICS	24
4.1 The necessity of Pharmacoeconomics	25
4.2 Types of cost in pharmacoeconomic evaluation	. 26
4.3 Outcomes of pharmacoeconomic evaluation	. 26
4.4 Pharmacoeconomic evaluation methods	. 27
4.5 The role of pharmacoeconomics in pharmaceutical research and development	33
4.6 Reducing health expenditures with the application of pharmacoeconomics	. 34
CHAPTER 5: CONCLUSION	. 36
REFERENCES	. 37

# **LIST OF FIGURES**

FIGURE 1: Healthcare costs	8
FIGURE 2: Health expenditure as a percentage of GDP	. 11
FIGURE 3: OECD estimates for 2019 & 2020	. 14
FIGURE 4: Deaths from NCDs per year	. 15
FIGURE 5: Total cost of diabetes in the US	. 22

# **LIST OF TABLES**

TABLE 1: QALY-based costs and results of treatments A & B	10
TABLE 2: Healthcare costs of major cancer types	18
TABLE 3: The cost of cancer in Europe	19
TABLE 4: Applications of pharmacoeconomics	25
TABLE 5: Cost-effectiveness ratio	29
TABLE 6: ICER equation	31
TABLE 7: Distribution of monthly values saved with the replacement of	
administration route	35

## **1.INTRODUCTION**

Economics is based on three key principles: scarcity, choice, and opportunity cost. Scarcity exists when the resources available (e.g., number of doctors) fall short of the resources required to accomplish all of our goals (e.g., provide effective healthcare to everyone). Thus, decisions must be made on how to use the existing resources. These decisions are often challenging. Should we spend money on a more effective, but costlier, hypertension medication if this would result in better regulation of the blood pressure? Furthermore, increasing the availability of resources for health care does not eliminate the need to make decisions on diverting extra resources from their present usage and maximizing the use of these new resources. Opportunity cost (the most valuable alternative use of resources) is the economic foundation for making these decisions. We have used our resources optimally if the benefits of the way we chose to use them outweigh the benefits of using the same resources in their most productive alternative uses (i.e., the opportunity cost).

Health economics is the application of these ideas to health care issues. However, health care presents unique obstacles for the application of economic principles since it differs from products and services typically purchased and sold in private markets. Economists need to pay close attention to health care issues in order to figure out how well resources are being used to provide sufficient health care and improve the overall health.

To assess the economic effects of health and health care, it is necessary to determine the direct costs (treatment expenses), indirect costs (productivity losses due to work absence), and intangible costs (detrimental effects on the quality of life of individuals). Direct costs can be calculated by adding hospitalization costs to treatment (pharmaceutical, surgical, etc.) costs. Indirect costs can be measured by counting the days that the patient as well as his or her caregivers miss from work and their general productivity loss, even on working days because of their condition. The most complex part of health economics is the estimation of the quality of life in numbers. This is the part where QALYs are used to quantify the patient's state of health and quality of life.

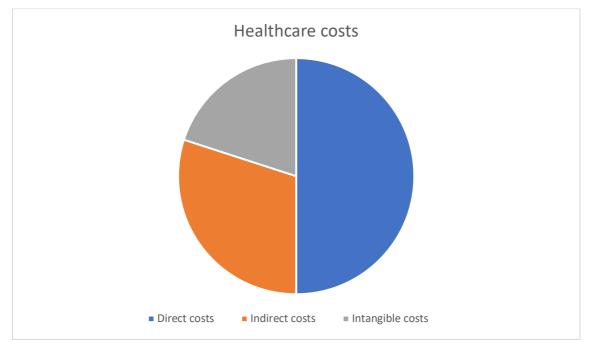


Figure 1 Healthcare costs

# 2. QUALITY ADJUSTED LIFE YEARS (QALY)

To make allocation decisions on the priority of healthcare resources across competing therapies, both costs and health outcomes must be evaluated. To demonstrate the efficacy of a treatment, healthcare research uses a variety of health outcome metrics. For example, one research may report on survival rates, while another may concentrate on the incidence of pressure ulcers and the number of pain-free days. It is challenging to establish where healthcare resources should be allocated most efficiently when there are so many distinct types of outcome indicators resulting from various interventions. If just survival is used to discriminate between healthcare interventions, any influence on quality of life linked with an intervention is disregarded.

A standardized metric is required to permit comparisons across diverse healthcare domains. This metric should ideally capture the influence of a therapy on a patient's life expectancy as well as the impact on their health-related quality of life (HRQoL), which is a recognized critical indication of treatment results. To capture both of these effects, the quality-adjusted life year (QALY) has been established and is extensively used in health economics as a summary measure of health outcome that may guide healthcare resource allocation choices. (Whitehead & Shehzad, 2010)

Developed in the 1960s, the QALY reflects the products of years lived and the corresponding utility values, ranging from 0 (dead) to 1 (perfect health). Utility estimates indicate the viewpoint of an individual's values or preferences, based on the core concept of "welfarist" economics—that people are the greatest judges of their own wellbeing, with the sum of these individual utilities as the ultimate aim. However, QALYs also incorporate so-called "extra-welfarist" aspects, such as the contribution of specific states of health, functionality, and patient preferences to utility estimation, into utility evaluation. Since its inception, the major application of QALYs has been to compare the benefits and hazards of medical therapies. (Feng, Kim, Cohen, Neumann, & Ollendorf, 2020)

A year of life spent in perfect health is equal to 1 QALY (1 Year of Life 1 Utility = 1 QALY), while a year of life spent in less than perfect health is equal to less than 1. To determine the precise QALY value, multiply the utility value associated with a certain state of health by the number of years lived in that condition. Therefore, QALYs are represented in terms of "years lived in perfect health": half a year spent in perfect health is equivalent to 0.5 QALYs (0.5 years 1 Utility), which is the same as 1 year of life lived in a circumstance with utility 0.5 (e.g., paralysis) (1 year 0.5 Utility).

The DALYs on the other hand, was established in the 1990s by the Global Burden of Diseases, Injuries, and Risk Factors (GBD) effort in order to quantify disease burden at the population level, identify main causes of health loss globally, and compare population health across geographic contexts. DALYs represent the total number of years of life lost as a result of early mortality and years lived with disability. The disability weights used to calculate DALYs are the inverse of utility weights, with "0" signifying no impairment and "1" representing the condition of death. DALYs also do not explicitly incorporate extra-welfarist concepts; for instance, disability weights are defined not on the basis of individual surveys but on the basis of expert opinion, as its developers believed that a single set of weights anchored to specific diseases facilitated cross-cultural comparisons more effectively than any form of self-assessment. In addition, only age and gender are associated with non-health consequences. In recent years, GBD has attempted to separate health loss from welfare loss and social context by refining its disability weights; these weights are supposed to be universal and independent of location or population but are currently undergoing testing. (Murray & Acharya, 1997)

9

During the last 20 years, QALYs have become progressively employed as a measure of health outcomes. This is largely owing to three crucial qualities. Firstly, the QALY integrates changes in morbidity (quality) and mortality (amount) in a single statistic. Secondly, QALYs are easy to compute by basic multiplication, however the prior calculation of utilities associated with particular health statuses is a more difficult issue. Finally, QALYs form an intrinsic aspect of one specific sort of economic analysis within healthcare, i.e., cost-utility analysis (CUA). (Prieto & Sacristán, 2003)

In Cost-Effectiveness Analysis (CEA), incremental impacts are quantified in natural measures such as lives saved, years of life gained, blood pressure measured in millimeters of mercury (mm Hg), etc., but in CUA, incremental health gains are measured in quality-adjusted life years (QALYs). A further benefit of QALYs is that they permit the comparison of the efficacy and cost-effectiveness of medicines provided in very different disease regions, even when, because to their differing outcomes, they could not be compared within a CEA. (Prieto & Sacristán, 2003)

Table 1 displays the QALY-based costs and results of two alternative therapies (A and B) for a specific medical condition. In a cost-utility analysis, costs and outcomes are compared by dividing the incremental cost by the incremental outcome of one therapy over another, which reveals the cost of each extra quality-adjusted life year (QALY) acquired with the new treatment. According to the data in Table 1, the cost-utility ratio for therapy A is 400€ for every extra QALY gained.

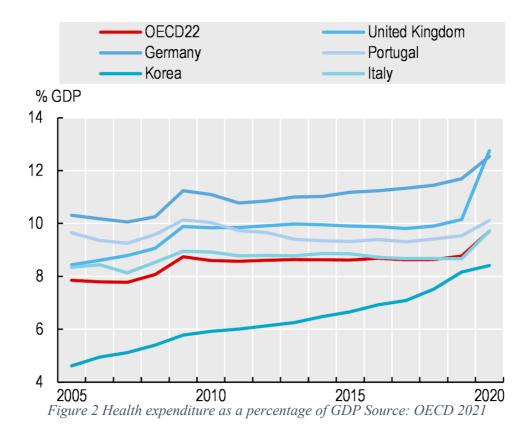
Treatment	Cost	QALY's
Α	2000€	3
В	1200€	1
Increment	800€	2
Incremental	800€/2=400€ per QALY	
cost/Incremental		
outcome		

Table 1 QALY-based costs and results of treatments A and B

# **<u>3. HEALTH EXPENDITURE</u>**

Changes in the internal and external environment have a substantial impact on open systems, such as healthcare organizations. Population aging and the associated increase in chronic illnesses, advancements in medicine and technology, shifting competitive patterns in the healthcare market, changes in healthcare laws, and a shifting healthcare workforce structure have all contributed to rising health costs. In addition to attempting to address rising healthcare expenses, nations also attempt to provide residents with access to comprehensive, non-discriminatory healthcare services and shield them from intolerably high healthcare expenditures. (Plümper & Neumayer, 2013)

In OECD (Organization for Economic Cooperation and Development) nations, health expenditures as a proportion of GDP increase annually. According to projections, this trend will continue for the next 50 years, and OECD nations' health expenditures will reach around 14 percent in 2060 but might be decreased to 9.5 percent with controls in national healthcare programs. The amount of national health expenditures is a significant concern for developed, developing, and underdeveloped nations. (Akca, Sonmez, & Yilmaz, 2017)



To determine a country's health spending, the following question must be posed: "How much should the country spend on health, taking into account the current epidemiological characteristics and the desired level of health status, accounting for the effectiveness of health inputs that would be purchased at existing prices, and accounting for the comparative value and cost of other demands on social resources?" Consequently, the process of determining a country's health expenditures needs consideration of several criteria. (Savedoff, 2003)

Investigation of the determinants of health spending has become a key concern for health policymakers and planners because of its steady growth. Numerous research has been conducted to uncover these factors. According to previous research, the income (GDP) is the most influential factor in determining health spending. Age dependency ratio and epidemiological needs, advances in medical technology, health system characteristics, out-of-pocket health expenditures, population disease pattern, health insurance system, number of physicians, number of prescribed drugs per person, number of hospitals, crude birth rate, literacy rate, and life expectancy are also considered to be determinants of health expenditure. (Akca, Sonmez, & Yilmaz, 2017)

# 3.1 Health expenditure in relation to GDP before and after the COVID-19 pandemic in OECD nations

Organization for Economic Cooperation and Development (OECD) is an economic association with 38 members, the vast majority of which are high-income nations devoted to democratic values and market economy. This makes OECD data more comparable to developed and developing country statistics. Health economics is highly important for the OECD, especially now that rising healthcare expenses have become a concern for many developed nations.

The ratio of health care expenditure to the size of the economy fluctuates throughout time due to variances in health spending growth and overall economic growth. During the 1990s and early 2000s, health spending in OECD nations usually outpaced the rest of the economy, resulting in an almost continuous increase in the ratio of health expenditure to gross domestic product (GDP). After the instability of the 2008 economic crisis, the proportion remained rather consistent, as the rise in health

expenditures in OECD nations mirrored the overall economic performance. With the COVID-19 issue severely limiting economic activity and health expenditures on the rise, the ratio of health expenditures to GDP will undergo a substantial shift. (OECD, 2021)

Prior to the COVID-19 pandemic, OECD nations spent an average of 8.8 percent of their GDP on health care in 2019 — a level that has been relatively stable since 2013. The United States spent the most on health care, equal to 16.8 percent of its GDP — far more than Germany, which spent the second-most at 11.7 percent. A greater proportion of the nation's gross domestic product allocated to health care, however, does not always result in a more efficient health system. In the example of the United States, excessive expenditure is mostly attributable to rising expenses and prices, and not to increased use. For instance, physician pay in the United States are much greater than in similar nations. A physician in the United States makes almost twice the salary of a typical German physician. The United States has far larger pharmaceutical expenditures per capita. Moreover, compared to other rich nations, the United States spends more on health administration expenditures. After the United States and Germany, eight high-income nations, including France, Canada, Japan, and the United Kingdom, spent over 10 percent of their GDP on health care. A further dozen OECD nations, including Brazil and South Africa, spend between 8 and 10 percent of their gross domestic product on health care. The next group of countries spending between 6 and 8 percent of their GDP on health care includes a number of central and eastern European OECD nations as well as Colombia and Costa Rica, two newer Latin American members. Mexico and Turkey, along with the People's Republic of China (China) and India, spend less than six percent of their gross domestic product on health care. (Statista, 2022)

Several OECD nations' first projections for 2020 indicate a large rise in the ratio of health expenditures to GDP. This is a result of both the increased health expenditures necessary to battle COVID-19 and the decreases in GDP resulting from constraints on economic activities. Based on the early statistics, it is predicted that the average proportion of GDP devoted to health has increased from 8.8 percent in 2019 to 9.7 percent in 2020. Those nations most hit by the epidemic reported extraordinary increases in the proportion of their GDP dedicated to health. The United Kingdom

predicted a rise from 10.2 percent in 2019 to 12.8 percent in 2020, while Slovenia anticipated a rise from 8.5 percent to more than 10 percent. (OECD, 2021)

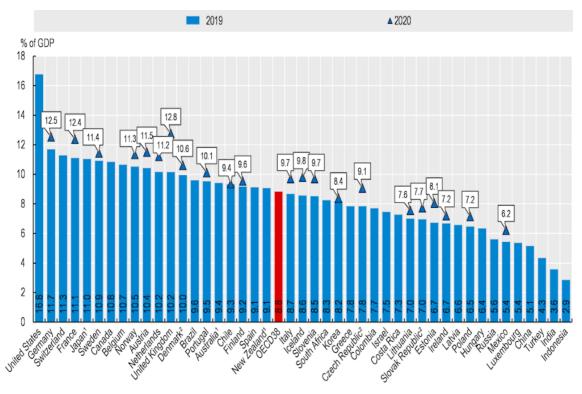


Figure 3 OECD estimates for 2019 & 2020 Source: OECD

Analysis of the patterns in per capita health expenditures and GDP over the last 15 years reveals two shocks: the 2008 economic crisis and the recent effect of COVID-19 in 2020. While OECD economies declined dramatically in 2008 and 2009, health spending growth was maintained for a while before also decreasing – growth hovered just around zero between 2010 and 2012 – as a variety of legislative initiatives to rein in public health expenditures were implemented. Throughout the remainder of the 2010s, the average rate of health expenditure increases in OECD nations tended to closely follow economic expansion. In 2019, the disparity worsened due to a higher increase in health expenditures. In 2020, several OECD economies collapsed due to widespread lockdowns and other public health measures that drastically restricted economic productivity and consumer spending. Average GDP per capita decreased by more than 4.5 percent, with Spain and the United Kingdom registering GDP declines in double digits. According to early statistics for several OECD countries, the necessity to raise health expenditure, notably by governments, in response to the pandemic drove average per capita increases in spending near to 5 percent. This will likely be the fastest increase in OECD health expenditures over the last 15 years. (OECD, 2021)

The increases in health expenditures and GDP throughout this time have resulted in a unique pattern, with big rises in the ratio in 2009 and 2020, followed by a period of stability. Italy and the United Kingdom closely followed this pattern, with the latter seeing an even more significant increase in 2020. Germany and Portugal underwent a more seamless transition, with Portuguese health expenditures anticipated to be just 0.4% higher than in 2005. Despite the shocks, Korea's annual health expenditures have risen steadily from 4.8% to 8.4% during the last 15 years. (OECD, 2021)

# 3.2 Health expenditure and chronic non-communicative diseases

While the COVID-19 resulted in 6.3 million deaths since its outbreak, the majority of deaths every year are the result of chronic noncommunicable diseases. Noncommunicable diseases (NCDs) account for 71 percent of all fatalities worldwide, or 41 million deaths annually. Moreover, Noncommunicable diseases (NCDs) are responsible for more than 60 percent of disability-adjusted life years (DALYs), and more than 80 percent of years lived with disability worldwide (YLD). (WHO, 2022)

Every year, 17.9 million people die from cardiovascular diseases, followed by 9.3 million from cancer, 4.1 million from respiratory disease, and 1.5 million from diabetes. These four types of illnesses account for more than 80 percent of premature NCD fatalities. (WHO, 2022)

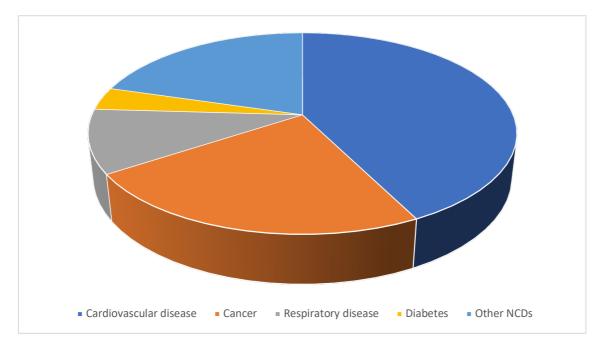


Figure 4 Deaths from NCDs per year

### 3.2.1 Cardiovascular diseases

Cardiovascular disease affects the heart and blood arteries. Smoking, high blood pressure, high cholesterol, a poor diet, lack of exercise and obesity may raise the risk of certain cardiovascular diseases. The most prevalent cardiovascular illness is coronary artery disease (narrow or obstructed coronary arteries), which may cause chest discomfort, heart attacks, and stroke. Congestive heart failure, heart rhythm disorders, congenital heart disease (heart illness at birth), and endocarditis are further cardiovascular diseases (inflamed inner layer of the heart). Also known as heart disease. (National Cancer Institute, n.d.)

Cardiovascular diseases are the leading cause of death around the world and one of the major burdens in health expenditure. The worldwide cost of cardiovascular disease was estimated to be \$863 billion in 2010 and is projected to increase to \$1044 billion by 2030. (Bloom, Cafiero, & Jané-Lopis, 2011)

A 25% of current yearly health costs in the United States are attributable to cardiovascular diseases. The American Heart Association projects that between 2012 and 2030, the national total direct medical expenses associated with CVDs would almost triple, from \$309 billion to \$830 billion. (Roger & Lloyd-Jones, 2012)

Annually, Cardiovascular diseases calculated to cost the EU 169 billion euros, with healthcare accounting for 62 percent of expenditures. Losses in productivity and informal care accounted for 21 and 17 percent of expenses, respectively. congenital heart defects accounted for 27% and cerebrovascular disorders for 20% of total CVD expenses. (Leal, Fernandez, Gray, Petersen, & Rayner, 2006)

# 3.2.2 Cancer

Cancer is a disease characterized by the uncontrolled multiplication and spread of bodily cells. Cancer may begin practically anywhere in the billions of cells that make up the human body. Human cells divide and multiply (a process known as cell division) to create new cells when the body requires them. When cells age or get damaged, they die and are replaced by new ones. Occasionally, this ordered process breaks down, and aberrant or damaged cells proliferate and reproduce inappropriately. These cells can become tumors, which are tissue masses. Tumors may or may not be malignant (benign). Cancerous tumors may move to distant areas of the body and develop new tumors there. Tumors can also infiltrate surrounding tissues (a process called metastasis). Malignant tumors are another name for cancerous tumors. Blood malignancies, including leukemias, often do not develop solid tumors. (National Cancer Institute, n.d.)

In 2020 approximately 18.1 million new cases of cancer were diagnosed, 51.4 percent in men and 48.6 percent in women. Among the most common cancers were breast cancer (12.5% of all cases), lung cancer (12.2% of all cases), colorectal cancer (10.7% of all cases) and prostate cancer (7.8% of all cases). (World Cancer Research Fund International, n.d.)

Cancer is the second most common cause of death after cardiovascular disease. It is estimated that in 2020, 10 million people died from different types of cancer. The enormous global economical cost of cancer is nearly impossible to estimate. However, there are some statistics of US and Europe that represent the effect of cancer in health expenditure.

In 2015, the national cost of cancer care reached \$190.2 billion dollars in the U.S. Costs are projected to reach \$208.9 billion dollars in 2020, an increase of 10 percent attributable only to the aging and growing of the U.S. population. These cost estimates cover medical services and oral prescription medicines associated with cancer. Those diagnosed with breast, colorectal, lung, prostate, and non-Hodgkin lymphomas had the highest national medical care expenses. Those with breast, leukemia, lung, and prostate cancers had the greatest national expenses for oral prescription medications. The variances in national expenses are a result of the disease's prevalence, treatment patterns, and the cost of different forms of care for the various cancer locations. (National Cancer Institute, 2015)

Cancer Site	2015	2020
All sites	\$190.2	\$208.9
Bladder	\$8.3	\$9.4
Female Breast	\$26.8	\$29.8
Cervix Uteri	\$2.2	\$2.3
Colorectal	\$22.3	\$24.3
Hodgkin Lymphoma	\$3.2	\$3.5
Kidney	\$8.2	\$9.7
Leukemia	\$11.7	\$13.6
Lung	\$21.1	\$23.8
Melanoma	\$4.9	\$5.7
Non-Hodgkin Lymphoma	\$16.2	\$18.6
Oral Cavity	\$5.4	\$6.0
Ovary	\$5.9	\$6.4
Prostate	\$19.4	\$22.3
Thyroid	\$5.2	\$6.1
Uterus	\$5.3	\$5.8

Table 2 Healthcare costs of major cancer types. Source: (National Cancer Institute, 2015)

In 2018, the overall cost of cancer in Europe, (EU-27 plus Iceland, Norway, and Switzerland) was 199 billion euros. Total expenses per capita varied from 160 euros in Romania to 578 euros in Switzerland (after adjustment for price differentials). 103 billion euros were spent on cancer treatment, of which 32 billion euros were spent on cancer medications. The cost of informal care was 26 billion euros. The entire loss of production was 70 billion euros, of which 50 billion was attributable to premature death and 20 billion to illness. (Hofmarcher, Lindgren, Wilking, & Jönsson, 2020)

Country	Direct costs			Informal care	Indirect costs	Indirect costs	
	Health expenditure on cancer care	Share of total health expenditure	Cancer drugs <sup>a</sup>	costs	Productivity loss from premature mortality	Productivity loss from morbidity	costs
Austria	2553	6.4% <sup>b</sup>	952	398	1080	281	4312
Belgium	3240	6.9% <sup>b</sup>	1024	693	1406	1244	6583
Bulgaria	320	7.1% <sup>b</sup>	216	43	174	49	587
Croatia	249	6.8% <sup>b</sup>	149	94	200	427	969
Cyprus	90	6.3%	-	24	40	9	163
Czechia	1084	7.0%	174	192	436	341	2053
Denmark	1499	4.8%	513	764	946	726	3934
Estonia	96	5.8%	5	24	61	75	255
Finland	844	4.0%	331	337	559	154	1895
France	18,707	7.1%	5184	3288	7116	4542	33,652
Germany	25,537	6.8%	7584	5141	11,516	4370	46,564
Greece	942	6.5%	44	314	607	159	2022
Hungary	618	7.1%	388	167	497	91	1372
Iceland	69	3.8%	21	20	44	40	173
Ireland	1139	5.0% <sup>b</sup>	308	180	526	113	1957
Italy	10,374	6.7%	4517	5165	4924	284	20,748
Latvia	111	6.4% <sup>b</sup>	26	33	92	39	274
Lithuania	196	6.4% <sup>b</sup>	55	34	113	82	426
Luxembourg	221	6.9% <sup>b</sup>	7	33	90	37	380
Malta	74	6.5% <sup>b</sup>	_	12	26	2	114
Netherlands	5309	6.9%	1072	982	2485	1387	10,163
Norway	1575	4.2%	366	362	609	666	3212
Poland	2185	7.0%	583	582	1775	784	5327
Portugal	991	5.4%	404	371	655	192	2208
Romania	712	7.1% <sup>b</sup>	351	159	598	160	1629
Slovakia	428	7.1% <sup>b</sup>	166	72	257	173	930
Slovenia	234	6.4%	105	77	166	139	616
Spain	5245	4.9%	2841	2529	3440	950	12,164
Sweden	1907	3.7%	572	491	830	960	4189
Switzerland	4366	6.0%	801	597	1716	477	7157
United Kingdom	11,691	5.0%	3249	3213	6633	1465	23,002
Europe	102,607	6.2%	32,008	26,389	49,615	20,418	199.029

Table 3 The cost of cancer in Europe. Source: (Hofmarcher, Lindgren, Wilking, & Jönsson,2020)

# 3.2.3 Non-communicative respiratory diseases

As the name suggests, respiratory disease affects the lungs and other respiratory system components. Infections, cigarette use, secondhand smoke, radon, asbestos, and other air pollutants may all cause respiratory disorders. Asthma, Chronic obstructive pulmonary disease, pneumonia, and lung cancer are the main categories of respiratory illnesses. Also known as pulmonary illness and lung disorder. Since this study is concentrated on noncommunicative diseases pneumonia will not be addressed, as well as lung cancer which was analyzed above. (National Cancer Institute, n.d.)

• Asthma

Asthma is a chronic disease that affects both children and adults. Due to inflammation and contraction of the muscles around the narrow airways, the airways in the lungs become constricted. This results in asthma symptoms as coughing, wheezing, shortness of breath, and chest pains. These symptoms occur intermittently and are frequently worse at night or after physical activity. Other frequent asthma causes may exacerbate asthma symptoms. There is a vast number of allergens including viral illnesses (colds), dust, smoke, fumes, weather fluctuations, grass and tree pollen, animal hair and feathers, harsh soaps, and scent. Asthma affects roughly 260 million people per year, causing 450.000 deaths and a major economic impact in healthcare systems around the world. (WHO, 2018)

According to study published online in the Annals of the American Thoracic Society, asthma costs the U.S. economy about 80 billion U.S. dollars annually in medical bills, days lost from work and school, and fatalities. Researchers from the Centers for Disease Control and Prevention (CDC) only counted "treated asthma," which is defined as having at least one medical interaction for asthma or having a prescription for at least one asthma medication filled during the calendar year.

The annual burden of asthma in EU economy is estimated at 72.2 billion euros. The direct medical costs are roughly 19.5 billion euros and the indirect 14.4 billion euros. The major cost of asthma is the loss of DALY's which is estimated at 38.3 billion euros per year. (Accordini, Corsico, & Braggion, 2013)

• Chronic Obstructive Pulmonary Disease (COPD)

Chronic Obstructive Pulmonary Disease is a form of lung illness characterized by irreversible lung tissue deterioration, making it difficult to breathe. COPD comprises chronic bronchitis, in which the bronchi (large air channels) are inflamed and scarred, and emphysema, in which the alveoli (small air sacs) are destroyed. It develops gradually and is often caused by smoking cigarettes. Chronic obstructive pulmonary disease is the third greatest cause of mortality globally, accounting for 3.2 million fatalities per year. (National Cancer Institute, n.d.) (WHO, 2022)

Studies have shown that only 21–25% of those identified during screening as suffering COPD had previously been diagnosed with the condition. Undiagnosed COPD patients may incur indirect expenses linked to morbidity, but as the vast majority of these patients have minor illness, it is thought that undiagnosed COPD patients incur neither direct nor indirect costs attributed to COPD. However, the absence of data on this topic may result in severe cost underestimate. (Jansson, Lindberg, & Ericsson, 2005)

Over 12 million individuals in the United States have Chronic Obstructive Pulmonary Disease (COPD), which is the third highest cause of 30-day readmissions. COPD is

pricey, with yearly direct expenses of over \$50 billion due to comorbid condition and other indirect expenses, such as absenteeism, the total expenditures associated with COPD might be up to twice the direct costs. (Press, Konetzka, & White, 2018)

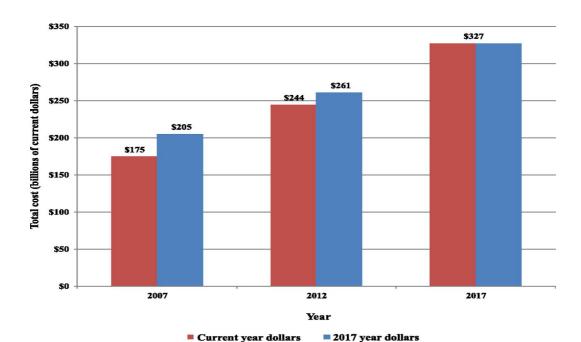
Each year Chronic Obstructive Pulmonary Disease burdens the EU economy by 141.4 billion euros. The majority of this cost is due to lost of DALYs (93 billion euros), followed by indirect costs (25.1 billion euros) and direct costs (23.3 billion euros). (Jansson, Lindberg, & Ericsson, 2005)

#### 3.2.4 Diabetes

Diabetes is a chronic disease resulting in high blood glucose levels, which result in serious heart, eyes, kidneys, and nerve damage. Type 2 diabetes, which often affects adults, happens when the body develops insulin-resistance or does not produce enough insulin. In the last three decades, the incidence of type 2 diabetes has skyrocketed across all socioeconomic levels. Type 1 diabetes, also known as insulin-dependent diabetes, is a chronic condition in which the pancreas does not produce insulin, or the amount of insulin produced is not sufficient for the regulation of the patients' blood sugar. Access to cheap treatment, particularly insulin, is essential for the survival of diabetes patients. (WHO, 2022)

Diabetes affects about 422 million people globally, the majority of whom reside in lowand middle-income countries; annually, diabetes is directly responsible for 1.5 million fatalities. Over the last few decades, both the incidence and prevalence of diabetes have gradually increased, as well as its' economic burden. (WHO, 2022)

More than 34 million U.S. citizens (about 1 in 10) have diabetes, and 88 million adults (1 in 3) have pre-diabetes. Young individuals ages 18 to 44 and middle-aged adults ages 45 to 64 are seeing an increase in diabetes complications. Diabetes is more prevalent among Asian, non-Hispanic Black, and Hispanic individuals than it is among non-Hispanic White individuals. Pre-diabetes affects about 1 in 5 adolescents aged 12 to 18 and 1 in 4 young adults aged 19 to 34. Diabetes is the chronic disease that has the highest economic burden in the United States. One dollar out of every four dollars spent on health care in the United States goes on diabetes treatment. Each year, 237 billion dollars is spent on direct medical expenditures, and another 90 billion dollars is spent on lost productivity. From 2007 to 2017, the entire economic cost of diabetes increased by



60 percent. (National Center for Chronic Disease Prevention and Health Promotion, 2017)

Figure 5 Total cost of diabetes in the US. Source: (National Center for Chronic Disease Prevention and Health Promotion, 2017)

Approximately 60 million European citizens today suffer from diabetes. The expense of controlling diabetes accounts for roughly 9 percent of the healthcare budgets of European Union Member states in 2019, reaching 149 billion euros. There is no treatment for diabetes, and each year 114.000 Europeans die from complications connected to diabetes. Care for patients with diabetes is very complicated, requiring the coordination of a large number of main, secondary, and specialty care experts. Currently, in the healthcare systems of the majority of Member States, this complex ecosystem of care is scattered, resulting in significantly greater expenditures and lower health outcomes. (https://www.europarl.europa.eu/, 2020)

# 3.3 Health expenditure and unsafe care

Unsafe care resulting in preventable patient injury imposes a substantial burden on people, health systems, and economies. Based on prior and current data, health care-related harm is a serious worldwide public health concern. Each year, unsafe care contributes to more than three million fatalities worldwide and has a comparable impact on global health as HIV/AIDS and car accidents. It incurs significant financial and economic expenses as well. In industrialized nations, about one dollar out of every ten spent on health care is redirected to addressing the impacts of safety failings. Patient

injury due to unsafe care, affects global economic productivity by trillions of dollars every year. (Slawomirski, Auraaen, & Klazinga, 2018)

In recent years, the appreciation of patient safety and its significance has increased. The World Health Organization (WHO), the European Union (EU), and the G20 have put the problem to the forefront of the public health agenda. Individuals and communities pay a hefty price for patient damage, but most of it is preventable via changes in practice and behavior, improved legislation, and prudent investment. There is the possibility for positive economic benefits and creation of value. Recent focus, however, has not yet translated into sufficient action to solve the global patient safety problem, and considering the scope of the issue, intervention and investment remain very small.

The COVID19 pandemic proved that, when it is required health systems and individuals can work together and succeed. A vast quantity of resources has been mobilized to safeguard the public and economy. As a result of the danger, health systems have been rapidly reorganized (and in some cases nationalized) to combat it. There is more cooperation across sectors, locations, and divisions. Immediate considerations have centered on ensuring adequate and timely capacity for controlling infection risk (protective equipment), diagnosing (tests), and treating (ventilators/intensive care units/skilled experts), while concurrently developing vaccinations and medicines. (OECD, 2020)

The pandemic has also highlighted the dangers involved with healthcare. A comprehensive study by OECD, using data through March 31, 2020, indicated that 44% of covid-19 cases were nosocomial, or acquired in hospitals by patients treated for other reasons. In the earlier SARS and MERS pandemics, 33% and 56% of all identified cases were hospital-acquired, respectively. Other studies put the percentage of nosocomial covid-19 cases at 15%. (Rickman, et al., 2020)

The financial and economic implications of substandard treatment are also substantial. The direct treatment costs of patients who have been injured during their treatment reaches 13% of health expenditure in developed nations. Excluding safety breaches that may not be avoided reduces this percentage to 8.7% of health expenditures. This equates to 606 billion dollars per year, or little more than 1% of the overall economic output of OECD nations. Even higher is the indirect economic and social impact of hazardous treatment, which exerts a significant drag on productivity and development. Based on willingness to pay, the annual societal cost of patient damage may be estimated to be between one and two trillion dollars. A human capital model implies that eradicating damage may increase annual economic expansion by more than 0.7%. In a decade, this will amount to more than 29 trillion dollars, or around 36% of current world GDP. (OECD, 2020)

# **4.PHARMACOECONOMICS**

Pharmacoeconomics is a branch of economics that uses studies of cost-benefit, costeffectiveness, cost-minimization, cost-of-illness, cost-utility, budget-impact, and costconsequence analysis to compare pharmaceutical products and treatment methods. The relevance of pharmacoeconomic and clinical outcomes research in guiding clinical innovation and market access choices of new novel medications is growing. It focuses mostly on health economics, with an emphasis on the economic impacts of medication treatment. (Brinsmead, 2003)

Pharmacoeconomics is the field of health economics concerned with the economic assessment of medications. Health outcomes research, and patient-reported outcomes (PRO) specifically, seek to comprehend patient value in terms of the effect of illness and its treatment on functional capacity and psychological well-being, also referred to as "health-related quality of life" (HRQL). It is the description and study of drug treatment costs to healthcare systems and societies.

Depending on the perspective from which the research is done, the value of pharmacoeconomic data to healthcare decision makers will vary. In the managed care system, pharmacoeconomic research is expanding. It is now used to construct illness management plans and measure the cost-effectiveness of managed care therapies and initiatives. As health technology develop and become more sophisticated, both the demand for and expense of health care are rising in all nations. Greater life expectancy, better technology, increasing standard of living, and increased demand for health care quality and services are the primary contributors to the rise in health care costs. (Lopert, 2003)

Medicines account up a tiny but important component of the entire cost of health care. To commercialize any novel chemical substance as a medicine, pharmaceutical firms must invest a substantial amount of money and time in order to satisfy different research standards. This explains the high pricing of medicines especially before the patent expiration. Prescription writing is the most frequent therapeutic action in medicine. As novel medications are sold and governed by patent law, as drug treatment is favored over invasive therapy, as many off-label applications of current pharmaceuticals are discovered, and as illogical drug prescriptions are made, the cost of medicines continues to rise. (Needy, Nachtmann, Roztocki, Warner, & Bidanda, 2003)

# **4.1 The necessity of Pharmacoeconomics**

Pharmacoeconomics examines and evaluates the costs and outcomes of pharmaceuticals and health services, as well as describing the economic link between drug research, medication manufacture, distribution, storage, pricing, and human usage. It is woven into the fabric of our societal structure, which governs and impacts all pharmaceuticals-related industries. (Rowlings, 2004)

As health technology advances, both the demand and the expense of health care increase in every country. Patients everywhere are impacted by the rising cost of medications. In Greece the household expenses for medications vary between 0% and 25%. However, these percentages concern the cheapest generic drug available. If a physician decides to prescribe the brand name drug or a generic with higher cost, the patient can be charged with up to 75% of the medicine's cost. As a result, a significant part of the community especially older people with low incomes- is unable to comprehend with the costs. So pharmaceutical costs do matter. The importance of pharmacoeconomics has increased over the last three decades owing to a greater focus on efficient medication treatments for illness, which raise health care costs.

Pharmacoeconomics is a subfield of health economics resulting from the maturation of that field from consolidation to specialization. Health economics is a very new subfield of economics. (Greenberg, et al., 2012) Essentially, pharmacoeconomics is important in the following manner:

In governments	In the pharmaceutical industry	In the private insurance industry
<ul> <li>Determining the</li></ul>	<ul> <li>Choosing between</li></ul>	<ul> <li>Designing insurance</li></ul>
advantages and costs	certain research and	coverage for
of a program.	development options	beneficiaries

Table 4 Applications of pharmacoeconomics

## 4.2 Types of cost in pharmacoeconomic evaluation

Cost is the first fundamental component of Pharmacoeconomic evaluations. The costs associated with pharmacoeconomic assessment may be categorized primarily as financial cost (mandated expenditure) and economic cost (resource for which no payment is required). The opportunity cost is the gain forgone while choosing one therapeutic option over the next-best one. When calculating the cost of an innovation, a number of variables might be considered. Identification of the different expenses is the first phase in any cost study. These may be direct, indirect, or intangible. (Marshall Raj & Raveendran, 2019)

- Direct costs from the standpoint of the healthcare provider, including personnel expenses, capital expenditures, and medication purchasing expenses. It covers medical fees, the cost of providing the prescription, and the cost of managing adverse drug reactions, among other expenses.
- Indirect expenses from the viewpoint of society as a whole: for instance, they may include loss of wages, reduced productivity, loss of recreational time, and cost of transport to hospital. This would involve not just the patient, but also their family and the larger community.
- Intangible costs: the agony, anxiety, or other discomfort that a patient or his or her family may endure. These may be unquantifiable in financial terms, but they are often reflected in measurements of life quality.

# **4.3 Outcomes of pharmacoeconomic evaluation**

Outcomes is the second fundamental component of a Pharmacoeconomic evaluation. The result of a cost-benefit analysis is stated in monetary terms. Cost-benefit analysis enables researchers to compare a diverse array of possibilities. It compares the expenses associated with implementing a program with its benefits. Since the outcomes are quantified in monetary terms, various endpoints, such as a surgical treatment vs a pharmacological intervention, may be compared. The anticipated benefits of a treatment might be assessed in terms of:

- 1. Physical units: for example, cancers healed, heart attacks prevented, years of life gained.
- 2. Utility units: Utility is the term used by economists to describe contentment or a feeling of well-being. It is an effort to analyze the quality of a condition of

health, not merely its quantity. Estimates of utility may be derived by direct measurement (using methods such as time trade-off or standard gambles) or by inferring them from the literature or the opinion of an expert. They are often guided by quality of life measurements in various illness conditions. (Sanchez, 1999)

# 4.4 Pharmacoeconomic evaluation methods

Pharmacoeconomic assessments include any research aimed to examine the costs (consumed resources) and outcomes (clinical, humanistic) of alternative treatments. The outlined assessment procedures were often useful for proving the financial effect of novel therapies, hence increasing their acceptability among healthcare professionals, administrators, and the general public.

The most important types of pharmacoeconomic evaluations are:

- 1. Cost-minimization analysis
- 2. Cost-benefit analysis
- 3. Cost-effectiveness analysis
- 4. Cost-utility analysis
- 5. Cost-of-illness analysis
- 6. Budget-impact analysis
- 7. Cost-consequence analysis

#### 4.4.1 Cost-minimization analysis

Cost-minimization analysis (CMA) identifies the least expensive treatment option when the results of two or more treatments are almost equivalent. Cost-minimization analysis includes assessing drug prices in order to determine the least expensive medicine. In addition, it includes the price of preparing and dispensing a dosage. This approach is used most often for determining the cost of a particular medicine. This approach is only used to evaluate two products whose dosage and therapeutic efficacy have been proved to be equal. Consequently, this strategy is particularly appropriate for comparing therapeutic equivalents and generic medications. If therapeutic equivalence cannot be proved, then cost-minimization analysis is improper. Numerous forms of clinical data may be used to assist economic analysis; however, the "gold standard" is often the randomized controlled trial (RCT), which maintains all variables constant except for the medicine being assessed. As the findings of clinical trials cannot be predicted in advance, it is difficult to organize a cost-minimization analysis alongside a randomized controlled trial because there is no assurance that the compared health outcomes would be equal. Therefore, no future economic review begins as a cost-minimization analysis; the health economist will only accept the cost-minimization analysis as a suitable approach when the health outcomes created are experimentally proved to be "same or comparable." (Donaldson, Hundley, & McIntosh, 1996)

The cost-minimization analysis is usually depicted as the "poor relative" of health economic approaches since its seeming simplicity renders it undeserving of consideration alongside more conceptually demanding health economic methodologies. Nonetheless, it is crucial that health economists realize and admit that the theoretical foundations of cost-minimization analysis are equally as rigorous as those of other economic assessment methodologies.

#### 4.4.2 Cost-benefit analysis

Cost-benefit analysis is the most challenging of all economic assessment methods. This approach assigns a monetary value to the advantages so that benefits and costs may be readily compared. Thus, it is possible to compare various interventions, making it an effective tool for resource allocation by policymakers. It is a fundamental tool for identifying, measuring, and comparing the costs and benefits of a treatment option. When comparing treatment options for which costs and benefits do not take place simultaneously, cost-benefit analysis should be utilized. Cost - benefit analysis can also be utilized to evaluate a single application or compare multiple programs, as all benefits are converted to monetary values. The expenses of delivering a program or alternative therapy are weighed against its advantages. In the same year that the costs and benefits will occur, both are quantified and translated into equal cash values. Future expenses and benefits are discounted to their present-day worth. These costs and benefits are described as the benefit to cost ratio. The most complex and difficult aspect of costbenefit analysis is evaluating the advantages in economic terms. Some advantages are easily convertible, while others need subjective evaluation. Cost - benefit analysis may disregard intangible advantages (pain, worry, stress) which are difficult to calculate monetarily. (Bootman, Townsend, & McGhan, 2004)

## 4.4.3 Cost-effectiveness analysis

When two or more therapy options vary in their efficacy, cost-effectiveness analysis (CEA) is used. The numerator represents the expenses of all direct medical use for the treatment of the ailment as well as the indirect costs (work effect), while the denominator represents the patient-level unit of benefit assessed in temporal units (life-years gained). In addition, incremental cost-effectiveness evaluations compare the two treatments.



#### Table 5 Cost-effectiveness ratio

The cost-effectiveness analysis (CEA) entails a comprehensive examination of pharmacological expenses. Cost is recorded in monetary terms, but efficacy is examined separately and may be quantified in terms of a clinical result, such as the number of lives saved, problems avoided, or illnesses cured [4]. Thus, CEA evaluates the incremental cost of delivering an additional health benefit stated as a specific health outcome that changes based on the indication of the medicine. CEA offers a framework for comparing two or more choice alternatives by assessing the ratio of cost and health effectiveness differences between options. The purpose of CEA is to give a single metric, the incremental cost-effectiveness ratio (ICER), that connects the amount of benefit obtained from an alternative therapy choice to the differentiated cost of that option. When comparing two choices, the ICER is computed using the formula:

 $Cost_2 - Cost_1 \, / \, Effectiveness_2 - Effectiveness_1$ 

In pharmacoeconomic cost-effectiveness analysis, medication costs (the numerator) are expressed in monetary terms and indicate the cost difference between selecting treatment 1 or treatment 2. In cost-effectiveness analysis, the non-monetary differential advantages of the various alternatives (the denominator) indicate the change in health effectiveness values suggested by selecting treatment 1 over treatment 2. Typically, these clinical or health outcomes are assessed in terms of lives saved, life years gained, sickness occurrences averted, or a number of other metrics. Unlike cost-effectiveness analysis, cost-benefit analysis quantifies both the costs and advantages of initiatives. CEA examines medical intervention techniques by calculating the incremental cost-effectiveness ratio (ICER), a measure of the cost of changes in health outcomes. When information on both costs and efficacy is available, these assessments may be done using clinical trial data or, more typically, by using decision analytic models to integrate data from many sources. Due to the multiplicity of health outcomes that may be used as the performance criteria in CEAs and the lack of a precise criterion for "cost-effective," interpreting CEA findings can be difficult. (Gold, Russel, & Siegel, 1996)

### 4.4.4 Cost-Utility Analysis

Cost utility analysis (CUA) is the economic evaluation in which the additional cost of a program is compared to the incremental health gain indicated in quality adjusted life years (QALYs). Cost-utility analysis is used to calculate the cost of utilities, or the amount and standard of living. Cost-utility analysis differs from cost-benefit analysis in that it is used to analyze two medications or treatments whose benefits may vary. Cost-utility analysis defines good value in terms of a specific kind of health outcome. The ICER in this instance is often represented as the incremental cost per additional QALY gained. This method includes both gains in life expectancy and alterations in quality of life into a single measurement. A higher quality of life (QoL) is represented as a utility value on a scale ranging from 0 (dead) to 1 (excellent) (perfect quality of life). Utilizing incremental cost-utility ratios allows the expense of getting a health benefit via the usage of a medicine to be compared to comparable ratios determined for other health treatments (e.g., surgery). Therefore, it gives a larger framework for evaluating the cost-effectiveness of utilizing a specific medicine.

# $ICER = \frac{C2 - C1}{Q2 - Q1}$

(C1, C2 are the costs of the different treatments and Q1, Q2 are their QALYs)

# Table 6 ICER equation

Cost-utility analysis is a specific instance of Cost-effectiveness analysis in which the numerator is a cost measure, and the denominator is normally quantified using the QALY metric. A QALY accounts for both the survival and quality of life advantages of a treatment. This kind of CEA is referred to as a cost-utility analysis since the QoL component of the QALY is quantified using a metric known as health utility. Given that the QALY may be used to quantify the survival and QoL advantages of a treatment, it can serve as a standard tool for comparing the benefits of very diverse treatments. (Phillips, 2009)

# 4.4.5 Cost-of-illness analysis

Cost of illness analysis is a popular form of economic analysis in the medical journals, especially in clinical journals of specialization. The objective of a cost of sickness research is to identify and quantify the direct, indirect, and intangible expenses of a given condition. The output is a monetary assessment of the overall societal cost imposed by a given illness. It is generally recognized that assessing the overall societal cost of a disease is a helpful tool for informing policy decisions, and organizations such as the World Health Organization use such research commonly. (Rice, 1996)

There are two ways to calculate the cost of a disease: the prevalence and incidence approaches. The prevalence technique is the most prevalent and is used to assess the overall annual expense of a condition. The more data-intensive incidence-based method calculates the lifetime costs of newly diagnosed cases in a given year, giving a benchmark against which novel therapies may be assessed. (Rice, 1996)

31

It is argued that determining the overall cost of a disease provides numerous helpful pieces of information. First, it shows us the burden of a certain sickness to society, and by extension, how much might be saved if the condition were eradicated. Second, it identifies the various cost components and the extent of each sector's contribution to society. Such information, it is believed, may assist in determining research and funding targets by revealing areas where inefficiencies occur and where cost reductions might be realized. (Ament & Evers, 1993)

The Cost-of-illness analysis is insufficient to support optimal healthcare allocation for coverage and reimbursement choices pertaining to a specific intervention. In this instance, a Budget-impact analysis (BIA) is preferred, since affordability is essential for short-term economic reasons. (Greenberg, Mohamed Ibrahim, & Boncz, 2014)

## 4.4.6 Budget-impact analysis

A Budget-impact analysis evaluates the influence on yearly healthcare usage and expenditures for the national or health insurance population in the first, second, and successive years after the launch of a new product. A Budget-impact analysis gives an assessment of a drug's impact based on its rate of acceptance as well as the degree and timing of its effect on medical use and expenditures. Financial planning requires such estimations of the effect of a new medicine on yearly drug and overall health system expenses. Decision-makers are also interested in the effect of a new medicine on yearly healthcare service use at the system level, as they must comprehend how the new drug will affect the system based on service supply. For instance, a novel therapy for influenza might have a significant influence on health system performance by encouraging more individuals to seek primary care for influenza symptoms, thus overburdening already overworked general practitioners. (Mauskopf & Earnshaw, Budget impact analysis: review of the state of the art, 2005)

## 4.4.7 Cost-consequence analysis

Cost-consequence analysis (CCA) is a kind of Cost-effectiveness analysis that displays expenses and health outcomes in individual categories without aggregating or weighting them.

When a patient visits a physician, after a diagnosis has been established, the physician often has a variety of treatment choices (including no therapy at all) from which to select. Depending on the selected treatment approach, a variety of outcomes or repercussions will occur. These outcomes can be divided into three major categories:

- 1. Direct medical care and other resource use and costs, such as doctor visits, hospitalizations, drug treatment, and paid nurse time.
- 2. Indirect resource use and costs, such as patient and family loss of productivity, work time lost and costs.
- Clinical or symptom impact, which includes life expectancy and quality of life loss. (Stergachis, 1995)

The cost-consequence matrix is an effort to collect as much information as possible, including the expenses of all medical procedures necessary for each alternative therapy, direct and indirect resource use consequences, clinical or symptom outcomes, and the effect on quality of life. The optimal CCA would include all conceivable health outcomes or repercussions, as well as utility ratings for each of the mentioned health outcomes. A Cost-consequence analysis should also include the effect of the new medication on distinct disease groups. Comparable populations may comprise, for instance, all individuals who get the illness, those in certain age ranges, or those with varying disease severity. The value of a novel therapy is highly variable among subgroups of a population; consequently, it is crucial for a decision-maker to have information on as many subcategories as possible. (Mauskopf, Paul, Grant, & Stergachis, 1998)

## 4.5 The role of pharmacoeconomics in pharmaceutical research and development

Pharmacoeconomics is important for pharmaceutical companies in order to communicate the value of their products to external decision-makers, securing regulatory and reimbursement approval, and contributing to commercial success. Given that the development of new pharmaceuticals is long, costly, and dangerous, and that choices must be made about the allocation of large research and development (R&D) resources, pharmacoeconomics plays a crucial role in guiding internal business decision-making throughout drug development. (Miller, 2005)

Utilizing pharmacoeconomics in the early phases of drug development is likely to improve R&D resource utilization and provide a solid foundation for communicating product value to external decision-makers later on, thereby increasing the probability of regulatory (reimbursement) approval and commercial success. There are five techniques (clinical trial simulation [CTS], option pricing [OP], investment appraisal [IA], threshold analysis [TA], and value of information [VOI] analysis) that can contribute to the design of clinical development programs, optimal pricing strategies, and portfolio management. CTS may evaluate efficacy and acceptability profiles before clinical data are available. OP is able to illustrate the utility of different clinical program designs, study sequencing, and termination options. IA is possible to compare the net present value (NPV) projections of alternative product profiles or research strategies. Given limited data, TA may be applied to appreciate the profile requirements for medication development. VOI may assist in risk management by quantifying uncertainty and assessing the economic viability of getting further information on a drug in development. (Miller, 2005)

No amount of pharmacoeconomic data will improve a subpar pharmaceutical, but it may enhance the drug developer's understanding of the treatment's features. In light of this information, decisions are likely to be superior to those made without it, whether it leads to the speedier termination of unprofitable enterprises or the allocation of more appropriate resources to attractive ones.

## 4.6 Reducing health expenditures with the application of pharmacoeconomics

The pharmacoeconomics discipline provides useful tools that can help reduce health expenditures around the globe. From government decisions on healthcare to the choice of a generic drug at the pharmacy, a pharmacoeconomics analysis provides useful information and helps reduce the cost of treatment without compromising the patients' health and quality of life. Hospitals are a great example on how pharmacoeconomics can be applied and produce results.

In a study conducted by (Silva, et al., 2021) in Brazil's Fundação Hospital, the use of pharmacoeconomics and especially cost minimization analysis is described and

evaluated. The research sample included 377 pharmacoeconomic interventions. The cost minimization analysis was conducted to determine if the change of the administration route from intravenous to oral could reduce the cost of treatment. In addition to reducing costs, substituting an intravenous therapy with an oral therapy increases patient safety minimizing the odds of an infection at the vein access point. (Silva, et al., 2021)

In patients who utilize a nasoenteric or nasogastric tube, interchangeability is not conducted; thus, the pharmacist undertakes a study of the prescription for injectable pharmaceuticals, monitoring technical aspects such as the patient's diet. In addition, the administration route swap becomes untenable for tracheostomized patients and those using mechanical ventilation. After this evaluation, the intervention is undertaken in conjunction with the prescribing physician to determine the potential of each patient's administration route being interchangeable. In 41.37 percent (156 patients) of the 377 pharmacoeconomic interventions conducted, the intravenous method was replaced with the oral. This outcome is affected by the patient's clinical state. The patient must be stabilized before the exchange is feasible. As the table below demonstrates, the pharmacoeconomic interventions reduced the cost of treatment, saving the hospital approximately 26000 Reais in the year that the study was conducted. (Silva, et al., 2021)

Month	Expected costs	Amounts spend	Money saved
January	R\$ 1208.14	R\$ 179.49	R\$ 1028.65
February	R\$ 2406.8	R\$ 123.59	R\$ 2283.21
March	R\$ 4152.38	R\$ 216.66	R\$ 3935,72
April	R\$ 3309.94	R\$ 278.96	R\$ 3030.98
May	R\$ 1656.2	R\$ 189.84	R\$ 1466.36
June	R\$ 3623.82	R\$ 116.04	R\$ 3507.78
July	R\$ 1205.17	R\$ 73.5	R\$ 1131.67
August	R\$ 1729.8	R\$ 83.1	R\$ 1646.7
September	R\$ 3786.8	R\$ 182.72	R\$ 3604.08
October	R\$ 2178.7	R\$ 178.53	R\$ 2000.17
November	R\$ 807.96	R\$ 112.68	R\$ 695.28
December	R\$ 1626.36	R\$ 58.85	R\$ 1567.51
Total	R\$ 27692.07	R\$ 1793.96	R\$ 25898.11

Table 7 Distribution of monthly values saved with the replacement of administration route.

Source: Silva RF, et al., 2021

# **5.CONCLUSION**

The importance of the study of health economics, and more specifically the subfield of pharmacoeconomics, was addressed in this Master of Business Administration thesis. In light of the fact that the COVID-19 epidemic is still going strong, it is especially important to have instruments at our disposal that may assist in the management of health expenditures.

The importance of the study of health economics, and more specifically the subfield of pharmacoeconomics, was addressed in this Master of Business Administration thesis. In light of the fact that the COVID-19 epidemic is still going strong, it is especially important to have instruments at our disposal that may assist in the management of health expenditures.

In the second section the subfield of pharmacoeconomics was analyzed, as well as their significance for cost reduction in pharmaceutical companies as well as worldwide health expenditures.

In conclusion, the fields of health economics and pharmacoeconomics have shown considerable cost-reduction outcomes and have assisted decision-makers in governments and the health industry. It is crucial that these disciplines continue to be studied and advanced, since they are the key to winning the war known as health expenditure.

#### **REFERENCES**

- Accordini, S., Corsico, A. G., Braggion, M., Gerbase, M. W., Gislason, D., Gulsvik, A., Heinrich, J., Janson, C., Jarvis, D., Jõgi, R., Pin, I., Schoefer, Y., Bugiani, M., Cazzoletti, L., Cerveri, I., Marcon, A., & de Marco, R. (2012). The cost of persistent asthma in Europe: An international population-based study in adults. *International Archives of Allergy and Immunology*, *160*(1), 93–101. https://doi.org/10.1159/000338998
- Akca, N., Sönmez, S., & Yılmaz, A. (2017). Determinants of health expenditure in OECD countries: A decision tree model. *Pakistan Journal of Medical Sciences*, 33(6). https://doi.org/10.12669/pjms.336.13300
- 3. Ament, A., & Evers, S. (1993). Cost of illness studies in health care: A comparison of two cases. *Health Policy*, *26*(1), 29–42. https://doi.org/10.1016/0168-8510(93)90076-2
- 4. Forum, W. E., & Health, H. S. of P. (2011). *The global economic burden of non-communicable diseases: A report.*
- 5. Bootman, J. L., Townsend, R. J., & McGhan, W. F. (1991). *Principles of pharmacoeconomics*. Harvey Whitney Books.
- Brinsmead, R., & Hill, S. (2003). Use of pharmacoeconomics in prescribing research. Part 4: Is cost-utility analysis a useful tool? *Journal of Clinical Pharmacy and Therapeutics*, 28(4), 339–346. https://doi.org/10.1046/j.1365-2710.2003.00469.x
- 7. Donaldson, C., Hundley, V., & McIntosh, E. (1996). Using economics alongside clinical trials: Why we cannot choose the evaluation technique in advance. *Health Economics*, 5(3), 267–269. https://doi.org/10.1002/(sici)1099-1050(199605)5:3<267::aid-hec209>3.0.co;2-x
- 8. Drummond, M., Sculpher, M. J., Claxton, K., Stoddart, G. L., & Torrance, G. W. (2015). *Methods for the economic evaluation of health care programmes*. Oxford University Press, USA.
- Edlin, R., Round, J., Hulme, C., & McCabe, C. (2010). Cost-effectiveness analysis and efficient use of the pharmaceutical budget: The key role of clinical pharmacologists. *British Journal of Clinical Pharmacology*, 70(3), 350–355. https://doi.org/10.1111/j.1365-2125.2010.03617.x
- Feng, X., Ollendorf, D. A., Kim, D. D., Cohen, J. T., & Neumann, P. J. (2019). CO2 USING QALYS VERSUS DALYS TO MEASURE COST-EFFECTIVENESS: DOES IT MATTER? *Value in Health*, 22, S36. https://doi.org/10.1016/j.jval.2019.04.020
- Gold, M. R., Siegel, O. of the A. S. for P. H. J. E., Siegel, J. E., Russell, L. B., Weinstein, M. C., Russell, P. at the C. for H. E. L. B., & Weinstein, P. in the D. of H. P. & M. S. of P. H. M. C. (1996). Cost-Effectiveness in health and medicine. Oxford University Press.
- Greenberg, D., Mohamed Ibrahim, M. I. B., & Boncz, I. (2014). What are the challenges in conducting cost-of-illness studies? *Value in Health Regional Issues*, 4, 115–116. https://doi.org/10.1016/j.vhri.2014.08.003
- Greenberg, P. E., Arcelus, A., Birnbaum, H. G., Cremieux, P.-Y., LeLorier, J., Ouellette, P., & Slavin, M. B. (1999). Pharmacoeconomics and health policy. *PharmacoEconomics*, 16(5), 425–432. https://doi.org/10.2165/00019053-199916050-00001
- Hofmarcher, T., Lindgren, P., Wilking, N., & Jönsson, B. (2020). The cost of cancer in Europe 2018. European Journal of Cancer, 129, 41–49. https://doi.org/10.1016/j.ejca.2020.01.011
- Jansson, S.-A., Lindberg, A., Ericsson, Å., Borg, S., Rönmark, E., Andersson, F., & Lundbäck, B. (2005). Cost differences for COPD with and without physician-diagnosis. *COPD: Journal of Chronic Obstructive Pulmonary Disease*, 2(4), 427–434. https://doi.org/10.1080/15412550500346501
- Leal, J., Luengo-Fernández, R., Gray, A., Petersen, S., & Rayner, M. (2006). Economic burden of cardiovascular diseases in the enlarged European Union. *European Heart Journal*, 27(13), 1610–1619. https://doi.org/10.1093/eurheartj/ehi733
- Lopert, R., Lang, D. L., & Hill, S. R. (2003). Use of pharmacoeconomics in prescribing research. Part 3: Cost-effectiveness analysis - A technique for decision-making at the margin. *Journal of Clinical Pharmacy and Therapeutics*, 28(3), 243–249. https://doi.org/10.1046/j.1365-2710.2003.00465.x
- 18. Raj, G. M., & Raveendran, R. (2019). Introduction to basics of pharmacology and toxicology: Volume 1: General and molecular pharmacology: Principles of drug action. Springer Nature.
- Mauskopf, J. A., Earnshaw, S., & Mullins, C. D. (2005). Budget impact analysis: Review of the state of the art. *Expert Review of Pharmacoeconomics & amp; Outcomes Research*, 5(1), 65–79. https://doi.org/10.1586/14737167.5.1.65
- Mauskopf, J. A., Paul, J. E., Grant, D. M., & Stergachis, A. (1998). The role of cost-consequence analysis in healthcare decision-making. *PharmacoEconomics*, 13(3), 277–288. https://doi.org/10.2165/00019053-199813030-00002
- 21. Miller, P. (2005). Role of pharmacoeconomic analysis in R&D decision making. *PharmacoEconomics*, 23(1), 1–12. https://doi.org/10.2165/00019053-200523010-00001
- Murray, C. J. L., & Acharya, A. K. (1997). Understanding dalys. *Journal of Health Economics*, 16(6), 703–730. https://doi.org/10.1016/s0167-6296(97)00004-0
- 23. Comprehensive cancer information. (n.d.). National Cancer Institute. Retrieved August 6, 2022, from https://www.cancer.gov/
- Li, R., & Zhang, P. (n.d.). Cost-Effectiveness of interventions for the prevention and control of diabetes. In *The Evidence Base for Diabetes Care* (pp. 449–470). John Wiley & Sons, Ltd. Retrieved August 6, 2022, from http://dx.doi.org/10.1002/9780470682807.ch27

- Needy, K. L., Nachtmann, H., Roztocki, N., Warner, R. C., & Bidanda, B. (2003). Implementing activitybased costing systems in small manufacturing firms: A field study. *Engineering Management Journal*, 15(1), 3–10. https://doi.org/10.1080/10429247.2003.11415190
- 26. Health at a glance 2021. (2021). OECD. http://dx.doi.org/10.1787/ae3016b9-en
- 27. The economics of patient safety Part III: Long-term care. (2020). In *OECD Health Working Papers*. Organisation for Economic Co-Operation and Development (OECD). http://dx.doi.org/10.1787/be07475c-en
- Plümper, T., & Neumayer, E. (2011). Health spending, out-of-pocket contributions, and mortality rates. SSRN Electronic Journal. https://doi.org/10.2139/ssrn.1759508
- Press, V. G., Konetzka, R. T., & White, S. R. (2018). Insights about the economic impact of chronic obstructive pulmonary disease readmissions post implementation of the hospital readmission reduction program. *Current Opinion in Pulmonary Medicine*, 24(2), 138–146. https://doi.org/10.1097/mcp.00000000000454
- 30. Rice, DorothyP. (1994). Cost-of-illness studies: Fact or fiction? *The Lancet*, *344*(8936), 1519–1520. https://doi.org/10.1016/s0140-6736(94)90342-5
- Rickman, H. M., Rampling, T., Shaw, K., Martinez-Garcia, G., Hail, L., Coen, P., Shahmanesh, M., Shin, G. Y., Nastouli, E., & Houlihan, C. F. (2020). Nosocomial transmission of coronavirus disease 2019: A retrospective study of 66 hospital-acquired cases in a London teaching hospital. *Clinical Infectious Diseases*, 72(4), 690–693. https://doi.org/10.1093/cid/ciaa816
- 32. Sanchez, R. (1999). Modular architectures in the marketing process. *Journal of Marketing*, 63, 92. https://doi.org/10.2307/1252104
- 33. Savedoff, W. D. (2007). What should A country spend on health care? *Health Affairs*, 26(4), 962–970. https://doi.org/10.1377/hlthaff.26.4.962
- Silva, R. F., Leite, F. P., Severino, K. S. A. F., Costa, J. B., Soares, W. D., & Cruz, A. F. P. da. (2021). Pharmacoeconomics: The impact of its applicability in a hospital foundation. *Revista Eletrônica Acervo Saúde*, 13(6), e7804. https://doi.org/10.25248/reas.e7804.2021
- 35. The economics of patient safety in primary and ambulatory care. (2018). In *OECD Health Working Papers*. Organisation for Economic Co-Operation and Development (OECD). http://dx.doi.org/10.1787/baf425ad-en
- 36. Statista The statistics portal. (n.d.). Statista. Retrieved August 6, 2022, from http://statista.com
- 37. Home. (n.d.). World Health Organization. Retrieved August 6, 2022, from http://who.int
- 38. WHO initiative aims to halve medication errors globally. (2017). *Reactions Weekly*, *1646*(1), 6–6. https://doi.org/10.1007/s40278-017-28370-5
- 39. Cancer Prevention Organisation. (2020, October 21). WCRF International. http://wcrf.org
- 40. (N.d.). Retrieved August 6, 2022, from https://www.europarl.europa.eu/