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Economic crises impact on the consumption of antidiabetic drugs

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ECONOMIC CRISES IMPACT ON THE CONSUMPTION OF ANTIDIABETIC DRUGS

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Biographical note

Daniela Marques Finteiro, pharmacist, daughter of Carlos Vicente de Carvalho Finteiro and Alzira da Conceição Rodrigues Marques Finteiro, was born on October 5th, 1994, in Porto. She completed the undergraduate course in Pharmaceutical Sciences in 2016 and the Master's Degree in Pharmaceutical Sciences in 2018, at the Faculty of Pharmacy of the University of Porto.

She began her professional activity, at the pharmacy ("Farmácia Ferreira" in Vila Nova de Gaia) where she completed her professional internship in 2018, and continues today as a pharmacist.

The importance of the area of management and economics in her professional activity motivated her to apply for the Masters in Management and Economics of Health Services (MMEHS) at the Faculty of Economics of the University of Porto, having started in 2020.

In 2023, she completed her dissertation for the MMEHS under the title "Economic crises impact on the consumption of antidiabetic drugs".

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Abstract

This dissertation examines the behaviour of the demand for antidiabetic drugs, distinguishing between non-insulin medicines and insulin, as well as measuring the demands for both these categories of drugs with the National Health Service (NHS) and the consumers' expenditure, and with the number of units sold in the pharmacies across the Portuguese territory. The main objective of this study is to prove that, in 'normal' macroeconomic environments, the demand for antidiabetic drugs behaves differently from the demand for normal goods and services but, in times of economic hardship, when recession reduces income, jobs and savings, the demand behaviour for life-saving medicines is fairly similar to the one expected from normal goods and services, that is, there will be a contraction, even if of smaller proportions, in the expenditure allocated to the purchasing of such drugs. However, the same may not be true when the demand is measured in number of units for, if there are no substitutes available as it is the case with insulin, the decrease in the demand during an economic recession, may be insignificant.

Keywords: antidiabetics; demand determinants; NHS expenditure; economic recession.

Resumo

Esta dissertação examina o comportamento da procura de medicamentos antidiabéticos, distinguindo entre medicamentos não-insulínicos e insulina, e mede a procura por ambas as categorias de medicamentos com base na despesa do Serviço Nacional de Saúde (SNS) e dos consumidores, e com base no número de unidades vendidas nas farmácias em todo o território português. O objetivo principal deste estudo é comprovar que, em ambientes macroeconómicos "normais", a procura de medicamentos antidiabéticos se comporta de forma diferente da procura de bens e serviços normais mas, em tempos de dificuldades económicas, quando a recessão reduz o rendimento, empregos e poupanças, o comportamento da procura por medicamentos vitais para a vida humana é bastante semelhante ao esperado para bens e serviços normais, ou seja, haverá uma contração, mesmo que em menor proporção, na despesa alocada à compra desses medicamentos. No entanto, o mesmo pode não ser verdade quando a procura é medida em número de unidades, pois, se não houver substitutos disponíveis, como é o caso da insulina, a diminuição na procura durante uma recessão económica pode ser insignificante.

Palavras-chave: antidiabéticos; determinantes da procura; despesa do SNS; recessão económica.

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1. Introduction

Diabetes *mellitus*, known simply as diabetes, is one of the largest worldwide health emergencies of this century. Currently, there are 422 million people suffering with diabetes in the world and 1.5 million deaths per year are attributed to this disease. In Portugal, at the beginning of the century, the prevalence of diabetes (number of diabetic patients) was just below 398 thousand, but two decades later, this number increased to about 1.1 million patients. This extraordinary growth has to do with two main factors – people live longer with the disease, and are diagnosed earlier.

Diabetes is a chronic, metabolic disease in which blood sugar levels are abnormally high, leading, over time, to serious impairment of the body's main functions affecting mainly, the heart, blood vessels, nervous system, kidneys, and the eyes. The most common form of this disease is the type 2 diabetes, which is characterized by the body's insufficient production of insulin. The other known form of this disease is the type 1 diabetes, which main feature is the total inability of the body to produce insulin.

Since diabetes is a chronic disease, the only way diabetic patients are able to live longer and better lives is to control their blood glucose levels. This can only be achieved if the patients follow the doctors' prescriptions to the letter, taking the mandatory medication regularly. Thus, as the number of patients increases, so does the demand for antidiabetic drugs and, consequently, the burden on the budget of both the national health system (NHS) and the taxpayers. The fast growing share of the expenditure with antidiabetic drugs has been responsible for the escalating interest in uncovering the main factors that determine the behaviour of their demand.

Following this line of thought, and recognising the scarcity of informed published studies in the available literature, the main objective of this dissertation is to investigate the behaviour of the demand for antidiabetics, focusing in particular, on the eventual differences that may arise between this demand behaviour and that of the demand for normal goods and services. Consequently, our purpose is to prove that the demand for antidiabetic drugs behaves differently from the demand for normal goods and services within 'normal' macroeconomic conditions. However, in times of economic recession, when income shrinks and unemployment grows, the demand for antidiabetics is expected to behave in a similar way to those of the demand for normal goods and services, meaning that a contraction of expenditure is expected although, when the demand for antidiabetic drugs is measured in units or boxes sold, this expected contraction may not be as expressive as the one observed for the demand measured in millions of euros.

Indeed, the results of the regressions estimated in the empirical part of this dissertation allow the conclusion that, contrary to what usually happens with the demand for normal goods and services, the consumers' income and the poverty rate are not relevant determinants of the demand for antidiabetics and the impact of changes in their average price on the public expenditure with these drugs is, in general, positive, contradicting the usual negative sign that would be expected in the price response of the demand for normal goods. Still regarding the impact of prices on the demand for antidiabetics we observe two different behaviours linked with the two main categories of antidiabetics dealt within this research: non-insulin antidiabetics (NIA) and insulin. In the case of the NIA drugs, the response of their demand to changes in its own price is always the opposite of what would be expected in the normal goods' demand, that is, the price changes response is always positive. In both the cases of the demand measured in expenditure and in units, the response to price changes is significant and positive on the linear form of the regression while, in the log form, the price elasticity of the demand is still positive but not significantly different from unit when measured by the expenditure, and is positive but inelastic when measured in units. In the case of insulin, the price changes impact on demand are not significant when the demand is measured by the expenditure and it is negative and significant when measured in units. In the log form of the model, the demand price elasticity for insulin is negative and inelastic, constituting the only case, of the eight regressions estimated, in which the demand behaviour for antidiabetics is similar to that for normal necessary goods.

An additional objective of this dissertation is also to examine the response of the demand behaviour for antidiabetics when economic, social and financial hardship hit the population, as it was the case in both the aftermath of the 2008 GFC and in the years of the SARS-CoV-2 pandemic. We found that the demand for antidiabetics in these cases of economic recession behaves similarly to the expected results from normal goods and services demands. Indeed, for both NIA and insulin demands, in both linear and log forms of the econometric models, and for both measures of expenditure and units, we observed a negative response of the antidiabetics' demand measured by the significant and negative coefficients estimates of the dummy variables included in the models to account for the eventual structural breaks that would arise from the economic recession experienced by the country in the aftermath of the 2008 global financial crisis (GFC) and of the intervention of the troika from 2011 to 2014.

The econometric methodology is carried out using the OLS estimation method in linear and log-linear static models to decide which are the best specifications explaining the demand behaviour for antidiabetic drugs. The EViews© programme has been used throughout all the estimations. The data used in the estimations are all time series of observations for the sample period [2000-2021]. The different sources from where all the data were gathered are appropriately mentioned across the dissertation.

We believe that this study greatly contributes to a better understanding of what influences the patients' behaviour in their purchasing of antidiabetic medicines when surrounded with 'normal' macroeconomic circumstances and when confronted with periods of economic adversity.

The remainder of this dissertation is structured in the following five chapters. In chapter 2, we provide a literature review that gathers an overview of the available studies on the influence of economic crises on the management of several National Health Systems (NHS) budgets, with particular focus on the 2008 financial global crisis and its consequences for the Portuguese NHS. Also we offer a summary of studies dealing with diabetes as a chronic disease and its ever increasing weight on the healthcare budgets of the NHS across Western developed countries. We also add a review of studies about the women's influence in education for healthier lifestyles as it is considered a relevant determinant of the demand for antidiabetic drugs. In chapter 3, we present a statistical analysis of the relevant variables to be included in the empirical models. In chapter 4, we present the estimation results of 8 specifications for which we interpret and critically discuss the coefficients estimates of the relevant factors that explain demand behaviour for antidiabetic drugs. In chapter 5 we draw some conclusions.

2. Literature review

2.1. Introduction

To illustrate the empirical part of this work it is necessary to produce a narrative that describes the economic and social environment in Portugal during the last two decades, which includes the aftermath of the global financial crisis (GFC) that hit the country in the third quarter of 2008 and lasted up until 2014. We concentrate this narrative on the health sector given that the main topic of this dissertation is to compare the features of the demand for antidiabetic drugs, with those of the demand for normal goods and services. In particular, we intend to explain the factors that influence the national demand for antidiabetic drugs given that, being diabetes a chronic disease increasingly common in the present century, the resources that have to be allocated to its management are of substantive dimension and also rapidly increasing, weighing each year more on the ever scarce national health budget.

We are particularly interested in investigating what happens to the demand of antidiabetic drugs when an economic recession, such as the one that followed the financial crisis of 2008, affects the people's livelihoods in such ways that they have to drastically restrict their consumption of goods and services. The global financial crisis of 2008 on the one hand, followed by the sovereign debt crises of 2011-2014 and the SARS-CoV-2 pandemic of 2020 and 2021 are cases that we would like to analyse, examining the response of the demand for diabetic drugs to the economic predicaments brought about by these economic, financial and social constraints.

We are also interested in including as determinants of the demand for antidiabetics, policy measures that were implemented to prevent or, at least, alleviate the social and economic burden that this chronical disease has in the pockets of both patients and taxpayers. Specifically, in the case of type 2 diabetes, which may be prevented or, at least, alleviated, by the adoption of simple measures conducing to healthier lifestyles. For that matter, we think that educators, particularly women (given that in Portugal, women are still the main responsible for the youngsters' education, both at home and at schools), may have an important role in shaping children's behaviour for healthier lifestyles that, hopefully, will last them a lifetime. Thus, besides the consensual variables that may explain the demand for antidiabetic drugs, it is important to include measures that can translate the influence of education on the adoption of healthier lifestyles, which may be converted into significant decreases in the long-run consumption of antidiabetic drugs.

In the remainder of this chapter, we supply an overview of the literature that examines the more recent trends of the health budgets in developed countries, with special emphasis on the case of the Portuguese demand behaviour for health goods and services in the last two decades, which includes the economic recession of the post 2008 crises and the economic and social crises of the SARS-CoV-2 pandemic. Section 2.2 gives an overview of the 2008 financial crisis and its consequences for the Portuguese economy; section 2.3 analyses the time trends of the Portuguese public health budget, with particular attention given to the explaining of the expenditure share allocated to the chronic disease of diabetes; section 2.4 addresses the possible influence of education on the consumption of antidiabetic medication exploring, in particular, the role of the population health literacy in the management of this chronic disease.

2.2. The global financial crisis: effects in the Portuguese economy

The so-called 2008 global financial crisis (GFC) started with the downturn of the United States of America (USA) housing market, which, in a domino-like effect, collapsed most of the USA financial system and that of the rest of the world, in less than two years.

The crisis was already brewing in the USA with the housing market mitigation driven by a massive credit expansion in 2007, but erupted visibly with the bankruptcy of Lehman Brothers' investment bank. At this point, many banks in the USA and around the world incurred in large losses and had to rely on their governments' support to avoid insolvency. Governments around the world withdraw large international loans, which caused increasing deficits and national debts in many countries (Helleiner, 2011). Japan, United Kingdom, China and Canada, were badly hit, spreading the crisis to other developed countries and their markets, which gave way to a global recession (Lin & Treichel, 2012). Millions of people lost their jobs, as the majority of the advanced economies experienced their most severe recession since the Great Depression.

The European smaller open economies with substantial foreign debts, such as Cyprus, Croatia, Greece, Czech Republic, Portugal, Italy, Spain and Slovenia, were the most affected.

These countries registered a negative growth of their Gross Domestic Product (GDP), for more than three consecutive years, after 2008 (Thomson et al., 2014). Portugal, alongside with Italy, Greece and Spain, had also to endure the sovereign debt crisis in the aftermath of the 2008 GFC. This new crisis was so severe that, to avoid defaulting, the Portuguese government required an emergency bailout package of 78 billion € in May of 2011, from a triad of international institutions known as "troika" and composed by the International Monetary Fund, European Central Bank and European Commission. The tradeoff for the bailout demanded from the Portuguese government the promise to adopt severe austerity measures included in the troika's *Adjustment Programme* (AP)[1] and to accept the troika's intervention and monitoring of the country's efforts to remain viable, during the next four years (IMF & Government, 2011; Portuguese Observatory on Health Systems, 2012; Sakellarides et al., 2014). These measures were mainly focus on increasing taxes and reducing public spending in order to reduce the country's budget deficit. Also included in the troika's "package" was the adoption of structural reforms in several sectors such as housing, consumption, labour and wages, for the period 2011 to 2014 (Maresso et al., 2015).

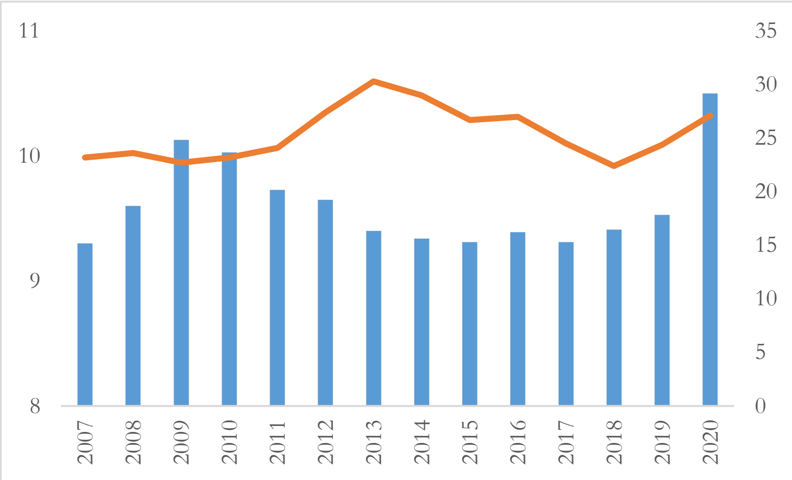
The AP draconian measures prolonged the already evident economic crisis of the Portuguese economy into a deep recession that lasted until 2014 with increasing deficits and national debt, which grew almost uncontrollably due to the exorbitant interest rates that the international markets demanded for lending money to the country's economy (European Commission, 2011; IMF, 2014). Indeed, the national GDP growth rates in the years 2011 to 2014 were, respectively, −1.7%; −4.1%; −0.92% and +0.79% (The World Bank, 2022). The average negative growth of these four years (−1.5%), was well below the corresponding average for the Eurozone (+0.7%) in the same period (Eurostat, 2017). During these difficult times, the national unemployment rose from 7.7% in 2008 to 16.7% in 2013 (Eurostat, 2013). This meant that families consumption had to be reduced and, by 2012, the healthcare share of this consumption had shrunk 22.2% (SEDES, 2012).

Figure 2.1 shows the annual share of the national health expenditure in the GDP (blue columns) and the poverty rate (orange line), from 2007 to 2020. It is interesting to notice that the poverty rate raises from its lower ever value of 23.6% in 2008 to its highest value ever of 30.3% in 2013, meaning that the economic recession in Portugal made poverty grow by close to 7 percentage points in just five years. By the same token, the highest health

[1] The AP agreed to a 75 billion euros' loan in exchange to the signing of a Memorandum of Understanding which included a set of measures to be implemented throughout a three years' period, from 2011 to 2014.

expenditure share ever recorded was attained in 2020, during the COVID pandemic, with the value of 10.5%.

Figure 2.1. Poverty rate and the share of health expenditure in GDP (%); (2007 - 2020).



According to Barros (2012), Karanikolos et al. (2013) and Maresso et al. (2015), the austerity policies implemented with the AP program to the Portuguese health sector included measures to reduce hospitals operating costs, public spending on medicines and general healthcare. These measures, that included cuts in the resources allocated to the health sector, increase fees to access hospital services, augmented waiting lists to be assisted in the NHS and extended waiting times for appointments and surgical interventions, were designed to make it more difficult and expensive to access the national healthcare system, (Cylus et al., 2012; Dauderstadt & Keltek, 2015; Karanikolos et al., 2016; Legido-Quigley et al., 2016). An immediate consequence of the implementation of these measures is the 668 million € decrease in the national spending on drugs, between 2010 and 2012 (Directorate-General of Budget, 2012; Maresso et al., 2015; Portuguese Observatory on Health Systems, 2012). Moreover, the Barros et al. (2013) study about the impact of the global financial crisis on the demand for healthcare services of the Portuguese population above 15 years old, concludes that 15.1% of the interviewed were not able to purchase some or even all of their compulsory medicines. Also, Da Costa et al. (2015) survey discloses that, between 2011 and 2013, 22.8% of people with chronic diseases did not purchase part or all of their medication due to financial problems, a fact also shown in Legido-Quigley et al. (2016).

2.3. Total health expenditure in Portugal

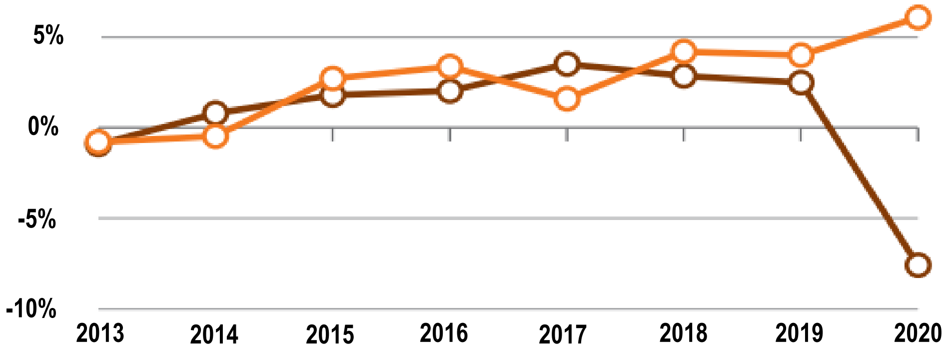
Health expenditure is defined as the total public and private spending on medical goods and services, public health, emergency aid, prevention proceedings and administrative procedures of health care provision (OECD/EU, 2020). In general, health expenditure is measured as a percentage of GDP, which allows comparison across countries health profiles (WHO, 2022a). Kleiman (1974) and Newhouse (1977), consider per capita income and economic growth as the main factors explaining differences in the healthcare expenditure levels across countries. Agreeing with this point of view, Beylik et al. (2022), sustain that healthcare expenditure is the most important economic indicator for measuring a country's development level. Additionally, WHO (2022a) states that as per capita income increases, so does the expenditure on health. Accordingly, European countries with the higher income per capita also show the highest levels of expenditure on health. This may imply that, in times of economic, financial and/or social crises, when economic growth is negative and income per capita decreases, expenditure in healthcare is bound to be reduced, worsening the living standards of the populations during those periods. It is also an empirical finding that, in the aftermath of economical or financial crises, developed countries tend to compensate the under budgeting of social expenditure with significant increases in this type of spending privileging in particular the healthcare bottom line. Indeed, since 2012, OECD countries have been spending a growing amount of funds to reinforce their health systems in order to compensate the cuts made during the 2008 GFC, keeping up with an ageing population in growing need of assistance and with the breakthroughs of medical science and technology in new and more efficient treatments.

Figure 2.2 complements the information in Figure 2.1 above, showing the national real annual growth of GDP (brown line) and of total public health spending (orange line) between 2013 and 2020. The graph shows a continuously positive growth of the health expenditure between 2013 and 2019 (excluding the 2020 atypical growth, due to the COVID pandemic), from a negative number in 2013 to just below 5% in 2019. Moreover, we also observe the counter-cycle growth pattern of the health expenditure compared with that of the GDP, as the health budget decided each year is based on the GDP growth of previous years.

Figure 2.3 compares the ratio of the health expenditure to the GDP for the Portuguese economy (blue line) with the corresponding ratio for the EU (green line), between 2000 and 2012. The graph shows that, the Portuguese expenditure ratio is always above that of the EU and, at its peak in 2009, the healthcare expenditure in Portugal reached 10.8% of the national

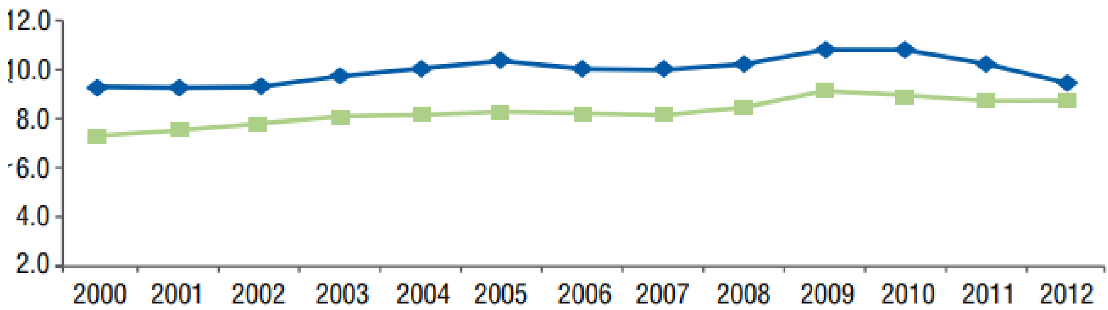
GDP, still above the corresponding EU ratio, which also peaked in the same year with the value of 9.5%. From 2009 onwards both ratios decrease and converge, until they both attain practically the same percentage in 2012. Nevertheless, both the national and the EU ratios increased after 2012, attaining 9.5% and 9.9%, respectively, by 2019. However, it is important to note that, although the ratios are similar, the national spending per capita in healthcare is 2 314€, which is only 1/3 of the EU corresponding spending of 3 521€ (OECD/European Observatory on Health Systems and Policies, 2021)

Figure 2.2. Real annual growth of GDP and of national public health spending; (2013-2020).



Source: OECD Portugal: Country Health Profile 2021, State of Health in the EU.

Figure 2.3. Portugal and EU average health expenditure ratio to GDP; (2000–2012)



Source: WHO Regional Office for Europe, 2014.

2.3.1. The main components of the Portuguese health expenditure

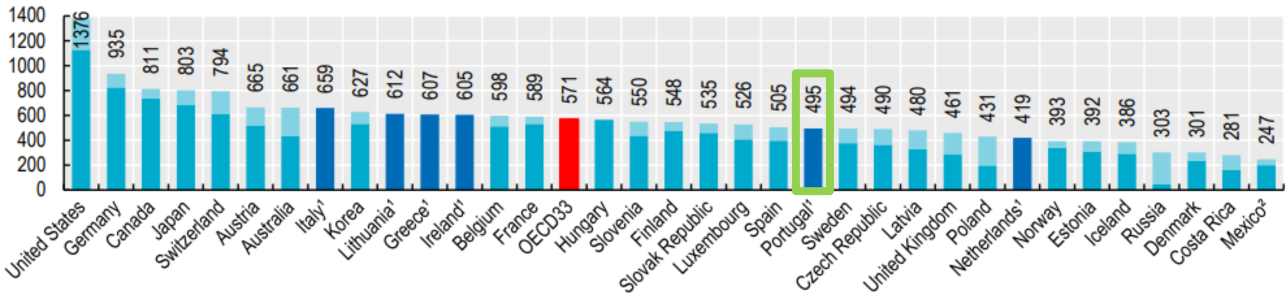
Health expenditure can be divided into three main categories: *inpatient* or *hospital care*, meaning admission in hospitals with overnight staying and rehabilitative care; *outpatient care*, which refers to all services or treatments that do not require hospitalization (except for dental care); and *medical goods*, where prescribed and over-the-counter pharmaceutical drugs, are included.

In the past decades, the healthcare costs have been growing due to the emergence of new diseases, new medicines, new lifestyles, population ageing, technical progress and the consistent growing need for more and better healthcare services (Machado & et al., 2011; Mossialos & Oliver, 2005). Accordingly, the consumption of pharmaceutical drugs has also been growing, mostly due to the dominance of chronic diseases associated with the general growth of life expectancy, less healthy environment, lifestyles and habits (Belloni et al., 2016).

The cost of medical drugs, which represent a significant share of the health budget, includes four main categories: the cost of research and development, the cost of manufacturing and distribution, the cost of patent registration and the cost of the administrative procedures involved in the developing and post-approval surveillance of the drugs (Moon et al., 2020). When a patent expires, generic copies of the original medicine can be produce and sold, significantly lowering the original price.

Figure 2.4 shows the per capita retail pharmaceutical expenditure of OECD countries in 2019, in US Purchasing Power Parities ($USPPP). The light blue bars correspond to over-the-counter medicines; the medium blue to the prescription medicines and the dark blue to the sum of the two. The OECD average (red bar) of 571 $PPP (326€) is higher than the Portugal's one (in green) of 495 $PPP (283€).

Figure 2.4. OECD expenditures ($USPPP) on retail pharmaceuticals per capita; (2019)[2]



Source: OECD Health Statistics 2021.

In 2019, Portugal spent 46% of total health expenditure in outpatient care, ranking the highest value share in EU. The shares corresponding to inpatient care (26%), medical goods including pharmaceuticals (19%) and collective services[3] (4%) are on pair with OECD-31 average (28%, 19% and 6%, respectively). However, the share of long-term care (5%) is, below the OECD-31 average (14%) (OECD, 2021b).

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[2] The upper-scripted numbers 1 and 2 in some of the countries names mean, respectively: "medical non-durables (resulting in an overestimation of around 5-10%)" and "includes only private expenditure".
[3] Refers to prevention and administration and includes unknown or unallocated services.

Included in the austerity measures of the AP for Portugal was the reduction of the public spending on medicines from 1.47% of the GDP (its value in 2010) to 1.25% in 2012 and to 1% in 2013 (Simões et al., 2017). To achieve this goal, a set of decisions was implemented concerning the price of pharmaceutical drugs: first, the maximum price of the first generic of any branded drug entering the market should be set at 60% of the branded price (adjusted to 50% right after the first revision of the Memorandum of Understanding); second, the homogenization of most of the drug prices across the national territory by adopting reference prices, based on a periodically updated list of averaged different prices observed across the country; third, the encouragement of physicians to prescribe more generics than branded medicines (Maresso et al., 2015). With these policies, the average retail prices of medicines decreased from 16.77€ in 2010, to 13.25€ in 2012, thus contributing for the reduction of the NHS per capita expenditure from 200.65€ to 144.78€ (INFARMED, 2014). However, the objective of decreasing the public spending on medicines to 1.25% of GDP was only attained in 2013 and not in 2012 as required.

Figure 2.5 shows the number of boxes of all medicines sold in Portugal, between 2006 and 2021. It is apparent that sales are relatively stable around 250 million boxes between 2006 and 2012, but suffer a visible break of about one hundred million boxes in 2013. Afterwards, the sales remain stable with a slight increase upwards until 2019.

Figure 2.6 shows the five main therapeutic groups of medicines consumed in Portugal (in thousands of boxes) between 2015 and 2021 (INFARMED, 2018, 2019, 2020, 2021). The light blue line corresponds to the anti-dyslipidemia drugs (for diseases related with high levels of lipids, e.g. cholesterol), the orange line depicts the consumption of acting agents renin-angiotensin-system (RAR) (for hypertension), the grey line describes the alpha-glucosidase inhibitors, dipeptidyl-peptidase-4 inhibitors and insulins (for diabetes treatment), the yellow line relates to the hypnotics, antidepressants and sedatives (for neurologic impairments), and the dark blue line represents antidepressants medicines. It is apparent from Figure 2.6 that, except for the neurologic drugs (yellow line) and the anti-hypertension drugs (orange line), the consumption of the other three groups of pharmaceuticals grew sharply within the period under analysis, with a particular steep increase for the antidiabetic drugs, second only to the anti-high-cholesterol drugs. The RAS-acting agents for hypertension decrease until 2017 and from then on, had a moderate growth, while the consumption of the neurological drugs decreased for the whole period, exception made for 2020, most likely due to the SARS-CoV-2 pandemic. The antidepressants steady rise (dark blue line) has been a constant across time and in developed countries, since the beginning of the century, with no signs of pattern change anywhere, anytime.

Figure 2.5. Quantity of all medicines consumed (10^6 units) in Portugal; (2006-2021).

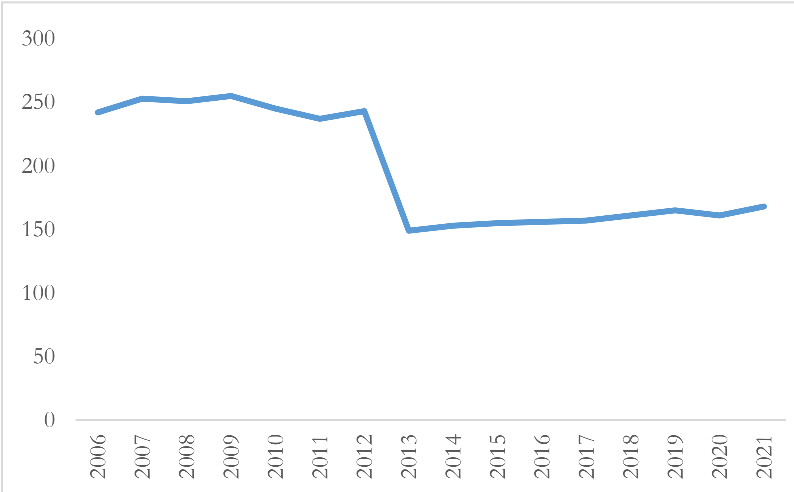
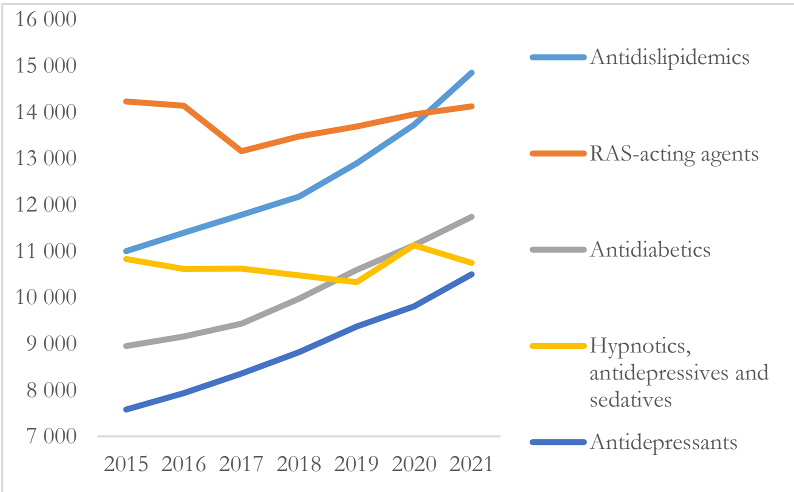


Figure 2.6. Main therapeutic classes of medicines (10^3 units) in Portugal; (2015-2021).



This dissertation is mainly concerned with the consumption of antidiabetic drugs (grey line). Although the grey line in Fig. 2.6 shows values only from 2015 to 2021, the truth is that for the full sample period, the same line would show a much faster average growth of 7.9% per year in the first half of the sample period (2000 to 2010), than the one observed in the second half, which average annual growth is -3.3% (2.5 times less), from 2011 to 2019 (excluding the pandemic years). The reason for this difference may lie on the increase of diabetes prevalence, which grew faster in the first half of the sample period, on the prescribed doses per capita, and of the proportion of antidiabetics' treatment involving combinations of drugs, instead of one sole drug per box. All these factors contribute to increasing the number of dispensed boxes for the treatment of diabetics in Portugal.

2.3.2. Main components of national expenditure with diabetes treatment

According to the WHO, the so called "*non-communicable*" diseases (NCDs) (*vulgo*, "chronical" diseases) are defined as ailments of "*long duration and generally slow progression*" (Busse et al., 2010, p. 9), which include cancer, mental and respiratory disorders and endocrine and cardiovascular conditions. Globally, these maladies represent more than 60% of deaths in patients under 70 years old, and it is estimated that one in five people in Western countries are currently suffering from one or more of these chronic illness (WHO, 2017). These are the health issues mainly responsible for the expansion of the healthcare budgets of high income countries, justifying more than one third of the funds allocated to their NHS systems (Garg & Evans, 2011). In addition, the predominance of NCDs worldwide is responsible for the projected increase of health budgets for most of these healthcare institutions (Devaux & Sassi, 2015; Ghebreyesus, 2018; Sassi, 2010).

Diabetes *mellitus* is one of the leading ailments within the NCD group that affects Western populations. In 2019, NCDs were responsible for 74% of all deaths globally, where diabetes represented 4% of those fatalities (WHO, 2022b). Moreover, there is a rapid increase of the indirect costs associated with the treatment of diabetes (Wild et al., 2004), which include the loss of salaries and working days, affecting not only the patients and their families, but also the businesses owners and the taxpayers (Seuring et al., 2015).

Diabetes includes three main types of diseases: type 1, type 2, and gestational diabetes (GDM). Type 1 diabetes is caused by an autoimmune process in which the body's immune system attacks the pancreas cells that produce insulin, meaning that these patients need daily insulin to survive. Type 1 diabetes is more common in children, affecting 8.75 million people worldwide (International Diabetes Federation, 2022). Type 2 diabetes triggers hyperglycaemia (high blood sugar levels) because the body produces little or no insulin. In this case, the first approach is to attempt to change the patient's lifestyle but, if that is not sufficient to control the glucose levels, oral medication is added. GDM is usually a transitory disorder that solves itself once the pregnancy ends (International Diabetes Federation, 2021). Type 2 diabetes is the most common condition, with 90-95% of the existing cases (American Diabetes Association, 2020). In Portugal, the Observatório Nacional da Diabetes (2019), estimates more than one million patients between 20 and 79 years old, suffering from type 2 diabetes.

The first-line pharmacologic treatment for type 2 diabetes is a drug called metformin[4]. However, if this single drug does not control the disease, a second drug must be added, such as sulphonylurea, glitazone, or glucagon-like peptide-1 inhibitor. If this combination of drugs is still not effective, it is possible to add a third non-insulin antidiabetic, that may produce the desired effect (Furtado & Oliveira, 2014; Moura et al., 2021). Due to the broadening of recommended drugs, solo or combined, the introduction of new therapeutic procedures and the growing number of new diabetes patients, the Portuguese NHS spending with diabetes increased from 210 million € in 2013, to 352 million € in 2020. In 2022, this cost is estimated to be 379 million € (INFARMED, 2022).

Figure 2.7 shows the NHS expenditure (10^6€) with antidiabetics (non-insulin and insulin), in the last two decades, where four different growth patterns can be observed across the period. First, until 2007, the expenditure grows at an annual average of 10.12%. Then, in the next seven years, the NHS spending grows, on average, 38.91% per year; finally, between 2014 and 2021, the annual growth rate is 5.20%. The sharp increase of the NHS expenditure between 2007 and 2014, quadrupling the previous period value, is mainly due, besides the increase of this disease prevalence, to the popularity of new antidiabetic drugs that enter the market in that period. Indeed, after 2007, the prescription pattern of non-insulin antidiabetic drugs changed, as the majority of prescriptions included more recent and expensive medicines, causing a rise in NHS expenditure. The negative growth rate in the following period is likely to be due to the economic recession happening in the aftermath of the troika intervention in the country.

For the non-insulin antidiabetics (NIA), the NHS contributes 90% of their total prices, meaning that only 10% of those prices are payed by the patients. It is important to clarify that the NHS subsidizes all antidiabetic medicines in Portugal, irrespective of Portuguese population income as long as the patient is either Portuguese or residing in Portugal. Thus, for patients under the so called "general regimen", which applies to the general population, their contribution is 10% of the price; for patients within the "pensioner regimen", which applies to senior citizens with pensions, the contribution is only 5% of the price.

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[4] Diabetic patients can take single drugs (e.g. metformin, canagliflozin, sitagliptin) or combinations of drugs (e.g. metformin+canaglifozin, metformin+sitagliptin), which include two or more classes of antidiabetic agents (with different action mechanisms) in one single pill or dose.

Figure 2.7. NHS expenditure (10⁶€) with antidiabetics (non-insulin and insulin); (2000-2021).

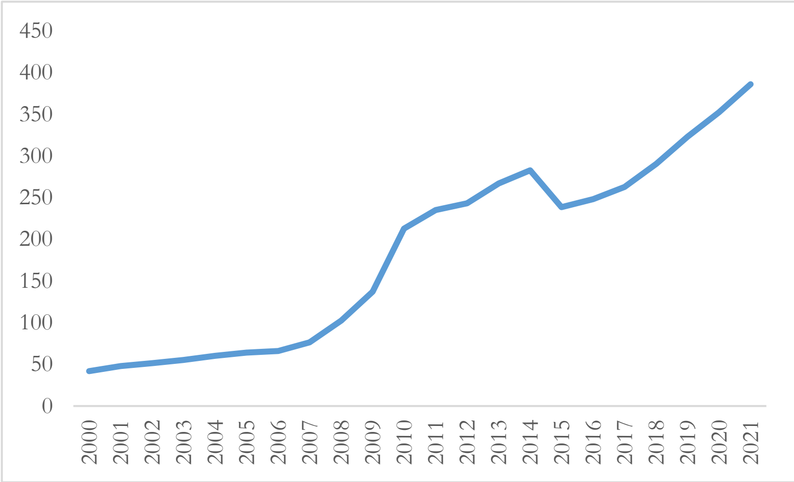


Figure 2.8 shows the NHS (dark blue) + patients (light blue) expenditures (10^6€) within [2006-2018], where it is observed that this sum grew 347%, from 70.8 million € in 2006 to 316.3 million € in 2018, with a considerable higher share for the NHS (Programa Nacional para a Diabetes, 2020). However, the NHS share has been decreasing from 93.1% in 2006 (65.9 million/70.8 million) to 91.9% in 2018 (290.7 million/316.3 million), regardless of the growth in the total expenditure level. Just as an illustrative example, the expenditure with non-insulin antidiabetics in 2021, rose from 273 to 314 million € (13%) relative to the previous year (INFARMED, 2023). These type of drugs represent 22% of the NHS total budget for all drugs sold at the community pharmacies (INFARMED, 2020, 2021).

Figure 2.8. NHS + patients' spending (10^6€) with all antidiabetics in Portugal (2006-2018).

(*) in the 2010 NHS share where it is 71.2, should be 171.2

Source: Programa Nacional da Diabetes (2020) and INFARMED, CCF (Centro de Conferência de Faturas).

2.4. Education and its influence on antidiabetic drugs consumption

The traditional feminine education model sustains that the women's social role is that of the home keeper ensuring the well-being and harmony of the whole family structure by taking care of the house management and children's education (Pintassilgo & Mogarro, 2013).

The women's path to access higher schooling and education, allowing them a different and more prominent role in society has been hard, long and slow.

Table 2.1 shows the women and men' schooling rate (%) for higher education in Portugal, by age group (25-34 and 35-64 years old), from 2011 to 2021. It is patent that women with higher education are more than men in both group ages and for all the years in the sample. However, it can also be seen that it took ten years to bring the weight of younger women with higher education from one third in 2011 (33.1%), to more than half in 2021 (56.5%).

The same metric for the OECD countries is given in Table 2.2, where the main indicator is population with tertiary education – meaning bachelors, masters, doctoral or equivalent degrees – by age group (25-34 and 35-64 years old), comparing the national tertiary education rates for women and men, with the corresponding OECD averages in 2021. The percentages of Portuguese younger and older men with higher education is smaller than the corresponding ones of the OECD, but more so for older men. However, women with tertiary education are more than men for both age groups and for both Portugal and the OECD countries. The only category for which Portugal is ahead of the OECD countries is that of younger women with tertiary education, meaning that Portugal has been catching up and even surpassing the OECD countries. This fact is more visible for the group of younger women where Portugal is already above the OECD average (56.5% vs. 53.7%).

Table 2.1. Women and men national tertiary education rate (%) by age groups (2011-2021).

Year	25-34 years old (%)		35-64 years old (%)	
	Men	Women	Men	Women
2011	21.8	33.1	11.9	15.7
2012	23.5	34.2	12.8	17.6
2013	22.3	37.4	13.2	19.0
2014	23.5	39.0	15.4	22.3
2015	25.4	40.6	16.5	23.3
2016	26.9	42.9	17.3	24.1
2017	25.6	42.3	17.5	25.0
2018	25.7	44.3	18.1	26.3
2019	29.5	45.1	19.4	27.2
2020	34.6	49.0	19.7	29.1
2021	38.3	56.5	21.6	31.7

Source: INE, 2021 – *Taxa de escolaridade do ensino superior na população entre os 25 e 64 anos, por sexo e grupo etário.*

Table 2.2. Women and men national and OECD's tertiary education rate in 2021, by age groups (25 to 34 and 55 to 64 years old).

	MEN		WOMEN	
Age group	Portugal (%)	OECD average (%)	Portugal (%)	OECD average (%)
25-34 years old	38.3	40.8	56.5	53.7
55-64 years old	15.1	28.6	19.9	30.6

Source: OECD Population with tertiary education (indicator) 2023.

Higher levels of education positively correlates with higher levels of income and with value-added working conditions, improving health quality (Benach & Muntaner, 2011; Virtanen et al., 2005). Higher levels of education are also associated with improved cognitive skills and with the will to obtain more and better information in order to assess improved health. Individuals with higher levels of education are more propitious to show healthier behaviors (Cowell, 2006): they smoke less (Stewart et al., 2013), consume less alcohol (Murakami & Hashimoto, 2019) and practice more physical exercise than the less educated people (Pinillos-Franco & García-Prieto, 2017). Higher education is associated with higher health literacy (Jansen et al., 2018), which implies competence, motivation, and knowledge to comprehend, evaluate, access and apply health data needed to make decisions about daily life health issues, in order to prevent diseases and achieve an improved quality of life (Sørensen et al., 2012). It is known that people with higher levels of health literacy are able of making wiser decisions and maintain better health indexes (Ayaz-Alkaya & Ozturk, 2021; Ho et al., 2018; Tehrani et al., 2018). Some studies (e.g. Curtis et al., 2012; DeWalt et al., 2004; DeWalt & Hink, 2009;

Howard et al., 2006; Kim, 2009; Wolf et al., 2005), indicate that lower levels of health literacy are related with higher prevalence of NCDs, playing an important role when it comes to prevention of chronic diseases (Liu et al., 2020). For Poureslami et al. (2017), health literacy is associated with risk-averse behaviour associated with NCDs and with a better "*health status*" that diminishes the average number of hospitalizations. Liu et al. (2020) study confirms that people with "*adequate health literacy*" has lower prevalence of NCDs. They also associated this conclusion with wealthier and higher educated younger people.

Although health literacy involves all of society, women play a more important role, since they are more likely than men to see a physician when they feel sick and advise others to do the same. Moreover, women are more likely than men to follow the prescribed treatments to the letter, and to do the follow up for any health conditions (Cuesta, 2003; Tehrani et al., 2018).

Norcross et al. (1996), state that adult married patients are more likely to seek healthcare influenced by their partners, and more so being male patients than the female partners (Marcell et al., 2010). In addition, studies by Bergeron-Boucher et al. (2022) and Drefahl (2012) state that life expectancy of married men is longer than that of single men. Wang et al. (2020) also concluded that unmarried men have higher risk of stroke and all-cause mortality, comparing to women. Moreover, Ackard & Neumark-Sztainer (2001) and Aten et al. (1996) state that mothers are the main source of healthcare information in the family core. Fox (1991) showed that, irrespective of sex, race, age, intellectual skills and socioeconomic status, adolescents are more prone to care about their health and seek for medical care, by the influence of their mothers.

Patients with diabetes require a daily self-care based on verbal instructions, leaflets, and medical instructions, which are likely to require an advanced health literacy. Powell et al. (2007); Sarkar et al. (2010); Schillinger et al. (2002), reported that a low level of health literacy has a negative impact on diabetes. However, Bains & Egede (2011) and Mancuso (2010), studies do not find significant links between health literacy and diabetes. Nevertheless, we believe that there is sufficient empirical evidence for considering the possibility of education having a significant impact on the prevention and treatment of diabetes. Thus, we will include in the econometric model to be estimated in chapter 4, explanatory variables that take under consideration the impact of education on the consumption of drugs for the treatment of diabetic conditions.

3. Data analysis

3.1. Introduction

Demand theory states that the main determinants of the demand for any normal good or service are the consumers' disposable income, the good or service own price and the price of any substitutes or complements associated with the consumption of the good or service under analysis. This dissertation aims to investigate what are the main determinants of the demand for antidiabetic drugs in Portugal during the last two decades. However, antidiabetic drugs are not "normal" goods in the sense that, being part of the treatment for a life-threatening disease, their demand responses to price and income changes should be different from the corresponding demand responses for normal goods and services, particularly those with numerous substitutes. More so, and for the same reason, the antidiabetics demand response in times of economic and/or social crises, when unemployment increases and per capita income diminishes, is also expected to be different from the normal goods and services' demand behavior facing the same type of economic environment. How different and by how much is the main issue to be answered in this dissertation.

Within the period under analysis (2000 to 2021), two major events shook the very structure of the national economy: the deep recession that followed the 2008 GFC and the SARS-CoV-2 pandemic in 2020 and 2021. For the latter, there is not enough data yet for a credible analysis of its full effects on the demand for antidiabetics. However, we intend to provide a reliable and consistent estimation of the demand behavior within the period [2000-2019] with the purpose of using it to forecast the consumption of antidiabetics in the years of the SARS-CoV-2 pandemic 2020 and 2021. In this way, we expect to obtain a fairly precise measure of the impact that the pandemic crises had on the demand for these drugs. Nevertheless, the main subject of this dissertation is a comprehensive analysis of the effects of the former crisis on the demand for antidiabetic drugs.

In the following sections, we discuss all the relevant variables to be included in the empirical models of the demand for antidiabetic drugs, estimated within sub-periods that coincide with the times before, during and after the economic recession that followed the GFC of 2008. In the next section, we discuss the dependent variables, namely, the national total expenditure with antidiabetic drugs, and the number of units of antidiabetic drugs consumed in Portugal. Section 3.3 gives an overview of all the independent quantitative variables that may justify the behaviour of the demand for antidiabetic drugs. Section 3.4 concludes.

3.2. Dependent variables: (1) expenditure with antidiabetics and (2) units sold of antidiabetics

Diabetes is a chronical disease manifested in two main categories: type 1 and type 2 diabetes. Type 1 diabetes is generally revealed earlier in life, with most of the first diagnostics being made for youngsters within a range of ages between 0 and 20 years old. Once detected, the patients have to endure the symptoms and treatment for this malaise their whole lives, as there is no cure for type 1 diabetes. The type 2 diabetes is mainly diagnosed later in life affecting older people within a wider range of ages. It can be just a temporary ailment as, for instances, during pregnancy, but these are very rare cases. The fact is that type 2 diabetes is also an incurable disease that afflicts the patients for the rest of their lives. Depending on the diabetes type, the pharmacological treatment may be different. With type 1 diabetes, insulin is the exclusive drug, essential for survival. With type 2 diabetes, there is a range of possible treatments that include single or combinations of antidiabetic drugs although, in particularly difficult cases, insulin may also be recommended as a complement treatment. Therefore, it is informative to analyse separately the demand for insulin from the demand for all the other antidiabetic drugs.

The decision to use two alternative metrics for measuring the antidiabetics demand, namely the expenditure with antidiabetics and the number of units consumed of these drugs, has to do with the fact that they are life-saving medicines and to interrupt treatment is not a rational option for those who want to live, even if prices increase and/or income diminishes. Consequently, the rise of expenditure with these type of drugs does not necessarily mean an escalation of the quantities demanded, but rather may simply reflect increases in prices that make expenditure rise, independently of the number of units consumed. Given this possibility, it seems appropriate to consider both the expenditure with antidiabetics and the number of units consumed, as alternative measures of the demand for antidiabetic drugs. Consequently, the econometric analysis in the next chapter aims to explain the behaviour of the demand for antidiabetics measured by two main aggregates: the one associated with the expenditure[5], and the one related with the number of units sold. Additionally, these two main aggregates are further divided into other variables that are also analysed separately. For the expenditure aggregate, we examine two dependent variables: the expenditure with *all* non-insulin antidiabetic drugs (NIA), and the expenditure with insulin only. This separate treatment has to do with the fact that the non-insulin drugs are paid by both the NHS and the patients, while the insulin cost is fully covered by the NHS only, meaning that the patients pay nothing for the insulin they use. In what concerns the number of antidiabetics units consumed, the corresponding dependent variables are also separated in the same ways. Furthermore, the econometric models specified in the next chapter also explain the demand behaviour of two groups of "consumers": first, the NHS + patients demand for NIA drugs, which alternative dependent variables are the total expenditure (NHS + patients spending), on the one hand, and the number of units sold, on the other hand; second, the NHS demand for insulin, which alternative dependent variables are, the total expenditure (NHS spending) with insulin, on the one hand and, the number of insulin units sold, on the other hand. Figure 3.1 shows the tree of options concerning the choice of dependent variables where the main four are clearly identified.

Figure 3.1. Tree of options for the dependent variables to be estimated.

Dependent variables
- Expenditure (10^6 €)
  - Non-insulin antidiabetics (NIA) ⇒ NHS + Patients
  - Insulin ⇒ NHS
- Number of units (10^3)
  - Non-insulin antidiabetics (NIA) ⇒ Patients
  - Insulin ⇒ Patients

In the next four subsections, we carefully analyse each of these four dependent variables.

3.2.1. Dependent variable: (1) patients + NHS expenditure with NIA drugs

The expenditure with non-insulin antidiabetics (NIA) is a relevant portion of the national sum spent with all medicines. To illustrate this, Figure 3.2 shows the NHS expenditure with all medicines (blue line), NIA (orange line) and insulin (grey line) in the period [2000-2021], and Figure 3.3 shows the patients' expenditure with all medicines (blue line), and NIA (orange line), in the same period. Figure 3.2 displays the values of the first two aggregates

[5] The source of the data for patients and NHS expenditure with antidiabetic drugs is the *Centro de Informação do Medicamento e Produtos de Saúde* (CIMI - INFARMED).

(expenditure with *all* medicines, and with NIA) on the left-hand side axe of the graph, while the values of the insulin aggregate are shown on the right-hand side axe. Figure 3.3 displays the expenditure values with *all* medicines on the left-hand side axe of the graph, and the expenditure values with NIA on the right-hand side axe.

Figure 3.2. NHS spending (10^6€) with all medicines (blue), NIA (orange) and insulin (grey); (2000-2021).

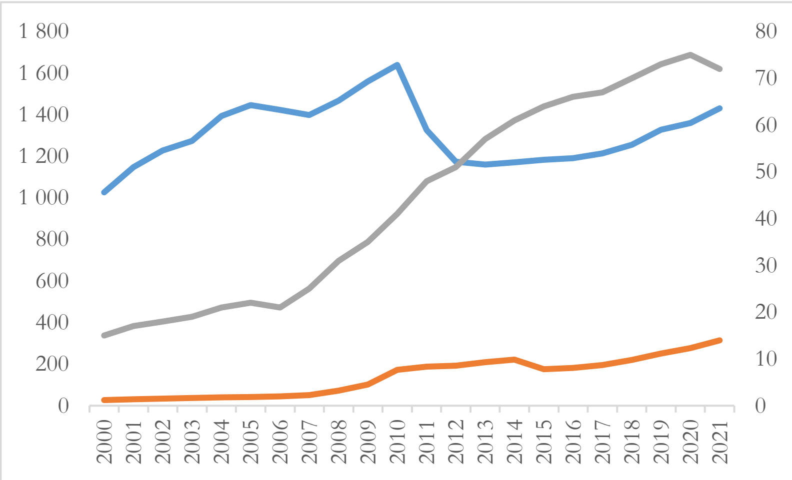
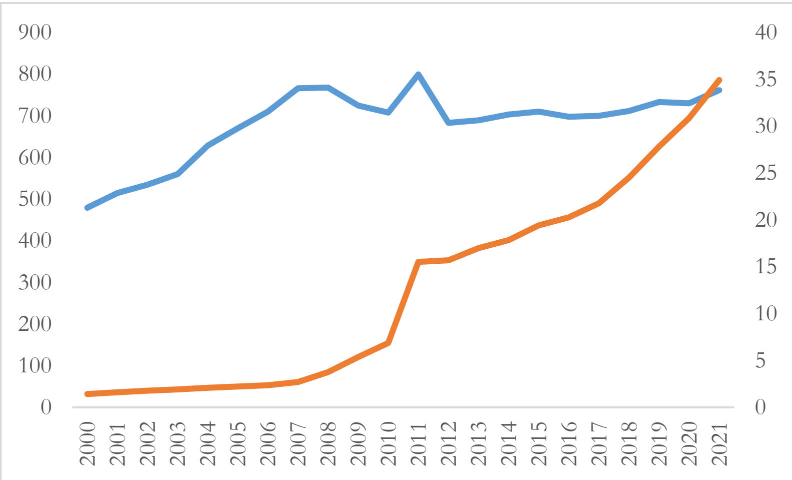


Figure 3.3. Patients spending (10^6€) with all medicines (blue) and NIA (orange); (2000-2021).



The all medicines expenditure (blue line) presents a three stages growth pace along the two decades under analysis. Between 2000 and 2010, its average annual growth is 5.43%; in the following two years' period, the NHS spending with all medicines sharply decreases to a negative average growth of -14.22%, most likely due to the implementation of the troika's policies. Finally, between 2012 and 2021, this aggregate returns to a positive growth (2.43%

per year), but at a much lesser rate than in the first period and attaining, in 2021, a level of expenditure as low as the one observed 10 years ago.

The trends of the other two aggregates, although also presenting three stages growth patterns, diverge from the "all medicines" expenditure in several aspects. For instances, up until 2006, the expenditure with NIA drugs grows at an average rate of 9.52% per annum; then, between 2006 and 2014, the NIA expenditure presents an average annual growth of 49.17%, which is more than 4 times the growth of the previous period. Finally, between 2014 and 2021, the average growth of this aggregate drops to 5.92% per year. In what concerns the insulin expenditure, we can identify an annual average growth of 5.71% between 2000 and 2006; an annual average growth of 21.43% between 2006 and 2014 - more than three times the growth of the previous period - and an average growth of 3.76% per year, between 2014 and 2021, lesser than that of the first period. We may conclude that, although the expenditure with all medicines have been growing at a modest pace in the last decade, the expenditure with antidiabetics grew much faster, thus expanding its annual weight in the national health care budget.

Figure 3.3 shows the patients corresponding expenditures with all medicines (blue line) and with NIA drugs (orange line), from 2000 to 2021[6]. Again, like in the NHS expenditure aggregates of Figure 3.2, we can identify three growth stages in the two aggregates of the patients' expenditure. For the "all medicines" expenditure, we compute an average growth of 7.49% annually, between 2000 and 2007. In the next period, up until 2012, we find a negative average growth of -2.17%, reflecting the restrictive policies imposed by the troika already described in the previous chapter. Within this period, we ignore the sharp raise of the expenditure in 2011, because was not sustained and was rapidly absorbed by the following consistent reductions of expenditure. In the last period, between 2012 and 2021, we compute a modest average growth of 1.27%, most likely due to the price policies and wider use of generics that justify the slower pace of the all medicines' spending growth in this period. So much so that, in 2021, the level of expenditure with this aggregate was lesser than that of 13 years ago, demonstrating the success of the policies initiated with the troika memorandum and maintained throughout this last decade. However, the aggregate of the patients' expenditure with NIA does not follow the same pattern, where we identify a much steeper growth rate up until 2014 and a significant growth after that, although not as prominent. In fact, this aggregate shows an average annual growth of 14.3% between 2000 and 2006. Then,

[6] Recall that the NHS fully covers the insulin cost implying no expenditure for the patients with this drug.

its growth increases more than 6 times in the next period showing a staggering average growth of 87.5% per year, up until 2014. After 2014, its average growth reduces to 16.96%, a little above the average growth rate of the first period. Thus, although the national expenditure growth with all medicines have been contained and has been evolving at a slower pace in the last decade, the same cannot be said about the expenditure with NIA drugs and insulin, which have been growing at a much steeper pace, consistently increasing their shares and annual weights in the national health care budget.

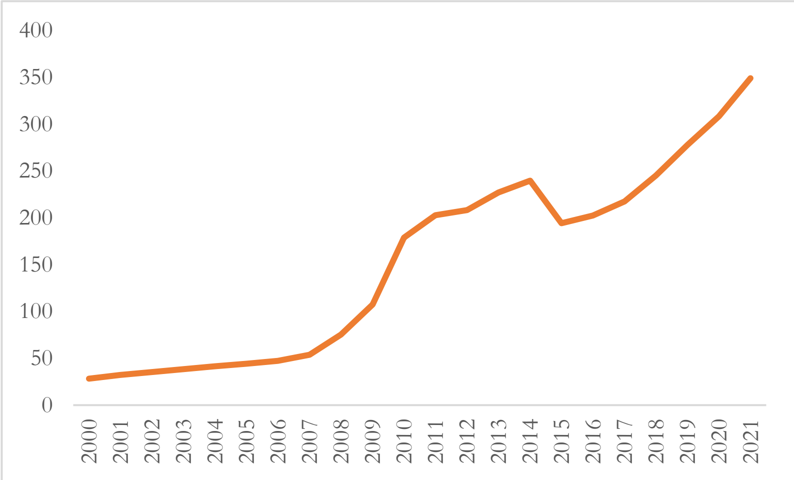
For comparison purposes, Table 3.1 summarizes the previous findings showing the average growth rates of patients and NHS expenditure aggregates, within the identifiable three sub-periods within the two decades under analysis. It is noteworthy that up until 2014, the patients have been supporting a steeper growing burden than that of the NHS, particularly during the recession that followed the 2008 GFC and entailed the troika intervention in the country. It is also interesting to note that from 2012 onwards, the growing pace of all expenditure aggregates slowed down significantly when compared to the initial period of [2000-2010], except for the patients' expenditure with NIA, which increased about 3 pp relative to the same aggregate in the initial period.

Table 3.1. Patients and NHS expenditures with all medicines, non-insulin antidiabetics (NIA) and insulin within the periods before, during and after the 2008 GFC.

	2000 - 2010			**2006 - 2014**			**2012 - 2021**		
	All Meds	**NIA drugs**	**Insulin**	**All Meds**	**NIA drugs**	**Insulin**	**All Meds**	**NIA drugs**	**Insulin**
NHS	5.43%	9.52%	5.71%	-14.22%	49.17%	21.43%	2.43%	5.92%	3.76%
Patients	7.49%	14.30%	×	-2.17%	87.50%	×	1.27%	16.96%	×

Given that the relevant dependent variable is the demand for NIA drugs measured by the NHS + patients' expenditures, we include Figure 3.4 depicting the observations of this variable across the sample period.

Figure 3.4. NHS + patient spending (10^6€) with NIA drugs; (2000-2021).

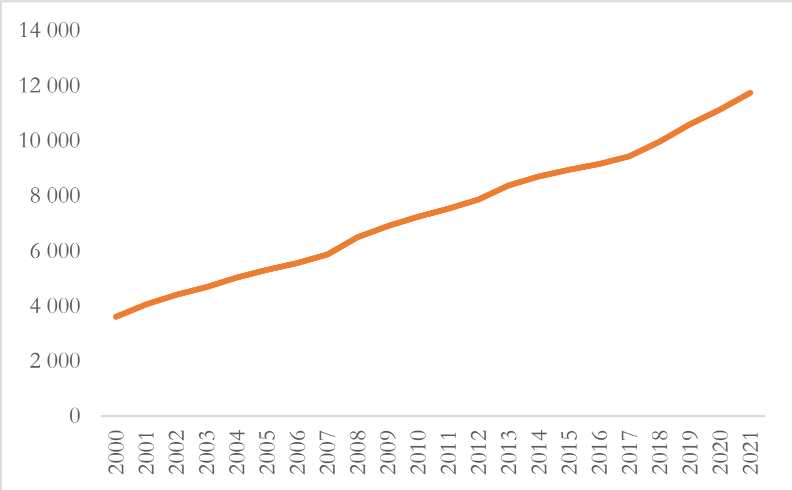


Similarly, to the previous figures, the NHS + patient's expenditure also presents three different growth stages: first, between 2000 and 2006, the variable's average growth is 9.69% per year; in the next period, up until 2014, the aggregate annual average growth increases to 51.33%; finally, between 2014 and 2021, the growth of the NHS + patients spending attains an average of 6.49% per year. These different growth stages have to be included in the empirical models using dummy variables that can divide the full sample period into the relevant sub-periods.

3.2.2. Dependent variable: (2) units of NIA drugs consumed

As stated before, it is also important to analyse the demand for antidiabetic drugs using the number of units sold, instead of the amount of euros spent. Thus, Figure 3.5 displays the number of units sold to the Portuguese patients in the last two decades. It is noteworthy the striking difference of profiles of the line in this figure when compared with the corresponding line depicting the NHS + patients' expenditure in Figure 3.4. Here we can spot an almost straight line creeping up at a relatively constant pace throughout the all period, while in the case of the NHS + patients' expenditure there is a very irregular growing pace. This means that, as expected, the expenditure reflects the change in prices as well as the demand itself. This seems to justify the need for analysing both metrics, when estimating the demand for antidiabetic drugs. Just like with the NHS + patients' expenditure, we also identify, in Figure 3.5, three different growth stages in the number of NIA units sold, although within somewhat diverse sub-periods. Between 2000 and 2007, the average annual growth of the number of NIA units consumed is 7.73%; in the next period, up until 2015, its average growth reduces to 6.76% per year; finally, between 2015 and 2021, its growth average reduces even further to 5.17%.

Figure 3.5. Number of NIA units consumed by patients; (2000-2021).

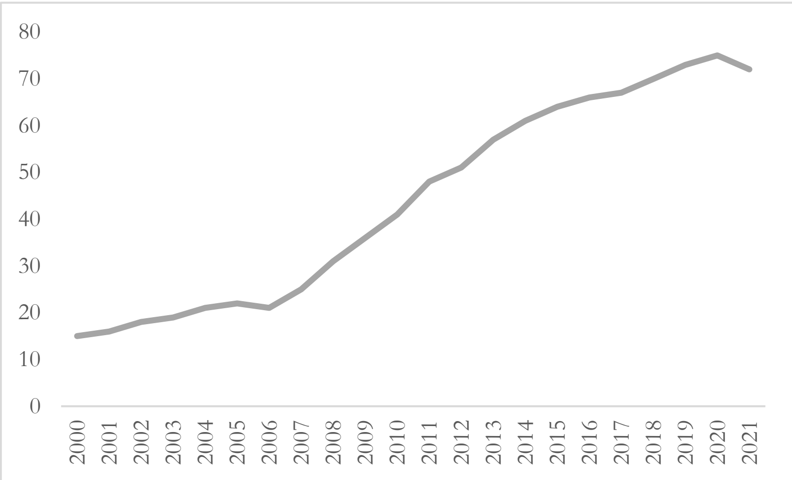


We cannot be too optimistic about these numbers, since the consistent reduction of the growth rate in Figure 3.5 may not only be due to the effective control of the disease, but also to new ways of treatment involving lesser numbers of single drugs or combination of drugs (implying less units sold), which may have appeared in the market in more recent years and proven to be more effective than a larger number of different drugs. Nevertheless, it also has to be acknowledged that the growth of the type 2 diabetics prevalence has stabilized after 2010 (see Figure 3.10 ahead), possibly contributing to the mild growth of NIA units sold in the last decade.

3.2.3. Dependent variable: (3) expenditure with insulin

In the treatment of diabetes, one pivotal drug is insulin. For type 1 diabetes, insulin is a *sine qua non* condition for survival; for type 2 diabetes, it is a complement of the therapeutic treatment. Consequently, it seems important to analyse separately the demand behaviour for this specific drug in the two forms previously defined: the NHS expenditure and the number of units sold. Figure 3.6 shows the NHS spending (10^6€) with insulin between 2000 and 2021. Again, we can identify three different paces for the growth of this expenditure. Between 2000 and 2006, we compute an average growth of 5.71% per annum. In the following period up until 2014, we register an average growth of 23.81%, more than 4 times the average of the previous period. In the third sub-period from 2014 to 2021, we compute an annual average growth of 2.58%, noticeably smaller than the one of the first period. The different growth patterns of the NHS insulin expenditure showed in Figure 3.6 are mostly justifiable by the increases of its average price. Indeed, in the first half of the sample period, between 2000 and 2011, the average growth of the insulin price was 12.44% per year whereas, from 2012 to 2021, its price grew at an average rate of only 0.49%.

Figure 3.6. NHS expenditure share (10^6€) with insulin; (2000-2021).



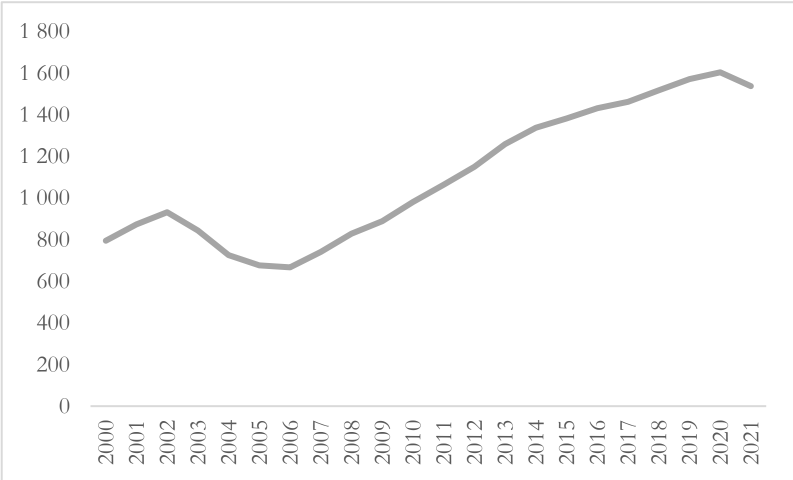
An additional explanation for the growth patterns of the expenditure with insulin, may lay with the preference of the NHS physicians to prescribe the newer non-insulin injectable drugs recommended for type 2 diabetes, which appeared in the market in the second half of the [2000-2021] period. These drugs have the additional advantage of providing cardiovascular protection, since diabetes is also a main risk factor also for heart diseases.

3.2.4. Dependent variable: (4) number of units of insulin sold

Figure 3.7 displays the number of insulin units sold within in the last two decades. In this case, the difference of the growth profiles in this figure, compared with that of the NHS expenditure with insulin in Figure 3.6, is as evident as in the NIA's case. At first, between 2000 and 2006, the average growth of insulin units purchased is -2.28% per year. This negative rate is probably due to the low number of type 1 diabetics in the early 2000 and the substitution of insulin with other antidiabetic drugs for the treatment of type 2 diabetes, given the then very high price of insulin. Then, between 2006 and 2014, the growth rate of insulin units sold increases drastically to a yearly average of 12.56%. Here the justification may be linked with the rise in the number of type 1 patients since the beginning of the century and with the 9.92% annual average growth of type 2 diabetes in just two years (2007 and

2009). Finally, between 2014 and 2021, the growth in the number of insulin units sold decreases sharply to less than 1/6 of the previous period rate, to 2.14% per year, probably due to the moderate increase of the type 1 cases and the stability of the number of type 2 patients.

Figure 3.7. Number of insulin units dispensed to patients; (2000-2021).



3.3. Independent variables

As stated above, demand theory defines as main determinants of the demand for normal goods or services, the own price, the price of substitutes and/or complements, and the consumers' disposable income. In the case of the demand for antidiabetic drugs, there are few substitutes and, in the case of insulin when applied to type 1 diabetics, there are no substitutes at all. Thus, the determinants of the national demand for antidiabetics include the average price of the recommended drugs and the consumers' purchasing power, measured by the real GDP per capita. However, there are other variables that should also be included as explanatory of the dependent variables. For instances, the national poverty rate is a variable that can complement the information about the purchasing power of the population, as well as suppling additional information about the vulnerable fringes of population more susceptible to endure poor health conditions. Another potentially relevant variable to explain the demand behavior for antidiabetics is the prevalence of the disease in the population. The prevalence of diabetes is measured by the number of diagnosed cases that, once detected, remains a challenging condition throughout all the patients' lives, needing permanent attention and treatment, particularly with the cases of type 1 diabetes.

Another potentially pertinent explanatory variable determining the behavior of the demand for antidiabetics is the literacy level of the Portuguese population, particularly that of women, as a proxy for the national health literacy. Assuming that women are more likely to be relevant in teaching children the behaviour that will keep them healthier throughout their lives, the women's literacy may be of particular interest in the explanation of antidiabetics' consumption, given that, at least in the type 2 diabetes case, this disease can be controlled or even prevented with changes in lifestyles and behavioural options. Consequently, the additional determinant of the demand for antidiabetics is the national level of women's literacy.

In sum, the quantitative explanatory variables included in the empirical models estimated in chapter 4 are the following: the annual levels of the GDP per capita; the annual poverty rate; the annual average price of all antidiabetic drugs excluding insulin; the annual average price of insulin; the prevalence of type 1 and type 2 diabetes; and the literacy level of the Portuguese women[7].

3.3.1. Independent variables: (1) real GDP per capita and poverty rate

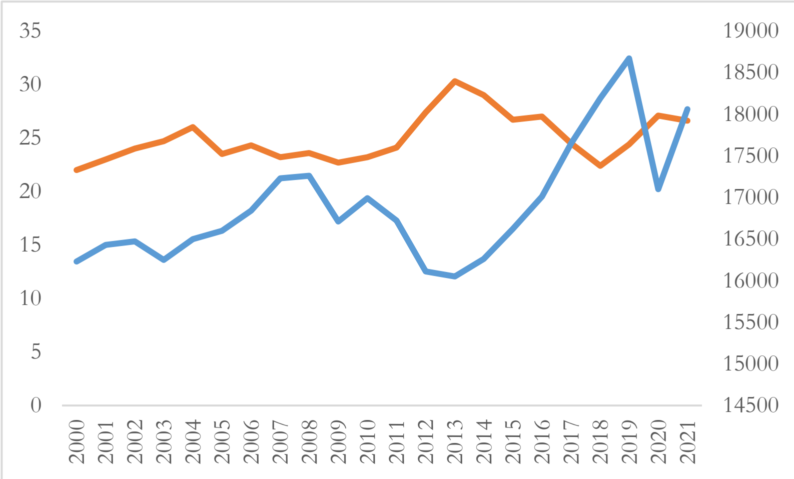
Figure 3.8 shows a graph with the real GDP per capita in euros (blue line), measured on the right-hand side vertical axe, and the poverty rate in percentage (orange line), measured on the left-hand side vertical axe, between 2000 and 2021[8]. The expected mirror-like behaviour of the two lines attest the quasi symmetry of both measures given that it is likely that when the real GDP per capita raises, the poverty rate falls and vice-versa. Thus, in the aftermath of the 2008 financial crisis, an increase of the poverty rate is observed from 22.7% in 2009 to 30.3% in 2013, its highest value since the beginning of the century. Matching this movement, the real GDP per capita registered its lowest value in the same year and for the same period. The poverty rate decreases consistently after 2013, up until the next crises in 2020, with the outbreak of SARS-CoV-2 pandemic. For the last two years of the sample

[7] The data sources for these variables are the following: for prices and total expenditure with antidiabetic drugs is the *Centro de Informação do Medicamento e Produtos de Saúde* (CIMI – INFARMED). For real GDP per capita is Eurostat – Real GDP per capita (in "Goal 8 – Decent work and economic growth"); the indicator is calculated as the ratio of real GDP to the average population of a specific year; GDP measures the value of total final output of goods and services produced by an economy within a certain period of time: the online data code is SDG_08_10. For women's literacy level is the *Pordata* website; for the poverty rate is the *Instituto Nacional de Estatística* (INE)

[8] The poverty rate is measured by the proportion of the population whose equivalent income, after social transfers, is below a limit, called "poverty line" defining the level of income for which a person is considered "poor". In Portugal, the poverty line is set at 60% of the median of the national equivalent disposable income, after social transfers.

period, the economic activity came almost to a halt with the expected consequences of unemployment increases, salaries and consumption decreases and income contractions.

Figure 3.8. Real GDP per capita (€) (blue) and poverty rate (%) (orange); (2000-2021).

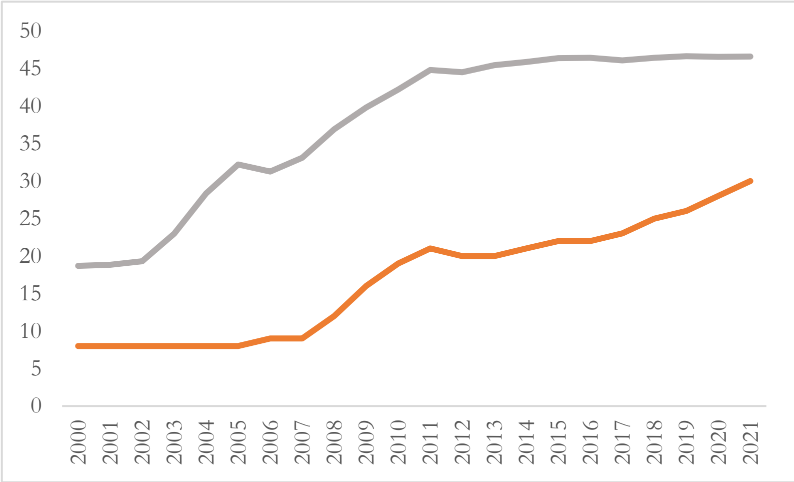


3.3.2. Independent variables: (2) average prices of insulin and NIA drugs

The information about the NHS and patients expenditure with each antidiabetic medicine and the number of units consumed of each one of these drugs was given by CIMI[9]. Within the "*all* antidiabetics" aggregate, we think that it is important to separate the insulin consumption from the consumption of all the other antidiabetics, given that the price of the former is fully covered by the NHS so that patients do not pay for accessing this drug. Thus, the average weighted annual price for the NIA drugs is obtained by computing a weighted average of the set of individual prices of all NIAs for each year. In what concerns the price of insulin, we simply use the annual average price information supplied by CIMI. Figure 3.9 shows the annual weighted average price of the NIA drugs (orange line) and that of the insulin (grey line) across the two decades under investigation.

[9] The data source for the prices of antidiabetic drugs is the *Centro de Informação do Medicamento e Produtos de Saúde* (CIMI – INFARMED), obtained through personal contacts via e-mail. The data is available if request.

Figure 3.9. Average annual price (€) of insulin (grey) and NIA drugs (orange); (2000-2021).



It is apparent in Figure 3.9 that, although the price variables of both categories increase along the whole period, they have a different pace for their respective growth rates within distinctive sub-periods. For instance, the insulin price increases sharply at an average annual rate of 11.00%, in the first half of the sample period while, in the second half of the sample period, between 2011 and 2021, the insulin price remains practically constant around 46€ per unit, showing a modest average growth of 0.44% per annum. On the other hand, the average price of the NIA drugs is relatively constant around 8€ per unit between 2000 and 2007, slightly growing at an average rate of 1.56% yearly. However, in the next period up until 2011, we compute an average growth rate of 33.33% per year, more than 20 times the previous average growth. Finally, within the period 2011 and 2021 the average annual growth of the NIAs price drops to a much lower rate of 4.29% per year, even so, more than doubling the average rate of the first period. The drastic increases of these two average prices variables, particularly in the case of the NIA drugs, are the main cause for the increase of the national expenditure with these types of drugs.

3.3.3. Independent variables: (3) prevalence of type 2 and type 1 diabetes

The prevalence of diabetes in a population is measured by the number of diagnosed cases per period, usually a year. Until 2009, the available data on the diabetes prevalence in the Portuguese territory were estimates based on the Inquérito Nacional de Saúde (2006)[10] and

[10] The *Inquérito Nacional de Saúde* is a health survey using interviews to collect population-based data to generate estimates on the state of health of the Portuguese population, providing the prevalence numbers for chronic diseases, like diabetes, by group age and sex. Since it is published every 10 years it does not provide the annual prevalence data for our sample of 22 years.

on the extrapolations of numbers from the Spanish region of Cataluña. The first study about the prevalence of the type 2 diabetes exclusively for Portugal is that of Gardete-Correia et al. (2010). The authors use the 2001 Portuguese Census to gather a random sample of residents aged between 20 to 79 years old, with which they estimate the prevalence of type 2 diabetes among the Portuguese population. This study is the database for all the estimated prevalence series published in the *Relatório Anual do Observatório Nacional da Diabetes*[11], which information we use. The data about type 2 diabetes prevalence in Portugal is scarce and the official data available is obtained from the Gardete-Correia et al. (2010) study as the source of all the published estimates.

However, according to the American Diabetes Association (2020), the Centers for Disease Control and Prevention (CDC) (2023) and the Direção Geral de Saúde (2011), there is a relatively stable relationship between the prevalence of diabetes type 2 and type 1 that is found across all Western countries. This empirical regularity establishing a percentage relationship between the number of patients with type 1 diabetes with the number of patients diagnoses with type 2 diabetes, may change from country to country, but it is accepted, as far as we can say, as a reliable and steady relationship. Thus, when confronted with the absence of published annual data for the prevalence of type 2 diabetes for the years 2001, 2002, 2004, 2005, 2006, 2016, 2017, 2019 and 2020, and having the official data for type 1 diabetes for the full sample period, we applied this "rule of thumb" to obtain estimates for the missing data on the type 2 diabetes prevalence, based on the prevalence of type 1 diabetes[12]. Figures 3.10 and 3.11 depict, respectively, the prevalence numbers for type 2 and type 1 diabetes. The information in Figure 3.11 about type 1 diabetes prevalence is retrieved from official published data. The information in Figure 3.10 about type 2 diabetes prevalence is partly retrieved from official published data, and partly extrapolated from the prevalence of type 1 diabetes, in accordance with the above mentioned "rule of thumb".

Figure 3.10 shows the number of cases of type 2 diabetes (prevalence) in the Portuguese population with ages between 20 and 79 years old, for the period [2000-2021]. We can see from the graph that there are two distinctive growth paces for this variable. Up until 2010,

[11] In Portugal, the official data source for diabetes prevalence is the *Relatorio Anual do Observatório Nacional da Diabetes*, published by *Sociedade Portuguesa de Diabetologia*. All the information supplied by this "*Relatório*" is based on the primary study of Gardete-Correia et. al (2010)

[12] The data for the prevalence of type 1diabetes is relatively more abundant, complete and regularly published. The source for the data on the type 1 diabetes prevalence is the *Programa Nacional para a Diabetes* 2017 and 2021. The source for the data on the prevalence of type 2 diabetes in 2000, 2003 and 2007, is the IDF Diabetes Atlas; the source for the data on the same variable in 2008 to 2015 and 2018 is the *Relatório Anual do Observatório Nacional da Diabetes*. For the way in which we used the official data on the prevalence of type 1 diabetes to estimate the missing values of the type 2 prevalence, please see Appendix 1.

the type 2 diabetes prevalence grows fast, at an average rate of 13.6% per year. But, in the next decade, the growth rate of this variable drops sharply to a modest 0.7% per year.[13]

Figure 3.10. Prevalence of type 2 diabetes in the Portuguese population; (2000-2021).

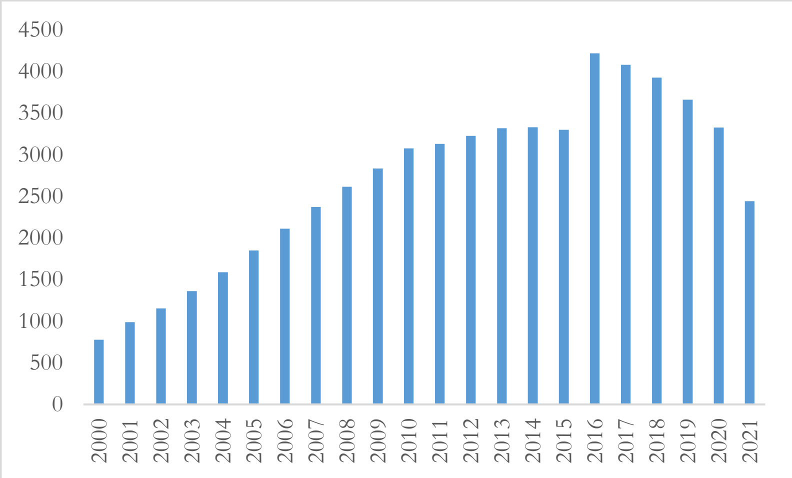
This steady maintenance of the number of cases in the second decade of the sample period may be the effect of preventive medicine and the availability of more information, as well as the efforts of the health and education authorities to limit the consumption of sugar and "junk food" at earlier ages, more recently converted into law with these three documents approved in Parliament: *Despacho n.º 11418/2017*, *Lei n.º 30/2019* and *Despacho n.º 8127/2021*[14]. Additionally, it should be mentioned that Western countries' populations are nowadays more aware of what may be the main causes of type 2 diabetes and are more likely to act accordingly, making more conscientious and consistent efforts to adopt healthier lifestyles.

Figure 3.11 shows the prevalence (number of cases) of type 1 diabetes for sample period of two decades, from 2000 to 2021.

[13] Given that chronic diabetic cases cannot "disappear" from one year to the other, we choose to ignore the "jump" of more than 700 thousand cases added in 2016, because they rapidly decrease 2 years later. These variations could probably be due to fluctuations of the migrating population. The same must be said about the 250 thousand cases that "disappear" in 2007 and "reappear" in 2008.

[14] The *Despacho nº11418/2017* sets the implementation of measures for the prevention of the disease, in particular, promoting healthier eating habits; the *Lei nº30/2019*: introduces restrictions on advertising for children under 16 of foods and beverages containing high energy values, salt content, sugar, saturated fatty acids and processed fatty acids; the *Despacho nº8127/2021* establishes the rules for the preparation of menus and the food items sold in buffets and vending machines in the public network of schools managed by the Ministry of Education.

Figure 3.11. Prevalence of type 1 diabetes in the Portuguese population; (2000-2021).



We can observe that, although displaying smaller numbers, the type 1 diabetes prevalence has also been increasing during the sample period, but in a different way from that of the type 2 diabetes. Indeed, we can identify in the graph of Figure 3.11, three different growth rhythms throughout the period under analysis. First, up until 2007, we observe that the prevalence of type 1 diabetes is growing at an increasing rate (concave shape of the trend), attaining a shocking annual average growth of 25.6% (triplicating the number of cases from 777 in 2000, to 2371 in 2007). After 2007 and up until 2014, the variable increases at a decreasing pace (convex shape of the trend), reducing its annual average growth to 5.8%, less than four times the rate of the previous period. From then on, there appears to be a decreasing trend up until the end of the period. Indeed, the number of cases reduces from 3331 in 2014 to 2443 cases in 2021, implying a negative average growth of -3.8% per year. However, it is difficult to justify the dubious "*jump*" of 917 cases in the 2016, relative to the previous year (a 27.8% increase, when the annual average growth rate of the previous 6 years is 1.2%). Even with the incoming flux of migrants that enter the country after 2015, this "*jump*" is difficult to validate[15].

Additionally, knowing that this disease is chronic, the only explanation for the decreasing in the number of cases in the last 7 years (excluding the abnormal increase of more than 900 cases in 2016) is emigration, given that death is not plausible for people this young and benefitting from all the modern medicine progresses and dedicated public health assistance currently offered to the population. Even assuming that, during the years of the pandemic,

[15] As it may be obvious, the information on the prevalence of type 1 diabetes must be taken with a "grain of salt", even if it is 'official' and 'published' information. Consequently, the data for the type 2 prevalence extrapolated from the "official" one on the type 1 prevalence, should also be taken with the same "grain of salt" given that the former is retrieved from the latter.

the virus could have ripped a few lives of the most vulnerable among the type 1 diabetic patients, there is no reasonable way to accommodate the loss of 888 type 1 diabetic patients since 2015. However, the decrease of the number of cases in 2019 and 2020 may be partially justified by the ongoing pandemic, which led to draconian movement restrictions onto the population implying, therefore, less doctors' appointments scheduled, less patients attended, meaning less cases detected, less reports made and less cases registrations in the support platforms of the clinical practice. It is also important to recall that during the years of the pandemic (2020 to 2022) all tasks, duties and obligations that were not directly or indirectly related to the prevention, assistance and registration of the SARS-CoV-2 cases, were relegated to a second or third order of priority, if not destined to total obliviousness. Thus, the lack of reliable published data for the prevalence of chronic diseases after 2015, is probably also due to the disruption of the official registration of the diabetes cases during the pandemic[16].

3.3.4. Independent variables: (4) health literacy of the Portuguese population

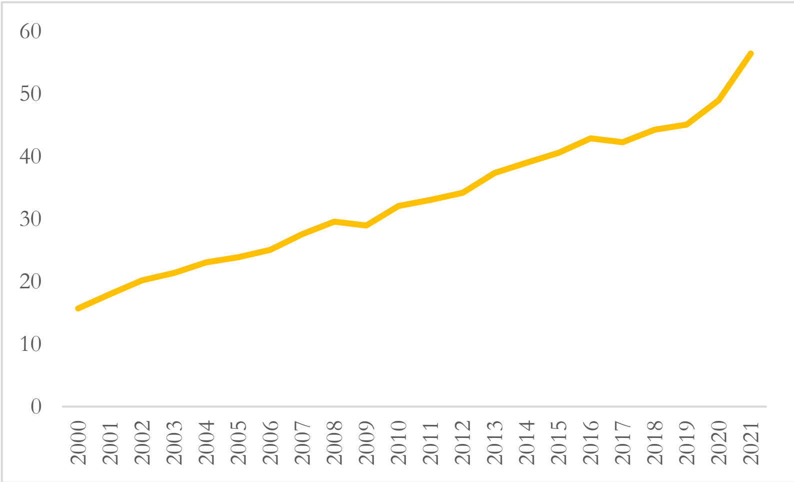
We believe that the best proxy for measuring the health literacy of the Portuguese population is the literacy level of Portuguese women, given that women are more likely to be actively involved with the health problems of their families[17]. Thus, the variable to be considered as the appropriate measure of the Portuguese health literacy is the share of the female population aged 25-34, who successfully completed tertiary studies (e.g. university, higher technical institution, etc.)[18]. Figure 3.12 shows this variable's observations for the years of the sample period.

[16] As reported by *Agência Lusa* in *Diário de Notícias* of March 13th, 2023, under the title: "*Limite ao acesso de registos hospitalares na pandemia prejudicou conhecimento da diabetes*." Available online in: https://www.dnoticias.pt/2023/3/13/351802-limite-ao-acesso-a-registos-hospitalares-na-pandemia-prejudicou-conhecimento-da-diabetes/

[17] In most empirical research work concerning economic growth and development and other social development indicators, women's literacy is typically the preferred variable to measure the impact of human capital on those social indicators.

[18] The source for the data on the literacy level of Portuguese women is Eurostat – Tertiary educational attainment by sex (in "Goal 4 – Quality education" from "Sustainable development indicators"). The educational attainment refers to ISCED (International Standard Classification of Education) 2011 level 5-8 for data from 2014 onwards and to ISCED 1997 level 5-6 for data up to 2013; the indicator is based on the EU Labour Force Survey (EU-LFS). The online data code is SDG_04_20.

Figure 3.12. Portuguese women aged 25-34 with tertiary education (%); (2000-2021).



It is perceptible in Figure 3.12 the consistent growth of the variable across the full period, with identifiable different paces. For instances, between 2000 and 2008, we compute an annual average growth of graduate young women of 9.72%. In the next period, between 2008 and 2017, the growth of the percentage of young women with tertiary education slows down to an average of 4.44% per year, with a drastic drop of -3.33%, right after the 2008 GFC, which is compatible with the diminishing disposable income, the rise of unemployment and the increase of tuition fees that took place within that recession period. Finally, between 2017 and 2021, the growth of the women's literacy variable realigns with that of the first period attaining an average rate of 8.93% per annum.

Concerning this variable, we came across the interesting fact that the percentage of Portuguese women aged 25-34 years old with a higher education degree has been growing fast and consistently since the beginning of the century and that, between 2019 and 2021, nearly 60% of young Portuguese women are graduated from universities, which favourably compares with the OECD average of 52%[19].

3.4. Conclusion

In this chapter, we conducted a detailed analysis of the variables that are going to be used in the econometric models estimated in chapter 4. These variables have been categorized into dependent and independent variables. The dependent variables include the NHS + patients' expenditure with NIA drugs; the quantity of NIA drugs consumed; the expenditure with

[19] OECD (2021a), Education at a glance 2021. OECD Indicators. The website is available in the References.

insulin, and the number of insulin units sold. Regarding the independent variables, income and prices are the generally accepted determinants of demand behaviour. So, we include, as representative of these determinants, the national real income per capita and the average prices of insulin and NIA drugs. Additionally, we also consider as explanatory variables, the national poverty rate, the prevalence of both type 1 and type 2 diabetes and the health literacy level of the Portuguese population.

A noteworthy fact about all the above mentioned variables is that all of them present a growth pattern in stages that more or less coincide with the sub-periods of before the 2008 GFC, during the recession that followed the 2008 GFC crisis and after the dismissal of the troika that managed the country within that period. These facts imply the use of dummy variables that are able to separate these sub-periods, allowing for a differentiation of the determinants' estimated impacts on the demand behaviour for antidiabetics within the different periods, which is one of the objectives of this dissertation.

In the next chapter, we employ all the aforementioned variables to estimate the econometric models that explain the behaviour of the national demand for antidiabetic drugs. We estimate eight regressions corresponding to the linear and log forms of four specifications, which dependent variables are: (1) the NHS + patients' expenditure with NIA drugs; (2) the number of units of NIA drugs purchased; (3) the NHS expenditure with insulin and (4) the number of insulin units sold.

4. Empirical models: derivation, estimation and results

4.1. Introduction

This chapter deals with the empirical analysis of the factors that are relevant for explaining the Portuguese demand behaviour for antidiabetic drugs, within the period 2000 to 2021, using linear and log-linear models. The estimation and quality evaluation of the several econometric models is carried out in order to select the specifications that best translate the data generation process of the demand for antidiabetics. Once the best models are selected their results are comprehensively discussed and interpreted to give a theory consistent and statistically robust view of the above mentioned demand behaviour, particularly in the period of economic recession that followed the financial global crisis of 2008. By the end of this chapter, some conclusions are drawn supporting the view that the demand for drugs that are health preservers behaves in different ways from the demand for normal good and services.

The demand equations for antidiabetic medicines involve nonstationary time series, which may lead to spurious regressions unless the variables are cointegrated. Cointegration among variables in an econometric specification indicates the existence of a genuine long-run equilibrium relationship among the time series involved. For the current analysis of all estimated models, we assess the existence of such relationship by testing the presence of a unit root in the residuals series of the estimated models. If the null hypothesis of a unit root in the residuals series is rejected, we conclude that each of the static estimated regressions represent the steady state long run equilibrium relationship between the demand for antidiabetics and its explanatory factors, excluding the possibility of a spurious association between the dependent variable and its determinants.

As previously stated, we analyse the demand for antidiabetic drugs by estimating the linear and log-linear forms of four different demand models: the demand for NIA drugs, where the dependent variable is either the expenditure or the number of units consumed and the demand for insulin, where the dependent variable is also either the expenditure or the number of units consumed. In the linear form, the estimated coefficients are interpreted as the absolute change in the dependent variable per unit absolute change of each determinant, *ceteris paribus*, that is, everything else constant. In the log-linear form, the estimated coefficients represent the relative change of the dependent variable per unit relative change of each determinant, that is, the elasticity of the dependent variable relative to each determinant, *ceteris paribus*. Both forms provide different insights into the impact of changes in the regressors on the demand for these medicines. However, for these two alternative forms, standard econometric criteria cannot be directly employed to compare them given that the dependent variable is in the linear form on one case, and in the log form on the other. Furthermore, since the coefficients represent different concepts (absolute changes in the linear case and relative changes or elasticities in the log-linear case), direct comparisons between them are also not feasible.

To allow for a comprehensive evaluation of the models' statistical performances and an informative interpretation of the coefficients' estimates, we report the estimations' results of both the linear and log-linear forms of the four specifications of the demand for antidiabetics in the following way: section 4.2.1 reports the estimation results, statistical quality and coefficients interpretation of the demand for NIA drugs, measured by the national expenditure with this type of drugs on the one hand, and by the number of units consumed, on the other hand; section 4.2.2 reports the same features for the insulin demand also using both measures of national expenditure and number of units consumed; section 4.2.3 concludes the chapter.

4.2.1. The demand for NIA drugs

1. Expenditure with NIA drugs

The linear and log forms of the regressions for the demand of NIA drugs measured by the NHS + patients' expenditure are, respectively:

$$NIA_t = \alpha_0 + \alpha_1 PNIA_t + \alpha_2 GDP_t + \alpha_3 POV_t + \alpha_4 T2D_t + \alpha_5 PTD_t \times T2D_t + \\ + \alpha_6 LIT_t + \alpha_7 GFC_t + \mu_t \tag{4.1}$$

$$lnNIA_t = \alpha'_0 + \alpha'_1 lnPNIA_t + \alpha'_2 lnGDP_t + \alpha'_3 lnPOV_t + \alpha'_4 lnT2D_t + \\ + \alpha'_5 PTD'_t \times lnT2D_t + \alpha'_6 lnLIT_t + \alpha'_7 GFC'_t + \mu'_t \tag{4.2}$$

Where, on the left hand side, NIA_t and $lnNIA_t$ are, respectively, the linear and log-linear forms of the dependent variables representing the demand for NIA drugs and measured by the disbursement of both NHS and the patients (in millions of euros). On the right hand side of Equations (4.1) and (4.2) are the independent variables $PNIA_t$ and $lnPNIA_t$, representing the average price (in euros) of the NIA drugs; GDP_t and $lnGDP_t$, expressing the real GDP per capita (in euros); POV_t and $lnPOV_t$, standing for the poverty rate (in percentage); $T2D_t$ and $lnT2D_t$, signifying the prevalence of type 2 diabetes (in thousands of patients) during the whole sample period; $PTD_t \times T2D_t$ and $PTD'_t \times lnT2D_t$, standing for the prevalence of type 2 diabetes between 2009 and 2017 and between 2006 and 2017, respectively[20]; LIT_t and $lnLIT_t$, representing the national health literacy, measured by the percentage of women, aged 25 to 34, that successfully completed tertiary education. GFC_t and GFC'_t are dummy variables that assume value 1 between 2006 and 2011 in the linear model and 2009 and 2015 in the log-linear model respectively, and 0 otherwise, standing for the period that includes the economic recession that followed the 2008 GFC crisis. Finally, μ_t and μ'_t are the assumed well-behaved (*i.i.d.*) disturbance terms of, respectively, equations (4.1) and (4.2).

Tables 4.1 and 4.2 show the estimation results of, respectively, Equation (4.1) and (4.2), using the Henry's (1995) general to specific methodology, which entails the estimation of a broader (general) model with all the potential relevant determinants of the dependent variable and a reduced (specific) model, which includes uniquely the statistically significant explanatory variables, using a threshold significance level[21].

Tables 4.1 and 4.2 are divided into an upper part and a bottom part.[22] In the upper parts of the tables, the first columns show the constant and explanatory variables of, respectively, Equations (4.1) and (4.2) right-hand-sides; the second columns show the estimated values of the explanatory variables' coefficients (p-values in brackets) for the 'general' (initial) models and the third columns contain the same information for the 'specific' (final) regression. The bottom parts of Tables 4.1 and 4.2 show the statistical robustness of the regressions including the following items: R^2 and adjusted R^2 (AdjR^2) statistics, measuring the models' goodness of fit; the F-statistics (p-values in brackets), measuring the regressions' overall significance; the White (1980) test statistic (p-values in brackets), which null hypothesis is the homoscedasticity of the disturbance terms; the Breusch-Godfrey (1978) serial correlation

[20] PTD and PTD' are dummy variables that take value 1 within [2009-2017] for Equation (4.1), and within [2006-2017] for Equation (4.2) and 0 otherwise. The multiplication of T2D by these dummies (PTD and PTD') – called cross-dummy variable – splits into two the behaviour of the type 2 diabetes prevalence (T2D) across the sample period. In this way, the different behaviour of the T2D, growing faster in the middle of the sample period and slower outside this period, can be accommodated in the respective equations.

[21] This same methodology is used throughout the estimations of all subsequent models, using the threshold of 10% as the minimum significance level.

[22] Hereafter, all the tables containing the estimation results for all the subsequent estimated models have the same structure (*mutandis mutatis*) described for Tables 4.1 and 4.2.

LM test statistics (p-values in brackets), which null hypothesis is the absence of serial correlation of the disturbance terms and the Augmented Dickey-Fuller (1979) t-test (p-values in brackets), which null hypothesis is the presence of a unit root in the residuals series of the regression. In this last test, if the null is rejected, the residuals series is stationary, which means that the variables are cointegrated and the regression represents a steady-state long run equilibrium between the dependent variable and its determinants. The interpretation of the results in Tables 4.1 and 4.2 (as in all the remaining tables hereafter) is focused solely on the estimates of the final regression, ignoring the estimates of the initial equation, which are only included for informative reasons about the variables' individual significance in the process of progressing from the 'general' initial model to the 'specific' final one. This final model is, in general, a statistically more robust reduced form of the initial specification.

Figures 4.1 and 4.2 depict the residuals (blue line) actual (orange line) and fitted (green line) values of the final (specific) regressions in, respectively, Tables 4.1 and 4.2, showing an almost perfect fit between the actual and the fitted values for both the linear and log-linear models of the NIA drugs' demand, measured as the NHS + patients' expenditure with their acquisition.

Table 4.1. Estimation results for Equation (4.1).

Variables	Initial (general) regression	Final (specific) regression
C	-34.9299 (0.7768)	-82.1394 (0.0000)
PNIA	10.7070 (0.0000)	10.4010 (0.0000)
GDP	-0.0031 (0.6199)	-
POV	0.0383 (0.9794)	-
T2D	-0.0330 (0.1092)	-0.04140 (0.0179)
PTD×T2D	0.0438 (0.0617)	0.04206 (0.0573)
LIT	2.6550 (0.0095)	2.83000 (0.0005)
GFC	-71.2514 (0.0097)	-64.8933 (0.0081)
R^2	0.9970	0.9969
AdjR^2	0.9955	0.9959
F-statistic	671.963 (0.0000)	1025.661 (0.0000)
White heteroscedasticity test	-	21.7533 (0.1513)
Breusch-Godfrey serial correlation test	-	0.4422 (0.5061)
Augmented Dickey-Fuller	-	-4.7131 (0.0014)

Table 4.2. Estimation results for Equation (4.2).

Variables	Initial (general) regression	Final (specific) regression
C	-3.724541 (0.3661)	-1.665219 (0.0000)
ln PNIA	1.195143 (0.0000)	1.180706 (0.0000)
ln GDP	0.192528 (0.6183)	-
ln POV	0.079921 (0.6289)	-
ln T2D	0.135634 (0.0719)	0.126730 (0.0456)
ln PTD×T2D	-0.131451 (0.0943)	-0.122629 (0.0598)
ln LIT	0.612220 (0.0003)	0.662061 (0.0000)
GFC	0.880278 (0.0966)	0.818020 (0.0630)
R^2	0.9994	0.9994
AdjR^2	0.9991	0.9992
F-statistic	3388.24 (0.0000)	5317.47 (0.0000)
White heteroscedasticity test	-	19.91310 (0.2242)
Breusch-Godfrey serial correlation test	-	1.1320 (0.2874)
Augmented Dickey-Fuller	-	-4.327032 (0.0033)

Figure 4.1. Residuals, actual and fitted values of Equation (4.1); (2000-2021).

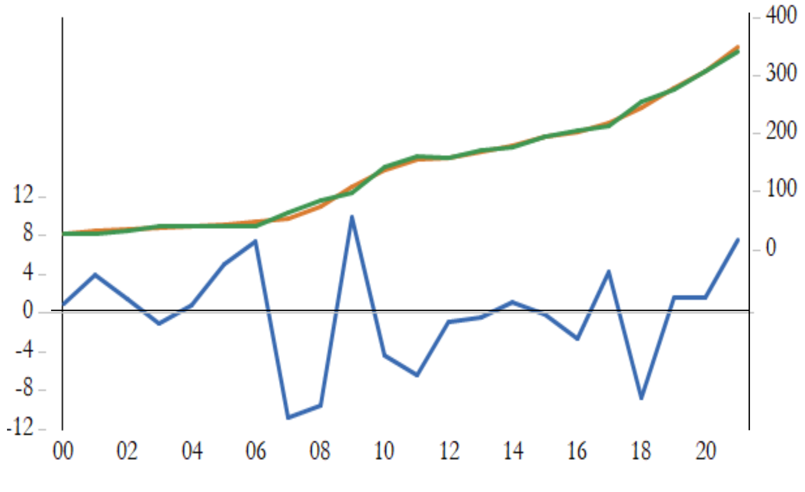
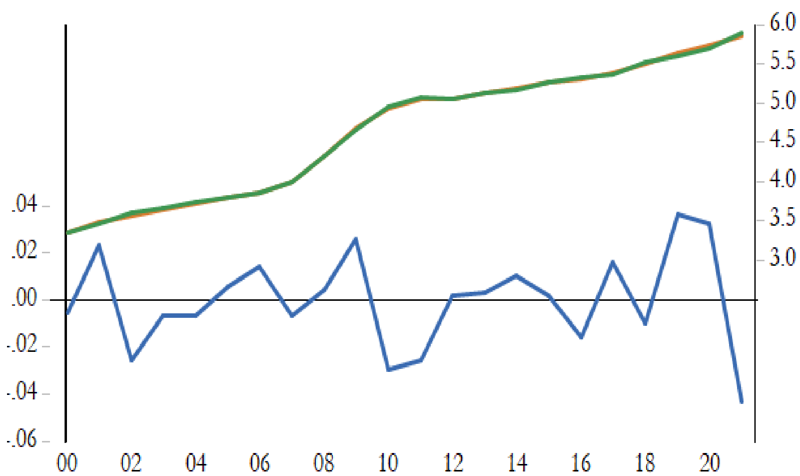


Figure 4.2. Residuals, actual and fitted values of Equation (4.2); (2000-2021).



Interpretation of the coefficients estimates of the (final) linear model in Table 4.1

All the explanatory variables in Table 4.1 are individually significant at the 2% level, except for the cross variable PTD×T2D, which is individually significant at the 6% significance level. The model explains 99.7% of the dependent variable variations and is overall significant at less than 1% significance level. Also, there is no evidence of heteroscedasticity or serial correlation in the disturbances and the variables are cointegrated, as demonstrated by the Augmented Dickey-Fuller (ADF) test that rejects the null of a unit root in the residuals series, with a higher than 99% confidence level. We may, therefore proceed with the interpretation of the coefficients' estimates given the statistical robustness of the model.

Everything else constant, a 1€ increase (decrease) in the average price of the NIA drugs implies an increase (decrease) of 10.4 million € in the national expenditure with this type of drugs. It is apparent that the demand for NIA drugs does not behave as the demand for normal goods, where the decrease of expenditure is expected when the price increases. Here, because we are dealing with life-saving medicines, the rise in prices will not deter demand enough and, consequently, the level of expenditure will increase. Also, an increase of 1 percentage point (1pp) in the population's health literacy level conduces to a 2.83 million € increase in the NIA's national expenditure. The health literacy of the population may have two opposite effects on the expenditure level with NIA drugs for if, on the one hand, the more informed a population is, the more likely will be to choose healthier life styles conducing to a reduction of the prevalence of the disease and, therefore, to the shrinking of the expenditure with antidiabetic drugs, on the other hand, the more informed a population is, the more likely will be that patients will follow the doctors' instructions to the letter, taking the prescribed drugs in the recommended quantities, not skipping the medication doses, even when income diminishes and unemployment increases, inducing a positive relationship between health literacy and expenditure with medication. That seems to be the case here, as the latter impact appears to surpass the former.

Regarding the prevalence variable, there are two stages in its impact on the expenditure, given the combined behaviours of the NIA's average price (relatively constant around 8€ up until 2008 and a sharp rise afterwards) on the one hand, and that of the type 2 prevalence (a sharp increase up until 2010 and a very small average growth thereafter). These two counterweights actions seem to give rise to different impacts of the type 2 diabetes prevalence on the expenditure with NIA drugs. First, from 2000 to 2008 and from 2018 to 2021 (when PTD=0), the impact is small, statistically significant and negative of 41 400€ (–0.04140 ×

10^6€) per each 1 000 additional patients, meaning that, in these periods, the national expenditure diminishes, on average, 41€ per patient and per year, which is a relatively small impact. However, the impact of T2D on the expenditure between 2009 and 2017 (when PTD=1), is statistically significant, positive, but even smaller, of 660€ [(0.04206 – 0.04140) × 10^6€ = 660€) per each additional 1 000 patients, meaning that in this period, the impact of each additional patient on the national expenditure with NIA drugs is 66 cents, on average and per year, everything else constant.

The impact of the economic recession that followed the 2008 GFC crisis, on the national expenditure with NIA drugs is measured by the coefficient estimate of GFC. In fact, when GFC=1, within the period [2006-2011], the annual average expenditure with NIA decreases 64.9 million €, everything else constant. As expected, in times of hardship, with reduced income and high unemployment, people try to reduce their consumption of goods, even if these goods are life-saving drugs, by reducing doses and/or skipping treatments.

Interpretation of the coefficients estimates of the (final) log model in Table 4.2

All variables are individually significance at the 5% level or less, except for variables PTD'×lnT2D and GFC', which display significance levels of 6% and 7%, respectively. This econometric model explains 99.9% of the observed variations in the dependent variable and it is overall significant at less than 1% significance level. Moreover, the White (1980) and the Breusch-Godfrey (1978) LM test statistics reveal the absence of both heteroscedasticity and serial correlation in the model's disturbances terms. Finally, the Augmented Dickey-Fuller (ADF) test indicates the absence of a unit root in the regression residuals with a confidence level higher than 99%, which implies the presence of a cointegrated association between the dependent variable and its determinants. Therefore, we may proceed with the interpretation of the coefficients' estimates.

Everything else constant, an increase of 1% in the average price of NIA drugs induces a rise of 1.1807% in the national expenditure with this type of drugs. This means that, in contrast with what happens when dealing with normal goods, the price elasticity of demand is positive and elastic, meaning a more than proportional response of the expenditure to price increases. This contradicts the values of the demand price elasticity for normal goods, which is always negative and often inelastic, particularly for necessary goods. On the contrary, the behaviour of the expenditure to changes in the number of patients is expected, since, for each 1% additional in the prevalence of type 2 diabetes patients, the national expenditure with NIA drugs always increases: 0.12673% on average and per year, until 2005 and after 2017 (when PTD'=0) and 0.0041% (0.12673 − 0.122629 = 0.0041) between 2006 and 2017 (when PTD'=1). The inelastic expenditure response (particularly in the period of economic recession) to increases in the number of patients may have to do with the reasons pointed out above. The patients increase their expenditure but in a very parsimonious way.

In what concerns the population's health literacy we observe that an increase of 1% in this variable conduces to a 0.6621% increase in the NIA's national expenditure. The justifications for this small, positive and inelastic elasticity estimate is identical to that given for the corresponding coefficient in Equation 4.1.

The impact on the national expenditure with NIA of the economic recession that followed the 2008 GFC crisis is measured here differently from the what it was in Equation 4.1, due to the log-linear nature of Equation 4.2. In this case, the impact when GFC'=1, within the [2009-2015], must be measured alongside the intercept value. So, the average expenditure with NIA in the hypothetical case of all quantitative variables being unit (1€ for the price, 1000 for the type 2 diabetics patients, 1% for the health literacy variable), meaning that all log variables are zero, and 0 for all the dummies, would be measured by the exponential of the intercept, $e^{-1.66522} = 0.189149$, that is, 189.15€. This value is to be added to any other scenario of different values for the variables when GFC'=0, that is, outside the period [2009-2015]. However, what we want to measure is the impact of the post 2008 crisis on the expenditure, which is given by $e^{-1.66522 + 0.81802} = 0.428614$, that is, 428.61€. This value is added to any scenario of different values for the variables when GFC'=1, that is, in [2009-2015]. In this case, therefore, the model points out to an increase of the expenditure within the period post 2008 crisis, but the value added is so small (the difference between 428.61 − 189.15 = 239.46€), that safely can be considered irrelevant. Nevertheless, is still positive and statistically significant, contradicting all the other results obtained in all the other models.

2. Units consumed of NIA drugs

The linear and log forms of the regressions for the demand of NIA drugs measured by the number of units consumed by the patients are, respectively:

$$nia_t = \gamma_0 + \gamma_1 Pnia_t + \gamma_2 GDP_t + \gamma_3 POV_t + \gamma_4 T2D_t + \gamma_5 PTD_t \times T2D_t + \gamma_6 LIT_t + \gamma_7 GFC_t + \mu_t \tag{4.3}$$

$$lnnia_t = \gamma'_0 + \gamma'_1 lnPnia_t + \gamma'_2 lnGDP_t + \gamma'_3 lnPOV_t + \gamma'_4 lnT2D_t + + \gamma'_5 PTD'_t \times lnT2D_t + \gamma'_6 lnLIT_t + \gamma'_7 GFC'_t + \mu'_t \quad (4.4)$$

Where, on the left hand side, nia_t and $lnnia_t$ are, respectively, the linear and log forms of the dependent variables representing the demand for units of NIA drugs (in millions). On the right hand side are the independent variables $Pnia_t$ and $lnPnia_t$, representing the average price (in euros) of the NIA drugs; GDP_t and $lnGDP_t$, expressing the real GDP per capita (in euros); POV_t and $lnPOV_t$, standing for the poverty rate (in percentage); $T2D_t$ and $lnT2D_t$, signifying the prevalence of type 2 diabetes (in thousands of patients) during the whole sample period; $PTD_t \times T2D_t$ and $PTD'_t \times lnT2D_t$, standing for the type 2 diabetes prevalence between 2010 and 2017 for both variables; LIT_t and $lnLIT_t$, expressing the national health literacy (in %) and GFC_t and GFC'_t, which are both dummy variables assuming value 1 in [2012-2015] and 0 otherwise, standing for the recession period that followed the 2008 GFC crisis. Finally, μ_t and μ'_t are assumed well-behaved (*i.i.d*) disturbance terms of, respectively, Equations (4.3) and (4.4). Tables 4.3 and 4.4 show the estimation results of, respectively, Equation (4.3) and (4.4) and Figures 4.3 and 4.4 depict the residuals (blue line) actual (orange line) and fitted (green line) values of the final (specific) regressions in, respectively, Tables 4.3 and 4.4.

Table 4.3. Estimation results for Equation (4.3).

Variables	Initial (general) regression	Final (specific) regression
C	-4.05709 (0.2146)	0.35797 (0.1025)
PNIA	0.12388 (0.0002)	0.113278 (0.0001)
GDP	0.00023 (0.1693)	-
POV	0.04440 (0.3485)	-
T2D	0.00106 (0.0298)	0.001093 (0.0194)
PTD×T2D	-0.000413 (0.0196)	-0.000453 (0.0066)
LIT	0.10835 (0.0006)	0.129136 (0.0000)
GFC	0.28822 (0.1240)	0.249876 (0.0824)
R^2	0.9959	0.9953
AdjR^2	0.9938	0.9938
F-statistic	483.0412 (0.0000)	671.5204 (0.0000)
White heteroscedasticity test	-	21.48640 (0.2053)
Breusch-Godfrey serial correlation test	-	1.776906 (0.1825)
Augmented Dickey-Fuller	-	-5.977157 (0.0001)

Table 4.4. Estimation results for Equation (4.4).

Variables	Initial (general) regression	Final (specific) regression
C	-2.393095 (0.4646)	-1.621949 (0.0000)
ln PNIA	0.182559 (0.0003)	0.187102 (0.0000)
ln GDP	0.089483 (0.7758)	-
ln POV	-0.023303 (0.8568)	-
ln T2D	0.109860 (0.0169)	0.112654 (0.0064)
PTD×ln T2D	-0.00760(0.0099)	-0.008097 (0.0026)
ln LIT	0.672631 (0.0000)	0.671593 (0.0000)
GFC	0.037103 (0.0814)	0.029827 (0.0558)
R^2	0.9976	0.9976
AdjR^2	0.9964	0.9968
F-statistic	841.8047 (0.0000)	1315.078 (0.0000)
White heteroscedasticity test	-	14.69316 (0.0118)
Breusch-Godfrey serial correlation test	-	1.993331 (0.1580)
Augmented Dickey-Fuller	-	-3.915727 (0.0089)

Figure 4.3. Residuals, actual and fitted values of Equation (4.3); (2000-2021).

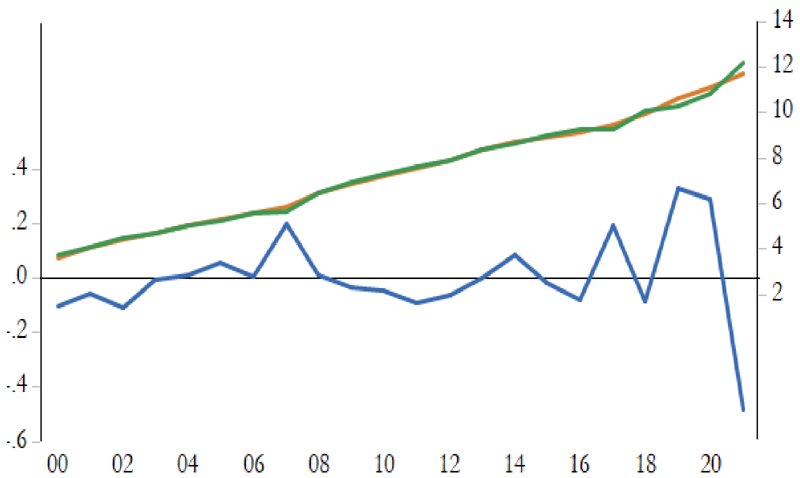
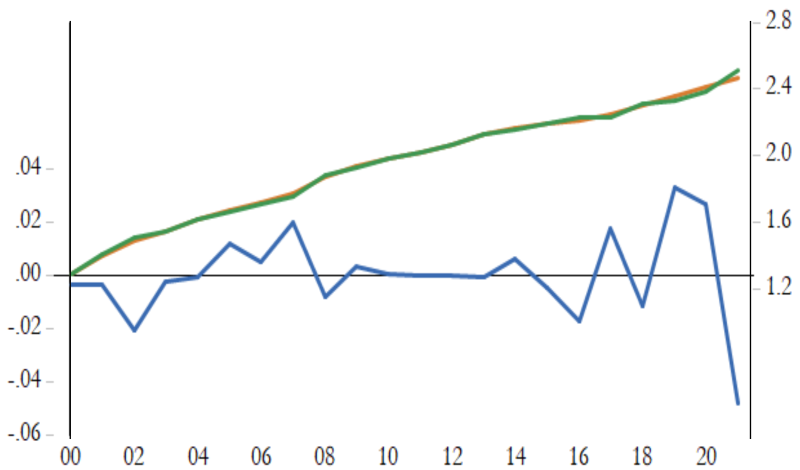


Figure 4.4. Residuals, actual and fitted values of Equation (4.4); (2000-2021).



Interpretation of the coefficients estimates of the (final) linear model in Table 4.3

All the explanatory variables in Table 4.3 are individually significant at the 2% level, except for the dummy variable GFC, which is individually significant at the 9% level. The model explains 99.6% of the dependent variable variations and is overall significant at less than the 1% significance level. Furthermore, there is no evidence of heteroscedasticity or serial correlation in the disturbances and the variables are cointegrated.

The interpretations of the coefficients' estimates of variables Pnia and LIT are the same (*mutatis mutandis*) as those of the of PNIA and LIT coefficients in Table 4.1, since their signs are identical. The impact of T2D on the dependent variable during the periods when PTD=0 (i.e. [2000-2009] and [2018-2021]), is positive and significant of 1 093 (0.0011×10^6) units per each 1 000 additional type 2 diabetic patients. This represents an additional estimated average of 1.1 packs per patient, per year, during those periods. However, within the period when PTD=1, that is, within [2010-2017], the T2D impact diminishes by a relatively minor yet statistically significant, amount of 453 units (-0.000453×10^6) on average, per each 1 000 additional patients and per year. This implies that, within this period, the estimated average of the annual number of NIA units purchased would be 640 units per additional 1 000 patients, instead of the 1 093 units/1 000 patients observed before and after the recession period of the post 2008 financial crisis. This means that, on average, within the recession period, the national consumption of NIA packages reduces to an average of 0.64 packs per patient per year, whereas within the non-recession periods, that average consumption is 1.1 packs/patient/year, everything else constant.

As for the interpretation of the GFC coefficient, the average annual increase of the number of NIA units consumed in the period [2012-2015] (when GFC=1), is positive, statistically significant and of 0.2499 millions of units (249 876 units), everything else constant. Contrary of what was concluded for the corresponding coefficient in Table 4.1, where the estimate is negative, meaning that there is a decrease of the NIA expenditure during the recession that followed the 2008 financial crisis, the GFC coefficient in Table 4.3, is positive and significant indicating an increase of the number of units consumed during this period. However, the contradiction is merely apparent, since the modest increase in the average number of units consumed annually (about 250 thousand), associated with a decrease of the average annual expenditure of about 65 million €, must simply mean that consumers may have swap the branded, more expensive, medicines for the corresponding less expensive generics, as well as purchasing more of the cheaper 1-month treatment packages containing less pills, and less of the 2-months treatment packages that are more expensive. These actions would increase the number of units consumed, while reducing the expenditure with NIA drugs.

Interpretation of the coefficients estimates of the (final) log model in Table 4.4

All the explanatory variables in Table 4.4 are individually significant at less than the 1% level, except for the dummy variable GFC', which is individually significant at the 6% level. The model explains 99.8% of the dependent variable variations and it is overall significant at less than 1% level of significance. Also, there is no evidence of heteroscedasticity or serial correlation in the disturbances and the variables are cointegrated, as demonstrated by the Augmented Dickey-Fuller (ADF) test that rejects the null of a unit root in the residuals series with a confidence level of more than 99%.

Maintaining everything else constant, a 1% increase (decrease) in the average price of the NIA drugs induces an increase (decrease) of 0.1871% in the number of NIA boxes consumed. The reason for a positive and inelastic price elasticity for the number of units consumed, in contrast with the positive and elastic elasticity of the expenditure is straightforward. Although one can swap expensive branded medicine for cheaper generics, it is substantially more difficult to swap from the correct dose of the medicine to a lesser number of pills, without putting at risk one's own well-being. So, the response of the NIA demand measured in units is less than proportional (inelastic) to unit percentage changes in its price, while the NIA demand measured in euros is more than proportional (elastic) to the same unit percentage change in the price.

Regarding the estimated impact of the type 2 diabetes prevalence on the number of NIA units consumed we can say that, for each additional 1% in the number of patients, the number of NIA drugs consumed increases 0.1127% on average, within the periods [2000-2009] and [2018-2021], that is, when PTD'=0. However, the impact of this variable between 2010 and 2017, (when PTD'=1) on the dependent variable is slightly reduced to 0.1046% ($0.112654 - 0.008097 = 0.1046$). Thus, the impact of type 2 diabetes prevalence across the sample period is always positive, significant, although inelastic, and more so within the recession period that followed the 2008 financial crisis. This means that the response of the demand for of NIA drugs is less than proportional to unit percentage changes in the number of patients, which may have to do with the different dimensions of the respective variables (millions of units vs. thousands of patients). Additionally, the impact of a 1% increase in the population's health literacy is a 0.672% increase in the number of NIA boxes consumed. Again, an inelastic response of the demand to a unit relative change in the literacy variable, which is a suitable estimate given the ambivalence of effects that this variable can cause to the demand of life-saving drugs.

4.2.2. The demand for insulin

1. National expenditure with insulin

The linear and log forms of the regressions for the demand of insulin measured by the national expenditure (NHS) are, respectively:

$$INS_t = \beta_0 + \beta_1 PINS_t + \beta_2 GDP_t + \beta_3 POV_T + \beta_4 T1D_t + \beta_5 PTD \times T1D_t + + \beta_6 LIT_t + \beta_7 GFC + \beta_8 OUT_t + w_t \tag{4.5}$$

$$lnINS_t = \beta'_0 + \beta'_1 lnPINS_t + \beta'_2 lnGDP_t + \beta'_3 lnPOV_t + \beta'_4 lnT1D_t + \beta'_5 PTD' \times T1D_t + \beta'_6 lnLIT_t + \beta'_7 GFC'_t + \beta'_8 OUT'_t + w'_t \tag{4.6}$$

Where, on the left hand side, INS_t and $lnINS_t$ are, respectively, the linear and log forms of the dependent variables representing the demand for insulin and measured by the national (NHS) expenditure (in 10^6€). On the right hand side of Equations (4.5) and (4.6) are the independent variables identical to those described previously in Equations (4.1) and (4.2) except for variables $T1D_t$ and $lnT1D_t$, now standing for the prevalence of type 1 diabetes (in thousands) during the whole sample period, while $PTD_t \times T1D_t$ and $PTD'_t \times lnT1D_t$, represent the prevalence of type 1 diabetes between 2006 and 2015. The dummy variables GFC_t and GFC'_t, assuming value 1 in [2006-2015], and 0 otherwise, stand for the time spell where the economic recession that followed the 2008 financial crises occurred; the dummy variables OUT_t and OUT'_t, assuming value 1 for [2003-2005] and 0 otherwise, express the "outlier" behaviour of the insulin demand within this 3 years period. Finally, μ_t and μ'_t are the *i.i.d* disturbance terms of, respectively, Equations (4.5) and (4.6).

Tables 4.5 and 4.6 show the estimation results for Equations (4.5) and (4.6), respectively, and Figures 4.5 and 4.6 depict the residuals (blue line), actual (orange line) and fitted (green line) values of the final (specific) regressions showed in Tables 4.5 and 4.6, respectively.

Table 4.5. Estimation results for Equation (4.5).

Variables	Initial (general) regression	Final (specific) regression
C	-38.61658 (0.4834)	-12.83685 (0.0002)
PINS	-0.022132 (0.9692)	-
GDP	0.001046 (0.6988)	-
POV	0.456249 (0.5191)	-
T1D	6.869431 (0.0321)	6.674894 (0.0000)
PTD×T1D	13.32850 (0.0036)	13.41083 (0.0000)
LIT	1.184589 (0.0103)	1.271992 (0.0000)
GFC	-44.13513 (0.0005)	-44.29502 (0.0000)
OUT	-6.671933 (0.0617)	-6.253218 (0.0094)
R^2	0.988069	0.987535
AdjR^2	0.980726	0.983639
F-statistic	134.5716 (0.0000)	253.5098 (0.0000)
White heteroscedasticity test	-	6.310406 (0.9341)
Breusch-Godfrey serial correlation test	-	0.003414 (0.9534)
Augmented Dickey-Fuller	-	-4.255721 (0.003)

Table 4.6. Estimation results for Equation (4.6).

Variables	Initial (general) regression	Final (specific) regression
C	-0.497113 (0.9603)	-0.114770 (0.6902)
ln PINS	0.302859 (0.2950)	-
ln GDP	-0.033666 (0.9722)	-
ln POV	0.094121 (0.7965)	-
ln T1D	0.271064 (0.0295)	0.359185 (0.0001)
PTD×ln T1D	1.048680 (0.0001)	1.121060 (0.0000)
ln LIT	0.851592 (0.0037)	1.018897 (0.0000)
GFC	-1.262278 (0.0000)	-1.298381 (0.0000)
OUT	-0.246078 (0.0006)	-0.212304 (0.0001)
R^2	0.993547	0.992931
AdjR^2	0.989575	0.990722
F-statistic	250.1824 (0.0000)	449.4765 (0.0000)
White heteroscedasticity test	-	19.02504 (0.0523)
Breusch-Godfrey serial correlation test	-	1.347962 (0.2456)
Augmented Dickey-Fuller	-	-6.055600 (0.0001)

Figure 4.5. Residuals, actual and fitted values of Equation (4.5); (2000-2021).

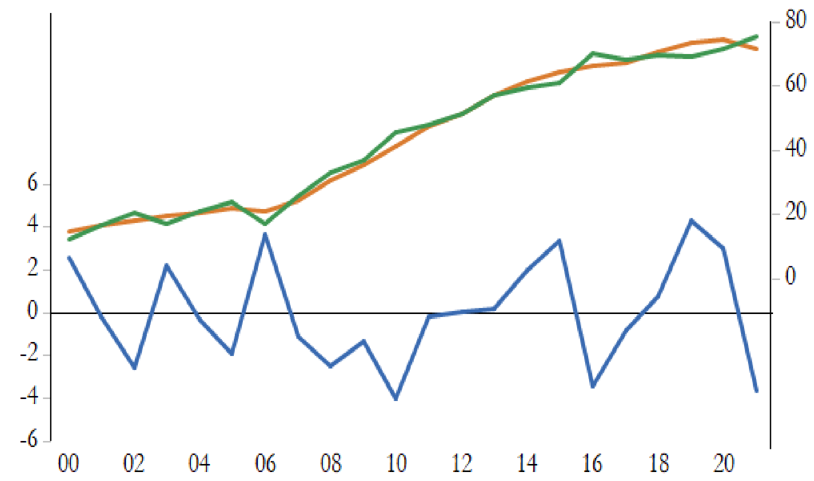
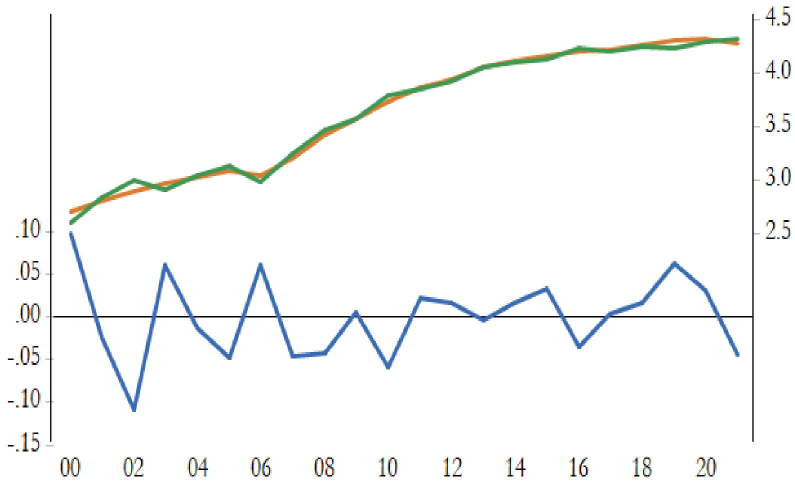


Figure 4.6. Residuals, actual and fitted values of Equation (4.6); (2000-2021).



Interpretation of the coefficients estimates of the (final) linear model in Table 4.5

All the explanatory variables in Table 4.5 are individually significant at the 1% level. The model explains 98.8% of the dependent variable variations and it is overall significant at less than the 1% significance level. Also, there is no evidence of heteroscedasticity or serial correlation in the disturbances and the variables are cointegrated, as established by the ADF test that rejects the null of a unit root in the residuals, with a higher than 99% confidence level. Thus, we proceed with the interpretation of the coefficients' estimates given the statistical robustness of the model.

Concerning the coefficients estimates of the population's health literacy, we observe that a 1pp increase in this variable conduces to a 1.27 million € increase in the national expenditure with insulin. We endorse here the same justification given previously for the corresponding estimate in regression (4.1), where we affirmed that the more knowledgeable people are about their health condition, the more likely they are to follow the doctor's prescribed treatment to the letter, whatever the costs.

Regarding the effect of T1D prevalence on the dependent variable, we have to consider two different periods: within [2000-2005] and [2016-2021], when PTD=0, the effect is positive, significant and of 6 674 894 € (6.674894×10^6€) per each 1 000 additional type 1 diabetic patients. This represents, on average, an additional 6 675€, per patient and per year, during those periods. Yet, within [2006-2015], when PTD=1, the impact of the T1D prevalence on the demand for insulin increases, to 20 085 724€ [$(6.674894 + 13.41083) \times 10^6$€], per each 1 000 additional patients. This means that, on average, within the time spell of [2006-2015], which includes the economic recession and the troika intervention, the national expenditure with insulin increases to 20 086€ per patient and per year, whereas within the time spells before and after the recession period, the national expenditure with insulin was, on average, less than 1/3 of that in the recession period at 6 675€/patient/year, everything else constant.

The substantial increase of the average expenditure with insulin during the recession period, compared with that of the periods before and after, has to do mainly with two reasons: first, the average annual number of patients within the first 5 years of the sample is below 1.3 million whereas, within the period 2006 to 2015, this average increases to close to 3 million patients, which is more than double the previous average; second, the insulin average price increased from 23€ per unit before 2005, to 41€ per unit between 2006 and 2015, which is almost double of the previous average price. This two effects combined catapulted the expenditure to the estimated values we report above.

Regarding the coefficients estimates of the dummy variables GFC and OUT, we have to recall the periods when those variables are active, meaning, when they assume value 1. The GFC=1 between 2006 and 2015, which includes the recession period that followed the 2008 financial crisis, as well as the escalations of both the insulin price and the prevalence of type 1 diabetics. These three factors made the national expenditure with insulin shoot up showing a structural break on its sample average that is accounted for by the inclusion of the GFC dummy variable. The OUT dummy variable is 1 during the 3 years' period of 2003 to 2005, within which the demand levels are obvious outliers, when compared with the rest of the sample period behaviour. The insulin demand grows consistently throughout the sample period, except during those 3 years when it stagnates or even decreases. That is the reason for the inclusion of the dummy OUT, which coefficient estimate indicates a significant decrease of more than 6 million € in the dependent variable annual average. Moreover, the average annual decrease observed in the national expenditure with insulin during [2006-2015] is 44.3 million €, indicating that the consumers that could dispense or substitute the use of insulin (namely, type 2 diabetic patients to whom this drug may have been prescribed) during this period of high insulin price, reduced income, and increasing unemployment may have been persuaded to do so, driving the annual average expenditure down. The corresponding coefficient in Table 4.1 holds the same negative signal, meaning that there is a reduction of both insulin and NIA drugs' expenditure during the recession that followed the 2008 financial crises.

Interpretation of the coefficients estimates of the (final) log model in Table 4.6

All the explanatory variables in Table 4.6 are individually significant at less than the 1% level. The model explains 99.3% of the dependent variable variations and it is overall significant at less than 1% level of significance. In addition, there is no evidence of heteroscedasticity or serial correlation in the disturbances and the variables are cointegrated, as demonstrated by the Augmented Dickey-Fuller (ADF) test that rejects the null of a unit root in the residuals series with a confidence level of more than 99%.

In what concerns the estimated impact of the type 1 diabetes prevalence on the national expenditure with insulin we can say that, within the periods [2000-2005] and [2016-2021], when the dummy variable PTD' = 0, each additional 1% increase in the number of patients makes the expenditure increase 0.359185%. This is an inelastic response of the demand for insulin, relative to the type 1 diabetes prevalence. However, within the period [2006-2015], when the dummy PTD' = 1, the impact of T1D prevalence on the demand for insulin is elastic, of 1.4802% (1.121060 + 0.359185 = 1.4802). This means that the demand for insulin is more responsive to changes in the type 1 diabetes prevalence within the time spell that includes the recession period, which confirms the tendency of an easier abandonment (or re-acquisition) of insulin treatments, for those who can do without it, when the number of those who cannot increases, given that type 1 diabetic patients are the priority for treatments involving a scarce, expensive and with no substitutes medicine. So, when recession hits, bringing unemployment and income reductions, those who can do without insulin will be willing to reduce or substitute its use, making demand more sensitive to changes in the prevalence of type 1 diabetes.

Regarding the impact of the population's health literacy level on the demand for insulin we can say that a 1% increase in this determinant conduces to a 1.018897% increase in the national expenditure with insulin, meaning that the demand elasticity relative to the health literacy is unit[23], that is, the demand response is proportional to the percentage unit changes of the Portuguese health awareness. This proportional demand response seems adequate, given that it is expected a better manage of health condition from patients with higher levels of health literacy, with proportional responses of their demand for life-saving drugs.

Due to the log-linear nature of Equation 4.6, the estimated impact of the occurrences that took place in [2006-2015], measured by the coefficient of GFC', is given by the difference between the exponential of the intercept, $e^{-0.114770}$ = 0.891571 million € (891 571 €) and the exponential of the intercept plus the dummy coefficient, $e^{-0.0114770-1.298381}$ = 0.243375 million € (243 375€). Thus, this model shows that the national expenditure with insulin decreased 648 196€ (891 571€ – 243375€ = 648 196€), on average and per year within [2006-2015], which includes the years of recession and troika intervention in the country.

Similarly, the impact of occurrences that took place in [2003-2005], measured by the coefficient of the dummy OUT is given by the difference between the exponential of the intercept, $e^{-0.114770}$ = 0.891571 million € (891 571 €) and the exponential of the intercept plus the dummy coefficient, $e^{-0.0114770-0.212304}$ = 0.721030 million € (721 030€). So, the national expenditure with insulin shows an average decrease of 170 541€ (891 571 − 721 030 = 170 541€), during the three outlier years of 2003 to 2005.

2. Units consumed of insulin

The linear and log forms of the regressions for the demand of insulin measured by the number of units sold to patients are, respectively:

$$ins_t = \delta_0 + \delta_1 Pins_t + \delta_2 GDP_t + \delta_3 POV_T + \delta_4 T1D_t + \delta_5 PTD \times T1D_t + + \delta_6 LIT_t + \delta_7 GFC_t + \delta_8 OUT_t + w_t \quad (4.7)$$

[23] The Wald test for H_0: $\beta'_6 = 1$, does not reject the null, with a p-value of 0.844.

$$lnins_t = \delta_0 + \delta'_1 lnPins_t + \delta'_2 lnGDP_t + \delta'_3 lnPOV + \delta'_4 lnT1D_t + + \delta'_5 PTD' \times lnT1D_t + \delta'_6 lnLIT_t + \delta'_7 GFC'_t + \delta'_8 OUT'_t + \mu'_t \quad (4.8)$$

Where, on the left hand side, ins_t and $lnins_t$ are, respectively, the linear and log forms of the dependent variables representing the demand for insulin (in thousands of units). On the right hand side are the independent variables identical to those described previously for Equations (4.5) and (4.6), respectively. Also, similarly to all previous equations, μ_t and μ'_t are the disturbance terms which are supposed to be *i.i.d.* variables.

Tables 4.7 and 4.8 show the estimation results for, respectively, Equations (4.7) and (4.8), and Figures 4.7 and 4.8 depict the residuals (blue line), actual (orange line) and fitted (green line) values of the final (specific) regressions showed in Tables 4.7 and 4.8, respectively.

Table 4.7. Estimation results for Equation (4.7).

Variables	**Initial (general) regression**	**Final (specific) regression**
C	160.1841 (0.8801)	643.2481 (0.0000)
Pins	-27.18158 (0.0275)	-28.68839 (0.0073)
GDP	0.022332 (0.6714)	-
POV	6.037902 (0.6596)	-
T1D	186.4366 (0.0052)	193.6049 (0.0013)
PTD×T1D	370.2575 (0.0002)	365.4367 (0.0000)
LIT	29.97432 (0.0018)	32.35727 (0.0000)
GFC	-1155.270 (0.0000)	-1135.346 (0.0000)
OUT	-152.7326 (0.0318)	-142.9275 (0.0151)
R^2	0.979230	0.978867
AdjR^2	0.966448	0.970414
F-statistic	76.61100 (0.0000)	115.8002 (0.0000)
White heteroscedasticity test	-	7.504980 (0.2767)
Breusch-Godfrey serial correlation test	-	0.328641 (0.5665)
Augmented Dickey-Fuller	-	-4.617471 (0.0016)

Table 4.8. Estimation results for Equation (4.8).

Variables	Initial (general) regression	Final (specific) regression
C	6.410718 (0.5240)	6.382307 (0.0000)
ln Pins	-0.696782 (0.0261)	-0.739660 (0.0079)
ln GDP	-0.033762 (0.9721)	-
ln POV	0.094222 (0.7963)	-
ln T1D	0.271041 (0.0295)	0.274569 (0.0184)
PTD×ln T1D	1.048821 (0.0001)	1.086176 (0.0000)
ln LIT	0.851377 (0.0037)	0.893744 (0.0000)
GFC	-1.262434 (0.0000)	-1.289762 (0.0000)
OUT	-0.246023 (0.0006)	-0.234993 (0.0001)
R^2	0.976469	0.976069
AdjR^2	0.961989	0.966497
F-statistic	67.43375 (0.0000)	101.9681 (0.0000)
White heteroscedasticity test	-	9.172827 (0.1641)
Breusch-Godfrey serial correlation test	-	1.594328 (0.2067)
Augmented Dickey-Fuller	-	-5.774213 (0.0001)

Figure 4.7. Residuals, actual and fitted values of Equation (4.7); (2000-2021).

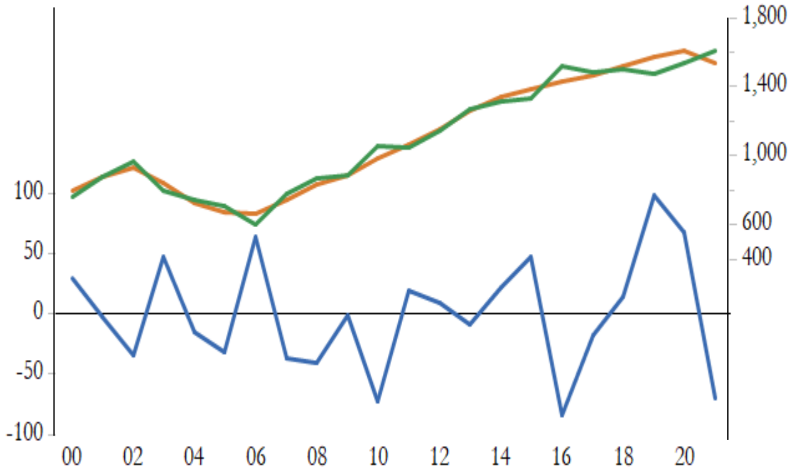
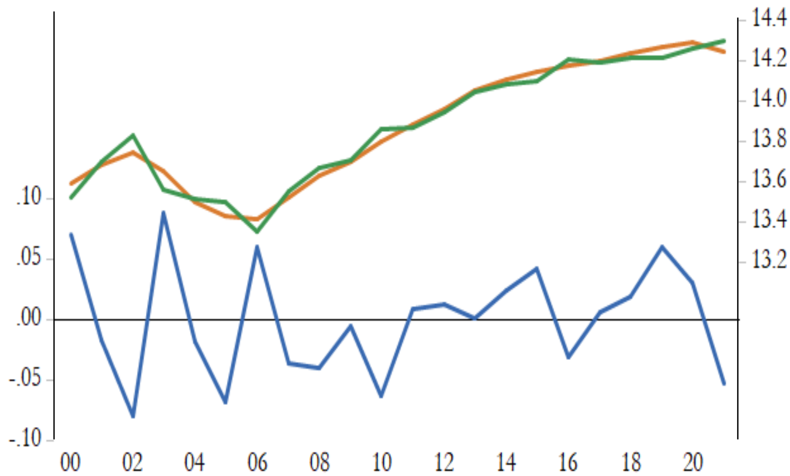


Figure 4.8. Residuals, actual and fitted values of Equation (4.8); (2000-2021).



Interpretation of the coefficients estimates of the (final) linear model in Table 4.7

All the explanatory variables in Table 4.7 are individually significant at the 1% level, except for the dummy variable OUT, which is individually significant at the 2% level. The model explains 97.9% of the dependent variable variations and is overall significant at the 1% significance level. Furthermore, there is no evidence of heteroscedasticity or serial correlation in the disturbances and the variables are cointegrated as showed by the ADF test that rejects the null of a unit root in the residuals series, with a higher than 99% confidence level. So, we may proceed with the interpretation of the coefficients' estimates given the statistical robustness of the model.

As we can see in Table 4.7 (and 4.8), the final model of the demand for insulin, displays a significant, negative and sizable impact of its price on the number of units demanded. This does not happen to any of the other demand models estimated previously, where the price impacts were always insignificant. Therefore, in this case, the demand for units of insulin shows a behaviour similar to that of normal goods, where the response to own-price increases is also significant and negative. So, concerning the coefficient estimate of the average insulin price (Pins), we can say that a 1€ increase in this variable implies an annual average decrease of 28.7 thousand units of insulin demanded, everything else constant.

Regarding the effect of the population's health literacy on the demand for insulin we can say that a 1 percentage point increase (1pp) in the literacy variable conduces to an average increase of 32.4 thousand units (32 357) of insulin consumed per year.

Concerning the impact of T1D on the dependent variable we observe that during the periods when PTD=0, across the periods [2000-2005] and [2016-2021], the increase of 1 000 type 1 diabetic patients brings an average increase of 194 thousand units consumed per year. However, in [2006-2015], when PTD=1, the impact of 1 000 additional type 1 diabetics on the insulin demand is an increase of 559 thousand units sold (193.6049 + 365.4367 = 559.05). This means that, on average, across [2006-2015], when the type 1 diabetics prevalence grows at an average annual rate of 10%, the national consumption of insulin increases to an average of 559 units per patient per year, whereas within the periods outside that time interval, the average quantity of units sold is below 200 packages/patient/year, everything else constant.

As for the interpretation of the dummy GFC coefficient, representing the structural break on the demand for insulin during the period [2006-2015], which includes the economic recession and the troika intervention in the national economy, we observe that the average consumption of insulin reduces by 1 135 thousand units. Similarly, the coefficient of the dummy OUT, representing the outlier behaviour of the demand for insulin within the 3 years' period of 2003 to 2005, indicates a decrease of the average consumption of insulin in 143 thousand units, *ceteris paribus*.

Interpretation of the coefficients estimates of the (final) log model in Table 4.8

All the explanatory variables in Table 4.8 are individually significant at the 1% level, except for the T1D prevalence variable, which is significant at less than the 2% level. The model explains 97.6% of the dependent variable variations and it is overall significant at less than 1% significance level. Also, there is no evidence of heteroscedasticity or serial correlation in the disturbances and the variables are cointegrated, as confirmed by the ADF test that rejects the null of a unit root in the residuals series with a confidence level of more than 99%.

As reported earlier for the linear model, the log model also shows a significant and negative impact of the insulin price on its demand given that, a 1% increase in the average price of insulin induces a decrease of 0.7397% in its demand. The features of the price elasticity observed in the log-linear model are compatible to those of the price elasticity of the demand for necessary goods or services with few substitutes, since it is negative and inelastic[24] as it would be the case for the price elasticity of such goods and services. Regarding, the impact of the health literacy variable on the demand for insulin we observe that a 1% increase in this determinant causes a 0.8937% increase in the number of insulin units consumed. Given that, this estimate is not significantly different from 1[25], the justification for this unit response of the demand is similar to the one given for the corresponding estimate of Table 4.4.

In what concerns the estimated impact of the type 1 diabetes prevalence on the dependent variable we can say that, for each additional 1% in the number of patients, the consumption of insulin increases 0.274569%, on average, across the periods [2000-2005] and [2016-2021], that is, when PTD'=0. This is a clearly inelastic response of the demand to changes in the number of patients in a period when the type 1 diabetes prevalence is relatively small. However, the impact of this variable when PTD'=1, that is, across [2006-2015], when the

[24]However, the Wald test for the null of $\delta'_1=-1$ (negative unit elasticity), against the alternative $\delta'_1>-1$ (inelastic elasticity, between −1 and 0), does not reject the null of a unit price elasticity, given that the test statistic for this null hypothesis is t_{obs} = 1.077, which is smaller than the 5% level critical value of 1.7531 (p-value = 0.2985). This means that a proportional response of the demand for insulin to changes in its price cannot be ruled out.
[25] The Wald test for the null of $\delta'_6=1$, is not rejected with the t statistic of -0.711 and the p-value of 0.488.

type 1 diabetes prevalence has an average growth of 10% every year, the response of the demand is clearly elastic, increasing to 1.361% (0.274569 + 1.086176 = 1.3607) per each additional 1% increase in the number of patients.

Due to the log-linear nature of Equation (4.8), the estimated impact of the events in [2006-2015], which include the economic recession and subsequent troika intervention, embodied by the dummy variable GFC', is given by the difference between the exponential of the intercept ($e^{6.38231}$ = 591.3) and the exponential of the intercept plus the GFC' coefficient ($e^{6.38231-1.28976}$ = 162.8). Thus, the events represented by the GFC' variable induced an estimated decrease of 429 thousand units (591.3 – 162.8 = 428.5) in the average demand of insulin within [2006-2015], relative to the average demand for insulin outside this period, everything else constant. Similarly, the impact of events occurring in [2003-2005], which are represented by the dummy variable OUT ', is given by the difference between the exponential of the intercept $e^{6.38231}$ = 591.3 and the exponential of the intercept plus the coefficient of the OUT' variable, $e^{6.38231-0.234993}$ = 467.5. Thus, the demand for insulin within the period [2003-2005], decreases 124 thousand units (591.3 − 467.5 = 123.83), relative to the demand level outside the same period, everything else constant.

4.3. Conclusion

In this chapter, we conducted the estimations of the econometric models that explain the behaviour of the national demand for antidiabetic drugs. The analysis is carried out through the interpretation of the estimation results obtained from eight econometric models that explain the demand for antidiabetic drugs. The first four models are related to the demand of NIA drugs and the last four to the demand of insulin. These models have provided valuable insights into the factors influencing the demand for these medicines, which is of paramount importance in the context of the management of healthcare resource planning for diabetes.

The aim of all these estimations is to prove that antidiabetics demand behave differently from the demand for normal goods and services, particularly in periods of economic recession as it was the case in Portugal after the 2008 global financial crisis. Indeed, in all the eight models, the explanatory variables representing income and poverty rate are statistically insignificance contradicting the demands' behaviour for any normal goods or services where this determinant is usually positive and significant.

In the case of the demand response to changes in prices, both linear and log-linear demand models for NIA show a positive and significant impact. In fact, the response of the expenditure in NIA increases 10.4 million € per each additional 1€ increase in its average price, while, the response of the units' demand for NIA is an increase of 113 000 units per each additional 1€ increase. This is in contrast with the usual demand response to changes in prices of normal goods, where it is expected a decrease of the demand to price increases. Moreover, the log-linear form results for the price elasticities of the demand for NIA are also contradictory to what is expected of the demand behaviour for normal goods. Indeed, in the case of the NIA demand measured in expenditure, the price elasticity is positive and elastic (+1.2) and in the case of the demand measured in units, the price elasticity is positive but inelastic (+0.19). Thus, both price elasticities are significant and positive, whereas in the case of the demand for normal goods the price elasticities are expected to be negative. This is coherent with the fact that NIA are life-saving medicines, but with some substitutes that are possibly less expensive. So, while one can substitute a more expensive antidiabetic for a cheaper option, the number of units cannot be relevantly reduced.

Regarding the demand for insulin, we also observe major differences in its responses to price changes, when compared with those of normal goods' demands. Actually, the responses of the demand for insulin to price changes, when measured in expenditure, are not significant in both the linear and log-linear forms. However, when the demand for insulin is measured in units, its price responses in both linear and log-linear models, are significant and negative. In fact, in the linear form, the demand response to one additional euro in the average price of insulin is a reduction of 28.7 thousands units sold while, in the case of the log-linear model, the demand price elasticity is −0.74, meaning that an increase of 1% in the average price of insulin leads to a 0.74% decrease in the number of units sold. This negative response is justifiable because each unit of insulin contains 5 "pens" of medicine that can be mindfully or loosely used[26]. But note that the price elasticity is inelastic so the response for increases in price is still less than proportional.

As expected, both type 1 and type 2 diabetes prevalence affect significantly the demand for antidiabetics. In the case the expenditure, in the linear form and in the period when the PTD=0, it decreases slightly by 41 400€, while in the period where PTD=1, it increases by

[26] There are five types of insulin: the rapid-acting, the short-acting, intermediate-acting, the mixed insulin and the long-acting insulin. The administration of the different types depends on the patient and, in the case of type 1 diabetes, on the type of food ingested. Consequently, the consumption of the "pens"' can be mindfully managed by each patient leading to some insulin units lasting more time than others, according to the standards of whom is using them.

the modest amount of 660€. Both values are relatively small enough to be considered irrelevant. The same can be said about the expenditure response in the log-linear model, which is of 0.13 in the period when PTD=0 and -0.0041 in the period when PTD=1. In conclusion, the NIA expenditure response to increases in the prevalence is of minor dimension. As for the linear response of the demand measured in units, we can say it is also of minor concern since, in the linear case, when PTD=0, it increases 1 093 units per 1 000 additional patients, while when PTD=1, it increases 640 units/1 000 patients. In the same way, the response of the log-linear demand in units is minor and similar in both periods: 0.1127 when PTD=0 and 0.1046 when PTD=1. So, inelastic and relatively modest responses.

In the case of the prevalence impact on the insulin demand, the linear expenditure shows positive impacts in both periods when PTD=0 and when PTD=1. In the former, the impact is positive of 7 million €, increasing to 20 million € in the latter. Similarly, the linear case for the demand in units shows a positive impact of 194 thousand units when PTD=0, increasing to 550 thousand units, when PTD=1. Concerning the log-linear form of the insulin demand, we observe that in both cases of the demand being measured by either in expenditure or in units, the elasticity is significant, positive and inelastic, when PTD=0 (0.36 in the expenditure case and 0.97 in the units' case), while when PTD=1 is, in both cases, significant, positive and elastic of 1.46 in the case of expenditure and 1.36 in the case of units.

Regarding the influence of the health literacy on the demand for both NIA and insulin, it is always positive and significant. In the linear cases of the demand for NIA measured by both expenditure and units, we observed increases of 2.83 million € on the expenditure and of 129 thousand on the number of units sold. In the log-linear form we observe elasticities that are positive, significant and inelastic of 0.66 in the expenditure case and of 0.67 in the units' case. On the other hand, concerning the demand for insulin, we observed, in the linear case, a 1.27 million € impact in the expenditure case and a 32 thousand in the units' case. For the log-linear form, in both cases of expenditure and units, the elasticities are positive, and not significantly different from unit, which implies a proportional response of the demand for each additional 1% change in the health literacy.

Finally, the general response of the demand for antidiabetics is significant and negative in all models, concerning the period that includes the economic recession following the 2008 financial crisis. Indeed, the demand for NIA drugs, when measured in expenditure, shows a decrease of 65 million € and, when measured in units, a decrease of 250 thousand units. Moreover, in the case of the demand for insulin, we observe a decrease of 44 million € in the expenditure and of 1135 thousand in units sold, across the period that includes the economic recession. Therefore, we may conclude that in periods of economic crises, the demand for life-saving drugs, no matter how inelastic, still shows a decrease of consumption, as it would be expected for normal goods.

In summary, the econometric models collectively provide a comprehensive understanding of the determinants of the demand for both NIA drugs and insulin, showing the significance of price, prevalence, health literacy and economic recession. These findings can help healthcare policies, resource allocation, and different strategies for managing diabetes and drugs-related healthcare services.

5. Conclusion

The significant burden of the ever growing expenditure with antidiabetic medications on the national healthcare budget is widely recognized and dreaded. Consequently, there has been a growing interest in researching the economic, social and financial aspects of the demand for antidiabetic treatments and drugs, given the persistent increase in the prevalence of diabetes worldwide. This dissertation is an example of a valuable contribution to the literature given that it focus on the impact of economic recessions on the demand for life-saving medicines.

Throughout this research, it has become evident that the demand for antidiabetic drugs defies conventional economic expectations given that, unlike the demand for normal goods, factors such as the consumers' income have minimal or none influence on the demand for these type of life-saving medicines. Instead, the average price of these drugs bears a positive impact on demand, contrary to conventional economic demand laws. This phenomenon highlights the non-negotiable priority that diabetic patients assign to their health, even amidst economic hardships.

Our study contributes to a deeper understanding of the intricate factors shaping the purchasing decisions of diabetic patients during times of economic distress. By employing linear and log-linear models, we have sought to provide valuable insights into the dynamics of this crucial aspect of healthcare demand. These models yielded critical comprehensions into the factors influencing the demand for these medications, particularly during economic recessions like the post-2008 global financial crisis in Portugal. Notably, our findings diverged from typical demand patterns for ordinary goods and services, with income and poverty rate variables proving statistically insignificant. Price elasticity also exhibited unconventional behaviour, as NIA drug demand responded positively to price increases, contrary to what would be expected. Furthermore, the prevalence of type 1 and type 2 diabetes played a role in demand variations, though with minor impacts. Health literacy consistently had a positive and significant influence on demand. During economic crises, demand for these life-saving drugs decreased, underscoring the nuanced nature of antidiabetic drug demand.

With our findings, we can infer that, unlike the typical behaviour of demand for normal goods and services, patients' income does not significantly influence the demand for antidiabetic medication. Furthermore, it is noteworthy that the average price of these medicines tends to have a positive impact on the amount spent by the NHS + patient, contradicting the conventional expectation of a negative relationship between expenditure and price of normal goods.

Regarding the intention of providing a consistent and steady estimation of the demand behaviour within the SARS-CoV-2 pandemic' years, laid out in the introduction of chapter 3, data, time and space restrictions prevented the fulfilment of this additional task but we intend to address this issue in future research when more reliable data is available.

In essence, this dissertation serves as a vital step toward comprehending the complex relationship between economic crises, healthcare behaviour, and the demand for antidiabetic drugs. It is our hope that this research contributes to informed policy-making and aids in devising strategies to ensure accessible and effective healthcare for diabetic patients, even in the face of economic adversity. However, given the multiple sources for the prevalence of type 1 and type 2 diabetes, which can carry some doubts about the precision of the published data we want to issue a cautionary note about the impacts of prevalence on the demand for antidiabetic drugs, both in the cases of NIA and insulin.

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Appendix A.1.

The source for the data on the type 1 diabetes prevalence in Table A.1 is the *Programa Nacional para a Diabetes* 2017 and 2021, for all the sample period under analysis. The source for the data on the prevalence of type 2 diabetes for 2000, 2003 and 2007 (in bold green) is the IDF Diabetes Atlas; the source on the same variable for the years of 2008 to 2015, 2018 and 2021 (in bold blue) is the *Relatório Anual do Observatório Nacional da Diabetes*. For the remaining missing values of the type 2 diabetes prevalence (in bold red), we apply the "rule of thumb" that consists on extrapolating the percentage relationship between type 1 and type 2 prevalence computed with the official data available in the previous year. For example, the first number in the 5th column of Table A.1 is 504 297. This number is obtained with the rule of three simple $(987 \times 397\,000)/777 = 504\,297$. All the other estimated values for type 2 prevalence in the 5th column were obtained in the same way.

Table A.1. *Official data on the prevalence of type 1 and official and estimated (according with "rule of thumb" described above) data of type 2 diabetes prevalence.*

Year	Official data on prevalence of type 1 diabetes	Official data on prevalence of type 2 diabetes	% relationship between types 1 and 2 diabetics	Extrapolated data for type 2 diabetes
2000	**777**	**397 000**	**0.196%**	**-**
2001	**987**	**-**	**-**	**504 297**
2002	**1 153**	**-**	**-**	**589 113**
2003	**1 360**	**584 500**	**0.233%**	**-**
2004	**1 589**	**-**	**-**	**682 919**
2005	**1 849**	**-**	**-**	**794 662**
2006	**2 111**	**-**	**-**	**907 264**
2007	**2 371**	**648 300**	**0.366%**	**-**
2008	**2 616**	**905 000**	**0.289%**	**-**
2009	**2 835**	**983 000**	**0.288%**	**-**
2010	**3 074**	**991 000**	**0.310%**	**-**
2011	**3 131**	**1 021 400**	**0.307%**	**-**
2012	**3 227**	**1 006 200**	**0.321%**	**-**
2013	**3 317**	**1 014 000**	**0.327%**	**-**
2014	**3 331**	**1 008 700**	**0.330%**	**-**
2015	**3 300**	**1 024 100**	**0.322%**	**-**
2016	**4 217**	**-**	**-**	**1 308 676**
2017	**4 080**	**-**	**-**	**1 266 160**
2018	**3 927**	**1 088 000**	**0.361%**	**-**
2019	**3 660**	**-**	**-**	**1 014 026**
2020	**3 324**	**-**	**-**	**920 935**
2021	**2 443**	**1 099 800**	**0.222%**	**-**

Given the absence of official data on type 2 diabetes prevalence, for almost half the sample period, and the fact that those values had to be extrapolated based on a questionable "rule of thumb", we had to issue a cautionary note about the influence of type 2 prevalence on the demand for NIA drugs. Even the "official" data available for type 1 are hardly justifiable for there are several examples of "disappearing" patients from one year to the next, when it is well known that type 1 diabetes is a chronical disease that affect the youngsters, difficultly susceptible to sudden death. This would be the case of 881 patients that "disappear" from 2020 to 2021 and the case of 137 patients also "disappear" from 2016 to 2017.