

# Pharmaceutical consumption, economic growth and life expectancy in the OECD: the application of a new causal direction from dependency algorithm and a DeepNet process

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Received 1 February 2024  
Revised 14 May 2024  
Accepted 16 May 2024

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## Abstract

**Purpose** – The objective of this study is to reevaluate the correlation among pharmaceutical consumption, per capita income, and life expectancy across different age groups (at birth, middle age, and advanced age) within the OECD countries between 1998 and 2018.

**Design/methodology/approach** – We employ a two-step methodology, utilizing two independent approaches. Firstly, we conduct the Dumitrescu-Hurlin pairwise panel causality test, followed by Machine Learning (ML) experiments employing the Causal Direction from Dependency (D2C) Prediction algorithm and a DeepNet process, thought to deliver robust inferences with respect to the nature, sign, direction, and significance of the causal relationships revealed in the econometric procedure.

**Findings** – Our findings reveal a two-way positive bidirectional causal relationship between GDP and total pharmaceutical sales per capita. This contradicts the conventional notion that health expenditures decrease with economic development due to general health improvements. Furthermore, we observe that GDP per capita positively correlates with life expectancy at birth, 40, and 60, consistently generating positive and statistically significant predictive values. Nonetheless, the value generated by the input life expectancy at 60 on the target income per capita is negative (–61.89%), shedding light on the asymmetric and nonlinear nature of this nexus.

## JEL Classification — C33, H51, O47

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**Ethical statement:** This article does not contain any studies involving human participants performed by any of the authors.

**Competing interests:** The authors declare that they have no competing interests.

**Funding:** The authors declare that they did not receive any funds for this publication.

The author read and approved the final manuscript.



Finally, pharmaceutical sales per capita improve life expectancy at birth, 40, and 60, with higher magnitudes compared to those generated by the income input.

**Practical implications** – These results offer valuable insights into the intricate dynamics between economic development, pharmaceutical consumption, and life expectancy, providing important implications for health policy formulation.

**Originality/value** – Very few studies shed light on the nature and the direction of the causal relationships that operate among these indicators. Exiting from the standard procedures of cross-country regressions and panel estimations, the present manuscript strives to promote the relevance of using causality tests and Machine Learning (ML) methods on this topic. Therefore, this paper seeks to contribute to the literature in three important ways. First, this is the first study analyzing the long-run interactions among pharmaceutical consumption, per capita income, and life expectancy for the Organization for Economic Co-operation and Development (OECD) area. Second, this research contrasts with previous ones as it employs a complete causality testing framework able to depict causality flows among multiple variables (Dumitrescu-Hurlin causality tests). Third, this study displays a last competitive edge as the panel data procedures are complemented with an advanced data testing method derived from AI. Indeed, using an ML experiment (i.e. Causal Direction from Dependency, D2C and algorithm) it is believed to deliver robust inferences regarding the nature and the direction of the causality. All in all, the present paper is believed to represent a fruitful methodological research orientation. Coupled with accurate data, this seeks to complement the literature with novel evidence and inclusive knowledge on this topic. Finally, to bring accurate results, data cover the most recent and available period for 22 OECD countries: from 1998 to 2018.

**Keywords** Pharmaceutical consumption, Economic growth, Life expectancy, Causality, Machine learning, OECD

**Paper type** Research paper

## 1. Introduction

The relationship between pharmaceutical consumption and healthcare is empirically ambiguous. While pharmaceutical consumption considerably varies across countries (also in advanced economies), its direct health return lacks evidence. On the one hand, per capita pharmaceutical consumption reached 759 US\$ (in Purchasing Power Parity, PPP) in Belgium in 2018, whereas it represented only 454 US\$ PPP in Estonia (OECD, 2020a). Similarly, per capita pharmaceutical consumption in Germany was roughly twice that of the Netherlands for the same year (OECD, 2020a). On the other hand, the indicators of life expectancy (at birth, 40, and 60) do not seem to follow a linear relationship with pharmaceutical consumption. Looking back at previous data, life expectancy values sensibly differ in Belgium, Estonia, Germany, and the Netherlands, ranging from 78.4 to 81.9 years old (at birth), from 39.5 to 42.6 years old (at 40), 21.9 to 24.8 years old (at 60), in 2018 (OECD, 2020b). Accordingly, this raises interesting questions: is there a causal linkage between pharmaceutical consumption and healthcare, and thus an effective health return in the supply of pharmaceutical products? Does income interact with these indicators, and how? Without empirical analysis, it appears impossible to infer which causality inference matters in practice.

As mentioned in Miller and Frech (2000), while the drivers of healthcare expenditure have attracted growing attention, estimating the determinants of healthcare itself remains largely overlooked, and more effort should be devoted to filling this gap. Pharmaceuticals increase life expectancy (i.e. leukaemia, lymphoma, and HIV/AIDS) and improve quality of life, impacting depression, pain, and anaemia (Crémieux *et al.*, 2005). And, far from being a coincidence, such a level and variability of life expectancy induces major implications for individuals (fertility behaviours), which, in turn, might affect the fragile equilibrium of some macroeconomic indicators over the long period (i.e. human productivity, employment level, the aggregate amount of pension benefit claims, intergenerational transfers, investments) (Arora, 2001; Zhang *et al.*, 2001; Coile *et al.*, 2002; Shaw *et al.*, 2005; Acemoglu and Johnson, 2007). From the policy side, it is now admitted

that economic policy affects health (Drakopoulos, 2011). Increasing longevity is positively correlated with public expenditure for education (Gradstein and Kaganovich, 2004). Meanwhile, alongside early retirement, such a longevity improvement is known to put pressure on the financing of the healthcare system and pension schemes (Cremer *et al.*, 2004). Thus, while often considered as an exogenous indicator, seminal studies have operated a break with this view, arguing that life expectancy is predetermined by socioeconomic factors. In doing so, they suggested estimating a new production function for health using aggregate-level indicators (Auster *et al.*, 1969; Miller and Frech, 2000; Shaw *et al.*, 2005). This is of high interest because relying on a modified version of a conventional economic model allows for the use of a wide range of empirical tools that might draw high value-added results and promising conclusions.

In this paper, we consider pharmaceutical consumption and assess whether it improves health outcomes. In addition, economic growth is included within our theoretical framework to investigate its interlinkages with the above-mentioned indicators. Indeed, while economic development is said to drive life expectancy, the feedback channel (that health might be a non-negligible factor in economic growth) should not be omitted. Having reached a supposed threshold level, the growth of per capita income is thought to influence the supply and the demand for pharmaceuticals. In turn, it might create the conditions allowing for the performance of the whole sector. Based on this trivariate model, this research aims to identify causal inferences and directions using a new causality testing framework, due to the design and implementation of an innovative algorithm. In a public debate where the surge against rising pharmaceutical costs has become predominant, a focus on their potential health and economic benefits is necessary to guide policy decisions. Thus, the aim of this study is not to estimate the marginal true return derived from pharmaceutical consumption on health outcomes. However, it seeks to provide a consistent picture of the existing causal linkages that operate among pharmaceuticals, income growth, and life expectancy. Moreover, with our new algorithm, we can measure the magnitude of this causality flow. Artificial Intelligence (AI) is fundamental for new scientific discoveries and applications in the field of medicine.

Therefore, very few studies shed light on the nature and the direction of the causal relationships that operate among these indicators. Exiting from the standard procedures of cross-country regressions and panel estimations, the present manuscript strives to promote the relevance of using causality tests and Machine Learning (ML) methods on this topic. Therefore, this paper seeks to contribute to the literature in three important ways. First, this is the first study analyzing the long-run interactions among pharmaceutical consumption, per capita income, and life expectancy for the Organization for Economic Co-operation and Development (OECD) area. Second, this research contrasts with previous ones as it employs a complete causality testing framework able to depict causality flows among multiple variables (Dumitrescu-Hurlin causality tests). Third, this study displays a last competitive edge as the panel data procedures are complemented with an advanced data testing method derived from AI. Indeed, using an ML experiment (i.e. Causal Direction from Dependency, D2C and algorithm) it is believed to deliver robust inferences regarding the nature and the direction of the causality. All in all, the present paper is believed to represent a fruitful methodological research orientation. Coupled with accurate data, this seeks to complement the literature with novel evidence and inclusive knowledge on this topic. Finally, to bring accurate results, data cover the most recent and available period for 22 OECD countries: from 1998 to 2018.

The rest of the paper is organized as follows. Section 2 presents the relevant literature. Section 3 describes the data and the empirical methodology. Section 4 displays and discusses the empirical results. Section 5 gives concluding remarks and policy implications, as well as prospects for future studies.

## 2. Literature review

Research in health economics has extensively explored the complex interplay between pharmaceutical consumption, economic development, and life expectancy across different countries. Although there are substantial differences in pharmaceutical consumption among countries, the direct relationship between health expenditures – including pharmaceutical spending – and improvements in life expectancy remains empirically ambiguous. Studies have focused on determining long-run relationships between life expectancy, healthcare, and pharmaceutical expenditures across OECD countries (Hermanowski *et al.*, 2015). Economic growth and advancements in medical knowledge notably play crucial roles in driving gains in life expectancy. Research from rapidly growing economies suggests that public cost containment policies have been largely ineffective in curbing ever-rising healthcare costs, with population ageing being a key driver of this phenomenon (Jakovljević, 2014, 2015; Lakdawalla, 2018). Given these important results, this literature review also examines the findings in emerging markets and traces the evolution of research methods within this domain.

The exploration of the health impact of pharmaceutical consumption began with influential studies like Miller and Frech (2000). They examined the health production function across 21 OECD countries, incorporating pharmaceutical consumption along with three lifestyle measures: alcohol consumption, smoking prevalence, and dietary richness. Their methodology relied primarily on Ordinary Least Squares (OLS) regression for a single year (1996), laying the groundwork for further research despite limitations in capturing long-run trends. The study found that high pharmaceutical consumption correlates with increased life expectancy at middle and advanced ages across OECD countries, a significant effect even when adjusting for variables such as obesity and using alternative health indicators like Disability-Adjusted Life Expectancy.

Subsequent research has built upon these initial findings, providing both confirmation and new insights. Studies have specifically focused on the impact of pharmaceuticals in OECD countries. Shaw *et al.* (2005) and Miller and Frech (2002) used sophisticated analytical frameworks to assess how pharmaceutical expenditures influence life expectancy. Further analyses continue to confirm the beneficial effects of pharmaceuticals on health, as demonstrated by studies such as Crémieux *et al.* (2005) for Canada; Caliskan (2009) for 21 OECD countries; Kim and Lane (2013) for 17 OECD countries; Linden and Ray (2017) for 34 OECD countries; Blazquez-Fernández *et al.* (2017) for both OECD and Asia/Pacific regions, collectively emphasizing the positive relationship between pharmaceutical spending and improved health outcomes. More recently, Xiong *et al.* (2019), Bölükbaşı *et al.* (2020), and Poças *et al.* (2020) reinforced these findings by offering new evidence using various methodologies – including Granger causality tests and Spearman correlation analysis – across different populations healthcare systems. Contrasting perspectives emerged from Babazono and Hillman (1994), emphasizing the complex interplay between healthcare spending and actual health benefits using 1988 OECD data. These studies also underscored the variability in outcomes based on demographic and socioeconomic factors such as population age and density, education, income, pharmaceutical consumption or private health expenditure, and sometimes other lifestyle indexes such as alcohol, tobacco, or vegetable consumption.

The literature then broadened to examine how economic growth and health expenditure relate to life expectancy. Early foundational work by Sachs and Warner (1997) uncovered a nonlinear relationship between economic growth and human capital accumulation, with life expectancy serving as a critical proxy for human capital. This pioneering analysis set the groundwork for subsequent investigations into the bidirectional impacts of health improvements and economic expansion. Extending this framework, Arora (2001) demonstrated the significant influence of health on the growth trajectories of

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industrialized nations, reinforcing the dual role of health as both an outcome and a catalyst of economic prosperity.

Further contributions by [Liao \(2011\)](#) through a General Equilibrium Model (GEM) and Taiwanese data, and [Gonzalez-Eiras and Niepelt \(2012\)](#) examination of demographic ageing within OECD countries, expanded the discussion to include the economic implications of demographic trends and policy adjustments necessitated by an ageing population. These explorations reveal how the demographic dynamics intersect with economic development.

Focusing on the relationship between health expenditure and life expectancy, a series of empirical studies provides valuable insights. [Shi et al. \(2014\)](#) and [Zaman et al. \(2017\)](#) identified significant connections between pharmaceutical expenditure, GDP growth, and health expenditure in China and Bangladesh, respectively. This line of inquiry was extended further by [Linden and Ray \(2017\)](#), as well as [Blazquez-Fernández et al. \(2017\)](#), who observed a positive correlation between private health expenditures and life expectancy in OECD countries, despite varying empirical methodologies and mixed results.

Building on these empirical analyses, recent research has shed further light on the dynamic interplay between health and economic development. For instance, [Dutton et al. \(2020\)](#) presented a counterintuitive model linking economic prosperity to mortality rates in OECD nations. Meanwhile, [Yıldırım et al. \(2020\)](#) emphasized the positive correlation between increased life expectancy and economic growth within the context of sustainable development. Furthermore, [Özler and Ağırbaş \(2023\)](#) analyzed the effects of pharmaceutical consumption on health status among European Federation of Pharmaceutical Industries and Associations (EFPIA) member countries and advocated for strategic health interventions to enhance public health outcomes. [Jakovljević et al. \(2023\)](#) broadened the perspective and provided a comprehensive analysis of the impact of healthcare reform in China on the pharmaceutical sector. The Chinese national health system plays a critical role in shaping the healthcare landscape not only in the Global South and low- and middle-income countries but also in the expanding market of Brazil, Russia, India, China, and South Africa (BRICS) nations. China's economy recently surpassed the combined economy of the European Union, reflecting its significant global influence ([Jakovljević et al., 2023](#)).

The growth in international trade between China and Southeast Asia has contributed to the rise in global demand and supply of medical goods, services, and pharmaceuticals driven by China's internal market developments. The expanding middle class in East Asia is contributing to overall real GDP growth with significant increases in purchasing power evident. These developments suggest that the Chinese health system and economy will continue to be a decisive force in the global healthcare market. [Jakovljević et al. \(2023\)](#) noted that although the policy measures introduced by the healthcare reform in China effectively reduced drug expenses by 40–50%, they unintendedly hindered innovation within domestic pharmaceutical companies. The intense price negotiations, while effective in reducing costs, made foreign market players hesitant and raised concerns about the sustainability of China's pharmaceutical system. This analysis provides a comprehensive view of the connection between healthcare reform initiatives and the intricacies of the pharmaceutical industry, aiding in a better grasp of health expenditures, economic growth, and life expectancy. However, it also uncovers the varied methodologies and occasionally conflicting outcomes that characterize this area of study.

In the Balkans, for instance, efforts to promote cost awareness among healthcare providers have yielded mixed results. [Jakovljević et al. \(2021\)](#) analysis in the Serbian context suggests that while austerity measures in healthcare have been widely adopted their impact on clinical decision-making remains limited. Consequently, the pursuit of efficient care is often seen as conflicting with resource constraints, thus impacting patient care quality. These findings from emerging markets serve as a warning about the intricate relationship between cost-cutting strategies and effective healthcare delivery in developing economies.

Further research shows the crucial need for a unified and systematic approach to healthcare reforms. This approach should consider a range of factors, including patient needs, industry dynamics, and policy implications. [Pourkavoos \(2012\)](#), highlights the interconnected nature of these components, emphasizing the importance of a comprehensive strategy that anticipates and addresses resource limitations while promoting cost-conscious healthcare practices.

In conclusion, these studies stimulate a discussion regarding a new approach to healthcare reforms, one that integrates patient care, pharmaceutical innovation, and health policy harmoniously. The complex relationship between health spending, economic factors and life expectancy highlights the importance of thorough economic analyses and compassionate policy development that consider the wide socioeconomic contexts they seek to address.

Furthermore, there has been significant attention on the impact of health expenditure on life expectancy, specifically on the intricate relationship between public and private contributions to healthcare and their effects on population health outcomes. Early research by [Kim and Lane \(2013\)](#) offers valuable insights into the positive influence of public health expenditure on life expectancy among 17 OECD countries. Their study highlights a significant negative correlation with infant mortality rates using panel data and mix effect model and observation from 1973 to 2000. This line of inquiry is further expanded upon by [Jaba et al. \(2014\)](#), who broadened the analysis to include 175 countries over the period 1995–2010, confirming a strong association between health expenditure and life expectancy despite variations across different nations.

[Jakovljević et al. \(2016\)](#) used Difference-in-Difference (DiD) and Data Envelopment Analysis (DEA) methods to show a strong link between health expenditure and longevity, particularly in early European Union (EU) member states. This indicates that increased spending on healthcare is connected to better longevity outcomes. Their study covered three main sub-regions of Eastern Europe from 1989 to 2012, including 24 countries in the EU, the Commonwealth of Independent States (CIS), and South-East Europe (SEE).

The relationship between private health expenditure and its impact on life expectancy has been less straightforward. According to [Shahraki \(2019\)](#), there appears to be bidirectional causality between public expenditure and life expectancy in Iran from 2000 to 2017, with a one-way causality from private health expenditure to life expectancy. This discovery, obtained using a Vector Error Correction Model (VECM), suggests that while public health investments directly affect life expectancy, the influence of private health expenditure may be more complex and warrants further investigation.

The literature also emphasizes the significant role of socio-economic factors and PPPs in mediating the relationship between health expenditure and life expectancy. According to [Linden and Ray \(2017\)](#) and [Blazquez-Fernández et al. \(2017\)](#), socioeconomic conditions like income levels and unemployment rates play critical roles in this dynamic. Based on data from 1970 to 2012, [Linden and Ray \(2017\)](#) have presented results for 34 OECD countries. Additionally, [Blazquez-Fernández et al. \(2017\)](#) offer new evidence regarding this relationship for 26 European countries over the period 1995–2014 using econometric panel time series methods.

Additionally, [Xiong et al. \(2021\)](#) offered valuable perspectives on the potential impact of state-owned enterprises' strategic participation in public-private partnerships (PPPs), particularly within China, highlighting a wider contextual framework for understanding the influence of health expenditure on health outcomes.

The pharmaceutical industry faces particular challenges when developing drug-drug combination products. These include addressing unmet patient needs, navigating patent expiration pressures, and ensuring a vital product pipeline. A comprehensive risk assessment framework is thus required throughout all stages of drug development to address these complexities and sustain innovation and market competitiveness ([Pourkavoos, 2012](#)). This

perspective aligns with broader discussions on healthcare expenditure, demonstrating the direct influence of pharmaceutical innovations on health outcomes and life expectancy.

Recent methodological innovations have introduced new ways of estimating the effects of health expenditure on health outcomes, offering exciting opportunities for future research. The Healthy Life Years Lost Methodology by [Skiadas and Skiadas \(2020\)](#) provides a sophisticated tool for analyzing the efficiency of health expenditure and its impact on population health. [Kara and Ersin \(2020\)](#), employing Kao's panel cointegration and [\(Dumitrescu and Hurlin, 2012\)](#) causality tests, investigated the relationship between health expenditure and infant mortality across 20 OECD countries from 1980 to 2017. Their analysis revealed a direct causal link, showing that increased healthcare spending significantly reduces infant mortality rates. In another study, [Akbar et al. \(2020\)](#) explored the impact of healthcare investment on the Human Development Index (HDI) across 33 OECD countries. Their findings highlighted bidirectional causality, emphasizing the crucial role of healthcare expenditure in promoting overall human development.

Despite these advancements, the literature reveals significant methodological gaps, particularly the need for approaches that account for cross-sectional dependence and heterogeneity in panel data analyses. The limited use of studies employing ML models and advanced causality tests to explore these relationships indicates a critical area for further research. These methodologies have shown promise in exploring macroeconomic dynamics, including the nexus between financial development and energy consumption ([Durusu-Ciftci et al., 2020](#)), the correlation between energy consumption and GDP ([Magazzino and Schneider, 2020](#)), the links between price and volatility ([Nazlioglu et al., 2020](#)), and the relationship between energy use and CO<sub>2</sub> emissions ([Magazzino et al., 2021](#)).

To bridge these gaps and uncover the intricate dynamics among pharmaceutical consumption, economic growth, and life expectancy, our study proposes a pioneering framework that merges ML algorithms with sophisticated causality testing.

By leveraging this innovative approach, our research aims to make a significant contribution to the existing body of literature, offering new directions for health policy and economic development strategies.

### 3. Data and methodology

#### 3.1 Data collection

We selected a sample of 22 OECD countries [\[1\]](#). For all series, data cover the largest available period (1998–2018), totalling 465 observations. Following the pioneer contributions of [Miller and Frech \(2000\)](#), [Frech and Miller \(2004\)](#), and [Shaw et al. \(2005\)](#), we proxy health with life expectancy (expressed in years) and distinguish between measures at birth (*LEb*), at age 40 (*LE40*), and age 60 (*LE60*). Data are derived from [OECD Health Statistics \(2020a\)](#) [\[2\]](#). Facing data availability constraints, pharmaceutical consumption is proxied by total pharmaceutical sales per capita (PPC), expressed in US\$ PPP [\[3\]](#). Economic growth is proxied by per capita income (*GDPp*) expressed in constant 2017 international dollars, taken from the World Development Indicators ([WDI, 2020](#)) [\[4\]](#). Data sources and definitions are summarized in [Table 1](#).

*3.1.1 Model set-up.* We first conduct panel data causality tests, using the Dumitrescu-Hurlin procedure, which allows for heterogeneity within the sample. This causality test considers the following linear regression model:

$$y_{it} = \alpha_i + \sum_{i=1}^K \gamma_i^{(k)} y_{i,t-k} + \sum_{i=1}^K \beta_i^{(k)} x_{i,t-k} + \varepsilon_{it} \quad (1)$$

where  $x$  and  $y$  are two stationary variables for  $N$  entities and  $T$  periods. The lag orders are represented by  $K \in \mathbb{N}^+$ , and assumed to be identical for all countries in the sample. This

**Table 1.**  
Data description

Indicator	Variable	Acronym	Measure	Source
Pharmaceutical consumption	Total pharmaceutical sales per capita	<i>PPC</i>	US\$ PPP	OECD Health Statistics (2020a)
Economic growth	Real GDP per capita	<i>GDPp</i>	Constant 2017 international \$	World Development Indicators (WDI, 2020)
Health	1. Life expectancy at birth	<i>LEb</i>	Years	OECD Health Statistics (2020b)
	2. Life expectancy at 40	<i>LE40</i>	Years	OECD Health Statistics (2020b)
	3. Life expectancy at 60	<i>LE60</i>	Years	OECD Health Statistics (2020b)
<b>Source(s):</b> Our elaborations				

model incorporates heterogeneity among panel members by allowing the coefficients  $\alpha_i, \gamma_i^{(k)}$ , and  $\beta_i^{(k)}$  to vary among cross-country units. Hence, the standardized test statistic  $\tilde{Z}_N^{Hnc}$  for a fixed sample period is expressed as follows:

$$\tilde{Z}_N^{Hnc} = \sqrt{\frac{N}{2K} * \frac{(T - 2K - 3)}{(T - K - 3)}} * \left[ \frac{(T - 2K - 3)}{(T - 2K - 1)} W_{N,T}^{Hnc} - K \right] \quad (2)$$

where  $W_{N,T}^{Hnc}$  refers to the arithmetic averaged individual Wald statistics of Granger non-causality. The null and alternative hypotheses are defined as:  $H_0: \beta_{i1} = \dots = \beta_{iK} = 0 \forall i = 1, \dots, N$  and  $H_1: \beta_{i1} = \dots = \beta_{iK} = 0 \forall i = 1, \dots, N_1$ ; or  $\beta_{i1} \neq 0$  or  $\dots$  or  $\beta_{iK} \neq 0 \forall i = N_1 + 1, \dots, N$ ; and where  $N_1 \in [0, N - 1]$  is unknown. Accordingly, rejecting the null hypothesis indicates the existence of a causal relationship running from  $x$  to  $y$  in some entities of the sample, but not necessarily all.

Following, this study extends the standard panel estimations and investigates the causal relationships operating among the selected variables using an ML algorithm derived from AI. In particular, we try to identify an unsupervised link between the “target” (life expectancy at birth, life expectancy at 40 and life expectancy at 60) and the “input” (GDP per capita, total pharmaceutical sales per capita) through an innovative methodology that we call “D2C Prediction”. Furthermore, to guarantee the Oryx software is able to work on a large dataset, we have carried out numerous mathematical transformations for each variable: logarithm, squared, first difference, and first logarithmic difference.

Starting from Pearl and Mackenzie (2018) approach, we tried to overcome the limitations of predicting causal links in ML. Indeed, the problem of predicting a causal link arises from the need to build numerous models with different architectures capable of comparing each other automatically. The problem, however, lies in the computational upgrading of any undergoing model comparison (ML-D2C, ANN, Cluster ML, etc.). The result that the researcher would arrive at would be an unattainable model, whose interpretation could appear wrong. Therefore, we combined several approaches by writing an algorithm to eliminate the comparison process between various ML applications. Thus, from the well-known setting due to Pearl and Mackenzie (2018), we derived the possibility of using the results of Peters et al. (2015), also extending the approach with the prediction of Grath et al. (2018).

At the mathematical level, we derived the functions  $M_i$  and  $M_j$  and the subsets [5]:



$$\frac{M_j}{z_i} = [m^k, k_i = 1 \dots, K_i] \text{ and } \frac{M_j}{z_j} = [m^k, k_j = 1 \dots, K_j]$$

where  $m^k$  is a generic component in Markov Blankets (MB);  $M_i$  is an MB of  $z_i$  (or  $j$ ) that minimizes the subset:

$$I \left( z_i \left( \frac{Z}{M_i} \cap z_i \right) \right) | M_i = 0 \tag{3}$$

$z_i$  and  $z_j$  in terms of dependence produce the following expression:

$$I = \left[ (z_i; z_j), \left( z_j; \frac{z_i | M_i}{z_i} \right), I \left( z_i; \frac{z_j | M_i}{z_j} \right) \right] \tag{4}$$

Since we have five variables, we can imagine them as subclasses ( $D$ ):

$$D_{i,j}^1 = [I(z_i; m_i^{kj} | z_j), k_j = 1 \dots K_j] \tag{5}$$

$$D_{j,i}^2 = [I(z_j; m_j^{ki} | z_i), k_i = 1 \dots K_i] \tag{6}$$

$$D_{i,j}^3 = [I(m_i^{ki}; m_j^{kj} | z_i), k_i = 1 \dots K_i, k_j = 1 \dots K_j] \tag{7}$$

$$D_{j,i}^4 = [I(m_i^{ki}; m_j^{kj} | z_j), k_i = 1 \dots K_i, k_j = 1 \dots K_j] \tag{8}$$

$$D_{i,j}^5 = [I(m_i^{kj}; m_j^{ki} | z_i), k_i = 1 \dots K_i, k_j = 1 \dots K_j] \tag{9}$$

$$\text{where } k_i = 1 \dots K_i, k_j = 1 \dots K_j \tag{10}$$

Now, our new approach can be inserted. First, we apply the set of equations in [Peters et al. \(2015\)](#) following [Pearl and Mackenzie \(2018\)](#) approach:

$$Y_k : X_m^k \approx Y'_k : X'_m \tag{11}$$

$$\nabla k, k' \in 1, \dots, \delta \tag{12}$$

$$\arg \min \max \left( \rho \cdot \left( \hat{f}(x') - y' \right)^2 + \delta(x, x') \right) \tag{13}$$

$$\delta(x, x') = \sum_{k \in f} \frac{|x_k - x'_k|}{G \perp \delta_k} \tag{14}$$

$$G \perp \delta_k = \text{median}_{j \in p} \left( |X_{j,k} - \text{median}_{l \in p} (X_{l,k})| \right) \tag{15}$$

We represent what was previously demonstrated through the [Grath et al. \(2018\)](#) function:

$$\hat{f}_{X_D, S}(X_{D, S}) = \tau_{x_d, s} \left[ \hat{f}(x_s, X_D) \right] = \int \hat{f}(x_s, X_D) p(X_D) dX_D \tag{16}$$

Thus, our D2C Prediction can be written as:

$$\left\{ \begin{array}{l} \frac{-\square^2}{k} \sum_{i=1}^k \text{dist} \left( \int \widehat{f}(x_s, X_D) p(X_D) dX_D \right) \\ \frac{\square^2}{G_2^k} \sum_{i=1}^{k-1} \sum_{j=i+1}^k \text{dist} \int \widehat{f}(x_s, X_D) p(X_S) dX_S \\ 1 - \frac{\square^2}{k \cdot d} \sum_{i=1}^k \sum_{i+1}^d \text{dist} \int \widehat{f}(x_s, X_D) p(X_S) dX_S \neq dX_D \end{array} \right. \quad (17)$$

**4. Empirical results and discussion**

As a preliminary analysis, some descriptive statistics are summarized in Table 2. The skewness value of all variables is negative, indicating that the distribution is right-skewed, with more observations on the left. Given the fact that, for each variable, 10-Trim values are near the mean and pseudo standard deviation, the Inter-Quartile Range (IQR) describes the absence of significant outliers in the observed sample.

Table 3 displays the results of the Dumitrescu-Hurlin pairwise panel causality tests. The null hypothesis of no causality can be rejected between GDPp and PPC as findings exhibit a

Variable	Mean	Median	Std. dev.	Skewness	Kurtosis	IQR
GDPp	10.6118	10.6493	0.3822	-0.1187	4.1406	0.4065
PPC	5.8603	5.9474	0.4253	-1.0573	4.1445	0.4779
LEb	4.3720	4.3808	0.0393	-1.1045	3.7351	0.0465
LE40	3.6993	3.7184	0.0689	-1.0780	3.5085	0.0784
LE60	3.1166	3.1420	0.0935	-0.7964	2.8446	0.1162

**Table 2.**  
Descriptive statistics

**Note(s):** \*\*\*p < 0.01, \*\*p < 0.05, \*p < 0.10  
**Source(s):** Our elaborations

Null hypothesis	W statistic	Z-bar statistic	p-value
GDPp→PPC	5.9065	5.6865	0.0000***
PPC→GDPp	3.7325	2.1801	0.0292**
GDPp→LEb	2.6593	0.5334	0.5938
LEb→GDPp	5.5812	5.4502	0.0000***
GDPp→LE40	2.7892	0.7586	0.4481
LE40→GDPp	3.5812	2.0953	0.0361**
GDPp→LE60	2.7367	0.6637	0.5069
LE60→GDPp	4.2587	3.2248	0.0013***
PPC→LEb	3.9985	2.5926	0.0095***
LEb→PPC	2.9392	0.8909	0.3730
PPC→LE40	3.8293	2.3312	0.0197**
LE40→PPC	3.3784	1.6049	0.1085
PPC→LE60	3.4546	1.7189	0.0856*
LE60→PPC	2.5806	0.3148	0.7529

**Table 3.**  
Pairwise Dumitrescu-Hurlin panel causality tests results

**Note(s):** Two lags. Null Hypothesis: the former does not homogeneously cause the latter. \*\*\*p < 0.01, \*\*p < 0.05, \*p < 0.10  
**Source(s):** Our elaborations

two-way bidirectional causality among those two variables. Also, with a  $p$ -value of 0.000, the lagged value of  $LEb$  is found to cause  $GDPp$ , while no significant causal relationship is depicted in the reverse direction. Furthermore, results pointed out to a one-way unidirectional causal relationship running from  $PPC$  to  $LEb$ , from  $LE40$  to  $GDPp$ , from  $LE60$  to  $GDPp$ , from  $PPC$  to  $LE40$ , and from  $PPC$  to  $LE60$ . This confirms our initial intuition that there exists a bidirectional causal relationship between pharmaceutical consumption and economic growth, thus highlighting the economic benefits derived from pharmaceutical sales. While results underline the well-established conclusion that a higher average life expectancy drives the changes in aggregate income over the long-run, they interestingly stress that total pharmaceutical sales per capita statistically determine changes in both life expectancy at 40 and 60. This is the first key contribution of this paper. Nonetheless, one limit of standard panel econometric methods is that they offer insights with regards to the existence and the direction of causalities among variables but fail to supply information regarding the sign and the robustness (in percentage % probability) of this relation. This is where the D2C algorithm derived from AI finds its contribution.

According to Magazzino *et al.* (2020a, b) and Mele and Magazzino (2020, 2021), our analysis begins using a standard D2C model to which the D3S algorithm (a three-level decomposition of Markov's process) is added. The algorithm returns, as a result, six simulations of scenarios concerning three states representing the ML core: "AVG.Scscs", "AVG.peak", "AVG.CPU time". The three scenarios identify the causality between the chosen target variable and the chosen input capable of generating the process. The variables used have been parameterized using the acronym in Table 1.

The subset of AVG.Scscs composed of Scsum and Scspec shows that the Scsum values, for each hypothesized scenario, are more significant than the hypothetical situations (*hidden*) unknown values that could generate bias effects in the algorithm. The values of the Scspec, which represent the causal links of random sub-descriptors, are more significant for each scenario than the hidden values. Furthermore, the value of the e-c ratio relative to the AVG peak stage shows real scenario values turn out to be higher again than hidden situations.

Tables 2–7 all have a one-way causal link. The only exception concerns Table 7. Table 2 shows, for each hypothesized scenario, a high causal link between GDP per capita and life expectancy at birth. At the computation level, we can see that the loss of information is less than 50% (% reduction). This result underlines how the algorithm could perfectly interact with each data aggregate, generated in an unsupervised context. At an economic level, the explanation of the strong causal link can be the following: life expectancy at birth indicates how many years a newborn is destined to live on average. A specific age denotes the remaining years that one can still expect to live onwards. Our model has shown how the number of years that each inhabitant (of the countries under analysis) can expect to live at birth is caused by the variation in economic income and grows as GDP per capita increases. The reasons for this result can be traced back to the following explanation. Citizens of advanced countries have better nutrition, have access to plenty of water and food, are vaccinated against various diseases, live in cities with sewage systems, and have highly advanced health and drug systems. These factors reduce infant mortality, extending the life of adults. Therefore, this result would also explain the causal link discovered in Table 3, which relates total pharmaceutical sales per capita with life expectancy at birth. Tables 4 and 5 causally relate GDP per capita with life expectancy at 40 and total pharmaceutical sales per capita with life expectancy at 40, respectively. Compared to the first two scenarios previously examined, we can see how a one-way causal relationship emerges, although, in this case, the relationship is less strong. One can observe this result by looking at the Scsum and % reduction values. Even though the former is lower than Tables 2 and 3, the latter shows a more significant reduction. This phenomenon, in an ML environment, suggests the existence of a causal relationship of the "real but weak" type.

Nonetheless, the Scspec and e-c ratio values show that these scenarios are also empirically correct. The major weakness of these causal links could be the result of the existence of a steady state between the target variable (*LE40*) and the selected inputs in the algorithm (*GDPp* and *PPC*). In other words, the effect of per capita GDP growth and pharmaceutical sales is less important than *LEb*. However, the link is always evident. In particular, in [Table 4](#), we can state that the link between *GDPp* and *LE40* could lie in the fact that there is a progressive increase in jobs in services and a decrease in employment in agriculture and industry for advanced countries. In wealthier countries, therefore, the share of the population that carries out tiring and life-threatening jobs gradually decreases. The results of [Tables 6–8](#) are very interesting. A strong causal link between GDP per capita and life expectancy at 60 and for total pharmaceutical sales per capita and life expectancy at 60 emerges. Indeed, the Scsum and % reduction values precisely respect the theory of ML in D2C: high values close to zero for Scsum and low values below 40% for % reduction. These results clarify that higher per capita economic growth translates into better health care for those who become elderly. According to [Table 9](#), higher spending on drugs guarantees a longer life expectancy for people aged 60 and over. Of great importance is the result we obtained in [Table 6](#) under the item Scsum. As can be noticed, it has both positive and negative signs. In other words, it shows us a negative two-way sense of randomness. The explanation could be that the progressive ageing of the population generates an increase in public spending on pensions, health, and assistance that could have adverse effects on potential GDP growth in the long-run.

**Table 4.**  
Predicted causality  
from *GDPp* to *LEb*

	Scsum	AVG.ScS	Application scenario 1 (1020 repetitions)		
			Scspec	AVG.peack e-c ratio	AVG.CPU time Reduction%
<i>GDPp</i>	0.94		0.90	64.32%	46%
Hidden	0.90		0.60	2.10%	91.66%

**Note(s):** Our elaborations in Oryx

**Table 5.**  
Predicted causality  
from *PPC* on *LEb*

	Scsum	AVG.ScS	Application scenario 2 (1020 repetitions)		
			Scspec	AVG.peack e-c ratio	AVG.CPU time Reduction%
<i>PPC</i>	0.97		0.93	71.15%	48%
Hidden	0.84		0.37	4.5%	96.26%

**Note(s):** Our elaborations in Oryx

**Table 6.**  
Predicted causality  
from *GDPp* on *LE40*

	Scsum	AVG.ScS	Application scenario 3 (1020 repetitions)		
			Scspec	AVG.peack e-c ratio	AVG.CPU time Reduction%
<i>GDPp</i>	0.76		0.82	60.14%	51%
Hidden	0.85		0.49	7.39%	91.2%

**Note(s):** Our elaborations in Oryx

After verifying the existence of a causal link between the inputs and target variables, it would be helpful to know to what extent this causal link exists in ML. As we have previously anticipated, such a procedure requires the use of a different algorithm that we have called D2C Prediction. Indeed, both in standard econometrics and ML, it is not easy to understand the precise value of a causal link. Especially when we analyze extensive aggregate data with an unsupervised (ML) technique, we always have difficulty extracting an accurate causality value. Therefore, the novelty of this work is to use a predictive randomness algorithm connected to a DeepNet process. To this end, we have chosen to adapt our algorithm to the BigML platform. Following the theoretical indications (also expressed by the manufacturer of the ML platform), we generated a dataset from our file containing a training equal to 80% and a test of 20% by inserting, in addition, a linear split. The next step represents the adaptation of our algorithm. First of all, we chose to use a DeepNet configuration with the target variables identical to the D2C model. Then, we set up an automatic optimization process, with a maximum training time of 5 h. In this way, we generated an average of 30,000 iterations (the maximum value was 38,649). Finally, we choose Adam’s algorithm to estimate the Gradient Descent and set the following values: Beta1 = 20,000 and Beta2 = 40,000. The results obtained are appealing, as we can see in [Figures 1–4](#).

[Figures 1–4](#) show very interesting results. Each of them represents a predictive causality in ML adapted to a DeepNet model. It can synthesize our D2C Predict. For the international scientific literature, our model represents a novelty. We can explain at least two types of reasons. The first is to generate a causal prediction in ML by comparing two inputs (*GDPp* and *PPC*) concerning a predetermined target (*LEb*, *LE40*, *LE60*). The second, on the other hand, is due to the ability of our model to generate a precise value of the causality between the

	Scsum	AVG.Scsc	Application scenario 4 (1020 repetitions)		
			Scspec	AVG.peak e-c ratio	AVG.CPU time Reduction%
PPC	0.75		0.80	58.26%	52%
Hidden	0.21		0.27	1.24%	91.3%

**Note(s):** Our elaborations in Oryx

**Table 7.**  
Predicted causality  
from PPC on LE40

	Scsum	AVG.Scsc	Application scenario 5 (1020 repetitions)		
			Scspec	AVG.peak e-c ratio	AVG.CPU time Reduction%
GDPp	±0.91		0.89	87.03%	38%
Hidden	0.10		0.15	0.74%	97%

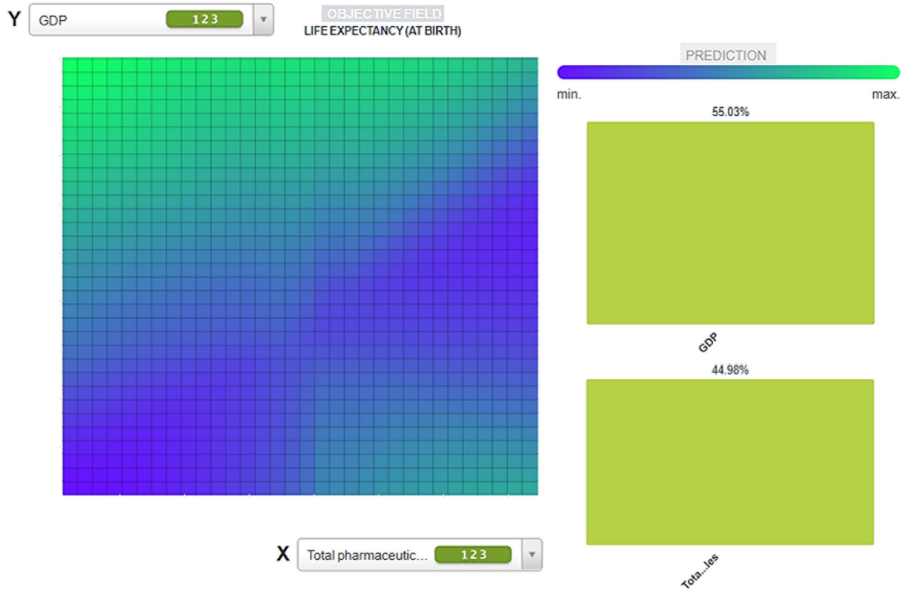
**Note(s):** Our elaborations in Oryx

**Table 8.**  
Predicted causality  
from GDPp on LE60

	Scsum	AVG.Scsc	Application scenario 6 (1020 repetitions)		
			Scspec	AVG.peak e-c ratio	AVG.CPU time Reduction%
PPC	0.95		0.96	90.01%	39%
Hidden	0.10		0.15	0.74%	97%

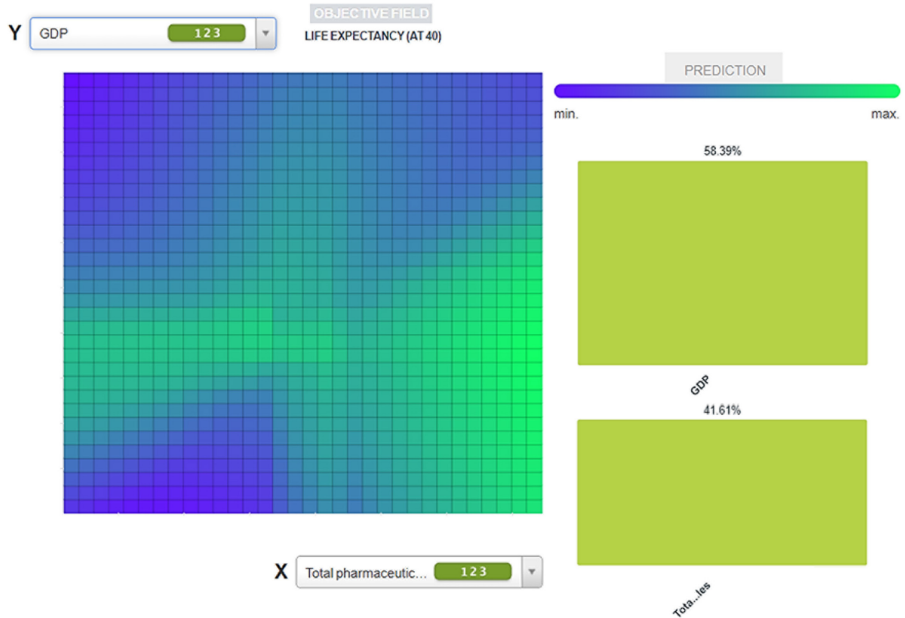
**Note(s):** Our elaborations in Oryx

**Table 9.**  
Predicted causality  
from PPC on LE60



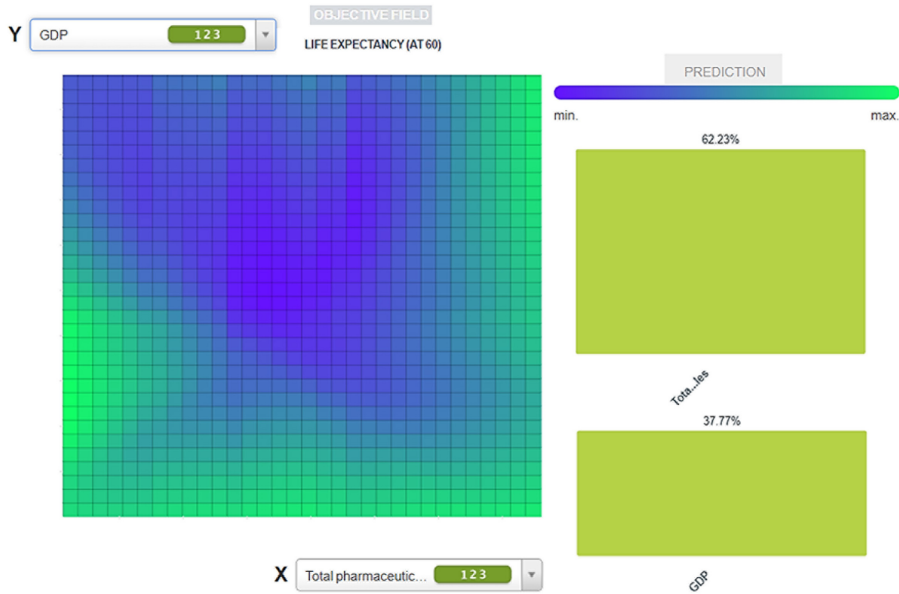
**Figure 1.**  
DeepNet "D2C Predict"  
on LEB

Source(s): Authors own work in BigML



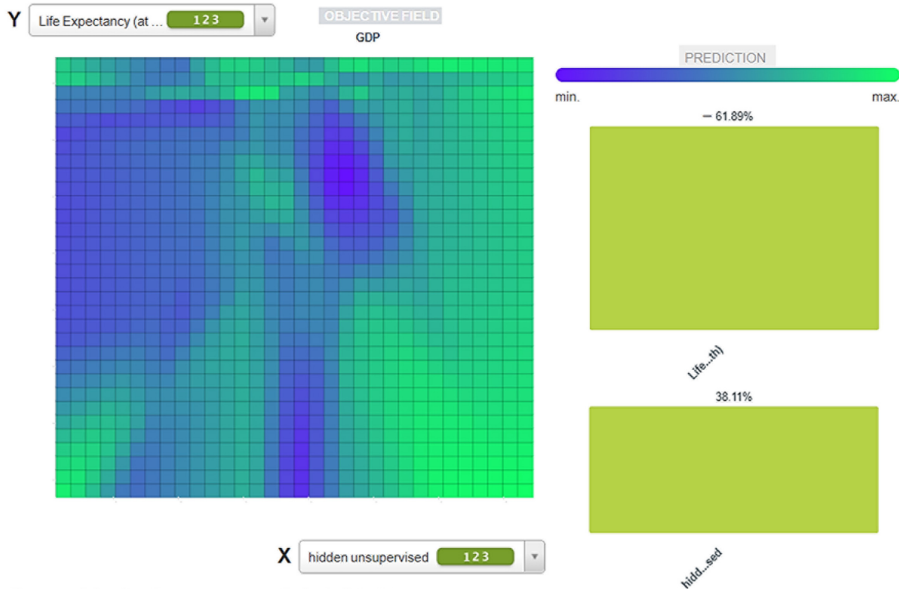
**Figure 2.**  
DeepNet "D2C Predict"  
on LE40

Source(s): Authors own work in BigML



Source(s): Authors own work in BigML

Figure 3.  
DeepNet "D2C Predict"  
on LE60



Source(s): Authors own work in BigML

Figure 4.  
DeepNet "D2C Predict"  
LE60-hidden  
unsupervised on GDP

input and the target. This operation is almost impossible with standard econometric procedures. In each figure, the large square on the left is the process between two inputs on the target within a DeepNet. If an input has an increasingly lighter colour, the more significant the causal prediction over time concerning the target. On the right, instead, two histograms are represented with the precise value of the causal link between input and target. The results obtained confirm those present in the ML D2C model. In [Figure 1](#), we can see a robust causal relationship between the two inputs and the life expectancy at birth. Our model, however, is able to show how the change in GDP per capita causes the target to be higher than total pharmaceutical sales per capita: 55.03 versus 44.98%. Therefore, more significant economic growth sets in motion all those known to the theory of development capable of guaranteeing a higher survival rate and a higher average standard of living as per capita income increases. In addition, per capita economic growth would assist the family's spending capacity for drugs capable of fighting infections and various health problems. The higher GDP per capita and life expectancy at birth coincide with a better welfare state towards an efficient health system at the macroeconomic level. [Figure 2](#) shows similar results to those found in [Figure 1](#). However, we can see the greater importance of GDP per capita in causing the life expectancy at 40 (*LE40*): GDP = 58.39% and total pharmaceutical sales per capita = 41.61%. In other words, the prediction of per capita GDP generates social phenomena (education, employment, wage variation, psychological security at work), which cause a higher life expectancy. Finally, [Figures 3 and 4](#) confirm the results obtained from [Tables 6 and 7](#). First of all, we can note in [Figure 3](#) that the total pharmaceutical sales per capita generate a predictive causal effect on life expectancy at 60, equal to 62.23% compared to a change in GDP per capita of 37.77%. Therefore, an increase in pharmaceutical sales generates a strong relationship on life expectancy regarding the variation in economic growth. [Figure 4](#), on the other hand, represents our further experiment concerning the inverse sense of causality obtained in [Table 6](#) (Scsum:  $GDPp = \pm 0.91$ ). We wanted to verify when life expectancy at 60 influenced (negatively or positively) GDP per capita. To do this, we adapted the dataset through Python processing, capable of generating  $n+1$  hidden variables affecting the GDP. Next, we processed the DeepNet model by targeting GDP per capita, using life expectancy at 60 as input and hidden unsupervised. The result obtained is impressive: the model returned a precise result with a negative value: life expectancy at 60 generates a predictive causal link on GDP per capita equal to  $-61.89\%$ . This result confirms the starting hypothesis: advancing age requires more assistance from the state. Under certain preconditions, they can turn into burdens for economic growth.

All in all, while the results of the pairwise Dumitrescu-Hurlin causality test supplied information with regard to the existence and the direction of causalities among variables, the D2C algorithm complemented with a DeepNet model underlined the sign and magnitude of these effects and provided a precise measure of the relationship operating between the input and the target. First, a two-way bidirectional causal relationship is revealed between GDP per capita and total pharmaceutical sales per capita, which indicate that these variables improve each other. Also, findings show that GDP per capita positively enhances life expectancy at birth, 40, and 60, with a systematic positive and significant generated predictive value, although a greater value is found for life expectancy at 40. This validates [Dutton et al. \(2020\)](#) who modelled the existence of a negative impact of economic growth on changes in death rates for 5 OECD countries. Similarly, pharmaceutical sales per capita do substantially trigger improvements in life expectancy, with an associated magnitude higher compared to the one produced when GDP is the input target. This echoes the panel econometric results of [Kim and Lane \(2013\)](#) for 17 OECD countries; and [Jaba et al. \(2014\)](#) for 175 countries. Such inferences also connect with those of [Jakovljević et al. \(2016\)](#) who employed DiD and DEA methods and underlined that in countries where the highest health expenditures are recorded, a surprisingly similar longevity increase arises. Nonetheless, while panel econometric



findings claimed evidence of a significant causal relationship between life expectancy at 60 and GDP per capita, ML results pointed out that such linkage is negative. Therefore, the nature of this relationship is asymmetric and non-linear, showing that life expectancy at 60 does require more assistance than it generated economic benefits, whereas the reverse is not true. This latter insight supports the conclusions drawn in [De la Croix and Licandro \(1999\)](#), [Boucekkine \*et al.\* \(2002\)](#), and [Kunze \(2014\)](#). Our panel econometrics and D2C findings are in line with those of [Shi \*et al.\* \(2014\)](#) who showed that pharmaceutical expenditure increased over time along with GDP growth for China. Also, the present study corroborates those of [Linden and Ray \(2017\)](#), [Blazquez-Fernández \*et al.\* \(2017\)](#), and [Sunday and Adeleye \(2017\)](#) who stressed that private health (including pharmaceutical) expenditures enhance life expectancy for a sample of OECD and Asia-Pacific samples, as well as Nigeria, respectively. Besides, our conclusions connect to those of [Kara and Ersin \(2020\)](#) whose Kao panel cointegration and Dumitrescu-Hurlin causality test performed on 20 OECD countries point out the presence of a unidirectional causal linkage from health expenditure to infant mortality rate. Slightly connected to this result, [Akbar \*et al.\* \(2020\)](#) supplied evidence of a two-way bidirectional causality between healthcare expenditures and the Human Development Index (HDI), which is partially in line with our conclusions. However, we fail to confirm the results of [Arora \(2001\)](#) who explored the influence of health on the growth paths of 10 industrialized countries over 125 years. Changes in health are found to increase their pace of growth by 30–40%, which contradicts our conclusions. Similarly, [Futagami and Nakajima \(2001\)](#) showed how population ageing can positively enhance economic growth using a GE model of life cycle savings combined with endogenous growth, which again contradicts our ML estimates as life expectancy at 60 generates a predictive causal link on GDP per capita equal to  $-61.89\%$ . Conversely, our results extend those of [Auerbach \*et al.\* \(2017\)](#) as they demonstrated how the growing gap in life expectancy affects retirement benefits and reforms. Using predicted mortality as an instrument, while a 1% increase in life expectancy is associated with a 2% increase in population, they also failed to supply evidence that life expectancy improvement raises per capita income.

## 5. Concluding remarks and policy implications

The aim of this study is to reassess the relationship among pharmaceutical consumption, per capita income, and life expectancy (distinguishing at birth, middle, and advanced ages) in the Data spanning from 1998 to 2018 from 22 member countries have been collected for analysis. Two distinct independent methodologies are applied. Firstly, we run the Dumitrescu-Hurlin pairwise panel causality test, followed by an ML experiment: the Causal Direction from the Dependency (D2C) Prediction algorithm. This algorithm is believed to provide robust insights into the nature, sign, direction, and significance of the causal relationships revealed by the econometric procedure.

Our analysis reveals a two-way positive bidirectional causal relationship between GDP and total pharmaceutical sales per capita, indicating that these indicators improve each other. Additionally, we find that GDP per capita positively correlates with life expectancy at birth, 40, and 60, consistently generating positive and statistically significant predictive values. Nonetheless, the value generated by the input life expectancy at 60 on the target income per capita is negative, shedding light on the asymmetric and non-linear nature characterizing this nexus. Lastly, pharmaceutical sales per capita positively impact life expectancy at birth, 40, and 60, with a higher associated magnitude than the one generated when economic growth is employed as the input target. By contributing to existing literature, our findings offer valuable conclusions and insights for health policy formulation.

The empirical investigation reveals a fundamental link between pharmaceutical sales and aggregate value-added, as evidenced by both panel econometric and ML analyses.

Consequently, any negative shock affecting one indicator is expected to produce an adverse impact on the other, and *vice versa*. Interestingly, such inference contradicts the general statement that, when GDP increases, health expenditures decrease due to general health improvements (Baltagi and Moscone, 2010). Instead, it underscores the perspective that health expenditures should be viewed as an investment in human capital, yielding subsequent economic benefits. However, the study clearly demonstrates that the health benefits derived from pharmaceutical use outweigh those resulting from aggregate income growth. Therefore, policymakers should consider this evidence and recognize that solely raising income may prove an inconsistent strategy unless accompanied by enhancements in affordable healthcare access. This holds particularly true for countries with predominantly private health systems, where there exists a risk of low-income groups falling into the health poverty trap due to inadequate healthcare access. Therefore, it is strongly recommended to implement appropriate frameworks that promote health insurance schemes tailored for low socio-economic groups. Additionally, there should be stringent controls on the profits obtained by pharmaceutical manufacturers, distributors, and providers in this context, namely each stage of the health supply chain. Furthermore, adequate regulation measures reducing the chronic gap between drug price indices and pharmaceutical costs are necessary. However, it is important for these reforms to anticipate that reduced prices of the pharmaceuticals on the restrictive list may lead to decreased sales revenues for manufacturers. This, in turn, may incentivize providers to purchase off-list high-priced pharmaceuticals to maintain or gain high marginal revenues.

In light of this, public regulations should internalize pharmaceutical producers' anticipations and set public subsidies equivalent to the marginal loss for producers. Finally, despite an increase in pharmaceutical consumption, a rise in life expectancy at 60 is associated with a negative impact on aggregate income. This indicates that increased longevity in the highest quantile does require more financial public assistance than it generates economic benefits. This well-established result should serve as a cautionary note for policy planners, highlighting that productivity declines, employment losses, and retirement supports should be rather regarded as unavoidable public costs. They call for comprehensive economic and societal support rather than being seen as the emergence of a promising market share for pharmaceutical industries.

The study is subject to several limitations. Firstly, while our results offer general macro-based insights for the OECD, future research should aim to provide country-specific and regional evidence if data availability permits. Secondly, due to chronic constraints in data availability, we were unable to identify which pharmaceutical products within the global set of sales create health and economic benefits, and which do not. Similarly, identifying which socio-economic categories benefit more from marginal changes in pharmaceutical sales could provide valuable insights to complement our current conclusions. Thirdly, the utilization of a two-step approach involving independent methodologies, including panel econometric estimators and ML algorithms is still in its nascent stages. Systematizing this approach should enrich the literature with robust findings and pave the way for further technical advancements in the field.

### Nomenclature

AI	Artificial Intelligence
ARDL	Auto-Regressive Distributed Lags
BRICS	Brazil, Russia, India, China, South Africa
CCEMG	Common Correlated Effects Mean Group
CIS	Commonwealth of Independent States
D2C	Causal Direction from Dependency

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DALE	Disability-Adjusted Life Expectancy
DEA	Data Envelopment Analysis
DH	Dumitrescu-Hurlin
DiD	Difference-in-Difference
EFPIA	European Federation of Pharmaceutical Industries and Associations
EU	European Union
GEM	General Equilibrium Model
GMM	Generalized Method of Moments
HDI	Human Development Index
IRFs	Impulse Response Functions
MB	Markov Blankets
MG	Mean Group
ML:	Machine Learning
OECD	Organization for Economic Co-operation and Development
OLS	Ordinary Least Squares
PPP	Purchasing Power Parity
PPPs	Public-Private Partnerships
SEE	South-Eastern European countries
PVAR	Panel Vector Auto-Regressions
VECM	Vector Error Correction Model
WDI	World Development Indicators

### Notes

1. This sample comprises Australia, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Japan, Latvia, Luxembourg, the Netherlands, New Zealand, Norway, Portugal, Slovak Republic, Spain, Sweden, Switzerland, and the United Kingdom.
2. Life expectancies data (at birth, at 40 and at 60) are available at: <https://doi.org/10.1787/data-00540-en>
3. Pharmaceutical sales per capita data are available at: <https://doi.org/10.1787/data-00545-en>
4. Per capita GDP data are available at: <https://databank.worldbank.org/source/world-development-indicators>
5. We start with Pearl and Mackenzie (2018) approach and the MB network.

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