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Research Article

Evolution of the Consumption of Proton Pump Inhibitors in Morocco (2020-2024): Pharmacoepidemiological Analysis and International Comparison

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Abstract

Introduction: Acid-related disorders are common, and the arrival of proton pump inhibitors (PPIs) has revolutionized their treatment. Their efficacy and good tolerance have led to widespread adoption, particularly in Europe, with a significant increase in healthcare spending. This study aims to analyze the evolution of PPI consumption in Morocco between 2020 and 2024, and to compare it with international trends.

Materials and Methods: This is a retrospective descriptive study, based on private sales data of PPIs in Morocco from 2020 to 2024, provided by IQVIA. The analysis is based on the defined daily dose (DDD) indicator.

Results: Between 2020 and 2024, PPI sales in Morocco increased from 11.7 to 16.5 million units, representing a compound annual growth rate (CAGR) of 9.1%. DDIs increased from 471 to 645 million (CAGR of 8.5%). Consumption per 1,000 inhabitants/day increased from 35 to 48 DDIs, representing an increase of 37.1%. All PPI classes show increasing consumption, with the exception of Lansoprazole and Rabeprazole. Omeprazole remains dominant, but its share is decreasing in favor of Esomeprazole, which is growing strongly (+78.4%).

Conclusion: The increasing use of PPIs raises concerns about cost and misuse. Strategies such as treatment reassessment, deprescribing, or reimbursement reforms have been shown to be effective in several countries.

Keywords: *Proton Pump Inhibitors; Consumption; Pharmacoepidemiology; Morocco; IQVIA; Trends; Health Expenditure; Misuse; Deprescription*

Introduction

Pathologies related to gastric acidity including GERD are common and their severity varies [1].

Progress in medical research in this area has made it possible to expand therapeutic options, particularly thanks to gastric antisecretory drugs such as proton pump inhibitors (PPIs) and H2 receptor antagonists (H2RAs) [2]. Their consumption is increasing in several European countries given their effectiveness and good short-term tolerance.

However, this increased use raises concerns, particularly regarding misuse and prolonged use, as demonstrated by several studies. Indeed, adverse effects can appear as a result of this: fractures, renal toxicity, cognitive disorders and certain cancers [3,4].

Objectives of the Study

- Describe the trend of PPI consumption in Morocco over the period 2020-2024.
- Compare national consumption data with data from international literature.
- Identify the main PPIs used and analyze their evolution over time.
- Evaluate the economic impact of this consumption.

Materials and Methods

Data source

The data analyzed in this study come from the Iqvia database and concern pharmacy sales of PPIs, measured in boxes sold and translated into Ddj (defined daily dose).

Unit of measurement of consumption

Number of boxes or units sold

This unit allows for a crude quantification of sales, but remains poorly suited to comparisons due to variations in dosage, galenic form and packaging.

Defined daily dose (DDD)

The DDJ, defined by the WHO, represents the theoretical daily intake for the primary indication in adults. It constitutes a standardized reference for comparing consumption on a national or international scale. The indicator used is: DDJ per 1000 inhabitants per day (DID).

Products concerned

The PPIs studied are classified according to the ATC (Anatomical Therapeutic Chemical) nomenclature:

• A02BC01: Omeprazole	• A02BC05: Esomeprazole
• A02BC02: Pantoprazole	• A02BC06: Dexlansoprazole
• A02BC03: Lansoprazole	• A02BC07: Dexrabeprazole
• A02BC04: Rabeprazole	• A02BC53/54: Forms in association

Table

Data analysis

The analysis is of type retrospective description, based on IPP sales data in Morocco between 2020 and 2024. It includes:

- The consumption volume expressed in DDJ.
- The evolution of trends by molecule and by year.
- The economic impact through the study of costs related to consumption.
- Graphical representation of data via histograms to visualize interannual variations.
- An international comparison of Moroccan data with those of other countries, allowing a global contextualization of prescription and use habits.

Results

Consumption of canned PPIs in Morocco from 2020 to 2024

During the years 2020 to 2024, statistical analysis reveals a significant upward trend in IPP sales in Morocco with a constant growth in the number of boxes sold, from 11,693,522 in 2020 to 16,525,748 in 2024 and an average annual growth rate (AAGR) of approximately 9.1%, thus highlighting a substantial average annual increase in sales during this period.

The analysis of absolute annual variations highlights an absolute increase of 4,832,226 boxes between 2020 and 2024, while the most remarkable increase was observed between 2020 and 2021, with an absolute increase of 1,601,271, representing a growth rate of 13.7%. This progression continued in the following years, reflecting a growing dynamic in IPP sales. Figure 1 illustrates this.

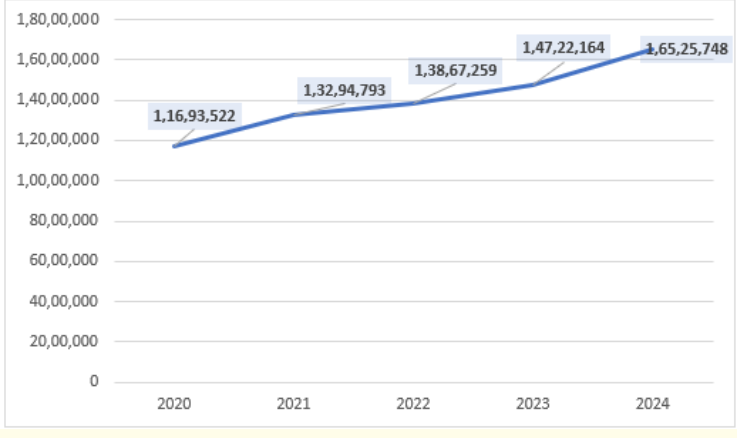

Figure 1: *Annual consumption in number of boxes of IPPs in Morocco between 2020 and 2024.*

Consumption of IPP in DDJ in Morocco from 2020 to 2024

Detailed analysis of data on annual private consumption of PPIs between 2020 and 2024 revealed significant upward trends, with a volume of 471 million DDJ in 2020 compared to 645 million DDJ in 2024, highlighting an increase over the years, with an average annual growth rate of 8.5%, reflecting a growing demand for PPIs. Figure 2 represents this.

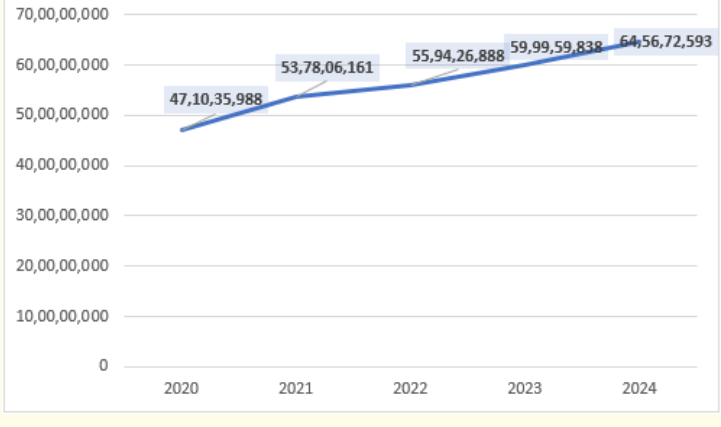

Figure 2: *Annual consumption in volume of DDJ/Year of IPPs in Morocco between 2020 and 2024.*

Related to the population, PPI consumption was 35 DDJ/day per 1000 inhabitants in 2020, and increased to 48 DDJ/day per 1000 inhabitants in 2024, a growth rate of 37.1%. This means that during 2020, on average, 35 inhabitants out of 1000 took a daily dose of PPI, and this average increased significantly in 2024 to reach 48 inhabitants out of 1000. Figure 3 illustrates this.

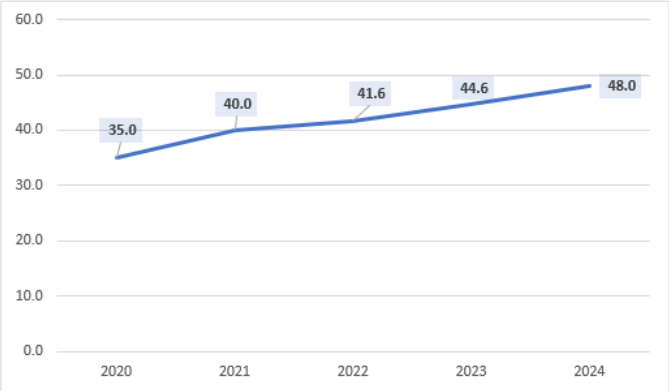

Figure 3: *Consumption DDJ/Day per 1000 inhabitants of IPPs in Morocco between 2020 and 2024.*

Consumption of PPIs by DCI in Morocco from 2020 to 2024

Statistical analysis of the evolution of PPI sales in boxes and in DDJ value according to the International Common Denomination (INN) finds an upward trend in consumption of all classes of PPI with an average annual growth rate (AAGR) of 6.6% (boxes) 4.5% (DDJ) for Omeprazole, 16.6% (boxes) 13.8% (DDJ) for Esomeprazole, 6.9% (boxes) 5% (DDJ) for Lansoprazole, 18.6% (boxes) 19.1% (DDJ) for Pantoprazole and 11.5% (boxes) 12.2% (DDJ) for Rabeprazole. It is noted that Pantoprazole is the PPI with the highest average annual growth rate, highlighting the increase in its use/prescription in recent years at the national level.

In 2020 as in 2024, Omeprazole was the most consumed PPI with a volume of 8,340,526 boxes or 272,482,327 DDJ in 2020 and 10,753,599 boxes or 323,904,452 DDJ.

Other PPIs have similarly experienced sustained growth. Figure 4 and 5 show the evolution of IPP sales in boxes and in DDJ value according to the International Common Denomination (INN) in Morocco from 2020 to 2024.

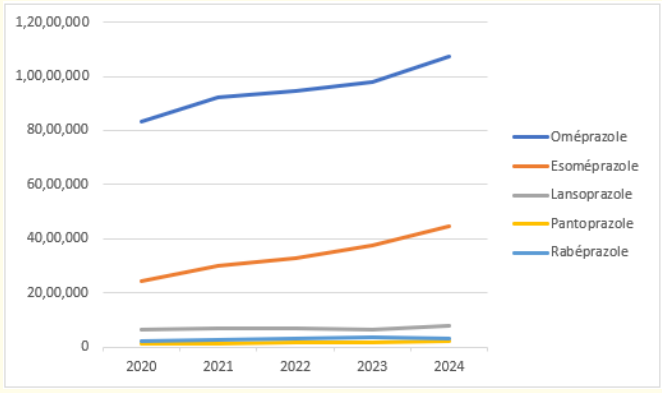

Figure 4: *Annual consumption of IPPs per class in Morocco between 2020 and 2024.*

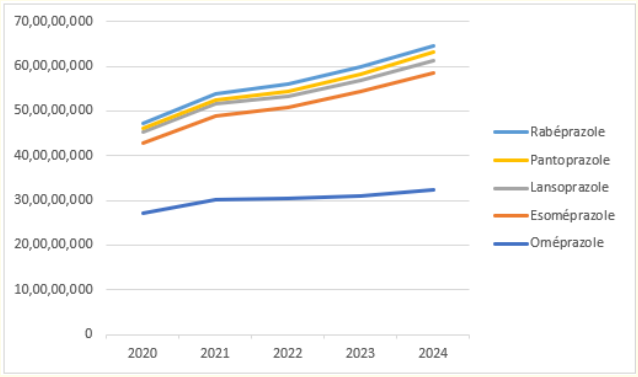

Figure 5: *Annual consumption in volume of DDJ/Year of IPPs by class in Morocco between 2020 and 2024.*

Figure 6 shows the percentage of each PPI by INN of the total volume consumed for each year in DDD volume. Omeprazole is the most consumed PPI in Morocco with 57.9% in 2020 and 50.2% in 2024 followed by Esomeprazole. Rabeprazole (2.1% in 2020 and 2.4% in 2024) and Pantoprazole (1.8% in 2020 and 2.6% in 2024) are the least consumed PPIs.

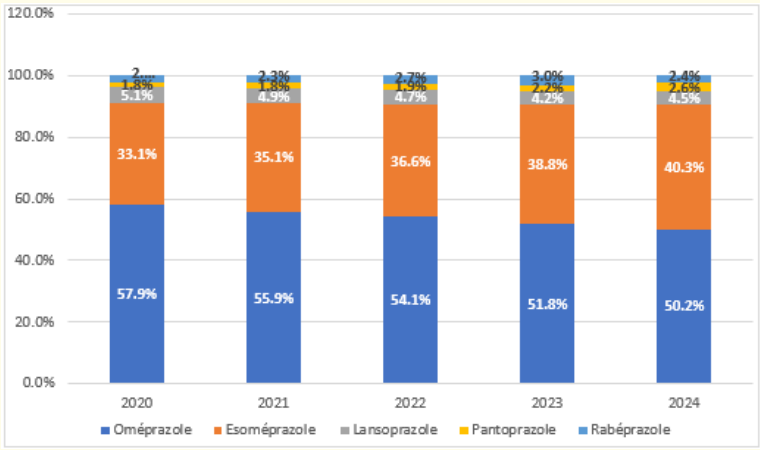

Figure 6: *Annual consumption in volume of DDJ/Year of IPPs by DCI in Morocco between 2020 and 2024.*

However, we note an increasing trend for other PPIs except Lansoprazole, especially Esomeprazole which increased from 33.1% in 2020 to 40.3% in 2024. On the other hand, we note a decrease in the percentage of Lansoprazole which increased from 5.1% in 2020 to 4.5% in 2024.

Evolution of IPP consumption by class in Morocco 2020-2024

There is an overall upward trend in annual canned consumption for all PPIs with an overall compound annual growth rate (CAGR) of 9.1%. Their consumption increases year on year: 13.7% from 2020 to 2021, 4.3% from 2021 to 2022, 6.2% from 2022 to 2023 and 12.3% from 2023 to 2024. Consumption of canned PPIs increased by 41.3% from 2020 to 2024.

Table 1 and 2 summarize the evolution of the consumption of canned and DDJ PPIs in Morocco from 2020 to 2024.

DCI	From 2020 to 2021	From 2021 to 2022	From 2022 to 2023	From 2023 to 2024	From 2020 to 2024	TCAM
Omeprazole	↑ 10.4%	↑ 2.8%	↑ 3.4%	↑ 9.8%	↑ 28.9%	↑ 6.6%
Esomeprazole	↑ 24.6%	↑ 9%	↑ 15%	↑ 18%	↑ 84.4%	↑ 16.6%
Lansoprazole	↑ 10%	↑ 0.7%	↓ 6.3%	↑ 23.3%	↑ 28%	↑ 6.9%
Pantoprazole	↑ 15.1%	↑ 6%	↑ 23.3%	↑ 30.2%	↑ 95.9%	↑ 18.6%
Rabeprazole	↑ 29.8%	↑ 12.6%	↑ 16.5%	↓ 12.7%	↑ 48.6%	↑ 11.5%
In total	↑ 13.7%	↑ 4.3%	↑ 6.2%	↑ 12.3%	↑ 41.3%	↑ 9.1%

Table 1: *Evolution of the consumption of canned PPIs in Morocco from 2020 to 2024.*

DCI	From 2020 to 2021	From 2021 to 2022	From 2022 to 2023	From 2023 to 2024	From 2020 to 2024	TCAM
Omeprazole	↑ 10.3%	↑ 0.8%	↑ 2.6%	↑ 4.2%	↑ 18.9%	↑ 4.5%
Esomeprazole	↑ 21.1%	↑ 8.4%	↑ 13.9%	↑ 11.8%	↑ 67.2%	↑ 13.8%
Lansoprazole	↑ 8.4%	↓ 0.06%	↓ 5.3%	↑ 17%	↑ 20.1%	↑ 5%
Pantoprazole	↑ 17%	↑ 6.6%	↑ 26.9%	↑ 26%	↑ 99.5%	↑ 19.1%
Rabeprazole	↑ 24%	↑ 21.6%	↑ 17.7%	↓ 14.5%	↑ 51.7%	↑ 12.2%
In total	↑ 14.2%	↑ 4%	↑ 7.2%	↑ 7.6%	↑ 37%	↑ 8.25%

Table 2: *Evolution of the consumption of IPPs in DDJ in Morocco from 2020 to 2024.*

Annual expenditure on IPP in Morocco from 2020 to 2024

The evolution of annual expenditure on IPP in Morocco from 2020 to 2024 shows a continuous growth. In 2020, expenditure was estimated at 736,553,543 MAD, and in 2024 it reached 1,063,418,486 MAD, a growth rate of 44.4%. Figure 7 illustrates this.

Annual IPP expenditure by DCI in Morocco from 2020 to 2024

There is a steady increase in spending for each class from year to year except for Lansoprazole whose spending fell from 2022 to 2023 and Rabeprazole from 2023 to 2024.

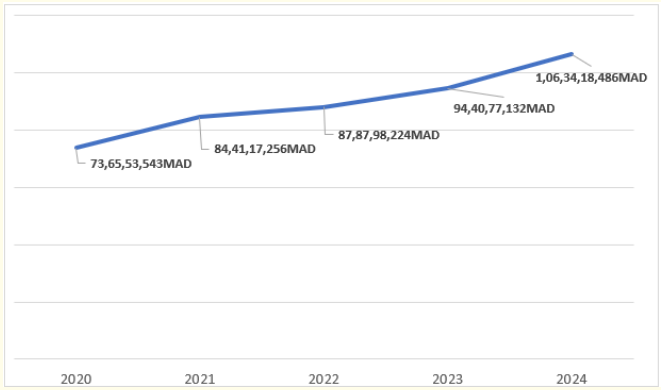

Figure 7: *Annual expenditure in MAD of IPPs in Morocco between 2020 and 2024.*

In 2020, Omeprazole dominated expenditure, with an amount of 428,292,878 MAD, or approximately 58.1% of the total. Expenditure increased steadily to reach 532,673,780 MAD in 2024, or 50.1% of total expenditure, with a growth rate of 24.4%.

Esomeprazole saw a significant increase in expenditure between 2020 and 2024, increasing from 241,089,538 MAD (32.7% of total expenditure) in 2020 to 430,017,017,512 MAD (40.4% of total expenditure) in 2024, a growth rate of 78.4%.

The other PPIs have similarly experienced sustained growth, Lansoprazole increased from 38,013,100 MAD (5.2% of the total) in 2020 to 47,753,840 MAD (4.5%) in 2024, a growth rate of 25.6%, Pantoprazole from 13,260,788 MAD (1.8% of the total) in 2020 to 27,698,606 MAD (2.6%) in 2024, a growth rate of 108.9% and Rabeprazole is from 15,897,237 MAD (2.2% of the total) in 2020 to 25,274,746 MAD (2.4%) in 2024, a growth rate of 59%.

Figure 8 illustrates the evolution of annual expenditure by DCI with amounts expressed in MAD and figure 9 shows the percentage distribution of spending by DCI.

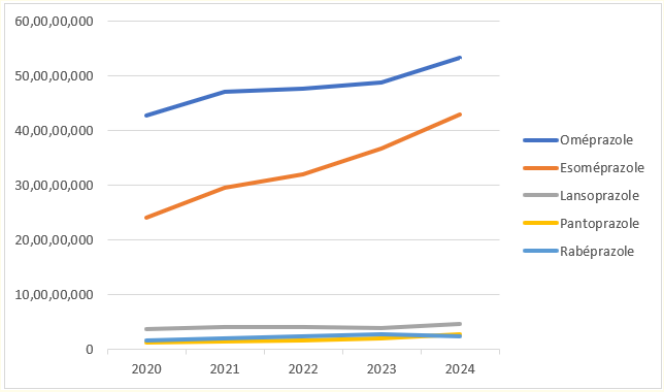

Figure 8: *Annual expenditure in MAD of IPPs by DCI in Morocco between 2020 and 2024.*

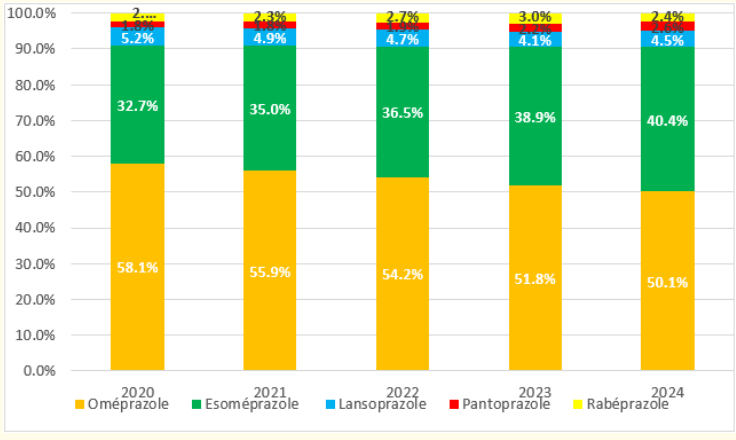

Figure 9: *Percentage distribution of annual IPP expenditure by DCI in Morocco from 2020 to 2024.*

Evolution of annual expenditure on IPP by DCI in Morocco from 2020 to 2024

There is an overall upward trend in annual expenditure for all PPIs with an overall compound annual growth rate (CAGR) of 9.7%. Expenditures have increased steadily year over year: 14.6% from 2020 to 2021, 41% from 2021 to 2022, 7.4% from 2022 to 2023 and 12.6% from 2023 to 2024.

Annual PPI spending increased by 41.3% from 2020 to 2024.

Spending on omeprazole, esomeprazole and pantoprazole has been steadily increasing year on year with an average annual growth rate of 5.7%, 15.7% and 20.6% respectively. From 2020 to 2024, growth rates were found to be 24.4% for omeprazole, 78.4% for esomeprazole and 108.9% for pantoprazole.

Lansoprazole and Rabeprazole experienced an increase in expenditure from 2020 to 2024 with a CAGR of 6.4% and 13.3% respectively. The growth rate from 2020 to 2024 was 25.6% for Lansoprazole and 59% for Rabeprazole. However, there is a decrease in expenditure for Lansoprazole from 2021 to 2022 of -0.06% and from 2022 to 2023 of -5.3% and for Rabeprazole from 2023 to 2024 of -10.4%.

Table 3 illustrates this data.

DCI	From 2020 to 2021	From 2021 to 2022	From 2022 to 2023	From 2023 to 2024	From 2020 to 2024	TCAM
Omeprazole	↑ 10.2%	↑ 0.9%	↑ 2.6%	↑ 9%	↑ 24.4%	↑ 5.7%
Esomeprazole	↑ 22.7%	↑ 8.5%	↑ 14.4%	↑ 17.1%	↑ 78.4%	↑ 15.7%
Lansoprazole	↑ 8.4%	↓ - 0.06%	↓ - 5.3%	↑ 22.4%	↑ 25.6%	↑ 6.4%
Pantoprazole	↑ 17%	↑ 6.6%	↑ 26.9%	↑ 32%	↑ 108.9%	↑ 20.6%
Rabeprazole	↑ 24%	↑ 21.6%	↑ 17.8%	↓ -10.4%	↑ 59%	↑ 13.3%
In total	↑ 14.6%	↑ 4.1%	↑ 7.4%	↑ 12.6%	↑ 44.4%	↑ 9.7%

Table 3: *Evolution of annual expenditure on IPP by DCI in Morocco from 2020 to 2024.*

Share of generics in the PPI market

Trends in boxes and DDJ

The Moroccan PPI market is dominated by generic drugs, it should be noted that only 3 originators were present on the market during the study, represented by Mopral* (Omeprazole), Inexium (Esomeprazole) and Lanzor* (Lansoprazole) marketed until 2021.

There is a decrease in the share of PPI generics consumed from 2020 to 2024, going from 95.2% to 93.8% in boxes and from 92.2% to 90.6% in DDJ.

Figure 10 illustrates the share of generic drugs consumed as a percentage of boxes sold and DDJ between 2020 and 2024 in Morocco.

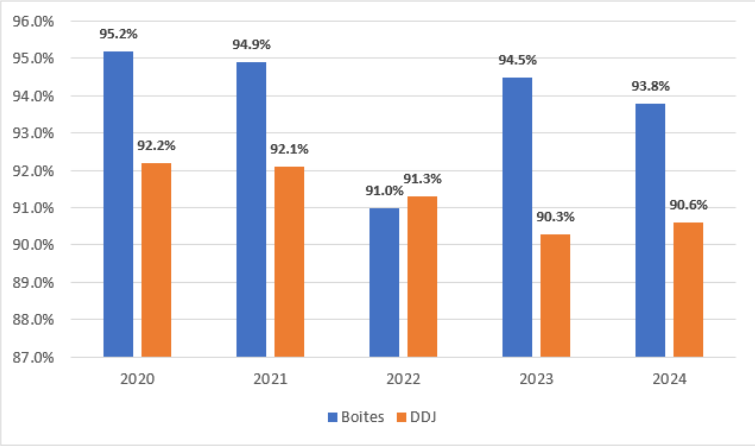

Figure 10: *Share of PPI generics consumed in boxes and in DDJ in Morocco from 2020 to 2024.*

It is noted that generic Esomeprazole are the least consumed compared to other PPIs with a percentage of 77.66% (boxes), 77.53% (DDJ) in 2020 and 77.03% (boxes), 76.95% (DDJ) in 2024.

Figure 11 and 12 show the share of generics consumed for each INN in number of boxes and in DDJ.

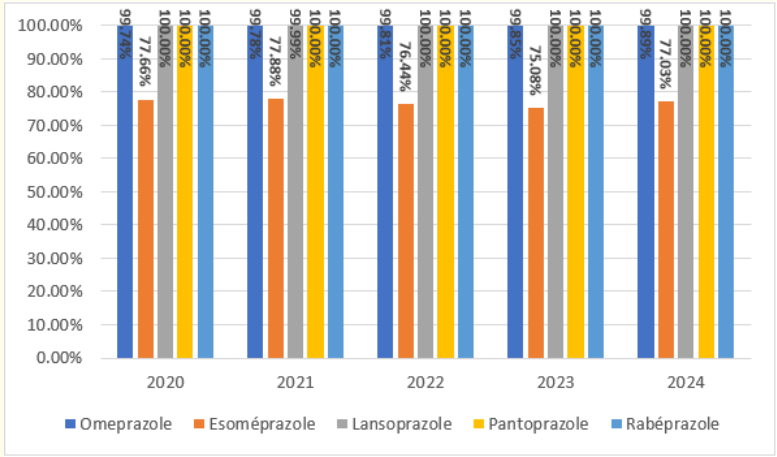

Figure 11: *Share of PPI generics consumed in boxes by INN in Morocco from 2020 to 2024.*

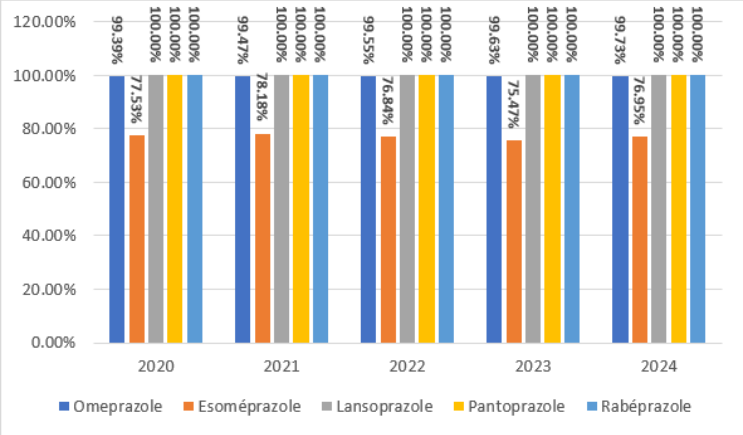

Figure 12: *Share of PPI generics consumed in DDJ by DCI in Morocco from 2020 to 2024.*

Spending trends

Generic drugs account for the majority of spending. However, their percentage decreased slightly from 2020 to 2024, falling from 92.37% to 90.65%.

Generic Esomeprazole represents the lowest expenditure with a percentage of 77.74% in 2020 and 77.20 in 2024. It is deduced that the original Esomeprazole is responsible for the majority of sales of reference PPI specialties on the Moroccan market.

Figure 13 and 14 illustrate the share of generic expenditure as a percentage of total expenditure and expenditure for each INN.

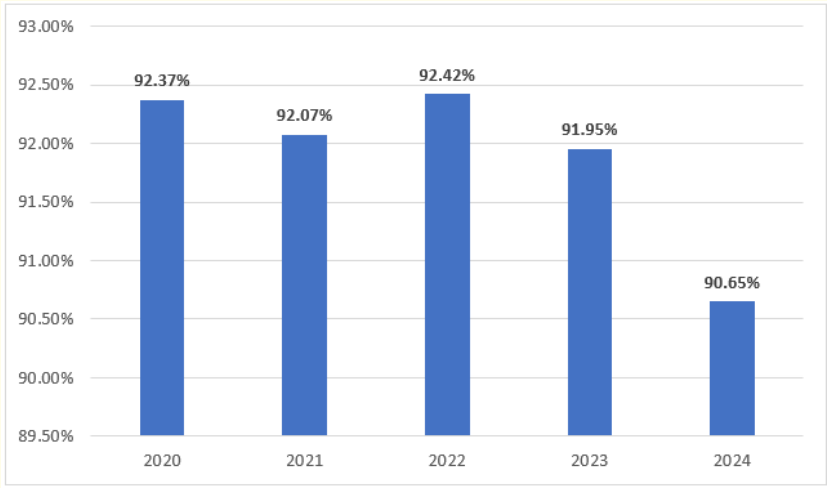

Figure 13: *Percentages of expenditure on generic PPIs in Morocco from 2020 to 2024.*

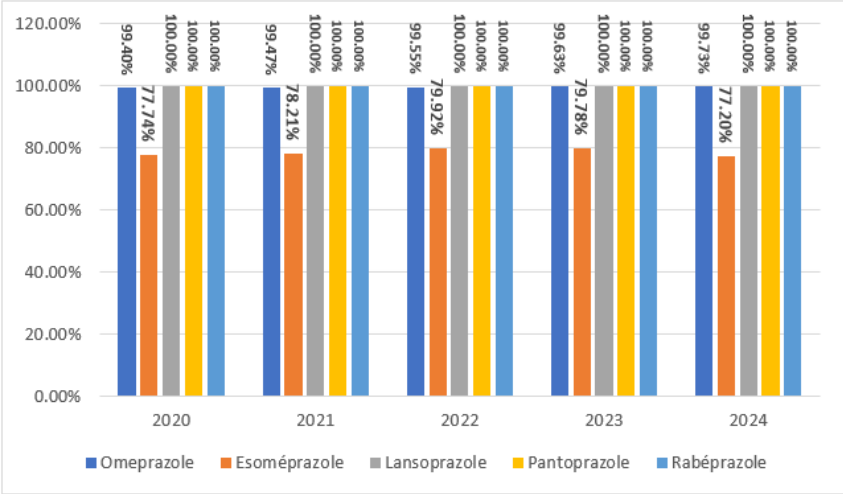

Figure 14: *Percentages of expenditure on generic PPIs by INN in Morocco from 2020 to 2024.*

Discussion

Consumption of PPIs

Comparison of PPI consumption trends

2011 and 2019 in France, PPIs were the second category of drugs most sold by pharmacies after paracetamol [5]. In 2013, Esomeprazole, Omeprazole, and Pantoprazole were ranked among the 30 most sold substances in pharmacies [6]. In five years, sales of PPIs, all markets combined, increased by approximately 27%, from 67 million boxes sold in 2010 to more than 85 million in 2015 [6].

A study conducted by Boucherie., *et al*. [7] from 2006 to 2016, identified 286,878 patients under the general scheme (GS) who had at least one PPI reimbursement. Omeprazole was the most widely used PPI, followed by esomeprazole (41%). PPI consumption was constantly increasing.

In another study conducted by Torres-bondia., *et al.* [8] between 2002 and 2015 in the Lleida health region over a period of 14 years, the use of PPIs increased during this period despite a decrease in 2011, and remained particularly high in the elderly population, which is more sensitive to the side effects of these drugs. While the consumption of Pantoprazole, Lansoprazole and Rabeprazole decreased, the consumption of Omeprazole and, to a lesser extent, Esomeprazole increased significantly during the period studied.

According to another study conducted by Garuolienė., *et al.* [9] in 2016, the total use of PPIs in the IMS (Intercontinental Marketing Services Health) database increased from 4.9 DID (defined daily doses per 1000 inhabitants per day) in 2004 to 21.2 DID in 2012, representing an average increase of 41.5% in annualized percentage. The use of reimbursed PPIs also increased, with a similar average annual percentage change.

A study conducted by Luo., *et al.* [10] between January 2007 and December 2016 at Southwest University Hospital in China shows an increasing trend in PPI consumption. PPI use increased 5.32-fold during the study period from 135,808 DDJ in 2007 to 722,943 DDJ in 2016.

The proportion of generic PPI use has remained stable at around 70% over the past ten years. Use of all forms of lansoprazole increased 6.97-fold during the study, compared to 6.73 for esomeprazole, 5.20 for rabeprazole, 4.38 for pantoprazole, and 3.32 for omeprazole. In addition, Rabeprazole dominated PPI use.

Omeprazole dominated hospital PPI use, with its percentage of all PPIs increasing from 33% in 2007 to 44% in 2010; however, it declined dramatically to 19% in 2012 due to drug interaction considerations. However, this rate increased sharply to 46% in 2015. Fortunately, after the implementation of the pharmaceutical intervention, omeprazole use declined (35%) in 2016.

Similar results are found in the study by Bennie., *et al.* [11] conducted in Scotland between 2001 and 2010 to evaluate the consumption of statins and PPIs in terms of DDD and DDD/1000 inhabitants/day, which found an increasing trend for all PPI subclasses.

Martínez Gorostiaga., *et al*. [12] conducted a descriptive study based on prescriptions billed by pharmacies during the years 2009-2014 in the Araba de Osakidetza region of Spain. They found that the prescription of PPIs increased by 23.75% (from 78.14 DD/1000 inhabitants/day in 2009 to 96.70 DD/1000 inhabitants/day in 2014), its use being much higher than that of other European countries. During the same period, the relative percentage of prescriptions for Omeprazole compared to other PPIs decreased by 4.56%.

In the United States, a study conducted by Mishuk., *et al*. [13] collecting PPI prescription data between 2002 and 2017 found that PPI use in the American population increased from 5.70% in 2002-2003 to 6.73% in 2016-2017, representing an overall increase of 18.07% in PPI use.

In Romania, Farcas., *et al*. [14] conducted a retrospective analysis of PPI pharmacy sales data provided by IQVIA Romania between January 2012 and December 2018. According to this study, the overall use of PPIs increased from 29.53 DD/1000/day in 2012 to 50.20 DDD/1000/day in 2018 (a 70% increase) with a 23% increase in costs. A continuous increase in use over successive years was observed for all PPIs (except Lansoprazole). The largest increase was for Pantoprazole (269%), followed by Esomeprazole (191%), while Lansoprazole consumption decreased by 37%. Overall, PPI consumption increased the most between 2015 and 2016 (13%).

According to data from IMS-Health (Intercontinental Marketing Services Health) and OECD (Organisation for Economic Co-operation and Development), there is a growing trend in the consumption of PPIs in several European countries including Germany, Italy and France between 2011 and 2018, which is consistent with previous results.

Overall, our results are consistent with those in the literature. During the years 2020 to 2024 in Morocco, there was a significant upward trend in IPP sales with a growth rate of 13.7% between 2020 and 2024, i.e. a volume of 471 million DDJ in 2020 compared to 645 million DDJ in 2024, or 35 DDJ per day per 1000 inhabitants in 2020, increasing to 48 DDJ per day per 1000 inhabitants in 2024 (growth rate of 37.1%).

Omeprazole was the most consumed PPI in our study, which is consistent with the literature, except for the study by Luo., *et al*. [10] conducted in China, where Rabeprazole was the most consumed PPI in outpatients.

Pantoprazole was the PPI that experienced the most significant increase in our study, which is consistent with the results of Farcas., *et al*. [14].

Although we find decreases in consumption over a few years in certain studies after the implementation of pharmaceutical reforms or the change of brands available on the market (Princeps vs generic), the overall trend is still upward in all the studies consulted, which underlines the global scale of the problem.

Expenses

In the study by Martínez Gorostiaga., *et al*. [12] the evolution of the expenditure on IPP in the Araba region during the study period (2009-2014) went from 2,972,502 euros in 2009 to 2,449,283 euros in 2014, a reduction of 17.60%.

Similarly, a decrease in expenditure corresponding to Omeprazole was observed, going from 804,405 euros in 2009 to 563,559 euros in 2014 (reduction of 36.20%) and an increase in Pantoprazole which went from 1,095,356 euros in 2009 to 1,189,860 in 2014.

In the United States, in the study by Mishuk., *et al*. [13] collecting PPI prescription data between 2002 and 2017, total expenditures for PPIs were $28.43 billion in 2002-2003 and peaked at $36.71 billion in 2008-2009.

PPI expenditures declined gradually after 2008-09 and were reduced to $19.99 billion in 2016-17. Although total PPI expenditures declined by 45.56% between 2002-03 and 2016-17, the trend was not statistically significant.

However, average PPI expenditure per patient decreased by 39.01% ($174.69 in 2002-2003 to $106.54 in 2016-2017), and the downward trend in average PPI expenditure was statistically significant.

We find this same downward trend in France between 2010 and 2023 according to health insurance reimbursement data, going from approximately 1.13 billion euros in 2010 to approximately 300 million euros in 2023 [6].

In the study by Bennie., *et al*. [11], expenditure per DDJ for generic omeprazole in 2010 was 91% lower than the price of the originator in 2001, meaning that expenditure per 1000 inhabitants for PPIs in 2010 was 56% lower than in 2001, despite use being three times higher.

In our study, there was a 44.4% increase in expenditure between 2020 and 2024 (736,553,543 MAD in 2020, and 1,063,418,486 MAD in 2024). This result diverges from those found in the literature where the trend in expenditure is decreasing, although it has previously increased, and this can be explained by the different strategies implemented in these countries to limit the overprescription and misuse of PPIs.

Misuse of PPIs

In most countries, the PPI market continues to grow. Excessive and incorrect use of PPIs is considerable in both hospital and outpatient settings. The main impacts of this include increased medical costs and the danger of long-term adverse effects. Continuing education and specialized expertise are therefore essential to guide physicians, the healthcare team, and patients towards the implementation of recognized principles regarding balanced use of PPIs [15].

Savarino., *et al*. [16] estimated in a 2020 assessment that inappropriate use accounted for 50% of PPI prescriptions in urban areas of advanced economies.

According to current knowledge, the use of PPIs in France is considered inappropriate in the following cases [1]:

- Prevention of gastroduodenal lesions during treatment with NSAIDs, prevention in conjunction with treatments of unverified gastrotoxicity: antiplatelets, anticoagulants or corticosteroids; prevention of mucositis or gastroduodenal lesions in cancer patients receiving chemotherapy or radiotherapy; functional dyspepsia not accompanied by GERD or ulceration; isolated extra-digestive signs without diagnosis of GERD.
- The absence of documented evidence or the unjustified continuation of prolonged treatment are considered abusive [16,17].

Causes

- Poor knowledge of risks: A study conducted in Jordan by Alameri., *et al*. [18] demonstrated that the population is not informed about the dangers associated with misuse of PPIs and the adverse effects. 43.1% of participants who used PPIs identified vitamin B12 deficiency as the most common adverse effect. The knowledge assessment conducted for the participants gave an overall knowledge score that was low.
- Inappropriate use: A study conducted by Chau., *et al*. [19] in the Netherlands to assess the extent of inappropriate use of PPIs: as protective co-medication with continued use after stopping NSAID or Aspirin treatment. It sought to estimate the potential cost savings and effect gains from stopping inappropriate use of PPIs and reducing adverse effects and their harmful consequences.

After one year, the total cost of banning the incorrect use of PPIs in NSAID/aspirin therapy in the Netherlands could reach approximately €1,050,000. Therefore, effective actions to stop a patient's inappropriate use would cost up to €29 and would likely pay off over several years.

Solutions

Periodic re-evaluation of prescriptions

According to the literature review conducted by Shanika., *et al.* [20], collecting data from 23 countries from 65 articles, essential clinical measures were recommended to healthcare professionals to limit the overuse of PPIs. Thus, these prescriptions should be periodically re-evaluated and the reasons for their continued use recorded [20].

The National Institute for Health and Care Excellence (NICE) also recommends annual reassessment of PPI prescriptions to discontinue or reduce any unjustified treatment [21]. This helps to minimize treatment costs and avoid significant drug interactions, including cases where co-administration of Omeprazole intensifies the effect (as with Mavacamten) or reduces the impact (as with Clopidogrel) of certain drugs.

Deprescribing: The cessation, reduction, or tapering of intermittent PPI use is recommended when no appropriate ongoing indication or evidence of benefit is present [21,22].

Patient awareness: The risk of rebound acid hypersecretion after sudden discontinuation of long-term treatment discourages patients from discontinuing their treatment [23]. Dills., *et al*. [24] identified in their comprehensive review that PPIs are among the drugs most resistant to discontinuation. It is therefore essential to inform and educate patients.

Conclusion

Since their introduction to the market in the late 1980s, PPIs have transformed the treatment of conditions related to gastric acidity thanks to their effectiveness and good tolerance.

However, they do have side effects, and research shows they can be very serious, especially in older people. Moreover, the financial impact associated with this misuse is not insignificant.

Our research revealed that the use of PPIs is continuously increasing nationally and also globally.

Thus, strategies such as the introduction of prescription scores, reimbursement reforms or even awareness raising on the importance of regular reassessment of patients on long-term treatment and deprescribing in the absence of proven benefit, have already been implemented in certain countries, giving positive results, particularly in France, Lithuania and the United States where PPI expenditure is decreasing.

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