

Can savings induced by off-patent drugs balance the increase of pharmaceutical expense associated with the high ageing rate of the Italian population?

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Abstract

Background: The predicted ageing rate of the Italian population is one of the highest worldwide and this condition is expected to produce a growing increase in pharmaceutical expenditure. The objective of this study was to assess whether or not off-patent drugs could counterbalance the economic effects generated by the aging of the Italian population in the next ten years.

Methods: On the basis of the predicted ageing rate of the Italian population for the period 2008-2018, the average annual cumulative increase of pharmaceutical expenditure and potential savings generated by the future loss of patent coverage have been considered in order to identify the year of the *Break-even Point*.

Results: The economic effect induced by the progressive ageing of population produces an average of 0.94% cumulative increase in local pharmaceutical expenditure per year, corresponding to an incremental pharmaceutical expenditure of about € 116 millions per year.

A number of 509 brands (103 active substances) will lose their patent coverage in the next 10 years. Considering both the present legislation and a level of price reduction, after patent expiration, corresponding to 40%, it is predicted that the *Break-even Point* will be achieved at the end of 2011.

Conclusions: In this study, a long term balance between the predictable increase of pharmaceutical expenditure induced by the ageing of Italian population and savings produced by future off-patent drugs was not established. In order to assure the future sustainability of pharmaceutical expenditure, this study supports the need for the development of new health policy strategies.

Key words: *off-patent drugs, population ageing, pharmaceutical expenditure*

Introduction

The pharmaceutical spending primarily depends on therapeutic demand, which relies on the following factors: drug consuming, new drugs offering, healthcare organisation, and pharmaceutical policy decisions [1]. The dynamics of the ageing of population is one of the main drivers influencing drug consuming in a medium-long time horizon. A recent Italian study showed that per capita pharmaceutical expenditure for people over 65 year old are two to three-fold higher than the average amount calculated for the entire population, and even five to eight times higher compared to that of people under 45 years old [2].

The ageing rate of Italian population is at the highest rates worldwide [3]. As a consequence, the pharmaceutical expenditure born by the

Italian National Health Service (NHS) for the elderly population has increased, and according to the Italian law regulating the financing of pharmaceutical expenditure [4], the savings from the loss of patent coverage is the only compensation measure.

In Italy, a specific regulation concerning off-patent drugs has been introduced since 2001, when a reference price among products containing the same active substances was settled at the lowest value [5]. The reference price is suitable within the product category containing the same active substance, with the same number of posological units and the same unit dose. Hence, just after the patent's expiration, the Italian NHS reimburses the product at the reference price, whereas for any product above the reference price, the difference is paid by the

patient. The introduction of every off-patent product after its patent expiration date can further contribute in reducing the reference price, producing additional savings for the Italian NHS.

As soon as this regulation mechanism was implemented, the off-patent drug market rapidly raised to around 20.3% of total expenditure and 30.7% of the overall number of doses consumed in 2007 [6]. As previously mentioned, the recent regulation states that potential savings generated by new off-patent drugs must be considered in the calculation of incremental resources available for the next year [4]. In detail, the forecast of incremental resources depends on the price difference between the branded and the equivalent *unbranded* product at the lowest price. The current price reduction is regulated by law at a minimum difference of 20% [7]; however, after negotiation procedures with the Italian Medicines Agency (AIFA), this difference usually reaches a value of 40% or greater [8].

It is worth noting that the number of new drugs authorized by the European Medicine Agency (EMEA) is substantially flat over time (approximately 50 every year) [9], and the offer of new drugs continue to have a limited economic impact on local pharmaceutical expenditure. The objective of this study was to identify the time required to achieve a balance between the economic consequences originating from the ageing of the Italian population and savings generated by products losing their patent coverage in the next ten years. The current

analysis was specifically focused on reimbursed drugs (A class) dispensed by retail pharmacies.

Methods

The indicator developed in this analysis depends on two elements:

1. Potential increase in pharmaceutical expenditure per year (ΔE_t) produced by the expected Italian population ageing in the next 10 years (until 2018);
2. Potential savings per year associated with drugs that will lose their patent coverage in the next 10 years (S_t).

These two elements have been combined in order to identify the time (in year) when the Breakeven Point (BEP) between increased expenses and savings is achieved:

$$BEP_t = \Delta E_t - S_t \approx 0 \quad (1)$$

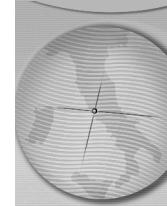
The equation (1) is applicable for $t \in N$ and $t \in [2008, 2018]$, where t is the year of the BEP, while N is a natural number. Parameters of the equation have been calculated using discrete data sources; therefore, they will be described individually.

Impact of population ageing on pharmaceutical expenditure

The effect of the ageing of the population on the pharmaceutical expenditure was calculated on the basis of the mean value of pharmaceutical spending and dynamic changes of Italian population as predicted for the next 10 years by the Italian Institute of Statistics (ISTAT) [3]. The

Table 1. Local pharmaceutical expenditure by age and sex. Data drawn from the ASSET study [2].

Age groups	Women		Men	
	Source	Adjusted	Source	Adjusted
<4 yrs	31.59	36.36	36.11	41.56
5-14 yrs	37.53	43.19	43.66	50.25
15-24 yrs	40.94	47.12	44.93	51.71
25-34 yrs	62.75	72.22	52.75	60.71
35-44 yrs	90.52	104.18	80.89	93.10
45-54 yrs	149.62	172.20	146.20	168.26
55-64 yrs	277.40	319.26	300.88	346.29
65-74 yrs	431.13	496.19	505.77	582.10
≥75	481.20	553.82	652.75	751.26



following equation was used:

$$E_t = \sum_{Sex=M}^F \sum_{Age=0-4yrs}^{\geq 75yrs} \bar{E}_{Sex,Age} \times {}^tP_{Sex,Age} \quad (2)$$

where ${}^tP_{Sex,Age}$ indicates the population projection by sex and age estimated by ISTAT from the year $t=2008$ to the year $t=2018$ [3], whereas $\bar{E}_{Sex,Age}$ is the average pharmaceutical expense by sex and age group as reported in the ASSET study [2]. The value of ΔE_t is given by the difference $E_t - E_{t-1}$.

The average pharmaceutical spending calculated by the ASSET study (table 1) was related to the sum of costs per person born by the Italian NHS (class A) for drugs distributed through retail pharmacies during the 12 months between October 2004 and September 2005 [2]. The value of expenditure charged to the Italian NHS was given by the prices of drug actually distributed to patients, including any co-payment. The population analysed in the ASSET study included citizens registered in the Local Health Unit of Monza, Regional Health Units of Marche and Basilicata, totally 3.2 million inhabitants (5.4% of the whole Italian population). Since the expenditure per capita in these regions was lower compared with the national mean value (Euro 213.4 [6]), the average expenditure by age-sex group found in the ASSET study was proportionally increased by 15% in order to make the whole calculated expenditure corresponding to the real pharmaceutical spending recorded in 2008 which amounted to 12.724 million Euro [6]. The adjustment procedure did not minimally affect the variability existing between age-sex groups, since it was dependent on the prevalence of drug utilization by groups for the treatment of chronic pathologies.

To assess the reliability in the identification of the BEP, a sensitivity analysis with a $\pm 10\%$ variation of the mean expenditure by age-sex group observed in the base case was carried out.

Impact on pharmaceutical expenditure of off-patent drugs

The potential savings generated during the next ten years from off-patent drugs were estimated on the basis of pharmaceutical expense recorded in 2008. The whole range of products included in the analysis meet the criteria of being in-patent on December 31, 2007 and becoming off-patent in the period between January 1, 2008 and December 31,

2018. Among all of the available drugs (pharmacological active substances), we considered exclusively all those refunded by the Italian NHS (drugs belonging to A class). The costs for drugs distributed through hospital pharmacies (and/or indirect distribution) and out-of-pocket expenses for drugs not refunded by the Italian NHS (C class) were not included. Moreover, all products associated with a patent protecting a process (i.e. salts, complexes, and so on) were also excluded.

The time limit of patent expirations refers to the so-called Complementary Protection Certificates (CCP - Law No. 349/1991) and Supplementary Protection Certificate (SPC - Regulation No. 1768/92/EEC) for drugs covered by patents and deposited within February 7, 2003. For CCPs granted on the basis of the Law No. 349/91, the expiration date of the complementary coverage was recalculated by the Italian Patent and Trademark Office (Ministry of Economic Development), in accordance with the Law No. 112/2002.

Each active substance was associated with all of the brand originator products included in the national pharmaceutical formulary and currently commercialised in Italy (including any co-marketing products containing the same active substance). Subsequently, each product identified through this procedure was linked to their national pharmaceutical expenditure in 2008.

The potential savings S_t induced by off-patent drugs in the t -th year were calculated through the following equation:

$$S_t = \sum_{t=2008}^{2018} \sum_{j=1}^n \frac{{}^tE_{j,2008}}{12} \times K \times (13 - {}^tM_j) \quad (3)$$

with ${}^tE_{j,2008}$ is the pharmaceutical expenditure in 2008 of the j -th product losing its patent coverage during the year t ; tM_j is the number of the month in the year t , starting from which the j -th product is no longer covered by a patent. Finally, K is the price reduction rate of the active substance after it lost its patent coverage and succeeding inclusion in the AIFA transparency lists [5]. The K value of the base case was set at 40%, as it matches the average discount rate on *unbranded* product prices - as compared with *brand originator* - negotiated by the AIFA during the last years [8]. To assess the reliability in the identification of the BEP, a sensitivity analysis on a range of K values between 20%

and 80% was performed. The highest and lowest values in this range was set up on the basis of the minimum discount level provided for by the Law [7] and the maximum hypothetic value.

This calculation model includes four assumptions:

- (i) For each active substance losing its patent coverage during the years after 2008, it is assumed that at least one *unbranded* product is authorised by the AIFA. The overall expenditure for all products containing the same active substance (i.e. brands already commercialised and *new unbranded* products) was bound to the reference price indicated in transparency lists [3];
- (ii) The price reduction rate K was indistinctly applied to all products with an expired patent;
- (iii) The expected savings during the year t was calculated in a conservative way: the calculation model just considered the months of the year t in which there was no more patent coverage. Therefore, the potential dragging effect of savings - on the next year - derived from products that have lost their patent coverage in the previous year (t-1) was not taken into account. This approach is totally consistent with the procedure reported under the Law 222/2007 [4];
- (iv) Savings originating from off-patent drugs was calculated assuming a market share value corresponding to that recorded in 2008.

Each assumption can influence the estimation of potential savings in both directions: either overestimating or underestimating them. Assumptions (ii) and (iii) tend to produce an underestimation, while assumptions (i) and (iv) produce an opposite effect. In particular, the (iv) - concerning the stability of market shares - is an optimistic assumption considering the frequent reduction of drugs utilization after their patent expiration [8]. The stability of market shares is also a realistic assumption, especially taking into account that off-patent drugs represent a growing market in Italy, with non-negligible differences as compared with other countries [6, 10]. Therefore, a sensitivity analysis was also designed to assess the reliability in identifying the year of BEP by $\pm 10\%$ variation of market shares of off-patent

drugs in the next years, in comparison with those recorded in 2008. This simulation was carried out by keeping fixed both the expenditure per capita, and the price reduction rate at the base case, corresponding to Euro 213.4 and K=40%, respectively.

Statistical analysis

The correlation of the annual series of potential savings with both the number of active substances losing their patent coverage per year, and the total number of products containing active substances with expired patent have been performed by Spearman's rank test.

In the sensitivity analysis, in order to fit the net differences of pharmaceutical expenditure per year obtained after every variation of price reduction rate (i.e. the K value in equation 3) a polynomial fitting was used.

Results

The ISTAT projections show a 0.31% decrease in the Italian population in 2018 (baseline 2008). On the contrary, the growth rate of the population aged ≥ 65 years is almost 14% and it is expected to be composed by over 13 million people [3]. With regard to the estimation of savings after patent expirations, 509 *brand originators* (including *co-marketing* products) refunded by the Italian NHS were analysed. These products contain 103 active substances, which lose their patent coverage in the period between 2008 and 2018.

Figure 1 shows the economic effects on pharmaceutical expenditure as a result of the progressive ageing of Italian population. In the overall population, the pharmaceutical spending achieves a mean cumulative increase of 0.94% per year, while in people aged over 65 year this increase corresponds to 1.5%. Therefore, the average incremental variation of pharmaceutical expenditure is almost Euro 116 million per year (interval 2008-2018), and this is largely (84%) due to ageing rate of Italian population.

Figure 2 shows the potential savings induced by off-patent drugs after 2008. Worthy of note is the progressive decrease in savings, which tends to increase with price discount rates. Also, potential savings for the Italian NHS are higher when off-patent drugs have the highest proportion of the pharmaceutical expenditure. Indeed, there is a strong correlation between

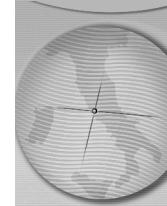


Figure 1. Cumulative increase of pharmaceutical expenditure (%) in the period 2008-2018 compared with the baseline value recorded in 2008. Projections of population data are provided by ISTAT.

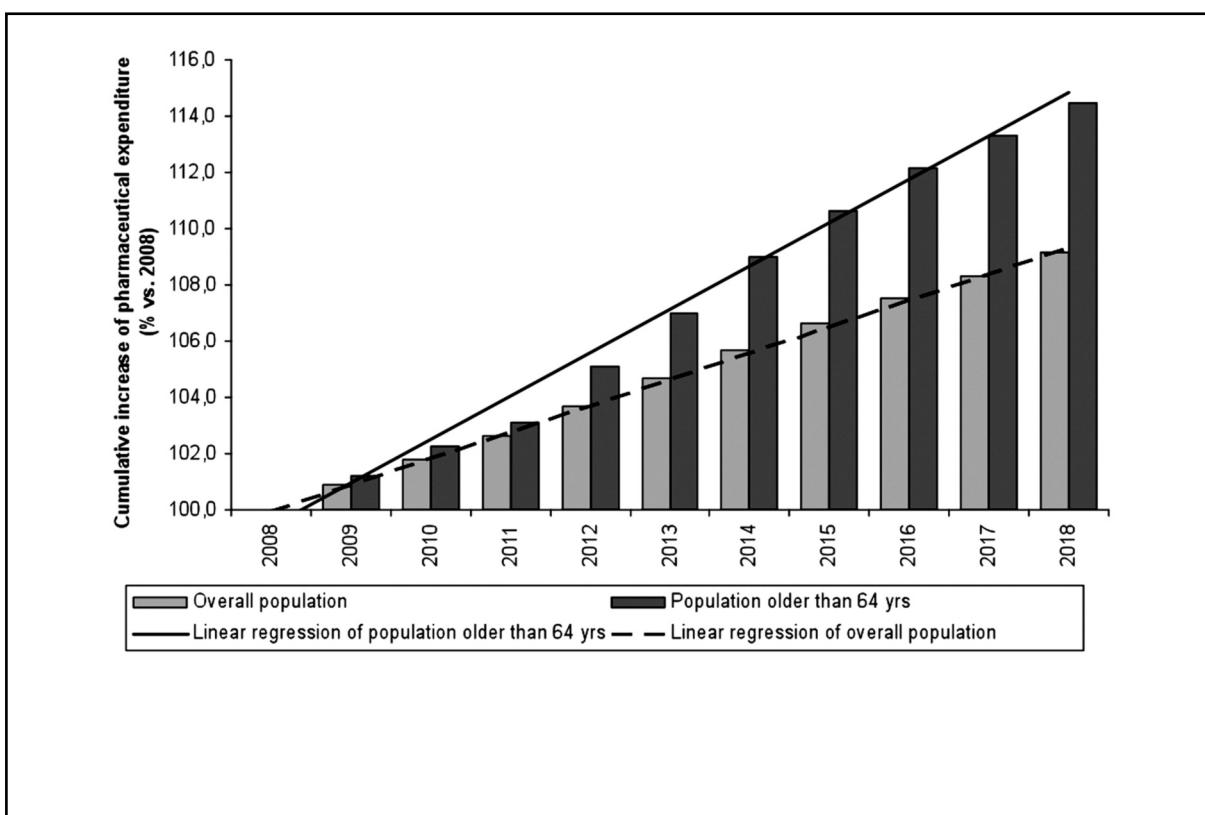
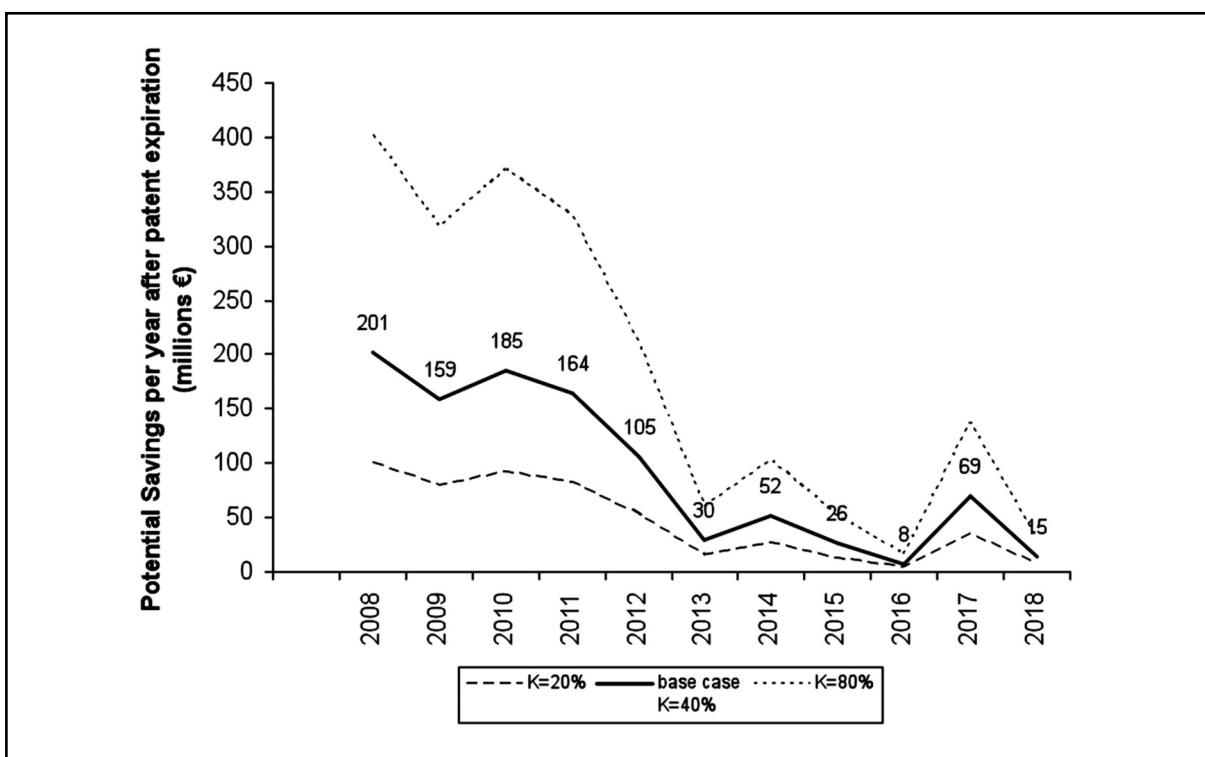


Figure 2. Potential savings associates with the price reduction of drugs with patent expired in the period 2008-2018.



the annual series of savings and the number of active substances losing their patent coverage per year (Spearman's $R = 0.86$; $p < 0.001$), and the total number of products containing active substances with expired patent (Spearman's $R = 0.91$; $p < 0.001$).

The trend in the difference between potential increase in pharmaceutical expenditure per year (due to population ageing) and potential savings induced by off-patent drugs during the next 10 years is reported in figure 3. Based on present regulation and considering a 40% price reduction after patent expiration, it is predictable that the BEP is reached at the end of 2011. In fact, after this period, the combined effect of population ageing and lower counterbalancing expense reduction generated by off-patent drug will produce net incremental effects on pharmaceutical expenditure, in a range between 26 and 108 million Euro.

The sensitivity analysis concerning the variation of expenditure per citizen showed that the BEP is quite insensitive to this parameter. In other words, considering $\pm 10\%$ variation of mean expenditure by age-sex group based on ASSET study, the BEP is always achieved at the end of 2011.

As far as the price reduction rate variation is concerned, the sensitivity analysis demonstrated how the BEP is strongly influenced by this parameter. In the base case ($K = 40\%$), the BEP is reached at the end of 2011; on the contrary, when price reduction rates get over 40% the BEP moved forward to 2015 (i.e. the upper limit of 95% confidence interval of polynomial fitting) (figure 4).

Finally, compared with the base case, a potential change in market share did not determine a shift in the time required to achieve the BEP. As it was expected, a 10% increase of market share of off-patent drugs enhanced savings between 2008 and 2011, and constrained the incremental spending associated with the ageing of population in the period between 2012 and 2018. However, the time to get the BEP was not affected.

Discussion

Healthcare planning often needs reliable indicators and information to efficiently direct the use of resources and health governance strategies. In this analysis, discrete variables are combined for the first time with the specific purpose of identifying useful time references

for healthcare planning in general and pharmaceutical planning in particular. In this respect, Italy can be considered a particularly interesting reference case, due to the presence of a universalistic NHS and population dynamics characterised by one of the highest ageing rates worldwide [11].

In the current situation, this study showed that the Italian NHS could counterbalance the incremental effects on expenditure due to population ageing with savings induced by off-patent drugs up to the end of 2011. Beyond this time limit, maintaining the present conditions, it will not be possible to contrast the growth of pharmaceutical spending.

A possible solution that may move the BEP forward is given by the reduction in the percentage of public coverage of pharmaceutical expenditure; however, this proposal appears not really feasible in the short term in the Italian context, which is characterised by a strong universalistic approach. With an increased price discount rate above 40%, the BEP would be moved forward up to 2015.

The breakeven point is one of feasible indicators supporting health governance, in addition to those that may appear from the accurate description of expenditure dynamics. It is qualitatively intuitive that population ageing produces incremental effects on pharmaceutical expenditure, and off-patent drugs may generate savings; however, the quantitative mode adopted in this study is a useful benchmark also for other healthcare systems.

There are several reasons why there is a specific need for identifying useful benchmarks in health governance in the Italian context. The first reason is the relevant ageing of our population. Eurostat population statistics of the European Commission show that Italy will be the European nation with the highest elderly population rate in 2020 [11]. This forecast will have important consequences on the *welfare state*. A second reason is the presence in Italy of a pharmaceutical expenditure ceiling [4]. Thus the current limited resources context requires careful planning, in order to ensure the compatibility between the offer extent (i.e., new innovative treatments, emerging treatment, health prevention, and so on) and the increasing demand generated by the ageing of population.

Last but not least, one of the reasons is

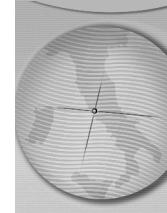


Figure 3. Annual differences between the increase of pharmaceutical expenditure due to population ageing and potential savings induced by off-patent drugs.

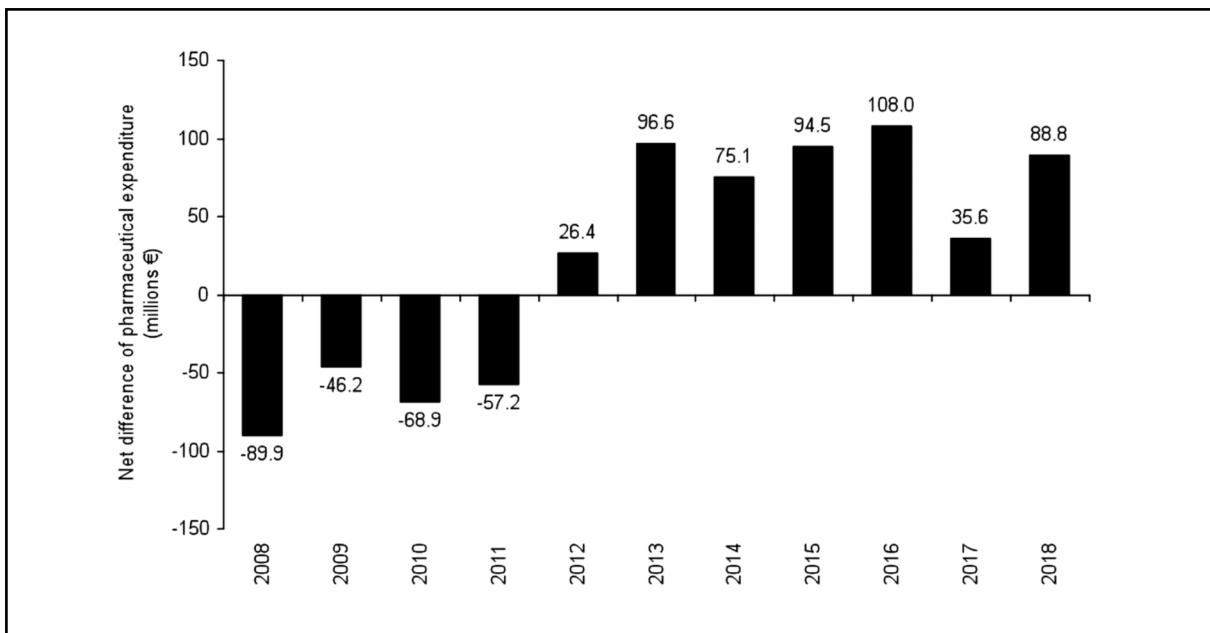
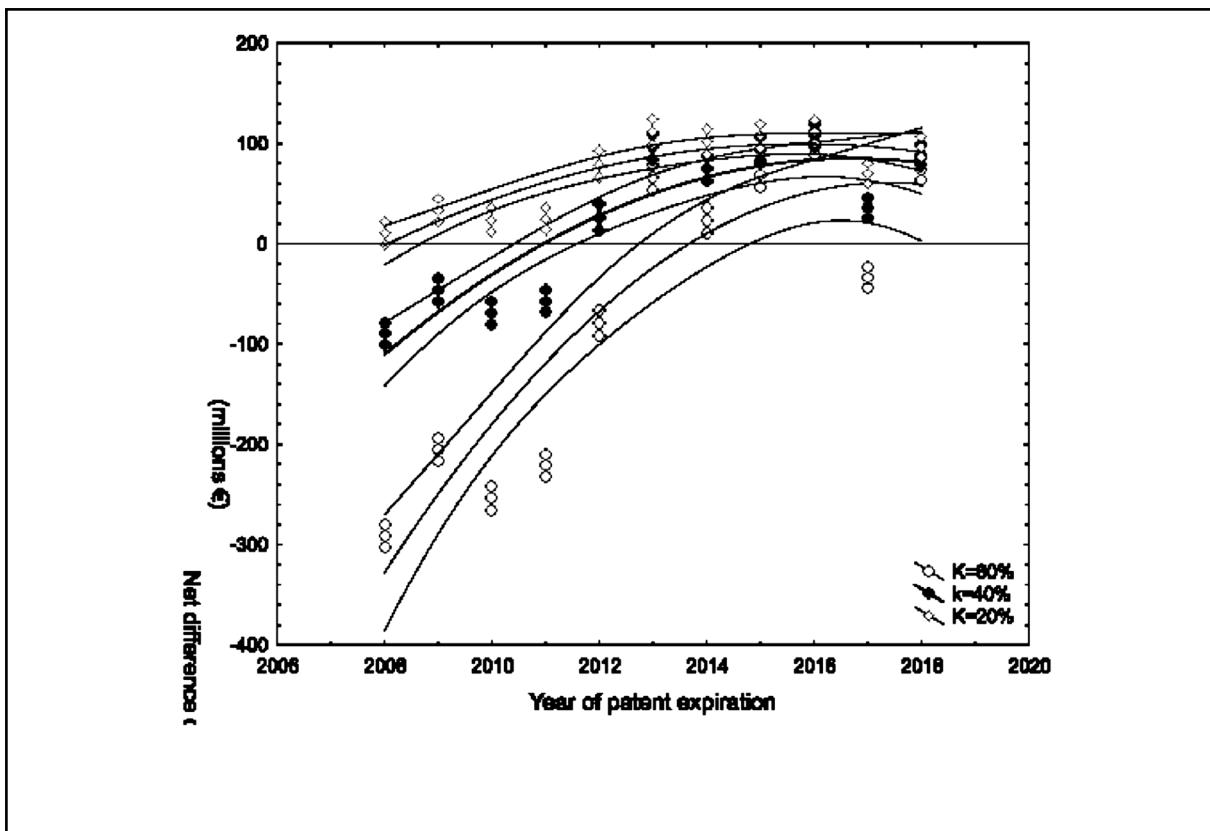
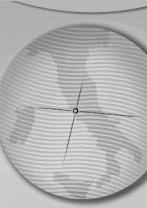


Figure 4. Sensitivity analysis of the price reduction rate between off-patent drugs and the brand *originator* on the pharmaceutical expenditure.





related to the federal organization of the Italian NHS, which came into force in 2001 [12]. This new system required regional benchmarks to be developed in order to monitor the efficiency of the local allocation of healthcare resources. In this respect, our study provides a useful methodological framework which could be implemented also at the Regional level, in full accordance with existing pharmaceutical rules [4]. For example, since the price reduction rate has been shown to influence the shift of the BEP, the same procedure applied at the regional level could help in verifying if the BEP is higher or lower than the national value estimated in the present study.

Furthermore, the optimal use of every indicator for Regional benchmark (such as the BEP) should be deployed in a context which is rapidly evolving for the following reasons: regional funding of healthcare system, monitoring of pharmaceutical expenditure, incentives to the distribution chain for *off-patent* drugs, overcoming the fragmentation of the national formulary in its transfer to regional level, and finally the introduction of *health technology assessment* procedures for health decision-making process.

Although most of the assumptions reported in the method have been evaluated by sensitivity analyses, some study limitations must be examined. First, this analysis did not consider the ageing effect on hospital expenditure. This limit - although it is economically significant - could produce a variation on a spending which currently

represents 17.7% of the total pharmaceutical expenditure [4]. Since these drugs are purchased by hospitals through tenders, the price for a given drug would not be the same. Hence, savings for the Italian NHS originating from patent expirations can not be calculated accurately.

Another potential limit may be associated with any possible modification of drug reimbursability or co-payment levels which could determine a change in the mean pharmaceutical expenditure by sex and age group. Whether or not the mean expenditure increased, the net effect would be neutral since it affects both the economic impact due to population ageing and the magnitude of savings originating from the loss of patent coverage.

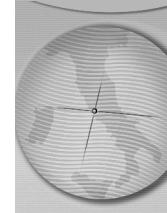
In this study, a long term balance between the predictable increase of pharmaceutical expenditure induced by the ageing of Italian population and savings produced by future off-patent drugs has not been proven. In order to assure the future sustainability of pharmaceutical expenditure, this study supports the need for the development of new health policy strategies.

Acknowledgments

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