

A budget impact analysis of Spiromax[®] compared with Turbuhaler[®] for the treatment of moderate to severe asthma: a potential improvement in the inhalation technique to strengthen medication adherence could represent savings for the Spanish Healthcare System and five Spanish regions

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Objective: To assess the economic impact of the introduction of DuoResp[®] Spiromax[®] by focusing on a potential improvement in the inhalation technique to strengthen medication adherence for the treatment of moderate to severe asthmatics in Spain and five Spanish regions including Andalusia, Catalonia, Galicia, Madrid, and Valencia.

Methods: A 4-year budget impact model was developed for the period 2015–2018 from the Spanish Healthcare System perspective. Budesonide–formoterol fixed-dose combination delivered by Turbuhaler[®] was considered to be the most appropriate comparator for assessing the budget impact with the introduction of DuoResp[®] Spiromax[®]. National and regional data on asthma prevalence were obtained from the literature. Input parameters on health care resources were obtained by consulting experts from different Spanish hospitals. Resources used included medical visits, emergency room visits, and hospitalizations. The average numbers of primary care and specialist visits per year were also gathered. Based on health care resource use per patient, the total treatment cost per patient was estimated.

Results: The population with moderate to severe asthma treated with budesonide–formoterol fixed-dose combinations delivered by Turbuhaler[®] in 2015 was estimated to be 166,985 in Spain. Region-specific prevalence data resulted in 25,081, 12,392, 16,097, 17,829, and 15,148 patients in Andalusia, Catalonia, Galicia, Madrid, and Valencia, respectively. Based on the forecast uptake of DuoResp[®] Spiromax[®], the total budget savings in Spain were expected to be €1.509 million over the next 4 years. Region-specific rates imply that the total savings were expected to be €229,706 in Andalusia, €90,145 in Catalonia, €188,327 in Galicia, €122,669 in Madrid, and €165,796 in Valencia over 2015–2018.

Conclusion: The introduction of DuoResp[®] Spiromax[®], which represents a potential improvement in the inhalation technique to strengthen medication adherence for the treatment of moderate to severe asthma, could represent savings for the Spanish National Health Society and five Spanish regions.

Keywords: dry powder inhaler, economic evaluation, region-specific estimates, payers perspective

Introduction

Asthma is a leading cause of morbidity, mortality, and economic burden and a significant public health problem worldwide.^{1,2} This chronic condition is characterized by inflammation of respiratory airways, hypersensitivity of airway path, and variable airflow limitation for short periods of time.

Daily medication is used to prevent or improve asthma symptoms. Inhaler therapy for asthma delivers therapeutic drug doses into the airways, leading to local efficacy within the lungs.³ Effective use of inhaler requires proper inhalation technique, which implies a good medication adherence, because it is a critical factor of self-management of the disease. Dry powder inhalers (DPIs) overcome the difficulties between inhaler actuation and inspiration, one of the most common errors with pressurized metered dry powder; however, recent reviews have shown that misuse of DPIs is also common in real life.^{4,5}

There are factors such as low inhaler complexity and patient preferences that can help to optimize the inhaler device by improving adherence to medication.⁶ Strengthening these factors would contribute to good disease management and better use of health care resources, given the excessive costs required to treat chronic obstructive lung diseases.

Asthma is a significant public health problem among inner city populations. In Spain, asthma prevalence varies widely, and studies have shown that divergence is explained by genetic factors, proportion of immigrants, and environmental, organizational, and health care factors of regional health care services.⁷ It has been reported that half of the treated patients do not comply correctly with their treatment.⁸ Medication adherence is a key factor for controlling progression of chronic disease.

The lack of adherence is associated with increased health care costs due to emergency room visits and hospitalizations as well as additional diagnostic tests and stepping up therapy compared to the original less costly therapy, which also indicates higher consumption of primary care (PC) and specialist consultations.^{5,9} Given the developments in inhalation devices such as pressurized metered dry powder and DPI, one would expect that these imply better clinical outcomes; however, most of the current inhalers are often poorly used and are not intuitive, which implies that an extensive training is needed in the long term.^{10,11} Therefore, optimization of the inhaler device needs to be oriented to meet the current unmet needs associated with medication adherence in the management of obstructive lung disease.

In the current study, we evaluated the expected economic impact from the increase in the market share of Spiromax[®], a brand-new inhalation device, for the maintenance therapy with budesonide–formoterol fixed-dose combination (FDC), by

using a budget impact model. This new inhalation device has been shown to reduce common utilization errors such as dose preparation errors, adequate flow rates, and even environmental conditions that might limit the delivery of the drug directly to the lungs.¹² We included data from the perspective of the Spanish Healthcare System (NHS) as well as regional data from five Spanish Autonomous Communities (hereafter known as regions): Andalusia, Catalonia, Galicia, Madrid, and Valencia.

Methods

Model development and structure

According to legislation of scientific studies (SAS/3470/2009 Order of December 16, to make public guidelines on post-authorization studies that are observational for drugs for human use) this project did not require approval from an ethical review board as we did not have access to patient level data, we did not need to interview patients to obtain estimates, and this was not a clinical study. The budget impact model was developed in Microsoft Excel from the perspective of the Spanish NHS, and for this purpose a time horizon of 4 years (2015–2018) was used. Spain and five Spanish regions were included in our analysis. Budesonide–formoterol FDCs delivered by Turbuhaler[®] whose complete brand names can be Rilast[®] Turbuhaler[®] and Symbicort[®] Turbuhaler[®] were considered to be the most appropriate comparator for assessing the budget impact with the introduction of DuoResp[®] Spiromax[®], a new inhaler for delivering budesonide–formoterol FDC. We decided to compare these two different inhalation devices that delivered budesonide–formoterol FDC because changes in prescription regimens were not hypothesized in this study.

Input parameters were obtained by expert panel consultation from different Spanish hospitals. Therefore, the model analyzed health care resource utilization per patient based on their daily maintenance treatment for asthma and the number of days with events such as hospitalizations and visits to the emergency room, PC visits, and specialist visits. All cost estimates were reported in Euros (EUR 2015), and a discount rate of 3% was applied.

It is worth mentioning that during the time this study was being completed, there was a significant change in prices of the drugs included in this analysis. From October 2015 onward, prices of both drugs were set at the same level by the Spanish Ministry of Health; therefore, price effect was no longer useful to calculate the economic impact of the introduction of DuoResp[®] Spiromax[®].¹³

This model included diagnosed patients who control asthma with a maintenance therapy. Proportion of FDC of budesonide–formoterol utilization that was delivered by

a DPI was based on the national and regional sales data for Spain reported by IMS. Therefore, data on Symbicort[®] Turbuhaler[®] and Rilast[®] Turbuhaler[®] utilization were used to estimate the target population. Forecast of DuoResp[®] Spiromax[®] uptake rates was reported by Teva Pharma.

The model generated estimates for the costs per patient and the total direct costs of treatment including drug and medical cost based on market shares and other input parameters. The potential effect of a strengthening of adherence to the total costs of asthma was generated from savings in medical resources utilization associated with an improvement in the inhalation technique. All patients were assumed to receive treatment during the whole year.

Model input variables

Target population

To estimate the target population diagnosed with a maintenance therapy with budesonide–formoterol FDC, the following algorithm was applied, as shown in Figure 1. A literature review was performed to identify the prevalence of asthma among the adult population of Spain and regions included in this analysis.^{14–17} Estimates for asthma were extrapolated to the adult populations obtained from the population projections conducted by the National Institute of

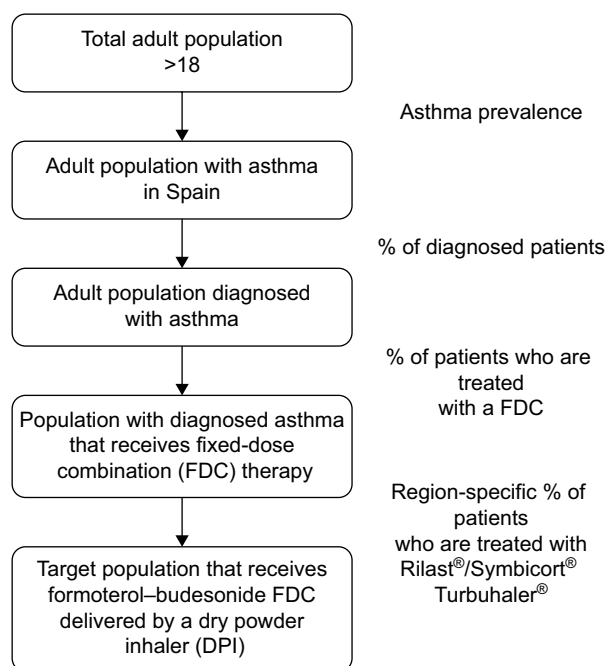


Figure 1 Target population of the study.

Notes: Asthma prevalence: Spain 9.90%, Andalusia 9.90%, Catalonia 5.60%, Galicia 12.90%, Madrid 7.00%, Valencia 9.80%; region-specific % of patients who are treated with Rilast[®]–Symbicort[®] Turbuhaler[®]: Spain 34.99%, Andalusia 33.35%, Catalonia 31.53%, Galicia 34.97%, Madrid 36.46%, and Valencia 34.26% of patients who are treated with a fixed-dose combination: Spain 35.85%, Andalusia 31.23%, Catalonia 33.42%, Galicia 42.86%, Madrid 38.17%, and Valencia 31.64%.

Statistics (INE).¹⁸ We had to take into account that >50% of asthmatic patients are not diagnosed and 26% of those do not receive treatment.¹⁹ A percentage was applied to distinguish patients using an FDC and among these patients, those who take budesonide–formoterol FDC delivered by DPI were determined.²⁰ The proxy for capturing these patients was the percentage of patients using Symbicort[®]/Rilast[®] Turbuhaler[®].

Inhalation technique, medication adherence, medical resource utilization, and costs

Before identifying directly variations in health care resources associated with the use of each inhaler, experts were asked to specify percentage of utilization errors with Spiromax[®] and Turbuhaler[®], and the differences between use of inhalation devices were mainly those regarding the incorrect dose loading and keeping the inhaler inclined not >45° from the vertical axis (Table 1). These results were not used for calculations, but they were relevant to confirm that the misuse of inhaler is seen in clinical practice.

Obtaining input data on health care resource utilization associated with potential strengthening of adherence was the basis to estimate the economic consequences of the introduction of Spiromax[®] in Spain. The use of health care resources was estimated based on data from clinical practice by consulting a panel of five clinical experts in pneumology, allergy, and a general practitioner from different Spanish hospitals. Accordingly with our expert panel, the proportions of patients who visit the emergency room and those who are hospitalized due to suboptimal inhalation are estimated to be 6.96% and 2.64%, respectively. Among these patients we also observed whether there were differences in the number of these events between patients using Turbuhaler[®] versus patients using Spiromax[®] (Table 2).

Table 1 Errors observed in daily practice

| Checklist of inhalation technique errors | % of patients using Symbicort [®] /Rilast [®] Turbuhaler [®] | % of patients using DuoResp [®] Spiromax [®] |
|--|---|--|
| Failure of loading | 17.17 | 0.83 |
| No breath holding after inhalation | 37.00 | 36.67 |
| Keep the inhaler inclined not >45° from the vertical axis during loading | 22.33 | 5.83 |
| No exhale prior to inhale | 35.83 | 28.67 |
| Stop inhaling prematurely | 27.67 | 22.50 |
| Exhaling into the device mouthpiece after inhalation | 12.17 | 8.83 |

Note: These percentages were not used for calculation. Estimates were sourced from a clinical expert panel of pneumologists, allergists, and a general practitioner and were prepared by the authors.

Table 2 Input data on drug cost, medical resource utilization, unit costs, and average cost per patient per year in Euro (€) 2015

| | Symbicort® Turbuhaler® | Rilast® Turbuhaler® | DuoResp® Spiromax® | Mean of regional unit costs in € 2015 ^a |
|---|---------------------------|------------------------|-----------------------|---|
| Annual resources of medical resource | | | | |
| Medical visits | | | | |
| Average number of PC visits per patient per year | 4.80 | 4.80 | 4.60 | 52.62 |
| Average number of specialist physician visits per patient per year | 2.00 | 2.00 | 2.00 | 75.15 |
| Average number of emergency visits per patient per year | 0.014 | 0.014 | 0.014 | 173.31 |
| Hospital resource utilization | | | | |
| Average number of hospitalization per patient per year ^b | 0.003 | 0.003 | 0.003 | 492.39 |
| Average days of length of stay per patient per year | 3.60 | 3.60 | 2.80 | – |
| Other interventions | | | | |
| Average number of spirometries per patient per year | 3.5 | 3.5 | 3.5 | 31.69 |
| Average number of thorax radiography per patient per year | 1.3 | 1.3 | 1.3 | 20.98 |
| Total healthcare cost per patient per year | | | | |
| Drug cost (€) ^c | 221 | 221 | 219 | – |
| Cost of medical visits (€) | 405 | 405 | 395 | – |
| Cost of hospital resource utilization (€) ^b | 5 | 5 | 4 | – |
| Cost of other interventions (€) | 138 | 138 | 138 | – |
| Cost per patient (€) | 769 | 769 | 756 | – |

Notes: ^aMean of unit costs of 12 Spanish regions. Region-specific unit costs of health care resources were used to estimate economic impact for five regions included. ^bThe proportions of patients who visit the emergency room and those who are hospitalized due to suboptimal inhaler utilization are 6.96% and 2.64%, respectively. Among patients who visited the emergency room we observed that on average the number of these events with Turbuhaler® were 0.2 and with Spiromax® were 0.2, which result in 0.014 times €173.71. We performed same calculations with number of hospitalizations, which resulted in 0.003 times €492.39. ^cDifferences in drug cost are due to differences in distributions of doses. However, drug cost was not associated with adherence, so this variation was offset for calculation of adherence effect. Data is sourced from a clinical expert panel of pneumologists, allergists, and a general practitioner and were prepared by the authors.

Abbreviation: PC, primary care.

Regarding number of PC visits and specialist visits, it was not possible to obtain a direct percentage of visits due to problems with the inhalers. One visit to a PC provider can be used to solve various patients' concerns, including problems with the device. Thus, it was necessary to ask the overall number of PC and specialist visits that a regular asthmatic patient has. On average patients who used Turbuhaler® should not be different from those using Spiromax® because they share indication with the same FDC of budesonide–formoterol.²¹ Therefore, we assume that this variation between health care resource utilization associated with Spiromax® versus Turbuhaler® might be related to the inhalation device (Table 2). Given that there is no scientific literature published on this topic, experts' consultation was needed to obtain input data on health care resource utilization. Monitoring test and its cost were also included in the model. This information was used to calculate the costs for medical resources associated with each drug.

Costs of health care resources included in this analysis were obtained from regional tariff lists.^{22–33} Cost of health care resources at the national level are the mean of 12 regions, including those in this analysis.

Table 3 Distribution of treatments (%): base case analysis and alternative scenario

| | Year | | | |
|-----------------------------|--------|--------|--------|--------|
| | 2015 | 2016 | 2017 | 2018 |
| Base case analysis | | | | |
| Symbicort® Turbuhaler® | 50.00% | 50.00% | 50.00% | 50.00% |
| Rilast® Turbuhaler® | 50.00% | 50.00% | 50.00% | 50.00% |
| DuoResp® Spiromax® | 0% | 0% | 0% | 0% |
| Alternative scenario | | | | |
| Symbicort® Turbuhaler® | 44.50% | 41.00% | 39.00% | 37.50% |
| Rilast® Turbuhaler® | 44.50% | 41.00% | 39.00% | 37.50% |
| DuoResp® Spiromax® | 11.00% | 18.00% | 22.00% | 25.00% |

Note: Data provided by Teva Pharma and it was prepared by the authors (unpublished data, 2015).

Budgetary impact analysis

Based on the annual drug cost and health care resource use per patient, the total treatment cost per patient was estimated in EUR 2015. With the annual average cost per patient for each treatment option, the target population, and the market shares for budesonide–formoterol FDC delivered by Turbuhaler®, the overall economic impact of the maintenance treatment of asthma for 2015–2018 was obtained. In the base case scenario or current scenario, a market without

DuoResp[®] Spiromax[®] was estimated. The current scenario was compared with an alternative in which the economic impact was calculated by taking into account DuoResp[®] Spiromax[®] and its potential effects toward improved medication adherence. The budget impact model was based on differences between a scenario without DuoResp[®] Spiromax[®], current scenario, and an alternative scenario (Table 3). The

uptake of DuoResp[®] Spiromax[®] increases during the period of study.

Results

In our model, region-specific prevalence data were used, which vary across all five regions. Prevalence of asthma in Spain (9.90%) differs substantially from Catalonia (5.60%),

Table 4 Target population (n) for asthma treatment

| Target population | Year | | | |
|--|-----------|-----------|-----------|-----------|
| | 2015 | 2016 | 2017 | 2018 |
| Spain | | | | |
| Adult patients with asthma | 3,748,190 | 3,726,486 | 3,705,397 | 3,686,296 |
| Adult patients who are diagnosed and treated | 1,331,357 | 1,323,648 | 1,316,157 | 1,309,373 |
| Adult patients treated with an FDC | 477,289 | 474,526 | 471,840 | 469,408 |
| Adult patients treated with budesonide–formoterol delivered by a DPI | 166,985 | 166,018 | 165,078 | 164,227 |
| Andalusia | | | | |
| Adult patients with asthma | 667,977 | 668,182 | 668,377 | 668,753 |
| Adult patients who are diagnosed and treated | 237,266 | 237,338 | 237,407 | 237,541 |
| Adult patients treated with an FDC | 74,093 | 74,116 | 74,137 | 74,179 |
| Adult patients treated with budesonide–formoterol delivered by a DPI | 25,081 | 25,089 | 25,096 | 25,110 |
| Catalonia | | | | |
| Adult patients with asthma | 331,090 | 326,955 | 323,031 | 319,444 |
| Adult patients who are diagnosed and treated | 117,603 | 116,134 | 114,741 | 113,466 |
| Adult patients treated with an FDC | 39,302 | 38,811 | 38,345 | 37,919 |
| Adult patients treated with budesonide–formoterol delivered by a DPI | 12,392 | 12,237 | 12,090 | 11,956 |
| Galicia | | | | |
| Adult patients with asthma | 302,391 | 300,709 | 299,044 | 297,444 |
| Adult patients who are diagnosed and treated | 107,409 | 106,812 | 106,220 | 105,652 |
| Adult patients treated with an FDC | 46,033 | 45,777 | 45,523 | 45,280 |
| Adult patients treated with budesonide–formoterol delivered by a DPI | 16,097 | 16,007 | 15,918 | 15,833 |
| Madrid | | | | |
| Adult patients with asthma | 360,702 | 358,131 | 355,641 | 353,387 |
| Adult patients who are diagnosed and treated | 128,121 | 127,208 | 126,324 | 125,523 |
| Adult patients treated with an FDC | 48,902 | 48,554 | 48,216 | 47,911 |
| Adult patients treated with budesonide–formoterol delivered by a DPI | 17,829 | 17,702 | 17,579 | 17,468 |
| Valencia | | | | |
| Adult patients with asthma | 393,305 | 389,855 | 386,517 | 383,421 |
| Adult patients who are diagnosed and treated | 139,702 | 138,476 | 137,291 | 136,191 |
| Adult patients treated with an FDC | 44,207 | 43,820 | 43,444 | 43,096 |
| Adult patients treated with budesonide–formoterol delivered by a DPI | 15,148 | 15,015 | 14,886 | 14,767 |

Abbreviations: FDC, fixed-dose combination; DPI, dry powder inhaler.

Table 5 Results of the base case budget impact analysis in Euro 2015 (€)

| | | Year | | | | Present value |
|--------------|--|-------------|-------------|-------------|-------------|---------------|
| | | 2015 | 2016 | 2017 | 2018 | |
| Spain | Current scenario | | | | | |
| | Symbicort [®] Turbuhaler [®] | 64,210,549 | 65,753,902 | 69,363,528 | 75,404,694 | 262,437,044 |
| | Rilast [®] Turbuhaler [®] | 64,210,549 | 65,753,902 | 69,363,528 | 75,404,694 | 262,437,044 |
| | Total cost | 128,421,098 | 131,507,804 | 138,727,057 | 150,809,389 | 524,874,089 |
| | Alternative scenario | | | | | |
| | Symbicort [®] Turbuhaler [®] | 57,147,388 | 53,918,199 | 54,103,552 | 56,553,521 | 212,247,425 |
| | Rilast [®] Turbuhaler [®] | 57,147,388 | 53,918,199 | 54,103,552 | 56,553,521 | 212,247,425 |
| | DuoResp [®] Spiromax [®] | 13,913,892 | 23,315,439 | 30,061,000 | 37,135,388 | 98,869,759 |
| | Total cost | 128,208,670 | 131,151,839 | 138,268,105 | 150,242,430 | 523,364,611 |
| | Budget impact savings | -212,428 | -355,965 | -458,952 | -566,959 | -1,509,479 |

Table 5 (Continued)

| | | Year | | | | |
|------------------|-----------------------------|------------|------------|------------|------------|---------------|
| | | 2015 | 2016 | 2017 | 2018 | Present value |
| Andalusia | Current scenario | | | | | |
| | Symbicort® Turbuhaler® | 10,157,509 | 10,465,439 | 11,106,022 | 12,142,679 | 41,898,894 |
| | Rilast® Turbuhaler® | 10,157,509 | 10,465,439 | 11,106,022 | 12,142,679 | 41,898,894 |
| | Total cost | 20,315,019 | 20,930,879 | 22,212,045 | 24,285,359 | 83,797,789 |
| | Alternative scenario | | | | | |
| | Symbicort® Turbuhaler® | 9,040,183 | 8,581,660 | 8,662,697 | 9,107,009 | 33,871,520 |
| | Rilast® Turbuhaler® | 9,040,183 | 8,581,660 | 8,662,697 | 9,107,009 | 33,871,520 |
| | DuoResp® Spiromax® | 2,202,679 | 3,713,653 | 4,816,733 | 5,984,473 | 15,825,042 |
| | Total cost | 20,283,046 | 20,876,974 | 22,142,128 | 24,198,492 | 83,568,083 |
| | Budget impact savings | -31,973 | -53,905 | -69,917 | -86,867 | -229,706 |
| Catania | Current scenario | | | | | |
| | Symbicort® Turbuhaler® | 3,709,673 | 3,773,245 | 3,954,990 | 4,273,736 | 15,012,050 |
| | Rilast® Turbuhaler® | 3,709,673 | 3,773,245 | 3,954,990 | 4,273,736 | 15,012,050 |
| | Total cost | 7,419,346 | 7,546,491 | 7,909,980 | 8,547,472 | 30,024,100 |
| | Alternative scenario | | | | | |
| | Symbicort® Turbuhaler® | 3,301,608 | 3,094,061 | 3,084,892 | 3,205,302 | 12,146,664 |
| | Rilast® Turbuhaler® | 3,301,608 | 3,094,061 | 3,084,892 | 3,205,302 | 12,146,664 |
| | DuoResp® Spiromax® | 803,290 | 1,337,001 | 1,712,822 | 2,103,255 | 5,640,625 |
| | Total cost | 7,406,508 | 7,525,124 | 7,882,607 | 8,513,859 | 29,933,955 |
| | Budget impact savings | -12,838 | -21,367 | -27,373 | -33,613 | -90,145 |
| Galicia | Current scenario | | | | | |
| | Symbicort® Turbuhaler® | 7,167,402 | 7,341,370 | 7,745,338 | 8,418,268 | 29,299,579 |
| | Rilast® Turbuhaler® | 7,167,402 | 7,341,370 | 7,745,338 | 8,418,268 | 29,299,579 |
| | Total cost | 14,334,805 | 14,682,740 | 15,490,677 | 16,836,537 | 58,599,159 |
| | Alternative scenario | | | | | |
| | Symbicort® Turbuhaler® | 6,378,988 | 6,019,923 | 6,041,364 | 6,313,701 | 23,696,070 |
| | Rilast® Turbuhaler® | 6,378,988 | 6,019,923 | 6,041,364 | 6,313,701 | 23,696,070 |
| | DuoResp® Spiromax® | 1,550,330 | 2,598,480 | 3,350,680 | 4,138,402 | 11,018,690 |
| | Total cost | 14,308,307 | 14,638,327 | 15,433,408 | 16,765,805 | 58,410,831 |
| | Budget impact savings | -26,498 | -44,412 | -57,269 | -70,732 | -188,327 |
| Madrid | Current scenario | | | | | |
| | Symbicort® Turbuhaler® | 6,332,212 | 6,475,696 | 6,822,304 | 7,407,674 | 25,829,043 |
| | Rilast® Turbuhaler® | 6,332,212 | 6,475,696 | 6,822,304 | 7,407,674 | 25,829,043 |
| | Total cost | 12,664,425 | 12,951,393 | 13,644,608 | 14,815,348 | 51,658,087 |
| | Alternative scenario | | | | | |
| | Symbicort® Turbuhaler® | 5,635,669 | 5,310,071 | 5,321,397 | 5,555,755 | 20,891,308 |
| | Rilast® Turbuhaler® | 5,635,669 | 5,310,071 | 5,321,397 | 5,555,755 | 20,891,308 |
| | DuoResp® Spiromax® | 1,375,782 | 2,302,292 | 2,964,526 | 3,657,829 | 9,752,800 |
| | Total cost | 12,647,120 | 12,922,435 | 13,607,320 | 14,769,340 | 51,535,418 |
| | Budget impact savings | -17,304 | -28,958 | -37,287 | -46,008 | -122,669 |
| Valencia | Current scenario | | | | | |
| | Symbicort® Turbuhaler® | 6,427,529 | 6,562,282 | 6,902,318 | 7,481,939 | 26,151,808 |
| | Rilast® Turbuhaler® | 6,427,529 | 6,562,282 | 6,902,318 | 7,481,939 | 26,151,808 |
| | Total cost | 12,855,058 | 13,124,565 | 13,804,637 | 14,963,878 | 52,303,617 |
| | Alternative scenario | | | | | |
| | Symbicort® Turbuhaler® | 5,720,500 | 5,381,071 | 5,383,808 | 5,611,454 | 21,154,873 |
| | Rilast® Turbuhaler® | 5,720,500 | 5,381,071 | 5,383,808 | 5,611,454 | 21,154,873 |
| | DuoResp® Spiromax® | 1,390,597 | 2,323,229 | 2,986,636 | 3,678,907 | 9,828,073 |
| | Total cost | 12,831,599 | 13,085,372 | 13,754,253 | 14,901,816 | 52,137,820 |
| | Budget impact savings | -23,459 | -39,192 | -50,384 | -62,062 | -165,796 |

Madrid (7%), or Galicia (12.9%), while it is similar to Andalusia (9.90%) and Valencia (9.80%).¹⁴⁻¹⁷ Based on demographics, the only region where slight increases in the asthmatic population were observed was Andalusia (Table 4).

Asthma treatment resulted to be very costly for the Spanish NHS. For instance, it has been estimated that treating patients using Symbicort® Turbuhaler® cost €64.21 million in 2015. Specifically, in the base case analysis of Spain

Table 6 Specific results: savings due to reduction in health care resource utilization Euro 2015 (€)

| Regions and savings in Euros | Year | | | | |
|--|----------|----------|----------|----------|---------------|
| | 2015 | 2016 | 2017 | 2018 | Present value |
| Spain | | | | | |
| Savings due to fewer days of hospital stay | -19,102 | -32,009 | -41,269 | -50,982 | -135,734 |
| Savings due to avoided PC visits | -193,326 | -323,956 | -417,682 | -515,977 | -1,373,745 |
| Total savings, Spain | -212,428 | -355,965 | -458,952 | -566,959 | -1,509,479 |
| Andalusia | | | | | |
| Savings due to fewer days of hospital stay | -3,434 | -5,789 | -7,508 | -9,329 | -24,668 |
| Savings due to avoided PC visits | -28,539 | -48,116 | -62,408 | -77,538 | -205,038 |
| Total savings, Andalusia | -31,973 | -53,905 | -69,917 | -86,867 | -229,706 |
| Catalonia | | | | | |
| Savings due to fewer days of hospital stay | -1,549 | -2,578 | -3,302 | -4,055 | -10,875 |
| Savings due to avoided PC visits | -11,289 | -18,789 | -24,071 | -29,558 | -79,270 |
| Total savings, Catalonia | -12,838 | -21,367 | -27,373 | -33,613 | -90,145 |
| Galicia | | | | | |
| Savings due to fewer days of hospital stay | -1,978 | -3,315 | -4,275 | -5,280 | -14,059 |
| Savings due to avoided PC visits | -24,520 | -41,097 | -52,993 | -65,452 | -174,269 |
| Total savings, Galicia | -26,498 | -44,412 | -57,269 | -70,732 | -188,327 |
| Madrid | | | | | |
| Savings due to fewer days of hospital stay | -1,961 | -3,282 | -4,225 | -5,214 | -13,901 |
| Savings due to avoided PC visits | -15,343 | -25,676 | -33,062 | -40,794 | -108,768 |
| Total savings, Madrid | -17,304 | -28,958 | -37,287 | -46,008 | -122,669 |
| Valencia | | | | | |
| Savings due to fewer days of hospital stay | -1,138 | -1,902 | -2,445 | -3,012 | -8,045 |
| Savings due to avoided PC visits | -22,321 | -37,290 | -47,939 | -59,050 | -157,751 |
| Total savings, Valencia | -23,459 | -39,192 | -50,384 | -62,062 | -165,796 |

Note: negative quantities mean savings.

Abbreviation: PC, primary care.

before the introduction of DuoResp[®] Spiromax[®], the total economic impact was estimated to be €524.87 million over 4 years (Table 5). Taking into account the increasing market share of DuoResp[®] Spiromax[®] in the alternative scenario, the total economic impact for Spain was calculated to be €523.36 million. Overall, at the national level the total budget savings with the market share of DuoResp[®] Spiromax[®] was expected to be €1.509 million over the next 4 years, given the difference in number of days of hospital stay and PC visits (Table 6).

This model also provides region-specific estimates. In the case of Andalusia, treating patients who take budesonide–formoterol FDC delivered by Turbuhaler[®] would lead to a health care expenditure of €83.79 million between 2015 and 2020 (Table 5). In the alternative scenario, costs were estimated to be €83.56 million in the same time period. Differences between both scenarios would allow Andalusia to save €229,706, which might be due to assumption of fewer PC visits and shorter hospital stays, associated with an assumption of better medication

adherence (Tables 6 and 7). Savings of Andalusia are higher compared with the results of the rest of the regions included in this study.

Regarding Catalonia, the total economic impact of the current scenario was estimated to be €30.02 million, while in the alternative scenario, we estimated €29.93 million over 2015–2018. Health care expenditure for asthma in Catalonia is the smallest one compared with the other regions included in this analysis. Given the results of both scenarios, the overall savings in Catalonia were estimated to be €90,145, which are obtained through reduction of health care resource, specifically fewer days of hospital stay and PC visits (Table 6).

The total economic impact without the introduction of DuoResp[®] Spiromax[®] in Galicia was estimated to be €58.59 million between 2015 and 2018, while in the alternative scenario was calculated to be €58.41 million (Table 5). Therefore, Galicia might save €188,327, principally due to fewer PC visits and a small proportion of fewer days of hospital stay (Table 6).

Referring to Madrid, the total economic impact for the current scenario throughout 2015–2018 was €51.66 million; meanwhile, the economic impact with the introduction of DuoResp® Spiromax® summed up to €51.53 million (Table 5). The total savings were expected to be €122,669 over the next 4 years, given the potentially positive effect of DuoResp® Spiromax® by reducing the days of hospitalization and PC visits (Table 6).

Finally, with regard to Valencia, economic impact without DuoResp® Spiromax® onto the market leads to €52.30 million throughout 2015–2018, while economic impact with DuoResp® Spiromax® is estimated to be €52.14 million (Table 5). Differences between both scenarios gave total savings of €165,796 (Table 5). These savings might be due to a reduction of hospitalization resource (length of stay) and PC visits (Table 6).

Discussion

Treating asthma is very costly for the regional health care budget, given the results illustrated in Table 5. Health care resources used in clinical practice included drug cost, medical visits, hospital resource utilization, and other interventions. However, a potential improvement in medication adherence due to a more intuitive device could impact economically by reducing medical visits and hospital resource use. Therefore, any intervention that could enhance medication adherence in asthmatic patients would be important to lower the economic impact of the disease. If the inhalation technique related to the inhaler does not help the drug-taking pattern because of lack of easy-to-use design, the drug-taking history does not coincide with the prescribed treatment. Indeed, we took into account the use of different inhalers in order to quantify the economic impact, keeping constant the drug effect (budesonide–formoterol). Finally, Turbuhaler presentations (Rilast® and Symbicort® Turbuhaler®) presented higher proportion of errors compared to DuoResp® Spiromax® according to our expert panel.

This study compares the cost of budesonide–formoterol FDC delivered by two different DPIs and estimates the budget impact for the asthma treatment in Spain. Results suggest that the increasing utilization of budesonide–formoterol FDC delivered by Spiromax®, that is DuoResp® Spiromax®, would result in a saving for the Spanish NHS of €1.509 million as well as savings for Andalusia, Catalonia, Galicia, Madrid, and Valencia of €229,706, €90,145, €188,327, €122,669, and €165,796, respectively.

Maintenance treatments are widely known and FDCs have become an advantage for controlling progression and

symptomatology of the disease.³⁴ As with any treatment for a chronic condition adherence is a requirement to achieve pharmacological efficacy, delay the progression of the disease, and avoid health care resource waste. Our results suggest that savings for Spain and five Spanish regions are possible given the estimate parameters based on clinical expert consultation. These outcomes are in line with the results of former studies that investigated the relationship between nonadherence and the use of health care resources in a population suffering from a pulmonary disease.^{5,8,35} A proportion of events such as hospitalization and excessive PC visits are avoidable and could provide cost savings if current adherence problems are addressed (Table 1).

One of the strengths for our analysis is that due to the lack of published clinical input data from Spanish populations, this study was based on the real-world utilization of these treatments and consequences of nonadherence, considering that input data were based on the expert opinion of specialists working in different Spanish hospitals. Furthermore, our analysis also includes results of five representative regions in Spain, which allowed us to have various regions involved by providing input to the estimated real-world utilization. Differences in asthma prevalence rates are significant and, for instance, health care resources for treating asthmatics in Catalonia are lower than those expended in Galicia although its population is smaller than the Catalonia population. Furthermore, Galicia might obtain greater savings if adherence improves in their population by using a more intuitive inhaler according to our estimations.

There are several limitations that should be noted. First, the model was developed to estimate the potential budget impact when increasing the market share of DuoResp® Spiromax® due to a reduced utilization of Symbicort® Turbuhaler® and Rilast® Turbuhaler®, whose FDC is budesonide–formoterol. This outcome may not reflect totally real-world change. Moreover, there are other FDCs such as salmeterol–fluticasone and formoterol/beclomethasone whose delivery system is also a DPI, for which Spiromax® could be an alternative although we did not hypothesize switching prescriptions. The quantification of gains in adherence leads to conservative quantities in our study, which in the end may be acceptable because we understand that the lack of adherence involves many factors,^{5,8,10,36} besides problems with the inhalation technique. Additionally, underdiagnosis of asthma is frequent, which is barrier for avoiding increasing prevalence rates of severe asthma. In Spain, underdiagnosis rates are high and half of the asthmatic population remains unaware of their condition.³¹ This would imply that asthma

health care expenditure might be even higher as only a proportion of asthmatics are currently treated.

Conclusion

Enhancement of adherence is a key factor to guarantee the efficacy of treatment in multiple diseases, especially those with a chronic profile. In our study, we quantify the economic impact of a potential improvement in the inhalation technique in order to strengthen medication adherence. Results from our analysis suggest that an increase in utilization of DuoResp[®] Spiromax[®], while the use of budesonide–formoterol FDC delivered by other devices Turbuhaler[®] (Symbicort[®] Turbuhaler[®] and Rilast[®] Turbuhaler[®]) decreases, could result in €1.509 million decrease in the overall budget over the period 2015–2018. These results could also be possible in the five Spanish regions included in this analysis, which are Andalusia, Catalonia, Galicia, Madrid, and Valencia.

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Disclosure

JD is an employee of the University of Barcelona. GR is an employee of BCN Health Economics & Outcomes Research SL, Barcelona, Spain, an independent contract health economic organization. AB is an employee of Teva Pharma SLU. The authors report no other conflicts of interest in this work.

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