ORIGINAL ARTICLES

Cost-Effectiveness Analysis of Tiotropium Compared to Ipratropium and Salmeterol

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OBJECTIVE: The constant increase in health care costs, in a context of limited resources and the appearance of more costly though more effective drugs, justifies an assessment of the pharmacoeconomics of these drugs. The objective of this study was to evaluate the cost-effectiveness of one of the newest drugs for the treatment of chronic obstructive pulmonary disease (COPD)-tiotropium.

MATERIAL AND METHOD: A cost-effectiveness analysis (costs and outcomes) within the framework of the Spanish National Health System was done. The alternatives to tiotropium analyzed were ipratropium and salmeterol. Direct health care costs associated with hospital treatment were calculated. Forced expiratory volume in 1 second, quality of life (with the Saint George's Respiratory Questionnaire), dyspnea transitional index, mean stay in hospital, and exacerbations were the variables used to measure effectiveness. Values for these variables were taken from the main reviews and randomized clinical trials published for tiotropium.

RESULTS: For COPD patients, treatment with tiotropium leads to a greater reduction in exacerbations (37% compared to ipratropium and 25% compared to salmeterol 25%), and a reduction in the number of days in hospital (33% compared to ipratropium and 14% compared to salmeterol). Therefore, use of tiotropium could save €100 000 for the current rates of admission and lengths of hospital stay in Spain.

CONCLUSIONS: Tiotropium was more effective than ipratropium and salmeterol as measured by objective clinical variables (forced expiratory volume in 1 second) and subjective ones (the Saint George's Respiratory Questionnaire and dyspnea transitional index). Hospital stays were shorter and exacerbations fewer with tiotropium. In all cases, tiotropium was more cost-effective than the alternatives, thus use of tiotropium could help hospitals to save money.

Key words: *Cost-effectiveness analysis. Tiotropium. Pharmacoeconomics. Effectiveness.*

Análisis del coste-eficacia del tiotropio frente al ipratropio y salmeterol

OBJETIVO: El incesante incremento de los costes en un marco en el que los recursos son limitados, así como la aparición de nuevos medicamentos más costosos y a la vez más eficaces, justifica la evaluación económica de los medicamentos. El objetivo de este trabajo es evaluar el coste-eficacia de uno de los fármacos más novedosos para el tratamiento de la enfermedad pulmonar obstructiva crónica (EPOC), el tiotropio.

MATERIAL Y MÉTODO: Se ha realizado un análisis de coste-eficacia (costes y consecuencias) desde la perspectiva del Sistema Nacional de Salud. Las alternativas analizadas han sido ipratropio y salmeterol. Se han considerado sólo costes sanitarios directos en el ámbito hospitalario. Los parámetros de eficacia analizados han sido: volumen espiratorio forzado en el primer segundo, calidad de vida (mediante el Saint George's Respiratory Questionnaire), índice transicional de disnea, estancias medias y exacerbaciones. Dichos parámetros se han obtenido de las principales revisiones y ensayos clínicos aleatorizados publicados sobre el tiotropio.

RESULTADOS: Teniendo en cuenta la reducción del número de exacerbaciones conseguida con el tiotropio frente al ipratropio y salmeterol (el 37 y el 25%, respectivamente) y del número de días de estancia hospitalaria (el 33 y el 14%, respectivamente), su utilización puede suponer un ahorro superior a los 100.000 € para las cifras actuales de tasa de ingresos y días de estancia hospitalaria de los pacientes con EPOC en España.

CONCLUSIONES: El tiotropio ha sido más efectivo que el ipratropio y salmeterol tanto en parámetros clínicos (objetivos, como el volumen espiratorio forzado en el primer segundo, y subjetivos, como el Saint George's Respiratory Questionnaire y el índice transicional de disnea) como en disminución de estancias hospitalarias y exacerbaciones. En todos los casos resulta más coste-efectivo que sus alternativas, lo que supone importantes ahorros en el ámbito hospitalario.

Palabras clave: *Análisis coste-eficacia. Tiotropio. Farmacoeconomía. Efectividad.*

Introduction

Chronic obstructive pulmonary disease (COPD) is currently one of the respiratory diseases associated with high morbidity and mortality.[1-5] Therapeutic approaches vary widely and the recommendations of the main

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Spanish and international respiratory societies are not strictly observed.[6,7] This increases the burden on health care resources and, as a result, there is a need to assess different treatment options, not only in terms of effectiveness but also in terms of efficiency.

It is calculated that the mean health care cost of a COPD patient, from the moment of diagnosis at around 50 years of age, until the end of his or her life is around €30 050[8]; thus COPD is an important health and social problem. One study that evaluated the economics of COPD interventions found a series of indicators suggesting that health care for these patients was not as effective or efficient as might be hoped.[9]

The constant increase in health care costs in a context of limited resources and the appearance of more costly though more effective drugs justify an assessment of the pharmacoeconomics of these new treatments. The ultimate aim of this type of assessment is to select the options that have the greatest positive health impact. This means that the findings of a pharmacoeconomic study should be an instrument used for making treatment decisions. An assessment of a new treatment should investigate not just the safety and efficacy (effectiveness in an ideal setting such as a clinical trial) of the drug, but also its efficiency, that is, the ratio of health benefit to unit cost, and compare it with existing effective options. The best method for assessing the degree of efficiency or the cost-efficacy or effectiveness ratio is a pharmacoeconomic analysis, that is, a systematic assessment and comparison of 2 treatments in terms of costs and outcomes. The cost-effectiveness ratios compare the cost of each intervention with a unit of health benefit obtained or, in an incremental cost analysis, allow the additional cost of each additional unit of benefit to be determined. The application of costs of different health effects or benefits is known as cost-effectiveness analysis.[10,11]

For the present economic evaluation, we have followed the recommendations in the Guidelines for Incorporation of New Drugs, published by the Andalusian Public Health System. The recommendations are based on those in the Guidelines for the Incorporation and Acquisition of New Health Technologies, published by the Andalusian Agency for Health Technologies.[12]

The process of assessment and evaluation to which new drugs are submitted before being included in drug directories or guides should include not just an efficacy and effectiveness analysis but also a pharmacoeconomic analysis. For this analysis, the mean cost-effectiveness, incremental cost-effectiveness, sensitivity analysis, and, finally, the estimated outcomes (number of candidates for in-hospital treatment during a given period) and overall impact on hospital economics should be calculated using the current precepts of evidence-based medicine.

Material and Methods

A cost-effectiveness analysis was done in the setting of the Spanish National Health System (the body that finances health care). This analysis therefore only took into account direct health care costs.

Therapeutic Options Assessed

To streamline the analysis, we compared tiotropium with the current most effective alternatives, combining the points of view of the patients and the Spanish National Health System. Such an approach is recommended in the current international guidelines and consensus statements,[13,14] the guidelines of the Spanish Society for Pulmonology and Thoracic Surgery (SEPAR),[15] and those issued jointly by SEPAR and the Spanish Society for Family and Community Medicine (semFYC).[16] The most appropriate drugs for comparison with tiotropium were ipratropium and salmeterol. Ipratropium is analogous to tiotropium and belongs to the same therapeutic subgroup (anticholinergics), whereas salmeterol (a long-acting β agonist) is one of the most common comparator drugs in international studies of efficacy in the treatment of COPD.

Cost Analysis

The costs used in the following analysis were taken from different publications on costs of COPD in Spain[17] and from studies published by our group,[18,19] including a previous study in one of the referral hospitals of our province (Hospital Regional Universitario Carlos Haya, Malaga, Spain).[19,20] These values included all direct medical costs of the hospital (attendance in the emergency room, stay in intensive care units and/or admission to the pulmonology ward, cost of specific pharmacological treatment for COPD, diagnostic tests, oxygen therapy, and specific antibiotic treatment for exacerbations).

The costs of the drugs used were assessed according to their "recommended retail price" as published in the Catalogue of Medicinal Products of the General Council of Associated Pharmacists.[21]

This study assessed mean cost-effectiveness and incremental cost-effectiveness as pharmacoeconomic variables.

Determination of Outcomes

The outcome measures and the use of resources in this pharmacoeconomic analysis were obtained from all patients randomized in clinical trials (by intention-to-treat analysis). We based our selection of clinical trials to be analyzed on the following: *a)* a recent systematic review of tiotropium[22] from 2003; *b)* a previous report of the Regional Drug and Therapeutics Centre published in accordance with the criteria of the National Institute for Clinical Excellence by the British National Health Service[23]; and *c)* analysis of the most relevant clinical trials that provide the best clinical evidence to date.[24-29]

The clinical efficacy of the drugs was determined for all clinical trials analyzed by criteria with clear clinical relevance such as improvement (increase of more than 12%) in trough forced expiratory volume in 1 second at the end of the study with respect to the baseline value[30] and decrease in score on the St George's Respiratory Questionnaire, a specific quality-of-life questionnaire. A decrease in health-related quality of life score was considered clinically significant if the change was more than 4 points (an objective improvement if observed by the physician, and a subjective one if perceived by the patient). The increase in the transitional dyspnea index score was also recorded and considered clinically relevant if it exceeded 1 point.[32,33]

TABLE 1
Mean Cost-Effectiveness of Tiotropium Compared to Ipratropium and Salmeterol*

	Ipratropium[27]	Tiotropium[27]	Salmeterol[28]	Tiotropium[28]
Duration of RCT	1 year		6 months	
No. of patients	535		623	
Dose administered	40 µg/6 h	18 µg/day	50 µg/12 h	18 µg/day
Cost of medication per patient, €	135.78†	689.28	231.42	344.64
SGRQ score	–0.44	–3.74	–3.54	–5.14
CE: 4 points SGRQ, €‡	1234.36	737.20	261.49	268.20
Increase in TDI	0.12	1.02	0.24	1.02
CE: 1 point TDI, €‡	1131.50	675.76	964.25	337.88
Trough FEV_1 at baseline, mL	1180	1250	1070	1110
Final trough FEV_1, mL	-30	+120	+85	+137
CE 12% trough FEV_1 at baseline, €‡	NA	861.6	349.58	335.08
CE 12% final trough FEV_1, €‡	NA	5.74	2.72	2.51

*RCT indicates randomized clinical trial; SGRQ, St George's Respiratory Questionnaire; CE, cost-effectiveness (lower cost-effectiveness ratio corresponds to greater efficiency); TDI, transitional dyspnea index; trough FEV_1, forced expiratory volume in 1 second measured 1 hour before drug administration; NA, not applicable (reference drug).
†Cost of the medication per patient-year according to the weighted cost of national sales of ipratropium (pressurized cartridge and inhaler) in Spain in 2002.
‡Considered clinically relevant scores and data.

TABLE 2
Differences in the Effectiveness of Tiotropium, Ipratropium, and Salmeterol*

	Tiotropium vs Placebo[25]	Tiotropium vs Ipratropium[27]	Tiotropium vs Salmeterol[29]
Patients with ≥4-point decrease on SGRQ, %	49/30†	52/35 (*P*<.01)	49/43
No. of exacerbations per patient-year	0.76/0.95†	0.73/0.96 (*P*=.006)	1.07/1.23
Patients with ≥1 exacerbation per year, %	36/42†	35/46 (*P*=.14)	32/35†
No. hospitalizations per patient for exacerbation	0.9/0.6	0.0/0.6 (*P*=.08)	0.10/0.17†
Patients hospitalized, %	5.5/9.4†	7.3/11.7 (*P*=.11)	12/16
Length of stay in hospital, days	0.6/1.2†	1.42/2.13 (*P*=.09)	0.98/1.14
No. days of inactivity due to exacerbation	–	–	8.3/11.1
Patients discontinuing study for any reason, %	18.7/27.8†	15.2/21.2 (*P*=.08)	–
Discontinuation due to adverse drug reaction, %‡	9.6/13.7†	10.1/12.8 (*P*=.089)	–
Discontinuation due to lack of efficacy, %	2.4/7.0†	0.8/1.7 (NG)	–

*SGRQ indicates St George's Respiratory Questionnaire; NG, not given.
†*P*<.05
‡Except dry mouth: 9.3% for tiotropium compared to 1.6% for placebo (*P*<.05),[24,25] and 14.7% for tiotropium compared to 10.3% for ipratropium (not significant).[26,27]

Results

Mean Cost-Effectiveness

Table 1 compares the net cost-effectiveness of tiotropium with that of ipratropium and salmeterol.[27,28] The analysis, done in accordance with the methods described earlier, considered only direct costs of medication at the "recommended retail price." Tiotropium was more cost-effective in the setting of the Spanish National Health System than the other two options (salmeterol and ipratropium), particularly if the limitations of the first analysis are taken into account. That is, the differences between tiotropium and the other options would have been larger still if the analysis had accounted for the effectiveness criteria presented in Table 2.[24-27,29]

Incremental Cost-Effectiveness Analysis

Table 3 shows the findings of the incremental cost-effectiveness analysis for tiotropium compared to the other options studied.[27-29] Incremental cost refers to the cost incurred to achieve an additional unit effect on health upon changing from one of the alternatives assessed (ipratropium or salmeterol) to tiotropium.

Evaluation of the Cost-Effectiveness of Tiotropium

The day-to-day reality of the hospital is more closely reflected by an analysis that takes into account the decrease in the number of admissions to hospital of these patients for exacerbations and the decrease in the

TABLE 3
Incremental Cost-Effectiveness Ratio (ICER), in Euro, of Tiotropium Versus the Comparator Therapeutic Options*

	Ipratropium for 1 Year[27]	Salmeterol for 6 Months[28,29]
ICER SGRQ	182.67	75.48
ICER TDI	615.00	191.90
ICER trough FEV_1, mL	3.69	2.76

*SGRQ indicates St George's Respiratory Questionnaire; TDI, transitional dyspnea index; trough FEV_1, forced expiratory volume in 1 second measured 1 hour before drug administration. ICER is the cost of attaining an additional unit of health benefit on changing from the option analyzed (ipratropium or salmeterol) to tiotropium.

TABLE 4
Prevalence of Patients With Chronic Obstructive Pulmonary Disease (COPD) in Malaga, Spain, and Number of Cost-Generating Patients With Moderate-Severe Disease According to SEPAR Guidelines*

Population	
Total	1 287 017
40-69 years	432 403
>69 years	121 219
No. of patients with COPD[34]	63 592 (prevalence: 9.1% among 40 to 69 year-olds; 20% >69 year-olds)
Patients diagnosed[35]	13 990 (22%)
Moderate or Severe COPD (FEV_1<80% reference)	8674 (62% of all patients with COPD)
Rate per 100 000 inhabitants	674

*SEPAR indicates the Spanish Society of Pulmonology and Thoracic Surgery; FEV_1, forced expiratory volume in 1 second.

length of hospital stay—a factor that is more important for the hospital once the exacerbation has occurred. According to our analysis of the findings of the IBERPOC study,[34] there are 9100 patients with COPD for every 100 000 inhabitants. Only 22% of the patients with COPD (2002 patients) have been diagnosed and generate health care costs.[35] Of these diagnosed patients, 62% have moderate or severe disease, according to the criteria of the European Respiratory Society. We therefore have a total of 1241 patients (Table 4). The population data were obtained from the 2001 census conducted by the National Institute of Statistics.[36]

In-hospital savings: decrease in hospital stay. Table 5 compares data on hospital savings for tiotropium treatment with the other two reference treatments.[25,27,29] According to these data, for every 100 000 inhabitants in a hospital catchment area, the savings in costs (due to hospital stays) for treatment with tiotropium compared to placebo (no maintenance bronchodilator treatment) would be more than €137 000. From the point of view of the hospital, this means that for every 100 patients attended (that is, admitted to hospital) and treated with tiotropium, €20 400 can be saved in hospital costs compared to the therapeutic option of "doing nothing" (that is, no maintenance bronchodilator treatment). The savings are thanks to a shortening of hospital stays by 60 days.

One of the therapeutic options most widely used instead of tiotropium is ipratropium. We therefore performed an analysis comparing these two options to assess the costs generated and the possible savings obtained. We found that for every 100 000 inhabitants in the catchment area, the savings produced due to both a shorter stay in hospital and a decrease in percentage of exacerbations achieved with tiotropium compared to ipratropium would be €102 548 (due to a decrease in hospital stays of 479 days per year) (Table 5). From the point of view of the hospital, this means that, for every 100 patients admitted to hospital and treated with tiotropium instead of ipratropium, €15 193 a year can be saved for hospital stays, derived from saving more than 126 days/year in hospital stays.

Another therapeutic option commonly used as a comparator in controlled clinical trials of tiotropium is salmeterol. Table 5 shows the pharmacoeconomic analysis taking into account the hospital stays in each group of patients; in this case the final assessment was for 6 months. The savings corresponding to the decrease in the number of days in hospital for an exacerbation with use of tiotropium compared to salmeterol would be €45 420 for every 100 000 inhabitants in a hospital catchment area in Spain, due to a saving in hospital stays of 107 days during 6 months. From the point of view of the hospital, this means that for every 100 patients admitted to hospital and treated with tiotropium instead of salmeterol, €6780 can be saved every 6 months, due to a decrease in hospital stays of 16 days every 6 months.

Savings in the Spanish National Health System thanks to fewer exacerbations. A previous study retrospectively collected the medical histories of patients with acute COPD exacerbations (of moderate or severe intensity according to SEPAR criteria).[19] The study assessed a total of 246 cases from 4 tertiary hospitals in Spain (including our own referral hospital) between 1999 and 2001. The mean length of hospital stay was 7.77 days per patient, with a mean daily cost of €258.75 (mean cost per exacerbation of €2011). This included all costs derived from hospitalization of these patients (room and board, intensive care unit, admission to the ward, medication, and diagnostic tests), and was the number we used as the mean cost per exacerbation and patient in Spain. For tiotropium, the

TABLE 5
Hospital Stays and Costs of Using Tiotropium Versus the Other Treatment Options*

Drug	Mean Length of Hospital Stay in Days per Patient With Moderate or Severe COPD[25,27,29]	Mean Daily Cost, €	Per 100 000 Inhabitants	
			Length of Stay in Days	Cost, €
Placebo†	1.2/year	340	809	275 060
Tiotropium	0.6/year	340	404	137 360
Ipratropium	2.13/year	298	1436	427 928
Tiotropium	1.42/year	340	957	325 380
Salmeterol	1.14/6 months	338	768	259 584
Tiotropium	0.98/6 months	324	661	214 164

*COPD indicates chronic obstructive pulmonary disease.
†Any COPD treatment other than maintenance bronchodilator treatment.

daily cost of this medication at recommended retail prices (€1.91) was added to the mean daily cost of each patient.

Table 6 presents the results of the pharmacoeconomic analysis done for the number of exacerbations experienced by patients included in the clinical trials analyzed.[25,27,29] The number of exacerbations per 100 patients with COPD in the tiotropium group was 41% lower than in the placebo group (any medication except long-acting bronchodilators), corresponding to a saving per 100 patients treated with tiotropium versus placebo of more than €7200. The number of exacerbations decreased by more than 37% with tiotropium, compared with ipratropium, corresponding to a saving of more than €8000 per 100 patients. The saving when tiotropium was used instead of salmeterol was more than €6600, due to a 25% decrease in the number of exacerbations.

Discussion

Economic pressures on the health care system[37] and the undeniable increase in consumption (and cost) of medications[38] have stimulated the development of methods for assessing the costs and outcomes of health care. Pharmacoeconomics has become an essential tool for economic assessment of drugs. In the pharmacoeconomic assessment used here (cost-effectiveness analysis), positive effects (benefits) are compared with negative ones (costs) for 3 options within the same type of health intervention (long-acting bronchodilators). The benefits were assessed in natural units of effectiveness and were clinically relevant for the disease under study (COPD).[23,30,32,33] Variables included easily measured objective ones, such as change in forced expiratory volume in 1 second compared to baseline, and other subjective variables such as health-related quality of life determined with the St George's Respiratory Questionnaire. The reasons for measuring the quality of life of patients with this disease (or indeed with any other) are to determine the efficacy or effectiveness of medical interventions, improve clinical decisions, assess the quality of health care, estimate the needs of the population, and finally, determine the causes and consequences of differences in state of health between individuals or groups of individuals.[37]

The cost-effectiveness analysis is applicable when the pharmacological treatments compared have a different degree of effectiveness (as has been shown) but share the same therapeutic goals, and so can be measured with the same units of effectiveness.[39,40] Clearly, the main constraint on such analysis is that only treatments whose outcomes can be expressed in the same health units can be compared. Furthermore, cost-effectiveness analysis only allows relative comparisons; it cannot provide information on whether the costs exceed benefits or vice versa, that is, the intrinsic value of health care programs or interventions is not investigated.[41] However, such an analysis is a good tool that may help physicians to make better clinical decisions, above all, when a variety of similar treatments are available.[42]

The present analysis is subject to a number of other limitations. For example, the clinical trials used in the analysis were relatively short; therefore efficacy results beyond 1 year are not available. This could be important in a chronic (and, at present, irreversible) disease such as COPD. Furthermore, we have no data on indirect costs (related essentially to productivity). Even so, for the comparison of tiotropium with salmeterol, the number of days of inactivity due to exacerbations (8.3 days for tiotropium vs 11.1 days for salmeterol[29]) could provide an indication of indirect costs (using, for example, the minimum wage). Nevertheless, given our methodology and the fact that many of the hospital patients affected by this disease have retired (mean age >65 years),[20,43,44] these indirect costs will not be particularly relevant to the final analysis.

Despite these limitations, our study has sufficient external validity for its findings to be taken into account when long-acting bronchodilators are prescribed because we have used up-to-date costs available for Spain and the best level of scientific evidence currently available.

The external validity of the analysis is further supported by the fact that we have compared the most widely used drugs, assessing their impact in the hospital setting (both with regard to shorter stay in hospital and number of admissions for exacerbations).

For the sensitivity analysis, our study population comprised patients with moderate or severe COPD in our province of Spain (2965 patients). The findings of

TABLE 6
Exacerbations per Patient and Associated Hospital Costs[25,27,29]

Drug	No. of Exacerbations per 100 Patients[25,27,29]	Decrease in Exacerbations, %	Mean Daily Cost per Hospitalization for Exacerbation, €	Per 100 Patients, €
Placebo*	9.4	41.49	259	18 917
Tiotropium	5.5		274	11 709
Ipratropium	11.7	37.60	259	23 545
Tiotropium	7.3		274	15 542
Salmeterol	16.0	25.00	259	32 199
Tiotropium	12.0		274	25 548

*Any treatment of chronic obstructive pulmonary disease other than maintenance bronchodilator treatment.

TABLE 7
Savings Due to Use of Tiotropium Compared to the Other Therapeutic Options

Drugs	Decrease in Number of Exacerbations, %[25,27,29]	Decrease in Number of Days in Hospital, %[25,27,29]	Mean Daily Cost, €	Per 100 000 Inhabitants Covered by Hospital†		
				Rate of Admission[44]	Days in Hospital[44]	Saving, €
Placebo*	41.5	50.0	233	118.35	11	213 838
Tiotropium			235‡	69.24	5.5	
Ipratropium	37.6	33.3	233	118.35	11	174 906
Tiotropium			235‡	73.85	7.4	
Salmeterol	25.0	14.0	233	118.35	11	105 174
Tiotropium			235‡	88.76	9.5	

*Any treatment of chronic obstructive pulmonary disease other than maintenance bronchodilator treatment.
†The mean daily cost per patient-day in hospital was €233. This figure includes direct health costs (drugs, oxygen, hospital supplies, health staff, diagnostic tests, etc) and indirect costs (arising from admission to a public institution, such as cleaning, administration, security, etc).[44]
‡The recommended retail price of tiotropium was used (€1.91/day)

this sensitivity analysis might have been different if we had analyzed the number of patients admitted to hospital for COPD, that is, the rate of hospital admission for COPD exacerbations, instead of the prevalence of the disease. Table 7 compares the savings for hospitals derived from use of tiotropium instead of the other therapeutic options in terms of fewer hospital admissions (rate of exacerbations per patient) and shorter hospital stays,[25,27,29] using the findings of a previous study in Andalusia.[44] In that study, which analyzed the total number of admissions due to COPD (related diagnostic groups 088 and 541 with an admission diagnosis corresponding to least one of the following codes of the International Classification of Diseases: 491, 492, 493.2, 494, and 496) in Andalusian hospitals, the mean hospital stay in Andalusia was 11×8.4 days, the rate of admission was 118.35 patients per 100 000 inhabitants, and a minimum cost of €233 per day was generated.

According to these data (rate of admission, mean stay, and cost per day in hospital) for our province of Andalusia, the savings associated with use of tiotropium compared to the option of "any COPD treatment, other than bronchodilator maintenance treatment" may have exceeded €210 000. These savings were somewhat lower when tiotropium was compared with ipratropium (€174 000) and salmeterol (€105 000) (Table 7), but they are still substantial. The mean savings achieved by avoiding admission to hospital due to a decrease in the number of exacerbations per patient[27] would, on its own, be greater than €570 per patient treated with tiotropium instead of ipratropium.

In conclusion, this study has shown that tiotropium is more cost-effective than the other two treatments considered clinically effective, although we must remember that, strictly speaking, in pharmacoeconomics, a treatment is better if the cost-effectiveness ratio is smaller than that of the comparator option. Effectiveness was measured with the following variables of proven clinical relevance in COPD patients: *a)* forced expiratory volume in 1 second (larger increase vs ipratropium and salmeterol); *b)* clinically measurable health-related quality of life (better in patients treated with tiotropium than in those who took ipratropium or salmeterol); and *c)* decrease in dyspnea (less severe dyspnea in patients treated with tiotropium compared to those who took ipratropium or salmeterol). Although tiotropium is more expensive, its cost-effectiveness ratio was better for the aforementioned variables, as measured by mean cost-effectiveness. Finally, tiotropium is more effective than ipratropium and salmeterol at reducing the number of admissions to hospital for exacerbations and decreasing the length of hospital stay in COPD patients. In all cases, tiotropium was more cost-effective than the other comparator options, and so use of this drug provides considerable savings in a hospital setting.

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