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Probabilistic cost-minimisation analysis of darbepoetin alpha versus epoetin alpha in treating anaemia secondary to chronic renal failure. Assessment in Spanish clinical practice

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Abstract
Introduction: The direct transfer of the results of pharmaco-economic studies between countries may not be suitable if the proper adaptations are not made to take into account differences in treatment patterns, resource use, and costs from country to country.
Objective: To estimate the cost in Spain of treating anaemia secondary to chronic renal failure with darbepoetin alpha or epoetin alpha from a review and analysis of available current information. In addition, the role of the route of administration as a main driver of the cost will be analysed.
Method: Population: patients with chronic renal failure induced anaemia. Data: Medline and Embase search of studies directly comparing erythropoiesis stimulating agents. Analysis: Cost minimization analysis from the perspective of a hospital pharmacy department. The main outcome chosen was the difference between the average cost per patient undergoing a 30-day treatment with epoetin alpha versus darbepoetin alpha.
Results: a) Haemodialysis: changing from epoetin alpha to darbepoetin alpha is associated with a cost reduction of 8.67%; 95% CI, −1.34 to 17.92 (€uro17.48; 95% CI, −2.70 to 36.13); probabilistic analysis showed that the use of darbepoetin alpha could be associated with a cost-saving probability of 94.9%. The IV administration yielded a decrease in costs of about 16.00%; 95% CI, −2.38 to 36.77 (€uro41.78, 95% CI: −6.21 to 96.04); *b)* Pre-dialysis: darbepoetin alpha is associated with a cost reduction of about 11%-32%.

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Conclusions: The use of darbepoetin alpha for the treatment of chronic renal failure induced anaemia (haemodialysis and pre-dialysis) shows higher cost efficiency than epoetin alpha in Spain; these differences increase with IV administration.

PALABRAS CLAVE
Darbepoetina alfa;
Epoetina alfa;
Anemia;
Insuficiencia renal crónica;
Minimización de costes;
Modelo probabilístico

Análisis probabilístico de minimización de costes de darbepoetin alfa frente a epoetina alfa en el tratamiento de la anemia secundaria a insuficiencia renal crónica. Valoración en la práctica clínica española

Resumen
Introducción: La transferencia directa de los resultados de estudios farmacoeconómicos de un país a otro no es adecuada si no se procede previamente a una adaptación de los datos a cada territorio, debido a la diversidad de utilización de recursos así como a las diferencias de costes entre países.
Objetivo: Estimar el coste en España del tratamiento de la anemia secundaria a insuficiencia renal crónica con epoetina alfa o darbepoetin alfa, a partir de una revisión y un análisis de la información actualmente disponible. Además, se analiza el papel de la vía de administración como factor modulador del coste del tratamiento.
Método: Población: pacientes con anemia secundaria a insuficiencia renal crónica. Extracción de datos: búsqueda en Medline y Embase de estudios de comparación directa de los agentes estimulantes de eritropoyesis. Tipo de análisis: análisis probabilístico de minimización de costes. Perspectiva: servicio de farmacia del hospital (costes farmacológicos). Variable principal: diferencia del coste medio por paciente del tratamiento de 30 días con epoetina alfa respecto de darbepoetin alfa.
Resultados: a) Hemodiálisis: la sustitución de epoetina alfa por darbepoetin alfa se asocia a una reducción mensual de costes del 8,67 %; intervalo de confianza (IC) del 95 %, −1,34 a 17,92 (17,48 €; IC del 95 %, −1,38 a 36,13); el análisis probabilístico mostró una probabilidad del 94,9 % de que la utilización de darbepoetin alfa estuviera asociada a una reducción del coste. Mediante la administración por vía intravenosa, la disminución es del 16,00 %; IC del 95 %, −2,38 a 36,77 (41,78 €; IC del 95 %, −6,21 a 96,04). *b)* Prediálisis: la reducción de costes con darbe- poetin alfa se sitúa en el rango más probable del 11-32 %.
Conclusiones: La utilización en España de darbepoetin alfa en el tratamiento de la anemia secundaria a insuficiencia renal crónica (hemodiálisis y prediálisis) presenta una eficiencia superior a la estimada con epoetina alfa; esta diferencia en costes aumenta con la administración por vía intravenosa.

Introduction

Chronic renal failure (CRF) is a remarkably relevant health problem in Spain, particularly in its terminal stage.[1] Anaemia, a common complication of this condition, requires frequent blood transfusions which decrease patients' quality of life and puts them at risk for catching viral infections.

The appearance of erythropoesis-stimulating agents (ESAs) reduced the need for transfusions and increased patient well-being, resulting in widespread use of these drugs. Epoetin alpha (EPO) was the first ESA to appear in the therapeutic line-up. It was followed by other similar agents, such as epoetin beta, darbepoetin alpha (DBT) or epoetin delta, and most recently by pegylated epoetin. Both EPO and endogenous erythropoietin possess 3 sugar chains, while DBT has 5 chains. This variation has a decisive influence on its average life; as a result, epoetins can be administered weekly, and DBT monthly. Another factor that sets them apart is the route of administration used: both epoetins and DBT may be used by the subcutaneous (SC) or intravenous (IV) routes; however, epoetins are less efficient when administered IV in respect with the SC route,[2] while DBT's efficiency is similar by both routes.

Many pharmacoeconomic analyses have been performed in order to determine which is the most efficient way to use ESAs. However, nearly all studies were carried out in such countries as the United States. It has been shown that geographical extrapolation of pharmacoeconomic

assessments is not possible, mainly because there are such important differences in clinical practice between different countries.[3-6] In the particular case of the ESAs, obvious differences can be observed between economic results arising from different clinical procedures from country to country, including neighbouring ones,[7] or due to temporary relevant differences in cost determination factors.[8] Several authors[9-11] have reviewed the existing clinical trials with EPO and DBT in order to compare the efficiency of the two by means of a cost minimisation analysis. In that analysis, the evaluation of pharmacological costs was done based on values taken from the Average Wholesale Price (AWP) representing the mean sale cost of drugs in the United States, which is very different from the cost established in Spain. Not only are the costs of 1U EPO and 1 µg DBT in that country clearly higher than in our own (159 and 298, respectively, but in addition, the cost relationship (1 µg DBT: 200U EPO) is 1.87 in the USA, and 1.00 in Spain. For all of these reasons, the results of these pharmacoeconomic assessments cannot be applied in Spain without making adjustments for normal practice and prices in our country.

The objective of this study is to estimate the cost, in Spain, of treating anaemia secondary to CRF using either EPO or DBT by reviewing and analysing current information. A secondary objective is to analyse factors that affect the cost of both treatment alternatives.

Method

Study design

The study was carried out in patients who presented anaemia secondary to CRF. Two different patient subgroups were formed: *a)* in dialysis and *b)* in pre-dialysis. In the first group, given that most of the dialysis patients were undergoing HD (7.85:1 compared with those undergoing PD), we only counted HD patients. For all patients, the ESA was dispensed through the pharmacy service of the corresponding hospital in accordance with Spanish law. The patients were either naïve (pre-dialysis group) or those who, once stable with respect to the dosage of one ESA and their haemoglobin levels (Hb), would change to a different drug (dialysis group).

As there were no significant differences with respect to the effectiveness of different ESAs for treating anaemia secondary to CRF, the pharmacoeconomic analysis used in this study was a cost minimisation model which assumed similar results and established the efficiency difference based on those costs.

In Spain, ESAs are only dispensed through hospital pharmacies. For that reason, the study was performed from a hospital pharmacy perspective. That fact means that the costs incorporated into the study are those of acquiring the ESAS that were administered.

The time horizon for treating anaemia was adjusted to that found in published studies: normally, 24 weeks.

The treatment alternatives that were initially considered were all ESAs indicated for treating CKD-associated anaemia (EPO, epoetin beta, epoetin delta, pegylated epoetin, and DBT), requiring only that they be evaluated simultaneously

in the same study for a direct comparison to be permitted. The analysed routes of administration were the ones that are generally used: IV and SC. Dosage guidelines correspond with those authorised in each ESA's package leaflet.

Data extraction

A bibliographic search was run on Medline, Embase and the *Índice Bibliográfico Español en Ciencias de la Salud* with no time, publication or language limits. We extracted studies that met the direct comparison criteria, whether parallel or consecutive, of treatment costs with ESAs, as well as those that performed an efficiency analysis for each treatment alternative, making express mention of the doses that were administered to reach a target Hb and using the doses recommended in our country. Studies carried out using doses that are not authorised according to package leaflets approved in Spain were excluded. We subsequently reviewed the bibliographical references in the selected articles and also extracted any studies that met the criteria specified above. Given the limited information found in conference presentations, these were not used in the study.

Data for Hb levels and the doses that were used were then extracted from the studies that had been selected. Data on the size of each analysed sample and the route of administration were also extracted.

Efficiency data

In the dialysis subgroup, the resulting variable was the Hb level at the time of changing the ESA, as well as the final recorded level; both were measured in g/dL. These values were finally combined in a weighted form in order to establish a median value of Hb at the time of the change and at the end of the study. Lastly, we verified efficiency equality between both parameters, which justifies choosing the cost minimisation analysis.

Cost estimation

Given the perspective of the present study, the model incorporates only the cost of those ESA used in treating anaemia (see Appendix).

Probabilistic analysis

In order to incorporate not only the uncertainty arising from the results (first-order uncertainty), but also that associated with their probability distributions (second-order uncertainty), we then performed a probabilistic analysis.

Subgroup analysis

EPO and epoetin beta have shown themselves to behave differently depending on the route of administration in use,[2] however, DBT can be used in with both IV and SC delivery with the same efficiency.[12] This distinguishing factor justifies a differentiated analysis of patients according to the route of administration used in each study. Therefore, after an analysis of the total patient group, we proceeded to a subanalysis for each of the 2 routes, SC and IV.

Table 1 Summary of results of using erythropoesis-stimulating agents and the haemoglobin values reached in clinical trials to evaluate effectiveness

Author	Ref.	n[a]	Route	DBT		EPO		Dose ratio
				Dose/week, µg	Hb, g/dL	Dose/week, U	Hb, g/dL	
Nissenson et al	13	169	IV	54.18	11.4	12 636	11.2	248
Vanrenterhem et al	14	134	IV	27	10.94	6700	11.0	233
		213	SC	28	10.97	5000	11.0	179
Locatelli et al	15	76	IV	21.5	11.9	5040	11.3	234
		267	SC	22.7	11.2	4160	11.2	183

DBT indicates darbepoetin alpha; EPO, epoetin alpha; Hb, haemoglobin; IV, intravenous; SC, subcutaneous.
[a]Sample size.

Table 2 Summary of results of using erythropoesis-stimulating agents and the haemoglobin values reached in treatment substitution studies, intravenous route

Author	Ref.	n[a]	DBT		EPO		Dose ratio
			Dose/week, µg	Hb, g/dL	Dose/week, U	Hb, g/dL	
Martínez et al	17	260	29.63	11.8	7407	11.6	250
Del Vecchio et al	18	146	28.56	11.3	5793	11.1	203
Molina et al	19	20	62.58	12.1	12 315	11.3	197
Brunkhorst et al	20	900	19.92	11.7	4659	11.5	234
Ardèvol et al	21	34	35	12.1	11 081	12.0	317
Kessler et al	22	217	22.32	11.6	5452	11.4	244
Pérez et al	23	24	34.6	13.0	8697	12.6	251
Mann et al	24	196	13.3	11.4	2520	11.4	189
Icardi et al	25	40	24.6	11.4	8000	11.4	325
Raymond et al	26	482	53.1	11.4	12 939	11.4	244
Bock et al	27	29	24.3	11.8	6758	11.9	278

DBT indicates darbepoetin alpha; EPO, epoetin alpha; Hb, haemoglobin.
[a]Sample size.

Results

Haemodialysis

Included studies
The pharmacoeconomic analysis was carried out based on the studies that directly compared EPO to DBT, whether they were clinical trials[13-15] or observational studies in which we substituted treatment with DBT[16-28] once the patients were stabilised with respect to the EPO dose administered and their Hb levels in order to minimise the statistical regression.

Epoetin beta could not be included in the analysis because only one study evaluated the 3 ESAs as a group.[27] Pegylated epoetin and epoetin delta were not included either because there were no available comparison studies with DBT, added to the fact that the latter had not yet been marketed in Spain at the time this study was carried out. Data extracted from pharmacological resources are shown in Tables 1-3.

Cost analysis
The analysis was carried out from a hospital pharmacy perspective. For this reason, only those costs associated with the ESAs are included as relevant, and they are expressed as the 2008 manufacturer sale price (MSP) in euros (€).[29] In this way, the estimated monthly cost per patient receiving EPO treatment in the Spanish health care system was € 201.56, while for DBT it was € 183.97 and we can calculate a monthly EPO-DBT cost increment of € 17.59.

Probabilistic analysis
The Monte Carlo simulation with 1000 repetitions (Figure 1) showed equality in the clinical result ({Prob [Hb_{DBT} – Hb_{EPO}] > 0} = 0.516; {Prob [Hb_{EPO} – Hb_{EBT}] > 0} = 0.484), which justifies choosing the cost minimisation analysis, while also showing a cost difference of €uro17.48 between EPO and DBT (95% CI, −2.7 to 36.13) (Table 4).

The probability analysis for reducing costs by substituting EPO treatment with DBT showed a 94.9% probability that

Table 3 Summary of results of using erythropoesis-stimulating agents and the haemoglobin values reached in treatment substitution studies, subcutaneous route

Author	Ref	n[a]	DBT		EPO		Dose ratio
			Dose/week, µg	Hb, g/dL	Dose/week, µg	Hb, g/dL	
Martínez et al	17	566	24.74	11.5	5124	11.6	207
Del Vecchio et al	18	804	25.43	11.2	5122	11.4	201
Molina et al	18	19	33.74	12.4	8753	12.1	259
Brunkhorst et al	20	602	21.61	11.4	4632	11.4	214
Kessler et al	22	791	23.32	11.3	4585	11.4	197
Shaheen et al	28	33	20.8	12.8	7454	11.6	358
Mann et al	24	905	16.1	11.3	3080	11.6	191

DBT indicates darbepoetin alpha; EPO, epoetin alpha; Hb, haemoglobin.
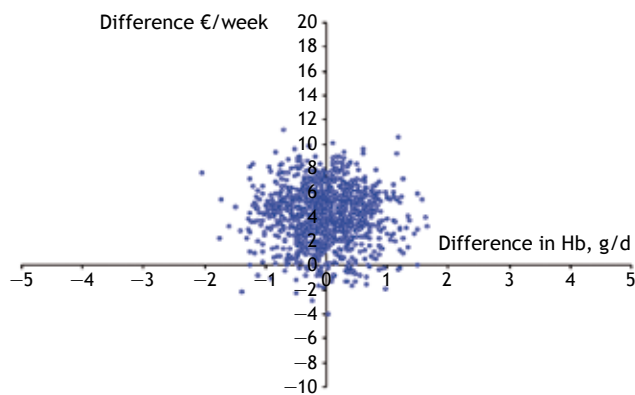[a]Sample size.

Figure 1 Graph of the cost difference values compared to results after the 1000-repetition sample of the results that were obtained. Hb indicates haemoglobin.
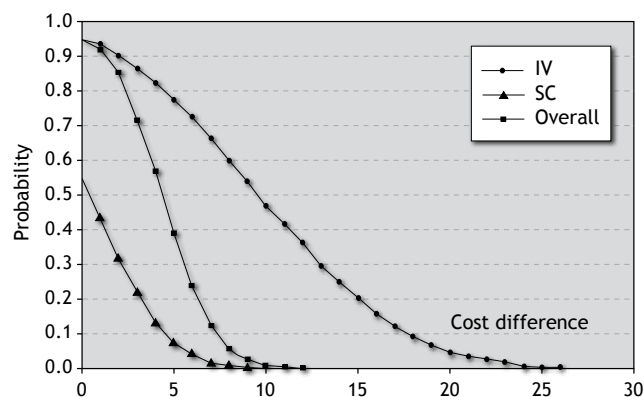
Table 4 Estimated average monthly cost per patient for treatment with EPO and DBT

Drug	Cost/ patient/ 30 days, €	95% CI, €
DBT	184.16	171.73 to 197.87
EPO	201.64	187.20 to 215.87
Cost difference (EPO-DBT)	17.48	−2.7 to 36.13
IV DBT	219.38	188.70 to 253.38
IV EPO	261.17	293.93 to 301.11
Cost difference (EPO-DBT)	41.78	−6.21 to 96.04
SC DBT	162.81	145.80 to 183.25
SC EPO	164.61	146.01 to 184.71
Cost difference (EPO-DBT)	1.80	−25.84 to 28.02

DBT indicates darbepoetin alpha; EPO, epoetin alpha; IV, intravenous; SC, subcutaneous.

Figure 2 Probability curve showing the reduction of mean weakly cost with darbepoetin alpha compared with epoetin alpha depending on the route of administration. SC indicates subcutaneous; IV, intravenous.

administering DBT would be less expensive. Consequently, we can deduce from its graph that there is a 50% probability that monthly costs will decrease by €uro17.91 per patient (Figure 2).

Subgroup analysis

Disaggregating the data extracted for the route of ESA administration demonstrated that the analysed medications behave differently. A new probabilistic analysis using a Monte Carlo simulation with 1000 repetitions per subgroup, showed that changing from IV EPO to IV DBT resulted in substantial savings in the DBT dose (€uro41.78/patient/month; 95% CI −6.21 to 96.04) (Table 4), while change from SC EPO to SC DBT revealed a cost difference that was not significant (€uro1.80/patient/month; 95% CI, −25.84 to 28.02).

The graph of the cost reduction probability curve determined that there was a 94.9% probability of generating savings by substituting EPO with DBT (Figure 2). Savings were estimated at €uro40.84 with a probability of 50% for the IV route.

Sensitivity analysis

Given that the relevant variable is the cost of the ESAs, we performed a sensitivity analysis to reduce the cost of the least efficient ESA (EPO) by 50% (Figure 3). When delivered by the IV or SC route, EPO needs an additional discount of

8.7% in order to reach the same efficiency as DBT. In the case of IV delivery, the additional price reduction would have to reach 16.1%.

Pre-dialysis

Included studies

For the pre-dialysis patient subgroup, we analysed the data from studies evaluating the DBT efficiency vs. EPO efficiency[26,30-38](Table 5). However, it was not possible to properly combine the results we obtained because of their heterogeneity, especially referring to the different doses that were administered.

Cost analysis

For that reason, the analysis focussed on estimating the EPO/DBT dose ratio. We observed that it was in the 200-293 range in most cases, which indicates that the theoretical relationship of 200U EPO: 1 µg DBT is not maintained in clinical practice. We subsequently evaluated the costs and estimated a DBT/EPO cost ratio of 0.68-0.89 (Table 5) which translates into an 11%-32% cost reduction by using DBT rather than EPO.

Discussion

The cost minimisation analysis that examines how DBT and EPO are used in Spanish clinical practice for treating anaemia secondary to CKD shows that costs are reduced by using DBT rather than EPO, and that this applies both to group of patients undergoing haemodialysis and to pre-dialysis patients; in the first group, IV delivery is a more efficient route.

Consequently, in a hospital attending 100 of these patients annually, the estimated savings would be € 20 976 (8.67%
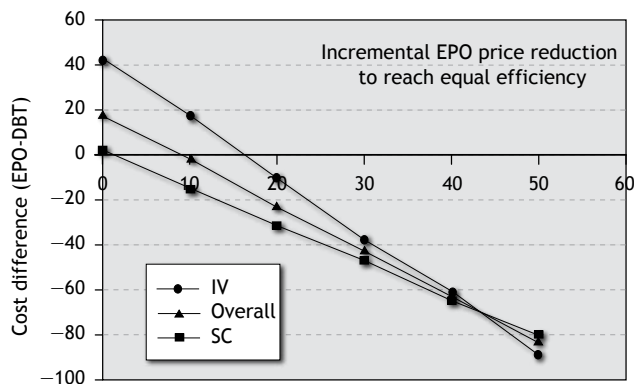

Figura 3 Sensitivity analysis. Cost variation for EPO. DBT indicates darbepoetin alpha; EPO, epoetin alpha; IV, intravenous; SC, subcutaneous.

less; 95% CI, −1.34 to 17.92), and could reach € 50 136 yearly (16.01%; 95% CI, –2.38 to 36.77) if delivered exclusively by the IV route in haemodialysis patients. Furthermore, the cost of EPO should be 8.7% less than that of DBT to reach the same efficiency level in the overall context of SC and IV delivery; if delivery is by the IV route, that incremental discount would reach 16.1%.

This result is significantly different from conclusions in other geographic areas, which proves that direct geographic extrapolation of economic assessment data is not possible.[39] In this manner, Morreale et al[9] determined that the mean annual cost with DBT is 1.2-3.0 times higher than EPO, which is mainly due to the fact that those prices are significantly higher than the ones in our country. Therefore, if we adapt

Table 5 Summary of results of DBT and EPO for treating anaemia secondary to CKD during pre-dialysis

	Ref	N.º (EPO/DBT)	EPO		DBT		Cost ratio[a]	Cost ratio[b]
			Dose/week, U	Cost, €	Dose/week, U	Cost, €		
Vekeman et al[c]	30	66 822	26 509	228.8	118.6	198.5	0.89	223
Locatelli et al[d]	31	129/37	7000	58.83	31.5	52.70	0.89	200
			3.983	33.47	23.8	39.81	1.19	167
Papatheofanis et al[d]	32	396/393	11 639	97.81	45.2	75.56	0.77	257
Duh et al[d]	33	595/260	11 536	96.95	42.5	71.10	0.73	271
Duh et al[d]	34	293/102	12 748	107.10	43.5	72.77	0.68	293
Papatheofanis et al[d]	35	200/200	10 155	85.34	37.6	62.87	0.74	270
Molina et al[e]	36	39	2500	21.02	11.20	18.73	0.89	223
Raymond et al[e]	26	111	5516	46.36	25.20	42.16	0.91	219
Hertel et al[e]	37	524	10 369	87.14	24.5	40.90	0.47	423
Hymes et al[e]	38	153	7090	59.58	24.7	41.32	0.69	287

DBT indicates darbepoetin alpha; EPO, epoetin alpha.
[a]DBT/EPO cost ratio.
[b]EPO/DBT dose ratio.
[c]Hospitalised patients.
[d]Outpatients.
[e]Patients changing treatment.

that review to Spanish prices, the result becomes inverted, and the DBT/EPO cost ratio of 1.49 becomes 0.79 in one of the studies that we analysed, and changes from 1.40 to 0.72 in another. A budget impact analysis published after the present study was completed also indicates that DBT could create savings in the Spanish health care system. However, the price difference alone does not completely explain the cost savings from DBT use. Earlier, Scott 41 pointed out that above a certain EPO dosage threshold, which he established at 7000 U, transferring patients from EPO to DBT requires a smaller dose than the theoretical equivalent indicated by the classic 200 U EPO: 1 μg BT relationship; he observed a ratio of nearly 280:1 with initial EPO doses of 7000-15000 U. That modification to the ratio stated above has been corroborated in other geographical areas, such as Australia, Asia or Europe,[23,27,28] including Spain as well.[21]

In addition, the route of administration has a decisive influence on increasing DBT efficiency compared with that of EPO. IV administration contributes increased efficiency to DBT use.

This study has certain limitations. The first is that the cost estimates for Spain were calculated based on the mean cost of 1 U of EPO and 1 μg DBT, and not to the number of vials that are used, because this information is not described in published studies. However, this skewing tendency is minimised because it affects both drugs equally and the unit cost was included in a log-normal probability distribution function. The second limitation is that the mean cost per patient was based on global consumption without considering the variations occurring from dosage adjustment. This entails a loss of information, although it does not affect the overall result. The third is that real-life practice patterns may be noticeably different from those observed in the studies that were evaluated; however, there were some Spanish observational studies that did reflect that situation, and the doses that were used were included in a log-normal probability distribution function which minimises that effect.

This study's strengths include the exhaustive overall review and update of all of the available literature, with no geographical, linguistic or time limits. We also used the methodology that is currently recommended for probabilistic analysis, which enables us to analyse second-order uncertainty associated with the probability distributions of the relevant parameters.

To conclude, this study clearly shows that it is not possible to transfer the results of pharmacoeconomic studies from country to country without readapting those results according to the differences that are normally present. In this case, substituting EPO for DBT to treat anaemia secondary to CKD would generate a cost reduction in Spain. For haemodialysis patients, the annual yearly savings is estimated at €uro20 976 per 100 patients (8.7% reduction) and could reach €uro50 136 with IV delivery (16.1%); in the pre-dialysis group, the most probable relationship is between 11% and 32%. These results should be confirmed by naturalistic studies in our country, in which the effectiveness and efficiency of the described therapeutic strategies can be described.

Conflict of interest

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Appendix

The cost of treating anaemia (C_{ESAi}) was estimated using:

$$C_{ESAi} = DU_{ESAi} \times MSP_{ESAi}$$

where D_{UESAi} is the number of administered dosage units (µg or international unit [U]) for each ESA in 30 days and MSP_{ESAi} is the mean unit price of each ESA. This was calculated as the mean cost of each µg or IU estimated according to:

$$MSP_{ESAi} = \Sigma[(MSP_{ESAz})/n_z]$$

where MSP_{ESAz} is the MSP of each marketed format of each product z and nz is the number of units contained in these formats.

In the dialysis subgroup, the C_{ESAi} were as follows: for EPO (C_{EPO}), it was the cost corresponding to the dose used at the moment the patient changed to DBT, once the patient was stabilised with respect to the drug dose administered and his/her Hb level to minimise the statistical regression effect, and for DBT (C_{DBT}) it corresponded to the cost of the DBT used at the time of the last evaluation.

The end result was expressed as a cost per patient per month. Subsequently, we combined the weighted results from each study to estimate the mean cost per patient and per month for every ESA that was analysed.

Lastly, we calculated the treatment cost ratio CR_{ESA} as:

$$CR_{ESA} = [C_{ESA1}/C_{ESA2}]$$

where 1 corresponds to DBT and 2 to other ESAs. In this way, a ratio lower than 1 indicates a lower cost for DBT, ad therefore, better relative efficiency, and a higher ratio would favour the ESA being evaluated.

To express efficiency in an absolute manner, we estimated the cost differences (ΔC_{ESA}) using the following:

$$\Delta C_{ESA} = [C_{ESA2} - C_{ESA1}]$$

here, a value greater than 0 indicates a higher cost for EPO, and therefore, less absolute efficiency; if it is less than 0, it shows greater efficiency for DBT.

The probabilistic analysis was carried out by designing distribution functions corresponding to each variable pertaining to cost (C) and result (R) (Table A1). Next, we performed a Monte Carlo simulation with 1000 random samples, estimating new values for each variable (C_{ESAi}^{*}, R_{ESAi}^{*}) and then proceeding to calculate the mean values ($\check{C}_{ESAi}$, $\check{R}_{ESAi}$) and their corresponding dispersion measurements. Lastly, we estimated the cost difference (ΔC_{ESA}) using:
$\Delta C_{ESA} = [\check{C}_{ESA2} - \check{C}_{ESA1}]$.

Table A1   Probability functions for the parameters in the model

Parameter	Value	SD	Distribution
cEPO	0.0084044	0.00013	Log normal
cDBT	1.67292	0.015	Log normal
nEPO	5.596	192.22	Log normal
Hbt0	11.44	0.4	Normal
nDBT	25.39	0.86	Log normal
Hbte	11.44	0.39	Normal

cDBT indicates cost of 1 µg DBT (at MSP); cEPO, cost of 1 U EPO (at MSP); Hbt0, haemoglobin level at time of change; Hbte, haemoglobin level at 24 weeks; nDBT, DBT dose at 24 weeks; nEPO, EPO dose replaced (in 200:1 proportion compared with DBT).