Departament de Psiquiatria i Psicobiologia Clínica
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COST-EFECTIVITAT DEL TRACTAMENT ANTIDEPRESSIU

Avaluació del cost-efectivitat i cost-utilitat dels antidepressius en el tractament de persones amb trastorns depressius en Atenció Primària de Salut a Catalunya

Tesi doctoral presentada per Antoni Serrano Blanco
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Cost–utility of selective serotonin reuptake inhibitors for depression in primary care in Catalonia

Serrano-Blanco A, Pinto-Meza A, Suárez D, Peñarrubia MT, Haro JM. Cost–utility of selective serotonin reuptake inhibitors for depression in primary care in Catalonia.

Objective: To determine the cost–utility of selective serotonin reuptake inhibitors (SSRIs) for treating depressive disorders prescribed in primary care (PC).
Method: A total of 301 participants beginning antidepressant treatment with an SSRI were enrolled in a prospective 6-month follow-up naturalistic study. Incremental cost–utility ratios (ICUR) were obtained for several comparisons among different SSRIs. To address uncertainty in the ICUR's sampling distribution, non-parametric bootstrapping was carried out.
Results: Taking into account adjusted total costs and incremental quality of life gained, fluoxetine dominated paroxetine and citalopram with 63.4% and 79.3% of the bootstrap replications in the dominance quadrant, respectively. Additionally, fluoxetine was cost-effective over sertraline with 83.4% of the bootstrap replications below the threshold of 33,936 US$/quality-adjusted life year (30,000 €/QALY).
Conclusion: Fluoxetine seems to be a better cost–utility SSRI option for treating depressive disorders in PC.

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Key words: depressive disorder; antidepressive agents; primary health care; economics

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Significant outcomes

- There were no statistically significant differences in effectiveness among fluoxetine, paroxetine, sertraline and citalopram.
- Fluoxetine seems to be a better cost–utility option for treating depressive disorders in primary care.
- There were no differences in dropping-out or switching among treatment groups ($P = 0.8123$).

Limitations

- The study was observational and not randomized, inter-subject variability may limit the ability to detect differences.
- Most of the participants were women. This has to be taken into account when referring results to men.
- The duration of follow-up could be shorter than those expected for long-term economic analyses.

Introduction

Depressive disorders are the most prevalent mental disorders (1–3), generating severe personal burden (4, 5) and high economic costs (6–8). Most individuals with depressive disorders are treated in primary care (PC) (9), usually with selective serotonin reuptake inhibitors (SSRI) (10, 11).

Most of the research comparing different antidepressant options has focused on efficacy and

safety (12). However, cost-effectiveness (13, 14) and cost–utility analyses are attracting increasing attention because they include a wider view of the effects of treatments (15). When analysing cost–utility, costs and effectiveness of the available antidepressant options are measured using quality of life measures (16). Commonly, results are expressed in ratios measuring economic costs and quality-adjusted life years (QALYs) from each of the evaluated options. Cost–utility analyses of the different therapeutical options are crucial to policy makers and clinicians.

Despite the growing amount of cost–utility studies (17), only a few have focused on depressive disorders (15). Among these, pharmacological and psychotherapeutical treatments (18, 19), or different antidepressant medications have been compared. To our knowledge, comparisons of different antidepressant medications have considered SSRI and trycyclics (TCAs) (20–24). It remains unclear if there are differences regarding cost–utility among different SSRIs.

Aims of the study

The aim of the present study was to compare cost–utility among citalopram, fluoxetine, paroxetine, and sertraline prescribed in PC for treating depressive disorders.

Material and methods

Participants

Eligible for participation were patients (aged 18–75 years old) from 16 PC centres from the Barcelona area (Spain), beginning pharmacological antidepressant treatment for treating a depressive disorder from December 2001 to December 2002. Exclusion criteria included i) being under pharmacological or psychotherapeutical antidepressant treatment in the previous 2 months; ii) cognitive impairment as assessed by the PC physician; iii) history of psychotic or bipolar disorder; and iv) history of alcohol or drug abuse or dependence.

Measurements

Current diagnosis and past history of major depressive episodes (MDE) were established using the MDE and the dysthymic disorder (DD) modules of the research version of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I, 25).

Depression severity was evaluated by means of the Patient Health Questionnaire 9-item depression module (PHQ-9) (26). The PHQ-9 is a 9-item self-report questionnaire designed to evaluate the presence and severity of depressive symptoms during the previous 2 weeks. Each of the nine items corresponds to each of the DSM-IV MDE diagnostic criteria, and can be scored from 0 (not at all) to 3 (nearly every day). The final score can range from 0 (absence of depressive symptoms) to 27 (severe depressive symptoms). It has been suggested that scores between 0 and 4 reveal minimal depressive symptoms; scores between 5 and 9 reveal mild symptoms; scores between 10 and 14 reveal moderate symptoms; scores between 15 and 19 reveal moderately severe symptoms; and scores between 20 and 27 reveal severe depressive symptoms (26). Additionally, the PHQ-9 has demonstrated sensitivity to change in depressive status (27).

Health-related quality of life was evaluated using the Spanish version of the EuroQol-5D (28). The EuroQol-5D is a non-disease-specific, generic, societal based instrument for describing and evaluating health-related quality of life. It may be administered in several ways (i.e. self-administered, during an interview or by mail), and consists of a classification system for a population-based preference score or societal index (SI) and a self-assessment score that reveals patient-derived evaluations. The EuroQol-5D classification system comprises five domains of health: mobility, self-care, everyday activities, pain/discomfort and anxiety/depression. Each domain comprises three levels (some, moderate, extreme problems), generating a total of 243 theoretically possible health states on the basis of which the SI is calculated. Values range from 1 (best health state) to 0 (death). However, this index may also provide negative values that correspond to health states perceived as worse than death. Utility scores for these health states were assigned using the readily available Spanish population tariffs (29).

Additionally, sociodemographic information was collected and patients were asked about treatment compliance and use of health-related services. Health-related services included general practitioner sessions, specialized medical sessions (e.g. psychiatry, cardiology, etc.), emergency room sessions and hospital in-patient stay.

Procedure

Participating PC physicians selected consecutively all patients (aged 18–75 years old), to whom they prescribed any antidepressant medication for treating a depressive disorder and which did not fulfil any exclusion criteria. The day the antidepressant

was prescribed was considered day 1, and baseline assessment was performed within the following 7 days.

During these 7 days, a trained clinical psychologist assessed the patients to be included. During a telephone interview: i) exclusion criteria were checked; ii) SCID-I MDE and DD modules, PHQ-9 and EuroQol-5D were administered; and iii) questions related to sociodemographics, treatment compliance, and use of services were asked. Patients correctly selected according to inclusion/exclusion criteria were included and followed-up during 6 months. Patients were re-interviewed in the same way after 3 and 6 months.

An effort was made to preserve the natural course of events. PC physicians prescribed antidepressants and doses based on their own diagnostic assessment (blind to our DSM-IV diagnosis), and performed patient follow-up according to their usual practice. Assessment of patients was performed over the telephone in order to minimize researcher interference (30). Except for reasons of patient safety (suicidal ideation), information gathered by telephone was not disclosed to PC physicians. The validity of telephone assessment of depressive disorder diagnosis and symptom severity has been established elsewhere (31, 32). The study protocol was approved by the ethics committee of Fundació Jordi Gol i Gorina (ref. 1/08/01-411). All participating patients gave their written consent.

Descriptions of costing procedure

Societal cost perspective was used for the calculation of costs. Direct costs were calculated by adding the costs derived from antidepressant and anxiolytic/hypnotic medication and use of health-related services (general practitioner sessions, specialized medical sessions, emergency room sessions, and hospital in-patient stay). The cost of medications was calculated by determining the price per milligram during the study, according to the International Vademecum (Red Book) 2003, and included value-added tax (Appendix 2). Total costs of antidepressant and anxiolytic/hypnotic treatment were calculated by multiplying the price per milligram by the daily dose in milligrams and the number of days receiving such treatment. Costs derived from the use of health-related services were calculated considering the SOIKOS unitary costs database (33). Original costs were calculated in euros (2003 value) but transformed to US$ in order to make data understandable worldwide (1 euro = US$1.1312).

Indirect costs were calculated considering the days under sick leave and by multiplying them by the minimum daily wage in Spain for 2003. Finally, total costs were calculated by adding direct and indirect costs. In Spain, the National Healthcare Service (NHS) is financed by the general taxes levied by the state and, in the municipalities where the study was carried out, it is administered by the autonomous government of Catalonia. Medical visits and hospital admissions are fully covered by the NHS. Medications prescribed are fully covered for retired persons, and partially for those still employed. Sick leave requires a physician's authorization, and patients unable to work continue receiving most of their salary.

When performing cost–utility analyses, two or more therapeutical options are compared in order to determine which one is the best for maximizing the benefits considering the available resources (16). This is achieved by calculating the relationship between the costs of a given intervention (e.g. A) and its consequences, expressed in QALYs, compared with another (e.g. B). This relative value is called incremental cost–utility ratio (ICUR), and it expresses the relationship between the costs and effects of one intervention compared with another. As the duration of the study was only 6 months, neither costs nor outcomes were subject to discounting (16).

Treatment costs during 6 months follow-up were modelled by a multivariate gamma regression with a log link. Gamma modelling has been suggested as a suitable choice for analysing cost data, taking into account the skewness of the distribution of the cost data (34, 35).

QALYs gained over the 6-month period for each treatment comparison were approximated by measuring the 'area under the curve':

$$\text{QALY gained over 6 months} = \begin{cases} \left(\frac{3}{12}\delta_{0-3}\right)0.5 & \text{for } 0-3 \text{ months} \\ +\frac{3}{12}\delta_{0-3} + \left(\frac{3}{12}\delta_{3-6}\right)0.5 & \text{for } 3-6 \text{ months} \end{cases}'$$

where δ_{0-3} is the incremental treatment effect on change in EQ-5D utility score for the first 3 months and δ_{3-6} the incremental treatment effect on change in EQ-5D utility score for the last 3 months. These incremental treatment effects were estimated using multivariate ordinary least squares regressions, adjusting for baseline differences among treatment groups. The covariates included in the models were: age, gender, years of education, employment and marital status, previous MDE, baseline PHQ-9 and EQ-5D utility scores, and antidepressant prescribed.

To address uncertainty in the ICUR's sampling distribution, non-parametric bootstrapping was carried out (36). Five thousand replications were carried out for each treatment comparison. All analyses were performed using SAS software (SAS Institute Inc., Cary, NC, USA; 1999, Ver. 8.00, 4th edn).

Results

Patient characteristics

Of the total 333 participants included, 301 (90.39%) were prescribed with an SSRI (citalopram, fluoxetine, paroxetine or sertraline), comprising the sample of the present study. The other 32 patients received other antidepressants and were not included for the small number of patients per group.

Table 1 describes the sociodemographic and clinical characteristics of the 301 patients included. There were no statistically significant differences among groups in gender, mean age, marital status, employment status, years of education, history of previous MD episodes, baseline PHQ-9, and baseline EuroQol-5D SI mean scores. Most of the participants under sick leave were unable to work because of their depressive state. The mean dosage for fluoxetine at baseline was 19.8 mg; for paroxetine, it was 20.0 mg; for sertraline, 50.0 mg; and for citalopram, 20.0 mg.

A total of 272 (90.3%) of 301 patients completed the 6-month follow-up. Of those lost during follow-up, 12 were prescribed with fluoxetine, nine with paroxetine, five with sertraline, and three with citalopram. Patients lost in follow-up did not show significant clinical and sociodemographic differences when compared with patients completing the follow-up.

A total of 175 patients dropped out or switched to antidepressant treatment during the 6 month follow-up. Among these, 60 were initially in the fluoxetine group (60.2% of this group), 59 in the paroxetine group (53.3% of this group), 32 in the sertraline group (58.8% of this group) and 24 in the citalopram group (62.9% of this group). There were no differences in dropping out or switching among treatment groups ($P = 0.8123$).

Quality of life

All four groups improved their health-related quality of life (Table 2). Table 3 summarizes the results, comparing EuroQol-5D utility scores among antidepressant groups.

Table 1. Sociodemographic characteristics of participants by baseline antidepressant prescription

	Antidepressant prescription at baseline				
	Fluoxetine ($n = 100$)	Paroxetine ($n = 110$)	Citalopram ($n = 38$)	Sertraline ($n = 53$)	Total ($n = 301$)
Gender					
Female (%)	82.0	79.1	79.0	77.4	79.7
Age in years					
Mean (SD)	42.6 (13.2)	45.4 (14.7)	47.3 (17.1)	46.1 (13.5)	44.8 (14.4)
Marital status (%)					
Married/living with a partner	64.0	69.1	60.5	58.5	64.5
Single/divorced/separated/widow/widower	36.0	30.9	39.5	41.5	35.6
Employment status (%)					
Active (currently working, sick leave, unemployed)	69.0	67.3	57.9	64.2	66.1
Not active (retired, student, homemaker)	31.0	32.7	42.1	35.9	33.9
Years of education (%)					
0–8	45.0	53.6	44.7	58.5	53.8
> 9	55.0	46.4	55.3	41.5	46.2
Current diagnosis *n* (%)					
Major depressive episode	40 (40.0)	37 (33.6)	17 (44.7)	15 (28.3)	109 (36.2)
Dysthymic disorder	6 (6.0)	4 (3.6)	1 (2.6)	3 (5.7)	14 (4.7)
Minor depression	16 (16.0)	30 (28.0)	10 (26.3)	16 (30.2)	72 (23.9)
Depressive disorder not otherwise specified	38 (38.0)	39 (35.5)	10 (26.3)	19 (35.9)	106 (35.2)
History of previous MDE (%)					
No	72.0	88.1	81.6	88.7	82.0
Clinical characteristics at baseline (mean [SD])					
PHQ-9	14.7 (5.5)	15.0 (5.3)	16.2 (4.7)	13.9 (5.3)	14.8 (5.3)
EuroQoL-5D societal index	0.48 (0.31)	0.46 (0.29)	0.46 (0.32)	0.40 (0.27)	0.45 (0.30)

SD, standard deviation.

Table 2. Mean change in EuroQol-5D utility scores between 0–3 and 3–6 months by treatment (least squares estimates)

	0–3 months			3–6 months		
Treatment	Estimate	Lower 95% CL	Upper 95% CL	Estimate	Lower 95% CL	Upper 95% CL
Fluoxetine	0.3170	0.2506	0.3834	0.0680	0.0151	0.1210
Paroxetine	0.2992	0.2293	0.3691	0.0893	0.0336	0.1450
Sertraline	0.2780	0.1909	0.3651	−0.0051	−0.0746	0.0644
Citalopram	0.2655	0.1661	0.3649	0.0773	−0.0020	0.1565

CL, confidence limit.

Costs

Six-month total costs (direct plus indirect costs) are summarized in Fig. 1. The adjusted costs for sertraline were US$511.1 per patient, lower than those observed for fluoxetine (US$633.8), citalopram (US$937.7) or paroxetine (US$958.0). This figure also shows the proportions attributable to each type of resource use, taking into account unadjusted data. The majority of costs emerged from days under sick leave, representing 41% of costs obtained for the sertraline group, 54% for the citalopram, 69% for the fluoxetine, and 73% for the paroxetine. When analysing costs derived from the antidepressant prescribed, patients initially prescribed sertraline showed 20% of their costs derived from that antidepressant. Patients prescribed with fluoxetine, paroxetine, and citalopram had somewhat lower costs derived from the antidepressant prescribed (11%, 11%, and 12% respectively). Direct costs (not showed in tables) were lower for the fluoxetine group (US$315.5) when compared with paroxetine (US$395.8), sertraline (US$397.3) and citalopram (US$484.1).

Cost–utility

Bootstrap replications of the incremental costs and QALYs gained with each treatment comparison were plotted (Figs 2–7). As can be seen, fluoxetine dominated paroxetine and citalopram because it was associated to a better cost and quality of life relationship. When comparing fluoxetine to paroxetine, 63.4% of the bootstrap replications were in the fluoxetine dominance quadrant. When comparing fluoxetine with citalopram, 79.3% of the bootstrap replications were in the fluoxetine

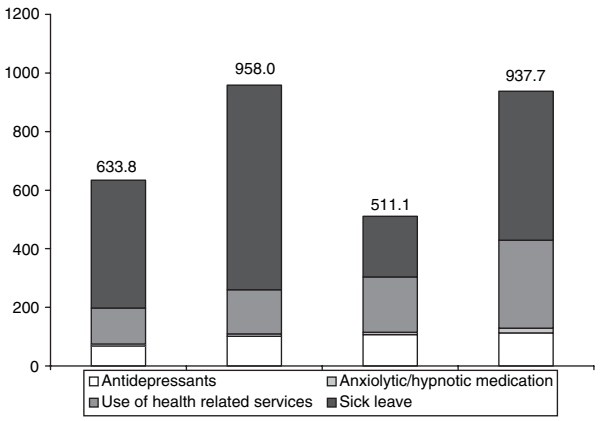

Fig. 1. Total adjusted costs over 6 months (proportions attributed to resource use are based on unadjusted costs).

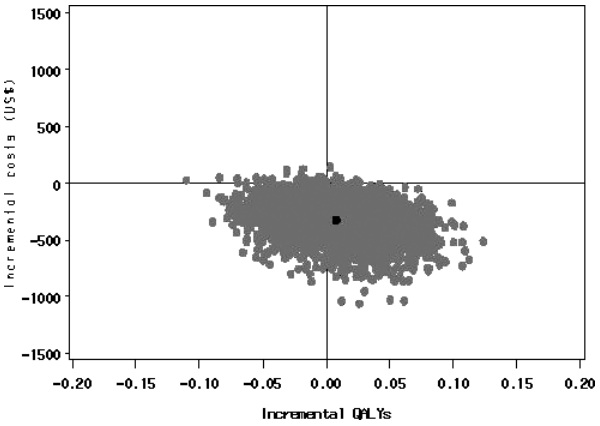

Fig. 2. The point estimate (in black) and 5000 bootstrap replications (in grey) of the total cost and quality-adjusted life year differences between treatment with fluoxetine and paroxetine.

Table 3. Treatment effect on change in EQ5D utility score between 0–3 and 0–6 months (OLS regression) and incremental QALY gained

Treatment comparison		0–3 months				3–6 months				Incremental QALY gained Area under curve
		Estimate	Lower 95% CL	Upper 95% CL	*P*-value	Estimate	Lower 95% CL	Upper 95% CL	*P*-value	
Fluoxetine	Paroxetine	0.0178	−0.0601	0.0957	0.6543	−0.0213	−0.0836	0.0411	0.5035	0.0040165
Fluoxetine	Sertraline	0.0390	−0.0564	0.1345	0.4229	0.0731	−0.0028	0.1490	0.0591	0.0237725
Fluoxetine	Citalopram	0.0515	−0.0558	0.1588	0.3468	−0.0092	−0.0951	0.0766	0.8330	0.018158
Paroxetine	Sertraline	0.0212	−0.0712	0.1137	0.6528	0.0944	0.0210	0.1677	0.0117	0.0197555
Paroxetine	Citalopram	0.0337	−0.0696	0.1369	0.5224	0.0120	−0.0705	0.0946	0.7752	0.014141
Sertraline	Citalopram	0.0125	−0.1056	0.1305	0.8360	−0.0823	−0.1760	0.0114	0.0850	−0.0056145

OLS, ordinary least squares; QALY, quality-adjusted life year; CL, confidence limit.

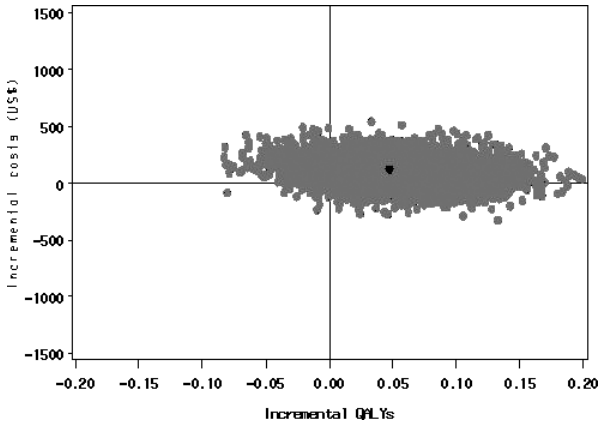

Fig. 3. The point estimate (in black) and 5000 bootstrap replications (in grey) of the total cost and quality-adjusted life year differences between treatment with fluoxetine and sertraline.

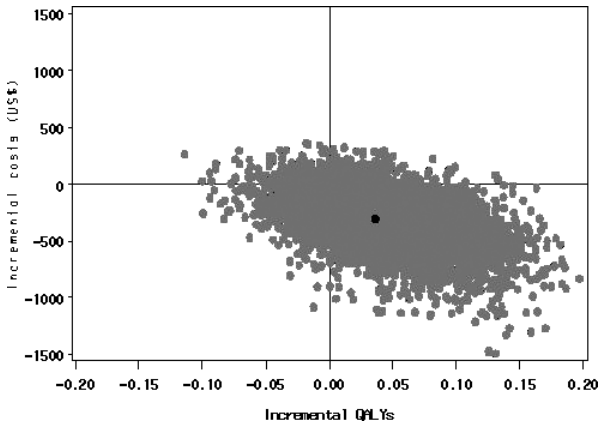

Fig. 4. The point estimate (in black) and 5000 bootstrap replications (in grey) of the total cost and quality-adjusted life year differences between treatment with fluoxetine and citalopram.

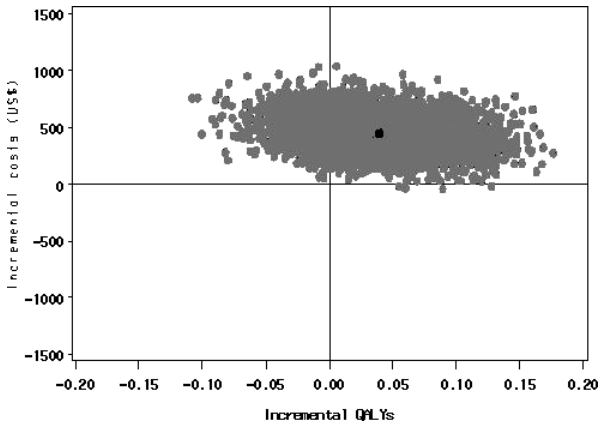

Fig. 5. The point estimate (in black) and 5000 bootstrap replications (in grey) of the total cost and quality-adjusted life year differences between treatment with paroxetine and sertraline.

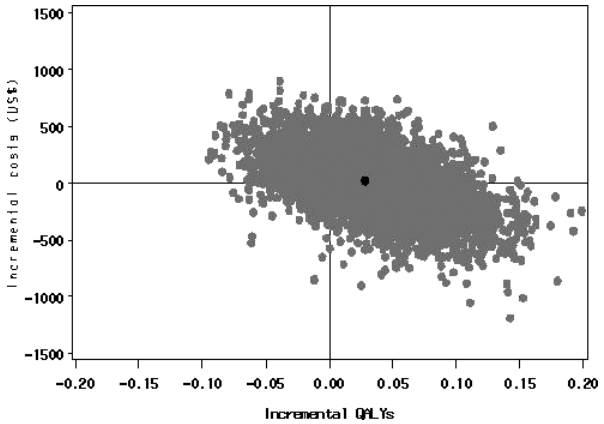

Fig. 6. The point estimate (in black) and 5000 bootstrap replications (in grey) of the total cost and quality-adjusted life year differences between treatment with paroxetine and citalopram.

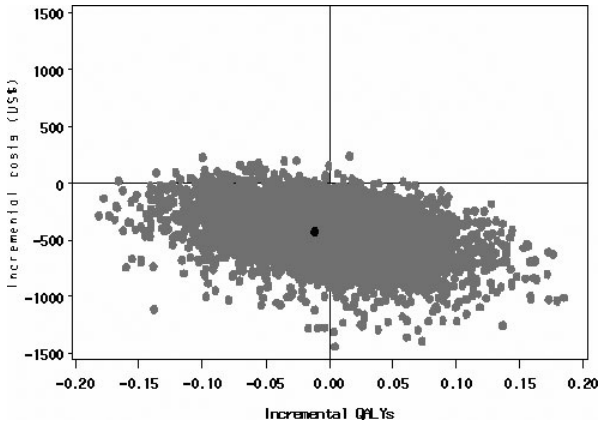

Fig. 7. The point estimate (in black) and 5000 bootstrap replications (in grey) of the total cost and quality-adjusted life year differences between treatment with sertraline and citalopram.

dominance quadrant. Additionally, fluoxetine costs were higher than sertraline, but it generated better quality of life outcomes (ICUR = 5160.1). As 83.4% of the bootstrap replications fell below the threshold of 33 936 US$/QALY (=30 000 €/QALY) proposed by others (37), fluoxetine could be considered to be more cost-effective than sertraline.

When paroxetine was compared with sertraline and citalopram, the first showed higher total costs but better quality of life outcomes (ICUR for sertraline comparison = 22621.8; and for citalopram = 1440.0), highlighting that paroxetine was more cost-effective than sertraline and citalopram. When paroxetine was compared with sertraline, 62.0% of the bootstrap replications fell below the threshold of 33 936 US$/QALY (=30 000 €/QALY), and 72.1% when it was compared with citalopram.

Sensitivity analyses

Considering direct costs, again fluoxetine was dominant over paroxetine, sertraline and citalopram (data not shown).

Discussion

The main finding of the present study is that, during the first 6 months of antidepressant treatment in PC, fluoxetine seems to have cost–utility benefits compared with paroxetine, sertraline or citalopram for treating a depressive disorder.

Previous studies comparing cost–utility of antidepressants have focused on TCAs vs. SSRIs. Hatziandreu et al. (20) found that maintenance antidepressant treatment with sertraline was a better cost–utility option when compared with episodic treatment with dothiepin for participants at high risk of recurrent depression. In 1995, Revicki et al. suggested that nefazodone was a better cost–utility option for treating MDE, when compared with imipramine and fluoxetine, both during a 20-year or lifetime period (21, 22). A report by the Canadian Co-ordinating Office for Technology Assessment suggested that SSRIs should be preferred over TCAs, given their better performance in relation to QALYs (23).

All of these studies used clinical decision analysis techniques. Therefore, considering their low external validity (as they were based on theoretical assumptions), their results should be generalized with caution (38). Recently, Peveler et al. (24) carried out a randomized controlled trial with a preference arm in PC in the UK. Results suggest that SSRIs are a better cost–utility option when compared with TCAs and lofepramine (24). Unfortunately, possible differences among SSRIs were not reported.

This study has included patients who were treated by their PC physician for depressive disorder. Their diagnosis is heterogeneous: they suffered from major depression but also from other depressive disorders (DD, minor depression, depressive disorder not otherwise specified). Previous research has found that these groups may not be qualitative different as many subjects with minor depression later develop major depression (39–41).

Two strong points of the present study are that the outcome assessment was performed during both acute and continuation phases of depression pharmacotherapy, and data were collected in PC settings, under 'usual care' conditions. These characteristics may increase the external validity of the present findings.

Several limitations should be mentioned, however. First, as the study was observational and not randomized, inter-subject variability may limit the ability to detect differences among SSRIs. Secondly, because the choice of antidepressants was not randomized, we had to consider several reasons for a particular physician choosing one antidepressant in preference to another. Physicians might have selected certain antidepressants based on their evaluation of which would be the most effective. If they were good at making such predictions, this could have affected effectiveness of individual antidepressants in individual patients, thus affecting our results. We should also highlight that 72 PC physicians from 16 centres participated in our study. Thus, a wide range of professionals could represent a wide range of expertise. Thirdly, as it is commonly observed in studies about depressive disorders, most participants were women. This has to be taken into account when referring our results to men. Fourthly, the informed consent requirement may have influenced the selection of patients, though this is true for all studies considering human participants. Fifthly, the consideration of exclusion criteria, though both necessary and less restrictive than in randomized controlled trials, could limit the generalization of findings. Finally, the duration of follow-up (6 months) could be shorter than those expected for economic analyses. Nevertheless, it is the minimum expected for treating a depressive episode (42).

To conclude, the present results indicate that fluoxetine has several cost–utility advantages for treating depressive disorders in PC. However, when deciding which antidepressant should be prescribed, it is also important to take into account antidepressant clinical profile, safety and tolerability.

Considering the few data comparing cost–utility among different SSRIs, more research is needed, with larger samples and longer follow-up periods. In order to increase knowledge about cost–utility, it could also be necessary to compare SSRIs with other antidepressants such as venlafaxine, mirtazapine or the most recently commercialized duloxetine.

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Appendix 1

The ETAPS group is a multidisciplinary group of researchers studying depressive disorders in primary care. The members of the ETAPS group are: Beatriz Arizaga (MD), Eva Bellerino (MD), Elena Blanco García (MD), Pilar Boncompte (MD), Belen Brun Alonso (MD), José Luis Caballé (MD), Mila Campos (MD), Emilia Caramés Duran (MD), José M Castillejo (MD), Eva Comin (MD), Ana M Cuenca (MD), Carmen Delgado (MD), Ángel Espín (MD), Montserrat Espuga (MD), Alicia Ezpeleta (MD), Rita Fernández Vergel (MD), Manel Ferran (MD), Lluisa Gardeñes (MD), Inmaculada García Bayo (MD), Francisco J Gómez (MD), Josep M. Haro Abad (PhD), Adelina Herrera (MD), Nuria Lara Suriñac (MD), Cristina Moliner (MD), Maria L. Morató (MD), Sonia Moreno (MD), Jesús Muniesa (MD), Juli Muñoz (MD), Maria A. Orús Escolà (MD), Maria T Peñarrubia María (MD), Carmen Pérez (MD), Judith Pertiñez (MD), Alejandra Pinto-Meza (PhD), Laura Pons (MD), Pilar Postigo (MD), Amelia Prieto (MD), Anna Rispau Falgàs (MD), Pere Reig (MD), Purificación Robles Raya (MD), José M Rodríguez Galipienzo (MD), Maria D. Ruiz Blanes (MD), Manel Segarra (MD), Oscar Seoane (MD), Antoni Serrano-Blanco (MD), Mariona Soler Vila (MD), David Suárez (MSc), Paloma Urbina (MD) and Enric Vicens Pons (PhD).

Appendix 2. Drug acquisition costs in US$, 2003

Drug	Brand name	Dose (mg)/tablet	Tablets	2003 price
Antidepressants				
Amitriptiline	Tryptizol	50	30	3.3
Citalopram	Prisdal	20	28	34.0
Clomipramine	Anafranil	25	40	4.1
Fluoxetine	Prozac	20	28	26.3
Fluvoxamine	Dumirox	50	30	10.8
Imipramine	Tofranil	25	50	2.4
Maprotiline	Ludiomil	10	30	2.5
Mianserine	Lantanon	10	50	4.9
Mianserine	Lantanon	30	30	8.7
Mirtazapine	Rexer	15	30	31.1
Moclobemide	Manerix	150	30	16.5
Paroxetine	Seroxat	20	28	37.5
Reboxetine	Norebox	4	20	15.8
Sertraline	Besitran	50	30	36.2
Anxiolytic/hypnotic				
Alprazolam	Trankimazin	0.25	30	2.7
Bromazepam	Lexatin	1.5	30	1.8
Clorazepato	Tranxilium	5	30	2.1
Clotiazepam	Distensan	5	30	3.0
Diazepam	Valium	5	30	1.7
Halazepam	Alapryl	40	30	4.1
Lorazepam	Orfidal	1	25	2.3
Lormetazepam	Loramet	1	30	3.3
Zolpidem	Stilnox	10	30	6.8
Zopiclone	Limovan	7.5	30	5.9