Clinical Trials and Regulatory Science in Cardiology 14 (2016) 1–3

Contents lists available at ScienceDirect

Clinical Trials and Regulatory Science in Cardiology

journal homepage: http://www.elsevier.com/locate/ctrsc

Cost-effectiveness analysis of smoking-cessation treatment using electronic medical records in a cardiovascular hospital

Jaqueline Scholz [a,*], Luana D. Portela [b], Tania Maria Ogawa Abe [a], Patricia Viviane Gaya [a], Valter G. Santos [b], Cristina Ferreira [b], Clarice Amorim [a], Alexandre Costa Pereira [c], Paulo Caleb Junior Lima Santos [c,**]

[a] Smoking Cessation Program Department, Heart Institute (InCor), University of Sao Paulo Medical School, Sao Paulo, Brazil
[b] Pharmacy Department, Heart Institute (InCor), University of Sao Paulo Medical School, Sao Paulo, Brazil
[c] Laboratory of Genetics and Molecular Cardiology, Heart Institute (InCor), University of Sao Paulo Medical School, Sao Paulo, Brazil

ARTICLE INFO

Article history:
Received 5 November 2015
Accepted 25 January 2016
Available online 4 February 2016

Keywords:
Pharmacoeconomic
Smoking
Nicotine dependence
Varenicline
Bupropion

ABSTRACT

Purpose: Evaluating the cost-effectiveness of a first-line smoking cessation drug using an electronic medical record system is very important for defining the best decision-making tree to use in the Brazilian National Health System (SUS). This study aimed to evaluate the cost effectiveness of varenicline compared with bupropion and nicotine replacement therapy (NRT) (gum and patches) in a smoking cessation program.
Methods: We included 940 patients admitted to a smoking cessation program. Smokers had access to medical consultations and prescription of nicotine replacement therapies (NRT — patch and gum), bupropion, and varenicline. Incremental cost-effectiveness ratios (ICERs) were estimated in the perspective of the Brazilian Public Health System (SUS).
Results: We were able to show that the best cost-effectiveness for one participant to quit smoking was BRL R$ 1.546,40 with varenicline plus bupropion BRL R$ 1.650,00 with varenicline alone; BRL R$ 1.971,32 with bupropion plus gum; BRL R$ 2.413,81 with bupropion plus NRT; and BRL R$ 2.414,26 with NRT alone.
Conclusion: Treatment with varenicline showed to be dominant and cost saving compared to NRT and/or bupropion.

1. Introduction

Smoking can be described as an epidemic that kills 5.4 million people every year, primarily due to lung cancer and cardiovascular disease. This makes smoking a key modifiable risk factor for increased morbidity and mortality [1], which generates a substantial burden to the economy of countries as well as loss of productivity due to morbidity and early death [2].

The use of medications is an additional resource in smoking cessation, being particularly useful when behavioral interventions are ineffective, usually due to a high level of nicotine dependence [3]. Nonetheless, the use of medications adds considerable cost to the overall expenditure of smoking cessation programs. Cost-effectiveness analyses have been marginally conducted to guide widespread use of different smoking cessation treatments in developing countries. The Brazilian National Health System (SUS) offers bupropion and nicotine replacement therapy for free. Varenicline is not available for SUS patients. Evaluating the cost-effectiveness of a first-line smoking cessation drug using an electronic medical record system is very important for defining the best decision-making tree to use in the Brazilian National Health System (SUS) [4].

2. Study aims

This study aimed to evaluate the cost effectiveness of varenicline compared with bupropion and nicotine replacement therapy (NRT) (gum and patches) in a smoking cessation program at the Heart Institute (InCor), which is part of the University of São Paulo's medical complex and offers treatment for SUS patients and private patients. The decision to choose varenicline as the reference treatment was based on the superior efficacy of this drug compared to that of bupropion or NRT.

The secondary aim was to determine the incremental cost of using multiple medications to identify the treatment that offers the greatest cost savings.

* Correspondence to: J. Scholz, Heart Institute (InCor), University of Sao Paulo Medical School, Av. Dr. Eneas de Carvalho Aguiar 44, Cerqueira Cesar, 05403-000 São Paulo, SP, Brazil.
** Corresponding author.
E-mail addresses: jaquelineissa@yahoo.com.br (J. Scholz), pacaleb@usp.br (P.C.J.L. Santos).

http://dx.doi.org/10.1016/j.ctrsc.2016.01.006

3. Methods

We conducted an outcome research from patients treated in the smoking cessation program at InCor, using the Program of Assistance to Smokers (Programa de Assistência do Fumante—PAFWEB) database available at http://www.pafweb.com.br. Data were collected between 2008 and 2011, and the Ethics Committee of the Hospital das Clínicas, University of São Paulo Medical School (CAPpesq) approved the study.

Inclusion criteria were smokers, over 18 years of age, undergoing smoking cessation treatment with a first-line medication, and consenting to have personal data analyzed. Individuals who did not match the inclusion criteria were excluded. First-line medications for smoking cessation included in this study were nicotine replacement therapy (NRT) (either gum or patch), bupropion, and varenicline.

Patients were divided into 5 groups: group 1 received varenicline only, group 2 received both varenicline and bupropion, group 3 received bupropion and NRT gum, group 4 received bupropion and NRT gum and patches, and group 5 received NRT (gum and/or patch) alone.

NRT and bupropion were available for free for all patients in the Brazilian National Health System (SUS). Varenicline is not available for SUS patients yet, but we obtained free samples for some patients from SUS (108 from 585 SUS patients received varenicline—18% of this sample). We prescribed varenicline to the majority of private patients (246 of 355 private patients—70% of this sample). The study population was divided into groups according to the medication used. The patients who wished to begin smoking cessation treatment received an individual medical approach and prescription for smoking cessation drugs for at least 12 weeks. These drugs were initiated as monotherapy according to the nicotine dependence level of the patient; previous use of smoking cessation medication; availability of medication, and contraindications. NRT was prescribed preferentially to SUS patients, who were men who smoked at least 20 cigarettes per day. Bupropion was prescribed to SUS patients who smoked more than 20 cigarettes per day or women who smoked at least 20 cigarettes per day. These study drugs could be combined to help a patient achieve the smoke-free status or decrease withdrawal symptoms. For this study, varenicline was made available for use by SUS patients. In this case, varenicline was used in patients who failed to stop smoking in previous attempts with NRT and/or bupropion, or who smoked one or more pack(s) of cigarettes per day. Varenicline was the first choice for private patients. Our indication to start providing bupropion at 150 mg/day was if the patient did not achieve complete abstinence 2 or 3 weeks after starting varenicline, or if the patient achieved complete abstinence, but experienced moderate or intense withdrawal symptoms.

The costs evaluated in this study refer to first-line medications used for smoking cessation in the Brazilian National Health System and were verified using the Health Prices Bank (BPS). The effectiveness of treatment was calculated separately for each of the five treatment groups, by dividing the number of patients that successfully quit smoking by the total number of patients in the group. The cost-effectiveness was assessed through a comparison of all treatment options: the incremental clinical benefit (the cost per patient treated) was obtained by dividing the cost of each treatment by its effectiveness.

To estimate the costs and results of each treatment, we developed a model in the form of a decision-making tree, representing the effectiveness of each of the five treatment groups and the direct cost of the medication. Initially, all patients were in the clinical condition of "smokers" from this initial point, five branches represent each of the five treatment groups. In each branch, two clinical outcomes are possible: "success", characterized by continuous abstinence for 52 weeks, or "failure", in which the patient remains as a smoker. Analyses for this study were conducted using SPSS version 16 software.

4. Results

Five groups were identified based on drugs used: group 1 included 246 patients using only varenicline, group 2 included 108 patients using both varenicline and bupropion, group 3 included 183 patients using bupropion and NRT gum, group 4 included 101 patients using bupropion and NRT gum and patches, group 5 included 302 patients using NRT (gum and/or patch) alone.

Table 1 shows the demographic profile of the study population by treatment group. In total, 940 patients were followed for 52 weeks, 585 were patients from SUS and 355 were private patients. We were able to compare success to the anti-smoking treatment received between private and SUS patients. We did not find a significant difference in success rates for the varenicline and varenicline plus bupropion groups ($p = 0.36$ and $p = 0.10$, respectively, and Private vs SUS).

Table 2 shows cost, effectiveness, and cost-effectiveness according to drugs used. We found the lower values for cost-effectiveness in groups 1 and 2 (varenicline alone or combined with bupropion) compared with groups 3, 4, and 5 (without varenicline).

In addition, results of the cost-effectiveness analysis comparing different treatments are presented as incremental cost-effectiveness ratios (ICER), i.e., the difference in the cost of two treatments divided by the difference in their effectiveness. Using group 1 (varenicline only) as the reference group, we observed the following values: BR$

Table 1
Demographic profile of the study population by treatment group (n = 940).

	Varenicline (n = 246)	Varenicline plus bupropion (n = 108)	Bupropion plus gum (n = 183)	Bupropion plus patch + gum (n = 101)	NRT alone (n = 302)	p value
SUS patients (n = 585)	81 (32.9)	27 (25.0)	145 (79.2)	81 (80.2)	251 (83.1)	
Private patients (n = 355)	165 (67.1)	81 (75.0)	38 (20.8)	20 (19.8)	51 (16.9)	
Age (years)	54 ± 11	51 ± 11	53 ± 10	53 ± 10	54 ± 11	0.87
Gender, female (%)	54.1	56.5	78.7	58.4	32.8	<0.01
Ethnicity, White (%)	89.5	86.6	59.4	62.8	67.9	<0.01
Fagerstrom score	7.3 ± 2.5[a]	7.7 ± 2.5[a]	5.9 ± 2.3[b,c]	6.4 ± 2.8[b]	5.3 ± 2.5[c]	<0.01
Hypertension (%)	36.6	34.3	55.7	58.4	62.3	<0.01
Coronary artery disease (%)	12.2	12.0	21.9	26.7	29.5	<0.01
Acute myocardial infarction (%)	12.2	9.3	23.0	27.7	34.1	<0.01
Dyslipidemia (%)	32.9	37.0	49.7	49.5	55.3	<0.01
Type 2 diabetes mellitus (%)	9.3	14.8	15.3	7.9	13.9	0.16
Depression (%)	23.8	26.9	25.6	23.8	20.2	0.52
Anxiety (%)	15.4	20.4	27.9	20.8	14.2	<0.01
Obstructive pulmonary chronic disease (%)	14.6	23.1	21.9	20.8	20.2	0.24
Asthma (%)	2.8	3.7	3.3	2.0	4.0	0.88
Number of diagnosed diseases	2.2 ± 1.5[a]	2.0 ± 1.7[a]	2.9 ± 1.9[b]	2.7 ± 1.7[b]	3.2 ± 1.9[b]	<0.01
Number of other medications	2.2 ± 2.6[a]	2.0 ± 3.1[a]	4.0 ± 3.3[b]	4.3 ± 3.9[b]	4.5 ± 3.2[b]	<0.01

Different superscript letters mean values significantly different (*post-hoc* test).

Table 2
Cost, effectiveness, and cost-effectiveness according to treatment options.

Drug	Effectiveness (%)	Cost	Cost-effectiveness
Varenicline	39.4	BR$ 650.10	BR$ 1650.00
Varenicline + bupropion	47.2	BR$ 729.90	BR$ 1546.40
Bupropion + gum	31.7	BR$ 624.91	BR$ 1971.32
Bupropion + NRT	39.6	BR$ 955.87	BR$ 2413.81
NRT	33.1	BR$ 799.12	BR$ 2414.26

2365.40 for NRT, BR$ 1528.85 for bupropion plus NRT, BR$ 327.14 for bupropion plus gum, and BR$ 1023.08 for varenicline plus bupropion.

5. Discussion

The decision to select the varenicline group as the reference group was considered based on the superior efficacy of this drug compared with bupropion [5] or with NRT [6].

The decision-making tree in this study indicates that the greatest cost-effective values were observed in patients who used varenicline or varenicline plus bupropion. In addition, it was an important finding that the cost-effectiveness of varenicline alone was BR$ 1650.00, while the cost-effectiveness of varenicline plus bupropion was BR$ 1546.40. Both drug therapies had lower values than the alternatives (bupropion and NRT gum, bupropion and NRT gum and/or patch, and NRT alone), which cost BR$ 1971.32, BR$ 2413.81, and BR$ 2414.26, respectively. In a previous study from our group, we showed a higher success rate in the patient group using varenicline plus bupropion compared with the patient group using varenicline as monotherapy [7].

Furthermore, another current randomized, placebo-controlled trial also identified the superiority of co-administration compared to varenicline as monotherapy in patients with a high dependency [8].

The incremental cost-effectiveness analysis found that varenicline alone, compared to NRT alone, saved BR$ 2365.40, and compared to bupropion associated with NRT that saved BR$ 327.14. The cost-effectiveness of varenicline in association with bupropion was BR$ 1023.08, and for bupropion associated with NRT, it was BR$ 1528.85. Therefore, varenicline seems to be cost-effective regardless of whether it is prescribed alone or in combination with bupropion.

This evidence aligns with study results from other continents. A study conducted in Finland compared the effectiveness of varenicline, bupropion, and no treatment over 12 weeks, and found that varenicline was the most effective and resulted in cost savings compared to bupropion or no treatment [9]. Another study conducted in Greece found that when comparing varenicline, bupropion, NRT and no treatment, varenicline improved the chances of successful smoking cessation and significantly reduced the overall costs of smoking cessation treatment in the health care system [10]. Other researchers also evaluated the cost-effectiveness of varenicline compared to other medications available for smoking cessation and concluded that varenicline was considered cost-effective in South Korea [11].

In the United States, a study compared varenicline, bupropion with NRT, and no treatment; results indicated that varenicline is a low-cost first-line medication alternative for smoking cessation [12]. Another study concluded that, for each of the paying parties (health care system, health insurance, and the patient), the use of varenicline substantially reduced health care costs [13].

A study in four European countries compared the cost-effectiveness of varenicline with that of NRT for smoking cessation in adults between the ages of 18 and 75. Under a smoking cessation benefits model (BENESCO), the incremental cost of varenicline compared to NRT went from EUR $54,522.00 to EUR $200,200.00, demonstrating that varenicline was cost-effective for the health care system [14].The initial cost of varenicline is offset by savings associated with less morbidity and mortality due to diseases associated with smoking. Despite its limitations, cost-effectiveness analyses are already available in several countries, all of which support the use of varenicline for 12 to 24 weeks as a low-cost treatment option to assist smokers in achieving successful cessation [15].

In conclusion, this study is an outcome research of real-world observations; therefore, it has intrinsic limitations including the lack of a controlled environment and randomization. Despite that, these results indicate that, in the clinical environment and under evaluation criteria by an electronic medical records system, varenicline alone or when co-administered had lower values of cost-effectiveness. Smoking is a risk factor for several chronic diseases and is responsible for a myriad of health problems that generate excessive health care expenses (including treatments, medications, and hospitalizations); therefore, efforts to control and reduce smoking such as treatment with drugs are extremely important in assisting smokers to achieve successful cessation.

References

[1] Bolliger CT, Issa JS, Valay RP, et al. Effects of varenicline in adult smokers: a multinational, 24-week, randomized, double-blind, placebo-controlled study. Clin Ther 2011;33(4):465–77.
[2] Portes LH, Silva JA, Teixeira MTB, et al. Internações por condições sensíveis à atenção ambulatorial tabaco-relacionadas: perfil de um município de grande porte. J Manag Prim Health Care 2013;4(2):94–101.
[3] Reichert J, Araújo AJ, Gonçalves CMC, et al. Diretrizes para cessação do tabagismo – 2008. J Bras Pneumol 2008;34(10):845–80.
[4] Nita EM, Secoli SR, Nombre MRC, et al. Avaliação de tecnologia em saúde: evidência clínica, análise econômica e análise decisão. Porto Alegre: Ed Artmed; 2010.
[5] Nides M, Glover ED, Reus VI, Christen AG, Make BJ, Billing Jr CB, et al. Varenicline versus bupropion SR or placebo for smoking cessation: a pooled analysis. Am J Health Behav 2008;32:664–75.
[6] Aubin HJ, Bobak A, Britton JR, Oncken C, Billing Jr CB, Gong J, et al. Varenicline versus transdermal nicotine patch for smoking cessation: results from a randomised open-label trial. Thorax 2008;63:717–24.
[7] Ebbert JO, Hatsukami DK, Croghan IT, et al. Combination varenicline and bupropion SR for tobacco-dependence treatment in cigarette smokers: a randomized trial. J Am Med Assoc 2014;311(2):155–63. http://dx.doi.org/10.1001/jama.2013.283185).
[8] Issa JS, Abe TO, Simone Moura Santos PCJL, Pereira AC. Effectiveness of co-administration of varenicline, bupropion, and serotonin reuptake inhibitors in a smoking cessation program in the real-life setting. Nicotine Tob Res 2013;15(6):1146–50.
[9] Linden K, Jormanainen V, Linna M, et al. Cost effectiveness of varenicline versus bupropion and unaided cessation for smoking cessation in a cohort of Finnish adult smokers. Curr Med Res Opin 2010;26(3):549–60.
[10] Athanasakis K, Igoumenidis M, Karampli E, et al. Cost-effectiveness of varenicline versus bupropion, nicotine-replacement therapy, and unaided cessation in Greece. Clin Ther 2012;34(8):1803–14.
[11] Bae JY, Kim CH, Lee EK. Evaluation of cost-utility of varenicline compared with existing smoking cessation therapies in South Korea. Value Health 2009;12(Suppl. 3):S70–3.
[12] Howard P, Knight C, Boler A, Baker C. Cost-utility analysis of varenicline versus existing smoking cessation strategies using the BENESCO simulation model: application to a population of US adult smokers. PharmacoEconomics 2008;26(6):497–511.
[13] Halpern MT, Dirani R, Schmier JK. The cost effectiveness of varenicline for smoking cessation. Manag Care Interface 2007;20(10):18–25.
[14] Bolin K, Wilson K, Benhaddi H, et al. Cost-effectiveness of varenicline compared with nicotine patches for smoking cessation: results from four European countries. Eur J Pub Health 2009;19(6):650–4.
[15] Keating GM, Lyseng-Williamson KA. Varenicline: a pharmacoeconomic review of its use as an aid to smoking cessation. PharmacoEconomics 2010;28(3):231–54.