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Original Article

Comparative Analysis of Three Different Drug Distribution Schemes for Smoking Cessation

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Abstract

OBJECTIVE: This study aimed to compare the success rate of 3 different drug prescription policies: Free drugs with online system prescription, free drugs with doctor's prescription, and drugs paid for by patients with doctor's prescription.

MATERIAL AND METHODS: The effect of 2 different Ministry of Health (MoH) projects with free-of-charge and self-payment pharmacotherapies for smoking cessation were compared. Patients who completed 6 months of pharmacotherapy and follow-up were evaluated. The first period was free-of-charge medication, which was determined by an online system, the following period was the self-payment period, and the third period was free medication, which was prescribed by a doctor. In all the groups, smoking habits in pack years and comorbidities of the patients were recorded, and pulmonary function tests (PFTs) and expiratory carbon dioxide (CO2) measurements were performed. Patients who had an expiratory CO2 level >5 ppm at the control visits were accepted as quitters.

RESULTS: A total of 829 patients with 438 patients in the first free-of-charge period (group 1), 111 in the self-payment period (group 2), and 280 in the second free-of-charge period (group 3) were enrolled in the study. Smoking cessation rates were significantly higher in the self-payment medication group (25%) according to the MoH's free-of-charge project groups. There was no difference in smoking cessation rates between the 2 free-of-charge medication project groups (15% in group 1 and 11% of group 3). Among all the patients, we compared 124 patients who quit smoking with 705 patients who did not. The quitters were older, mostly male, and heavier smokers. In addition, the number of patients with chronic obstructive pulmonary disease and obstructive PFT rates were higher among the quitters. Their dependency score, PFTs, and the use of free medication was lower, and treatment duration was longer. Independent factors that increased smoking cessation success were longer treatment duration, lower dependency score, and self-payment of medication.

CONCLUSION: Free medications provided via 2 different modalities did not increase the smoking cessation success. Paying for the medication, lower dependency score, and longer treatment duration increased smoking cessation success independently.

KEYWORDS: Smoking pharmacological treatment, smoking cessation success, reimbursement of smoking cessation treatments

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INTRODUCTION

Tobacco use is a major preventable risk factor for many diseases and death. In the 20th century, 100 million deaths occurred because of tobacco use. It is estimated that 8 million tobacco deaths may occur in 2030 if tobacco use continues in the same way [1]. Smoking cessation is one of the important components of tobacco control. The most effective method for smoking cessation is a multidisciplinary approach, which includes pharmacological therapies with psychological treatment (problem solving skills training and supportive treatments). Nicotine replacement therapy (NRT), varenicline, and bupropion are the first-line pharmacological treatments recommended for smoking cessation [2-7]. Long-term cessation rates in smokers were reported to be 15%–29%, 27%–29%, and 43%-48% for NRT, bupropion, and varenicline, respectively [6]. Psychological treatment increases this success rate up to 70% according to the results of a meta-analysis [8].

An effective smoking cessation strategy includes reimbursement for smoking cessation therapy, which seems to increase quitting rates. Clinical practice guidelines urge health insurances to provide coverage for effective counseling and pharmacological therapy [3, 9]. In the United States (US), Medicare provides intermediate or intensive smoking cessation counseling and pharmacotherapy for tobacco users who have a tobacco-use-related disease [9]. The smoking cessation reimbursement spectrum range changes within states in the US [10].

In Turkey, according to a global adult tobacco survey 2012 report, 41.5% of men and 13.1% of women are currently smokers [11]. The national tobacco control program's action plan has been used for the past 10 years in Turkey. Cessation counseling and supportive interventions by physicians at smoking cessation clinics were paid for by the social security

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institution as a component of this program. In addition, the social security instruction had decided to add the reimbursement of pharmacological treatment of smoking cessation to this action plan [12-14]. However, today, the costs of pharmacological treatments are not yet included in the reimbursement programs of either the government or private health insurance companies. In 2011, the Ministry of Health (MoH) of Turkey bought bupropion and varenicline in the context of a research project. These medications were distributed to smoking cessation clinics to be prescribed free of charge, but which medicine was to be given to which patient was decided by an online computer system [15]. In this project, 247,435 boxes of drugs were delivered to 164,733 participants for smoking cessation. Quit rates for 1 year were found 29.6% in those prescribed varenicline and 25.1% in those prescribed bupropion [16]. In our smoking cessation clinic, 604 participants were given bupropion or varenicline in the same project, and we found the quit rate for 1 year to be 10.7%. After this project, the quit rate for 1 year was 18.3% for the patients who paid for the medication on their own, and success rate was lower than the period in which patients paid for their medications. We concluded that the introduction of a computer-based system that restricts the physicians' decision making reduced the success rate of treatments for smoking cessation in our clinic [17]. There was a significant difference in the success rates of smoking cessation between our clinic and the MoH countrywide projects [16].

In 2015, (second project) the MoH purchased bupropion and varenicline again. At this time, the physicians who treated the patients at smoking cessation clinics were allowed to decide which medicine to prescribe. In a recent report given by Karadoğan et al. [18], the 3-month quit rate seemed to be higher in the free medication group (in the first and second projects of the MoH) than in the self-payment group, but there was no statistically significant difference in the multivariate analysis. There are 3 surveys [16-18], 1 from our clinic about this subject, which showed contradictory results. Therefore, this study aimed to compare the success rate of the 3 different drug prescription policies: Free drugs with online system prescription (the first MoH project), free drugs with a doctor's prescription (the second MoH project), and drugs paid for by the patient with a doctor's prescription. We hoped to see the effects of these different systems and to determine factors other than reimbursement of medication that affect the cessation rate in 6 months.

MAIN POINTS

- In Turkey, the costs of pharmacological treatments are not yet included in the reimbursement programs.
- In 2011 and 2015, smoking cessation medications were distributed as Ministry of Health (MoH) projects with free-of-charge.
- We compared the smoking quit rates of two different MoH project groups and self payment group.
- The rate of smoking cessation was significantly higher in self-payment medication group (25%) according to the MoH's free-of-charge project groups.

MATERIAL AND METHODS

The study was planned according to the World Medical Association Declaration of Helsinki (2008). It was a retrospective cohort research that compared the effect of 2 different MoH projects and a self-payment method for drugs for smoking cessation. The research was conducted at the smoking cessation clinic of a government educational and research hospital. In the first period of free-of-charge medication (from April to December 2011), 604 patients (group 1); in the following period of self-payment (from January to June 2012), 332 patients (group 2); and in the second free-of-charge medication period (from April 2015 to June 2016), 304 patients (group 3) were admitted. A total of 1,240 patients were included, as seen in Figure 1. Patients who used pharmacological treatment and completed 6 months' follow-up were enrolled in the study. Patients without any medical treatment were not included.

Smoking habits (pack years) and comorbidities were recorded among the groups, and informed consents were obtained from all the patients on their first visit. The Fagerstrom test was used to determine nicotine addiction [19], and physical examination and pulmonary function tests (PFTs) were performed (Sensor Medics Vmax22, CareFusion, San Diego, California, USA). Expiratory carbon dioxide (CO_2) levels were measured (piCO Smokerlyzer, Bedfont Scientific Ltd, Harrietsham Maidstone Kent, England). Both the first evaluation and the follow-up of the patients were carried out by the same pulmonary specialist.

In group 1, patient information was recorded both on the online system of the MoH and on the hospital system on their first visit. Their second visit was an informative meeting of 10-12 people each. Visual education with slides about the harmful effects of smoking, the advantages of quitting, and smoking cessation methods was performed, and the patients were informed about motivational and behavioral approaches [4, 5]. The third visit was face-to-face with the doctor to determine the quitting date and prescribed drug. In this visit, either varenicline or bupropion, which was determined by the online system of the MoH according to the information recorded about the patient, was given [15]. If the patient had a history of depression, the system refused to provide any medication. The doctors were not allowed to decide about the medication in this group. Free-of-charge NRT was not included in this project; thus, the patients who needed nicotine replacement had to pay for it.

In group 2, patient information was recorded only on the hospital system during the first visit. The second visit was again an informative meeting of 10-12 people. In the third visit, quitting date was determined with the prescription of bupropion, varenicline, or nicotine replacement according to the doctors' decision. The patients paid for their drugs themselves.

In group 3, patient information was recorded again both on the online system of the MoH and the hospital. Face-to-face communication was the main system on all visits. On the first visit, harmful effects of smoking, advantages of quitting, and helpful behavioral techniques were explained, and a quit-

ting date was determined. Bupropion or varenicline was prescribed according to the doctors' decision free of charge and recorded on the online system. The patients received their medication from the community health centers with their prescriptions. Free-of-charge NRT was not included in this project, and thus the patients who needed nicotine replacement had to pay for it.

Patients in all the groups had to come for follow-up visits twice in the first month and once in the second, third, and sixth months. They were inquired about their smoking habit and the side effects of medication during each visit, and expiratory CO_2 measurements were performed. An expiratory CO_2 level ≤6 ppm was accepted as no smoking, and a level >6 ppm was accepted as still smoking [20]. Patients who missed the follow-up visits were assumed to have not quit.

Statistical Analysis

Patients who received medical treatment and completed 6 months of follow-up were analyzed. Comparisons were made among the 3 groups and patients who quit or did not quit smoking at the end of 6 months. In addition, independent risk factors that affect smoking cessation in 6 months were analyzed. Data from the standardized medical reports were transferred to the Statistical Package for the Social Sciences version 25.0 (IBM SPSS Corp.; Armonk, NY, USA) software program by the lead researcher. Descriptive analyses were presented using means and standard deviations for continuous data. Frequencies and percentages were used for categorical data.

The variables were investigated using the Kolmogorov-Smirnov test to determine whether or not they are normally distributed. Homogeneity of variances assumption was evaluated using the Levene test. When the variables were normally distributed, two independent samples t test was used to compare the quitters and non-quitters. When the variables were not normally distributed, the Mann-Whitney U test was used to compare these groups. The chi-square test was used to compare the proportions of the groups. Analysis of variance was used to compare the means of the study groups for normally distributed data. The Tukey test was performed to test the significance of pairwise differences. When the data were not normally distributed, the Kruskal-Wallis test was conducted to compare medians of the study groups. The Mann-Whitney U test was performed to test the significance of pairwise differences using the Bonferroni correction adjusted for multiple comparisons. Multivariate analysis was performed using 2 methods. First, binary logistic regression with enter method was applied to predict the factors for quitting smoking. Then, binary logistic regression analysis with backward conditional method was applied to find a reduced model that best explains the independent predictors of quitters' outcome adjusting the confounders. The Hosmer-Lemeshow goodness of fit statistics was used to assess model fit. Multinomial logistic regression analysis was performed taking group 2 as the reference group to show the differences among periods by considering the confounders. A 5% type-I error level was used to infer a statistical significance.

RESULTS

Patients who received pharmacological treatment and who completed 6 months of follow-up were enrolled in the study. Of a total of 829 patients, 438 (72.5%) of 604 patients in group 1, 111 (33.4%) of 332 patients in group 2, and 280 (92%) of 304 patients in group 3 were found eligible (Figure 1).

Comparing the 3 groups, we observed the oldest age and the highest prevalence of COPD and obstructive PFT in group 2 (p<0.001, p=0.006, p=0.001, respectively) as well as the lowest FEV1%, FVC %, FEV1/FVC, FEF25%-75% (p=0.005, p=0.057, p=0.002, p=0.008, respectively). Group 3 had the most number of men and comorbidities (p=0.033, p<0.001, respectively) (Table 1). Among the whole study population, rate of smoking cessation at the 6th month was 124 (15%) out of 829. The highest rate of smoking cessation was in group 2 (15% in group 1, 25% in group 2, and 11% in group 3; p=0.002). There was no statistically significant difference between groups 1 and 3 according to smoking cessation rates (p>0.05), but there was a statistically significant difference between the groups 1 and 2 and between groups 2 and 3 (p=0.008, p=0.001, respectively). The lowest rate of varenicline use and the shortest duration of the treatment (days) was in group 2 (p<0.001, p<0.001, respectively), whereas NRT use was the highest in this group (p<0.001). There were no differences among the groups according to the mean Fagerstrom score, mean smoking rate as pack years, and bupropion use (p>0.05) (Table 1).

For multivariate analysis, statistically significant factors, which were obtained from univariate analysis, were included in the model. The multinomial logit estimates of covariates for group 1 relative to group 2 were not statistically significant (p<0.001). The multinomial logit estimates of covariates for group 3 relative to group 2 were statistically significant (p<0.001). If the patient's age increased by 1 point, the multinomial log-odds of preferring group 3 to group 2 would be expected to decrease by 0.033 unit, with all the other variables in the model as constant. If a patient's FEV1 increased by 1 point, the multinomial log-odds of preferring group 3 to group 2 would be expected to increase by 0.026 unit, holding all the other variables in the model constant. The multinomial logit for non-comorbities relative to the presence of comorbities is 2.232 units lower for preferring group 3 relative to group 2 given all the other predictor variables in the model are constant. The multinomial logit for non-obstruction relative to the presence of obstruction is 1.471 unit higher for preferring group 3 relative to group 2 given all other predic-

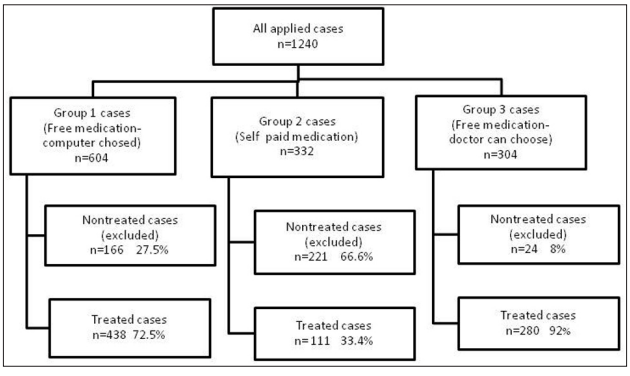

Figure 1. Distribution of the cases

Table 1. Comparison of patients from groups 1, 2, and 3

Patients	Group 1 n=438	Group 2 n=111	Group 3 n=280	p
Mean age (years)	43±10[¶, µ]	47±13[¶]	41±12[µ]	<0.001[a]*
Sex (male), n (%)	245 (56%)[µ]	70 (63%)	183 (65%)[µ]	0.016[b]*
Mean Fagerstrom score	6.2±2.3	6.3±2.4	6.3±2.4	0.496[a]
Mean pack years	27.4±17.6	30.7±18.1	26.8±18.3	0.065[a]
Comorbidities, n (%)	117 (26.7)[¶, µ]	53 (47.7)[¶]	153 (54.6)[µ]	<0.001[b]*
COPD, n (%)	24 (5.4)[¶, µ]	14 (12.6)[¶]	31 (11)[µ]	0.006[b]*
Obstruction in PFT, n (%)	62 (14.1)[¶,#]	30 (27)[¶]	38 (13.5)[#]	0.001[b]*
Mean FEV1 %	88.9±18.4	84.2±20.2[#]	92.6±16.4[#]	0.005[a]*
Mean FVC %	96.2±14.8	93.8±16	100.6±40.5	0.057
Mean FEV1/FVC	78.7±11.6[¶]	74.2±12.6[¶,#]	79±9.2[#]	0.002[a]*
Mean FEF-25%-75 %	71.6±30.2	63.7±28[#]	74.9±27.6[#]	0.008[c]*
Quitters in the 6th month, n (%)	65 (14.8)[¶]	28 (25.2)[¶,#]	31 (11)[#]	0.002[b]*
Bupropion usage, n (%)	139 (31.7)	38 (34.2)	72 (25.7)	0.110[b]
Varenicline usage, n (%)	294 (67.1)[¶]	36 (32.4)[¶,#]	185 (66)[#]	<0.001[b]*
NRT usage, n (%)	5 (1.2)[¶, µ, #]	37 (33.4)[¶, µ, #]	23 (8.3)[¶, µ, #]	<0.001[b]*
Mean duration of the treatment (days)	49.2±24.2[¶]	35.4±17.6[¶,#]	49.8±29.8[#]	<0.001[a]*

COPD: Chronic obstructive pulmonary disease; PFT: Pulmonary function tests; FEV1: Forced expiratory volume in the first second; FVC: Forced vital capacity; FEF: Forced expiratory flow; NRT: Nicotine replacement therapy
[a]Kruskal-Wallis test, [b]chi-square test, [c]analysis of variance,*p<0,05 statistically significant
[¶]Significance between groups 1 and 2, [#]significance between groups 2 and 3, [µ]significance between groups 1 and 3. Bold p values: statistically significant

Table 2. Multivariate analysis to find the difference among groups considering the confounders

							95% confidence interval for exp(B)		
Group[a]		B	Std. error	Wald	df	Odds ratio	Lower bound	Upper bound	p
Group 1	Intercept	-0.629	1.813	0.120	1				0.729
	Age	-0.024	0.013	3.398	1	0.976	0.951	1.002	0.065
	FEV1%	0.001	0.013	0.003	1	1.001	0.976	1.026	0.953
	FEV1/FVC	0.036	0.026	2.002	1	1.037	0.986	1.090	0.157
	FEF 25-75	-0.009	0.011	0.769	1	0.991	0.970	1.012	0.380
	Sex (female/male)	0.115	0.298	0.148	1	1.122	0.625	2.012	0.700
	Comorbid. (No/yes)	0.492	0.305	2.614	1	1.636	0.901	2.972	0.106
	COPD (no/yes)	-0.423	0.589	0.516	1	0.655	0.207	2.078	0.473
	Obstruction in PFTs(no/yes)	0.060	0.524	0.013	1	1.062	0.380	2.966	0.908
	Quitters in the 6th month (no/yes)	0.434	0.336	1.666	1	1.543	0.799	2.982	0.197
Group 3	Intercept	-0.598	1.803	0.110	1				0.740
	Age	-0.033	0.013	6.718	1	0.967	0.943	0.992	0.010
	FEV1	0.026	0.013	4.441	1	1.027	1.002	1.052	0.035
	FEV1/FVC	0.028	0.025	1.211	1	1.028	0.979	1.080	0.271
	FEF 25-75	-0.016	0.010	2.354	1	0.984	0.964	1.004	0.125
	Sex (female/male)	-0.230	0.295	0.608	1	0.795	0.446	1.417	0.436
	Comorbid. (No/yes)	-0.235	0.299	0.618	1	0.790	0.440	1.421	0.432
	COPD (no/yes)	-2.232	0.630	12.565	1	0.107	0.031	0.369	0.000
	Obstruction in PFT (no/yes)	1.471	0.591	6.186	1	4.352	1.366	13.864	0.013
	Quitters in the 6th month (no/yes)	1.000	0.348	8.242	1	2.719	1.374	5.383	0.004

[a]reference category is: group2. Multinomial logistic regression. Goodness of fit Pearson's test p=0.199, deviance p=0.774. Cox and Snell R^2: 0.131; Negelkerke R2: 0.151. Final likelihood ratio test: p<0.001. Bold p values: statistically significant

Table 3. Comparison of quitters and non-quitters in the 6th month

	Quitters in the 6th month (n=124)	Non-quitters in the 6th month (n=705)	p
Mean age (years)	49±11	41±11	<0.001[a]*
Sex (male), %	70	58	0.013[b]*
Mean Fagerstrom score	5±2	6±2	0.003[c]*
Mean pack years	33±19	26±17	<0.001[c]*
Comorbidities, %	43.5	38	0.273
COPD, %	14.5	7	0.012[b]*
Obstruction in PFT, %	29	16	0.001[b]*
Mean FEV1, %	84±20	91±17	0.002[a]*
Mean FVC, %	93±15	98±32	0.152[c]
Mean FEV1/FVC	74±13	78±10	0.002[a]*
Mean FEF 25%–75%	65±29	73±18	0.028[a]*
Free medication, %	77	88	0.002[b]*
Varenicline usage, %	64	62	0.685[b]
Bupropion usage, %	28	30	0.668[b]
Mean duration of the treatment (days)	63±25	43±25	<0.001[a]*

COPD: Chronic obstructive pulmonary disease; PFT: Pulmonary function tests;FEV1: Forced expiratory volume in the first second; FVC: Forced vital capacity; FEF: Forced expiratory flow
NRT: Nicotine replacement therapy
[a]two independent samples t test, [b]chi-square test, [c]Mann-Whitney U test *p<0.05 statistically significant

Table 4. The effector factors on quit success in multivariate analysis

							95% CI for odds ratio	
Variables in the Equation	**B**	**S.E.**	**Wald**	**df**	**p**	**Odds ratio**	**Lower**	**Upper**
Age	0.021	0.022	0.899	1	0.343	10.021	0.978	10.065
Sex (female/male)	-0.434	0.351	10.530	1	0.216	0.648	0.325	10.289
Fagerstrom score	-0.157	0.070	40.953	1	0.026	0.855	0.745	0.981
Pack years	-0.008	0.017	0.215	1	0.643	0.992	0.960	1.026
Comorbidities (no/yes)	0.285	0.349	0.666	1	0.415	1.330	0.671	2.637
COPD (no/yes)	-0.033	0.620	0.003	1	0.957	0.967	0.287	3.263
Obstruction in PFT (no/yes)	-0.722	0.636	1.291	1	0.256	0.486	0.140	1.688
FEV1 %	-0.018	0.035	0.260	1	0.610	0.982	0.916	1.053
FVC %	0.003	0.028	0.014	1	0.905	1.003	0.950	1.060
FEV1/FVC	0.014	0.028	0.243	1	0.622	1.014	0.960	1.071
FEF25%–75%	0.009	0.013	0.457	1	0.499	10.009	0.983	10.036
Self-payment (no/yes)	-1.177	0.408	8.325	1	0.004	0.308	0.139	0.686
Varenicline (no/yes)	-0.924	0.680	1.846	1	0.174	0.397	0.105	1.505
Bupropion (no/yes)	-0.799	0.687	1.353	1	0.245	0.450	0.117	1.729
Duration of the treatment	0.025	0.006	15.304	1	0.000	1.025	1.013	1.038
Constant	-0.525	2.636	0.040	1	0.842	0.591		

[#]Binary logistic regression Method: Enter (likelihood ratio): –2 Log likelihood: 279.35; Cox and Snell R^2: 0.121; Negelkerke R^2: 0.195, Omnibus test of model coefficients: p<0.001. B: regression coefficient, S.E: standard error, df: degree of freedom, bold p values: statistically significant

tor variables in the model are constant. The multinomial logit for non-quitters relative to quitters is 1.000 unit higher for preferring group 3 relative to group 2 given all other predictor variables in the model are constant (Table 2).

Comparing 124 (15%) patients who quit smoking at the end of the 6 months period with 705 (85%) patients who did not, we found older age, male sex, median cigarette consumption (pack years), prevalence of COPD, and obstructive PFTs were higher among the groups who quit (p<0.001, p=0.013, p<0.001, p=0.012, p=0.001, respectively). The Fagerstrom score, FEV1, FEV1/FVC, FEF 25%–75%, and free-of-charge medication use were significantly lower in the quitters group

Table 5. The effector factors on quit success in multivariate analysis adjusted for confounders

							95% CI for exp (B)	
Variables in the equation	**B**	**S.E.**	**Wald**	**df**	**p**	**Odds ratio**	**Lower**	**Upper**
Fagerstrom score	-0.160	0.061	6.923	1	0.009	0.852	0.756	0.960
Duration of treatment	0.026	0.006	20.355	1	0.000	1.027	1.015	1.039
Self-payment	-1.173	0.363	10.463	1	0.001	0.309	0.152	0.630
Constant	-0.962	0.514	3.510	1	0.061	0.382		

*Binary logistic regression method: Backward stepwise (likelihood ratio): –2 Log likelihood: 287,923; Cox and Snell R2: 0,098; Negelkerke R2: 0.158, Omnibus test of model coefficients: p<0.001.*Adjusted with all the variables: age, sex, Fagerstrom score, pack years, presence of comorbidities, chronic obstructive pulmonary disease, obstruction in pulmonary function tests, duration of the treatment, and quit status. B: regression coefficient, S.E: standard error, df: degree of freedom, bold p values: statistically significant

(p=0.003, p=0.002, p=0.002, p=0.028, p=0.002, respectively). There were no differences among the groups according to the prevalence of comorbidities and varenicline and bupropion use (p>0.05) (Table 3).

In multivariate analysis, the factors that increased the 6-month smoking cessation success were lower Fagerstrom score (p=0.026), longer duration of treatment (p<0.001), and higher self-payment of medications (p=0.004) (Table 4). Adjusting for confounders in the multivariate analysis results; for every 1-unit increase in the Fagerstorm score, we expect a 0.157 decrease in the log-odds of quitting, holding all other independent variables constant. For every 1-unit increase in duration of the treatment, we expect a 0.025 increase in the log-odds of quitting, holding all other independent variables constant. The logit for free medication relative to self-payment medication is 1.177 units lower for the preferring group quitters relative to non-quitters given all other predictor variables in the model are held constant (Table 5).

DISCUSSION

In this study, the rate of smoking cessation was significantly higher in self-payment medication group (25%) according to the MoH's free-of-charge project groups. There was no difference between the 2 free-of-charge medication project groups (15% of group 1 and 11% of group 3). The smoking cessation rate among all patients was 15%. In the quitters group, older age, male sex, Fagerstrom score, cigarette consumption in pack years, COPD prevalence, percentage of obstructive PFT, and mean duration of treatment were higher and use of free medication was lower than in the non-quitters group. In multivariate analysis, lower Fagerstrom score, higher self-payment medication, and longer duration of treatment were found to be the independent factors that increased the 6-month smoking cessation success. The results of this study are important in determining the reimbursement strategy for pharmacological treatment of smoking cessation in Turkey.

Reimbursement of the medications for smoking cessation by social security or the private insurance systems is advised in smoking cessation treatment guidelines [3, 9, 10]; however, reimbursement is not yet accepted in our country, either by social security or the private insurance systems. The MoH conducted 2 different projects of free medication in 2011 and 2015. Approximately, 250,000 boxes of medicine were distributed to the smoking cessation clinics in the first project, and an online system decided which drug will be given to which patient without allowing the doctor's intervention. In this project, only varenicline and bupropion were given free of charge but not NRT [15]. At the end of the first year of this project, Çelik et al. [16] conducted a survey and randomly selected 164,733 patients who were contacted by phone to detect the success rates. It was 29.6 % among the ones who used varenicline and 25.1% in the bupropion group. During the same project period, 604 patients were admitted in our clinic; of whom, 438 received their medication determined by the system, and overall, the quit rate at 1 year was 10.7%. After the end of this project, our patients began to pay for their medication; 99/316 patients of our clinic used medical treatment, and the quit rate at 1 year was 18.2%. In this group, the 6-month quit rate was significantly higher than that in the group with free medication (27.3% versus 14.8%). In both the groups, after the first educational seminar, the patients were consulted by a certain doctor in control visits, and face-to-face behavioral treatment was performed. During the MoH's project, more patients were admitted for pharmacological treatment but success rate was low [17]. There was also a significant difference in the 1-year quit rates between the results of Çelik et al. [16] and those of our study during the same period. Çelik et al. [16] contacted their patients via telephone at the end of 1 year to inquire about the quit rate. We measured expiratory CO_2 levels at control visits to determine the quit rate, and the patients who missed these visits were accepted as those who did not quit. This survey in our clinic was conducted in 2015 during the period of the second MoH project. During this period, varenicline and bupropion were again distributed free but not NRT. The doctors were allowed to decide which medication to prescribe, and it was provided free of charge by the community health centers. The patients who were prescribed NRT had to pay for it. Controls were performed by the same doctor, and educational and behavioral support was given face-to-face and not by a common seminar. Although the drug distribution system was revised in this second project, there was no statistically significant difference in the 6-month quit rates from the first project (11% versus 15%). Although the number of patients enrolled was lower than the other groups, 6-month quit rates were the highest in the self-payment group at 25%.

In this study, univariate and multivariate analysis revealed that self-payment was an independent factor that increased the smoking cessation rate. In a recent report by Karadoğan et al. [18] from Turkey, 346 patients who had free medications and 71 patients who paid for them were compared, and 3-month

quit rates were recorded via phone calls. Contradictory to our results, the patients who had free medications had a higher quit rate in the univariate analysis, but no statistically significant difference was detected among the groups in multivariate analysis.

In the US, Medicare provides smoking cessation therapies, but the range of reimbursement changes within the states [10]. Curry et al. [21] had conducted a survey at the end of 1990s comparing 4 different reimbursement systems, including full coverage of NRT (pharmacological) and behavioral treatment; 50% of behavioral treatment and full NRT (standard); 50% of both; and full behavioral treatment with 50% of NRT. The 6-month quit rate of smoking was 28% in the group in which both NRT and behavioral treatment were fully covered and 38% in the standard group. It was 31% and 33% in the other groups. The authors concluded that the lack of motivation in the full coverage group was probably the reason for the low rate of success [21]. In our previous research, the 6-month quit rate was significantly higher in the self-payment group according to the project group. Moreover, mean age in the self-payment and quitters group was significantly higher than that in the project group. In that research, we concluded that older age was a factor which increased smoking cessation success, and the younger project group was less motivated [17]. In this study, the mean age of the self-payment and the quitters group was higher than that of the non-quitters group; however, in multivariate analysis, older age is not an independent factor that increases smoking cessation success. The study by Karadoğan et al. [18] reported no age difference between the self-payment and the free medication group, but old age was found to be an effective factor in the success of smoking cessation in both univariate and multivariate analyses. In our study, 35% of the patients in the self-payment group received bupropion, 32% received varenicline, and 33% received NRT. During the free-of-charge project periods, varenicline and bupropion were free of charge but the patients had to pay for NRT. Therefore, NRT could not be used during these projects as the patients preferred not to pay. In the Cochrane analysis, varenicline seems to be the most efficient medicine in smoking cessation success [6]. In our results, there was no difference between different pharmacological therapies, but the cessation rate was higher among the group who used the medicine for a longer period of time. Karadoğan et al. [18] concluded that compliance to treatment is the most effective factor in quitting, and varenicline also increases the success rates.

In this survey, another independent factor that increased smoking cessation success was lower Fagerstrom score. Similarly, Yaşar et al. [22] found that Fagerstrom score was lower in quitters [22]. Fagerstrom et al. showed that in a pooled analysis of clinical trial data, abstinence rates decreased with increasing dependence scores [23].

In our study, patients who successfully quit were older, heavier smokers, predominantly male and had higher COPD prevalence and lower PFTs. In another study conducted in our clinic, older age and obstructive pulmonary functions were found as effective independent factors for 3-month quitting success rates [24]. Similarly, Kaminsky et al. [25] also found increased success rate among patients with a higher lung age. In a meta-analysis about smoking cessation strategies in patients with COPD, the success rate increases when pharmacological treatment is combined with behavioral treatment [26]. In the US, Medicare covers smoking cessation therapies in tobacco users who have a disease related to tobacco [9, 10]. Although COPD and obstructive PFTs were not independent factors in success rates in our study, it was higher among the self-payment and the quitters groups. Therefore, we conclude from all these results that older patients with COPD are more successful in smoking cessation. We foresee an increase in success rates, especially in this group of patients, if the reimbursement program is applied.

Our research is a retrospective study in which some data may be missing. Also as it was not a multicentered study, the results may not be representative of the community. The patients who missed the control visits were accepted as non-quitters, but some of them might have quit smoking.. In our opinion these are the limitations of our research.

In conclusion, reimbursement of pharmacological treatment of smoking cessation is neither covered by the MoH nor by private insurance companies in Turkey. Limited time projects of free medications have increased the number of patients admitted to smoking cessation programs but could not increase the success rate of quitting to a desired level. In our previous study performed during the first free-of-charge medication period of the MoH, smoking cessation rates were found to be lower than those in the period of self-payment [17]. In this study, we also found that the smoking cessation rate was higher during the self-payment period compared with that of the first and second MoH projects periods. We could not find statistically significant differences in smoking cessation rates between 2 free-of-charge medications by different methods. In addition, age and the percentage of patients with obstructive pulmonary disease were found to be higher in the quitters group in this study and both of our previous studies [17, 24]. We found that lower score of dependence and longer period of pharmacological treatment also increased the success rate. Therefore, we advise that pharmacological treatment of smoking cessation be included permanently in the reimbursement system of the government rather than limited project periods, and older patients and those with COPD should be the primary target group.

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Informed Consent: Informed consents were obtained from all the patients.

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