

Evaluation of factors affecting smoking cessation in people treated with Varenicline

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ABSTRACT

Objective: Aim of the study is to evaluate factors affecting treatment success among individuals receiving varenicline therapy for smoking cessation.

Material and Methods: This research was carried out at Istanbul Medeniyet University Göztepe Training and Research Hospital between January 2018 and January 2019. A total of 209 patients in the smoking cessation outpatient clinic who were treated with varenicline Varenicline were constituted into the study group. The Fagerstrom Nicotine Dependence Level Test (FTND) was used to determine individuals' nicotine addiction levels, and the Hospital Anxiety and Depression Scale (HADS) was used to evaluate anxiety and depression levels.

Results: There were 90 (43.1%) women and 119 (56.9%) men in the study group and mean age was 41.34 ± 10.93 (21-64) years. Overall, 63.2% (n=132) of varenicline recipients quit smoking. The frequency of quitting smoking due to physician advice was higher in those who quit than those who did not ($p=0.011$). Multiple logistic regression revealed that the independent factors associated with the lower likelihood of smoking cessation were higher number of cigarettes per day ($p=0.008$), higher HADS-Total score ($p<0.001$), post-treatment nervousness ($p=0.046$), and post-treatment depressive mood ($p=0.007$), whereas being able to remain smoke-free for longer periods in previous quitting attempts was associated with higher likelihood of success ($p=0.005$).

Conclusion: The success of smoking cessation with varenicline therapy is lower in the presence of the following factors: having high risk for anxiety and depression, smoking a greater number of cigarettes per day, shorter periods of remaining smoke-free in previous quitting attempts, and experiencing nervousness during withdrawal. Receiving physician advice to quit also appears to increase the chance of quitting smoking.

Keywords: Smoking; Smoking Cessation; Smoking Cessation Agents; Varenicline; Anxiety; Depression

INTRODUCTION

Smoking causes oxidative stress and leads to a wide variety of chronic diseases and cancers that place a significant burden on health systems (1). It is reported that life expectancy in smokers is shortened by more than 10 years compared to those who have never smoked. On the other hand, quitting smoking before age 40 reduces the risk of smoking-related death by approximately 90% (2). With smoking cessation, risks for cardiovascular events and mortality decrease remarkably (3).

Professional support while quitting makes it easier to quit smoking (4). Varenicline is an FDA-approved cost-effective smoking cessation therapeutic that works by countering the effects of nicotine on nAChRs (5, 6). Although possible neuropsychiatric events with varenicline treatment were reported in earlier years, current evidence shows that such a relationship does not exist (7).

Most smokers state that they smoke in response to stress or other negative mood disorders, which makes it challenging to quit smoking (8). Smoking remains the most important modifiable risk factor for health disparities; therefore, identifying factors associated with the success of smoking cessation therapy in different regions and populations are critical to ensure that smokers can reliably quit this extremely dangerous addiction (9). As such, we aimed to determine factors affecting smoking cessation among individuals who received varenicline treatment.

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MATERIAL AND METHODS

This retrospective study was carried out in Istanbul Medeniyet University Göztepe Training and Research Hospital Family Medicine Clinic, Smoking Cessation Outpatient Clinic between January 2018 and January 2019. Ethics committee approval was obtained for the study, and the research was carried out in accordance with the Declaration of Helsinki (Approval date: June, 2018, no:2018/0255).

Within the scope of the study, the files of patients who applied to the smoking cessation outpatient clinic between January 2017 and January 2018 to quit smoking were analyzed retrospectively. Among the 970 files examined, patients who were started on varenicline treatment for smoking cessation and continued the treatment for at least 1 month were selected for evaluation. In order to be able to assess smoking cessation accurately, we only included patients in which at least 6 months of post-treatment data (after varenicline treatment) were available. This inclusion/exclusion assessment resulted in the identification of 327 patients; 209 of these patients who could be reached by phone and agreed to participate in the study constituted the study group. Sociodemographic variables, comorbidities, alcohol consumption, smoking-related characteristics (starting age, pack-years, previous quitting attempts etc.) and other relevant parameters were questioned and analyzed.

The smoking cessation polyclinic is operated by a family medicine specialist with a "Tobacco Addiction Treatment Training" certificate. Patients can apply to the clinic as walk-in patients by making an appointment with the 171 smoking cessation hotline or being referred with a smoking cessation recommendation from other clinics. At the first admission to the clinic, electrocardiogram (ECG), pulmonary function tests (PFTs), postero-anterior chest X-ray, brief biochemistry and hemogram examinations are performed. Patients are called for routine control once a month, but if they need earlier support or want to get feedback on any side effects, they can also apply to the center at their discretion. Patients are informed about the health hazards of smoking and the economic burden it brings, and brochures about these issues are distributed.

Sociodemographic characteristics, medical history, smoking behaviors and attitudes, reasons for quitting smoking, nicotine addiction levels, and anxiety and depression status were recorded from the patients' medical records. In order to obtain the most up-to-date information about the smoking cessation status of the patients in the study group, each patient was contacted by phone to record data. Among the patients, those who quit smoking within 3 or 6 months and stated that they started smoking again at the 6th or 12th month, respectively, were defined to have experienced relapse.

The Fagerström test for nicotine dependence (FTND): The FTND was applied to determine the nicotine addiction levels of individuals. This test was developed in 1978 by Fagerström and colleagues. The score that can be obtained from the test consisted of six questions ranging from 1 to 10. If the total score is 0-2, it is evaluated as very low addiction, 3-4 low-level addiction, 5 medium-level addiction, 6-7 high-level addiction, and 8-10 very high-level nicotine addiction (10, 11).

The Hospital Anxiety and Depression Scale (HADS): The HADS, developed by Zigmond and Snaith, was used to evaluate anxiety and depression levels. Anxiety (items 1, 3, 5, 7, 9, 11 and 13) and depression (items 2, 4, 6, 8, 10, 12 and 14) were evaluated. In the Turkish version of the HADS, the cut-off value was reported as 10 for the anxiety sub-domain and 7 for the depression sub-domain. In addition, by summing both subfield scores, the patients' mood can be classified as euthymic, minor depressive, or major depressive (12, 13).

Statistical Analysis: All analyses were subject to the classical significance testing threshold ($p \leq 0.05$) and were performed on version 25.0 of the SPSS software (IBM, Armonk, NY, USA). For the normality check, histograms and Q-Q plots were used and continuous variables were described with mean \pm standard deviation or median (1st quartile - 3rd quartile) according to the presence or absence of normal distribution (respectively). Nominal data were reported with counts and relative frequency. Normally distributed variable comparisons were performed with the independent samples t-test. Non-normally distributed variable comparisons were performed with the Mann-Whitney U test. Categorical variable distributions were compared with appropriate chi-square tests or the Fisher's exact test. Multivariable (multiple) logistic regression analysis was performed with the forward conditional method to determine factors independently associated with unsuccessful treatment.

RESULTS

There were 90 (43.1%) women, and 119 (56.9%) men in the study group and the mean age of the group was 41.34 ± 10.93 (21-64) years. The frequency of smoking cessation was determined to be 63.2% ($n=132$) among varenicline recipients. The groups were similar in terms of age ($p=0.188$), sex ($p=0.737$), marital status ($p=0.569$), occupation ($p=0.966$), education status ($p=0.197$), comorbidities ($p=0.308$) and alcohol use (0.923). The median HADS-anxiety ($p<0.001$), HADS-depression ($p<0.001$) and HADS-total ($p<0.001$) scores were higher in quitters. The frequency of anxiety ($p<0.001$), depression ($p<0.001$), and major depression ($p<0.001$) was significantly higher in those who could not quit smoking (**Table 1**).

Age at onset of smoking ($p=0.238$) and number of pack-years ($p=0.620$) were similar between the groups. The median number of cigarettes smoked per day was significantly lower in those who stopped smoking ($p=0.011$). The frequency of patients who had previously attempted to quit smoking was similar in the two groups ($p=0.816$). Patients who quit smoking after varenicline treatment reported longer periods of remaining smoke-free (months) during their prior attempts to quit ($p<0.001$). The groups were similar in terms of seeking professional support ($p=0.421$). The three most common reasons for quitting smoking were fear of contracting a disease (71.8%), economic reasons (48.8%), and being bothered by bad odor (37.8%). There was no difference between the groups in terms of existing diseases ($p=0.582$), anxiety to contract a disease ($p=0.174$), harm to the environment ($p=0.373$), economic reasons ($p=0.059$), beliefs ($p=0.330$), aspiring to be a model individual ($p=0.128$), social pressure ($p=0.196$), embarrassment ($p=0.366$), and being bothered by bad odor ($p=0.694$).

Table 1. Summary of patient characteristics with regard to smoking status after treatment.

	Total (n=209)	Smoking (n=77)	Quit (n=132)	p
	Mean ± SD.	Mean ± SD.	Mean ± SD.	
Age	41.34 ± 10.93	40.04 ± 10.38	42.11 ± 11.2	0.188
	n (%)	n (%)	n (%)	
Sex				
Female	90 (43.1)	32 (41.6)	58 (43.9)	0.737
Male	119 (56.9)	45 (58.4)	74 (56.1)	
Marital status				
Married	125 (59.8)	48 (62.3)	77 (58.3)	0.569
Single	84 (40.2)	29 (37.7)	55 (41.7)	
Occupation				
Working	151 (72.2)	55 (71.4)	96 (72.7)	0.966
Not-working	58 (27.8)	22 (28.6)	36 (27.3)	
Education status				
Illiterate	1 (0.5)	0 (0.0)	1 (0.8)	0.197
Primary school	48 (23.0)	21 (27.3)	27 (20.5)	
Secondary school	31 (14.8)	12 (15.6)	19 (14.4)	
High school	72 (34.4)	30 (39.0)	42 (31.8)	
University	57 (27.3)	14 (18.2)	43 (32.6)	
Comorbidities	91 (43.5)	30 (39.0)	61 (46.2)	0.308
Chronic obstructive pulmonary disease	12 (5.7)	6 (7.8)	6 (4.5)	0.365
Diabetes mellitus	33 (15.8)	14 (18.2)	19 (14.4)	0.598
Hypertension	27 (12.9)	10 (13.0)	17 (12.9)	1
IM	9 (4.3)	3 (3.9)	6 (4.5)	1
Coronary artery disease	20 (9.6)	6 (7.8)	14 (10.6)	0.672
Other	32 (15.3)	9 (11.7)	23 (17.4)	0.362
Alcohol use	51 (24.4)	18 (23.4)	33 (25.0)	0.923
HADS-anxiety score (Mean ± SD.)	7.83 ± 3.95	9.69 ± 3.91	6.75 ± 3.57	<0.001
<10	141 (67.5)	41 (53.2)	100 (75.8)	0.001
≥10	68 (32.5)	36 (46.8)	32 (24.2)	
HADS-depression score (Mean ± SD.)	6.74 ± 3.56	8.17 ± 3.54	5.90 ± 3.31	<0.001
<7	114 (54.5)	29 (37.7)	85 (64.4)	<0.001
≥7	95 (45.5)	48 (62.3)	47 (35.6)	
HADS-total score (Mean ± SD.)	14.55 ± 6.66	17.86 ± 6.37	12.61 ± 6.06	<0.001
Euthymic (≤12)	92 (44.0)	16 (20.8)	76 (57.6)	<0.001
Minor depressive (13-18)	56 (26.8)	26 (33.8)	30 (22.7)	
Major depressive (≥19)	61 (29.2)	35 (45.5)	26 (19.7)	

HADS: Hospital Anxiety and Depression Scale, SD.: Standard deviation, n: number, %: percent, Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables

The frequency of quitting smoking after receiving physician advice was higher in those who could quit ($p=0.011$), and the frequency of quitting due to workplace pressure was higher in those who could not quit ($p=0.006$).

The median FTND score was significantly higher among non-quitters compared to those who had quit ($p<0.001$). According to the FTND score, the frequency of being 'highly dependent' was higher in those who could not quit smoking ($p=0.024$). The frequency of people who took nicotine replacement therapy in addition to varenicline treatment was similar between the two groups ($p=1.000$).

There was no difference between the groups in terms of treatment duration ($p=0.115$). The three most common symptoms found after treatment was uneasiness (20.6%), insomnia (16.7%), and nervousness (15.8%). The frequency of nervousness ($p=0.004$), uneasiness ($p=0.018$), and depressive mood ($p=0.011$) were significantly higher among non-quitters. There was no difference between the groups in terms of other symptoms. The frequency of side effects after treatment was 23.4%, and there was no difference between the two groups ($p=0.182$). The groups were similar in terms of treatment follow-up time ($p=0.182$). The median time spent without smoking was higher in those who quit smoking ($p<0.001$, **Table 2**).

Table 2. Summary of patients' smoking and quitting characteristics with regard to smoking status after treatment.

	Total (n=209) Median (IQR)	Smoking (n=77) Median (IQR)	Quit (n=132) Median (IQR)	p
Age at onset of smoking	18 (15 - 19)	17 (15 - 19)	18 (16 - 19)	0.238
Number of cigarettes, in a day	20 (20 - 30)	30 (20 - 40)	20 (20 - 30)	0.011
Number of pack-years	24 (16 - 36)	24 (16 - 38)	24.5 (16 - 36)	0.62
Tried to quit before	174 (83.3%)	63 (81.8%)	111 (84.1%)	0.816
Longest period without smoking, month, before treatment	1 (0.1 - 3)	0.25 (0.1 - 1)	1.42 (0.25 - 6)	<0.001
	n (%)	n (%)	n (%)	
Professional help for quitting	57 (27.3)	18 (23.4)	39 (29.5)	0.421
Pharmacological	46 (22.0)	16 (20.8)	30 (22.7)	
Acupuncture	4 (1.9)	0 (0.0)	4 (3.0)	0.411
Psychiatric	7 (3.3)	2 (2.6)	5 (3.8)	
Reason to quit				
Existing diseases	52 (24.9)	17 (22.1)	35 (26.5)	0.582
Anxiety to catch a disease	150 (71.8)	51 (66.2)	99 (75.0)	0.174
Harm to environment	69 (33.0)	22 (28.6)	47 (35.6)	0.373
Economic reasons	102 (48.8)	31 (40.3)	71 (53.8)	0.059
Beliefs	10 (4.8)	2 (2.6)	8 (6.1)	0.33
To be a model individual	39 (18.7)	19 (24.7)	20 (15.2)	0.128
Social pressure	6 (2.9)	4 (5.2)	2 (1.5)	0.196
Embarrassment	23 (11.0)	6 (7.8)	17 (12.9)	0.366
Bothered by the smell	96 (45.9)	34 (44.2)	62 (47.0)	0.694
Doctor advice	79 (37.8)	20 (26.0)	59 (44.7)	0.011
Workplace pressure	15 (7.2)	11 (14.3)	4 (3.0)	0.006
	n (%)	n (%)	n (%)	
Factors increasing smoking				
Tea/Coffee	112 (53.6)	43 (55.8)	69 (52.3)	0.617
Alcohol	17 (8.1)	5 (6.5)	12 (9.1)	0.689
Postprandial	148 (70.8)	55 (71.4)	93 (70.5)	1
Stress	153 (73.2)	58 (75.3)	95 (72)	0.714
Other	18 (8.6)	8 (10.4)	10 (7.6)	0.657
Another smoker at home	132 (63.2)	50 (64.9)	82 (62.1)	0.684
Anybody non-smoker at home	143 (68.4)	51 (66.2)	92 (69.7)	0.603
FTND score (Mean \pm SD.)	6.88 \pm 1.98	7.48 \pm 1.57	6.53 \pm 2.12	<0.001
Minimally dependent (0-3)	8 (3.8)	0 (0.0)	8 (6.1)	
Moderately dependent (4-6)	74 (35.4)	23 (29.9)	51 (38.6)	0.024
Highly dependent (7-10)	127 (60.8)	54 (70.1)	73 (55.3)	
Treatment				
Varenicline	176 (84.2)	65 (84.4)	111 (84.1)	1
Varenicline + NRT	33 (15.8)	12 (15.6)	21 (15.9)	
Duration of treatment				
One month	11 (5.3)	1 (1.3)	10 (7.6)	0.115
Two months	79 (37.8)	28 (36.4)	51 (38.6)	
Three months	119 (56.9)	48 (62.3)	71 (53.8)	
Symptoms after treatment				
Nervousness	33 (15.8)	20 (26.0)	13 (9.8)	0.004
Uneasiness	43 (20.6)	23 (29.9)	20 (15.2)	0.018
Concentration problems	26 (12.4)	14 (18.2)	12 (9.1)	0.088
Insomnia	35 (16.7)	10 (13.0)	25 (18.9)	0.358
Anxiety	6 (2.9)	2 (2.6)	4 (3.0)	1
Fatigue	23 (11.0)	13 (16.9)	10 (7.6)	0.065
Abnormal dreams	18 (8.6)	3 (3.9)	15 (11.4)	0.109
Tremor/Shivering	4 (1.9)	2 (2.6)	2 (1.5)	0.626
Drowsiness	12 (5.7)	7 (9.1)	5 (3.8)	0.13
Oral aphthae	17 (8.1)	7 (9.1)	10 (7.6)	0.901
Constipation	30 (14.4)	10 (13.0)	20 (15.2)	0.821
Palpitation	2 (1.0)	1 (1.3)	1 (0.8)	1
Depressive mood	7 (3.3)	6 (7.8)	1 (0.8)	0.011
Other	49 (23.4)	17 (22.1)	32 (24.2)	0.852
Side effect	49 (23.4)	17 (22.1)	32 (24.2)	0.852
Follow-up time, month (range 6-21)	10 (8 - 16)	10 (9 - 18)	9 (8 - 14)	0.182
Quit smoking and restart	69 (33.0)	69 (89.6)	-	N/A
Duration without smoking, month	8 (4 - 9)	3 (3 - 5)	9 (8 - 11)	<0.001
Re-apply	14 (6.7)	14 (18.2)	-	N/A

FTND: Fagerström Test for Nicotine Dependence, n: number, %: percent, SD.: Standard deviation, N/A: Not-Applicable, IQR: Interquartile range. Data are given as mean \pm standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables

We performed multiple logistic regression analyses to determine significant factors independently associated with relapse after treatment. We found that higher daily cigarette count ($p=0.008$), higher HADS-Total score ($p<0.001$), nervousness ($p=0.046$) and depressive mood ($p=0.007$) were independently associated with unsuccessful treatment. In addition, we found that individuals who were able to remain

smoke-free for longer periods before treatment ($p=0.005$) were more likely to quit smoking. Other variables included in the model, trying to quit due to doctor advice ($p=0.160$), trying to quit due to workplace pressure ($p=0.309$), HADS-Anxiety score ($p=0.908$), HADS-Depression score ($p=0.770$), FTND score ($p=0.450$) and uneasiness after treatment ($p=0.105$) were found to be non-significant (**Table 3**).

Table 3. Significant factors of the unsuccessful Varenicline treatment, multiple logistic regression analysis.

	β coefficient	Standard Error	p	Exp(β)	95.0% CI for Exp(β)	
Number of cigarette, in a day	0.048	0.018	0.008	1.049	1.013	1.086
Longest period without smoking, month	-0.194	0.07	0.005	0.823	0.718	0.944
HADS Total score	0.145	0.03	<0.001	1.156	1.089	1.227
Nervousness after treatment	0.882	0.443	0.046	2.416	1.014	5.756
Depressive mood after treatment	3.673	1.368	0.007	39.353	2.693	575.129
Constant	-3.73	0.716	<0.001	0.024		

Dependent variable: Continue/restart smoking; Nagelkerke R²=0.422, CI: Confidence Interval, %: percent

DISCUSSION

Varenicline, which relieves withdrawal and craving symptoms that occur when not smoking, has been demonstrated to increase smoking cessation rates compared to other pharmacotherapeutics (14). In this study, we examined factors affecting the success of smoking cessation with Varenicline.

In the current study, 63.2% of varenicline recipients successfully quit smoking. This is a remarkable result because various studies have reported 12-month cessation rates of 35.3% and 24.5% in varenicline recipients (15,16). The high success found in our study may be explained by various characteristics of the study group, including sociodemographics, comorbidities, motivation to quit, health literacy and the differences in the interventions and methods applied for smoking cessation.

In this study, the three most common motivations were fear of disease (71.8%), economic reasons (48.8%), and being bothered by bad odor (37.8%). In the study of Buczkowski et al., the three most common motivations to quit smoking were reported as a smoking ban at home or work, high cigarette prices, and influences of peers (17). In the study by Dickens et al., it was reported that health concerns were the primary reason for quitting smoking (18). Concerns regarding physical fitness are also reported in different populations and the cost of tobacco products (19). In a study from Turkey by Yaşar et al., the three most common reasons for quitting smoking were reported as medical advice, current illness and fear of illness, indicating that fear of disease and physician advice appears to be effective on patients in Turkey (20). It was concluded that the motivation to quit smoking could be increased by providing knowledge regarding the effects of smoking on health, keeping the price of tobacco products high, and ensuring that physicians advise patients whenever possible, especially in Turkey.

In this study, the frequency of quitting smoking due to physician advice was significantly higher in those who successfully quit smoking with Varenicline. This again shows the importance of positive health behavior recommendations about smoking, especially when received from physicians.

Nicotine replacement therapy is based on the controlled administration of nicotine, which facilitates tobacco abstinence by partially replacing the nicotine obtained from previous tobacco use. With nicotine replacement therapy, nicotine receptors are stimulated, reducing the desire to smoke and withdrawal symptoms (4). In the current study, we found that adding nicotine replacement therapy to Varenicline was not independently effective in smoking cessation success. According to a meta-analysis by Guo et al., in which randomized controlled trials of varenicline therapy were assessed, it was reported that combined treatments with Varenicline, bupropion and nicotine replacement therapy produced more positive results than monotherapies (21). According to the results of another study, it was reported that Varenicline in combination with nicotine replacement was more effective than Varenicline alone in the treatment of tobacco withdrawal (22). In the study of Baker et al., there was no significant difference in the prevalence of smoking cessation between those treated with varenicline and nicotine patches and those treated with varenicline monotherapy (23). Therefore, it appears that adding nicotine replacement therapy to varenicline treatment should be decided on

Those with high nicotine addiction have difficulty quitting smoking compared to those with lower addiction levels (24). In some previous studies, it was reported that the median FTND score was higher in those who could not quit smoking, similar to our study (20,25). The main feature of nicotine addiction is the desire to feel the positive pharmacological effects of nicotine, such as psychoactive stimulation, and to avoid possible withdrawal symptoms (4). Withdrawal symptoms such as depressed mood, insomnia, and irritability occur when the target nAChR receptors are no longer occupied by nicotine. These negative feelings are reported to facilitate the urge to continue smoking (26). In this study, the three most common symptoms found after treatment were uneasiness (20.6%), insomnia (16.7%) and nervousness (15.8%). The frequency of these symptoms was higher among those who could not quit smoking. In another study, the most common withdrawal symptoms were reported as nervousness, craving for cigarettes, and loss of concentration (20). Smoking cessation rates may be increased by supporting

patients who report these symptoms at greater frequency or severity.

In this study, a lower cigarette count per day was one of the independent predictors of smoking cessation, which was a replication of the findings from the study by Klemperer and colleagues (27).

Of note, a study from Turkey reported conflicting results to the literature and found no relationships between depression or anxiety among those who did and did not quit smoking (20).

CONCLUSION

This study shows that a higher HADS-Total score, higher number of daily cigarettes, suffering from nervousness after treatment initiation, and having depressive mood were independently associated with unsuccessful varenicline therapy; whereas being able to quit smoking for longer periods in prior attempts to quit was associated with higher likelihood of successful cessation. Following up on individuals who will receive Varenicline for smoking cessation in terms of anxiety and depression and treating these diseases in at-risk individuals may increase treatment success. It also appears that receiving physician advice increased the motivation to quit smoking and the success of cessation therapy, which might be important factors to consider in patients from Turkey. We conclude that prospective and more comprehensive studies evaluating factors affecting smoking cessation success with Varenicline are required, especially in Turkey.

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REFERENCES

- WHO, Assessment of the Economic Costs of Smoking Available from: http://apps.who.int/iris/bitstream/handle/10665/44596/9789241501576_eng.pdf;jsessionid=AE2D3D8F6FFD7926B13820E6DA2E4F96?sequence=1, access date: 22.05.2022.
- Jha, P., et al., 21st-century hazards of smoking and benefits of cessation in the United States. *New England Journal of Medicine*. 2013;368(4):341-50.
- Ferri, C., Strategies for reducing the risk of cardiovascular disease in patients with chronic obstructive pulmonary disease. *High Blood Pressure & Cardiovascular Prevention*. 2015;22(2):103-11.
- Giulietti, F., et al., Pharmacological Approach to Smoking Cessation: An Updated Review for Daily Clinical Practice. *High Blood Press Cardiovasc Prev*. 2020;27(5):349-62.
- Cahill, K., et al., Nicotine receptor partial agonists for smoking cessation. *Cochrane database of systematic reviews*. 2016;9(5):CD006103.
- Baker, C.L. and G. Pietri, A cost-effectiveness analysis of varenicline for smoking cessation using data from the EAGLES trial. *Clinico Economics and Outcomes Research*. 2018;10:67-74.
- Anthenelli, R.M., et al., Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *The Lancet*. 2016; 387(10037):2507-20.
- Kalkhoran, S., N.L. Benowitz, and N.A. Rigotti, Prevention and Treatment of Tobacco Use: JACC Health Promotion Series. *Journal of the American College of Cardiology*. 2018;72(9):1030-45.
- Gilbody, S., et al., Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. *The Lancet Psychiatry*. 2019;6(5):379-90.
- Uysal, M.A., et al., Fagerstrom test for nicotine dependence: reliability in a Turkish sample and factor analysis. *Tuberk Toraks J*. 2004;52(2):115-21.
- Heatherton, T.F., et al., The Fagerström test for nicotine dependence: a revision of the Fagerstrom Tolerance Questionnaire. *British journal of addiction*. 1991;86(9):1119-27.
- Zigmond, A.S. and R.P. Snaith, The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*. 1983;67(6):361-70.
- Aydemir, O., Hastane anksiyete ve depresyon olcegi Turkce formunun gecerlilik ve guvenilirliigi. *Turk Psikiyatri Derg*. 1997;8:187-280.
- Perez-Paramo, Y.X. and P. Lazarus, Pharmacogenetics factors influencing smoking cessation success; the importance of nicotine metabolism. *Expert Opinion on Drug Metabolism & Toxicology*. 2021;17(3):333-49.
- Lieberman, J.N., et al., Adherence to Varenicline and Associated Smoking Cessation in a Community-Based Patient Setting. *Journal of Managed Care Pharmacy*. 2013;19(2):125-31.
- Ebbert, J.O., et al., Effect of Varenicline on Smoking Cessation Through Smoking Reduction: A Randomized Clinical Trial. *JAMA*. 2015;313(7):687-94.
- Buczkowski, K., et al., Motivations toward smoking cessation, reasons for relapse, and modes of quitting: results from a qualitative study among former and current smokers. *Patient Preference Adherence*. 2014;8:1353-63.
- Dickens, G.L., J. Staniford, and C.G. Long, Smoking behaviour, motives, motivation to quit and self-efficacy among patients in a secure mental health service: comparison with staff controls. *Journal of Psychiatric and Mental Health Nursing*. 2014;21(6):483-90.
- Villanti, A.C., et al., Reasons to quit and barriers to quitting smoking in US young adults. *Family Practice*. 2016;33(2):133-9.
- Yaşar, Z., et al., One-year follow-up results of smoking cessation outpatient clinic: factors affecting the cessation of smoking. *Eurasian J Pulmonol*. 2014;16(2):99-104.
- Guo, K., et al., The effect of Varenicline and Bupropion on smoking cessation: A network meta-analysis of 20 randomized controlled trials. *Addictive Behaviors*. 2022;131:107329.
- Koegelenberg, C.F., et al., Efficacy of varenicline combined with nicotine replacement therapy vs varenicline alone for smoking cessation: a randomized clinical trial. *JAMA*. 2014;312(2):155-161.
- Baker, T.B., et al., Effects of Combined Varenicline With Nicotine Patch and of Extended Treatment Duration on Smoking Cessation: A Randomized Clinical Trial. *JAMA*. 2021;326(15):1485-93.

24. Lindberg, A., et al., Low nicotine dependence and high self-efficacy can predict smoking cessation independent of the presence of chronic obstructive pulmonary disease: a three year follow up of a population-based study. *Tobacco Induced Diseases*. 2015;13(1):27.
25. Eum, Y.H., et al., Factors related to the success of smoking cessation: A retrospective cohort study in Korea. *Tobacco Induced Diseases*. 2022;20:15.
26. Minichino, A., et al., Smoking behaviour and mental health disorders--mutual influences and implications for therapy. *International Journal of Environmental Research and Public Health*. 2013;10(10):4790-811.
27. Klemperer, E.M., et al., Predictors of Smoking Cessation Attempts and Success Following Motivation-Phase Interventions Among People Initially Unwilling to Quit Smoking. *Nicotine & Tobacco Research*. 2020;22(9):1446-52.