

Juan M. Molina-Linde¹

Effectiveness of smoking cessation programs for seriously mentally ill

¹Agencia de Evaluación de Tecnologías Sanitarias de Andalucía (AETSA), Sevilla

Introduction. Many studies have supported the significant association between mental illness and smoking habit, with relative independence of socio-cultural factors. The aim of this study was to review effective strategies for smoking cessation of adults with major depression, schizophrenia and psychosis.

Material and methods. An extensive literature search was performed in Medline, Embase, PsycINFO, Cochrane Library, Center for Reviews and Dissemination, ECRI, clinicaltrials.gov, UK National Research Register, Current Controlled Trials, Trip Database, NLM Gateway, Networked Digital Library of Theses and Dissertations (electronic theses and dissertations (ETDs)), TESEO, Dialnet, Lilacs, SciELO, EMI, Doyma, and Catalogue et Index des Sites Medical Francophones. We selected all systematic reviews, comprehensive reports, clinical trials, observational studies and recommendations, which had evaluated smoking cessation programs in patients with severe mental illness.

Results. Few studies focusing on smoking cessation in severe mental illness were found. In the treatment of smokers who suffer these mental disorders, it is recommended to increase and prolong the treatment period, to implement joint psychoeducation techniques, cognitive-behavioral techniques and the use of any drug treatment that helps to control and / or reduce the occurrence of relapses in tobacco consumption or baseline psychiatric symptoms. However, there is great heterogeneity in the recommendations given by the studies.

Conclusions. It remains unclear whether people with severe mental illness could benefit from access to smoking cessation treatments. In the best of the scenarios, it was

seen that drug therapy and psychosocial interventions have indicated abstinence at 6 months for a few patients.

Key words:

Smoking, psychopathology, depression, psychosis, schizophrenia.

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Efectividad de los programas de deshabituación tabáquica para enfermos mentales graves

Introducción. Numerosas investigaciones señalan la asociación significativa entre enfermedad mental y fumar, relativamente independiente de factores socioculturales. El objeto de este estudio fue examinar las estrategias eficaces para la deshabituación tabáquica en adultos con depresión mayor, esquizofrenia y psicosis.

Material y métodos. Se ha realizado una búsqueda bibliográfica extensa en Medline, Embase, PsycINFO, Cochrane Library, Centre for Reviews and Dissemination, ECRI, clinicaltrials.gov, UK National Research Register, Current Controlled Trials, Trip Database, NLM Gateway, Networked Digital Library of Theses and Dissertations (electronic theses and dissertations (ETDs)), TESEO, Dialnet, Lilacs, Scielo, IME, Doyma y Catalogue et Index des Sites Médicaux Francophones. Se seleccionaron todas las revisiones sistemáticas, informes completos, ensayos clínicos, estudios observacionales y recomendaciones, que hubieran evaluado programas de deshabituación tabáquica en enfermos con patología mental grave.

Resultados. Existen pocos estudios que se centren en la deshabituación tabáquica en enfermos mentales graves. En el tratamiento del tabaquismo en pacientes que padecen alguna de estas patologías mentales es conveniente: incrementar y prolongar el tiempo de tratamiento, poner en práctica técnicas conjuntas de psicoeducación, cognitivo-conductuales y la utilización de algún tratamiento farmacológico que ayude a controlar y/o reducir la aparición de recaídas en el consumo de tabaco o en la sintomatología psiquiátrica de base. No obstante, existe una gran heterogeneidad en las recomendaciones de los estudios.

Correspondence:

Juan Máximo Molina Linde
Avda. de la Innovación, s/n
Edificio RENTA SEVILLA. 2ª planta.
Sevilla (Spain)
41020
E-mail: juanm.molina.ext@juntadeandalucia.es

Conclusiones. Permanece confuso si las personas con enfermedad mental grave pueden beneficiarse del acceso a tratamientos de deshabituación tabáquica. En el mejor de los casos, la terapia farmacológica y las intervenciones psicosociales apuntan a la abstinencia a los 6 meses para muy pocos pacientes.

Palabras clave:

Fumar, psicopatología, depresión, psicosis, esquizofrenia.

INTRODUCTION

Smoking is a serious public health problem both nationally and worldwide. It is estimated that smoking is responsible for almost 5,000,000 premature deaths per year worldwide, mainly because of the etiological role of smoking on cardiovascular diseases, chronic obstructive pulmonary disease and lung disease.¹ In our country, it is estimated that more than 50,000 deaths occur per year due to smoking. This accounts for 15.5% of all the deaths in persons over 35 years.²

Tobacco dependence is recognized as a mental and behavioral disorder in the International Classification of Disease of the WHO (ICD-10)³ and in the Diagnostic and Statistical Manual of Mental Disorders of the American Association of Psychiatry (DSM-IV-TR).⁴

Patients with serious mental disorders have a greater prevalence of smoking than in the general population.⁵ Therefore, it has been observed that the likelihood that a person who smokes may have a mental disorder is twice that of a person who does not have one.^{6,7} These patients more frequently meet the nicotine dependence criteria, this also being more intense, when they are measured by the usually established criteria.⁸ In general, there is a directly proportional relationship between the intensity of the psychiatric symptoms and the severity of the smoking dependence.^{9,10}

Furthermore, in mental patients, smoking has special scientific connotations: due to the effect they have on the nicotine receptors in the pathophysiology of diseases such as schizophrenia.¹¹ In other words, the cholinergic stimulating effect of the nicotine can be interpreted as a self-medication measure aimed at decreasing the cognitive defect and the stimulus on the mesolimbic dopaminergic pathway could improve tolerance to undesirable effects of the antipsychotics.¹² It is also speculated that there would be a common vulnerability that would link tobacco usage and that of other substances with the mood state and anxiety disorders,¹³ and, on the other part, culture ones, since smoking is something embedded in the culture of the mental health services.

In the management of these patients, this is a generally accepted fact, even though the tests show that tobacco is especially harmful for mental patients.¹⁴ Both the patients as well as the staff¹⁵ have demonstrated limited preparation and an attitude that is not favorable for the approach to nicotine dependence.¹⁶ Because of these circumstances, the problem of smoking has been overlooked, depriving mental patients of the necessary interventions for its control and prevention.¹⁷ This is especially serious if it is considered that the data show that reduction or discontinuation of smoking is important to improve the quality of life and its longevity.¹⁸ However, more recent initiatives have focused their objectives on improving the physical health of persons with severe mental disease and guidelines have been published on the smoking cessation interventions in these patients.¹⁹⁻²¹

The prevention of morbidity and mortality related with tobacco requires effective interventions aimed at smoking cessation.

The purpose of this research consisted in gathering the most relevant documents and summarizing their conclusions in order to provide information on smoking cessation in severe mental patients: major depression, schizophrenia and psychosis.

MATERIAL AND METHODS

A search was made to locate the principal documents on smoking cessation in severe mental patients. To do so, the following reference databases were used: MedLine (including PRE-MEDLINE by OVID), Embase (Evidence Based Medicine) and PsycINFO, as well as the Cochrane Library, Centre for Reviews and Dissemination, ECRI, clinicaltrials.gov, UK National Research Register, Current Controlled Trials, Trip Database, NLM Gateway, Networked Digital Library of Theses and Dissertations (electronic theses and dissertations (ETDs)), TESEO, Dialnet, Lilacs, Scielo, IME, Doyma and Catalogue et Index des Sites Médicaux Francophones.

The search strategies used in MedLine, Embase and PsycINFO are shown in Tables 1, 2 and 3, respectively. Very open strategies in free text were used in the remaining databases. Furthermore, manual searches were made in the list of references.

All of the systematic reviews, complete reports, clinical trials, observational studies and recommendations that had evaluated smoking cessation programs in patients with a severe mental condition were selected.

The review of the literature to identify original studies and pertinent reviews was made without time limitation.

Table 1	Search strategy used in MEDLINE
1.	exp affective disorders, psychotic/ or depressive disorder, major/ or exp "schizophrenia and disorders with psychotic features"/ (137640)
2.	(schizo\$ or hebephreni\$ or psychotic\$ or psychos?s or (depression adj1 major) or bipolar).ti. (93232)
3.	1 or 2 (156292)
4.	exp "Tobacco Use Cessation"/ (16279)
5.	((tobacco or smok\$) and (cessation or reduction or quit\$ or intervention\$ or abstinence)).ti. (8659)
6.	4 or 5 (18172)
7.	3 and 6 (258)
8.	limit 7 to (clinical trial, all or comparative study or controlled clinical trial or meta analysis or multicenter study or randomized controlled trial) (96)
9.	limit 7 to systematic reviews (11)
10.	(trial or random\$ or blind\$ or review).mp. (2900464)
11.	7 and 10 (131)
12.	8 or 9 or 11 (146)

Table 3	Search strategy used in PsycINFO
1.	exp bipolar disorder/ (15197)
2.	exp Major Depression/ (72564)
3.	psychosis/ or affective psychosis/ or chronic psychosis/ or exp "paranoia (psychosis)"/ or exp schizophrenia/ (74769)
4.	(psychosis or psychotic or schizophrenia or bipolar or 'major depression').id. (83556)
5.	1 or 2 or 3 or 4 (164923)
6.	smoking cessation/ or nicotine withdrawal/ (6835)
7.	("smoking cessation" or abstinence or "quit smoking" or "stop smoking" or "nicotine withdrawal").id. (7269)
8.	5 and (6 or 7) (361)
9.	(schizophrenia or psychosis).ti. (41113)
10.	((major or bipolar or psychotic) and (depression or disorder)).ti. (13007)
11.	9 or 10 (53441)
12.	((tobacco or smok*) and (cessation or stop or withdrawal or quit* or abstinence)).ti. (3939)
13.	11 and 12 (59)
14.	8 or 13 (365)
15.	("Treatment Outcome/Clinical Trial" or "empirical study" or "quantitative study" or "Followup study" or "meta analysis").md. (567157)
16.	((randomi*ed or blind or clinical or controlled) and study) or trial or meta*analysis or 'systematic review'.ti. (22100)
17.	15 or 16 (578174)
18.	14 and 17 (160)

Table 2	Search strategy used in EMBASE
1.	'psychosis'/exp OR 'major affective disorder'/exp OR 'mania'/exp (199576)
2.	schizo*:ti OR hebephreni*:ti OR psychotic*:ti OR psychos?s:ti OR ('depression' NEXT/2 'major'):ti OR bipolar:ti (205516)
3.	#1 OR #2 (217300)
4.	'smoking cessation'/exp (26726)
5.	tobacco:ti OR smok*:ti AND (cessation:ti OR reduction:ti OR quit*:ti OR intervention*:ti OR abstinence:ti) (9399)
6.	#4 OR #5 (28176)
7.	#3 AND #6 (516)
8.	schizo*:ti OR hebephreni*:ti OR psychotic*:ti OR psychos?s:ti OR ('depression' NEXT/2 'major'):ti OR bipolar:ti (205520)
9.	#1 OR #8 (217304)
10.	#6 AND #9 (516)
11.	'randomized controlled trial':it OR 'meta analysis':it OR 'controlled clinical trial'/exp OR 'controlled clinical trial' OR trial:ti OR ('clinical trial':it AND (('double' NEXT/3 'blind'):ab,ti OR ('phase' NEXT/4 'study'):ab,ti OR random*:ab,ti)) (439067)
12.	#6 AND #9 AND ([cochrane review]/lim OR [controlled clinical trial]/lim OR [meta analysis]/lim OR [randomized controlled trial]/lim OR [systematic review]/lim) (71)
13.	#10 AND #11 (49)
14.	#12 OR #13 (76)

RESULTS

Most of the interventions with severe mental patients use a combination of pharmacological treatment together with an educational approach or cognitive-behavioral treatment, an approach similar to that used in the nonpsychiatric population.

Major depression

In regards to the population with major depression, we have found studies with different approaches.

Thus, Glassman et al.²² performed a study with 100 smokers with a history of major depression. When they began treatment, none of the subjects were depressed and they had been antidepressant treatment-free for at least 6 months. The subjects were randomly assigned to the sertraline-treated group and to another group with placebo for 9 weeks. In the follow-up at 6 months, data were obtained on 76 out of the 100 smokers. Of these, 42 had quit

smoking and 34 continued to smoke. Of those who continued to smoke, 2 (6%) had symptoms of major depression. Of those who had quit smoking, 13 (31%) had symptoms of major depression. The odds ratio for the latter group was very significant: 7.17.

In a randomized clinical trial²³ with 179 smokers who had suffered major depressive disorder in the past, the benefits were compared between on group with a cognitive-behavioral program for smoking cessation and another group in which the same program was performed with the addition of another cognitive-behavioral program for the treatment of depression. The study recruited smokers with a background of major depressive determined by structured interviews, using the Diagnostic and Statistical Manual of Mental Disorders Manual (DSM-III). In this study, no drug was administered to the participants. The abstinence rates at one month were 33.3% for the cognitive-behavior therapy group for smoking cessation and 37.6% for the group with the addition of therapy for the depression. At one year, the rates were 24.7% and 32.5%, respectively, there being no significant differences found between the treatments. However, a secondary analysis revealed that smokers with recurrent major depression and those who smoked a significant amount had significantly greater likelihood of smoking cessation if they attended both treatment programs and not only the standard program (odds ratio = 2.3 [95% CI= 1.05 to 5.03] and 2.62 [95% CI= 1.18 to 5.83]). The authors point out that the additional program for the treatment of depression can provide some benefits for smokers with major depression.

In contrast to the study of Glassman et al.,²² Cox et al.²⁴ state that the use of the pharmacological treatment, in this case bupropion, seems to be effective to avoid relapses in all range of smokers with and without a history of major depression. They observed significant differences between the smokers who had received the drug versus the control group ($p = 0.007$), independently of whether they had a background or not of major depression.

Along the same line, Kim et al.,²⁵ administered bupropion (150-300 mg/day) to 37 patients for 8 weeks. A total of 28 patients maintained continuous abstinence from the first week to the fourth and 19 patients had successfully abstinence at the eighth week. The authors state that bupropion is useful as a treatment for nicotine dependence in patients with major depressive disorder.

McClure et al.²⁶ used varenicline and behavioral treatment for persons with or without a background of major depression who had intention to quit smoking. The analyses did not show differences for smoking cessation at 21 days between patients with major depression and those who did not have major depression (48.6% for patients with depression. 47.3% for patients without depression; OR = 1.05; 95% CI = 0.84-1.33;

$p = 0.66$) and at three months (44.8% for patients with depression vs. 41.98% for patients without depression; OR = 1.13; 95% CI = 0.89-1.42; $p = 0.32$).

Kinnunen et al.²⁷ recruited 608 participants who received brief therapy plus nicotine replacement treatment, nicotine gum or placebo. A total of 32% of the participants were classified as depressed at the onset of the study. At 12 months of follow-up, the nondepressed participants and those with nicotine replacement therapy were more successful (20.1%) while the depressed patients with placebo had the least success (5.7%) ($p = 0.004$). However, although the participants with depression and nicotine replacement treatment (15.1%) were less successful than the nondepressed with nicotine replacement therapy (20.1%), this difference was not statistically significant ($p = 0.23$).

Schizophrenia

In regards to smoking cessation in patients with schizophrenia, the results are heterogeneous.

The studies show permanence rates of 50% to 94% at the end of the treatment.

In five studies²⁸⁻³² in which the participants received nicotine replacement treatment (NRT) together with attendance to support groups, the smoking cessation rates at the end of the treatment were 42-50%, and at 6 months of follow-up 12-17%.

Of the five studies previously mentioned, Addington et al.²⁸ conducted a study with 50 outpatients with schizophrenia. They divided them into 5 groups that met separately for seven weekly sessions in a smoking cessation program. The program included a positive reinforcement group, learning and role-playing of alternative behaviors, strategies aimed at reduction in control of anxiety as well as nicotine patches. A total of 42% of the participants quit smoking at the end of the group sessions, 16% had maintained abstinence at 3 months and 12% at 6 months. These changes were statistically significant. There were no changes in the positive or negative symptoms of the schizophrenia.

Along this same line, a randomized clinical trial³⁰ was conducted with 45 smokers diagnosed of schizophrenia or schizoaffective disorder. They were assigned to a standard smoking cessation therapy group ($n=17$) or to a specialized group therapy program for smokers with schizophrenia ($n=28$). All the subjects participated in 10 weekly group therapy sessions and were administered nicotine patch treatment (21 mg/day) in addition to receiving their antipsychotic medication. The abstinence rate did not differ

between the two types of group therapy programs, although the smoking cessation rate in the final four weeks of the trial was greater with the specialized program. However, the atypical antipsychotic medications combined with the nicotine patch significantly improved the smoking habit cessation rate (56% with atypical antipsychotics vs 22% with conventional antipsychotics at the end of the program). At 6 months, the results were 16.7% with atypical antipsychotics and 7.4% with conventional antipsychotics. In the atypical antipsychotic group, the carbon monoxide levels significantly decreased. Risperidone and olanzapine were associated with higher rates of dropout, although the sample size was very small in these cases. No changes in the psychiatric symptoms were observed during the evaluations.

Other studies have examined the effect of the nicotine patches together with non-pharmacological interventions. Gallagher et al.³² evaluated the effects of a contingent reward with money (with and without additional nicotine patches), in comparison with a minimum intervention in a group of patients with severe mental diseases. They conducted an analysis of subgroups for the participants with diagnosis of schizophrenia or schizoaffective disorder ($n=80$). A total of 32.5% of the participants expressed their interest to quit smoking. The abstinence rates at week 20 and week 36 (at the end of the study) were significantly greater in the group with contingent reward and nicotine patches compared to the group with contingent reward without nicotine patches (week 20: 56.3% vs. 27.8%; week 36: 50% vs. 27.8%) and also in comparison with the minimum intervention group (week 20: 10%; week 36: 10%).

In another study³³ with 23 patients who attended individual and group therapy together with NRT and behavioral techniques, the results showed a smoking cessation rate of 35% after treatment and 21% at one year of the program.

In studies in which psychosocial treatment was not possible, but that allowed for treatment with NRT^{34, 35} and bupropion,³⁶ reductions were seen in the smoking behavior but not in the drop-out. Similarly, combined positive reinforcement techniques, without the drug treatments seemed to be effective for short-term reduction of the smoking rates, but smoking abstinence was not completed.³⁷

There are several studies that have used bupropion as part of the smoking cessation treatment with schizophrenics. In the Williams et al.³⁸ study, it is seen how bupropion may help to reduce smoking consumption in persons with schizophrenia, and it does not show deterioration of the clinical symptoms of the disease.³⁹ This fact, which occurred with the participation of 53 persons, was not maintained after the treatment when the relapse rate was high.

In a subsequent study,⁴⁰ a combination of NRT and bupropion improved the abstinence and there was reduction of cigarette smoking during the treatment. Fifty-one subjects were randomly assigned to receive bupropion 150 mg or placebo once a day for 7 days, and then twice a day for 11 weeks. The participants attended a smoking cessation program for 12 1-hour group sessions held weekly. In the fourth week, they were provided nicotine patches (Habitrol) and polacrilex nicotine gum (Nicorette). From the onset to week 12, the subjects with bupropion plus NRT had a mean change of -21 cigarettes per day (95% CI = 29-15), and those with placebo had a mean change of -11 cigarettes per day (95% CI = -26 to 4.8). At week 24, those who were in the bupropion + NRT group had a change compared to the baseline of -9.5 (95% CI = -19 to -0.4) cigarettes per day and those of the placebo group plus NRT reported a mean change of -2.9 (95% CI = -24 to 18) cigarettes per day. No effect of the antipsychotics (atypical vs. conventional) on the results of the abstinence was detected. It is important to point out that the incremental benefit of bupropion for smoking cessation and its reduction was only seen during the 12 weeks of duration, that is, during the treatment period. However, the relapse rates in the subjects with bupropion plus NRT was 31% (weeks 8-12) and 77% at 12 months of follow-up.

In another trial of George et al.,⁴¹ 32 subjects diagnosed of schizophrenia or schizoaffective disorder and nicotine dependence with DSM-IV criteria were randomly assigned to a group with bupropion (300 mg/day) or placebo. Those of the bupropion group had a significant increase in the prevalence of smoking cessation at 7 days of treatment compared to those with placebo [Bupropion, 8 / 16 (50.0%), Placebo, 2 / 16 (12.5%); $\chi^2 = 5.24$, $df = 1$, $p = < 0.05$], and the reduction of the carbon monoxide (CO) levels during the evaluation (Medication $\times$ Interaction time; $Z = 3.09$, $p = < 0.01$). The positive symptoms of the schizophrenia were not altered with the use of bupropion, however the negative symptoms decreased significantly.

A recent double blind trial of George et al.⁴² studied whether the combination of bupropion (300 mg/day) together with the nicotine transdermal patch (21 mg/24h) is well-tolerated and superior to placebo plus the patch to achieve smoking cessation in schizophrenia. The study was performed for 10 weeks with 58 outpatients with schizophrenia who smoked. The smokers assigned to the treatment group ($n=29$) had more probability of being successful with smoking cessation (8 / 29, 27.6%) than the placebo group ($n=29$, 1 / 29, 3.4%) (Fisher's exact test, $p = < 0.05$) at 4 weeks of the trial and at 6 months of the treatment, 4 / 29 (13.8%) compared to 0 / 29 (0.0%) ($p = 0.11$). Neither bupropion nor having abandoned the smoking habit significantly altered the positive or negative symptoms of schizophrenia. The side effects of the combination were, in general, few, and included lack of concentration, muscular stiffness and insomnia.

Jun et al.⁴³ evaluated the efficacy and safety of bupropion for smoking cessation in a randomized and double-blind study. The treatment had a time period of 4 weeks and a follow-up of 8 weeks with an experimental group (n=36) treated with bupropion and a control group (n=33) with placebo. A statistically significant decrease was found in cigarette smoking in the experimental group ($p = < 0.01$) after one week and the efficacy rates of treatment at the end of weeks 4 and 8 of the experimental group were 33.3% and 27.8%, respectively, these showing significant differences with the control group (9.1% and 6.1%, respectively) ($p = < 0.01$). More common adverse reactions were found in the experimental group, such as insomnia, dry mouth, restlessness, headache, nausea and diaphoresis ($p = < 0.05$). The authors concluded that tolerability of bupropion, even though it caused mild reactions, was effective and safe for smoking cessation in patients with schizophrenia.

In other studies that have used bupropion but that had very few subjects, one with 10 subjects⁴⁴ and another one with 8 subjects,⁴⁵ similar findings were found.⁴¹⁻⁴³ Bupropion is a safe medication that can be administered to patients with schizophrenia without exacerbating the positive symptoms.

There is no evidence for varenicline in smokers with schizophrenia, except for one case⁴⁶ that describes the exacerbation of the symptoms of the disorder during its use.

In a study with a 2-year follow-up,⁴⁷ it was demonstrated that persons with schizophrenia who reduced the amount of tobacco would probably quit smoking a posteriori.

Psychosis

Only one trial with patients who smoke and who had a psychotic disorder has been found.⁴⁸ The authors recruited 298 regular smokers who lived in the community and who were randomly assigned to the comparison group, that included baseline treatment and educational leaflets (n=151) or to the treatment group, that included eight individual 1 hour sessions with motivational interviews and cognitive-behavior therapy plus NRT, in addition to baseline treatment for their disorder and the supplying of leaflets to quit smoking (n=147). Although they did not find differences between the treatment group and the comparison group in the smoking cessation rates, a significantly greater proportion of the smokers who completed all of the treatment sessions quit smoking in each one of the follow-up evaluations (cessation prevalence rates: at 3 months, 30.0 % vs. 6.0%; at 6 months, 18.6% vs. 4.0%, and at 12 months, 18.6% vs. 6.6%). No changes in the symptoms of the disease were detected.

Our experience in our country is scarce in this type of patients although there are experiences with NRT,⁴⁹ with anti-smoking advice,⁵⁰ or with prohibiting smoking in a psychiatric hospitalization unit.¹¹ However, the results cannot be generalized because of the methodology used.

Finally, it is important to indicate that the studies that analyze the effects of the reduction of smoking are limited to very short-term results. Therefore, the need exists to have trials that evaluate if these results can be maintained and, if they are maintained, if this reduction in the smoking habit could reduce the harm from exposition and/or produce a cessation of the habit at a later date.

Some investigations have evaluated if it is feasible to limit access to smoking within the psychiatric premises due to the fear that such restrictions may incite problematic behaviors among the patient population. Specifically, they have proven the effects of smoking restriction in designated areas or in psychiatric hospitals,^{14, 51} although the methodological limitations do not make it possible to draw solid conclusions.

Although there are investigators who outline possible negative consequences of this approach,^{52, 53} less than 10% of those who smoke and have a psychiatric disease find it difficult to adapt to these restrictions.⁵²

DISCUSSION

Few studies that approach smoking cessation in patients with severe mental disorders as a primary study population have been found and those that have been found do not have high methodology quality. In general, there are methodological difficulties in grouping and interpreting the results due to the high rates of dropout, variability of the interventions and the measurements of the results, contexts, samples and comparison groups.

Although the strength of the evidence is relatively weak, with wide confidence intervals, especially for the long-term benefits, the studies support the efficacy of bupropion in smoking cessation and the reduction of the smoking habit in patients with such incapacitating mental diseases such as schizophrenia. For smoking cessation with other therapeutic options such as NRT and psychosocial interventions, sufficient and robust tests have not been found in this review to support their use in the clinical practice.⁵⁴

The scarcity of quality studies may be explained, at least partially, by the non-scientifically based beliefs on the calming effect of nicotine, especially intense in persons with psychiatric disorders,⁵⁵ in which it also reduces inhibition and social withdrawal (above all, in patients with

schizophrenia). On the other hand, for some mentally-ill patients, smoking is one of their principal occupations in their daily routine, it providing a structure for them within their day few activities. Smoking has been considered as a comprehensive part of the psychiatric culture and a belief that the patient with these diseases is not capable of smoking cessation.⁵⁶

The recent clinical trials and those in the on-going phase, as the one that is being conducted in Spain,⁵⁷ show the growing scientific interest on the subject and the documents recovered manifest the capacity and need that the mentally ill patient has. In recent years, a change in attitudes towards the disease has been occurring. In general, there is a more human view, that is less restrictive and less authoritarian than before. However, the attitude is still very paternalistic with these patients.⁵⁸

Smoking cessation campaigns and social awareness have considerably reduced the prevalence of smoking in the last 20 years. Future projections propose that a high percentage of the population who smoke will have psychiatric comorbidity in the next years. The decrease of the prevalence of smoking from this point on will be slower since the population without mental disorder is already giving up smoking.⁵⁹

Thus, by way of conclusions, the following points could be emphasized:

- The trials on treatment available for smokers with a serious mental disorder have methodological limitations, including the heterogeneous nature of the samples of the participants, the small sample sizes, lack of a definition of the interventions and lack of control groups.
- The smoking habit should be approached in these patients because in addition to it meaning a serious risk of morbidity-mortality, it significantly affects their quality of life.
- There is little data that conclude when the smoking habit should be approached in the recovery of the mental disorder, although it seems to be recommendable to do so when the disorder is stabilized.
- A strategy that should often be considered as the best is that of reducing consumption.
- It is not clear if those persons with serious mental disease can benefit from access to smoking cessation treatments. In the best of the cases, pharmacological therapy (e.g. NRT) and psychosocial interventions point to abstinence at 6 months for very few patients.
- In general, although the smoking cessation rates of patients with serious mental disease may be inferior to those of the non-psychiatric populations, the reasons to quite smoking, such as health and concerns and costs, are comparable.

REFERENCES

1. Ezzati M, López A. Estimates of global mortality attributable to smoking in 2000. *Lancet* 2003;362:847-52.
2. Banegas JR, Díez L, González J, Villar F, Rodríguez F. La mortalidad atribuible al tabaquismo comienza a descender en España. *Med Clin (Barc)* 2005;24:769-71.
3. World Health Organization. International Statistical Classification of Diseases and related Health problems, 10th revision. Geneva: World Health Organization; 1992.
4. American Psychiatric Association. DSM-IV-TR. Manual diagnóstico y estadístico de los trastornos mentales IV. Barcelona: Masson; 2003.
5. De León J, Díaz FJ. A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviours. *Schizophr Res* 2005;76:135-57.
6. Brown C. Tobacco and mental health: a review of the literature. Edinburgh: ASH Scotland; 2004.
7. Lasser K, Boyd W, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: a population based prevalence study. *JAMA* 2000;284:2606-10.
8. West R. Theory of addiction. Oxford: Blackwell Publishing; 2006.
9. Coney JL, Stevens TA, Conney NL. Comorbidity of nicotine dependence with psychiatric and substance-use disorders. In: Kranzler HR, Rounsaville BJ, editors. Dual diagnosis and treatment. New York: Marcel Dekker; 1998. p. 223-61.
10. John U, Meyer C, Rumpf HJ, Hapke U. Smoking, nicotine dependence and psychiatric comorbidity--a population-based study including smoking cessation after three years. *Drug Alcohol Depend* 2004;76:287-95.
11. Knott V, McIntosh J, Millar A, Fisher D, Villeneuve C, Ilivitsky V, et al. Nicotine and smoker status moderate brain electric and mood activation induced by ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist. *Pharmacol Biochem Behav* 2006;85:228-42.
12. Punnoose S, Belgamwar MR. Nicotine for schizophrenia. *The Cochrane Database of Systematic Reviews* 2006;1:CD004838.
13. Farrell M, Howes S, Bebbington P, Brugha T, Jenkins R, Lewis G, et al. Nicotine, alcohol and drug dependence and psychiatric comorbidity. *Br J Psychiatr* 2001;179:432-7.
14. Iglesias C, López G, Alonso MJ. Efectos de la prohibición de fumar en una unidad de hospitalización psiquiátrica. *Actas Esp Psiquiatr* 2008;36:60-2.
15. Reilly P, Murphy L, Alderton D. Challenging the smoking culture within a mental health service supportively. *Int J Ment Health Nurs* 2006;15:272-8.
16. Prochaska JJ, Fromont SC, Hall SM. How prepared are psychiatry residents for treating nicotine dependence? *Acad Psychiatry* 2005;29:256-61.
17. Bron C, Zullino D, Besson J, Borgeat F. Smoking in psychiatry, a neglected problem. *Schweiz Rundsch Med Prax* 2000;89:1695-9.
18. Strasser K, Moeller-Saxone K, Meadows G, Hocking B, Stanton J, Kee P. Smoking cessation in schizophrenia. General practice guidelines. *Aust Fam Physician* 2002;31:21-4.
19. Fiore MC, Jaén CR, Baker TB, Bailey WC, Benowitz NL, Curry SJ, et al. Treating tobacco use and dependence: 2008 Update - Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service; 2008.
20. Dixon L, Perkins D, Calmes C. Guideline Watch (September 2009): Practice Guideline for the Treatment of Patients with

- Schizophrenia. American Psychiatric Publishing; 2009.
21. Buchanan RW, Kreyenbuhl J, Kelly DL, Noel JM, Boggs DL, Fischer BA, et al. The 2009 Schizophrenia PORT Psychopharmacological Treatment Recommendations and Summary Statements. *Schizophr Bull* 2010;36:71-93.
22. Glassman AH, Covey LS, Stetner F, Rivelli S. Smoking cessation and the course of major depression: A follow-up study. *Lancet* 2001;357:1929-32.
23. Brown RA, Kahler CW, Niaura R, Abrams DB, Sales SD, Ramsey SE, et al. Cognitive-behavioral treatment for depression in smoking cessation. *J Consult Clin Psychol* 2001;69:471-80.
24. Cox LS, Patten CA, Niaura RS, Decker PA, Rigotti N, Sachs DP, et al. Efficacy of bupropion for relapse prevention in smokers with and without a past history of major depression. *J Gen Intern Med* 2004;19:893-5.
25. Kim H, Lee KJ. Effect of bupropion for nicotine dependence in patients with major depressive. *J Cancer Educ* 2009;24(Suppl.1):S375-S376.
26. McClure JB, Swan GE, Jack L, Catz SL, Zbikowski SM, McAfee TA, et al. Mood, side-effects and smoking outcomes among persons with and without probable lifetime depression taking varenicline. *J Gen Intern Med* 2009;24:563-9.
27. Kinnunen T, Korhonen T, Garvey AJ. Role of nicotine gum and pretreatment depressive symptoms in smoking cessation: twelve-month results of a randomized placebo controlled trial. *Int J Psychiatry Med* 2008;38:373-89.
28. Addington J, el-Guebaly N, Campbell W, Hodgins DC, Addington D. Smoking cessation treatment for patients with schizophrenia. *Am J Psychiatr* 1998;155:974-6.
29. Ziedonis DM, George TP. Schizophrenia and nicotine use: report of a pilot smoking cessation program and review of neurobiological and clinical issues. *Schizophr Bull* 1997;23:247-54.
30. George TP, Ziedonis DM, Feingold A, Pepper WT, Satterburg CA, Winkel J, et al. Nicotine transdermal patch and atypical antipsychotic medications for smoking cessation in schizophrenia. *Am J Psychiatry* 2000;157:1835-42.
31. Evins AE, Mays VK, Rigotti NA, Tisdale T, Cather C, Schoenfeld D, et al. A pilot trial of bupropion added to cognitive behavioral therapy for smoking cessation in schizophrenia. *Nicotine Tob Res* 2001;3:397-403.
32. Gallagher SM, Penn PE, Schindler E, Layne W. A comparison of smoking cessation treatments for persons with schizophrenia and other serious mental illnesses. *J Psychoactive Drugs* 2007;39:487-97.
33. Breckenridge JS. Smoking by outpatients. *Hosp Community Psychiatry* 1990;41:454-5.
34. Hartman N, Leong GB, Glynn SM, Wilkins JN, Jarvik ME. Transdermal nicotine and smoking behavior in psychiatric patients. *Am J Psychiatry* 1991;148:374-5.
35. Dalack GW, Meador-Woodruff JH. Smoking, smoking withdrawal, and schizophrenia: case reports and a review of the literature. *Schizophr Res* 1996;22:133-41.
36. Evins AE, Tisdale T. Bupropion and smoking cessation. *Am J Psychiatry* 1999;156:798-9.
37. Roll JM, Higgins ST, Steingard S, McGinley M. Use of monetary reinforcement to reduce the cigarette smoking of persons with schizophrenia: a feasibility study. *Exp Clin Psychopharmacol* 1998;6:157-61.
38. Williams JM, Hughes JR. Addressing tobacco use in mental health and addiction settings. *Psychiatr Ann* 2003;33:457-66.
39. Evins AE, Cather C, Deckersbach T, Freudenreich O, Culhane MA, Olm-Shipman CM, et al. A double-blind placebo-controlled trial of bupropion sustained-release for smoking cessation in schizophrenia. *J Clin Psychopharmacol* 2005;25:218-25.
40. Evins AE, Cather C, Culhane MA, Birnbaum A, Horowitz J, Hsieh E, et al. A 12-week double-blind, placebo-controlled study of bupropion SR added to high-dose dual nicotine replacement therapy for smoking cessation or reduction in schizophrenia. *J Clin Psychopharmacol* 2007;27:380-6.
41. George TP, Vessicchio JC, Termine A, Bregartner TA, Feingold A, Rounsaville BJ, et al. A placebo controlled trial of bupropion for smoking cessation in schizophrenia. *Biol Psychiatry* 2002;52:53-61.
42. George TP, Vessicchio JC, Sacco KA, Weinberger AH, Dudas MM, Allen TM, et al. A placebo-controlled trial of bupropion combined with nicotine patch for smoking cessation in schizophrenia. *Biol Psychiatry* 2008;63:1092-6.
43. Jun L, Tian-liang Z, Bin W, Xian-wei L. An efficacy analysis of bupropion for smoking cessation in schizophrenia. *Chin J New Drugs Clin Remedies* 2009;28:231-4.
44. Fatemi S, Sary J, Hatsukami D, Murphy D. A double-blind placebo-controlled cross over trial of bupropion in smoking reduction in schizophrenia. *Schizophr Res* 2005;76:353-6.
45. Weiner E, Ball MP, Summerfelt A, Gold J, Buchanan RW. Effects of sustained-release bupropion and supportive group therapy on cigarette consumption in patients with schizophrenia. *Am J Psych* 2001;158:635-7.
46. Freedman R. Exacerbation of schizophrenia by varenicline. *Am J Psych* 2007;164:1269.
47. Evins E, Cather C, Rigotti NA, Freudenreich O, Henderson DC, Olm-Shipman CM, et al. Two-year follow-up of a smoking cessation trial in patients with schizophrenia increased rates of smoking cessation and reduction. *J Clin Psychiatry* 2004;65:307-11.
48. Baker A, Richmond R, Haile M, Lewin TJ, Carr VJ, Taylor RL, et al. A randomized controlled trial of a smoking cessation intervention among people with a psychotic disorder. *Am J Psychiatry* 2006;163:1934-42.
49. De Vicente T, Porcel A. Supresión del consumo de tabaco durante el ingreso hospitalario en psiquiatría. *Med Clin (Barc)* 2006;127:756.
50. Dueñas RM, Aleu M, González I, San L, Salavert J, Arranz B. El papel del consejo antitabaco en el proceso de deshabituación en enfermos mentales. *Actas Esp Psiquiatr* 2004;32:287-92.
51. American Psychiatric Association. Practice guideline for the treatment of patients with nicotine dependence. *Am J Psychiatry* 1996;153(Suppl.10):1-31.
52. Hughes JR. Possible effects of smoke-free inpatient units on psychiatric diagnosis and treatment. *J Clin Psychiatry* 1993;54:109-14.
53. Greeman M, McClellan TA. Negative effects of a smoking ban on an inpatient psychiatry service. *Hosp Community Psychiatry* 1991;42:408-12.
54. Tsoi DT, Porwal M, Webster AC. Interventions for smoking cessation and reduction in individuals with schizophrenia. *Cochrane Database Syst Rev* 2010;16(6):CD007253.
55. Guebaly N, Cathcart J, Currie S, Brown D, Gloster S. Public health and therapeutic aspects of smoking bans in mental health and addiction settings. *Psychiatric Services* 2002;53:1617-22.
56. Van Dogen C. Smoking and persistent mental illness: an exploratory study. *J Psychosocial Nurs* 1999;37:26-34.
57. García Campayo J, Sobradie N, Alda M, Mas A, Andrés E, Magallón R, et al. Effectiveness of topiramate for tobacco dependence in patients with depression; a randomised, controlled trial. *BMC Fam Pract* 2008;9:28.
58. Campo Revilla I, Yllá Segura L, González-Pinto Arrillaga L,

Bardaji Suárez P. Actitud de la familia hacia el enfermo mental.
Actas Esp Psiquiatr 2010;38:57-64.

59. Gree MA. Tobacco cessation. A hospital based survey of
outpatients' attitudes. J Psychosoc Nurs 2005;43:33-6.