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EDITORIAL

Smoking cessation programs for persons with schizophrenia: An urgent unmet need[☆]

Programas de cesación tabáquica para personas con esquizofrenia: una necesidad urgente no cubierta

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It is well-known that persons with schizophrenia are almost twice more likely to smoke than people in the general population, with worldwide prevalence rates of around 60%,¹ even in first episode psychosis.² In Spain the reported tobacco use rate in patients with schizophrenia is 54.4%,³ almost double that of the Spanish general population (26.4%).⁴ In addition, their smoking pattern is more pernicious and characterized by habit commencement about 5 years on average prior to illness onset,⁵ use of a greater number of cigarettes per day,^{5,6} higher plasma nicotine levels^{7,8} and more nicotine-dependence than general population.^{9–11}

Tobacco impact on the health of persons with schizophrenia

The high prevalence and specificity of the smoking pattern, which are attributed to several biological^{12–14} and psychosocial^{15,16} factors, play an important role in the high rates of medical morbidity and mortality found in this particular population,^{3,15,17} with cardiovascular disease being the major contributor to excess death.^{18,19} Furthermore,

tobacco has recently been identified as a predictor of natural mortality in schizophrenia.²⁰

In addition to its negative impact on physical health, tobacco use in patients with schizophrenia has been associated with more excitement and agitation symptoms,^{21,22} greater severity of global psychopathology as measured by the Clinical General Impression (CGI) scale,³ and positive psychotic symptoms,^{3,23} although the effect size was small.³ Moreover, it is necessary to point out that tobacco smoking was found to be associated with higher rates of suicidal behaviours in patients with schizophrenia.²⁴ Quite the opposite, beneficial effects of tobacco on patients' mental health have also been reported for negative symptoms.^{23,25} Eventually, the pro-cognitive (attention, spatial working memory and sensory gating) effects claimed in different studies,^{26,27} have been recently questioned by Núñez et al.,²⁸ so further research in this area is needed.²⁹ In either case, we believe that the potential beneficial effects of tobacco use do not warrant the maintenance of the smoking habit, as tobacco is associated with more than 4000 toxins including more than 60 carcinogens,³⁰ and, if proven necessary, nicotine can be more safely delivered through approved drugs.

Smoking cessation treatments: effective and safe

Bucking the downward trend in smoking incidence observed in the general population, despite awareness-raising campaigns to quit the habit, people with mental disorders continue to smoke at the same rate. However, in the last

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years, there is growing evidence on the efficacy, safety and tolerability of available pharmacological treatments for smoking cessation in persons with schizophrenia.

Several meta-analysis and reviews³¹⁻³⁵ as well as double-blind and pragmatic studies³⁶⁻⁴² have demonstrated that, in stabilized patients, available pharmacological treatments are effective and well-tolerated, being varenicline the drug with a greater body of evidence. Furthermore, recent reviews demonstrate that psychiatrists' concerns about psychopathological exacerbations induced by these prescription medicines seemed to be unjustified.^{32,35,38-40,43,44} Moreover, data on the beneficial cognitive effects of varenicline have been reported in persons with schizophrenia.^{45,46} However, Smith et al.⁴² using the MATRICS did not find this influence, so further studies are needed in order to clearly determine this effect.

Concerning safety, the overwhelming data from the EAGLES study in the subgroup of persons with mental disorders³⁹ led the EMA⁴⁷ to lift the warning on possible suicidal risk for varenicline. As a matter of fact, they stated that this medicine does not have dangerous psychiatric adverse effects both in the general population and in persons with mental disorders. The FDA is awaiting final approval for an amendment to its warning in the same direction.

Barriers that prevent tobacco cessation among people with schizophrenia

In spite of all the evidence above described, a study described that only a third of clinicians give guidance about smoking cessation⁴⁸ to their patients with bipolar disorder, although the emerging findings show that people with severe mental disorders are motivated to quit.^{49,50} Among the possible hurdles we would like to highlight: (1) the lack of resources, both by the health system (lack of specific programmes for this patients) and by the patients (unfeasibility to afford the cost of the medicines); (2) the negligence and old prejudices of psychiatrists; and (3) the medical stigma that suffer such patients. Thus, the main challenge consists of how to proceed to motivate health managers and psychiatrists to follow ethic norms and leave behind long-standing biases,⁵¹ in order to implement and rely upon specific resources for helping patients to quit smoking. In this sense, guidance for psychiatrists on strategies for tobacco use cessation in people with mental illness has been published⁵²⁻⁵⁶ as a tool to encourage eradication of the therapeutic nihilism in this area.

In conclusion, given the aforementioned factors, we believe we are now ready to bend the curve of this hidden public health problem and provide a boost against tobacco cessation, and the current therapeutic nihilism that prevails in Psychiatry. Thereby, we shall be able to prevent the onset/worsening of cardiovascular diseases, and to improve the general health and life expectancy of our patients with schizophrenia.

References

- De Hert M, Correll CU, Bobes J, Cetkovich-Bakmas M, Cohen D, Asai I, et al. Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World Psychiatry*. 2011;10:52-77.
- Myles N, Newall HD, Curtis J, Niesssen O, Shiers D, Large M. Tobacco use before, at, and after first-episode psychosis: a systematic meta-analysis. *J Clin Psychiatry*. 2012;73:468-75.
- Bobes J, Arango C, Garcia-Garcia M, Rejas J. Healthy lifestyle habits and 10-year cardiovascular risk in schizophrenia spectrum disorders: an analysis of the impact of smoking tobacco in the CLAMORS schizophrenia cohort. *Schizophr Res*. 2010;119:101-9.
- Ministry of Health. Encuesta nacional de salud [National health survey]. Madrid: Ministry of Health; 2006.
- Baker A, Richmond R, Haile M, Lewin TJ, Carr VJ, Taylor RL, et al. Characteristics of smokers with a psychotic disorder and implications for smoking interventions. *Psychiatry Res*. 2007;150:141-52.
- Levander S, Eberhard J, Lindstrom E. Nicotine use and its correlates in patients with psychosis. *Acta Psychiatr Scand Suppl*. 2007;435:27-32.
- Strand JE, Nyback H. Tobacco use in schizophrenia: a study of cotinine concentrations in the saliva of patients and controls. *Eur Psychiatry*. 2005;20:50-4.
- McKee SA, Weinberger AH, Harrison EL, Coppola S, George TP. Effects of the nicotinic receptor antagonist mecamylamine on ad-lib smoking behavior, topography, and nicotine levels in smokers with and without schizophrenia: a preliminary study. *Schizophr Res*. 2009;115:317-24.
- Williams JM, Ziedonis D. Addressing tobacco among individuals with a mental illness or an addiction. *Addict Behav*. 2004;29:1067-83.
- De Leon J, Diaz FJ. A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. *Schizophr Res*. 2005;76:135-57.
- Weinberger AH, Sacco KA, Creeden CL, Vessicchio JC, Jallow PI, George TP. Effects of acute abstinence, reinstatement, and mecamylamine on biochemical and behavioral measures of cigarette smoking in schizophrenia. *Schizophr Res*. 2007;91:217-25.
- Brunzell DH, McIntosh JM. Alpha7 nicotinic acetylcholine receptors modulate motivation to self-administer nicotine: implications for smoking and schizophrenia. *Neuropsychopharmacology*. 2012;37:1134-43.
- Berg SA, Sentur AM, Cooley BS, Engleman EA, Chambers RA. Nicotine is more addictive, not more cognitively therapeutic in a neurodevelopmental model of schizophrenia produced by neonatal ventral hippocampal lesions. *Addict Biol*. 2014;19:1020-31.
- Chen J, Bacanu SA, Yu J, Zhao Z, Jia P, Lendler KS, et al. Genetic relationship between schizophrenia and nicotine dependence. *Sci Rep*. 2016;6:25671.
- Ziedonis D, Hitsman B, Beckham JC, Zvolensky M, Adler LE, Audrain-McGovern J, et al. Tobacco use and cessation in psychiatric disorders: National Institute of Mental Health report. *Nicotine Tob Res*. 2008;10:1691-715.
- Tidey JW, Miller ME. Smoking cessation and reduction in people with chronic mental illness. *BMJ*. 2015;351:h4065.
- Pérez-Piñar M, Mathur R, Foguet Q, Ayis S, Robson J, Ayerbe L. Cardiovascular risk factors among patients with schizophrenia, bipolar, depressive, anxiety, and personality disorders. *Eur Psychiatry*. 2016;35:8-15.
- Olfson M, Gerhard T, Huang C, Crystal S, Stroup S. Premature mortality among adults with schizophrenia in the United States. *JAMA Psychiatry*. 2015;72:1172-81.
- Andrade C. Cardiometabolic risks in schizophrenia and directions for intervention, 1: Magnitude and moderators of the problem. *J Clin Psychiatry*. 2016;77:e844-7.

20. Dickerson F, Origoni A, Schroeder J, Schweinfurth LA, Stallings C, Savage CL, et al. Mortality in schizophrenia and bipolar disorder: clinical and serological predictors. *Schizophr Res.* 2016;170:177–83.
21. Aguilar MC, Gurpegui M, Diaz FJ, de Leon J. Nicotine dependence and symptoms in schizophrenia: naturalistic study of complex interactions. *Br J Psychiatry.* 2005;186: 215–21.
22. De Leon J, Diaz FJ, Aguilar MC, Jurado D, Gurpegui M. Does smoking reduce akathisia? Testing a narrow version of the self-medication hypothesis. *Schizophr Res.* 2006;86: 256–68.
23. Ziedonis DM, Kosten TR, Glazer WM, Frances RJ. Nicotine dependence and schizophrenia. *Hosp Community Psychiatry.* 1994;45:204–6.
24. Altamura AC, Bassetti R, Bignotti S, Pioli R, Mundo E. Clinical variables related to suicide attempts in schizophrenic patients: a retrospective study. *Schizophr Res.* 2003;60: 47–55.
25. De Leon J. Smoking and vulnerability for schizophrenia. *Schizophr Bull.* 1996;22:405–9.
26. Sacco KA, Termine A, Seyal A, Dudas MM, Vessicchio JC, Krishnan-Sarin S, et al. Effects of cigarette smoking on spatial working memory and attentional deficits in schizophrenia: involvement of nicotinic receptor mechanisms. *Arch Gen Psychiatry.* 2005;62:649–59.
27. Leonard S, Adams CE. Smoking cessation and schizophrenia. *Am J Psychiatry.* 2006;163:1877.
28. Núñez C, Stephean-Otto C, Cuevas-Esteban J, Haro JM, Huerta-Ramos E, Ochoa S, et al. Effects of caffeine intake and smoking on neurocognition in schizophrenia. *Psychiatry Res.* 2015;230:924–31.
29. Al-Halabi S, Fernández-Artamendi S, Díaz-Mesa EM, García-Álvarez L, Flórez G, Martínez-Santamaría E, et al. Tobacco and cognitive performance in schizophrenia patients: the design of the COGNICO study. *Adicciones.* 2016;724 [Article in English, Spanish].
30. International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans. Lyon: IARC; 2004.
31. Yousefi MK, Folsom TD, Fatemi SH. A review of varenicline's efficacy and tolerability in smoking cessation in subjects with schizophrenia. *J Addict Res Ther.* 2011;Suppl 4:pii: 3045.
32. Weiner E, Ball MP, Buchholz AS, Gold JM, Evins AE, McMahon RP, et al. Bupropion sustained release added to group support for smoking cessation in schizophrenia: a new randomized trial and a meta-analysis. *J Clin Psychiatry.* 2012;73: 95–102.
33. Tsoi DT, Porwal M, Webster AC. Interventions for smoking cessation and reduction in individuals with schizophrenia (Review). *Cochrane Database of Systematic Reviews.* 2013, <http://dx.doi.org/10.1002/14651858.CD007253.pub3>.
34. Evins AE, Cather C. Effective cessation strategies for smokers with schizophrenia. *Int Rev Neurobiol.* 2015;124:133–47.
35. Roberts E, Eden Evins A, McNeill A, Robson D. Efficacy and tolerability of pharmacotherapy for smoking cessation in adults with serious mental illness: a systematic review and network meta-analysis. *Addiction.* 2016;111:599–612.
36. Pachas GN, Cather C, Pratt SA, Hoeppner B, Nino J, Carlini SV, et al. Varenicline for smoking cessation in schizophrenia: safety and effectiveness in a 12-week, open-label trial. *J Dual Diagn.* 2012;8:117–25.
37. Williams JM, Anthenelli RM, Morris CD, Treadow J, Thompson JR, Yunis C, et al. A randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of varenicline for smoking cessation in patients with schizophrenia or schizoaffective disorder. *J Clin Psychiatry.* 2012;73:654–60.
38. Fatemi SH, Yousefi MK, Kneeland RE, Liesch SB, Folsom TD, Thuras PD. Antismoking and potential antipsychotic effects of varenicline in subjects with schizophrenia or schizoaffective disorder: a double-blind placebo and bupropion-controlled study. *Schizophr Res.* 2013;146:376–8.
39. Anthenelli RM, Benowitz NL, West R, St Aubin L, McRae T, Lawrence D, 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. *Lancet.* 2016;387:2507–20.
40. Brody AL, Zorick T, Hubert R, Hellemann GS, Balali S, Kawasaki SS, et al. Combination extended smoking cessation treatment plus home visits for smokers with schizophrenia: a randomized controlled trial. *Nicotine Tob Res.* 2016, pii: ntw190.
41. Garcia-Portilla MP, Garcia-Alvarez L, Sarramea F, Galvan G, Diaz-Mesa E, Bobes-Bascaran T, et al. It is feasible and effective to help patients with severe mental disorders to quit smoking: an ecological pragmatic clinical trial with transdermal nicotine patches and varenicline. *Schizophr Res.* 2016;176: 272–80.
42. Smith RC, Amiaz R, Si TM, Maayan L, Jin H, Boules S, et al. Varenicline effects on smoking, cognition, and psychiatric symptoms in schizophrenia: a double-blind randomized trial. *PLOS ONE.* 2016;11:e0143490.
43. Cerimele JM, Durango A. Does varenicline worsen psychiatric symptoms in patients with schizophrenia or schizoaffective disorder? A review of published studies. *J Clin Psychiatry.* 2012;73:e1039–47.
44. Gibbons RD, Mann JJ. Varenicline, smoking cessation and neuropsychiatric adverse events. *Am J Psychiatry.* 2013;170:1460–7.
45. Hong LE, Thaker GK, McMahon RP, Summerfelt A, Rachbeisel J, Fuller RL, et al. Effects of moderate-dose treatment with varenicline on neurobiological and cognitive biomarkers in smokers and nonsmokers with schizophrenia or schizoaffective disorder. *Arch Gen Psychiatry.* 2011;68: 1195–206.
46. Shim JC, Jung DU, Jung SS, Seo YS, Cho DM, Lee JH, et al. Adjunctive varenicline treatment with antipsychotic medications for cognitive impairments in people with schizophrenia: a randomized double-blind placebo-controlled trial. *Neuropsychopharmacology.* 2012;37:660–8.
47. European Medicines Agency. Champix, INN Varenicline tartrate – Europa.eu. Available from: http://www.ema.europa.eu/docs/es_ES/document_library/EPAR_-_Product_Information/human/000699/WC500025251.pdf.
48. Prochaska JJ, Reyes RS, Schroeder SA, Daniels AS, Doederlein A, Bergeson B. An online survey of tobacco use, intentions to quit, and cessation strategies among people living with bipolar disorder. *Bipolar Disord.* 2011;13:466–73.
49. Siru R, Hulse GK, Tait RJ. Assessing motivation to quit smoking in people with mental illness: a review. *Addiction.* 2009;104:719–33.
50. Ashton M, Miller CL, Bowden JA, Bertossa S. People with mental illness can tackle tobacco. *Aust N Z J Psychiatry.* 2010;44:1021–8.
51. Lolas-Stepke F. Tendencias y necesidad clínica de los principios éticos. *Rev Psiquiatr Salud Ment (Barc).* 2015;8:1–2.
52. 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.
53. Rüther T, Bobes J, de Hert M, Svensson TH, Mann K, Batra A, et al. EPA guidance on tobacco dependence and strategies for smoking cessation in people with mental illness. *Eur Psychiatry.* 2014;29:65–82.

54. Evins AE, Cather C, Laffer A. Treatment of tobacco use disorders in smokers with serious mental illness: toward clinical best practices. *Harv Rev Psychiatry*. 2015;23:90–8.
55. Stubbs B, Vancampfort D, Bobes J, de Hert M, Mitchell AJ. How can we promote smoking cessation in people with schizophrenia in practice? A clinical overview. *Acta Psychiatr Scand*. 2015;132:122–30.
56. Schroeder SA. Smoking cessation should be an integral part of serious mental illness treatment. *World Psychiatry*. 2016;15:175–6.