

Smoking cessation, anxiety, mood and quality of life: reassuring evidences

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A close and complex relationship between smoking and mental health problems was found. Different hypotheses have been proposed to explain these associations: 1) smoking and poor mental health may share common causes (genetic factors or environmental mechanisms); 2) for people with poor mental health smoking is a coping strategy to regulate psychiatric symptoms; 3) smokings worsen mental health. Moreover, smokers with psychiatric disorders may have more difficulty quitting and patients with mental diseases who received mental health treatment within the previous year were more likely to stop smoking than those not receiving treatment. Taylor *et al.* hypothesized that quitting smoking might improve rather than exacerbate mental health, because it allows to avoid multiple episodes of negative affect induced by withdrawal. With the aim to verify this hypothesis, they conducted a systematic review and meta-analysis on longitudinal studies (randomized controlled trials and cohort studies) in which the difference in change in mental health between subjects who stop smoking and subjects who continue to smoke has been explored. A total of 26 longitudinal studies evaluating anxiety, depression, mixed anxiety and depression, positive effect, psychological quality of life, and stress have been included. The study results provided enough evidence to assure that quitting smoking is associated with a reduction of depression, anxiety, and stress, with an improvement of psychological quality of life

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and positive affect compared with continuing to smoke. The strength of association was similar for both the general population and study enrolled populations, including those with mental health disorders. The results of this meta-analysis have direct clinical implications: the benefits for mental health could motivate physicians and patients to take into account the possibility of smoking cessation.

KEY WORDS: Smoking cessation - Mental health - Mood disorders - Stress, psychological - Quality of life.

Tobacco smoking represents a global epidemic of public health concern. It is the leading preventable cause of disability, morbidity and death worldwide. Despite detrimental effects from smoking on health are well known, a substantial portion of the population smokes cigarettes regularly. In

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particular, it has been shown that tobacco dependence is more frequent in people suffering from mental diseases and these patients find quitting more difficult than other smokers.¹ For this reason, the close and complex relationship between smoking and mental health problems is increasingly explored and recognized.² Smoking cigarette has been described as a coping strategy that aims to regulate negative affects and to reduce feelings of anxiety, depression and distress. This cognitive process is common to smokers with and without mental disorders³ and has a negatively reinforcing effect, leading to think that smoking allows to guarantee mental health benefits. Smokers consider smoking as a way to feel comfortable in social situations, stabilize mood, maintain a better concentration, enhance stimulation and reduce anxiety and distress.³

Nevertheless, an association between smoke and poor mental health has been found in recent epidemiological studies. People suffering from a psychiatric disease are twice as likely to be current smokers compared to the general population⁴ and represent more than a half of nicotine-dependent smokers.⁵ Moreover, they are heavier consumers of cigarettes and have poorer cessation outcomes.⁶

The bidirectional association between smoking and mental disorders is supported by the fact that smokers have an increased probability to meet current diagnostic criteria for psychiatric disorders than non-smokers. Several clinical and population-based studies have found an association between smoking or nicotine dependence and various mental illnesses including depression,² suicidal behavior,⁷ anxiety,⁸ bipolar disorder,⁶ personality disorders,⁹ schizophrenia,¹⁰ attention-deficit/hyperactivity disorders,¹¹ alcohol abuse and dependence.¹² As a consequence, tobacco-related morbidity and mortality result higher among subject with mental health diseases.¹³ Moreover, the experience of stressful events and the resulting emotional or psychological distress play a critical role in cigarette use:¹⁴ a substantial amount of research has documented that smoking is more common among subjects

who report high levels of strain in different life domains (work, family, social relationship, financial condition) or that have experienced stressful life events or childhood adversity.¹⁵ Mental diseases not only represent an independent risk factor for smoking, but are associated with smoking-related risk factors such as lower income, lower education and unemployment.⁵

Different hypotheses have been proposed to explain these complex associations: 1) smoking and poor mental health may share common causes (genetic factors or environmental mechanisms); 2) people with poor mental health smoke to self-medicate their psychiatric symptoms and to manage the affective dysregulation; 3) or smoking might bring to the development of secondary mental disorders or worsen mental health.¹⁶ Moreover, literature data also suggest that smokers with psychiatric disorders may have more difficulty quitting, providing at least a partial explanation for why smoking rates are higher in this population.¹⁷ The effects on mental health often represent an impediment to successful quitting and may constitute the cause of smoking relapse. When tobacco use is stopped, nicotine withdrawal syndrome emerges in the first 24-48 hours. It is characterized by somatic and affective symptoms such as irritability, anger, frustration, restlessness, sleep disturbances, anxiety, depressed mood, difficulty concentrating, increased appetite, and craving for tobacco which may interfere with social relationships and daily life functioning.¹⁸ This syndrome constitutes an important obstruction to successful quitting and may lead to smoking relapse.¹⁹ Smokers may be less likely to stop because they fear they will experience mental health problems and professionals often do not encourage some patients to quit because they believe that quitting might exacerbate psychiatric symptoms.²⁰

The role of concomitant psychiatric diseases in smoking cessation has been underlined in a recent meta-analysis: individuals with mental diseases who received mental health treatment within the previous year were more likely to stop smoking than those not receiving treatment.⁵

Taylor *et al.*¹⁶ hypothesized that smoking quitting might improve rather than exacerbate mental health, because it helps avoid multiple episodes of negative affect induced by withdrawal. With the aim to test this hypothesis, they conducted a systematic review and meta-analysis on longitudinal studies (randomized controlled studies and cohort studies) in which the difference in change in mental health between subjects who stop smoking and subjects who continue has been explored.¹⁶

Authors using a broad eligibility criteria selected 26 longitudinal studies in general population and in clinical selected populations including smokers with current psychiatric diseases, with the aim to capture all potentially relevant data. What emerges from the analysis conducted by Taylor *et al.* provides useful suggestions for clinical practice. Health professionals and patients must be aware about the links among smoking cessation, mental health and psychological well-being. In fact, both the physician's decision to intervene and the patient's motivation to quit may be influenced by incorrect beliefs and negative expectations regarding the detrimental effects of smoking cessation on mental health.

The effect measured by the meta-analysis has been calculated from a difference in standardized change in symptom scores from baseline. They compared those who were able to quit smoking to those who continued or restarted smoking after quitting. Findings are clinically very relevant as they show improvement in those who were able to quit smoking ranging from 0.37 of the standardized mean deviation (SMD) for anxiety, 0.31 for mixed anxiety/depression, 0.25 for depression, 0.27 for stress, 0.22 for psychological quality of life, 0.40 for positive affect; *i.e.*, the change in mental health is similar to the effect expected with the use of antidepressant drugs as it has been remarked by the authors in their conclusion of the abstract and discussion of possible mechanisms and by comments to the article published in the BMJ.²¹ It is noteworthy that the effect on mild to severe depression of selective serotonin reuptake inhibitors

is between 0.11 and 0.17, smaller than the 0.25 seen with smoking cessation.²² Similarly the effect on anxiety disorder of all type of antidepressant drugs ranges from 0.25 to 0.50;²³ this is comparable to the improvement seen with smoking cessation: 0.31 for mixed anxiety/depression and 0.37 for anxiety. Moreover, the results of the meta-analysis have implications for research: starting from the available evidence, future studies are suggested to allow drawing causal inferences of the determinants of mental health after smoking cessation.

Smoking cessation in people with mental disorders has always been a source of concern for both the healthcare providers and the patients. The idea that smoking alleviate stress and anxiety provide a major obstacle for smokers to quit, and for physicians to recommend quitting.²⁴ Many health professionals also believe that smoking is anxiolytic and that smoking cessation usually worsens mood.^{25, 26} The belief about the relationship between smoking and mental health is particularly damaging for subjects with psychiatric disorders, who are less likely than other smokers to be offered cessation advice and support.²⁷ It is no coincidence that in many countries, smoking is allowed in the psychiatric hospital wards. Nevertheless, smokers with mental disorders have a life expectancy around 20 years lower than people without such a problem, and much of the excess mortality is attributed to cigarette smoking, which is highly prevalent in this group.²⁸

It is known that nicotine absorbed by smoking stimulates the release of various neurotransmitters involved in feelings of pleasure and relaxation, such as dopamine,²⁹ norepinephrine, serotonin, β -endorphin, and GABA.³⁰ Eventually, smoking can affect pharmacokinetics of psychotropic medications in part by interfering with cytochrome CYP 450 system.³¹ On the other hand, the abrupt discontinuation of nicotine causes withdrawal symptoms including irritability, anxiety, difficulty concentrating, and depressed mood. It has been recently reported that about half the smokers in England cite stress relief as one

of the main reasons for smoking.³² McDermott *et al.* recently observed that people who quit smoking experience a marked reduction in anxiety, whereas those who fail to achieve abstinence experience a modest long-term increase of anxiety. These data contradict the assumption that smoking is a stress reliever, but suggest that failure of a quit attempt may generate anxiety.³³

Smoking does not seem to decrease stress in smokers who are not nicotine deprived; on the other hand, the intensity of stress in smokers after smoking is similar to those of non-smokers.³⁴ It has been suggested, therefore, that the perceived beneficial effects of smoking upon stress are actually a misattribution of withdrawal relief.^{35, 36} Withdrawal symptoms are usually experienced most acutely in the first 24-48 hours after quitting smoking and resolve within two to four weeks after cessation, when the neurological functioning of quitters returns to the same level as non-smokers.^{19, 37} There is further research suggesting that smoking may actually cause stress and is a risk factor for the development of anxiety-related disorders.³⁸

Nicotine's ability to quickly reverse the symptoms of withdrawal induces in smokers the feeling that it alleviates stress.³⁹ Though depression is one of the less common symptoms of nicotine withdrawal, one of the biggest concerns about smoking cessation regards the fear of worsening mood or triggering a full-blown depression. This often leads to discourage smokers from trying to quit and physicians from intervening, particularly when smokers have current or past mental illness.² However, many studies failed to show mood enhancing effects of nicotine.⁴⁰

The main studies which analyzed the relationship between cigarette smoking and mental health, were focused on six mind disorders: anxiety, depression, mixed anxiety and depression, positive affect, psychological quality of life, and stress. Several studies have differences in methodology, analyzed population and length of follow-up, but with appropriate adjustments Taylor and coworkers have obtained interesting

global information.¹⁶ The study provided enough evidence to assure that quitting smoking is associated with a reduction of depression, anxiety, and stress, with an improvement of psychological quality of life and positive affect compared with continuing to smoke. The strength of association was similar for both the general population and clinical populations, including patients with mental health disorders.

The possible interpretations of this association are basically three: 1) smoking cessation may be the real cause of the improvement of mental health; 2) an improvement in mental health can facilitate attempts to smoking cessation; 3) a common factor (*e.g.*, a positive life event) may cause both the improvement of mental health and the facilitation of smoking cessation. Even if these observational data cannot prove causality, they can at least reassure doctors and patients, even in the case of individuals with mental illness, that quitting smoking is likely to improve mental health.

As general rule, meta-analysis reflect the limitations of the included studies. For the meta-analysis of Taylor *et al.* the first limitation is the heterogeneity of the studies evaluated, *i.e.* study design (cohort studies, secondary analyzes, randomized trials), evaluated sample (general population, patients suffering from a chronic physical disease, post-operative patients, pregnant women, people suffering from physical and/or psychiatric chronic diseases), age of patients, number of cigarettes smoked, degree of dependence, number of cigarettes smoked a day, smoking cessation interventions (psychological and/or pharmacological), duration of follow-up (from 7 weeks to 6 years). Moreover, depending on the studies, several outcomes were analyzed (anxiety and/or depression, health related quality of life, health status, stress) with different tools, some of which are not validated. For example, the study of Hajek *et al.* evaluated the presence of perceived stress by two simple questions that explore the use of smoking as a coping strategy and the level of stress, with two different response Likert scales.⁴¹ The absence of proved psychomet-

ric characteristics of validity, reliability and responsiveness of a questionnaire, limits the meaning of the results. Moreover, for some of the included studies, the Authors provide an incomplete analysis of the available collected data. For example, for the cohort study of Croghan *et al.*,⁴² that evaluated health status by a generic questionnaire (SF-36), only the score of a domain (energy/vitality) has been considered for the meta-analysis. Neither the other components of mental health status evaluated by the SF-36 (role limitations due to emotional problems, social functioning and general mental health) nor the mental component summary (that aggregates these four domains) have been considered. Also for the study of Mitra *et al.*,⁴³ partial results have been reported: authors take into account for their analysis only two scores of SF-36 (general health and energy/vitality). Similarly, analyzing the study by Balduyck⁴⁴ on the effect of smoking cessation on quality of life after lung cancer surgery, Taylor *et al.* considered only the emotional functioning subscale of the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire. The scores of subscales that evaluate cognitive, role functioning and social functioning, that are domains strictly related to mental health status, were not considered.

In their discussion the authors explored causal effects from all plausible point of view. Although they state even that observational longitudinal studies do not allow to draw firm statement on the causal condition of the observed event (*i.e.*, an improvement in mental health status in smokers who succeed in quitting compared to those who continue to smoke), they indeed discarded the hypothesis that improvement in mental health is the primary cause of successful smoking cessation. In fact, subgroup analysis did not support the statement that improvement in mental health status prompts people to attempt cessation. Attempting smoking cessation is very different from succeeding in smoking cessation and eventually people who attempt and fail show a deterioration of their mental health status.

It is noteworthy that other studies support the relationship between mental health status and successful quitting,⁴⁵ but authors fail to recognise this difference.⁴⁶ Other authors remarked this forced interpretation of causality⁴⁷ and suggest the possibility that change in lifestyle rather than smoking cessation itself might have played a role in mental health improvement in successful quitters.

Authors also do not take into account the possible beneficial effect of smoking cessation drugs as varenicline or bupropion on mental health⁴⁸ as this was beyond the clinical question explored by the meta-analysis. Benefit seen on mental health in successful quitters might well be related to the modality of the smoking cessation process rather than to the cessation itself. This acquires even more clinical relevance in the view of the recent data on the use of varenicline in patients with stable depression and schizophrenia.^{49, 50} Finally, gender is not considered in this meta-analysis despite suggesting evidence support the correlation between gender and different abstinence behavior,^{51, 52} mental health⁵³ and response to cessation program.⁵⁴

Many questions remain open, and it is necessary to have more available data to answer them. First of all, studies that investigate the personal factors that influence the risk of developing a mental disorder after the cessation of smoking - coping strategies, distress tolerance,⁵⁵ alexithymia, temperament traits, self-efficacy - are needed. This would help to develop targeted interventions and to evaluate their effectiveness in improving the success of cessation programs.

In addition, as recently pointed out by Leventhal,⁵⁶ depression, as well as anxiety, stress, psychological well-being, include cognitive, behavioral, affective and autonomic symptoms. It is possible that some symptomatic expressions may be associated more than others both to smoking habits and smoking cessation. Considering a single descriptive label could make it harder to understand the complex variability of subjective reactions to smoking cessation.

Moreover, data on populations at increased risk of depression and anxiety, such as adolescents and the elderly are missing.

The link between smoking cessation and improved mental health condition brings up the question if smoking surrogates, like e-cigarettes with or without nicotine supplementation, have an impact on Taylor and co-workers findings.²¹ The topic is likely to gain more clinical relevance with an expanding market for these products, and enforces the need to understand the causality relation between gesture, life style, nicotine and mental health

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