

## "Health outcomes in COPD smokers using heated tobacco products: a 3-year follow-up: comment"

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Dear Editor,

There is no doubt that smoking increases the risk of cardiovascular disease, lung disease and several types of cancer. It is estimated that smoking is one of the most noteworthy causes of death in the world. In 2005, Anthonisen et al. reported the effect of smoking cessation intervention on a 14.5-year mortality in COPD patients. An intensive, 10-week smoking cessation program was used on the intervention group compared to the regular treatment group. After 5 years, 21.7% of patients in the intervention group had quit smoking and only 5.4% in the control group. The patients were then further observed for 14.5 years, and in the control group, the risk ratio of death due to respiratory and cardiovascular diseases was 1.18. Stopping smoking permanently or even temporarily reduces the risk of death. However, the fact that the intensive smoking cessation program was only effective in 21.7% of patients should not be considered very effective. It is imperative to seek more effective treatments for cigarette addiction.

Polosa et al. recently published the study "Health outcomes in COPD smokers using heated tobacco products" [1]. The study aimed to compare health parameters [COPD exacerbations, patient-reported outcomes (CAT scores) and 6-min walk distance (6MWD)] for 3 years in 19 patients with COPD who attenuated or ceased cigarette consumption after switching to heated tobacco products (HTPs) and 19 patients with COPD who continued smoking. They have observed that patients using HTPs had a substantial decrease in annualized COPD exacerbations, improvements in CAT scores and 6MWD. The study confirmed the thesis that avoiding exposure to chemicals generated from the combustion of tobacco cigarettes by switching to heated tobacco products might improve patients' health. Moreover, switching from traditional cigarettes to HTPs might be a bridge to permanent smoking cessation.

Despite the widespread awareness of the fatal consequences, a large number of patients continue smoking. The US Preventive Services Task Force (USPSTF) recently published recommendation statements, titled "Interventions for Tobacco Smoking Cessation in Adults Including Pregnant Persons", which evaluates the benefits and harms of primary care interventions on tobacco use cessation in adults [2]. The USPSTF recommends that "clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioural interventions and US Food and Drug Administration (FDA)-approved pharmacotherapy for a cessation to nonpregnant adults who use tobacco" [2]. As pharmacotherapy for tobacco smoking cessation, the authors of the recommendation listed nicotine replacement therapy (NRT), bupropion and varenicline. Regrettably, the authors did not mention cytisine-partial nicotine receptor agonist-whose effect is to bind selectively to nicotine receptors, with sevenfold greater affinity to the receptor than nicotine. Moreover, the USPSTF concludes that "the current evidence is insufficient to assess the balance of benefits and harms of e-cigarettes for tobacco cessation in adults".

The role of cytisine in smoking cessation is well established, and it has been safely used in Europe since the 1960s. In a randomized, single-center, double-blind, placebo-controlled study of 25 days of cytisine treatment versus placebo in a group of 740 smokers, it was shown that during the 12-month follow-up, 8.4% of the subjects did not smoke in the cytisine group and only 2.4% in the placebo group. Side effects, mainly gastrointestinal, were more common in the cytisine group [3]. A meta-analysis of eight controlled

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trials involving 4020 adult smokers reported that cytisine was significantly more effective than placebo treatments in smoking cessation [4]. According to an article published in 2014, the result of an open-label trial conducted among 1310 adult smokers (who were randomly assigned to receive cytisine or nicotine-replacement therapy) was that cytisine was superior to nicotine-replacement therapy in helping smokers quit smoking. After 1 month, 40% of participants receiving cytisine and only 31% of participants receiving nicotine replacement therapy reported continuous abstinence. Also, at 6 months, the self-reported abstinence rate was higher among participants taking cytisine (22%) compared to nicotine replacement therapy (15%). Furthermore, there were similar rates of serious adverse events in the cytisine (6.9%) and the NRT (6.0%) groups. Moreover, it should be noted, the cost of cytisine treatment course is the lowest compared to nicotine replacement therapy, bupropion or varenicline.

In summary, based on the current state of the art, the Task Force of the Polish Society of Civilization Diseases recommends that interventions for tobacco smoking cessation in adults should involve cytisine as a safe and effective pharmacotherapy intervention. An algorithm prepared by an interdisciplinary Task Force of the Polish Society of Civilization Diseases for smoking cessation includes a new approach to the old scheme (proposed by The US Preventive Services Task Force) and can be seen in Fig. 1. In patients who, despite many attempts, fail to execute all methods of tobacco dependence treatment, the Panel of Experts decided to include a recommendation to switch from regular cigarettes to heated tobacco, in line with the 2020 FDA's opinion that such an approach could help addicted adult smokers quit smoking and reduce their exposure to harmful chemicals, but only if they switch completely.

Nevertheless, managing smokers who relapse during the smoking cessation program can be more challenging. In these situations, very important is to consider different counseling strategy, review dosing of pharmacological treatment, add a nicotine-free inhaler (for smokers with a strong behavioral component of tobacco dependence) or encourage the patient to switch to a less harmful source of nicotine (tobacco harm reduction options, THR) [5].

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## Declarations

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