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SPECIAL PAPER/PRACA SPECJALNA

## Is there an optimal management system for nicotine-dependent patients with chronic obstructive pulmonary disease and asthma? Expert consensus

Czy istnieje optymalne postępowanie z pacjentami uzależnionymi od nikotyny w przebiegu przewlekłej obturacyjnej choroby płuc i astmy?  
Konsensus ekspertów

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### ABSTRACT

Nicotinism remains one of the main causes of morbidity and mortality in Poland and worldwide. A particularly vulnerable group of patients are those with respiratory diseases – especially chronic obstructive pulmonary disease and asthma. Smoking cigarettes is associated with a poorer prognosis and a difficult treatment process for the underlying disease. Anti-smoking therapy has limited effectiveness. One of the strategies that breaks through to the mainstream is harm reduction management. Some of the methods available today include systems for heating tobacco. However, attention is drawn to the risks associated with the smoking of traditional cigarettes and the use of ‘heat-not-burn’ systems. The management of nicotine-dependent patients and lung disease requires a multi-profile, holistic approach, individually tailored to each patient.

### KEY WORDS

tobacco smoking, nicotine addiction, chronic obstructive pulmonary disease, asthma, heat-not-burn, modified risk tobacco products.

## STRESZCZENIE

Nikotynizm stanowi jedną z głównych przyczyn chorobowości i śmiertelności w Polsce oraz na świecie. Szczególnie narażoną grupą pacjentów są osoby z chorobami układu oddechowego w postaci przewlekłej obturacyjnej choroby płuc oraz astmy. Palenie papierosów wiąże się z gorszym rokowaniem oraz utrudnionym procesem leczniczym choroby podstawowej. Farmakoterapia antynikotynowa ma ograniczoną skuteczność. Jedną z przebijających się do głównego nurtu strategii jest postępowanie oparte na kompleksowej farmakoterapii uzupełnionej redukcją szkód. Wśród dostępnych metod wymienia się obecnie między innymi systemy służące do podgrzewania tytoniu. Zwraca się jednak uwagę na ryzyko związane z podwójnym używaniem zarówno tradycyjnych papierosów, jak również podgrzewaczy. Postępowanie z pacjentami z przewlekłą chorobą płuc i uzależnionymi od nikotyny wymaga wieloprofilowego, holistycznego podejścia indywidualnie dostosowanego do każdego chorego.

## SŁOWA KLUCZOWE

palenie tytoniu, uzależnienie od nikotyny, przewlekła obturacyjna choroba płuc, astma, heat-not-burn, produkty tytoniowe o obniżonym ryzyku.

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## EPIDEMIOLOGY OF NICOTINISM IN PATIENTS WITH ASTHMA AND/OR CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Nicotinism has been one of the main diseases in civilisation for many years. Due to its numerous negative health consequences and its prevalence in society, nicotine is associated with a significant burden on health-care systems, increased mortality rates and decreased productivity as expressed by gross domestic product etc. According to the International Classification of Diseases and Related Health Problems (ICD-10), nicotine is the addiction to nicotine, a substance found in cigarettes, which can also be taken in other forms. Smoking traditional cigarettes increases the cardiovascular risk, promotes the development of chronic obstructive pulmonary disease and has significant implications for the treatment of asthma. Chronic exposure to tobacco smoke is a risk factor for several malignant tumours, especially lung cancer. Patients with respiratory system diseases who are nicotine-dependent represent a particular group of patients as nicotine significantly hinders their effective treatment. Consequently, the cessation or significant reduction of smoking is the primary recommendation.

According to the available data, over 480,000 deaths per year are caused by nicotine in the United States [1]. According to a World Health Organisation (WHO) report, there are approx. 8 million deaths

worldwide [2]. The annual number of deaths in Poland caused by tobacco smoking is over 80,000 [3]. However, the exact number is unknown due to the lack of reliable reports. Tobacco smoking is the leading cause of death for men (26.6% of all deaths in 2019) and the second leading cause of death for women (13.7% of all deaths in 2019) [4]. The indirect costs associated with the loss of productivity due to premature mortality among smokers in Poland amounted to PLN 6.4 billion in 2017. It is estimated that premature deaths related to tobacco smoking in 2017 accounted for a loss of 0.33% of Poland's GDP [5].

Currently, the percentage of people who smoke is decreasing, but considering the absolute increase in the global population, more patients smoke [6]. It is worth emphasizing that it is usually young and economically active people who die, which confirms the relationship between nicotine and productivity along with tangible economic losses. Based on the data from the National Institute of Hygiene – National Institute of Public Health, 29.8% of men and 17.6% of women regularly use nicotine products. Additionally, 2.5% of men and 1.9% of women declare occasional smoking [7]. Epidemiological studies suggest that cigarettes are more often smoked by people with a low social status, lower income, from small locations and the unemployed [5].

In a study conducted in 2021 on behalf of the Bureau for Chemical Substances, it was demonstrated that regular users of tobacco heating systems and

e-cigarettes constitute, respectively, 1.6% and 0.9% of the adult population in Poland. The results of the study suggest a growing interest among smokers in systems for heating processed tobacco as these devices have only been available on the Polish market since 2017. Most users declared limiting themselves to a maximum of 10 cartridges per day (an average of 12.3 cartridges). Both e-cigarettes and tobacco heating systems were often used by the respondents as a method for ceasing to smoke conventional cigarettes. The statements by respondents may indicate that the effectiveness of tobacco heating systems is slightly higher than that of e-cigarettes, although this data needs to be confirmed in further studies [8]. It is also worth noting that the increase in nicotine consumption during the COVID-19 pandemic can be attributed partly to the stress and tension associated with the epidemiological situation.

There is a strong correlation between smoking cigarettes and chronic obstructive pulmonary disease (COPD). Depending on the available analysis, 10-15% of people who start smoking cigarettes will develop COPD. Among those people who have quit smoking cigarettes, 7-8% will be diagnosed with COPD as a consequence of their earlier addiction. Of course, the risk depends on the intensity of smoking prior to the onset of abstinence. For comparison, in the group of people who never smoked cigarettes, the risk of developing COPD is 2-3% and it is most likely related to air pollution and personal predispositions [9]. However, among patients with COPD, approx. 65% of them smoke or have smoked cigarettes in the past. This percentage is even higher among patients with COPD who have accompanying mental disorders, such as depression (75.5%), anxiety disorders (72%), schizophrenia (85.2%), or sleep disorders (73.7%) [10].

Until recently, not much attention has been paid to asthma patients who smoke cigarettes, although new studies on the subject have emerged. Cigarette smoking in asthmatics is a problem because it significantly complicates the treatment of the underlying disease and it also affects the course of the disease. Cigarette smoking activates certain cellular and cytokine pathways, causing asthma, which is an inflammatory disease, to progress and require more intensive treatment. It is believed that smokers require about twice the amount of medication for asthma therapy in comparison to non-smokers. Nicotinism also contributes to the accelerated remodelling of the airways in asthma. It is worth emphasizing that the problem of asthma in society is underestimated due to the reporting system of deaths. Asthma is usually omitted in the report, although it often contributes to the death. The exact number of smokers among asthma patients is unknown. In a study

conducted a few years ago on the Polish population, it was found that as many as 35% of asthmatics smoke. Interesting data were presented in a study based on the data from the United States, where it was observed that the frequency of smoking among teenagers with asthma was twice as high as among non-smoking teenagers. It is important to emphasize the health and financial implications for both patients and social security systems. Asthma as a chronic disease is associated with periods of better and worse symptom control. Is it noteworthy that cigarette smoking almost quadruples the risk of asthma exacerbation, and passive exposure to cigarette smoke increases this risk by 75% [11].

### CONSEQUENCES OF NICOTINISM IN PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE OR ASTHMA

Nicotinism is associated with a number of adverse consequences. Most of the evidence has been collected through research on traditional cigarettes. The number of reports on e-cigarettes or heat-not-burn products is significantly lower, but further research is ongoing. Tobacco smoke generated during smoking contains over 70 carcinogenic substances, mainly nitrosamines, polycyclic aromatic hydrocarbons, cadmium, methanol, acetone, carbon monoxide, butane, and polonium [12]. Some of these compounds are also present in the aerosol produced during the tobacco heating process: nitrosamines, polycyclic aromatic hydrocarbons, and carbon monoxide, but at significantly lower concentrations [13]. No presence of cadmium, methanol, acetone, hydrogen cyanide, or polonium was observed. Nevertheless, the authors of numerous studies note that the concentration of these substances is lower in tobacco heating products. The active forms of oxygen and nitrogen, present in tobacco smoke, also play a significant role in the development of chronic diseases, cancer, and dynamics of their course. As the research results suggest, the level of free radicals in nicotine aerosols emitted by heat-not-burn products and electronic nicotine delivery systems is 100 times lower compared to cigarette smoke [14]. Currently, there is no evidence of the carcinogenicity of nicotine, which has been available in pharmacies in Europe for over 40 years in various forms as an over-the-counter medicinal product [15]. However, there are ongoing discussions regarding the potential carcinogenicity of nicotine metabolites.

Nicotinism affects the functioning of practically every system in the human body. About 5% of all deaths could be prevented if patients quit smoking, and smoking in individuals under 50 years of age is equivalent to shortening life expectancy by about 10 years [16]. This

effect is more visible in younger patients. Smoking cigarettes promotes the development of tumours, which develop in the respiratory, digestive and urinary systems or on the skin, among other places. Active or passive tobacco smoking is responsible for approx. 85–90% of lung cancer cases. Reducing the exposure to tobacco smoke is the only way to significantly reduce the incidence and mortality rates [17]. According to various data, the risk of developing cancer is 2–20 times higher compared to the non-smoking population.

The leading cause of death on a global scale is cardiovascular diseases, including acute coronary syndromes, heart failure, and arrhythmias. Nicotinism leads to the development of atherosclerosis and the steady progression of cardiovascular diseases [4].

### CURRENT METHODS TO SUPPORT THE CESSATION OF TOBACCO SMOKING

Treating addictions is an exceptionally demanding task, and often the desired results cannot be achieved. According to the WHO data, only 4% of smokers manage to successfully quit without smoking cessation aids [1]. The treatment process should primarily involve not only the patient, but also his or her physician, a psychologist and a psychotherapist. There are many regimens aimed at reducing stimulant use. Available scientific data indicate that regularly repeated anti-smoking intervention (advice) consisting of implementing 5 questions (5A rule) provided by a healthcare worker to a smoker can bring some benefits compared to not providing this advice [18].

Based on the historical data, it can be inferred that the goal defined as the complete abstinence is very difficult to achieve. Currently, the goal is to reduce the amount of psychoactive substance taken, in this case, nicotine.

One of the elements of treatment is the use of nicotine replacement therapy (NRT), which involves taking nicotine in the form of skin patches, chewing gum, tablets, and inhalers. In this case, the goal is to gradually reduce the amount of nicotine taken. Nevertheless, alternative ways of taking nicotine can also cause adverse effects. The most common side effects of popular nicotine patches include: nightmares, insomnia, headache, dizziness, nausea, vomiting, nervousness, trembling, shortness of breath, throat inflammation, cough, indigestion, diarrhoea, constipation, joint pain, muscle pain, chest pain, weakness, and reactions at the patch application sites.

In the case of chewing gum, irritation of the oral cavity, hiccups, and nausea are emphasized. However, it has been demonstrated that the use of a combina-

tion of different forms of NRT (patches combined with short-acting NRT in another form) increases the likelihood of smoking cessation for at least 6 months compared to a single form of NRT, with similar frequencies of serious adverse events occurrence and withdrawal from the study due to medication use. However, no favourable or unfavourable differences were observed regarding the longer or shorter use of the combination of NRT [19].

Another treatment option is bupropion, a dopamine reuptake inhibitor. This drug is responsible for simulating the reward effect by increasing dopamine and noradrenaline concentrations. Bupropion should be recommended to patients who report symptoms suggesting a decrease in mood during the interview and to individuals with previous depressive episodes. Therefore, the drug can be used in people with COPD or atherosclerosis, who often have a decreased mood. Since bupropion reduces carbohydrate cravings and limits weight gain after smoking cessation, it can be used in individuals who express concern about excessive weight gain. In highly nicotine-dependent patients, it is worth considering to combine bupropion with NRT. The most common adverse effects include insomnia, agitation, headache, dry mouth, weight loss and the risk of seizures.

Another drug used as a support during tobacco smoking cessation is varenicline – a partial selective agonist of nicotine receptors. According to the mechanism of partial antagonism of this drug towards nicotine receptors, satisfaction from smoking and psychological reward are significantly reduced in smokers taking varenicline compared to a placebo. Tashkin *et al.* have shown that varenicline is well tolerated by patients with mild to moderate forms of COPD, with a continuous abstinence rate of 18.6% vs. 5.6% in the placebo group in the period of 9–52 weeks [20]. In a prospective, open-label study, Politis *et al.* evaluated the maintenance of complete abstinence from tobacco smoking in patients hospitalized earlier due to COPD exacerbation, asthma exacerbation or community-acquired pneumonia [21]. The percentage of patients who maintained abstinence from tobacco smoking after 52 weeks in the group treated with varenicline combined with behavioural therapy and in the group receiving one session of anti-smoking therapy (5A method) were 52.3% and 14.0%, respectively.

The effectiveness of varenicline has also been studied in a group of young patients (18–40 years old) with asthma, with a history of at least 10 pack-years of the addiction and smoking at least 10 cigarettes a day. Westergaard *et al.* in a randomized, double-blinded, placebo controlled study have demonstrated a slight

advantage of varenicline over a placebo in terms of the percentage of patients maintaining smoking abstinence at 24 weeks of the follow-up: 19% and 16%, respectively (ITT analysis). A significant improvement in the over-reactivity of the respiratory tract has also been observed in the group receiving varenicline compared to the placebo group [22]. Severely addicted smokers may benefit from varenicline treatment combined with NRT, because varenicline does not completely saturate the nicotine receptors as the dose increases [23]. Concurrent use of NRT in this case leads to more complete receptor saturation and weaker cigarette craving.

Another drug used to alleviate withdrawal syndrome in nicotine-dependent individuals is cystine, a natural alkaloid extracted from the seeds of plants such as *Cytisus carturum* and *Sophora tetraptera*. Like varenicline, cystine is a partial agonist of the nicotine receptors, reducing the satisfaction and reward associated with tobacco use [24]. The drug was introduced to the market in the 1960s in Bulgaria as a smoking cessation aid, and later in other Eastern European countries. The largest study to date evaluating the efficacy of cystine was conducted by Walker *et al.* in 2014 [25]. It was a randomized, open-label, controlled trial involving 1,360 participants in which the efficacy of cystine was compared to NRT. All participants received telephone-based behavioural support. Although the study was designed as a non-inferiority test, it demonstrated a significant advantage of cystine over NRT in terms of continuous smoking abstinence after 6 months of the follow-up: 22% vs. 15%, respectively (RR = 1.4, 95% CI: 1.1–1.8). However, the validation measure was self-reported abstinence without biochemical verification.

Despite the limited effectiveness, the use of the drug is associated with the risk of adverse effects such as feeling unwell, anxiety, dizziness, increased blood pressure, watery eyes, sleep disturbances, rash, muscle pain, shortness of breath, or decreased libido. Contraindications for the use of this drug include a history of heart attack, age over 65 or under 18, as well as kidney or liver failure and hyperthyroidism [26].

In practically every case, the methods of supporting patients described above should be accompanied by behavioural counselling. In some patients, brief anti-smoking advice aimed at smoking cessation can be an effective method for giving up smoking and it can be easily used by physicians in their practice. Treatment options include individual, group, or telephone counselling. Comprehensive therapy has a better chance of success. The crucial element that should not be overlooked is the patient's own commitment and willingness to break the addiction.

What is also worth mentioning is the harm reduction program, which is used as a method of treating tobacco smoking addiction. The underlying rationale is that providing nicotine in a form other than cigarettes poses lower health risks and reduces the absorption of toxins, including many carcinogens.

Numerous smoking cessation strategies have been developed, but their effectiveness is often unsatisfactory. It seems that the best chance of quitting the addiction is an integrative approach that combines psychological therapy with nicotine replacement therapy. Such therapy can be effective in up to 3/4 of patients. Counselling in primary health care offices is difficult due to the lack of additional time for anti-smoking advice during the visits.

A separate issue is patients referred to as dual users, who smoke traditional cigarettes and use tobacco heating systems or electronic cigarettes. Some people using tobacco heating systems also smoke traditional cigarettes [27]. The consequences of such a combination are unknown. Young people who often use multiple products simultaneously are particularly vulnerable to this type of exposure. Another problem is the initiation of smoking through the use of heat-not-burn systems.

## WHAT IS MRTP?

MRTP stands for a modified risk tobacco product, and it is a separate category of tobacco products established by the U.S. Food and Drug Administration (FDA), which includes a group of FDA-verified and tested products that support the reduction of tobacco smoking and the significant reduction of passive exposure to the toxins present in the smoke. The use of MRTP by patients strongly addicted to tobacco smoking involves one of the above-mentioned procedures, which is a harm reduction program. It involves the use of products that are still harmful but to a lesser extent than cigarettes, which gives an opportunity to completely quit smoking. Harm reduction involves much less exposure to the harmful substances that are directly associated with exposure to cigarette smoke. There is also much less exposure to reactive forms of oxygen and nitrogen that contribute to the development of chronic diseases, including malignant tumours [28]. Reducing smoking means a lower number of all the substances present in cigarette smoke. Furthermore, by using this approach, there is also an increased chance of breaking the addiction.

Patients who switched from traditional cigarettes to another form of nicotine delivery observed an improvement in asthma control after just one year. In addition, there is a decrease in bronchial hyperreactivity, but the



effect is observed later, even up to 3 years after the intervention [29]. In a study of 230 patients who were observed for a year, the change from smoking traditional cigarettes to tobacco heating systems was compared. The results indicated an improvement in asthma control test scores, and the results were statistically significant.

Since the introduction of the new category of products towards the end of 2022, the FDA has granted MRTP status to only a few of these types of products. These include: oral snus, nicotine-free “cigarettes” VLN King, and a system for heating processed tobacco, which is also available on the European market [30]. The new methods of nicotine consumption are a response to the growing need to reduce the health risks associated with smoking traditional cigarettes.

Oral snus is only allowed for sale in Scandinavian countries in Europe. Population studies conducted in Sweden have shown that this product can play a beneficial role as an aid to quitting smoking. Over 70% of smokers who started using snus completely quit smoking cigarettes, including about 30% who stopped using any form of tobacco [31].

The tobacco heating system is currently the only device available on the European Union market to which the FDA has granted the MRTP status. The FDA indicated that this product is intended only for adult smokers, suitable for promoting public health, but that does not mean it is risk-free. After several years of research and analysis, the FDA allowed the possibility of informing adult smokers in the United States about the difference between the tobacco heating system and cigarettes, as well as the potential health benefits associated with a complete switch from traditional cigarettes to heat-not-burn tobacco products. At the same time, it was emphasized that the greatest health benefits come from complete withdrawal from nicotine and that MRTPs are not harmless products, so people who do not use tobacco products should never reach for them [32]. Thus, MRTPs can serve as a substitute for cigarettes for heavily addicted smokers who are resistant to pharmacotherapy or in case of intolerance to the medications used in nicotine addiction treatment. A significant reduction in exposure to toxins when cigarettes are completely replaced with tobacco heating systems has also been confirmed by public scientific institutions in the Netherlands, Germany and Japan [33–35].

In an independent study with a 3-year follow-up conducted by the University of Catania, it was shown that changing the way nicotine is consumed to tobacco heating systems may result in tangible benefits for patients with COPD. They include a consistent improvement in respiratory symptoms, exercise tolerance

and quality of life, and a reduction in exacerbation frequency. These benefits were observed in COPD patients who completely quit smoking or significantly reduced smoking by switching to tobacco heating systems [36]. The study results suggest that heat-not-burn tobacco products may support smoking cessation, and the effect appears by the end of a 12-month period.

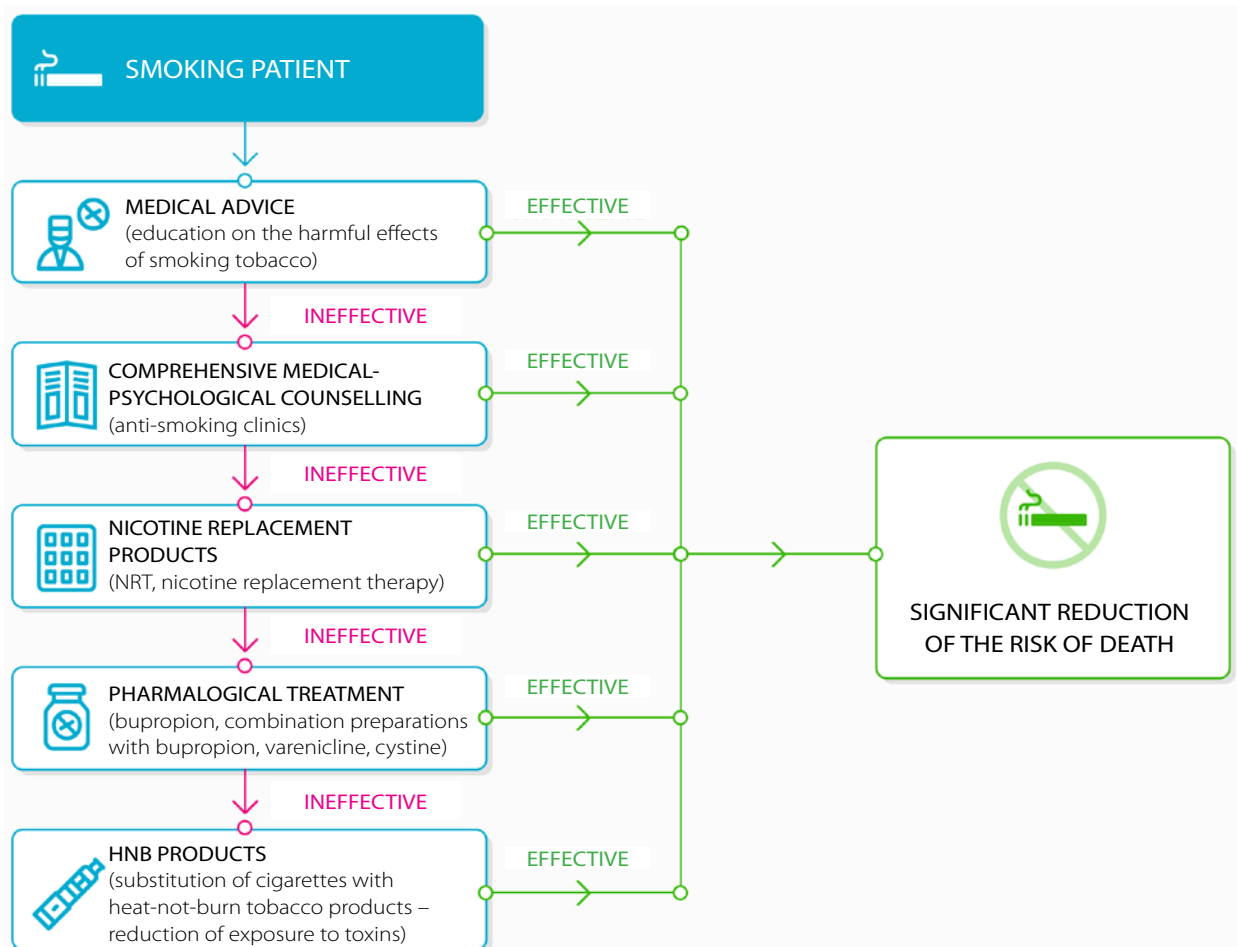
Interesting observational data was presented based on analyses conducted in Japan, which was the first country in the world to introduce systems for heating processed tobacco into the market in 2016. Since then, the number of conventional cigarettes sold in that country has significantly decreased. From 2011 to 2019, the sales of cigarettes decreased by 38%, whereas the sales of cigarettes and heating cartridges in conjunction dropped by 19%, which may indicate that around 19% of tobacco users withdrew from the addiction at that time period [37]. However, it should be noted that Japan is a culturally distant country, so these results should not be directly translated into effects in the European population. By 2022, tobacco heating systems were authorized for sale in about 70 countries worldwide.

In the guidelines of the European Society of Cardiology regarding cardiovascular prevention, the use of heat-not-burn products was discouraged due to the presence of nicotine in them [38]. There is not enough data on cardiovascular prognosis in patients using heat-not-burn tobacco systems. However, it has been proven that in patients who have switched from traditional cigarettes to tobacco heating systems, the coronary reserve has increased, which means that the heart muscle can be better oxygenated [39].

On the other hand, the British Royal College of Physicians states in its position that taking nicotine in a form where smoke has been eliminated reduces the harm to smokers who completely quit smoking in favour of nicotine vaporisation [40]. Polish scientific societies also recognise the rationale for using innovative products to reduce exposure to tobacco smoke, both for smokers and bystanders previously exposed to passive smoking. At the same time, they emphasize that these products still contain nicotine, which is harmful to the human body in itself (Figure 1) [41, 42].

Analysing the FDA's foregoing approach to MRTP products, it should be noted that by the end of 2022, the agency did not include any e-cigarettes in this category [43]. The use of these devices as aids in smoking cessation is currently controversial, due to the lack of proper standardization, the presence of unwanted substances in some nicotine fluids, and frequent misinformation on the packaging [44–46].

In 2019–2020, a number of cases of toxic lung damage were reported in the United States due to the use



**FIGURE 1.** Algorithm for smoking cessation management in patients with COPD or asthma (based on Szymański F.M., Kuna P., Płatek A.E., Kowalik R., Gotlib J., Filipiak K.J. Heat-not-burn tobacco products and patient health: Expert Group opinion. *Choroby Serca i Naczyń* 2019, volume 16, issue 2, pp. 135-142)

of e-cigarettes containing liquids with added tocopherol acetate [47, 48]. Another controversial issue is a frequent self-preparation of nicotine fluid mixtures at home using many premixes available for sale [49].

### POTENTIAL RISKS ASSOCIATED WITH MRTP PRODUCTS: SIMULTANEOUS USE OF CIGARETTES AND MRTP, AND THEIR ATTRACTIVENESS TO TEENAGERS

The use of heat-not-burn tobacco products is associated with a reduction in exposure to smoke from cigarettes. However, the long-term effects of using such solutions are still unknown as there has not been enough time since the introduction of heated tobacco products to the market, and there are no scientific studies confirming the assumption that it will actually bring long-term benefits to smokers. It is also worth noting that more experts now emphasize new risks associated with heat-not-burn products. It seems that the use of heat-not-burn products may be associated with

the potential risk of developing an addiction to traditional cigarettes in individuals who perceive smoke-free products as the beginning of their nicotine addiction adventure. Based on the available data, it can be inferred that the main users of heated tobacco products are currently those who used to smoke traditional cigarettes. This is also supported by the results of a study conducted among Polish teenagers by the National Institute of Public Health – National Institute of Hygiene, where it was investigated which product had initiated their nicotine use. In 53% of respondents it was traditional cigarettes, in 30% it was e-cigarettes, while in 0.2% it was tobacco heating systems [50]. Analogous conclusions were drawn in a report prepared for the European Commission (Eurobarometer 2021), according to which traditional cigarettes and roll-your-own cigarettes accounted for 87% of cases of nicotine use initiation (other products: waterpipes with tobacco – 4%, e-cigarettes – 2%, snus and heat-not-burn tobacco products < 1%) [51]. Also according to the FDA, the risk of regular use of heat-not-burn products by

non-smokers and minors is low as is the risk of them being used by former smokers. It is also worth adding that the declared motives for consuming nicotine in the form of e-cigarettes and heated tobacco products include: lower harmfulness, reduced smoking of traditional cigarettes, belonging to a social group, the possibility of use in places where traditional smoking is prohibited, and, in the case of e-cigarettes, also the relatively low price [52].

## REGULATORY ASPECTS

The act of 9 November 1995 on protection of health against the consequences of the consumption of tobacco and tobacco products (Journal of Laws of 2015, item 298, and 1916 and of 2016, item 960) does not identify any category of nicotine product as having a reduced level of exposure to toxins. The act distinguishes between tobacco products for smoking, smokeless products (chewing tobacco, snuff and oral tobacco), and innovative ones (tobacco heating systems). There is also a separate category for non-tobacco products that deliver nicotine (electronic cigarettes used for the inhalation of nicotine-containing vapour through a mouthpiece). Legal requirements for the listed groups of products related to marketing authorisation are diversified. In the case of innovative products, the manufacturer is obliged to provide additional available scientific research on the toxicity, addictive properties, and attractiveness of the product, as well as an analysis of the risk-benefit ratio associated with such a product [53]. By the end of 2022, the Bureau for Chemical Substances approved the sale of innovative products (cartridges with processed tobacco) designed for electronically controlled tobacco heating in 4 different systems.

In the case of reporting electronic cigarettes and nicotine liquids to the Bureau for Chemical Substances, the manufacturer is obliged to provide a list of all substances released as a result of using the product, along with their quantities, toxicological data, taking into account, in particular, the addictive properties of the product and a description of the production process [54]. Despite the fact that several thousand different e-liquids have been authorised for sale in Poland, the results of these studies have not been published by the authority, which makes it impossible to make a detailed risk assessment for a given product [55].

The provisions of the law (Article 8(4)) prohibit the placement on the labels of tobacco products the information regarding the content of nicotine, tar substances, or carbon monoxide in the product, which can make it difficult to use certain products as a form of harm reduction for addicted smokers. It is also prohibited to

place information suggesting that a given tobacco product is less harmful than others or that its purpose is to reduce the effects of certain harmful cigarette smoke components.

The issue is regulated differently in many countries. The British agency responsible for the registration of medicines allows for electronic nicotine delivery devices to be registered as medicinal products, provided that clinical trials have demonstrated a benefit for smokers [56]. A report published in 2022 by the British Office for Health Improvement and Disparities summarizes the state of knowledge on electronic devices delivering nicotine, which are widely used in the British public health system as a form of harm reduction for smokers [57]. The authors of the report drew attention to the results of the clinical trial with a 5-year follow-up, which showed improved spirometry results in smokers with COPD who completely switched from smoking to nicotine vaporisation in comparison with continued smoking of tobacco [58, 59].

In terms of the incidence of COPD in a given country, the percentage of tobacco smokers in the population has the greatest impact [60]. Over the past 30 years, the largest reduction in the percentage of smokers in Europe has been observed in Sweden, where the use of oral smokeless tobacco (snus) has become widespread. This has been accompanied by a significant decrease in the incidence of lung cancer and COPD in that country [28].

The approach to substitution of cigarettes with oral nicotine pouches adopted in Germany is also noteworthy. According to the position statement of the German Federal Institute for Risk Assessment (BfR) published in 2022, the non-tobacco oral pouches containing nicotine can be classified by local authorities as a novel food in the country. These products are subject to control, and in the event of exceeding the maximum allowable dose of nicotine, they must be withdrawn from the market [61]. These arguments should be taken into account when redefining existing anti-tobacco policies.

## CONCLUSIONS

Management of nicotine addiction poses a challenge in daily medical practice. Patients with COPD or asthma are a special group of patients as in their case addiction directly affects the course of disease. Thus far, a universal method for supporting patients in smoking cessation has not been developed, but in the case of highly dependent smokers, an approach based on comprehensive pharmacotherapy complemented by harm reduction is gaining popularity.



In view of the results of a study conducted by the European Lung Foundation and the European Respiratory Society (ERS) in 26 European countries involving smoking patients with COPD, asthma and other lung diseases, patients considered NRT (12% of participants) and electronic nicotine delivery systems (11% of participants) to be the most effective methods to quit smoking of tobacco. Varenicline therapy and bupropion therapy were considered effective by 5.9% and 2.8% of participants, respectively. Both organizations recommend regular anti-smoking counselling and providing smokers with access to a wide range of pharmacotherapy options and non-pharmacological interventions [62]. In the case of patients with chronic lung diseases who report significant difficulties in tobacco smoking cessation despite attempts made, the ERS recommends combining two or more NRT products at doses higher than usual, prolonged use of these products before and after smoking cessation, as well as the combination of NRT with varenicline. Harm reduction based on reducing the number of smoked cigarettes (by at least 50% and for a longer period of time) can also provide some benefits to the patient [63].

According to the WHO Framework Convention on Tobacco Control, tobacco control means *a range of supply, demand, and harm reduction strategies that aim to improve the health of a population by eliminating or reducing their consumption of tobacco products and exposure to tobacco smoke* [64]. Replacing cigarette smoking with tested nicotine vaping systems, especially in patients resistant to pharmacotherapy for nicotine dependence, seems to be in line with this approach. However, the substitution of tobacco smoking with MRTP should not interrupt the patient's efforts to completely break nicotine dependence. In 2020, WHO emphasized the need for a modern approach to addressing the consequences of tobacco smoking.

In a report on electronic nicotine delivery systems, WHO summarized that these products as dangerous for youths, pregnant women, and adults who have never smoked [65]. At the same time, WHO predicts that the use of these products by adult smokers, excluding pregnant women, can reduce their health risks, provided they completely switch from conventional tobacco cigarettes to properly regulated and uncontaminated electronic nicotine delivery systems and nicotine-free vaping devices.

However, the risks associated with simultaneous and excessive nicotine intake using different methods and the risk of nicotine initiation among adolescents should not be overlooked. Further industry-independent research and standardisation of electronic nicotine delivery systems is required to position the tested nicotine

vaping systems within the scheme of nicotine addiction treatment and to reduce the health consequences caused by this addiction.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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