

Awareness and Acceptance of Nicotine-free Smoking Intervention Methods (Acetium® Lozenge) Increased Among Health Care Professionals by Targeted E-training as Confirmed by Post-training Surveys

KARI SYRJÄNEN¹, ILARI PATRAKKA², ESA PALONIEMI³,
AARNI SOPPI³, PANU HENDOLIN² and OSMO SUOVANIEMI²

¹SMW Consultants Ltd, Kaarina, Finland;

²Department of Clinical Research, Biohit Oyj, Helsinki, Finland;

³Success Clinic Oy, Helsinki, Finland

Abstract. *Background/Aim:* To increase the awareness and acceptance of the new nicotine-free smoking intervention method (Acetium® lozenge; Biohit Oyj, Finland), targeted E-Training with accompanying surveys were conducted in 2018, 2020 and 2023. *Patients and Methods:* The target groups were derived from the General Data Protection Regulation (GDPR)-compliant registers of Finnish physicians, pharmacy staff and nurses owned by Success Clinic Oy. The post-training surveys recorded 1) awareness of the responders on Acetium® lozenge, 2) their attitude to nicotine-free smoking intervention methods in general as well as 3) their readiness for recommending this new tool to their patients. *Results:* The three surveys accumulated a total of 1.892 responders. There was a constantly increasing awareness on Acetium® lozenge, increased interest in nicotine-free smoking intervention methods in general and a substantially increased readiness to recommend Acetium® acceptance to the smoking patients. The impact of E-Training, as measured by the increased interest in nicotine-free methods (56%) and readiness to endorse Acetium® acceptance (58%), was most marked among nurses who had the least awareness on Acetium® lozenge beforehand, exceeding the respective increase among medical doctors by

20% and 10% and among pharmacy staff by 30% and 20%, respectively. *Conclusion:* This E-Training had a favorable effect 1) on the responders' interest in nicotine-free smoking intervention method in general, 2) on increasing the awareness of Acetium® lozenge as a novel innovative method to quit smoking, as well as 3) on increasing the responders' readiness to introduce the new device to their smoking patients who are motivated to stop smoking nicotine-free.

In many Western countries, smoking rates have been constantly declining since the 1970's-1980's but during the recent years, this trend seems to be leveling off and smoking is even increasing in some countries, e.g., China (1-3). According to recent estimates, there are over 1.1 billion adults regular smokers, and smoking-related annual economic losses exceed 500 billion dollars (4-7). This emphasizes the urgent need of more effective tools for smoking intervention (3-7).

According to several interviews, at least 60% of regular smokers have a desire to quit smoking, but as generally known, cessation of smoking is extremely difficult (8). According to a recent WHO report, "more than a billion people worldwide continue to use tobacco products, and the toll of illness, death and other harms will continue to be staggering unless we accelerate the trajectory of progress demonstrated in this report" (9). The most lethal consequence of smoking is lung cancer, the risk of which remains increased for several years after smoking cessation (4, 5, 10, 11). However, this risk is gradually decreasing to the level of never-smokers, which further emphasizes that smoking cessation is justified even after long-term smoking (6, 12, 13).

Principally two different approaches are available for assisting smoking cessation: methods i) with and ii) without assistance by healthcare professionals (8, 14). Dispute continues which of the numerous intervention methods is the

Correspondence to: Prof. Kari Syrjänen, MD, Ph.D., FIAC, SMW Consultants Ltd, Kylläisentie 9, FI-21620 Kuusisto, Finland. Tel: +358 405566810, e-mail: kasyrja@saunalahti.fi

Key Words: Acetium® lozenge, E-Training, smoking intervention, nicotine-free, nicotine replacement therapy (NRT), post-training survey, health care professionals, medical doctor, nurse, pharmacy staff, awareness, interest, acceptance.



This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY-NC-ND) 4.0 international license (<https://creativecommons.org/licenses/by-nc-nd/4.0>).

most effective (15, 16). The most widespread are the products based on nicotine replacement therapy (NRT). The global market for NRT products (gums, lozenges, patches, inhalers) exceeded 2.7 billion USD in 2021, with the projected annual growth of 8.3% (17). Despite their popularity, NRT-based smoking interventions are only moderately effective; in large-scale RCTs, odds ratio (OR) for smoking cessation levels were around 1.5 (14, 15).

Recently, an innovative new method for nicotine-free smoking intervention was introduced by a Finnish biotechnology company (Biohit Oyj, Helsinki, Finland), based on elimination of cigarette smoke-derived acetaldehyde in the saliva by a patented formulation of slow-release L-cysteine (Acetium® lozenge) (18, 19). The theoretical basis of this concept is derived from experimental studies suggesting that acetaldehyde, the most common carcinogenic compound in tobacco smoke (20, 21), enhances behavioral, endocrine and neuronal responses to nicotine (22-24). Acetaldehyde in the saliva can be effectively eliminated by slow-release L-cysteine converting it to inactive MTCA (2-methylthiazolidine-4-carboxylic acid) compound (25-27), and elimination of acetaldehyde in the saliva during cigarette smoking by Acetium® lozenge can be expected to effectively minimize the reinforcing effects of acetaldehyde on smoking dependence (18, 19, 25-27). This concept was patented by Biohit Oyj (19) soon after the feedback from the smokers who i) lost their level of pleasure achieved from smoking, and ii) felt that sensations of smoking were changed, after a short testing of Acetium® lozenge (18).

To clinically validate the new device, two randomized, placebo-controlled clinical trials (RCT) were designed, where Acetium® lozenge was confirmed to be clearly superior to placebo, with the efficacy in assisting smoking cessation being equivalent to that reported for NRT and only slightly inferior to the results obtained by the two most popular medications (bupropion and varenicline) (28, 29).

A focused E-Training was designed and realized in 2018, 2020 and 2023, aiming to increase the awareness and acceptance of Acetium® lozenge as a novel nicotine-free smoking intervention method among general practitioners (in 2023), occupational health physicians (2018, 2020, 2023), nurses (2018, 2020, 2023), nutritionists (2018), personal trainers (2018) and pharmacists (2018, 2023) (30). The present communication reports the results of this targeted E-Training, with special reference to the increase in awareness and acceptance of the novel nicotine-free smoking intervention method, tested by repeated surveys linked with the E-Training sessions (30).

Patients and Methods

Study design. The present data are derived from three E-Training sets, organized in 2018, 2020 and 2023, focused on slightly different target groups in each year. The purpose of the E-Training was to survey (before and after training) the awareness about tobacco and

Table I. *The participants in the three E-Training sets (2018, 2020, 2023).*

Category of professionals	Survey conducted in:					
	2018		2020		2023	
	N	%	N	%	N	%
Physician	130	12.9	121	40.0	167	28.7
Nurse	529	52.5	181	60.0	196	33.7
Pharmacist	300	29.7			219	37.6
Other professional	49	5.9				
	1008	100.0	302	100.0	582	100.0

nicotine addiction and smoking intervention methods among general practitioners (in 2023), occupational health specialists (2018, 2020, 2023), nurses (2018, 2020, 2023), nutritionists (2018), personal trainers (2018) and pharmacists (2018, 2023), actively working in this country (Finland).

Study subjects. The target groups (with contact information) were derived from the registries of Finnish physicians, pharmacists and nurses of the Success Clinic Oy. All these panels are General Data Protection Regulation (GDPR)-compliant registers, property of Success Clinic, and governed under the Business ID of the company. The panel of physicians contains information on their medical specialty, and here were used to target the E-Training referrals to general practitioners and occupational health specialists. The pharmacy panel includes both pharmacists with pharmaceutical training and technical staff of the pharmacies.

E-Training materials. The questionnaires were prepared in cooperation between the experts of Biohit Oyj and Success Clinic Oy. The questionnaires recorded the awareness of the responders on the optional treatment modalities available for tobacco and nicotine addiction and smoking intervention. E-Training introduced the key items on Acetium® lozenge and its use in smoking intervention presented on the company (Biohit Oyj) website (18). In addition, the E-Training material included short articles (with references) and videos about tobacco and nicotine addiction as well as the role of Acetium® lozenge as a novel nicotine-free method for smoking cessation. In some of the questions, the respondents were asked to judge if the statements are true or false. The full E-Training set of 2023 is found in (30).

Data collection. The data collection was carried out as an electronic survey, which was distributed to the selected responders by e-mail. The survey was targeted to all those general practitioners (2023), occupational health specialists (2018, 2020, 2023), nurses (2018, 2020, 2023), pharmacy staff (2018, 2023) and nutrition specialists (2018) who were listed in the registries of Success Clinic Oy. The short introduction to the survey explained the purpose of the survey, including the estimated time needed to complete it.

Statistical analysis. Analyses of all data was performed anonymously, and the identity of the responders could not be linked with the answers. All statistical analyses were performed using the SPSS 29.0.1.0 for Windows (IBM, Armonk, NY, USA). The descriptive statistics were performed according to routine

Table II. The specific questions included in the three E-Training sets.

Questions	Survey in:		
	2018	2020	2023
Date of completing the E-training	Y	Y	Y
Medical profession	Y	Y	Y
Region, site, type and professional title of employment	Y	Y	Y
Brand name of the pharmacy chain (if pharmacist)	Y		Y
Specialty (if medical doctor) (GP, OHS, Other)	Y	Y	Y
How many patients who are motivated to quit smoking do you meet per month?	Y	Y	Y
How well do you know the issues related to smoking and nicotine dependence and the smoking intervention methods?	Y	Y	Y
Specify the reasons that prevent you from actively practicing smoking prevention for your patients?		Y	Y
Have you observed adverse effects in smoking intervention devices?			Y
Have you heard about Acetium® lozenge as a smoking intervention method?	Y	Y	Y
How interesting do you consider nicotine-free methods of smoking intervention?			
Regarding smoking intervention methods, which one is more important: proven efficacy or being free of adverse effects?			Y
True or false: Acetium® lozenge contains cysteine?	Y	Y	Y
True or false: Acetium® lozenge contains nicotine?	Y	Y	Y
True or false: Acetium® lozenge leads to a changed taste of cigarette and a decreased pleasure produced by smoking?	Y	Y	Y
Your best guess how many of your patients might have a chance to commit themselves for smoking intervention of 3+ months duration			Y
Which of the following statements are false?	Y		Y
Acetaldehyde is not normally present in the saliva?	Y		Y
Acetaldehyde is Class I human carcinogen comparable to asbestos and tobacco	Y		Y
Acetaldehyde is not transported with saliva but remains acting locally in oral cavity	Y		Y
Smoking and pregnancy: which of the following are true or false?			Y
Smoking during pregnancy has undeniable immediate and long-term effects on the health and development of the foetus			Y
Nicotine and carbon monoxide are the most harmful substances for foetal development			Y
In Sweden, more people smoke during pregnancy than in Finland			Y
Quitting smoking reduces the risk of pregnancy complications			Y
Did this E-Training increase your willingness to recommend Acetium® lozenge for your patients?	Y	Y	Y
What makes you still doubtful about Acetium® lozenge?			Y
True or false statement: Acetium® is a Finnish innovation?	Y		
Adverse effects of Acetium® are similar as those of NRT devices	Y		
Acetium® is developed and produced in Finland	Y		

Y: Yes, the question included in the E-Training set; GP: general practitioner; OHS: occupational health specialist; NRT: nicotine replacement therapy.

procedures. Frequency tables were analysed using the χ^2 test, with the likelihood ratio (LR) or Fisher-Freeman-Halton exact test for categorical variables. Differences in the means of continuous variables were analysed using ANOVA or a non-parametric (Mann-Whitney) test for two independent samples. All statistical tests were two-sided and declared significant at p -value <0.05 level.

Results

Table I summarizes the number of participants in the three post-E-Training surveys as stratified by the profession of the responders. The data collection periods for the three surveys were as follows: 1) October 17, 2018-March 24, 2019; 2) May 1, 2020-June 16, 2020, and 3) March 30, 2023-June 5, 2023. Regular reminders were sent to non-responders. Altogether, the three surveys accumulated a total of 1.892 responders.

The surveys were continuously modified by adding new questions and/or leaving out those that proved to be redundant or otherwise inappropriate to solicit meaningful responses. Table

II lists the specific questions and their use in the three surveys.

The responses to the core questions on awareness, interest, and acceptance of Acetium® lozenge in the three surveys are depicted in Table III. The differences in the response pattern were statistically significant between the three surveys. As to the awareness on Acetium® lozenge, there was a substantial decline in the number of responders who had never heard about the device, from the 2018 survey up to the 2023 survey (from 50% to 39.4%). This coincides with the increase of 1) responders, who had already recommended Acetium® for their smoking patients (from 7.6% to 11.4%), respectively, and most importantly, 2) the responders who regularly recommend Acetium® (from 0.1% to 1.3%, increased by a factor of 10) (Table III).

Also, the interest in nicotine-free (natural) smoking intervention methods showed an increasing trend across the surveys from 2018 until 2023, the proportion of moderately or very interested increasing from 87.6% to 92.2% and was most

Table III. The responses to the key questions on awareness, interest and acceptance of Acetium® lozenge in the three surveys.

Core questions on awareness, interest and acceptance of Acetium® lozenge	Survey in:					
	2018		2020		2023	
Q 1: Have you heard about Acetium® lozenge as a smoking intervention method?	N	%	N	%	N	%
Never heard about	401	50.0	133	62.4	177	39.4
Yes, and recommended to my smoking patients	61	7.6	9	4.2	51	11.4
Yes, but not yet recommended to my patients	339	42.3	69	32.4	215	47.9
Yes, and recommend regularly to my smoking patients	1	0.1	2	0.9	6	1.3
* $p < 0.001$						
Q 2: How interesting are the natural (nicotine-free) smoking intervention methods for you?	N	%	N	%	N	%
Not interesting	25	3.1	3	1.4	14	3.1
Very interesting	295	36.9	96	45.3	186	41.4
Moderately interesting	406	50.7	90	42.5	228	50.8
No opinion	74	9.3	23	10.8	21	4.7
* $p = 0.004$						
Q 3: Did this E-Training increase your readiness to recommend Acetium® lozenge for your patients?	N	%	N	%	N	%
Did not increase at all	37	6.0	6	4.3	10	2.8
Increased to some extent	318	51.7	69	50.0	185	51.1
Increased substantially	221	35.9	49	35.5	163	45.0
No opinion	39	6.3	14	10.1	4	1.1
* $p < 0.001$						

*Significance calculated using Fisher-Freeman-Halton exact test.

marked between the surveys of 2020 and 2023. These trends parallel the decline of responders with no opinion on this subject.

As to the responders' readiness to recommend Acetium® lozenge for their patients, the proportion of those with no effect (training did not increase the readiness) declined constantly from 6.0% (in 2018) down to 2.8% (in 2023). Most marked is the increased proportion of the responders whose readiness increased substantially, *i.e.*, almost by 10 percentage points from 35.9% to 45.0%. The difference in the overall response patterns across the surveys is statistically significantly ($p < 0.001$).

Figure 1 summarizes the awareness on the Acetium® lozenge clustered by the responders' professional status in the 2023 survey. The numbers with – or + prefix indicate %-decrease or %-increase in the last (2023) survey as compared with the highest/lowest percentage in the two previous surveys (2018 and 2020). Among medical doctors, there was an 8% increase in those who had already recommended the device to their patients, and an 1% increase both in those who are aware but not yet recommended and those who recommend Acetium® lozenge regularly to their smoking patients. Among the staff of pharmacies, the responses remain stable, whereas among nurses, there seems to be a substantial increase of the response “never heard” about the product, at the expense of the other response categories.

Figure 2 is tracking the general attitudes of the responders to the nicotine-free smoking intervention methods. The proportion of those who did not have any firm opinion of the subject declined to a very low level (5%) among both nurses and physicians and remained even lower (3%) among pharmacy staff. Among physicians, a bimodal trend was observed; on one hand, a 5% increase of those who responded “very interesting”, and a 3% of those not interested, and on the other hand, a 3% decrease of those who were only modestly interested.

The impact of E-Training in the responders' readiness to recommend Acetium® lozenge for their patients is depicted in Figure 3. Of the nurses, 56%, and of the doctors 45% responded that the training increased substantially their readiness to recommend Acetium® lozenge. Compared with the two previous surveys, the total increase in this response category was 20 and 9 percentage points, respectively, among the nurses and doctors. In addition, 50% of the physicians felt that the training increased their willingness to recommend the device to some extent.

Discussion

At present, the global markets of smoking intervention methods are dominated by devices based on the NRT concept (17). As compared to the most effective special medications, however,

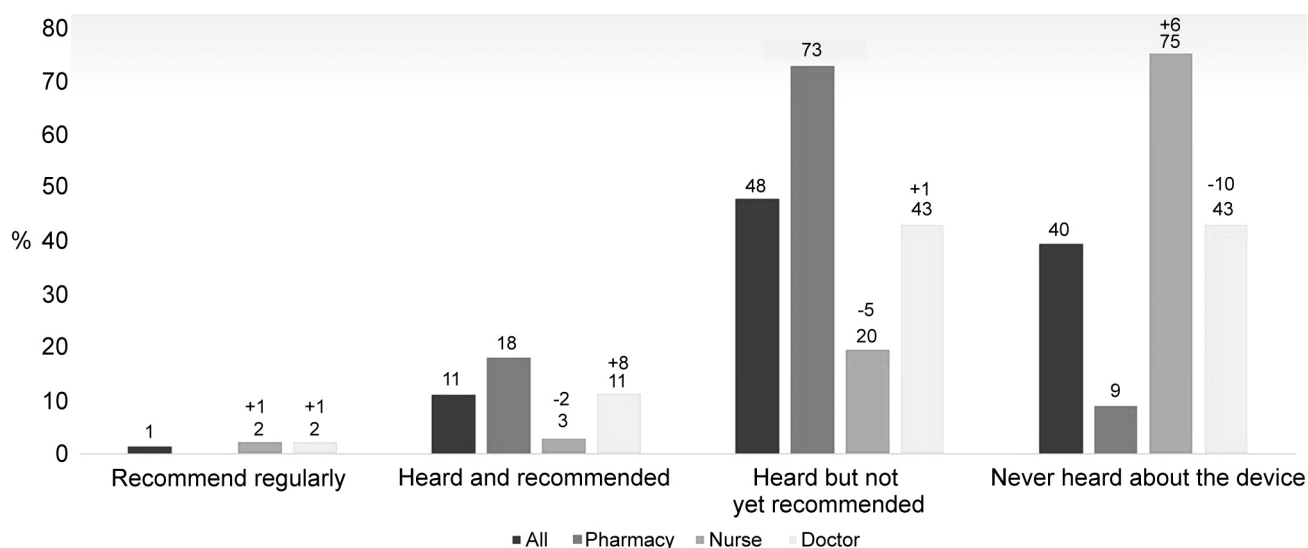


Figure 1. Changes in awareness about Acetium® lozenge across the surveys. Numbers with – or + prefix indicate % decrease or % increase in the last (2023) survey as compared with the highest/lowest percentage in the two previous surveys (2018, 2020).

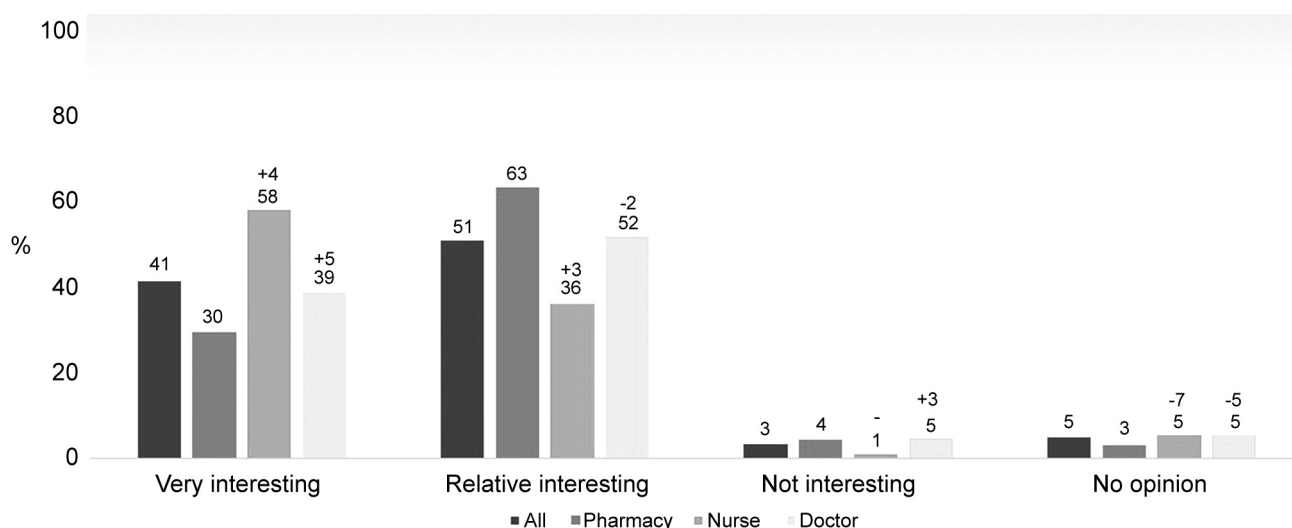


Figure 2. Attitudes of the responders to the natural (nicotine-free) smoking intervention methods. Numbers with – or + prefix indicate % decrease or % increase in the last (2023) survey as compared with the highest/lowest percentage in the two previous surveys (2018, 2020).

the efficacy of NRT is only moderate (15, 16). Importantly, NRT is associated with a wide variety of severe side effects, as recently disclosed in a systematic review and meta-analysis of 120 studies including 177,390 smokers (31). The report concludes that the patients should be clearly informed of all potential side effects of NRT (31). Given these concerns on NRT, the side effect-free Acetium® lozenge recently introduced by Biohit Oyj (Helsinki) appears as a logical choice to assist in nicotine-free smoking cessation (18, 28, 29).

As compared with the NRT products, Acetium® lozenge has several indisputable advantages (18, 19, 28, 29, 31). The most

important of these are: 1) no nicotine-dependence and side effects of NRT; 2) no upper daily dose (one lozenge for each smoked cigarette); 3) the efficacy is equivalent to NRT; 4) tolerability is superior to NRT; 5) extremely high user compliance; 6) favorable effect achieved within 3–4 months (among the responders); 7) total costs of a quit attempt are significantly lower (no need to continue after successful smoking cessation); 8) improving oral hygiene by its xylitol component; 9) a nicotine-free alternative to quit smoking without transferring the nicotine addiction from cigarette to an NRT device; 10) protected by European Patent; EP 2 197 436

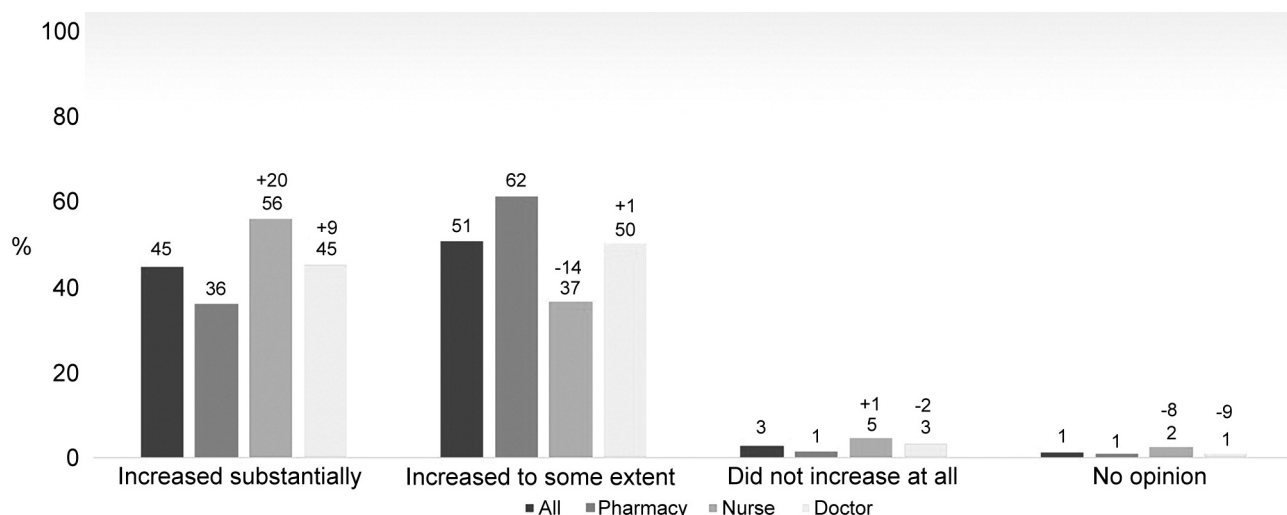


Figure 3. The impact of E-Training in the responders' readiness to recommend Acetium® lozenge for their patients. Numbers with – or + prefix indicate % decrease or % increase in the last (2023) survey as compared with the highest/lowest percentage in the two previous surveys (2018, 2020).

B1 (19); 11) other bonus effect is harm reduction: L-cysteine binds carcinogenic acetaldehyde in the saliva. Accordingly, Acetium® lozenge represents a major breakthrough in the development of smoking intervention methods.

Because one cannot anticipate achieving adequate dissemination of the awareness of this novel tool among health care professionals exclusively by the original reports on the RCTs (28, 29), the company decided to take advantage of the modern applications of E-Learning. As a joint effort between the experts of Biohit Oyj and Success Clinic Oy, a set of E-Training was repeated three times (2018, 2020 and 2023), distributed to the responders by e-mail. The target groups in the three surveys were slightly different (Table I). Nurses and physicians were invited to all three surveys, whereas pharmacy staff were surveyed twice and other professionals only once (2018). This difference in the targets of these surveys precludes a direct comparison of the responses at a level of the profession. Such a direct comparison is possible, however, for medical doctors and nurses who are included in all three surveys. Similarly, the number of participants varied between the three surveys, the first one receiving the highest number of responders (n=1,008), followed by the last one (n=582). The explanation is to be found in the length of the data collection period (2018: 5 months; 2020: 1.5 months; 2023: 2 months) which was positively related to the number of responders in the survey. Another factor in favor of the 2018 survey is the annual season when the data were collected (late autumn to mid-winter), as compared to early and late springtime in the two others.

Another feature that makes the three surveys non-identical is the content of the included questions (Table II). As a natural development of the process, the contents of the E-Training materials were modified by the feedback from the

preceding survey. The most comprehensive in its content is the last survey that was realized only recently (data collection between March 30, 2023-June 5, 2023). With the added important questions on smoking and pregnancy, including false/true statements, this latest survey provides the most comprehensive information on the responders' recognition of this important subject. Furthermore, some of the questions that received almost unanimous correct responses in the 2018 survey were omitted from the two subsequent E-training sets as redundant.

Three core questions tracking the awareness, importance and acceptance of the new device were included in all three surveys (Table III). The response patterns in the three surveys, respectively, were significantly ($p<0.001$; $p=0.004$; $p<0.001$) different, implicating the effect achieved by the E-Training. Starting from responder's awareness on Acetium® lozenge, the proportion of responders who had never heard about the device decreased from 50% (in 2018), and 62.4% (in 2020) down to 39.4% in the last survey. This increased awareness was mostly contributed by the responders who knew the product but had not yet recommended it for their patients: from 32.4% (in 2020) to 47.9% (in 2023). However, the proportion of responders who have already recommended Acetium® (11.4%) or who regularly recommend it (1.3%) for their smoking patients is still too low to support a widespread nationwide acceptance of this device. However, because the first survey was done only a year after the last RCT was published (29), the proportion of responders who already knew Acetium® lozenge (50.0%) in 2018 can be regarded unexpectedly high.

As to the responders' attitude to nicotine-free intervention methods, all three surveys must be considered reassuring. In the 2023 survey, above 90% of the responders consider

nicotine-free smoking intervention methods highly interesting or at least moderately interesting, and only 3% consider them “not interesting”. Also, the proportion of those with no opinion has declined to one half (4.7%) from the 2018 survey (9.3%). This development certainly reflects an increased awareness among the health care professionals on i) the many side effects of NRT (31) and ii) the fact that these products only transfer the nicotine-dependence from cigarette smoking to NRT-products. Highly unfortunate, these attitudes do not yet parallel the acceptance of nicotine-free intervention methods among smokers, as evidenced by the ever-increasing global sales of the NRT products (17).

Regarding the expected future acceptance of Acetium® lozenge, the responses are most rewarding (Table III). In all three surveys, over 80% up to 96% of the responders reported that the E-Training increased (either substantially or to some extent), their readiness to recommend Acetium® lozenge to their smoking patients. Only very few responded the contrary (*i.e.*, not increased at all), and even fewer had no opinion on the subject. These results indicate that the information given in the E-Training sets was well taken by the participants whose responses implicate that the vast majority are ready to endorse Acetium® lozenge to their smoker patients who are motivated to stop smoking.

Between the groups of professionals, interesting differences in these key responses were noticed in the 2023 survey (Figure 1, Figure 2, Figure 3). This was not unexpected, given the differences between these groups particularly in their contact with the patients. Starting with the awareness of Acetium® lozenge (Figure 1), the highest degree of awareness was reported by the pharmacy staff (>85%) whereas the vast majority (95%) of nurses reported having never heard about the product. The awareness among the physicians (56%) was intermediate between these two extremes. These results implicate pharmacists’ high degree of familiarity of the new products on sale in their pharmacy, including Acetium®. Additional efforts are still needed to increase the awareness of the device among physicians, of whom a substantial proportion was not yet aware of Acetium® lozenge in the 2023 survey.

As to the attitudes towards nicotine-free smoking intervention methods, most of the responders among each profession considered those either very interesting or moderately interesting (Figure 2). Interestingly, the nurses reporting very low awareness on Acetium® lozenge, did express the highest interest in nicotine-free methods, 58% considering these “very interesting”, which is roughly 20 percent points more than that among doctors and 30 percent points more than that among pharmacy staff. This is another indication of the usefulness of these E-Training sets, which clearly succeeded in arousing the interest in nicotine-free intervention methods among those who were least aware of this novel method in advance.

This increased interest in nicotine-free methods (Figure 2) closely parallels the responders’ readiness to recommend Acetium® lozenge (Figure 3). The difference in the response pattern between the profession categories was no longer highly significant but only slightly different ($p=0.025$). Again, the increase in the willingness to recommend the method to motivated smokers was highest among the nurses, of whom 56% responded “substantial increase”. This is >10 percent points more than reported by doctors (45%), and 20 percent points more than among the pharmacy staff (36%). The almost similar response rates were received for the category “increased to some extent” leaves few for whom this E-Training was not useful or stimulating.

This E-Training focused on increasing the awareness, interest and acceptance of a novel nicotine-free smoking intervention method (Acetium® lozenge) among health care professionals working in Finland was well received among the responders. The training-accompanied surveys repeated three times at 2-year intervals confirmed the great potentials of E-Training in promoting this type of professional information, as an additional tool to the company website (18) and original research reports (28, 29). The response rates are clearly related to the length of the data collection period, and also the annual season seems to have an effect. When repeated at regular intervals, the survey was constantly updated by omitting the questions that received almost unanimous responses, *i.e.*, are too obvious to respond. The repeated surveys also offer an opportunity to follow-up the trends in awareness, interest and acceptance of the target method (Acetium® lozenge in this case).

Taken together, as determined from the three surveys, the E-Training sets had a favorable effect 1) on the responders interest in nicotine-free smoking intervention method in general, 2) in increasing the awareness of Acetium® lozenge as a novel innovative method to quit smoking nicotine-free, as well as 3) in substantially increasing the responders’ (doctors, nurses, pharmacy staff) readiness to introduce the new device to their smoking patients who are motivated to stop smoking nicotine-free. Widespread adaptation of any new method necessitates continuous dissemination of the expert information to medical professionals, and modern E-Training has major potential in reaching the right target groups and adequate number of responders.

References

- 1 Mackay JL: The fight against tobacco in developing countries. *Tuber Lung Dis* 75(1): 8-24, 1994. DOI: 10.1016/0962-8479(94)90097-3
- 2 Samet JM: Tobacco smoking. *Thorac Surg Clin* 23(2): 103-112, 2013. DOI: 10.1016/j.thorsurg.2013.01.009
- 3 Chen ZM, Peto R, Iona A, Guo Y, Chen YP, Bian Z, Yang L, Zhang WY, Lu F, Chen JS, Collins R, Li LM, China Kadoorie Biobank Collaborative Group: Emerging tobacco-related cancer risks in China: A nationwide, prospective study of 0.5 million adults. *Cancer* 121(Suppl 17): 3097-3106, 2015. DOI: 10.1002/cncr.29560

- 4 Thun MJ, Carter BD, Feskanich D, Freedman ND, Prentice R, Lopez AD, Hartge P, Gapstur SM: 50-year trends in smoking-related mortality in the United States. *N Engl J Med* 368(4): 351-364, 2013. DOI: 10.1056/NEJMsa1211127
- 5 Peto R, Lopez AD, Boreham J, Thun M, Heath C Jr: Mortality from tobacco in developed countries: indirect estimation from national vital statistics. *Lancet* 339(8804): 1268-1278, 1992. DOI: 10.1016/0140-6736(92)91600-d
- 6 Pirie K, Peto R, Reeves GK, Green J, Beral V, Million Women Study Collaborators: The 21st century hazards of smoking and benefits of stopping: a prospective study of one million women in the UK. *Lancet* 381(9861): 133-141, 2013. DOI: 10.1016/S0140-6736(12)61720-6
- 7 Ekpu VU, Brown AK: The economic impact of smoking and of reducing smoking prevalence: review of evidence. *Tob Use Insights* 8: 1-35, 2015. DOI: 10.4137/TUI.S15628
- 8 Guide to quitting smoking. American Cancer Society. Available at: http://www.cancer.org/docroot/ped/content/ped_10_13x_guide_for_quitting_smoking [Last accessed on August 10, 2023]
- 9 WHO report on the global tobacco epidemic, 2017. Monitoring tobacco use and prevention policies. Available at: <https://apps.who.int/iris/bitstream/handle/10665/255874/9789241512824-eng.pdf?sequence=1&isAllowed=y> [Last accessed on August 10, 2023]
- 10 Doll R, Peto R, Boreham J, Sutherland I: Mortality in relation to smoking: 50 years' observations on male British doctors. *BMJ* 328(7455): 1519, 2004. DOI: 10.1136/bmj.38142.554479.AE
- 11 Thun MJ, Henley SJ, Calle EE: Tobacco use and cancer: an epidemiologic perspective for geneticists. *Oncogene* 21(48): 7307-7325, 2002. DOI: 10.1038/sj.onc.1205807
- 12 Peto R, Darby S, Deo H, Silcocks P, Whitley E, Doll R: Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies. *BMJ* 321(7257): 323-329, 2000. DOI: 10.1136/bmj.321.7257.323
- 13 Doll R, Peto R, Wheatley K, Gray R, Sutherland I: Mortality in relation to smoking: 40 years' observations on male British doctors. *BMJ* 309(6959): 901-911, 1994. DOI: 10.1136/bmj.309.6959.901
- 14 Chapman S, MacKenzie R: The global research neglect of unassisted smoking cessation: causes and consequences. *PLoS Med* 7(2): e1000216, 2010. DOI: 10.1371/journal.pmed.1000216
- 15 Lemmens V, Oenema A, Knut IK, Brug J: Effectiveness of smoking cessation interventions among adults: a systematic review of reviews. *Eur J Cancer Prev* 17(6): 535-544, 2008. DOI: 10.1097/CEJ.0b013e3282f75e48
- 16 Stead LF, Perera R, Bullen C, Mant D, Lancaster T: Nicotine replacement therapy for smoking cessation. *Cochrane Database System Rev* (1): CD000146, 2008. DOI: 10.1002/14651858.CD000146.pub3
- 17 Allied Market Research. Available at: <https://www.alliedmarketresearch.com/nicotine-replacement-therapy-market-A31526> [Last accessed on August 10, 2023]
- 18 Acetium. Available at: <https://www.acetium.com/en/quit-smoking/acetium-lozenge/> [Last accessed on August 10, 2023]
- 19 Suovaniemi O, Salaspuro M, Salaspuro V, Marvola M: Sucking tablet for use in reducing tobacco and/or alcohol dependence. European Patent Office - EP 2197436 B1 - EPO. Available at: <https://data.epo.org/publication-server/document?iDocId=5473994&iFormat=0> [Last accessed on September 19, 2023]
- 20 Secretan B, Straif K, Baan R, Grosse Y, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Coglian V: A review of human carcinogens – Part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. *Lancet Oncol* 10(11): 1033-1034, 2009. DOI: 10.1016/s1470-2045(09)70326-2
- 21 Haussman HJ: Use of hazard indices for a theoretical evaluation of cigarette smoke composition. *Chem Res Toxicol* 25(4): 794-810, 2012. DOI: 10.1021/tx200536w
- 22 Cao J, Belluzzi JD, Loughlin SE, Keyler DE, Pentel PR, Leslie FM: Acetaldehyde, a major constituent of tobacco smoke, enhances behavioral, endocrine, and neuronal responses to nicotine in adolescent and adult rats. *Neuropsychopharmacol* 32(9): 2025-2035, 2007. DOI: 10.1038/sj.npp.1301327
- 23 Belluzzi JD, Wang R, Leslie FM: Acetaldehyde enhances acquisition of nicotine self-administration in adolescent rats. *Neuropsychopharmacol* 30(4): 705-712, 2005. DOI: 10.1038/sj.npp.1300586
- 24 Quertemont E, Tambour S, Tirelli E: The role of acetaldehyde in the neurobehavioral effects of ethanol: A comprehensive review of animal studies. *Prog Neurobiol* 75(4): 247-274, 2005. DOI: 10.1016/j.pneurobio.2005.03.003
- 25 Sprince H, Parker CM, Smith GG, Gonzales LJ: Protective action of ascorbic acid and sulfur compounds against acetaldehyde toxicity: Implications in alcoholism and smoking. *Agents Actions* 5(2): 164-173, 1975. DOI: 10.1007/BF02027359
- 26 Salaspuro V, Hietala J, Kaihovaara P, Pihlajarinne L, Marvola M, Salaspuro M: Removal of acetaldehyde from saliva by a slow-release buccal tablet of L-cysteine. *Int J Cancer* 97(3): 361-364, 2002. DOI: 10.1002/ijc.1620
- 27 Salaspuro VJ, Hietala JM, Marvola ML, Salaspuro MP: Eliminating carcinogenic acetaldehyde by cysteine from saliva during smoking. *Cancer Epidemiol Biomarkers Prev* 15(1): 146-149, 2006. DOI: 10.1158/1055-9965.EPI-05-0248
- 28 Syrjänen K, Salminen J, Aresvuo U, Hendolin P, Paloheimo L, Eklund C, Salaspuro M, Suovaniemi O: Elimination of cigarette smoke-derived acetaldehyde in saliva by slow-release L-cysteine lozenge is an effective new method to assist smoking cessation. A randomised, double-blind, placebo-controlled intervention. *Anticancer Res* 36: 2297-2306, 2016.
- 29 Syrjänen K, Eronen K, Hendolin P, Paloheimo L, Eklund C, Bäckström A, Suovaniemi O: Slow-release L-cysteine (Acetium®) lozenge is an effective new method in smoking cessation. A randomized, double-blind, placebo-controlled intervention. *Anticancer Res* 37: 3639-3648, 2017. DOI: 10.21873/anticancer.11734
- 30 Koulutus tupakoinnin lopettamisesta ilman nikotiinia. Miten estää tupakoitsijan siirtyminen nikotiinin käyttäjäksi vuosikausiksi. Available at: [https://fi.eu.research.net/r/TNDZJK2?2023=\[2023_value](https://fi.eu.research.net/r/TNDZJK2?2023=[2023_value) [Last accessed on August 10, 2023]
- 31 Mills EJ, Wu P, Lockhart I, Wilson K, Ebbert JO: Adverse events associated with nicotine replacement therapy (NRT) for smoking cessation. A systematic review and meta-analysis of one hundred and twenty studies involving 177,390 individuals. *Tob Induc Dis* 8(1): 8, 2010. DOI: 10.1186/1617-9625-8-8

Received August 20, 2023

Revised September 15, 2023

Accepted September 19, 2023