

SMOKING CESSATION – WHAT’S NEW?

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Abstract

Tobacco cessation represents a multifaceted approach involving patients who often don't neatly fit into classic prototypes. Researchers found that current smokers experience a more than 10-year reduction in life expectancy compared to non-smokers, and more than half make an attempt each year, but less than 10% manage to stay smoke-free for at least 6 months. Therefore, it's recommended to employ a combination of methods and strategies, ranging from questionnaires to established medications. The role of the medical staff is and remains vital in this context. Nicotine is a potent drug due to its rapid absorption and swift diffusion into the central nervous system, and quitting nicotine leads to important consequences, such as craving, drug-seeking behaviour and withdrawal symptoms. Negative affective states also emerge, characterized by symptoms like depressed mood, anxiety, irritability and insomnia. Hierarchical multiple regression models have revealed that extraversion, neuroticism, conscientiousness and age are among the predictors of daily cigarette consumption. The authors discuss both traditional and innovative opportunities to expedite this process, while analysing the potential to enhance the compliance of healthcare providers and patients. Smoking cessation, the process of quitting smoking, can be approached through both pharmacological (medication-based) and non-pharmacological (behavioural and supportive) methods. The choice of approach or combination of approaches depends on individual preferences and needs.

Rezumat

Renunțarea la fumat reprezintă o abordare complexă a unui pacient care adesea nu se încadrează în prototipurile clasice. Cercetările au evidențiat că fumătorii se confruntă cu o reducere de peste 10 ani a speranței de viață în comparație cu nefumătorii și mai mult de jumătate fac o încercare de a renunța în fiecare an, dar mai puțin de 10% reușesc să rămână abștinenți cel puțin 6 luni. Prin urmare, se recomandă utilizarea unei combinații de metode și strategii, de la chestionare la medicamente deja stabilite, iar rolul personalului medical este și rămâne vital în acest context. Nicotina este un drog puternic datorită absorbției și difuzării rapide în sistemul nervos central, iar renunțarea conduce la efecte secundare importante, precum dorința arzătoare, comportamentul de căutare a drogului și simptomele de sevraj. Apar și stări afective negative, caracterizate prin simptome precum depresie, anxietate, iritabilitate și insomnie. Modelele ierarhice de regresie multiplă au dezvăluit că extraversia, nevroticismul, conștiinciozitatea și vârsta se numără printre predictorii consumului zilnic de țigări. Autorii discută oportunități vechi și noi de a accelera acest proces analizând posibilitatea de a îmbunătăți complianța furnizorilor de servicii medicale și a pacienților. Procesul de renunțare la fumat, poate fi abordat atât prin metode farmacologice, cât și prin metode comportamentale și de susținere. Alegerea abordării sau combinația de abordări depinde de preferințele și nevoile individuale.

Keywords: tobacco cessation, strategies in quitting smoking, counselling, primary care physician

Introduction

Epidemiological data concerning tobacco consumption

Tobacco consumption persists as a major risk factor for numerous diseases and stands as a leading cause of preventable deaths worldwide (WHO, 2017). The survival of smokers has been extensively studied, revealing a clear pattern. In a sampled group aged 25 to 79 years, the rate of all-cause mortality among current smokers was approximately three times higher than among those who had never smoked. Moreover, the probability of surviving from ages 25 to 79 was about twice as high in non-smokers (70% vs. 38% for women and 61% vs. 26% for men). This indicates that current smokers experience a more than 10-year reduction in life expectancy compared to non-smokers [1]. This explains why a substantial number of smokers express

a desire to quit. While effective treatments for smoking cessation are available, even the most intensive evidence-based treatments conducted in tightly controlled conditions often result in frequent relapses, occurring at a rate of around 70% within 6 months [2, 3]. The desire to quit is an important objective, as the majority of cigarette smokers indeed wish to quit. Despite this, more than half make an attempt each year, but less than 10% manage to stay smoke-free for at least 6 months [4].

Every country adopts its own strategy for smoking cessation. In Germany, for instance, only one in five smokers attempts to quit annually [5]. Among these, 13.0% employ at least one evidence-based method during their cessation attempts. Notably, individuals with stronger tobacco dependence are more likely to

use these evidence-based methods. Electronic cigarettes are the most commonly used form of smoking cessation support (10.2%).

In the United States, between 2006 and 2015, lower rates of physicians offering advice to quit smoking were observed, as well as reduced uptake of known prescription smoking cessation medications. These trends were prominent among men, younger adults, uninsured individuals, racial/ethnic minority groups and those without smoking-related comorbidities. This discrepancy explains the higher smoking rates within these subgroups, despite an overall decline in smoking prevalence across the United States [6].

The Nicotine dependency process

Nicotine is a potent drug due to its rapid absorption and swift diffusion into the central nervous system within seconds after inhalation from tobacco smoke or electronic cigarettes [7, 8]. Upon entry, it triggers the activation of nicotinic acetylcholine receptors, resulting in a quick rise in blood nicotine levels. This mechanism underscores the reinforcing properties and potential for abuse associated with these products [9]. The reinforcing effects of nicotine primarily stem from its binding to $\beta 2$ -containing nicotinic acetylcholine receptors (nAChRs) [10], particularly those with $\alpha 4\beta 2$ subunits, which exhibit the highest affinity for nicotine [11]. Upon activation of $\alpha 4\beta 2$ nAChRs by nicotine, a cascade of events unfolds, including the release of dopamine in key brain regions such as the prefrontal cortex, ventral striatum and nucleus accumbens [12]. This dopamine release leads to positive reinforcement, a common factor in the addictive potential of various substances, including nicotine, which is linked to the mesolimbic dopamine system [13]. Additional factors contributing to the development of addiction include the $\alpha 5$, $\alpha 3$ and $\beta 4$ subunits [14], changes in receptors within the central nervous system and musculoskeletal system, resulting in the development of tolerance, negative reinforcing effects and withdrawal symptoms upon cessation [15]. Additionally, environmental cues associated with substance use play a significant role, contributing to the habitual nature of drug intake and a high rate of relapse [16]. Quitting nicotine dependence leads to important consequences, such as craving, drug-seeking behaviour and withdrawal symptoms [17]. Negative affective states also emerge, characterized by symptoms like depressed mood, anxiety, irritability and insomnia [18].

Challenges in Smoking Cessation

Challenges in smoking cessation arise not only from patients but also from healthcare providers.

Smokers' Personality and Smoking Cessation Factors Personality traits, self-esteem, self-efficacy and coping mechanisms within different groups—non-smokers, ex-smokers and current smokers—are subjects of intense research interest. When examining predictive

factors, researchers have identified significant differences in extraversion between smokers and non-smokers [19]. Hierarchical multiple regression models have revealed that extraversion, neuroticism, conscientiousness and age are among the predictors of daily cigarette consumption. Importantly, stable personality traits tend to be better predictors of smoking behaviour compared to more transient variables like self-esteem and self-efficacy.

In the context of self-identity, researchers studied the effects of two types: self-identity related to smoking and self-identity related to quitting. They observed that recent quit attempts somewhat alleviate the negative impact of smoking-related identity on attempts to quit [20]. Among Turkish teenagers, self-concept and social comparison were examined in relation to smoking and alcohol consumption. The study found higher social comparison scores among adolescents who consume alcohol and tobacco, while self-concept scores were lower [21]. Patient beliefs are also significant. Despite the entrenchment of addiction over years, beliefs regarding willpower, ability to quit and treatment use consistently predict quit attempts, abstinence duration and cessation aid usage [22]. Among these beliefs, notions of willpower's necessity and sufficiency for quitting were commonly endorsed, while beliefs about quitting anytime or being too addicted to quit were endorsed less consistently. Additionally, the belief that using aids indicates weakness was rarely endorsed. This research highlights the need for clinical and media interventions to counter these willpower-related beliefs and boost quit attempts.

Regarding temperament traits and character traits linked to addiction, a study involving non-motivated and motivated patients in a smoking cessation program discovered a positive correlation between novelty seeking, persistence, cooperativeness and motivation to quit smoking. However, no correlation was found between harm avoidance, reward dependence, self-directedness, self-transcendence and motivation to quit smoking [22, 23]. Researchers are striving to develop a comprehensive smoking scale for evaluating motivation to quit. A Brazilian team's study indicated that females scored significantly higher than males in addiction, tension reduction, handling, weight control and affiliative attachment. The Fagerstrom test exhibited positive correlations with addiction, tension reduction, stimulation, automatism, social smoking and affiliative attachment. Moreover, the number of cigarettes smoked *per day* correlated positively with several factors including addiction, tension reduction, stimulation, automatism, affiliative attachment and handling. Additionally, the level of exhaled carbon monoxide (CO) was positively correlated with addiction, automatism and affiliative attachment [24].

For university students, a correlation exists between perceived self-efficacy and motivation to quit smoking, with high self-efficacy associated with increased

motivation to quit [25]. Other *predictive factors* for cessation include various psychological factors, such as mood and self-efficacy [26], as well as delay discounting—the reduction in reward value as a function of the delay to receipt. This mechanism accurately identified the smoking status of 80% of participants post-treatment [27].

Age and smokers' personality are notable factors. A study conducted on Brazilian students revealed that nicotine-dependent smokers were less extroverted than non-dependent smokers [28]. Other research explores the relationship between the “Big Five” personality traits and cigarette use over a ten-year period among adults in the United States [29]. Findings indicated that only two traits—openness to experience and neuroticism—were significantly associated with an increased risk of any lifetime cigarette use. Neuroticism was also linked to an increased risk of progressing from occasional smoking to daily smoking and maintaining daily smoking. Conversely, conscientiousness was linked to a decreased risk of lifetime cigarette use, progression to daily smoking and smoking persistence. The nicotine dependency process appears multifaceted, with current smoking associated with higher extraversion, higher neuroticism and lower conscientiousness. Smoking cessation was negatively associated with neuroticism, and initiation into smoking correlated with higher extraversion and lower conscientiousness. Relapse to smoking among ex-smokers was associated with higher neuroticism [30].

Regarding gender and tobacco consumption among university students, significant gender differences were found in the patterns of tobacco consumption, the number of smoking peers, opinions about tobacco-free outdoor spaces and knowledge of new forms of tobacco/nicotine consumption. Students classified the university campus as the second-most prevalent location for consuming tobacco products and encountering tobacco smoke. This underscores the need for strategies to create a healthier university environment [31].

The profile of smokers in primary care also provides insights. In Ontario, readiness to quit was positively associated with higher self-efficacy, male sex, the presence of chronic obstructive pulmonary disease and longer years of tobacco use. Conversely, the presence of anxiety and/or depression was linked to lower cessation self-efficacy and smoking within 30 minutes of waking didn't predict readiness to quit [32]. Self-efficacy in smoking cessation remains a topic of ongoing discussion. Researchers from Qatar found that the number of cigarettes smoked, at least one quit attempt in the past year, and reporting a complete home smoking ban were significantly associated with higher self-efficacy to quit smoking [33].

Multiple studies highlight the adverse effects of smoking not only on biological aspects but also on psychological, social and spiritual aspects. Researchers discovered that these various dimensions play a crucial

role in determining smokers' motivation to quit holistically [34].

Healthcare professionals (HCPs) behaviours, attitudes and cessation therapy

The prevalence of smoking among healthcare professionals (HCPs) varies across specialties and countries. Increased smoking rates among HCPs can hinder their ability to provide effective counselling to patients struggling with addiction. This issue is becoming more prominent in some countries. Successful methods for quitting smoking among healthcare professionals include using nicotine patches and other cessation medications, participating in educational programs and engaging in discussions with fellow healthcare providers. Notably, a study found a significant association between smoking and non-smoking medical staff regarding feelings of self-respect and loneliness [35].

Very brief opportunistic interventions for smoking cessation, delivered by clinicians like general practitioners (GPs), are not only effective but also cost-saving for healthcare systems. However, clinicians often face resistance from both patients and themselves [36]. Patients may resist discussing their smoking habits or downplay their smoking, especially when quantifying their smoking behaviour or linking it to their medical conditions. Only a minority of patients (12%) are interested in receiving advice on quitting smoking. Optometrists have been shown to effectively provide brief advice interventions to smokers in the community, emphasizing the importance of training specialists in delivering such interventions [37]. Other specialists like lung physicians and cardiologists can also play a crucial role in smoking cessation efforts.

Assessing readiness to quit and facilitating constructive conversations between healthcare workers and patients attempting to quit smoking can be achieved using tools like the *Willingness to Quit smoking questionnaire* [38, 39]. The *Smoking Abstinence Questionnaire* (SAQ) is another tool that captures smokers' expectancies for abstinence and the success of a quit attempt [40]. A higher score on the SAQ is associated with factors such as tobacco dependence, motivation to quit, abstinence self-efficacy, withdrawal symptoms, dietary restraint, body image concerns and tobacco use expectations.

Healthcare professionals face several barriers when providing optimal smoking cessation advice, including a perception of its ineffectiveness, time constraints, lack of cessation skills, reluctance due to perceived patient sensitivity and doubts about patient motivation [41].

Cessation Impact and Other Patients or Diseases Characteristics

Cessation before the age of 40 significantly reduces the risk of death associated with continued smoking

by approximately 90% compared to individuals who ignore medical advice [1]. Patients who participated in an inpatient smoking cessation program in Singapore exhibited certain characteristics linked to successful quitting. Older age, being married, initiating smoking at a later age, higher education levels and lower Fagerström Test for Nicotine Dependence scores were associated with successful quitting. Those who planned to quit abruptly (“cold turkey”) and those who quit due to social pressures had higher success rates. Nicotine dependence was identified as the only independent predictor of smoking cessation [42]. In the context of a Smoking Cessation Clinic in China, achieving a high quit rate was associated with factors such as participants' prior quit attempts, three or more follow-ups and the decision to quit either immediately or within seven days [43].

Behavioural support and its components are crucial for successful smoking cessation. Behavioural counselling and financial incentives guaranteed through Short Message Service (SMS) (with a tailored focus on how to quit) were linked to the highest success rate (OR of 2.94) [44]. Various combinations of delivery modes were associated with increased odds of quitting, including face-to-face counselling combined with telephone counselling, tailored internet-based interventions combined with non-tailored SMS interventions and SMS delivery outperforming telephone or print delivery. Primary care providers play a pivotal role; if all routinely ask about tobacco use and advise tobacco users to quit, they could potentially reach over 80% of all tobacco users annually. Their interventions have the capacity to trigger quit attempts in 40% of cases and help 2 - 3% of those receiving brief advice quit successfully [45].

In mild Chronic obstructive pulmonary disease (COPD) cases, repeated smoking cessation efforts over a 5-year period achieved a quit rate of 37%. Benefits of cessation included improved lung function and higher survival rates after 14.5 years. Notably, new nicotine formulations like mouth sprays and medications like varenicline showed high efficacy. Smoking cessation should be prioritized in the treatment of COPD [46].

Advances in Smoking Cessation Pharmacotherapy

Very Brief Advice (VBA) regarding smoking remains an effective approach for promoting quit attempts among patients who smoke. Approximately one quarter of patients reported being motivated to attempt quitting smoking after receiving VBA from their General Practitioner (GP) [47]. Patients with existing smoking-related illnesses were more inclined to express intentions to act on their GP's VBA. Offering brief advice to quit smoking based on medical reasons can result in a 47% increase in long-term smoking abstinence, a finding supported by other researchers as well [48]. However, time constraints pose a significant challenge

when healthcare professionals are tasked with engaging in smoking cessation efforts.

Implementing approaches like the *Ask-Advice-Connect* (AAC) method comes with its own set of barriers. Challenges include addressing the accountability of smokers, the responsibilities of healthcare providers, the roles of healthcare providers and the perceived lack of time on the part of healthcare providers [49]. A gap persists between the behaviour reported by practitioners and the rates of advice reported by patients. Interventions aimed at increasing smoking cessation efforts, such as sending emails to all healthcare providers in a cardiology department, conducting live presentations for staff to emphasize the importance of smoking cessation and sending text messages containing smoking-related facts, did not lead to increased numbers of patients being asked about smoking by healthcare providers or the identification of more smokers connected to external smoking cessation programs. This lack of effectiveness is likely due to the inadequate time available to healthcare providers during patient consultations for AAC, in addition to their existing clinical responsibilities [50].

While there's significant pressure from smokers seeking to quit, there has been a lack of new nicotine cessation pharmacotherapies introduced to the market in the past decade. The United States Food and Drug Administration has approved nicotine replacement therapy (acting on nicotinic acetylcholine receptors), varenicline (an $\alpha 4\beta 2$ and $\alpha 7$ nAChR partial agonist) and the atypical antidepressant bupropion (a blocker of dopamine and norepinephrine transporters, along with nicotinic acetylcholine receptors) for nicotine cessation. However, the challenge with these drugs lies in their relatively low rates of success in achieving nicotine cessation in clinical trials [51].

Evidence from trials in adults, as reviewed by Cochrane, suggests that interactive and tailored *Internet-based interventions* with or without additional behavioural support are moderately more effective than non-active controls at six months or more. However, there's no conclusive evidence that these interventions are superior to other active smoking treatments. The effectiveness of such treatments in younger individuals remains uncertain [52].

E-cigarettes have emerged as an alternative for smoking cessation in some countries [53]. The true effects of e-cigarettes became clearer about a decade after their launch. Research indicates that nicotine-containing electronic cigarette liquids induce a similar reduction in intracranial self-stimulation (ICSS) reward thresholds as nicotine alone in rats [54]. The evidence also suggests, but doesn't definitively establish, that more frequent use of e-cigarettes might be associated with increased smoking cessation compared to less frequent use and that e-cigarettes containing nicotine might be more effective for smoking cessation than those without nicotine [55].

Non-Pharmacological Approaches

Behavioural Counselling

This involves working with a therapist or counsellor to identify triggers, develop coping strategies and set up a plan for quitting. It may include individual, group, or telephone counselling.

Rewards and Incentives

Some people find it motivating to set up a system of rewards for themselves when they achieve specific milestones in their smoking cessation journey. In a study, the one-year smoking cessation rate was found to be higher in an intervention group (receiving additional *spirometry and lung age announcement* along with the standard cessation program) compared to a control group (receiving only the standard cessation program) (25.5% versus 16.5%). This difference was statistically significant ($p = 0.019$). These findings suggest that interventions involving spirometry and lung age announcement could serve as additional motivators for individuals to quit smoking [56].

Self-Help Materials

There are various self-help resources available, such as books, websites and mobile apps, that provide information, tips and strategies for quitting smoking. When examining the effectiveness and cost-effectiveness of computer and other electronic aids for smoking cessation, researchers have discovered that such aids increase the likelihood of cessation when compared to no intervention or generic self-help materials. However, the effect size is relatively small [57]. The integration of electronic support alongside brief advice or more intensive counselling for smokers seeking to quit appears to be highly cost-effective.

Another potential avenue is the use of chatbots or conversational agents, which are novel digital tools that simulate real-time human conversation. Several studies have indicated benefits related to smoking cessation and participant engagement when utilizing chatbots. However, a review paper concludes that more research is needed to definitively determine the efficacy of chatbots for smoking cessation [58].

Mindfulness and Relaxation Techniques

Practices like meditation, deep breathing exercises and yoga can help manage stress and reduce the urge to smoke. In a Cochrane Review from 2022, the authors found no clear evidence of benefit or harm in terms of changing mental health and well-being from mindfulness training interventions (which involve mindfulness-based meditation) compared to intensity-matched smoking cessation treatments. Similarly, no clear benefit was observed for ACT (acceptance and commitment therapy), which encourages individuals to embrace their thoughts and feelings, or for distress tolerance training, which exposes individuals to situations triggering their desire to smoke. The same lack of clear benefit was noted for yoga interventions [59].

Support Groups

Joining a smoking cessation support group can provide a sense of community and encouragement. Many people find it helpful to share their experiences with others who are also trying to quit. Parent-tailored smoking cessation telephone counselling has been shown to be effective in assisting parents to quit smoking. At three months post-intervention, the 7-day point-prevalence abstinence rate was significantly higher for parents who received telephone counselling compared to those who received a self-help brochure [60].

Lifestyle Changes

Adopting a healthier lifestyle can complement smoking cessation efforts. This includes regular exercise, a balanced diet and avoiding situations or triggers associated with smoking. Regarding exercise interventions for smoking cessation, no evidence suggests that adding exercise to smoking cessation support leads to improved abstinence rates compared to support alone [61].

Family and Social Support

Enlisting the support of friends and family can make a significant difference. Informing loved ones of your intention to quit can help create a supportive environment. In the ongoing debate of quitting abruptly *versus* gradually reducing smoking before quitting, moderate-certainty evidence indicates that neither approach is superior in terms of long-term quit rates when compared to each other [62]. Access to and engagement with social support is a potentially crucial factor for successfully reducing and quitting smoking, as well as preventing relapse.

Avoiding Triggers

Identifying and avoiding situations, places, or people that trigger the urge to smoke is essential. This may involve changes in routine or environment.

Pharmacological Approaches

From a pharmacological perspective, nicotine replacement therapy (NRT) and bupropion exhibit an increase in smoking cessation rates of more than 80% at the six-month mark when compared to a placebo, while varenicline more than doubles the likelihood of successfully quitting smoking. To provide a clearer picture comparing the effectiveness of different methods for quitting smoking, for every 1 person who quits smoking using a placebo, 1.8 individuals quit using nicotine replacement therapy and 22.5 individuals quit using Varenicline. Notably, varenicline's effectiveness is 50% greater than that of a transdermal patch-type NRT, and it is 70% more effective compared to nicotine gums. It's worth mentioning that the combined use of two types of NRTs demonstrates a similar efficacy to varenicline, making this combination preferable to using a single type of NRT. Additionally, there is no discernible difference in cardiovascular and neuro-

psychiatric tolerance between these three treatments and a placebo [63].

Strategies to Improve Smoking Cessation Rates in Primary Care

There is moderate-certainty evidence supporting the strategy of increasing quit rates through various means, including counselling provided by healthcare professionals other than primary care physicians, cost-free medications and tailored print materials provided alongside standard smoking cessation care in primary care practice [64, 65]. However, there is no definitive evidence indicating a significant increase in long-term smoking quit rates when providing biomedical feedback to patients or when healthcare providers receive training or incentives to offer smoking cessation support in addition to standard care. Some evidence does suggest that provider training might enhance the implementation of smoking cessation support.

In a study conducted between 2008 and 2018 [66], some authors attempted to compare two behavioural intervention models for smoking cessation—the Transtheoretical Model (TTM) and the Health Belief Model (HBM). They found a statistically significant difference in smoking cessation rates between the TTM-based interventional group and the control group. However, there was no statistically significant difference in smoking cessation rates when comparing the HBM-based interventional group and the control group. Both the HBM and TTM-based trainings demonstrated positive effects on smoking cessation and progression through the different stages.

Smoking cessation and the challenges within health systems are also important considerations [67]. Offering cessation services as part of cancer treatment is crucial, but the implementation of such programs has encountered delays. Other opportunities for improvement include integrating cessation programs with tuberculosis control services and standardizing peri-operative care to incorporate smoking cessation interventions, potentially utilizing mobile phones for interactive cessation programming.

Probability and Predictors of Relapse

The risk of relapse among individuals who had been smoke-free for up to 12 months at the baseline assessment exceeded 50% [68], gradually stabilizing at approximately 10% after sustaining abstinence for 30 years. Through a multivariable analysis, it was established that a younger age at cessation and a shorter duration of abstinence were the sole independent predictors of relapse risk. The first year subsequent to a quit attempt consistently remains the period of greatest susceptibility to relapse. Notably, the discontinuation of cessation therapy consultations remains prevalent. In addressing this kind of risk, certain

subsets of smokers, including women, those of younger age, individuals experiencing depression or anxiety, those with lower smoking frequency and those initiating treatment during the initial appointment, have been identified as predictors of follow-up loss [69]. These specific patients could potentially benefit from more frequent assessments and an intensive cognitive approach.

Future Therapeutical Areas

In animal models, non-nicotinic pharmacological approaches are being explored to enhance the effectiveness of nicotine cessation. These approaches can be categorized into two main directions: immunopharmacological and enzymatic interventions, both of which aim to either limit nicotine within the peripheral system or break down nicotine before it exerts psychoactive effects on the central nervous system. Recent advancements in this field revolve around two biotherapeutic strategies: nicotine vaccines and nicotine-degrading enzymes. These strategies are designed to act peripherally, thereby reducing the concentration of nicotine in the central nervous system and subsequently diminishing its psychoactive impact [51].

Conclusions

Tobacco cessation is a complex endeavour that involves addressing patients who often don't neatly fit into standard molds. This is why a multifaceted approach, ranging from utilizing questionnaires to established medications, is recommended. The pivotal role of medical professionals in guiding and supporting patients through this process remains crucial and indispensable.

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Conflict of interest

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