Lifestyle Vaccines and Public Health: Exploring Policy Options for a Vaccine to Stop Smoking

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Experimental vaccines are being developed for the treatment of ‘unhealthy lifestyles’ and associated chronic illnesses. Policymakers and other stakeholders will have to deal with the ethical issues that this innovation path raises: are there morally justified reasons to integrate these innovative biotechnologies in future health policies? Should public money be invested in further research? Focusing on the case of an experimental nicotine vaccine, this article explores the ethical aspects of ‘lifestyle vaccines’ for public health. Based on findings from a qualitative study into a vaccine for smoking cessation, the article articulates possible value conflicts related to nicotine vaccination as an intervention in tobacco control. The ‘vaccinization’ of lifestyle disease piggybacks on the achievements of classic vaccines. Contrary to expectations of simplicity and success, quitting smoking with a vaccine requires a complex supportive network. Social justice and public trust may become important ethical challenges when deciding whether to use further public funds for research or whether to implement these innovative vaccines in the future.

Introduction

Vaccination for combating the ‘new epidemics’, such as smoking, hypertension, diabetes and obesity (Fulurija *et al.*, 2008; Bachmann and Jennings, 2011) is an innovative, experimental strategy that might become available for public health goals. Traditionally, vaccines have been a tool to protect individuals and groups from the ‘old epidemics’ of contagious diseases. Now that the vaccination technique emerges for ‘unhealthy’ lifestyles and chronic disease, policymakers and other stakeholders will have to confront the ethical issues that this innovation path raises.

To explore the public health ethics of lifestyle vaccines, this article concentrates on the case of nicotine vaccination (NV). Due to its hypothesized contribution

to public health goals, authorities have given financial and administrative support to the development of NV (Vocci and Chiang, 2001; NIDA, 2009). In the past 15 years, its potential has inspired high expectations in research groups (Lockner and Janda, 2013), while the mass media have reported on NV as a ‘medical dream [that] is about to become a reality!’ (Faint, 2007). The enthusiasm refers to the assumed simplicity and ‘automatic’ protection offered by these vaccines.

The scientific rationale for NV is derived from a neurobiological understanding of smoking as an addiction to nicotine. The nicotine molecule is so small that it is able to enter the brain, where it is said to cause a feeling of reward. From a neurobiological viewpoint, it is the search for this rush that makes smoking addictive and quitting smoking so difficult. NV aims to eliminate

the role of nicotine. After vaccination, antibodies in the blood are expected to bind to the nicotine molecule, creating a new particle that is too large to pass the blood-brain barrier. Without nicotine in the brain, the addictive 'reward' would not occur. Thus, NV would only 'work' if and when a cigarette is smoked. NV is not designed to combat withdrawal or craving (Cerny and Cerny, 2009).

Smoking is a contentious issue that has been related in many different ways to the well-being of individuals and populations. While people seem to find psychological and other advantages in smoking, the behaviour is associated with nicotine addiction, disease and premature death. For more than half a century, smoking has been part of the public health agenda (1964). Since the 1950s, the percentage of smokers in Western countries has halved, yet not at the expected pace and a further reduction is difficult to achieve. Worldwide, the number of smokers is growing, especially in less affluent regions (Ng *et al.*, 2014). Both nationally and globally, the smoking-related health gap is widening (WHO, 2015). It is in this context of smoking cessation and health disparities that a nicotine vaccine is being developed.

Two hypothetical uses of NV are discussed in the literature. One is for the prevention of nicotine addiction in, for instance, children and 'adolescent smokers before they become confirmed smokers' (Vocci and Chiang, 2001: 505). Administering a preventive NV to minors has never been the subject of clinical trials, and yet, it has inspired much ethical analysis. Recurrent themes are the balance between the neurobiological, socio-economic and psychological sides of adolescent smoking (Kosten and Owens, 2005; Lev *et al.*, 2013), the autonomy and well-being of children, including their 'right to an open future' (Hasman and Holm, 2004) and the role and obligations of parents (Feldman, 2013). Furthermore, the necessity, utility and unintended social consequences of preventive vaccination campaigns have been discussed (Gartner *et al.*, 2012; Lieber and Millum, 2013). At this point, the ongoing ethical debate tends towards a rejection of preventive NV for minors.

The second possible use of NV is smoking cessation therapy for current smokers. Several nicotine vaccines have been tested, often with public funding and support (Hartmann-Boyce *et al.*, 2012). To date, therapeutic NV has not performed better than placebos. Unsuccessful vaccines have been withdrawn, but a new generation of nicotine vaccines is in the early stages of development (Pfizer, 2015; SelectaBiosciences, 2015).

The immature stage of the normative debate on therapeutic NV is in stark contrast to these efforts. Although points are often subsidiary or hidden amidst

other foci, the scholarly literature contains some interesting starting material for a discussion on therapeutic NV. Examples are the drawbacks of seeing NV as a miracle cure (Hall, 2002), problems of distributive justice (Hall and Gartner, 2011; Janda and Treweek, 2012), respect for users in offering the treatment (Hasman and Holm, 2004; McMahon-Parkes, 2011) and the role of the vaccinated quitter (Wolters *et al.*, 2014b). As yet, and compared to the advanced debate on the ethics of preventive NV, the ethical picture of therapeutic NV is far from complete.

It is thus vital to conduct a more in-depth exploration of what experimental therapeutic NV could mean for public health, notably for the two above points on the tobacco control agenda: increasing smoking cessation and bridging the smoking-related health gap. Given the epidemiological context and the content of the ethical debate, two paths present themselves. One focuses on the therapy itself and its benefit to individual smokers, in and after the test phase. The second path focuses on researching the smoking-related health divide and the issue of equity. The paths converge with the overall research question: from a public health ethics viewpoint, are there morally justified reasons to integrate future NV in public health policies and to invest public money in its present development?

We approach that question with a combination of practical public health ethics and social sciences. Public health ethics has a tradition of exploring whether policy proposals conflict with important societal values and how to minimize possible negative effects. Multiple justificatory frameworks with a theoretical or empirical basis have been developed to facilitate the exploration (Lee, 2012). The social sciences, notably its Science, Technology and Society (STS) branch, have a track record in grasping the normativities inherent in health research and innovative health technologies (Epstein, 1996; De Vries and Horstman, 2007; Brown, 2011; Blume, 2013). The important STS claim is that norms and values start playing their role long before the implementation phase of a technology (Keulartz *et al.*, 2002; Jasanoff, 2004).

Combining the strengths and methods of ethics with those of empirical STS research is even more strongly advocated for evaluating health care and innovations (Petersen, 2013; Taebi *et al.*, 2014). The interdisciplinary approach avoids the frequent criticisms that ethics are decontextualized and neglect the normative dimensions of a technology itself (Borry *et al.*, 2005; Hedgcock, 2007). It also adds the ethics and policy aspect that is often missing in STS, despite its critical potential (Reuzel *et al.*, 2004; Mamo and Fishman, 2013). In

our article, ethics and STS are united by an interest in the interaction of technologies and people's values. Our methods and presentation reflect the interdisciplinary theoretical background. To gain insights into NV as a therapy, we qualitatively studied the scholarly literature on NV, did fieldwork at an NV trial site and collected perspectives from the stakeholders who matter for the public health context. An analysis of these sources sensitized us to possible moral issues. As a next step, we assessed our qualitative material with the help of values that are central in public health ethics frameworks: proportionality, respect for persons and justice.

Determining the best moment for the ethical exploration raises what is termed the Collingridge dilemma (Collingridge, 1980). Indeed, in very early stages of a technological development, the ethical analysis is highly speculative because empirical material is lacking. Performed later, the ethical exploration follows the technology more closely, but has less of an impact on an innovation that is gaining momentum (Grunwald, 2013). We dealt with the Collingridge dilemma by choosing to evaluate therapeutic NV at a moment when it has been richly described (Hartmann-Boyce *et al.*, 2012; Wolters *et al.*, 2014a,b), but is still far from entering the market.

The methods section presents the qualitative study that has engendered our understanding of the social and ethical aspects of therapeutic NV. The findings describe what NV means for smoking cessation on the one hand and for decreasing the health gap on the other. It starts by exploring NV as therapy in two largely empirical subsections: how does it work, what do vaccinated smokers do, what happens in trials and how do differences between test and 'real world' conditions matter? The results of that exploration are used in the third subsection, which weighs the possible pros and cons of therapeutic NV for public health. We then elaborate on relations between NV and the equity problem of the smoking-related health gap. Integrating the previous findings, we explore three policy proposals. In the conclusions, we review whether there are morally justifiable reasons to continue collective funding for NV research and to, eventually, integrate the innovative vaccine in public health policies. We also indicate how our evaluation may apply to the development of vaccines against other 'unhealthy' lifestyles.

Methods

This article has an interdisciplinary scope and combines methods of public health ethics and qualitative research

into innovative health technologies. It reports on a publicly funded research project on the ethical and social aspects of therapeutic NV. The first author, a qualitative researcher by training, was the embedded social scientist in the Dutch clinical trial that has been described by Hoogsteder and colleagues (2012, 2014). It tested the safety and efficacy of therapeutic NV. A total of 556 people who wished to quit smoking volunteered to receive six injections with the experimental vaccine or a placebo. All the volunteers also received behavioural counselling and pills (varenicline) to help them quit smoking.

Empirical material was collected with participatory observation, semi-structured interviews, discussion groups and a study of texts. Between 2009 and 2013, the first author did fieldwork at the trial site and conducted 75 in-depth interviews with staff, research participants and their relatives. Recurring themes in all interviews were the meanings of NV, smoking, quitting and trial involvement. Ethical approval for this part of our study was obtained from the Netherlands Central Committee for Research involving Human Subjects (CCMO). The first author also organized two meetings (one international) at which 26 policymakers, health care professionals and scientists discussed their expectations and experiences with regard to therapeutic NV as a public health strategy. Interview and discussion quotes are included in this article; pseudonyms were used for all quotes. On top of the ethnographic research, we performed a literature analysis of 64 peer-reviewed academic papers on the science and ethics of NV, published between 2001 and 2014.

For the question of whether NV can be a justified strategy for smoking cessation, we refer to central values in public health ethics frameworks. Rather than prioritizing one specific framework, we embrace three values that they have in common: proportionality, respect for people and social justice (Lee, 2012). This set of values allows us to grasp ethical issues around NV as a public health strategy for smoking cessation. We enriched the exploration by comparing NV with both classic vaccination and widely used tobacco control strategies (nicotine replacement, medication). We pay special attention to the smoking-related health divide by referring to health and justice theories, notably the work of Venkatapuram (Venkatapuram and Marmot, 2009; Venkatapuram, 2011).

Findings

Our findings describe what is expected from NV and the quitter, before comparing possible positive trial outcomes

to a 'real world' context. Next, this section balances pros and cons and elaborates on social justice issues. It ends by reviewing three public health policy modalities.

Expected and Experienced Roles and Activities in a Vaccinated Quit Attempt

NV is an emerging technology that may one day be added to the range of strategies offered to support smoking cessation. Normatively and empirically, the benefits of such aids for people have been contested. Regardless of whether smokers use support, the vast majority of attempts to quit smoking fail (Casella *et al.*, 2010). In one line of thinking, support is undesirable because it makes people unnecessarily dependent on caregivers or the pharmaceutical industry. The empirical backing of this argument is that 'unaided cessation is by far the most common method used by most successful ex-smokers' (Chapman and MacKenzie, 2010). Other researchers claim, however, that external support increases success (Cahill *et al.*, 2014) and that non-assisted attempts too often end in disappointment for the individual quitter (West *et al.*, 2010). It is against the background of this debate that we study the expected and experienced roles of smoker and vaccine in the smoking cessation process.

The rationale for NV differs significantly from that of other tools, which address craving or withdrawal. NV aims to prevent the neurochemical 'reward' that is associated with nicotine addiction.

[F]or the [vaccinated] smoker the impression is comparable to smoking a cigarette without nicotine. (...) The antibodies don't have any effect on withdrawal symptoms. The craving of the smoker for nicotine is not affected but smoking can't satisfy anymore the craving. (Cerny and Cerny, 2009: 201)

According to the scientific hypothesis, it makes no sense to smoke if the addictive, good feeling of nicotine is lacking. The absence of satisfaction is expected to help ex-smokers avoid relapse.

However, the focus on the rewarding nicotine rush might need to be put in perspective. NV developers view smoking and quitting as a problem caused by nicotine. Yet, for other researchers, the effects of nicotine do not fully explain the behaviour. Smokers also seem to be highly attached to the cigarette stick, smoking rituals and perceived social benefits, such as peer group belonging (Klein, 1993; Paul *et al.*, 2010; Fagerström, 2011; Elam, 2012). That more complex picture also transpired in the stories of people who undertook a vaccinated quit

attempt. These interviewees said they mainly experienced smoking as a tenacious habit, including but not limited to the search for nicotine. They struggled to change that pattern in their lives.

The views and experiences of trial volunteers seldom reflected the scientific rationale for NV. Trial participant Don was an exception, as can be seen in his account of a meeting with friends after he had stopped smoking. Craving a cigarette after a couple of alcoholic drinks, Don lit one up. There was no absence of pleasure, according to Don; indeed, quite the contrary:

It was such a thrill, that cigarette after eight or nine weeks. (...) This vaccine should ensure that I cannot get that kick at all. They explained to me that the nicotine particles would bind to cells and those cells would become so large that they could no longer pass the brain barrier.

Don experienced enjoyment and felt unprotected by the vaccine. He then concluded that he had received the placebo injection and he slowly relapsed. Since the trial was double-blinded, it was only after its completion that Don discovered, to his great surprise, that he had received the 'real' vaccine. Yet much more interesting than how 'true' Don's delight was, are the morally relevant insights about what the vaccine and the quitter are expected to do.

In contrast to vaccination against disease germs, the protection of NV also depends on the actions of the vaccinee. Only at the moment of relapse can NV antibodies start their work of binding to nicotine and preventing its passage to the brain. At the same time, however, the quitter has to become active in preventing relapse. He or she should extinguish the cigarette or not light a second one. How this behaviour can be achieved is not explained in papers on NV. As Don's case suggests, NV does not 'automatically' protect the smoker, but requires behavioural control similar to the period before the relapse. While the NV rationale heavily stresses the neurobiological reward of nicotine, it remains an open question whether individuals in a real quit attempt should, can or do notice the presence or absence of that good feeling, and how this relates to consequent smoking behaviour.

In a quit attempt with NV, smokers still have to deal with withdrawal and craving (Cerny and Cerny, 2009). To handle these difficulties, research volunteers in the trial of our case study received behavioural counselling and medication. It was this total package, together with the obligatory visits and personal techniques, which many volunteers experienced as helpful. As Myriam stated:

You have to go there every week, you have those conversations. . . You're getting the injections, the tests, the tablets. That entire treatment is what counts, for me. If you only have an effective vaccine and nothing else, then the chance of success is much smaller than when you get the whole package. (. . .) [The fact that I no longer smoke is mainly due] to my own will, the stimulation of my surroundings and the trial team. You are the key. (. . .) They can give you three vaccines, even ten, but if you don't have—or don't want—all the rest, you're not going to stop smoking.

Myriam emphasized the interaction between external help and her own role. She and other research volunteers framed quitting as an endeavour for which they benefited from multifaceted support.

Brainstorming about how to offer NV in practice, experts in our discussion groups also anticipated quitters taking an active role and pleaded for combination therapy:

Zack (representing nurses in respiratory care): So that pleads, above all, for therapeutic behavioural support on top of the vaccine. . . [Tamar: Yes, just like. . .] . . . similar to what we would have done anyway.

Tamar (addiction physician): What we usually do is: pills and talking. In case of nicotine vaccination, we would also notify: it includes a counselling track.

In arguing for additional forms of support, professionals treated NV as other smoking cessation tools. They also emphasized the relevance of a context for use. Next to proposing dual therapy, they linked NV treatment to types of smokers (with multiple addictions; hardened smokers; pregnant women) and conditions (prison, illness). They also specified the role of caregivers in delivering the injections, providing counselling and managing expectations:

Pauline (official from the Ministry of Public Health): it is a kind of stepped care, [nicotine vaccination] as a more radical step in a series of quit tools, but always with accompanying support [someone interjects: quite right!]. There is also always behaviour involved. It is not a panacea [interjection: exactly!]. That might also avoid the risk of: 'Oh I can go back to smoking and when I want to get rid of it again, I'll have that jab and then it's settled'.

People in the field of smoking cessation noted that multiple ingredients are needed for individuals to benefit from NV. This stance reflects a general trend, in the literature and in reimbursement stipulations alike, of offering a multipronged approach to people who wish

to quit smoking (Stead and Lancaster, 2012; Hartmann-Boyce *et al.*, 2014; Nagelhout *et al.*, 2015).

In summary, for quitters to benefit from NV, they need much more than antibodies preventing the nicotine rush. With or without additional support, vaccinees will have to develop strategies to both avoid and overcome a lapse. The working of NV seems more dependent on the vaccinated quitter than the other way round.

From Testing Conditions to the Real World

This part reflects on the clinical testing of NV, also as experienced by research volunteers, and the translation from trials to the 'real world'. The literature distinguishes between 'efficacy' as the result in trial conditions and 'effectiveness' as the working of an intervention in the 'real world' (Kotz *et al.*, 2014). We review both.

The first way to grasp whether NV 'works' is to evaluate its efficacy. In other words, do more trial volunteers quit smoking when they receive an active vaccine than when they receive a placebo treatment? At this time, the answer is no. There has been no difference in results between vaccine and placebo groups in the various clinical trials of the past decade. Surprisingly, and despite the inefficacy of NV, many smokers managed to quit when smoking cessation medication (varenicline) and counselling were offered on top of the experimental product (Tonstad *et al.*, 2013; Hoogsteder *et al.*, 2014). For instance, in our case study, one of three participants ceased to smoke. This was as much as what was hoped the vaccine would minimally achieve (Hoogsteder *et al.*, 2014: 1255, 34 % abstinence in the group testing the real product; in the 2006 application for the Dutch grant 'at least 40% quitters' were expected). The overall high numbers of quitters were, however, not given much attention in the reports of the respective studies.

A second way to evaluate the effectiveness of a health intervention is to look at its 'real life' result. Huge gaps have been identified between the efficacy and effectiveness of smoking cessation aids. For instance, the effectiveness of standardized counselling programmes in the UK has proven very uneven, even after identical training and use of identical protocols (Brose *et al.*, 2012). Another example is nicotine replacement therapy (e.g. nicotine gum). When used as a stand-alone treatment, it is not more effective than stopping smoking without any aids (Stead and Lancaster, 2012; Kotz *et al.*, 2014). Effectiveness problems are also anticipated for NV as a stand-alone treatment:

Monotherapy with a nicotine vaccine does not appear to be a promising tool to overcome the

complex physiological and psychosocial alterations observed in smokers (Raupach *et al.*, 2012: e12).

For NV to be of benefit, researchers argue, one or two other aids may have to be added. In fact, a dual therapy of vaccination and counselling was offered in all the NV efficacy trials. The studies that also gave smoking cessation medication produced remarkably high abstinence rates, as we noted above. Moreover, research participants said they found this total package to be beneficial.

In the translation from efficacy to effectiveness, the high expectations of NV as a magical cure cannot be neglected. The prospect of having a vaccine gave research participants an impetus to undertake their first or a novel quit attempt. Vaccination was often associated with ‘an easy opportunity for many people to quit smoking’, as the partner of a volunteer told us. That perceived promise of a quick fix was also present in the popular media (Faint, 2007), while the vaccination concept was well received by the scientific press (Hartmann-Boyce *et al.*, 2012), evoking connotations with public health progress in the fight against infectious diseases (Gartner *et al.*, 2012).

The experts in our discussion meetings took issue with the adequacy of the term ‘vaccination’. Some felt it was incorrect to talk of vaccination if its efficacy was only short term. Others went beyond definition criteria and anticipated on the effect of the word on the target groups:

Ralph (tobacco control researcher): I think it’s great. I think you should call it a vaccine, because that’s what makes it attractive to smokers. It’s a bit like hypnotherapy. Even if it doesn’t work, if it encourages people to have a go at something, then there is a public health benefit. I think there will be vaccines that will work [ultimately]... but if it grasps the fascination of the public—which it clearly does, you can’t stop the press from being interested in vaccines...

Jan (public health consultant): Then people will have more expectations, if you say ‘vaccine’.

Pierre (clinical researcher): Good!!

(...)

Hank (physician and smoking cessation consultant): Would the name have an effect on whether people choose to use it or not? People are quite used to getting ‘vaccinations’... but something that is a little bit out of left field perhaps, would that put them off using it perhaps?

The discussants clearly expected that the term ‘vaccination’ would affect beliefs and decisions of potential users.

The high expectations of NV were derived from implicit comparisons with classic vaccines. What ‘old’ and

‘new’ vaccines have in common is that people show an immune response, which lies outside an individual’s sphere of influence. Some vaccinees make a lot of antibodies, others relatively few (CDC, 2015). This is also the case with NV (Hatsukami *et al.*, 2011). A fundamental difference, however, concerns the link between the protection of the individual and the group. Triumphs of classic vaccines are significantly connected to ‘herd immunization’; if the aggregate immune response against a disease germ in a group is high, the risk of disease outbreaks seriously decreases (Malone and Hinman, 2007). Yet, in the case of vaccination against a nicotine molecule, which does not spread, the possible immunological benefit is always only for the individual and never for the group. In that sense, the protective mechanism of the innovative vaccine is very dissimilar from classic vaccination. Herd immunity cannot and should not be expected from NV.

Thus, the question of whether NV ‘works’ has different meanings and therefore different answers. A quit attempt with NV alone is unlikely to succeed but requires multiple support. Furthermore, trial successes are not a guarantee that NV will function well outside the lab. Lastly, societal disappointment lurks in so far as the high expectations around NV are based on unjustified parallels with classic vaccines.

Balancing Pros and Cons

Taking into account the above empirical sections, what are the possible benefits and negative effects of NV, assuming that future clinical trials yield positive results? We will start with the benefits. For smokers desiring to quit, we discern two possible advantages in the specific character of NV. First, the ‘reward’ blocking principle may help the quitter overcome a lapse and persist in the quit attempt. Secondly, in case of injections, smokers will have to visit a health professional, which might open a window to additional helpful support. A more general advantage is that NV brings more variety to the available strategies, which may raise the number of successful quit attempts and, eventually, decrease the prevalence of smoking.

NV may also be burdensome to users for multiple reasons. First, vaccination does not support the quitter in relieving craving and withdrawal and the sociocultural difficulties of quitting. In that sense, NV has similarities to stopping ‘cold turkey’. Also, it takes several weeks for the immunity level to peak (Hoogsteder *et al.*, 2012). In that interval, people may lose the motivation to quit, or interrupt the vaccination routine (Raupach *et al.*, 2012). Moreover, in case of injections,

the smoker must find the time and money to visit a trained professional. Physically, NV is not painless; research participants frequently reported persistent pain in the arm at the injection site (Hoogsteder *et al.*, 2014). An additional negative feature is worries about the unknown long-term effects of NV, including its interference with the immune system and with other vaccines. A similar uncertainty applies to public health effects. While clinical trials are designed to test the safety of NV during a relatively short period of use, future public health strategies will have a longer time horizon. If, moreover, expectations of NV as a technological fix were to persist, many quit attempts would be bound to fail, which may make people feel hopeless and perceive public health policies as a failure. For smokers and for tobacco control more generally, a possible drawback is that the neurobiological framing of NV steers away from the psycho-social-cultural sides of smoking that play a crucial role in any quit attempt. In line with this, the availability of a new ‘medical aid’ may increase the pressure to ‘treat’ this ‘disease’, which may work as a catalyst for stigmatizing smokers as sick (Lupton, 1995) (see the next section for an elaboration of this point). Budget wise, there is a risk that the opportunity costs for NV may be high; this precludes expenditure for other, possibly more effective, smoking cessation aids. Furthermore, how necessary NV will have been in achieving abstinence can only be determined afterwards; if the user does not smoke during the quit attempt, the treatment and its burdens will have been superfluous. Finally, use of NV may increase inequalities if it mainly responds to the needs of the smaller group of affluent smokers.

Possibly negative features may, however, be avoidable. The adverse physical effects of NV may be circumvented by the novel generation of vaccines that are said to come in delivery forms other than injections (NIDA, 2011). The risk of quit attempts ending in failure can be reduced by adding medication and counselling to NV. Input of professionals and smokers in the further development of NV would diminish negative user experiences. Expenses are also partly avoidable. Future NVs may be synthetic and come in the form of a nasal spray, less difficult to handle and therefore less costly than biological vaccines. Waste of money may be limited by not only emphasizing efficacy, but also effectiveness. This could be done by providing multiple support, which, of course, requires additional expenditures. Talking with users about the role of NV in relation to their own role and that of a supportive environment will also increase effectiveness.

When the possible pros and cons are balanced, future NV may add a new dimension to smoking cessation aids. If NV is used in combination with medication and counselling, smokers may profit from a treatment that covers many difficult aspects of quitting. At least two important challenges remain. One is dealing with the expectations invoked by the term ‘vaccine’; we will come back to this when exploring policy options. A second challenge is reaching, in a morally sound way, groups of smokers that have not yet been able to benefit from tobacco control policies. The next section elaborates on this latter point.

NV and the Smoking-Related Health Gap

The majority of smokers are from disadvantaged populations. They have seen the fewest benefits from smoking cessation strategies (Passey and Bonevski, 2014). At national levels, smoking prevalence shows a strong social gradient; people who are economically deprived and less educated constitute the largest group of smokers (Hiscock *et al.*, 2012). Globally, 80 per cent of smokers live in the poorer parts of the world (WHO, 2015). These general tobacco control considerations apply *a fortiori* for NV. Assuming for the sake of argument that this novel vaccine meets the prerequisites of proportionality, the question arises of whether developing NV (and related public health policies) can be justified from the global health perspective. Papers that have reviewed NV often refer to its future significance for health worldwide:

[Since] [t]obacco smoking causes (...) disease, and stopping smoking is among the key medical interventions to lower the worldwide burden of these disorders, (...) more effective treatment options are needed. An intriguing novel therapeutic concept is vaccination against nicotine. (Raupach *et al.*, 2012: e1)

Epidemiologically, to achieve a reduction in smoking-related disease and death, it would be necessary for large groups of people to use NV, assuming it is efficacious. Due to reasons related to infrastructure, budget and culture, however, it may prove difficult for NV to reach these groups. For instance, the nicotine vaccines that have been tested thus far were biological and required sophisticated handling conditions, such as cold transport and storage, which may not be available in less affluent countries. Moreover, funds targeting tobacco use and non-communicable diseases are levelling off in those regions (Venkatapuram *et al.*, 2012; Stoklosa and Ross, 2014). If these trends continue and

if NV is used by numerically small groups, the impact on smoking prevalence will be accordingly small.

From a public health ethics viewpoint as well, a socio-economic differentiation in the use of NV is problematic. NV is being developed at a time when the better-off profit more from tobacco control policies (e.g. price increases of tobacco and quit support) than those who might need it most (Over *et al.*, 2014). It is the type of development that Tudor Hart coined ‘the inverse care law’ in *The Lancet* (1971: 412): ‘The availability of good medical care tends to vary inversely with the need for the population served’. A large health gap between affluent and disadvantaged smokers has been identified, also in adolescents (Kuipers *et al.*, 2014). The subsequent call is to reduce that divide (Nuffield Council, 2007). But if some groups were to benefit more from NV than others, its uptake in tobacco control would conflict with the value of distributive justice.

At the same time, the advent of NV revives social justice questions that go beyond fair distribution and equal access. Simply conceiving of NV as a possible solution for a health problem leaves out the fact that the very notion of ‘health’ is replete with moral assumptions. As Metzl and Kirkland (2010: 2) wrote:

‘Health is a desired state, but it is also a prescribed state and an ideological position.’

In line with Zola (1975), they argue that ‘health’ speaks about well-being as much as it speaks about rhetoric, control and power. Smoking denormalization is a good example. In many places, smoking has been made to shift from a standard behaviour to a deviation from the norm. Increasingly, smokers themselves and not only their behaviour are seen as irresponsible, resulting in their stigmatization and social disqualification (Bell *et al.*, 2010). On the one hand, smokers are seen as victims of an ‘addiction disease’. Biomedical ‘remedies’, of which NV is an example, reinforce an approach to smoking in which smokers are viewed as sick and in need of help (Dingel *et al.*, 2011). On the other hand, smokers are blamed for refusing to or not being able to end the ‘disorder’ (Lupton, 1995). Some contributors to the debate defend stigmatization to discourage unhealthy behaviour (Kulik and Glantz, 2015) or make a call to not reject it at face value but to look for morally acceptable forms of stigmatization (Bayer, 2008). Others, however, develop an argument in which stigmatization is considered ethically contentious in its own right (Cartwright, 2012; Voigt, 2012; Wardrope, 2014). Content and timing of denormalization strategies

have been criticized as unjust because they hit disadvantaged groups harder than others (Voigt, 2010; Mair, 2011).

Inevitably, future decisions about NV will interact with social justice aspects in tobacco control. As a representative of the nicotine addiction discourse that has contributed to the stigmatization of socio-economically deprived groups, NV risks increasing that social injustice unless proper policies are proposed.

Policy Options

Given the above ethical analysis, and assuming that the vaccine has an acceptable degree of safety and efficacy: What are possible public health policy modalities for future therapeutic NV? We first explore two options that have NV as a starting point. Guiding the third option is the smoking-related health gap.

(1) Doing nothing after market approval of NV

If NV were to obtain market approval after successful clinical trials, governments could choose to refrain from developing NV-specific public health policies like including it in insurance packages or launching information campaigns. However, abstaining from action does not mean that no value conflicts arise. As the Nuffield Council (2007, p. 42) formulates it, doing nothing ‘is in itself a value judgment and may have adverse consequences for some’. Not developing a policy for NV implies that economic forces will determine the usage of this novel tool (Scherer, 2004). It is unpredictable if and how this commercial option would reach groups who smoke the most, and how it would contribute to decreasing smoking prevalence. If, moreover, NV were expensive, it would most likely increase the smoking cessation options for affluent people mainly. Consequently, a policy of ‘doing nothing’ is bound to conflict not only with values of justice and fairness, but also with proportionality.

(2) Offering the NV

A preliminary consideration when reviewing policy options is that positive trial results are a necessary but insufficient condition for ‘real world’ effectiveness. Management of the high expectations around NV will be crucial in this respect. Before exploring policies, we therefore review the designation ‘vaccine’ and will propose to rename the innovation.

NV cannot live up to expectations that are based on successes of classic vaccines. First, while smokers and

caregivers expect that vaccination offers automatic and easy protection, the opposite is true. NV deals with only one aspect of the quit attempt and requires active involvement of all parties to cover the remaining points. Second, smoking-related diseases are triggered by tar and other agents in tobacco smoke, not by nicotine. Unlike classic vaccines, NV thus only indirectly contributes to disease prevention. Third, although ‘old’ and ‘new’ epidemics may have a similar massive spread, disease outbreak and fatalities are much more rapid for infections than for smoking. That lower level of immediacy allows for interventions that are less urgent and intrusive than vaccination. Finally, classic vaccination campaigns raise the immunity of the group, but the gain of NV is limited to single cases. In conclusion, continuing to speak of a nicotine ‘vaccine’ despite these critical differences might harm public health, damage public belief in this and other vaccines and affect the credibility of health authorities. Abandoning the term ‘vaccine’ would be a good way to avoid flawed parallels and their harmful consequences.

Cutting the associative links with classic vaccination orients our exploration to policy decisions for other smoking cessation tools. These include making the strategy known (e.g. information campaigns, expectation management), available (e.g. where and how NV is offered) and affordable (e.g. reimbursement). A decisive overall consideration is that stand-alone smoking cessation strategies are not considered to be effective for smoking cessation in general and for NV in particular (Raupach *et al.*, 2012). Thus, public health benefits can only be expected from policies that combine NV with other support, like counselling or medication.

When reflecting on how to offer NV, context matters. Socio-economic disparities are a case in point. To combat inequity, one option is to make NV affordable for people with a low household income. This type of policy is common practice in a number of countries. Comparisons of equity impact in tobacco control found that more people from lower income groups make a quit attempt when they do not have to shoulder all the costs. When treatment is offered ‘free’ of charge, entitlement is nevertheless restricted to people who can afford to have health insurance and to pay pre-deductible expenses. The net effect of free cessation treatment is still unclear (Brown *et al.*, 2014; Hill *et al.*, 2014; Nagelhout *et al.*, 2015). Moreover, smoking cessation programmes are not suitable for everyone in any circumstance, as Kotz and West (2009) have argued. Their quantitative research suggests that poor socio-economic settings lead to poor quit results; disadvantaged people often end the quit attempt prematurely.

Thus, a NV policy that responds to the difficult financial situation of many smokers is a just policy, yet it does not necessarily repair inequalities.

Policymakers also need to reflect on the level of pressure that is justifiable to promulgate the use of NV. Societal norms and values have impacted tobacco control ever since the 1950s (Brandt, 2007). Liberal countries have tended to put the emphasis on non-paternalistic measures that are, as Childress noted (2007: 226), ‘more palatable to the public in a society committed to individualism’. If governments make smoking cessation tools known, available and affordable, they are not totally eschewing interference in people’s private lives. This has often been termed ‘soft paternalism’ if the moral underpinning is that cessation is the smoker’s desire, and ‘weak paternalism’ if, due to the addiction, the smoker were deemed unable to act in his or her own interest (but there is a confusion of terms, e.g. Feinberg, 1984, vol. 3: 377; Gaare Bernheim *et al.*, 2015: 37). The framing of smoking as a neurobiological addiction might strengthen the view that smokers are incapable of wanting to do what is for their own good. In addition, the present debate on tobacco control progress (or the lack thereof) also seems to announce a shift towards more paternalism.

While some authors have claimed that laws and regulations have reached their moral limits or that more urgent public health problems have arisen, other voices are pleading for a ‘tobacco endgame’ (2013; van der Eijk, 2015). In that plea, smoking is conceptualized as a deviation from societal norms. Denormalization (see the above section) has been an incentive for quitting, but mainly among groups with a higher socio-economic status (Graham, 2012). Ethically and epidemiologically, the effect on disadvantaged populations has been less positive (Clare *et al.*, 2014; Frohlich and Abel, 2014). If NV policies also have more success among wealthier people, the smoking-related health gap will widen even more.

Given the neurobiological rationale of NV and an increased demand for smoking denormalization, it may be asked whether NV should be offered with a higher level of pressure than for previous smoking cessation tools. From the standpoint of equal treatment for equal cases, treating potential users of NV with less respect for their autonomy than other or former smokers cannot be justified. Moreover, if a more pressing policy were applied to all current smokers, it would chiefly affect those with a lower socio-economic status, due to their numbers. An alternative approach, prioritizing NV for the disadvantaged groups, comes with similar ethical downsides. Targeted health interventions have been

criticized for constantly aiming, with increasing moral pressure, at the same ‘unhealthy’ groups, holding them accountable for disadvantages that appear, in essence, to be socio-economically determined (Mair, 2011). It is unlikely that these groups will support a differential treatment that increases stigma. Consequently, their trust in public health policies is likely to suffer.

In sum, public health policymaking for NV poses a dilemma. If the term ‘vaccine’ is abandoned and future NV is offered as part of a combination therapy, policies similar to those used for other smoking cessation tools are conceivable, but not necessarily just. Without NV policies for disadvantaged populations, the quantitative smoking-related health gap may increase. With targeted policies, however, the moral divide between societal groups is likely to widen. Thus, policies for NV come with serious ethical drawbacks.

(3) Taking the smoking-related health gap as the starting point

The above dilemma has inspired us to take a new approach: to base our reflection on the smoking-related health gap rather than on the innovative vaccine. This different emphasis is in line with pressing calls to address health inequities (Buchanan, 2000; Marmot, 2006; Powers and Faden, 2006; Ruger, 2006; Wolff and De-Shalit, 2007). What position could NV have in policies that aim first and foremost at reducing the gap between smoking and health?

A fresh perspective on the equity challenges in tobacco control may be inspired by Sridhar Venkatapuram’s (2011, 2013) philosophy on ‘health justice’. His work combines respect for people with a critical perspective on the health divide. While drawing on the capabilities approach (Nussbaum and Sen, 1993), it differs from this and other normative theories in foregrounding health as the very basis of social justice. People have a right to health, Venkatapuram states. They are entitled to the social and political arrangements that make health feasible. Being healthy is understood as having the capability ‘to be and do things that make up a minimally good, flourishing, and non-humiliating life’. So the claim is not directly to health outcomes, but rather to ‘social policies that take steps towards making the claim feasible’ (Venkatapuram, 2011: 19–20). Venkatapuram rejects value-free, statistical or scientific definitions of health. Having the health capability cannot be boiled down to health care or individual volition; it is the interplay of biological and environmental conditions. Also, the process of taking actions counts, as is illustrated in a thought experiment

by Breton and Sherlaw (2011). They rephrased smoking cessation as ‘to be able to quit smoking if one wishes to’ and linked the diverse capabilities of smokers to their living conditions. The authors proposed unorthodox new interventions, such as access to pleasant activities where people who make a quit attempt can ‘refocus thoughts on something else than smoking’, especially those ‘who spend most of their time at home’ (p. 155). Policymakers might use the health capabilities approach as a philosophical guide to try and find ways out of the ethical quandaries as regards issues of justice and respect for people in tobacco control. The offer of NV or any other smoking cessation tool would then be subsidiary to the social claim. In a view on health that puts the dignity and diversity of people first, smokers should of course be included in policy deliberations concerning their lives and bodies.

Discussion

Our qualitative, interdisciplinary study suggests that future NV only might ‘work’—both at the individual and population level—if users also receive support to deal with craving, withdrawal and sociocultural difficulties. Policies similar to those for other smoking cessation tools are conceivable for NV, and yet, they risk widening the smoking-related gap between affluent and deprived groups, ethically if not epidemiologically. We will discuss three critical issues emanating from our analysis.

For public health problems with a strong social gradient, such as smoking, a remedy-driven policy falls short. In concentrating on drug efficacy, the larger social issues are *de facto* discounted. Moreover, resulting policies may unintentionally contribute to the continuation of an undesirable status quo. This is bound to happen if vaccination is considered to be a justified way to change health behaviour without addressing compelling socio-economic aspects of people’s lives. The perspective of ‘health justice’ (Venkatapuram, 2011), which is respectful of social justice, diversity and people’s capabilities, might guide policymakers, smokers and other relevant stakeholders in finding new ways to deal with the hardening inequity problem in tobacco control.

Public trust is central for future decision processes around NV and other lifestyle vaccines. To elucidate this point, we introduce the concept *vaccinization*¹. Vaccinization capitalizes on the public health successes of classic vaccines and therefore differs from ‘medicalization’ (Zola, 1975), ‘biomedicalization’ (Clarke,

2010) and ‘pharmaceuticalization’ (Bell and Figert, 2012; Mamo and Epstein, 2014). Vaccinization refers to processes in which ‘unhealthy’ lifestyles and related afflictions are redefined as conditions that can be prevented or cured with vaccines. In the case of smoking, nicotine is singled out as the cause of the ‘unhealthy’ or ‘addictive’ behaviour (Elam, 2014) and, consequently, as the target of antibodies. The implied promise that a behaviour change requires little more than antibodies taking care of a molecular or biological culprit obscures the complexities of the lifestyle at issue. It pushes acknowledged psychological, social or cultural aspects of the behaviour to the background, makes individuals accountable and comes with a lack of transparency about what the vaccine can and cannot do. The reductionist side of vaccinization risks backlash against public trust in tobacco control and other lifestyle-related policies, all the more because it discourages the active participation of relevant stakeholders in product development and decision processes. Yet, the phenomenon also jeopardizes public trust in vaccines. The vaccinization of lifestyle disease piggybacks on the achievements of classic vaccines, which have a reputation for assuring easy, long-lasting and automatic protection against specific disease germs. Parties, subconsciously or deliberately, transfer these ‘magic bullet’ expectations to preventive and therapeutic lifestyle vaccines. Due to the many differences between classic and novel vaccines, and also between contagious and chronic diseases, the high expectations are likely to end in disappointment. As noted earlier, replacing the term ‘vaccine’ and managing expectations are ways to counter undesirable connotations.

Our third point concerns the content and representation of research. Decision-making around NV for public health may benefit from input on not only efficacy, but also on roles, usage, unexpected results, etc. The focus in trial reports is on the comparison between placebo and NV; we recall that the serendipity of the extraordinary quit rates in our case study was hardly mentioned. Although trial conditions, including the effect of placebos (Bishop *et al.*, 2012) and the high quality of staff and offer (Timmermans and McKay, 2009) may explain results, the high number of quitters in our study also opens a window to a more fruitful use of existing smoking cessation tools in societal conditions.

The analysis has focused on a vaccine for which clinical trials have as yet not produced evidence. Yet one might ask: Would the ethical analysis still hold if the experimental vaccine, one day, proved to be highly efficacious and ‘really work’? While it might be tempting to

pose that question, it does not adequately frame the issues at hand. Our analysis has shown that the meaning of what ‘works’ is complex in the context of lifestyle vaccines. For sure, notions like efficacy are never neutral, and yet, the analysis suggests that this applies all the more to lifestyle vaccines, which are, moreover, an elusive concept. Are they to be compared to classic vaccines? Or to medication? Or to still other therapies or interventions? It depends on the option whether an efficacy percentage of let us say 40 (in terms of continuous abstinence) will be considered poor or impressive, regardless of its being labelled in trial reports as ‘significant’, statistical jargon for outcomes that are not due to chance. ‘Efficacy’ and ‘lifestyle vaccines’ are constructions that cannot be weighed without knowledge of how, why and by whom this or that benchmark was chosen. Carefully discriminating between types of vaccines, conditions and situations will be vital for public health evaluations of this emerging technology.

Our interdisciplinary paper suggests that social justice and vaccinization should be put on the public agenda. Involving a broad range of relevant parties in the discussion about the ethical issues of lifestyle vaccines would be a way to work on public trust, as would diversifying research populations with people from disadvantaged populations and designing pragmatic, ‘real world’ trials. Most importantly, glaring health gaps should be the start and end points of any justifiable public health decisions related to matters of lifestyle and chronic disease.

Note

1. The word ‘vaccinization’ once was used in a very different sense. According to the Oxford English dictionary it referred to a now obsolete type of continued vaccination.

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