

Online Journal of Health Ethics

Volume 14 | Issue 2

Article 5

Nicotine Vaccines for Smoking Prevention and Treatment from Utilitarian and Deontological Ethical Perspectives

Enam A. Alsayheen

University of New Brunswick, ealsrayh@unb.ca

Khaldoun Aldiabat

University of New Brunswick, kaldiaba@unb.ca

Follow this and additional works at: <https://aquila.usm.edu/ojhe>

 Part of the [Medicine and Health Sciences Commons](#)

Recommended Citation

Alsayheen, E. A., & Aldiabat, K. (2018). Nicotine Vaccines for Smoking Prevention and Treatment from Utilitarian and Deontological Ethical Perspectives. *Online Journal of Health Ethics*, 14(2). <http://dx.doi.org/10.18785/ojhe.1402.05>

This Article is brought to you for free and open access by The Aquila Digital Community. It has been accepted for inclusion in Online Journal of Health Ethics by an authorized editor of The Aquila Digital Community. For more information, please contact Joshua.Cromwell@usm.edu.

Nicotine Vaccines for Smoking Prevention and Treatment from Utilitarian and Deontological Ethical Perspectives

Enam A. Alsayheen, PhD & Khaldoun M. Aldiabat, PhD

University of New Brunswick

ABSTRACT

Nicotine vaccines are a new prevention and treatment method for smoking addiction. They are promoted as a method to cease smoking among those who smoke and possibly prevent this behaviour from taking place among those who do not smoke. However, offering these vaccines to adults, adolescents, and children will undoubtedly raise an ethical debate among policy-makers, health professionals, and the public. This paper discusses the possibility of using nicotine vaccines to treat and prevent smoking among adults/children/adolescents through the lenses of two ethical theories: utilitarianism and deontology (Kantianism). From an utilitarian perspective, nicotine vaccines are good for society because they provide the greatest benefit for the greatest number of individuals. Authors perceive them as a healthy ethical choice to prevent and treat smoking. And, from the deontological perspective, nicotine vaccines are justified because individuals can prevent the harm of nicotine addiction by choosing vaccines or any other smoking prevention and treatment methods.

Key Words: Nicotine Vaccine, Smoking, Utilitarianism, Deontology, Ethics, Children

1. Introduction

Smoking behaviour is an unhealthy behaviour that increases morbidity rates and adverse health outcomes (Hasman & Holm, 2004). Evidence from research demonstrates that smoking behaviour causes lung cancer, emphysema, and coronary disease; and, contributes significantly to increased mortality rates (Baliunas, Patra, Rehm, Popova, & Taylor, 2007). In Canada, lung cancer is the leading cause of cancer death. Smoking behavior caused 85% of these deaths. (Canadian Cancer Society's Advisory Committee on Cancer Statistics, 2017). Although Canada has advanced policies to prevent smoking and lower smoking rates (Government of Canada, 2012), the latest Canadian statistics indicate that 16.9% of Canadians aged 12 and older (about 5.2 million people) smoke every day or occasionally (Statistics Canada, 2017). A study conducted in the United States of America (USA) by Eaton et al. (2010) found that 46.3% of people experimented with tobacco when they were adolescents. Despite these statistics, mortality and morbidity rates related to smoking behaviour in Canada remain high. Clearly, innovative, evidence-based smoking cessation and prevention methods are needed to minimize the risk of smoking behaviour in Canada.

One of the latest innovative methods for treatment and prevention of smoking behaviour is the nicotine vaccine. Many researchers are looking forward to investigating nicotine vaccines as an immunological therapy to prevent and treat smoking. Nicotine vaccines provide protection against tempting pleasures that lead to smoking addiction (Lieber & Millum, 2013). These vaccines stimulate the production of antibodies that bind to nicotine molecules and prevent nicotine from reaching the brain (Cornuz et al., 2008; Goniewicz & Delijewski, 2013). Some studies even suggest that these vaccines can probably combat smoking addiction before it starts by offering it to children by the age of 10 years (Lev, Wilfond, & McBride,

2013). Therefore, using these vaccines for adults, adolescents and children will undoubtedly raise an ethical debate among policy-makers, health professionals, and the public. In this paper, the authors will drive an argumentative ethical analysis using the utilitarianism and deontology (Kantianism) ethical philosophies to discuss the ethical implications of using these vaccines to prevent and treat smoking behaviour. Specifically, topics discussed are: effectiveness of nicotine vaccines, ethical analysis of using nicotine vaccines, and concludes with implications for future inquiry.

2. Effectiveness of Nicotine Vaccines

Pharmaceutical companies have developed and tested three nicotine vaccines: NicVAX, CYT002-NicQb, and TA-NIC (Cornuz et al., 2008; Goniewicz & Delijewski, 2013; Lieber & Millum, 2013). Clinical trials have been carried out to study the effectiveness of these vaccines on adults as a smoking cessation tool. They have passed phase I and II testing by showing a positive efficacy, identification of side effects, and by determination of appropriate dosages (Lieber & Millum, 2013). Experimental studies indicated that after 12 months of providing the nicotine vaccines for adult smokers, smoking cessation rates were between 16-42%, depending on the type and dose of vaccines (Cornuz et al., 2008; Lieber & Millum, 2013). Also reported is that nicotine vaccines are safe and well tolerated. The most observed side effects were a temporary mild pain at the injection site (tenderness swelling, and ache), flu-like symptoms, dry mouth, and headache (Cornuz et al., 2008; Goniewicz & Delijewski, 2013). Conversely, phase III testing demonstrated that some vaccines have cessation rates comparable to other smoking cessation methods such as nicotine patches and bupropion. It is important to note that the regular smoking cessation methods work on the brain to change the nicotine addiction process, while nicotine vaccines target nicotine molecules in the bloodstream. When the body is injected with the nicotine vaccines, plasma cells produce nicotine-specific antibodies that circulate in the bloodstream and prepare to bind to nicotine molecules. When nicotine enters the body by inhaling smoking, these antibodies bind to nicotine molecules and form complex compounds that are too large to cross the blood-brain barrier, leading to a lower nicotine action (Goniewicz & Delijewski, 2013). It has been found that the nicotine vaccines can reduce nicotine permeability into the brain by up to 65% (Leader, Lerman, & Cappella, 2010). Stage III results indicate that nicotine vaccines may not wholly prevent nicotine from reaching the brain. Therefore, it has been recommended that the combination of vaccine treatments with nicotine replacement therapy products may be compatible to treat smoking behaviour (Goniewicz & Delijewski, 2013).

Many researchers agree that nicotine vaccines are a promising tool for smoking cessation (Goniewicz & Delijewski, 2013; Hasman & Holm, 2004) The vaccines have been developed as an active immunization treatment that helps smokers quit by ensuring that cessation is effective (Hasman & Holm, 2004). Leader, Lerman, and Cappella (2010) declared that 53% of adult smokers would likely try the nicotine vaccines to quit smoking when the vaccines are available. These vaccines have the potential to provide an opportunity to prevent nicotine addiction among adolescents and children who do not smoke to immunize them against potential future smoking behaviour. In this case, the vaccine will prevent smoking in two ways. First, adolescents and children will less likely experiment with tobacco. Second, if adolescents and children decide to experiment with smoking, nicotine addiction will not follow, and it will be easy for them to quit because nicotine will not cross their brain barriers (Hasman & Holm, 2004). However, no studies (e.g., longitudinal studies) could be found showing the effect of these vaccines on adults, adolescents and children who have never smoked tobacco. Researchers only speculated that using vaccines as a preventative method for

smoking behaviour if it is given to adults, adolescents and children who never smoked would prevent those populations from involving themselves in smoking behaviour in the future or quit smoking if they currently smoke (Lieber & Millum, 2013).

Vaccinating adults who smoke with the nicotine vaccines is likely going to be accepted by the majority of smokers who are willing to quit. Whereas vaccinating adolescents and children to immunize them against smoking behavior will have critical and needed ethical scrutiny by the parents/legal guardians (Lieber & Millum, 2013). Consequently, ethical analysis is required before policy-makers and health professionals make any decisions about offering nicotine vaccines for adults, adolescents and children. The ethical inquiry and debate will provide researchers with guidance for researchers regarding scientific support for the effectiveness and long-term implications (Lev et al., 2013). Ethical analysis of nicotine vaccines also provides policy makers, healthcare providers, and the public with ethical direction about usefulness and safety of these products. Using nicotine vaccines to prevent and treat smoking will be discussed next from two ethical models: utilitarianism and deontology (Kantianism).

3. Ethical Analysis of Using Nicotine Vaccines

3.1 Utilitarianism Model

“The doctrine that the basis of morals is utility, or the greatest happiness principle, holds that actions are right in proportion as they tend to promote happiness, wrong in proportion as they tend to produce the reverse of happiness. By ‘happiness’ is meant pleasure and the absence of pain; by ‘unhappiness’ is meant pain and the lack of pleasure (Mill, 1863/2017, p.4).”

Utilitarian ethics is characterized as the ethics of duty where morality of an action policy, or program is based on the greatest amount of benefit obtained for the greatest number of individuals (Bellefleur & Keeling, 2016; Kahane, Everett, Earp, Farias, & Savulescu, 2015 ; Mandal, Ponnambath, & Parija, 2016). Albeit, utilitarian ethics is a society-centered philosophy because the outcomes of utilitarian philosophy provide the greatest benefit expected for the society. This philosophy has two approaches; act utilitarianism and rule utilitarianism. Act utilitarianism is the process of making decisions for each case by analyzing the benefits and harms promoting general better consequences. Rule utilitarianism is the process of making decision that is guided by performed rules and based on evidence. However, the outcomes of utilitarian approaches may cause harm to some individuals because they may conflict with their moral or religious beliefs (Mandal et al., 2016).

Nicotine vaccines will not only reduce the smoking prevalence, but it has economic impacts, environmental impacts, and social impacts (Venkatesh, 2013). However, discussing the impact is beyond the scope of this paper. From a utilitarianism perspective, vaccination against smoking behaviour may have the probability of reducing smoking rates in the society and reducing the adverse health outcomes of smoking. Although the long-term side effects of nicotine vaccines are not studied yet, the current scientific studies suggest that giving these vaccines to adults is likely safe with mild temporary side effects that are comparable to any other vaccines. Nicotine vaccines also have low cost, which is likely to facilitate their widespread distribution for public health purposes in healthcare systems (Goniewicz & Delijewski, 2013). Consequently, if public health offers these vaccines for adults as a smoking cessation tool, the greatest benefit for the society will be achieved by reducing the smoking rate and its adverse outcomes (morbidity and mortality) (Lieber & Millum, 2013).

Eaton et al. (2010) indicated that children start experimenting with smoking at the age of 11-17 years. If we assume that the nicotine vaccine is an effective intervention for children with minimum side effects, it will, therefore, reduce the possibility for them to become smokers and protect children from being smokers in future. Consequently, the expected harm from nicotine vaccines is far lower than the harm of nicotine addiction (Lieber & Millum, 2013). From the utilitarian view, vaccinating children against smoking will lead to the greatest benefit to the society. Smoking vaccination programs are also going to be highly efficient in low socio-economic societies where children are at high risk to become smokers in their lives (Goniewicz & Delijewski, 2013). In this case, the greatest benefit for the society can be achieved by empowering parents/legal guardians to vaccinate their children against smoking as a healthy choice for them.

A further benefit of nicotine vaccination is that the economic costs of smoking are far more significant than nicotine vaccination costs (Goniewicz & Delijewski, 2013). In Canada, smoking costs about 16.2 billion per year in direct and indirect costs (Dobrescu, Bhandari, Sutherland, & Dinh, 2017). When adult smokers and children with high risks of becoming smokers are immunized against smoking, a large number of the community will be protected against nicotine addiction and its consequence of harm. A lot of money can be saved and may be spent on other beneficial community projects. From utilitarianism's perspective, the nicotine vaccines can be ethical to be provided through public health prevention programs as it provides the greatest good for the greatest number of individuals. Therefore, if the Canadian public healthcare system adopts a cost-effective nicotine vaccines program, there is a possibility that mortality and morbidity rates caused by smoking will be decreased, and as a result, health services will be enhanced.

3.2 Deontology (Kantianism) Model

In contrast to utilitarian, deontological ethics is defined as "the ethics of duty where the morality of an action depends on the nature of the action" (Mandal, Ponnambath, & Parija, 2016, para. 3). That is, some of human acts are considered wrong and some are considered right because their nature is wrong or right and not because they lead to wrong or good outcomes (Kant, 2014/1875). Based on this premise of deontology, deontologists judge human acts regardless of their consequences, inclinations, intentions, desires and emotions. The human acts are considered "good will" when they are good in and of themselves. According to Kant, because the human being is the only creature who can rationalize wrong and right actions; human beings must act within the moral law or duty that gives him/her the guidance to do "good will". However, consequences of our acts cannot be totally ignored when we assess and perform some acts: they are still relevant to give us a framework for our duty.

The decisions of deontological philosophy are probably suitable for an individual, but not suitable for all the population. This means that the deontological ethics are patient-centered or individual centered philosophy (Mandal, Ponnambath, & Parija, 2016). Hence, decisions based on deontological approaches are not easy to explain because very often, they are subjective. Deontology has two types: deontological universalism and deontological relativism. In deontological universalism, the rules apply to everyone, under all circumstances. In deontological relativism, the rules apply to people under certain circumstances, or under certain conditions (Kant, 1875).

In the case of nicotine vaccination, deontological ethics would support the individual choice to prevent harm by taking the vaccination or using any other smoking prevention methods, despite the consequences of the decision. For example, a social survey for nicotine vaccination has revealed that 66% of smokers, who had tried five smoking cessation methods before, are probably going to use the nicotine vaccines (Leader et al., 2010). This result indicates that adult smokers, who are willing to quit smoking, may find nicotine vaccines a new healthy option for them to stop the unhealthy behaviour. For more elaboration, adult smokers are willing to accept the side effect of nicotine vaccines because the expected harm of the nicotine vaccines is less than that of nicotine addiction. From deontological lens, the motivations for these smokers to use nicotine vaccines are to reduce the harm of nicotine addiction and give up a harmful behaviour. On the other hand, the same survey also revealed that 28% of adult smokers are not willing to try the nicotine vaccines (Leader et al., 2010). The motivations of these smokers to refuse the nicotine vaccines are that they likely consider smoking as a lifestyle choice, can use any other smoking cessation method, or have a pleasurable feeling that reduces their stress when they smoke (Hasman & Holm, 2004; Lieber & Millum, 2013). From a deontological aspect, adults have the duty to prevent the harm of nicotine addiction by taking moral actions that prevent any negative consequences.

There is an ethical discussion regarding the parents'/legal guardians' power over their children. This argument suggests that parents'/legal guardians' authority is likely preventing children from having freedom regarding their future choices. Since nicotine vaccination is irreversible, it does, therefore, limit the children's future option in exploring the social functions of smoking (Hasman & Holm, 2004). However, as a society, parents/legal guardians are entrusted to prevent and protect their children from being caught in harmful behaviours like smoking (Lev et al., 2013). Since nicotine addiction causes preventable diseases, parents/legal guardians have the power to decide whether or not to vaccinate their children. Let us take the assumption that the nicotine vaccines as an effective and safe intervention for children and adolescents, reducing the probability that they become smokers in their lifetimes. By applying the concepts of deontology on children immunization against smoking, parents/legal guardians immunize their kids against smoking because smoking behaviour is a harmful and unacceptable regardless of its consequences. The parents'/legal guardians' decision to immunize their children is appropriate for individual child and it is not necessary to make positive outcomes on society (Mandal, Ponnambath, & Parija, 2016). For more elaboration, the relationship between parents/legal guardians and their children is a deontological one because one of expected roles for parents/legal guardians is to protect their children against harmful products or behaviours. When this expected role of parents/legal guardians is not appropriately performed, their children will be at higher risk to harmful products and behaviours. This result will encourage parents/legal guardians to do the right action (e.g., immunize their kids against smoking) to keep their children healthy and safe. It is vital to note that nicotine vaccines are not like any other infectious disease vaccines as nicotine vaccines are used for behavioural enhancement to prevent nicotine addiction (Lev et al., 2013).

From the deontological perspective, parents/legal guardians can have practical reasons to agree or refuse to give nicotine vaccines to their children. At the same time, parents/legal guardians have the duty to take moral action to prevent and protect their children from harmful products and behaviours. Parents/legal guardians may not agree on vaccinating their children against smoking because it may affect the well being of their children (Lev et al., 2013). Some other arguments suggest that parents/legal guardians think that vaccination might cause harm to their children and put them at risk that is preventable (Lieber & Millum,

2013). From a deontological perspective, parents'/legal guardians' motivation to refuse to vaccinate their children is to prevent harm and not undermine the children's rights. On the other hand, parents/legal guardians who smoke and tried different smoking cessation methods will likely accept vaccinating their children against smoking because they do not want their children to fall in the same unhealthy behaviour in the future (Hasman & Holm, 2004). Also, children who live in low socio-economic conditions have a higher chance to become tobacco smokers (Bethell, Simpson, Stumbo, Carle, & Gombojav, 2010). Therefore, parents/legal guardians who live in low socio-economic conditions may also find vaccinating their children against smoking is an effective method to prevent their children from being involved in current or future smoking behaviour. In conclusion, from the deontological view, parents'/legal guardians' motivation to vaccinate their children is only to prevent the harm of nicotine addiction, but they do not take in consideration other consequences of their decision.

4. Comparison of Utilitarianism and Deontology Perspectives

The utilitarian and deontological approaches to the nicotine vaccines have essential ethical views on providing vaccines against smoking for adults, adolescents, and children. For example, utilitarianism argues that giving nicotine vaccines to adult smokers and children will lead to the greatest benefit to the society by decreasing smoking rates and its adverse health outcomes. On the other hand, deontology (Kantianism) ethics argues that it is an individual responsibility to make a moral judgment about taking or refusing the vaccines to prevent harm. Both deontology and utilitarianism support the nicotine vaccines from their perspectives. Through the deontological lens, adult smokers can make their choice to accept the nicotine vaccines with its temporary side effects, or refuse nicotine vaccination and use other smoking cessation methods. Through the deontological lens, parents/legal guardians have the choice to accept to vaccinate their children, if they ensure it is safe, efficient, and will prevent their children from becoming smokers in the future. They also have the choice to refuse to vaccinate their children to avoid harmful side effects, threats to well-being, and violation of their children's autonomy.

5. Implications for Future Inquiry

The most critical issue about nicotine vaccines is their health effectiveness and safety on adult smokers, adolescents, and children. In this case, future research and random control trials are needed to investigate the effectiveness of nicotine vaccines on adolescents and children in preventing nicotine addiction in future. Cost-effectiveness analysis is also required to decide whether the implementation of the nicotine vaccines in public health is affordable. The social acceptance of nicotine vaccines also needs to be assessed in the society.

6. Conclusion

Active nicotine vaccines as a new smoking treatment and prevention method will provide opportunities for adult smokers to quit nicotine addiction or prevent them from involving in this harmful behaviour. Nicotine vaccines also have the potential to provide an opportunity to prevent nicotine addiction among children and young adults who do not smoke from being smokers in the current time or in the future. However, vaccinating children and adolescents against smoking will encumber a tremendous ethical debate among policy-makers, health professionals, and the public. The authors of this paper discussed the offering of nicotine vaccination for adults, children, and adolescents from utilitarian and deontological ethical

models. It is evident that preventing harm and acting toward individuals' best interest are common across the two ethical perspectives. From utilitarian perspective, nicotine vaccination is good for the society as it provides the greatest benefit for the greatest number of individuals as a healthy choice to prevent smoking among adult and children. However, the deontological perspective of nicotine vaccines is more acceptable because an individual has the duty to prevent the harm of nicotine addiction by choosing nicotine vaccines or any other smoking cessation methods. Parents/legal guardians have the duty also to protect their children from the harm of nicotine addiction by making reasonable moral judgments that prevent any negative consequences. The ethical analysis provides researchers with guidance to improve research outcomes. Future studies need to be conducted to study the effectiveness of nicotine vaccines in preventing nicotine addiction among adolescents and children.

References

- Baliunas, D., Patra, J., Rehm, J., Popova, S., & Taylor, B. (2007). Smoking-attributable morbidity: acute care hospital diagnoses and days of treatment in Canada, 2002. *BMC Public Health*, 7, 1-8. Retrieved from <https://doi.org/10.1186/1471-2458-7-247>
- Bellefleur, O., & Keeling, M. (2016). Utilitarianism in Public Health. Retrieved from http://www.ncchpp.ca/docs/2016_Ethics_Utilitarianism_En.pdf
- Bethell, C., Simpson, L., Stumbo, S., Carle, A. C. & Gombojav, N. (2010). National, state, and local disparities in childhood obesity. *Health Affairs*, 29, 347–356. doi: 10.1377/hlthaff.2009.0762.
- Canadian Cancer Society's Advisory Committee on Cancer Statistics (2017). Canadian Cancer Statistics 2107. Retrieved Oct. 27, 2107, from cancer.ca/Canadian-Cancer-Statistics-2017-EN.pdf
- Cornuz, J., Zwahlen, S., Jungi, W. F., Osterwalder, J., Klingler, K., Van Melle, G., . . . Willers, J. (2008). A vaccine against nicotine for smoking cessation: a randomized controlled trial. *PloS one*, 3(6), e2547. doi: <https://doi.org/10.1371/journal.pone.0002547>
- Dobrescu, A., Bhandari, A., Sutherland, G., & Dinh, T. (2017). The Costs of Tobacco Use in Canada, 2012 (pp. 174). Ottawa, ON: The Conference Board of Canada. Retrieved from <http://www.conferenceboard.ca/e-library/abstract.aspx?did=9185>
- Eaton, D. K., Kann, L., Kinchen, S., Shanklin, S., Ross, J., Hawkins, J., ... Wechsler, H. (2010). Youth risk behavior surveillance-United States, 2009. *Morbidity and Mortality Weekly Report*, 59, 1–142, Retrieved from <http://www.cdc.gov/mmwr/pdf/ss/ss5905.pdf>
- Goniewicz, M. L., & Delijewski, M. (2013). Nicotine vaccines to treat tobacco dependence. *Human Vaccines & Immunotherapeutics*, 9(1), 13-25. doi: 10.4161/hv.22060
- Government, of Canada. (2012). Strong Foundation, Renewed Focus: An Overview of Canada's Federal Tobacco Control Strategy 2012-17. Retrieved from <https://www.canada.ca/en/health-canada/services/publications/healthy-living/strong->

foundation-renewed-focus-overview-canada-federal-tobacco-control-strategy-2012-17.html

- Hasman, A., & Holm, S. (2004). Nicotine conjugate vaccine: is there a right to a smoking future? *Journal of Medical Ethics*, 30(4), 344. Retrieved from <http://jme.bmj.com/content/30/4/344>
- Kahane, G., Everett, J. A. C., Earp, B. D., Farias, M., & Savulescu, J. (2015). "Utilitarian" judgments in sacrificial moral dilemmas do not reflect impartial concern for the greater good. *Cognition*, 134, 193–209. doi: <http://doi.org/10.1016/j.cognition.2014.10.005>
- Kant I. (2014). *Fundamental principles of the metaphysic of morals* [trans. Thomas Kingsmill Abbott]. University of Adelaide, Australia. The Electronic Classics Series (original work published 1875). Retrieved from <https://ebooks.adelaide.edu.au/k/kant/immanuel/k16prm/>
- Leader, A. E., Lerman, C., & Cappella, J. N. (2010). Nicotine vaccines: Will smokers take a shot at quitting? *Nicotine & Tobacco Research*, 12(4), 390-397. doi: 10.1093/ntr/ntq015
- Lev, O., Wilfond, B. S., & McBride, C. M. (2013). Enhancing Children against Unhealthy Behaviors—An Ethical and Policy Assessment of Using a Nicotine Vaccine. *Public Health Ethics*, 6(2), 197-206. doi: 10.1093/phe/pht006
- Lieber, S. R., & Millum, J. (2013). Preventing Sin: The Ethics of Vaccines against Smoking. *The Hastings Center Report*, 43(3), 23-33. doi: 10.1002/hast.159
- Mandal, J., Ponnambath, D., & Parija, S. (2016). Utilitarian and deontological ethics in medicine. *Tropical Parasitology*, 6(1), 5-7. doi: 10.4103/tp.TP_4_17
- Mill, J. (2017). *Utilitarianism*. [Trans. Jonathan Bennett]. 2nd ed. ebook (original work published 1863). Retrieved from <http://www.earlymoderntexts.com/assets/pdfs/mill1863.pdf>
- Venkatesh, N. (2013). Impact of Smoking: Influence on the society and global business. *International Journal of Business and Management Invention*, 2(3), 46-53. Retrieved from [https://www.ijbmi.org/papers/Vol\(2\)3/Version-2/H234653.pdf](https://www.ijbmi.org/papers/Vol(2)3/Version-2/H234653.pdf)