

# **Chantix® versus NicoDerm®: How Different Drug Delivery Methods affect One's Ability to Quit Smoking**

Principle Investigator - Harin Shah

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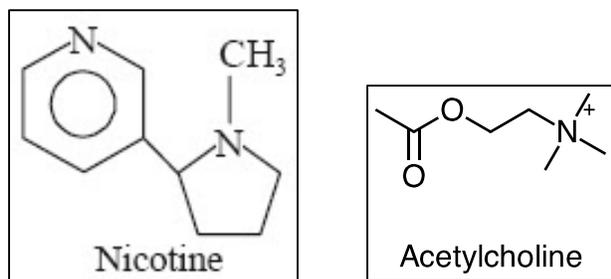
## **ABSTRACT**

As tobacco-related fatalities are on the rise, there is a push by consumers to quit smoking. Pharmaceutical companies have realized this billion-dollar opportunity to cash in and have been developing nicotine replacement therapy (NRT) drugs. The two main classes of NRTs are medications through oral administration, such as Chantix®, and medications through transdermal patches, such as NicoDerm®. There have been numerous studies conducted by independent agencies and pharmaceutical companies to ascertain the famous question: which drug therapy works best and how do we improve our current drug design? When comparing Chantix and NicoDerm, it appears that long-term smoking cessation is more likely with Chantix (though both are promising in the short-term).<sup>1</sup> However, while once seen as dangerous, researchers have been using combined NRTs and found that there is a synergetic effect when participants use both therapies concurrently (55% users on combined therapy quit smoking versus 41% users on placebo).<sup>2</sup> The future for NRTs is very promising as nearly seven out of ten smokers wish they hadn't started smoking and many of them are attempting to quit.<sup>3</sup> Researchers are working on new charged nanoparticles to be the future of medicine as they are better at targeting their destination and easier to administer.<sup>4</sup>

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In the United States, the largest preventable cause of death is tobacco-related. Annually, firsthand exposure claims just under half a million lives (~480,000) while secondhand exposure is responsible for just over 41,000 deaths. The problem with smoking cigarettes, besides the fact that it contains over 7,000 chemicals of which 70 are carcinogens, is that they are purposely filled with nicotine.<sup>1</sup> Nicotine influx in the body triggers a release of the neurotransmitter dopamine. This can lead to a combination positive, negative feedback loop system that goes awry. Nicotine is also related to a neurotransmitter called acetylcholine (ACh), which is involved in many homeostatic functions such as muscle movement / respiration and corresponds with dopamine levels; an increase of which can lead to a sense of euphoria in the human body. However, once the brain stops releasing dopamine as nicotine levels fall, the body goes into a state of withdrawal causing many people to become anxious and crave a cigarette (a

nicotine source).<sup>8</sup> Hence, we have addiction. In this paper we will study the effects of two different drug delivery systems by comparing Chantix\* and NicoDerm, an oral pill and transdermal patch, respectively.



**Figure 1:** Nicotine ( $C_{10}H_{14}N_2$ ) and Acetylcholine ( $C_7H_{16}NO_2^+$ ) are both organic substances that are involved in addiction. Nicotine is an extremely toxic alkaloid, which explains why nitrogen is present. Acetylcholine is an ester of choline which is a nitrogen-containing alcohol related to B vitamins.<sup>8</sup>

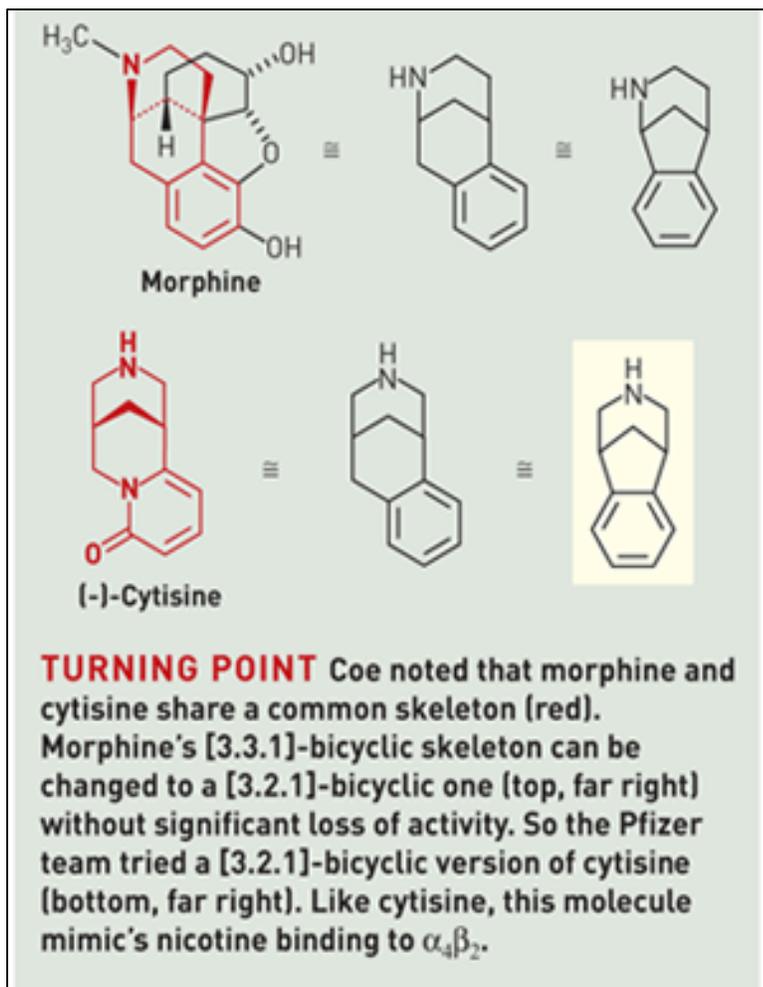
To begin, there are many forms of NRT such as patches, gums, inhalers, pills, etc. A popular therapy is NicoDerm: a transdermal patch. NicoDerm works by “[controlling] the release of nicotine into your bloodstream through your skin. The level of nicotine uptake is lower than that of cigarettes, and the program is designed to allow your body to gradually adjust to having less nicotine until you don’t need any.” This makes it relatively difficult for a user to accidentally overdose on the drug or to take it incorrectly.<sup>5</sup>

While once the most widely used vehicle for nicotine replacement therapy, there have been conflicting reports as to whether NicoDerm has any significant effects in the long-term. In the scientifically peer-reviewed journal *JAMA Intern Med*, a study is conducted entitled “Long-term Nicotine Replacement Therapy: A Randomized Clinical Trial”. Participants on the patch (sample size,  $n = 525$  smokers) for 8, 24, and 52 weeks were evaluated to see if they had successfully stopped smoking. The findings indicated that there is some success of cessation in the short-term, but effectiveness is questioned in the long-term as success rates sharply drop after the 24-week mark.<sup>7</sup> There are also numerous side effects such as skin irritation, headache, racing heartbeat, and nausea.<sup>6</sup>

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\* Note that the Chantix is also known by its generic name – varenicline – which for the purposes of this paper will be used interchangeably

In addition to nicotine replacement therapy via transdermal means, another popular antismoking medicine – called varenicline – is the “first nonnicotine antismoking medicine designed specifically to help smokers stop smoking,” according to researcher Jotham W. Coe of the biopharmaceutical company Pfizer.<sup>9</sup> If we recall from earlier, the phenomenon of becoming addicted to cigarettes is because nicotine binds to a class of ion channels in the



central nervous system (CNS). These channels (nAChRs) bind to acetylcholine (recall **Figure 1**). As a result, these receptors in the brain, which also happen to respond to pleasurable and “reinforcing” stimuli, trigger the release of dopamine, which is the neurotransmitter that is related to addiction.<sup>8</sup>

Simply put, once a user becomes accustomed to these frequent bursts of dopamine, it becomes increasingly difficult to quit smoking. Varenicline is a drug that “partially mimic[s] nicotine’s ability to activate  $\alpha_4\beta_2$ ” -  $\alpha_4\beta_2$  being an abundant nAChR subtype. This drug works two-fold: first by activating  $\alpha_4\beta_2$  and thereby releasing dopamine to distract any cravings and by also directly blocking nicotine’s access to these receptors which makes it more likely

**Figure 2:** Varenicline ( $C_{13}H_{13}N_3$ ) resembles morphine and is being touted as revolutionary breakthrough for smokers wanting to quit.<sup>9</sup>

for users to wean off nicotine completely. Varenicline was mimicked to resemble a significantly larger alkaloid morphine. In fact, the two structures are only different by the position of one nitrogen atom (see **Figure 2**).<sup>9</sup>

Perhaps instead of comparing Chantix and NicoDerm directly, both therapies can be combined to create a synergistic experience for the user. Such is the idea presented in a WebMD article, which finds that “combining two anti-smoking approaches -- the medication Chantix and nicotine patches -- improves the odds you’ll quit

smoking over the short term.” Although this approach can be financially taxing, Dr. Koegelenberg of Stellenbosch University and Tygerberg Academic Hospital in South Africa claims that combination therapy is only for a short while and will ultimately reduce smoking-related costs if/once the user quits smoking completely.<sup>2</sup>

While not without its fair incidences of side effects, a study was conducted by Chantix and nicotine patch makers that was published in the *Journal of the American Medical Association*. After 12 weeks, 55% of users who had combined therapy had stopped smoking compared to 41% of users who were on a placebo. After 6 months these percentages swayed to 49 and 33, respectively. Previously thought to have been dangerous, researchers have hypothesized that these medicines work well in unison because of “something to do with how they combine to disrupt the way the brain processes nicotine”.<sup>2</sup> These facts seem to be supported in scientifically peer-reviewed article *Addiction* in a study called “An exploratory short-term double-blind randomized trial of varenicline versus nicotine patch for smoking cessation in women”. Obviously this study is gender biased, but the results give us more insight as to how users deal with various drug therapies. In this study, the subjects were females, aged 18-45, who averaged more than or equal to ten cigarettes per day. In the two treatment groups, these women were either given varenicline and placebo pills, or a nicotine patch and placebo pills. At the end of the 4-week period, varenicline had 2:1 odds of end-of-treatment abstinence compared to the nicotine patch.<sup>3</sup> This begs the question whether or not a combination therapy would yield better results than any individual treatment alone, and it is probably not incorrect to speculate the combined therapy would have been better considering that the results were somewhat diminished during a standard post-treatment follow-up.

It is important to note that tobacco addiction affects all races, both sexes, all age groups, people in every education bracket and is otherwise not specific to any group of people. More research needs to be conducted to manufacture better drug designs and therapies.<sup>1</sup> There is substantial R&D giving insight in drug therapies that are better at targeting their desired destination as “researchers at Boston University have been working on packaging drugs into tiny charged nanoparticles, and then applying a small electric field to the skin that would open up pores...one day, such technology could be a way to give people shots without needles, and in a way that would be much faster-acting than current methods”.<sup>4</sup>

In conclusion, both varenicline and NicoDerm are decorously promising in the short-run with varenicline having a slight advantage when both drugs are directly compared. However, the most successful smoking cessation results were obtained in groups of people who are on a combined therapy of both an oral pill and transdermal patch.

As we have explored in this paper, both means of drug transportation work differently in the body but can prove to have significant success rates if done concurrently. Ultimately, overcoming addiction occurs when one is able to regain control of their dopamine and acetylcholine levels and not be consumed by the thought of smoking to alleviate a nicotine craving. For some it may be too late, but for others perhaps it is best to quit smoking by never starting in the first place. The future of drug design looks promising, however, and for those who have already started, it looks like medicine may help them stop.

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\* Journal volume / page #s are not yet available