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Tobacco Industry Research on Nicotine Replacement Therapy: "If Anyone Is Going to Take Away Our Business It Should Be Us"

Nicotine replacement therapy (NRT) is recommended for tobacco cessation on the basis of pharmaceutical industry research showing its effectiveness when combined with counseling. The tobacco industry opposed NRT when it first appeared in the 1980s but by 2016 was marketing its own NRT products.

We used internal tobacco industry documents dated 1960 through 2010 to identify the industry's perceptions of NRT. As early as the 1950s, tobacco companies developed nonsmoked nicotine replacements for cigarettes, but they stopped out of concern that marketing such products would trigger Food and Drug Administration regulation of cigarettes. In the 1990s, after pharmaceutical companies began selling prescription NRT, tobacco companies found that many smokers used NRT to supplement smoking rather than to quit. In 2009, once the Food and Drug Administration began regulating tobacco, tobacco companies restarted their plans to capture the nicotine market.

Although the tobacco industry initially viewed NRT as a threat, it found that smokers often combined NRT with smoking rather than using it as a replacement and began marketing their own NRT products. (*Am J Public Health*. 2017;107:1636–1642. doi: 10.2105/AJPH.2017.303935)

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Prescription nicotine replacement therapy (NRT) gum was approved by the US Food and Drug Administration (FDA) for cessation in 1984. The tobacco industry perceived it as a threat and successfully pressured the first drug company to sell NRT to change marketing that recommended cessation.[1] In 1996, pharmaceutical companies successfully advocated to make NRT an over-the-counter (OTC) drug, arguing that cigarettes were available without prescription and cessation aids should be as well.[2,3] Although tobacco companies initially opposed NRT, by the 21st century they had begun marketing their own NRT products.[4–6] We sought to understand why tobacco companies shifted from viewing NRT as a threat in the 1980s to a business opportunity in the 21st century.

The 2013 clinical practice guideline on smoking cessation recommends NRT for tobacco cessation on the basis of placebo-controlled randomized clinical trials[7] of smokers motivated to quit who tapered NRT over time and received counseling.[8–10] Additional randomized clinical trials and a Cochrane meta-analysis reported that NRT was effective in simulated OTC settings, even with less intensive behavioral support.[11–16] By contrast, population studies have found that NRT does not increase, and may depress, cessation, likely because it is not used in monitored populations, as clinical trials are.[8–10,17,18]

Internal industry documents reveal that the tobacco industry changed its approach to NRT because of internal research showing that NRT was often used to supplement smoking rather than for cessation, or NRT replaced quitting smoking outright—and in response to 2009 changes in federal law that allowed tobacco companies to sell NRT without triggering FDA regulation of cigarettes. In these documents, tobacco companies stated that their new products could successfully compete with pharmaceutical NRT and indicated that their goal was to gain market control of all products containing nicotine.

METHODS

Between August and December 2015 we searched the Truth Tobacco Industry Documents Library using established methods.[19–24] (The online supplemental file [available as a supplement to the online version of this article at http://www.ajph.org] contains details about the library and our search strategy.) When our research revealed that smokers were not necessarily using NRT for cessation, we reviewed contemporaneous medical literature addressing the role of NRT in smoking cessation to contextualize these findings.[25] We used a snowball strategy,[22] beginning with the keywords "nicotine patch," "NRT," and "nicotine gum," and then we refined search terms and dates using named individuals, organizations, and products and adjacent (by Bates numbers) documents. We searched PubMed for medical literature using comparable search terms and compared studies that used surveillance data to those that used clinical trials to assess the use of NRT at the population level.

We considered the effects of NRT use under real-world conditions as well as under the idealized conditions of clinical trials, which recruit smokers

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highly motivated to quit, often provide counseling as well as NRT, monitor behavior and outcomes, simulate OTC drug status, and taper use under the supervision of medical professionals. We analyzed approximately 100 tobacco industry documents dated between 1960 and 2010.

TIMELINE OF TOBACCO INDUSTRY NRT RESEARCH AND PRODUCT DEVELOPMENT

Years	Research and Development
1950s	Philip Morris research and development division works on development of nicotine gum.
1960	Philip Morris abandons research on nicotine gum to avoid FDA regulation.
1960s	RJ Reynolds begins development of nicotine gum, beverages, inhalers, edibles, and "artificial cigarettes."
1970	RJ Reynolds abandons research on nicotine gum, beverages, and candy to avoid FDA regulation.
1970s	Brown & Williamson develops nicotine gum.
1970s	Tobacco industry research shows consumers perceive nicotine to be dangerous.
1978	Brown & Williamson abandons research on nicotine gum to avoid FDA regulation.
1980s	Tobacco companies begin research on reduced nicotine products.
1984	FDA approves Nicorette (nicotine gum) for smoking cessation.
1987	Tobacco industry research shows consumers no longer perceive nicotine to be dangerous because of NRT marketing.
1991	Philip Morris terminates research on reduced nicotine products.
1991	FDA approves nicotine patches for smoking cessation.
1992	Philip Morris research reveals that use of nicotine patches has no effect on real-world quit rates.
1992	Philip Morris develops strategy to position NRT as a complement to smoking.
1992	British American Tobacco considers purchase of nicotine patch company but decides against it to avoid FDA regulation.
1994	Philip Morris classifies NRT as a competitor product (comparable to cigars) in internal strategy memos.
2000	Philip Morris begins advocating FDA regulation of cigarettes.
2008	RJ Reynolds classifies Zonnic nicotine gum as comparable to smokeless tobacco products.
2009	FDA begins regulation of cigarettes under the Family Smoking Prevention and Tobacco Control Act.
2014	RJ Reynolds begins marketing Zonnic nicotine gum.
2016	Philip Morris begins marketing Verve nicotine lozenges.

Note. FDA = US Food and Drug Administration; NRT = nicotine replacement therapy.

RESULTS

As indicated in the timeline in the box on this page tobacco companies considered marketing nicotine replacement products between the 1950s and 1980s as extensions of their cigarette product lines, but they did not do so for fear of triggering FDA regulation of cigarettes. In the 1990s, industry-internal research found that many smokers were using NRT to supplement smoking or in lieu of quitting outright. After the FDA began regulating cigarettes in 2009, tobacco companies launched their own nicotine product lines, which they defined as a single category that included nicotine gum, patches, lozenges, and e-cigarettes.[26]

1950s to 1983

Philip Morris. In 1959, Philip Morris researchers considered developing a nicotine gum to be used concurrently with or as a substitute for cigarettes.[27] In October 1960, the director of research Helmut Wakeham wrote the vice-president of the research and development department, saying, "[We wanted to] provide nicotine to the consumer in the form of a chewing gum, providing all the satisfaction of smoking while circumventing the whole area of health."[27] Philip Morris decided not to pursue this idea because "such a product would place us directly under the Food and Drug Administration, a rather undesirable relationship."[27] Philip Morris sought to avoid FDA regulation until 2000, when it decided it was politically expedient to embrace FDA regulation to mitigate uncertainty and allow the marketing of new "safer" tobacco products.[28–30]

RJ Reynolds. In 1969, Claude Teague, assistant chief of the RJ Reynolds (RJR) research and development department, wrote a strategy document suggesting that although "nicotine is considered to be a sine qua non in smoking satisfaction," there was no "safe" cigarette that would address the health risks of smoking. RJR's "new strategy . . . should be . . . to devise and market profitable new products—away from conventional cigarettes—that will provide those same gratifications."[31] Alternatives included a hypothetical "no tobacco" cigarette using "nicotine-flavor-water" (comparable to the nicotine solution that was later used in e-cigarettes[26,30]) and nicotine gum, beverages, inhalers, and "edible products."[31]

RJR addressed Teague's proposal in 1970 by producing a Cigarette "Substitute" Concept Study that observed, "Smoking and health propaganda . . . forces [that] have influenced many smokers to quit . . . may have reduced the number of new smokers entering the market."[32] RJR hoped a "a cigarette 'substitute' . . . would provide some of the same satisfactions as cigarettes" but be hopefully less vulnerable to heavy taxation or health criticism. "The problem," the report continued, was "just what product [to develop]."[32] Smokers RJR surveyed in the 1970s preferred "gum (43%), beverage (39%), candy (33%), and artificial cigarette (23%)."[32] The report observed, however, that these smokers felt nicotine was harmful to health and wondered "whether nicotine should be promoted as an ingredient in a substitute cigarette without also mounting a strong support campaign in nicotine's favor and defense," considering that nicotine is addictive and its

inclusion was critical to maintaining a tobacco habit.[32] The report said that using this hypothetical product, targeted at "former smokers and those who were inclined to, but didn't start smoking (probably because of the health controversy),"[32] RJR could capture more of a shrinking nicotine market.

In 1970, despite the expected marketing potential of such substitutes, RJR abandoned this research, except work on artificial cigarettes, in part because it believed:

> the Food and Drug Administration might frown on the use of nicotine in those items classified as food products such as gum, beverage, and candy which received the highest attitude ratings in the concept study.[33]

Brown & Williamson. Brown & Williamson, then British American Tobacco's (BAT) US subsidiary, started developing nicotine gum in the 1970s. A 1978 letter from the BAT marketing department to BAT's research and development center stated, "Several years ago we did some work on tobacco based chewing gum . . . which was terminated for obvious reasons."[34] Like other tobacco companies, Brown & Williamson wanted to avoid FDA regulation.[28]

1984–1991

The FDA approved Nicorette gum, the first pharmaceutical NRT, for use by prescription as a tobacco cessation aid in 1984,[35] with nicotine patches following in 1991.[35,36] In July 1984, a US Tobacco Company consumer marketing representative wrote the manager of sales communication, noting "similarities between the effects and sensations of the gum[s] with smokeless tobacco" in an article on Nicorette in *Consumer Reports*. This observation reflected the understanding inside the tobacco industry that NRT was not a cessation aid, as consumers perceived it to be, but a different kind of tobacco product.[37]

Tobacco companies abandoned the idea of producing nicotine replacement products when internal industry research conducted in the 1970s found that consumers believed nicotine was dangerous.[32,33] As a result, in the 1980s Philip Morris focused on reduced nicotine products. Project ART, for example, sought to develop low-nicotine tobacco products, and Project Extra aimed to create increased tar products.[38] However, focus groups testing these products, convened by the Leo Burnett Advertising Agency in 1987, revealed that smokers no longer viewed nicotine in cigarettes as a health risk; the spread of NRT had changed public opinion about nicotine.[39] Burnett reported, "The fact that nicotine gum was prescribed by their doctors and endorsed by their pharmacy led some people to conclude that nicotine must not be all that bad for them."[40]

Burnett's summary continued:

> Groups were not overly concerned about being "addicted" to nicotine. It appeared that they believed that "addiction" was the price they paid for enjoying smoking. In fact, because they did not understand nicotine's effects, or—at most—believed that nicotine passed through their bodies quickly, they had fewer concerns about it.[40]

Philip Morris research on potential reduced nicotine products found:

> Nicotine was perceived to be the substance which was key to overall smoking satisfaction. Importantly it was what many smokers sought from cigarettes . . . Health implications of nicotine were acknowledged, but its effects were thought to be short-term, and sometimes pleasant and desirable.[41]

In 1988, the US surgeon general report *Nicotine Addiction* concluded that nicotine was the addictive constituent of cigarettes that kept people smoking.[42] By the late 1980s, Philip Morris had returned to studying alternative tobacco products marketed by other companies. A 1988 memo noted:

> The average nicotine concentration for [Chewbacco, a recreational nicotine gum containing tobacco sold by an independent company] was 0.45 mg/piece before chewing. . . . The amount of tobacco material in the gum was estimated to be less than 1% by weight. . . . Subjectively, the gum was reported by five volunteers to leave a "hot or peppery" taste in the mouth.[43]

In 1991, Philip Morris terminated its development efforts on reduced nicotine products.[44] Internal reports leading to this decision concluded:

> On the surface, the development of a nicotine-free cigarette would seem to be the most dramatic technological advance[ment] since the filter, and with it potential for a major new entry in an otherwise stagnant industry. Smoker awareness of the reported risks associated with smoking has never been higher . . . [however] consumers [*sic*] awareness of the perceived negatives of nicotine as distinct from tar is not as high as is thought.[45]

1992–2008

British American Tobacco. In 1992, BAT considered purchasing a manufacturer of nicotine patches, Stowic, and to assess the potential market for the patches they compared nicotine delivery rates between cigarettes and patches.[28] BAT's research and development department compared the Stowic patch to other patches for Imasco, a BAT subsidiary that owned a Canadian drugstore chain. A 1992 memorandum to the director of Imasco discussed the benefits of a strategy that included entering the alternative nicotine product market:

> Studies of the efficacy of nicotine gum or transdermal patches on smoking cessation invariably show a significant benefit in the short term, but only a small advantage (if any) over placebo in the long term (6+ months). . . . One could make an argument for the industry supporting development of alternative nicotine delivery systems by considering them in the same philosophical light as brand extensions, or in this case, a business extension. The rationale is that if anyone is going to take away our business it should be us.[46]

BAT continued its research on the Stowic patch, which included a 1992 discussion on nicotine patches' market potential:

> The fact that people use snuff and chewing tobacco indicates that administration routes other than the inhalation route can deliver tobacco satisfaction. . . . There is currently a void in the market for a product that provides tobacco satisfaction in a form that is acceptable and available to many segments of the market. The tobacco industry currently does not have such a product. A critical turning point for the nicotine patch will be whether the current product fulfills the regulatory requirements to become available over the counter.[47]

The company decided against entering the nicotine patch market because the legal department said, "If we did anything which suggested we were

simply in the nicotine delivery business, we would run a serious risk of facing FDA jurisdiction."[48]

Philip Morris. From at least 1987 to 2003 Philip Morris surveyed population samples of smokers monthly through its Smoker Tracking Surveys. Their interests included smokers' brand preferences and quit attempts. The April 1992 survey included an effort to "gauge the initial impact of the Nicotine Patch on smoker quitting."[49] It showed that using nicotine patches had no effect on real-world quit rates:

> 301 past two year quitters (out of a sample of 551 quitters identified in January–February) were reinterviewed . . . to determine their usage of and reactions to the Nicotine Patch. . . . Roper [the polling organization Philip Morris hired to track smoking trends] data through December indicate that quitting rates on a 12 [month] basis have been roughly flat.[49]

Philip Morris continued to monitor nicotine patch use and quit attempts throughout 1992. The June survey found:

> Monthly and 12 [month] quitting rates have been roughly flat through April. The use of Nicotine Patch as a way to stop smoking jumped dramatically in April (8% - 26%). . . . The results seem to suggest that Nicotine Patch [use for quit attempts] evidenced growth at the expense of 'stopped all at once' quitting.[50]

The monthly tracking surveys did not report on whether quit attempts using different methods were more or less successful.

In August 1992, Doron Stern, a researcher who had been reporting the results from surveys of smokers regarding their nicotine patch use, wrote Altria (which owned Philip Morris) president and chief operating officer David Beran, summarizing pharmaceutical industry clinical trials and Philip Morris surveys and focus groups:

> Clinical results indicate the nicotine patch was more effective against placebos. . . . It is important to keep in mind, however, that in objectively validated tests (1 full year after quitting) nicotine patch scores were less impressive vs placebos. . . . Some sort of behavior modification was administered during the clinical tests. Without some degree of psychological therapy, many experts warn that the nicotine patch is powerless [as a method of smoking cessation].[51]

He noted, "The explosive growth of nicotine patch sales has not seemed to increase rate[s] of quitting (currently holding at 6.7% for 12 [month period] ending June [1992])."[51]

Findings from focus groups conducted for Philip Morris in 1992, summarized in a PowerPoint presentation, reviewed how smokers obtained and used NRT: nicotine patches were not prescribed in combination with behavioral therapy as advised to maximize effectiveness, nor were they offered with the same care as other prescription drugs. The presentation listed how entering the alternative nicotine market could benefit Philip Morris:

- The process of acquisition [of the nicotine patch] is easy. Apparently, any type of doctor will write a prescription without an examination nor will be expect [*sic*] any interim appointments.
- While doctors seem to readily encourage patch usage, few get any more involved—offering advice, discussing side effects, suggesting behavior modification.[52]

The presentation noted that nicotine patches were being used as adjuncts to smoking, which had implications for Philip Morris in terms of an alternative product line that would complement cigarette sales:

- There appears to be an extremely casual approach to the medical requirements surrounding patch usage typical of an OTC mentality [even though the patch is only available by prescription]. Users . . .
- Physically cut the patch to reduce dosage
- Change number of hours to wear
- Share patches with friends/family
- Removal [*sic*] of the patch for occasional smoking.[52]

Stern reported further on these findings in another memo to Beran in October 1992: "Almost all the men we spoke to [who used NRT patches] went back to smoking."[53] He proposed that interest in trying the patch might begin to decline, noting, "Some believe that the novelty [of the nicotine patch] has started to wear off."[53] He continued to update Beran, stating in December 1992 that Philip Morris smoker surveys reported that use of NRT had declined as anticipated:

> Based on the attached results from our Continuous Tracking Study [Roper polls of smokers], it appears that usage of the nicotine patch has dropped steadily since it peaked in June. . . . [A] possible explanation for the patch's loss in popularity may relate to the difficulty quitter's [*sic*] experience in adhering to the strict, but necessary, regimen prescribed for the patch treatment.[54]

Philip Morris continued to study alternative nicotine products as a strategy for smokers to deal with increased workplace smoking restrictions. A 1992 presentation titled "Nicotine Patch Overview" in the Philip Morris documents stated that Philip Morris could use alternate market approaches for nicotine patches, which included:

> target[ing] smokers with alternate to smoking message rather than cessation strategy. . . . [Because of that] approximately half of all smokers [are] subject to some restrictions in the workplace and one of ten face complete bans.[55]

The proposal suggested that nicotine gum could be a bridge between cigarettes. It stated that this change in strategy would be profitable, and because of that, "Profit margins [for the nicotine patch were] estimated at 15% after taxes—roughly in line with cigarette industry."[55] It observed that marketing NRT as a cessation aid for smokers was challenging. Taking nicotine gum as an example:

> Nicotine gum achieved comparable results [to the nicotine patch] vis a vis placebos [in clinical trials]. Yet, treatment is often demanding.
>
> - Up to 30 sticks/day
> - Very gradual dose reduction
> - Required to keep product between cheek and gum.[55]

The presentation reported that new NRT products delivered nicotine more effectively than the patch and similarly to cigarettes:

> New products: Several other smoking cessation devices are being explored for market consideration including nasal sprays and vapor inhalers. Both systems do a better job than the nicotine patch in achieving absorption rates comparable to cigarettes.[55]

Philip Morris continued to monitor NRT sales and use. In 1994 Philip Morris included producers of nicotine gum and

nicotine patches in its regular "competitor review" reports developed by its business planning department in the same category as cigar sales, despite the fact that NRT was still available only by prescription and was not technically a tobacco product.[56] An example noted details such as distributor agreements, attempts to obtain FDA approval for new products, and the history of and research on nicotine nasal spray, indicating that the industry viewed these products, from a business perspective, as comparable to their cigarette brands.[56]

2009–2016

In 2009, the FDA began regulating nontherapeutic tobacco products under the Family Smoking Prevention and Tobacco Control Act. This new law meant tobacco companies could focus on developing and marketing alternative tobacco and nicotine delivery products without triggering FDA authority to regulate cigarettes. In 2008 RJR acquired Niconovum, the Swedish producer of Zonnic nicotine gum, as an avenue into the NRT market. RJR began test marketing it in Des Moines, Iowa, and Omaha, Nebraska.[4] The goals of this product expansion were described in an internal planning document describing RJR's product development project Craving Relief:

> Objectives:
>
> - Develop a new nicotine replacement gum for cessation to state of market launch readiness
> - Use learning from NRT development to develop a superior Craving Relief [nicotine delivery] product to branded readiness for FDA evaluation
> - Use learning from CR [Craving Relief] product development to establish development project for enhanced next-generation CR product.[57]

RJR compared the use of NRT to its "traditional moist, snus, and dissolvables"[57] smokeless tobacco product lines:

> Preliminary data indicate that about 15% of smokers use NRT off label for situational coping—not for cessation. . . . It is plausible that current NRT manufacturers have already conducted the necessary research to gain approval for the reclassification of the gum and lozenge products for unlimited extended use. . . . The primary goal is to develop a superior Craving Relief product to successfully compete in what is expected to be a large and growing CR category.[57]

RJR planned to develop a preliminary business case for new Craving Relief products of its own that addressed product options, market volume, profit estimates, and brand development.[57]

In 2012, Altria (Philip Morris) developed the nicotine lozenge Verve with the expectation that it would not be subject to the same restrictions as traditional tobacco products. Philip Morris believed it could market Verve without FDA-mandated warning labels because it contained nicotine extracted from tobacco, rather than whole tobacco, which it argued was not a cancer risk.[58] As of 2016, Verve products were marketed only in Virginia.[5,6]

DISCUSSION

Major tobacco companies in the United States and the United Kingdom viewed NRT, even when it was only available by prescription, as a recreational product that could maintain and possibly expand the use of nicotine as smoking became less socially acceptable. Although NRT was approved for cessation, tobacco industry research found in the early 1990s that many smokers used it in combination with cigarettes and that smokers who used NRT for cessation would otherwise have quit outright.[49–51,53,54]

In the 21st century, medical research began to find similar results. The majority of smokers who receive prescription NRT receive counseling on how to use the medication.[59] Initial clinical trials suggesting comparable effectiveness for OTC NRT relied on simulated OTC use rather than real-world OTC use.[11–16] Follow-up population studies of OTC NRT showed it did not improve—and could impede—cessation, without an organized cessation program.[8,9,17,18] Outside of monitored settings, NRT is often used for shorter periods than recommended and not combined with behavioral counseling.[10] These findings are consistent even among individuals motivated to quit: a follow-up study of participants enrolled in a clinical trial of nicotine patch users found that after 8 years, there was no statistically significant difference in abstinence for patch users than nonusers.[60] Moreover, smokers who used over-the-counter NRT were significantly less likely to quit than were smokers who did not use any cessation aids.[8,9]

Tobacco companies expressed interest in developing and marketing alternative products containing nicotine as early as the 1950s, but they were concerned about marketing them because doing so could lead to FDA regulation. In 2009, following new FDA regulation of cigarettes, tobacco companies began selling the alternative nicotine products they had first proposed decades earlier.[61] In 2014, RJ Reynolds Tobacco began selling its nicotine gum, Zonnic, throughout the United States. Internally, RJR classified Zonnic with its e-cigarette brand Vuse, considering both products to be part of its "quest toward becoming a 'total tobacco company.'"[4] Reflecting this ambition, marketing in 2015 for Zonnic suggested that smokers could use it with cigarettes: "Quitting doesn't have to feel like all or nothing."[61] This marketing is consistent with tobacco industry research that found many smokers used NRT in combination with cigarettes instead of as a means to quit smoking. Philip Morris began marketing nicotine lozenges in 2016.[5,6]

Limitations

The tobacco industry documents provide incomplete information about corporate activity.

In particular, our efforts to study recent tobacco industry development of NRT products was challenging because some potentially relevant documents were marked as privileged legal communication. Cigarette companies use attorney–client privilege as a strategy to avoid making internal documents public.[62,63]

Conclusions

Although NRT is marketed as a cessation aid, the tobacco industry has been aware since the 1990s that it is unlikely to increase quitting. Although pharmaceutical industry studies of NRT use in clinical trials showed it increased quit attempts, these results appear to have been driven in part by the monitoring inherent to trials themselves; multiple studies show that adherence

rates are higher in clinical trials than in real-world practice.[64–71] Medical research in the 21st century on population use of NRT has found results similar to those identified by the tobacco industry: NRT can expand nicotine use while maintaining smoking rates.

Tobacco industry research from the 1970s forward treated all products containing nicotine—including cigarettes, e-cigarettes and their precursors, and others (e.g., gums, patches, and candy)—as part of a single market: the nicotine delivery, or Craving Relief market. Industry marketing anticipates that noncigarette nicotine delivery products will be used by smokers for whom smoking is unacceptable, thus facilitating and normalizing lifelong nicotine addiction. These findings suggest that the least harmful way to sell nicotine delivery products is to restrict them to smokers whose quit attempts are medically supervised, consistent with the original studies of NRT for smoking cessation.[7] AJPH

CONTRIBUTORS

D. Apollonio conceptualized the study, did the primary data collection, and prepared the first draft of the essay. S. A. Glantz revised the essay. Both authors revised the essay in accordance with the reviewers' comments.

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HUMAN PARTICIPANT PROTECTION

No protocol approval was necessary because no human participants were involved in this study.

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