

Comments on Nicotine Replacement Therapies from the American Association for Cancer Research (AACR)

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- The American Association for Cancer Research (AACR), with over 37,000 members, is the oldest and largest scientific organization in the world dedicated to the prevention and cure of cancer through research, education, communication, and collaboration.

AACR Tobacco and Cancer Subcommittee

The AACR Tobacco and Cancer Subcommittee was convened in 2009 to foster scientific and policy initiatives to reduce the incidence of disease and mortality due to tobacco use.

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Outline

- Improving NRT
- Additional indications for NRT
- Labeling

Need for Improving NRT

- Historically, the approval of medicinal nicotine and other smoking cessation products has been rigorous and regulations restrictive.
- Efforts were made to minimize the abuse liability and appeal of medicinal products to prevent uptake among tobacco naïve individuals and sustained use among consumers.
- These efforts may have also minimized the uptake and possibly the efficacy of these products.

Need for Improving NRT

- Prior studies have shown that products with higher nicotine content are associated with greater substitution for cigarettes¹⁻³ and sensory aspects of smoking can provide positive and negative reinforcement.⁴
- Electronic nicotine delivery systems (ENDS) have the capability of delivering higher levels of nicotine and provide the sensory aspects of smoking.
- Compared to NRT, ENDS have greater appeal and lead to greater substitution for cigarettes⁵⁻⁸ and, more recently, have exhibited greater uptake for the purposes of smoking cessation.⁹
- A few clinical trials and epidemiological studies have suggested that ENDS can be an effective smoking cessation tool,¹⁰⁻¹² especially with frequent use,¹³⁻¹⁶ yet major impediments for conducting such trials exist in the U.S.

- A path to readily allow independent investigators to test ENDS products for smoking cessation should be considered.
- Evidence for the safety and efficacy of a medication for smoking cessation should be imperative.
- Safety should be determined relative to continued cigarette smoking.
- Randomized clinical trials should be conducted to determine the uptake and efficacy of the novel medication as compared to currently available nicotine replacement therapies.
- Consumer perception of the marketing and product itself among tobacco naïve individuals should be conducted to determine ways to minimize uptake in this population.
- Post-marketing surveillance must be in place.

Additional Indications for NRT

- Combination NRT medications
 - Studies show that combination medications are safe and more effective than monotherapy.²⁰⁻²¹
 - Recommendation for use of short-acting and long-acting medications have been made by:
 1. Cochrane report²
 2. The U.S. Department of Health and Human Services Guideline for Tobacco Use and Dependence¹
 3. National Comprehensive Cancer Network²²

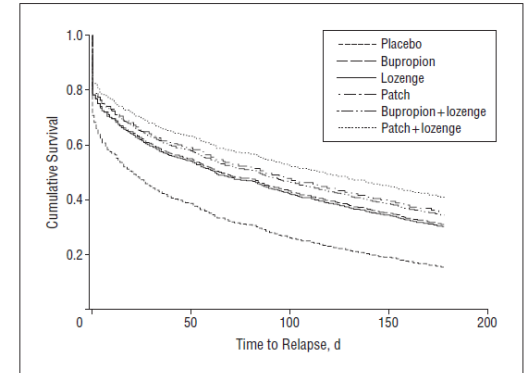


Figure 3. Survival curves for latency to relapse, or the number of days until the participants smoked on 7 consecutive days following the target quit day for the 6 treatment conditions.

Piper et al.²¹

Additional Indications for NRT to Consider

- Long term use of NRT for harm reduction - use of NRT to completely substitute for cigarettes in order to reduce harm to health:
 - Some smokers find it difficult to quit using nicotine-containing products.
 - Swedish experience with snus supports the use of non-combusted product to reduce mortality and morbidity.¹⁷⁻¹⁹

Table 2 Ratios of death rates attributable to tobacco

Age group	Cause of death		
	All causes	Lung cancer	All cardiovascular
45-59	0.15	0.24	0.13
60-69	0.27	0.38	0.19
70-79	0.42	0.49	0.33

Men in Sweden vs. men in Europe as a whole 2004. Ramstrom & Wikmans¹⁸

Daily tobacco use by Swedish males, ages 16-84, 2016

Tobacco type	Prevalence (%)
Smoking only	7
Snus only	17
Smoking + snus (dual use)	1
Any tobacco use	25

Source: Public Health Agency of Sweden

- Nicotine replacement products are substantially less toxic than snus.
- The AACR is not recommending cigarette reduction as a harm reduction approach.

Additional Indications for NRT to Consider

- Long term use of NRT for cessation
 - Need to frame nicotine addiction as a medical condition that may warrant more long-term treatment
 - Psychiatric disorders involve long-term medication treatment
 - Extended duration of NRT might increase quit rates and recovery from smoking relapse in some smokers^{1-2,20}

Additional Indications for NRT to Consider

- Pre-quit NRT use
 - Reduce to quit
 - Not all smokers are ready to quit smoking.
 - Almost half planning to quit in next 12 months were interested in gradual reduction.²⁴
 - Reducing to quit with NRT is more effective than placebo.²⁰
 - Reduce to quit results in comparable quit rates as abrupt cessation.²⁶

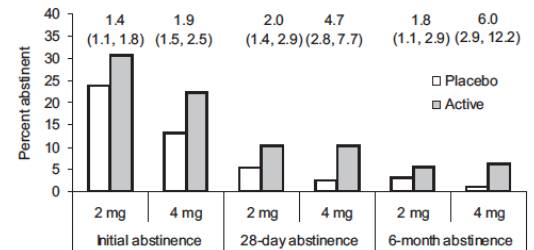
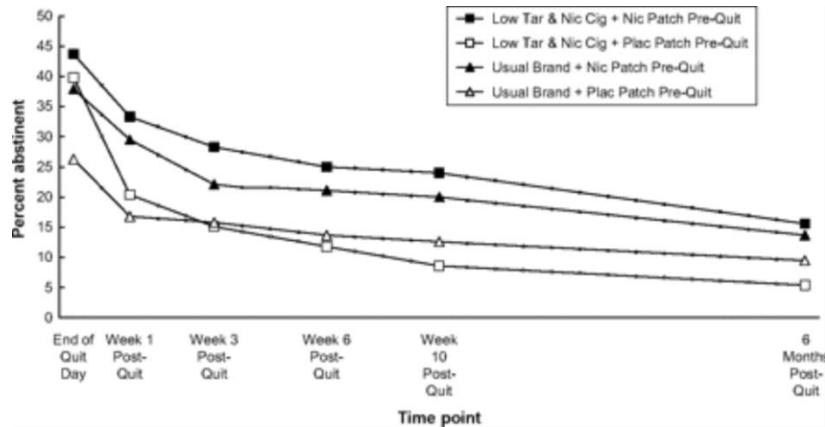


Figure 2. Initial abstinence percentages and 28-day and 6-month continuous smoking cessation percentages, by treatment and dose group. Figures above each set of bars represent the OR for active treatment versus placebo, and its 95% CI.

Additional Indications for NRT to Consider

- Pre-quit NRT use
 - Preloading, particularly with nicotine patch, might increase abstinence success.^{2,20,23}



Rose et al.²³

Product Labeling and Reduced Risk Claim

- “Nicotine replacement therapy is substantially less harmful to health than cigarette smoking”
 - There are significant misperceptions or lack of knowledge of harm of nicotine and NRT in smokers²⁷⁻³⁰ and healthcare providers.³¹⁻³²
 - Misperceptions have been associated with reduced uptake and optimal use of NRT.²⁷
 - Reduced optimal NRT use results in less efficacy.

Summary

- Improve appeal and nicotine delivery of NRT to increase uptake and efficacy
- Approve NRT for combination treatments (short plus long-acting NRT)
- Consider approval for:
 1. harm reduction
 2. extended use
 3. reduce to quit and pre-quit
- Add claim on package to clarify misperceptions of the relative harm or harm of NRT

For questions, please contact Nicole Boschi, PhD, Senior Science Policy Analyst, at 215-446-7275 or nicole.boschi@aacr.org

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