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Short communication

Use of nicotine replacement therapy among never smokers in the 1999–2006 National Health and Nutrition Examination Surveys

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Abstract

Nicotine replacement therapies (NRT) have been available without a prescription in the United States since 1996. Given that nicotine, at least as it is delivered through tobacco products, is addictive, we examined whether NRT was being used by individuals who have never smoked cigarettes. Adults ($n = 18{,}986$) and adolescents ($n = 9187$) who participated in the in-home survey and physical examination components of the 1999–2006 National Health and Nutrition Examination Surveys were assessed for cigarette smoking status, other tobacco use or exposure, and use of NRT. Among the 8415 adults (ages 20 and older) who reported never having smoked 100 cigarettes and who provided a blood sample during their physical exam, 3 (0.08%; 95% CI = 0.02–0.28%) reported using NRT within the 5 days prior to being examined. Among the 5510 adolescents (aged 12–19 years) who reported never smoking and who provided a blood sample, 5 (0.12%; 95% CI = 0.04%–0.36%) reported using NRT. Analyses of cotinine (a metabolite of nicotine) from their blood samples, along with analysis of their other survey responses regarding additional nicotine exposures suggest that it is unlikely that any of the adults were never smokers using NRT and perhaps 2 adolescents may have been never smokers who used NRT. Based on these assessments, the re-estimated prevalence of NRT use by never smokers would be 0% among adults and 0.05% (95% CI = 0.01–0.27%) among adolescents.

Keywords: Cotinine; Nicotine replacement therapy; Smoking

1. Introduction

More than 45 million adults in the United States (U.S.) currently smoke cigarettes, and about 40% reported attempting to quit smoking in 2005 (Centers for Disease Control and Prevention, 2006a). Nicotine replacement therapy (NRT) is a class of medication developed to assist smokers in quitting. Nicotine gum and patch have been available without a prescription in the U.S. since 1996 (Centers for Disease Control and Prevention, 2000a). Given the wider availability of NRT and the addictiveness of nicotine, at least as it is delivered via tobacco products, there has been concern about persistent use of or dependence on NRT products (Shiffman and Sweeney, 2008). Among smokers, about 6% who use nicotine gum for quitting used it for longer than 6 months, and less than 2% used nicotine patches for more than 6 months (Shiffman et al., 2003a,b). Hughes et al. (2004) estimated that only 0.7–1.4% of all nicotine gum users would transfer their nicotine dependence to the nicotine in the gum.

Two studies have noted use of NRT by nonsmokers. Klesges and colleagues (2003) administered a school survey in Memphis, Tennessee and found that less than 2 percent of nonsmokers reported ever using NRT. Etter (2007) reported that a solicitation on a number of Internet sites drew reports from 5 persons claiming to be nonsmokers who used nicotine gum daily. However, respondents' reports could not be verified, and the survey method (volunteer respondents who happened to find the website with the survey) did not allow for an estimation of the prevalence of NRT use among nonsmokers. However, both reports raise concern about NRT use by nonsmokers.

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Although it is unlikely that use of NRT by nonsmokers would exert significant harm, use by nonsmokers is inappropriate and raises concern that, once exposed to nicotine, the nonsmoker might turn to smoking or other forms of tobacco to obtain higher doses of nicotine. We sought to examine the use of NRT products by adult and adolescent never smokers in a nationally representative survey that included biochemical indicators of nicotine exposure against which to compare reports of nonsmoking and NRT use. We analyzed data from the National Health and Nutrition Examination Survey (NHANES) (Centers for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS), 2000b, 2002, 2004, 2006b) for the years 1999–2006. NHANES is a written survey conducted in the home that is followed by a physical examination conducted in mobile examination centers (93% of adults participated in both for 1999–2006 as did 97% of adolescents). Participants who completed the physical examination were asked about their use of tobacco and NRT products in the 5 days prior to their examination.

Blood samples drawn during the examination were analyzed for cotinine, a metabolite of nicotine. Cotinine has a half-life in serum of approximately 17 h (Tutka et al., 2005), which makes it suitable for assessing nicotine exposure over the past several days. We sought to use the observed cotinine levels to substantiate reports of nonsmoking and NRT use. Cotinine values can vary by smoking status, by amount smoked, by use of other tobacco products, by exposure to secondhand smoke, and by the use of NRT. Individuals with no exposure to nicotine would be expected to have non-detectable cotinine levels. Adult nonsmokers exposed to secondhand smoke at home and/or at work had mean serum cotinine levels between 0.32 and 0.93 ng/mL in NHANES III, which was conducted between 1988 and 1991 (Pirkle et al., 1996). Plasma cotinine levels above 10–15 ng/mL have been considered to indicate active smoking (Caraballo et al., 2001; Pirkle et al., 2006). Levels averaged 78 ng/mL among adults who smoked fewer than 10 cigarettes per day, and 301 ng/mL among those smoking more (Wall et al., 1988). In a group smoking 22 cigarettes per day, Benowitz and Jacob (1994) observed levels that remained above 200 ng/mL. Adolescents who smoked lightly in the previous 4 days demonstrated mean levels of 24 ng/mL in saliva (Rubinstein et al., 2007). Continuous use of nicotine gum for 5 days was associated with average plasma levels of 33 ng/mL (Oncken et al., 1996), and use of nicotine patches (15 and 25 mg) for cessation resulted in levels between 110 and 155 ng/mL after 12 weeks of treatment among abstinent smokers (Paoletti et al., 1996). Thus, while cotinine levels due to various exposures to tobacco or NRT products overlap, they do help discriminate among degrees of nicotine exposure.

2. Methods

We analyzed data from 4 waves of NHANES (1999–2000, 2001–2002, 2003–2004, and 2005–2006). Adults (20 years old or older) who denied smoking at least 100 cigarettes in their lifetime were considered never smokers. Adolescents (12–19 years old) who denied ever smoking a whole cigarette were considered never smokers. All respondents who participated in the physical examination were asked if they had used any tobacco products or NRT products in the 5 days prior to their exam. Those who responded "yes" were asked which tobacco products had been used, how much of each, how often in the past 5 days, and how long ago the products had been used. Questions regarding NRT use assessed how many days in the past 5 days NRT was used and when it was last used. The type of NRT used (gum, patch, etc.) was not assessed. Data from the four surveys were combined, and analysis weights were created according to the NHANES Analytic and Reporting Guidelines (CDC, 2006c). Proportions and their associated confidence intervals were generated on weighted data using the SUDAAN software package (Research Triangle Institute, 2004).

3. Results

There were 18,986 adults (age 20+) and 9187 adolescents (12–19 years old) surveyed and physically examined in the 1999–2006 waves of the NHANES. Among the 8415 adults who reported never having smoked 100 cigarettes and for whom cotinine data were available, 3 (0.08%; 95% CI = 0.02–0.28%) reported using NRT within the 5 days prior to being examined. Among the 5510 adolescents who reported never smoking a whole cigarette and for whom cotinine data were available, 5 (0.12%; 95% CI = 0.04–0.36%) reported using NRT[1]. Detailed information on these 8 subjects is presented in Table 1.

Among the adults, none of them had cotinine values consistent with their reported behaviors. The first adult, a male, had barely detectable cotinine (0.035 ng/mL), indicative of little, if any, exposure to a nicotine-containing substance; these levels are below those associated with passive smoke exposure. The second male had cotinine consistent with substantial smoking or smokeless tobacco use (583.0 ng/mL) but unlikely to result from NRT use. The third adult, a female, had cotinine in the range of what would be expected from patch use (117.52 ng/mL), but she reported smoking the day prior to her exam, and was diagnosed with chronic bronchitis, which is prevalent among smokers (Cerveri et al., 2001). It is likely that she is a smoker.

There were 2 of 5 adolescents whose cotinine levels provided some support for their reported NRT use. The first was a 13 year old who had a cotinine level of 12.60 ng/mL. The second was a 17 year old with a cotinine of 2.32 ng/mL. Missing or contradictory data from these 2 respondents regarding how often NRT was used or when it was last used reduce the ability to further assess the validity of their reports of use.

The reported use of NRT by the other 3 adolescents was not supported by their cotinine levels. The 14 year old had a level too low (0.03 ng/mL) to be consistent with the reported NRT use. The two 18 year olds had levels higher than would be expected from just NRT exposure, and, in fact, one reported substantial use of smokeless tobacco and cigar smoking.

4. Discussion

The findings from this analysis of multiple years of national data indicate that use of NRT among never smokers was very rare. Among adults, the prevalence estimated purely from

[1] There was only one nonsmoker (an adolescent male) who claimed to have used NRT but for whom cotinine data were not available. This participant was excluded from all analyses.

Table 1
Subjects who reported never smoking cigarettes and recent use of Nicotine Replacement Therapy (NRT) National Health and Nutrition Examination Survey (1999–2006)

	Adults			Adolescents				
Subject #	5214	27693	8109	24833	38165	4219	13267	9871
Survey year	1999–2000	2003–2004	1999–2000	2003–2004	2005–2006	1999–2000	2001–2002	1999–2000
Age	21	32	47	13	14	17	18	18
Gender	Male	Male	Female	Male	Male	Male	Male	Male
Race/ethnicity	Other hispanic	Non-hispanic white	Non-hispanic white	Non-hispanic white	Mexican American	Non-hispanic black	Non-hispanic black	Non-hispanic white
Nicotine exposures reported								
NRT use	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Duration of NRT use and day of most recent use	**Used all 5 of past 5 days**	Used 4 of last 5 days; last used 1 day prior to exam	Used all 5 of past 5 days	No information on number of days used; last used 3–5 days prior to exam	Used on 1 day; last used 3–5 days prior to exam	Used on all of the past 5 days but reports last used 3–5 days prior to exam	Used on 1 day; last used 3–5 days prior to exam	Used on 3 of the past 5 days; last used 1 day before the exam
Cigarette smoking	No	No	**Yes**	No	No	No	No	No
Amount of cigarette smoking and when last used	n/a	n/a	Smoked 3 cigarettes the day prior to exam	n/a	n/a	n/a	n/a	n/a
Smokeless tobacco use	No	No	No	No	No	No	No	**Yes**
Amount of smokeless tobacco use and when last used	n/a	n/a	n/a	n/a	n/a	n/a	n/a	Used 2 of the past 5 days and last use was 1 day before the exam
Cigar smoking	No	No	No	No	No	No	No	**Yes**
Amount of cigar smoking and when last used	n/a	n/a	n/a	n/a	n/a	n/a	n/a	Smoked 6 cigars in the 5 days prior to the exam and last use was 1 day before the exam
Does anyone smoke in the home?	No	No	No	No	No	No	Yes	No
Plasma cotinine (ng/mL)	**0.035**	**583.00**	117.52	12.60	**0.03**	2.32	**58.60**	416.16
Interpretation of cotinine based on all information provided	Too low for reported NRT use, below values associated even with passive exposure to cigarette smoke	More consistent with substantial smoking or smokeless tobacco use than with reported NRT use	Consistent with use of nicotine patch; subject's report of smoking and chronic bronchitis suggest this is likely a smoker	Possibly consistent with NRT use and/or smoking; missing data on days of use prevents more definitive interpretation	Too low for reported NRT use, below values associated even with passive exposure to cigarette smoke	Consistent with low level nicotine exposure; contradictory information provided on NRT use prevents more definitive interpretation	Consistent with tobacco use, too high for NRT use 3–5 days before	Consistent with subject's reported use of smokeless tobacco and cigars

Note: Items in bold highlight information of particular importance in evaluating the respondent's report of being a never smoker using NRT; see text.

self-report was 0.08%; among adolescents, it was 0.12%. Examination of other self-reported data, and objective data from serum cotinine levels, suggested that some of the reports of smoking status and/or NRT use were in error: some of the "never smokers" reported recent smoking or tobacco use, and others demonstrated cotinine levels inconsistent with their self-reported behaviors. Thus, it seems likely that the true prevalence of NRT use among never smokers is lower than estimated from self-report. Indeed, only two individuals' reports of using NRT while being a never smoker were consistent with their other survey and examination data. Re-estimated on this basis, the prevalence among adults would be 0% and the prevalence among adolescents would be 0.05% (95% CI = 0.01–0.27%).

These findings are somewhat consistent with the only other reports of NRT use in nonsmokers. Klesges et al. (2003) reported prevalence of ever use by never smoking adolescents of 1.7% in a school-based survey conducted in one city; the reports were unverified. Etter (2007) collected self-reports of use from 5 individuals via an Internet survey, but there was no valid denominator against which prevalence could be assessed, and no biochemical validation. The present study has some important elements that the previous two studies did not have. The survey upon which the findings are based is representative of the U.S. population (both youth and adults) and so allows for the estimation of population prevalence of NRT use. It also provides an objective measure of nicotine exposure against which to assess reports of use.

The finding that nonsmokers do not take up use of NRT is consistent with studies showing that the abuse liability of NRT products is very low (Henningfield and Keenan, 1993; Houtsmuller et al., 2002). Those studies showed that smoking, which rapidly delivers nicotine to the brain, demonstrates abuse and addiction potential, while NRT products did not. With wide availability and affordability of cigarettes in the U.S., there would be little incentive for nonsmokers to take up use of NRT.

There are some limitations to this study. First, the data on smoking status and NRT use were based on self-reported information, which is subject to misreporting, whether in error or deliberately. As discussed, many self-reports were contradicted by the observed cotinine values. Second, we examined only self-reported nonsmokers who reported using NRT. It is conceivable that some respondents who self-reported that they smoked were, in fact, nonsmokers; however, misclassification of a nonsmoker as a smoker is less likely, given the social undesirability of smoking. Further, NHANES only assessed NRT use during the 5 days preceding the physical exam, so earlier use would have been missed. However, regular or ongoing use would have been observed. Finally, cotinine values do not provide perfect validation of self-reports of smoking or NRT use, though they did provide unambiguous contradiction of self-reports in some cases.

The availability of over-the-counter NRT products to assist smokers in quitting has greatly increased their use by smokers attempting to quit (Hyland et al., 2005; Reed et al., 2005). The NHANES data suggest that this increase in appropriate use has not been accompanied by misuse by nonsmokers, which was very rare.

Conflict of interest

All authors serve as consultants to GlaxoSmithKline Consumer Healthcare (GSKCH) on an exclusive basis regarding matters relating to smoking cessation. Dr. Shiffman and Mr. Gitchell also have a financial interest in a venture to develop a new nicotine replacement medication.

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Contributors: Dr. Shiffman and Mr. Gitchell conceived of this study and provided significant guidance in the drafting and interpretation of the results. Dr. Gerlach wrote the manuscript, and Mr. Rohay conducted all the statistical analyses. All authors have approved the final manuscript.

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