BURNING Issues
TRDRP Newsletter
Special Edition, November 2003

# To Patch or Not to Patch

*by Phillip Gardiner, Dr. P.H.*

## A Three Tiered Controversy

The clinical efficacy of Nicotine Replacement Therapy (NRT) has been documented by many researchers.[1,2,3] However, the actual public health effectiveness of these products purchased over the counter (OTC) for long-term smoking cessation was called into question by John Pierce and Elizabeth Gilpin's 2002 article in the Journal of the American Medical Association, "Impact of the Over the Counter Sales on Effectiveness of Pharmaceutical Aids for Smoking Cessation."[4] The author's conclusions: "In 1999, although collectively pharmaceutical aids helped moderate to heavy smokers discontinue using cigarettes longer, they were not associated with a clinically meaningful long-term improvement in successful cessation, and no benefit was observed for light smokers," created much controversy among tobacco cessation scientists.[4] Moreover, the press release that accompanied the article sensationalized and potentially distorted the findings.[5] To further complicate matters, a scientist with an advance copy of the article posted it on the Society for Research on Nicotine and Tobacco (SRNT) listserve, prior to the lifting of the embargo, and without the author's permission, generating in and of itself another controversy. Below, I review the conclusions of the Pierce/Glipin article; the methodological concerns voiced by other scientists responding on the SRNT listserve; the assertions of the University of California San Diego press release; and the issues involved in skirting the embargo.

**AIM 2003**
**8th Annual Investigator Meeting**

**Is over the counter (OTC) nicotine replacement therapy (NRT) effective for tobacco use cessation?**

**Attend TRDRP's Town Hall Meeting on Thursday, December 4th and lend your voice to this important discussion, details on back.**

## Long-Term Effectiveness?

The Pierce/Gilpin study, funded by the Tobacco Related Disease Research Program (TRDRP), was based on the California Tobacco Surveys (CTS). These surveys were conducted over the telephone and were based on respondent recall. Data were collected in 1992, 1996 and 1999, including 5247 (71.3% response rate), 9725 (72.9% response rate), and 6412 (68.4% response rate) respondents, respectively.[4] The authors stated in their method section that "because this is not a randomized study, individuals who choose to use a pharmaceutical aid likely differ from nonusers." They also noted that the surveys themselves were not exclusively designed to measure cessation aid use by smokers.[4]

Results showed that cessation attempts lasting a day or longer were up from 38.1% in 1992 to 61.5% in 1999, an increase of 61.4% in the 7-year period. Additionally, during smokers' most recent cessation attempt, use of assistance (self-help, counseling, NRT, or in 1999 an anti-depressant) rose from 18.4% in 1992 to 19.3% in 1996 to 22.1% in 1999, the latter increase from 1996 to 1999 being statistically significant. Also, one-on-one counseling and use of self-help materials was up during the 7 years the study covered.[4]

NRT use itself was up from 9.3% in 1992 to 14.0% in 1999, an increase of 50% ($p<.001$). The authors make the conservative estimate that 116,209 Californians used NRT in 1992, and that this figure rose to 423,290 in 1999, a 3.6-fold growth. It is important to note that even though the number of people using NRT was up, the duration of use was not statistically different between 1992 and 1999. Furthermore, the duration of use was related to payment mode; those smokers whose insurance covered NRT used it 6 weeks longer than smokers who had a co-pay or who had to pay for treatment on their own.[4]

While NRT use was up, it seems effectiveness was down. The authors report that "in contrast to with 1992 and 1996, the effect in 1999 was only short-term," lasting approximately 3 months. Regression analysis showed virtually no difference between those using NRT and those smokers not using any aid at all. As stated above, although collectively pharmaceuticals helped moderate to heavy smokers to quit for a while, still there was no "clinically meaningful long-term improvement in successful cessation." The authors suggest that the reason for this finding was that in 1992 and 1996, NRT was only available by prescription from a doctor and that "physicians or pharmacists

may have provided counseling about product use." Counseling, for the most part, was not required for smokers who in 1999 purchased NRT OTC.[4]

## Flaws in the Study?

As soon as this study was made public, serious questions about the methodology and conclusions were raised. Clive Bates, Director of Action on Smoking and Health (ASH) based in London, listed a series of concerns on the SRNT listserve that he and other tobacco control advocates and smoking cessation scientists had identified. First, reliance on memory and self-reported data was insufficient for Pierce and Gilpin's "heroic assumptions and sweeping generalizations." Second, "retrospective self-reports of quitting like these are biased and tend to suffer from a marked recency effect." Third, the absence of a control group was identified as a particularly problematic feature of the study. "We just don't know how comparable the NRT users are with the non-users – controlling for smoking rate is not really enough." Fourth, "People are more likely to remember salient quit efforts – e.g., those where they spent big bucks buying an NRT product, or those that were fairly serious or long-lived. Short, unaided, unsuccessful efforts seem less likely to be remembered."[6]

The following quote may best sum up the concerns voiced by many scientists concerning this study: "We have to be very wary of letting one survey of this sort, somehow negate over 100 controlled trials on NRT showing good effectiveness - though not that many in OTC use. It's always good to challenge the evidence base, but it is a mistake to jump to hastily to conclusions based on one result when there are so many possible explanations for the results measured in California."[6]

Not all responding on this topic concurred with the concerns and criticisms mentioned above. David Antonuccio, Director of the Stop Smoking Program at the Veteran's Administration in Reno Nevada, stated that "the data from the Pierce and Gilpin (2002) ARE consistent with the few prior MINIMAL INTERVENTION [upper case in the original] efficacy studies using the patch (e.g., Foulds et al., 1993; Jorenby et al., 1999; Joseph et al., 1996."[7] Moreover, in a sample of 600 cardiac patients who were smokers, the patch was found to be no more effective than placebo; "at 48 weeks follow-up, 10% of patients in the active patch condition were abstinent while 12% in the placebo were abstinent."[8] It has also been pointed out that it is difficult to interpret the efficacy of NRT independently of behavioral regiments, since the majority of published studies include some form of behavioral intervention.[9]

## UCSD Press Fans the Flames

The Pierce/Gilpin article made some strong statements concerning OTC NRT and at the same time pointed out some of the shortcomings in the study methods. On the other hand, the UCSD press release was quite a bit less balanced, going for sensation value and in the process exaggerating the study's findings. Many tobacco cessation re-searchers were left with a bad taste in their mouths. While the press release headline, "OTC sales of smoking cessation aids up, effectiveness down. . ." was not in and of itself bad, the take home message from the lead sentence essentially fanned the fire: "Cancer re-searchers at the University of California, San Diego (UCSD) School of Medicine report in the September 11 issue of the Journal of the American Medical Association that nicotine replacement therapies (NRT) such as the nicotine patch and nicotine gum are *no longer effective in helping smokers quit* (my emphasis) for the long term. They cite over-the-counter availability of these products starting in mid-1996 as the turning point."[5]

Many were just as outraged by the press-release as by the Pierce/Gilpin study, itself. Clive Bate's irritation is clear: "[the quote above] is designed to lead the story and be the take-home message. . . one of the main drugs in use in the treatment of tobacco dependence does not work. Period. Delivered as a bolt of lightening from the Mount Olympus of tobacco control California, and straight to thousands of journalists world wide."[10]

"UCSD crossed the line from scientific discourse to the much more adversarial arena of public opinion with this press release . . . I can only conclude that they are trying to get a complete repudiation of the evidence base on NRT into the headlines."[10]

"The press release - either by accident or design - is formulated to create mayhem and is a gift to many of tobacco control's critics. To argue that this should be addressed by a few letters to JAMA that will be published in 3 months while the news today might actually put smokers, health care providers and governments off NRT altogether is frankly laughable."[10]

The strong reaction to this press release may have been muted if the sentence that the press release ends with was instead the opening sentence introducing the public to the study's findings: "The researchers write that this study highlights the need for more research nationwide concerning the barriers to more appropriate use of NRT, and they suggest that NRTs should be used in combination with other types of smoking-cessation assistance, such as behavioralcounseling."[5] But then, perhaps this more balanced assessment would not have been so newsworthy.

## Posting Prior to Lifting the Embargo: Egregious or Necessary?

Not only were the Pierce/Glipin findings controversial and the UCSD press release overstated, but both were posted on the Society for Research on Nicotine and Tobacco (SRNT) prior to the lifting of the publishing embargo. Some felt that many in the tobacco cessation community would be "disoriented and challenged by journalists to respond, while the authors did little to give guidance on the implications of the article or to promote debate before hand."[10] On the other hand, John Pierce in response stated: "I gave everyone who reads SRNT and Globallink listserves a heads up on the paper and major results. I copied the full text of the article to numerous scientists . . . I made sure everyone knew of the embargo times . . . these data were part of a SRNT poster session at the last conference."[11]

Opinions on the appropriateness of posting this prior to the lifting of the embargo were all over the map. One respondent stated: "We need to grow up

and smell the coffee someone broke the article to help those who know how to use such information no bad intentions, just good old 'help thy neighbor."[12] Another commenter said: "the alleged sin here (unauthorized circulation of an embargoed article) is trivial when placed in the context of the potential sub-optimal response that experts might make when asked to comment in ignorance of an important paper's actual strengths and weaknesses. Let's be straight here: this paper HAS major potential to do huge damage to public confidence in NRT." [13]

On the other hand, another person stated that "From the point of view of a potential author myself, I think I would be quite distressed at the distribution of my embargoed article without my consent. . . . My consistent experience has been that when such a request is made [TV or media interview], the media person will fax me a copy of the article in question and, if there is one, the press release. If they do not offer it I ask for the material, not wanting to speak on something I have not read; it has not yet happened that they did not or could not provide it."[14]

Still another respondent pointed out that it is improper to distribute the full text of an article via a listserve or website without the publisher's permission, either before or after the lifting of an embargo.[15]

This topic excited some and incensed others; some felt it was necessary to break the embargo and post it on the website, others felt that this action was egregious. However, the SRNT Executive Committee had the last word and brought this part of the controversy to a close by stating unequivocally that: "The Society for Research on Nicotine and Tobacco respects and supports copyright protections and the embargo policies of other journals, and the Society prohibits the use of its listserv or website for postings or electronic links that violate copyright protections and journal embargo policies. However, free and open discussion of scientific issues is a major goal of our Society and this policy is in no way intended to discourage such discussion."[16]

## Much Ado About Nothing?

Stepping back from this multi-tiered issue, it seems clear in hindsight that much of the rancor produced was created by the UCSD press release. The sound bite that NRT was "no longer effective" failed to grasp the complexity of the issue and ultimately was misleading. Crafting the perfect sound bite, in this case, did more to obscure the important and thorny issues addressed by the Pierce/Gilpin article, than to illuminate them. The concerns voiced by members of the SRNT listserve about the Pierce/Gilpin article should not be dismissed lightly. However, in all the hoopla that has surrounded this article many have failed to take a very important and salient fact into account: Nowhere in the article do the authors call for practitioners to stop prescribing or for consumers to stop buying OTC NRT for smoking cessation. As the authors say themselves, "The present study highlights the need for more research nationwide concerning barriers to more appropriate use of NRT in the nonclinical setting."[4] The call for more appropriate use is a far cry from calling on people to stop using OTC NRT.

While there may be some methodological shortcomings with the study, the fact that literally thousands of people taking OTC NRT for smoking cessation are only showing short term results, the same as those who used no support at all, should give all in the field pause. Even if the NRT users are not comparable to non-NRT users, it still is vitally important that we understand why thousands of people were not successful in quitting using OTC products. Additionally, it has been pointed out by numerous people that we should not place all our eggs in the basket of one study. If the findings of the Pierce/Gilpin study are true, then certainly these results will be replicable in other specifically designed studies. Indeed, further research is what the authors themselves have called for.

John Pierce and Betsy Gilpin are not the only scientists to find some shortcomings in OTC NRT. David Antonuccio stated that: "My read on all of this is that slapping on a patch by itself without any behavioral intervention just doesn't work very well, no more than detoxing an alcoholic with IV alcohol, in the absence of strategies to change drinking behavior, would work."[7]

The real take home message, I believe, is that addiction to smoking will not necessarily be overcome by just taking a pill or slapping on a patch. Larry Williams put it thusly: "Does it surprise me that the effect of NRT may be lost – no. The US populace is always looking for the quick fix diet, brain booster, 1-minute abs, etc. What makes us think that those quick fixers won't try NRT and be disappointed? Simply stated, those that want to quit will (probably with NRT or placebo) and those that are looking for an effortless existence/quick fix will show no effect."[12]

*I would like to extend a special thank you to Beth Kipling of the SRNT Listserve for help in compiling the numerous emails that framed this debate.*

*References*

1. Hughes JR, Shiffman S, Callas P, Zhang J. "A meta-analysis of the efficacy of over-the-counter nicotine replacement." Tobacco Control, Mar; 12(1):21-7, 2003.
2. Hays JT, Croghan IT, Schroeder DR, Offord KP, Hurt RD, Wolter TD, Nides MA, Davidson M. "Over-the-counter nicotine patch therapy for smoking cessation: results from randomized, double-blind, placebo-controlled, and open label trials." American Journal of Public Health, Nov; 89(11):1701-7, 1999.
3. Shiffman S, Corsline J, Gorodetzky CW. "Efficacy of over-the-counter nicotine patch." Nicotine & Tobacco Research, Nov; 4(4):477-83, 2002.
4. Pierce JP, Gilpin EA. "Impact of Over-the-Counter Sales on Effectiveness of Pharmaceutical Aids for Smoking Cessation." Journal of the American Medical Association, Sept;288(10), 1260-1264,2002.
5. Stringer N. "OTC sales of smoking cessation aids up, effectiveness down Moores UCSD Cancer Center study." University of California San Diego Press Release, September 10th, 2002.
6. Bates C. "Re: JAMA report on California NRT use – response." SRNT Listserve, September 10th, 2002.
7. Antonuccio D. "Pierce & Gilpin (2002)." SRNT Listserve, September 14th, 2002.
8. Joseph AM, Antonuccio D. "Lack of efficacy of transdermal nicotine in smoking cessation." New England Journal of Medicine, 341: 1157-1158, 1999.

*"Patch" continued from page 3*

See "Patch" page 4

Tobacco-Related Disease Research Program
University of California—Office of the President
300 Lakeside Drive, 6th Floor
Oakland, CA 94612-3550
1952

# AIM 2003 Special Edition

9. Klesges RC, Ward KD, DeBon M. "Smoking cessation: A successful behavioral/pharmacologic interface." Clinical Psychology Review, 16(6): 479-496, 1996.
10. Bates C. "Posting copyrighted material: J JAMA NRT paper." SRNT Listserve, September 11th, 2002.
11. Pierce J. "Posting copyrighted material: JAMA NRT paper." SRNT Listserve, September 11th, 2002.
12. Williams L. "JAMA art." SRNT Listserve, September 11th, 2002.
13. Chapman S. "Comments from Simon Chapman on embargo, copyright, etc." SRNT Listserve, September 12th, 2002.
14. Covey L."Re: Use of SRNT listserve to post embargoed material." SRNT Listserve, September 11th, 2002.
15. Davis R. "Posting copyrighted material: JAMA NRT paper." SRNT Listserve, September 10th, 2002.
16. Lando H. "Re: Use of listserve." SRNT Listserve, September 18th, 2002.

## TRDRP STAFF

**Acting Director**
***Charles L. Gruder, Ph.D.***

**Research Administrators**
***M.F. Bowen, Ph.D.***
Cancer and Pulmonary Disease

***Francisco Buchting, Ph.D.***
Epidemiology, Policy and Economic Sciences

***Phillip Gardiner, Dr.P.H.***
Social and Behavioral Sciences; Nicotine Dependence

***Kamlesh Asotra, Ph.D.***
Cardiovascular Disease and General Biomedical Sciences

**Administrative Staff**
Shana Amenaghawon
Jewel Charles
Carlin Colbert
Sharon L. Davis
Teresa E. Johnson
Jessica Ratcliff
Christine Tasto

## TRDRP 8TH ANNUAL INVESTIGATOR MEETING

**INVESTIGATE**
**TRANSLATE**
**DISSEMINATE**

***Research for a Healthier Tomorrow***

## AIM TOWN HALL MEETING

**Thursday, December 4, 12:30-2:20 PM**

### Nicotine Replacement Therapy

*To Patch or Not to Patch?*

***Moderator***

**Thomas Scott, Ph.D.**
Dean, College of Sciences, San Diego State University

***Featured Participants***

**John Pierce, Ph.D.**
Professor, University of California, San Diego

**Betsy Gilpin, Ph.D.**
Director, Biostatistics Shared Resource
University of California, San Diego

**Saul Shiffman, Ph.D.**
Professor of Psychology, University of Pittsburgh
Principal, Pinney Associates

Is over the counter (OTC) nicotine replacement therapy (NRT) effective for tobacco use cessation? Do patches, gums, lozenges, inhalers, and/or anti-depressants work to promote smoking cessation? Drs. John Pierce and Betsy Gilpin have published data that question the effectiveness of OTC NRT. Dr. Saul Shiffman, on the other hand, maintains that NRT is clinically tested and proven to be an effective treatment for smoking cessation.

*WHAT DO YOU THINK?*

Join these researchers along with moderator Dr. Thomas Scott, Dean of the College of Sciences at San Diego State University and member of the TRDRP Scientific Advisory Committee, for a lively debate and discussion on the efficacy and/or effectiveness of NRT for smoking cessation.