Center for Regulatory Effectiveness (CRE) assessment of the following research report:

"Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns"

by:

Pebbles Fagan, Eric T. Moolchan, Alton Hart, Jr., Allison Rose, Deirdre Lawrence, Vicki L. Shavers, & James Todd Gibson

December 2010

References:

a. Research Report: "Nicotine dependence and quitting behaviors among menthol and non-menthol smokers with similar consumptive patterns" Society for the Study of Addiction, No. 105, Supplement 1, September 7, 2010, pp. 55-74, by Pebbles Fagan, et al.

b. Research Report: "Relationship between menthol cigarettes and smoking cessation among African American light smokers" Society for the Study of Addiction, No. 102, May 2007, pp. 1979-1986, by Dr. Kolawole S Okuyemi, et al.

c. National Cancer Institute website, www.cancer.gov

Background

On June 22, 2009, President Obama signed into law the Family Smoking Prevention and Tobacco Control Act, which gives the Food and Drug Administration the power to further regulate the tobacco industry. One element of the law imposes new warnings and labels on tobacco packaging, with the goal of discouraging minors and young adults from smoking. The bill bans flavored cigarettes, including cloves, cinnamon, candy, and fruit flavors, with a special exception for menthol cigarettes. There is a need to investigate possible health hazards of smoking menthol cigarettes as well as cessation (quitting) efforts.

The Tobacco Products Scientific Advisory Committee (TPSAC) provisioned under the bill is to submit a recommendation on menthol cigarettes to the United States Secretary of Health and Human Services no later than March 23, 2012. The intent of this CRE assessment is to consider the merits and shortfalls of the study as well as present the reader with topics for further discussion and investigation.

The report at reference (a) was identified for review and public discussion due to its focus on smoking cessation rates among menthol smokers. The researchers presented the following primary results:
- Menthol smokers reported a mean of 13.05 compared with 15.01 cigarettes per day among non-menthol smokers;
- Among smokers consuming 6-10 cigarettes per day, menthol smokers were significantly more likely than non-menthol smokers to consume their first cigarette within 5 minutes after waking (odds ratio = 1.22, 95% confidence interval = 1.05, 1.43).

The researchers concluded "…that menthol smokers in the United States who report consuming 6-10 cigarettes per day, show greater signs of nicotine dependence than comparable non-menthol smokers." [p. 55]

The authors cite reference (b) findings as a motivator for further exploring the supposed association between light-smoking (less than 10 cigarettes per day) smokers and significantly lower quit rates. CRE would like to point out that reference (b) has been assessed as having significant shortfalls (i.e. disproportionate comparisons between menthol and non-menthol treatment and control groups; and the lack of accounting for no-show patients by week 26). See Okuyemi, 2007.

The CRE conducted a limited assessment which included a review of the referenced primary survey study, The Tobacco Use Supplements to the Current Population Surveys (TUS CPS). Under the Data [Information] Quality Act, the FDA is prohibited from using any information from a third-party, such as TPSAC, unless it meets the requirements of the DQA. CRE has reviewed the study by Fagan et al., and has identified the following shortcomings, which if valid after outside peer review, would deem it non-compliant with the DQA. CRE is requesting public comment for the material set forth herein.

Summary of Findings and Issues

Publicly available information partially supports the requirements of the Data [Information] Quality Act.

The reader should be advised that the research completed by Fagan, et al., is considered a secondary study, meaning that the analysis was conducted on data from previously completed surveys in 2003 and 2006/2007. The Tobacco Use Supplements to the Current Population Surveys (TUS CPS) is periodically administered by the U.S. Census Bureau. The surveys and selected analysis is available to the public at reference (c). The complete data is available to the public via an order request. The TUS CPS survey process and partial data analysis provided at the National Cancer Institute website was assessed as partially meeting the DQA objectives for quality, objectiveness, utility, and integrity.

Since the data was not directly available to the public, CRE was not able to independently check the statistical findings reported in the subject report.

The Design Experiment (use of the TUS CPS survey data) does not support the researcher's conclusions.

A significant shortfall in this study is that the researcher's conclusion and associated statements are not supported by the survey data. Specifically, the researchers conclude: "…menthol smokers …who report consuming 6-10 cigarettes per day, show greater signs of nicotine dependence than comparable non-menthol smokers." [p. 55] The researchers go on to state "[t]ime to first cigarette is associated significantly with cotinine levels and has higher predictability of nicotine uptake within the first five minutes after waking than other categorical measures." [p. 67] The TUS CPS data is strictly survey (qualitative) data and does not include measurement (quantitative) data. Indeed, the authors state the lack of measurement data (e.g. no biochemical measures, no menthol concentrations, etc.) as a limitation. [p. 67]

Are the statistical models valid?

Since the survey data was not available for an independent verification of the analysis, CRE checked the reported statistics. Inconsistencies in the results were found which leads to concerns regarding data quality and reliability.

For example, the researchers hypothesized that "…daily menthol smokers would report …fewer quit attempts compared with daily non-menthol smokers with similar smoking intensity." [p. 56] The researchers used "Odds Ratios" to report menthol smokers as being less likely to have quit attempts of one day or longer versus non-menthol smokers, in the 6-10 cigarettes per day category. The authors report an odds ratio of 0.92 for menthol smokers and 1.0 for non-menthol smokers, which appears to confirm their hypothesis. However, CRE was able to calculate the Odds Ratio based on the category data provided at page 61, and found the Odds Ratio to be the opposite: 1.02 for menthol smokers and 0.976 for non-menthol smokers, which would mean that menthol smokers are more likely to have quit attempts of one day or longer versus non-menthol smokers.

Furthermore, the difference between the Odds is not statistically significant. CRE found a similar disparity with respect to Odds Rations computed for the category (variable): longest quit attempt in past 12 months.

Technical details regarding these discrepancies are provided below.

Technical Details

Inaccurate calculations found in Table 1 of the reference report.

Table 1 of the report provided some of the underlying data for the Odds Ratio calculations. The figures below illustrate how some of the data was not calculated correctly, which may subsequently lead to an inaccurate Odds Ratio calculation for the Quit Attempts category.

from Table 1, p.61, of reference report				
	Menthol smokers		Non-menthol smokers	
Variable	n	%	n	%
Quit Attempt 1 day or longer in past 12 months				
Yes	3,825	33.79%	10,848	31.94%
No	7,846	66.21%	22,796	68.06%
Number of quit attempts one day or longer in past 12 months				
0	7,846	66.21%	22,796	68.06%
1-3	3,253	25.88%	8,486	24.85%
4 +	872	7.91%	2,362	7.09%

The data in the bottom half of the table are sub-category counts for the upper half of the table. For example, among the menthol smokers, there were a grand sample total of 7,846 who reported no quit attempts. Consequently, "7846" correctly appears in the bottom half of the table, under the sub-category of zero quit attempts. This was likewise correctly computed for the non-menthol smokers. However, notice that there were a grand sample total of 3,825 menthol smokers who self-reported "yes" to quit attempts. Thus, the aggregate total for the sub-categories of "1-3" quit attempts and "4 +" quit attempts should have summed to 3825. Instead, the sum is 4,125. This raises into question the accuracy of the statistical models.

4

Within the discriminator: 6-10 cigarettes smoked per day, and the variable: Quit Attempts of one day or longer, the researchers reported an Odds Ratio of 0.92 for menthol smokers and Odds Ratio of 1.00 for non-menthol smokers. This would imply (and support their hypothesis) that menthol smokers are less likely to have quit attempts of one day or longer; and that the Odds are significant (that there is a significant difference). Since data was not available for the sample sizes (n) of those menthol and non-menthol smokers who attempted to quit, given they only smoked 6-10 cigarettes per day, CRE could not independently calculate the Odds Ratio. However, the Odds Ratio was calculated for the total menthol and non-menthol smokers who attempted to quit:

Menthol Odds Ratio: $(3825/7846) \div (10848/22796) = 1.02$
Non-menthol Odds Ratio: $(10848/22796) \div (3825/7846) = 0.976$

This infers that overall non-menthol smokers are less likely to have quit attempts of one day or longer. Furthermore, the difference between the two odds are not statistically significant. Meaning, if you randomly sample again, the odds may swing in favor of the other category.