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

“Lower quit rates among African American and Latino menthol cigarette smokers at a tobacco treatment clinic”

by:


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References:


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 African American and Latino menthol smokers. The researchers presented the following primary results:

- Compared to White menthol smokers, African American and Latino menthol smokers had lower quit rates at a four-week follow-up point;
- African American and Latino menthol smokers had significantly lower odds (approx 1-to-3) of quitting than their non-menthol counterparts;
- Compared to African American non-menthol smokers, African American menthol smokers had half the odds of being abstinent at a six-month follow-up point.

The researchers concluded “[d]espite smoking fewer cigarettes per day, African American and Latino menthol smokers experienced reduced success in quitting as compared with non-menthol smokers within the same ethnic/racial groups.” [p. 360]

The authors cite reference (b) findings as a motivator for further exploring the supposed association between light-smoking (less than 10 cigarettes per day) minority group menthol 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 comprised a review of the report and the referenced primary clinical study (cohort data). 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 Ghandi 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**

The cohort study described in reference (c) lacked control and replication, key elements to a valid experiment. A data utility concern.

This report, performed by Ghandi, was described as a …“retrospective cohort analysis of 1688 consecutive patients who set a quit date and attempted to quit smoking between January 1, 2001 and June 30, 2005. They all attended a specialist tobacco dependence treatment outpatient clinic in New Jersey.” This cohort study group scheme had very similar study characteristics as the clinical trials that were used by the secondary Okuyemi (2007) report. However, unlike in the clinical set-up re-used by the Okuyemi report, the cohort patients were largely observed (as it should be with a cohort study). The cohort group of patients were given the opportunity to receive medications, but no formal statistical treatment and control groups (i.e. such as an administered placebo) were established. Furthermore, review of reference (c) does not include statistics on accepted treatments within menthol versus non-menthol smokers. Regarding replication (the ability of an independent researcher to re-create the experimental setting), the Ghandi report cites 1688 consecutive patients studied between the period January 2001 and June 2005. However, a review of reference (c) indicates only an “…analysis of the first 1021 patients, …from [the study’s] inception in January 2001.”

*Are the statistical models valid?*

The researchers reported that “African American and Latino menthol smokers had significantly lower odds of quitting (Odds Ratio of 0.34; 95% Confidence Interval of 0.17 to 0.69 for African Americans, and Odds Ratio of 0.32; 95% Confidence Interval of 0.16 to 0.62 for Latinos). All confidence intervals are built with the assumption of data being Normally distributed or that a researcher has a sufficient data size in its mean (average) tends to be Normal. In the Statistical vernacular, the Central Limit Theorem is used to establish confidence interval conditions. In particular, if the pedigree of a data set is unknown, then the Theorem states that the sample size must be greater than or equal to 30 in order for the mean to approximate a Normal-like distribution.

CRE reviewed reference (c), the source of the clinical data, and found the following statistics for Latino smokers (African American statistics are also shown for comparison sake):
<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>valid number N</th>
<th>%</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>1021</td>
<td>100%</td>
<td>463</td>
<td>45.3%</td>
<td>320</td>
<td>31.3%</td>
</tr>
<tr>
<td>African American</td>
<td>219</td>
<td>21.4%</td>
<td>78</td>
<td>35.6%</td>
<td>48</td>
<td>21.9%</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>80</td>
<td>7.8%</td>
<td>21</td>
<td>26.3%</td>
<td>16</td>
<td>20%</td>
</tr>
</tbody>
</table>

Notice that the 4-week and 26-week sample sizes (n) for the Latino group are smaller than the required size of 30, in order to form confidence intervals. The main point is that when the sample size is small (less than 30), then confidence intervals cannot be relied upon, regardless of whether one is expressing intervals in terms of odds ratios or sample means.

What should be the most meaningful milestone for assessing cessation results, 4 weeks or 6 months?
The researchers computed statistics for reported abstinence responses, across three ethnic groups, at 4 weeks as well as 6 months. Their results were similar to that of the Okuyemi 2007 report (e.g. lower abstinence rates among menthol smokers versus non-menthol smokers). However, as was the case in the Okuyemi report, there appears to be a higher relapse rate among non-menthol smokers over the longer period of time. This should be investigated further.