Review of: "IQOS® Cross-Sectional and Cohort US Study Documentation"

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Potential competing interests: No potential competing interests to declare.

Summary

The “IQOS Cross-Sectional Study and Cohort US Study Documentation” outlines the post-market surveillance studies (PMSS) mandated of the FDA granted Modified Risk Tobacco Product (MRTPA) order for IQOS Tobacco Heating System and Marlboro Heatsticks. Thusly, the IQOS cross-sectional (CS) and longitudinal cohort (LC) studies aim to 1) characterize IQOS users and their tobacco use patterns, 2) characterize risk perceptions, 3) describe IQOS initiation, cigarette to IQOS transition(s), and cessation, and 4) [in the case of LC,] compare self-reported health and quality of life measures between IQOS and cigarette users. Participant recruitment for both studies is based on IQOS consumer database participants age 21 years and older, with supplemental sampling through third-party commercial market recruitment in IQOS sales geographies if initial recruitment does not reach necessary sample size. The CS study will include annual samples of 250 ever established IQOS users over the course of four years; with amenable CS participants recruited for LC enrollment in addition to a never-IQOS, cigarette smoker reference group. Results of the CS and LC studies are intended to substantiate the MRTP order granted by the FDA, with the ultimate goal of expanding on tobacco harm reduction initiatives for cigarette users unwilling or unable to achieve complete cessation of tobacco use.

Authors detail rigorous study methodology, with thorough plans for assessing descriptive profiles of IQOS users, and their associated health outcomes and risk perceptions relative to cigarette users. Authors are commended for taking on the weighty and noble charge of investigating harm reduction initiatives aimed at improving population health among cigarette smokers.

Feedback

1. The recruitment of IQOS users within six months of their IQOS initiation is of potential concern, especially if these users tend to be naïve to tobacco use, as may be the case with the relatively younger populations drawn to smokeless products. In comparing these new initiates to a cigarette smoker reference group, my concern is that the severity and duration of tobacco use is not comparable between the groups and may bias health outcome measures away from the null; in favor of a protective association with IQOS use. I understand authors plan on adjusting for years of smoking cigarettes, though I might suggest adjusting on years of tobacco exposure rather.
2. A possible concern is the recruitment of participants predominantly from the IQOS consumer database. It is encouraging that third-party markets may be used for sampling, though in the event of insufficient sample size. With

70% of all IQOS consumers registering in the database, I am curious about the differences between consumers who register and consumers who do not. IQOS consumers who register in the database may be more favorable toward IQOS products and/or more regular users of IQOS/tobacco products than users in general, potentially attenuating descriptives estimates and associations regarding risk perceptions and health. Thus, it may be beneficial to include targeted sampling of those not registered in the consumer database.

3. While IQOS sales geographies are limited to southeastern US markets, I wonder about the geographic distribution across the region. With cardiovascular disease, including hypertension, being relatively more prevalent in the ‘stroke belt’, southeastern region of the US, I wonder whether these risk perceptions of IQOS and/or cigarette smokers generalize to other regions of the US.
4. Lastly, it may be worthwhile to perform hierarchical modeling with environmental factors (e.g., air quality) considered in the pool of candidate confounders for model selection, as they may potentially confound the relationship between IQOS/cigarette use and respiratory outcomes. Likewise, social factors (e.g., state/local policy) may potentially confound the relationship between IQOS/cigarette use and hypertension/risk perceptions.