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Intention to Switch to Smokeless Tobacco Use among South African Smokers: Results from the 2007 South African Social Attitudes Survey

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Abstract

**Background:** Some smokeless tobacco products (SLT) have been shown to be associated with only a fraction of the risks of cigarettes. This study assessed South African smokers’ interest in switching to a hypothetical reduced harm SLT product.

**Methods:** The 2007 South African Social Attitudes Survey was analysed for 678 exclusive cigarette smokers. Respondents were asked about their perceptions about relative harm of snuff compared to cigarettes, and their interest in switching to snuff if informed it was 99% less harmful than cigarettes.

**Results:** About 49.7% of exclusive cigarette smokers believed that snuff was equally as harmful as cigarettes; 12.9% thought snuff was more harmful; 5.7% thought snuff was less harmful; while 31.8% did not know if there was a difference in harm between snuff and cigarettes. Approximately 24.2% of exclusive cigarette smokers indicated interest in switching to snuff, with significantly greater interest observed among those exposed to 100% smoke-free work environment. Interest in switching was highest (34.7%) among smokers who believed a priori that using snuff was more harmful than cigarettes, and lowest (14.5%) among those who did not know if there was a difference in harm. In a multi-variable adjusted logistic regression model, this latter group remained less likely to be interested in harm reduction switching (adjusted odds ratio = 0.42; 95% CI: 0.19–0.91).

**Conclusion:** About a quarter of smokers indicated interest in harm reduction switching to snuff. SLT products have a potential role in reducing the harm from smoking in South Africa, but only if they are not used to circumvent smoke-free laws that have been associated with reduced smoking.

Introduction

Smokeless tobacco (SLT) is a small category within the South African tobacco market, with the majority of users being black females of low socio-economic status. [1] Unlike India and several Western countries where most SLT products are used orally (e.g., chewing tobacco and Swedish-style snus), most commercial and traditional SLT products in South Africa are used nasally. A recent study showed that the levels of carcinogenic tobacco-specific nitrosamines in traditional South African SLT products are up to 19 times higher than those in Swedish-style snus. [2] Although low-nitrosamine, Swedish-style snus was introduced into the South African SLT market in 2005 for situational use - ‘where you can’t smoke’ and as a reduced risk product, [3] uptake of the product has remained low in South Africa.

“First, do no harm” remains one of the guiding principles in medicine and public health. However, the definition of what constitutes population-level “harm” regarding use of modified-risk tobacco products remains controversial in the tobacco control community. Proponents of harm reduction hold that it is paternalistic and unethical for public health authorities to fail to provide comprehensive information to smokers that SLT products are relatively less harmful than cigarettes.[4–6] On the other hand, the counter-argument is made that no tobacco product is safe, and that it is harmful to promote a product that has significant potential for addiction, abuse liability, and disease, including oral cancer. [7,8] Hence the sale and use of SLT products has remained banned in several regions including Australia and parts of Europe. [9,10] Nonetheless, based on scientific evidence on relatively lower content of tobacco carcinogens in certain SLT products compared to combustible tobacco products, and also evidence from countries such as Sweden where low-nitrosamine snus has been widely used as a harm reduction strategy, the potential role of SLT products in reducing smoking-attributable morbidity and mortality must be acknowledged. [11,12] However, this potential benefit of SLT can only be optimal in an
environment where the use of combustible tobacco products is at a minimum, with SLT being used in lieu of cigarettes and other combustible tobacco products, rather than in dual fashion.

Similar to the United States, SLT manufacturers in South Africa are required by law (since 1995) to include the phrase “causes cancer” on every can of SLT. [13] In recent years, some have however maintained that such federally mandated warnings on SLT products negate harm reduction messages, [14] and that given correct information about the relative harm of SLT products compared to cigarettes, smokers would be motivated towards harm reduction switching. [4] Although Biener et al previously showed that U.S. smokers’ interest in trying low-nitrosamine snus was higher among those who correctly believed it was less harmful than cigarettes, [15] other studies conducted mainly in developed countries suggested that only about one-third or less of smokers expressed interest in using SLT products. [16,17] Despite these developments, very little information exists on the interest of smokers from low and middle income countries in switching to SLT if informed it is relatively less harmful than cigarettes.

| Characteristics | Sample % (n) | Current smoking prevalence *n=689% (95% CI) | Current Snuffing prevalence n=119% (95% CI) | % of current exclusive cigarette smokers 1 interested in harm reduction switching to snuff n=678 |
|-----------------|-------------|-------------------------------------------|----------------------------------------|--------------------------------------------------|
| Race            |             |                                           |                                        |                                                  |
| Black African   | 76.7 (1812) | 17.2 (14.8–19.5) | 6.5 (4.8–8.2) | 32.0 (24.9–39.1) |
| Colored         | 9.4 (434)   | 40.9 (33.2–48.7) | – 1 | 9.3 (4.2–14.4) |
| Indian or Asian | 2.7 (326)   | 27.6 (18.9–36.3) | – 1 | 17.1 (6.6–27.7) |
| White           | 11.2 (335)  | 28.7 (21.9–35.6) | – 1 | 12.0 (3.4–20.5) |
| Sex             |             |                                           |                                        |                                                  |
| Male            | 48.7 (1221) | 33 (29.3–36.6) | 1.4 (0.6–2.3) | 27.7 (21.6–33.7) |
| Female          | 51.3 (1686) | 9.5 (7.3–11.6) | 8.4 (6.1–10.7) | 12.8 (7.5–18.0) |
| Age, years      |             |                                           |                                        |                                                  |
| 16–24           | 27.4 (686)  | 17.5 (13.6–21.4) | 1.2 (0.2–2.2) | 16.2 (8.1–24.2) |
| 25–34           | 26.0 (633)  | 21.7 (17.4–26.1) | 3.3 (1.6–5.0) | 27.9 (18.4–37.4) |
| 35–44           | 17.0 (614)  | 26.3 (20.9–31.8) | 3.6 (0.9–6.3) | 24.2 (13.7–34.7) |
| 45–54           | 13.5 (440)  | 23.3 (17.3–29.3) | 8.7 (5.0–12.4) | 36.3 (20.3–52.4) |
| ≥55             | 16.2 (526)  | 17.8 (12.9–22.6) | 12.7 (7.9–17.5) | 17.2 (8.8–25.7) |
| Education       |             |                                           |                                        |                                                  |
| <12 year of schooling | 61.9 (1798) | 21.3 (18.5–24.1) | 7.2 (5.2–9.2) | 28.5 (21.5–35.4) |
| =12 year of schooling | 28.2 (762)  | 20.5 (16.3–24.6) | 1.1 (0.3–1.9) | 13.0 (6.6–19.4) |
| >12 year of schooling | 9.9 (336)   | 20.7 (14.3–27.0) | 1.0 (0.1–2.1) | 28.8 (13.6–44.1) |
| Marital Status  |             |                                           |                                        |                                                  |
| Never married   | 54.0 (1378) | 20.8 (17.7–23.8) | 2.8 (1.6–4.0) | 24.1 (17.4–30.7) |
| Widowed, divorced, or separated | 12.3 (436)  | 21.4 (15.0–27.9) | 14.7 (8.9–20.4) | 18.0 (8.2–27.8) |
| Married         | 33.8 (1086) | 21.2 (17.9–24.6) | 5.2 (3.2–7.2) | 26.7 (17.5–35.8) |
| Employment      |             |                                           |                                        |                                                  |
| Unemployed      | 32.6 (1037) | 29.4 (25.1–33.7) | 3.1 (1.8–4.5) | 23.3 (15.8–30.8) |
| Pensioner/student/housewife | 44.0 (1177) | 19.3 (16.1–22.6) | 7.0 (5.0–9.0) | 28.6 (20.4–36.8) |
| Employed        | 23.4 (680)  | 12.5 (8.9–16.1) | 3.9 (1.3–6.6) | 14.7 (4.5–24.9) |
| Region          |             |                                           |                                        |                                                  |
| Urban           | 67.5 (2011) | 21.7 (18.8–24.5) | 4.5 (2.9–6.1) | 21.5 (15.5–27.5) |
| Rural           | 32.5 (896)  | 19.4 (15.9–22.9) | 6.0 (3.6–8.4) | 30.8 (22.2–39.3) |
| Overall         | 100.0 (2907)| 20.9 (18.7–23.1) | 5.0 (3.7–6.4) | 24.2 (19.3–29.2) |

Note: All samples (n) were unweighted while all percentages (%) were weighted to account for the complex survey design. CI = Confidence interval. *Respondents who reported smoking hand-rolled or manufactured cigarettes daily or on some days. 1Respondents who reported using nasal or oral snuff daily or on some days. By race, virtually 100% of current snuffers were Black Africans. *Exclusive cigarette smokers were defined as current smokers that did not report current use of oral or nasal snuff.

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**Methods**

**Survey Design/sample**

The SASAS is a household survey which uses a multi-stage probability sampling strategy with census enumeration areas as the primary sampling unit. The original protocols for the SASAS were approved by the South African Human Sciences Research Council (HSRC). In 2007, a sample of 3500 households was drawn from the master sample of the HSRC. This SASAS sample was stratified by socio-demographic domain for each province and geographical subtypes, namely tribal areas, formal rural, formal urban and informal urban. This stratification is designed to ensure sufficient geographical distribution across all nine provinces, and adequate distribution between South Africa’s four race groups. From each of the households, one eligible person (≥16 years old) was randomly selected for participation in the survey. [18] In 2007, the pre-tested survey questionnaires were administered by trained interviewers in the respondents’ preferred language, which was selected from among all eleven South African official languages (questionnaires were available in all official languages). The survey was completed by 2907 respondents, yielding an overall response rate of 83.1%.

This study was performed on de-identified secondary data. These data are deposited with the HSRC. While the tobacco use supplement of the SASAS is not publicly available, the data can however be obtained upon special request through the HSRC or its primary collaborator—the University of Pretoria.

**Measures**

**Socio-demographic characteristics.** Socio-demographic characteristics assessed included race (Black African; Colored; Indian or Asian; or White); sex (male or female); age (16–24; 25–34; 35–44; 45–54 or ≥55 years), educational attainment (<12; ≥12; or >12 years of schooling), marital status (single; married; or widowed/divorced/separated); employment status (unemployed; pensioner/housewife/student; or employed) and region (urban or rural).

**Tobacco use.** Current cigarette smokers were respondents who reported smoking roll-your-own cigarettes or factory-made cigarettes daily or on some days. Current snuff users were respondents who reported using nasal or oral snuff daily or on some days. Data were also collected among smokers on lifetime duration of smoking, number of cigarettes smoked per day (CPD) (1–10; 11–20; 21–30; or >30 cigarettes) and the time from waking up to smoking first cigarette (≤5, 6–30, 31–60, or >60 minutes). We also measured smoking restrictions in the home and work environments.

**Lifetime quit attempts and quit intentions.** A lifetime quit attempt among current smokers was defined as any response of “once”, “twice”, “three times or more” to the question: “Have you ever tried to quit smoking?”.

Among current smokers that had made a past quit attempt, methods employed to quit smoking were assessed and included: cold turkey (i.e., just stopped smoking one day without using any smoking cessation aids), cutting-down, use of nicotine replacement therapy (e.g. patch, gum) or prescription medication (e.g. Zyban), or switching to light cigarettes, snuff or snus.

A quit intention was defined as any response of “within the next month”, within the next 6 months”, or “sometime in the future, beyond 6 months” to the question: “Are you planning to quit smoking?” Smokers’ self-efficacy about successfully giving up smoking if they were to try quitting in the next six months was measured on a four-point of “Very likely”; “Fairly likely”; “Not very likely”; or “Not at all likely”.

**Reasons for smoking and for past quit attempts.** Considering that reasons for smoking may influence the level of interest in switching to snuff, smokers were asked reasons why they smoked, which were then categorized into four themes namely; 1) cost of smoking; 2) smoking-related health problems or concern for the health of household members; 3) motivation from family and friends; 4) changing social environment towards smoking (i.e., proliferation of smoke-free laws and societal denormalization of smoking); 5) advice from a healthcare professional and; 6) reaction to cigarette health warning labels.

**Perception about relative harm of snuff compared to cigarettes.** Perception about the relative harm of snuff and cigarettes was assessed using the question: “Do you believe that snuff is a safer alternative to smoking cigarettes?” Categorical responses included: “Using snuff is less harmful than smoking”, “Using snuff is equally as harmful as smoking”, “Using snuff is more harmful than smoking”, and “Do not know”.

**Interest in switching to snuff.** Interest in harm reduction switching to snuff was assessed with the question: “If you currently smoke and were told that snuff is 99% safer than smoking and it would give you the same amount of nicotine you crave from your cigarette, how likely would you be to switch?” Responses of “Very likely” or “Somewhat likely” were categorized together as an affirmative response, while responses of “Somewhat unlikely” or “Very unlikely” were categorized together as a dissenting response.

It is pertinent to note that the survey first asked current smokers about their knowledge of the relative harm of snuff and cigarettes earlier on in the survey and then later asked if they would be interested in switching to snuff if they were told it was 99% safer than cigarettes. Pre-testing of the questionnaire used showed that keeping the phrase ‘99% safer’ also conveyed a local layman’s lingua of ‘confidently’ or ‘surely’, or ‘certainly’ safer.

**Statistical Analysis**

Prevalence of current smoking and SLT use were calculated overall and by socio-demographic variables. Comparison of estimates was performed using $\chi^2$ tests ($p<0.05$).

Level of nicotine dependence among current smokers was assessed using the Heaviness of Smoking Index—a six-point scale calculated from CPD and the time to first cigarette after waking. [19] Scores of 0–1 were categorized as low nicotine dependence; 2–4 as moderate nicotine dependence; and 5–6 as high nicotine dependence. For the purposes of these analyses, moderate nicotine dependent smokers were analyzed together as one category because of the small sample among the latter.

The primary analysis which assessed smokers’ interest in switching to snuff if informed that snuff was 99% less harmful than cigarettes, was restricted to exclusive cigarette smokers, defined as current smokers who did not report using oral or nasal snuff. However, in a secondary analysis, we also explored the role of snuff in modifying cigarette smoking behavior, by comparing CPD and quit attempts between exclusive cigarette smokers and dual users of cigarettes and snuff.
In order to explore factors independently associated with exclusive smokers’ interest in harm reduction switching, we fitted a multivariate logistic regression model that assessed for presence of smoke-free homes and workplaces, reasons for smoking, heaviness of smoking, lifetime duration of smoking, perceptions about relative harm of snuff and cigarettes, past quit attempts, self-efficacy towards quitting, race, sex, age and education ($p<0.05$). Data were weighted using the “svyset” function in STATA 11 to account for the complex survey design characteristics, and also included the “psu” and “strata” options since the population was sampled by stratifying it first and then randomly selecting several clusters for each stratum.
Interest in Harm Reduction Switching

About 24.2% of all exclusive cigarette smokers indicated interest in harm reduction switching to snuff. This proportion was highest (34.7%) among exclusive cigarette smokers who believed a priori that snuff is more harmful than cigarettes, and lowest (14.5%) among those who did not know if there was a difference in harm between snuff and cigarettes. After adjusting for all other factors, this latter group remained less likely to be interested in harm reduction switching (adjusted odds ratio \( \text{aOR} = 0.42; 95\% \text{ CI}: 0.19–0.91 \)). Other factors associated with interest in harm reduction switching included: presence of 100% smoke-free policies at work (\( \text{aOR} = 2.05; 95\% \text{ CI}: 1.09–3.97 \)); increasing self-efficacy towards successfully quitting (\( \text{aOR} = 1.49; 95\% \text{ CI}: 1.21–1.84 \)) and smoking cigarettes primarily to enhance concentration or cope with everyday life (\( \text{aOR} = 1.58; 95\% \text{ CI}: 1.02–2.46 \)).

Discussion

Similar to findings in the literature, [20] this study demonstrated that about a quarter of exclusive cigarette smokers indicated interest in harm reduction switching to SLT products. The fact that only a relatively small fraction of smokers were interested in harm reduction switching may attest to the fact that while nicotine is the primary addictive agent in tobacco, the role of smoking sensory experience (e.g., taste, flavor, and mouth-feel of tobacco smoke), as well as behavioral addictions (e.g., the hand-to-mouth motions of smoking) as secondary reinforcers of smoking behavior cannot be under-estimated. Thus, a lack of interest among smokers in switching to SLT products may not necessarily indicate a lack of awareness about the risks of smoking. For example, among smokers that had made a quit attempt, 70% had done so out of concern for smoking related health problems, indicating that ignorance about the health risks of smoking is not likely an issue among this population. Taken together, this might suggest that promotion of snuff use among this predominant group of smokers not interested in harm reduction switching may only encourage dual use of cigarettes and SLT (i.e. using SLT only where smoking is not allowed), which might cause net population harm, especially if it reduces the impact of smoke-free laws in promoting tobacco cessation. [8] This is particularly pertinent in the studied population considering that a significantly higher...
### Table 4. Logistic regression analyses of factors associated with interest in harm reduction switching to snuff among current exclusive cigarette smokers (n=678), South African Social Attitudes Survey, 2007.

| Characteristic                               | Categories                                      | Crude odds ratios, 95% CI                           | Adjusted odds ratios, 95% CI                         |
|----------------------------------------------|-------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|
| **Smoke-free environments**                  |                                                 |                                                     |                                                     |
| Smoke-free home regulations                  | Absent (Referent)                               | 1.60 (1.12–2.29)                                    | 1.35 (0.83–2.20)                                     |
|                                             | Present                                         |                                                     |                                                     |
| Smoke-free policies at work                  | No smoke-free policy at work (Referent)         | 1.24 (0.72–2.14)                                    | 1.30 (0.65–2.59)                                     |
|                                             | Partial bans on workplace smoking               |                                                     |                                                     |
|                                             | 100% smoke-free policies at work                | 2.14 (1.35–3.39)                                    | 2.05 (1.09–3.87)                                     |
|                                             | Did not know/did not answer                      | 0.71 (0.38–1.34)                                    | 1.14 (0.52–2.49)                                     |
| **Self-reported reasons for Smoking**        |                                                 |                                                     |                                                     |
| For pleasure or enjoyment (i.e., hedonistic reward) | No (Referent)                                   | 0.43 (0.27–0.69)                                    | 0.67 (0.38–1.17)                                     |
|                                              | Yes                                             |                                                     |                                                     |
| To enhance concentration or cope with everyday life | No (Referent)                                   | 1.74 (1.19–2.54)                                    | 1.58 (1.02–2.46)                                     |
|                                              | Yes                                             |                                                     |                                                     |
| Difficulty quitting or lack of willpower to try | No (Referent)                                   | 0.66 (0.45–0.98)                                    | 1.20 (0.74–1.93)                                     |
|                                              | Yes                                             |                                                     |                                                     |
| **Social influences**                         |                                                 |                                                     |                                                     |
|                                              | No (Referent)                                   | 0.84 (0.53–1.33)                                    | 0.79 (0.46–1.34)                                     |
|                                              | Yes                                             |                                                     |                                                     |
| **Tobacco use characteristics and perception**|                                                 |                                                     |                                                     |
| Heaviness of smoking index                   | Low dependence (Referent)                       | 0.62 (0.43–0.91)                                    | 0.76 (0.48–1.21)                                     |
|                                             | Moderate to heavy dependence                    |                                                     |                                                     |
| Duration of smoking, years                   | (Per unit increase)                             | 1.00 (0.98–1.02)                                    | 1.02 (0.99–1.05)                                     |
| Perception of relative harm from snuff use   | Snuff is safer than smoking (Referent)          |                                                     |                                                     |
|                                             | Snuff equally harmful as smoking                 | 0.76 (0.40–1.44)                                    | 0.64 (0.31–1.32)                                     |
|                                             | Snuff more harmful than smoking                 | 1.00 (0.49–2.06)                                    | 1.04 (0.43–2.52)                                     |
|                                             | Did not know                                    | 0.39 (0.20–0.76)                                    | 0.42 (0.19–0.91)                                     |
| **Lifetime Quit attempts**                   |                                                 |                                                     |                                                     |
| Past quit attempt                            | None (Referent)                                 | 0.79 (0.55–1.13)                                    | 0.58 (0.35–0.95)                                     |
|                                              | ≥1                                              |                                                     |                                                     |
| Number of past quit attempts (among past quit attempters) | 1 (Referent)                                   | 0.51 (0.20–1.28)                                    | 0.47 (0.18–1.20)                                     |
|                                              | 2                                              |                                                     |                                                     |
|                                              | ≥3                                              | 0.33 (0.14–0.75)                                    | 0.30 (0.12–0.71)                                     |
| Self efficacy to quit                        | (Per unit increase)                             | 1.43 (1.20–1.70)                                    | 1.49 (1.21–1.84)                                     |
| **Socio-demographic characteristics**        |                                                 |                                                     |                                                     |
| Race                                         | Black African (Referent)                        |                                                     |                                                     |
|                                             | Colored                                         | 0.38 (0.22–0.64)                                    | 0.48 (0.23–1.02)                                     |
|                                             | Indian or Asian                                 | 0.39 (0.21–0.72)                                    | 0.59 (0.28–1.27)                                     |
|                                             | White                                           | 0.30 (0.15–0.59)                                    | 0.57 (0.22–1.43)                                     |
| Gender                                       | Male (Referent)                                 |                                                     |                                                     |
|                                             | Female                                          | 0.54 (0.36–0.80)                                    | 0.75 (0.43–1.30)                                     |
| Age, years                                   | 16–24 (Referent)                                |                                                     |                                                     |
|                                             | 25–34                                          | 1.29 (0.75–2.20)                                    | 1.59 (0.80–3.19)                                     |
|                                             | 35–44                                          | 0.94 (0.53–1.66)                                    | 1.10 (0.51–2.39)                                     |
|                                             | 45–54                                          | 1.39 (0.78–2.48)                                    | 1.67 (0.73–3.83)                                     |
|                                             | ≥55                                            | 1.01 (0.56–1.82)                                    | 1.00 (0.34–2.95)                                     |
| Education                                    | <12 year of schooling (Referent)                |                                                     |                                                     |
|                                             | =12 year of schooling                           | 0.58 (0.36–0.93)                                    | 0.57 (0.31–1.03)                                     |
|                                             | >12 year of schooling                           | 0.69 (0.36–1.33)                                    | 0.69 (0.33–1.47)                                     |

**Note:** All analyses were weighted to account for the complex survey design. CI = Confidence interval. *Statistical significant after adjusting for all other factors listed in table (P<0.05).
multi-national cigarette companies have invested significantly in oral and esophageal cancers. [23] More so, given that several that are more affordable in low and middle income countries. [2] alternative to cigarettes, especially so for the traditional products in no way implies that SLT products are harmless or a safe and other toxins compared to combustible tobacco products, this that SLT products contain relatively lower levels of nitrosamines of SLT products. Although the body of scientific evidence shows that SLT products have a potential role in reducing the harm from SLT manufacture and several cigarette-branded SLT products are available, [24] the potential of the tobacco industry promoting dual use rather smoking cessation needs to be given consideration. This is important considering that dual use among current cigarette smokers is a significant public health problem, with over a fifth of cigarette smokers in 28 of 44 countries assessed in a recent study reporting concurrent use of at least one other non-cigarette tobacco product. [25] Interestingly, our study showed that while Colored respondents (i.e. those of mixed ancestry) as well as Whites had the highest smoking prevalence, they paradoxically had the lowest proportion indicating interest in harm reduction switching to snuff. This may suggest that the Swedish experience may not be transferable to societies without a strong SLT culture or those with unique tobacco use habits or patterns. [3].

This study has some limitations. First, we did not make a distinction as to the application route of this hypothetical reduced harm SLT product. However, given that the aim was to explore the interest of South African smokers in switching to a considerably less harmful product and considering that the level of interest in harm reduction switching in this study was comparable to that reported in similar studies elsewhere; [20] it is likely that the conclusions reached in this study will not differ even if the route of application had been specified. Second, self-reported tobacco use status and the cross-sectional study design may have resulted in a mis-reporting of tobacco use and may also preclude drawing causal inferences. Third, the fact that smokers expressed interest in switching to snuff does not necessarily mean they may actually switch—especially inveterate smokers or heavy smokers—considering the interplay between neurobiological and behavioral factors in smoking addiction. Fourth, it is possible that the phrasing of our survey question which suggested complete switching to cigarettes may not capture smokers who may not wish to switch completely, but rather be interested in SLT only to reduce their smoking intensity. Finally, since data were collected in 2007, it is possible that smokers’ views or perceptions may have changed.

Conclusion

This study demonstrated that about a quarter of South African exclusive cigarette smokers sampled in a 2007 population-based survey indicated interest in harm reduction switching to snuff. SLT products have a potential role in reducing the harm from cigarettes smoking but only if they are not used to circumvent smoke-free laws that have been associated with significant reductions in smoking prevalence.

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Author Contributions
Conceived and designed the experiments: OAA-Y. Analyzed the data: ITA OAA-Y. Wrote the paper: ITA OAA-Y.

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