

# EVALUATION OF CARDIOVASCULAR DISEASE BIOMARKERS IN ADULT TOBACCO CONSUMERS: A COMPARISON BETWEEN THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY AND A SINGLE SITE CROSS-SECTIONAL STUDY

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## INTRODUCTION

Cardiovascular disease is a leading cause of morbidity and mortality worldwide.

Cigarette smoking is a major modifiable risk factor for cardiovascular disease.

Cigarette smoking is associated with biological markers of cardiovascular disease.

The tobacco harm reduction concept is based on the idea that cigarette smoking-related morbidity and mortality might be decreased without completely eliminating the use of tobacco products (Stratton et al. 2001).

Non-combustible tobacco products are considered to be less hazardous than cigarette smoking (Zeller et al. 2009).

Biomarkers are useful for assessment of harm reduction (Hatsukami et al. 2007).

Few data are available on the relationship between smokeless tobacco consumption and biological markers of cardiovascular disease.

The primary objective of this analysis was to evaluate and compare levels of various cardiovascular disease biomarkers of potential harm in cigarette smokers, smokeless tobacco consumers, and non-consumers of tobacco in three different data sets (Table 1).

**Table 1: Description of the three data sets**

<b>Data Set 1</b> NHANES full data set n=21851	<b>NHANES 1999-2008</b> <b>US males and females</b> <b>ages ≥20 years</b>  Cigarette smokers, n=5040 Chewing tobacco & snuff consumers, n=368 Non-consumers of tobacco, n=16443
<b>Data Set 2</b> NHANES subset n=4010	<b>NHANES 1999-2008</b> <b>US males</b> <b>ages 26-49 years</b>  Cigarette smokers, n=1440 Snuff consumers, n=69 Non-consumers of tobacco, n=2501
<b>Data Set 3</b> Cross-sectional study n=168	<b>Single site, cross-sectional study</b> <b>US males</b> <b>ages 26-49 years</b>  Cigarette smokers, n=60 Snuff consumers, n=48 Non-consumers of tobacco, n=60

NHANES, National Health and Nutrition Examination Survey (United States)

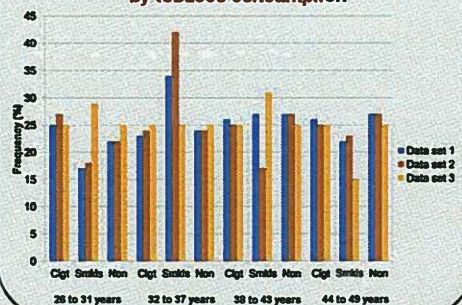
## METHODS

NHANES is conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) and is designed to annually assess the health and nutritional status of adults and children in the US. Data are publicly available and are representative of the civilian, non-institutionalized US population (CDC 2010).

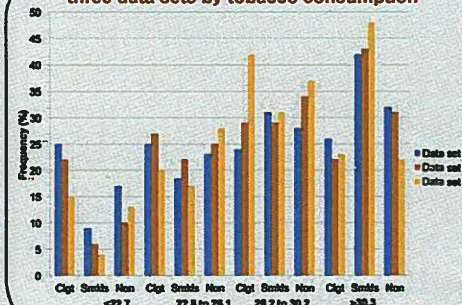
A single site, cross-sectional study was conducted in the US to evaluate biological markers of cardiovascular disease in cigarette smokers, moist snuff consumers, and never smokers/never consumers of smokeless tobacco.

In all three data sets, to identify statistically significant differences in biological markers between cigarette smokers, smokeless tobacco consumers, and non-consumers of tobacco, multiplicative factors and corresponding 95% confidence intervals were calculated. Multiplicative factors were computed by exponentiation of the exposure-specific regression coefficients from multiple linear regression models for the natural log transformed mean biological marker values.

**Figure 1: Distribution of age in three data sets by tobacco consumption**



**Figure 2: Distribution of body mass index in three data sets by tobacco consumption**



**Table 2: Statistically significant differences in biological markers between tobacco consumption groups, NHANES and cross-sectional study**

Biological markers	Cigt smokers versus non-consumers			Cigt smokers versus smokeless tobacco consumers			Smokeless tobacco consumers versus non-consumers		
	Data set 1	Data set 2	Data set 3	Data set 1	Data set 2	Data set 3	Data set 1	Data set 2	Data set 3
Cholesterol	↑								
HDL	↓								
Triglycerides	↑	↑		↑	↑				
Hemucyteline	↑	↑		↑	↑		↑		
Fibrinogen	↑	↑		↑	↑		↑		
C-Reactive Protein	↑	↑		↑	↑		↑		
Hematocrit	↑	↑		↑	↑				
Platelets (#)	↑								
Red Cell Dist Width	↑								
Mean Cell Volume	↑	↑		↑	↑		↑		
Mean Cell Hemoglobin	↑	↑		↑	↑		↑		
Hemoglobin	↑	↑		↑	↑				
White Blood Cells (#)	↑	↑		↑	↑		↑		
Eosinophils (#)	↑	↑		↑	↑				
Monocytes (#)	↑	↑		↑	↑		↑		
Lymphocytes (#)	↑	↑		↑	↑		↑		
Neutrophils (#)	↑	↑		↑	↑		↑		
Apolipoprotein B	↑			↑					
Folate	↓			↓			↓		
Ankle Brachial Index	↓			↓			↓		

Results based on multiplicative factors and corresponding 95% confidence intervals that do not include 1.00

## RESULTS

Data set 3 was largely homogenous (e.g., all male, equal distribution between age groups, equal distribution between tobacco consumption categories) by design.

Based on data sets 1 & 2, the highest percentage of smokeless tobacco users were aged 32-37 years; the smallest percentage was 26-31 years (Figure 1).

In all three data sets, a higher percentage of smokeless tobacco consumers (than cigarette smokers and non-consumers) were categorized with BMI ≥30.3 (than with other BMI categories) (Figure 2).

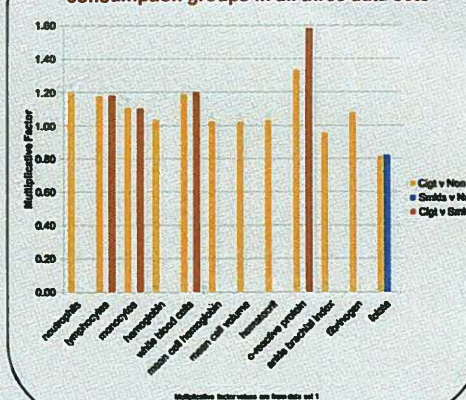
Median values for all biological markers in all data sets were within clinical reference ranges (data not shown).

In all three data sets, in cigarette smokers versus non-consumers, the following biological markers were different: fibrinogen, c-reactive protein, hematocrit, mean cell volume, mean cell hemoglobin, hemoglobin, white blood cells, monocytes, lymphocytes, neutrophils, folate, ankle brachial index (Table 2, Figure 3).

In all three data sets, in cigarette smokers versus smokeless tobacco consumers, the following biological markers were different: c-reactive protein, white blood cells, monocytes, lymphocytes (Table 2, Figure 3).

In all three data sets, in smokeless tobacco consumers versus non-consumers, the following biological marker was different: folate (Table 2, Figure 3).

**Figure 3: Biological markers with statistically significant differences between tobacco consumption groups in all three data sets**



## SUMMARY & CONCLUSIONS

These findings are consistent with previous reports of differences in biological markers of cardiovascular disease in cigarette smokers compared with non-smokers (USDHHS 2004).

These findings are generally consistent with the limited data available on biological markers of cardiovascular disease in smokeless tobacco consumers compared with cigarette smokers and non-consumers of tobacco (e.g., Eliasson et al. 1991; Emster et al. 1990).

In this analysis of cigarette smokers compared with non-consumers of tobacco, consistent differences in 12 biological markers were observed. With the exception of folate, these differences were not observed in comparisons of smokeless tobacco consumers and non-consumers.

These results support the tobacco harm reduction concept, that cigarette smoking related morbidity might be decreased with migration to non-combustible tobacco products.

## ACKNOWLEDGEMENTS

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