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Classification of frequent snoring from routine medical examinations using the NHANES Database

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ABSTRACT

Increased upper airway resistance during sleep, or snoring, is a risk factor for health problems affecting individuals of all ages, such as increased obesity, hypertension, alterations in glucose metabolism, dyslipidemia, and inflammation. A logistic regression model was employed to investigate how well routine physiological and laboratory measures predict frequent snoring using survey and clinical data derived from 2005-2008 National Health and Nutrition Examination Survey (NHANES). Gender, age, BMI, diastolic blood pressure, triglycerides, total cholesterol, and alanine aminotransferase level were associated with frequent snoring. Our findings suggest that frequent snorers may be at increased risk for the development of cardiovascular disease, metabolic dysfunction, and liver damage.

INTRODUCTION

Sleep-Disordered breathing (SDB) describes a spectrum of disorders characterized by abnormalities of breathing patterns or the degree of ventilation during sleep. Increased upper airway resistance during sleep, or snoring, is a risk factor for Obstructive sleep apnea (OSA), the most common form of sleep disordered breathing [1]. SDB, and OSA in particular, have been implicated in the development of adverse cardiovascular outcomes (hypertension) and may contribute to development of components of the metabolic syndrome such as obesity, insulin resistance, and dyslipidemia [2-3]. In addition, milder forms of sleep disordered breathing, such as snoring, are also now recognized to themselves have significant health sequelae [4]. Despite increasing awareness of SDB and its potentially adverse consequences, the majority of patients remain undiagnosed due to the need for expensive, inconvenient, and highly labor intensive procedures such as overnight polysomnography (sleep studies). Furthermore, many patients may even be unaware of snoring, especially if they are living alone. For this reason, we examined whether routinely administered physiological and laboratory exams would prove useful in predicting habitual, or frequent, snoring, a symptom of increased upper airway resistance during sleep and commonly used surrogate marker for SDB in the absence of available sleep studies [4]. Gender, age, BMI, diastolic blood pressure, triglycerides, total cholesterol, and alanine aminotransferase level were found to be associated with frequent snoring and indicate that mild forms of SDB are likely to have important physiological consequences that may impact future health, such as the development of cardiovascular disease, metabolic dysregulation, and liver dysfunction.

METHODS

Data Source

In this study, we used a 2005-2008 data set obtained from the National Health and Nutrition Examination Survey (NHANES). NHANES is an ongoing, continuous program from the National Center for Health Statistics (NCHS) and the Centers for Disease Control and Prevention (CDC) designed to assess the health and nutritional status of adults and children in the United States. Currently, The NHANES collects demographic, health history and behavioral information from a nationally representative sample of about 5,000 persons each year. In addition, some participants are also given detailed medical, dental, and physiological exams, as well as laboratory tests administered by highly trained medical personnel. The NHANES is continually evolving to reflect emerging health issues, and a sleep disorders component was added to the NHANES survey starting in 2005. The present study was limited to non-pregnant participants aged 16 and older, for which sleep survey data were available, and who were not previously diagnosed with sleep apnea. This data subset consisted of 10,482 individuals from the dataset.

Variable Selection and Data Preprocessing

All preprocessing and analyses were performed with SAS® Enterprise Guide and SAS® Enterprise Miner. Frequent snoring was defined as 5 or more nights per week. Individual sleep survey, demographic, and physiological data were merged with the standard NHANES biochemistry profile, which contains a battery of measurements used in the diagnosis and treatment of certain liver, heart, and kidney diseases, acid-base imbalances in the respiratory and metabolic systems, other diseases involving lipid metabolism and various endocrine disorders, as well as metabolic or nutritional disorders.

Prior to our analysis, data sets were merged and numerical data were standardized to a mean of 0 with a standard deviation of 1 using SAS® Enterprise Guide 4.2. Following standardization, demographic, physiological, and biochemical variables for our model were selected using the variable selection node in SAS® Enterprise Miner, which

uses R-squared tests in order to determine the explanatory variables that have the greatest degree of correlation with the target variable. Figure 1 shows the demographic, physiological, and biochemical variables processed by the variable selection node.

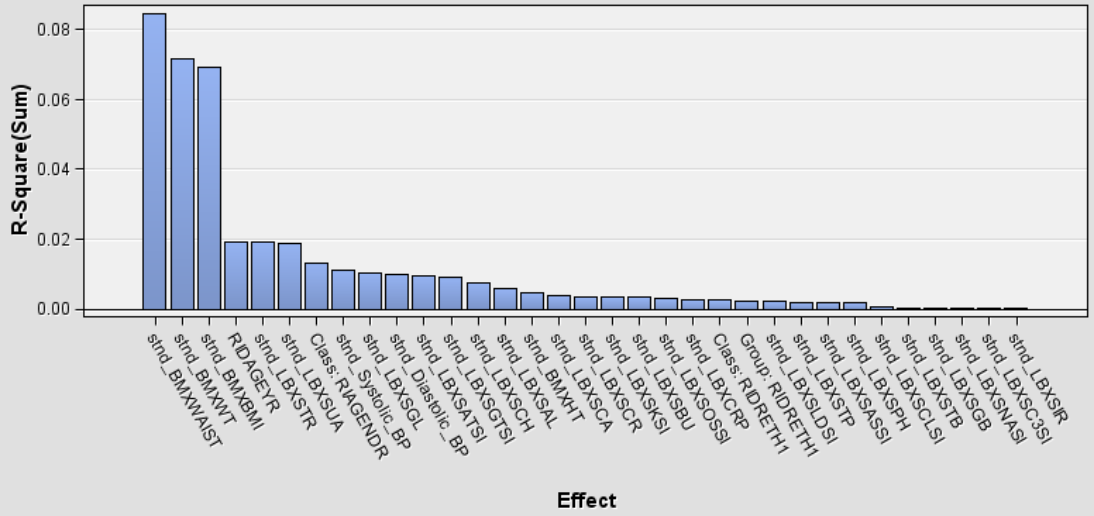

Figure 1. R-Square (Sum) of demographic, physiological, and biochemical variables examined.

The final variables selected for our model are shown in Figure 2.

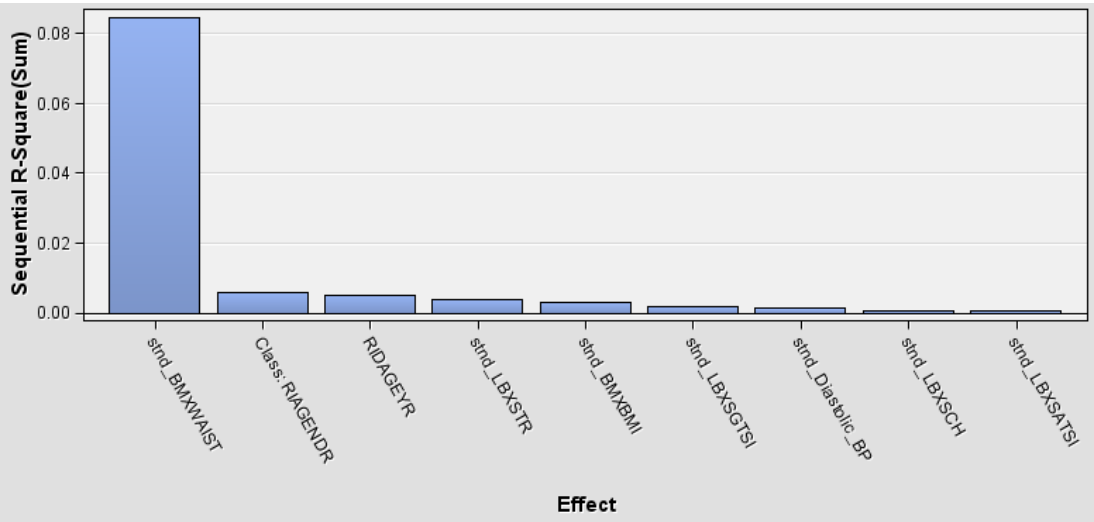

Figure 2. Sequential R-Square (sum) for demographic, physiological, and biochemical variables retained.

RESULTS

A total of 10,482 subjects satisfied our selection criteria. Summary statistics prior to standardization and code translations for our model variables are provided in Tables 1 and 2. Initial distributions were examined with table analyses for the categorical variable gender, and via kernel density estimation for the numerical variables selected for our model.

Gender	N Obs	Variable	Label	Mean	Std Dev	N	N Miss
Male	3484	RIDAGEYR	Age at Screening Adjudicated - Recode	43.1470	21.4183	3484	0
		BMXBMI	Body Mass Index (kg/m**2)	26.9420	5.5533	3425	59
		BMXWAIST	Waist Circumference (cm)	95.4387	15.7284	3315	169
		Systolic_BP	Systolic Blood Pressure	123.2684	16.2739	3319	165

Gender	N Obs	Variable	Label	Mean	Std Dev	N	N Miss
		Diastolic_BP	Diastolic Blood Pressure	68.6456	13.3184	3319	165
		LBXSCH	Cholesterol (mg/dL)	186.1263	40.6383	3223	261
		LBXSTR	Triglycerides (mg/dL)	151.3606	136.4209	3222	262
		LBXSGTSI	Gamma glutamyl transferase (U/L)	31.5602	49.0044	3222	262
		LBXSATSI	Alanine aminotransferase ALT (U/L)	27.6873	18.1020	3198	286
Female	3776	RIDAGEYR	Age at Screening Adjudicated - Recode	43.1663	20.4944	3776	0
		BMXBMI	Body Mass Index (kg/m**2)	27.3820	6.6538	3699	77
		BMXWAIST	Waist Circumference (cm)	91.3409	15.5085	3564	212
		Systolic_BP	Systolic Blood Pressure	119.8023	20.2729	3576	200
		Diastolic_BP	Diastolic Blood Pressure	67.3181	12.5569	3576	200
		LBXSCH	Cholesterol (mg/dL)	194.2605	41.3768	3474	302
		LBXSTR	Triglycerides (mg/dL)	126.0469	104.6028	3473	303
		LBXSGTSI	Gamma glutamyl transferase (U/L)	22.2216	27.9114	3474	302
		LBXSATSI	Alanine aminotransferase ALT (U/L)	20.8253	20.2217	3451	325

Table 1. Summary statistics for normal subjects.

Gender	N Obs	Variable	Label	Mean	Std Dev	N	N Miss
Male	1946	RIDAGEYR	Age at Screening Adjudicated - Recode	48.6228	17.4855	1946	0
		BMXBMI	Body Mass Index (kg/m**2)	30.2178	6.7522	1915	31
		BMXWAIST	Waist Circumference (cm)	104.8905	15.8069	1846	100
		Systolic_BP	Systolic Blood Pressure	126.4624	16.7802	1855	91
		Diastolic_BP	Diastolic Blood Pressure	72.1535	13.4294	1855	91
		LBXSCH	Cholesterol (mg/dL)	197.3743	43.9558	1838	108
		LBXSTR	Triglycerides (mg/dL)	190.8851	161.0737	1837	109
		LBXSGTSI	Gamma glutamyl transferase (U/L)	41.0054	62.2065	1840	106
		LBXSATSI	Alanine aminotransferase ALT (U/L)	32.0202	28.8497	1828	118
Female	1276	RIDAGEYR	Age at Screening Adjudicated - Recode	50.0556	17.4698	1276	0
		BMXBMI	Body Mass Index (kg/m**2)	32.4372	8.2084	1256	20
		BMXWAIST	Waist Circumference (cm)	102.8733	16.4342	1204	72
		Systolic_BP	Systolic Blood Pressure	124.8961	20.2148	1213	63
		Diastolic_BP	Diastolic Blood Pressure	68.9610	13.4615	1213	63
		LBXSCH	Cholesterol (mg/dL)	200.1575	44.6539	1200	76
		LBXSTR	Triglycerides (mg/dL)	159.1435	109.0079	1199	77
		LBXSGTSI	Gamma glutamyl transferase (U/L)	29.3433	39.5119	1200	76
		LBXSATSI	Alanine aminotransferase ALT (U/L)	24.0436	18.0951	1192	84

Table 2. Summary statistics for frequently snoring subjects.

Table 3 shows the distribution of snoring frequency by gender. Males had a higher percentage of individuals classified as frequent snorers, which is also illustrated graphically in Figure 3.

Table of SNORING by RIAGENDR				
		Gender		
		Male	Female	Total
SNORING				
Normal	Frequency	3484	3776	7260
	Percent	33.24	36.02	69.26
	Row Pct	47.99	52.01	
	Col Pct	64.16	74.74	
	Cumulative Col%	64.16	74.74	69.26
Freq Snoring	Frequency	1946	1276	3222
	Percent	18.57	12.17	30.74

Table of SNORING by RIAGENDR				
		Gender		
		Male	Female	Total
	Row Pct	60.40	39.60	
	Col Pct	35.84	25.26	
	Cumulative Col%	100.00	100.00	100.00
Total	Frequency	5430	5052	10482
	Percent	51.80	48.20	100.00

Table 3. Summary statistics for frequently snoring subjects.

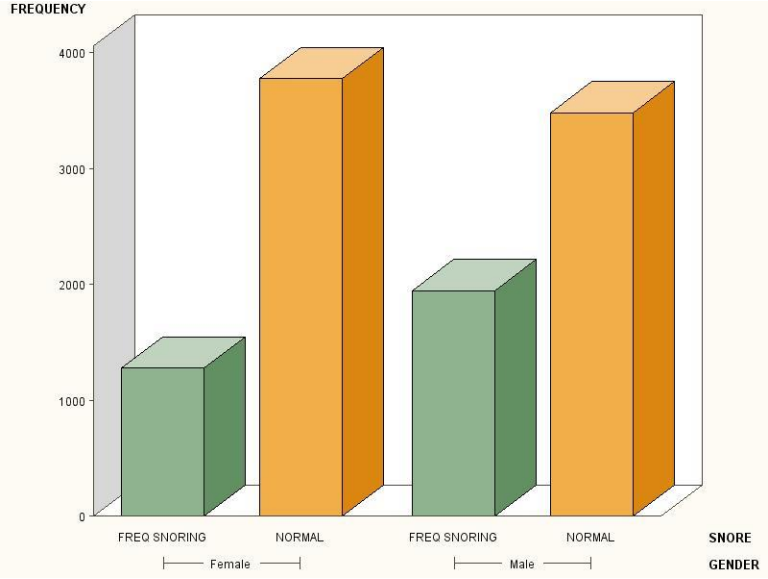

Figure 3. Snoring classification in males and females.

Kernel density estimates were used to compare the distribution of numerical data across groups and are given in Figures 4-11. Kernel density estimates were generated through the use of SAS® code nodes and the PROC KDE in Enterprise Guide.

Figure 4 shows the distribution of BMI by snoring classification (0=normal, 1=frequently snoring). It can be seen from figure 4 that the distribution of BMI is shifted to the right (higher) in frequently snoring individuals.

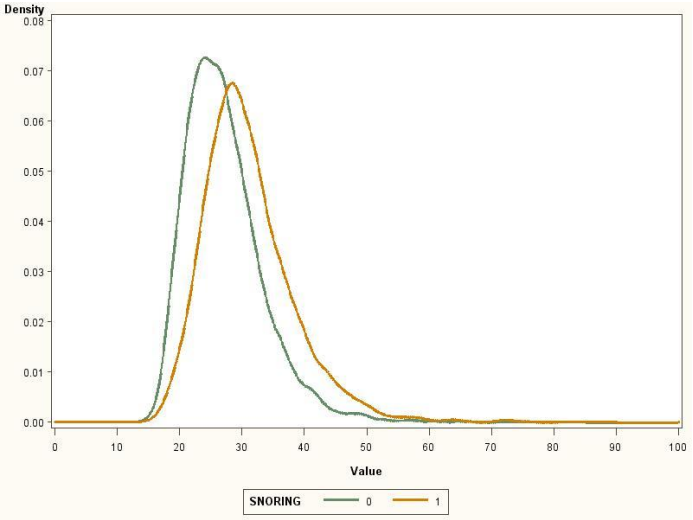

Figure 4. Kernel density of BMI by snoring classification.

Figure 5 shows the distribution of waist circumference by snoring classification (0=normal, 1=frequently snoring). It can be seen from figure 5 that the distribution of waist circumference is shifted to the right (higher) in frequently snoring individuals.

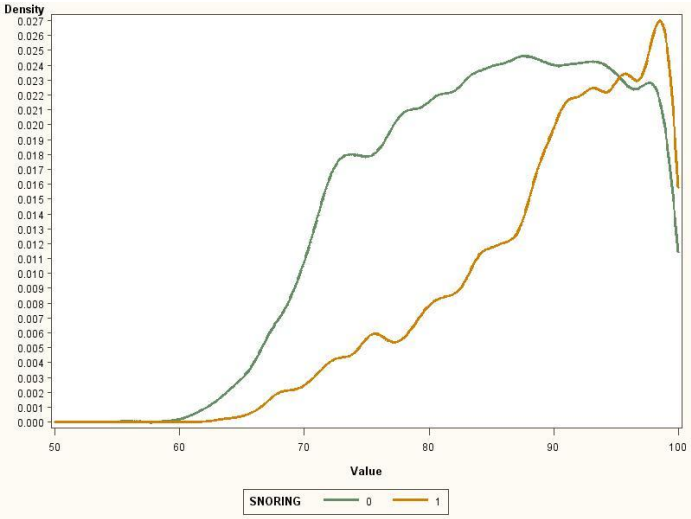

Figure 5. Kernel density of Waist circumference (cm) by snoring classification.

Figure 6 shows the distribution of age by snoring classification (0=normal, 1=frequently snoring). It can be seen from figure 6 that the peak distribution of age is shifted to the left (lower) in normal individuals.

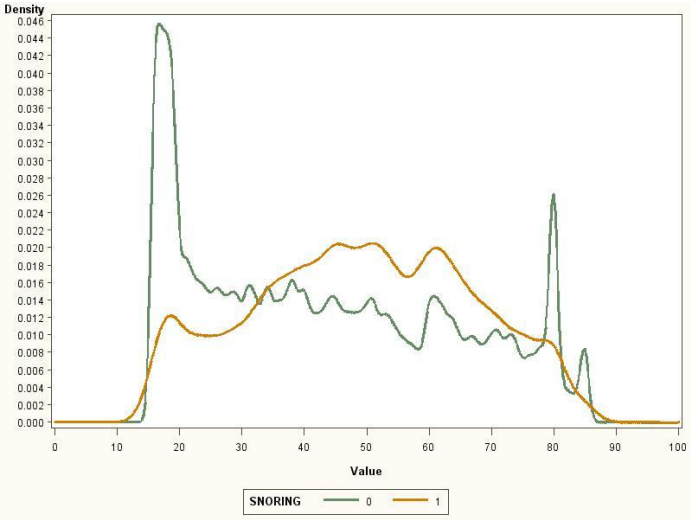

Figure 6. Kernel density of Age (years) by snoring classification.

Figure 7 shows the distribution of triglyceride level by snoring classification (0=normal, 1=frequently snoring). It can be seen from figure 7 that the peak distribution of is again shifted to the right (higher) in frequently snoring individuals.

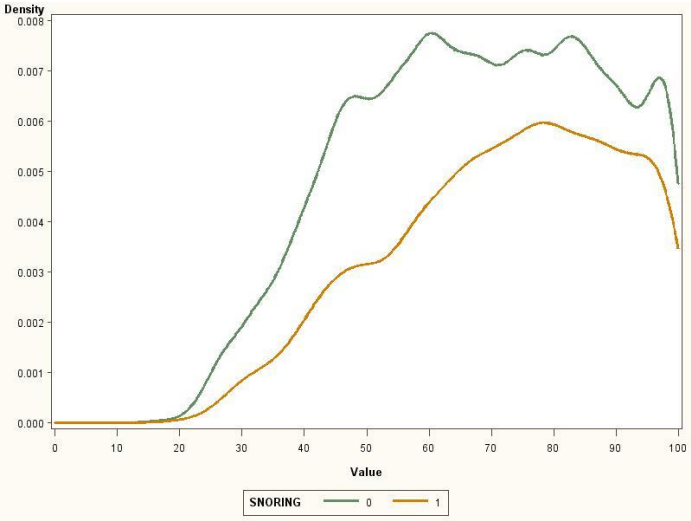

Figure 7. Kernel density of triglycerides by snoring classification.

Figure 8 shows the distribution of cholesterol level by snoring classification (0=normal, 1=frequently snoring). It can be seen from figure 8 that there is increased variability in normal individuals.

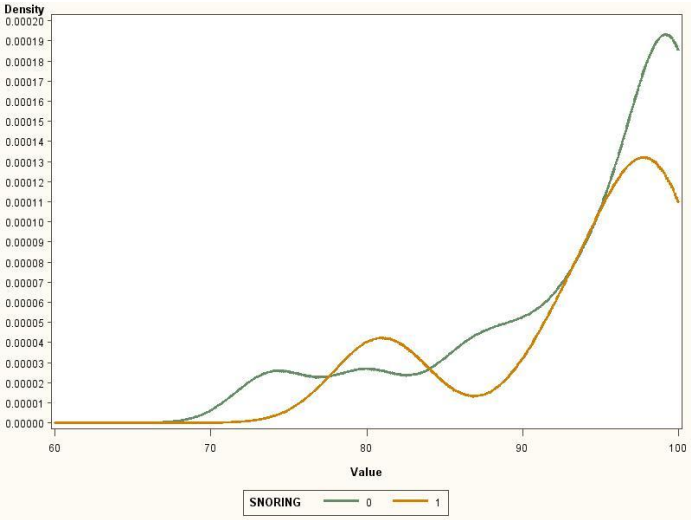

Figure 8. Kernel density of cholesterol by snoring classification.

Figure 9 shows the distribution of gamma glutamyl transferase level by snoring classification (0=normal, 1=frequently snoring). It can be seen from figure 9 that the peak distribution of is again shifted to the right (higher) in frequently snoring individuals.

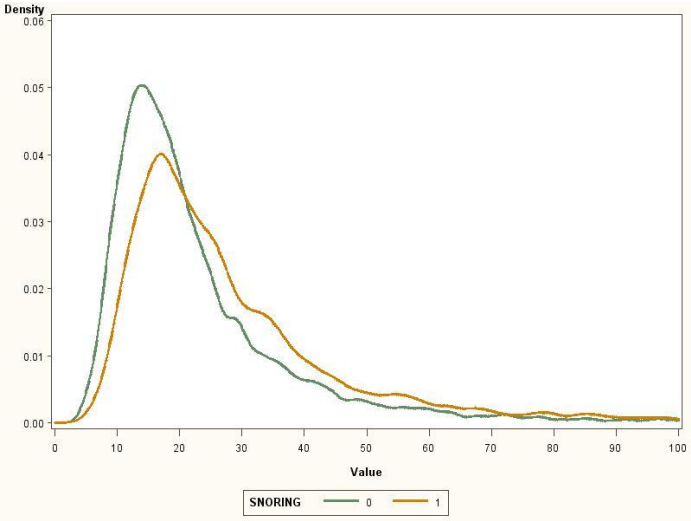

Figure 9. Kernel density of gamma glutamyl transferase by snoring classification.

Figure 10 shows the distribution of diastolic blood pressure by snoring classification (0=normal, 1=frequently snoring). It can be seen from figure 10 that the peak distribution of is again shifted to the right (higher) in frequently snoring individuals.

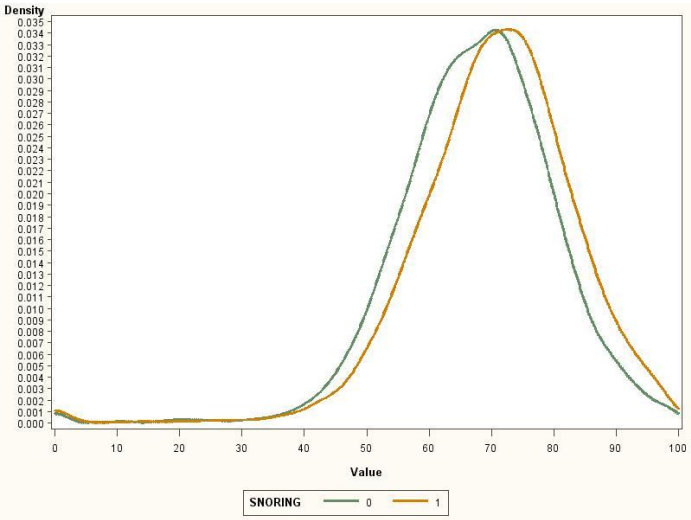

Figure 10. Kernel density of diastolic blood pressure by snoring classification.

Figure 11 shows the distribution of alanine aminotransferase by snoring classification (0=normal, 1=frequently snoring). It can be seen from figure 11 that the peak distribution of is again shifted to the right (higher) and is more variable in frequently snoring individuals.

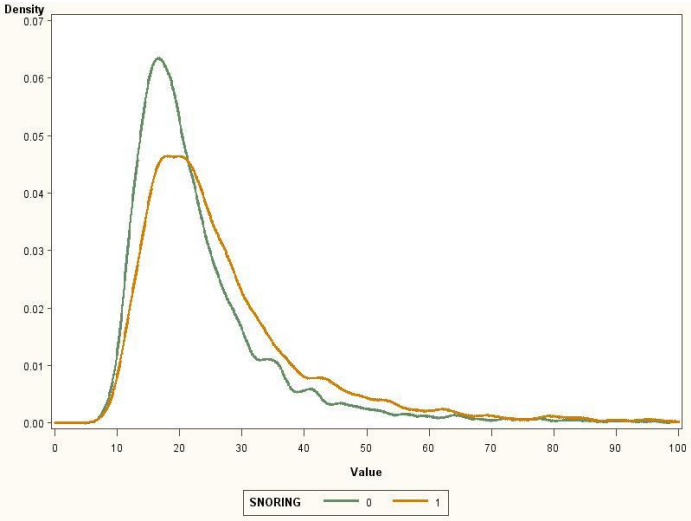

Figure 11. Kernel density of alanine aminotransferase by snoring classification.

Logistic Regression

A total of 9011 observations were used from the 10,482 subjects who satisfied our selection criteria, with 1471 observations omitted due to missing response values. The response profile of the logistic regression is given in table 4 below (0 = Normal, 1 = Frequently Snoring).

Response Profile		
Ordered Value	SNORING	Total Frequency
1	0	6205
2	1	2806

Table 4. Response profile of normal (0) and frequently snoring (1) subjects.

The overall statistical significance of the logistic regression is shown in Table 5. Each of the three types of Chi-Square results were significant, with Pr > Chi-Square < 0.0001.

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	988.8684	9	<.0001
Score	947.9730	9	<.0001
Wald	839.9953	9	<.0001

Table 5. Statistical significance of the logistic regression

The Type 3 analysis of effects for each explanatory variable is listed in Table 6 below. A Chi Squared value less than 0.05 was considered statistically significant. Significant effects were seen for gender (RIAGENDR), age (RIDAGEYR), body mass index (stnd_BMXBMI), diastolic blood pressure (stnd_Diastolic_BP), triglycerides (stnd_LBXSTR), total cholesterol (stnd_LBXSCH), and alanine aminotransferase (stnd_LBXSATSI). No significant effect was observed for gamma glutamyl transferase (stnd_LBXSGTSI).

Type 3 Analysis of Effects			
Effect	DF	Wald Chi-Square	Pr > ChiSq
RIDAGEYR	1	54.6545	<.0001
stnd_BMXBMI	1	27.5964	<.0001
stnd_BMXWAIST	1	11.7951	0.0006
stnd_Diastolic_BP	1	10.1299	0.0015
stnd_LBXSTR	1	15.9933	<.0001
stnd_LBXSGTSI	1	2.6839	0.1014
stnd_LBXSATSI	1	6.2941	0.0121

Type 3 Analysis of Effects			
Effect	DF	Wald Chi-Square	Pr > ChiSq
stnd_LBXSCH	1	12.2089	0.0005
RIAGENDR	1	60.7634	<.0001

Table 6. Type 3 analysis of effects

The odds ratio estimates are shown in table 7. Examination of the Odds ratio estimates shows that gender (RIAGENDR), age (RIDAGEYR), body mass index (stnd_BMXBMI), diastolic blood pressure (stnd_Diastolic_BP), triglycerides (stnd_LBXSTR), total cholesterol (stnd_LBXSCH), and alanine aminotransferase (stnd_LBXSATSI) did not contain the 1 in their respective intervals, consistent with their significant chi-square values. This is illustrated graphically in Figure 12.

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
RIDAGEYR	0.989	0.987	0.992
stnd_BMXBMI	0.683	0.593	0.788
stnd_BMXWAIST	0.736	0.618	0.877
stnd_Diastolic_BP	0.918	0.871	0.968
stnd_LBXSTR	0.904	0.860	0.950
stnd_LBXSGTSI	0.960	0.914	1.008
stnd_LBXSATSI	0.937	0.891	0.986
stnd_LBXSCH	0.910	0.863	0.959
RIAGENDR 1 vs 2	0.645	0.577	0.720

Table 7. Odds ratio estimates

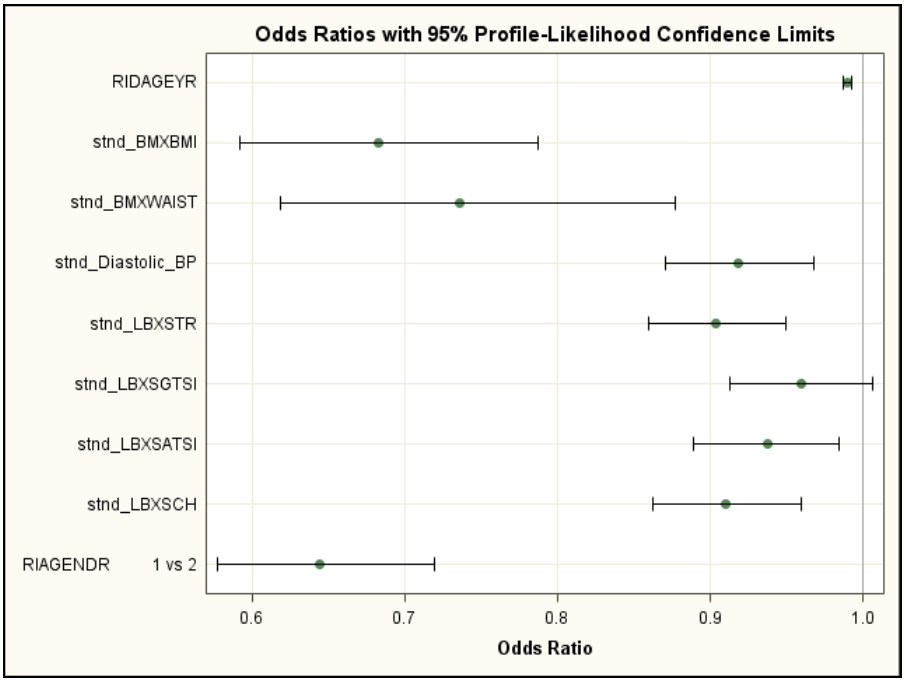

Figure 12. Odds ratio estimates

The overall accuracy of the model is summarized in Table 8. Examination of the model statistics model shows that the model is 70.5% concordant, with a c statistic of 0.705. The c statistic is equivalent to the area under the ROC (receiver operator characteristic) curve, which is shown in figure 13.

Association of Predicted Probabilities and Observed Responses			
Percent Concordant	70.5	**Somers' D**	0.411
Percent Discordant	29.5	**Gamma**	0.411
Percent Tied	0.0	**Tau-a**	0.176
Pairs	17411230	**c**	0.705

Table 8. Association of Predicted Probabilities and Observed Responses

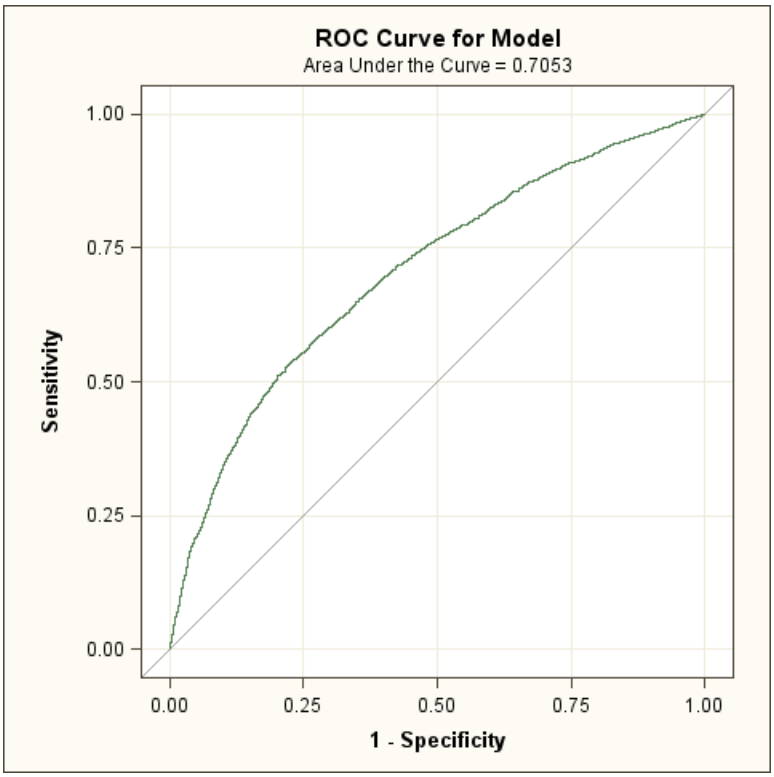

Figure 13. ROC curve for the logistic regression model.

CONCLUSION

The results of our logistic regression model confirm that gender, BMI, age, and waist circumference are risk factors for the presence of increased upper airway resistance during sleep (frequent snoring). Our findings also indicate that frequent snoring has a significant impact on diastolic blood pressure and cholesterol levels (both total cholesterol and triglycerides). Surprisingly, we found also found that frequent snoring was associated with changes in serum alanine aminotransferase, which is a commonly used marker of liver damage that has been reported to be elevated in sleep apnea patients [5]. These findings suggest that even seemingly innocuous levels of sleep disordered breathing, such as frequent snoring, have important physiological consequences that may impact future health, such as the development of obesity, cardiovascular disease, metabolic dysfunction, and liver damage. Furthermore, our results illustrate how SAS Enterprise Guide and SAS Enterprise Miner, in conjunction with continually evolving databases and programs such as the NHANES, can provide a valuable tool for health research.

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