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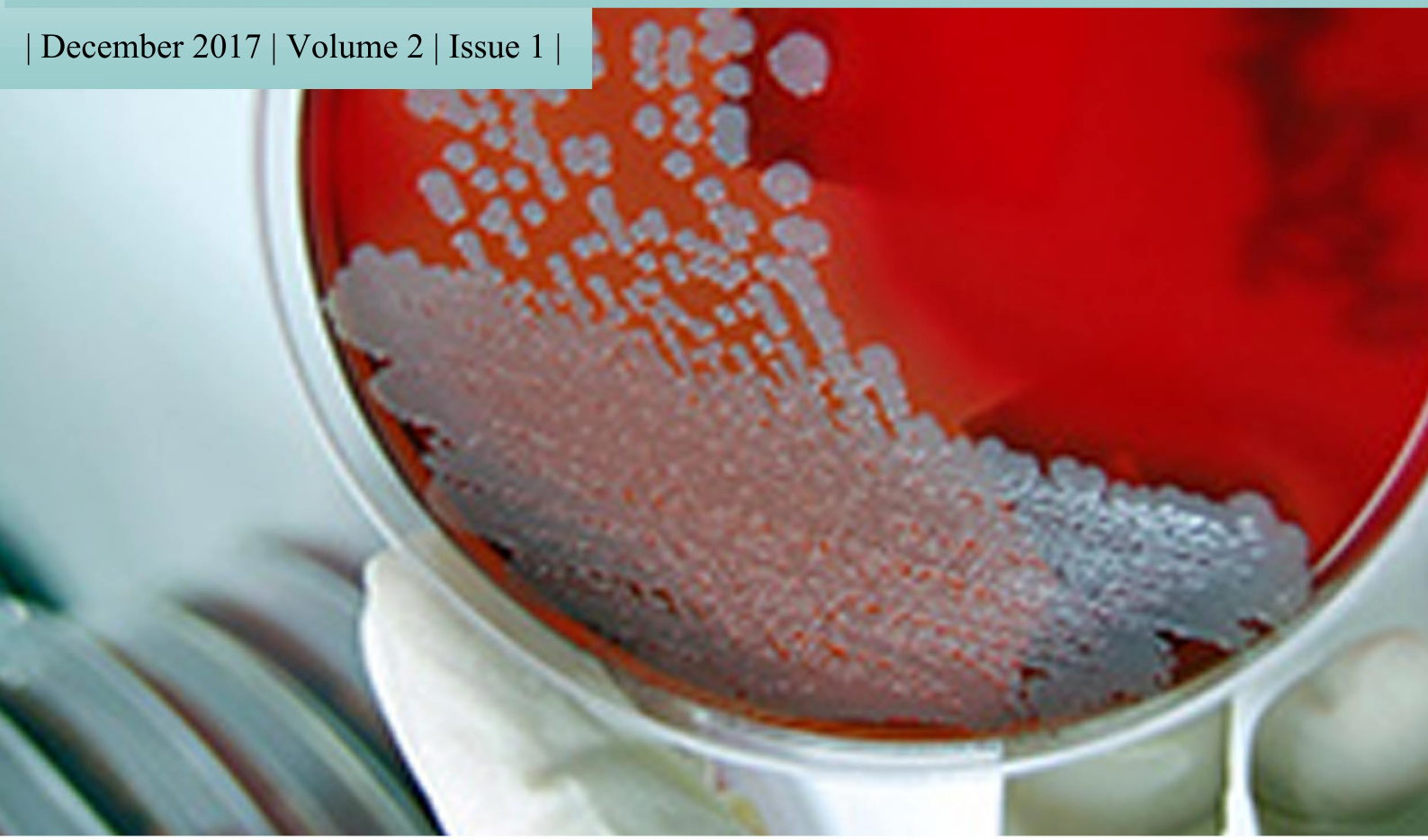
ISSN 2473-4780

EPIDEMIOLOGY

Open Journal

| December 2017 | Volume 2 | Issue 1 |



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EPIDEMIOLOGY

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ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-107

Brief Research

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Volume 2 : Issue 1
Article Ref. #: 1000EPOJ2107

Article History
Received: June 2nd, 2016
Accepted: July 11th, 2016
Published: July 12th, 2016

Citation
Burleson C, Anderson K, Copeland Z, Karcs C, Sullivan KL. Consumption of sugar-sweetened beverages associated with increased odds of depression. *Epidemiol Open J*. 2016; 2(1): 1-6. doi: 10.17140/EPOJ-2-107

Consumption of Sugar-Sweetened Beverages Associated With Increased Odds of Depression

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ABSTRACT

Objective: To evaluate the association between depression and sugary drink intake using participant data from the Behavioral Risk Factor Surveillance Survey (BRFSS).
Design: Cross-sectional data from the 2012 and 2013 BRFSS were examined (N=44,603). Depression was based on self-report of symptoms within the past 30 days. Covariates included age, sex, race, employment status, body mass index (BMI), education level, and exercise in the past 30 days.
Setting: Data from a national telephone survey (BRFSS) were used to assess risk factors associated with health of the participants.
Subjects: Participants in the 2012 and 2013 BRFSS were included in this analysis (N=44,603).
Results: Adjusting for confounders, the odds of depression increased by 5% for every sugary drink consumed (odds ratio (OR)=1.06, 95% confidence interval (CI)=1.02-1.10). Depression was also associated with race, with non-Hispanic blacks being 60% more likely to be depressed than non-Hispanic whites. Unemployment and having a high school or less education were independently associated with depression. The association of depression and consumption of sugar sweetened beverages was stronger among women than men.
Conclusion: This study indicates that consuming sugary drinks are associated with an increased odds of depression. These findings support advocacy efforts for an overall healthy lifestyle. In addition, future research should evaluate this association using a cohort design in order to establish the temporality of this association.

KEYWORDS: Mental health; Epidemiology; Diet; Soda.

ABBREVIATIONS: BRFSS: Behavioral Risk Factor Surveillance Survey; USDA: United States Department of Agriculture; NIH: National Institutes of Health; BMI: Body Mass Index; IRB: Institutional Review Board.

INTRODUCTION

Increased sugar intake has become a major concern in the United States over the past few decades, with particular concern related to sugar sweetened beverages. Between 1977 and 1996 all age groups in the United States (US) more than doubled their consumption of sugary beverages.[1] In 2000, the average American citizen consumed 260 grams of sugar per day, although the United States Department of Agriculture (USDA) recommends no more than 40 grams per day. This recommended amount would be equivalent to one 12-ounce soft drink.[2] The United States also has an increasing rate of mental health disorders, especially depression and anxiety. According to the National Institutes of Health (NIH), 15.7 million adults reported having at least one major depressive episode in 2013, accounting for 6.7% of the overall US population. The NIH also reported that an estimated 18% of the adult population identifies themselves as having an anxiety disorder, with 4% of these being classified as "severe".[3] The increased levels of sugar intake and increased reporting of mental illness are both major public health concerns

ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-107

in the US.

Overwhelming evidence suggests that added dietary sugar has a negative impact on an individual's mental health. Research has provided many examples of sugar consumed excessively leading to altered mental health, however the association between the concentrated sugar contents in manufactured sugary beverages and depressive symptoms has not been examined. With the current increase in both sugary beverage intake as well as reported depression in the US, the objective of this study was to evaluate the possible association between sugary beverage intake and reported depression symptoms using data from the Behavioral Risk Factor Surveillance System (BRFSS).

METHODS

The BRFSS is a national telephone survey used to assess risk factors associated with health of the participants.[4] It is conducted on an annual basis throughout the US. Response data for the years 2012 and 2013 were included in this analysis.

Inclusion and Exclusion Criteria

For participants to be included in this analysis, answers for both the outcome and exposure variables (described below) must have been valid. Any missing responses to the aforementioned variables excluded the participant from the analysis.

Outcome

BRFSS participants were asked how often during the past month they felt "so depressed that nothing could cheer (them) up?".[4,5] Participants who self-reported depression in this manner were categorized as depressed.

Exposure

The primary exposure for this analysis was intake of sugar sweetened beverages. Two questions in the BRFSS provide these data, asking participants to report their consumption in the past 30 days:

1. "About how often do you drink regular soda or pop that contains sugar?."[4,5]
2. How often did you drink sugar-sweetened fruit drinks (such as Kool-aid and lemonade), sweet tea, and sports or energy drinks (such as Gatorade and Red Bull)?".[4,5]

Participants were asked to not include 100 percent fruit juice, diet drinks, or artificially sweetened drinks such as diet soda or diet pop. Responses to these questions were standardized to the number of drinks consumed per day and this variable was considered continuous.

Covariates

Covariates for the study included participant's age, sex, race, employment status, body mass index (BMI), education level, and exercise in the past 30 days. Age was categorized as 18-24, 25-34, 35-44, 45-54, 55-64, and 65+ years. Race was classified as Non-Hispanic white (reference group), Non-Hispanic black, or other; employment status was categorized as employed (employed for pay or self-employed) or not employed (retired, student, homemaker or looking for work); education was coded as high school or less or more than high school, and exercise was dichotomized to indicate if the participant exercised at all outside of their employment during the past month. BMI was treated as a continuous variable and was calculated by BRFSS based on participants' self-reported weight and height. These covariates were considered as possible confounders.

Analysis

The bivariate association between each covariate and depression and sugar sweetened beverages (separately) was evaluated using *t*-tests and Chi-square tests, as appropriate. Means and standard errors (SE) were calculated for continuous variables and frequencies were obtained for categorical variables. A logistic regression model was constructed to evaluate the association between sugar sweetened beverages and depression, controlling for confounders. In addition to the model for the entire sample, separate models were evaluated stratified by sex in order to assess possible effect modification. Survey weights were used throughout the analysis, which was performed using SAS version 9.4.[6] Survey procedures were used for mean, frequency and logistic procedures.

RESULTS

Table 1 shows the unadjusted demographic distribution by depression status. Among those depressed, more than 60% of the study population was 44 years of age or older, income level was fairly evenly distributed among the participants, education was also fairly even for those obtaining a high school degree and higher, some college or technical school and finishing college. Those not participating in exercise reported depression more frequently than those who did exercise (32.8% crude fibre (cf.) 20.1%, respectively), although the majority of both groups did not exercise. There was also a lower percentage of employed and retired individuals in the depressed group (43.5% of depressed participants were employed and 18.7% were retired cf. 56.8% employment and 28.0% retirement among non-depressed participants); however in the depressed group there was also a large percentage (18%) of individuals classified as "unable to work".

After adjusting for confounders using logistic regression, it was found that drinking one sugary beverage per day increases the likelihood of depression by 6% (OR=1.06, 95% CI=1.02-1.10) (Table 2). Among other covariates, race was most strongly associated with depression, with black non-Hispanics being approximately 60% more likely to be depressed (OR=1.62, 95% CI=1.19-2.20) and other races being more than twice as likely to be depressed (OR=2.16, 95% CI 1.79-2.62) compared to white non-Hispanics. Being unemployed and hav-

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Variables	Depressed (N=5,439)	Non-Depressed (N=39,164)	*p*-Value (crude)
	N (%)	N (%)	
Sex			
Male	2,119 (39.0%)	16,498 (42.1%)	<0.0001
Female	3,320 (61.0%)	22,666 (57.9%)	
Age (years)			
18-24	377 (6.9%)	1,829 (4.7%)	<0.0001
25-34	659 (12.1%)	3,869 (9.9%)	
35-44	794 (14.6%)	5,068 (12.9%)	
45-54	1,236 (22.7%)	6,991 (17.6%)	
55-64	1,246 (22.9%)	9,020 (23.0%)	
65 and Older	1,127 (20.1%)	12,387 (31.6%)	
Employment Status			
Employed for Wages	1,988 (36.6%)	18,439 (47.1%)	<0.0001
Self-employed	373 (6.9%)	3,805 (9.7%)	
Out of work for more than 1 year	354 (6.5%)	756 (1.9%)	
Out of work for less than a year	269 (4.9%)	778 (2.0%)	
A homemaker	273 (5.0%)	2,101 (5.4%)	
A student	170 (3.1%)	857 (2.2%)	
Retired	1,018 (18.7%)	10,980 (28.0%)	
Unable to work	981 (18.0%)	1,332 (3.4%)	
Missing=129			
Income Level (Household, $/year)			
Less than 10,000	603 (11.1%)	1,114 (2.8%)	<0.0001
Less than 15,000	518 (9.5%)	1,451 (3.7%)	
Less than 20,000	593 (10.9%)	2,229 (5.7%)	
Less than 25,000	636 (11.7%)	3,086 (7.9%)	
Less than 35,000	607 (11.2%)	3,834 (9.8%)	
Less than 50,000	616 (11.3%)	5,477 (14.0%)	
Less than 75,000	557 (10.2%)	6,239 (15.9%)	
75,000 or more	729 (13.4%)	11,199 (28.6%)	
Missing=5,115			
Education			
Never attended school or only kindergarten	16 (0.3%)	33 (0%)	<0.0001
Grades 1 through 8 (elementary)	209 (3.8%)	538 (1.4%)	
Grades 9 through 11 (some high school)	466 (8.6%)	1,321 (3.4%)	
Grade 12 or GED (high school graduate)	1,722 (31.7%)	10,211 (26.1%)	
College 1 to 3 years	1,608 (29.6%)	11,494 (29.3%)	
College 4 years or more years	1,408 (25.9%)	15,482 (39.5%)	
Missing=95			
Race			
White non-Hispanic	4,186 (80.0%)	34,561 (88.2%)	<0.0001
Black non-Hispanic	308 (5.7%)	1,142 (2.9%)	
Asian non-Hispanic	95 (1.7%)	530 (1.4%)	
American Indian/Alaskan Native	182 (3.3%)	631 (1.6%)	
Hispanic	473 (8.7%)	1,444 (3.7%)	
Other race non-Hispanic	195 (3.9%)	856 (2.2%)	
Exercise			
Yes	1,783 (32.8%)	7,864 (20.1%)	<0.0001
No	3,642 (67.2%)	31,248 (79.9%)	
Missing=66			
Continuous Variables	**Mean±SE**	**Mean±SE**	***p*-value**
BMI	27.87±0.19	27.16±0.07	0.0004
Sugary-drink consumption (#/day)	1.12±0.13	0.62±0.02	<0.0001

SE: Standard Error.

Table 1: Demographics.

ing a high school education or less were also associated with depression status (OR=2.12, 95% CI=1.80-2.51; OR=1.89, 95% CI=1.62-2.18, respectively).

Consistent with prior research, there also was a protective factor associated with exercise, as those who did not partake in regular exercise, outside of their profession, were 71% more likely to be depressed in comparison with their counterparts who did exercise. This protective factor was also seen in individuals of "retirement age" in the 65 years and older category, which is also consistent with a greater percentage of non-depressed retirees seen (Table 1).

It should also be noted that there was a greater percentage of women that self-reported depression with women having a 17% greater chance of depressive symptoms. In the sex-stratified analysis, the odds of depression was higher among women than men, although the confidence intervals overlapped (Table 3). Contrary to the whole-group findings, age was not independently associated with depression among women.

ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-107

	Odds Ratio	95% CI
Sugary Beverages (#per day)	1.06	1.02-1.10
Sex		
Male	Ref	
Female	1.17	1.01-1.36
Age		
18-24 years	Ref	
25-34 years	1.50	1.10-2.02
35-44 years	1.18	0.88-1.58
45-54 years	1.25	0.94-1.65
55-64 years	0.99	0.74-1.33
65+ years	0.43	0.31-0.59
Race		
White, non-Hispanic	Ref	
Black, non-Hispanic	1.61	1.18-2.19
Other	2.06	1.70-2.50
BMI	1.01	1.00-1.03
Employment		
Employed for pay	Ref	
Not employed	2.12	1.79-2.51
Education		
More than high school	Ref	
High school graduate or less	1.78	1.53-2.02
Exercise	1.71	1.45-2.02
Yes	Ref	
No	1.71	1.45-2.02

*Each measure is adjusted for other variables in table.
CI: Confidence Interval; Ref: Reference group.

Table 2: Odds of depression (adjusted*) (n=44,243).

	Men	Women
	Odds Ratio (95% CI)	**Odds Ratio (95% CI)**
Sugary Beverages (#per day)	1.05 (1.02-1.08)	1.11 (1.01-1.22)
Age		
18-24 years	Ref	
25-34 years	2.19 (1.34-3.57)	1.09 (0.75-1.58)
35-44 years	1.47 (0.92-2.35)	1.03 (0.70-1.50)
45-54 years	1.75 (1.12-2.73)	0.97 (0.68-1.39)
55-64 years	1.64 (1.05-2.57)	0.66 (0.46-0.96)
65+ years	0.65 (0.40-1.05)	0.32 (0.21-0.49)
Race		
White, non-Hispanic	Ref	
Black, non-Hispanic	1.28 (0.78-2.12)	1.85 (1.24-2.76)
Other	1.96 (1.47-2.61)	2.03 (1.58-2.60)
BMI	1.00 (0.97-1.02)	1.02 (1.01-1.04)
Employment		
Employed for pay	Ref	
Not employed	2.19 (1.66-2.88)	2.11 (1.71-2.60)
Education		
More than high school	Ref	
High school graduate or less	2.05 (1.66-2.53)	1.59 (1.28-1.97)
Exercise		
Yes	Ref	
No	1.30 (1.02-1.65)	2.05 (1.63-2.57)

*Each measure is adjusted for other variables in table.
CI: Confidence Interval; Ref: Reference group.

Table 3: Sex-specific Odds of Depression (adjusted*).

ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-107

DISCUSSION

We found that sugary drink consumption was positively associated with depression, controlling for age, sex, and measures of socio-economic status. For every sugary drink consumed daily, the odds of depression increased by 5%. Depression was also independently associated with younger age as well as race, with non-Hispanic blacks being 60% more likely to be depressed than non-Hispanic whites. There also appeared to be an effect modification showing sugary sweetened beverages may have a greater effect on women than men (OR=1.17).

This study is one of the few to compare men and women of all adult age groups, as well as to examine the direct association between sugary drinks and depression. Previous studies have typically focused solely on youth or women, as well as specific diets.[7-14] An ecologic study evaluated the association between major depression and national sugar consumption in Korea, the US, France, Germany, Canada, and New Zealand and found a positive correlation (p=0.004).[7] Whitaker et al[8] found a significant association between depressive symptoms and saturated fat and sugar intake (<0.05) and, although not statistically significant, a positive association between depressive symptoms and sweetened beverage consumption (p=0.06).

The association between sugar and depression is especially concerning in children and adolescents, as rates for both are dramatically increasing in this age group. An Australian study reported that individuals who consumed more than a half litre of soft drinks per day had approximately a 60% greater risk of having depression, stress, suicidal ideation, and psychological distress than those who did not consume soft drinks.[9] A cross-sectional study in China of 12-19 year old students found an association between soda intake and suicidal plans or attempts. Individuals who consumed at least three soft drinks per day were 80% more likely to attempt suicide than non-consumers.[10] Additionally, a survey in 2005 in California reported 40% of 2-11 year old children consumed at least one soda per day.[11] A significant association between soda consumption and withdrawn behavior, attention, and aggressive behaviors (p<0.05) has been reported among urban 5-year olds, which may influence the occurrence of mental disorders as the children grow.[12]

High consumption of sugar may also affect women differently than men. Women who consumed a traditional diet based on vegetables, meats, fish, fruits, and whole grains were shown to have a lower risk of having depression while those who consumed a Western diet consisting of processed or fried foods, refined grains, sugary products, and beer were more likely to have depression (OR=1.52).[13] An examination of BMI, specific food intake, and severity of depression reported that greater consumption of high-calorie sweet food, such as chocolate, soda, and sweetened fruit drinks, were associated with depressive symptoms (p<0.01) but not BMI. The opposite was true for high-calorie non-sweet food, such as fried foods, hamburgers, and whole-milk, where there was an association between BMI but not with depressive symptoms. This may suggest sugar and not caloric surplus plays a more significant role in depression.[14]

The large, nationally representative sample included in the BRFSS is the primary strength of this study. However, there were limitations in the methodology. Importantly, the survey did not clearly define an amount for what constituted one drink. Variables such as the particular sugar sweetened beverage, the volume of beverage or sugar content contained in the beverage can vary widely, leading to information bias. The results are further limited by participants' self-report of depressive symptoms in lieu of a validated measure of depression. The BRFSS is a national survey in which questions are categorized in modules and many modules are only offered semi-annually. Additionally, variables included in the survey are generally limited to specific options for response. Expanding these options would enhance analytic options in future research. Due to the cross-sectional nature of the data, the temporal relation between consumption of sugary drinks and depression cannot be established and should be further investigated.

Another limitation is that the BRFSS does not account for the effects of caffeine. Caffeine can be found in many sugar sweetened beverages, especially sodas and pops. The association between sugar consumption and depression may be confounded by caffeine intake. In 2011, Lucas et al[15] investigated this issue, surveying 50,739 US women with a mean age of 63 years who were free from depressive symptoms at baseline. They prospectively assessed caffeine and coffee consumption and depressive symptoms. During the 10 year follow-up 2,607 incident cases of depression were observed.

Consistent with established risk factors for depression, we found employment status (OR=2.12), race (non-Hispanic blacks (OR=1.61), and races other than non-Hispanic white (OR=2.06)) accounted for the highest odds for development of depression. Further analysis of these sub-populations could establish more demographically deterministic information on sugar and depression. Furthermore, because women were shown to be an effect modifier, in the future it might be advantageous to look at gender specifically when doing research on the topic.

CONCLUSIONS

The association among consumption of sugary sweetened beverages and depression adds to the volume of evidence negatively linking health and sugar. As policymakers look to advocate against high sugar contents in both foods and beverages, this data can provide additional support for their recommendations. Lowering the allowable sizes of sugar sweetened beverages available for purchase or informing consumers of the health consequences of their beverage choices is important to begin to reduce the prevalence and incidence of preventable morbidities.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-107

ETHICAL APPROVAL

This study was approved by the Institutional Review Board (IRB) of Georgia Southern University.

REFERENCES

1. Nielsen SJ, Popkin BM. Changes in beverage intake between 1977 and 2001. *Am J Prev Med.* 2004; 27(3): 205-210. doi: 10.1016/j.amepre.2004.05.005

2. USDA, United States Department of Agriculture. 2015. Web site. http://www.usda.gov/wps/portal/usda/usdahome. Accessed June 1, 2016

3. NIH, National Institutes of Health. Turning Discovery into Health. 2015. Web site. https://www.nih.gov/. Accessed June 1, 2016

4. CDC, Centers for Disease Control and Prevention. *Behavioral Risk Factor Surveillance System Survey Questionnaire*. Atlanta, Georgia, USA: Department of Health and Human Services, Centers for Disease Control and Prevention; 2012, 2013.

5. CDC, Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System. 2015. Web site. http://www.cdc.gov/brfss/. Accessed June 1, 2016

6. SAS. Analytics, Business Intelligence and Data Management. 2015. Web site. https://www.sas.com/en_us/home.html. Accessed June 1, 2016

7. Westover AN, Marangell LB. A cross-national relationship between sugar consumption and major depression? *Depression and Anxiety*. 2002; 16(3): 118-120. doi: 10.1002/da.10054

8. Whitaker KM, Sharpe PA, Wilcox S, Hutto BE. Depressive symptoms are associated with dietary intake but not physical activity among overweight and obese women from disadvantaged neighborhoods. *Nutr Res.* 2014; 34(4): 294-301. doi: 10.1016/j.nutres.2014.01.007

9. Shi Z, Taylor AW, Wittert G, et al. Soft drink consumption and mental health problems among adults in Australia. *Public Health Nutr*. 2010; 13(7): 1073-1079. doi: 10.1017/S1368980009993132

10. Pan X, Zhang C, Shi Z. Soft drink and sweet food consumption and suicidal behaviours among Chinese adolescents. *Acta Paediatr.* 2011; 100(11): e215-e222. doi: 10.1111/j.1651-2227.2011.02369.x

11. Babey SH, Jones M, Yu H, et al. Bubbling over: Soda consumption and its link to obesity in California. *Policy Brief UCLA Cent Health Policy Res.* 2009; (PB2009-5): 1-8. Web site. https://escholarship.org/uc/item/1fj3h5cj. Accessed June 1, 2016

12. Suglia SF, SolnickS, Hemenway D. Soft drinks consumption is associated with behavior problems in 5-year-olds. *J Pediatr*. 2013; 163(5): 1323-1328. doi: 10.1016/j.jpeds.2013.06.023

13. Jacka F, Pasco J, Mykletun A, et al. Association of western and traditional diets with depression and anxiety in women. *Am J Psychiatry.* 2009; 167(3): 305-311. doi: 10.1176/appi.ajp.2009.09060881

14. Jeffery RW, Linde JA, Simon GE, et al. Reported food choices in older women in relation to body mass index and depressive symptoms. *Appetite.* 2009; 52: 238-240. doi: 10.1016/j.appet.2008.08.008

15. Lucas M, Mirzaei F, Pan A, et al. Coffee, caffeine, and risk of depression among women. *Arch Intern Med.* 2011; 171(17): 1571-1578. doi: 10.1001/archinternmed.2011.393

EPIDEMIOLOGY

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ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-108

Research

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Volume 2 : Issue 1
Article Ref. #: 1000EPOJ2108

Article History
Received: July 11th, 2016
Accepted: August 5th, 2016
Published: August 8th, 2016

Citation
Gómez-Elipe A, Aguirre-Jaime A. Another approach to detect malaria epidemics and to evaluate the impact of their control measures in situation of lack of information. *Epidemiol Open J.* 2016; 2(1): 7-15. doi: 10.17140/EPOJ-2-108

Another Approach to Detect Malaria Epidemics and to Evaluate the Impact of their Control Measures in Situation of Lack of Information

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ABSTRACT

The purpose of this study is to establish a theoretical epidemiologic threshold for the rate of reported malaria cases in order to detect epidemics and evaluate the impact of control measures. To create this epidemiologic threshold it has been used an multiple cross-over time series autoregressive integrated moving average forecasting model that reflects the dependence of the magnitude of the rate of malaria reports on the past levels of rain, temperature and vegetation density according to factors related with malaria transmission described by the MacDonald's theory. Information available for the model derivation and accuracy testing was obtained from Médecins Sans Frontières in Karuzi, a Burundi's province, with a health network of a 100-bed hospital and 11 health centers, that consists in the monthly malaria incidence rate estimated from clinical diagnostics in medical consultations with a 5-20% of clinical cases with microbiological confirmation in non-epidemic periods and less than 2% during outbreaks, the cumulative monthly level of precipitation and the minimum and maximum mean monthly temperature recorded by the local meteorological stations, as well as the NDVI provided by the National Oceanographic and Atmospheric Administration satellites. This available information covers the 1997-2003 period. The obtained model makes it possible to create a curve of expected non-epidemic case reports with a reliability of 95%. This model identified four epidemics in the 7-year study period and detected the impact of a malaria control campaign in the last year. The application of this methodological tool permits the timely detection of malaria epidemics and the evaluation of the impact of measures for its control.

KEYWORDS: Autoregressive integrated moving average modeling (ARIMA); Malaria; Malaria epidemiologic surveillance system.

ABBRIVATIONS: ARIMA: Autoregressive integrated moving average modeling; ACF: Sample autocorrelation function; PACF: Partial autocorrelation function; NDVI: Normalized Difference Vegetation Index.

HIGHLIGHTS

- Malaria is rampant in Africa and causes significant mortality and morbidity
- Malaria transmission is complex and is believed to be associated with local climate changes
- We propose a tool of malaria incidence forecasting for their epidemiological surveillance
- The proposed model could be useful for detecting and preventing malaria epidemics

INTRODUCTION

Malaria epidemics are an important public health problem for the populations of Sub-Saharan Africa.[1-5] The influence of climatic factors on the genesis of malaria epidemics has

ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-108

been described in numerous studies.[6-9] Early detection of these epidemics has been difficult; however, giving rise to high rates of morbidity and mortality that could be avoided with timely and effective detection and intervention measures.[10-11] Initiatives such as the Malaria Early Warning Systems[12] have been undertaken to develop and evaluate more precise methods for the definition, detection, early warning and forecasting of malaria epidemics.[13-15] Both the definition and methods of detection of malaria epidemics are generally based on the estimation of measures of central tendency and dispersion of historic malaria morbidity to establish epidemic thresholds in order to make decisions about the application of contingency measures to control its spread.[16,17] This approach suffers from serious methodological weaknesses, however, such as the arbitrary manner of deciding what morbidity rates to exclude from the calculation of the threshold because they are considered epidemic values, thus defining "epidemic" before hand in order to make a supposedly objective determination of what constitutes an epidemic. Another limitation is the use of statistical procedures for the treatment of random variables for measurements of incidence, when the variables are auto-correlated, because of these kinds of weaknesses; the epidemiologic thresholds for epidemic detection obtained by such methods are not reliable.

Our starting hypothesis is that environmental factors such as temperature, precipitation and vegetation levels, as estimators of the population density and infectivity of the vector and the development of the parasite, on the one hand, combined with the level of malaria incidence in a recent period, as an estimator of the magnitude of the parasite reservoir and population susceptibility, on the other, could explain variations in malaria incidence. This study aims to create a theoretical epidemiologic threshold i.e, endemic, non-epidemic, usually expected, normally, incidence, based on the behavior of the incidence rate predicted by a model that establishes the relations among the variables. The purpose is to obtain a simple and easily applied tool that provides a practical and reliable way to identify epidemics, so that health services can implement timely control measures to interrupt the spread of the disease or mitigate its effects, and to assess the effectiveness of health interventions to these ends. Considering the methodological purpose of this study we use only real data in order to verify the validity and accuracy of our theoretical elaboration. This verification uses as empirical material the available reports of monthly malaria cases treated by the medical services routinely collected by the surveillance system, together with monthly levels of rain, temperature and vegetation density in the province of Karuzi, Burundi, during a seven years period.

MATERIAL AND METHODS

Our model is based on factors related with malaria transmission described by MacDonald.[18] According to this relation; the determining factors are vector population density, transmission capacity based on vector survival and duration of the extrinsic incubation period, and immunity in the susceptible human host. Rainfall influences the vector population by affecting larvae production and maturation capacity, and is reflected in the vegetation index; and temperature influences transmission capacity by affecting the extrinsic incubation period. Our hypothesis is based on the fact that in tropical areas at altitudes over 1,200 m, the most important factor limiting malaria transmission is minimum temperature, since under 16 ºC inhibit parasite maturation, sexual reproduction and sporozoite development. Tropical areas between latitudes 25 ºN and 25 ºS and at altitudes of 1,000-2,000 m have enough monthly precipitation to maintain abundant marshy areas where vector larvae can develop. In an epidemic situation, factors that can most plausibly explain fluctuations in transmission are: i) increased minimum temperature, which would permit a prolongation of seasonal transmission and a "staircase" effect of repeated superinfections with increasing parasitemia and anemia up to clinical thresholds; ii) increased maximum temperature, shortening the extrinsic incubation period with an exponential effect on vector transmission capacity; iii) increased rainfall, with consequent increase in vegetation density, resulting in a larger vector population and a transmission increase; and iv) increased population reservoir of the parasite, which induces faster transmission.

One way of symbolically representing these assumptions can be obtained by taking I_t to mean the malaria incidence rate in month t; R_t as the cumulative level of precipitation in that month; T_t as the mean temperature in that month; V_t as the mean vegetation density in that month; p as the seasonal oscillation period for the previous three variables; and I_{t+k} as the malaria incidence rate for a future month that is k months from month t. These variables would then be interrelated as follows:

$$\sum \alpha I_t^* \sum \beta \sin(2\pi / p)\left(R_t^* T_t^* V_t\right) \rightarrow I_{t+k} \qquad \text{(a)}$$

This relation represents a cumulative linear combination of previous values of the incidence rate, as an estimator of immunity or population reservoir, and the combination of past levels of rainfall, temperature and vegetation density, as estimators of vector capacity, combined to influence future values of the incidence rate. The term that includes rainfall, temperature and vegetation confers an oscillation in the malaria incidence with a period according to their common seasonality. In expression (a) α is the coefficient for the incidence rate, and β for the amplitude of seasonal oscillation estimated by regression. The use of * as an operator to link the components expresses the lack of *a priori* knowledge of how they are interrelated. The model combines all those terms having significant autocorrelation and cross-correlation coefficients with the incidence rate in their corresponding lags.

Data Processing

First we explored malaria rate series, together with temperature, precipitation and vegetation levels series, to identify regularities. Incidence rate trend analysis and periodogram obtained with Fast Fourier and Tukey Transforms help to identify the periodic oscillations to be modeled. The sub-series of the last seasonal

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period are separated. The shortened series is called "base" and the separate sub-series "complement". Rainfall, temperature and vegetation series are shortened to the base period. Simple autocorrelation function (ACF) and partial autocorrelation function (PACF) graphics are obtained for these bases, with lags equal to their oscillation period. Then, we identified, adjusted and evaluated autoregressive integrated moving average (ARIMA) models, which explains the malaria rate by its past values, to introduce as a term in model (a). Periodograms are obtained for the bases of precipitation, temperature and vegetation series to identify seasonal oscillations and their period p in (a). Cross-correlations are obtained of these three series with the ARIMA model residual in the malaria rate base series, to identify lags in the relationship. The ARIMA and oscillatory component terms are combined to form model (a). The coefficients of the terms and goodness-of-fit of the model are estimated. The model works by successively entering the previous rates predicted by the model itself, and the observed values for precipitation, temperature and vegetation in their corresponding lags, thereby obtaining each expected non-epidemic rate in the time series window. The 95% confidence thresholds are estimated with the base rate series white-noise residuals. Data processing was performed using the SPSS™ 21.0 and Statgraphics Plus™ 5.1. The usual two-tailed statistical significance level of $p \leq 0.05$ was established for all these tests.

Information available for the model derivation and accuracy testing was obtained from Médecins Sans Frontières in Karuzi. Karuzi is a Burundi's province located in the central-eastern area of the country, with a population around 300,000 inhabitants, at an altitude of 1,500-1,900 m, with mean annual temperatures ranging from 10.5-13 ºC to 25.5-28.5 ºC. The area is characterized by a October-May wet season, with 141 mm mean monthly precipitation, and a June-September dry season, with 30 mm mean precipitation. The vegetation mass varies with a mean monthly Normalized Difference Vegetation Index (NDVI) of 0.36 in July-October, and 0.53 in November-June. In Figure 1 shows a typical Burundi vegetation map. Karuzi has a health network consisting of a 100-bed hospital and 11 health centers with a total of 311 beds.[19] The monthly malaria incidence rate is estimated from medical consultations considering as a case the patient seeking medical care with a fever over 38 ºC, after excluding other causes. five hundred twenty percent of clinical cases had microbiological confirmation in non-epidemic

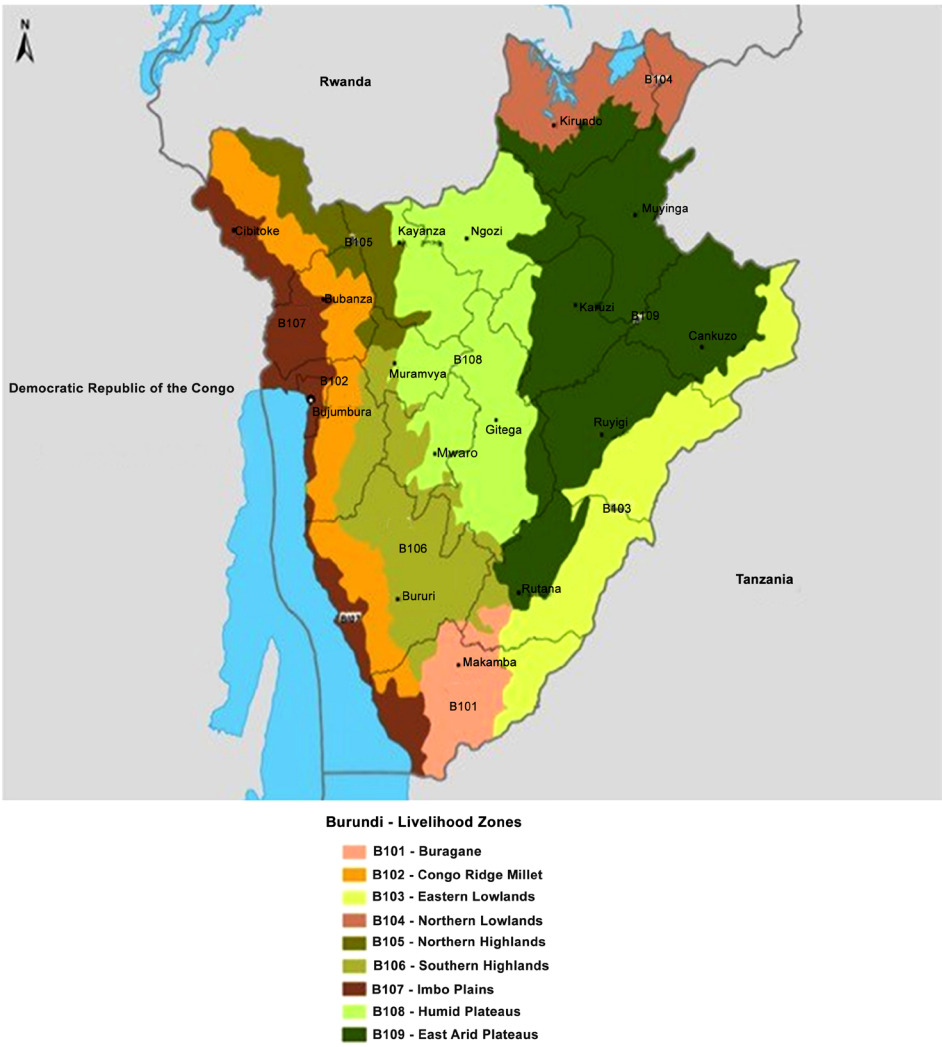

Figure 1: Burundi map of vegetation.

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periods, and <2% during outbreaks, depending on the health facility. For the incidence rate the monthly cumulative reports is the numerator and the denominator is the total population of the province according to the census adjusted for the growth factor. We use the cumulative monthly level of precipitation and the minimum and maximum mean monthly temperature recorded by the local meteorological stations, as well as the NDVI provided by the National Oceanographic and Atmospheric Administration satellites.[20] The images of the vegetation index were processed using WinDisp 4. This available information covers the January 1997 through December 2003 period. During this period various epidemic events occurred in Karuzi.[17,21] Moreover, at the end of 2003, Médecins Sans Frontières together with the Burundi Ministry of Health, launched an intervention to reduce transmission consisted of implementing a new protocol to diagnose and treat malaria, including rapid serologic diagnosis of suspected cases and first-line treatment with artemisinin compounds drugs[22] that produced an important reduction in disease transmission, which is still under evaluation.[23] To test the accuracy of the forecast obtained with the model, the expected and observed endemic rates are compared for the periods in which the epidemic events and reduced incidence occurred.

RESULTS

Figure 2 shows the 1997-2003 series used to construct the model. Its visual exploration does not seem to indicate any trend; for rain, temperature and vegetation, there is a certain seasonal-type oscillation with a 0, 5-1 year period. The results of the trend analysis and periodograms show neither trend nor periodic oscillation in the cumulative monthly rate of malaria reports, while for the rest of the series they confirm the trend absence, and yearly period seasonality. Consequently, for rainfall, temperature and vegetation series the 1997-2002 period is taken as the base, reserving their values during 2003 as the complement, and the malaria rate series is forced to the same cut-offs to form its base and complement.

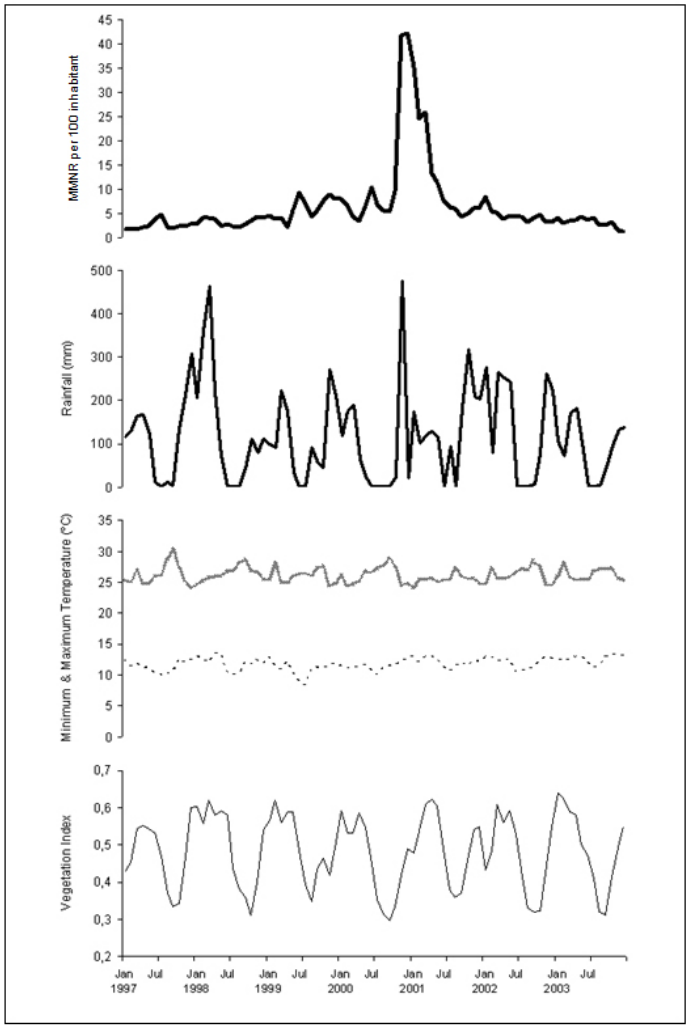

Figure 2: Monthly Malaria Notification Rate per 100 inhabitants in Karuzi province, Burundi, from January 1997 to December 2003 (MMNR, first picture in heavy bold solid line); Monthly cumulative rainfall in mm (Rainfall, second pictures in light bold solid line); Maximum and Maximum monthly temperature in ºC (Maximum Temperature, third picture in bold dashed line; Minimum monthly, fourth picture in light dashed line); and Normalized Difference Vegetation Index (Vegetation Index, fifth picture in light solid line).

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Correlograms of the base malaria rates show a non-seasonal configuration with significant coefficients only in lag 1 (ACF=0.82, PACF=0.82, both $p<0.05$) which indicates that ARIMA model (1, 0, 0) represents the influence of each preceding value on the following one. This model fits with a coefficient of 0.80 ($p<0.0001$) and explains 80% of the observed variability in the rate, leaving a residual that is nearly white noise, but with hints of regular patterns.

The base periodograms of precipitation, temperature and vegetation show, similar to complete series, a seasonal oscillation with a period of 12 months, therefore term[1] of the model takes the form $\sin\beta(0.52\ R_t\ T_t\ V_t)$. Cross-correlation of this term with the residuals of ARIMA (1,0,0) shows that only the lag 1 coefficient is significant, therefore the environmental influence on the malaria rate becomes $\sin\beta(0.52R_{t-1}\ T_{t-1}\ V_{t-1})$. With the addition of the term for the influence of the environmental variables to the autoregressive term, and after fitting the model, it takes the form:

$$I_t = 0.80I_{t-1} + 0.99\sin(0.52R_{t-1}\ T_{t-1}\ V_{t-1}) \qquad \text{(b)}$$

This model explains a 82% of the observed variability in the malaria rate (R^2_{adj}, $p<0.0001$) with a 95% CI of 0.68-0.95 ($p<0.0001$) for the coefficient of the autoregressive term and of 0.97-1.00 ($p<0.0001$) for the environmental term. Model (b) leaves a white noise residual on the base malaria rates, normally distributed with a mean of 0 and 0.98 SD.

Figure 3 depicts the expected epidemiologic threshold for the malaria rate, with its 95% confidence interval, that is obtained with this model for the period February 1997-December 2002, using the rate for January 1997 as the initial value, and the precipitation, maximum temperature and vegetation density for each preceding month. Table 1 shows the expected non-epidemic monthly cumulative malaria case-reported rate for the base malaria series, the epidemiologic threshold, and the observed value for each month in the period 1997-2002. This epidemiologic threshold identifies four periods of an excess in malaria incidence rates: June-July 1999, October 1999-January 2000, June-July 2000, and October 2000-June 2001, corresponding to the four epidemics that occurred in the study period.[13,19] The two values of the rate that exceeds the threshold of the epidemiologic threshold during a single month (July 1997 and January 2002) were not considered epidemic outbreaks, following the Serf ling's criteria.[24]

The epidemiologic threshold predicted for the cumulative rate of malaria monthly reports for 2003, with its 95% threshold, is shown in Figure 4 and in Table 2. A change in the trend in the observed rate can be seen beginning in November 2003, with a more than 60% reduction with respect to the preceding month, which can be attributed to the health intervention that began in October of that year.[22] This unusual decline in the months of November and December 2003 is captured by the lower threshold of the epidemiologic threshold obtained with the model, which reflects chance fluctuation in the rate.

DISCUSSION

In this work we propose a tool for malaria surveillance that is simple in conception and easy to use in defining and detecting malaria epidemics, and to evaluate the impact of the measures for their control. Direct information about variables related to the intensity of malaria transmission, as anopheline density in relation to man, about the probability of mosquito survival or about the duration of the extrinsic cycle of the parasite in the mosquito is not available nor information regarding the state of the human population reservoir. This tool makes it possible to

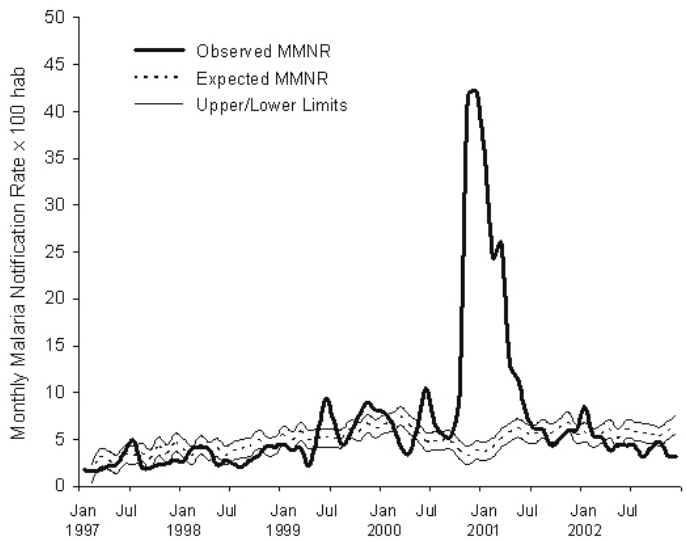

Figure 3: Expected and observed values for the Monthly Malaria Notification Rate (MMNR) per 100 inhabitants in Karuzi, Burundi, from January 1997 to December 2002. The upper and lower limits of the expected values are estimated for a 95% confidence endemic threshold.

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Month	Expected	Max	Observed	Month	Expected	Max	Observed
Jan 1997	---	---	1.7	Jan 2000	6.6	7.5	7.9
Feb	1.3	2.3	1.6	Feb	6.8	7.8	6.5
Mar	3.0	4.0	1.7	Mar	7.4	8.4	4.2
Apr	2.7	3.7	2.2	Apr	6.5	7.5	3.5
May	2.3	3.3	2.3	May	5.8	6.8	6.5
Jun	3.3	4.3	3.8	Jun	4.7	5.7	10.4
Jul	3.2	4.2	4.9	Jul	4.8	5.8	6.8
Aug	3.6	4.6	2.1	Aug	4.8	5.8	5.6
Sep	2.9	3.9	1.9	Sep	4.8	5.8	5.4
Oct	4.2	5.2	2.3	Oct	3.9	4.8	9.5
Nov	3.4	4.4	2.4	Nov	3.2	4.2	41.6
Dec	4.6	5.6	2.8	Dec	3.8	4.7	42.2
Jan 1998	4.0	5.0	2.7	Jan 2001	3.6	4.6	35.3
Feb	3.2	4.2	4.1	Feb	4.0	5.0	24.4
Mar	4.3	5.3	4.1	Mar	5.1	6.0	25.9
Apr	3.7	4.7	4.0	Apr	5.7	6.6	13.2
May	4.0	5.0	2.3	May	6.1	7.1	11.4
Jun	3.2	4.2	2.7	Jun	5.6	6.6	7.7
Jul	3.7	4.7	2.4	Jul	5.5	6.5	6.2
Aug	4.0	5.0	2.1	Aug	6.1	7.1	6.0
Sep	4.2	5.1	2.8	Sep	5.6	6.6	4.3
Oct	5.0	5.9	3.4	Oct	6.2	7.1	5.0
Nov	4.2	5.2	4.3	Nov	6.8	7.8	5.9
Dec	4.3	5.3	4.2	Dec	5.5	6.5	6.0
Jan 1999	5.4	6.4	4.5	Jan 2002	5.7	6.7	8.4
Feb	4.8	5.8	3.8	Feb	5.1	6.1	5.4
Mar	5.8	6.7	4.1	Mar	5.5	6.5	5.2
Apr	4.9	5.9	2.2	Apr	6.1	7.0	3.8
May	5.1	6.1	5.6	May	5.1	6.0	4.4
Jun	5.1	6.1	9.4	Jun	6.0	7.0	4.3
Jul	5.1	6.1	6.9	Jul	5.8	6.8	4.3
Aug	5.1	6.0	4.4	Aug	5.6	6.6	3.1
Sep	6.0	7.0	5.7	Sep	5.5	6.5	4.1
Oct	5.8	6.8	7.6	Oct	5.3	6.3	4.7
Nov	6.6	7.6	8.9	Nov	5.9	6.9	3.2
Dec	6.1	7.1	8.1	Dec	6.6	7.6	3.2

Table 1: Values predicted for the expected endemic cumulative monthly rate of malaria case reports per 100 inhabitants in Karuzi with the Upper Limit at 95% confidence for the epidemic threshold (Max) obtained by the forecasting model and the corresponding rates of monthly malaria cases reported during 1997-2002.

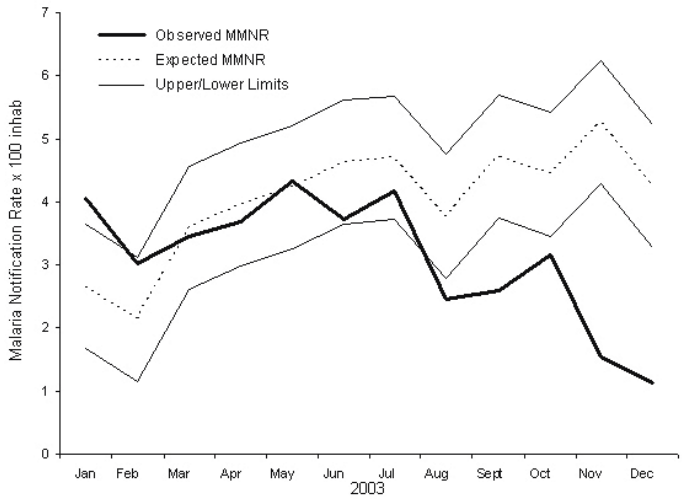

Figure 4: Expected and observed values for the Monthly Malaria Notification Rate per 100 inhabitants (MMNR) in Karuzi, Burundi in 2003. The Upper and Lower Limits of the expected values are estimated for a 95% confidence epidemiologic threshold.

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Month (2003)	Threshold Lower Limit	Expected	Threshold Upper Limit	Observed
January	1.6	2.6	3.6	4.0
February	1.1	2.1	3.1	3.0
March	2.6	3.5	4.5	3.4
April	2.9	3.9	4.9	3.6
May	3.2	4.2	5.2	4.3
June	3.6	4.6	5.6	3.7
July	3.7	4.7	5.6	4.1
August	2.7	3.7	4.7	2.4
September	3.7	4.7	5.7	2.6
October	3.4	4.4	5.4	3.1
November	4.2	5.2	6.2	1.5
December	3.2	4.2	5.2	1.1

Table 2. Endemic values predicted for the expected cumulative monthly rate of malaria case reports per 100 population in Karuzi in 2003 according to the forecasting model, with the upper and lower 95% confidence limits of the epidemiologic threshold and the observed values for the period.

forecast an epidemiologic threshold for the cumulative monthly consultations rate of malaria for one year period based on the values preceding months and on the combination of temperature, rainfall and vegetation data observed in the preceding months. The estimation of the epidemiologic threshold with our model is based on the hypothesis that the malaria incidence rate is an estimator of the volume of the parasite reservoir in the human population, while rainfall, temperature and vegetation density are an estimator of vector transmission capacity.

Different methods for the definition and early detection of malaria epidemics, such as those proposed by Cullen[25], Najera[26] and CDC,[27] use the monthly mean and median with their confidence intervals for preceding years, with a minimum of 5 years required, to identify an excess of reported cases. An evaluation of these methods in Kenya raises considerable doubts about their precision: their sensitivity and transparency are reduced when rates are transformed into logarithms; alert thresholds are established based on small samples (n=5) for which standard deviations are calculated; and they arbitrarily exclude "epidemic years" in these samples.[10-11] From our point of view, moreover, these techniques do not consider the influence of an environmental component reflecting parasite and vector conditions that may result in increased malaria transmission due to climatic variations.

Our model for estimating the endemic, non-epidemic, threshold offers an explanation for much of the variability observed in the malaria rate. Its reliability was shown by the ability to identify four empirically-defined epidemics in 1997-2002 and to detect the impact of a control program in 2003. It could generally be said that the expected incidence threshold through which the malaria consultations rate in Karuzi should pass between 1997 and 2003 is a theoretical representation of how this variable would behave, beginning with a particular initial number, given the influence of the environmental factors observed in that period. This implies that fluctuations in the incidence rate "outside" this threshold are not due to important variations in these climatic factors, but to factors related with other types of events that also determine the triggering and magnitude of malaria epidemics. Thus, for the same area and time period, Checchi have suggested as triggering factors for malaria epidemics: i) armed civil conflict with the consequent displacement of the non-immune population, and ii) the progressive expansion of rice cultivation in the valleys of central Burundi.[28] This would explain why the expected rate in our model for the months of the large epidemic between October 2000 and June 2001 is lower than the expected rate for preceding months, so that the model would be able to detect epidemics that are produced mainly by increased transmission related with human activity rather than climatic variability. The same thing occurs with the identification in the model of an important decrease in the observed rate in the months of November and December 2003, when the previously mentioned health intervention was carried out. Again, a reduction in the base rate of reproduction, or mean number of secondary infections produced from a single infected individual, would lead to an incidence rate much lower than expected by the model, by reducing the population reservoir of gametocytes as a result of treatment with artemisinin derivatives, and not because of the influence of climatic variables.

The proposed model for the detection of epidemic events in this area can be evaluated using the CDC criteria for evaluating surveillance systems.[27] That is, a) simplicity: health units routinely report malaria cases to the provincial office of the Ministry of Health; rigorous and ongoing collection of rainfall and temperature data which are relayed to the area epidemiologist; collection of vegetation data is not complex for a person with minimum training; channels for the flow of information are well established and have been improved; and the expected endemic threshold obtained for the province can easily be computed by putting all the components into the model; b) flexibility: Since the system is based on a computer program, it would be flexible enough to include changes in data collection that may occur among the different actors involved; c) acceptability: the malaria epidemic detection system would clearly be accepted since the persons involved in the process understand the repercussions of these events in their area; d) sensitivity: confirmation of cases

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by serological testing increases specificity, but not sensitivity; in contrast, using reports of suspected malaria cases would detect epidemics with higher sensitivity, albeit with a higher number of "false positives"; e) Positive Predictive Value (PVP): this system may detect epidemics that are not true epidemics, but if we use Serfling's criteria,[24] considering at least two consecutive months with an incidence above the established threshold, the PVP of the system increases considerably since this area is prone to malaria epidemics; f) representativeness: this may be limited when using reports of consultations for suspected malaria instead of microbiological confirmation; what is most important, however, is the historic stability of this form of reporting or notification that may be affected during period of conflicts or other issues outside the scope of the model; and g) timeliness: a limitation of the model is the minimum surveillance period it offers for the detection of epidemics but, as occurs in most epidemiological surveillance systems in rural areas of Africa, it is very difficult to obtain weekly reports of malaria cases that would permit earlier alerts. With appropriate changes in the forecasting model, the same methodology could be used with weekly cumulated reporting rates, and this approach would improve the timeliness of the epidemic early warning if this data would be obtained by the surveillance system of Burundi.

The combination of two modeling tools to predict malaria endemic-epidemic incidence rates, the described in this work for endemic, and another previously published for epidemic forecasting[29] offers a complete surveillance system for detection and development prediction of malaria epidemics and the evaluation of control measures. Thus, the model establishing endemic thresholds makes it possible to know when an epidemic took place, at which time the epidemic forecasting model can be applied to estimate its magnitude and plan the type and intensity of control measures. Finally, the results of these measures can be evaluated using the expected endemic thresholds.

The design and development of these types of models constitute one more tool—and not the only on—in what should be an appropriate and balanced policy for preventive action in areas prone to malaria epidemics. Because the multifactorial nature of these epidemics makes them difficult to detect, Malaria Early Warning Systems are needed that take into account variables related with climate, environment and population susceptibility.[14] With regard to the latter point, these Malaria Early Warning Systems should include components that go from rigorous and timely epidemiological surveillance and improved access to health services with adequate diagnostic and therapeutic measures, to monitoring the factors that may affect waning individual immunity, i.e. movements of the non-immune population or malnutrition.

Our model would need to be tested and evaluated before being proposed as an operational tool for malaria surveillance. Meanwhile, our research continues to focus on these techniques and their refinement in order to be able to define precisely when an excess of reported cases is a true malaria epidemic. Early warning of such epidemics would make allow time on time implementation of activities to reduce the suffering caused by these events. We can conclude that the application of this methodological tool permits the timely detection of malaria epidemics and the evaluation of the impact of measures for its prevention and control.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. Brown V, Isaac MA, Rossi M, Barboza P, Paugam A. Epidemic of malaria in North-eastern Kenya. *Lancet*. 1998; 352: 1356-1357.

2. Lindblade KA, Walker ED, Onapa AW, Katungu J, Wilson ML. Highland malaria in Uganda: Prospective analysis of an epidemic associated with El Niño. *Trans R Soc Trop Med Hyg*. 1999; 93(5): 480-487. doi: 10.1016/S0035-9203(99)90344-9

3. Kilian AHD, Langi P, Talisuna A, Kabagambe G. Rainfall pattern, El Niño and malaria in Uganda. *Trans R Soc Trop Med Hygiene*. 1999; 93(1): 22-23.

4. Protopopoff N, Van Bortel W, Speybroeck N, et al. Ranking Malaria Factors to Guide Malaria Control Efforts in African Highlands. *Plos ONE*. 2009; 4(11): e8022. doi: 10.1371/journal.pone.0008022

5. Nkurunziza H, Gebhardt A, Jürgen P. Bayesian modeling of the effect of climate on malaria in Burundi. *Malaria J*. 2010; 9: 114-122. doi: 10.1186/1475-2875-9-114

6. Hay SI, Snow RW, Rogers DJ. From predicting mosquito habitat to malaria seasons using remote sensed data: practice, problems and perspectives. *Parasitol Today*. 1998; 14: 306-313. doi: 10.1016/S0169-4758(98)01285-X

7. Connor SJ, Thomson MC, Molyneux DH. Forecasting and prevention of epidemic malaria: New perspectives on an old problem. *Parasitol*. 1999; 41(1-3): 439-448. Web site. http://europepmc.org/abstract/med/10697900. Accessed July 10, 2016

8. Abeku TA, van Oortmarssen GJ, Borsboom G, de Vlas SJ, Habbema JD. Spatial and temporal variations of malaria epidemic risk in Ethiopia: factors involved and implications. *Acta Trop*. 2003; 87(3): 331-340. doi: 10.1016/S0001-706X(03)00123-2

9. Zhoua G, Minakawab N, Andrew K. Githekoc, Yan G. Climate variability and malaria epidemics in the highlands of East Africa. *Trends Parasitol*. 2005; 21(2): 54-56. doi: 10.1016/j.pt.2004.11.002

10. Hay SI, Simba M, Busolo M, et al. Defining and detecting malaria epidemics in the highlands of western Kenya. *Emerg*

ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-108

Infect Dis. 2002; 8(6): 555-562. doi: 10.3201/eid0806.010310

11. Hay SI, Were EC, Renshaw M, Noor AM, Ochola SA, Olusanmi I. Forecasting, warning, and detection of malaria epidemics: a case study. *Lancet*. 2003; 361(9370): 1705-1706. doi: 10.1016/S0140-6736(03)13366-1

12. Thomson MC, Connor SJ, Milligan PJW, Flasse S. Mapping malaria risk in Africa-what can satellite contribute? *Parasitol Today*. 1997; 13(8): 313-318. doi: 10.1016/S0169-4758(97)01097-1

13. World Health Organization. 20th WHO Expert Committee report on Malaria. Technical Report Series, No 892. Geneva: WHO; 2000.

14. World Health Organization. Malaria Early Warning Systems. Concepts, Indicators and Partners. A framework for field Research in Africa. WHO/CDS/RBM/2001.32. Geneva: WHO; 2001.

15. World Health Organization. Field guide for malaria epidemic assessment and reporting. WHO/HTM/MAL/2004.1097. Geneva: WHO; 2004.

16. World Health Organization. Malaria Epidemics: Forecasting, Prevention, Early Detection and Control. From policy to practice. Report of an Informal consultation, Leysin, Switzerland 8-10 December 2003. WHO/HTM/MAL/2004.1098. Geneva: WHO; 2004.

17. Dantoine F. Epidémie de paludisme. Evaluation des systèmes de surveillance épidémiologiques. Secteur de santé de Buhiga, province de Karuzi, Burundi, décembre 2000 [In French]. Rapport Epicentre 378. Paris, France; 2000.

18. MacDonald G. *The epidemiology and control of malaria*. London, USA; Oxford University Press; 1957.

19. United Nation Population Division-2000 World Population Prospects: Population Database. The 2002 Revision.

20. Africa Data Dissemination Service. Dekadal Normalised Difference Vegetation Index.

21. Legros D, Dantoine F. Epidémie de paludisme du Burundi. Septembre 2000-Mai 2001. Rapport Epicentre 395. París, France; 2001.

22. Ndayiragije A, Niyungeko D, Karenzo J, et al. Efficacité de combinaisons thérapeutiques avec des dérivés de l'artémisinine dans le traitement de l'accès palustre non-compliqué au Burundi [In French]. *Trop Med Int Health*. 2004; 9(6): 673-679. doi: 10.1111/j.1365-3156.2004.01255.x

23. Protopopoff N, Van Herp M, Maes P, Reid T, Baza D, D'Alessandro U. Vector control in a malaria epidemic occurring within a complex emergency situation in Burundi: A case study. *Malar J*. 2007; 6: 93-98. doi: 10.1186/1475-2875-6-93

24. Serfling RE. Methods for current statistical analysis of excess pneumonia-influenza deaths. *Public Health Rep*. 1963; 78(6): 494-506.

25. Cullen JR, Chitprarop U, Doberstyn EB, Sombatwattanangkul K. An epidemiological early warning system for malaria control in northern Thailand. *Bull World Health Organ*. 1984; 62(1): 107-114.

26. Najera JA, Kouznetzsov RL, Delacollette C. Malaria epidemics. Detection and control, forecasting and prevention. WHO/MAL/98.1084. Geneva: WHO; 1998. Web site. http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.391.8509&rep=rep1&type=pdf. Accessed July 10, 2016

27. Centers for Disease Control and Prevention. Updated guidelines for evaluating public health surveillance systems: Recommendations from the guidelines working group. MMWR 2001; 50 (No. RR-13): 1-35.

28. Checchi F, Cox J, Balkan S, Tamrat A, Priotto G, Alberti KP. Malaria epidemics and interventions, Kenya, Burundi, southern Sudan, and Ethiopia, 1999-2004. *Emerg Infect Dis*. 2006; 12(10): 1477-1485. Web site. http://wwwnc.cdc.gov/eid/article/12/10/06-0540_article. Accessed July 10, 2016

29. Gomez-Elipe A, Otero A, van Herp M, Aguirre-Jaime A. Forecasting malaria incidence based on monthly case reports and environmental factors in Karuzi, Burundi, 1997-2003. *Malar J*. 2007; 6: 129-139. doi: 10.1186/1475-2875-6-129

EPIDEMIOLOGY

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ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-109

Short Communication

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Volume 2 : Issue 1
Article Ref. #: 1000EPOJ2109

Article History
Received: December 12th, 2016
Accepted: January 4th, 2017
Published: January 6th, 2017

Citation
Guimarães MLR, Hermont AP. Obstructive sleep apnea and oral appliances. *Epidemiol Open J*. 2017; 2(1): 16-18. doi: 10.17140/EPOJ-2-109

Obstructive Sleep Apnea and Oral Appliances

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Central sleep apnea is a sleep-related breathing disorder characterized by repetitive cessation or decrease of both airflow and respiratory effort during sleep.[1] Conversely, in obstructive sleep apnea (OSA) there is a respiratory effort against a closed upper airway evidencing that patients who suffer from OSA have anatomic/functional deficits in the upper airways.[2] When associated with clinical signs and symptoms such as excessive daytime sleepiness, cognitive deficit, decreased quality of life (QoL) and increased cardiovascular morbidity it is called obstructive sleep apnea syndrome (OSAS).[3-5]

In clinical practice it is noticeable that rarely do patients suffer from pure OSAS, the majority of them exhibits some proportion of central and/or mixed events. The coexistence of two types of apnea indicates more complex underlying disorders than just increased resistance in the upper airway. In fact, unstable respiratory control has been implicated in the pathogenesis of both central and obstructive sleep apnea.[2]

Oral appliances (OA) are recommended exclusively as a treatment option for OSAS. In the literature, 3 large groups of OA are found: tongue retaining devices, anterior mandibular repositioning devices and lifting devices of the soft palate and uvula. Combined therapy using intraoral positive-pressure devices can also be used.[6] Nowadays, the category of anterior mandibular repositioning devices is by far the most common type of OA in use.[7]

Many different device designs have contributed towards the misunderstanding related to the success of the treatment. In order to correct these deficiencies, a consensus conference was held to develop an evidence-based definition of an effective OA for the treatment of sleep-related breathing disorders and to establish a standard reference for research and clinical practice. Thus, the American Academy of Dental Sleep Medicine (AADSM) has determined that the OA terminology refers to mandibular advancement devices because they are the most effective and widely used in clinical practice. However, this definition will be re-evaluated and revised as new methods and evidences become available. Innovations have been released in OSA treatments, including advances in relation to OA treatment.[8-11]

Although OA are indicated exclusively for the treatment of OSA, a study published in 1991 showed two cases of patients with central apnea treated with this device.[12] The pathophysiology of central sleep apnea syndrome has not yet been fully clarified, but obstruction of the upper airway may be one of the causes.[13] This relationship between central sleep apnea and partial obstruction of the upper airway was suggested in a study in which a continuous positive airway pressure device (CPAP), administered to improve respiratory load during sleep, eliminated central sleep apnea in patients who had narrow upper airways, but it had no positive effect on central apnea in patients with brainstem lesions.[14]

Central sleep apnea emergent to the treatment of OSA has been described, especially after therapy with positive airway pressure (PAP) device. However, it is important to be aware that central apneas can also arise by treatment with OA.[15] Thomas et al[16] has used OA

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ISSN 2473-4780 http://dx.doi.org/10.17140/EPOJ-2-109

in patients with complex apnea and who are intolerant to PAP with reasonable success. According to these authors, residual sleep apnea may occur when using OA and it requires adjuvant therapy. Once OA are less likely to induce hypocapnia and are also less effective in treating obstructions, the researcher has used "cocktails" in the treatments including OA. He has used a combination with acetazolamide, or a benzodiazepine, or supplemental oxygen.

In our clinical routine we have observed that the polysomnography of patients with OSA often does not exhibit central and mixed events in the reports. We believe it happens due to the fact that scores of respiratory events in patients with sleep apnea have traditionally been inclined to an obstructive phenotype, although the recent 2007 update of the AASM guidelines established some criteria to quantify central hypopneas and short sequences of periodic breathing/cheyne-stokes respiration.[17]

Scoring guidelines for respiratory events predict that central hypopneas should not be marked in the presence of flow limitation, but obstruction is a common feature of central events.[16] Direct visualization of the upper airway commonly shows collapse in the nadir of the cycle, even in polysomnography of the "central" disease. Narrowing of the pharynx on expiration occurs during central hipocapnic hypopnea, supporting the concept that the presence of flow limitation by itself cannot be used to distinguish between obstructive and central hypopnea.[18-20]

We consider that scoring central and mixed events in polysomnography is important not only in the baseline assessment of sleep-related breathing disorders, but it should also be taken into account by the criteria used to estimate the therapies success.

More studies are needed to better evaluate and clarify the relationship between obstructive, central and mixed events and the impact of OA on the treatment of these sleep-related respiratory events.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. 3rd ed. Darien, IL, USA; American Academy of Sleep Medicine; 2014.

2. Xie A, Bedekar A, Skatrud JB, Teodorescu M, Gong Y, Dempsey JA. The heterogeneity of obstructive sleep apnea (predominant obstructive vs pure obstructive apnea). *Sleep*. 2011; 34(6): 745-750. doi: 10.5665/SLEEP.1040

3. Barbé, Pericas J, Munoz A, Findley L, Anto JM, Agusti AG. Automobile accidents in patients with sleep apnea syndrome. An epidemiological and mechanistic study. *Am J Respir Crit Care Med*. 1998; 158(1): 18-22. doi: 10.1164/ajrccm.158.1.9709135

4. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med*. 2005; 353: 2034-2041. doi: 10.1056/NEJMoa043104

5. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. *Sleep*. 1999; 22: 667-689.

6. SD Smith. Oral appliances in the treatment of obstructive sleep apnea-hypopnea syndrome. *RCOE*. 2002; 7(4): 391-402.

7. Hoffstein V. Review of oral appliances for treatment of sleep-disordered breathing. *Sleep Breath*. 2007; 11(1): 1-22. doi: 10.1007/s11325-006-0084-8

8. Scherr SC, Dort LC, Almeida FR. Definition of an effective oral appliance for the treatment of obstructive sleep apnea and snoring: A report of the American Academy of Dental Sleep Medicine. *J Dent Sleep Med*. 2014; 1(1): 39-50. Web site. http://www.aadsm.org/resources/pdf/consesusReport.pdf. Accessed December 11, 2016.

9. Singh GD, Keropian B, Pillar G. Effects of the full breath solution appliance for the treatment of obstructive sleep apnea: A preliminary study. *Cranio*. 2009; 27(2): 109-117. doi: 10.1179/crn.2009.017

10. Ngiam J, Kyung HM. Microimplant-based mandibular advancement therapy for the treatment of snoring and obstructive sleep apnea: A prospective study. *Angle Orthod*. 2012; 82(6): 978-984. doi: 10.2319/071311-449.1

11. Dort L, Remmers J. A combination appliance for obstructive sleep apnea: The effectiveness of mandibular advancement and tongue retention. *J Clin Sleep Med*. 2012; 8(3): 265-269. doi: 10.5664/jcsm.1910

12. Farrow SJ. Successful treatment of central sleep apnea with an oral prosthesis. *Chest*. 1991; 100(5): 1461-1462. doi: 10.1378/chest.100.5.1461

13. Bradley TD, McNicholas WT, Rutherford R, Popkin J, Zamel N, Phillipson EA. Clinical and physiologic heterogeneity of the central sleep apnea syndrome. *Am Rev Respir Dis*. 1986; 134(2): 217-221. Web site. http://www.atsjournals.org/doi/abs/10.1164/arrd.1986.134.2.217. Accessed December 11, 2016.

14. Guilleminault C, Quera-Salva MA, Nino-Murcia G, Partinen M. Central sleep apnea and partial obstruction of the upper airway. *Ann Neurol*. 1987; 21(5): 465-469. doi: 10.1002/

ISSN 2473-4780 http://dx.doi.org/10.17140/EPOJ-2-109

ana.410210509

15. Mohan A, Henderson J, Mador MJ. Mandibular advancement device-emergent central sleep apnea can resolve spontaneously: A case report. *J Clin Sleep Med*. 2016; 12(1): 137-138. doi: 10.5664/jcsm.5414

16. Thomas RJ. Alternative approaches to treatment of central sleep apnea. *Sleep Med Clin*. 2014; 9(1): 87-104. doi: 10.1016/j.jsmc.2013.10.008

17. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: Update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med*. 2012; 8(5): 597-619. doi: 10.5664/jcsm.2172

18. Badr MS, Toiber F, Skatrud JB, Dempsey J. Pharyngeal narrowing/occlusion during central sleep apnea. *J Appl Physiol (1985)*. 1995; 78(5): 1806-1815. Web site. http://jap.physiology.org/content/78/5/1806.long. Accessed December 11, 2016.

19. Thomas RJ, Tamisier R, Boucher J, et al. Nocturnal hypoxia exposure with simulated altitude for 14 days does not significantly alter working memory or vigilance in humans. *Sleep*. 2007; 30(9): 1195-1203.

20. Sankri-Tarbichi AG, Rowley JA, Badr MS. Expiratory pharyngeal narrowing during central hypocapnic hypopnea. *Am J Respir Crit Care Med*. 2009; 179(4): 313-319. doi: 10.1164/rccm.200805-741OC

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ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-110

Brief Research Report

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Volume 2 : Issue 1
Article Ref. #: 1000EPOJ2110

Article History
Received: June 23rd, 2017
Accepted: July 17th, 2017
Published: July 18th, 2017

Citation
Liu J, Tan H. The association of weight status with dental caries and trachoma among school children in cities of Changsha and Shenzhen, China. *Epidemiol Open J*. 2017; 2(1): 19-23. doi: 10.17140/EPOJ-2-110

The Association of Weight Status with Dental Caries and Trachoma Among School Children in Cities of Changsha and Shenzhen, China

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ABSTRACT

Dental caries and trachoma are two common diseases among children in developing countries. To examine whether weight status is associated with these two diseases, we used data from two screening surveys conducted in Changsha and Shenzhen, two cities in China. The screening surveys were part of a case-control study examining risk factors related to childhood obesity. Approximately 5,900 children (3,794 from Changsha and 2,193 from Shenzhen) participated in the screening survey in which weight and height were measured. Decayed or filled tooth counts (primary dentition) and trachoma infection status were obtained from school general health examination records (SGER). After excluding those who had missing information on weight, height, and SGER, a total of 4,073 (2,185 boys and 1,888 girls) aged 5-9 years old were included in the analysis. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2) and standardized for age and sex, then converted to a BMI *z*-score. Using BMI *z*-score, subjects were categorized into 4 groups as underweight (<-2), normal weight (~1.03), overweight (~1.64), or obese (>1.64). Overall, approximately 5.5% of children (6.2% girls and 4.6% boys) were underweight and 18% (11% girls and 23% boys) were overweight or obese. Comparing normal weight to underweight, overweight and obese subjects, after adjusting for age, gender, grade, and city of survey, the odds ratios (OR, [95% CI]) for dental caries were 1.12 (0.84-1.49), 0.70 (0.56-0.86), and 0.62 (0.48-0.79), (p for trends <0.001) while the ORs for trachoma were 1.65 (0.94-2.89), 0.90 (0.52-1.57), and 1.92 (1.20 -3.06). This suggests that weight status is associated with dental caries and trachoma among these Chinese children. Further study is warranted to explore the underlying mechanism(s).

KEY WORDS: Childhood obesity; Dental caries; Trachoma; Epidemiological study.

INTRODUCTION

The global accelerated increase in obesity among children and adolescents is alarming.[1] Dental caries and trachoma are two common diseases among children in developing countries as well as among children from economically disadvantaged rural and aboriginal areas.[2-7] Information regarding the relationship between obesity and these two diseases of childhood is inconclusive or scarce. For dental caries, some studies showed a positive relationship,[8-10] but others show no relationship[11-14] or even an inverse relationship.[15,16] Our search turned up no study having examined the relationship between childhood obesity and trachoma. Since the prevalence of childhood obesity is on the rise and both dental caries and trachoma are prevalent among Chinese children, it is worth understanding whether and what relationship might exist between obesity and these two diseases when we keep intervention in mind.

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ISSN 2473-4780 http://dx.doi.org/10.17140/EPOJ-2-110

METHODS

Survey Method and Participants

The data used in this analysis came from a survey conducted between March and June, 2005 in the cities of Changsha and Shenzhen, China(Footnote 1). A two-stage cluster sampling method was used in the survey: in stage one, one out of nine districts in the city of Changsha and one out of ten districts in the city of Shenzhen were randomly selected; in stage two, 10 out of 62 elementary schools from the chosen district of the city of Changsha and 5 of 45 elementary schools from the chosen district of the city of Shenzhen were randomly selected for the survey. A combined total of 5,987 children aged 5-9 years were surveyed at the time as they underwent a school health screening examination. After cleaning the dataset for missing information, a total of 4,073 children (2,185 boys and 1,888 girls) were included in this analysis.

Measurements Related to Obesity Status

Weight and height were measured using a portable stadiometer and weight scale with each participant wearing light clothing without shoes. Body mass index (BMI) were calculated as weight (kg) divided by height (m^2) and converted to an age and sex specific BMI *z*-score. Using BMI *z*-score, subjects were categorized as either underweight (≤-2), normal weight (~1.03), overweight (~1.64), of obese (≥1.64), which correspond to the ≤5th, ~85th, ~95th, and ≥95th age and sex-specific percentiles.[17]

Examination of Dental Caries and Trachoma

Information on dental caries and trachoma was obtained from a school health screening examination conducted by dentists and eye specialists. Oral health examination from schools in the city of Shenzhen recorded decayed (d), missing (m) and filled (f) teeth (t) for primary and permanent dentition; while the health examination at schools in the city of Changsha only recorded a positive finding of dental caries. Therefore, in this analysis, dental caries was defined as positive if either the health examination records showed 'yes' for students from the city of Changsha or dft>0 for primary dentition and dmft>0 for permanent dentition for students from the city of Shenzhen. Trachoma was assessed using the simplified grading scheme proposed by the World Health Organization (WHO),[18] and recorded as 'yes' in the health examination records when positive.

Statistical Analysis

Data was analyzed using SAS 9.4 with significance level set at two-sided α=0.05. A *t*-test was used to compare the mean level of continuous variables and a Chi-square test was used to compare the distribution of category variables. A multiple logistic regression model was used to evaluate the association between dental caries and trachoma with weight status. Covariates controlled in the analysis were age (year), sex (1-male, 0-female), grade (1~4), and city (1-Changsha, 2-Shenzhen).

1. At the time these surveys were conducted there was no requirement for a research ethics review.

RESULTS AND DISCUSSION

Overall, 717 children (17.6%) were categorized as overweight (9.8%) or obese (7.8%). 48.4% (1,973) of children had dental caries and 4.7% (192) screened positive for trachoma. There was no gender difference in age, survey location, or the proportion of positive dental records and incidence of trachoma. However, the distribution of grades, and mean BMI distribution varied by gender (Table 1).

Table 1: Characteristics of 4,073 Children by Gender.

	Girls	Boys
N	1,888	2,185
Age (yr, mean (SD))	7.5 (0.9)	7.5 (0.9)
Grade (%)		
1	17.7	19.9 **
2	35.8	36.8
3	35.9	35.4
4	10.7	7.8
City from (%)		
Changsha	47.3	46.1
Shenzhen	52.7	53.9
BMI (kg/m^2, mean (SD))	15.5 (2.1)	16.4 (2.6)***
Weight status^ (%)		
Underweight	6.3	4.5***
Normal weight	82.3	72.6
Overweight	7.9	11.4
Obese	3.6	11.4
Dental Caries (%)	46.3	53.7
Trachoma (%)	5.2	4.2

^based on BMI *z*-score. Underweight: BMI *z*-score <-2, Normal weight: -2<BMI *z*-score<1.03,
Overweight: 1.03<BMI *z*-score<1.96, Obese: BMI *z*-score >1.96
**p<0.001, ***p<0.0001

Univariate analysis found that the proportion of dental caries in underweight, normal weight, overweight, and obese groups was 51.6%, 50.0%, 41.3%, and 39.8% (p<0.01) respectively, with trachoma frequencies by weight category of 6.9%, 3.4%, 3.7%, and 7.5% (p=0.02).

Multiple logistic regression used normal weight as comparator group, adjusting for age, gender, grade, and survey location. For dental caries by weight category, our model found odds ratios (OR, [95% CI]) of 1.12 (0.84, 1.49), 0.70 (0.56, 0.86), and 0.62 (0.48, 0.79), (p-value for trends <0.001) (Figure 1a) corresponding to underweight, overweight, and obese; for trachoma the respective ORs (95% CI) were 1.65 (0.94, 2.89), 0.90 (0.52, 1.57), and 1.92 (1.20, 3.06) (p-value for trends=0.19) (Figure 1b).

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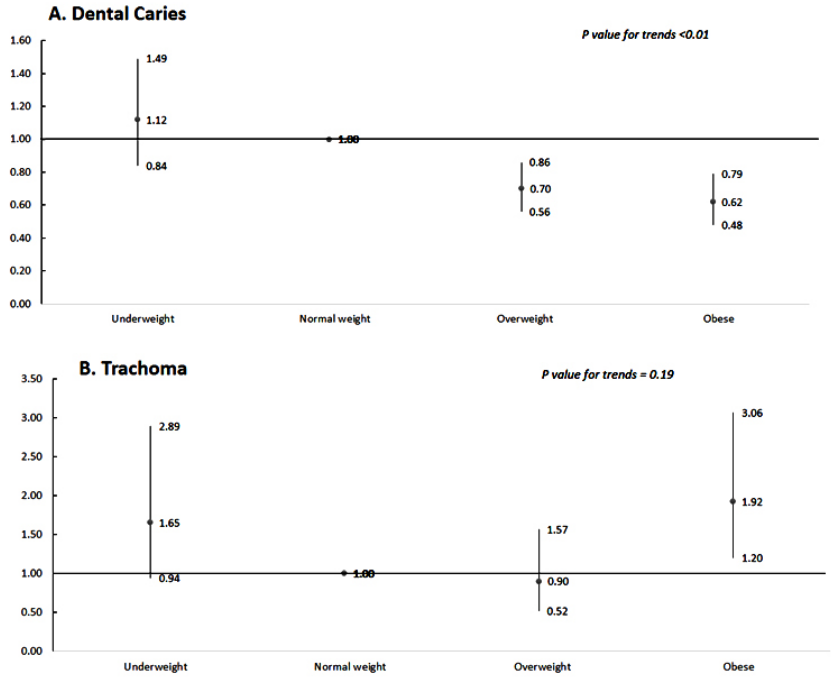
ISSN 2473-4780 http://dx.doi.org/10.17140/EPOJ-2-110

Figure 1: Odds Ratios for Dental Caries (A) and Trachoma (B) by Weight Status in Children, Adjusting for Age, Gender, Grade, and Survey City.



With economic progress and modernization in China the prevalence of obesity in Chinese children has increased dramatically over the past two decades.[19,20] Although, there is no information on the trends of dental caries among Chinese children, population-based cross-sectional studies suggest that the prevalence of dental caries is high among Chinese children with significant geographical variation.[21,22] While the prevalence of blindness caused by trachoma is happily on the decline, it remains endemic, nonetheless, among school children, particularly in rural areas.[23-26] Prevalence rates for obesity, dental caries, and trachoma in this study are comparable to those from other national metropolis samples. In the current study, we observed a negative association between weight status and the odds of dental caries and a "U" shaped relationship between weight status and the odds of trachoma.

Although, this is not the first study to find a negative relationship between weight status and dental caries we believe this to be the first report of a "U" shaped relationship between weight status and trachoma. The underlying mechanism that accounts for this remains uncertain. It is biologically quite plausible that childhood obesity could correlate with dental caries since they share risk factors, e.g., too much free sugar intake,[27] though the evidence to support such a hypothesis is weak and inconclusive. The relationship between weight status and dental caries among children may be more complicated than we think. The aforementioned studies[8-16] are to some extent contradictory which suggests that each may only be seeing part of the bigger picture. The pathogenic mechanism for the link between underweight status and dental caries may well differ from that for overweight/obese children and finding a common solution may be improbable. In the case of trachoma, some increased risk was observed in children who were underweight as well as for those categorized as obese, though the difference only reached significance for the obese. Why there should be such an association and by what biological mechanism is not at all clear.

The main limitations of this study include 1) the data originate from cross-sectional surveys, which cannot determine causality; 2) there was no information on family socio-economic status which would be an important risk factor in the study of childhood obesity, dental caries, and trachoma; and 3) no sampling weight information was available since the number of students in the excluded clusters is unknown. Although, the sampling probability for individual students is indeterminate, we have no reason to think that the sample in the study was not representative of the population since the sampling method ensured representativeness by region; furthermore, results are based on the analysis of a very large sample of carefully scrutinized anthropometric measurements.

CONCLUSION

In conclusion, given the fact that the childhood obesity is a growing problem in China, and that dental caries and trachoma are still endemic health concerns among children, more studies are needed to examine the complex relationships between weight status oral health and trachoma among children.

ISSN 2473-4780 http://dx.doi.org/10.17140/EPOJ-2-110

ACKNOWLEDGEMENT

The authors wish to thank John MacIntyre MD, Burlington, Ontario, Canada for providing editorial assistance.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. Broyles ST, Denstel KD, Church TS, et al. The epidemiological transition and the global childhood obesity epidemic. *Int J Obes Suppl*. 2015; 5(Suppl 2): S3-S8. doi: 10.1038/ijosup.2015.12

2. Zhang S, Man Lo EC, Liu J, Chu CH. A review of the dental caries status of ethnic minority children in China. *J Immigr Minor Health*. 2015; 17(1): 285-297. doi: 10.1007/s10903-013-9916-3

3. Cleaton-Jones P, Fatti P, Bonecker M. Dental caries trends in 5- to 6-year-old and 11- to 13-year-old children in three UNICEF designated regions--Sub Saharan Africa, Middle East and North Africa, Latin America and Caribbean: 1970-2004. *Int Dent J*. 2006; 56(5): 294-300. doi: 10.1111/j.1875-595X.2006.tb00104.x

4. Christian B, Blinkhorn AS. A review of dental caries in Australian Aboriginal children: The health inequalities perspective. *Rural Remote Health*. 2012; 12(4): 2032.

5. Wang LH, Wang B, Wang HY, et al. Prevalence of trachoma in rural primary school children in Tengzhou City of Shandong Province in China [In Chinese]. *Zhonghua Yan Ke Za Zhi*. 2010; 46(5): 395-399. doi: 10.3760/cma.j.issn.0412-4081.2010.05.004

6. Alemayehu M, Koye DN, Tariku A, Yimam K. Prevalence of active trachoma and its associated factors among rural and urban children in Dera Woreda, Northwest Ethiopia: A comparative cross-sectional study. *Biomed Res Int*. 2015; 2015: 570898. doi: 10.1155/2015/570898

7. Mengistu K, Shegaze M, Woldemichael K, Gesesew H, Markos Y. Prevalence and factors associated with trachoma among children aged 1-9 years in Zala district, Gamo Gofa Zone, Southern Ethiopia. *Clin Ophthalmol*. 2016; 10: 1663-1670. doi: 10.2147/OPTH.S107619

8. Yao Y, Ren X, Song X, et al. The relationship between dental caries and obesity among primary school children aged 5 to 14 years. *Nutr Hosp*. 2014; 30(1): 60-65. doi: 10.3305/nh.2014.30.1.7552

9. Vázquez-Nava F, Vázquez-Rodríguez EM, Saldívar-González AH, Lin-Ochoa D, Martinez-Perales GM, Joffre-Velázquez VM. Association between obesity and dental caries in a group of preschool children in Mexico. *J Public Health Dent*. 2010; 70(2): 124-130. doi: 10.1111/j.1752-7325.2009.00152.x

10. Honne T, Pentapati K, Kumar N, Acharya S. Relationship between obesity/overweight status, sugar consumption and dental caries among adolescents in South India. *Int J Dent Hyg*. 2012; 10(4): 240-244. doi: 10.1111/j.1601-5037.2011.00534.x

11. Chen W, Chen P, Chen SC, Shih WT, Hu HC. Lack of association between obesity and dental caries in three-year-old children. *Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi*. 1998; 39(2): 109-111.

12. D'Mello G, Chia L, Hamilton SD, Thomson WM, Drummon BK. Childhood obesity and dental caries among paediatric dental clinic attenders. *Int J Paediatr Dent*. 2011; 21(3): 217-222. doi: 10.1111/j.1365-263X.2011.01112.x

13. Granville-Garcia AF, de Menezes VA, de Lira PI, Ferreira JM, Leite-Cavalcanti. A Obesity and dental caries among preschool children in Brazil. *Rev Salud Publica (Bogota)*. 2008; 10(5): 788-795. doi: 10.1590/S0124-00642008000500011

14. Wu L, Chang R, Mu Y, et al. Association between obesity and dental caries in Chinese children. *Caries Res*. 2013; 47(2): 171-176. doi: 10.1159/000344017

15. Farsi DJ, Elkhodary HM, Merdad LA, et al., Prevalence of obesity in elementary school children and its association with dental caries. *Saudi Med J*. 2016; 37(12): 1387-1394. doi: 10.15537/smj.2016.12.15904

16. Prashanth ST, Bhatnagar S, Das UM, Gopu H. Oral health knowledge, practice, oral hygiene status, and dental caries prevalence among visually impaired children in Bangalore. *J Indian Soc Pedod Prev Dent*. 2011; 29(2): 102-105. doi: 10.4103/0970-4388.84680

17. Kuczmarski RJ, Ogden CL, Guo SS, et al, 2000 CDC growth charts for the United States: Methods and development. N.C.f.H. Statistics. Centers for Disease Control and Prevention; 2002. Web site. http://europepmc.org/abstract/med/12043359. Accessed June 22, 2017.

18. Thylefors B, Dawson CR, Jones BR, West SK, Taylor HR. A simple system for the assessment of trachoma and its complications. *Bull World Health Organ*. 1987; 65(4): 477-483.

19. Liang YJ, Xi B, Song AQ, Liu JX, Mi J. Trends in general and abdominal obesity among Chinese children and adolescents 1993-2009. *Pediatr Obes*. 2012; 7(5): 355-364. doi: 10.1111/j.2047-6310.2012.00066.x

20. Song Y, Wang HJ, Dong B, Ma J, Wang Z, Agardh A. 25-year trends in gender disparity for obesity and overweight by

ISSN 2473-4780 http://dx.doi.org/10.17140/EPOJ-2-110

using WHO and IOTF definitions among Chinese school-aged children: A multiple cross-sectional study. *BMJ Open*. 2016; 6(9): e011904. doi: 10.1136/bmjopen-2016-011904

21. Wang HY, Petersen PE, Bian JY, Zhang BX. The second national survey of oral health status of children and adults in China. *Int Dent J*. 2002; 52(4): 283-290. doi: 10.1111/j.1875-595X.2002.tb00632.x

22. Shen A, Zeng X, Cheng M, Tai B, Huang R, Bernabé E. Inequalities in dental caries among 12-year-old Chinese children. *J Public Health Dent*. 2015; 75(3): 210-217. doi: 10.1111/jphd.12091

23. Hu A, Cai X, Qiao L, Wang N. Comparison of visual impairment caused by trachoma in China between 1978 and 2006. *Zhonghua Yan Ke Za Zhi*. 2015; 51(10): 768-772.

24. Ren Z, Liang QF, Guo S, Zhou YM, Li R, Sun XG. Prevalence and risk factors for trachoma in primary school children in Datong City in China [In Chinese]. *Zhonghua Yan Ke Za Zhi*. 2008; 44(6): 507-510. doi: 10.3321/j.issn:0412-4081.2008.06.007

25. Xue W, Lina Lu, Zhu J, et al. A cross-sectional population-based survey of trachoma among migrant school aged children in Shanghai, China. *Biomed Res Int*. 2016; 2016: 8692685. doi: 10.1155/2016/8692685

26. Wang N, Deng S, Tian L. A review of trachoma history in China: research, prevention, and control. *Sci China Life Sci*. 2016; 59(6): 541-547.

27. Scientific Advisory Committee on Nutrition: Carbohydrates and Health. London: T.S. Office, Editor; 2015.

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ISSN 2473-4780 Open Journal http://dx.doi.org/10.17140/EPOJ-2-111

Observational Study

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Volume 2 : Issue 1
Article Ref. #: 1000EPOJ2111

Article History
Received: August 4th, 2017
Accepted: September 6th, 2017
Published: September 6th, 2017

Citation
Ahmed NU, Delgado ME, Degarege A. HPV vaccination and knowledge of cervical cancer among female University Students in a Multiethnic Institution, USA. *Epidemiol Open J.* 2017; 2(1): 24-31. doi: 10.17140/EPOJ-2-111

HPV Vaccination and Knowledge of Cervical Cancer among Female University Students in a Multiethnic Institution, USA

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ABSTRACT

Objective: College-aged women are at high-risk of Human Papillomavirus (HPV) infection. Although, HPV vaccination is most effective, its rates remain quite low among college students. It may be due to inadequate understanding of the relationship between HPV and cervical cancer. Therefore, the objective of this study was to examine the level of knowledge about HPV, cervical cancer and their associations with HPV vaccination among female college students.
Methods: Cross-sectional questionnaire based survey was conducted among female students in a Multiethnic University in Florida. We assessed HPV vaccination status, annual health checkup status, knowledge about HPV and cervical cancer among the students. The response rate for the survey was 91.5%.
Results: Out of 141 students, 39.7% received HPV vaccine, and 38.3% did annual medical checkup within a year. Out of 4, the mean and the median knowledge score of students about cervical cancer was 2.87 and 3.0, respectively. A greater percentage of students who did annual health checkup (44%) received HPV vaccine than those who did not (15%). The odds of receiving HPV vaccine was nearly 5 times as much for the students who achieved knowledge scores about causes of cervical cancer greater than or equal to the median compared with the students with knowledge scores below the median (adjusted odds ratio [aOR]:4.85, 95% confidence interval [CI]:2.15, 10.92). The odds of receiving HPV vaccine was almost three times as much of students who knew that HPV causes cervical cancer than those who did not know it to be so (aOR:2.9, 95% CI:1.1, 8.2).
Conclusion: Receipt of HPV vaccination was associated with knowing that HPV infection is a cause of cervical cancer and that it's preventable. HPV vaccination was also associated with annual health checkup status.

KEY WORDS: College students; HPV; Cervical cancer; Knowledge; HPV vaccine; Vaccination.

ABBREVIATIONS: HPV: Human papillomaviru; STI: Sexually Transmitted Infection; STDs: Sexually Transmitted Diseases; MSP: Multiple Sexual Partners.

INTRODUCTION

Human papillomavirus (HPV) infection is the most commonly occurring sexually transmitted infection (STI) in the United States. Approximately, 79 million women in the country are infected with HPV, and 14 million new infections occur annually.[1] More than 80% of American women will have contracted at least one strain of genital HPV by the time they reach 50 years of age.[2] Sexually active women below the age of 25 such as college students have the highest rates of genital HPV infection.[3] College students are considered to be a high-risk group for contracting STIs because they are likely to have multiple sexual partners (MSP) and have unprotected sexual intercourse.[4,5]

While HPV infection is usually benign or asymptomatic, it can result in serious health consequences, such as genital warts and even cervical cancer.[6] HPV infection is necessary

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ISSN 2473-4780 http://dx.doi.org/10.17140/EPOJ-2-111

for cervical cancer to develop.[7,8] Cervical cancer is the second most commonly occurring female-specific cancer worldwide, accounting for about 8% of total cancer cases and total cancer deaths among women.[9] This disease claims 2,66,000 lives worldwide[10] and over 4,217 in the USA annually.[11]

HPV vaccination is an effective method of preventing cervical cancer. Three HPV vaccines namely; Gardasil, Cervarix, and Gardasil-9 are licensed to combat cervical cancer in women in the USA.[12] The HPV vaccination is recommended for males and females of ages 11 to 26-years-old.[1] Gardasil and Cervarix have been shown to be efficacious, safe, and well-tolerated.[12] Gardasil reduced the combined incidence of infection with types 16 or 18 by 94.5% in participants.[13] The protection against types 16 and 18 lasts for at least eight years after vaccination with Gardasil and more than 9 years after vaccination with Cervarix.[12] After the introduction of the vaccines, the prevalence of HPV infection (types 6, 11, 16, and/or 18) fallen by about 88% among vaccinated women in United States, and the annual cost of cervical cancer treatment decreased from $6,000 million to approximately $400 million in the country.[14,15]

However, about 60% among college-aged women did not receive HPV vaccination in the USA.[16] This may be due to inadequate understanding of HPV infection, cervical cancer and the vaccine. As the American college students are at high risk for HPV infection, their sufficient awareness and accurate information about cervical cancer, HPV transmission, and its prevention are imperative to increase HPV vaccination coverage. Therefore, the objectives of this study were to examine the level of knowledge about HPV, cervical cancer and its association with HPV vaccination among college students in the USA.

METHODS

Study Participants and Sample Size Determination

This study was conducted at a large multiethnic public university in the state of Florida, in January-May 2013. In 2013, there were 21,287 female undergraduate students in the Institute. There were 55 required university core courses offered in the institute in 2013 spring semester in the areas of Global Learning, English Composition, Humanities with Writing, Quantitative Reasoning, Social Inquiry, Societies and Identities, Natural Sciences, Life Sciences, Physical Sciences, and Arts. Out of the 55 courses (which we treated as clusters), 10 courses/clusters were randomly selected for this study. On average there were 42 students registered for each course selected for this study. All female students who were attending classes in the aforementioned courses during the study period were eligible for this study. In those clusters, a total of 151 female students present on the day of the survey, were approached, and 141 female students completed the survey. The sample size (n=141) was determined based on the Rules of Thumb (n>104+m) for studying the relationships of an outcome with individual 'm' predictors as suggested by Harris, 1985 and Green, 1991.[17,18]

Questionnaire

The questionnaire consisted of 24 items, most of which were multiple-choice questions in which students were asked to choose one among several predefined categories. Items were selected from the previously published peer-juried literature that assessed knowledge about HPV and cervical cancer.[19-21] The questionnaire was divided into four sets. The first set contained questions on socio-demographic variables (e.g., Year spent in college, Major subject, Race/ethnicity). The second set consisted of items used to assess information about the participants' knowledge about HPV and cervical cancer and the participants' primary source of health-related information (Sexual activity is a risk for cervical cancer, sexually transmitted diseases (STDs) and MSP are risk factors for cervical cancer, Human Papilloma virus causes cervical cancer, Cervical cancer is preventable). The third set contained items asking participants about their own preventive behaviors concerning HPV and cervical cancer (e.g., When did you have a most recent medical check-up from the day of the survey?). The fourth set consisted of items used to assess if students received an HPV vaccine or will consider receiving in the future (considering receiving the vaccine in the future) it in the future (e.g., Received HPV vaccine at least one dose).

Data Collection Procedures

Before data collection, the course instructors briefly introduced the survey team to their students. There were five graduate students that were trained to administer the questionnaire. After the instructor introduced the survey, one of the two team members described the research objective and importance of the study, confidentiality and that no personal information is part of the survey. Then, students who agreed to participate in the study completed a questionnaire in a period of 10-12 minutes at the beginning or end of their class. By the Course Instructors' plan either at the beginning or during the end part of the class the survey was conducted. In the case of students, who were attending two courses, data were collected only once when they were contacted for the first time.

Data Analysis

The data for this study were analyzed in the Statistical Package for the Social Sciences (SPSS).[22] The outcome variable was HPV vaccination status (0=not received any dose or 1=vaccinated at least partially). The explanatory variables were age (continuous), health insurance (0=no or 1=yes), race/ethnicity (non-Hispanic White, Hispanic white, Black, and other) and knowledge about cervical cancer (0=incorrect or 1=correct). The knowledge about cervical cancer was assessed using four items: a) Sexual activity is a risk for cervical cancer; b) STDs and MSP are risk factors for cervical cancer; c) Human Papilloma virus causes cervical cancer; and d) Cervical cancer is preventable. Responses for each item was recorded as 'incorrect' or 'correct.' For each participant, a composite knowledge score was calculated by adding their responses to the four items. Total scores can range from 0 through 4, and the composite score achieved

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an acceptable reliability measuring knowledge (Cronbach's alpha=0.68, p=0.0001). Then a dichotomous variable was created from the composite knowledge score (0=knowledge scores less than the median; 1=knowledge scores greater or equal to the median) to be included in the regression models. A Chi-square test was used to test the relationship of race/ethnicity, health information sources, health insurance status with annual health checkup and HPV vaccination status. A multiple logistic regression model was used to estimate the association between participants' knowledge about cervical cancer and HPV vaccination status.

Ethical Consideration

The Institutional Review Board approved the study, and consent was obtained from each participant. No personal information about the study participants (e.g., name, address, phone number) was recorded.

RESULTS

A total of 153 female students, who were attending 10 major courses in a Multiethnic Institute, were contacted. However, 12 students could not complete the questionnaire because arrived late in class, less time to complete the questionnaire, or had some other time commitment. Thus, the sample for our study consisted of 141 female undergraduate students. The response rate was 91.5%. The mean age of the sample was 21.7 years. The majority of the participants were non-Hispanic Whites (51.5%), followed by Hispanic Whites (30.8%). Higher percent (41.2%), of the students were in their junior year of college and the commonly reported (40.0%) majors were subjects in the health sciences. About 60% of the students did not receive HPV vaccine. Of those students who had not received an HPV vaccine, 68% listed a lack of trust, apathy, and fear of side-effects as reasons for not being vaccinated (Table 1).

Table 1: Selected Sociodemographic Characteristics of the Study Participants and Health Seeking Behaviors.

Variable	Categories	Number	Percentage
Year in college	Freshman	31	22.8
	Sophomore	23	16.9
	Junior	56	41.2
	Senior	26	19.1
Majoring in	Health sciences	56	40.0
	Basic sciences	38	27.1
	Arts	30	21.4
	Business	12	8.6
	Engineering	4	2.9
Race/ethnicity	White (non-Hispanic)	70	51.5
	White (Hispanic)	42	30.8
	Black (non-Hispanic)	14	10.3
	Other	10	7.4
Health information source(s)	Online	87	61.7
	Print media	20	14.2
	Online (& others)	18	12.8
	TV (& others)	15	10.6
Top two major health issues*	STDs± & mental health disorders	56	39.7
	STDs±& overweight	49	34.8
	Mental health disorders & overweight	36	25.5
Health insurance status	Yes	101	71.6
When most recent medical check-up from the day of survey	Within 12 months	54	38.3
	In 13-24 months	55	39.0
	In 25-36 months	18	12.8
	Never or do not remember	14	9.9
HPV vaccine received at least one dose	Yes	56	39.7
Reason for not receiving HPV vaccine	Lack of trust in effectiveness, fear of side-effects, or apathy	28	68.3
	Overaged or not sexually active	9	22.0
	Doctor did not advise them to receive the vaccine	4	9.8
Considering receiving vaccine in the future	Yes	25	29.4

Note: *Students were asked to choose which two health issues they felt were most important for their age group.STDs±= sexual transmitted disease

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Annual Health Check-Ups and HPV Vaccination

Of 141 students, 39.7% of the students had received an HPV vaccine and 38.3% had undergone a medical checkup in the year prior to completing the questionnaire. The percentage of students who received an HPV vaccine was greater among those who attended an annual health check-up within the last three years from the day of the survey (43.8%) as compared to those who did not (15.4%) (p=0.04). The percentage of students who attended an annual health check-up during the three years prior to the survey were greater among those who had insurance coverage (93.1%) than those who lacked insurance (82.5%) (p=0.05) (Table 2).

Knowledge about Cervical Cancer and HPV Vaccination

The mean and the median knowledge score of students about cervical cancer/HPV on the basis of four points was 2.87 and 3.0, respectively. Most students understood that HPV (75.7%) and having MSP and other STDs (83.0%) were each risk factors for developing cervical cancer. However, there were key areas of misunderstanding among participants. More than one-third of the students were unaware that cervical cancer is preventable. In general, the participants were not thoroughly knowledgeable about cervical cancer, with only 13.5% of participants reporting that they knew of all the causes of cervical cancer and 9.9% reporting that they knew about all the aspects of cervical cancer.

The prevalence of HPV vaccination was significantly positively associated with knowledge scores, with 70.3% of those students in the highest quartile of scores having been vaccinated as opposed to 25.0% in the lowest quartile (p=0.001) (Figure 1). The odds of receiving HPV vaccine was nearly five times as much for the students who achieved knowledge scores about the causes of cervical cancer greater than or equal to the median compared with the students with knowledge scores about the causes of cervical cancer below the median (adjusted odds ratio [aOR]:4.85, 95% confidence interval [CI]:2.15, 10.92). Particularly, students who knew that HPV is a cause of cervical cancer were almost three-times odds of receiving HPV vaccine as compared to students who did not know that HPV is cause for cervical cancer (aOR:2.90, CI:1.1, 8.2). Those who knew that cervical cancer is preventable were over 2.5-times odds of getting HPV vaccine as compared to those who did not know; however, after adjusting for other variables, the difference was not statistically significant (Table 3).

DISCUSSION

Vaccination is one of the most effective and least complex ways to address the public health problems especially cervical cancer. Cervical cancer is one of most preventable types of cancer, and HPV vaccination plays a central role in this effort. Despite the safety, effectiveness, and simplicity of the vaccination program, the uptake remained quite low among the high-risk group-college students. This study showed that HPV vaccination is positively associated with students' knowledge about cervical cancer. The association of HPV vaccination with knowledge about cervical cancer was particularly strong among students who knew that HPV infection is a causal factor for cervical cancer and cervical cancer is preventable. This finding is consistent with several other studies which showed a significant positive association be-

Table 2. Annual Checkup, HPV Vaccination, and Median Knowledge Score by Selected Characteristics of Students (n=141).

Variable	Category	Annual health checkup within the 3 years (%)	Received HPV vaccine (%)	Knowledge score ≥median (%)
Race/ethnicity	White (non-Hispanic)	88.6	48.6	28.6
	White (Hispanic)	90.5	35.7	33.3
	Black (non-Hispanic)	100.0	35.7	35.7
	Other	90.0	20.0	10.0
Health insurance status	Yes	93.1*	42.7	28.7
	No	82.5	36.8	32.5
Majoring in	Health sciences	92.9	33.9	35.7
	Basic sciences	94.7	52.6	31.6
	Arts	83.3	33.3	31.6
	Business	83.3	33.3	25.0
	Engineering	75.0	50.0	0.0
Health information sources	Online only	90.8	36.8	32.7
	Print media	85.0	40.0	25.0
	Online (& others)	94.4	44.4	38.9
	TV (& others)	86.7	53.3	13.3
Most recent medical check-up	Within 3 years	---	43.8*	29.1***
	Never or do not remember	---	15.4	0.0

Note: *p=0.05, **p=0.01, ***p=0.001
STDs & multiple sexual partners are risk factors of cervical cancer

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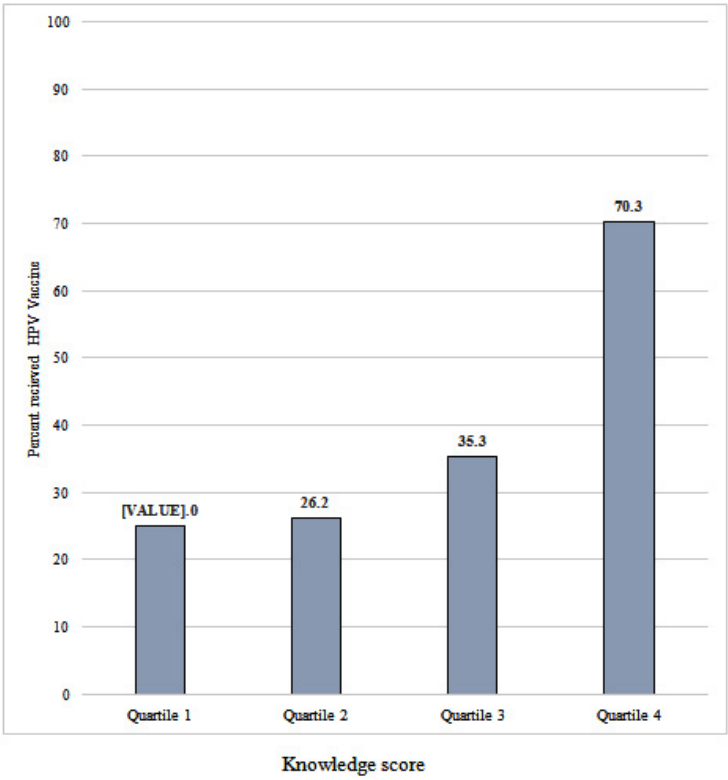
Figure 1: HPV Vaccination Status among Students based on Knowledge Score Level.



Note: The trend is statistically significant at *p*=0.001

Table 3: Odds Ratios of Receipt of HPV Vaccine for the Knowledge of Students about Cervical Cancer (n=141).

Knowledge assessment item	Response	Frequency	Receipt of HPV vaccine (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Sexual activity is a risk for Cervical cancer	Yes	95	46.3*	2.1 (0.9, 4.6)	2.1 (0.90, 5.8)
	No	41	29.3	---	---
STDs & multiple sexual partners are risk factors of cervical cancer	Yes	117	41.0	1.4 (0.6, 3.5)	0.4 (0.1, 1.5)
	No	24	33.3	----	---
Human Papilloma virus causes cervical cancer	Yes	103	47.6***	3.4 (1.3, 8.4)	2.9 (1.1, 8.2)
	No	33	21.2	---	---
Cervical cancer is preventable	Yes	90	47.8**	2.7 (1.3, 5.7)	2.1 (0.9, 5.8)
	No	51	25.5	---	---
Knowledge assessment	Yes	37	70.3***	5.8 (2.6, 13.2)	4.8 (2.2, 10.9)
Score ≥median	No	104	28.8	---	---

Note: Multiple logistic model, variable controlled for in the model are Age, Insurance, and Race/ethnicity.
**p*=0.05; ***p*=0.01; ****p*=0.001
Nasar fix the decimal point for odds .00

tween knowledge of college students about HPV and/or cervical cancer and intention to accept HPV vaccine or actual receiving of the HPV vaccine.[23-25] Studies had also shown that members of communities at higher risk for HPV infection tend to be less knowledgeable about the transmission mechanisms of HPV and its impacted morbidities.[23,26]

In addition to knowledge about causes of cervical cancer, annual health checkup attendance played a significant role in HPV vaccination in the study. This finding is corroborated by previous studies conducted in Germany[27] and the United States.[28] Possible reasons for this finding could be because healthcare providers recommend the HPV vaccination to their patients during their visits for a medical checkup. Physicians have a greater opportunity to teach their patients one-on-one about the importance of HPV vaccination during annual check-ups, which usually last much longer than other visits. Studies consistently showed that healthcare providers' recommendations strongly

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predict HPV vaccination,[29,30] suggesting that recommendation and subsequent administration of the vaccine when adolescents visit healthcare providers for check-ups are crucial to increase the HPV vaccination rate.[31,32] However, only 38% of the students had undergone the annual health checkup within a year before the survey was conducted. This shows that larger number of students had missed the opportunity of recommendation and/or administration of the HPV vaccine, and this might also explain the finding of the low percentage of students who received HPV vaccine in the current study (39.7%). In fact, the percent received HPV vaccine in the current study is similar to the recent national percentage estimate (40.2%) among females aged 19-26 years in the USA.[16]

However, as college students are at higher risk of HPV infection, increased HPV vaccination coverage in this age group would be more useful. Health education efforts which help increase students' interest in attending regular health check-ups and receiving pap smearsis necessary to increase HPV vaccine coverage among college students. Additionally, physicians should be encouraged to counsel their female patients more frequently about receiving the HPV vaccine and address HPV-related issues.

Majority of the study participants who did not receive HPV vaccine claimed lack of trust, fear of side effect, being careless as the reasons why they did not get the HPV vaccine. Consistent with our findings, other studies have also documented lack of trust, fear of adverse effects, and general apathy as common barriers to HPV vaccination in a variety of communities.[33,34] The lack of trust and fear of side effect of HPV vaccination among college students could be due to the low level of knowledge of about HPV, cervical cancer, and HPV vaccination. Indeed, the median knowledge score of these students about risk factors of cervical cancer based on eight points was quite low. The literature also indicates most sexually active people-college students know little about HPV and were not practicing appropriate cervical cancer preventive behaviors.[35] Hence provision of information about cervical cancer prevention emphasizing HPV vaccine is safe and effective may help to increase HPV vaccination coverage. Information campaigns about the benefits of the HPV vaccine and the risks that result from infection with HPV have shown some success in correcting misperceptions about the vaccine.[36] In addition, the proportion of students who received HPV vaccine was almost three times higher among students who attended an annual checkup than those who did not attend an annual checkup. This perhaps indicates that students are more likely to receive the HPV vaccine if they have an opportunity to discuss their risk of HPV infection and the benefits of vaccination with their physician. The discussion with the physician could address many of their concerns including trust, barriers, and effectiveness of the vaccine.

Implication for Policy and Practice

The current study findings have several implications for planning public health policy and practices. The results suggest that HPV vaccination programs should include education of young women about the benefits of HPV vaccination and causes and methods of prevention of cervical cancer. The education program needs to be designed to reduce the lack of trust, fear of side effect and other concerns about HPV vaccine among college students. In effecting this, provision of information that HPV vaccine is safe and effective might be useful. This can be implemented during the annual health checkups where doctors will have the opportunity to deal details with their patients.

LIMITATIONS

The current study involved college students with highly diversified ethnic backgrounds. Thus, the present study provides information on the relationship between HPV vaccination and knowledge of individuals about HPV or cervical cancer among-students with the heterogeneous ethnic background. The findings of this study are based on a cross-sectional design and should be interpreted in light of several limitations. Data were from all self-reported response. Additionally, poor memory about annual medical checkups, pap smears, and vaccination might have affected the results. Moreover, the sample was not very large, which might have limited power to detect true association between vaccination and several other variables. Also, while the sample had a heterogeneous composition, it consisted mostly of students majoring in the basic sciences or health sciences. Thus, the findings might not be fully representative of college women students in general. The results should be treated as correlational not as causational.

CONCLUSIONS

Receipt of HPV vaccination was associated with knowing that HPV infection is a cause of cervical cancer and that cervical cancer is a preventable disease. HPV vaccination was also associated with annual health checkup status. Educational efforts that create awareness about the linkage of HPV infection with cervical cancer and benefits HPV vaccine would help to increase uptake of HPV vaccination rates among college students in the USA.

AUTHOR DISCLOSURE STATEMENT

The authors declare that they have no conflicts of interest exist to report.

FUNDING

The study did not receive any external funding support.

REFERENCES

1. Centers for Disease Control and Prevention (CDC). Genital HPV Infection. Web site. http://www.cdc.gov/std/hpv/stdfact-hpv.htm. Accessed July 1, 2016.

2. Dunne EF, Unger ER, Sternberg M, et al. Prevalence of HPV

ISSN 2473-4780 http://dx.doi.org/10.17140/EPOJ-2-111

infection among females in the United States. *JAMA*. 2007; 297(8): 813-819. doi: 10.1001/jama.297.8.813

3. Satterwhite CL, Torrone E, Meites E, et al. Sexually transmitted infections among US women and men: Prevalence and incidence estimates, 2008. *Sex Trans Dis*. 2013; 40(3): 187-193. doi: 10.1097/OLQ.0b013e318286bb53

4. Abma JC, Martinez GM, Copen CE. Teenagers in the United States: Sexual activity, contraceptive use, and childbearing, National Survey of Family Growth 2006-2008. *Vital Health Stat*. 2010; 23(30): 1-47.

5. Trotter EC, Alderson KG. University students' definitions of having sex, sexual partner, and virginity loss: The influence of participant gender, sexual experience, and contextual factors. *Can J Hum Sex*. 2007; 16: 11-29.

6. Ljubojevic S, Skerlev M. HPV-associated diseases. *Clin Dermatol*. 2014; 32(2): 227-234. doi: 10.1016/j.clindermatol.2013.08.007

7. Gadducci A, Barsotti C, Cosio S, Domenici L, Riccardo Genazzani A. Smoking habit, immune suppression, oral contraceptive use, and hormone replacement therapy use and cervical carcinogenesis: A review of the literature. *Gynecol Endocrinol*. 2011; 27(8): 597-604. doi: 10.3109/09513590.2011.558953

8. Snijders PJ, Steenbergen RD, Heideman DA, Meijer CJ. HPV-Mediated cervical carcinogenesis: Concepts and clinical implications. *J Pathol*. 2006; 208(2): 152-164. doi: 10.1002/path.1866

9. World Health Organization (WHO). *World Cancer Report 2014*. Washington, DC, USA: World Health Organization Press; 2014.

10. GLOBOCAN Cancer Fact Sheets: Cervical cancer – IARC: Cervical Cancer: Estimated Incidence, Mortality and Prevalence Worldwide in 2012. Web site. http://globocan.iarc.fr/old/FactSheets/cancers/cervix-new.asp. Accessed August 18, 2016.

11. U.S. Cancer Statistics Working Group. United States Cancer Statistics: 1999-2013 Incidence and Mortality Web-based Report. Atlanta (GA): Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute; 2016. Web site. http://www.cdc.gov/uscs. Accessed August 18, 2016.

12. De Vicenzo R, Conte C, Ricci C, Scambia G, Capelli G. Long-term efficacy and safety of human papillomavirus vaccination. *Int J Wom Health*. 2014; 6: 999-1010. doi: 10.2147/IJWH.S50365

13. Yoshikawa H, Ebihara K, Tanaka Y, Noda K. Efficacy of quadrivalent human papillomavirus (types 6, 11, 16 and 18) vaccine (GARDASIL) in Japanese women aged 18-26 years. *Cancer Sci*. 2013; 104: 465-472. doi: 10.1111/cas.12106

14. Chesson HW, Ekwueme DU, Saraiya M, Watson M, Lowy DR, Markowitz LE. Estimates of the annual direct medical costs of the prevention and treatment of disease associated with human papillomavirus in the United States. *Vaccine*. 2012; 30: 6016-6019. doi: 10.1016/j.vaccine.2012.07.056

15. Markowitz LE, Hariri S, Lin C, et al. Reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in the United States, National Health and Nutrition Examination Surveys, 2003–2010. *J Infect Dis*. 2013; 208(3): 385-393. doi: 10.1093/infdis/jit192

16. CDC. Surveillance of vaccination coverage among adult populations — United States, 2014. 2016; *MMWR*. 65(1); 1-36.

17. Harris RJ. *A Primer of Multivariate Statistics*. 2nd ed. New York, USA: Academic Press; 1985.

18. Green SB. How many subjects does it take to do a regression Analysis. *Multivariate Behav Res*. 1991; 26(3): 499-510. doi: 10.1207/s15327906mbr2603_7

19. Gerend MA, Magloire ZF. Awareness, knowledge, and beliefs about human papillomavirus in a racially diverse sample of young adults. *J Adolesc Health*. 2008; 42(3): 237-242. doi: 10.1016/j.jadohealth.2007.08.022

20. Klug SJ, Hukelmann M, Blettner M. Knowledge about infection with human papillomavirus: A systematic review. *Prev Med*. 2008; 46(2): 87-98. doi: 10.1016/j.ypmed.2007.09.003

21. Yacobia E, Tennantb C, Ferranteb J, Palc N, Roetzheimb R. University students' knowledge and awareness of HPV. *Prev Med*. 1999; 28(6): 535-541. doi: 10.1006/pmed.1999.0486

22. BM Corp. *IBM SPSS Statistics for Windows, Version 21.0*. Armonk, NY, USA: IBM Corp.; 2012.

23. Jones M, Cook R. Intent to receive an HPV vaccine among university men and women and implications for vaccine administration. *J Am Coll Health*. 2008; 57(1): 23-32. doi: 10.3200/JACH.57.1.23-32

24. Wong LP, Sam I. Ethnically diverse female university students' knowledge and attitudestoward human papillomavirus (HPV), HPV vaccination and cervical cancer. *Eur J Obstet Gynecol Reprod Biol*. 2010; 148(1): 90-95. doi: 10.1016/j.ejogrb.2009.10.002

25. Iliyasu Z, Abubakar IS, Aliyu MH, et al. Cervical cancer risk perception and predictors of human papilloma virus vaccine acceptance among female university students in northern Nigeria. *J Obstet Gynaecol*. 2010; 30(8): 857-862. doi:

ISSN 2473-4780 http://dx.doi.org/10.17140/EPOJ-2-111

10.3109/01443615.2010.511724

26. Friedman AL, Shepeard H. Exploring the knowledge, attitudes, beliefs, and communication preferences of the general public regarding HPV: Findings from CDC focus group research and implications for practice. *Health Educ Behav*. 2007; 34(3): 471-485. doi: 10.1177/1090198106292022

27. Riecka T, Feigc M, Deleréa Y, Wichmannaa O. Utilization of administrative data to assess the association of an adolescent health check-up with human papillomavirus vaccine uptake in Germany. *Vaccine*. 2014; 32(43): 5564-5569. doi: 10.1016/j.vaccine.2014.07.105

28. Reiter PL, McRee AL. Correlates of receiving recommended adolescent vaccines among youth with special healthcare needs: Findings from a statewide survey. *Vaccine*. 2016; 34: 3125-3131. doi: 10.1016/j.vaccine.2016.04.062

29. Kessels SJ, Marshall HS, Watson M, Braunack-Mayer AJ, Reuzel R, Tooher RL. Factors associated with HPV vaccine uptake in teenage girls: A systematic review. *Vaccine*. 2016; 30(24): 3546-3556. doi: 10.1016/j.vaccine.2012.03.063

30. Holman DM, Benard V, Roland KB, Watson M, Liddon N, Stokley S. Barriers to human papillomavirus vaccination among US adolescents: A systematic review of the literature. *JAMA Pediatr*. 2014; 168(1): 76-82. doi: 10.1001/jamapediatrics.2013.2752

31. Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER. Quadrivalent human papillomavirus vaccine: recommendations of the Advisory Committee on Immunization Practices. *MMWR*. 2007; 56(RR02): 1-24.

32. Gilkey MB, Calo WA, Moss JL, Shah PD, Marciniak MW, Brewer NT. Provider communication and HPV vaccination: The impact of recommendation quality. *Vaccine*. 2016; 34: 1187-1192. doi: 10.1016/j.vaccine.2016.01.023

33. Zimet GD, Weiss TW, Rosenthal SL, Good MB, Vichnin MD. Reasons for non-vaccination against HPV and future vaccination intentions among 19-26 year-old women. *BMC Women's Health*. 2010; 10: 27. doi: 10.1186/1472-6874-10-27

34. Rand CM, Schaffer SJ, Humiston SG, et al. Patient-provider communication and human papillomavirus vaccine acceptance. *Clin Pediatr*. 2011; 50: 106-113. doi: 10.1177/0009922810379907

35. American College Health Association. American College Health Association-National College Health Assessment II: Reference group undergraduates' executive summary fall 2015.

36. Gerend MA, Magloire ZF. Awareness, knowledge, and beliefs about human papillomavirus in a racially diverse sample of young adults. *J Adolesc Health*. 2008; 42: 237-242.