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The Relationship of Breast and Gynecological Cancers with Smoking and Metabolic Syndrome - An Examination of NHANES Data 2001 - 2010

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Citation	Yankey, Barbara A. "The Relationship of Breast and Gynecological Cancers with Smoking and Metabolic Syndrome - An Examination of NHANES Data 2001 - 2010." Thesis, Georgia State University, 2012. https://doi.org/10.57709/2818792
DOI	https://doi.org/10.57709/2818792
Download date	2026-03-09 02:18:33
Link to Item	https://hdl.handle.net/20.500.14694/9214

**The Relationship of Breast and Gynecological Cancers with
Smoking and Metabolic Syndrome
- An Examination of NHANES Data 2001 - 2010**

**By
Barbara A. Yankey**

A Thesis Submitted to
The Graduate Faculty of Georgia State University
In Partial Fulfillment of the Requirements for the Degree

MASTER OF PUBLIC HEALTH

**Under the Direction of
Eriksen, M. P., Okosun, I. S., Rothenberg, R. B.**

ATLANTA, GEORGIA
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**The Relationship of Breast and Gynecological Cancers with
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**By
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Acknowledgement

I wish to extend my profound appreciation to all who have supported me in diverse ways; intellectually, emotionally, through scholarship, funding, leadership and prayers, during my academic journey in Georgia State University. I thank God Almighty for keeping me safe and sound.

I thank my family for their support especially, my Father, J.K. Yankey Snr. for his blessings, with emphasis that, my brother David Yankey would leave no stone unturned till I entered the MPH program. My training in Public Health at the Georgia State University is an exceptional experience; thank you David.

I thank Dr. Monica H. Swahn, my program Advisor for her true stewardship and encouragement.

I thank Dr. Michael P. Eriksen, Director of the Institute of Public Health, my professor and Chair of my Thesis committee who stimulated my interest in cancer research and prevention with words handed down to him; “if you must do something, do something about cancer” for his strong support and guidance. I thank Dr. Solomon I. Okosun, my professor and co-Chair of my Thesis committee for the immense support and thorough training he accorded me throughout my studies. I thank Dr. Richard B. Rothenberg, my professor and committee member for my Thesis for making me benefit from his dexterous knowledge.

I cannot find the words to thank Dr. Sheryl Strasser, my professor, for her extraordinary support and being there for me always. I thank Mdm. Courtney M. Burton, graduate coordinator, for being a sister, granting me great guidance and extra care. I thank all professors for their great direction and training, especially; Dr. Bruce Perry, Dr. Christine Stauber, Dr. Frances McCarthy, Dr. Greg Lewis, Dr. John R. Lutzker, Prof. John Steward and Dr. Karen Giesecker.

I wish to express my sincere appreciation to the Ministry of Health and Ghana Health Service for supporting my studies at Georgia State University.

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The Relationship of Breast and Gynecological Cancers with Smoking and Metabolic Syndrome - An Examination of NHANES Data 2001 - 2010

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ABSTRACT

Background: Breast and Gynecological cancers are a major public health problem. Smoking is a lifestyle associated with several chronic diseases including cancer, and is a cause of preventable death. Other lifestyles of public health concern like poor dietary habits and lack of exercise, predisposes many people to dyslipidemia, hypertension and obesity; which are risk factors for metabolic syndrome, and are associated with cancer.

Objectives: The purpose of this study is to find if those who smoke, and have the metabolic syndrome, are more likely to have breast or gynecological cancers, and to find the distribution by education, having health insurance, race/ethnicity and socio-economic status.

Methods: A case-control study of females aged 20 years and above who participated in the United States National Health and Nutrition Examination Survey (NHANES) 2001-2010.

Results: Adjusting for age, education, race, marriage, country of birth and income to poverty ratio, females who have smoked more than hundred cigarettes in life and still smoke; a) have a 42 percent less chance of having a breast cancer diagnosis (OR 0.58; 95% CI 0.36 – 0.93, p-value 0.025), and b) are 2.67 times as likely to report a cervical cancer diagnosis as females who have smoked less than hundred cigarettes in life (OR 2.67; 95% CI 1.72 – 4.13, p-value <.0001). The rate of cervical cancer diagnosis is highest among females who live below the federal poverty level and among females aged 30 - 39 years.

Conclusion: Smoking and metabolic syndrome are very important indicators of reproductive health and needs further study. Because smoking is associated with increased odds of having cervical cancer, smoking cessation interventions should be an integral part of cervical cancer prevention programs and these programs should be targeted at younger females as well as females who live below the federal poverty level.

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Student MPH/MPA, spring 2012

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Key words/Abbreviations:

BP	Blood Pressure
BCEO	Breast, Cervical, Endometrial and Ovarian
BC	Breast Cancer
CC	Cervical Cancer
EC	Endometrial Cancer
GC	Gynecological Cancer
HDL	High Density Lipoprotein
MetS	Metabolic Syndrome
NHANES	National Health And Nutrition Examination Survey
OR	Odds Ratio
OC	Ovarian Cancer

Caveat: The terms reported cancers and have cancers are used interchangeably only for purposes of emphasis from time to time that, this study uses reported cancer cases. The term valid respondent is used for study participants who gave answers to questions provided; those who did not give answers at all or answered “don’t know” are excluded. The term relevant female/participant is used in cases where results of examinations are available. Gynecological cancer in this study refers to the three common gynecological cancers (cervical, endometrial and ovarian). Nonsmokers in this study include ever smokers who have smoked less than 100 cigarettes in life.

INTRODUCTION

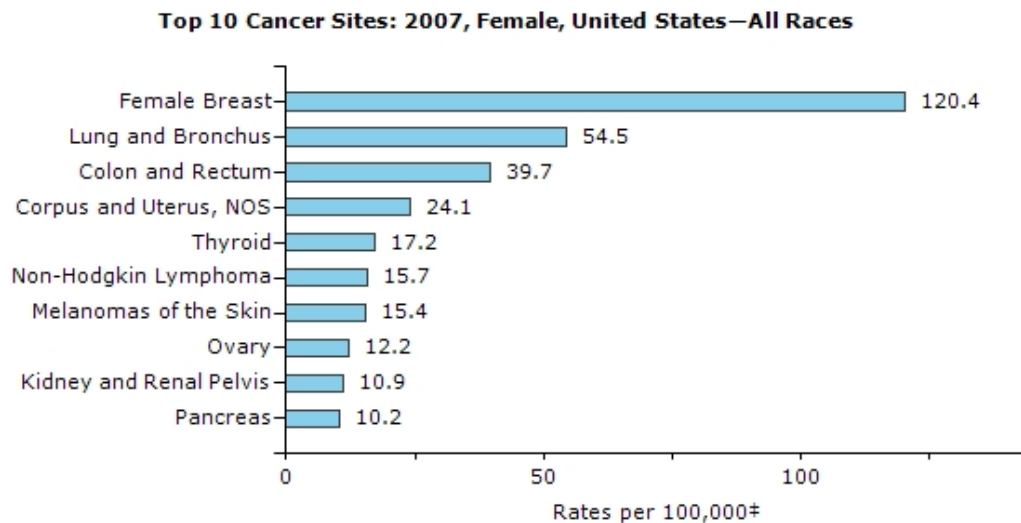
The epidemiologic transition of the causes of morbidity and mortality is from infections to chronic diseases because of lifestyle changes like poor dietary habits including consumption of high-fat foods (Omran 2001). The prevalence of chronic diseases is increasing and adding to the global disease burden already posed by infections (WMA, 2011). Chronic diseases alone account for almost 60% of all deaths in the world: dominant among the causes is heart disease and cancer (Sami M. 2010). Cancer is a very important public health concern globally and a major public health concern in the United States and several other countries, with about 7.6 million people dying each year in the world from cancer; cancer accounts for about 13% of all deaths worldwide (Siegel, Ward et al. 2011). Almost 24% of all deaths in the world are due to a cardiovascular disease and about 19% of all deaths in the world are due to infectious and parasitic diseases (lower respiratory infections (7.1%), diarrheal diseases (3.7%), HIV/AIDS (3.5%), tuberculosis (2.5%) and malaria (1.5%) (Dal-Ré 2011); cancer ranks second (13% vs. 24%) as the cause of deaths worldwide after cardiovascular disease and ranks second as the cause of death worldwide after infectious diseases (13% vs. 19%). It is noteworthy that each year, more people die from cancer globally than from HIV/AIDS, tuberculosis and malaria combined; as many as 12.7 million people were diagnosed with some kind of cancer in the year 2008 (Ferlay, Shin et al. 2010). In the United States of America, cancer ranks second after heart disease as the cause of deaths; being responsible for the death of 568,668 Americans in 2009 (Kochanek K.D et. al. 2011).

Cancers of the female reproductive organs are called gynecological cancers (GCs); the five major cancers that make up gynecological cancers are cervical, ovarian, endometrial, vaginal and vulvar cancers. Vulvar and vaginal cancers are rare, particularly among younger women.

Another reproductive tract cancer, found in the fallopian tubes, is quite rare and often is of the same cell type as endometrial cancers. Together these rare cancers constitute 6 – 7% of all GCs. Gynecological cancers account for almost 8% of all female tumors. Globally, out of the ten most common cancers in females; breast cancer is the first, cervical cancer ranks third, endometrial cancer is sixth and ovarian cancer is the seventh in rank (Jemal, Bray et al. 2011). In the year 2007; 80,976 women in the United States were diagnosed with a gynecologic cancer, and 27,739 died from a gynecologic cancer.

Breast cancer comes second in rank after lung cancer among all cancers: breast cancer accounts for as much as 10.9% of all cancers, occurs more commonly among all women worldwide with 1.38 million new cases diagnosed in 2008 (Ferlay, Shin et al. 2010). This is about 23% of all incident cancer cases. Breast cancer incidence rates (BCIR) are high in most of the developed regions of the world compared to the less developed regions of the world apart from Japan; BCIR are more than 80 per 100,000 in developed regions and less than 40 per 100,000 in less developed regions (GLOBOCAN 2008). On the other hand, mortality rates are 6 – 19 per 100,000 in developed regions much lower compared to incidence rates and this is due to effective intervention programs (screening and treatment) for breast cancer in the developed countries resulting in low overall mortality rates sending breast cancer to 5th place as the overall cause of deaths from cancer. Cervical cancer ranks seventh among all cancers and third among all cancers in women with 530, 000 incident cases worldwide in 2008 (Ferlay, Shin et al. 2010). Low and middle income countries carry the greatest burden about 85%; the European Union (EU- 27) about 5.9%; and the United States of America about 2.1% of the entire burden due to cervical cancer incident cases in 2008. Cervical cancer is not part of the top ten cancers in females in the United States; cervical cancer ranks 14th among cancers in females (Howlander N

et. al 2011). Globally uterine cancer is the most commonly diagnosed gynecological cancer and ranks third among cancers affecting females. In the United States, uterine cancer also ranks first among gynecological cancers but is the fourth most common cancer in females. The age-adjusted death rate for endometrial cancer based on patients who died in 2004-2008 in the United States was 4.2 per 100,000 women per year. Ovarian cancer accounts for only about three percent of all cancers in females, but is classified the deadliest of all gynecological cancers.



U.S. Cancer Statistics Working Group. *United States Cancer Statistics: 1999–2007 Incidence and Mortality Web-based Report*. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2010. Available at: www.cdc.gov/uscs. Assessed February 14, 2012

Five main risk factors associated with cancer are tobacco use, high body mass index, low fruit and vegetable intake, lack of physical activity and alcohol use. These risk factors account for about 30% of all cancer deaths globally. It is estimated that by the year 2030, the number of global cancer deaths will increase from 7.6 million deaths in 2008 to 13.1 million deaths (GLOBOCAN, 2008).

Smoking is a major cause of preventable death and disease; the US Surgeon General reports that smoking is associated with several chronic diseases including cancer and heart disease, and reports the possible mechanisms by which smoking causes these diseases (CDC, 2010). Globally, tobacco use kills almost six million people yearly. It is projected that tobacco use will kill more than eight million people worldwide if the current trend in tobacco use continues; 80% of these premature deaths will be in low and middle income countries. Tobacco use is the single most preventable cause of death in the United States; more than 440,000 premature deaths per year are attributed to tobacco use and this is about one out of every five deaths a year. People who smoke lose about 13 – 14 years of their life compared to those who do not smoke. In 2010, 21.5% of all adult males and 17.3% of adult females in the United States were current smokers and this differed by age, race, education and poverty status with about 52% of all current smokers attempting to quit smoking (CDC). People who are more educated smoke less than people who are less educated; 45.2% of adults with a GED diploma were current smokers, whilst 6.3% of people with a post graduate college degree, 9.9% with undergraduate degree, 23.8% with high school diploma, 28.9% of those below the poverty line and 18.3% of those who live at or above the poverty line were current smokers in 2010. People aged 65 years and older smoke less (9.5%) than people between the ages of 18 years and 64 years (21% on average). American Indians/Alaskan natives (AI/N) smoke the most ; 31.4% of AI/N followed by 21.0% of Whites, 20.0% of Blacks, 12.5% of Hispanics and 9.2% of Asians. Whereas there is enough evidence that tobacco causes cancer of the lungs and almost all organs in humans, about 25% of people living with cancer still smoke. This is quite unfortunate, especially when other people who do not smoke are exposed to second hand smoking putting them at risk for cancer as well.

Contemporary demands and changes in lifestyle results in reduced physical activity and poor diet which increases the incidence and prevalence of obesity; a major risk factor for several chronic diseases including cancer and the metabolic syndrome. Obesity in women has been linked to breast cancer and it is important to know if obesity increases the risk of having gynecological cancers as well. Metabolic syndrome (MetS) is a combination of metabolic factors that increases ones risk of developing cardiovascular diseases, diabetes, stroke or other diseases associated with atherosclerosis. The definition of metabolic syndrome includes the basic conditions: obesity, insulin resistance, dyslipidemia and hypertension, albeit, different expert groups have different clinical criteria for defining metabolic syndrome. Among the most widely accepted definitions of metabolic syndrome are those of the World Health Organization (WHO), European group for the Study of Insulin Resistance (EGIR) and the National Cholesterol Education Program – Third Adult Treatment Panel (NCEP ATP III). The WHO defines MetS as impaired glucose tolerance or diabetes with two or more of the following: blood pressure more than or equal to 140/90 mmHg, plasma triglycerides of more than or equal to 150mg/dl, lowered HDL cholesterol (< 35mg/dl for men or < 39mg/dl for women), waist to hip ratio of > 0.90 for men and > 0.85 for women and/or body mass index (BMI) of > 30kg/m², urinary albumin excretion rate of more than or equal to 20 micrograms/min or albumin:creatinine ratio of more than or equal to 30mg/g. (WHO 1999). The NCEP ATP III guidelines state that metabolic syndrome may be diagnosed in a person who has three or more of the following: central obesity (waist circumference of > 102cm for men and >88cm for women), an elevated triglyceride level (more than or equal to 150mg/dl), a reduced HDL- cholesterol level(< 40mg/dl for men and <50mg/dl for women), high blood pressure of more than or equal to 130/85mmHg, and high fasting glucose concentration of more than or equal to 100mg/dl (NCEP ATP III 2001).

Metabolic syndrome is quite prevalent among populations and is an increasing problem globally. The International Diabetes federation (IDF) identifies the current obesity epidemic as the main cause of the high prevalence of MetS. The WHO lists that obesity has more than doubled since 1980 worldwide; in 2008, about 1.5 billion adults 20 years and over were overweight. Out of this number, 200 million men and 300 million women were obese. Uterine and breast cancers are among the common consequences of being obese. According to the national Health Statistics Report about 34% of United States adults aged 20 years and above have the metabolic syndrome, the MetS increases with age, its prevalence varies by age and ethnicity and the pattern of MetS differs by gender (Ervin, 2009).

Breast and gynecological cancers are a major public health problem. Whereas screening programs help to reduce the incidence of female cancers through early detection and treatment, there is a disparity in access to these services. Screening programs in United States (U.S.) has helped to reduce the incidence and mortality due to cancer, but the U.S. does not provide a basic health benefit package to all of its citizens (Sankaranarayanan 2001). Medicare is a health benefit program for the elderly above 65 years and the disabled. Medicaid is for people with low income in the U.S. Other people must finance their healthcare through various Health Insurance (HI) programs/packages (Sigurdsson 2009). Whilst HI premiums are high, it does not pay for all the cost of accessing medical service. An insured client still faces co-payments and deductibles when he/she gets medical services. People who need healthcare services are not likely to access these services because they cannot afford it. A study conducted by Weaver et al concluded that more than two million cancer survivors in the US did not get one or more needed medical service during the period of 2003 – 2006 because of concern for cost (Weaver, et al., 2010). Evidence and information on the relationship between smoking, metabolic syndrome and gynecological

cancers as well as their distribution among certain demographic factors such as race/ethnicity, education, income and having health insurance can help plan effective intervention programs aimed at reducing the burden of gynecological cancers.

PURPOSE AND HYPOTHESIS

The purpose of this study is to find the association and rates of breast and gynecological cancers among females who: a) smoke, b) have metabolic syndrome and c) smoke and have metabolic syndrome, compared to females who do not have these conditions, and to look at the distribution by race/ethnicity, education, socioeconomic status and having health insurance. If among females with the above listed risk factors, breast and gynecological cancers are more prevalent, then it is likely there is a causal relationship which needs further study to help plan programs aimed at reducing the incidence and mortality due to cancers in females.

The hypothesis of this study is that in the United States:

- a) Breast and gynecological cancers are more prevalent among females who smoke than females who do not smoke.
- b) Breast and gynecological cancers are more prevalent among females who have the metabolic syndrome than among females who do not have the metabolic syndrome.
- c) Breast and gynecological cancers are more prevalent among females who smoke and have the metabolic syndrome than among females who smoke but do not have the metabolic syndrome.
- d) Breast and gynecological cancers are more prevalent among females who smoke and have the metabolic syndrome than among females who have the metabolic syndrome and do not smoke.

LITERATURE REVIEW

Antonio Russo et al. conducted a population based study to describe the link between metabolic syndrome and cancer risk. The study identified 16,677 records of participants aged 40 years and over in Milan's Health Information System from January 01, 1999 to December 31, 2005, resident in Milan, Italy, who had been concurrently prescribed at least an antihypertensive, a hypoglycemic and a hypolipemic with an average follow up period of 2.7 years (Russo, Autelitano et al. 2008). Records in the local cancer registry showed that 823 of the participants had cancer incident cases during this study period. The number of person years at risk was calculated from the index date (date when pharmacological treatment was started) to date of first malignant cancer diagnosis or date of death or date of migration or the last date of follow up (whichever came first). Standardized Incident Ratios (SIR) and Standardized Mortality Ratios (SMR) at 95% confidence intervals under the assumption of a Poisson distribution of observed cases were computed as the ratio between observed and expected numbers of site specific incident invasive cancer and mortality cases respectively. A significantly increased risk for pancreatic cancer in males and colorectal cancer in females was observed, however, they also found a non-significant increased risk of liver, gallbladder, biliary tract, breast and endometrial cancer among females and concluded that people who had the metabolic syndrome had an increased risk of developing several cancers (Russo, Autelitano et al. 2008). The expected number of invasive cancers calculated was 302 for females (SIR 104; 95% CI 93–116) and 492 for males (SIR 103; 95% CI 95–113). Colorectal cancer risk was statistically significant only in females (SIR 132; 95% CI 101–170) with a notable increase for rectal cancer sub-site (SIR 180; 95% CI 112–276). There was a significant increased risk for Pancreatic cancer observed in males

(SIR 178; 95% CI 114–266) and females had a similar but not significant risk increase (SIR 145; 95% CI 87–226). Concerning breast and gynecological cancers, non-significant increased risks were observed in females, for breast (SIR 117; 95% CI 95–143) and endometrial cancers (SIR 156; 95% CI 95–241). Mortality follow up was completed by January 1, 2006. Out of the 1,746 deaths, 867 deaths were caused by cardiovascular diseases: SMRs were 195 for males (95% CI 178–213) and 168 for females (95% CI 151–186) and invasive cancers accounted for 345 deaths: SMRs were 73 for males (95% CI 64–84) and 81 for females (95% CI 68–95), respectively.

Components of the metabolic syndrome have also been studied to assess their association with cancer. In the Metabolic syndrome and cancer project (Me-Can) the association between serum triglycerides and cancer risk was assessed. Concerning cancers among women, the study shows significant increases in the relative risk for total cancer, cervical, respiratory, non-melanoma skin cancers and other non-specified skin cancers in the top quintile compared to the bottom quintile of serum triglycerides (Borena, Stocks et al. 2011). The Metabolic syndrome and Cancer project (Me-Can) includes data from population-based cohorts in Norway (The Oslo study, the Norwegian Counties study-NCS, the Cohort of Norway-CONOR and the Age 40 programme-40-y), Austria (the Vorarlberg Health Monitoring and Prevention Programme-VHM&PP), and Sweden (The Vasterbotten Intervention Project-VIP and the Malmo Preventive Project-MPP) in 2006. Altogether, there were 940 060 subjects and 1 600 296 observations for the Me-Can dataset, however, the full Me-Can dataset includes 924,801 participants with 1,566,553 health examinations after an initial data cleaning process and ultimately data on 514,097 men and women were used for the serum triglyceride and cancer risk study after inclusion criteria were met. Incident cancer cases were identified through linkages with national cancer registries of the respective countries and categorized according to the International

Classification of Diseases, seventh revision (ICD-7). Taking whichever occurred first; the date of the first cancer diagnosis, emigration, death or December 31, 2003 (Austria), 2005 (Norway), and 2006 (Sweden), was used as an end-point. Cox proportional hazard regression was used to estimate hazard ratios, denoted as relative risks (RR), for triglyceride levels with risk of incident cancer. In women, for fasting compared to non-fasting serum triglyceride levels (STG) respectively, a significant association for non-melanoma skin cancer of (RR: 4.31; 95% CI, 1.56–11.9) versus (RR: 0.96; 95% CI, 0.40–2.36) and a borderline significant effect for corpus uteri (endometrial) of (RR: 1.74; 95% CI, 0.99–3.09) versus (RR: 1.07; 95% CI, 0.65–1.72) was observed and in contrast, only non-fasting STG showed a significant association with cervical cancer (RR: 2.64; 95% CI, 1.29–5.52) versus (RR: 1.04; 95% CI, 0.37–2.77).

A prospective cohort study examined the association between the metabolic syndrome and risk of incident endometrial and fatal uterine corpus cancer among female cohorts in the Me-Can study. In all, 287,320 women were enrolled during 1974–2005 and followed for ten years calculated as 2.9 million person-years on average (Bjørge, Stocks et al. 2010). A total of 917 endometrial carcinomas and 129 fatal cancers were identified. The metabolic syndrome was assessed as a composite Z score, as the standardized sum of Z scores for body mass index, blood pressure, blood/plasma/serum levels of glucose, total cholesterol, and triglycerides. BMI, blood pressure, glucose, cholesterol and triglycerides were standardized to Z score variables with mean = 0 and standard deviation (SD) = 1. Because data for glucose and triglycerides were skewed and had outliers, they were log-transformed before standardization. A score for the metabolic syndrome, was calculated by adding the individual Z scores and standardized to a Z score variable with mean = 0 and SD = 1. Cox proportional hazards regression models was fitted with age as the time variable to calculate relative risks and 95% confidence intervals for endometrial

carcinoma incidence and mortality. The models were stratified into six sub-cohorts and adjusted for year of birth (up to 1929, 1930–1939, 1940–1949, 1950–1959, and from 1960) and smoking status (never, former, and current smokers). Blood pressure, glucose, cholesterol, and triglycerides were further adjusted for quintile of body mass index BMI, which is known to be a strong risk factor for endometrial cancer. Parity, year(s) of childbirth(s), and physical activity were also adjusted for in the Norwegian cohorts, but this did not change the risk estimates by much and so these variable were not adjusted for in the final model. Relative risk of endometrial carcinoma increased with increasing BMI, blood pressure, glucose level, and triglyceride level. There was an increased risk of endometrial carcinoma for the metabolic syndrome (per 1-unit increment of Z score, RR = 1.37, 95% CI: 1.28, 1.46). An increased risk was also observed for fatal cancer in relation to the metabolic syndrome RR = 1.56, 95% CI: 1.32, 1.84; as well as increased risks for all of the individual Z scores except for cholesterol when stratifying for cohort and adjusting for year of birth and smoking, and there was increased risk for blood pressure after further adjustment for quintile of BMI.

The association between MetS and risk of breast cancer incidence and mortality was also examined in the Me-Can project. 4,862 incident cases of breast cancer with a mean age of 58 years at diagnosis and 633 deaths from breast cancer were identified (Bjørge, Lukanova et al. 2010). Interestingly, women below 50 years of age had a decreased risk of incident breast cancer for the MetS (per 1-unit increment of z-score; RR, 0.83; 95% CI, 0.76-0.90) and for the individual components examined, except for glucose. Stratifying by age, a decreasing risk of breast cancer incidence with increasing BMI (RR 0.70; 95% CI, 0.57-0.85) for the top versus bottom quintile was observed in women aged below 50 years. Of the continuous Z-score factors, increasing levels of blood pressure, glucose, and the MetS was associated with an increased risk

of breast cancer mortality in women above age 60 years. The RR for the MetS was 1.23 (95% CI, 1.04-1.45) per 1-unit increment of Z-score with the association for blood pressure and glucose being present even after adjustment for the other individual Z-scores. The highest RR was observed for glucose (RR, 1.50; 95% CI, 1.05- 2.14).

Nagel et al examined the association of metabolic syndrome with rare gynecological cancers in the Me-Can project (Nagel, Concin et al. 2011) and found that metabolic syndrome was associated with increased risk of vulvar (RR 1.78, 95% CI 1.30 – 2.41) and vaginal cancers (RR 1.87, 95% CI 1.07 – 3.35). Increased risk of vulvar cancer was also associated with blood glucose (RR 1.98, CI 1.10 – 3.58) and triglyceride levels (RR 2.09, 95% CI 1.39 – 3.15).

Experimental studies show that nicotine which is also the active ingredient in tobacco is associated with poor cancer prognosis. A randomized control study conducted by Davis et al demonstrated that nicotine can promote tumor growth and metastasis in immune-competent mice (Davis, Rizwani et al. 2009). In this study, to assess tumor growth under use of nicotine, mice were injected with cultured line-1 mouse adenocarcinoma cells and were randomized to control (n=8) and test (n=8) after 3-7 days of the injection. Nicotine was administered to test mice for two weeks by intraperitoneal injections at a dose of 1mg/kg three times daily weekly or transdermally at a daily dose of 25mg/kg using over the counter nicotine patches, control mice were given vehicle with no nicotine. The tumor growth was measured three times weekly. Mice that received intraperitoneal nicotine had significantly larger tumors ($2267 \pm 369 \text{ mm}^3$, p-value = .019) compared to controls tumors ($695 \pm 98 \text{ mm}^3$, p-value = .002) and for mice that had transdermal patch, average tumor volume was $871 \pm 106 \text{ mm}^3$ compared to controls $530 \pm 59 \text{ mm}^3$, p-value = 0.002. The tumor was removed and the mice were exposed to nicotine (test) or vehicle without nicotine (control) again for 14 days to test for regrowth. There was an average of

19 ± 7% tumor recurrence in the control group, as compared to an average of 59 ± 3% tumor recurrence in nicotine group (p-value = .01). To test for metastasis, the mice were injected with tumor cells, randomized to nicotine 1mg/kg injections (n = 16) or vehicle alone (n = 16) and observed for three weeks and tumor removed. The mice received their assigned injections for two more weeks. A histological examination of the lung tumors showed that the control group had average metastatic foci of 0.9 ± 0.2 compared to 8.1±1.7 in the test group (p-value = .001). Surprisingly, metastatic foci for the transdermal patch group was an average of 20.6 ± 4.9 (test group) and 6.7 ± 2.1 (control group) p-value = .02. The study concluded that while nicotine has limited capacity to initiate tumor formation, nicotine can promote the proliferation and spread of cancers which have been caused by other carcinogens in tobacco.

A hospital-based case-control study conducted to investigate common and site-specific risk factors among gynecologic cancers in females aged 30 years and over admitted to a hospital in Miyagi Cancer Center Hospital (MCCH), Miyagi Prefecture, Japan, from 1997 to 2003 concluded that smoking was significantly associated with an increased risk of cervical cancer (Fujita, Tase et al. 2008). Incident cancer cases were identified from a list of the patients linked with the hospital-based cancer registry files which records all cancer cases confirmed by clinical, cytological and/or histopathological examination at the MCCH; 151 women were diagnosed with cervical, 103 with endometrial and 141 with ovarian cancer. 2016 female patients who had no history of cancer and did not have cancer were selected as controls. A self-administered questionnaire was used to obtain information on reproductive factors, exogenous hormone use, and lifestyles including smoking. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for active and passive smoking, alcohol intake, marital status, reproductive factor and exogenous hormone use were estimated for each cancer site using an unconditional logistic regression

model, adjusting for age, year of survey, occupation and other related factors including family history of cancer in parents and siblings. Compared with never smokers, active smoking was significantly associated with an increased risk of cervical cancer (OR = 2.25, 95% CI, 1.47 – 3.43). A significant dose-response relationship was found between the numbers of cigarettes smoked per day and the odds of having cervical cancer compared to never smokers: among those who smoke less than 10 cigarettes a day (OR= 2.00, 95% CI, 1.12-3.58), among those who smoke from 11- 20 cigarettes a day (OR= 2.51, 95% CI, 1.42-4.56), however, among those who smoked 20 or more cigarettes a day (OR =1.56, 95% CI, 0.74-3.31) p-value for the trend = 0.004. A high odds for cervical cancer was also observed (OR = 3.20, CI, 1.22-8.44) in women who started smoking before 20 years of age, compared to women who started smoking between the age of 20 – 24 years OR = 2.49, CI,1.38-4.51 and those who started smoking after 25 years OR =1.94, CI,1.05-3.61. For endometrial cancer, there was a significant decreased risk associated with passive smoking (OR = 0.54, CI, 0.32-0.93) and an insignificant decreased risk associated with active smoking (OR = 0.54, CI, 0.26-1.13. the odds of having ovarian cancer among active smokers was OR =1.04, CI, 0.62-1.72. Alcohol intake was significantly associated with a decreased risk of ovarian cancer compared with people who never drank alcohol, OR = 0.58, CI, 0.35-0.96.

Mammographic density (MD) is a strong indicator of breast cancer risk; Lesley Butler et al. assessed the associations between active smoking and secondhand smoke (SHS) exposure with mammographic density among 799 pre- and early peri-menopausal women who were enrolled in the Study of Women's Health Across the Nation (SWAN). Average percent mammographic density, significantly decreased consistently with increased tobacco smoke exposure at a 95% confidence interval: Never smoker/no SHS 48.5 (46.3, 50.6), Never smoker/with SHS: 43.1

(40.3, 45.8), Former smoker: 40.7 (37.7, 43.6), Current smoker: 38.4 (33.7, 43.0), p-value: 0.001 (Butler, Gold et al. 2010). Cigarette smoke may exert antiestrogenic effects by influencing estrogen metabolism. Estradiol 2-hydroxylation yields metabolites, such as [2-hydroxyestrone (2-OHE)], that have antiestrogenic properties; Lesley Butler et al have previously reported a statistically significant trend (p-value 0.0001) of increasing urinary 2-OHE level with increasing amount of smoking among pre- and early perimenopausal women in SWAN and as corollary concluded that the inverse association observed between smoking and breast density may be due to antiestrogenic but not the carcinogenic effects of smoking. Using seven questions adapted from the American Thoracic Society and validated self-administered questionnaires, active smoke exposure and SHS exposure were assessed at baseline and subsequent follow-up visit. The definition for active smoking is not explicitly explained in the study but ever-active smokers were defined as having smoked a total of at least 20 packs of cigarettes over one's lifetime, or at least one cigarette per day for at least one year and ever-active smokers who reported no longer smoking at the time of interview were classified as former-active smokers. Having SHS exposure was defined as at least one total person-hour of SHS exposure during the past seven days. Eligible mammograms were those taken as part of routine medical care during the period from two years prior to the baseline examination through two years after annual follow-up visit. The total area of the breast and the areas of dense breast were measured with a compensating polar planimeter (LASICO, Los Angeles, CA) on the craniocaudal view of the right breast or the left breast when films from the right breast were unavailable (n = 81). Percent density was calculated by dividing the area of dense breast by the total area of the breast and multiplying by 100. The study controlled for age, body mass index (BMI), race/ethnicity, study-site, age at menarche, oral-contraceptive use and alcohol consumption in the final model.

The SWAN study also evaluated the association between MetS and mammographic density (MD) in 790 enrolled premenopausal and early peri-menopausal women (Conroy, Butler et al. 2011) and observed a lower mean percent MD for women with the MetS (mean % MD 27.4, SD \pm 17.2) <0.001 and each component of the MetS, compared to those without the metabolic abnormality (mean % MD 47.4, SD \pm 19.3). The study showed modest inverse associations between percent MD and the MetS [β = -2.5, standard error (SE) = 1.9, p = 0.19], abdominal adiposity (β = -4.8, SE = 1.9, p = 0.01) and raised glucose (β = -3.7, SE = 2.4, p = 0.12) after adjusting for body mass index (BMI) in a cross sectional model; after adjusting for age and BMI in longitudinal models, abdominal adiposity (β = 0.34, SE = 0.17, p = 0.05) was significantly positively associated with β slower annual decline in percent MD with time. The study concluded that, the results do not support the hypothesis that, the MetS increases breast cancer risk via a mechanism of increase in percent MD, and gave an explanation that it is possible that the effects of abdominal adiposity on breast cancer risk are not mediated by MD but via alternative pathways that are not represented by MD.

A case-control study to examine the relation between smoking and breast cancer risk in non-Hispanic white women under the age of 50 years who carry a deleterious mutation in BRCA1 (195 cases and 302 controls) or BRCA2 (128 cases and 179 controls) indicates that history of ever smoking is associated with increased risk of breast cancer before age 50 years in BRCA1 and BRCA2 mutation carriers (2008). Compared to never smokers, the odds ratios for former and current smokers at 95% confidence interval were; OR 1.44 CI: 0.96–2.17 and OR 2.02 CI: 1.31–3.10 in BRCA1 carriers and OR 2.02 CI: 1.37–2.96 and OR 2.35 CI: 1.25–4.43 in BRCA2 carriers respectively. Information on selected demographics /lifestyles including smoking history, alcohol consumption, oral contraceptive (OC) use, and reproductive and other

risk factors were collected using a common structured questionnaire, and information on deleterious mutation in either BRCA1 or BRCA2 were ascertained from the Breast Cancer Family Registry (Breast CFR). Subjects with a first primary invasive breast cancer were defined as cases, and subjects without breast cancer were defined as controls.

A case-control study of 272 women attending Obstetrics and Gynecology clinics for cervical cytologic screening at the University of Texas Medical Branch in Galveston (UTMB) in the US and the Universidad Central in Caracas, Venezuela examined the differential risk contribution of sexual behavior and cigarette smoking to cervical cancer (CC) in the U.S. and Venezuela (Sierra-Torres, Tyring et al. 2003). The study reported that HPV infection was significantly associated with CC in both populations, but compared to US controls, the Venezuelan controls were twice as likely to be infected with HPV and that whereas having more than two lifetime sexual partners (OR = 4.7, 95% CI = 1.7-13.1) and initiation of sexual activities before the age of 18 (OR = 4.7, 95% CI = 1.6-13.7) were significant risk factors in a multivariate model for CC in Venezuela, current cigarette smoking was a significant risk factor only in the US (OR = 3.6, 95% CI = 1.7-7.7) and not in Venezuela (OR 1.0, 95% C.I. 0.5—2.4). Among all the subjects, compared to never smokers, the odds of having CC increased significantly in ever smokers (OR 1.8, 95% C.I. 1.1—2.9) and current smokers (OR 2.0, 95% C.I. 1.2—3.5) as well as pack-years; for ≤ 5 years (OR 1.2, 95% C.I. 0.7—2.3) and for > 15 years (OR 3.9, 95% C.I. 1.6—9.8). The study excluded women who had been exposed to chemotherapeutic drugs, had chronic illnesses, or sexually transmitted diseases. Cases consisted of 114 women with biopsy-confirmed high-grade cervical intraepithelial neoplasia (HGICIN; i.e., CIN 2-3) or invasive CC and controls consisted of 158 women with a history of normal Pap tests in the past than one year or less. Those who reported smoking at the time of study recruitment

where classified as current smokers and the number of packs of cigarettes smoked per day multiplied by the duration of cigarette smoking in years was calculated as the pack-years, an indicator of cumulative smoking dose.

A population-based study conducted to assess the risk associated with cigarette smoking, with a particular focus on tumor subgroups jointly classified according to the degree of invasiveness and histology, identified 812 women aged 35 – 75 years with ovarian cancer diagnosed in western Washington State from 2002–2005 through a population-based registry that is part of the Surveillance, Epidemiology, and End Results program of the US National Cancer Institute (Rossing, Cushing-Haugen et al. 2008). The study selected 1,313 controls with at least one ovary and no history of ovarian cancer by random digit dialing using stratified sampling in five-year age categories, one year calendar intervals and two county strata in a 2:1 ratio to women with invasive epithelial ovarian cancer and assessed the risk associated with cigarette smoking, with a particular focus on tumor subgroups jointly classified according to the degree of invasiveness and histology. The study established that, the incidence of both borderline and invasive mucinous ovarian tumors increased among women with a history of cigarette smoking (OR 1.8, 95% CIs = 1.2–2.9, and OR 1.8, 95% C.I. = 0.8–4.3, respectively). Increased smoking duration and pack-years of exposure among women increased the risk of having these tumor types especially among women who had smoked within the previous 15 years. Overall, smoking was associated with a 30% increase in risk of epithelial ovarian cancer. In this study, demographic and lifestyle characteristics, family history of cancer, and reproductive history were obtained through in-person interviews spanning the period of time before diagnosis (for cases) or before an assigned, comparable reference date (for controls). Smoking history was initiated by questions on whether a woman had smoked a total of 100 or more cigarettes; if she had,

information on age at starting to smoke, and, if not smoking at the reference date, age at stopping. Women who had smoked also reported the total number of years smoked which accounts for time periods of non-smoking of at least one year's duration as well as the typical number of cigarettes per day. Odds ratios (ORs) and 95% confidence intervals (CI) were calculated using unconditional logistic regression. The study adjusted for age (5-year intervals), county of residence (two strata), and year of diagnosis/reference date, number of full-term births, duration of hormonal contraception, education and other potential confounding factors.

Niwa Y. et al conducted a prospective study to examine the relation between cigarette smoking and the risk of ovarian cancer using data from the Japan Collaborative Cohort Study for Evaluation of Cancer Risk (Niwa 2005) from 1988 and found that cigarette smoking increases the risk of developing ovarian cancer in the Japanese population. 1990, 64 327 women from 45 areas of Japan and aged 40–79 years registered based on a basic health examination conducted under the Health and Medical Service Law for the Aged. Over an average of 7.6 years (range = 0 – 10.0 years) which calculates as 266 366 person-years, a total of 39 women were diagnosed with ovarian cancer; fourteen cases with histologic diagnosis of serous carcinoma, four cases of endometrial carcinoma, two cases of mucinous carcinoma, and nineteen cases with no detailed histologic diagnosis. Proportions of those who had never smoked and former and current smokers were 93.1% of the study population had never smoked, 1.6%, were former smokers and 5.3% were current smokers. Cox proportional-hazards models were used to estimate relative risks (RR) and 95% confidence intervals (CI), adjusting for age at enrollment and study area; current smokers showed a significantly increased risk of ovarian cancer compared to those who had never smoked (RR = 2.63, 95% CI = 1.02–6.78). In another multivariate analysis, RR were estimated adjusting for: body mass index, height, hormone replacement therapy, family history

of breast cancer and/or ovarian cancer, age at menarche, age at menopause, parity, alcohol consumption and education; current smokers were associated with an increased though not significant risk of ovarian cancer (RR = 2.27, 95% CI = 0.85–6.08) and former smokers were also non significantly positively associated with the risk of ovarian cancer. Relative risk was estimated for ovarian cancer for cigarettes per day, years smoked, and consumption in pack-years among current smokers. Women who currently smoked 10–19 cigarettes per day had a significantly higher risk of developing ovarian cancer (RR = 3.50, 95% CI = 1.05–11.68) compared with those who had never smoked with risk also increased in women who were long-term smokers at enrollment. Women who smoked 10–19 years were more than four times as likely as never smokers to develop ovarian cancer (RR = 4.58, 95% CI = 1.07–19.59). Compared with those who had never smoked women who currently consumed 10–19 pack-years showed the highest relative risk (RR = 5.56, 95% CI = 1.68–19.06). Women who smoked at least 20 pack-years had an increased risk of ovarian cancer, but without statistical significance (RR = 1.86, 95% CI = 0.25–14.30).

A meta-analysis of epidemiologic studies conducted to examine the association of endometrial cancer risk with cigarette smoking concluded that cigarette smoking is associated with lower risk of endometrial cancer, especially among postmenopausal women (Bo, Li et al. 2008). The systematic literature search was limited to English-language articles up to June of 2007 and was performed in MEDLINE and EMBASE to identify relevant studies. Out of the 220 records identified from primary literature search, 48 articles were eventually selected as relevant for the study, but ten prospective and 24 case-control studies were included in the meta-analysis because six articles did not give risk estimates and 95% CIs, one publication was a duplicate of a previous report from the same study population and five articles did not adjust for any potential

risk factors. The included studies were conducted in United States (22), Canada (1), Europe (9) and Asia (2). Ever smoking was statistically significantly associated with a reduced risk of endometrial cancer among prospective studies (RR 0.81; 95% CI= 0.74-0.88) and case-control studies (OR 0.72; 95% CI=0.66-0.79). Pooled results of case-control studies found a statistically significant reduction in endometrial cancer risk for cigarette smoking among postmenopausal women (RR 0.71; 95% CI, 0.65-0.78) and not among premenopausal women (RR 1.06; 95% CI, 0.88-1.28). The difference between two estimates was statistically significant ($P = .01$). One prospective study and five case-control studies which examined the association between cigarette smoking and risk of endometrial cancer according to HRT status showed that risk reduction appears be stronger among HRT users (RR 0.45; 95% CI, 0.29-0.70) than among nonusers (RR 0.65; 95% CI, 0.51-0.84). An increase of 20 cigarettes smoked per day was significantly associated with 16% and 27% reduced risks of endometrial cancer in prospective and case-control studies respectively; however, trends with increasing duration of smoking were not noted to allow confirmation of a linear increase in this association.

A health survey conducted from 1984–1986 among men and women aged 20 years and above in Nord-Trøndelag county in Norway (the HUNT Study) initially had 85,100 eligible persons. Lindeman et al followed 36, 761 women with a mean age of 49 years at baseline for an average of 15.7 years (range 0–19 years) to examine the relationship of body mass index (BMI), diabetes and smoking to endometrial cancer risk and found that women with known diabetes at baseline were three times as likely as women without diabetes to develop endometrial cancer (RR 3.13, 95% CI: 1.92–5.11); women who reported current smoking at baseline were at reduced risk compared to never smokers (RR 0.55, 95% CI: 0.35–0.86). The study concluded that, the strong linear positive association of BMI with endometrial cancer risk as well as a strongly

increased risk of endometrial cancer among women with diabetes could mean that any increase in body mass in the female population will increase endometrial cancer incidence (Lindemann 2008). During follow-up, 222 endometrial cancers were diagnosed. Age-adjusted relative risks (RR) of BMI, diabetes and smoking with 95% confidence intervals was estimated using the Cox regression analysis whilst mutually adjusting for each study factor including alcohol use, physical activity and hypertension. Analysis showed a strong and consistent increase in risk with increasing BMI (P-trend = 0.001); compared to women with BMI of 20–24 kgm⁻², the age-adjusted RR for BMI < 20 kgm⁻² was 0.51 (95% CI: 0.19–1.40), and with BMI ≥ 40 kgm⁻² was 7.89 (95% CI: 3.90–15.94). After adjusting for diabetes, smoking status, alcohol use, physical activity and hypertension: adjusted RRs were: RR 6.36, 95% CI: 3.08–13.16; for BMI ≥ 40 kgm⁻²; RR 4.28, 95% CI: 2.58–7.09 for BMI 35–39 kgm⁻²; and RR 0.53, 95% CI: 0.19–1.47 for BMI > 20 kgm⁻². Among women with diabetes at baseline, 1.88% of the women were diagnosed with endometrial cancer during follow-up compared to 0.57% of women diagnosed with endometrial cancer without diabetes. After adjusting for confounders, diabetes was associated with a three-fold higher risk (RR 3.13, 95% CI: 1.92–5.11). Current smoking was inversely associated with endometrial cancer risk. After multivariable adjustment, a moderately reduced negative association with smoking was observed, RR 0.55, 95% CI: 0.35–0.86; for former smoking RR was 1.06, 95% CI: 0.71–1.61.

DATA AND METHODS

NHANES data:

This study analyzes data from the National Health and Nutrition Examination survey (NHANES) which is a program of the National Centre for Health Statistics (NCHS) under the Centers for Disease Control and Prevention (CDC). NHANES is a continuous program of studies designed to combine the use of interviews and physical examinations to assess the health and nutritional status of children and adults in the United States; it examines a nationally representative sample of about 5,000 people a year located in counties across the country; 15 of which are visited each year. NHANES selects samples to represent U.S. population of all ages and oversamples people over 60 years as well as African Americans and Hispanics to ensure reliable statistics. NHANES conducts interviews using the Computer-Assisted Personal Interviewing-CAPI (interviewer administered) system. Persons aged 16 years and older and emancipated minors are interviewed directly. Interviews are done in respondents' homes and examinations are done in mobile examination centers.

NHANES has collected information on a total of 52,195 people living in the United States from the year 2001 to 2010 [n = 25,702 (49.2%) males and n = 26,293 (50.8%) females]. This study analyzes data from female respondents who are 20 years and above and gave valid response to the question of ever having been diagnosed with cancer or not (n = 14,300). All questions which were refused to be answered or answered as "don't know" or had missing values are excluded from this study, apart from the question on smoking status. The sample size of the study is 6,407.

Main Dependent and Independent variable:

The main dependent variable is breast cancer and gynecological cancer (GC). Gynecological cancer in this study comprises the three main GCs; cervical, ovarian and endometrial cancers. The two rare vaginal and vulvar cancers are excluded because information is not available on these variables from NHANES during the specified period of study. To obtain information on these variables, participants were asked “have you ever been told by a doctor or other health professional that you had cancer or a malignancy of any kind?” If the answer was yes, then the participant was asked “what kind of cancer was it?” All respondents who answered yes to breast, cervical, ovarian and uterine cancers are identified as cases in this study and randomly selected female respondents who said they had never been diagnosed with any kind of cancer or malignancy were classified as controls.

Independent variables:

The main independent variables are cigarette smoking status and metabolic syndrome (MetS). Respondents are classified as current smokers if they answered yes to the question “have you smoked at least 100 cigarettes in life” and responded that they still smoke “every day” or “some days” as at the time of interview. Respondents who said they have not smoked up to 100 cigarettes in their life times are classified as non-smokers. Metabolic syndrome is defined according to the guidelines of NCEP ATP III. Females who have at least three of the following conditions: a waist circumference of more than 88 cm, an average blood pressure of 130/85 mmHg or more, triglyceride level of 150 mg/dl or more, HDL-cholesterol level of less than 50 mg/dl, and a fasting glucose concentration of 100mg/dl or more. A third independent variable is concurrently having the metabolic syndrome and being a current smoker.

Trained personnel take anthropometric measurements and study participants generally wear exam gowns otherwise a code is given to show that participants wore their own clothes; waist circumference is measured with measuring tape around the trunk in a horizontal plane of the midaxillary line of study participants in a standing position and holding their gowns up and at a minimal respiration to the nearest 0.1 cm. Certified BP examiners take the blood pressures of respondents/participants (R/P) in Mobile Examination Centers; after R/Ps have rested quietly in a sitting position for 5 minutes, the maximum inflation level (MIL) is determined and three consecutive blood pressure readings are obtained, a fourth reading may be taken if the BP measurement is interrupted or incomplete. The computer system is programmed by NHANES to capture; systolic blood pressure and maximum inflation level up to 300 mmHg, only even values of systolic and diastolic blood pressure and maximum inflation level, systolic blood pressure greater than diastolic blood pressure, a systolic blood pressure, only if there is diastolic blood pressure, and a diastolic blood pressure can be zero. In this study, average blood pressure is calculated by taking the average of the valid four blood pressure readings. In this study, average blood pressure is calculated by taking the average of the recorded blood pressure readings. Specimen collection for triglyceride levels, HDL-cholesterol levels, and fasting glucose concentrations are taken by trained NHANES laboratory staff at a mobile examination center.

Sample size and method of selection:

The total sample size for the study is 6407 females aged 20 years and above, who either have breast cancer, a gynecological cancer or said had not been diagnosed with a cancer and have valid values. From 2001 -2010, NHANES has records of 26,493 females and 14, 327 of them are aged 20 years and above. The study includes a total of 754 cases defined as 396 females who reported having breast cancer, 385 females who reported having a gynecological cancer; and 5653 randomly selected females who reported not having been diagnosed with any cancer. See diagram of selection criteria below.

Statistical Analysis:

PASW statistics version 18.0 (SPSS Inc) was used to download data, merge and code for cases and controls. Initial descriptive analysis was run using SPSS to ensure that merging had been done correctly. SAS program version 9.2 was used to analyze data. The code proc freq and proc means was used to obtain the distribution of the continuous variables; sample size, mean, standard deviation and 95% confidence limits were estimated. Only percentages and sample size were calculated for other variables that were coded as categorical or dichotomous. Proc freq was also used to run bivariate analysis, chi square test statistics was estimated to compare the difference in proportion rates, p- value <.05 was considered a statistically significant relationship among variables. Odds ratios were also obtained for unadjusted rates. Proc logistic was used to run a logistic regression of relationships that had statistical significance under the proc freq bivariate analysis; breast and cervical cancer with different combinations of smoking and metabolic syndrome. Age, education, race marriage, country of birth and income to poverty ratio were entered as covariates for the analysis. Adjusted odds ratios and at 95% confidence limits

were estimated. Backward selection was done, to find the best model with the covariates however, the result obtained from this process either removed the independent variable of interest at an early stage or did not show much difference after removing certain variables, so the odds ratios estimated from the initial model are reported in this study.

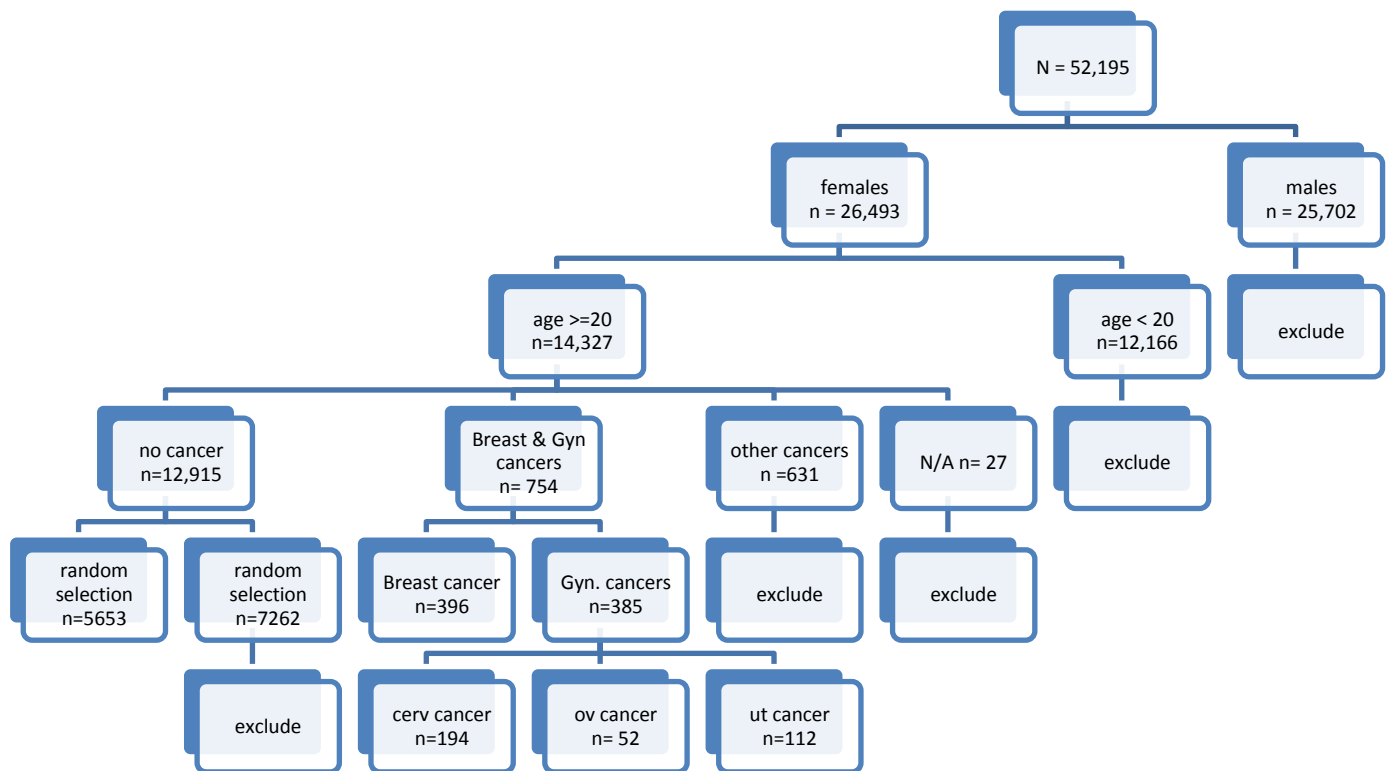


Figure 1: Diagram of selection process for females in the study

RESULTS

Baseline Characteristics of Study Population

Demographics (Table 1A): The mean age of the 6407 selected females in this study is 60.2 years (SD \pm 14.16). The mean annual family income and annual household income of valid respondents in this study ranges between 25,000 US dollars to 45,000 US dollars; NHANES classifies annual family income and annual household income into 15 categories, with 1 being the least income ranging from 0 – 4,999 dollars and 15 being the highest income; as 100,000 and over. On the average, females in the study earn a middle income; the mean income to poverty ratio is 2.6 ± 1.6 . At least 85% of the valid respondents said they had either emotional or financial support. The majority of the females; about 86% of the valid respondents are born in the United States and about 84% of valid respondents have lived in the United States for more than ten years. Nearly 87% of the valid respondents have some health insurance coverage. About 70 % of the valid respondents have completed at least high school education. Nearly 61% of the study participants are non-Hispanic whites and about 50% of the valid respondents are married. See all of Table 1 for comparison of demographic characteristics between cases and control groups.

Examination and lifestyle: On the average, relevant females in the study population (Table 1A) can be considered as having a normal diastolic blood pressure (< 85 mmHg; mean DBP, 60 ± 14) but high systolic blood pressure (> 130 mmHg; mean SBP, 131 ± 22), a normal plasma glucose level (< 110 mg/dl, mean PGL, 109.8 ± 37.8), a good HDL-cholesterol level (> 50 mg/dl; mean HDL, 58.8 ± 16.8), a normal triglyceride level of (< 150 mg/dl; mean TG, 142.2 ± 107.2) but a high measure of central obesity (> 88 cm; mean AO, 97.5 ± 15.1) by the NCEP ATP III

standard. According to the classification of the National Heart Lung and Blood Institute ($25.0 \leq \text{BMI} \leq 29.9$; mean BMI, 29.2 ± 6.9) and LCL-cholesterol in the near optimal/above optimal range ($100 \leq \text{LDL} \leq 129$ mg/dl; mean LDL, 120.3 ± 36.9); females in this study are on the average, in the overweight group. The reported mean number of cigarettes smoked daily among VRs is about 17.0 ± 9.0 (Table 1C) and the mean cotinine level measured in the relevant study participants is 50.7 ± 124.0 (Table 1B). About 43% of the 6401 study participants have smoked at least 100 cigarettes in life (ever smokers) and 41% of them said they still smoke cigarettes; 17.5% of the study participants are current smokers. About 15% of the valid respondents said they engage in work that involves at least ten minutes of vigorous activity like lifting heavy loads or climbing stairs daily, more than half of the VRs have had at least 12 alcoholic drinks /year in life and less than 40% of the VRs said they eat fewer high fat foods on their own. See table for comparison among cases and control groups. Overall, females in the control group seem to have better values for the risk factors listed.

Medical Conditions and Reported Cancer Diagnosis among the Study Population

Breast and Gynecological cancers (Table 2A): Out of the 754 females in this study who reported having been diagnosed with breast cancer or a gynecological cancer, 396 (52.5%) of the BCEO is breast cancer, 194 (25.7%) of them being cervical cancer, 112 (14.9%) of them is endometrial cancer and 52 (6.9%) of them is ovarian cancer. On average, cervical cancer is diagnosed during the youngest age in this population; the mean age at first diagnosis of cervical cancer is 30.8 ± 11.6 . Breast cancer is generally diagnosed at a later age among study participants; the mean age at first diagnosis of breast cancer is 58.1 ± 14.7 .

Metabolic syndrome and factors of metabolic syndrome (Table 2A): Almost 37% of the valid respondents have metabolic syndrome by the NCEP III standard. About; 28% of the

relevant females have a risky fasting plasma glucose level, 32% have a risky HDL cholesterol level, 34% have a risky triglyceride level, 47% classified as having a risky blood pressure measurement and 72% have abdominal obesity. Out of 2884 relevant participants, 6.7% of them smoke and have the metabolic syndrome, 11.2% of them smoke only, 30.2% of them have metabolic syndrome only and 52.0% of them neither smoke nor have the metabolic syndrome (not shown in the tables)

Reproductive health (Table 2B): Somewhere around 91% of valid respondents have been pregnant before, the average number of live births among VRs is three and almost 60% of VRs breastfed their children. Studies have associated age at menarche and menopause with BCEO. In this study, most (86.5%) of the VRs had their first menstrual period after age 15 years and 61.6% of VRs had their last menstrual period at or after 45 years of age. About 61.1% of VRs have used birth control pills before and the majority (80.3%) of VRs has used hormone pills with estrogen only. The least hormone pill used is progestin only (17.5%) of valid respondents. About 25% of VRs have at least one ovary removed and nearly 38% of VRs have a hysterectomy even though comparatively, only about 12% of VRs had been diagnosed with endometriosis and about 21% with uterine fibroid. See all of Table 2 for comparison among case and control groups.

Bivariate analysis

Smoking is highly significantly associated with breast and cervical cancer (p-value <.0001). Unadjusted results of bivariate analysis show that those who smoke are more likely to have been diagnosed with cervical cancer (OR 4.04; 95% CI, 3.02 – 5.40) than those who do not smoke. It seems that compared to those who do not smoke, those who smoke are less likely to have breast cancer (OR 0.58; 95% CI, 0.42 – 0.80). The odds of having an endometrial or ovarian cancer

diagnosis among those who smoke compared to those who do not smoke is 1.06; 95% CI, 0.65 – 1.72 and 1.02; 95% CI, 0.49 – 2.09 respectively (Table 3).

No statistically significant association is found between metabolic syndrome and breast cancer (p-value 0.42) or any of the gynecological cancers (p-value 0.44) in this study. Bivariate analysis shows no statistical significant association between having only one risk factor for metabolic syndrome, or having a combination of two or more risk factors of MetS and a BCEO cancer (Table 3). Observation from the population based study conducted by Antonio Russo et al. to describe the link between metabolic syndrome and cancer risk, also found a non-significant increased risk of breast and endometrial cancer among females. The association between BCEO and specific risk factors for metabolic syndrome was also considered (Table 4). Bivariate analysis shows that: a) fasting plasma glucose, HDL- cholesterol level and blood pressure are significantly associated with cervical cancer; p-value 0.012, <.0001 and <.0001 respectively, with increased odds of having cervical cancer associated with high levels of triglycerides and low levels of HDL cholesterol, b) the existence of both hypertension and risky levels of plasma glucose are significantly associated with cervical cancer; p-value 0.029, c) fasting plasma glucose is significantly associated with endometrial cancer; p-value 0.046, d) a coexistence of hypertension and high HDL-cholesterol in a female, is associated with endometrial cancer; p-value 0.036. In the Metabolic syndrome and cancer project (Me-Can) Borena et al observed significant increases in the relative risk for total cancer, as well as cervical cancers in the top quintile compared to the bottom quintile of serum triglycerides (Borena et al., 2011).

The association between smoking as well as metabolic syndrome and all the independent variables described above was also assessed. Bivariate analysis shows that: a) smoking is significantly associated with the following a) demographic variables: age, income to poverty

ratio, education, marital status and race; with average level of physical activity and b) medical conditions: abdominal obesity, HDL-cholesterol, blood pressure and a coexistence of high blood pressure and high blood glucose levels; and reproductive health factors like use of birth control pills, hysterectomy and HPV 18. Metabolic syndrome is significantly associated with the following factors: age, income to poverty ratio, country of birth, education, race/ethnicity; average level of physical activity, alcohol use, perceived health condition, use of birth control pills, hysterectomy and having at least one ovary removed. The significant associations were determined for the purposes of identifying which variables to adjust for, in the regression model.

Distribution of BCEO by selected demographic variables (Table 5): The highest prevalence of reported cervical cancer diagnosis is observed in females between the ages of 30 – 39 years; as many as about 24% of VRs between the ages of 30 – 39 years reported having a cervical cancer diagnosis and only about eight percent of females in this group reported not having a cervical cancer diagnosis. The reverse is seen after age 70 years, only about nine percent of females in this age group reported having cervical cancer diagnosis whilst about 28% of females in this age group reported not having a diagnosis of cervical cancer. The percentage difference of females who reported diagnosis of breast cancer is highest among females after age 70 years; as much as about 54% of females who are 70 years and above reported a breast cancer diagnosis and only 30% did not report a breast cancer diagnosis in this age group (a difference of 24 percentage point), whereas the percentage difference is less than ten among all the other age groups and carries a negative sign as well. About 14% of females between the ages of 20 -29 years reported a cervical cancer diagnosis whereas about 0.2%, 6.2%, and 2.0% of females reported breast, endometrial and ovarian cancer respectively.

Only about seven percent (p-value 0.012) of females with less than 9th grade level of education reported a diagnosis of cervical cancer and this percentage increases with level of education up to some college (32.5%) and drops to about 12% of females who are at least college graduates. Compared to females without a diagnosis of breast cancer, breast cancer diagnosis is 4.2 percentage points less prevalent among females who are married, 5.0 percentage points less among females who are divorced, 0.9 percentage points less among separated, 2.7 percentage points less in never married females and 1.1 percentage points less in females who live with a partner, but as much as 14.1 percentage points more prevalent among widows (p-value <.001). Compared to females who do not have a diagnosis of cervical cancer, cervical cancer diagnosis is 13.3 percentage points less prevalent among widows, 8.9 percentage points less prevalent among married females, 6.5 percentage points more prevalent among divorced females, 2.0 percentage points more among females who are separated, 5.9 percentage points among never married females, and as much as 7.9 percentage points more among females who live with a partner (p-value <0.001).

Cervical and endometrial cancers are statistically significantly related to poverty level; p-value 0.0009 and 0.004 respectively. Cervical and endometrial cancers affect more females who live below the poverty level than females who live above the poverty level; the rates of reported diagnosis of these cancers decreases significantly with an increase in income (although for cervical cancer there seems to be a more decrease in rates of reports among middle income females than among high income females. Compared to those who do not have cervical cancer, females in low income, middle income and high income range are about 13.0 percentage points more, 6.9, and 6.1 percentage points less likely to be diagnosed with cervical cancer respectively. This pattern is observed in females who reported having a diagnosis for endometrial cancer;

compared to those who do not have endometrial cancer, females in low income, middle income and high income range are about 15.1 percentage points more, 4.8, and 10.3 percentage points less likely to be diagnosed with cervical cancer respectively.

Among the BCEO cancers, reported breast cancer diagnosis is significantly associated with race (p-value <.001). Non-Hispanic white and Non-Hispanic black females are more affected by breast cancer than females in other racial/ethnic groups; within racial groups, compared to those who do not have a breast cancer diagnosis, non-Hispanic whites are 11.0 percentage points more likely to have a breast cancer diagnosis and non-Hispanic blacks are about 1.0 percentage points more likely to have a breast cancer diagnosis. Mexican Americans, other Hispanics, and females of other/Multiracial groups are less likely by 4.9, 2.5, and 2.6 percentage points to have a breast cancer diagnosis compared to females in the respective groups who do not have breast cancer (Table 5).

There is a significant association between the prevalence of cervical cancers and different combinations of females who smoke and have metabolic syndrome (p-value 0.0004), however no significant association was observed between the rates of the other cancers (breast, endometrial and ovarian) and different combinations of females who smoke and have metabolic syndrome (p-value 0.104, 0.568, 0.818 respectively). Table 6C shows the rates of reported cancers among the different combinations of smoking and metabolic syndrome. Among those who smoke and do not have metabolic syndrome, the highest rates of reported BCEO cancer diagnoses was cervical cancer (32.5%), followed by ovarian cancer (11.1%), those who reported no cancer (10.9%), endometrial cancer (8.9%) and breast cancer (5.3%). Among those who neither smoke nor have the metabolic syndrome, the highest rate of reported cancer diagnosis is ovarian cancer (61.1%) and the lowest is cervical cancer (34.9%). There are higher rates of cervical cancer diagnosis

among females who have the metabolic syndrome and smoke (13.3%), compared to endometrial cancer (8.9%), having no cancer (6.4%), ovarian cancer (5.6%) and breast cancer (5.3%)

Consistent with findings in this study, below 45 years of age: a) less females have breast cancer (4.6%) compared to females who do not (15.9%) and these females have a 75% less chance of reporting a breast cancer diagnosis than females above 45 years (OR 0.25; 95% CI 3.51 – 6.71, p-value <.0001), b) more females have cervical cancer (49.9%) compared to females who do not (15.9%) and these females are almost five times as likely as females above 45 years to report a cervical cancer diagnosis (OR 4.69; 95% CI 3.51 – 6.27, p-value <.0001) (Table 7). Females born in the United States are about two times as likely as females not born in the United States to report a breast cancer diagnosis (OR 2.12; 95% CI 1.26 – 3.57, p-value < 0.001). Females who have health insurance are four times as likely as females who do not have health insurance to report a breast cancer diagnosis (OR 4.05; 95% CI 2.4 -6.82, p-value < .001) and a 47% less chance of reporting a cervical cancer diagnosis (OR 0.53; 95% CI 0.38 – 0.74, p-value < 0.001). This could be because females who do not have health insurance are economically challenged and since cervical cancer is more prevalent among females who are poor, it follows that more females who do not have health insurance will report a cervical cancer diagnosis. Females in the low income group are 76 percent more likely than females in middle and high income groups to report a cervical cancer diagnosis (OR 1.76; 95% CI 1.30 -2.37, p-value < .001). Married females have a 30 percent less chance of reporting a cervical cancer diagnosis than females in the other marriage categories described (OR 0.70; 95% CI 0.52 – 0.93, p-value <.0001). Whites are 63 percent more likely to report a breast cancer diagnosis than females of other racial/ethnic groups (OR 1.63, 95% CI 1.30 – 2.04, p-value < 0.0001). Females who are current smokers have a 53 percent less chance of reporting a breast cancer diagnosis than

females above 45 years (OR 0.47; 95% CI 0.33 - 0.68, p-value <.0001) and almost three times as likely as to have cervical cancer (OR 2.89; 95% CI 1.99 – 4.19, p-value <.0001). Females who are infected with the human papillomavirus 16 are almost four times as likely as uninfected females to have cervical cancer (OR 3.82; 95% CI 1.67 - 8.73, p-value <.001) and females infected with the human papillomavirus 18 are more than four times as likely as uninfected females to have cervical cancer (OR 4.35; 95% CI 1.23 - 15.31, p-value <.05).

Females who have a high blood pressure have a 66 percent less chance of reporting a cervical cancer diagnosis than females who have a normal blood pressure (OR 0.44; 95% CI 0.31 – 0.61, p-value <.0001). Females who have a high fasting plasma glucose level have a 49 percent less chance of reporting a cervical cancer diagnosis than females who have a normal fasting plasma glucose level (OR 0.51; 95% CI 0.29 – 0.87, p-value <.001). Females who have a high HDL-cholesterol levels are 65 percent more likely than females who have normal HDL-cholesterol levels to have cervical cancer (OR 1.65; 95% CI 1.22 – 2.23, p-value <.001)

Logistic Regression analysis

Adjusting for age, education, race, marriage, country of birth and income to poverty ratio: females who have smoked more than hundred cigarettes in life and still smoke; a) have a 42 percent less chance of having a breast cancer diagnosis than females who have smoked less than hundred cigarettes in life (OR 0.58; 95% CI 0.36 – 0.93, p-value 0.03), b) have a 2.67 increased odds of reporting a cervical cancer diagnosis than females who do not smoke (OR 2.67; 95% CI 1.72 – 4.13, p-value <.0001) (Table 8A and 8B). See all of Table 8 for the entire results of logistic regression analysis.

DISCUSSION

Family size was not taken into consideration so, the ratio of family income to poverty, was used as a more appropriate measure of income/poverty status. The cutoffs are based on the poverty guidelines recommended by the Department of Health and Human Services to categorize income to poverty ratio. Females having or living in a family with a ratio of income to poverty below 1.33 are classified as having a low income, from 1.33 to 3.22 as middle income and having more than 3.22 to 5.03 as having a high income, and above 5.03 as having a very high income. On the average, females in the study earned a middle income. There were no females in the very high income category. Because this study looks at patients diagnosed with cancer, having financial or emotional support was considered an important characteristic of the population because psychosocial problems can affect the diagnosis and treatment outcome of cancer (Easton 2010). At least 85% of the valid respondents said they had either emotional or financial support. This is a good indicator for health, well-being and success of treatment, especially when considering people afflicted by cancer. About 72% of the females in this study expressed that they had good to excellent health and nearly 87% of the valid respondents had some health insurance coverage. Singer recommends that because emotional support is an important aspect of patient satisfaction, several members of the oncological team must provide it (Singer, Götze et al. 2009); this should actually include friends and family. Looking at the demographics, it can be said that the study participants are on the average of good socio-economic status; averagely of middle income and at least 40% of the valid respondents have some college education and above. Because the mean age of the study population was 60.2 years, it was assumed that most of them had a higher possibility of having at least gone to college and the percentage cutoff for education was set for females in the study who had at least some

college education, however, less than half of the valid respondents had some education at college level or above, and about 70% of VRs had at least high school education. Zhu et al. explain that when assessing the relationship between smoking and education categorization is important because the relationship is not monotonic (Zhu, et al., 1996) and they list the recommended categories in years of education. The US Census Bureau reports that as at April 2010, non-Hispanic whites made up about 64% of the US population (US Census Bureau, 2010) so the representation of non-Hispanic whites (61%) in this study is somehow representative of this.

NHANES measures cotinine levels to for purposes of measuring the prevalence and extent of tobacco use or of exposure to environmental tobacco smoke (ETS), and to describe their relationships with chronic health conditions, including respiratory and cardiovascular diseases. Cotinine is a major metabolite of nicotine that may be used as a marker for both active smoking, and as an index to Environmental Tobacco Smoke (ETS) exposure, or "passive smoking". Plasma cotinine has substantially longer half-life (15-20 hours) than nicotine (0.5–3 hours). Urine cotinine concentrations tend to be higher (3–8 times) in urine than in serum; however, for studies requiring a quantitative assessment of exposure, plasma or serum cotinine levels is preferred. The foundation for blood research considers cotinine levels <10 ng/mL to be consistent with no active smoking, 10 ng/mL to 100 ng/mL with light smoking or moderate passive exposure, and levels above 300 ng/mL with heavy smoking - more than 20 cigarettes a day. Because smoking status of the females in this study is based on self-reports, average cotinine levels by the three levels of smoking described above was calculated to check consistency with smoking status reports. The reported mean number of cigarettes smoked daily among VRs was about 17 ± 9 (Table 1C) and the mean cotinine level measured in the relevant study participants was 50.7 ± 124.1 (Table 1B). This level is quite consistent with the reports;

however it must be noted that out of the 1123 current smokers only 503 participants gave the number of cigarettes smoked daily whilst cotinine levels were measured in 5405 study participants. In this study, females who reported having smoked at least 100 cigarettes in life and still smoke were considered current smokers and those who have smoked less than 100 cigarettes in life including those who have possibly not smoked at all were considered nonsmokers. This is because in the questionnaire, NHANES asked only people who are under 20 years if they have ever smoked or not. This means that some people classified as non-smokers include never smokers and ever smokers who may actually have smoked at some time in their life, or may be still smoking if they are recent light smokers. The assumption for this study therefore, is that, smoking less than 100 cigarettes in life may not be enough of a contributory factor to a BCEO cancer. In this study, smoking is more prevalent among females who reported a cancer diagnosis than among those who have no cancer (See Table 1)

Non-Hispanic white and Non-Hispanic black females are more affected by breast cancer than females in other racial/ethnic groups. Non-Hispanic white females generally have a comparatively high incidence rate of breast cancer (Gomez, Quach et al. 2010) so this observation is not unusual. The association between race and breast cancer is quite difficult to explain because not only are the risk factors for breast cancer diverse; e.g. biologic factors, socioeconomic status, education, and cultural perspectives, but in this case, it could partly explained by the fact that more non-Hispanic whites have the means to screen for breast cancer (e.g. have health insurance) resulting in more of them reporting a breast cancer diagnosis if they should have one and therefore are predominantly reporting early or localized stage breast cancer (Sue, Mary et al. 2005); early detection rates of breast cancer is reported in literature among non-Hispanic whites, (Summers, Saltzstein et al. 2010). Non-Hispanics blacks are normally

diagnosed with advanced stages of breast cancer probably because of inability to screen earlier, but because this study does not look at the stages of cancer, it cannot be certain if the increase in breast cancer diagnosis observed in this group is mainly due to advanced breast cancer diagnosis (Lantz, Mujahid et al. 2006). However, The high cases of cervical cancer diagnosis among females who do not have health insurance compared to females who have health insurance could be because females who do not have health insurance are economically challenged and since cervical cancer is more prevalent among females who are poor, it follows that more females who do not have health insurance report a cervical cancer diagnosis, and this may actually be an advanced case of cervical cancer.

Results in this study also demonstrate that females born in the United States have a higher likelihood of having a breast cancer than females not born in the United States. The association between breast cancer diagnosis and females born in the United States needs further study. About 15% of the valid respondents said they engage in work that involves at least ten minutes of vigorous activity like lifting heavy loads or climbing stairs daily, more than half of VRs reported having had at least 12 alcoholic drinks /year in life and less than 40% of the VRs said they eat fewer high fat foods on their own. This information was included as an attempt to characterize the level of conscious effort made by the study participants to live a healthy life by engaging in physical activity , avoiding alcohol and fatty foods; indicators which have been proven to improve blood lipid levels resulting in good cardiovascular health, general well-being and a reduced risk for certain cancers. Msolly et al. found that physical activity can reduce breast cancer risk among certain age group (Msolly, Gharbi et al. 2011), Nicolas et al. observed that moderate to intense physical activity like heavy housework can help reduce the risk of breast cancer in some women (Nicolas, Adrien et al. 2011), Moore et al. also conclude that physical

activity reduces the risk of endometrial cancer (Moore, Gierach et al. 2010), Gudrun et al, describe several lifestyle activities including alcohol use, and diet as risk factors for gynecological cancers (Gudrun and Alison 2006). Drinking alcohol for example increases the level of endogenous estrogens, a known risk for breast cancer (Coronado, Beasley et al. 2011). Because no significant relationship was observed between the personal choice to eat fewer high fat foods, or some of the above mentioned variables and any of the cancers of interest in this study, the variables remain only as descriptive variables for the population.

The overall high prevalence of breast cancer diagnosis among females is consistent with literature. Breast cancer is the most common cancer diagnosed among women in the United States (SEER). It is likely that most females have either endometrial or ovarian cancers as a second gynecological cancer diagnosis; even though 112 females are listed as having endometrial cancer, 123 females gave the age at which endometrial cancer was diagnosed and 61 females as against 52 females listed in the study gave the age at which ovarian cancer was diagnosed.

Waist circumference above 88 cm is the most prevalent health risk factor in the study population. This is a very important observation because, increase in waist circumference (abdominal obesity) is a metabolic factor associated not only with the risk of several chronic diseases, especially cardiovascular diseases, but increased healthcare utilization and healthcare costs (Wolf, Finer et al. 2008). Okosun et al., found a significant increase in waist circumference and other factors of metabolic syndrome among American adolescents and recommend early lifestyle intervention to prevent the onset of cardiovascular diseases in adulthood (Okosun, Seale et al. 2012). About 37% of the relevant females were classified as having the metabolic syndrome in this study. Even though the use of diabetic medications to control blood glucose

levels was assessed; this including the use of medications prescribed to control risky or high levels of factors associated with metabolic syndrome were not considered in the study. This means that the number of females with metabolic syndrome in this study could be higher than stated, however another assumption made is that, if medications were being used appropriately, then it would manage the risky health factors and such females could qualify as having normal levels of these factors.

The use of birth control pills and hormones was assessed among the study participants. The least hormone pill used is progestin only; this is also consistent with the observation that females in the study are averagely in their mid-60's and are not likely to use progestin only pills or even estrogen/progestin combination pills. Whereas the age at which these pills are used and for what purpose they are used is not a focus of this study, it is likely that because most of the females are in their mid-60's the medication is used to manage postmenopausal symptoms. The percentage (about 25%) of VRs who have at least one ovary removed is not unusual for females in the United States; given the fact that technology is available for purposes of diagnosis, treatment or management of reproductive problems and several other conditions, and that about 300,000 prophylactic oophorectomies (ovary removal) are performed annually in the United States (Parker, 2010). About 38% of VRs have had a hysterectomy even though comparatively, only about 12% of VRs have been diagnosed with endometriosis and about 21% with uterine fibroid before. Whereas there is a possibility that the diagnosis of an endometrial cancer may play a role in this, there may be other reasons which would be interesting to study. This information is also taken for descriptive purposes. Apart from the limitation posed by empty cells in running a regression with these variables, they were not adjusted for, because the study does not look at cancer incidence but cancer diagnosis at any point in life so correction rates for

ova removal or hysterectomy (Merrill 2006) are assumed not to affect results of the study. It must be noted that in this study, significant associations are observed between some reproductive health factors and BCEO which needs further study.

Bivariate analysis showed no significant association at $\alpha = 0.05$ between metabolic syndrome and gynecological cancers. Having metabolic syndrome seems to present a spurious relationship with BCEO cancer diagnosis. For example, even though some factors of metabolic syndrome are significantly associated with risk of cervical cancer, when they co-exist, the relationships between these variables change. From the findings, it is plausible that metabolic syndrome reduces the risk for example, breast cancer, but this is difficult to conclude because there may be other factors that contribute to this or confound this relationship, and this must be examined. One other observation is that significance changes when independent factors or certain combinations of factors of the metabolic syndrome are analyzed, as well as when certain cutoffs are used for categorization; for example whereas significance with age and BCEO is still consistent (p-value $<.0001$) after categorization, a significant association (p-value 0.012) which was not observed between education and cervical cancer and the significance between endometrial cancer and education (p-value 0.024) is not observed (p-value 0.342) after more levels of stratification is used (Table 5). A significant association is also observed between cervical cancer and hypertension or in combination with fasting plasma glucose. This could be a contributing factor to the absence of significance observed between metabolic syndrome and BCEO, because certain factors of the metabolic syndrome are significantly associated with some of the cancers of interest in this study. Metabolic syndrome is associated with several reproductive health factors (use of birth control pills, hysterectomy, ovary removal and probably more); this is an interesting area of research considering the observation that almost 40% of

females in this study have the metabolic syndrome and as much as 72% of women have abdominal obesity.

Far less females under 45 years reported having a diagnosis of breast cancer than cervical cancer (Figure 1). The highest prevalence of reported cervical cancer diagnosis is observed in females between the ages of 30 – 39 years and the least in females aged 70 years and older however, the percentage of females with a diagnosis of breast cancer increases consistently with age. Two reasons for this could be because increased age is a breast cancer risk or that; females are living longer after a breast cancer diagnosis because of available treatment. Endometrial cancer also increases consistently with an increase in age but with a much narrower gap between those who report having a diagnosis of endometrial cancer and those who report no diagnosis of endometrial cancer. Ovarian cancer shows much the same pattern as endometrial cancer but the increase is not consistent with increase in age. Of all the BCEO, cervical cancer is a cancer that is more prevalent during young age.

Because the cases are reported cancer diagnosis, a report of no diagnosis should not be taken as absence of cancer diagnosis. Some females especially in the low income and low educated group may have undiagnosed cancer cases. Only about 7% (p-value 0.012) of females with less than 9th grade level of education reported a diagnosis of cervical cancer and this percentage increases with level of education up to some college (32.5%) and drops to about 12% of females who are at least college graduates. The finding among females with less than ninth grade is more likely to do with knowledge about screening services or inability to afford screening services, because less education could mean a less gainful employment and therefore less income. Smoking is another factor that is predominant among people with less than high school education; Zhu et al observed that the less than high school grade group consist of two

distinct categories when it comes to smoking, and that persons with 9 – 11 years of education tend to be current smokers compared to persons with 0 -8 years of education and recommend a categories for education when considering the relationship with smoking, (Zhu, Giovino et al. 1996). Accordingly, females with less than 9th grade level of education may be smoking less, thus resulting in the observed reduced cervical cancer diagnosis among in this group.

The observation of a high prevalence of breast cancer diagnosis among widows most likely has to do with the fact that the majority of widows are in the older age group around 70 years of age and therefore more consistent with results observed in the stratified age groups. By far less widows reported having cervical cancer compared to all other females in the other marriage categories and cervical cancer is also less among married females. The observation that more unmarried females among the other four marriage categories have cervical cancer, undoubtedly points to the fact that cervical cancer is a disease associated with sexual behavior; females who are unmarried and not widowed are more likely to have different sexual partners putting them at risk of infection with possibly HPV, eventually leading to cervical cancer diagnosis. Rothenberg explains this transmission dynamics by demonstrating that people who change their friends may change themselves and that quite unfortunately, it oftentimes results in an increased risk to a negative factor; that for example drug users who change their drug contact have more than three times the likelihood to be exposed to increased risk of any factor say, crime, or infection compared to baseline. (Rothenberg 2006). The high risk associated with HPV 16, 18 infection and cervical cancer (Silvia de, Wim et al. 2010) is demonstrated in results of this study (even though it is an unadjusted bivariate analysis). Cervical and endometrial cancers affect more females who live below the poverty level than females who live above the poverty level. The high rate of reports of cervical cancer diagnosis among females in the low income group

indicates that cervical cancer is a problem of poverty. This is especially important because then, it is unlikely that females can afford to get screened for cervical cancer, detect precancerous changes early and have early treatment; an activity that is key to reducing the incidence and mortality due to cancer. Compared to cervical cancer, endometrial cancer hits females with low income more.

On the contrary, even though the differences in rates of reported diagnosis for breast and ovarian cancers across income to poverty ratios were not significant, breast cancer diagnosis seems to be less prevalent among females in the low income group than among females in middle and high income group, with less females in the low income group reporting a diagnosis of breast cancer compared to those who did not report a breast cancer diagnosis, and more people in the middle and high income group reporting a breast cancer diagnosis than those who did not. Reports of ovarian cancer diagnosis are however more prevalent among females in the low income group than females in the middle income group;

Smoking more than 30 cigarettes daily is consistently associated with an increase in cases of reported cancers compared to those who do not have these cancers. A paradoxical decrease in cases of reported endometrial cancers among females who smoke more than 30 cigarettes daily compared to absent cases of this cancer is observed. All these differences are however not significant for the specified categorization, all the p-values are above 0.05.

There is a significant association between cervical cancer and different combinations of females who smoke and have metabolic syndrome. Smoking is strongly associated with an increased probability of having cervical cancer, but a coexistence of metabolic syndrome and smoking seems to reduce the probability of having cervical cancer; this is an important observation which needs further study because some individual factors of the metabolic

syndrome (e.g increased triglycerides) are associated with increased odds of having some cancers including cervical cancer. In this study, no significant association was found between rates of diagnosis of the other cancers (breast, endometrial and ovarian) and different combinations of females who smoke and have metabolic syndrome, however certain factors like sample size and categorization may play a role in this, so further study is required.

The seemingly protective factor of smoking on breast cancer also needs further study, because research shows that smoking adversely affects almost all organ systems and nicotine has been shown to promote proliferation and metastatic properties of tumor cells. Several studies have found decreased odds of having breast cancer among those who smoke compared to those who do not smoke. Lesley Butler et al., explain that the apparent reduced risk of breast cancer among smokers is from the antiestrogenic but not the carcinogenic effects of smoking (Butler et al., 2010). The increased risk of breast cancer demonstrated among females under age 50 years who are BRCA1 and BRCA2 mutation carriers with a history of ever smoking, compared to never smokers (“Smoking and risk of breast cancer in carriers of mutations in BRCA1 or BRCA2 aged less than 50 years,” 2008) shows that smoking may actually not decrease the odds of breast cancer especially among breast cancer mutation carriers.

Figure 2 shows that during the midlife (50-59 years), breast and gynecological cancers are most likely to be diagnosed; females, who have not had any screening, should at least screen for breast and gynecological cancers at age 50 – 59 years. The strong significance found between hypertension and cervical cancer also requires further studies. The association between metabolic syndrome and reproductive indicators will be an important area of study in reproductive health.

STRENGTHS/LIMITATION

The strength of this study is the rigor with which NHANES collects data and the use of results from medical and laboratory examinations in certain cases. No self-reports were used in calculating metabolic syndrome among study participants. NHANES also collects rich information on the lifestyles and demographics of study participants and most of the variables relevant to this study are available from the NHANES data. Most studies looking at gynecological cancer were limited by the unavailability of such information.

One limitation of this study is the use of self-reported cancer diagnosis; ideally information on cancer diagnosis from a cancer registry is preferred because it is more reliable and gives information on the types and severity or grades of cancer however; the consistency of results with findings in literature makes these self-reports quite reliable.

One other limitation of this study is the inability to factor in time; the study looks at people who reported having been diagnosed with breast or a gynecological cancer from the year 2001 to 2010 as well as their cigarette smoking status and factors of metabolic syndrome, however the length of exposure to risk factors and time of diagnosis is not accounted for. Even though there is rich information on reproductive health in the study participants, some important variables like use of birth control pills and other hormones, use of hypoglycemic or antihypertensive and hypolipemic medications were not controlled for, because the number of valid respondents did not match the regression model (empty cells) and no significance was observed in the bivariate analysis with some variables. It is also assumed that since adjusting for parity, year(s) of childbirth(s), and physical activity in the Norwegian cohorts, of the Me-Can study (Bjørge, Stocks et al. 2010) did not change the risk estimates by much, not adjusting for these in this study may also not change the odds ratios by much. It is must be noted that the total

number of females who gave the age at which BCEO was diagnosed are more than the total number of BCEO cancer cases in the study because some females reported having been diagnosed with more than one kind of cancer. NHANES allowed entry for up to three cancers, put respondents with more than four cancers in another category coded four different variables of cancer diagnosis in a year [MCQ230A, MCQ230B, MCQ230C, MCQ230D; (NHANES data)] but only MCQ230A which recorded the first kind of cancer reported was used in the analysis. One limitation that arises from this is that, the results of the analysis could be confounded by the existence of more than one kind of cancer in some females. This was not accounted for.

CONCLUSION

The rates of breast and gynecological cancers reported among females with the different combinations of smoking and metabolic syndrome do not follow a pattern consistent with increasing coexistence of these risk factors. Of the gynecological cancers, the rate of cervical cancer diagnosis is significantly higher among females, who only smoke, than among females who both smoke and have the metabolic syndrome; there were no statistically significant odds of increase or decrease in endometrial or ovarian cancer diagnosis among females with different combinations of smoking or metabolic syndrome. Smoking is statistically significantly associated with increased odds of having cervical cancer diagnosis. More females who have neither of the risk factors (smoke and metabolic syndrome) reported a diagnosis of breast cancer, than females who only have the metabolic syndrome or females who only smoke. Smoking is statistically significantly associated with decreased odds of having a breast cancer diagnosis.

Significantly, more females who live below the poverty line and females who are below the age of 45 years reported cervical cancer diagnosis and more white females reported breast a cancer diagnosis and more females who reported having breast cancer diagnosis have health insurance. Smoking and metabolic syndrome are very important indicators of reproductive health and needs further study. Because smoking is associated with increased odds of having cervical cancer, smoking cessation interventions should be an integral part of cervical cancer prevention programs and these programs should be targeted at younger females as well as females who live below the federal poverty level.

Table 1A: Distribution of Study Participants by Demographics, Examination and Lifestyle**Characteristics**

I. Demographics	Sample size	Mean \pm SD	95% CL for mean
Age	6407	60.2 \pm 14.2	59.9 - 60.6
Annual Family Income	3160	6.6 \pm 3.2	6.5 - 6.8
Annual Household Income	3046	6.8 \pm 3.1	6.7 - 6.9
Family PIR	5893	2.6 \pm 1.6	2.6 - 2.7
	Sample size	Yes, %	
Anyone to help with emotional support	508	93.7	
Anyone to help with financial support	502	85.7	
Country of Birth(US)	3248	86.0	
Covered by health insurance	6387	86.6	
Education (high school and above)	6407	70.1	
Length of time in US (5+ yrs.)	1097	93.0	
Marital Status (Married)	6407	50.1	
Race/ethnicity (Whites)	6407	60.7	
II. Examination	Sample size	Mean \pm SD	95% CL for mean
Average diastolic blood pressure (mmHg)	6319	60 \pm 14	68.7 - 69.4
Average systolic blood pressure (mmHg)	6301	131 \pm 22	130.6 -131.6
Body Mass Index (kg/m ²)	6228	29.2 \pm 6.9	29.1 - 29.4
Cotinine (ng/mL)	5405	50.7 \pm 124.0	47.4 – 54.0
Glucose, plasma (mg/dL)	3080	109.8 \pm 37.8	108.4 - 111.1
HDL-cholesterol (mg/dL)	6297	58.8 \pm 16.8	58.4 - 59.2
LDL-cholesterol (mg/dL)	2983	120.3 \pm 36.9	119.0 - 121.6
Triglyceride (mg/dL)	3077	142.2 \pm 107.2	138.4 -146.0
Waist Circumference (cm)	6074	97.5 \pm 15.1	97.1 - 97.8
III. Lifestyle	Sample size	Mean \pm SD	95% CL for mean
Num. of cigarettes smoked per day now	503	16.8 \pm 9.7	15.9 - 17.6
	Sample size	Yes, %	
Ave. level of PA daily (Stairs or heavy load)	3246	15.3	
Eating fewer high fat foods on own	605	38.5	
Had at least 12 alcohol drinks/1 yr.?	867	54.1	
Smoked 100 cigarettes and still smoke	6406	17.5	
Smoked at least 100 cigarettes in life	6401	42.8	
Take diabetic pills to lower blood sugar	635	58.0	

Table 1B: Distribution of Participants Who Reported a Breast or Gynecological Cancer Diagnosis (Cases) by Demographics, Examination and Lifestyle Characteristics

I. Demographics	Sample size	Mean ± SD	95% CL for mean
Age	754	61.0±16.9	59.8 - 62.2
Annual Family Income	393	6.3±3.4	6.0 - 6.7
Annual Household Income	369	6.4±3.1	6.0 - 6.7
Family PIR	679	2.5±1.6	2.4 - 2.6
	Sample size	Yes, %	
Anyone to help with emotional support	80	96.3	
Anyone to help with financial support	80	88.8	
Country of Birth(US)	403	90.8	
Covered by health insurance	753	89.2	
Education (high school and above)	754	70.7	
Length of time in US (5+ yrs.)	90	93.3	
Marital Status (Married)	754	46.0	
Race/ethnicity (Whites)	754	65.8	
II. Examination	Sample size	Mean ± SD	95% CL for mean
Average diastolic blood pressure (mmHg)	666	67.7±14.6	66.6 - 68.8
Average systolic blood pressure (mmHg)	648	130.0±21.6	128.3 - 131.6
Body Mass Index (kg/m-2)	681	29.4±7.2	28.9 - 29.9
Cotinine (ng/mL)	541	67.1±140.9	55.2 - 78.9
Glucose, plasma (mg/dL)	331	109.2±36.0	105.3 - 113.1
HDL-cholesterol (mg/dL)	644	57.5±16.9	56.1 - 58.8
LDL-cholesterol (mg/dL)	306	116.9±37.0	112.8 - 121.1
Triglyceride (mg/dL)	321	150.7±105.0	139.1 - 162.2
Waist Circumference (cm)	649	98.0±16.0	96.7 - 99.2
III. Lifestyle	Sample size	Mean ± SD	95% CL for mean
Num. of cigarettes smoked per day now	72	18.0 ± 9.3	15.8 - 20.2
	Sample size	Yes, %	
Ave. level of PA daily (Stairs or heavy load)	403	15.6	
Eating fewer high fat foods on own	86	38.4	
Had at least 12 alcohol drinks/1 yr.?	105	61.0	
Smoked 100 cigarettes and still smoke	754	21.1	
Smoked at least 100 cigarettes in life	754	50.3	
Take diabetic pills to lower blood sugar	78	60.3	

Table 1C: Distribution of Participants Who Reported No Cancer Diagnosis (Controls) by Demographics, Examination and Lifestyle Characteristics

I. Demographics	Sample size	Mean ± SD	95% CL for mean
Age	5653	60.1±13.7	59.7 - 60.5
Annual Family Income	2767	6.7±3.2	6.6 - 6.8
Annual Household Income	2677	6.9±3.1	6.8 - 7.0
Family PIR	5214	2.6±1.6	2.6 - 2.7
	Sample size	Yes, %	
Anyone to help with emotional support	428	93.2	
Anyone to help with financial support	422	85.3	
Country of Birth(US)	2845	85.3	
Covered by health insurance	5634	86.2	
Education (high school and above)	5653	70.1	
Length of time in US (5+ yrs.)	1007	93.1	
Marital Status (Married)	5653	50.7	
Race/ethnicity (Whites)	5653	60.0	
II. Examination	Sample size	Mean ± SD	95% CL for mean
Average diastolic blood pressure (mmHg)	5653	69.2±14.3	68.8 - 69.6
Average systolic blood pressure (mmHg)	5653	131.3±21.8	130.7 - 131.8
Body Mass Index (kg/m-2)	5547	29.2±6.9	29.1 - 29.4
Cotinine (ng/mL)	4864	48.9±121.9	45.4 - 52.3
Glucose, plasma (mg/dL)	2749	109.8±38.0	108.4 - 111.2
HDL-cholesterol (mg/dL)	5653	58.9±16.8	58.5 - 59.4
LDL-cholesterol (mg/dL)	2677	120.7±36.9	119.3 - 122.1
Triglyceride (mg/dL)	2756	141.2±107.5	137.2 - 145.2
Waist Circumference (cm)	5425	97.4±15.0	97.0 - 97.8
III. Lifestyle	Sample size	Mean ± SD	95% CL for mean
Num. of cigarettes smoked per day now	431	16.5±9.8	15.6 - 17.5
	Sample size	Yes, %	
Ave. level of PA daily (Stairs or heavy load)	2843	15.2	
Eating fewer high fat foods on own	519	38.5	
Had at least 12 alcohol drinks/1 yr.?	763	53.1	
Smoked 100 cigarettes and still smoke	5652	17.1	
Smoked at least 100 cigarettes in life	5647	41.8	
Take diabetic pills to lower blood sugar	557	57.6	

Table 2A: Distribution of Study Participants by Medical Conditions, Type of Reported Cancer and Reproductive Health Indicators

I. Medical condition	Sample size	Mean ± SD	95% CL for mean
Age when breast cancer first diagnosed	397	58.1 ± 14.7	56.6 - 59.5
Age when cervical cancer first diagnosed	196	30.8 ± 11.6	29.1 - 32.4
Age when endometrial cancer first diagnosed	123	43.4 ± 16.9	40.4 - 46.4
Age when ovarian cancer first diagnosed	61	44.5 ± 16.1	40.3 - 48.6
	Sample size	Yes %	
Abdominal obesity	6074	71.7	
Breast cancer	6049	6.6	
Cervical cancer	5847	3.3	
Endometrial cancer	5765	1.9	
Ovarian cancer	5705	0.9	
General health condition (good to excellent)	6403	71.9	
Have cancer or not	6407	11.8	
Metabolic syndrome	2885	36.7	
Metabolic syndrome and smokes	2884	6.6	
Risky fasting plasma glucose	3080	27.9	
Risky HDL cholesterol level	6297	31.6	
Risky triglyceride level	3077	33.6	
Risky blood pressure	6179	47.3	
	Sample size	Mean ± SD	
II. Reproductive health	Sample size	Mean ± SD	
No of pregnancies resulting in live births	1804	3.1 ± 2.1	3.0 - 3.2
	Sample size	Yes %	
Age range at first menstrual period(15+)	89	86.5	
Age range at last menstrual period (45+)	258	61.6	
Breastfed any of your children?	2655	57.6	
Ever been pregnant?	866	91.2	
Ever taken birth control pills?	5957	61.1	
Had a hysterectomy	5421	37.9	
Had at least 1ovary removed	3032	25.2	
Told by doctor had endometriosis?	1070	11.6	
Told by doctor had uterine fibroids?	1071	21.3	
Use hormone pills w/estrogen only	1727	80.8	
Used estrogen/progestin combo pills	1719	23.3	
Used hormone pills w/progestin only	1712	17.5	

Table 2B: Distribution of Study Participants who reported a Breast or Gynecological Cancer (Cases) by Medical Conditions, Type of Reported Cancer and Reproductive Health Indicators

I. Medical conditions	Sample size	Yes %
Abdominal obesity	649	70.1
Breast cancer	754	52.5
Cervical cancer	754	25.7
Endometrial cancer	754	14.9
Ovarian cancer	754	6.9
General health condition (good to excellent)	754	65.5
Have cancer or not	754	100.0
Metabolic syndrome	278	37.4
Metabolic syndrome and smokes	278	8.3
Risky fasting plasma glucose	331	28.1
Risky HDL cholesterol level	644	35.4
Risky triglyceride level	321	36.8
Risky blood pressure	629	45.0

II. Reproductive health	Sample size	Mean \pm SD
No of pregnancies resulting in live births	196	2.8 \pm 1.8

	Sample size	Yes %
Age range at first menstrual period(15+)	12	0.0
Age range at last menstrual period (45+)	28	57.1
Breastfed any of your children?	289	59.5
Ever been pregnant?	105	90.5
Ever taken birth control pills?	643	59.3
Had a hysterectomy	593	54.0
Had at least 1ovary removed	331	38.1
Told by doctor had endometriosis?	117	15.4
Told by doctor had uterine fibroids?	115	25.2
Use hormone pills w/estrogen only	200	80.0
Used estrogen/progestin combo pills	195	21.0
Used hormone pills w/progestin only	197	15.7

Table 2C: Distribution of Study Participants Who Reported No Cancer (Controls) by Medical Conditions, Type of Reported Cancer and Reproductive Health Indicators

I. Medical Conditions	Sample size	Yes %
Abdominal obesity	5425	71.8
Breast cancer	0	0.0
Cervical cancer	0	0.0
Endometrial cancer	0	0.0
Ovarian cancer	0	0.0
General health condition (good to excellent)	5649	72.7
Have cancer or not	754	0.0
Metabolic syndrome	2607	36.7
Metabolic syndrome and smokes	2606	6.4
Risky fasting plasma glucose	2749	27.8
Risky HDL cholesterol level	5653	31.1
Risky triglyceride level	2756	33.3
Risky blood pressure	5550	47.5

II. Reproductive health	Sample size	Mean ± SD
No of pregnancies resulting in live births	1608	3.2 ± 2.1

	Sample size	Yes %
Age range at first menstrual period(15+)	77	15.6
Age range at last menstrual period (45+)	230	62.2
Breastfed any of your children?	2366	57.4
Ever been pregnant?	761	91.3
Ever taken birth control pills?	5310	61.3
Had a hysterectomy	4828	35.9
Had at least 1ovary removed	2701	23.6
Told by doctor had endometriosis?	953	11.1
Told by doctor had uterine fibroids?	956	20.8
Use hormone pills w/estrogen only	1527	80.9
Used estrogen/progestin combo pills	1524	24.3
Used hormone pills w/progestin only	1515	17.8

Table 3: Bivariate Analysis Showing the Direct Unadjusted Effect of Smoking Status, Metabolic Syndrome and Factors of Metabolic Syndrome with Reported Breast and Gynecological Cancers

	Odds Ratio	95% CI	P-value (Chi-square prob.)
Current Smokers			
Breast Cancer	0.58	0.42 - 0.80	< .001
Cervical Cancer	4.04	3.02 - 5.40	< .0001
Endometrial Cancer	1.06	0.65 - 1.72	0.82
Ovarian Cancer	1.02	0.49 - 2.09	0.96
Metabolic Syndrome			
Breast Cancer	1.16	0.81 - 1.66	0.42
Cervical Cancer	0.83	0.52 - 1.33	0.44
Endometrial Cancer	1.26	0.69 - 2.29	0.44
Ovarian Cancer	0.66	0.24 - 1.87	0.44
One MetS Risk only			
Breast Cancer	1.74	0.90 - 3.39	0.10
Cervical Cancer	0.85	0.42 - 1.69	0.64
Endometrial Cancer	1.13	0.38 - 3.34	0.82
Ovarian Cancer	0.85	0.14 - 5.01	0.86
Two MetS Risk only			
Breast Cancer	1.2	0.61 - 2.34	0.59
Cervical Cancer	0.72	0.36 - 1.44	0.35
Endometrial Cancer	1.06	0.36 - 3.08	0.91
Ovarian Cancer	1.93	0.41 - 9.13	0.40
Three MetS Risk only			
Breast Cancer	1.65	0.84 - 3.26	0.14
Cervical Cancer	0.82	0.40 - 1.67	0.59
Endometrial Cancer	*		
Ovarian Cancer	*		
Four MetS Risk only			
Breast Cancer	1.63	0.77 - 3.45	0.19
Cervical Cancer	0.39	0.14 - 1.09	0.06
Endometrial Cancer	2.18	0.74 - 6.44	0.15
Ovarian Cancer	*		

*some expected cell counts < 5 or unrealistically wide range of values; all five MetS risk have some expected cell counts < 5 so OR was not computed.

Table 4: Bivariate Analysis Showing Unadjusted Odds Ratios/ Significant Levels of Independent Variables of Interest with Reported Breast and Gynecological Cancers

Demographics	BC	CC	EC	OC	Smoke	MetS
Age < 45 years	0.25	4.69	1.22	1.59	2.28	0.39
Family PIR	0.90	1.76	1.92	1.25	2.59	1.55
Country of Birth(US)	2.12	2.07	1.07	0.73	2.77	0.75
Education (high school and above)	1.12	1.23	0.74	0.63	0.83	0.49
Length of time in US (5+ yrs.)	1.42	1.42	0.67	0.67	2.77	1.35
Marital Status (Married)	0.84	0.70	1.04	0.83	0.60	0.79
Race/ethnicity (Whites)	1.63	1.26	0.89	0.57	1.03	0.67
Have health insurance	4.05	0.53	1.03	1.22	0.42	-

Lifestyle	BC	CC	EC	OC	Smoke	MetS
Ave level of PA daily (Stairs or heavy load)	0.91	1.58	0.67	0.93	1.25	0.64

Medical condition	BC	CC	EC	OC	Smoke	MetS
Abdominal obesity	0.89	0.99	0.76	1.29	0.70	-
Risky fasting plasma glucose	1.24	0.51	1.76	0.72	0.83	-
Risky HDL cholesterol level	1.02	1.65	1.24	1.1	1.75	-
Risky triglyceride level	0.98	1.18	1.52	1.84	1.27	-
Risky blood pressure	1.17	0.44	1.30	0.8	0.55	-

Reproductive health	BC	CC	EC	OC	Smoke	MetS
Ever taken birth control pills?	0.61	3.52	0.74	0.74	2.03	0.73
HPV 16	2.39	3.82	-	-	5.00	1.03
HPV 18	2.14	4.34	-	-	1.45	0.39

	significant at <.0001 level
	significant at <.001 level
	significant at <.05 level

Table 5: Proportions of Reported Breast and Gynecological Cancer Diagnosis compared to Reports of No Breast or Gynecological Diagnosis (NC) by Selected Demographic Variables and their Levels of Significance

Age	NC	BC	CC	EC	OC
20-29yrs	0.2	0.3	13.9	6.2	1.9
30-39yrs	8.1	1.8	23.7	8.0	13.5
40-49yrs	15.8	7.6	21.7	9.8	15.4
50-59yrs	22.3	12.4	20.6	12.5	11.5
60-69yrs	25.7	24.9	10.8	27.7	32.7
> 70yrs	53.5	53.5	9.3	25.7	25.0
Education	NC	BC	CC	EC	OC
< 9th grade	14.4	10.1	7.2	18.8	17.3
9-11th grade	15.3	17.4	18.6	17.9	23.1
High School grad/GED	25.4	25.0	29.4	26.8	26.9
some college/AA	26.2	26.3	32.5	26.8	23.1
<= college graduate	18.5	21.2	12.4	9.8	9.6
Marriage	NC	BC	CC	EC	OC
Married	50.7	46.5	41.8	51.8	46.2
Widowed	21.0	35.1	7.7	21.4	23.1
Divorced	15.1	10.1	21.6	11.6	15.4
Separated	3.2	2.3	5.2	4.5	7.7
Never married	7.0	4.3	12.9	5.4	3.8
Live with Partner	2.9	1.8	10.8	5.4	3.8
PIR	NC	BC	CC	EC	OC
<1.33	29.9	27.6	42.9	45.0	34.8
1.33 - < 3.22	33.8	35.0	26.9	29.0	28.3
3.22 - < 5.03	36.3	37.3	30.2	26.0	37.0
Race/ethnicity	NC	BC	CC	EC	OC
Mexican American	12.7	7.8	10.3	15.2	19.2
Other Hispanic	5.5	3.0	7.2	8.9	5.8
Non-Hispanic White	60.0	71.0	65.5	57.1	46.2
Non-Hispanic Black	16.8	17.8	12.9	15.2	25.0
Other Race/Multiracial	5.1	2.5	4.1	3.6	3.8

Table 6A: Reported Breast and Gynecological Cancer Diagnosis Compared to Reports of No Breast or Gynecological Diagnosis by Number of Cigarettes Smoked Daily

Number of cigarettes	Sample size	Breast Cancer (n= 18)		No Cancer (n= 431)	
		Percentage	Percentage	Percentage	Percentage
1-9	91	2.2		97.8	
10-19	142	3.5		96.5	
20-29	155	4.5		95.5	
30+	61	6.6		93.4	
Total	449	4.0		96.0	

Number of cigarettes	Sample size	Cervical Cancer (n= 41)		No Cancer (n= 431)	
		Percentage	Percentage	Percentage	Percentage
1-9	93	4.3		95.7	
10-19	149	8.1		91.9	
20-29	169	12.4		87.6	
30+	61	6.6		93.4	
Total	472	8.7		91.3	

Number of cigarettes	Sample size	Endometrial Cancer (n =10)		No Cancer (n= 431)	
		Percentage	Percentage	Percentage	Percentage
1-9	92	3.3		96.7	
10-19	140	2.1		97.9	
20-29	149	0.7		99.3	
30+	60	5.0		95.0	
Total	441	2.3		97.7	

Number of cigarettes	Sample size	Ovarian Cancer (n=3)		No Cancer (n= 431)	
		Percentage	Percentage	Percentage	Percentage
1-9	89	0.0		100.0	
10-19	138	0.7		99.3	
20-29	150	1.3		98.7	
30+	57	0.0		100.0	
Total	434	0.7		99.3	

Table 6B: Breast and Gynecological Cancer Diagnosis Compared to No Breast or Gynecological Diagnosis by Presence (+) or Absence (-) of Smoking and Metabolic Syndrome

Smoke &MetS	Sample size	Breast Cancer (n= 132)		No Cancer (n= 2606)	
		Percentage	Percentage	Percentage	Percentage
Smoke Mets (+ ; -)	291	2.4		97.6	
Smoke Mets (- ; +)	835	5.5		95.5	
Smoke Mets (+; +)	174	4.0		96.0	
Smoke Mets (- ; -)	1438	5.0		95.0	
Total	2738	4.8		95.2	

Smoke &MetS	Sample size	Cervical cancer (n= 83)		No Cancer (n= 2606)	
		Percentage	Percentage	Percentage	Percentage
Smoke Mets (+ ; -)	311	8.7		91.3	
Smoke Mets (- ; +)	805	2.0		98.0	
Smoke Mets (+; +)	178	6.2		98.0	
Smoke Mets (- ; -)	1395	2.1		97.9	
Total	2689	3.1		96.9	

Smoke &MetS	Sample size	Endometrial cancer (n =45)		No Cancer (n= 2606)	
		Percentage	Percentage	Percentage	Percentage
Smoke Mets (+ ; -)	288	1.4		98.6	
Smoke Mets (- ; +)	804	1.9		98.1	
Smoke Mets (+; +)	171	2.3		97.7	
Smoke Mets (- ; -)	1388	1.6		98.4	
Total	2651	1.7		98.3	

Smoke &MetS	Sample size	Ovarian cancer (n=18)		No Cancer (n= 2606)	
		Percentage	Percentage	Percentage	Percentage
Smoke Mets (+ ; -)	286	0.7		99.3	
Smoke Mets (- ; +)	793	0.5		99.5	
Smoke Mets (+; +)	168	0.6		99.4	
Smoke Mets (- ; -)	1377	0.8		99.2	
Total	2624	0.7		99.3	

See Notes on page 65 for explanation of (SmokeMetS combinations)

Table 6C: Rates of Reported Breast and Gynecological Cancer Diagnosis compared to Reports of No Breast or Gynecological Diagnosis (NC) by Presence (+) or Absence (-) of Smoking and Metabolic Syndrome with their Levels of Significance

Smoke & MetS	NC	BC	CC	EC	OC
Smoke Mets (+; -)	10.9	5.3	32.5	8.9	11.1
Smoke Mets (-; +)	30.3	34.8	19.3	33.3	22.2
Smoke Mets (+ ; +)	6.4	5.3	13.3	8.9	5.6
Smoke Mets (- ; -)	52.4	54.6	34.9	48.9	61.1
Total	100	100	100	100	100

Note:

- BC: Females who reported a breast cancer diagnosis
- CC: Females who reported a cervical cancer diagnosis
- EC: Females who reported an endometrial cancer diagnosis
- OC: Females who reported an ovarian cancer diagnosis
- NC: Females who reported no cancer diagnosis

Note for Table 6B

- Smoke (+) vs Smoke (-): Females who smoke compared to females who do not smoke
- MetS (+) vs MetS (-): Females who have metabolic syndrome compared to females who do not have metabolic syndrome
- Smoke /MetS (+ / +): Females who smoke and have metabolic syndrome
- Smoke/ MetS (+ / -): Females who smoke and do not have metabolic syndrome.
- Smoke /MetS (- / +): Females who do not smoke and have metabolic syndrome.
- Smoke /MetS (- / -): Females who do not smoke and do not have metabolic syndrome.

Table 7A: Bivariate Analysis Showing Distribution of Reported Breast and Cervical Cancer Diagnosis (+) compared to No Cancer Diagnosis Among Selected: a)Confounding Variables and b) Main Independent Variables of Interest

Demographics	NC	BC	OR; 95%CI	CC	OR
Age; < 45yrs	15.9	4.6	0.25(0.16-0.41)	46.9	4.69(3.51-6.27)
Ave. PA; (Stairs, load)	15.2	14.1	0.91(0.61-1.36)	22.1	1.58(0.98-2.54)
Country of Birth; US	85.3	92.5	2.12(1.26-3.57)	92.3	2.07(1.00-4.28)
Educ.; > high school	70.7	72.5	1.12(0.90-1.41)	74.2	1.23(0.89-1.70)
Health Insurance, Yes	86.2	96.2	4.05(2.40-6.82)	76.8	0.53(0.38-0.74)
Marriage; Married	50.7	46.5	0.84(0.69-1.04)	41.8	0.70(0.52-0.93)
PIR <1.33	29.9	27.6	0.90(0.70-1.14)	42.9	1.76(1.30-2.37)
Race; Whites	60.0	71.0	1.63(1.30-2.04)	65.5	1.26(0.94-1.71)
Time in US; 5years+	93.0	95.0	1.42(0.34-6.00)	95.0	1.42(0.19-10.76)
HPV 16	1.5	3.5	2.40(0.72-7.92)	5.5	3.82(1.67-8.73)
HPV 18	0.6	1.2	2.14(0.28-16.44)	2.4	4.34(1.23-15.31)
Risk Factors	NC	BC	OR; 95%CI	CC	OR
Current Smoker	17.1	10.61	0.58(0.42-0.80)	45.4	4.04(3.02- 5.40)
Metabolic Syndrome	36.7	40.2	1.16(0.81-1.66)	32.5	0.83(0.52-1.33)
Hypertension	47.5	51.6	1.17(0.9-1.47)	28.3	0.44(0.31-0.61)
HDL Cholesterol	31.1	31.5	1.02(0.80-1.29)	42.7	1.65(1.22-2.23)
Fasting Glucose	27.8	32.3	1.23(0.89-1.74)	16.3	0.51(0.29-0.87)

Table 7B : Bivariate Analysis Showing Distribution of Reported Endometrial and Ovarian Cancer Diagnosis (+) compared to No Cancer Diagnosis Among Selected: a)Confounding Variables and b) Main Independent Variables of Interest

Demographics	NC	EC	OR; 95%CI	OC	OR; 95%CI
Age; < 45yrs	15.9	18.8	1.22(0.76-1.97)	23.1	1.59(0.83-3.05)
Ave. PA; (Stairs, load)	15.2	10.8	0.67(0.30-1.48)	14.3	0.93(0.27-3.16)
Country of Birth; US	85.3	86.2	1.07(0.53-2.18)	81	0.73(0.24-2.19)
Educ.; > high school	70.7	63.4	0.74(0.50-1.09)	59.7	0.63(0.36-1.10)
Health Insurance, Yes	86.2	86.6	1.03(0.60-1.79)	88.5	1.22(0.52-2.88)
Marriage; Married	50.7	51.8	1.04(0.72-1.52)	46.2	0.83(0.48-1.44)
PIR <1.33	29.9	45.0	1.92(1.29-2.86)	34.8	1.25(0.68-2.30)
Race; Whites*	60.0	57.1	0.89(0.61-1.30)	46.2	0.57(0.33-0.99)
Time in US; 5years+	93.0	90.0	0.67(0.15-2.96)	90	0.67(0.08-5.38)
HPV 16	1.5	0.0	-	0	-
HPV 18	0.6	0.0	-	0	-
Risk Factors	NC	EC	OR; 95%CI	OC	OR; 95%CI
Current Smoker	17.1	17.9	1.06(0.64-1.72)	17.3	1.02(0.49 - 2.09)
Metabolic Syndrome	36.7	42.2	1.26(0.69-2.29)	27.8	0.66(0.24-1.87)
Hypertension	47.5	54.2	1.30(0.87-1.96)	42.1	0.80(0.42-1.53)
HDL Cholesterol	31.1	36.0	1.24(0.82-1.88)	33.3	1.11(0.59-2.06)
Fasting Glucose	27.8	40.4	1.76(1.00-3.08)	21.7	0.72(0.27-1.95)

Table 8A: Logistic Regression of Reported Breast Cancer Diagnosis with Main Independent Variables and Selected Factors of Metabolic Syndrome Adjusting for Age, Education, Race, Marriage, Country of Birth and Income to Poverty Ratio

Risk Factors	OR	95% CI	p-value	Pearson Goodness of fit
Smoke (+) vs Smoke (-)	0.58	0.36 - 0.93	0.03	<0.01
MetS (+) vs MetS (-)	0.82	0.49 - 1.39	0.46	0.77
Smoke/MetS (+/+) vs Smoke/ MetS (-/-)	1.05	0.39 – 2.81	0.44	0.98
Smoke/ MetS (+ / -)/ Smoke/ MetS (-/-)	0.51	0.18 - 1.48	0.30	
Smoke /MetS (- / +)/ Smoke/ MetS (-/-)	0.70	0.40 – 1.25	0.67	

Table 8B: Logistic Regression of Reported Cervical Cancer Diagnosis with Main Independent Variables and Selected Factors of Metabolic Syndrome Adjusting for Age, Education, Race, Marriage, Country of Birth and Income to Poverty Ratio

Risk Factors	OR	95% CI	p-value	Pearson Goodness-of-fit
Smoke (+) vs Smoke (-)	2.67	1.72 – 4.13	<.0001	<0.0001
MetS (+) vs MetS (-)	0.46	0.20 -1.10	0.08	0.13
Smoke/MetS (+/+) vs Smoke/ MetS (-/-)	1.38	0.37-5.02	0.76	<0.0001
Smoke/ MetS (+ / -) vs Smoke/ MetS (-/-)	3.03	1.41- 6.53	<0.01	
Smoke /MetS (- / +) vs Smoke/ MetS (-/-)	0.47	0.15 – 1.44*	0.03	
Hypertension	0.72	0.44 -1.21	0.22	0.01
HDL Cholesterol	1.38	0.88 -2.16	0.16	0.01
Fasting Glucose	0.51	0.20 -1.35	0.18	0.23

Table 8C: Logistic Regression of Reported Endometrial Cancer Diagnosis with Main Independent Variables and Selected Factors of Metabolic Syndrome Adjusting for Age, Education, Race, Marriage, Country of Birth and Income to Poverty Ratio

Risk Factors	OR	95% CI	p-value	Pearson Goodness-of-fit
Smoke (+) vs Smoke (-)	1.01	0.52 - 1.97	0.98	<.0001
MetS (+) vs MetS (-)	1.16	0.48-2.76	0.74	0.02
Smoke/MetS (+/+) vs Smoke/ MetS (-/-)	1.03	0.22 - 4.98	0.80	0.14
Smoke/ MetS (+ / -) vs Smoke/ MetS (-/-)	0.57	0.12 - 2.67	0.45	
Smoke /MetS (- / +) vs Smoke/ MetS (-/-)	1.06	0.40 – 2.77	0.67	

Table 8D: Logistic Regression of Reported Ovarian Cancer Diagnosis with Main Independent Variables and Selected Factors of Metabolic Syndrome Adjusting for Age, Education, Race, Marriage, Country of Birth and Income to Poverty Ratio

Risk Factors	OR	95% CI	p-value	Pearson Goodness-of-fit
Smoke (+) vs Smoke (-)	0.90	0.25 - 3.18	0.86	0.09
MetS (+) vs MetS (-)	0.23	0.03-1.96	0.18	0.44
Smoke/MetS (+/+) vs Smoke/ MetS (-/-)	-	-	-	-
Smoke/ MetS (+ / -) vs Smoke/ MetS (-/-)	0.98	0.11 - 8.66	0.96	<.0001
Smoke /MetS (- / +) vs Smoke/ MetS (-/-)	0.27	0.03 - 2.30	0.97	

Note:

ORs are not estimated when the maximum likelihood for variables do not exist

Figure 1: Rates of Reported Breast and Cervical Cancers by Socio-demographic Factors

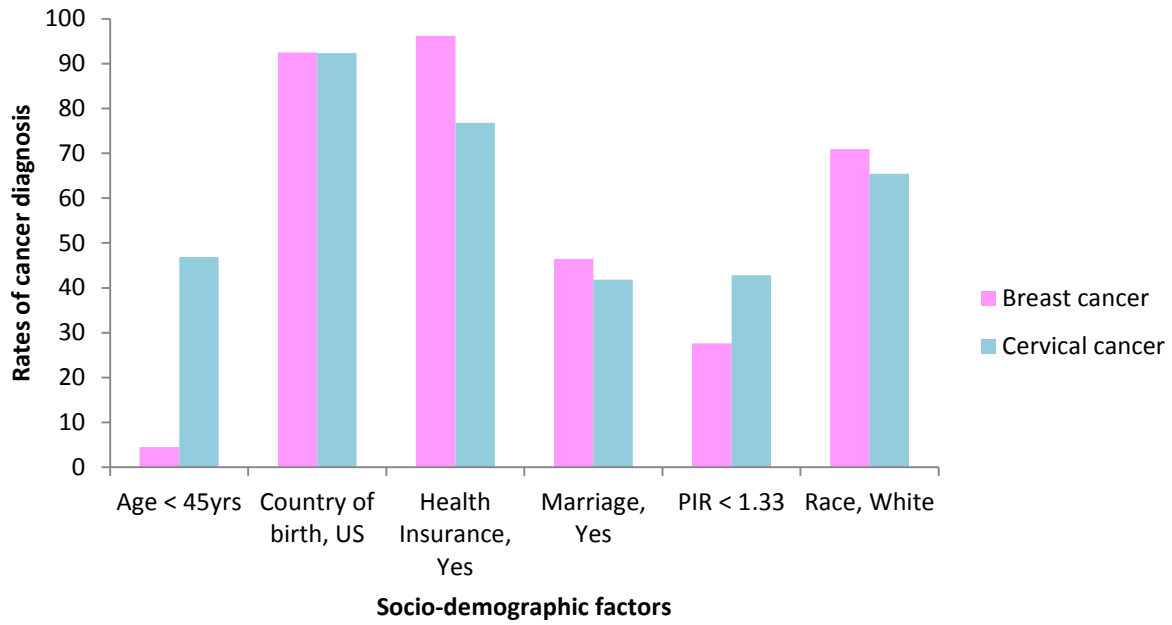
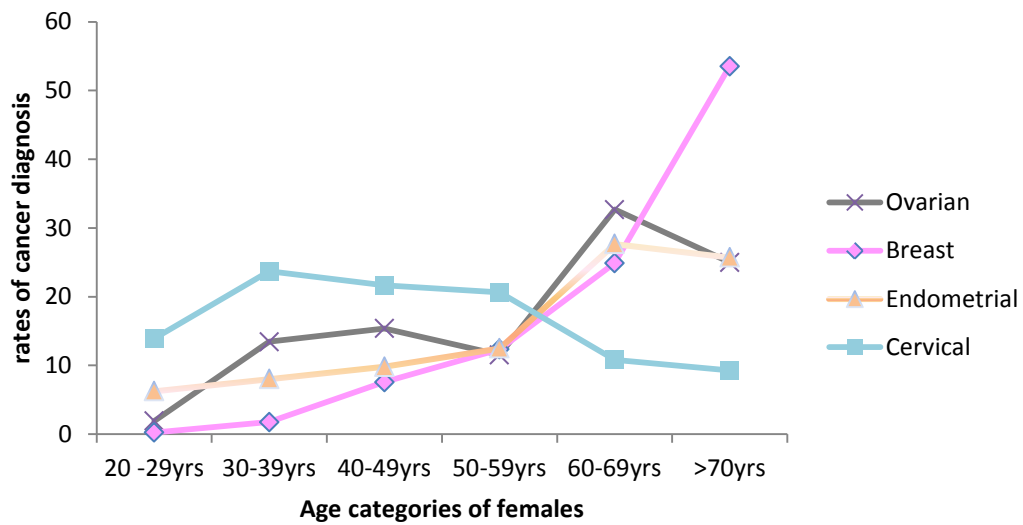


Figure 2: Rates of Reported Breast and Gynecological Cancers Stratified by Age.



SAS Code for Analysis

```
LIBNAME BABSTHES ";

PROC IMPORT OUT= BABSTHES.MYTHESISBABS
  DATAFILE= "THESIS\datatouse222.sav"
  DBMS=SPSS REPLACE;
RUN;

DATA BABSTHES.NEWTHESIS;
  SET BABSTHES.MYTHESISBABS;

  IF SMOKES = 1 THEN NEWSMOKE = 1;
  ELSE IF SMOKE NE . THEN NEWSMOKE = 2;

  NAGE = .;
  IF 20 <= AGE < 45 THEN NAGE = 1;
  ELSE IF 45 <= AGE <= 85 THEN NAGE = 2;

  IF AFI IN (77, 99) THEN AFI = .;

  IF AHI IN (77, 99) THEN AHI = .;

  IF EMOTIONALSUPP IN (7,9) THEN EMOTIONALSUPP = .;

  IF FINANCIALSUPP IN (7,9) THEN FINANCIALSUPP = .;

  IF HI IN (7,9) THEN HI = .;

  IF EDUCATION IN (7,9) THEN EDUCATION = .;

  NTIMEINUS = .;
  IF TIMEINUS IN (77,99) THEN TIMEINUS = .;
  IF 3 <= TIMEINUS <= 9 THEN NTIMEINUS = 1;
  ELSE IF TIMEINUS IN (1,2) THEN NTIMEINUS = 2;

  IF MARRIED IN (77,99) THEN MARRIED = .;
  IF MARRIED = 1 THEN NMARRIED = 1;
  ELSE NMARRIED = 2;

  IF WTC IN (7,9) THEN WTC = .;

  IF DIABPILLS IN (7,9) THEN DIABPILLS = .;

  IF SMOKE IN (7,9) THEN SMOKE = .;

  IF AGEBREAST IN (99999) THEN AGEBREAST = .;

  IF AGECERV IN (99999) THEN AGECERV = .;

  IF MENSRRANGE IN (7,9) THEN MENSRRANGE = .;

  IF LASTRRANGE IN (77,99) THEN LASTRRANGE = .;

  IF PREGNANT IN (7,9) THEN PREGNANT = .;
```

```
IF CONTRACEP IN (7,9) THEN CONTRACEP = .;

IF HYSTERECTOMY IN (7,9) THEN HYSTERECTOMY = .;

IF OVAREMOVE IN (7,9) THEN OVAREMOVE = .;

IF ENDO IN (7,9) THEN ENDO = .;

IF FIBROID IN (7,9) THEN FIBROID = .;

IF OESTROGEN IN (7,9) THEN OESTROGEN = .;

IF OESTRPROG IN (7,9) THEN OESTRPROG = .;

IF PROGESTIN IN (7,9) THEN PROGESTIN = .;

IF 0 <= POVERTYINC < 1.33162 THEN MYPOV = 1;
ELSE IF POVERTYINC >= 1.33162 THEN MYPOV = 2;

IF 0 <= POVERTYINC < 1.33162 THEN MYPOVNEW = 1;
ELSE IF 1.33162 <= POVERTYINC < 3.22046 THEN MYPOVNEW = 2;
ELSE IF 3.22046 <= POVERTYINC < 5.03326 THEN MYPOVNEW = 3;
ELSE IF POVERTYINC >= 5.03326 THEN MYPOVNEW = 4;

IF COUNTRYBORN = 1 THEN NCOUNTRYBORN = 1;
ELSE IF COUNTRYBORN >= 2 THEN NCOUNTRYBORN = 2;

IF EDUCATION >= 3 THEN NEDUC = 1;
ELSE IF EDUCATION < 3 THEN NEDUC = 2;

IF RACE = 3 THEN NRACE = 1;
ELSE NRACE = 2;

IF AVEPA IN (3,4) THEN NAVEPA = 1;
ELSE IF AVEPA IN (1,2) THEN NAVEPA = 2;

IF BMI < 18.5 THEN NBMI = 1;
ELSE IF 18.5 <= BMI <= 24.9 THEN NBMI = 2;
ELSE IF 25 <= BMI <= 29.9 THEN NBMI = 3;
ELSE IF BMI >= 30 THEN NBMI = 4;

IF 1 <= NUMCIG <= 9 THEN NNUMCIG = 1;
ELSE IF 10 <= NUMCIG <= 19 THEN NNUMCIG = 2;
ELSE IF 20 <= NUMCIG <= 29 THEN NNUMCIG = 3;
ELSE IF NUMCIG >= 30 THEN NNUMCIG = 4;

NEWBREASTCANCER = BREASTCANCER;
IF NEWBREASTCANCER = 2 THEN NEWBREASTCANCER = 0;

NEWCERVANCER = CERVANCER;
IF NEWCERVANCER = 2 THEN NEWCERVANCER = 0;

NEWOVACANCER = OVACANCER;
IF NEWOVACANCER = 2 THEN NEWOVACANCER = 0;

NEWUTERINECANCER = UTERINECANCER;
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```

IF NEWUTERINECANCER = 2 THEN NEWUTERINECANCER = 0;

SMOKMETSYN = .;
IF NEWSMOKE = 1 AND METSYN = 1 THEN SMOKMETSYN = 1;
ELSE IF NEWSMOKE = 1 AND METSYN = 2 THEN SMOKMETSYN = 2;
ELSE IF NEWSMOKE = 2 AND METSYN = 1 THEN SMOKMETSYN = 3;
ELSE IF NEWSMOKE = 2 AND METSYN = 2 THEN SMOKMETSYN = 4;

NHHPV16 = .;
IF HHPV16 = 1 THEN NHHPV16 = 1;
ELSE IF HHPV16 = 2 THEN NHHPV16 = 2;
ELSE IF HHPV16 = 3 THEN NHHPV16 = 2;
ELSE IF OHPV16 = 1 THEN NHHPV16 = 1;
ELSE IF OHPV16 = 2 THEN NHHPV16 = 2;
ELSE IF OHPV16 = 3 THEN NHHPV16 = 2;
ELSE IF RHPV16 = 1 THEN NHHPV16 = 1;
ELSE IF RHPV16 = 2 THEN NHHPV16 = 2;
ELSE IF RHPV16 = 3 THEN NHHPV16 = 2;

NHHPV18 = .;
IF HHPV18 = 1 THEN NHHPV18 = 1;
ELSE IF HHPV18 = 2 THEN NHHPV18 = 2;
ELSE IF HHPV18 = 3 THEN NHHPV18 = 2;
ELSE IF OHPV18 = 1 THEN NHHPV18 = 1;
ELSE IF OHPV18 = 2 THEN NHHPV18 = 2;
ELSE IF OHPV18 = 3 THEN NHHPV18 = 2;
ELSE IF RHPV18 = 1 THEN NHHPV18 = 1;
ELSE IF RHPV18 = 2 THEN NHHPV18 = 2;
ELSE IF RHPV18 = 3 THEN NHHPV18 = 2;

RUN;

PROC CONTENTS DATA = BABSTHES.NEWTHESIS;
RUN;

ods html file = 'THEESIS\NEWALLDEMOFREQ.xls';
PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  TITLE "MEANS, SD AND 95% CI OF DEMOGRAPHICS VARIABLES";
  VARS AGE AFI AHI POVERTYINC MYPOV;
RUN;

PROC FREQ DATA = BABSTHES.NEWTHESIS;
  TITLE "DISTRIBUTION OF DEMOGRAPHICS VARIABLES";
  TABLES NAGE MYPOV EMOTIONALSUPP FINANCIALSUPP HI NEDUC NTIMEINUS
  NMARRIED RACE NCOUNTRYBORN;
RUN;

PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  TITLE "MEANS, SD AND 95% CI OF EXAMINATION VARIABLES";
  VARS AVEDBP AVESBP BMI COTININE GLUCOSE HDL LDLCHOL HEIGHT TRIG WAISTCIR;
RUN;

PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  TITLE "MEANS, SD AND 95% CI OF LIFESTYLE VARIABLES";
  VARS NUMCIG;
RUN;

```

```

PROC FREQ DATA = BABSTHES.NEWTHESIS;
  TITLE "DISTRIBUTION OF LIFESTYLE VARIABLES";
  TABLES AVEPA WTC SMOKENOW FATCONTROL ALCOHOL NEWSMOKE DIABPILLS;
RUN;

PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  TITLE "MEANS, SD AND 95% CI OF MEDICAL CONDITION VARIABLES";
  VARS AGEBREAST AGECEVAGE AGEVARY AGEUTERINE;
RUN;

PROC FREQ DATA = BABSTHES.NEWTHESIS;
  TITLE "DISTRIBUTION OF MEDICAL CONDITION VARIABLES";
  TABLES ABDOBESITY BREASTCANCER CERVICANCER UTERINECANCER OVACANCER
HCONDITON CANCER METSYN SMOKMETSYN METSYNDROME
  FASTGLUCOSE HDLCHOLEST TRIGLYCERIDE HBP;
RUN;

PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  TITLE "MEANS, SD AND 95% CI OF REPRODUCTIVE HEALTH VARIABLES";
  VARS LIVEBIRTHS;
RUN;

PROC FREQ DATA = BABSTHES.NEWTHESIS;
  TITLE "DISTRIBUTION OF REPRODUCTIVE HEALTH VARIABLES";
  TABLES MENSRRANGE LSTRANGE BREASTFED PREGNANT CONTRACEP
HYSTERECTOMY OVAREMOVE ENDO FIBROID
  OESTROGEN OESTRPROG PROGESTIN;
RUN;

ods html file = 'THESES\NEWYESCANCERFREQ.xls';
PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  WHERE CANCER = 1;
  TITLE "MEANS, SD AND 95% CI OF DEMOGRAPHICS VARIABLES YES CANCER";
  VARS AGE AFI AHI POVERTYINC MYPOV;
RUN;

PROC FREQ DATA = BABSTHES.NEWTHESIS;
  WHERE CANCER = 1;
  TITLE "DISTRIBUTION OF DEMOGRAPHICS VARIABLES YES CANCER";
  TABLES NAGE MYPOV EMOTIONALSUPP FINANCIALSUPP HI NEDUC NTIMEINUS
NMARRIED RACE NCOUNTRYBORN;
RUN;

PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  WHERE CANCER = 1;
  TITLE "MEANS, SD AND 95% CI OF EXAMINATION VARIABLES YES CANCER";
  VARS AVEDBP AVESBP BMI COTININE GLUCOSE HDL LDLCHOL HEIGHT TRIG WAISTCIR;
RUN;

PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  WHERE CANCER = 1;
  TITLE "MEANS, SD AND 95% CI OF LIFESTYLE VARIABLES YES CANCER";
  VARS NUMCIG;
RUN;

```

```

PROC FREQ DATA = BABSTHES.NEWTHESIS;
  WHERE CANCER = 1;
  TITLE "DISTRIBUTION OF LIFESTYLE VARIABLES YES CANCER";
  TABLES AVEPA WTC SMOKENOW FATCONTROL ALCOHOL NEWSMOKE DIABPILLS;
RUN;

PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  WHERE CANCER = 1;
  TITLE "MEANS, SD AND 95% CI OF MEDICAL CONDITION VARIABLES YES CANCER";
  VARS AGEBREAST AGECEV AGEVARY AGEUTERINE;
RUN;

PROC FREQ DATA = BABSTHES.NEWTHESIS;
  WHERE CANCER = 1;
  TITLE "DISTRIBUTION OF MEDICAL CONDITION VARIABLES YES CANCER";
  TABLES ABDOBESITY BREASTCANCER CERVCANCER UTERINECANCER OVACANCER
HCONDITION METSYN SMOKMETSYN METSYNDROME
  FASTGLUCOSE HDLCHOLEST TRIGLYCERIDE HBP;
RUN;

PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  WHERE CANCER = 1;
  TITLE "MEANS, SD AND 95% CI OF REPRODUCTIVE HEALTH VARIABLES YES CANCER";
  VARS LIVEBIRTHS;
RUN;

PROC FREQ DATA = BABSTHES.NEWTHESIS;
  WHERE CANCER = 1;
  TITLE "DISTRIBUTION OF REPRODUCTIVE HEALTH VARIABLES YES CANCER";
  TABLES MENS RANGE LASTRANGE BREASTFED PREGNANT CONTRACEP
HYSTERECTOMY OVAREMOVE ENDO FIBROID
  OESTROGEN OESTRPROG PROGESTIN;
RUN;

ods html file = 'THESES\NEWNOCANCERFREQ.xls';
PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  WHERE CANCER = 2;
  TITLE "MEANS, SD AND 95% CI OF DEMOGRAPHICS VARIABLES NO CANCER";
  VARS AGE AFI AHI POVERTYINC MYPOV;
RUN;

PROC FREQ DATA = BABSTHES.NEWTHESIS;
  WHERE CANCER = 2;
  TITLE "DISTRIBUTION OF DEMOGRAPHICS VARIABLES NO CANCER";
  TABLES NAGE MYPOV EMOTIONALSUPP FINANCIALSUPP HI NEDUC NTIMEINUS
NMARRIED RACE NCOUNTRYBORN;
RUN;

PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  WHERE CANCER = 2;
  TITLE "MEANS, SD AND 95% CI OF EXAMINATION VARIABLES NO CANCER";
  VARS AVEDBP AVESBP BMI COTININE GLUCOSE HDL LDLCHOL HEIGHT TRIG WAISTCIR;
RUN;

PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
  WHERE CANCER = 2;

```

```

        TITLE "MEANS, SD AND 95% CI OF LIFESTYLE VARIABLES NO CANCER";
        VARS NUMCIG;
    RUN;

    PROC FREQ DATA = BABSTHES.NEWTHESIS;
        WHERE CANCER = 2;
        TITLE "DISTRIBUTION OF LIFESTYLE VARIABLES NO CANCER";
        TABLES AVEPA WTC SMOKENOW FATCONTROL ALCOHOL NEWSMOKE DIABPILLS;
    RUN;

    PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
        WHERE CANCER = 2;
        TITLE "MEANS, SD AND 95% CI OF MEDICAL CONDITION VARIABLES NO CANCER";
        VARS AGEBREAST AGECERV AGEOVARY AGEUTERINE;
    RUN;

    PROC FREQ DATA = BABSTHES.NEWTHESIS;
        WHERE CANCER = 2;
        TITLE "DISTRIBUTION OF MEDICAL CONDITION VARIABLES NO CANCER";
        TABLES ABDOBESITY BREASTCANCER CERVCANCER UTERINECANCER OVACANCER
        HCONDITON METSYN SMOKMETSYN METSYNDROME
        FASTGLUCOSE HDLCHOLEST TRIGLYCERIDE HBP;
    RUN;

    PROC MEANS DATA = BABSTHES.NEWTHESIS N MIN MAX MEAN STD CLM;
        WHERE CANCER = 2;
        TITLE "MEANS, SD AND 95% CI OF REPRODUCTIVE HEALTH VARIABLES NO CANCER";
        VARS LIVEBIRTHS;
    RUN;

    PROC FREQ DATA = BABSTHES.NEWTHESIS;
        WHERE CANCER = 2;
        TITLE "DISTRIBUTION OF REPRODUCTIVE HEALTH VARIABLES NO CANCER";
        TABLES MENS RANGE LASTRANGE BREASTFED PREGNANT CONTRACEP
        HYSTERECTOMY OVAREMOVE ENDO FIBROID
        OESTROGEN OESTRPROG PROGESTIN;
    RUN;

    ods html file = 'THESES \NEWSMOKEBIVARIATE.xls';
    PROC FREQ DATA = BABSTHES.NEWTHESIS;
        TITLE "BIVARIATE ANALYSIS WITH NEWSMOKE(UNADJUSTED)";
        TABLES NEWSMOKE*(BREASTCANCER CERVCANCER UTERINECANCER
        OVACANCER)/ALL;
    RUN;

    ods html file = 'THESES \NEWNNUMCIGBIVARIATE.xls';
    PROC FREQ DATA = BABSTHES.NEWTHESIS;
        TITLE "BIVARIATE ANALYSIS WITH NNUMCIG(UNADJUSTED)";
        TABLES NNUMCIG*(BREASTCANCER CERVCANCER UTERINECANCER OVACANCER)/ALL;
    RUN;

    ods html file = 'THESES \NEWSMOKMETSYNBIVARIATE.xls';
    PROC FREQ DATA = BABSTHES.NEWTHESIS;
        TITLE "BIVARIATE ANALYSIS WITH SMOKMETSYN(UNADJUSTED)";
        TABLES SMOKMETSYN*(BREASTCANCER CERVCANCER UTERINECANCER
        OVACANCER)/ALL;

```

RUN;

```
ods html file = 'THESES\ALLBIVARIATE.xls';
PROC FREQ DATA = BABSTHES.NEWTHESIS;
  TITLE "BIVARIATE ANALYSIS FOR TABLE 4.(UNADJUSTED)";
  TABLES (BREASTCANCER CERVCANCER UTERINECANCER OVACANCER NEWSMOKE
SMOKMETSYN)*
(NAGE MYPOV NCOUNTRYBORN NEDUC NTIMEINUS NMARRIED RACE HI AVEPA ABDOBESITY
HCONDITON FASTGLUCOSE HDLCHOLEST TRIGLYCERIDE HBP CONTRACEP) /ALL;
RUN;
```

```
ods html file = 'THESES \ALLBIVARIATENHHPV16.xls';
PROC FREQ DATA = BABSTHES.NEWTHESIS;
  TITLE "BIVARIATE ANALYSIS FOR TABLE 4 PART2(UNADJUSTED)";
  TABLES (BREASTCANCER CERVCANCER UTERINECANCER OVACANCER NEWSMOKE
SMOKMETSYN)*(NHHPV16 NHHPV18) /ALL;
RUN;
```

```
ods html file = 'THESES\BIVARIATETAB6C.xls';
PROC FREQ DATA = BABSTHES.NEWTHESIS;
  TITLE "BIVARIATE ANALYSIS FOR TABLE 4 PART2(UNADJUSTED)";
  TABLES (SMOKMETSYN)*(CANCER BREASTCANCER CERVCANCER UTERINECANCER
OVACANCER NEWSMOKE) /ALL;
RUN;
```

/******LOGISTIC REGRESSION FOR ADJUSTED RESULTS******/

/****** BREAST CANCER ******/

/**** NEWSMOKE *****/

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ods html file = 'THESES\NEWBREASTCANCERNEWSMOKELOGIS.xls';
PROC LOGISTIC DATA = BABSTHES.NEWTHESIS DESCENDING;
  TITLE "PREDICTING USING LOGISTICS REGRESSION BREAST CANCER
NEWSMOKE(ADJUSTED)";
  CLASS NEWBREASTCANCER NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
NEWSMOKE;
  MODEL NEWBREASTCANCER = NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
NEWSMOKE/
  SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
RUN;
QUIT;
```

```
ods html file = 'THESES\NEWBREASTCANCERNNUMCIGLOGIS.xls';
PROC LOGISTIC DATA = BABSTHES.NEWTHESIS DESCENDING;
  TITLE "PREDICTING USING LOGISTICS REGRESSION BREAST CANCER
NNUMCIG(ADJUSTED)";
  CLASS NEWBREASTCANCER NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
NNUMCIG;
  MODEL NEWBREASTCANCER = NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
NNUMCIG/
  SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
RUN;
QUIT;
```

```
ods html file = 'THESES\NEWBREASTCANCERSMOKMETSYNLOGIS.xls';
PROC LOGISTIC DATA = BABSTHES.NEWTHESIS DESCENDING;
```

```

    TITLE "PREDICTING USING LOGISTICS REGRESSION BREAST CANCER
SMOKMETSYN(ADJUSTED)";
    CLASS NEWBREASTCANCER NAGE MYPOV NOUNTRYBORN NEDUC NMARRIED NRACE
SMOKMETSYN;
    MODEL NEWBREASTCANCER = NAGE MYPOV NOUNTRYBORN NEDUC NMARRIED NRACE
SMOKMETSYN/
        SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
RUN;
QUIT;

```

```

/***** CERVICAL CANCER *****/

```

```

/**** NEWSMOKE ****/

```

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ods html file = 'THESES\NEWCERVANCANERNEWSMOKELOGIS.xls';
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NEWSMOKE(ADJUSTED)";
    CLASS NEWCERVANCANCER NAGE MYPOV NOUNTRYBORN NEDUC NMARRIED NRACE
NEWSMOKE;
    MODEL NEWCERVANCANCER = NAGE MYPOV NOUNTRYBORN NEDUC NMARRIED NRACE
NEWSMOKE/
        SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
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QUIT;

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ods html file = 'THESES\NEWCERVANCANERNNUMCIGLOGIS.xls';
PROC LOGISTIC DATA = BABSTHES.NEWTHESIS DESCENDING;
    TITLE "PREDICTING USING LOGISTICS REGRESSION CERVICAL CANCER
NNUMCIG(ADJUSTED)";
    CLASS NEWCERVANCANCER NAGE MYPOV NOUNTRYBORN NEDUC NMARRIED NRACE
NNUMCIG;
    MODEL NEWCERVANCANCER = NAGE MYPOV NOUNTRYBORN NEDUC NMARRIED NRACE
NNUMCIG/
        SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
RUN;
QUIT;

```

```

ods html file = 'THESES\NEWCERVANCANERSMOKMETSYNLOGIS.xls';
PROC LOGISTIC DATA = BABSTHES.NEWTHESIS DESCENDING;
    TITLE "PREDICTING USING LOGISTICS REGRESSION CERVICAL CANCER
SMOKMETSYN(ADJUSTED)";
    CLASS NEWCERVANCANCER NAGE MYPOV NOUNTRYBORN NEDUC NMARRIED NRACE
SMOKMETSYN;
    MODEL NEWCERVANCANCER = NAGE MYPOV NOUNTRYBORN NEDUC NMARRIED NRACE
SMOKMETSYN/
        SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
RUN;
QUIT;

```

```

/***** OVARIAN CANCER *****/

```

```

/**** NEWSMOKE ****/

```

```

ods html file = 'THESES\NEOVACANCERNEWSMOKELOGIS.xls';
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    TITLE "PREDICTING USING LOGISTICS REGRESSION OVARIAN CANCER
NEWSMOKE(ADJUSTED)";
    CLASS NEWOVACANCER NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
NEWSMOKE;
    MODEL NEWOVACANCER = NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
NEWSMOKE/
        SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
RUN;
QUIT;

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ods html file =THESES\NEWOVACANCERNNUMCIGLOGIS.xls';
PROC LOGISTIC DATA = BABSTHES.NEWTHESIS DESCENDING;
    TITLE "PREDICTING USING LOGISTICS REGRESSION OVARIAN CANCER
NNUMCIG(ADJUSTED)";
    CLASS NEWOVACANCER NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
NNUMCIG;
    MODEL NEWOVACANCER = NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
NNUMCIG/
        SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
RUN;
QUIT;

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ods html file =THESES\NEWOVACANCERSMOKMETSYNLOGIS.xls';
PROC LOGISTIC DATA = BABSTHES.NEWTHESIS DESCENDING;
    TITLE "PREDICTING USING LOGISTICS REGRESSION OVARIAN CANCER
SMOKMETSYN(ADJUSTED)";
    CLASS NEWOVACANCER NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
SMOKMETSYN;
    MODEL NEWOVACANCER = NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
SMOKMETSYN/
        SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
RUN;
QUIT;

```

```

/***** UTERINE CANCER *****/

```

```

/**** NEWSMOKE ****/
ods html file =THESES\NEWUTERINECANCERNEWSMOKELOGIS.xls';
PROC LOGISTIC DATA = BABSTHES.NEWTHESIS DESCENDING;
    TITLE "PREDICTING USING LOGISTICS REGRESSION UTERINE CANCER
NEWSMOKE(ADJUSTED)";
    CLASS NEWUTERINECANCER NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
NEWSMOKE;
    MODEL NEWUTERINECANCER = NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED
NRACE NEWSMOKE/
        SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
RUN;
QUIT;

```

```

ods html file =THESES\NEWUTERINECANCERNNUMCIGLOGIS.xls';
PROC LOGISTIC DATA = BABSTHES.NEWTHESIS DESCENDING;
    TITLE "PREDICTING USING LOGISTICS REGRESSION UTERINE CANCER
NNUMCIG(ADJUSTED)";
    CLASS NEWUTERINECANCER NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
NNUMCIG;

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MODEL NEWUTERINECANCER = NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED
NRACE NNUMCIG/
SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
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QUIT;

ods html file =THESES\NEWUTERINECANCERSMOKMETSYNLOGIS.xls';
PROC LOGISTIC DATA = BABSTHES.NEWTHESIS DESCENDING;
TITLE "PREDICTING USING LOGISTICS REGRESSION UTERINE CANCER
SMOKMETSYN(ADJUSTED)";
CLASS NEWUTERINECANCER NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED NRACE
SMOKMETSYN;
MODEL NEWUTERINECANCER = NAGE MYPOV NCOUNTRYBORN NEDUC NMARRIED
NRACE SMOKMETSYN/
SCALE=NONE AGGREGATE LACKFIT CLPARM=WALD LACKFIT RISKLIMITS;
RUN;
QUIT;
ods html close;
```

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