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Polyp Detection During Colonoscopy Among Uninsured Patients In South Carolina

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POLYP DETECTION DURING COLONOSCOPY AMONG UNINSURED PATIENTS IN SOUTH CAROLINA

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ABSTRACT

Little information is known on what demographic, behavioral, and procedural factors influence the number of polyps found during a colonoscopy screening for colorectal cancer (CRC). The main objective of this study is to describe the polyp detection rate (PDR), number of polyps removed, and predictors of polyp count overall and for high-risk polyps among uninsured patients undergoing colonoscopy in the Colorectal Cancer Prevention Network (CCPN) program of South Carolina. We performed a secondary data analysis on CCPN data for colonoscopies performed between May 2014 and May 2017. We assessed the association of polyp count with the following variables: age, race, gender, smoking status, alcohol use, BMI, family history of CRC, education status, NSAID use, physical activity, rural/urban residence, bowel preparation quality, and time of procedure. We hypothesized that since these variables have been shown to influence the risk of colonic polyps they will also influence the number of all polyps and number of high-risk polyps detected during colonoscopy. Total PDR within this study was 61.82%. Respective mean, median, and max number of polyps removed were 1.65, 1.00, and 15 for all polyps and 0.31, 0, and 13 for high-risk polyps. Multivariable analyses found male gender, current and former smokers, moderate alcohol use, family history of CRC, obesity, and never using NSAIDS to be positively associated with total number of polyps detected; rural residence was negatively associated with number of total polyps. Males, current smokers, and using NSAIDS 1-3 days/week,

occasionally, or never were found to have a higher number of high-risk polyps. A later procedure time resulted in a lower number of high-risk polyps than the earliest procedure times. This study demonstrates the effects that demographic, behavioral, and procedural influencers have on polyp detection and the number of polyps detected during a colonoscopy procedure. Based on these relationships, our findings may help to identify individuals who are at risk for a high number of polyps, which could possibly lead to better detection of polyps during their colonoscopy procedure.

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LIST OF ABBREVIATIONS

ACS ..... American Cancer Society

ADR ..... Adenoma Detection Rate

BMI ..... Body Mass Index

CCCR ..... Center for Colon Cancer Research

CCPN ..... Colorectal Cancer Prevention Network

CCSR ..... Colorectal Cancer Screening Registry

CDC ..... Centers for Disease Control

CI ..... Confidence Interval

CRC ..... Colorectal Cancer

IRR ..... Incidence Rate Ratio

NIAAA ..... National Institute on Alcohol Abuse and Alcoholism

NSAID ..... Non-Steroidal Anti-Inflammatory Drug

PDR ..... Polyp Detection Rate

RUCA ..... Rural-Urban Commuting Area

RR ..... Rate Ratio

USPSTF ..... U.S. Preventive Services Task Force

WHO ..... World Health Organization

CHAPTER 1

INTRODUCTION

Colorectal cancer (CRC) is the third most common type of cancer for men and women in the United States and in South Carolina.[1,2] The American Cancer Society (ACS) estimates that about 140,250 cases of colon and rectal cancer will be diagnosed in 2018.[2] Colonoscopies are an effective primary prevention method of CRC because they remove cancer-causing polyps and detect early signs of cancer.[3] These procedures have reduced CRC incidence and risk of death.[4–7]

Although colonoscopies are effective at reducing the risk for CRC, they can be expensive procedures. The cost for a colonoscopy screening averages between $586 to $2,146 depending on health insurance type and the facility in which the screening is performed.[8,9] Because of these high costs, colonoscopy screening rates for U.S. adults who are uninsured is lower than the rate for those who do have health insurance.[2,3,10–12] This makes the uninsured population more susceptible to colorectal polyps and CRC, and more likely to be diagnosed at an advanced stage than those who have health insurance.[2,13] About 10.0% of South Carolina residents did not have health insurance in 2016,[14] and only 71.3% of the state's adult residents aged 50+ have ever received a colorectal endoscopy (as of 2014)[15] which makes the uninsured individuals in this state of particular concern for colorectal polyps and CRC.

The U.S. Preventive Services Task Force (USPSTF) recommends CRC screening for those between the ages of 50 and 75, or sooner than 50 years if an individual is among a high-risk group for developing CRC- such as African-Americans.[1] However, the ACS now recommends screening for average-risk individuals aged 45-50.[16] Many different factors may contribute to an individual's risk status. These include race, age, gender, BMI, smoking, physical activity, family history of CRC, alcohol use, nonsteroidal anti-inflammatory drug (NSAID) use, rural vs. urban residence, and education, all which have all been found to be associated with the risk of adenoma polyps.[1,2,17–25]

Non-Hispanic blacks are more at risk to develop CRC when compared to non-Hispanic whites, and are also less likely to receive a colonoscopy screening.[1,10,18] From 2010 through 2014, non-Hispanic blacks had a 40% higher CRC death rate than non-Hispanic whites. Regardless of race, males have a higher incidence rate and mortality rate than women.[2,17,18] Additionally, the probability of developing CRC increases with age and is the highest among those who are 70 years or older.[2] Some types of NSAIDs, regular physical activity, and higher education levels have been shown to decrease the risk of colonic adenomas.[1,22,26] Smoking, having a high BMI, and frequently drinking alcohol are all well known risk factors for developing colorectal polyps.[18,26,27] Having a first-degree relative with a history of CRC can increase one's risk for developing CRC.[23] Additionally, colonoscopy screening rates are lower in rural areas than they are in urban areas.[21] Rural residents often have long travel distances to a screening provider which has been shown to have higher odds of being diagnosed with a late-stage CRC as compared to those who live closer to a provider.[20]

In an effort to improve upon the colorectal screening rates in South Carolina's uninsured population, the Center for Colon Cancer Research (CCCR) at the University of South Carolina established the Colorectal Cancer Prevention Network (CCPN) in 2008 which provides free colonoscopy screenings to those who are uninsured and meet the program's eligibility requirements. Between May 2014 and May 2016, the CCPN program completed 909 colonoscopies and found that 6.6% were normal, 41.6% were hyperplastic polyps, 28.0% were non-advanced adenomas, 22% were advanced adenomas, and about 1% of patients were diagnosed with CRC or carcinoid tumor.[28] The overall polyp detection rate (PDR) of the procedures was 63%, and the adenoma detection rate (ADR) was 36%.[28]

Studies have found that polyp count, or the number of polyps discovered in the colon during colonoscopy, has an influence on cancer risk. When polyp density increases, the risk of CRC also increases.[29] Although many studies have focused on what demographic and behavioral factors make people more at risk for high-risk polyps and colorectal cancer, there seems to be a knowledge gap on what specific factors may influence the *quantity* of polyps detected during a colonoscopy procedure.

The main objective of this study is to describe the polyp detection rate, number of polyps removed (overall and by risk type), and predictors of polyp count among uninsured patients undergoing colonoscopy in the CCPN program of South Carolina. We will be focusing on those patients who received colonoscopy procedures between May 2014 and May 2017. Our aims include (1) calculating the PDR overall and for each independent variable, (2) describing the mean, median, and max of polyps removed, and (3) determining the association of demographic and lifestyle characteristics on number of

polyps detected (overall and high-risk only) during colonoscopy for patients participating in the CCPN screening program.

Since our study sample consists of uninsured and low-income patients, we expect to see a relatively large PDR. Persons who are of older age, African-American, male, currently smoke, live in a rural area, participate in zero days of vigorous physical activity per week, have fair-to-poor quality of bowel preparation, family history of CRC, heavily drink alcohol, never use NSAIDs, have less than high school education, and who are obese/overweight are expected to have a significantly higher PDR than their counterparts. We also expect these individuals to have a larger number of polyps removed during colonoscopy. We hypothesize that these factors that have been shown to increase the risk of colonic polyps will also increase the risk of overall number of polyps detected during colonoscopy.

CHAPTER 2

LITERATURE REVIEW

2.1 COLORECTAL CANCER BURDEN IN THE U.S. AND SOUTH CAROLINA

According to the American Cancer Society (ACS), about 1.7 million new cases of cancer are expected to be diagnosed in 2018, with 140,250 of those being colon and rectal cancers.[2] The ACS estimated new cases of colorectal cancer (CRC) in 2018 to be higher among males (n= 75,610) than females (n= 64,640).[2] The death rates of CRC also tend to vary by sex. The 2011-2015 CRC death rate for males in the United States was about 17.3 per 100,000, whereas this rate was 12.2 per 100,000 for females.[2] These rates are slightly higher in the state of South Carolina, where the 2011-2015 CRC death rates for males and females were 18.0 and 12.6, respectively.[2] The ACS estimates that in 2018 the total number of deaths from CRC will be approximately 50,630 in the U.S. and 860 in South Carolina.[2]

Not only does sex influence CRC risk, but other factors such as age and race can have an effect. The probability of developing CRC increases with age, and is highest amongst those aged 70+.[1,2] African Americans have a higher CRC mortality rate and a lower screening rate than whites.[1,2,25,30] Moreover, the risk of CRC is affected by whether or not someone has had a CRC screening. Screening rates are higher among women, whites, and increase with age.[8] Only about 71.3% of South Carolina's eligible population had ever received a colorectal endoscopy in 2014, which is slightly higher than the U.S. value of 69.1%.[15] Due to the potentially high costs of CRC screening, screening rates are

affected by health insurance status. Those without health insurance are less likely to receive a CRC screening and more likely to be diagnosed with CRC than those with health insurance.[9,11] Therefore, the groups most at risk for developing CRC are males, African-Americans, those of older age, and those without health insurance.

2.2 TYPES OF HIGH-RISK POLYPS

The removal of an adenomatous colonic polyp reduces the risk of death from CRC by about 53%.[7] During a colonoscopy, the performing physician removes the high-risk polyps which have the potential to develop into cancer.[7] High-risk polyps are those that are neoplastic and have the potential to become malignant.[31,32] Polyps with high grades of dysplasia, increased percentage of villous tissues, and ≥1cm in diameter are associated with an increased risk of malignancy and considered advanced adenomas.[31–33]

There are multiple types of polyps which are all classified as either neoplastic (cancerous) or non-neoplastic (non-cancerous).[31–33] Non-neoplastic polyps are those with no malignant potential, such as hyperplastic polyps, hamartomas, lymphoid aggregates, and inflammatory polyps.[31,32] The more high-risk/malignant polyps are neoplastic polyps which are classified as tubular adenomas (0-25% villous tissue), tubulovillous adenomas (25-75% villous tissue), and villous adenoma (75-100% villous tissue).[31,32] Over 95% of colorectal cancers result from these types of neoplastic adenoma polyps.[32] Recent studies have also found that sessile serrated adenomas/polyps and traditional serrated adenomas that had previously been classified as low-risk hyperplastic polyps have potential to develop into cancer and should be treated as high-risk.[34] Small hyperplastic polyps (<1 cm in diameter) are generally considered low-risk as they rarely develop into cancer.[33,34]

2.3 RISK FACTORS FOR HIGH-RISK POLYPS AND CRC

Smoking

Smoking is a risk factor for colonic polyps, adenomas, and CRC.[2,19,24,26,35,36] Cigarettes release carcinogens into the blood stream which can cause malignancies in organs throughout the body.[18] In a study by Shrubsole et al., they found a strong dose-response association for years of smoking and risk of colonic polyps. The odds ratio (OR) of smoking for 35+ years compared to those who never smoked was 5.0 (95% CI 3.3-7.3) for hyperplastic polyps, 1.9 (95% CI 1.4-2.5) for adenoma polyps, and 6.9 (95% CI 4.4-11.1) for both adenomas and hyperplastic polyps.[35]

Another study by Fu et al., found that when compared to those who never smoke, those who currently smoke ≥30 pack-years had the strongest association for adenomatous polyp risk with an OR=2.05 (95% CI 1.62-2.61), while also finding significant associations for those who currently smoke <30 pack-years and former smokers.[26] Similar to Shrubsole et al.,[35] cigarette smoking was found to be more strongly associated with hyperplastic polyps than adenomatous polyps.[26] Overall, this study found the strongest association was between developing both adenomatous polyps and hyperplastic polyps for those who currently smoke ≥30 pack-years with an OR=7.01 (95% CI 5.02-9.79).[26]

BMI

Individuals who have a body-mass index (BMI) of ≥25 kg/m^2 ("overweight" or "obese") have higher odds than those with a BMI <25 kg/m^2 of developing adenomas and advanced adenomas.[2,18,19,24,26,36,37] When compared to those of normal weight, Shapero et

al., found significant ORs for adenoma among those who are overweight (OR=1.80, 95% CI 1.06-1.83) and those who are obese (OR=1.72, 95% CI 0.99-2.99), as well as advanced adenoma for those who are obese (OR=1.8, 95% CI 1.09-2.96).[19]

Furthermore, the association between BMI and colorectal polyps has been shown to be stronger among men than women.[37] In a study by Sato et al., the OR for colorectal polyps in obese men compared to non-obese men was 1.34 (95% CI 1.17-1.54) and increased as BMI increased.[37] The OR found for obese women was 1.13 (95% CI 0.92-1.39) and also increased with BMI, but was insignificant.[37]

Physical Activity

Many studies have found that those who engage in physical activity are less likely to develop colonic polyps.[2,22,36,38] One study found that physical activity is more strongly associated with reducing the risk of advanced adenomas than the risk of non-advanced adenomas.[38] In a study by Sanchez et al.,[22] those who exercised at least one hour per week had a significantly lower polyp prevalence compared to those do did not regularly exercise for both adenomas (13.8% vs 18.9%) and any polyps (25.2% vs 33.2%). They also assessed the relationship when active individuals were classified as those who exercised at least 3 hours a week and found that they still had a lower prevalence of adenomas and advanced adenomas.[22] When long-term exercisers were compared to those who only recently began regular exercise, those who had a history of exercising 5+ years tended to have fewer adenomas than their counterpart.[22]

The protective aspects of physical activity on polyp risk have also been shown to vary based on multiple demographic factors. The Sanchez et al., study found that

African-Americans and Hispanics benefit most from physical activity's effect on polyp risk, and whites and Asians were not found to have any large beneifts.[22] Some studies have found a stronger association between physical activity and reduced risk of adenoma among men than women.[38] However, a systematic literature review and meta-analysis found that these physical activity benefits are similar among male and females, with respective relative risks of adenoma at 0.81 and 0.87.[39] Lastly, among those who are overweight or obese, individuals who engaged in physical activity were significantly less likely to have adenomas and advanced adenomas (13.5%) than those who did not exercise (20.5%).[22]

Alcohol Consumption

The effect of alcohol consumption on the risk of adenoma polyps has varied across studies.[2,27,35,36] Some studies have found that those who drink alcohol are more likely to have adenomas or hyperplastic polyps,[27,36] while others have found no significant association between the two factors.[35] One study found that those who had consumed alcohol for 30+ years had a weak and non-significant increased risk for hyperplastic polyps, and found no dose-response relationship.[35] Overall, results showed alcohol was not associated with the risk of adenoma, hyperplastic polyp, or both.[35] Other study results oppose these findings. According to Song et al., the odds of advanced adenoma among those who drink alcohol are 2.70 (95% CI 1.44-5.06) times the odds of advanced adenoma among those who do not drink alcohol.[27]

Although there is some disagreement in the association between alcohol and risk of polyps, a systematic review and meta-analysis by Zhu et al. found that most studies

have confirmed alcohol to be a significant risk factor for polyps.[40] In general, alcohol drinkers were found to have a 17% increased risk for adenoma compared to those who do not drink, and the summarized relative risk for adenoma and alcohol consumption in the U.S. was found to be 1.12 (95% CI 1.05-1.20).[40]

Race

African-Americans are more likely to develop colorectal polyps and CRC than any other racial group.[1,2,18,22] A study by Sanchez et al., found African-Americans to have the greatest incidence of all polyps, adenoma, and advanced adenoma, and also have the highest detection rate for any polyp (30.8%), adenoma (20.8%), and advanced adenoma (6.7%).[22] Whites were found to be significantly less likely to have polyps detected compared any other race.[22]

According to Grahn et al., multiple studies have found that the odds of CRC are greatest for African-Americans and lowest for Hispanics and Asian-Americans when compared to Whites. Studies have also found African-Americans to have the highest incidence rates of CRC and cancer related mortality, and an increased risk for large polyps.[18] Lastly, some have found that there are significantly more African-Americans with CRC under the age of 50 than any other race.[1,18]

Age

The likelihood of a colonic adenoma has been shown to increase as age increases.[1,2,19,24,35] According to the American Cancer Society,[2] age increases the probability of developing CRC for both males and females. The age group 70+ has the

highest probability of CRC for both males (3.4%, or 1 in 29) and females (3.1%, or 1 in 32).[2] Those of older age have also been found to have a stronger association with advanced adenomas than with non-advanced adenomas.[24]

Gender

Males are more likely to develop a colonic adenoma than females.[18,19,26,35,36] Some studies have additionally found that men develop colonic lesions at an earlier age than women do.[18] A study by Burnett-Hartman et al., found that women had a 40% (95% CI 21-55%) decrease in odds of adenoma compared to men, but that the odds of a serrated polyp was not associated with gender (OR 1.06, 95% CI 0.99, 2.44).[24]

Education

Individuals with a lower education status have an increased risk of CRC compared to those who have a higher education status.[26,35,36,41] Those with a lower education level are also more likely to have adenoma polyps, hyperplastic polyps, and a combination of these two types.[26,35] Doubeni et al. found that the incidence of CRC increases with decreasing levels of educational level. Those with less than 12 years of education had a 42% higher risk of incidence of CRC (IRR 1.42, 95% CI 1.29-1.56) when compared to those with a postgraduate education.[41]

NSAID Use

Although regular NSAID use may be a risk factor for some adverse health events such as stomach bleeding, they are a protective factor for colonic polyps.[2,26,36,42] A study

by Murff et al. found a reduced risk of adenomas in regular users of aspirin or non-aspirin NSAIDs. Using non-NSAID users as the referent group, the OR for those who used baby aspirin was 0.79 (95% CI 0.66-0.93) and was 0.60 (95% CI 0.47-0.76) for those who used a combination of NSAIDs.[36] Additionally, there was a dose-response relationship for all aspirin and non-aspirin NSAID categories and risk of adenomas.[36]

Johnson et al. also performed a similar study and found regular use of aspirin only NSAIDs protective for hyperplastic polyps, adenomas, and advanced adenomas, while regular use of ibuprofen only NSAIDs was protective only for advanced adenomas.[42] A combined use of both aspirin and ibuprofen NSAIDs was associated with a lower prevalence of all three of these types of polyps. When assessed with age and BMI, the investigators found NSAID use provided stronger protection against polyps for those who were 70-74 years old compared to those who were 55-69 years old, and also slightly more protection for those with a BMI <25 compared to those ≥25 (overweight/obese).[42]

Family History of CRC

Family history of CRC has also been associated with high-risk polyps and colorectal cancer.[2,23,38] One study by Kerber et al. defined family history as one or more first degree relative(s) that had ever had cancer of the colon, rectum, or large bowel, and found that those with this description were positively associated with colon cancer risk (OR=1.77, 95% CI 1.47-2.13).[23] They discovered the increased risk of colon cancer for those with a family history of CRC was higher among males (RR=1.95, 95% CI 1.51-2.53) than females (RR=1.60, 95%CI 1.22-2.11), and was more strongly associated with

those <67 years old (OR=1.91, 95% CI 1.43-2.54) than those ≥67 years old (OR=1.65, 95% CI 1.29-2.11).[23]

Rural/Urban Residence

Residence location (urban or rural area) has been found to have an effect on CRC risk. A study by Kinney et al. found that rural residence is associated with an increased risk of colon cancer with an OR of 1.40 (95% CI 1.1-1.8).[43] Additionally, they found that those who resided in rural areas had an increased risk of local (OR 1.40 95% CI 1.0-2.1) and regional/advanced disease (OR 1.40 95% CI 1.0-1.9) at time of diagnosis than their urban-dwelling counterparts.[43]

Additional Factors

Not only are demographic and behavioral factors influential on the detection of polyps, but the colonoscopy results can be influenced by other outside factors as well. Colonoscopy procedure quality based on the performing physician's adenoma detection rates (ADR) can impact whether or not a high-risk polyp is detected as physician's with a higher ADR may have more enhanced detection of polyps.[44] ADR has been found to be inversely associated with the risk of subsequent CRC following colonoscopy.[44] Additionally, bowel preparation during colonoscopy can have an effect on polyp detection. According to Hong, et al., the rate of missed polyps and adenomas per-patient significantly increased as the quality of bowel preparation decreased.[45] Because of these findings, it is important to consider physician level variance and bowel preparation when assessing colonoscopy results.

2.4 PREDICTORS OF POLYP COUNT

The number of colonic polyps detected during colonoscopy has been associated with the risk of CRC. A study by Debenski et al. found that cancer risk increases with the amount of polyps detected. Among patients of the same ages who received a colectomy (a surgical resection of all or part of the colon) due to familial adenomatous polyposis, those with ≥1000 polyps had 2.3 (95% CI 1.3-4.1) times the cancer risk of those with <1000 polyps.[29] Therefore, the number of polyps detected during colonoscopy procedures is important in assessing CRC risk.

Few studies have assessed any associations with number of polyps detected during colonoscopy. Some have measured the association between number of polyps found and system based factors- such as time of day the colonoscopy is performed. A study by Chan et al. found that the time of day colonoscopy is performed is associated with the number of polyps discovered. Their results showed that physicians may be more likely to detect polyps at the beginning of the day rather than later in the day.[46] Bowel preparation status has also been shown to increase the risk of missing polyps and adenomas during colonoscopy.[45,47] The results from a study by Papanikolaou et al., found that bowel preparation quality effects the number of polyps detected during colonoscopy.[47] They assessed two preparation methods: full dose (4-L of polyethylene glycol "PEG" given on previous day of procedure) and split-dose (3-L of PEG given on previous day, 1-L on same day of procedure). They found that the split-dose method provided increased bowel cleanliness and the number of polyps that were detected.[47] **Table 2.1** demonstrates the evidence found from these two mentioned studies.

To our knowledge, no studies have assessed the relationship between other individual factors (such as those listed in section 2.3) and the quantity of polyps detected during colonoscopy. Therefore, our study aims to fill this knowledge gap. Our main purpose is to assess the association between the individual factors: smoking, BMI, physical activity, alcohol, race, age, gender, education, NSAID use, family history of CRC and rural/urban location and the number of polyps detected during colonoscopy Additionally, we will assess the effect of time of day procedure occurred and bowel preparation as predictors of polyp count based on the findings of the aforementioned studies.

Table 2.1: *Evidence Table for Predictors of Polyp Count*

Main Author	Year(s)	Setting	Main Outcome	Results
Chan, Michael	2006-2007	West Los Angeles Veteran's Administration Medical Center; (Los Angeles, CA)	Polyp yield	More polyps were detected in colonoscopies that received colonoscopies earlier in the day compared to later procedures; Reduction in adenoma detection as day progresses
Papanikolaou, Ioannis	2012	Attikon University General Hospital; (Athens, Greece)	Difference between number of polyps detected during colonoscopies prepared by split-dose bowel preparation and previous dose preparation	Split-dose bowel preparation significantly associated with an increased number of polyps detected; split-dose preparation improves colon cleansing and enhances polyp detection

CHAPTER 3

METHODS

3.1 STUDY POPULATION AND DATA SOURCE

We performed a secondary analysis on data obtained from the Center for Colon Cancer Research's (CCCR) Colorectal Cancer Prevention Network (CCPN) at the University of South Carolina. The program provides free colonoscopy screenings to those who are uninsured in South Carolina. All CCPN patients included within this study were those whose colonoscopies took place between May 2014 and May 2017.

To be eligible to participate in the CCPN program, participants must be between 50-64 years old (45-64 for African Americans), live at or below 150% of the poverty line, be asymptomatic of colorectal cancer, and pursuing medical care at participating free medical clinics, federally qualified health centers, or hospital indigent practices in SC. All CCPN screenings are performed by board-certified gastroenterologists.[28] Patients were excluded from the program if they had a previous colonoscopy within the past 10 years, had recent onset of CRC symptoms, a diagnosis of inherited CRC disorder, or a history of gastrointestinal disease or a cancer other than a non-melanoma skin cancer.[28]

Data on each individual's demographic, personal and family medical history, and behavioral factors was collected through an in-person interview 5-10 days before their colonoscopy procedure. During this time, the participants were also instructed on the process of colonoscopy and the colonic preparation process. After the colonoscopy, endoscopy and pathology report data are then stored in the same database which captured

all other patient information. All data are collected and managed in a HIPAA-compliant, cloud-based system by the CCPN navigators and staff.[28]

3.2 OUTCOME ASSESSMENT

Our main outcome of interest was the number of polyps found during colonoscopy which was treated as any type of polyp removed from colonoscopy and assessed as a count variable. Biopsies with a pathology report indicating the removed lesion as a carcinoid/cancerous were excluded from the study since we're assessing polyps that were removed in order to potentially prevent cancer. A lesion was considered a polyp if initially indicated by the physician at time of removal via the endoscopy report, rather than by pathologic examination outcome.

We first assessed the polyp detection rate (PDR) defined as the percentage of patients that underwent colonoscopy who had at least one polyp removed. We then calculated the mean, median, and max number of polyps for all polyps removed overall and by type of polyp removed. Type of polyp was classified as either: "low-risk polyp" (hyperplastic polyps <1cm in diameter and non-advanced polyps <1cm in diameter), or "high-risk polyp" (advanced polyps ≥1cm in diameter including hyperplastic, traditional serrated, sessile serrated, or any polyp with villous components and/ or high-grade dysplasia).[28,31,33,34] Furthermore, polyps which had pathology reports indicating inflammation or normal colonic mucosa were classified as low-risk. Patients that did not have a pathology report or were missing pathology information on lesion classification were excluded.

3.3 INDEPENDENT VARIABLES

Our independent variables included gender (male or female), race (Caucasian/white, African-American/black, or other), age (45-49, 50-54, 55-59, and 60-64 year olds), smokers (current, former, or non-smoker), alcohol consumption (heavy, moderate, or light/non-drinker), BMI (normal/underweight, overweight, or obese), residence location (rural/urban), family history of CRC (yes/no), highest educational level obtained (less than high school, high school diploma/GED, some college, or college degree). Family history of CRC was "yes" if at least one first-degree relative (mother, father, or sibling) had ever been diagnosed with CRC. Rural or urban status of residence location was categorized by the 2010 Rural-Urban Commuting Area (RUCA) U.S. census classification of the zip-code for which the participant resided at the time of enrollment in the CCPN program (in-person navigation appointment). Since the 45-49 age group only consisted of African-Americans, our reference group for age was 60-64. All other reference groups for these independent variables were those which research has shown to be the least at-risk for developing polyps: females, Caucasians, non-smokers, light/non-drinkers, normal/underweight BMI, urban residents, no family history of CRC, and college degree.

NSAID use was based on each participant's response to the amount of NSAIDs/Aspirin they took per week over the four months previous to their procedure. We categorized NSAID use into either "Never" take NSAIDs if never take them, "Occasionally" if they reported taking them either <1/week or <1/month, "1-3 days/week", "4-6 days/week", and "7 days/week". Since taking NSAIDs is considered a protective factor for CRC, we used the "7 days/week" category as our reference group.

Physical activity was assessed based on the number of days within the week prior to procedure which the participant engaged in vigorous physical activity for at least 10 minutes. The numbers of days were categorized into "0 days/week", "1-3 days/week", or "4-7 days/week". Since frequent exercisers are considered the most low-risk physical activity group, we used the "4-7 days/week" category as our reference group.

In accordance to CDC guidelines, smoking status was categorized for cigarette, pipe, cigar, and smokeless tobacco use based on each individual's current smoking status, whether they had smoked at least 100 units (of cigarettes, etc.) within their lifetime, and if they have smoked on a regular basis for more than a year.[48] Non-smokers were classified as those which had smoked less than 100 units in their lifetime. Current smokers were those which reported that they currently smoke. Former smokers were individuals who did not report smoking currently, have smoked at least 100 units in their lifetime, and/or smoked regularly for at least a year.

Alcohol use was defined by the number of drinks an individual had per week for all alcohol types (beer, wine, malt liquor, hard liquor/mixed drinks/shots/cocktails). In accordance with NIAAA guidelines,[49] alcohol use was categorized into either "heavy drinker," "moderate drinker," or "light/non-drinker" and took into account gender. For males: heavy drinkers consumed at least 14.5 drinks/week, moderate drinkers consumed >1 and <14.5 drinks/week, and light/non-drinkers consumed 1 or less drinks/week. For females: heavy drinkers consumed at least 7.5 drinks/week, moderate drinkers consumed >1 and <7.5 drinks/week, and light/non-drinkers consumed 1 or less drinks/week.

BMI measurements were expressed as kg/m^2 and defined in accordance with the World Health Organization (WHO) guidelines where <18.5 is "Underweight," 18.5-

24.99 “Normal,” 25-29.99 “Overweight,” and ≥30.0 “Obese.”[50] Normal and underweight BMI’s were combined into the category “Normal/underweight.” BMI was calculated by study investigators prior to our secondary analysis.

Since bowel preparation has been shown to affect our outcome of interest, we also included this variable in our analysis. The performing physician rated each individual’s preparation quality as either (1) “excellent” (REX scale D, only scattered, tiny particles and/or clear liquid, 100% visualization possible throughout colon), (2) “good” (REX scale C, “adequate”, easily removable small amounts of particles and/or liquid, very unlikely to impair visualization), (3) “fair” (REX scale B, residual feces and/or non-transparent fluid, possible impairing visualization), (4) “poor” (REX scale A, feces and/or non-transparent fluid, definitely impairing visualization), or (5) “other.” Bowel preparation quality was categorized into “Excellent/Good” for those which were rated excellent or good, and “Fair/Poor” for those which were considered fair or poor. Colonoscopies which were documented as “Other” or did not have bowel preparation quality documented were excluded from the study.

Procedure time was based on procedure start time and categorized as: before 10:00am, 10:00am-2:00pm, and after 2:00pm. Since previous studies have found the morning procedures to be the most successful at detecting polyps, the before 10:00am category served as our reference group.

3.5 ANALYSIS

We first described the characteristics of our study participants for each of our independent variables. Since all of our variables are categorical, we described them as the

total number and percentage. Next, we calculated the PDR as the proportion of colonoscopies which resulted in the removal of one or more polyps. To test for differences in PDR between independent variable categories, we performed a chi-squared analysis. P-values were compared to $\alpha=0.05$. We also described the number and percentage of colonoscopies which resulted in no polyps removed. Additionally, we described the mean, median, and max number of polyps overall and by risk type (low- and high-risk) for each independent variable.

We performed a univariate negative binomial regression analysis to assess the relationship between total number of polyps detected and each independent variable by itself. We then performed a multivariable negative binomial regression to assess the association between the number of polyps detected and all of our independent variables together. We repeated these univariate and multivariable negative binomial regression analyses for number of high-risk polyps detected. For all regression analyses, we calculated the rate ratio (RR) and 95% confidence intervals (95% CI). Finally, we tested for interaction in both multivariable models among variables which research showed may interact (BMI and gender; BMI and race; physical activity and gender; physical activity and race; NSAIDs and age; NSAIDs and BMI; family history of CRC and gender; family history of CRC and age). We first assessed the significance of these interaction terms individually within the multivariable model that contained all independent variables. Interaction terms that had a significant individual p-value ($\alpha=0.05$) were all initially added into the multivariable model together, and then the remaining significant interaction terms were included within our final model. All analyses were performed using SAS software version 9.4. The study was approved by the University of South

Carolina Institutional Review Board, and data usage approved by the CCSR Advisory Committee.

CHAPTER 4

RESULTS

4.1 SAMPLE CHARACTERISTICS

There were a total of 1,541 colonoscopies performed by the CCPN between May 2014 and May 2017. We then excluded patients who did not give consent to participate in the research data registry, whose colonoscopy procedure report was still pending, had an incomplete/aborted colonoscopy, had only cancerous/carcinoid lesions removed, had no pathology reports or missing pathology information, and individuals missing information on our independent variables (n=551). Our final sample consisted of 990 individuals. Additional details on sample inclusion are demonstrated in **Figure 4.1**. The independent variable categories with the highest proportions in our sample, as described in **Table 4.1,** were individuals aged 50-54 (44.75%), African-Americans (52.73%), females (60.81%), current smokers (40.10%), urban area residents (84.75%), light/non-drinkers (68.38%), zero days/week exercisers (74.44%), had no family history of CRC (91.11%), high school diploma/GED (42.22%), excellent/good bowel preparation quality (90.61%), had a scheduled endoscopy procedure time between 10:00am and 2:00pm (40.01%), obese (50.30%), and never took NSAIDs in the four months prior to procedure (42.53%).

4.2 POLYP DETECTION RATE

The overall PDR was 61.82% (**Table 4.1)**. Results from our chi-squared test of independence showed a significantly higher PDR in males than females (p=<.0001),

urban residents than rural residents (p=0.0029), and those with a family history of CRC than those without (p=0.0481). The age group with the highest PDR were those aged 55-59 years, and the lowest were those aged 50-54 (p=0.0444). For the smoking category, current smokers had the highest PDR and non-smokers had the lowest (p=<.0001). Heavy drinkers were the most likely to have a polyp detected while non/light drinkers were the least likely (p=0.0117). No significant differences in PDR were found between race, physical activity, education, bowel preparation quality, procedure time, BMI, or NSAID use.

4.3 MEAN, MEDIAN, AND MAX OF NUMBER OF POLYPS

The total respective mean, median, and max of number of polyps removed were 1.65, 1.00, and 15 for all polyps, 1.34, 1.00, and 13 for low-risk polyps, and 0.31, 0, and 13 for high-risk polyps (**Table 4.2**). The category with the highest mean number of all polyps and high-risk polyps, respectively, removed for each independent variable were: "other" race, males, current smokers, urban residents, family history of CRC, less than a high school education, and having a procedure time before 10:00am. Those who were 55-59 years old had the highest mean all polyps while 60-64 year old's had the highest mean of high-risk. Individuals who exercised 4-7 days/week had the highest mean for all polyps and zero days/week had the highest mean for high-risk. Overweight individuals had the highest mean for all polyps, and normal/underweight individuals had the highest mean for high-risk polyps. Highest mean for all polyps for NSAID use was among those who never took them, and among 1-3 days/week users for high-risk polyps. Patients who had excellent/good bowel preparation quality had a higher mean number of high-risk

polyps removed, but the mean for fair/poor preparation was higher for all polyps. Both moderate and heavy drinkers had the highest mean number of high-risk polyps, but only heavy drinkers had the highest mean for all polyps.

4.4 REGRESSION ANALYSIS FOR NUMBER OF ALL POLYPS

For our multivariable model, we performed a negative binomial regression analysis instead of a Poisson regression analysis as the deviance test showed a better fit for our data. We found significant rate ratios for gender, smoking, rural/urban residence, alcohol use, family history of CRC, BMI, and NSAIDs. Since our multivariable model contained all independent variables, findings for each variable were adjusted for all other variables. The rate of polyps detected for males is 1.26 times the rate of polyps detected among females (95% CI 1.07-1.48). Current smokers (RR=2.04, 95% CI 1.70-2.44) and former smokers (RR=1.57, 95% CI 1.28-1.94) both had significantly higher rate ratios when compared to non-smokers. The rate of polyps detected among rural residents is 0.62 times the rate of polyps among urban residents (95% CI 0.50-0.78). Moderate drinkers had a significantly higher rate ratio when compared to non/light drinkers (RR=1.22, 95% CI 1.02-1.46), but no difference was found between heavy and non/light drinkers. The rate of polyps among individuals with a family history of CRC was 1.34 times the rate of polyps among individuals with no family history of CRC (95% CI 1.04-1.74). When compared to normal/underweight individuals, obese individuals had a significantly higher rate ratio (RR=1.35, 95% CI 1.09-1.67), but no difference was detected between overweight and normal/underweight individuals. Lastly, the rate of polyps for those who never take NSAIDs was 1.40 times the rate of polyps for those who

take NSAIDs 7 days/week (95% CI 1.15-1.71). No significant associations were found between number of polyps and age, education, bowel preparation, or procedure time.

When testing for interaction within the multivariable analysis, we found a significant interaction between physical activity and race. In terms of race: among individuals who exercised 4-7 days/week, African-Americans had a mean number of polyps about 49% lower than whites (RR=0.51, 95% CI 0.33-0.79) (**Table 4.4)**. In terms of physical activity: among African-Americans, individuals who exercised zero days/week had a mean number of polyps about 49% higher than individuals who exercised 4-7 days/week (RR=1.49, 95% CI 1.04-2.11) (**Table 4.5**). No evidence of interaction was found among any other variables.

4.5 REGRESSION ANALYSIS FOR NUMBER OF HIGH-RISK POLYPS

We also performed a negative binomial regression analysis for high-risk polyp number since it better predicted the probability of detecting the large amount of zero high-risk polyps in our model than Poisson regression. Since no high-risk polyps were detected for individuals aged 45-49, we excluded this age group from our regression analysis assessing number of high-risk polyps (n=45). Therefore, our total sample size for this analysis was n=945. We found significant associations between number of high-risk polyps with gender, smoking, procedure time, and NSAIDs. Since our multivariable model contained all independent variables, findings for each variable were adjusted for all other variables. The rate of polyps removed for males were 1.82 times the rate of polyps removed for females (95% CI 1.15-2.89). The rate of polyps removed for current smokers is 2.53 times the rate for number of polyps removed among non-smokers (95%

CI 1.48-4.32). No difference was detected when comparing former smokers to non-smokers. The rate of polyps removed for procedure times that occurred after 2:00pm was 0.52 times the rate of polyps removed for procedures which took place before 10:00am (95% CI 0.29-0.94). Lastly, significant associations were found when individuals who took NSAIDs every day were compared to individuals who took them 1-3 days/week (RR=2.93, 95% CI 1.40-6.12), occasionally (RR=2.02, 95% CI 1.01-4.05), and never took them (RR=1.86, 95% CI 1.04-3.34). No significant associations were found between number of high-risk polyps and age, race, rural/urban location, alcohol, physical activity, family history of CRC, education, bowel preparation, or BMI. Additionally, no significant interaction between independent variables was found.

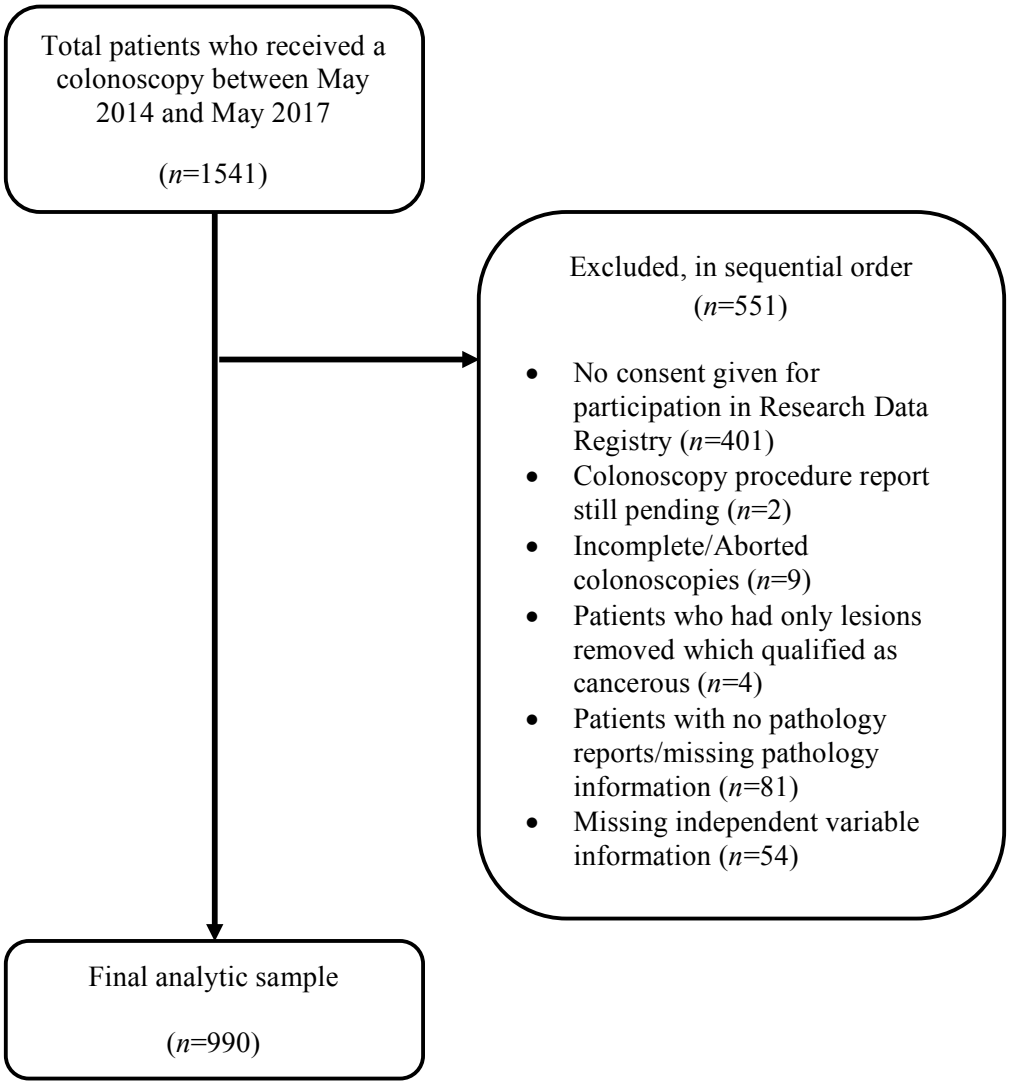

Figure 4.1: *Flow Diagram of Sample Inclusion*

Table 4.1: *PDR by Sample Characteristics, May 2014-May 2017*

Characteristics		*No Polyps Removed*	*≥ 1 Polyp Removed (PDR)*	*P-value*[a]
	N%	**n (%)**	**n (%)**	
Total	990	378 (38.18)	612 (61.82)	
Age[b]				***0.0444***
45-49	45 (4.55)[c]	19 (42.22)	26 (57.78)	
50-54	443 (44.75)	189 (42.66)	254 (57.34)	
55-59	307 (31.01)	103 (33.55)	204 (66.45)	
60-64	195 (19.70)	67 (34.36)	128 (65.64)	
Race				*0.2505*
Caucasian	443 (44.75)	157 (35.44)	286 (64.56)	
African-American	522 (52.73)	212 (40.61)	310 (59.39)	
Other	25 (2.53)	9 (36.00)	16 (64.00)	
Gender				***<.0001***
Female	602 (60.81)	259 (43.02)	343 (56.98)	
Male	388 (39.19)	119 (30.67)	269 (69.33)	
Smoking Status				***<.0001***
Non-Smoker	389 (39.29)	192 (49.36)	197 (50.64)	
Former	204 (20.61)	76 (37.25)	128 (62.75)	
Current	397 (40.10)	110 (27.71)	287 (72.29)	
Location				***0.0029***
Urban	839 (84.75)	304 (36.23)	535 (63.77)	
Rural	151 (15.25)	74 (49.01)	77 (50.99)	
Alcohol Use				***0.0117***
Non-Drinker/Light	677 (68.38)	278 (41.06)	399 (58.94)	
Moderate	264 (26.67)	88 (33.33)	176 (66.67)	
Heavy	49 (4.95)	12 (24.49)	37 (75.51)	
Physical Activity				*0.5514*
4-7 days/week	110 (11.11)	38 (34.55)	72 (65.45)	
1-3 days/week	143 (14.44)	59 (41.26)	84 (58.74)	
0 days/week	737 (74.44)	281 (38.13)	456 (61.87)	
Family History				***0.0481***
No	902 (91.11)	353 (39.14)	549 (60.86)	
Yes	88 (8.89)	25 (28.41)	63 (71.59)	
Education				*0.3417*
College Degree	136 (13.74)	57 (41.91)	79 (58.09)	
Some College	186 (18.79)	72 (38.71)	114 (61.29)	
HS Diploma/GED	418 (42.22)	165 (39.47)	253 (60.53)	
Less than HS	250 (25.25)	84 (33.60)	166 (66.40)	
Bowel Preparation				*0.4338*
Excellent/Good	897 (90.61)	339 (37.79)	558 (62.21)	
Fair/Poor	93 (9.39)	39 (41.94)	54 (58.06)	
Procedure Time				*0.7472*
Before 10:00am	244 (24.65)	98 (40.16)	146 (59.84)	
10:00am-2:00pm	406 (41.01)	151 (37.19)	255 (62.81)	
After 2:00pm	340 (34.34)	129 (37.94)	211 (62.06)	
BMI				*0.3299*
Normal/Underweight	190 (19.19)	66 (34.74)	124 (65.26)	
Overweight	302 (30.51)	111 (36.75)	191 (63.25)	
Obese	498 (50.30)	201 (40.36)	297 (59.64)	
NSAID Use				*0.1115*
Every Day	213 (21.52)	85 (39.91)	128 (60.09)	
4-6 days/ week	43 (4.34)	13 (30.23)	30 (69.77)	

1-3 days/week	137 (13.84)	49 (35.77)	88 (64.23)
Occasionally	176 (17.78)	81 (46.02)	95 (53.98)
Never	421 (42.53)	150 (35.63)	271 (64.37)

[a]P-values were calculated from a chi-square test and compare each patient characteristic (rows) to the outcomes (columns); [b]Age at inclusion; age group 45-49 includes African-American participants only; [c]all percentages rounded to two decimal points which may impact total percentage equaling 100%

Table 4.2: *Mean, Median, and Max of Polyp Count Overall and by Type*

Characteristics	*All Polyps*	*Low-Risk Polyps*[a]	*High-Risk Polyps*
	Mean[b]**, Median (Max)**	**Mean, Median (Max)**	**Mean, Median (Max)**
Total	1.65, 1.00 (15)	1.34, 1.00 (13)	0.31, 0 (13)
Age[c]			
45-49	1.29, 1.00 (8)	1.29, 1.00 (8)	0, 0 (0)[d]
50-54	1.54, 1.00 (15)	1.23, 0 (12)	0.31, 0 (13)
55-59	1.81, 1.00 (13)	1.49, 1.00 (13)	0.33, 0 (7)
60-64	1.72, 1.00 (11)	1.35, 1.00 (10)	0.36, 0 (8)
Race			
Caucasian	1.74, 1.00 (15)	1.39, 1.00 (13)	0.35, 0 (13)
African-American	1.55, 1.00 (13)	1.29, 1.00 (12)	0.27, 0 (13)
Other	2.00, 1.00 (12)	1.40, 1.00 (9)	0.60, 0 (5)
Gender			
Female	1.44, 1.00 (12)	1.23, 1.00 (12)	0.22, 0 (8)
Male	1.97, 1.00 (15)	1.51, 1.00 (13)	0.46, 0 (13)
Smoking Status			
Non-Smoker	1.08, 1.00 (12)	0.92, 0 (10)	0.16, 0 (6)
Former	1.75, 1.00 (13)	1.46, 1.00 (13)	0.30, 0 (7)
Current	2.15, 2.00 (15)	1.68, 1.00 (11)	0.47, 0 (13)
Location			
Urban	1.73, 1.00 (15)	1.41, 1.00 (13)	0.32, 0 (13)
Rural	1.20, 1.00 (10)	0.93, 0 (8)	0.27, 0 (4)
Alcohol Use			
Non-Drinker/Light	1.51, 1.00 (13)	1.24, 1.00 (13)	0.27, 0 (8)
Moderate	1.95, 1.00 (15)	1.55, 1.00 (11)	0.41, 0 (13)
Heavy	1.96, 2.00 (9)	1.55, 1.00 (9)	0.41, 0 (4)
Physical Activity			
4-7 days/week	1.93, 1.00 (13)	1.65, 1.00 (13)	0.28, 0 (4)
1-3 days/week	1.37, 1.00 (12)	1.16, 0 (12)	0.21, 0 (4)
0 days/week	1.66, 1.00 (15)	1.32, 1.00 (11)	0.34, 0 (13)
Family History			
No	1.61, 1.00 (15)	1.30, 1.00 (13)	0.30, 0 (13)
Yes	2.07, 1.00 (10)	1.67, 1.00 (8)	0.40, 0 (6)
Education			
College Degree	1.50, 1.00 (13)	1.31, 0 (13)	0.19, 0 (2)
Some College	1.58, 1.00 (12)	1.29, 1.00 (12)	0.29, 0 (8)
HS Diploma/GED	1.61, 1.00 (13)	1.35, 1.00 (9)	0.26, 0 (13)
Less than HS	1.84, 1.00 (15)	1.36, 1.00 (11)	0.48, 0 (13)
Bowel Preparation			
Excellent/Good	1.64, 1.00 (15)	1.32, 1.00 (13)	0.32, 0 (13)
Fair/Poor	1.72, 1.00 (11)	1.45, 1.00 (10)	0.27, 0 (6)
Procedure Time			
Before 10:00am	1.72, 1.00 (15)	1.32, 1.00 (9)	0.40, 0 (13)
10:00am-2:00pm	1.67, 1.00 (12)	1.34, 1.00 (12)	0.33, 0 (8)
After 2:00pm	1.57, 1.00 (13)	1.34, 1.00 (13)	0.23, 0 (7)
BMI			
Normal/Underweight	1.66, 1.00 (13)	1.28, 1.00 (13)	0.38, 0 (13)
Overweight	1.70, 1.00 (10)	1.37, 1.00 (9)	0.33, 0 (8)
Obese	1.61, 1.00 (15)	1.34, 1.00 (12)	0.28, 0 (13)
NSAID Use			
Every Day	1.38, 1.00 (11)	1.19, 1.00 (9)	0.19, 0 (6)
4-6 days/ week	1.65, 1.00 (9)	1.35, 1.00 (6)	0.30, 0 (6)

1-3 days/week	1.74, 1.00 (10)	1.34, 1.00 (10)	0.39, 0 (6)
Occasionally	1.40, 1.00 (13)	1.10, 0 (13)	0.30, 0 (6)
Never	1.86, 1.00 (15)	1.50, 1.00 (12)	0.36, 0 (13)

[a]Low-risk polyp group contains polyps classified as inflammation or normal colonic mucosa; [b]Some low-risk and high-risk polyp means do not sum to their respective all polyp mean due to rounding; [c]Age at inclusion; age group 45-49 includes African-American participants only; [d]No high-risk polyps were found among those aged 45-49

Table 4.3: *Negative Binomial Regression for Number of Polyps (Overall & High-Risk)*

	All Polyps (n=990)				***High-Risk Polyps (n=945)[b]***			
	Univariate		*Multivariable[a]*		*Univariate*		*Multivariable*	
Characteristic	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**
Age								
45-49	0.75	(0.49, 1.14)	0.84	(0.56, 1.27)	*NA*	*NA*	*NA*	*NA*
50-54	0.90	(0.73, 1.11)	0.88	(0.72, 1.07)	0.86	(0.50, 1.48)	0.62	(0.36, 1.07)
55-59	1.05	(0.84, 1.32)	1.04	(0.84, 1.28)	0.89	(0.50, 1.60)	0.71	(0.40, 1.24)
60-64	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
Race								
Caucasian	*REF*	*NA*	*NA[c]*	*NA*	*REF*	*NA*	*REF*	*NA*
African-American	0.89	(0.76, 1.05)	*NA*	*NA*	0.84	(0.55, 1.28)	0.72	(0.46, 1.12)
Other	1.15	(0.71, 1.87)	*NA*	*NA*	1.71	(0.50, 5.82)	2.64	(0.79, 8.79)
Gender								
Female	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
Male	1.36	**(1.16, 1.59)**	1.26	**(1.07, 1.48)**	2.13	**(1.41, 3.22)**	1.82	**(1.15, 2.89)**
Smoking Status								
Non-Smoker	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
Former	1.62	**(1.31, 2.00)**	1.57	**(1.28, 1.94)**	1.79	**(1.01, 3.18)**	1.60	(0.88, 2.91)
Current	1.99	**(1.67, 2.36)**	2.04	**(1.70, 2.44)**	2.78	**(1.74, 4.44)**	2.53	**(1.48, 4.32)**
Location								
Urban	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
Rural	0.69	**(0.55, 0.87)**	0.62	**(0.50, 0.78)**	0.81	(0.45, 1.46)	0.68	(0.36, 1.25)
Alcohol Use								
Non-Drinker/Light	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
Moderate	1.29	**(1.09, 1.54)**	1.22	**(1.02, 1.46)**	1.52	(0.96, 2.41)	1.24	(0.73, 2.11)
Heavy	1.30	(0.91, 1.85)	1.17	(0.83, 1.64)	1.58	(0.62, 4.05)	1.23	(0.48, 3.20)
Physical Activity								
4-7 days/week	*REF*	*NA*	*NA[c]*	*NA*	*REF*	*NA*	*REF*	*NA*
1-3 days/week	0.71	**(0.52, 0.97)**	*NA*	*NA*	0.76	(0.32, 1.79)	0.85	(0.36, 2.03)
0 days/week	0.86	(0.67, 1.10)	*NA*	*NA*	1.19	(0.61, 2.34)	1.79	(0.88, 3.66)
Family History								
No	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
Yes	1.29	(0.99, 1.68)	1.34	**(1.04, 1.74)**	1.29	(0.64, 2.61)	1.33	(0.64, 2.77)
Education								

College Degree	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
Some College	1.05	(0.80, 1.40)	0.85	(0.65, 1.12)	1.49	(0.70, 3.20)	1.18	(0.54, 2.57)
HS Diploma/GED	1.07	(0.84, 1.37)	0.90	(0.71, 1.15)	1.42	(0.72, 2.81)	1.16	(0.58, 2.32)
Less than HS	1.23	(0.95, 1.60)	0.95	(0.74, 1.24)	2.50	**(1.23, 5.08)**	1.77	(0.84, 3.71)
Bowel Preparation								
Excellent/Good	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
Fair/Poor	1.05	(0.80, 1.37)	1.05	(0.82, 1.36)	0.82	(0.40, 1.69)	1.01	(0.49, 2.10)
Procedure Time								
Before 10:00am	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
10:00am-2:00pm	0.97	(0.80, 1.19)	0.98	(0.81, 1.19)	0.83	(0.50, 1.38)	0.88	(0.52, 1.49)
After 2:00pm	0.91	(0.74, 1.12)	0.88	(0.72, 1.09)	0.59	(0.34, 1.02)	0.52	**(0.29, 0.94)**
BMI								
Normal/Underweight	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
Overweight	1.02	(0.82, 1.29)	1.24	(1.00, 1.56)	0.90	(0.50, 1.62)	1.34	(0.71, 2.52)
Obese	0.97	(0.79, 1.20)	1.35	**(1.09, 1.67)**	0.75	(0.43, 1.29)	1.30	(0.70, 2.43)
NSAID Use								
Every Day	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*	*REF*	*NA*
4-6 days/ week	1.19	(0.79, 1.80)	1.21	(0.82, 1.79)	1.54	(0.52, 4.60)	1.24	(0.40, 3.85)
1-3 days/week	1.25	(0.96, 1.64)	1.28	(0.99, 1.66)	2.07	**(1.01, 4.25)**	2.93	**(1.40, 6.12)**
Occasionally	1.01	(0.78, 1.31)	1.07	(0.84, 1.38)	1.54	(0.77, 3.06)	2.02	**(1.01, 4.05)**
Never	1.34	**(1.09, 1.65)**	1.40	**(1.15, 1.71)**	1.86	**(1.05, 3.30)**	1.86	**(1.04, 3.34)**

[a]Multivariable analysis for all polyps includes all independent variables and an interaction term for race and physical activity; [b]Individuals aged 45-49 were removed from our number of high-risk polyps analyses (n=45) due to no high-risk polyps being detected among this group- all independent variables included in analysis; [c]Since race and physical activity had significant interaction, the rate ratios for these variables are reported in subsequent tables

Table 4.4: *Rate Ratios for Number of All Polyps for Race by Physical Activity*

	Race					
	African-American		Other		White	
Physical Activity	**RR[a]**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**
0 days/week	1.02	(0.85, 1.22)	1.63	(0.94, 2.83)	*REF*	*NA*
1-3 days/week	0.92	(0.60, 1.40)	0.31	(0.06, 1.63)	*REF*	*NA*
4-7 days/week	0.51	**(0.33, 0.79)**	1.35	(0.46, 3.94)	*REF*	*NA*

[a]Rate ratios in these analyses compare the mean number of polyps removed

Table 4.5: *Rate Ratios for Number of All Polyps for Physical Activity by Race*

	Physical Activity					
	0 days/week		1-3 days/week		4-7 days/week	
Race	**RR[a]**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**
African-American	1.49	**(1.04, 2.11)**	1.19	(0.78, 1.81)	*REF*	*NA*
Other	0.90	(0.28, 2.88)	0.15	(0.02, 1.03)	*REF*	*NA*
White	0.74	(0.53, 1.04)	0.66	(0.42, 1.02)	*REF*	*NA*

[a]Rate ratios in these analyses compare the mean number of polyps removed

CHAPTER 5

DISCUSSION

5.1 KEY FINDINGS

The overall PDR found within this study (61.82%) is comparable to that found in the earlier CCPN study of May 2014-May 2016 patients (62.71%).[28] A previous study found a 37% PDR among uninsured individuals in New York.[51] To compare these numbers to insured individuals, the PDR in a national study among Medicare beneficiaries varied between 23.9% and 35.7% depending on the specificity of polyp definition.[52] Our higher PDR findings are likely due to 90.61% of our sample having good-to-excellent bowel preparation, having all procedures performed by board-certified gastroenterologists, and the distribution of individual characteristics in our SC sample. Our chi-squared analysis found significant differences in PDR among age, gender, smoking status, rural/urban residence, alcohol use, and family history of CRC.

Our multivariable negative binomial regression model showed significant associations between number of all polyps and gender, smoking, rural/urban residence, alcohol, family history of CRC, BMI, and NSAIDs. Additionally, significant interaction was found between race and physical activity. Our multivariable negative binomial model for high-risk polyps only found significant associations for gender, smoking, procedure time, and NSAIDs. No other significant associations were found in either model.

Age

Since previous literature has demonstrated that the risk for polyps increases with age,[1,2,19,24,35] we expected our PDR, and number of polyps to be highest among the 60-64 age group. Although the highest mean number of high-risk polyps was amongst this age group, the remaining results were highest among the 55-59 age group. However, the 60-64 age group still had higher results when compared to the two younger age groups. All regression models found age to be non-significant.

Race

Our results for race were not as expected since previous literature has found African-Americans more at risk for colonic polyps compared to all other races.[1,2,18,22] Our mean number of polyps found for all types were highest for other races and lowest for African-Americans. Furthermore, race was only significant in our all polyps model among individuals that exercised 4-7 days/week (RR=0.51, 95% CI 0.33-0.79), suggesting that African-Americans who exercise 4-7 days/week have a protective effect to number of polyps when compared to whites who exercise 4-7 days/week. Despite African-Americans being a high-risk group for colonic polyp development, this finding is only among those who frequently exercise; therefore, these individuals are likely of better health than other African-Americans who do not exercise as frequently. These findings further emphasize the results in a previous study which found African-Americans to be one of the racial/ethnic groups that benefit most from frequent exercise.[22] Further- race was insignificant elsewhere in our models which aligns with findings in the previous CCPN study.[28] Since our sample consisted of uninsured and poor individuals, race may

not be as significant within our study since socioeconomic status could be a proxy between race and polyp detection.

Gender

Previous literature has found the risk of polyps, and specifically high-risk polyps, to be higher among males than females.[18,19,26,35,36] Therefore, our results for gender were as expected as we also found males to have a significantly higher PDR, and a higher mean and max number of polyps. Both of our multivariable regression models also agree with previous findings as males were found to have a higher rate of polyps removed than females in our model of all polyps removed (RR=1.26, 95% CI 1.07-1.48) and in our model for high-risk polyps (RR=1.82, 95% CI 1.15-2.89).

Smoking

Our results for smoking status also reinforce findings from previous studies.[18,19,24,26,28,35,36] Current smokers had the largest PDR while non-smokers had the smallest PDR. This trend is further demonstrated by the mean number of overall, low-risk, and high-risk polyps found. Our regression models found that compared to non-smokers, both current (RR=2.04, 95% CI 1.70-2.44) and former smokers (RR=1.57, 95% CI 1.28-1.94) had a higher rate of overall polyps removed. For high-risk polyps, current smokers (RR=2.53, 95% CI 1.48-4.32) had higher rates of high-risk polyps removed when compared to non-smokers.

Urban/Rural Residence

Our findings for urban/rural residents were not expected based on previous literature that has shown rural residents more at risk for the development of CRC than urban residents.[43] However, a previous study on May 2014-May 2016 CCPN patients also found a higher PDR among urban residents compared to rural residents.[28] In addition, our multivariable model for number of all polyps removed found living in a rural area to be protective against number of polyps (RR= 0.62, 95% CI 0.50-0.78). These unexpected results may be due to the difference in quality of performance for the physician. However, we were unable to acquire this data in order to test any random effect from the performing physician. These results may also be due to most CCPN recruiting facilities being within urban areas, so the rural patients in our sample are those who were seeking healthcare which could potentially mean they have better health behaviors.

Alcohol Use

Previous studies have shown conflicting results on the relationship between alcohol use and polyp detection.[2,27,35,36,40] Our results found that heavy drinkers had the highest PDR while non-drinkers had the lowest PDR. This was also the case for mean number of overall polyps, low-risk polyps, and high-risk polyps. Our multivariable regression models found only moderate drinkers to be significantly associated with number of all polyps removed (RR=1.22, 95% CI 1.02-1.46) when compared to non-drinkers. No significant associations were found for heavy drinkers in either analysis, or for any category of alcohol use with high-risk polyps.

Physical Activity

Our findings for physical activity were unexpected since previous literature has shown frequent physical activity as a protective factor against colonic polyps.[22,28,36,38,39] In our study, individuals who reported exercising at least 4 days/week had the highest mean number of all polyps and low-risk polyps. These unexpected results could be explained by the fact that physical activity was assessed as how many days of vigorous activity the patient engaged in within the week prior to colonoscopy. Therefore, physical activity levels may not accurately reflect each patient's regular exercise habits. Additionally, there could be an inaccuracy within participant responses since they may not consider occupational or leisure activities that qualify as vigorous activity as such.

Within our multivariable analysis for number of all polyps, physical activity was found only significant among African-Americans who exercised zero days/week compared to African-Americans who exercised 4-7 days/week (RR=1.49, 95% CI 1.04-2.11). These findings support previous literature that African-Americans benefit more from the protective effects of physical activity on the detection of polyps than do whites.[22]

Family History of CRC

Family history of CRC has been strongly associated with an increased risk of CRC and colonic polyps.[2,23,38] Our results further reflect these findings as we found a significantly higher PDR for those with family history of CRC than those who did not have it. Additionally, our multivariable regression model found individuals with a family history of CRC to have a higher rate of all polyps removed (RR=1.34, 95% CI 1.04-1.74)

when compared to those with no family history of CRC. Family history was not significant in predicting number of high-risk polyps.

Education

We were unable to find any significant differences in PDR between education levels as previous studies have suggested.[26,35,36,41] Although, our univariate analysis found that those with less than a high school education had a higher rate of high-risk polyps detected than those who had a college degree (RR=2.50, 95% CI 1.23-5.08). However, when adjusting for all other independent variables, our multivariable regression model found education non-significant in predicting number of high-risk polyps. Education was not significant for either analysis assessing number of all polyps.

Bowel Preparation Quality

Our mean number of all polyps and low-risk polyps were the highest among those with fair/poor bowel preparation quality. These results were not expected since good-to-excellent quality provides more clarity during the procedure and therefore usually results in more polyps removed.[45,47] Because of this, we expected individuals with fair-to-poor bowel preparation to have a lower mean of polyps detected, and to find a significantly lower PDR. Bowel preparation was not found to be associated with number of all polyps removed or number of high-risk polyps removed. One possible explanation for this result could be that individuals in our sample who do not prepare their bowels to the good-to-excellent quality may also have poor health behaviors that could potentially cause more polyps.

Procedure Time

Our mean and max findings for procedure time were reflective of previous studies as morning procedure times have been found more likely to result in a polyp detected.[46] Procedure time after 2:00pm was found to result in a lower rate of high-risk polyps when compared to procedures before 10:00pm (RR=0.52, 95% CI 0.29-0.94) in our multivariable model. These results are likely due to morning procedures taking place at the beginning of the physician's shift when they are more alert. However, we would expect procedure time to also be significant in our number of all polyps removed model since high-risk polyps are generally larger[33,34] and may be easier to detect than low-risk polyps. Since we do not have information on the hours each physician worked during each colonoscopy they performed for our population, we were unable to assess this effect further.

BMI

Since previous literature has demonstrated that those who are overweight or obese are more at risk for colorectal polyps and advanced adenomas,[2,18,19,24,26,36,37] our mean number of high-risk polyps for BMI were unexpected since the highest mean was amongst the underweight/normal group. However, our multivariable regression model for all polyps showed that the rate ratio was significant for obese when compared to normal/underweight (RR=1.35, 95% CI 1.09-1.67) but was not significant for overweight individuals. Additionally, no significant associations were found between BMI and number of high-risk polyps or in either univariate analysis.

NSAIDS

The largest mean number of high-risk polyps among 1-3 day/week users was surprising since NSAIDs have been found to be preventive of high-risk polyps.[2,26,36,42] However, our regression analyses agreed with previous findings as those who never took NSAIDs had a higher rate of all polyps (RR=1.40, 95% CI 1.15-1.71) and number of high-risk polyps (RR=1.86, 95% CI 1.04-3.34). Our model for number of high-risk polyps also showed a higher rate among occasional NSAID users (RR=2.02, 95% CI 1.01-4.05) and 1-3 days/week users (RR=2.93, 95% CI 1.40-6.12) when compared to individuals who take NSAIDs 7 days/week. The higher rate ratio for 1-3 day/week users than that of never users was also unexpected. Nonetheless, these findings confirm that more frequent use of NSAIDs is a protective factor against number of all polyps and high-risk polyps.

5.2 LIMITATIONS AND STRENGTHS

One limitation to our study was that our sample consisted of only uninsured individuals; therefore, our results may not be generalizable to those who do have health insurance. Further, selection bias may be present since CCPN participants were referred to the program if they regularly received care from one of the participating federally-qualified health centers or free medical clinics; therefore, all participants are individuals who are seeking out healthcare. Recall bias may also be a concern since many of our independent variables (alcohol use, NSAID use, physical activity, and smoking) relied on patient self-reported information. Lastly, our lack of ability to test for random physician effect to explain the unexpected findings for urban/rural residence was also a limitation.

A strength of our study was that 90% of our included participants had good-to-excellent bowel preparation quality, and all procedures were performed by board-certified gastroenterologists that perform a high volume of colonoscopy procedures; thus, making ideal conditions for precise colonoscopy readings. Despite these limitations, we consider our results to be accurate and to add important findings to the literature gap.

CHAPTER 6

CONCLUSION

In conclusion, our results aligned with previous similar studies as our analyses showed that 55-59 year old individuals, males, current smokers, heavy drinkers, and individuals with a family history of CRC had a higher PDR that their counterparts. Differing from previous studies, our study found urban residents to be more likely to have a polyp detected than rural residents. We found gender, smoking habits, residence location (rural/urban), alcohol consumption, family history of CRC, BMI and NSAID use to be predictors of number of polyps removed during colonoscopy. Race was found significantly associated with number of all polyps only among individuals who exercised 4-7 days/week; and physical activity was also significant for only African-Americans who exercised zero days/week. Number of high-risk polyps removed was found to be significantly associated with gender, smoking, time of procedure, and NSAID use. Since no other studies, to our knowledge, have assessed the effects of all of these factors on number of polyps, we are unable to compare our findings with similar study findings.

Future studies are needed to further assess what may be influencing the higher rate of polyps detected among urban residents found here, in addition to focusing on populations which include insured individuals since our results here are not generalizable to that population. Overall, our study demonstrates the effects that demographic, behavioral, and procedural influencers have on polyp detection and the number of polyps

detected during a colonoscopy procedure. By assessing this relationship, our findings may help to identify individuals who are at risk for a large quantity of polyps which could perhaps improve the detection of more polyps during their colonoscopy procedure.

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