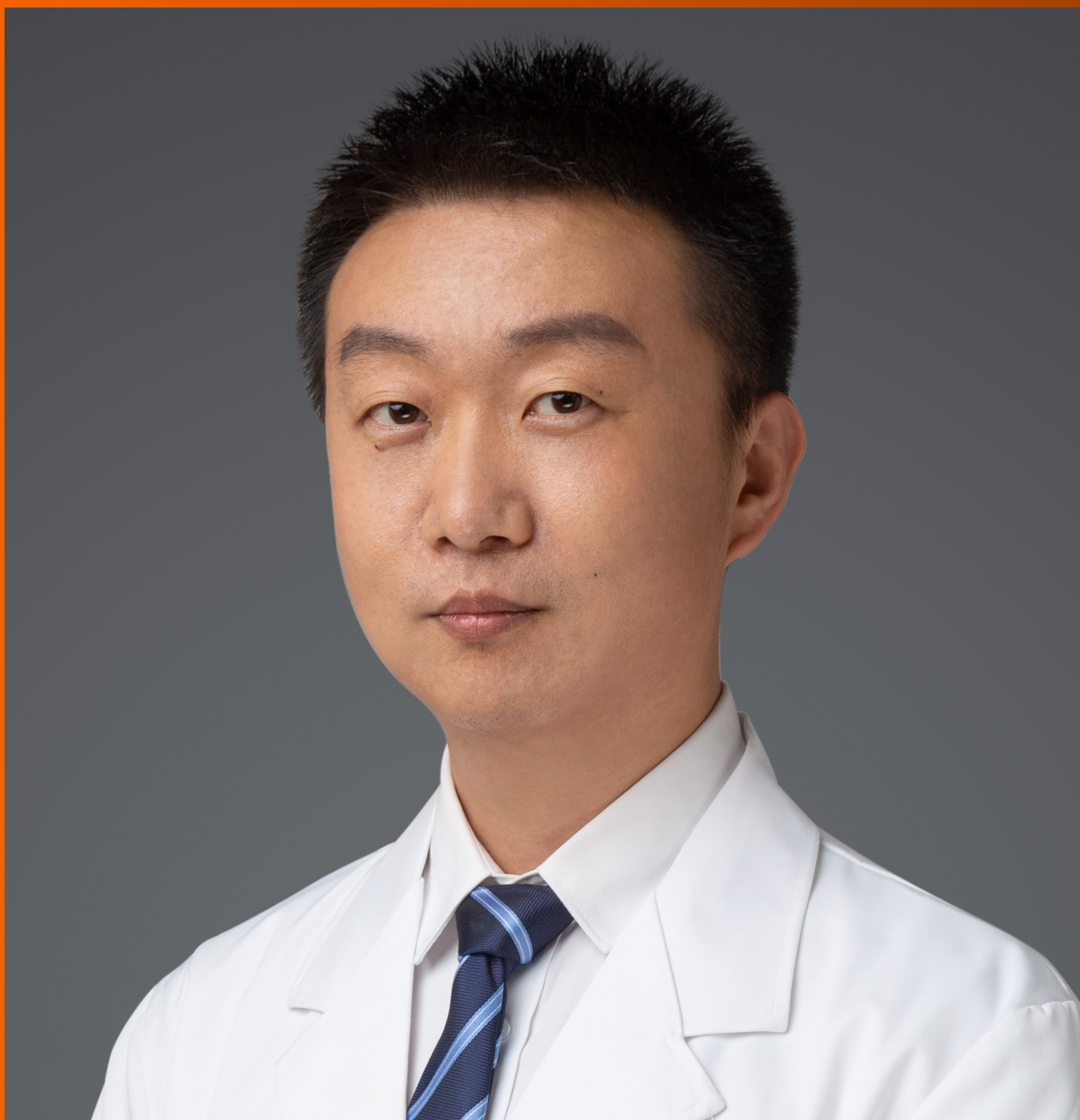


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## Retrospective Cohort Study

## Impact of type 2 diabetes on adenoma detection in screening colonoscopies performed in disparate populations

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## Abstract

## BACKGROUND

The Black/African Ancestry (AA) population has a higher prevalence of type 2 diabetes mellitus (T2DM) and a higher incidence and mortality rate for colorectal cancer (CRC) than all other races in the United States. T2DM has been shown to increase adenoma risk in predominantly white/European ancestry (EA) populations, but the effect of T2DM on adenoma risk in Black/AA individuals is

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**statement:** The study was reviewed and approved by the Stony Brook University Institutional Review Board, No. 180023; SUNY Downstate Medical Center Institutional Review Board, No. 802718.

**Informed consent statement:** A waiver of consent was obtained by both the SUNY DMC and Stony Brook University IRBs for retrospective collection and analysis of deidentified demographic and medical data.

**Conflict-of-interest statement:** The authors declare no competing interests.

**Data sharing statement:** Technical appendix, statistical code, and dataset available from the corresponding author at [ellen.li@stonybrookmedicine.edu](mailto:ellen.li@stonybrookmedicine.edu). A waiver of consent was obtained by both the SUNY DMC and Stony Brook University IRBs for retrospective collection and analysis of deidentified demographic and medical data. Because the presented data are deidentified, the risk of identification is low.

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less clear. We hypothesize that T2DM has a significant effect on adenoma risk in a predominantly Black/AA population.

#### AIM

To investigate the effect of T2DM and race on the adenoma detection rate (ADR) in screening colonoscopies in two disparate populations.

#### METHODS

A retrospective cohort study was conducted on ADR during index screening colonoscopies (age 45-75) performed at an urban public hospital serving a predominantly Black/AA population (92%) (2017-2018,  $n = 1606$ ). Clinical metadata collected included basic demographics, insurance, body mass index (BMI), family history of CRC, smoking, diabetes diagnosis, and aspirin use. This dataset was combined with a recently reported parallel retrospective cohort data set collected at a suburban university hospital serving a predominantly White/EA population (87%) (2012-2015,  $n = 2882$ ).

#### RESULTS

The ADR was higher in T2DM patients than in patients without T2DM or prediabetes (35.2% *vs* 27.9%,  $P = 0.0166$ ,  $n = 981$ ) at the urban public hospital. Multivariable analysis of the combined datasets showed that T2DM [odds ratio (OR) = 1.29, 95% confidence interval (CI): 1.08-1.55,  $P = 0.0049$ ], smoking (current *vs* never OR = 1.47, 95%CI: 1.18-1.82, current *vs* past OR = 1.32, 95%CI: 1.02-1.70,  $P = 0.0026$ ), older age (OR = 1.05 *per* year, 95%CI: 1.04-1.06,  $P < 0.0001$ ), higher BMI (OR = 1.02 *per* unit, 95%CI: 1.01-1.03,  $P = 0.0003$ ), and male sex (OR = 1.87, 95%CI: 1.62-2.15,  $P < 0.0001$ ) were associated with increased ADR in the combined datasets, but race, aspirin use and insurance were not.

#### CONCLUSION

T2DM, but not race, is significantly associated with increased ADR on index screening colonoscopy while controlling for other factors.

**Key Words:** Adenoma; Diabetes mellitus, type 2; African continental ancestry group; European continental ancestry group; Colonoscopy; Multivariate analysis

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**Core Tip:** This retrospective cohort study examines the factors associated with the adenoma detection rate (ADR) during initial screening colonoscopy in two disparate populations. One population comprised predominantly underinsured Black/African Ancestry individuals served by an urban public hospital, and the second population predominantly insured White/European Ancestry individuals served by a suburban university hospital. The results show that type 2 diabetes was significantly associated with increased ADR in both populations. In addition, while older age, higher body mass index, smoking and male sex were also associated with increased ADR, race, aspirin use and insurance were not significant in the multivariable analysis of the combined datasets.

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#### INTRODUCTION

Colorectal cancer (CRC) is the second leading cause of cancer death in the United States. However, there has been an overall downward trend in CRC incidence and

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mortality over the past two decades. This has been attributed to CRC screening with removal of precancerous polyps and detection of early-stage CRC during optical colonoscopy<sup>[1]</sup>. Despite this overall downward trend, the CRC incidence and mortality in individuals with black/African ancestry (AA) remain persistently higher than those in all other races<sup>[2,3]</sup>. Multiple factors, including both social determinants of health, such as access to quality healthcare, and biological gene-environment factors that may promote oncogenic transformation, have been implicated<sup>[4-9]</sup>.

Diabetes mellitus is a biological gene-environment factor of particular interest because diabetes is related both to Black/AA race and poverty<sup>[10]</sup> and has been associated with increased CRC risk<sup>[11]</sup>. Type 2 diabetes mellitus (T2DM) has been reported to increase the risk of adenoma, which is a benign neoplastic precursor to CRC, in predominantly White/European Ancestry (EA) populations<sup>[12]</sup>. However, there is a paucity of data reporting the effects of T2DM on adenoma risk in Black/AA individuals. Because a nested case-control study using data from the Black Women's Health Study failed to detect a significant effect, it is less clear whether an association of T2DM with increased adenoma risk is also present in Black/AA populations<sup>[13]</sup>.

We initiated a retrospective analysis of the adenoma detection rate (ADR) in index screening colonoscopies performed in 2012 on disparate populations served by three institutions: New York City Health and Hospitals/Kings County, the State University of New York (SUNY) Downstate Medical Center (DMC) and Stony Brook University Medical Center (SBUMC)<sup>[14]</sup>. SUNY DMC and SBUMC are funded by New York State, whereas Kings County is supported by the New York City Health and Hospital Corporation. DMC and Kings County are located in central Brooklyn, New York. SBUMC is located in Suffolk County on Long Island, New York. The procedures were carried out by full-time teaching gastroenterologists with and without the assistance of gastroenterology fellow trainees and by nonteaching gastroenterologists at all three institutions. Of the 2225 initial screening colonoscopies, 1495 (67.2%) were performed in 2012 on Black/AA individuals, and 566 (25.4%) were performed on white/EA individuals. Multivariable analysis revealed that older age, male sex, current smoking and teaching gastroenterologists were associated with a higher ADR. T2DM was much more prevalent in Black/AA individuals than in white/EA individuals (30% *vs* 10%), but the association with the detection of colonic neoplasia did not reach significance ( $P = 0.076$ ). Race, ethnicity, body mass index (BMI), human immunodeficiency virus (HIV) status, medical insurance and fellow trainee participation were also not significantly associated with ADR in this study. Because our findings were confounded by the low average ADR (< 20%) of some nonteaching gastroenterologists at one institution, an intense physician feedback program was initiated to rectify the problem before resuming data collection.

Multivariable analysis of an expanded retrospective cohort study (2012-2015) conducted on the predominantly insured White/EA population served by SBUMC revealed that T2DM was significantly associated with higher ADR ( $P = 0.0047$ ) while controlling for multiple other variables<sup>[15]</sup>. We now report a retrospective cohort study of index screening colonoscopies performed from 2017-2018 at Kings County Hospital to address the question of whether T2DM is significantly associated with an increased ADR during index screening colonoscopies performed in a predominantly underinsured Black/AA population. To further examine the role of T2DM and race, we conducted a multivariable analysis of this new dataset combined with the recently reported dataset collected on the predominantly insured White/EA population described above<sup>[15]</sup>.

## MATERIALS AND METHODS

### Collection of data

This retrospective cohort study was approved by the SUNY DMC and Stony Brook University Institutional Review Boards (IRB No. 802718 and 180023). All methods were performed in accordance with the guidelines and regulations of the SUNY DMC and Stony Brook University IRBs. A waiver of consent was obtained by both the SUNY DMC and Stony Brook University IRBs for the retrospective collection and analysis of deidentified demographic and medical data. Patients who underwent index screening colonoscopies at Kings County Hospital from January 1, 2017, until December 31, 2018, were identified using endoscopy reporting software. Patients aged < 45 years or > 75 years or with a history of previous colonoscopy, a history of inflammatory bowel diseases, known hereditary colorectal syndromes, detection of microscopic or macroscopic blood in stool and other alarm syndromes, or detection of colonic masses



or polyps in previous studies were excluded from this analysis as previously described<sup>[14,15]</sup>. Colonoscopies that were incomplete (did not reach the cecum) and those associated with poor bowel preparation were also excluded. Clinical metadata were manually collected on each patient using electronic medical records (EMRs) as documented at the time of screening colonoscopy and included (1) age at time of initial screening colonoscopy (year); (2) sex (Male, Female); (3) race (White/EA, Black/AA, Asian, Other); (4) Hispanic ethnicity; (5) Insurance (Commercial, Medicare, Medicaid, Self-pay); (6) BMI (kg/m<sup>2</sup>); and (7) Tobacco Exposure (Current within one year, Past greater than one year, Never)<sup>[14,15]</sup>. A family history of a first-degree relative of CRC was not included in the analysis because of incomplete documentation in the EMR.

Patients were categorized as T2DM if they were diagnosed with T2DM in the EMR or if a recent hemoglobin A1c (HbA1c) level was  $\geq 6.5\%$ <sup>[16]</sup>. They were phenotyped as nondiabetic (NoDM) if they were not diagnosed with T2DM in the EMR and their previous HbA1c levels were  $< 6.5\%$ . The NoDM patients were further classified as prediabetic (Pre-DM) if they were diagnosed as prediabetic in the EMR, if a recent HbA1c level was  $\geq 5.7\%$  and  $< 6.5\%$ , or control if a recent HbA1c level was  $< 5.7\%$ . NoDM patients without HbA1c levels were unclassified. Ten patients diagnosed with type 1 diabetes mellitus were also excluded from the analysis of the combined dataset (2 from Kings County Hospital and 8 from SBUMC dataset).

For T2DM patients, further data were collected using the EMR as documented at the time of screening colonoscopy and included (1) fasting plasma glucose on the day of screening colonoscopy; (2) HbA1c within 12 mo. of the procedure; (3) insulin use (Yes, No); (4) metformin use (Yes, No); (5) sulfonylurea use (Yes, No); (6) thiazolidinedione use (Yes, No); (7) meglitinide use (Yes, No); (8) glucagon-like peptide-1 agonist use (Yes, No); (9) dipeptidyl peptidase-4 (DPP-4) inhibitor use (Yes, No); (10) sodium-dependent glucose transporters 2 inhibitor use (Yes, No); and (11) acarbose use (Yes, No) as previously described<sup>[15]</sup>.

The colonoscopy report was reviewed to determine if a colonic biopsy or polypectomy was performed. If a biopsy or polypectomy was performed, the pathology report was reviewed to collect data on polyp type (hyperplastic *vs* adenoma, *vs* serrated adenoma *vs* adenocarcinoma) as previously described<sup>[15]</sup>. The right colonic location was defined as including the cecum, ascending colon, hepatic flexure, or transverse colon. The left colonic location was defined as including the splenic flexure, descending colon, sigmoid colon, rectosigmoid, or rectum. We defined an advanced adenoma as any adenomatous polyp containing at least one of the following features: villous or tubulovillous histology, high-grade dysplasia, and size  $\geq 1$  cm. We defined a high-risk adenoma as any adenomatous polyp containing at least one of the following features: Villous or tubulovillous histology, high-grade dysplasia, size  $\geq 1$  cm, and presence of  $\geq 3$  adenomatous polyps.

### Statistical analysis

Statistical analysis was performed utilizing the Biostatistics and Bioinformatics Shared Resource at the Stony Brook University Cancer Center. Demographics were compared between diabetes and nondiabetes patients using either the Wilcoxon rank sum test for continuous variables and the chi-square test with exact p-values from Monte Carlo simulations for categorical variables as previously described<sup>[15]</sup>. For the combined Kings County Hospital and SBUMC datasets, a multivariable generalized linear mixed model (GLMM) was conducted, with the primary outcome being the detection of at least one adenoma compared with patients who had no colonic neoplasia detected. Patients with serrated adenomas or CRCs in the combined dataset were therefore excluded from the analysis ( $n = 20$  from Kings County Hospital, and  $n = 45$  from SBUMC). The covariates that exhibited marginal significance in univariate GLMM analyses and Race were included in the multivariable GLMM analysis. We previously did not detect significant effects of Hispanic ethnicity, fellow participation, and family history of first-degree relative CRC in our previous analyses<sup>[14,15]</sup>. There was also a significant amount of missing data for Hispanic ethnicity and family history of first-degree relative CRC in the Kings County Hospital dataset. For these reasons, the multivariable GLMM did not include either Hispanic ethnicity or family history of a first degree relative with CRC in the multivariable GLMM. Physician and institutional sites (Kings County Hospital *vs* SBUMC) were both considered random effects in the multivariable GLMM analysis. Statistical analysis was performed using SAS 9.4, and the significance level was set at 0.05 (SAS Institute Inc., Cary, NC, United States).

## RESULTS

A total of 1606 index screening colonoscopies (January 1, 2017–December 31, 2018) performed on subjects aged 45–75 years with fair or good colonoscopic preps were identified after manual review of 4959 colonoscopy reports from Kings County Hospital. This number was reached after excluding 131 index screening colonoscopies from the analysis for (1) incomplete colonoscopies ( $n = 48$ ); (2) poor prep ( $n = 76$ ); (3) failure of biopsy retrieval ( $n = 5$ ); and (4) diagnosis of type 1 diabetes mellitus ( $n = 2$ ).

Because greater than 90% of all individuals undergoing index screening colonoscopies at Kings County Hospital had recent HbA1c results, the HbA1c values were used in addition to their diagnoses recorded in the EMR to categorize them with respect to their diabetes status<sup>[16]</sup>. As shown in Table 1, 529 (32.3%) patients were categorized as T2DM based on diagnoses in the EMR and/or recent HbA1c  $\geq 6.5\%$ . The median HbA1c was  $5.7 \pm 0.6\%$  for the NoDM category. The 1077 (67.7%) patients in the NoDM category was further subdivided based on recent HbA1c values as prediabetic or Pre-DM ( $n = 542$ , 33.7%) and controls ( $n = 452$ , 28.2%), with the remaining 83 (5%) individuals remaining as unclassified NoDM. The median HbA1c was  $7.2\% \pm 1.9\%$  (16 missing values) for the T2DM category,  $5.9\% \pm 0.3\%$  for the Pre-DM category and  $5.4\% \pm 0.3\%$  for the control group. The median preprocedure fasting glucose level in the T2DM group was  $6.9 \pm 3.4$  mmol/L (LX1) (75 missing values). The majority of the T2DM subjects (78.4%) were treated with at least one antidiabetic medication (see Table 2). A total of 24.4% of the T2DM patients were treated with insulin with and without oral antidiabetic medications. The most common oral antidiabetic medications prescribed were metformin, DPP-4 inhibitors and sulfonylureas. Many of the patients were treated with more than one antidiabetic medication.

The individuals undergoing index screening colonoscopies at this urban public hospital were predominantly Black/AA (92.7%) and underinsured (80.8%, on Medicaid or Self-pay without insurance). Proportionally fewer men (35.4%) than women (64.6%) underwent index screening colonoscopies. As shown in Table 3, significant differences in the T2DM group *vs* the NoDM group included older median age at the time of index colonoscopy, higher median BMI (missing 3 values), and higher intestinal solution of aspirin capsule (ASA) use in the T2DM group, possibly reflecting a higher prevalence of cardiovascular disease in this group. Overall, the percentage of individuals who endorsed current smoking was low (6.0%), but current smoking was lower in the T2DM group than in the NoDM group ( $P = 0.0494$ , missing 35 values). There was no significant difference between the two groups with respect to race, Hispanic ethnicity (missing 197 values), HIV status, glycemic index (GI) fellow participation in the procedure, quality of the colonoscopy prep, and medical insurance status.

As shown in Table 4, a significantly increased risk of total colonic neoplasias (adenomas, serrated adenomas and CRCs) was detected on index colonoscopy in T2DM *vs* NoDM ( $P = 0.0322$ ); however, the increased risk of adenoma only detection did not reach significance ( $P = 0.0581$ ). As shown in Table 5, when the T2DM group was compared instead with the control group (HbA1c  $< 5.7\%$ ), the increased ADR reached significance ( $P = 0.0166$ ). The number of advanced adenoma events was too low in this study to detect a significant difference between the T2DM advanced adenoma detection rate (AADR, 5.5%) and the control AADR (3.5%). The marginal  $P$ -value (0.053) suggests that increasing the sample size would likely result in detection of a significant effect of T2DM on AADR. In addition, the association of the right-sided location of colonic neoplastic lesions reached significance ( $P = 0.0359$ ) when the T2DM group was compared with the control group. When the pre-DM group (HbA1c  $\geq 5.7\%$  and  $< 6.5\%$ ) was compared with the control group (Table 6) and with the T2DM group (Table 7), no significant differences were observed.

To evaluate the role of T2DM while controlling for other factors, such as race and insurance, we combined the datasets collected on the two disparate populations served by SBUMC and Kings County Hospital. Because HbA1c values were not available for any of the NoDM and only approximately 50% of the T2DM subjects in the SBUMC dataset, it was not possible to subcategorize the NoDM subjects further as Pre-DM or Control in that dataset<sup>[15]</sup>. The univariate analysis of the combined data set comparing subjects with adenomas *vs* subjects with no neoplastic lesions detected is summarized in Table 7. T2DM, older age, increased BMI, male sex, current smoking, and ASA use were identified as variables associated with increased ADR with marginal significance. Commercial insurance was associated with a reduced ADR with marginal significance.

Multivariable analysis of the combined data sets (see Table 8) confirmed that T2DM

**Table 1 Glycemic status in the type 2 diabetes mellitus, nondiabetic, prediabetic and control groups at an urban public hospital**

	T2DM, <i>n</i> = 529	NoDM, <i>n</i> = 1077	Pre-DM, <i>n</i> = 542	Control, <i>n</i> = 452
HbA1c (%) median ± IQR	7.2 ± 1.9	5.7 ± 0.6	5.9 ± 0.3	5.4 ± 0.3
Fasting blood sugar (mmol/L) median ± IQR	6.9 ± 3.4	N/A	N/A	N/A

IQR: Interquartile range; T2DM: Type 2 diabetes mellitus; HbA1c: Hemoglobin A1c; Pre-DM: Prediabetic; NoDM: Nondiabetic.

**Table 2 Anti-diabetic medications in type 2 diabetes mellitus patients at an urban public hospital**

Anti-diabetes medications	No. of T2DM subjects (%) <i>n</i> = 529
None	114 (21.6)
Insulin	129 (24.4)
Metformin	359 (67.9)
Sulfonylureas	145 (27.4)
DPP4 inhibitors	158 (29.9)
Thiazolidinediones	2 (0.4)
GLP1 agonists	3 (0.6)
SGLT-2 inhibitors	0 (0.0)
Meglitinides	1 (0.2)
Acarbose	2 (0.4)

T2DM: Type 2 diabetes mellitus; DPP4: Dipeptidyl peptidase-4; GLP1: Glucagon-like peptide 1; SGLT-2: Sodium-dependent glucose transporters 2.

was significantly associated with increased ADR while controlling for other factors [odds ratio (OR) 1.29 95% confidence interval (CI): 1.08-1.55,  $P = 0.0049$ ]. Multivariable analysis also identified older age, higher BMI, male sex and current smoking as associated with increased ADR on index screening colonoscopies. However, neither race nor insurance nor ASA use were significantly associated when controlling for all other factors. ASA and nonsteroidal anti-inflammatory drug use have been associated with reduced adenoma risk<sup>[17]</sup>. The paradoxical observation in our univariate analysis that ASA use was associated with increased ADR may be related to the higher prevalence of ASA use in T2DM *vs* NoDM patients due to a higher prevalence of cardiovascular disease in these patients<sup>[18]</sup>.

## DISCUSSION

While it is clear that CRC incidence and mortality are increased in Black/AA compared with all other races in the United States, it remains to be determined whether the incidence of precursor lesions, such as adenomas, is also increased in Black/AA. While T2DM has been shown to increase adenoma risk in predominantly White/EA populations, there is a paucity of data reported on the effect of T2DM in Black/AA individuals. A nested case-controlled study on Black/AA women did not detect a significant effect of T2DM on adenomas<sup>[13]</sup>. In this retrospective cohort study, the effects of T2DM and race on ADR in index colonoscopies were studied in two disparate populations separated geographically by 50 miles within the same land mass in New York. In carrying out this study, it was first important to control for operator dependence in ADR during index colonoscopies, particularly because of previous reports that some Black/AA patients may undergo colonoscopy by physicians with lower polyp detection rates<sup>[14,19]</sup>. Both endoscopy units at the two institutions achieved recommended ADR benchmarks of 25% for all patients and sex-specific rates of 30% for men and 20% for women over the time period studied<sup>[20]</sup>.

We detected a significant effect of T2DM patients compared with control patients with normal glycemic status (HbA1c < 5.7%) in the predominantly Black/AA population served by the public urban hospital. In contrast, a significant effect of pre-

**Table 3 Comparison of patient characteristics between type 2 diabetes mellitus and nondiabetic patients at an urban public hospital**

Variables	T2DM, <i>n</i> = 529	NoDM, <i>n</i> = 1077	<i>P</i> value
Age (yr) median $\pm$ IQR	58 $\pm$ 11	55 $\pm$ 10	< 0.0001
Male sex, <i>n</i> (%)	189 (35.7)	379 (35.2)	0.8627
Race, <i>n</i> (%)			0.8741
Black/AA	493 (93.2)	995 (92.4)	
Non-Hispanic White/EA	2 (0.4)	3 (0.3)	
Asian	2 (0.4)	6 (0.6)	
Other	32 (6.0)	73 (6.8)	
Hispanic ethnicity, <i>n</i> (%)	26 (5.6)	43 (4.5)	0.4329
BMI (kg/m <sup>2</sup> ), median $\pm$ IQR	29.5 $\pm$ 7.5	28.3 $\pm$ 7.5	< 0.0001
Smoking, <i>n</i> (%)			0.0494
Current	20 (3.9)	75 (7.1)	
Past	20 (3.9)	39 (3.7)	
Never	471 (92.2)	946 (89.2)	
Aspirin use, <i>n</i> (%)	135 (25.5)	130 (12.1)	< 0.0001
HIV status, <i>n</i> (%)	26 (4.9)	64 (5.9)	0.4245
Fellow participation, <i>n</i> (%)	119 (22.5)	263 (24.4)	0.4125
Quality of colonoscopic prep			0.3346
Good	511 (96.6)	1050 (97.5)	
Fair	18 (3.4)	27 (2.5)	
Insurance, <i>n</i> (%)			0.2072
Commercial	85 (16.1)	180 (16.7)	
Medicare	20 (3.8)	23 (2.1)	
Medicaid	326 (61.6)	652 (60.5)	
Self-pay	98 (18.5)	222 (20.6)	

T2DM: Type 2 diabetes mellitus; AA: African ancestry; EA: European ancestry; IQR: Interquartile range; BMI: Body mass index; NoDM: Nondiabetics; HIV: Human immunodeficiency virus.

DM patients compared with control subjects in this population did not reach significance. The increased ADR in T2DM did not reach significance when compared with all NoDM patients, suggesting that inclusion of Pre-DM patients in the NoDM group could obscure the effect of T2DM. The current study differs from a previous nested case-control study focused on examining the effect of diabetes on ADR in Black/AA women<sup>[13]</sup> in that both men and women were included. This study also differed in design from the previous study on the effect of T2DM on ADR in Black/AA women in that all index colonoscopy reports were included in the analysis, thus eliminating potential selection bias in selecting control cases.

The availability of recent HbA1c values for > 90% of all Kings County Hospital patients allowed for further categorization of the Pre-DM and Control groups within the NoDM category. This was not, however, possible for the SBUMC population, where HbA1c values were available for only approximately 50% of the population<sup>[15]</sup>. For this reason, the effect of T2DM *vs* NoDM, the latter group, including prediabetics, on ADR was measured in the multivariable GLMM analysis of the combined dataset.

This retrospective cohort study is subject to several limitations. Family history of a first degree relative with CRC in the EMR was not included in the analysis because of incomplete documentation. Detection of this deficiency has prompted the adoption of family history intervention<sup>[21]</sup> at both institutions, which will hopefully result in increased uptake of CRC screening, particularly in the underserved Black/AA population. Another limitation is that only two institutions are included. The lack of a

**Table 4 Comparison of colonic lesions (polyps and colorectal cancer) in type 2 diabetes mellitus and nondiabetic patients at an urban public hospital, *n* (%)**

Variables	T2DM, <i>n</i> = 529	NoDM, <i>n</i> = 1077	<i>P</i> value
All colonic neoplastic lesions	195 (36.9)	338 (31.4)	0.0322
Location of neoplastic lesions			0.1688
Left-sided only	56 (10.6)	103 (9.6)	
Right-sided only	105 (19.8)	179 (16.6)	
Both	34 (6.4)	56 (5.2)	
Adenomas (not serrated or CRC)	186 (35.2)	327 (30.4)	0.0581
Sessile serrated adenoma	6 (1.1)	7 (0.6)	0.3769
Advanced adenoma (> 1 cm, villous, high grade dysplasia, not including CRC)	29 (5.5)	38 (3.5)	0.0887
High risk adenoma (> 3 adenomas and/or advanced adenoma)	45 (8.5)	75 (7.0)	0.3131
CRC	3 (0.6)	4 (0.4)	0.6923
Hyperplastic polyp only (no additional colonic neoplasia)	66 (12.5)	136 (12.6)	0.9347

CRC: Colorectal cancer; T2DM: Type 2 diabetes mellitus; NoDM: Nondiabetics.

**Table 5 Comparison of colonic lesions (polyps and colorectal cancer) in type 2 diabetes mellitus and control patients (hemoglobin A1c < 5.7%) at an urban public hospital, *n* (%)**

Variables	T2DM, <i>n</i> = 529	Control, <i>n</i> = 452	<i>P</i> value
All colonic neoplastic lesions	195 (36.9)	131 (29.0)	0.0092
Location of neoplastic lesions			0.0359
Left-sided only	56 (10.6)	47 (10.4)	
Right-sided only	105 (19.8)	63 (13.9)	
Both	34 (6.4)	21 (4.6)	
Adenomas (not serrated or CRC)	186 (35.2)	126 (27.9)	0.0166
Sessile serrated adenoma	6 (1.1)	3 (0.7)	0.5098
Advanced adenoma (> 1 cm, villous, high grade dysplasia, not including CRC)	29 (5.5)	13 (2.9)	0.0534
High risk adenoma (> 3 adenomas and/or advanced adenoma)	45 (8.5)	29 (6.4)	0.2275
CRC	3 (0.6)	2 (0.4)	1.0000
Hyperplastic polyp only (no additional colonic neoplasia)	66 (12.5)	59 (13.1)	0.8499

CRC: Colorectal cancer; T2DM: Type 2 diabetes mellitus.

racial effect on ADR observed in this study may not be applicable to other Black/AA populations in the United States because a substantial proportion of the population served by the urban public hospital in this study is Afro-Caribbean<sup>[22]</sup>.

To control for multiple confounding variables, the following variables were included as fixed effects in the GLMM in addition to diabetes status: (1) age; (2) sex; (3) race; (4) BMI; (5) smoking status; (6) insurance status; and (7) aspirin use (see Table 9). Institution and colonoscopists were included in the GLMM as random effects. Patient age was restricted in this study to 45-75 years based on recent recommendations for initiating CRC screening in the United States. The GI societies currently recommend initiation of average-risk CRC screening in Black/AA individuals at age 45, five years earlier than the general population<sup>[23]</sup>. More recently, the American Cancer Society has recommended that initiation of CRC screening be lowered universally to age 45 because of rising incidences of early onset CRC in other races<sup>[24]</sup>.



**Table 6 Comparison of colonic lesions (polyps and colorectal cancer) in prediabetic diabetes mellitus (hemoglobin A1c  $\geq 5.7\%$ ,  $< 6.5\%$ ) and control patients (hemoglobin A1c  $< 5.7\%$ ) at an urban public hospital, *n* (%)**

Variables	Pre-DM <i>n</i> = 542	Control <i>n</i> = 452	<i>P</i> value
All colonic neoplastic lesions	173 (31.9)	131 (29.0)	0.3310
Location of neoplastic lesions			0.5944
Left-sided only	54 (10.0)	47 (10.4)	
Right-sided only	92 (17.0)	63 (13.9)	
Both	27 (5.0)	21 (4.6)	
Adenomas (not serrated or CRC)	168 (31.0)	126 (27.9)	0.2916
Sessile serrated adenoma	3 (0.6)	3 (0.7)	1.0000
Advanced adenoma ( $> 1$ cm, villous, high grade dysplasia, not including CRC)	22 (4.1)	13 (2.9)	0.3894
High risk adenoma ( $> 3$ adenomas and/or advanced adenoma)	39 (7.2)	29 (6.4)	0.7058
CRC	2 (0.4)	2 (0.4)	1.0000
Hyperplastic polyp only (no additional colonic neoplasia)	68 (12.5)	59 (13.1)	0.8463

CRC: Colorectal cancer; Pre-DM: Prediabetics.

**Table 7 Comparison of colonic lesions (polyps and colorectal cancer) in type 2 diabetes mellitus and prediabetics mellitus (hemoglobin A1c  $\geq 5.7\%$ ,  $< 6.5\%$ ) patients at an urban public hospital, *n* (%)**

Variables	T2DM <i>n</i> = 529	Pre-DM <i>n</i> = 542	<i>P</i> value
All colonic neoplastic lesions	195 (36.9)	173 (31.9)	0.0959
Location of neoplastic lesions			0.3534
Left-sided only	56 (10.6)	54 (10.0)	
Right-sided only	105 (19.8)	92 (17.0)	
Both	34 (6.4)	27 (5.0)	
Adenomas (not serrated or CRC)	186 (35.2)	168 (31.0)	0.1515
Sessile serrated adenoma	6 (1.1)	3 (0.6)	0.3324
Advanced adenoma ( $> 1$ cm, villous, high grade dysplasia, not including CRC)	29 (5.5)	22 (4.1)	0.3137
High risk adenoma ( $> 3$ adenomas and/or advanced adenoma)	45 (8.5)	39 (7.2)	0.4321
CRC	3 (0.6)	2 (0.4)	0.6858
Hyperplastic polyp only (no additional colonic neoplasia)	66 (12.5)	68 (12.5)	1.0000

CRC: Colorectal cancer; T2DM: Type 2 diabetes mellitus; Pre-DM: Prediabetics.

## CONCLUSION

The results of our multivariable (GLMM) analysis of two disparate populations suggest that diabetes and obesity, which are more prevalent in the Black/AA population<sup>[10,25]</sup>, may be drivers of increased adenoma formation in many Black/AA individuals. The results also suggest that attention be devoted to stages subsequent to adenoma formation in the adenoma-CRC sequence to elucidate the biological basis for racial disparities in CRC incidence. This study reinforces the concept that these metabolic disorders should be taken into consideration in advising asymptomatic individuals whether to undergo optical colonoscopy or noninvasive stool testing for CRC screening<sup>[26]</sup>. In addition to continuing efforts to expand access to high-quality CRC screening among Black/AA individuals, it is important to intervene early to reduce the risks of forming adenomas. For this reason, we advocate integrating and coordinating CRC screening efforts with screening for diabetes mellitus<sup>[16]</sup> beginning at

**Table 8 Characteristics of patients with adenomas vs patients with no neoplasia detected on index screening colonoscopy from two disparate populations, *n* (%)**

Factors	Missing	Level	No neoplasia, <i>n</i> = 3138 (70.95%)	Adenoma, <i>n</i> = 1285 (29.05%)	<i>P</i> value
T2DM	0	Yes	501 (62.5)	300 (37.5)	< 0.0001
		No	2637 (72.8)	985 (27.2)	
Age (yr)	0		54.0 ± 8.9	57.0 ± 10.6	< 0.0001
BMI (kg/m <sup>2</sup> )	3		27.8 ± 7.0	28.5 ± 7.3	0.0004
Sex	0	Female	1953 (76.1)	612 (23.9)	< 0.0001
		Male	1185 (63.8)	673 (36.2)	
Race	0	White	1797 (72.7)	674 (27.3)	0.9310
		Black	1124 (68.6)	515 (31.4)	
		Asian	67 (71.3)	27 (28.7)	
		Other	150 (68.5)	69 (31.5)	
Smoking	35	Never	2206 (72.2)	850 (27.8)	< 0.0001
		Past	602 (69.8)	260 (30.2)	
		Current	305 (64.9)	165 (35.1)	
Insurance	0	Commercial	1673 (74.2)	583 (25.8)	0.0034
		Medicare	219 (66.4)	111 (33.6)	
		Medicaid	986 (67.6)	473 (32.4)	
		Self-Pay	260 (68.8)	118 (31.2)	
Fellow participation	0	Yes	605 (67.4)	293 (32.6)	0.2729
		No	2533 (71.9)	992 (28.1)	
Aspirin use	9	Yes	405 (65.5)	213 (34.5)	0.0038
		No	2727 (71.8)	1069 (28.2)	

BMI: Body mass index; T2DM: Type 2 diabetes mellitus.

age 45 particularly for Black/AA individuals.

**Table 9 Estimated odds ratios and 95% confidence intervals of the risk factors for adenoma detection rate based on a multivariable generalized linear mixed model**

Factors	Levels	OR with 95%CI	P value
T2DM	T2DM <i>vs</i> NoDM	1.29 (1.08-1.55)	0.0049
Age (yr)	Every 1 year increase in age	1.05 (1.04-1.06)	< 0.0001
BMI kg/m <sup>2</sup>	Every 1 unit increase in BMI	1.02 (1.01-1.03)	0.0003
Sex	Male <i>vs</i> Female	1.87 (1.62-2.15)	< 0.0001
Race	Black <i>vs</i> White	0.93 (0.69-1.24)	0.8020
	Asian <i>vs</i> White	1.19 (0.74-1.91)	
	Other <i>vs</i> White	1.02 (0.72-1.44)	
Insurance	Medicare <i>vs</i> Commercial	0.9 (0.68 -1.18)	0.0582
	Medicaid <i>vs</i> Commercial	1.25 (1.04-1.5)	
	Self-pay <i>vs</i> Commercial	1.1 (0.83-1.45)	
Aspirin use	Yes <i>vs</i> No	0.97 (0.80-1.18)	0.7966
Smoking	Current <i>vs</i> Past	1.32 (1.02-1.70)	0.0026
	Current <i>vs</i> Never	1.47 (1.18-1.82)	

CI: Confidence intervals; BMI: Body mass index; T2DM: Type 2 diabetes mellitus; NoDM: Nondiabetics; OR: Odds ratio.

## ARTICLE HIGHLIGHTS

### Research background

Multiple factors, including both social determinants of health (*e.g.*, access to quality healthcare) and biological gene-environment factors that may promote oncogenic transformation, have been implicated in the persistently increased colorectal cancer (CRC) incidence and mortality in Black/African Ancestry (AA) individuals compared with those of all other races in the United States.

### Research motivation

We explored how these multiple factors affect the risk of adenoma, a precursor stage for CRC, during index colonoscopies performed at two hospitals located 50 miles apart that serve two very disparate populations. While type 2 diabetes (T2DM) has been associated with increased adenoma detection in predominantly White/European Ancestry (EA), one of the few studies conducted on a predominantly Black/AA population detected no significant effect of T2DM on adenoma risk in Black/AA women.

### Research objectives

To measure the univariate effect of T2DM on the adenoma detection rate (ADR) in a predominantly Black/AA population, recent hemoglobin A1c (HbA1c) levels were used to further stratify the nondiabetic patients into prediabetic patients (pre-DM) and controls with normal glycemic status (control). To conduct a multivariable analysis of the effect of race and diabetes status in the combined datasets collected on a predominantly underinsured Black/AA population and a predominantly insured White/EA population while controlling for multiple factors.

### Research methods

The datasets were assembled by manual curation of endoscopy and clinical records in the electronic medical record at each hospital using the same vocabulary. Multivariable analysis utilized generalized linear mixed models, which incorporated both fixed effects (age, sex, race, diabetes status, obesity, smoking status, aspirin use and insurance status) and random effects (institution and individual colonoscopists).

### Research results

The ADR was significantly higher in the T2DM group than in the control group in the

predominantly underinsured Black/AA population, but no significant difference in the ADR was detected for the pre-DM group compared to both the T2DM group and the control group. T2DM along with age, obesity, smoking status, and male sex were significantly associated with a higher ADR after combining the datasets for the two disparate populations. Race, insurance status and aspirin use were not significant.

### Research conclusions

These results indicate that T2DM increases adenoma risk in both Black/AA and White/EA individuals.

### Research perspectives

We plan to conduct a prospective study recruiting patients scheduled for index screening colonoscopies at both institutions to measure HbA1c and fasting blood glucose preprocedure. We plan to refer individuals with abnormal levels for the management of prediabetes and diabetes.

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