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Original Contribution

Type 2 Diabetes and the Risk of Colorectal Adenomas: Black Women's Health Study

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Evidence for the association of type 2 diabetes mellitus (DM) with colorectal neoplasms is contradictory, and African Americans have been underrepresented in the studies published to date. In a nested case-control study (1995–2009), we examined DM and insulin therapy as risk factors for colorectal adenomas in African American women enrolled in the ongoing Black Women's Health Study. From women reporting ever having undergone a gastrointestinal endoscopy, 917 cases of colorectal adenoma were compared with 2,751 controls without a colorectal polyp, matched on age and follow-up time. Cases were verified by medical record review. We used multivariable logistic regression analyses that included DM exposures and selected confounders. There were no overall associations between DM and adenoma risk or between insulin use and adenoma risk. However, DM without insulin use was inversely associated with risk of colon adenomas (odds ratio (OR) = 0.71, 95% confidence interval (CI): 0.52, 0.97) but not rectal adenomas. DM was inversely associated with adenoma risk in women older than 55 years (OR = 0.64, 95% CI: 0.44, 0.91) but not in women 55 years or younger (OR = 1.24, 95% CI: 0.81, 1.89). Future research should attempt to replicate the unexpected inverse association of DM with colon adenoma risk among older African American women.

African American women; colorectal adenoma; colorectal cancer; diabetes; insulin

Abbreviations: BWHS, Black Women's Health Study; CI, confidence interval; CRC, colorectal cancer; DM, diabetes mellitus; OR, odds ratio.

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and cause of cancer death in the United States (1). Incidence and rates of death from CRC are disproportionately high in African Americans (1). The prevalence of colorectal adenoma, a premalignant polyp, is also high in African Americans (35%) (2), and African Americans are more likely to have larger and more advanced adenomas compared with whites (3).

Metabolic abnormalities resulting from diabetes mellitus (DM) were hypothesized to be mediators of colorectal carcinogenesis in the mid-1990s (4, 5) and, since then, numerous studies on the association of CRC with DM have been published. Pooled data from studies published before 2005 revealed a statistically significant 33% increased risk of CRC in women with a history of DM (6). However, evidence from recently published studies has been contradictory. Although 2 cohort studies in predominantly white populations showed a positive association between DM and CRC in men but not women (7, 8), other studies have reported a higher risk of CRC in women with DM than in those without (9–11).

There is limited information on the association of DM with colorectal adenomas. One hospital-based case-control study of women reported an increased risk of colorectal adenomas in diabetics compared with nondiabetics (12). Other studies of DM or impaired glucose tolerance and adenoma risk have not published sex-specific estimates. Data from case-control studies suggest an increased risk of colorectal adenomas in diabetics or those with impaired fasting blood glucose levels (100–125 mg/dL) or impaired glucose tolerance based on a 75-g glucose tolerance test (13–15). In contrast, 2 recently

published nested case-control studies failed to find an association between impaired glucose tolerance and colorectal adenomas (16, 17).

Animal studies have suggested that insulin administration leads to colonic tumors and aberrant-crypt foci, and that it promotes colonic epithelial cell proliferation (18–20). Limited data from epidemiologic studies on the association of insulin use with CRC are contradictory (7, 21–24), and a recent cross-sectional study of patients with DM did not show an increased risk of adenomas associated with insulin therapy (25). There are no data on the risk of colorectal adenomas in African Americans who use insulin.

It is estimated that 18.7% of African Americans over the age of 20 years have DM compared with 10.2% of European Americans (26). However, there is little information on the association of CRC with DM in African Americans (10), and no study has investigated DM as a risk factor for colorectal adenomas in African Americans.

Given the high prevalence of both DM and colorectal adenomas among African American women, we evaluated DM and insulin use as risk factors for colorectal adenomas in a case-control study nested within an ongoing prospective follow-up study, the Black Women's Health Study (BWHS).

MATERIALS AND METHODS

Study population

The BWHS is a prospective cohort study of African American women from across the United States. In 1995, 59,000 women aged 21–69 years enrolled by responding to health questionnaires mailed to subscribers of *Essence* magazine, members of several African American professional associations, and friends of early respondents (27). Approximately equal proportions were from the Northeast, South, Midwest, and West (28). Respondents completed 14-page questionnaires on demographic information, health status, and medical and lifestyle variables. The baseline questionnaire collected information on adult height, current weight, demographic characteristics, reproductive history, medical history, use of medications, use of cigarettes and alcohol, and usual diet. Since 1995, follow-up questionnaires have been sent every 2 years to update information on reproductive history and other exposures and to identify new occurrences of cancer and other serious illnesses. Eighty percent of the women in the baseline cohort have been followed through 2009. Approval for the study was obtained from Boston University's institutional review board.

Case and control ascertainment

We conducted a nested case-control study among participants in the ongoing BWHS. Participants were asked about a list of diseases and the date of first diagnosis on the baseline and follow-up questionnaires. In 1999, "colon or rectal polyps" was added to the list of illnesses for the following question: "Between March 1997 and March 1999, if you were diagnosed with any of the following conditions, please fill in the circle(s) and indicate the year it was first diagnosed" and included in all subsequent questionnaires. Participants were asked to mark "yes" if they had been diagnosed with colorectal polyps and to leave the question blank if they had not received a diagnosis of colorectal polyps in the preceding 2 years. The present analyses are based on self-reports from the 1999, 2001, 2003, 2005, 2007, and 2009 questionnaires. Medical records were obtained for women who self-reported the removal of a colon polyp or rectal polyp. Cases were participants whose pathology reports indicated a colorectal adenoma. Controls were participants who reported undergoing a colonoscopy or sigmoidoscopy during the period 1999–2009 and who had never reported a colorectal polyp or adenoma. It was not possible to distinguish from the questionnaire whether participants underwent colonoscopy or sigmoidoscopy. Three controls were matched to each case on age and follow-up time. Relevant exposure data for the controls were abstracted from the questionnaires prior to the "index period" (period during which the index case reported an incident adenoma diagnosis). Women with cancer (including CRC) or polyps other than adenomas and women in whom a medical record for polyp review could not be obtained were excluded from the analysis.

Assessment of DM

Type 2 DM and insulin use were ascertained through self-report on the baseline questionnaire (in 1995) and on follow-up questionnaires (in 1999–2007). Women who reported being diabetic or taking insulin/oral medications for DM were considered as having DM. We asked a random sample of women who had reported incident DM for access to their medical records and assessed the accuracy of self-reported DM among the 227 participants whose physicians provided data from their medical records (29). The sensitivity of self-reported type 2 DM was very high (96%) in the validation study (30). Participants who reported a diagnosis of DM before 30 years of age were excluded to reduce the likelihood of inclusion of women with type 1 DM. We also collected data on duration of DM from self-report of the year of DM diagnosis. For women who reported a new diagnosis of DM in their follow-up questionnaires but did not report a year of diagnosis, the midpoint of the 2-year follow-up interval was used as the year of diagnosis.

Assessment of covariates

Covariates for analysis were selected a priori from the literature. Data on cigarette smoking, regular (at least 3 days per week) aspirin use, alcohol intake, weight, height, menopausal status, and postmenopausal hormone therapy were collected on the baseline questionnaire (in 1995) and updated on the basis of data reported on the follow-up questionnaires. Body mass index, a measure of obesity, was calculated as weight (kg)/height $(m)^2$. In the 1997 and subsequent questionnaires, participants provided information on the number of hours spent each week on vigorous exercise such as basketball, swimming, running, and aerobics. Information on education was obtained in 1995 and on family history of CRC in a first-degree relative in 1999. Women were classified as premenopausal if they were still menstruating and as postmenopausal if they had experienced natural menopause (no periods for at least a year) or bilateral oophorectomy. Women with hysterectomy but without a bilateral oophorectomy were classified as postmenopausal if they were older than 56 years and as premenopausal if

they were younger than 43 years. Women who did not report menopausal status or who had undergone hysterectomy without a bilateral oophorectomy and were between the ages of 43–56 years were classified as having "unknown" menopausal status. Data on weekly servings of fruits and vegetables, total red meat intake, and total daily energy intake were derived from the 68-item modified version of the National Cancer Institute–Block food frequency questionnaire (31), which was administered to all participants at baseline (in 1995) and in the 2001 questionnaire. Time-varying covariates were reassigned for every 2 years of follow-up by using the Anderson-Gill data structure (32). This creates a new record for every follow-up cycle at which the participant is at risk and assigns covariate values for that specific questionnaire cycle. For cases, covariates were based on the questionnaires administered in the cycle prior to when they reported an adenoma (index period). Matched controls for each case also had their covariates updated on the basis of responses to the questionnaires administered during the index period. Dietary variables were derived from the food frequency questionnaire administered in 1995 if the index period was prior to 2001 and from the 2001 food frequency questionnaire if the index period was at or after the 2001 follow-up.

Statistical analysis

We used conditional logistic regression to estimate age-adjusted and multivariable-adjusted odds ratios and 95% confidence intervals for the risk of colorectal adenomas in association with DM. In the multivariable models, we adjusted for the following potential confounders selected a priori: age (in years), education (≤12, 13–15, ≥16 years), body mass index (<25, 25–29.9, 30–34.9, ≥35) (only 0.2% of the case-control sample had body mass index <18), smoking status (never, past, current), alcohol intake (nondrinker, 1–6 drinks/week, ≥7 drinks/week), family history of CRC in a first-degree relative, regular aspirin use (≥3 days/week), menopausal status, vigorous activity (none, ≤1 hour/week, 2–6 hours/week, ≥7 hours/week), total energy intake (in kcal), fruit and vegetable intake (in servings/week), and red meat intake (in servings/week). We assessed effect modification of the association between adenomas and DM by age, menopausal status, postmenopausal hormone therapy, family history of CRC, obesity, and aspirin use. We assessed interaction by using the log-likelihood ratio test, which compared models with and without the multiplicative interaction terms. All statistical analyses were performed by using SAS, version 9.2, software (SAS Institute Inc., Cary, North Carolina).

RESULTS

After the exclusion of participants with prevalent or incident cancer and prevalent colorectal polyps, there were 22,362 participants who reported having had a colonoscopy or sigmoidoscopy during the follow-up period. Of these, 4,078 (18%) reported having had a polyp removed. Medical records were obtained from 1,380 (34%) of those women, and 917 were found to have had a colorectal adenoma. Of these, 552 had at least 1 proximal adenoma, 359 had at least 1 distal adenoma, and 92 had rectal adenoma(s). Controls were randomly selected from the 18,284 women who had a colonoscopy or sigmoidoscopy and who never reported a diagnosis of colorectal polyp. Three controls were matched to each colorectal adenoma case by age, for a total of 2,751 controls.

The baseline characteristics of the cases and matched controls are presented in Table 1. Compared with controls, cases were more likely to be current smokers. They were also more likely to drink 7 or more alcoholic drinks per week and to have a family history of CRC in a first-degree relative. Cases reported consuming fewer servings of fruits and vegetables per week compared with controls. Body mass index, educational levels, regular aspirin use, self-reported vigorous physical activity, menopausal status, and red meat intake were not associated with case-control status in bivariate analyses.

Age- and multivariable-adjusted odds ratios for DM and colorectal adenomas are presented in Table 2. The multivariable-adjusted odds ratio for DM relative to no DM was 0.83 (95% CI: 0.64, 1.09). Diabetics who reported never having used insulin had a 25% lower risk of adenomas compared with

Table 1. Baseline Characteristics in a Matched Case-Control Study[a] Nested in the Black Women's Health Study, 1997–2009

Variable	Adenoma Cases ($n = 917$)		Polyp-Free Controls ($n = 2,751$)	
	Mean (SD)	%	Mean (SD)	%
Age, years	54.6 (8.5)		54.6 (8.5)	
Body mass index[b]	30.1 (6.7)		29.8 (6.4)	
Education				
≤12 years		17		19
13–15		30		32
≥16		53		49
Current smoker		16**		11**
Alcohol use (≥7 drinks/week)		7*		4*
Family history of colorectal cancer in first-degree relative		14**		8**
Regular aspirin use (≥3 days/week)		37		37
Vigorous physical activity (≥2 hours/week)		16		15
Postmenopausal		59		59
Total energy intake, kcal	1,338 (591)		1,323 (594)	
Red meat intake, servings/week	4.08 (3.90)		3.98 (4.09)	
Fruit and vegetable intake, servings/week	17.6 (12.9)**		19.0 (14.1)**	
Diabetes		12		14

Abbreviation: SD, standard deviation.

* $P < 0.05$ for difference between cases and controls; ** $P < 0.01$ for difference between cases and controls.

[a] Cases and controls were matched on age and follow-up time.

[b] Weight (kg)/height $(m)^2$.

Table 2. Odds Ratios for the Association Between DM and Risk of Colorectal Adenomas in a Matched Case-Control Study[a] Nested in the Black Women's Health Study, 1997–2009

DM Status by Adenoma Type	No. of Cases	No. of Controls	Age-adjusted OR[b]	95% CI	Multivariable-adjusted[c] OR[b]	95% CI
Colorectal adenoma						
No DM	804	2,378	1.00	Referent	1.00	Referent
DM	113	373	0.89	0.71, 1.12	0.83	0.64, 1.09
DM without insulin use	81	306	0.78	0.60, 1.01	0.75	0.56, 1.00
DM with insulin use	32	67	1.41	0.92, 2.17	1.23	0.75, 2.02
Colon adenoma						
No DM	734	2,160	1.00	Referent	1.00	Referent
DM	99	339	0.86	0.67, 1.09	0.80	0.60, 1.05
DM without insulin use	71	279	0.75	0.57, 0.99	0.71	0.52, 0.97
DM with insulin use	28	60	1.37	0.86, 2.17	1.21	0.71, 2.07
Distal adenoma						
No DM	318	940	1.00	Referent	1.00	Referent
DM	41	137	0.88	0.60, 1.29	0.81	0.52, 1.28
DM without insulin use	30	110	0.80	0.52, 1.23	0.76	0.46, 1.24
DM with insulin use	11	27	1.20	0.58, 2.45	1.07	0.45, 2.58
Proximal adenoma						
No DM	480	1,417	1.00	Referent	1.00	Referent
DM	72	239	0.89	0.67, 1.18	0.83	0.60, 1.14
DM without insulin use	52	198	0.78	0.56, 1.07	0.72	0.50, 1.04
DM with insulin use	20	41	1.45	0.83, 2.53	1.38	0.74, 2.59
Rectal adenoma						
No DM	80	237	1.00	Referent	1.00	Referent
DM	12	39	0.91	0.45, 1.84	0.99	0.41, 2.35
DM without insulin use	11	31	1.06	0.50, 2.24	1.40	0.56, 3.52
DM with insulin use	1	8	0.38	0.05, 3.02	0.11	0.01, 1.48

Abbreviations: CI, confidence interval; DM, diabetes mellitus; OR, odds ratio.

[a] Cases and controls were matched on age and follow-up time.

[b] Based on a conditional logistic regression model.

[c] Adjusted for age, educational status, body mass index (weight (kg)/height (m)^2), physical activity, family history of colorectal cancer in a first-degree relative, menopausal status, smoking status, alcohol intake, total energy intake, red meat intake, fruit and vegetable intake, and regular aspirin use.

nondiabetics (95% CI: 0.56, 1.00). However, those taking insulin had a 23% higher risk of adenomas compared with nondiabetics, but the result was not statistically significant. The inverse association between adenoma risk and DM among women not taking insulin was observed for colon adenomas (odds ratio (OR) = 0.71, 95% CI: 0.52, 0.97) but not rectal adenomas. The association of DM with adenoma risk did not differ by adenoma site within the colon (distal vs. proximal). Because the estimates for the association of DM with rectal adenomas were based on small numbers and were therefore unstable, additional analyses were restricted to colon adenomas.

There was a significant interaction between DM and age in colon adenoma risk ($P = 0.03$) (Table 3). The odds ratios for DM and colon adenomas were 0.64 (95% CI: 0.44, 0.91) among women over age 55 years and 1.24 (95% CI: 0.81, 1.89) among women at or under age 55 years. The odds ratio for insulin use in women at or under age 55 years (OR = 1.57, 95% CI: 0.70, 3.55) was also elevated but was not significantly different compared with that of women over age 55 years (OR = 1.16, 95% CI: 0.59, 2.26) (Table 3).

Duration of DM was inversely associated with colon adenoma risk (Table 4). Women with DM for 10 years or longer had a 40% lower risk of colon adenomas than those without DM (95% CI: 0.39, 0.94), whereas women with DM for 5 years or less had an odds ratio of 1.07 (95% CI: 0.73, 1.56) associated with colon adenoma risk compared with nondiabetic women. The reduction in colon adenoma risk with increasing DM duration was observed both for women over age 55 years and for women at or under age 55 years. However, odds ratios were consistently below 1 for women over age 55 years. In addition, the P value for the linear trend of decreasing risk over increasing DM duration was significant only among women over age 55 years. (Table 4)

Regular aspirin use, obesity, and family history of CRC did not modify the association between DM and colon adenoma risk among women in this study (data not shown). We have

Table 3. Odds Ratios for the Association Between DM With and Without Insulin Use and Risk of Colon[a] Adenomas Stratified by Age[b] in a Matched Case-Control Study[c] Nested in the Black Women's Health Study, 1997–2009

DM Status	Age ≤55 Years				Age >55 Years				$P_{interaction}$ With Age
	No. of Cases	No. of Controls	Multivariable-adjusted[d] OR[e]	95% CI	No. of Cases	No. of Controls	Multivariable-adjusted[d] OR[e]	95% CI	
No DM	401	1,234	1.00	Referent	347	978	1.00	Referent	
DM	48	113	1.24	0.81, 1.89	57	234	0.64	0.44, 0.91	0.03
DM without insulin use	38	100	1.15	0.71, 1.85	39	194	0.54	0.36, 0.81	0.03
DM with insulin use	14	24	1.57	0.70, 3.55	18	40	1.16	0.59, 2.26	0.72

Abbreviations: CI, confidence interval; DM, diabetes mellitus; OR, odds ratio.

[a] Cases with only rectal adenoma(s) and matched controls were excluded.

[b] Age was categorized on the basis of median age among controls.

[c] Cases and controls were matched on age and follow-up time.

[d] Adjusted for educational status, body mass index (weight (kg)/height (m)^2), physical activity, family history of colorectal cancer in a first-degree relative, menopausal status, smoking status, alcohol intake, total energy intake, red meat intake, fruit and vegetable intake, and regular aspirin use.

[e] Based on a conditional logistic regression model.

also not reported data on stratified analysis by menopausal status because determination of menopausal status was partially based on age and, therefore, the results were difficult to distinguish from age-stratified analyses. Among postmenopausal women who did not use hormone therapy, the odds ratios were 0.64 (95% CI: 0.40, 1.02) for the association of colon adenomas with DM and 1.14 (95% CI: 0.51, 2.59) for the association of colon adenomas with insulin use.

DISCUSSION

In this case-control study of African American women nested in a large ongoing cohort study, there was an inverse association of DM with colon adenomas in women not taking insulin but not in women using insulin therapy. The inverse association of DM with colon adenoma risk was restricted to women over the age of 55 years. There was also some evidence to suggest that increasing duration of DM was associated with decreasing risk of colon adenomas.

This is the first analysis from a prospective follow-up study of DM, insulin use, and colorectal adenomas in African American women. Our findings do not corroborate evidence from previous studies that suggested DM was a risk factor for colorectal adenomas in women (12, 14, 15). However, 2 of these were case-control studies that did not report sex-specific estimates (14, 15), and 1 was a hospital-based case-control study limited to hormone-negative postmenopausal women or women who had undergone a bilateral oophorectomy and who were not taking hormone therapy (12). When we restricted our analysis to postmenopausal women without hormone therapy, we did not observe an increased risk of colon adenomas with either DM or insulin use. Our results are consistent with those from recent population-based studies of adenoma risk with metabolic syndrome, which suggest that abnormal fasting blood glucose levels (≥110 mg/dL) are not an independent risk factor for colorectal adenomas (16, 17). Although a 2005 meta-analysis of epidemiologic studies conducted in the 1980s and 1990s (6), including results from large cohorts of women such as the Nurses' Health Study (33), reported a significantly increased risk of CRC in women with DM, studies published since the meta-analysis, with a large proportion of the follow-up conducted after 2000, have shown either null results for women or attenuated effect estimates compared with men.

Metabolic abnormalities in DM, such as insulin resistance and hyperinsulinemia, have been proposed to be involved in colorectal neoplasia risk associated with risk factors such as obesity and lack of physical activity (4, 5). There is sufficient biological plausibility and evidence to support the role of insulin and insulinlike growth factors in the adenoma-carcinoma sequence (18–20). Increased levels of endogenous insulin and insulinlike growth factor-1 have been shown to be associated with increased risk of adenomas (34, 35) and CRC (36, 37). Therefore, it is intriguing that recent large studies, including ours, have failed to show a positive association between DM and colorectal neoplasms. Contrary to our hypothesis, DM was associated with a lower risk of adenomas among older postmenopausal women. It has been suggested that the increased use of metformin as the first line of therapy for DM and better blood glucose control among diabetic women compared with men in recent years might explain the lack of association seen with DM and colorectal neoplasms (7). It is also likely that, compared with nondiabetic women, diabetic women are more likely to make lifestyle changes regarding nutrition, physical activity, and other factors that contribute to risk of colorectal adenomas as a result of their DM diagnoses and physician recommendations. Although we updated time-varying lifestyle covariates to capture the most recent self-reported lifestyle behavior prior to an adenoma diagnosis and adjusted for selected dietary and lifestyle factors in our regression models, it is possible that, for some women, the covariate information reflected the post-DM "healthy" lifestyle and, for others, the pre-DM "unhealthy" lifestyle. This is a possibility because not all covariates were assessed at all time points during the follow-up period. For example, diet was assessed only in the 1995 and

Table 4. Odds Ratios for the Association Between Duration of DM and Risk of Colon[a] Adenomas in a Matched Case-Control Study[b] Nested in the Black Women's Health Study, 1997–2009

DM Status and Duration, Years[c]	All Participants				Age ≤55 Years				Age >55 Years			
	No. of Cases	No. of Controls	Multivariable-adjusted[d] OR[e]	95% CI	No. of Cases	No. of Controls	Multivariable-adjusted[d] OR[e]	95% CI	No. of Cases	No. of Controls	Multivariable-adjusted[d] OR[e]	95% CI
No DM	748	2,212	1.00	Referent	401	1,234	1.00	Referent	347	978	1.00	Referent
Yes DM												
≤5	51	137	1.07	0.73, 1.56	26	54	1.42	0.80, 2.54	25	83	0.82	0.48, 1.39
5–9	21	71	0.87	0.50, 1.51	12	27	1.35	0.62, 2.92	9	44	0.59	0.26, 1.32
≥10	33	139	0.60	0.39, 0.94	10	32	0.85	0.37, 1.97	23	107	0.52	0.31, 0.89
P_{trend}			0.04				0.66				<0.01	

Abbreviations: CI, confidence interval; DM, diabetes mellitus; OR, odds ratio.

[a] Cases with only rectal adenoma(s) and matched controls were excluded.

[b] Cases and controls were matched on age and follow-up time.

[c] Duration of DM was calculated on the basis of the year of diagnosis reported by participants. For participants who did not report year of diagnosis but who reported a new diagnosis of DM on the follow-up questionnaire, the date of diagnosis was assumed to be the midpoint of the 2-year follow-up interval.

[d] Adjusted for age, educational status, body mass index (weight (kg)/height $(m)^2$), physical activity, family history of colorectal cancer in a first-degree relative, menopausal status, smoking status, alcohol intake, total energy intake, red meat intake, fruit and vegetable intake, and regular aspirin use.

[e] Based on a conditional logistic regression model.

2001 questionnaires. Therefore, the inverse association of DM and adenoma risk might be explained by changes in diet and lifestyle after a DM diagnosis. This hypothesis receives indirect support from the observation that the inverse association between DM and adenoma risk became stronger with increasing duration of DM. If lifestyle changes are indeed responsible for the lower risk of adenomas among diabetic women, we would expect these changes to be evident over a longer rather than a shorter timeframe.

Few studies have investigated the association of insulin use in DM as a risk factor for colorectal adenomas. In a hospital-based case-control study of postmenopausal women, insulin use was not associated with the risk of colorectal adenomas (12). A recent cross-sectional study of diabetic patients undergoing colonoscopy also did not find insulin therapy to be associated with adenoma risk (25). Campbell et al. (7) did not find an association between insulin use and CRC among women in the Cancer Prevention Study II cohort. Null results for older African American women in our study who reported taking insulin support findings from these studies. There was some evidence to suggest that insulin use might be associated with increased risk of adenomas in younger women, but the results were based on small numbers of cases and were not statistically significant.

The strengths of our study include the nested design within a large prospective cohort of African American women in the United States, adenoma outcomes verified by medical records, and detailed information on a large number of covariates. In addition, results from our study are generalizable to most African Americans in the United States. The rate of screening endoscopy in our cohort was 63% for women aged 50–64 years and 61% for women aged 65–74 years. These figures are very similar to the 60% colonoscopy screening rate reported in the 2010 Behavioral Risk Factor Surveillance System for African Americans aged 50–75 years (38).

Our study has limitations. As stated earlier, DM status and treatment for DM were self-reported and could have led to exposure misclassification, but the impact of such misclassification on our results is likely to be negligible. A validation substudy within the BWHS cohort observed excellent concordance of self-reported physician-diagnosed DM with medical records (29, 39). In addition, a validation study from the Women's Health Initiative concluded that "treated diabetes," defined as "self-report of physician diagnosis and treatment with insulin or oral anti-diabetic drugs," is sufficiently accurate for use in epidemiologic studies (40). A recent analysis from the Atherosclerosis Risk in Communities cohort also confirmed a high specificity of self-report for prevalent DM (96%–97%) (41). Participant-reported polyps were verified by medical record review in our study, but the absence of polyps was not verified. Misclassification in the adenoma outcomes in which participants diagnosed with adenomas failed to report polyps and were therefore included in the control group would attenuate the DM-adenoma association toward null. However, previous studies have shown that self-report of polyps has a high negative predictive value (94%–100%) for adenomas, and it is unlikely that this was a major source of bias in our study (42, 43). Although we found evidence of effect modification by age for the DM-adenoma association, we had no a priori reason for this analysis, and we looked within strata of several other factors, as well. The

stratified analyses in this study were based on small numbers and were thus underpowered. Results obtained for the effect modification by age for the DM-adenoma association should be considered a new hypothesis that needs to be confirmed in adequately powered analyses in the future. We also did not have details of medication use and, thus, could not assess the risk of adenomas associated with specific oral medications, such as metformin, which might reduce the risk of adenomas in diabetic women. Results from our study may not be generalizable to African American women with low educational attainment. More than 95% of the BWHS cohort had a high school education or more at enrollment compared with 83% of African American women in the general population (44). In addition, the prevalence of DM reported in our study, primarily for women 65 years of age and older, is lower than that reported for the general population of African American women (45).

In conclusion, in a nested case-control study of incident colorectal adenomas among African American women who have undergone screening colonoscopies or sigmoidoscopies, an inverse relationship was observed between DM and colon adenoma risk, primarily among older women who did not report taking insulin for DM management. We also observed a trend suggesting that increasing duration of DM might be associated with lower risk of colon adenomas. These unexpected findings suggest an intriguing hypothesis and warrant replication in future studies.

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