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Physical activity and risk of colon cancer among diabetic and non-diabetic US adults

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Abstract

OBJECTIVE: To determine whether moderate to vigorous physical activity is associated with decreased risk of colon cancer among diabetics.

RESEARCH DESIGN AND METHODS: We evaluated the association between physical activity and colon cancer among 25,753 individuals with self-reported history of diabetes and 274,965 non-diabetics of the National Institutes of Health-AARP Diet and Health Study who were aged 50–71 years in 1995–96. Moderate to vigorous physical activity was assessed at baseline using a self-administered questionnaire. Follow-up for colon cancer incidence extended to December 31, 2011.

RESULTS: During 13.0 years of follow-up, 480 diabetics and 4,151 non-diabetics developed colon cancer. Among diabetics, compared to never/rarely engaging in physical activity, >7 hours/week of physical activity showed a reduced risk of colon cancer in the age- and sex-adjusted model (Hazard ratio (HR)=0.74, 95% confidence interval (CI)=0.56–0.996, $P_{trend}=.16$). This association was attenuated and no longer statistically significant following additional control for other covariates (HR=0.78, 95% CI=0.58–1.05, $P_{trend}=.29$). By comparison, physical activity was inversely related to colon cancer risk in non-diabetic individuals (multivariable-adjusted HR=0.81, 95% CI=0.73–0.89, $P_{trend}<.001$).

CONCLUSIONS: In this investigation of the physical activity and colon cancer relation among diabetics, we found a statistically significant inverse relationship between physical activity and colon cancer among diabetics in the age- and sex-adjusted model which was no longer statistically significant in the multivariable-adjusted model. A reduced risk was noted among non-diabetics, irrespective of other covariates. Future studies with a larger number of participants are required to explore whether physical activity beneficially affects colon cancer risk among diabetics.

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Disclosure

The authors declare no conflicts of interest.

Keywords

diabetes; physical activity; colon cancer

INTRODUCTION

In 2014, the global number of individuals with diabetes mellitus was 387 million, and it is projected to increase 1.5-fold in the next 20 years.¹ That figure mirrors the climbing rates of obesity^{2–4} and physical inactivity,^{5,6} which greatly contribute to the increase in type 2 diabetes.⁷ Diabetic individuals are at greater risk of developing colon cancer than non-diabetic individuals.⁸ The proposed underlying biologic mechanisms linking diabetes to increased risk of colon cancer include insulin resistance⁹ and chronic inflammation.¹⁰ Physical activity plays an important role in protecting against colon cancer.^{11,12} High levels of physical activity are linked to improvements in insulin sensitivity^{13,14} and other physiologic conditions related to colon carcinogenesis, such as low-grade chronic inflammation,¹⁵ natural killer cell activity,¹⁶ vitamin D levels,¹⁷ and intestinal transit time.¹⁸

Despite the existence of potential interrelations between diabetes, physical activity, and colon cancer risk, the association between physical activity and colon cancer risk among diabetic individuals remains unknown. Previous research has focused primarily on physical activity and cancer incidence in the overall population. Howard et al.¹⁹ investigated the relationship of physical activity and colon cancer risk in the National Institutes of Health (NIH)-AARP Diet and Health Study and observed a statistically significant inverse association between moderate to vigorous physical activity and colon cancer among men (multivariable-adjusted hazard ratio (HR)=0.82, 95% confidence interval (CI)=0.67–0.99), whereas the relationship was less pronounced in women (HR=0.93, 95% CI=0.70–1.22).

Because diabetic patients are at greater risk of comorbidities and premature death than non-diabetic individuals,^{20–24} it is important to determine whether physical activity produces similar effects in diabetic and non-diabetic individuals. Evidence on reduced colon cancer risk through increased physical activity in individuals with diabetes may help guide specific recommendations for this high-risk population. Current physical activity guidelines for diabetic patients target the prevention of cardiovascular disease and mortality, but do not include recommendations for the prevention of cancer.^{25,26}

We therefore investigated 1) the association between physical activity and risk of colon cancer among participants with diabetes in the NIH-AARP Diet and Health Study; 2) whether relations differ by colonic anatomic subsite, including proximal and distal colon cancers, and 3) whether associations vary according to population subgroups.

To provide information about whether physical activity protects against colon cancer among individuals without diabetes, we also investigated the association between physical activity and colon cancer among non-diabetics.

METHODS

Study population

The NIH-AARP Diet and Health Study is a prospective cohort study²⁷ of 566,398 adults aged 50–71 years residing in six U.S. states (California, Florida, Pennsylvania, New Jersey, North Carolina, Louisiana) or two metropolitan areas (Atlanta, Georgia, and Detroit, Michigan) who satisfactorily completed a mailed questionnaire in 1995–1996. The questionnaire collected data about socio-demographic characteristics, medical conditions, and lifestyle factors. Within 6 months of that assessment, a second questionnaire (so-called risk factor questionnaire) inquired about more detailed information on risk factors including moderate to vigorous physical activity, and 334,905 men and women completed it. We excluded study members with prevalent cancer at the time the second questionnaire was returned, those with missing information on physical activity, those with missing data on body mass index (BMI), and those with a BMI < 18.5 kg/m² or > 65 kg/m², leaving a total of 300,718 individuals for analysis, of which 25,753 were diabetic. These diabetic and non-diabetic study members were followed up for colon cancer incidence.

The Special Studies Institutional Review Board of the US National Cancer Institute approved the NIH-AARP Diet and Health Study, and all participants gave informed consent by virtue of completing and returning the questionnaires.

Diabetes ascertainment

History of diabetes was assessed by self-report. Participants were asked if a doctor had ever told them that they had diabetes and an affirmative response was considered as having been diagnosed with diabetes. The questionnaire did not ask about the type or onset of diabetes, or about diabetes medications.

Colon cancer ascertainment

Vital status of the NIH-AARP Diet and Health Study cohort was determined by periodic linkage to the Social Security Administration Death Master File in the United States, the National Death Index Plus (for participants who could also be matched to the Death Master File), and cancer registry records. Questionnaire responses and other mailings were also used to confirm vital status. Incident colon cancer was identified through eight certified state cancer registries in which the study participants were recruited, and additionally through the cancer registries of Texas, Arizona, and Nevada to which study participants most frequently moved during follow-up. A pilot study was conducted in a subset of the NIH-AARP Diet and Health Study population to determine the accuracy of cancer case ascertainment through cancer registries.²⁸ A number of identifiers were used to match the members of the pilot study to cancer registries.²⁸ In addition, self-reports and confirmation through medical records were used to ascertain completeness of the cancer cases reporting from cancer registries.²⁸ The study estimated that the sensitivity for case ascertainment of the registries included in the NIH-AARP cohort is about 90% with a 4-year lag period between the end of follow-up of cancer incidence and the linkage date.²⁸

Colon cancer was defined using the International Classification of Diseases for Oncology codes for colon cancer (C180–C189, C260). Colonic anatomic subsites were classified as proximal colon (cecum through transverse colon; codes C180–184) and distal colon (splenic flexure through sigmoid colon; codes C185–187). Because most evidence indicates that physical activity is not related to rectal cancer, we did not include rectal cancer in our case definition.^{11,29}

Assessment of physical activity

In the second questionnaire, study members were asked to report how often they participated in moderate and vigorous activities in the past 10 years: never, rarely, weekly but <1 hour/week, 1–3 hours/week, 4–7 hours/week, or >7 hours/week. A list of examples of moderate and vigorous activities was provided including tennis, golf (walking), biking, swimming, heavy gardening, weight lifting, basketball/baseball, football/soccer, cheerleading/drill team, handball/racquetball, hiking/climbing mountains, fast walking/fast dancing, rowing, aerobics, jogging/running, and heavy housework. For our analysis, we collapsed the “never” and “rarely” response categories. The validity of these questions has not been evaluated, but they are similar to assessments of recreational moderate to vigorous activity noted to have acceptable validity,³⁰ and the moderate to vigorous physical activity question is inversely associated with total mortality,³¹ breast cancer,³² and endometrial cancer.³³

Statistical analysis

Cox proportional hazards models were applied to estimate HRs and 95% CIs for the relation of physical activity to colon cancer across different physical activity categories. The proportional hazards assumption was verified using Schoenfeld’s residuals.³⁴ Follow-up time extended from the scan date of the return of the second questionnaire to the date of diagnosis of colon cancer, date of death, relocation out of the cancer registry ascertainment area, or 31 December 2011, whichever came first. For the analyses of proximal or distal colon cancers, the other anatomic sub-type was censored.

The initial model adjusted for age (continuous) and sex. In a subsequent multivariable model, we additionally considered race/ethnicity (white, black, other, unknown), education (<12 years, high school graduate, college education or some vocational training, college graduate/postgraduate, unknown), smoking status (never smoker, former smoker with 20 cigarettes per day or less, former smoker with more than 20 cigarettes per day, current smoker with 20 cigarettes per day or less, current smoker with more than 20 cigarettes per day, missing), hormone replacement therapy use in women (never, past, current, unknown), family history of colon cancer (any first-degree relatives with colon cancer, yes, no, unknown), non-steroidal anti-inflammatory drug use (aspirin/ibuprofen, yes, no, missing), and intakes of red meat (quartiles of g/1,000 kcal per day), fiber (quartiles of g/1,000 kcal per day), and alcohol (0.0 g per day, 0.1–14.9 g per day, 15 g per day). In a third fully adjusted model, we entered BMI (18.5–24.9 kg/m², 25.0–29.9 kg/m², 30.0–34.9 kg/m², 35–65 kg/m²) in the model to explore whether BMI represents an intermediate variable of the relation of physical activity to colon cancer. The covariates were chosen *a priori* because they are considered risk factors for colon cancer^{35–37} and have been included as potential confounders in the available literature. All covariates were assessed in the baseline

questionnaire except age and non-steroidal anti-inflammatory drug use, which were queried about in the second questionnaire. We calculated age-standardized incidence rates of colon cancer per 100,000 person-years for different physical activity levels adjusting for sex.

Potential interactions between physical activity and covariates were evaluated using a likelihood ratio test. To determine whether undiagnosed colon cancer at baseline may have caused participants to report a lower physical activity level, thereby leading to potentially biased results, we performed sensitivity analyses that excluded colon cancer cases occurring during the first year of follow-up. All statistical tests were two-sided and *P* values were considered statistically significant at the .05 level. Analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

During 3,908,237 person-years of follow-up (mean follow-up duration: 13.0 years; SD: 3.96), 480 diabetic and 4,151 non-diabetic participants developed colon cancer. Characteristics of the study members according to ascending levels of physical activity are summarized in Table 1.

Among diabetic participants, compared to never/rarely participating in physical activity, >7 hours per week of moderate to vigorous physical activity showed an inverse relation to total colon cancer in the age- and sex-adjusted model (HR=0.74, 95% CI=0.56–0.996, $P_{trend}=0.16$, Table 2) that was attenuated and no longer statistically significant after further adjustment for other potential confounding variables (HR=0.78, 95% CI=0.58–1.05, $P_{trend}=0.29$; additional adjustment for BMI: HR=0.81, 95% CI=0.60–1.09, $P_{trend}=0.45$). We noted an inverse association between physical activity and colon cancer in nondiabetic-individuals (multivariable-adjusted HR=0.81, 95% CI=0.73–0.89, $P_{trend}<0.001$). Further adjustment for BMI had little impact on the results among non-diabetics.

Among diabetic individuals, exclusion of colon cancer cases that occurred during the first year of follow-up attenuated the association (multivariable-adjusted HR=0.87, 95% CI=0.64–1.19 comparing extreme physical activity groups, $P_{trend}=0.68$). Exclusion of colon cancer cases occurring during the first year of follow-up did not materially change the results in non-diabetic individuals (HR=0.77, 95% CI=0.70–0.86, $P_{trend}<0.001$).

To explore for possible differences in threshold levels of physical activity required for colon cancer risk reduction between diabetics and non-diabetics, we repeated our multivariable-adjusted analyses using varying cut-points for physical activity categories (Supplementary Table 1). Among diabetic individuals, comparing 1 versus <1 hour per week of physical activity (multivariable-adjusted HR=0.92, 95% CI=0.76–1.11) or 4 versus 3 hours per week of physical activity (HR=0.97, 95% CI=0.80–1.16) revealed a weaker association with colon cancer than comparing >7 versus 7 hours per week of physical activity (HR=0.80, 95% CI=0.63–1.03). Among non-diabetics, 1 versus <1 hour per week of physical activity was associated with a multivariable-adjusted HR for colon cancer of 0.85 (95% CI=0.80–0.91) in non-diabetics. Similarly, 4 versus 3 hours per week of physical activity was related to an HR for colon cancer of 0.85 (95% CI=0.80–0.91) in non-diabetics. The inverse

association among non-diabetics remained evident for >7 versus ≤7 hours per week of physical activity (HR=0.91, 95% CI=0.85–0.98).

On evaluation of colon cancer anatomic subtypes, high versus low physical activity was inversely related to proximal colon cancer in age- and sex-adjusted analysis in diabetics (HR=0.68, 95% CI=0.46–0.98, $P_{trend}=0.27$, Table 2), but the association was no longer statistically significant following adjustment for other covariates (multivariable-adjusted HR=0.69, 95% CI=0.47–1.01, $P_{trend}=0.32$; additional adjustment for BMI: HR=0.72, 95% CI=0.49–1.06, $P_{trend}=0.47$, Table 2). We observed a statistically significant inverse relation between physical activity and risk of proximal cancer in non-diabetics after full adjustment (HR=0.78, 95% CI=0.68–0.89, $P_{trend}<0.001$). The multivariable-adjusted relation of physical activity to distal colon cancer was statistically non-significant in both diabetics and non-diabetics (Table 2).

In analyses stratified by sex, a significant inverse association between physical activity and total colon cancer was noted in non-diabetic men (multivariable-adjusted HR=0.72, 95% CI=0.64–0.82; $P_{trend}<0.001$), but not women (HR=1.004, 95% CI=0.84–1.20; $P_{trend}=0.48$, $P_{interaction}=0.004$, Table 3).

We calculated age- and sex-adjusted incidence rates for colon cancer across increasing categories of physical activity (Figure 1). Within each category of physical activity, the incidence rate of colon cancer was higher in diabetics than non-diabetics.

DISCUSSION

In the present investigation, we observed a statistically significant inverse association between physical activity and total colon cancer risk in diabetics in age- and sex-adjusted analysis, but that association was attenuated and no longer statistically significant following adjustment for potential risk or protective factors for colon cancer. We found an approximately 20% statistically significant reduced risk of colon cancer among non-diabetics, irrespective of BMI and other covariates.

To the best of our knowledge, no study has examined physical activity in relation to colon cancer risk among individuals with diabetes. Two studies^{38,39} investigated the association between physical activity and colon cancer in the general population and reported that diabetes status did not modify the results, but did not provide risk estimates. The associations we observed for physical activity and colon cancer among non-diabetics are in line with those found in the general population, where high versus low overall or recreational physical activity is related to 14–24% lower risks of total colon cancer.^{11,40}

Intervention studies that investigated the effect of physical activity on glucose metabolism in diabetic and non-diabetic individuals have yielded heterogeneous findings. For example, one study found that a single bout of exercise at 65% maximal oxygen uptake (VO_{2max}) failed to improve glucose disposal upon insulin stimulation in diabetics and obese non-diabetics,⁴¹ whereas other studies reported significant improvements in glucose metabolic clearance rate in obese diabetics and obese non-diabetics after a single bout of exercise at 85% VO_{2max} ^{42,43} or until heart rate reached 150 to 160 beats/min.⁴⁴ Two studies

found that a single bout of exercise at 68% $\text{VO}_{2\text{max}}$ ⁴⁵ or 75% $\text{VO}_{2\text{max}}$ ⁴⁶ did not affect glucose metabolism among individuals with mild diabetes,⁴⁵ obese diabetics,⁴⁶ or obese non-diabetics,⁴⁶ but extending the exercise training to seven days resulted in metabolic improvements in the diabetic group in both studies.^{45,46} Another study with a seven-day exercise intervention at 70% $\text{VO}_{2\text{max}}$ or 70 minutes at 50% $\text{VO}_{2\text{max}}$ reported an improved insulin response to glucose ingestion in obese normoglycemic individuals after exercise at 70% $\text{VO}_{2\text{max}}$, but not in obese diabetics who were relatively hypoinsulinemic.⁴⁷ Three studies investigating exercise interventions at $\text{VO}_{2\text{max}}$ up to 70% for 6 weeks,⁴⁸ 8 weeks,⁴⁹ and 4 months⁵⁰ detected mild to significant improvements in glucose tolerance or disposal in diabetics⁵⁰ and overweight/mildly obese diabetics or non-diabetics,^{48,49} of which one study found greater improvements in obese individuals with mild diabetes⁴⁸ and another study did not find improved glucose metabolism in diabetic patients with poor metabolic control.⁵⁰ Taken together, exercise of appropriate intensity and duration can improve glucose metabolism among diabetic individuals.

The sample size of our study may have been insufficient to supply adequate power to detect a noticeable association between physical activity and colon cancer risk among diabetics, which is supported by the wide confidence interval of the multivariable-adjusted risk estimate for diabetics (HR=0.78, 95% CI=0.58–1.05). Thus, our study cannot rule out the possibility that a meaningful association exists.

In our study, moderate to vigorous physical activity during the past ten years was queried by the self-report method and we cannot exclude the possibility that our study failed to capture adequate physical activity measures that reflect regular exercise of sufficient intensity.

Whether there are biologic reasons for why the associations between physical activity and colon cancer risk may differ by diabetes status requires further research. Several biologic links between physical activity and colon cancer are plausible including improvements in the insulin and insulin-like growth factor axis,^{13,14,51} chronic inflammation,¹⁵ immune function,¹⁶ vitamin D levels,¹⁷ intestinal transit time,¹⁸ and inhibition of cox-derived prostaglandin E2 synthesis.⁵² As discussed above, increased physical activity may improve glucose metabolism and insulin sensitivity among diabetics and non-diabetics,^{13,42,43,48,49,53} thereby potentially reducing the risk of colon cancer. Moreover, physical activity may lower pro-inflammatory markers such as C-reactive protein, interleukin-6, and tumor necrosis factor-alpha, and it may increase anti-inflammatory adiponectin levels.⁵⁴ Although pro-inflammatory markers are higher in diabetics than non-diabetics,⁵⁵ improvements in interleukin-6 levels among type 2 diabetics have been observed in studies with 12 weeks and one year of exercise training depending on exercise modalities,^{56–58} but not in a study with a four-week exercise intervention.⁵⁹ Higher C-reactive protein levels have been found in diabetic men without physical activity participation as compared to men with diabetes who are regularly physically active.⁶⁰ Physical activity may also improve the immune system in the general population, specifically by increasing natural killer cell activity.¹⁶ Although diabetic individuals may be more prone to infectious diseases due to disturbances in cellular innate immunity,⁶¹ the effect of physical activity on immune function among diabetics remains unknown. In diabetic rats, physical exercise has been shown to improve immunologic parameters.⁶² Moreover, outdoor exercise provides sun

exposure and subsequently higher vitamin D levels, which have been suggested to protect against colon cancer,⁵² but results for circulating vitamin D and colon cancer have been mixed.⁶³ Individuals with diabetes have lower vitamin D levels than non-diabetics,^{64,65} although results are conflicting.^{66,67} To the best of our knowledge, no study has examined the impact of exercise on vitamin D levels among diabetics. Physical activity may affect colon cancer carcinogenesis by lowering intestinal transit time, thereby reducing contact to carcinogens in the colon.¹⁸ Diabetic individuals may have a lower intestinal transit time than non-diabetic individuals⁶⁸ and it remains to be elucidated whether physical activity improves intestinal transit time in diabetics.

Our analyses regarding colon cancer anatomic subsites showed that physical activity was related to 24% reduced risk of proximal colon cancer in non-diabetic individuals, whereas a statistically non-significant inverse association between physical activity and distal colon cancer was observed in both diabetics and non-diabetics. By comparison, a meta-analysis on physical activity and colon cancer showed similar summary risk estimates for proximal (summary risk estimate=0.73, 95% CI=0.66–0.81) and distal colon cancer (summary risk estimate=0.74, 95% CI=0.68–0.80).¹² Molecular evidence for a link between physical activity and colon cancer by anatomic subsite is unavailable. Physical activity may have a greater influence on metabolic factors and gut mobility in the proximal colon than distal colon.¹² On the other hand, physical activity could have a greater impact on intestinal transit time and constipation in the distal colon, which plays a main role in storage function.¹² Moreover, the relationships between physical activity, vitamin D levels, and colon cancer may be stronger for distal than proximal colon cancer.^{12,69}

Among non-diabetic individuals, analyses stratified by sex revealed an inverse graded association between physical activity and colon cancer in men, whereas the association was null in women. Previous studies reported stronger inverse relations between overall physical activity,⁷⁰ recreational physical activity,³⁸ or walking⁷¹ and colon cancer risk in men than women. Two meta-analyses on total¹¹ and recreational physical activity⁴⁰ and colon cancer reported that results did not materially vary by sex, although one of those meta-analyses¹¹ observed a stronger risk reduction in men (summary risk estimate=0.81, 95% CI=0.73–0.89) than women (summary risk estimate=0.89, 95% CI=0.81–0.99) in cohort studies, whereas in case-control studies the summary risk estimates were similar in both sexes (men: summary risk estimate =0.72, 95% CI=0.66–0.79, women=0.68, 95% CI=0.64–0.72). Another meta-analysis⁷² revealed significant inverse associations for recreational, occupational, and the combination of both recreational and occupational physical activity for both sexes in case-control studies, whereas in cohort studies significant inverse relations for occupational and the combination of occupational and recreational physical activity were detected in men but not women. Women spend about half their activity time doing household chores.⁷³ Our physical activity measure mostly captured exercise during recreation rather than household activity which may have reduced our ability to identify a significant association in women. On the other hand, household physical activity is more difficult to accurately capture by self-reported questionnaires than regular physical activity at work.⁷⁴

Our study has several strengths, including its prospective design, the large cohort size, and the method of case ascertainment through certified cancer registries. Another advantage is

the availability of information on lifestyle factors, which allowed for adjustments for both dietary and non-dietary risk factors for colon cancer.

Several limitations of this study deserve comment. Since we did not collect information about diabetes treatment at baseline, we cannot exclude the possibility that metabolic status and medications to treat diabetes may have influenced the results. For example, metformin, which is the most frequently used medication to treat type 2 diabetes, reduces glucose and insulin levels in individuals with hyperinsulinemia and insulin resistance⁷⁵ and may exert anti-neoplastic activities.⁷⁶ Insulin secretagogues including sulfonylureas, stimulate insulin secretion in the β -cells by binding to specific receptors, thereby increasing circulating insulin levels.^{75,77} A recent meta-analysis⁷⁸ reported that intake of sulfonylureas increases cancer risk, although an earlier meta-analysis did not support that notion.⁷⁹ Whether diabetes treatment counteracts the potential protective effects of physical activity on glucose and insulin levels remains unclear.

An additional shortcoming of our study is that history of diabetes was self-reported. However, self-reported assessment of prevalent diabetes at baseline has been shown to be an accurate measure.⁸⁰ We lacked information about the type of diabetes. Since type 2 diabetes accounts for more than 90% of diabetes in adults,⁸¹ our results apply to type 2 diabetes. The few studies that explored the association between diabetes type 1 and site-specific cancer incidence yielded risk estimates with wide confidence intervals due to the low sample size and studies that have not differentiated between diabetes type typically address type 2 diabetes.⁷⁷ Type 1 diabetes does not appear to be statistically significantly related to increased colorectal cancer⁷⁷ and the health benefits of physical activity are less clear among individuals with type 1 diabetes.⁸²

Moreover, our study lacked information regarding the onset and duration of diabetes. Of some concern is the possibility that symptoms of undiagnosed colon cancer may have led participants to reduce their physical activity level at baseline, leading to spurious results. Finally, the sample size of our study may have been insufficient to supply adequate power to detect a noticeable association between physical activity and colon cancer risk among diabetics.

Although our study was not able to identify a meaningful improvement in colon cancer risk through increased physical activity participation among diabetics, it is reasonable to recommend physicians to counsel patients with type 2 diabetes to adopt a physically active lifestyle along with optimal weight management and appropriate diabetes treatment. According to the American Diabetes Association and the American College of Sports Medicine, adults with type 2 diabetes should be advised to engage in at least 150 minutes of moderate aerobic physical activity at 3 days per week with no more than 2 sequential days of break between physical activity sessions.²⁵ In the National Health and Nutrition Examination Survey, only 28.2% individuals with diabetes engaged in at least 30 minutes of moderate to vigorous physical activity five or more times per week or vigorous physical activity three or more times per week.⁸³ Overweight or obese individuals with type 2 diabetes in particular should be encouraged to be physically active. A recent study reported that obese adolescents with or without insulin resistance showed lower levels of physical

activity than normal weight adolescents.⁸⁴ Nevertheless, healthy non-diabetic adults may also reduce their risk of colon cancer through increased physical activity participation.

Conclusion

In conclusion, physical activity was not significantly associated with reduced risk of colon cancer among diabetics in this cohort following adjustment for potential risk or protective factors of colon cancer. However, our results suggest that adherence to high levels of physical activity by individuals without diabetes represents an important means of preventing colon cancer. Because diabetic individuals carry an elevated risk for developing colon cancer and other comorbidities,^{8,20–24} the present study may build the base for more epidemiologic research on this topic among diabetics. Larger cohort studies are crucial to determine whether physical activity protects against colon cancer risk among diabetic individuals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

BMI
body mass index
CI
confidence interval
HR
hazard ratio

National Institutes of Health-AARP Diet and Health Study

NIH-AARP Diet and Health Study

$\text{VO}_{2\text{max}}$

maximal oxygen uptake

REFERENCES

1. International Diabetes Federation. Key findings 2014. Diabetes Atlas. 6th Edition. <http://www.idf.org/diabetesatlas/update-2014>. Accessed January 22, 2015. th Edition.
2. Finucane MM, Stevens GA, Cowan MJ, et al. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet*. 2011;377(9765):557–567. [PubMed: 21295846]
3. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2014;384(9945):766–781. [PubMed: 24880830]
4. Finkelstein EA, Khavjou OA, Thompson H, et al. Obesity and severe obesity forecasts through 2030. *Am J Prev Med*. 2012;42(6):563–570. [PubMed: 22608371]
5. Medina C, Janssen I, Campos I, Barquera S. Physical inactivity prevalence and trends among Mexican adults: results from the National Health and Nutrition Survey (ENSANUT) 2006 and 2012. *BMC Public Health*. 2013;13:1063. doi: 10.1186/1471-2458-13-1063. [PubMed: 24215173]
6. Hallal PC, Andersen LB, Bull FC, et al. Global physical activity levels: surveillance progress, pitfalls, and prospects. *Lancet*. 2012;380(9838):247–257. [PubMed: 22818937]
7. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk Factors Contributing to Type 2 Diabetes and Recent Advances in the Treatment and Prevention. *Int J Med Sci*. 2014;11(11):1185–1200. [PubMed: 25249787]
8. Deng L, Gui Z, Zhao L, Wang J, Shen L. Diabetes mellitus and the incidence of colorectal cancer: an updated systematic review and meta-analysis. *Dig Dis Sci*. 2012;57(6):1576–1585. [PubMed: 22350783]
9. Giovannucci E Insulin and colon cancer. *Cancer Causes Control*. 1995;6(2):164–179. [PubMed: 7749056]
10. Xu CX, Zhu HH, Zhu YM. Diabetes and cancer: Associations, mechanisms, and implications for medical practice. *World J Diabetes*. 2014;5(3):372–380. [PubMed: 24936258]
11. Wolin KY, Yan Y, Colditz GA, Lee IM. Physical activity and colon cancer prevention: a meta-analysis. *Br J Cancer*. 2009;100(4):611–616. [PubMed: 19209175]
12. Boyle T, Keegel T, Bull F, Heyworth J, Fritschi L. Physical activity and risks of proximal and distal colon cancers: a systematic review and meta-analysis. *J Natl Cancer Inst*. 2012;104(20):1548–1561. [PubMed: 22914790]
13. Mann S, Beedie C, Balducci S, et al. Changes in insulin sensitivity in response to different modalities of exercise: a review of the evidence. *Diabetes Metab Res Rev*. 2014;30(4):257–268. [PubMed: 24130081]
14. Dwyer T, Ponsonby AL, Ukoumunne OC, et al. Association of change in daily step count over five years with insulin sensitivity and adiposity: population based cohort study. *BMJ*. 2011;342:c7249. doi: 10.1136/bmj.c7249. [PubMed: 21233153]
15. Warnberg J, Cunningham K, Romeo J, Marcos A. Physical activity, exercise and low-grade systemic inflammation. *Proc Nutr Soc*. 2010;69(3):400–406. [PubMed: 20598198]
16. Pedersen BK, Ullum H. NK cell response to physical activity: possible mechanisms of action. *Med Sci Sports Exerc*. 1994;26(2):140–146. [PubMed: 8164530]
17. Gorham ED, Garland CF, Garland FC, et al. Vitamin D and prevention of colorectal cancer. *J Steroid Biochem Mol Biol*. 2005;97(1–2):179–194. [PubMed: 16236494]
18. Song BK, Cho KO, Jo Y, Oh JW, Kim YS. Colon transit time according to physical activity level in adults. *J Neurogastroenterol Motil*. 2012;18(1):64–69. [PubMed: 22323989]

19. Howard RA, Freedman DM, Park Y, et al. Physical activity, sedentary behavior, and the risk of colon and rectal cancer in the NIH-AARP Diet and Health Study. *Cancer Causes Control*. 2008;19(9):939–953. [PubMed: 18437512]
20. Carson JL, Scholz PM, Chen AY, et al. Diabetes mellitus increases short-term mortality and morbidity in patients undergoing coronary artery bypass graft surgery. *J Am Coll Cardiol*. 2002;40(3):418–423. [PubMed: 12142105]
21. Centers for Disease Control and Prevention (CDC). Diabetes, high blood pressure raise kidney disease risk. <http://www.cdc.gov/features/WorldKidneyDay/>. Accessed February 21, 2015.
22. Fox CS, Matsushita K, Woodward M, et al. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis. *Lancet*. 2012;380(9854):1662–1673. [PubMed: 23013602]
23. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. *JAMA*. 1979;241(19):2035–2038. [PubMed: 430798]
24. Marso SP, Hiatt WR. Peripheral arterial disease in patients with diabetes. *J Am Coll Cardiol*. 2006;47(5):921–929. [PubMed: 16516072]
25. Colberg SR, Sigal RJ, Fernhall B, et al. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. *Diabetes Care*. 2010;33(12):e147–167. [PubMed: 21115758]
26. Office of Disease Prevention and Health Promotion. 2008 Physical Activity Guidelines for Americans. <http://www.health.gov/paguidelines/guidelines/>. Accessed February 20, 2015.
27. Schatzkin A, Subar AF, Thompson FE, et al. Design and serendipity in establishing a large cohort with wide dietary intake distributions : the National Institutes of Health-American Association of Retired Persons Diet and Health Study. *Am J Epidemiol*. 2001;154(12):1119–1125. [PubMed: 11744517]
28. Michaud DSMD, Hermansen S, et al. Comparison of cancer registry case ascertainment with SEER estimates and self-reporting in a subset of the NIH–AARP Diet and Health Study. *J Regist Manag*. 2005;32(2):70–75.
29. World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Report. Food, Nutrition, Physical Activity, and the Prevention of Colorectal Cancer. 2011. <http://www.wcrf.org/int/research-we-fund/continuous-update-project-findings-reports/colorectal-bowel-cancer>. Accessed March 06, 2016.
30. Washburn RA, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. *J Clin Epidemiol*. 1993;46(2):153–162. [PubMed: 8437031]
31. Leitzmann MF, Park Y, Blair A, et al. Physical activity recommendations and decreased risk of mortality. *Arch Intern Med*. 2007;167(22):2453–2460. [PubMed: 18071167]
32. Peters TM, Moore SC, Gierach GL, et al. Intensity and timing of physical activity in relation to postmenopausal breast cancer risk: the prospective NIH-AARP diet and health study. *BMC Cancer*. 2009;9:349. doi: 10.1186/1471-2407-9-349. [PubMed: 19796379]
33. Gierach GL, Chang SC, Brinton LA, et al. Physical activity, sedentary behavior, and endometrial cancer risk in the NIH-AARP Diet and Health Study. *Int J Cancer*. 2009;124(9):2139–2147. [PubMed: 19123463]
34. Schoenfeld D Partial Residuals for the Proportional Hazards Regression-Model. *Biometrika*. 1982;69(1):239–241.
35. Giovannucci E Modifiable risk factors for colon cancer. *Gastroenterol Clin North Am*. 2002;31(4):925–943. [PubMed: 12489270]
36. Haggard FA, Boushey RP. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. *Clin Colon Rectal Surg*. 2009;22(4):191–197. [PubMed: 21037809]
37. Murphy G, Devesa SS, Cross AJ, et al. Sex disparities in colorectal cancer incidence by anatomic subsite, race and age. *Int J Cancer*. 2011;128(7):1668–1675. [PubMed: 20503269]
38. Chao A, Connell CJ, Jacobs EJ, et al. Amount, type, and timing of recreational physical activity in relation to colon and rectal cancer in older adults: the Cancer Prevention Study II Nutrition Cohort. *Cancer Epidemiol Biomarkers Prev*. 2004;13(12):2187–2195. [PubMed: 15598779]

39. Johnsen NF, Christensen J, Thomsen BL, et al. Physical activity and risk of colon cancer in a cohort of Danish middle-aged men and women. *Eur J Epidemiol*. 2006;21(12):877–884. [PubMed: 17160429]
40. Harriss DJ, Atkinson G, Batterham A, et al. Lifestyle factors and colorectal cancer risk (2): a systematic review and meta-analysis of associations with leisure-time physical activity. *Colorectal Dis*. 2009;11(7):689–701. [PubMed: 19207713]
41. Cusi K, Maezono K, Osman A, et al. Insulin resistance differentially affects the PI 3-kinase- and MAP kinase-mediated signaling in human muscle. *J Clin Invest*. 2000;105(3):311–320. [PubMed: 10675357]
42. Devlin JT, Horton ES. Effects of prior high-intensity exercise on glucose metabolism in normal and insulin-resistant men. *Diabetes*. 1985;34(10):973–979. [PubMed: 3930321]
43. Devlin JT, Hirshman M, Horton ED, Horton ES. Enhanced peripheral and splanchnic insulin sensitivity in NIDDM men after single bout of exercise. *Diabetes*. 1987;36(4):434–439. [PubMed: 3102297]
44. Burstein R, Epstein Y, Shapiro Y, Charuzi I, Karnieli E. Effect of an acute bout of exercise on glucose disposal in human obesity. *J Appl Physiol* (1985). 1990;69(1):299–304. [PubMed: 2203726]
45. Rogers MA. Acute effects of exercise on glucose tolerance in non-insulin-dependent diabetes. *Med Sci Sports Exerc*. 1989;21(4):362–368. [PubMed: 2674587]
46. O’Gorman DJ, Karlsson HK, McQuaid S, et al. Exercise training increases insulin-stimulated glucose disposal and GLUT4 (SLC2A4) protein content in patients with type 2 diabetes. *Diabetologia*. 2006;49(12):2983–2992. [PubMed: 17019595]
47. Kang J, Robertson RJ, Hagberg JM, et al. Effect of exercise intensity on glucose and insulin metabolism in obese individuals and obese NIDDM patients. *Diabetes Care*. 1996;19(4):341–349. [PubMed: 8729157]
48. Schneider SH, Amorosa LF, Khachadurian AK, Ruderman NB. Studies on the mechanism of improved glucose control during regular exercise in type 2 (non-insulin-dependent) diabetes. *Diabetologia*. 1984;26(5):355–360. [PubMed: 6376244]
49. Christ-Roberts CY, Pratipanawatr T, Pratipanawatr W, et al. Exercise training increases glycogen synthase activity and GLUT4 expression but not insulin signaling in overweight nondiabetic and type 2 diabetic subjects. *Metabolism*. 2004;53(9):1233–1242. [PubMed: 15334390]
50. Ronnema T, Matila K, Lehtonen A, Kallio V. A controlled randomized study on the effect of long-term physical exercise on the metabolic control in type 2 diabetic patients. *Acta Med Scand*. 1986;220(3):219–224. [PubMed: 3535397]
51. McTiernan A. Mechanisms linking physical activity with cancer. *Nat Rev Cancer*. 2008;8(3):205–211. [PubMed: 18235448]
52. Wolin KY, Tuchman H. Physical activity and gastrointestinal cancer prevention. *Recent Results Cancer Res*. 2011;186:73–100. doi: 10.1007/978-3-642-04231-7_4. [PubMed: 21113761]
53. Devlin JT. Effects of exercise on insulin sensitivity in humans. *Diabetes Care*. 1992;15(11):1690–1693. [PubMed: 1468302]
54. Hamer M, Sabia S, Batty GD, et al. Physical activity and inflammatory markers over 10 years: follow-up in men and women from the Whitehall II cohort study. *Circulation*. 2012;126(8):928–933. [PubMed: 22891048]
55. de Rekeneire N, Peila R, Ding J, et al. Diabetes, hyperglycemia, and inflammation in older individuals: the health, aging and body composition study. *Diabetes Care*. 2006;29(8):1902–1908. [PubMed: 16873800]
56. Kim KB. Effect of different training mode on Interleukin-6 (IL-6) and C-reactive protein (CRP) in type 2 diabetes mellitus (T2DM) patients. *J Exerc Nutrition Biochem*. 2014;18(4):371–378.
57. Dekker MJ, Lee S, Hudson R, et al. An exercise intervention without weight loss decreases circulating interleukin-6 in lean and obese men with and without type 2 diabetes mellitus. *Metabolism*. 2007;56(3):332–338. [PubMed: 17292721]
58. Balducci S, Zanuso S, Nicolucci A, et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities

- and independent of weight loss. *Nutr Metab Cardiovasc Dis.* 2010;20(8):608–617. [PubMed: 19695853]
59. Oberbach A, Tonjes A, Kloting N, et al. Effect of a 4 week physical training program on plasma concentrations of inflammatory markers in patients with abnormal glucose tolerance. *Eur J Endocrinol.* 2006;154(4):577–585. [PubMed: 16556721]
 60. Svensson E, Mor A, Rungby J, et al. Lifestyle and clinical factors associated with elevated C-reactive protein among newly diagnosed Type 2 diabetes mellitus patients: a cross-sectional study from the nationwide DD2 cohort. *BMC Endocr Disord.* 2014;14:74. pp. 1–7. doi: 10.1186/1472-6823-14-74. [PubMed: 25163828]
 61. Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus (DM). *FEMS Immunol Med Microbiol.* 1999;26(3–4):259–265. [PubMed: 10575137]
 62. Crespihlo DM, de Almeida Leme JA, de Mello MA, Luciano E. Effects of physical training on the immune system in diabetic rats. *Int J Diabetes Dev Ctries.* 2010;30(1):33–37. [PubMed: 20431804]
 63. Weinstein SJ, Yu K, Horst RL, et al. Serum 25-hydroxyvitamin D and risks of colon and rectal cancer in Finnish men. *Am J Epidemiol.* 2011;173(5):499–508. [PubMed: 21248311]
 64. Bayani MA, Akbari R, Banasaz B, Saeedi F. Status of Vitamin-D in diabetic patients. *Caspian J Intern Med.* 2014;5(1):40–42. [PubMed: 24490013]
 65. Gagnon C, Lu ZX, Magliano DJ, et al. Serum 25-hydroxyvitamin D, calcium intake, and risk of type 2 diabetes after 5 years: results from a national, population-based prospective study (the Australian Diabetes, Obesity and Lifestyle study). *Diabetes Care.* 2011;34(5):1133–1138. [PubMed: 21430082]
 66. Marzieh Kafeshani MZ, Sara Shokri-Moghaddam, Ali Ahmadi, Hamid Nasri. Serum 25-hydroxy vitamin D level in diabetic patients versus normal individuals; a pilot study. *Journal of Parathyroid Disease.* 2016;4(2):40–43.
 67. Taheri E, Saedisomeolia A, Djalali M, Qorbani M, Madani Civi M. The relationship between serum 25-hydroxy vitamin D concentration and obesity in type 2 diabetic patients and healthy subjects. *J Diabetes Metab Disord.* 2012;11(1):16. pp. 1–5. doi: 10.1186/2251-6581-11-16. [PubMed: 23497722]
 68. Jung HK, Kim DY, Moon IH, Hong YS. Colonic transit time in diabetic patients--comparison with healthy subjects and the effect of autonomic neuropathy. *Yonsei Med J.* 2003;44(2):265–272. [PubMed: 12728467]
 69. Boyle T, Heyworth J, Bull F, et al. Timing and intensity of recreational physical activity and the risk of subsite-specific colorectal cancer. *Cancer Causes Control.* 2011;22(12):1647–1658. [PubMed: 21922204]
 70. Lee KJ, Inoue M, Otani T, et al. Physical activity and risk of colorectal cancer in Japanese men and women: the Japan Public Health Center-based prospective study. *Cancer Causes Control.* 2007;18(2):199–209. [PubMed: 17206529]
 71. Takahashi H, Kuriyama S, Tsubono Y, et al. Time spent walking and risk of colorectal cancer in Japan: the Miyagi Cohort study. *Eur J Cancer Prev.* 2007;16(5):403–408. [PubMed: 17923810]
 72. Samad AK, Taylor RS, Marshall T, Chapman MA. A meta-analysis of the association of physical activity with reduced risk of colorectal cancer. *Colorectal Dis.* 2005;7(3):204–213. [PubMed: 15859955]
 73. Simons CC, Hughes LA, van Engeland M, et al. Physical activity, occupational sitting time, and colorectal cancer risk in the Netherlands cohort study. *Am J Epidemiol.* 2013;177(6):514–530. [PubMed: 23420352]
 74. Roeykens J, Rogers R, Meeusen R, et al. Validity and reliability in a Flemish population of the WHO-MONICA Optional Study of Physical Activity Questionnaire. *Med Sci Sports Exerc.* 1998;30(7):1071–1075. [PubMed: 9662675]
 75. Giovannucci E, Harlan DM, Archer MC, et al. Diabetes and cancer: a consensus report. *Diabetes Care.* 2010;33(7):1674–1685. [PubMed: 20587728]
 76. Gallagher EJ, LeRoith D. Diabetes, cancer, and metformin: connections of metabolism and cell proliferation. *Ann N Y Acad Sci.* 2011;1243:54–68. doi: 10.1111/j.1749-6632.2011.06285.x. [PubMed: 22211893]

77. Garcia-Jimenez C, Gutierrez-Salmeron M, Chocarro-Calvo A, et al. From obesity to diabetes and cancer: epidemiological links and role of therapies. *Br J Cancer*. 2016;114(7):716–722. [PubMed: 26908326]
78. Thakkar B, Aronis KN, Vamvini MT, Shields K, Mantzoros CS. Metformin and sulfonylureas in relation to cancer risk in type II diabetes patients: a meta-analysis using primary data of published studies. *Metabolism*. 2013;62(7):922–934. [PubMed: 23419783]
79. Soranna D, Scotti L, Zambon A, et al. Cancer risk associated with use of metformin and sulfonylurea in type 2 diabetes: a meta-analysis. *Oncologist*. 2012;17(6):813–822. [PubMed: 22643536]
80. Oksanen T, Kivimaki M, Pentti J, et al. Self-report as an indicator of incident disease. *Ann Epidemiol*. 2010;20(7):547–554. [PubMed: 20538198]
81. World Health Organization. Diabetes. 2015. <http://www.who.int/mediacentre/factsheets/fs312/en/>. Accessed March 06, 2016.
82. Chimen M, Kennedy A, Nirantharakumar K, et al. What are the health benefits of physical activity in type 1 diabetes mellitus? A literature review. *Diabetologia*. 2012;55(3):542–551. [PubMed: 22189486]
83. Resnick HE, Foster GL, Bardsley J, Ratner RE. Achievement of American Diabetes Association clinical practice recommendations among U.S. adults with diabetes, 1999–2002: the National Health and Nutrition Examination Survey. *Diabetes Care*. 2006;29(3):531–537. [PubMed: 16505501]
84. Velasquez-Rodriguez CM, Velasquez-Villa M, Gomez-Ocampo L, Bermudez-Cardona J. Abdominal obesity and low physical activity are associated with insulin resistance in overweight adolescents: a cross-sectional study. *BMC Pediatr*. 2014;14:258. pp. 1–9. doi: 10.1186/1471-2431-14-258 [PubMed: 25301371]

Figure 1. Age-standardized incidence rates of colon cancer for moderate to vigorous physical activity among diabetics and non-diabetics, adjusted for sex. The physical activity category “0” comprised individuals never or rarely engaging in moderate to vigorous physical activity.

Table 1.
Characteristics of NIH-AARP study participants with and without diabetes according to moderate to vigorous physical activity.

Characteristic*	Moderate to vigorous physical activity (hrs/wk)							
	Diabetics				Non-diabetics			
	Never/rarely	Never/rarely to <1 hr/wk	1 to 3 hrs/wk	4 to 7 hrs/wk	>7 hrs/wk	Never/rarely	1 to 3 hrs/wk	4 to 7 hrs/wk
Participants, number	6,057	3,239	6,474	5,462	4,521	28,623	69,490	71,854
Age, years	63.3	63.2	63.6	63.8	64.2	62.3	62.5	62.8
Sex, %								
Men	67.0	67.7	68.4	69.1	68.4	58.7	58.6	59.1
Women	33.0	32.3	31.6	30.9	31.6	41.3	41.4	40.9
White, %	87.2	87.9	88.1	89.1	89.7	91.8	93.4	93.9
Smoking status, %								
Never smoker	29.8	29.5	30.8	31.6	32.0	35.8	36.6	36.7
Past smoker	55.5	57.5	56.8	57.3	56.4	47.9	49.2	50.6
Current smoker	11.3	9.5	9.3	8.0	8.1	13.0	11.2	9.6
Hormone replacement therapy (women only), %								
Never	62.4	60.5	57.9	57.2	59.2	45.8	44.3	42.1
Past	9.9	8.8	9.3	10.0	8.7	9.3	9.2	8.7
Current	27.7	30.5	32.3	32.5	31.9	44.8	46.4	49.0
Non-steroidal anti-inflammatory drug use, %	82.4	84.7	84.6	85.3	83.8	86.4	86.8	87.0
Body mass index, kg/m ²	31.2	30.4	29.8	29.0	28.6	27.7	27.0	26.3
College graduate/postgraduate, %	29.5	32.4	35.0	36.3	31.2	39.7	43.2	45.1
Family history of colon cancer, %	8.2	8.6	8.1	8.3	8.5	8.4	9.1	9.2
Red meat intake, g/1000 kcal per day, mean	42.7	42.0	41.5	40.0	38.3	36.0	34.3	32.1
Total fiber intake, d/1000 kcal per day, mean	10.7	11.1	11.3	11.8	12.1	10.3	10.8	11.3
Alcohol intake, g/d, mean	8.2	7.9	8.2	9.1	8.8	13.5	13.0	13.3

* All values (except age) are standardized to the age distribution of the study population. Categories may not add up to 100% due to missing values.

HRs and 95% CIs of colon cancer according to moderate to vigorous physical activity among individuals with and without diabetes in the NIH-AARP Diet and Health Study.

Table 2.

		Moderate to vigorous physical activity					P trend	
		Never/rarely	Never/rarely to <1 hr/wk	1 to 3 hrs/wk	4 to 7 hrs/wk	>7 hrs/wk		
Diabetics								
Total colon cancer								
Person-years	64,678	36,930		75,983	64,837	54,888		
Cases	113	61		116	115	75		
Age- and sex-adjusted HR (95% CI)	1.00	0.95 (0.70–1.30)		0.86 (0.66–1.12)	0.99 (0.76–1.28)	0.74 (0.56–0.996)	.16	
Multivariable-adjusted HR (95% CI)	1.00	0.98 (0.72–1.34)		0.89 (0.69–1.16)	1.03 (0.80–1.35)	0.78 (0.58–1.05)	.29	
Multivariable- and BMI-adjusted HR (95% CI)	1.00	0.99 (0.72–1.35)		0.91 (0.70–1.19)	1.07 (0.82–1.39)	0.81 (0.60–1.09)	.45	
Proximal colon cancer								
Cases	72	40		59	76	44		
Age- and sex-adjusted HR (95% CI)	1.00	0.98 (0.66–1.44)		0.68 (0.48–0.96)	1.02 (0.74–1.40)	0.68 (0.46–0.98)	.27	
Multivariable-adjusted HR (95% CI)	1.00	0.98 (0.67–1.45)		0.69 (0.49–0.97)	1.03 (0.74–1.43)	0.69 (0.47–1.01)	.32	
Multivariable- and BMI-adjusted HR (95% CI)	1.00	0.99 (0.67–1.47)		0.71 (0.50–0.998)	1.07 (0.77–1.49)	0.72 (0.49–1.06)	.47	
Distal colon cancer								
Cases	36	20		52	33	28		
Age- and sex-adjusted HR (95% CI)	1.00	0.99 (0.57–1.70)		1.23 (0.80–1.88)	0.90 (0.56–1.45)	0.89 (0.55–1.47)	.37	
Multivariable-adjusted HR (95% CI)	1.00	1.04 (0.60–1.80)		1.32 (0.86–2.02)	0.98 (0.61–1.58)	0.96 (0.58–1.59)	.53	
Multivariable- and BMI-adjusted HR (95% CI)	1.00	1.05 (0.61–1.82)		1.34 (0.87–2.06)	1.01 (0.62–1.63)	0.996 (0.60–1.65)	.62	
Non-diabetics								
Total colon cancer								
Person-years	474,947	372,947		913,040	952,944	897,043		
Cases	664	462		1069	981	975		
Age- and sex-adjusted HR (95% CI)	1.00	0.91 (0.81–1.02)		0.84 (0.76–0.93)	0.72 (0.65–0.79)	0.74 (0.67–0.81)	<.001	
Multivariable-adjusted HR (95% CI)	1.00	0.94 (0.84–1.06)		0.90 (0.82–0.99)	0.79 (0.71–0.87)	0.81 (0.73–0.89)	<.001	
Multivariable- and BMI-adjusted HR (95% CI)	1.00	0.94 (0.84–1.06)		0.91 (0.82–1.002)	0.80 (0.73–0.89)	0.83 (0.75–0.91)	<.001	
Proximal colon cancer								
Cases	394	271		655	644	559		

Moderate to vigorous physical activity					
	Never/rarely	Never/rarely to <1 hr/wk	1 to 3 hrs/wk	4 to 7 hrs/wk	>7 hrs/wk
Age- and sex-adjusted HR (95% CI)	1.00	0.90 (0.77–1.05)	0.87 (0.77–0.98)	0.79 (0.70–0.90)	0.71 (0.62–0.81)
Multivariable-adjusted HR (95% CI)	1.00	0.93 (0.79–1.08)	0.92 (0.81–1.04)	0.85 (0.75–0.97)	0.76 (0.67–0.87)
Multivariable- and BMI-adjusted HR (95% CI)	1.00	0.93 (0.80–1.09)	0.93 (0.82–1.05)	0.87 (0.76–0.99)	0.78 (0.68–0.89)
Distal colon cancer					
Cases	242	174	381	314	382
Age- and sex-adjusted HR (95% CI)	1.00	0.94 (0.77–1.14)	0.83 (0.70–0.97)	0.64 (0.54–0.75)	0.80 (0.68–0.94)
Multivariable-adjusted HR (95% CI)	1.00	0.98 (0.81–1.19)	0.90 (0.77–1.06)	0.72 (0.61–0.85)	0.90 (0.76–1.06)
Multivariable- and BMI-adjusted HR (95% CI)	1.00	0.98 (0.81–1.20)	0.91 (0.77–1.07)	0.73 (0.62–0.87)	0.93 (0.78–1.09)

HR=hazard ratio; CI=confidence interval; BMI= body mass index. Multivariable-adjusted HRs (95% CIs) are adjusted for age, sex, race/ethnicity, education, smoking status, family history of colon cancer, hormone replacement therapy use (women only), non-steroidal anti-inflammatory drug use, total fiber intake, red meat intake, and alcohol consumption.

Table 3.

Multivariable HRs and 95% CIs of total colon cancer according to moderate to vigorous physical activity among individuals with and without diabetes in the NIH-AARP Diet and Health Study, stratified by selected study characteristics.

Physical activity									
	Cases	Never/rarely	Never/rarely to <1 hr/wk	1 to 3 hrs/wk	4 to 7 hrs/wk	>7 hrs/wk	P trend	P interaction	
Diabetics									
Age									
<65 years	217	1.00	1.34 (0.87–2.06)	1.03 (0.70–1.52)	0.98 (0.65–1.49)	0.96 (0.62–1.51)	.45		.15
65 years	263	1.00	0.70 (0.44–1.12)	0.80 (0.56–1.14)	1.06 (0.75–1.49)	0.68 (0.46–1.003)	.51		
Sex									
Men	327	1.00	0.86 (0.58–1.28)	0.94 (0.69–1.29)	1.07 (0.77–1.47)	0.77 (0.54–1.11)	.50		.62
Women	153	1.00	1.22 (0.73–2.02)	0.78 (0.48–1.25)	0.95 (0.59–1.51)	0.79 (0.47–1.32)	.34		
BMI									
18.5–25 kg/m ²	81	1.00	2.87 (1.20–6.88)	1.70 (0.74–3.94)	2.67 (1.20–5.91)	1.29 (0.53–3.14)	.91		.07
25.0–29.9 kg/m ²	190	1.00	0.70 (0.38–1.28)	1.04 (0.68–1.60)	1.11 (0.72–1.70)	0.83 (0.51–1.33)	.87		
30–65 kg/m ²	209	1.00	0.91 (0.60–1.38)	0.71 (0.49–1.04)	0.77 (0.51–1.16)	0.77 (0.49–1.20)	.23		
Non-diabetics									
Age									
<65 years	1936	1.00	0.85 (0.71–1.004)	0.89 (0.77–1.02)	0.79 (0.68–0.91)	0.79 (0.68–0.92)	.002		.44
65 years	2215	1.00	1.03 (0.87–1.21)	0.91 (0.79–1.04)	0.80 (0.69–0.92)	0.84 (0.73–0.96)	<.001		
Sex									
Men	2701	1.00	0.88 (0.76–1.02)	0.82 (0.73–0.92)	0.69 (0.61–0.78)	0.72 (0.64–0.82)	<.001		.004
Women	1450	1.00	1.07 (0.87–1.33)	1.09 (0.92–1.29)	1.02 (0.85–1.21)	1.004 (0.84–1.20)	.48		
BMI									
18.5–25 kg/m ²	1379	1.00	0.81 (0.64–1.03)	0.86 (0.72–1.04)	0.84 (0.70–1.01)	0.80 (0.67–0.96)	.09		.10
25.0–29.9 kg/m ²	1866	1.00	1.13 (0.95–1.35)	0.99 (0.86–1.15)	0.80 (0.69–0.94)	0.85 (0.73–0.995)	<.001		
30–65 kg/m ²	906	1.00	0.82 (0.66–1.02)	0.84 (0.70–1.004)	0.76 (0.62–0.92)	0.85 (0.69–1.05)	.11		

BMI=body mass index, HR=hazard ratio, CI=confidence interval. Multivariable-adjusted HRs (95% CIs) are adjusted for age, sex, race/ethnicity, education, smoking status, family history of colon cancer, hormone replacement therapy use (women only), non-steroidal anti-inflammatory drug use, total fiber intake, red meat intake, and alcohol consumption where appropriate.