Dietary Magnesium and Colorectal Cancer Risk in the Atherosclerosis Risk in Communities Cohort (ARIC)

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Introduction

- Colorectal cancer (CRC) is the second leading cause of cancer morbidity and mortality among men and women in the United States.
  - Novel prevention measures are important to decrease the CRC-related incidence and death.

- Previous meta-analyses of prospective cohort studies have found inverse associations between dietary magnesium and the risk of CRC development:
  - Increased magnesium intake has been inversely associated with an 11 to 19% decrease in CRC risk for the highest vs lowest category of magnesium intake.

- Magnesium is involved in multiple biochemical reactions that regulate key cell functions, such as cell proliferation and apoptosis.

Goal of the study

- **Hypothesis**: Participants who meet or exceed the daily dietary recommendations for magnesium intake (300 mg/day) will have a lower CRC risk, compared to those who do not.

- We prospectively evaluated the association of dietary magnesium with colorectal cancer risk in the Atherosclerosis Risk in Communities (ARIC) study, a cohort of middle-aged and older White and African-American men and women.

Methods

- The ARIC study is a prospective cohort study conducted in four centers: Forsyth County, NC; Jackson, Mississippi; Minneapolis, MN; Washington County, MD.

- Participants received five exams in 1987-89, 1990-92, 1993-95, 1996-98, and 2011-2013, which included medical examination and questionnaires.

- Follow-up was conducted via telephone calls annually from 1987-2012 and semi-annually since 2012.

  - Dietary magnesium consumption was determined using a 61-question food frequency questionnaire at Visit 1.

  - Colorectal cancers cases were ascertained by linkage to cancer registries and supplemented by hospital records.

  - A total of 374 incident colorectal cancer cases were identified through 2012 (317 colon, and 57 rectal).

- Cox proportional hazards regression was used to estimate hazard ratios (HR) of CRC and 95% confidence intervals (CI) across categories of dietary magnesium consumption.

- We examined participants who met US recommendations for dietary magnesium intake (>300 mg/day), versus those who did not (reference category).

- The models were adjusted for
  - Model 1: race, center, sex
  - Model 2: Model 1 plus total calorie intake, BMI, physical activity, alcohol intake, dietary calcium intake, dietary fiber intake, C-reactive protein level, aspirin use, cigarette smoking, and hormone replacement therapy for women

Table 1. Baseline participant characteristics stratified by meeting magnesium dietary recommendations in the ARIC Study.

	Meets dietary magnesium recommendation	Does not meet dietary magnesium recommendation	p-value
Dietary magnesium mange (mg/day)	300.01-863.86	31.27-300.00	
No. of participants	3452	10,316	
No. of cases	85	289	
Person-years	44,576	125,422	
Demographics			
Age (yrs), mean ± sd	54.2 ± 5.7	54.0 ± 5.7	0.08
BMI (kg), mean ± sd	27.6 ± 5.2	27.8 ± 5.4	0.09
Total calorie intake (kcal), mean ± sd	2267 ± 590	1416 ± 450	<.0001
Dietary calcium intake (mg), mean ± sd	1021 ± 456	5310 ± 248	<.0001
Dietary fiber intake (g), mean ± sd	25 ± 9	14 ± 6	<.0001
Alcohol intake (g/day), mean ± sd	9 ± 19	5 ± 11	<.0001
Physical activity (per week)	2.6 ± 0.8	2.5 ± 0.8	<.0001
CRP concentration (mg/L)	0.78 ± 1.07	0.87 ± 1.08	<.0001
Smokers n (%)	1279 (36.1)	4627 (44.6)	<.0001
African America n (%)	694 (19.6)	3091 (29.1)	<.0001
Men n(%)	1986 (56.1)	4472 (42.1)	<.0001
Recent aspirin use (%)	1694 (48.2)	4798 (45.6)	0.007

Figure 1. Incidence rates and hazard ratios for colorectal, colon and rectal cancers by daily magnesium intake below and above the US dietary recommendations in the ARIC study
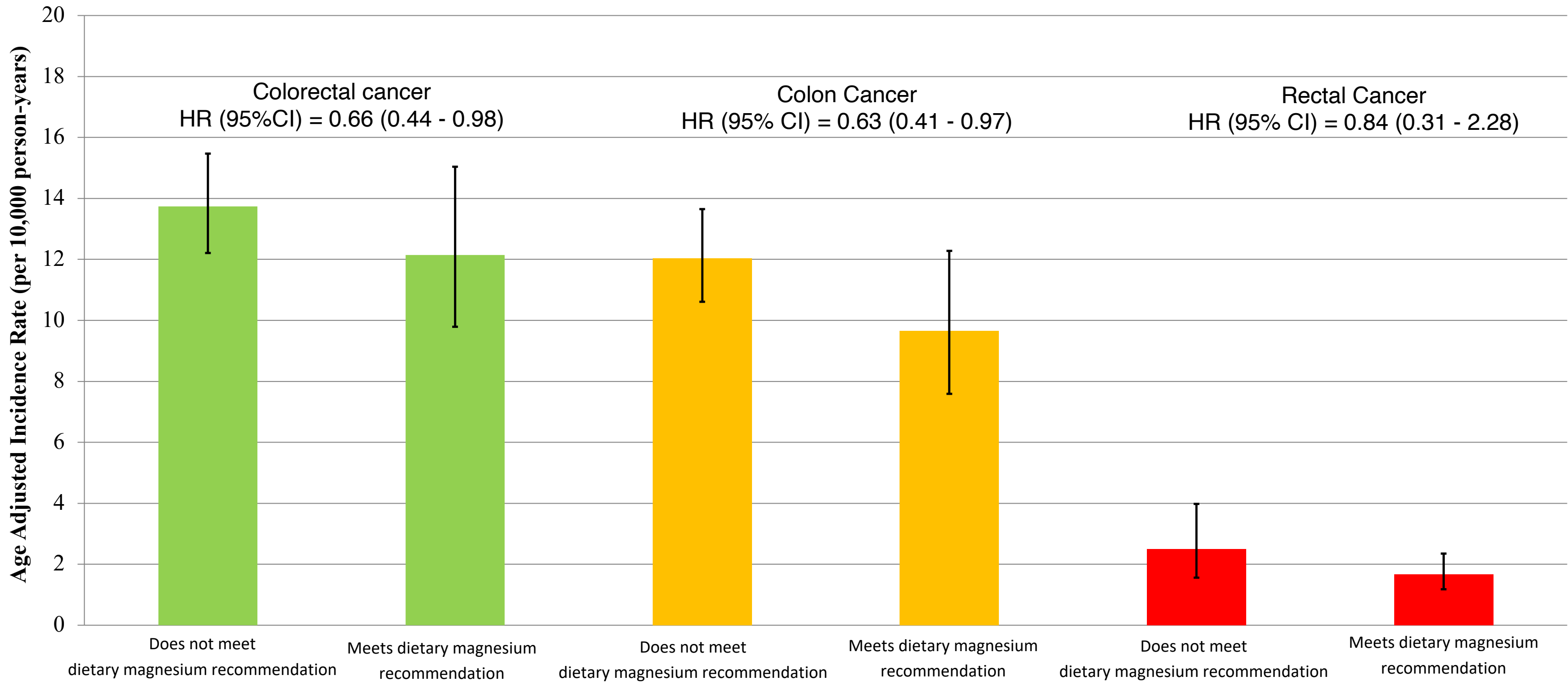

Figure 2. Sex-stratified incidence rates and hazard ratios for colorectal cancer by daily magnesium intake below and above the US dietary recommendations
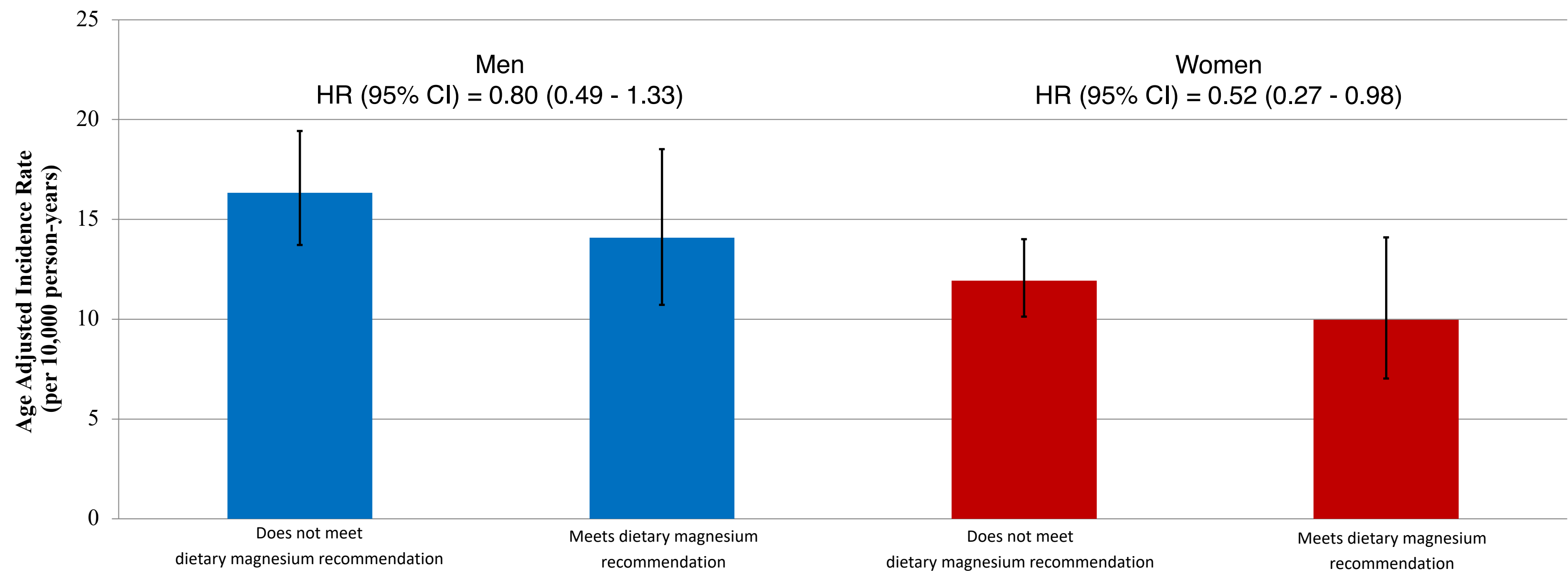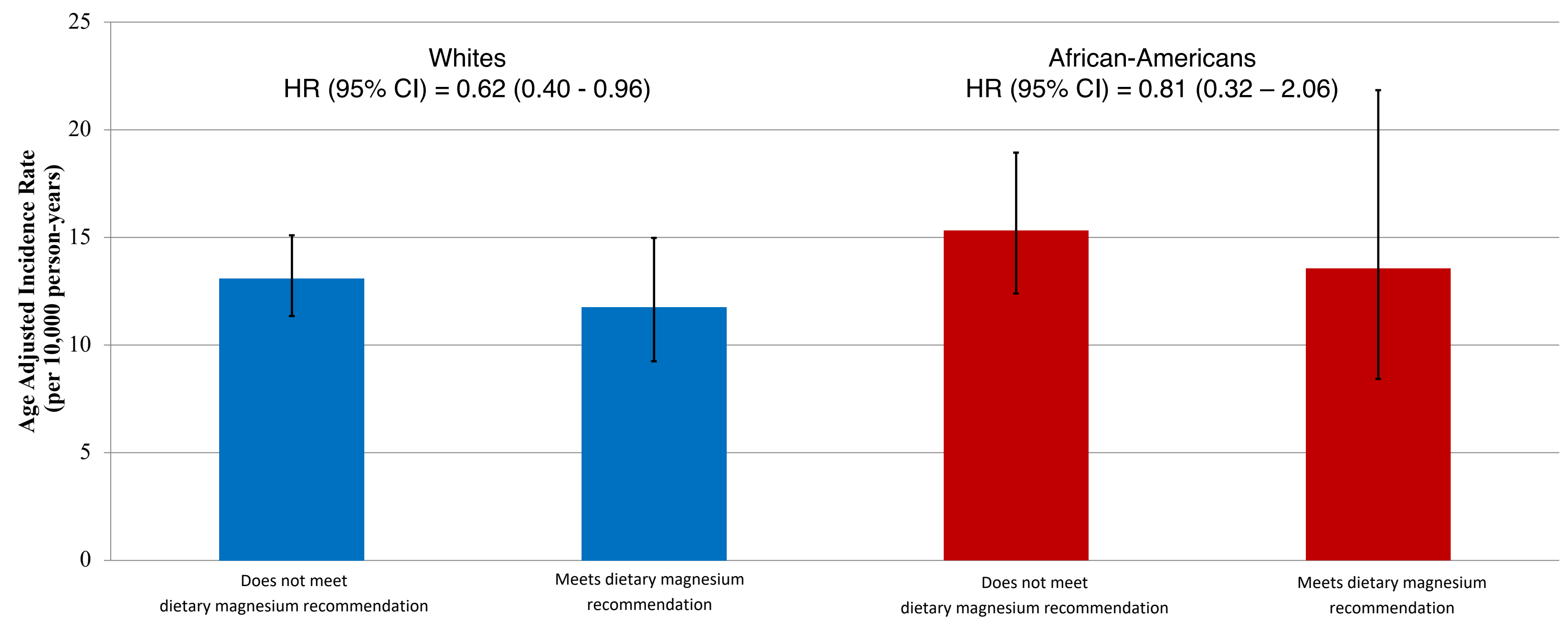

Figure 3. Race-stratified incidence rates and hazard ratios for colorectal cancer by daily magnesium intake below and above the US dietary recommendations

Results

- Participants (54.4% women, 26.7% African-American) were followed for a median of 19.2 years.

- Participants in the highest quartile of dietary magnesium intake had a lower risk of CRC (HR=0.66, 95% CI, 0.44 - 0.98, p-value=0.04) than those in lowest three quartiles combined.
  - There is an indication of an association for both colon and rectal cancer (Figure 1).

- The association for CRC appeared to be inverse for both men and women (Figure 2), and both Whites and African-Americans (Figure 3).
  - p-interaction = 0.74 for gender and 0.62 for race.

- Including lifestyle factors in the model had a significant impact on the association between dietary magnesium and CRC risk (Likelihood Ratio Test p-value < 0.05)
  - Model 1: HR (95% CI) = 0.83 (0.57-1.21).
  - Model 2: HR (95% CI) = 0.66 (0.44 - 0.98).

- We observed no evidence of a linear dose response for the association between dietary magnesium intake (on the logarithmic scale) and CRC risk (p-trend=0.59).

Conclusions

- Our findings support existing evidence of an inverse association between dietary magnesium and colorectal cancer across different populations subgroups, including men and women, Whites and African-Americans.

- A statistically significant inverse association was observed between dietary magnesium intake and colon cancer.

- Limitations
  - Low number of rectal cancer cases and African-Americans.
  - Unable to assess the impact of magnesium from supplement use.

Main citations

1. Chen, G. C., Pang, Z., & Liu, Q. F. (2012). Magnesium intake and risk of colorectal cancer: a meta-analysis of prospective studies. European Journal of Clinical Nutrition, 66(11), 1182–1186. https://doi.org/10.1038/ejcn.2012.135; 10.1038/ejcn.2012.135
2. Folsom, A. R., & Hong, C.-P. (2006). Magnesium intake and reduced risk of colon cancer in a prospective study of women. American Journal of Epidemiology, 163(3), 232–235. https://doi.org/10.1093/aje/kwj037

Acknowledgments