Associations of leg length with increased colorectal cancer incidence in the Atherosclerosis Risk in Communities (ARIC) Study

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Introduction

- Colorectal cancer is the third most common cancer diagnosed in both men and women in the United States, and the third leading cause of cancer-related deaths in the United States.
- Several epidemiologic studies reported an association between taller people and an increased risk of colorectal cancer[1].
- Possible physiologic explanations include:
  - an increased production of growth hormones during puberty
  - a larger pool of at-risk colonic cells.

Goal of the study

- **Hypothesis**: Long-bone growth, indicated by leg length, would be the component of height that is more strongly associated with colorectal cancer.
- We evaluated the association of leg length, sitting height and total height with colorectal cancer risk in Atherosclerosis Risk in Communities (ARIC) prospective cohort.

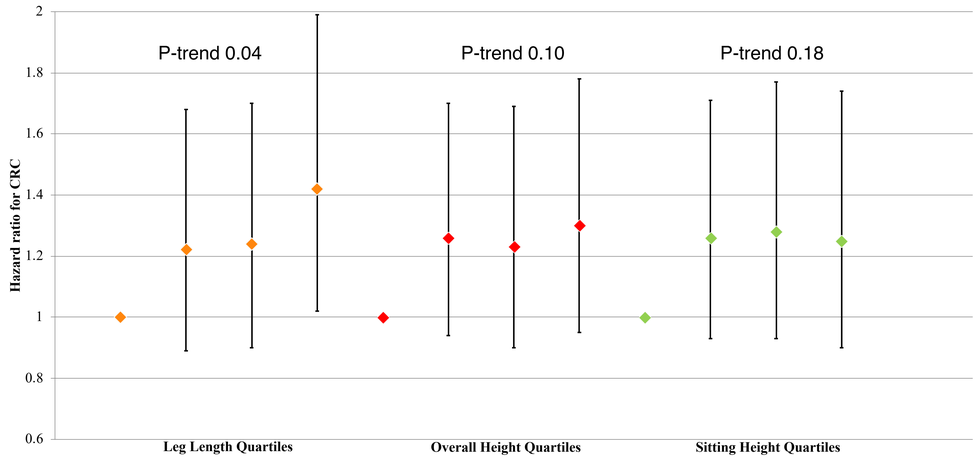
Methods

- The ARIC participants included 14,605 men and women, cancer-free at baseline (1987-1989), and followed until 2006.
  - Leg length was estimated as standing height minus sitting height; these measurements were performed by trained research staff.
  - Colorectal cancers cases were ascertained by linkage to cancer registries and supplemented by hospital records. A total of 344 Incident colorectal cancer cases were identified.
- Cox proportional hazards regression estimated hazard ratios (HR) of colorectal cancer and 95% confidence intervals (CI) across quartiles of height, leg length, and sitting height.
  - The final models were adjusted for age, sex, race, study center, education level, waist-to-hip ratio, female hormone replacement therapy use, and smoking status.

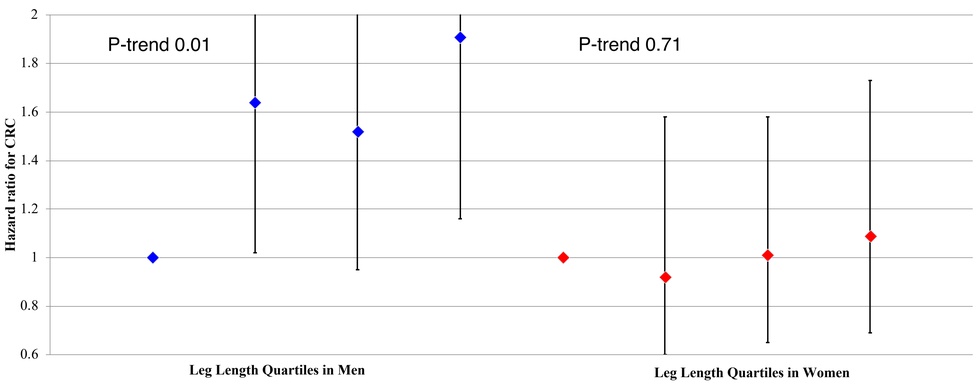
Baseline participant characteristics stratified by sex and leg length quartile in the ARIC Study.

	Sex Specific Leg Quartiles			
Men	Q1	Q2	Q3	Q4
N	1471	1666	2044	1457
Range	38 - 80	81 - 83	84 - 87	88 - 103
Height (cm), median ± sd	169 ± 4.39	174 ± 3.61	178 ± 3.74	183 ± 4.72
Sitting Height (cm), median ± sd	91 ± 3.65	92 ± 3.49	93 ± 3.52	93 ± 3.88
Leg length (cm), median ± sd	79 ± 2.43	82 ± 0.80	85 ± 1.09	90 ± 2.55
Demographics				
Age (yrs), mean ± sd	55.2 ± 5.7	54.4 ± 5.8	54.4 ± 5.7	54.0 ± 5.7
Weight (kg), mean ± sd	175.9 ± 29.1	184.6 ± 30.8	191.6 ± 31.5	198.0 ± 32.1
WHR, mean ± sd	.97 ± .05	.96 ± .05	.96 ± .05	.96 ± .05
Smokers n(%)	414 (22.3)	504 (27.2)	550 (29.7)	385 (20.8)
African American n(%)	167 (10.7)	280 (18.0)	485 (31.2)	622 (40.0)
Education Beyond High School n(%)	620 (19.3)	784 (24.4)	1069 (33.3)	741 (23.1)
Women	Q1	Q2	Q3	Q4
N	1905	2168	1951	1933
Range	37 – 73	74 – 76	77 – 79	80 – 97
Height (cm), median ± sd	156 ± 4.04	161 ± 3.40	164 ± 3.52	169 ± 4.33
Sitting Height (cm), median ± sd	85 ± 3.52	86 ± 3.25	86 ± 3.46	86 ± 3.60
Leg length (cm), median ± sd	72 ± 2.36	75 ± 0.81	78 ± 0.80	82 ± 2.44
Demographics				
Age (yrs), mean ± sd	54.0 ± 5.7	53.7 ± 5.7	53.7 ± 5.7	53.5 ± 5.6
Weight (kg), mean ± sd	150.5 ± 32.9	157.7 ± 35.0	163.9 ± 35.7	176.5 ± 39.9
WHR, mean ± sd	0.89 ± .08	0.89 ± 0.08	0.89 ± 0.08	0.90 ± 0.08
Smokers n(%)	1057 (24.9)	1119 (26.4)	1024 (24.1)	1042 (24.6)
African American n(%)	226 (9.1)	484 (19.6)	668 (27.0)	1095 (44.3)
Education Beyond High School n(%)	711 (22.6)	857 (27.3)	771 (24.6)	800 (25.5)

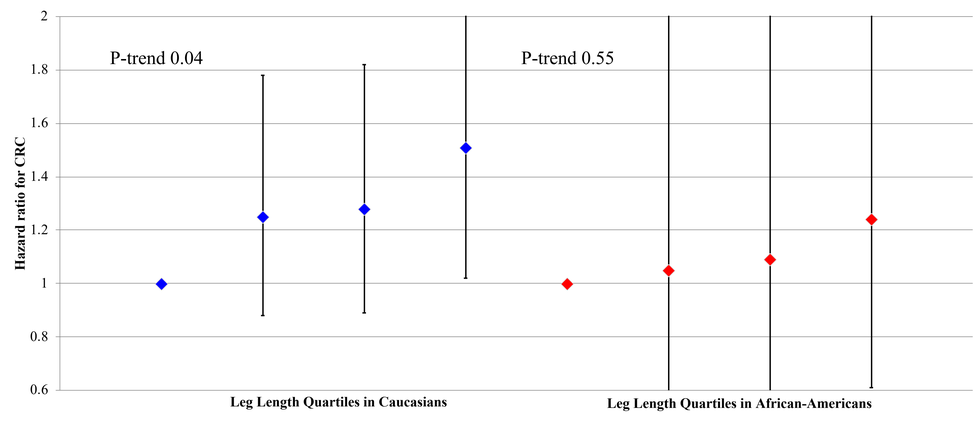
Association of Leg Length, Overall Height and Sitting Height with Incident Colorectal Cancer Cases



Sex-stratified Association of Leg Length with Incident Colorectal Cancer Cases



Race-stratified Association of Leg Length with Incident Colorectal Cancer Cases



Results

- Leg length was correlated with total (Pearson r=0.83), and sitting height (Pearson r=0.52) in the whole cohort.
- Participants in the highest quartile of leg length were at a 42% (95% CI, 1.02-1.99) greater risk of colorectal cancer, relative to the lowest quartile (p-trend=0.04).
- The associations were weaker for
  -- total height: HR=1.30, 95% CI, 0.95-1.78, p-trend=0.10
  -- sitting length: HR=1.25, 95% CI, 0.90-1.74, p-trend=0.18
- For the highest versus the lowest quartile of leg length:
  --Men: HR=1.91, 95% CI, 1.16-3.12
  --Women: HR=1.09, 95% CI, 0.69-1.73; p-interaction=0.16.

  -- Whites: HR=1.51, 95% CI, 1.02-2.26
  -- African-Americans: HR=1.21, 95% CI, 0.61-2.53; p-interaction=0.62.

Conclusions

- Longer leg length was more strongly associated with an increased risk of colorectal cancer than overall height or sitting height.
- This association is most likely driven by biological mechanisms correlated to long bone growth, such as insulin-like growth factor-1, a risk factor for colorectal cancer[2].
- The sex-specific association between longer leg length and CRC risk may be explained by differences in IGF-1 production between males and females during puberty.

Main citations

1. Engeland A, Tretli S, Austad G, Bjørge T. Height and body mass index in relation to colorectal and gallbladder cancer in two million Norwegian men and women. Cancer Causes Control. 2005 Oct;16(8):987-96.
2. Yamaji T, Iwasaki M, Sasazuki S, Tsugane S. Gender difference in the association of insulin and the insulin-like growth factor axis with colorectal neoplasia. Int J Obes (Lond). 2012 Mar;36(3):440-7.

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