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Original Contribution

Associations of Height With the Risks of Colorectal and Endometrial Cancer in Persons With Lynch Syndrome

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People with Lynch syndrome (LS), who carry a pathogenic mutation in a DNA mismatch repair gene, have increased risks of colorectal cancer (CRC) and endometrial cancer (EC). A high reported variability in cancer risk suggests the existence of factors that modify cancer risk for persons with LS. We aimed to investigate the associations between height and CRC and EC risk for persons with LS using data from 2 large studies. Information on 1,115 men and 1,553 women with LS from the Colon Cancer Family Registry (1998–2007) and the GEOLynch Cohort Study (2006–2017) was harmonized. We used weighted Cox proportional hazards regression models with age on the time axis to estimate adjusted hazard ratios and 95% confidence intervals for each 5-cm increment in self-reported height. CRC was diagnosed in 947 persons during 65,369 person-years of observation, and 171 women were diagnosed with EC during 39,227 person-years. Height was not associated with CRC for either men (per 5-cm increment, hazard ratio (HR) = 1.00, 95% confidence interval (CI): 0.91, 1.11) or women (per 5-cm increment, HR = 1.01, 95% CI: 0.92, 1.11), nor was height associated with EC (per 5-cm increment, HR = 1.08, 95% CI: 0.94, 1.24). Hence, we observed no evidence for an association of height with either CRC or EC among persons with LS.

body height; colorectal cancer; endometrial cancer; hereditary cancer; Lynch syndrome; mismatch repair; weighted cohort

Abbreviations: CCFR, Colon Cancer Family Registry; CI, confidence interval; CRC, colorectal cancer; EC, endometrial cancer; HR, hazard ratio; LS, Lynch syndrome; MMR, mismatch repair; PALGA, Nationwide Network and Registry of Histo- and Cytopathology in the Netherlands.

Lynch syndrome (LS) is defined by a germline mutation in one of the mismatch repair (MMR) genes mutL homolog 1 (*MLH1*), mutS homolog 2 (*MSH2*), mutS homolog 6 (*MSH6*), or PMS1 [postmeiotic segregation increased 1 (*S. cerevisiae*)] homolog 2, mismatch repair system component (*PMS2*) (1) or the epithelial cell adhesion molecule gene (*EPCAM*) (2). In persons with such MMR gene mutations, a disrupted DNA MMR system causes an increased risk of several types of cancer. Even though not all persons with LS develop cancer, LS is the most common cause of hereditary colorectal cancer (CRC) and endometrial cancer (EC) (3). LS also increases the risk of colorectal adenomas (a precursor lesion of CRC (4)), as well as the risks of ovarian, stomach, small bowel, pancreas, and several other cancers (2, 5–12).

Cancer risk estimates for people with LS are highly variable between and within families, even for those with the same mutated gene (2, 8, 13). This suggests that factors other than the germline mutation may also influence cancer risk for persons with LS (14).

Height is a factor of interest, since a person's tallness may be a surrogate for factors that could influence cancer development—that is, the number of a person's body cells, a person's genetic make-up, exposure to environmental factors, and exposure to several hormones and growth factors during maturation (15). For the general population, there

is strong evidence that height is associated with the risks of sporadic colorectal, kidney, pancreatic, prostate, ovarian, endometrial, and pre- and postmenopausal breast cancer and malignant melanoma (16). For instance, in the general population, a 5-cm increment of height has been associated with a 4% higher risk of CRC (17) and a 10-cm increment of height has been associated with a 15% increased risk of EC (18). LS-related tumors develop via a distinctive molecular pathway compared with non-LS-related tumors (19–28), and therefore study findings from the general population might not be directly translatable to persons with LS.

To our knowledge, only 2 studies have been published on the association between height and colorectal neoplasia risk for persons with LS, with conflicting results. For persons suspected to have LS on the basis of their family history, women taller than 1.55 m were found to have 47%–127% increased CRC risks compared with those shorter than 1.55 m in a Canadian study, while no evidence of an association was found for men (29). In contrast, for persons confirmed to have LS within a Dutch study (the GEOLynch Cohort Study), a 57% decreased risk of colorectal adenoma for each 5-cm increment of height was reported for men, while no association was found for women (30). The conflicting results might have been due to different study samples (persons with suspected LS vs. those confirmed to have LS), exposure measures (categorical vs. continuous), outcomes (CRC vs. colorectal adenoma), and study designs (case-control vs. prospective cohort). In these analyses, we aimed to investigate the associations of adult attained height with CRC and EC risk for men and women with LS separately, using data from a large sample of persons confirmed to have LS.

METHODS

Study population

For this study, we harmonized data on 2,849 persons confirmed to have LS from 2 separate studies: the GEOLynch Cohort Study (30) (ClinicalTrials.gov identifier NCT03303833) and the Colon Cancer Family Registry (CCFR) (31).

Briefly, within the GEOLynch Cohort Study, persons with LS—that is, a pathogenic variant in one of the MMR or *EPCAM* genes—have been actively recruited since 2006 through the Netherlands Foundation for the Detection of Hereditary Tumors (Leiden, the Netherlands) and 2 university medical centers (Radboud University Medical Center (Nijmegen, the Netherlands) and University Medical Center Groningen (Groningen, the Netherlands)). Since 2012, participants have also been passively recruited through information published in the magazine and on the website of the Lynch Polyposis Society, a Dutch patient association. Adults with LS were eligible for study inclusion regardless of whether they had ever had a cancer diagnosis before study enrollment (30).

The CCFR is an international consortium of 6 research centers in North America and Australia. Its design and recruitment have been described in detail by Newcomb et al. (31) and Jenkins et al. (32). Briefly, at all 6 centers, population-based probands were persons with recently diagnosed CRC identified via cancer registries. Additionally, 4 centers also used identified clinic-based probands, that is, cancer-affected and cancer-unaffected persons from families with multiple CRC cases presenting at familial cancer clinics. Population-based probands with MMR-deficient CRC and all clinic-based probands were tested for germline mutations in a DNA MMR gene. Possession of a pathogenic variant was defined as LS. Subsequently, where possible, first- and/or second-degree relatives of identified probands with LS were recruited for study participation and germline mutation testing of the variant found in their proband. In this study, we included population-based and clinic-based probands and their relatives with a confirmed germline MMR gene mutation.

Both studies were approved by local medical ethical review committees. Additionally, all individual participants provided informed consent.

Data collection

For both studies, self-reported height and other self-reported personal information (smoking habits, weight, and, for women, menstrual and reproductive history and menopausal status) and data on demographic characteristics (age, sex, ethnicity, educational level) were collected at recruitment via study- and/or center-specific standardized questionnaires. Clinical information regarding bowel diseases, colorectal surgeries, and hysterectomy was obtained from medical records and pathology reports and/or was self-reported (CCFR).

Cancer diagnoses

Cancer diagnoses were identified by several mechanisms. For GEOLynch, the majority of the participants (80.1%) provided consent for linkage with the Nationwide Network and Registry of Histo- and Cytopathology in the Netherlands (PALGA; now called the PALGA Foundation). PALGA has had full coverage of Dutch pathology tests since 1991. Reported cancer diagnoses within PALGA after 1991 were therefore used to identify any cancer diagnosis among GEOLynch participants with a linkage to PALGA. Cancer diagnoses obtained from medical records were used for persons who did not consent to linkage with PALGA and for persons with cancer diagnoses before 1991, which were not reported in PALGA.

In CCFR data, cancer diagnoses were obtained from cancer registries for population-based probands. Self-reports and/or secondhand reports by relatives of cancer patients at study enrollment and/or 5-year follow-up were confirmed, where possible, using pathology reports, medical records, and/or death certificates for all enrolled participants (31, 32).

Study sample

For this study, we included 757 persons with LS from the GEOLynch Cohort Study and 2,092 persons with LS from the CCFR. Subsequently, we excluded participants with missing information on the mutated gene (n = 3),

Table 1. Characteristics of Participants With Lynch Syndrome in a Study of Height and Colorectal and Endometrial Cancer Risk, by Sex-Specific Median Height, Colon Cancer Family Registry (Australasia, Canada, and United States; 1998–2007) and GEOLynch Cohort Study (the Netherlands; 2006–2017)[a]

Characteristic	Sex and Median Height, cm											
	Male ($n = 1,155$)						Female ($n = 1,553$)					
	<180.0 ($n = 577$)			≥180.0 ($n = 578$)			<165.0 ($n = 698$)			≥165.0 ($n = 855$)		
	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)
Age at study enrollment, years			50.2 (13.4)			46.3 (13.7)			50.8 (14.1)			46.5 (14.0)
Ever smoking at age 18 years	238	41.3		201	34.8		200	28.7		246	28.8	
Weight in young adulthood, kg[b,c]	70.0 (64.0–77.0)			79.0 (72.0–85.0)			54.0 (50.0–59.0)			60.0 (55.0–67.0)		
Age at menarche, years									12.8 (1.5)			13.2 (1.6)
Country-specific educational level[d]												
Low	144	25.0		100	17.3		223	32.0		164	19.2	
Medium	273	47.3		258	44.6		338	48.4		390	45.6	
High	157	27.2		216	37.4		133	19.1		296	34.6	
Mutated mismatch repair gene												
MLH1	201	34.8		211	36.5		263	37.7		299	35.0	
MSH2	271	47.0		243	42.0		306	43.8		362	42.3	
MSH6	69	12.0		84	14.5		90	12.9		122	14.3	
PMS2	31	5.4		33	5.7		29	4.2		61	7.1	
EPCAM	5	0.9		7	1.2		10	1.4		11	1.3	
Caucasian ethnicity	535	92.7		562	97.2		656	94.0		823	96.3	
Country of residence												
Australasia	257	44.5		202	35.0		345	49.4		274	32.1	
Canada	66	11.4		45	7.8		86	12.3		90	10.5	
The Netherlands	93	16.1		202	35.0		115	16.5		316	37.0	
United States	161	27.9		129	22.3		152	21.8		175	20.5	
Cohort												
CCFR	484	83.9		376	65.1		583	83.5		539	63.0	
GEOLynch	93	16.1		202	35.0		115	16.5		316	37.0	

Table continues

Table 1. Continued

Characteristic	Sex and Median Height, cm											
	Male ($n = 1,155$)						Female ($n = 1,553$)					
	<180.0 ($n = 577$)			≥180.0 ($n = 578$)			<165.0 ($n = 698$)			≥165.0 ($n = 855$)		
	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)
End of person-time due to CRC diagnosis	278	48.2		233	40.3		210	30.1		226	26.4	
End of person-time due to EC diagnosis[e,f]							90	13.0		81	9.5	
Age (years) at end of person-time for CRC[g]			44.4 (11.9)			40.6 (11.9)			43.8 (12.1)			40.3 (11.8)
Age (years) at end of person-time for EC[e,f,h]									44.5 (11.0)			42.5 (10.2)

Abbreviations: CCFR, Colon Cancer Family Registry, CRC, colorectal cancer, EC, endometrial cancer; *EPCAM*, epithelial cell adhesion molecule gene; *MLH1*, mutL homolog 1 gene; *MSH2*, mutS homolog 2 gene; *MSH6*, mutS homolog 6 gene; PALGA, Nationwide Network and Registry of Histo- and Cytopathology in the Netherlands; *PMS2*, PMS1 [postmeiotic segregation increased 1 (*S. cerevisiae*)] homolog 2, mismatch repair system component gene; SD, standard deviation.

[a] Characteristics are based on the number of participants included in CRC analyses ($n = 2,708$) unless otherwise specified.

[b] Weight in young adulthood reflects weight at age 18 years for GEOLynch participants and weight at age 20 years for CCFR participants.

[c] Values are expressed as median (interquartile range).

[d] Percentages do not add up to 100% because there were 7 and 9 missing values for educational level in men and women, respectively.

[e] Women with missing data on age at hysterectomy were excluded from the EC analyses (i.e., 7 of the 701 women with height <165.0 cm and 9 of the 860 women with height ≥165.0 cm). One woman with height ≥165.0 cm without data on person-time was also excluded.

[f] Based on the number of women for EC analyses ($n = 1,544$).

[g] Age at the first occurrence of one of the following events: first diagnosis of cancer (excluding nonmelanoma skin cancer), baseline interview (CCFR), first colonoscopy of the first series of regular colonoscopies (GEOLynch), last update of the medical records (GEOLynch), last linkage to PALGA (GEOLynch), or age at total proctocolectomy.

[h] Age at the first occurrence of one of the following events: first diagnosis of cancer (excluding nonmelanoma skin cancer), death, last contact (CCFR), last update of the medical records (GEOLynch), last linkage to PALGA (GEOLynch), trial inclusion (GEOLynch), age at study exclusion (GEOLynch), or age at hysterectomy.

Table 2. Hazard Ratio for Colorectal Cancer per 5-cm Increment of Height Among Men and Women in the Colon Cancer Family Registry (Australasia, Canada, and United States; 1998–2007) and the GEOLynch Cohort Study (the Netherlands; 2006–2017)

Sex	Total No. of Participants	No. of CRC Cases	Total No. of Person-Years	Crude Analysis			Multivariable Analysis[a]		
				HR	95% CI	*P* Value	HR	95% CI	*P* Value
Men[b]									
All men	1,155	511	28,279	0.95	0.87, 1.04	0.25	1.00	0.91, 1.11	1.00
Men aged <55 years	1,155	449	27,016	0.98	0.89, 1.07	0.58	1.03	0.93, 1.14	0.60
Men aged ≥55 years	171	62	1,263	0.68	0.50, 0.92	0.01	0.72	0.51, 1.02	0.06
Women	1,553	436	37,090	0.97	0.89, 1.05	0.41	1.01	0.92, 1.11	0.84

Abbreviations: CI, confidence interval; CRC, colorectal cancer; HR, hazard ratio.

[a] Results were adjusted for educational level, ethnicity, smoking at age 18 years, year of birth, and country of residence. Year of birth was added as a time-varying covariate because it violated the proportional hazards assumption.

[b] Violation of the proportional hazards assumption was observed for height in men. Therefore, CRC risk estimates for men were also partitioned at the age of 55 years.

persons who also carried a germline mutation in the breast cancer type 1 gene (*BRCA1*) (n = 1), persons with missing clinical data (n = 26) or missing data on height (n = 44) or age at cancer diagnosis (n = 14), persons who were under age 18 years at questionnaire completion (n = 1), persons with familial adenomatous polyposis (n = 35), and persons diagnosed with cancer before age 18 years (n = 5). Additionally, for CRC analyses, participants were excluded if they had a total proctocolectomy but were missing data on age at total proctocolectomy (n = 3) or if no person-time could be calculated (n = 9). For EC analyses, men (n = 1,159), women who had undergone hysterectomy but were missing data on age at hysterectomy (n = 16), and women without person-time (n = 1) were excluded. This resulted in the inclusion of 2,708 persons in the analyses for CRC risk and 1,544 women in the analyses for EC risk. Characteristics of the participants included in the analyses were similar to those of the total cohort (data not shown).

Statistical analyses

We used summary statistics to describe the study population across sex-specific median height values.

Cox proportional hazards regression with age as the time scale was used to calculate hazard ratios and 95% confidence intervals for the associations of height with CRC and EC. Height (cm) was modeled per 5-cm increase for both CRC and EC, since no evidence for any departure from a linear association was observed by using restricted cubic splines in Cox regression.

We chose to use a weighted model in the hazard ratio calculations to adjust for ascertainment bias, which may have occurred because of oversampling of cancer cases in our population (see Web Tables 1–3, available at https://academic.oup.com/aje) (33). Through the use of this method, ascertainment bias will be removed in the case of accurate specification of the expected incidence rates of the external referent population, and it will be reduced if specification is not completely accurate (33). Additionally, we applied a robust sandwich-covariance estimate by clustering on family membership to account for any dependence of observations within families (34, 35).

We used a retrospective approach to calculate CRC and EC risk estimates. For CRC, person-time started at the age of 18 years, since height plateaus around the age of 18 years for both men and women (36). Person-time ended at the age of the first occurrence of any of the following events: first diagnosed cancer (excluding nonmelanoma skin cancer), the baseline interview (i.e., the first interview after study enrollment; CCFR), first colonoscopy of the first series of regular colonoscopies (GEOLynch; defined as at least 2 colonoscopies performed with a maximum interval of 2.5 years between them), last update of the medical records (GEOLynch), last linkage to PALGA (GEOLynch), or age at total proctocolectomy, which diminishes the risk of developing CRC.

For calculation of EC risk estimates, person-time also started at the age of 18 years and ended at the age of the first occurrence of one of the following events: first diagnosed cancer (excluding nonmelanoma skin cancer), death, last contact (CCFR), clinical trial enrollment (GEOLynch), loss to follow-up (GEOLynch), last update of the medical records (GEOLynch), last linkage to PALGA (GEOLynch), or age at hysterectomy, since hysterectomy eliminates the risk of developing EC.

Risk estimates were adjusted for confounding covariates identified a priori (37): country-specific educational level (low, middle, or high), ethnicity (Caucasian vs. non-Caucasian), smoking status at age 18 years (ever smoking vs. never smoking), year of birth, and country of residence (Australasia, Canada, the Netherlands, or the United States). Estimates of EC risk were additionally adjusted for age at menarche. No adjustments were made for adulthood factors

(e.g., smoking status during adulthood) that may influence the risk of CRC or EC, because it is unlikely that adulthood factors causally affect adult height, which is reached in young adulthood. Furthermore, such factors may lie within the causal pathway between height and CRC or EC and therefore were not identified as confounding covariates in our a priori–created causal diagrams.

Schoenfeld residuals were used to judge whether the proportional hazards assumption was met. Violation of the assumption was observed for height in the association between height and CRC for men. Therefore, CRC risk estimates for men were additionally partitioned at the age of 55 years. Moreover, year of birth was added as a time-varying variable in regressions for CRC, and EC risk estimates were calculated with a stratified Cox procedure over strata of country of residence to correct for violation of the proportional hazards assumption seen for birth year and country of residence.

Heterogeneity in the effect of height on the 3 CRC risk estimates (i.e., for men aged <55 years, men aged ≥55 years, and women) was explored by adding a term for interaction between height and those 3 participant groups into the model. Moreover, to explore a potential differential effect by cohort (CCFR vs. GEOLynch), we added a term for interaction between height and cohort to the models for CRC and EC to determine heterogeneity by cohort.

Two sensitivity analyses were performed. At first, to assess whether self-reported cancer cases or cancer cases reported by relatives and/or spouses influenced the results, we excluded those cancer diagnoses (n = 399). Secondly, since Møller et al. (38) showed that the incidence of a second primary cancer diagnosis in persons with LS was similar to the incidence of a first primary cancer diagnosis, we performed a sensitivity analysis in which person-time ended at the first diagnosed CRC or EC only instead of the first diagnosed cancer.

All P values were 2-sided. Data analyses were performed in the SAS System for Windows using SAS 9.4 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Participants' characteristics

A total of 1,155 men and 1,553 women contributed 28,279 and 37,090 person-years to the study, respectively. Median height was 180.0 cm (range, 150.0–213.0 cm) for men and 165.0 cm (range, 134.0–190.0 cm) for women. Taller participants were heavier in young adulthood, more often highly educated, and more often enrolled in the GEOLynch Cohort Study than shorter participants. Ever smoking at the age of 18 years was less often reported by taller men than by shorter men. Person-time ended less often at CRC diagnosis for taller participants than for shorter participants. Person-time ended less often at the age of EC diagnosis for taller women than for shorter women (Table 1). Person-time ended more often at CRC diagnosis (40.9% vs. 18.7%), but not EC diagnosis (10.9% vs. 11.6%), for CCFR participants than for GEOLynch participants (data not shown).

Colorectal cancer

A 5-cm increment of height was not associated with the risk of CRC in men (hazard ratio (HR) = 1.00, 95% confidence interval (CI): 0.91, 1.11) (Table 2). When we partitioned CRC risk estimates for men because the proportional hazards assumption was violated for height, we observed a hazard ratio of 1.03 (95% CI: 0.93, 1.14) per 5-cm increment of height for CRC among men aged <55 years and a hazard ratio of 0.72 (95% CI: 0.51, 1.02) per 5-cm increment of height among men aged ≥55 years (Table 2). No evidence of an association between height and CRC was observed for women (HR = 1.01, 95% CI: 0.92, 1.11).

Heterogeneity in the effect of height on CRC between men aged <55 years, men aged ≥55 years, and women was not observed (P = 0.09). No evidence of heterogeneity by cohort was found (P = 0.58).

Endometrial cancer

A 5-cm increment of height was not associated with EC (HR = 1.08, 95% CI: 0.94, 1.24) (Table 3). No evidence for a differential effect of height on EC by cohort was observed (P = 0.40).

Sensitivity analyses

Excluding self-reported cancer diagnoses and cancer diagnoses reported by relatives or spouses and ending person-time at the first diagnosed CRC or EC only instead of the first diagnosis of any cancer did not result in different CRC or EC risk estimates for either men or women (data not shown).

DISCUSSION

In this study, which comprised a large number of persons with LS, we did not observe evidence for an association between height and CRC for men or women. Height was not associated with EC for women with LS.

To the best of our knowledge, this is the first study to have investigated the associations of height with both CRC and EC in persons confirmed to have LS. While we did not observe evidence for an association between height and CRC in this study, a 4% (95% CI: 1.02, 1.05) increased risk of CRC per 5-cm increment of height has been suggested for men and women in the general population (17). Moreover, being taller increased CRC risk for women but not for men in a Canadian study of persons with suspected LS based on their family cancer history (29). Our current analyses, carried out only among persons with a germline MMR gene mutation leading to LS, may have shown different results than analyses performed among persons suspected to have LS, since persons expected to have LS will comprise persons with LS but also persons with sporadic cancers or other familial cancer syndromes. Additionally, our observation of no association between height and CRC for men contrasts with the results of previous analyses in the GEOLynch Cohort Study in which a 5-cm increment of height was associated with a 57% decreased risk of colorectal adenoma

Table 3. Hazard Ratio for Endometrial Cancer per 5-cm Increment of Height Among Women in the Colon Cancer Family Registry (Australasia, Canada, and United States; 1998–2007) and the GEOLynch Cohort Study (the Netherlands; 2006–2017)

Total No. of Participants	No. of EC Cases	Total No. of Person-Years	Crude Analysis			Multivariable Analysis[a]		
			HR	95% CI	*P* Value	HR	95% CI	*P* Value
1,544	171	39,227	1.01	0.90, 1.14	0.81	1.08	0.94, 1.24	0.29

Abbreviations: CI, confidence interval; EC, endometrial cancer; HR, hazard ratio.
[a] Results were adjusted for educational level, ethnicity, smoking at age 18 years, year of birth, and age at menarche. Results were stratified for country of residence because of violation of the proportional hazards assumption.

for men with LS (30). However, for women, the results of the current study are consistent with the previous analyses in the GEOLynch Cohort Study, since no evidence for an association between height and colorectal adenoma risk was found for women with LS in the previous analysis (30).

For EC, we did not find evidence for an association between height and EC risk among persons with LS (per 5-cm increment of height, HR = 1.08, 95% CI: 0.94, 1.24). In the general population, meta-analysis evidence was presented for a 15% (95% CI: 1.09, 1.22) increased risk of EC for each 10-cm increment of height (18), which is similar to the risk estimate observed in our current analyses if a 10-cm increment of height is used instead of a 5-cm increment (per 10-cm increment of height, HR = 1.16, 95% CI: 0.88, 1.53).

Strengths of this study include the large number of persons confirmed to have LS from 3 continents. Additionally, we were able to adjust for confounding covariates; we used a weighted cohort approach to reduce potential ascertainment bias; and we used a robust covariance estimate to adjust for any dependence of observations within families.

It should be noted that the retrospective approach of our data analyses may have introduced survival bias, since the mean age at study enrollment was 48.4 years while person-time started at the age of 18 years. This may have influenced our results if many CRC- or EC-related deaths occurred between the age of 18 years and the moment of participant recruitment. However, survival of persons with LS after a colon cancer or EC diagnosis is high, with estimated 5- and 10-year survival of 96% and 88% for colon cancer and 93% and 93% for EC, respectively (39). Hence, we do not expect a large impact of this potential bias on our risk estimates. Additionally, height was self-reported instead of measured. The correlation between self-reported height and measured height is reported to be high ($r > 0.9$), but self-reporting of height may lead to an inflated height (40, 41). Nevertheless, even though an inflated report of height may have occurred, this is expected to have been nondifferential with respect to CRC/EC diagnosis, and therefore any estimates of associations would be expected to be biased toward the null. Moreover, participants were asked to report their current height instead of their height at the age of 18 years, which may not have reflected their tallest attained adult height, since aging comes with a decrease in height (42). As a consequence, height reported at study enrollment by older participants versus younger participants is more likely to be an underestimate of the tallest attained adult height. However, self-reported current height is not expected to be differentially reported for persons with a taller versus shorter attained adult height. Hence, using self-reported current height instead of height at the age of 18 years may have introduced a bias toward the null for our risk estimates. Finally, the majority of our participants were of Caucasian origin. Therefore, generalizability of our results to non-Caucasian LS populations may be hampered.

In conclusion, we observed no evidence for an association of height with either CRC or EC among men and women with LS.

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