Does insulin-like growth factor moderate the association between height and risk of cancer at 24 sites?

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ABSTRACT

BACKGROUND: Whether the association of height with cancers differ by insulin-like growth factors has not been fully elucidated. Therefore, this study aimed to investigate the sex-specific associations between height and 24 site-specific cancers to assess whether the association differed by IGF-1.

METHODS: 414 923 participants from the UK Biobank prospective cohort study were included. The association of height (per 5 cm increment) with incidence and mortality from 24 cancer sites was investigated by using Cox proportional hazards models.

RESULTS: The median follow-up was 6.0 years. In men, height was positively associated with incidence risk of all-cause cancer and at five sites (lung, lymphatic, leukaemia, non-Hodgkin lymphoma and melanoma). In women, it was associated with breast, melanoma, lymphatic, non-Hodgkin lymphomas and all-cause cancer. The association was stronger in women than men for all-cause cancer incidence. The strength of association did not differ by IGF-1 concentration.

CONCLUSIONS: Adult height was associated with risk of several cancer sites. However, some of these associations were sex specific. There was no strong evidence to support IGF-1 moderating the association between height and cancer.

Keyword: cancer, height, insulin-like growth factors

INTRODUCTION

Although simple to measure, height is a complex phenotype that is downstream of multiple biological and sociological determinants.[1] Height has been associated with many chronic diseases including cardiovascular diseases and cancer. Although height has a strong genetic component,[2,3] the environment, especially economic development and nutrition, play a major role in determining our height.[1] Recent evidence suggests that changes in a population's height also correlates with cancer estimates.[4]

Height has been robustly associated with a higher risk for many cancer sites, with most of this evidence derived from prospective cohort studies,[2,5,6] but also recently from Mendelian Randomization (MR) studies.[2,3,7] The last report from the World Cancer Research Fund (WCRF) showed that eight cancer-sites are positively associated with height (colorectum, breast, ovary, pancreas, endometrium, prostate, kidney and skin). However, five of these cancer sites have been labelled as having "probable evidence", therefore further research is required.[6] A recent study, published for Choi et al., investigated the association between height and cancer risk in a cohort of 23 million Korean adults. [8] This study reported an increased risk of cancers of the nervous system, thyroid, breast, lung, colon, rectum, prostate, ovary, testes, cervix, endometrium, skin, lymphoma, multiple myeloma and leukaemia. [8]

However, the mechanism underpinning how height confers a higher risk of cancer is complex because the biological determinants of height are multifactorial. Despite this, several hypotheses have been proposed: one of them relates to insulin-like growth factor (IGF-1), which has a direct effect on increasing cancer risk but also height. [9] IGF-1 is one of the most important determinants of height and organ size and it has been postulated as a potential moderator of the link between height and cancer risk. [10,11] A second hypothesis suggests that the increased risk conferred by height is attributable to more cells in taller, compared with shorter, people.[12-14] Taller individuals have more stem cells and therefore they are exposed to a higher number of cell divisions during which driver mutations may occur.[11,13,14] Moreover, the higher IGF-1 concentration and higher number of cells in taller people could, at least partly, explain differences in the cancer risk observed between men and women. However, whether IGF-1 modifies the association between height and cancer risk has not been fully elucidated. [11] Therefore, by using the UK Biobank prospective cohort study we aim to investigate the sex-specific association

between height and 24 site-specific cancers to assess whether the association differed by circulating concentrations of IGF-1.

METHODS

Data sources

502 536 participants (aged 37-73 years, 56.3% were women) were recruited into UK Biobank between 2006 and 2010. Participants attended one of 22 assessment centres across England, Scotland, and Wales, where they completed a touch screen questionnaire, had physical measurements taken, and provided biological samples, as described in detail elsewhere. [15,16] The outcomes in the study reported here were incidence of and mortality from 24 site-specific cancers, with the exposure variable being height (expressed in 5 cm increment). We treated sociodemographic factors (age, ethnicity, and area based socioeconomic status), smoking status, waist circumference, and self-reported physical activity, sedentary time, sleep and dietary intake as potential confounders, as well as prevalent comorbidities at baseline (diabetes, hypertension, cardiovascular diseases and longstanding illness). After excluding participants with prevalent cancer at baseline (n=41 437) and those with missing data on covariates, exposures or outcomes (n= 46 176), 414 923 (82.6%) participants with full data available were included in this study.

Procedures

The outcomes for this study were cancer incidence and mortality; overall and for 24 site-specific cancers. Date and cause of death was obtained from death certificates held within the National Health Service Information Centre (England and Wales) and the National Health Service Central Register Scotland (Scotland). Dates and cause of hospital admissions were obtained from the Health Episode Statistics (England and Wales) and Scottish Morbidity Records (Scotland). Detailed information about the record linkage procedures can be found at http://content.digital.nhs.uk/services. Incident cancer was defined as the first record of the cancer of interest, from hospitalisation or death records. At the time of analysis, mortality data were available up to 14 February 2018. Mortality analyses were therefore censored at this date or date of death, whichever occurred earlier. Hospital admission data were available until 31 March 2017. Therefore, analyses of incident cancer were censored at this date, or the date of first hospitalisation for the cancer of interest or death, whichever occurred earlier.

The International Classification of Diseases, 10th revision (ICD-10) was used to define the following 24 cancer-specific sites: all cancers (C00-C97, D37, D48), brain (C71), oral (C00-C14), oesophagus (C15), stomach (C16), liver (C22), gallbladder (C23), pancreas (C25), lung (C34), colorectal (C18, C19, and C20), kidney (C64-C65), bladder (C67), thyroid (C73), lymphatic and hematopoietic tissue (C81-C96), non-Hodgkin lymphoma (C82-C85), multiple myeloma (C90), malignant melanoma (C43), leukaemia (C91-C95), prostate (C61), testis (C62), breast (C50), ovary (C56), endometrium (C54), uterine (C55) and cervix (C53). Of these, 20 cancer sites were used for men and women, two sites were specific to men (testis and prostate) and five to women (breast, endometrium, uterine, cervix and ovary).

Exposure

Height was measured at baseline by trained staff using standardised protocols and a Seca 202 device (Seca, Hamburg, Germany).

Covariables

Potential confounders were identified a priori based on established relationships, with cancer and height (Supplementary figure 1). Age, ethnicity, smoking status (non-smokers, ex-smokers and current smokers), dietary intake of major food groups, alcohol intake and female-specific factors were self-reported at the baseline assessment via a touch-screen questionnaire. Comorbidities and past medical history were based on self-report of physician diagnosis and verified during the face-to-face interview. Townsend area deprivation index was derived from the postcode of residence using aggregated data on unemployment, car and homeownership, and household overcrowding, and was categorised into tertiles (low, middle and high) [17]. Physical activity level over a typical week was self-reported using the International Physical Activity Questionnaire and analysed as metabolic equivalent of task (MET) per week. [18] Sedentary behaviour included time spent watching TV or in front of a PC at leisure time. Sleep time was also self-reported and categorised in short (<7 h/day), normal (7-9 h/day) and long sleepers (>9 h/day). Waist circumference was measured by trained nurses using a standard protocol. In initial assessment visit (2006-2010), 467,041 participants were recruited and consent. Serum concentrations of insulin-like growth factor-1 (IGF-1) were measured using a DiaSorin Ltd (Beckman Coulter DXI 800) chemiluminescent immunoassay. The IGF-1 assays were externally validated with good correlation and coefficient of variations

were consistent across samples.[19] Further details of these measurements can be found in the UK Biobank online protocol (http://www.ukbiobank.ac.uk).

Statistical analyses

Cox proportional hazard models with follow-up time as the time-dependent variable were used to investigate sex-specific associations of height with incidence and mortality for 24 cancer sites and all-cause cancer. All analyses excluded participants who reported prevalent cancer at baseline. To minimise the potential contribution of reverse causality to the findings, we conducted a landmark analysis excluding people who had events within the two years after recruitment.

Descriptive variables are presented as mean and standard deviation for continuous variables and number and percentage of participants for categorical variables. Pearson correlation were performed to investigate the associations of IGF-1 with age and height by sex. To investigate whether the concentration of IGF-1 by age and height differed by sex, we interaction terms (age*sex and height*sex) were included in our linear regression models.

Sex-specific associations between height (expressed per 5 cm increment) and cancer outcomes were studied using Cox-proportional hazard models for both females and males independently. Results were reported as hazard ratios and their 95% CI. All analyses were incrementally adjusted for the following covariates: Model 1 included age, ethnicity, deprivation, and comorbidity (including prevalent hypertension, cardiovascular diseases, diabetes and long-standing illness); Model 2 included model 1 plus smoking, alcohol consumption, fruit and vegetables, processed meat, oily fish intake, sleep, physical activity and sedentary behaviours, and Model 3 (fully adjusted) included variables from model 2 plus waist circumference.

To investigate differences on cancer risk between sex, Men-to-women hazard ratios were then estimated using Cox models with height:sex interaction terms. This term represents the statistical interaction between sex and the predictor and can be interpreted as the ratio of HR between men to women ratio of HR.

To investigate whether the association between height and cancer differed by IGF-1 we fitted an interaction term between height (per 5 cm) and age- and sex-standarised IGF-1 concentration. We also investigated whether the association between 5-cm increment in

height and cancer differed by height (shorter or taller) by stratifying the analyses using the the sex-specific median of height as the cut-off: above or below 162 cm for women and 176 cm for men. We also conducted sensitivity analyses for lung and women-specific cancers. The association of height with lung cancers were stratified by smoking status (current, ex-smoker and non-smoker). For women, the association between height and cervix, ovary, uterus, breast and endometrium cancers were stratified by pre and postmenopausal status. Additionally, stomach and liver cancers were stratified by reported alcohol consumption (≤1 per week versus >1 per week). Finally, because of potentially inflated type-I errors due to multiple tests, All analyses were corrected for multiple testing using Holm's method, [20] which performed similarly as Bonferroni's method while retaining higher statistical power. [21] The multiple testing corrected p-value are denoted as P_{adj}.

All analyses were performed using R Statistical Software version 3.6.2 with the package survival. The proportional hazard assumption was verified by tests based on Schoenfeld residuals.

RESULTS

Characteristics of the study population

Of the 502 536 participants enrolled in UK Biobank, 414 923 were included in the current study. The median follow-up period was 6.03 (range 5.3 to 6.7) years for cancer incidence and 6.9 (range 6.3 to 7.5) years for cancer mortality. Over the follow-up period, 22 647 participants developed cancer and 4,539 died from it.

Baseline characteristics at baseline were described by sex in Table 1. The mean age was 53.6% were women and 94.8% were of White-European ethnic background. The mean of height was 1.69 cm (1.76 cm and 1.62 cm for men and women, respectively). The mean concentration of IGF-1 were 21.1 and 21.9 nmol/L for women and men, respectively. The Pearson correlation coefficient between IGF-1 and height was r=0.118 and r=0.107 for men and women, respectively (Supplementary Table S1). The associations of IGF-1 with age and height by sex are shown in Supplementary Figures S2 and S3. In summary, IGF-1 concentration decreased in a linear manner with age for both men and women. However, the reduction in IGF was higher in women than men with increasing age (p-interaction <0.0001) (Supplementary Figure S2). In contrast, IGF-

1 concentration increased in a linear fashion with increasing height, with no differences between men and women (p-interaction=0.114) (Supplementary Figure S3).

Height and cancer risk

In men, after correction for multiple testing, height was positively associated with increased risk of incident cancer overall and at five sites (lung, lymphatic, non-Hodgkins lymphoma, melanoma and leukaemia). The hazard ratios of these associations per 5-cm higher height ranged between 1.01 and 1.05 (Figure 1). Similar magnitudes of association were observed in women for breast cancer, melanoma, lymphatic and non-Hodgkin lymphomas and all-cause cancer (Figure 2). For cancer mortality, the associations became non-significant after controlling for multiple testing (Figure 1). For women, only all-cause cancer remained significant after controlling for multiple comparisons (Figure 2). The associations were similar in the three models studied (Supplementary Table S2 and S3).

Sex differences in the association of height and cancer

When adjusted for multiple testing, compared to men, women had a higher risk of incident all-cause cancer (HR: 0.99, 95% CI: 0.99; 0.99) per 5-cm higher height. No other differences in cancer risk were found between men and women (Figure 3).

Sensitivity analysis

In a sensitive analysis height was associated with breast cancer incidence in both premenopausal and postmenopausal women with similar effect sizes (HR 1.02, 95% CI:1.01; 1.02) and 1.02, 95%CI: 1.00; 1.02) respectively, $P_{interaction}$ 0.936) (Supplementary Table S4). Sensitivity analyses by smoking status are presented in Supplementary Table S5. Height was associated with lung cancer in current and ex-smokers ($P_{interaction}$ 0.720). Although similar hazard ratios were observed for smokers and non-smokers, these associations were no significant. Height was associated with liver cancer mortality only among women, no differences were found between those who consumed < or ≥ once a week (Supplementary Table S6).

When association between height and cancer was further stratified by tall v/s short individuals, no differences were observed among men for leukaemia, melanoma, non-Hodking lymphoma, lungand all-cause cancer (Supplementary Table S7). The

association were lost when the analyses were adjusted for multiple testing (Supplementary Table S7).

Moderator analysis by IGF-1

For men, the interaction between IGF-1 and cancer incidence is presented in Figure 4. IGF-1 did not modify the association between height and cancer incidence. HR of height among high IGF-1 group is presented in Supplementary Table S8. Similar results were found for women, no difference in the association were showed by IGF-1 levels (Figure 4, Supplementary Figure S4, Table S9).

DISCUSSION

The main findings of this study corroborate the associations of height with increased incidence risk of different cancer sites and overall cancer in men and women. However, some of these associations differ by sex. Women have a higher incidence risk than men for all-cause cancer. We also provide evidence that circulating concentrations of IGF-1 do not modify the association between height and cancer incidence and mortality.

Our findings are in line with previous prospective cohort evidence that suggests that height is associated with a higher risk of postmenopausal breast cancer, melanoma, non-Hodgkin lymphoma, lymphatic cancer and leukaemia.[5,6,8] However, we did not corroborate the association of height with colorectal, ovary, endometrium pancreas, prostate and kidney cancer. However, the magnitude and direction of the associations observed in our study agreed with previous evidence.[8] Therefore, the lack of significant association may be related to a lack of power rather than a lack of association. For all cause cancer Choi et al found HR: 1.088 (95% CI:1.086; 1.090), similar to our results: HR: 1.008 (95% CI: 1.005; 1.010) for men 1.010 (95% CI: 1.008; 1.013) for women.

Although our findings are in agreement with evidence derived from prospective studies,[5,6,8] these associations do not imply causality. An MR study reported a positive association for 17 cancers sites, only six (kidney, non-Hodgkin, colorectal, lung, melanoma and breast cancer) of these cancer sites were significantly associated with height.[22] Another MR study conducted in UK Biobank participants found a positive association between height and colorectal, endometrium and ovary cancer.[3] We did observe an association with colorectal cancer in minimally adjusted models however, no associations were observed for ovary and endometrium cancer in the fully adjusted

models. Besides, the magnitude of the association reported by our study were smaller than those reported by MR studies.[3,22] These differences between studies may be related to residual confounding or reverse causality, as well as effect sizes from MR studies representing a lifelong cumulative risk or lifelong exposure.

Evidence behind the associations of height with non-Hodgkins lymphoma, melanoma and leukaemia has been controversial. However, MR studies have provided evidence that the link between height and these cancers is causal. However, the exact mechanism behind these associations has not been fully elucidated. Some hypotheses suggests that genetic or early environment exposures may play a role in the link between height and these cancers.[23] Height during adulthood may reflect cumulative exposure to hormones/growth factors and nutritional status in early life.[5] However, it is biologically plausible that height may indirectly influence carcinogenesis through IGF-1 pathways or immune pathways. The IGF-1 pathways could be triggered by overnutrition, particularly by higher intake of energy-dense foods.[24] Moreover, recent studies have provided evidence that supports an association between IGF-1 and the risk of several cancers.[9,25,26] IGF-1 concentration is an important determinant of height and may be a determinant of organ size, and thus IGF-1 could be related to cancer through greater cell division.[27] Moreover, taller individuals have a greater number of cells, that are susceptible to conversion into neoplastic cells.[28] However, more research is necessary to understand the underlying mechanism.

Strengths and limitations

The strength of the paper is the comprehensive analysis of height and cancer stratified by sex, in one large cohort. Observational studies cannot determine causality, with confounding and reverse causation, However, to minimise the effect of reverse causation in our study, we excluded all participants with a self-reported medical history of cancer at baseline and those new cancer diagnoses within the first 2-years of follow up. UK Biobank is not representative of the general population; therefore, caution should be taken in generalising summary statistics to the general population, but estimates of the magnitude of the associations are generalisable.[29] Some of the sample sizes for cancer-specific sites were small (less than 30), therefore the association should be interpreted with caution. Our hazard estimate compares to MR study results share a similar trend but a smaller magnitude of the association.[3,22] However, we did not find an association between height

and cancers of the ovary and endometrium. Some of the conflicting results could be explained by a lack of power for some rare cancers with wide confidence intervals in our study and the MR evidence.

CONCLUSION

Height was positively associated with an increased risk of several cancer sites in men and women. However, women have a higher risk than men for all-cause cancer. IGF-1 does not modify the associations between height and cancer risk.

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Authors' contributions: Study conception and design: SPS, F.H. JPP and CCM. Data analysis: SPS, FH and CCM. Interpretation of results: SPS, F.H. JPP and CCM. Original draft preparation: SPS, F.H. JPP and CCM. Review, editing and approval of manuscript: SPS, F.H. JPP and CCM.

Ethics: UK Biobank has been reviewed and approved by the NHS Health Research Authority, North West – Haydock Research Ethics Committee (REC reference 16/NW/0274). All participants have read the volunteer information sheet and provide full consent to participate in the study. The study was performed in accordance with the Declaration of Helsinki.

Data availability: Data is available upon request from UK Biobank. Information about data access is available onlinehttp://www.ukbiobank.ac.uk/wp-content/uploads/2011/11/UK-Biobank-Protocol.pdf

Competing interests: The authors declare no conflict of interest.

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TABLE LEGENDS

Table 1: Characteristics of participants

	Females	Males	Overall
n (%)	222 635 (53.6%)	192 288 (46.3%)	414 923
Age (years), mean (SD)	56.1 (8.0)	56.5 (8.2)	56.3 (8.1)
IGF1 (nmol/L), mean (SD)	21.1 (5.8)	21.9 (5.5)	21.5 (5.7)
Townsend deprivation index, n (%)			
Lower	75 311 (33.8%)	65 557 (34.1%)	140 868 (34.0%)
Middle	75 622 (34.0%)	63 654 (33.1%)	139 276 (33.6%)
Higher	71 702 (32.2%)	63 077 (32.8%)	134 779 (32.5%)
Ethnicity, n (%)			
White	211 041 (94.8%)	182 334 (94.8%)	393 375 (94.8%)
Mixed	3 532 (1.6%)	2 529 (1.3%)	6 061 (1.5%)
South Asian	3 645 (1.6%)	4 309 (2.2%)	7 954 (1.9%)
Black	3 613 (1.6%)	2 622 (1.4%)	6 235 (1.5%)
Chinese	804 (0.4%)	494 (0.3%)	1 298 (0.3%)
Height (m), mean (SD)	1.62 (0.1)	1.76 (0.1)	1.69 (0.1)
Weight (Kg), mean (SD)	71.3 (14.0)	85.9 (14.2)	78.1 (15.9)
Waist (cm), mean (SD)	84.5 (12.4)	96.8 (11.2)	90.2 (13.4)
Body Mass index (kg/m^2) , mean (SD)	27.0 (5.1)	27.8 (4.2)	27.4 (4.7)
Nutritional status, n (%)			
Underweight	1 629 (0.7%)	427 (0.2%)	2 056 (0.5%)
Normal	87 856 (39.5%)	48 179 (25.1%)	136 035 (32.8%)
Overweight	81 755 (36.7%)	95 382 (49.6%)	177 137 (42.7%)
Obese	51 395 (23.1%)	48 300 (25.1%)	99 695 (24.0%)
Smoking, n (%)			
Never	133 852 (60.1%)	95 290 (49.6%)	229 142 (55.2%)
Ex-Smoker	69 315 (31.1%)	73 403 (38.2%)	142 718 (34.4%)
Current	19 468 (8.7%)	23 595 (12.3%)	43 063 (10.4%)
Alcohol intake, n (%)			
Daily or almost daily	36 136 (16.2%)	49 101 (25.5%)	85 237 (20.5%)
3-4 times a week	46 471 (20.9%)	51 095 (26.6%)	97 566 (23.5%)
Once or twice a week	57 861 (26.0%)	49 894 (25.9%)	107 755 (26.0%)
1-3 times a month	29 211 (13.1%)	17 053 (8.9%)	46 264 (11.2%)
Special occasions only	32 745 (14.7%)	13 614 (7.1%)	46 359 (11.2%)
Never	20 211 (9.1%)	11 531 (6.0%)	31 742 (7.7%)
Sleep time, n (%)			
Normal 7-9h.day	165 418 (74.3%)	140 733 (73.2%)	306 151 (73.8%)
Short sleep <7h.day	53 339 (24.0%)	48 480 (25.2%)	101 819 (24.5%)
Long sleep >9h.day	3 878 (1.7%)	3 075 (1.6%)	6 953 (1.7%)
Sedentary time (h/day), mean (SD)	4.66 (2.0)	5.46 (2.5)	5.03 (2.3)
Physical activity (MET h/week) mean (SD)	1.78 (1.7)	1.86 (1.6)	1.82 (1.7)
Diabetes, n (%)	7 185 (3.2%)	12 823 (6.7%)	20 008 (4.8%)
Hypertension, n (%)	50 661 (22.8%)	57 155 (29.7%)	107 816 (26.0%)
CVD, n (%)	55 743 (25.0%)	64 937 (33.8%)	120 680 (29.1%)
Long-standing illness, n (%)	156 193 (70.2%)	124 823 (64.9%)	281 016 (67.7%)

Data are presented as number of participants and their percentage (%) for categorical variables. Continuous variables are presented as mean and standard deviation. Data available for 414 923.

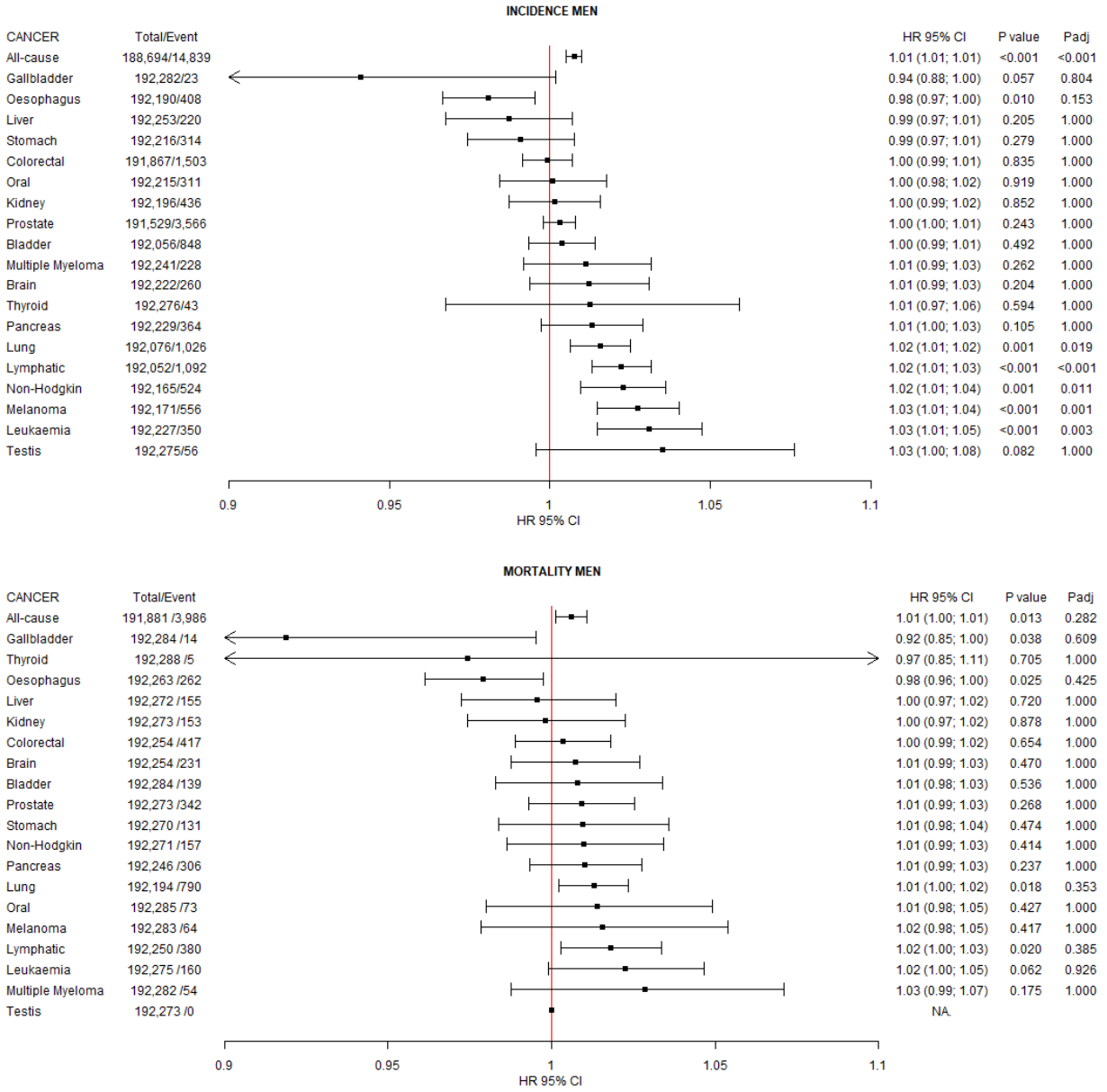


Figure 1. Association of height with the risk of incidence and mortality from 20 cancer sites in men.

Data presented as hazard ratio and their 95% CI per 5-cm increment in height. analyses were adjusted for age, sex, ethnicity, deprivation index, comorbidity, smoking, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity, sedentary behaviours and waist circumference.

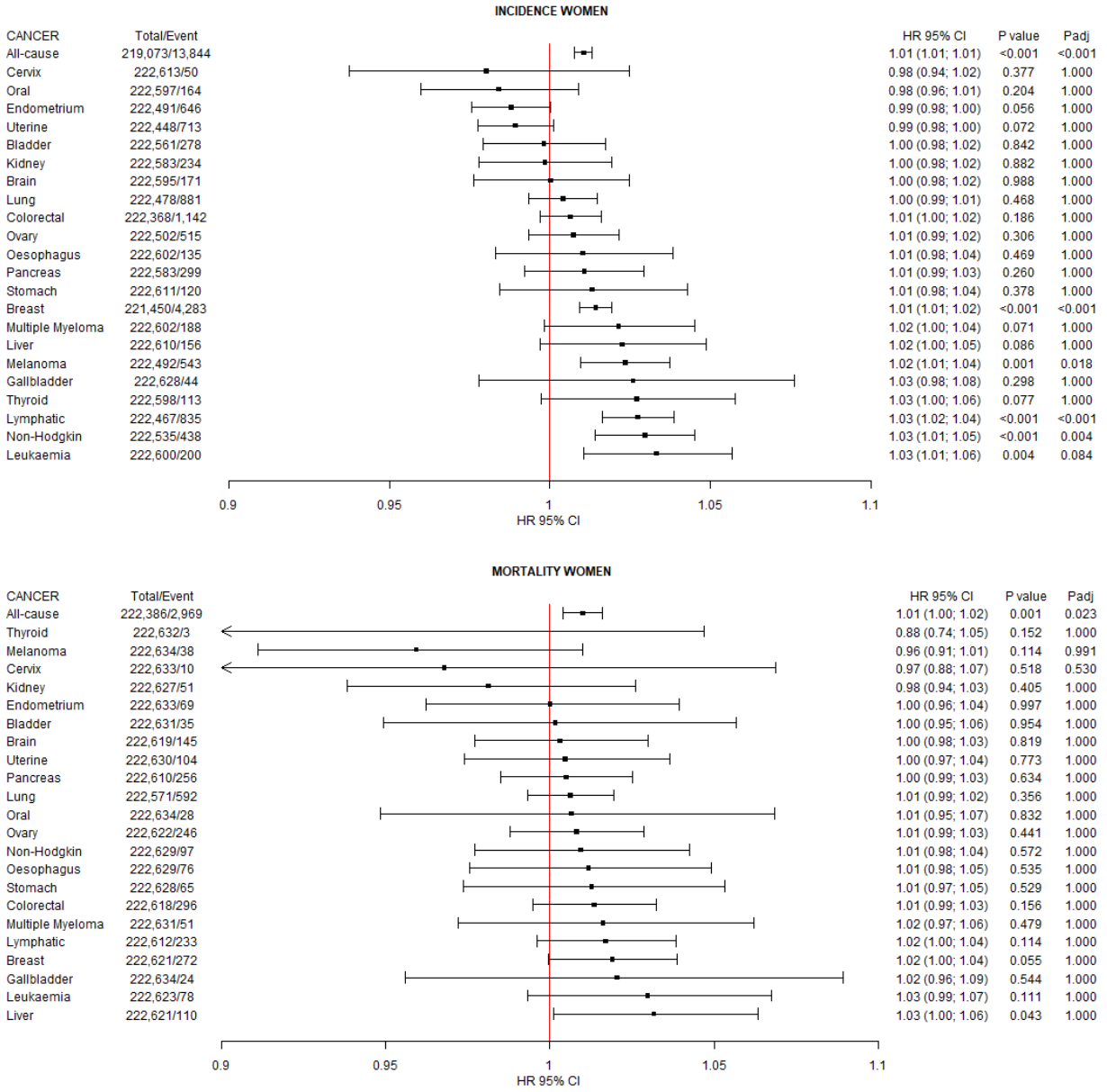


Figure 2. Association of height with the risk of incidence and mortality from 22 cancer sites in women.

Data presented as hazard ratio and their 95% CI per 5-cm increment in height. Analyses were adjusted for age, sex, ethnicity, deprivation index, comorbidity, smoking, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity, sedentary behaviours and waist circumference.

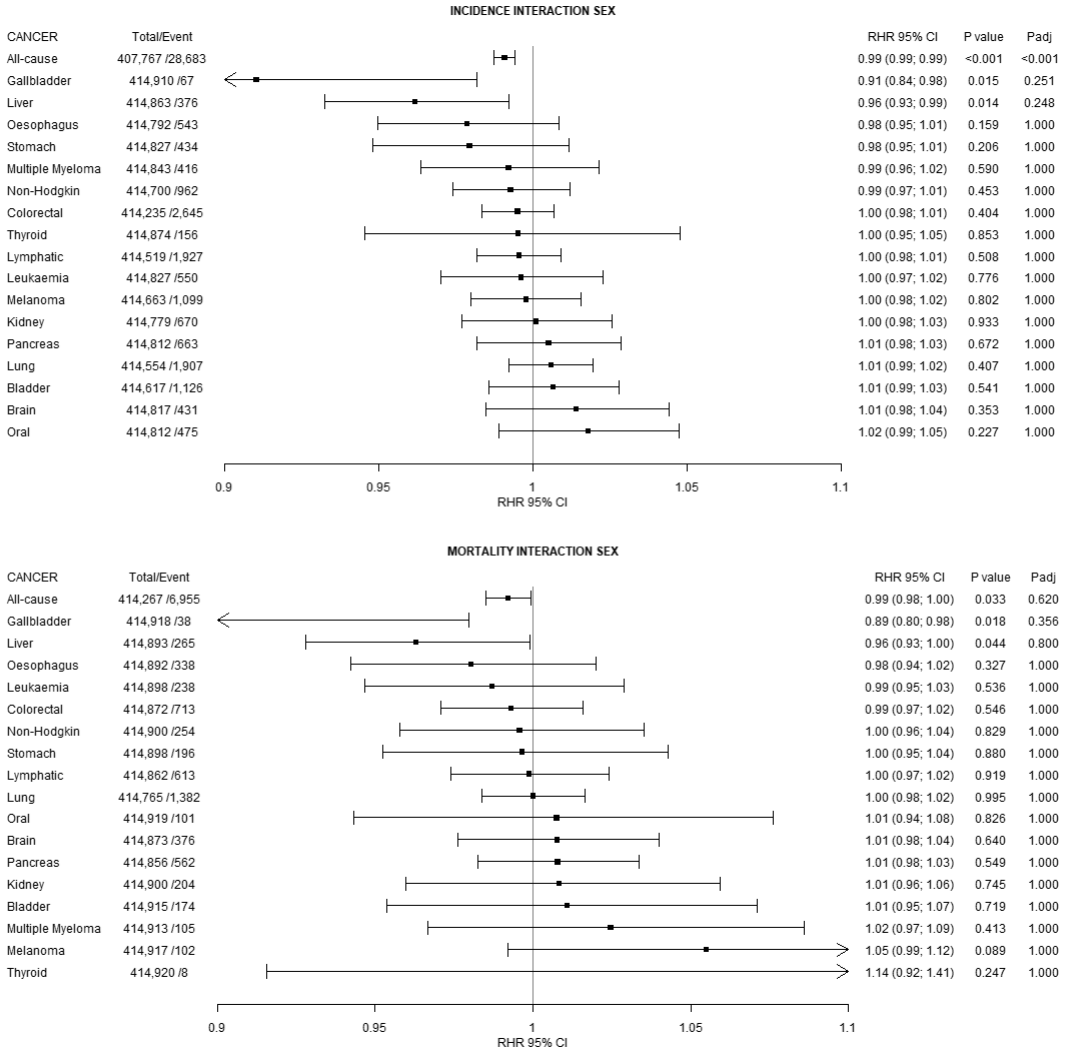


Figure 3. Ratios of HR of women to men for the association of height with incidence and mortality of 18 cancer sites.

Data presented as ratio of HR (interaction term sex and height) and their 95% CI per 5-cm increment in height. Models were adjusted for age, ethnicity, deprivation index, comorbidity, smoking, alcohol consumption, fruit & vegetable, processed meat intake, oil and fish, sleep, physical activity, sedentary behaviours and waist circumference.

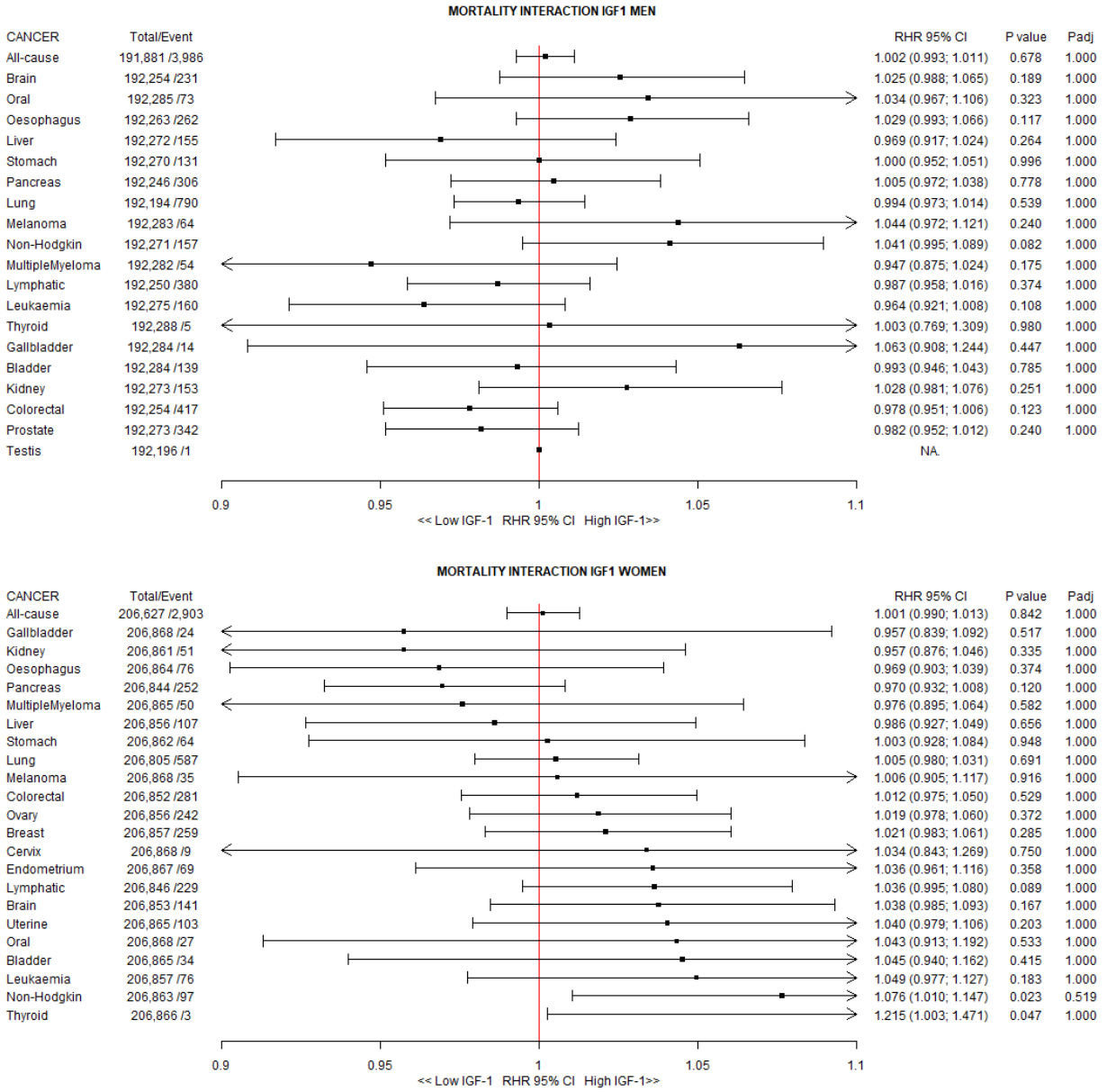
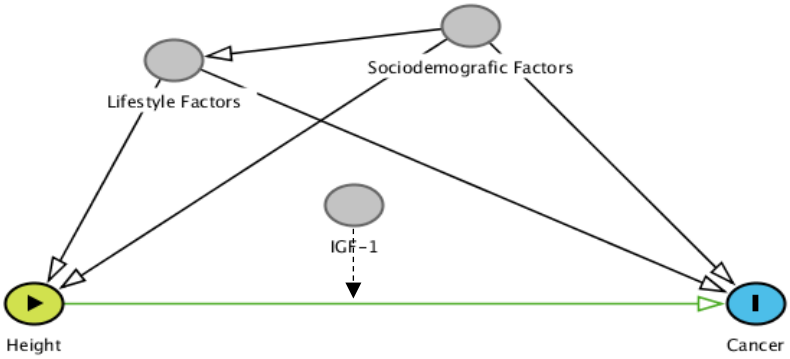


Figure 4. Ratio of HR of low to high IGF-1 level for the association of height with incidence of 24 cancer sites men and women.

Data presented as ratio of hazard ratio (interaction term of IGF-1 level and height) and their 95% CI per 5-cm increment in height. Models were adjusted for age, ethnicity, deprivation index, comorbidity, smoking, alcohol consumption, fruit & vegetable, processed meat intake, oil and fish, sleep, physical activity, sedentary behaviours and waist circumference.

Supplementary material: Does insulin-like growth factor moderate the association between height and risk of cancer at 24 sites?

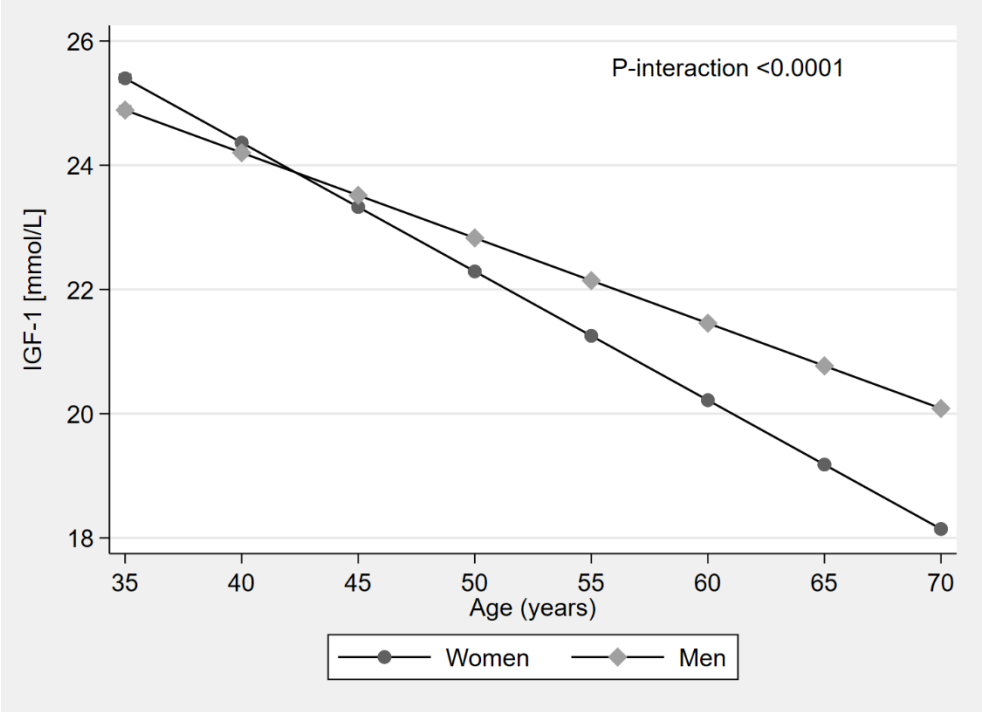


Supplementary Figure S1: Directed Acyclic Graphs Potential confounders identified a priori based on established relationships, with cancer and height.

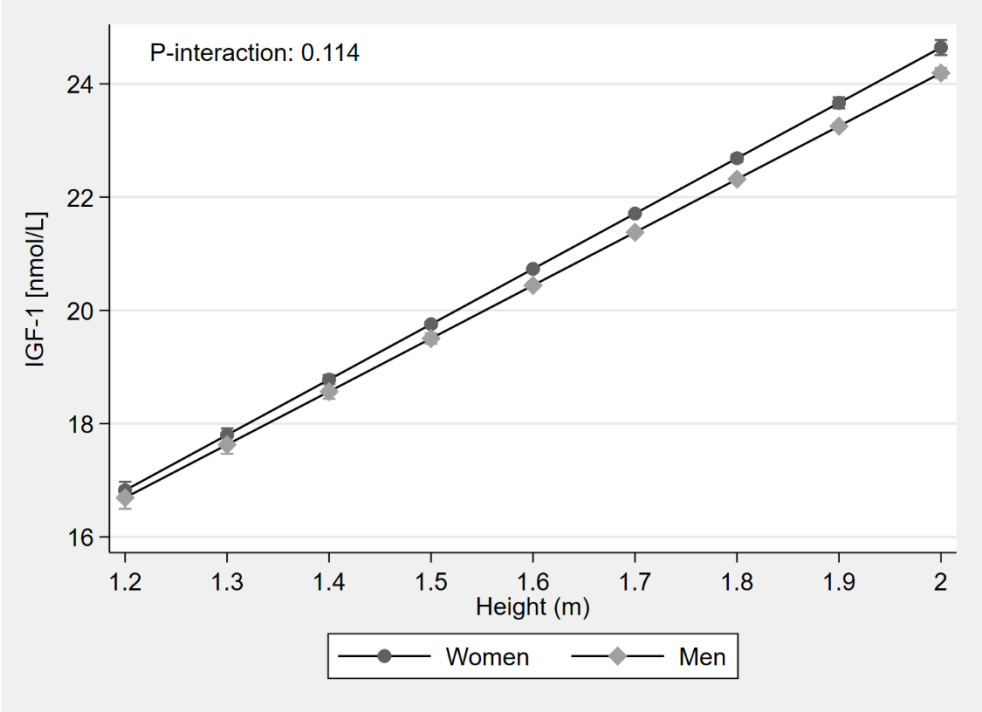
Sociodemographic factors: age, ethnicity, deprivation, Lifestyle factors: diet (fruits and vegetables, oily fish, alcohol, red and process meat intake), sleep, physical activity and sedentary behaviour.

Supplementary Table S1: Person Correlation IGF-1 and height by age and sex

	Both sex		Men		Women	
Height and IGF-1	**Coefficient**	**P value**	**Coefficient**	**P value**	**Coefficient**	**P value**
Overall	0.133	<0.001	0.118	<0.001	0.107	<0.001
<45 years	0.038	<0.001	0.106	<0.001	0.070	<0.001
45-50 years	0.083	<0.001	0.108	<0.001	0.080	<0.001
50-55 years	0.116	<0.001	0.095	<0.001	0.070	<0.001
55-60 years	0.119	<0.001	0.084	<0.001	0.050	<0.001
60-65 years	0.130	<0.001	0.082	<0.001	0.047	<0.001
>65 years	0.136	<0.001	0.066	<0.001	0.034	<0.001
>70 years	0.128	<0.001	0.028	0.389	0.016	0.628



Supplementary Figure S2: IGF-1 blood concentration by age and sex.



Supplementary Figure S3: IGF-1 blood concentration by height and sex.

Supplementary Table S2: Association height (per 5 cm) and cancer risk incidence, men and women.

Site cancer	Total	Event	Model 1	P-value	$P_{adjusted}$	Model 2	P-value	$P_{adjusted}$	Model 3	P-value	$P_{adjusted}$
MEN											
All-cause	188,694	14,839	**1.01 (1.01; 1.01)**	<0.001	<0.001	**1.01 (1.01; 1.01)**	<0.001	<0.001	**1.01 (1.01; 1.01)**	<0.001	<0.001
Bladder	192,056	848	1.01 (1.00; 1.02)	0.288	1.00	1.01 (1.00; 1.02)	0.230	1.00	1.00 (0.99; 1.01)	0.492	1.00
Brain	192,222	260	1.01 (0.99; 1.03)	0.241	1.00	1.01 (0.99; 1.03)	0.254	1.00	1.01 (0.99; 1.03)	0.204	1.00
Colorectal	191,867	1,503	1.00 (1.00; 1.01)	0.360	1.00	1.00 (1.00; 1.01)	0.378	1.00	1.00 (0.99; 1.01)	0.835	1.00
Gallbladder	192,282	23	0.95 (0.89; 1.01)	0.094	1.00	0.95 (0.89; 1.01)	0.083	1.00	0.94 (0.88; 1.00)	0.057	0.741
Kidney	192,196	436	1.00 (0.99; 1.02)	0.484	1.00	1.01 (0.99; 1.02)	0.347	1.00	1.00 (0.99; 1.02)	0.852	1.00
Leukaemia	192,227	350	**1.03 (1.01; 1.05)**	<0.001	<0.001	**1.03 (1.01; 1.05)**	<0.001	<0.001	**1.03 (1.01; 1.05)**	<0.001	<0.001
Liver	192,253	220	0.99 (0.97; 1.01)	0.405	1.00	0.99 (0.97; 1.01)	0.552	1.00	0.99 (0.97; 1.01)	0.205	1.00
Lung	192,076	1,026	1.01 (1.00; 1.02)	0.069	0.897	**1.01 (1.00; 1.02)**	0.005	0.075	**1.02 (1.01; 1.02)**	0.001	0.016
Lymphatic	192,052	1,092	**1.02 (1.01; 1.03)**	<0.001	<0.001	**1.02 (1.01; 1.03)**	<0.001	<0.001	**1.02 (1.01; 1.03)**	<0.001	<0.001
Melanoma	192,171	556	**1.03 (1.02; 1.04)**	<0.001	<0.001	**1.03 (1.02; 1.04)**	<0.001	<0.001	**1.03 (1.01; 1.04)**	<0.001	<0.001
Multiple Myeloma	192,241	228	1.01 (0.99; 1.03)	0.212	1.00	1.01 (0.99; 1.03)	0.215	1.00	1.01 (0.99; 1.03)	0.262	1.00
Non-Hodgkin	192,165	524	**1.02 (1.01; 1.03)**	0.002	0.032	**1.02 (1.01; 1.03)**	0.001	0.016	**1.02 (1.01; 1.04)**	0.001	0.016
Oesophagus	192,190	408	0.98 (0.97; 1.00)	0.039	0.585	0.99 (0.97; 1.00)	0.097	1.00	0.98 (0.97; 1.00)	0.010	0.140
Oral	192,215	311	1.00 (0.98; 1.01)	0.795	1.00	1.00 (0.98; 1.02)	0.872	1.00	1.00 (0.98; 1.02)	0.919	1.00
Pancreas	192,229	364	**1.02 (1.00; 1.03)**	0.043	0.602	1.02 (1.00; 1.03)	0.052	0.728	1.01 (1.00; 1.03)	0.105	1.00
Prostate	191,529	3,566	1.00 (1.00; 1.01)	0.357	1.00	1.00 (1.00; 1.01)	0.500	1.00	1.00 (1.00; 1.01)	0.243	1.00
Stomach	192,216	314	1.00 (0.98; 1.01)	0.597	1.00	1.00 (0.98; 1.01)	0.802	1.00	0.99 (0.97; 1.01)	0.279	1.00
Testis	192,275	56	1.04 (1.00; 1.08)	0.076	0.912	1.03 (1.00; 1.07)	0.080	1.00	1.03 (1.00; 1.08)	0.082	0.984
Thyroid	192,276	43	1.02 (0.97; 1.06)	0.415	1.00	1.01 (0.97; 1.06)	0.556	1.00	1.01 (0.97; 1.06)	0.594	1.00
WOMEN											
All-cause	219,073	13,844	**1.01 (1.01; 1.01)**	<0.001	<0.001	**1.01 (1.01; 1.01)**	<0.001	<0.001	**1.01 (1.01; 1.01)**	<0.001	<0.001
Bladder	222,561	278	1.00 (0.98; 1.02)	0.940	1.00	1.00 (0.98; 1.02)	0.899	1.00	1.00 (0.98; 1.02)	0.842	1.00
Brain	222,595	171	1.00 (0.98; 1.03)	0.887	1.00	1.00 (0.98; 1.02)	0.993	1.00	1.00 (0.98; 1.02)	0.988	1.00
Breast	221,450	4,283	**1.02 (1.01; 1.02)**	<0.001	<0.001	**1.02 (1.01; 1.02)**	<0.001	<0.001	**1.01 (1.01; 1.02)**	<0.001	<0.001
Cervix	222,613	50	0.98 (0.93; 1.02)	0.292	1.00	0.98 (0.94; 1.03)	0.413	1.00	0.98 (0.94; 1.02)	0.377	1.00
Colorectal	222,368	1,142	1.01 (1.00; 1.02)	0.193	1.00	1.01 (1.00; 1.02)	0.116	1.00	1.01 (1.00; 1.02)	0.186	1.00
Endometrium	222,491	646	0.99 (0.98; 1.00)	0.242	1.00	1.00 (0.98; 1.01)	0.500	1.00	0.99 (0.98; 1.00)	0.056	0.952
Gallbladder	222,628	44	1.03 (0.98; 1.08)	0.280	1.00	1.03 (0.98; 1.08)	0.236	1.00	1.03 (0.98; 1.08)	0.298	1.00
Kidney	222,583	234	1.00 (0.98; 1.02)	0.881	1.00	1.00 (0.98; 1.02)	0.777	1.00	1.00 (0.98; 1.02)	0.882	1.00
Leukaemia	222,600	200	1.03 (1.01; 1.06)	0.004	0.072	1.03 (1.01; 1.06)	0.003	0.054	1.03 (1.01; 1.06)	0.004	0.072
Liver	222,610	156	1.02 (1.00; 1.05)	0.115	1.00	1.02 (1.00; 1.05)	0.072	1.00	1.02 (1.00; 1.05)	0.086	1.00

Lung	222,478	881	1.00 (0.99; 1.01)	0.719	1.00	1.00 (0.99; 1.02)	0.399	1.00	1.00 (0.99; 1.01)	0.468	1.00
Lymphatic	222,467	835	**1.03 (1.01; 1.04)**	<0.001	<0.001	**1.03 (1.02; 1.04)**	<0.001	<0.001	**1.03 (1.02; 1.04)**	<0.001	<0.001
Melanoma	222,492	543	**1.02 (1.01; 1.04)**	0.001	0.019	**1.02 (1.01; 1.04)**	0.001	0.019	**1.02 (1.01; 1.04)**	0.001	0.019
Multiple Myeloma	222,602	188	1.02 (1.00; 1.04)	0.111	1.00	1.02 (1.00; 1.05)	0.050	0.800	1.02 (1.00; 1.04)	0.071	1.00
Non-Hodgkin	222,535	438	**1.03 (1.01; 1.04)**	<0.001	<0.001	**1.03 (1.01; 1.05)**	<0.001	<0.001	**1.03 (1.01; 1.05)**	<0.001	<0.001
Oesophagus	222,602	135	1.01 (0.98; 1.04)	0.544	1.00	1.01 (0.98; 1.04)	0.494	1.00	1.01 (0.98; 1.04)	0.469	1.00
Oral	222,597	164	0.98 (0.96; 1.01)	0.185	1.00	0.98 (0.96; 1.01)	0.172	1.00	0.98 (0.96; 1.01)	0.204	1.00
Ovary	222,502	515	1.01 (0.99; 1.02)	0.355	1.00	1.01 (0.99; 1.02)	0.318	1.00	1.01 (0.99; 1.02)	0.306	1.00
Pancreas	222,583	299	1.01 (0.99; 1.03)	0.211	1.00	1.01 (0.99; 1.03)	0.204	1.00	1.01 (0.99; 1.03)	0.260	1.00
Stomach	222,611	120	1.01 (0.98; 1.04)	0.392	1.00	1.01 (0.99; 1.04)	0.320	1.00	1.01 (0.98; 1.04)	0.378	1.00
Thyroid	222,598	113	1.03 (1.00; 1.06)	0.062	1.00	1.03 (1.00; 1.06)	0.047	0.799	1.03 (1.00; 1.06)	0.077	1.00
Uterine	222,448	713	0.99 (0.98; 1.01)	0.285	1.00	1.00 (0.99; 1.01)	0.582	1.00	0.99 (0.98; 1.00)	0.072	1.00

Data is presented as hazard ratio (HR) and their 95% confidence interval (95% CI) in men and women, $P_{adjusted}$: P-value adjusted for multiple testing

Model 1: Adjusted for age, ethnicity, deprivation index and comorbidity.

Model 2; Adjusted for model 1 plus smoking, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity and sedentary behaviours.

Model 3: Adjusted for model 2 plus waist circumference.

Supplementary Table S3: Association height (per 5 cm) and cancer risk mortality, men and women.

Site cancer	Total	Event	Model 1	P-value	$P_{adjusted}$	Model 2	P-value	$P_{adjusted}$	Model 3	P-value	$P_{adjusted}$
MEN											
All-cause	191,881	3,986	**1.01 (1.00; 1.01)**	0.019	0.361	**1.01 (1.00; 1.01)**	0.001	0.019	1.01 (1.00; 1.01)	0.013	0.247
Bladder	192,284	139	1.01 (0.98; 1.03)	0.522	1.00	1.01 (0.99; 1.04)	0.432	1.00	1.01 (0.98; 1.03)	0.536	1.00
Brain	192,254	231	1.01 (0.99; 1.03)	0.560	1.00	1.01 (0.99; 1.02)	0.592	1.00	1.01 (0.99; 1.03)	0.470	1.00
Colorectal	192,254	417	1.01 (1.00; 1.02)	0.200	1.00	1.01 (0.99; 1.02)	0.211	1.00	1.00 (0.99; 1.02)	0.654	1.00
Gallbladder	192,284	14	0.93 (0.86; 1.00)	0.059	1.00	0.93 (0.86; 1.00)	0.056	0.952	0.92 (0.85; 1.00)	0.038	0.570
Kidney	192,273	153	1.00 (0.98; 1.02)	0.981	1.00	1.00 (0.98; 1.03)	0.797	1.00	1.00 (0.97; 1.02)	0.878	1.00
Leukaemia	192,275	160	1.02 (1.00; 1.04)	0.082	1.00	1.02 (1.00; 1.05)	0.064	0.96	1.02 (1.00; 1.05)	0.062	0.868
Liver	192,272	155	1.00 (0.98; 1.02)	0.928	1.00	1.00 (0.98; 1.03)	0.754	1.00	1.00 (0.97; 1.02)	0.720	1.00
Lung	192,194	790	1.01 (1.00; 1.02)	0.295	1.00	1.01 (1.00; 1.02)	0.058	0.952	1.01 (1.00; 1.02)	0.018	0.324
Lymphatic	192,250	380	1.02 (1.00; 1.03)	0.024	0.432	1.02 (1.00; 1.03)	0.013	0.234	1.02 (1.00; 1.03)	0.020	0.340
Melanoma	192,283	64	1.02 (0.98; 1.05)	0.418	1.00	1.02 (0.98; 1.05)	0.384	1.00	1.02 (0.98; 1.05)	0.417	1.00
Multiple Myeloma	192,282	54	1.03 (0.99; 1.07)	0.114	1.00	1.03 (0.99; 1.07)	0.126	1.00	1.03 (0.99; 1.07)	0.175	1.00
Non-Hodgkin	192,271	157	1.01 (0.98; 1.03)	0.525	1.00	1.01 (0.99; 1.03)	0.365	1.00	1.01 (0.99; 1.03)	0.414	1.00
Oesophagus	192,263	262	0.98 (0.97; 1.00)	0.080	1.00	0.99 (0.97; 1.01)	0.182	1.00	0.98 (0.96; 1.00)	0.025	0.400
Oral	192,285	73	1.00 (0.97; 1.04)	0.811	1.00	1.01 (0.98; 1.04)	0.620	1.00	1.01 (0.98; 1.05)	0.427	1.00
Pancreas	192,246	306	1.01 (1.00; 1.03)	0.102	1.00	1.01 (1.00; 1.03)	0.110	1.00	1.01 (0.99; 1.03)	0.237	1.00
Prostate	192,273	342	1.01 (1.00; 1.03)	0.150	1.00	1.01 (1.00; 1.03)	0.122	1.00	1.01 (0.99; 1.03)	0.268	1.00
Stomach	192,270	131	1.01 (0.99; 1.04)	0.400	1.00	1.02 (0.99; 1.04)	0.238	1.00	1.01 (0.98; 1.04)	0.474	1.00
Testis	192,273	0	NA.		1.00	NA.		1.00	NA.		1.00
Thyroid	192,288	5	0.99 (0.87; 1.13)	0.903	1.00	0.99 (0.86; 1.13)	0.843	1.00	0.97 (0.85; 1.11)	0.705	0.247
WOMEN											
All-cause	222,386	2,969	**1.01 (1.00; 1.02)**	0.001	0.023	**1.01 (1.01; 1.02)**	<0.001	<0.001	**1.01 (1.00; 1.02)**	0.001	0.023
Bladder	222,631	35	1.00 (0.95; 1.06)	0.857	1.00	1.01 (0.95; 1.06)	0.811	1.00	1.00 (0.95; 1.06)	0.954	1.00
Brain	222,619	145	1.00 (0.98; 1.03)	0.817	1.00	1.00 (0.98; 1.03)	0.857	1.00	1.00 (0.98; 1.03)	0.819	1.00
Breast	222,621	272	1.02 (1.00; 1.04)	0.025	0.550	1.02 (1.00; 1.04)	0.035	0.735	1.02 (1.00; 1.04)	0.055	1.00
Cervix	222,633	10	0.96 (0.87; 1.06)	0.373	1.00	0.96 (0.87; 1.06)	0.457	1.00	0.97 (0.88; 1.07)	0.518	1.00
Colorectal	222,618	296	1.01 (0.99; 1.03)	0.188	1.00	1.01 (1.00; 1.03)	0.123	1.00	1.01 (0.99; 1.03)	0.156	1.00
Endometrium	222,633	69	1.01 (0.97; 1.05)	0.750	1.00	1.01 (0.97; 1.05)	0.634	1.00	1.00 (0.96; 1.04)	0.997	1.00
Gallbladder	222,634	24	1.02 (0.96; 1.09)	0.519	1.00	1.02 (0.96; 1.09)	0.476	1.00	1.02 (0.96; 1.09)	0.544	1.00
Kidney	222,627	51	0.99 (0.94; 1.03)	0.568	1.00	0.99 (0.94; 1.03)	0.594	1.00	0.98 (0.94; 1.03)	0.405	1.00
Leukaemia	222,623	78	1.03 (1.00; 1.07)	0.080	1.00	1.03 (1.00; 1.07)	0.080	1.00	1.03 (0.99; 1.07)	0.111	1.00

Liver	222,621	110	1.03 (1.00; 1.06)	0.046	0.966	1.03 (1.00; 1.07)	0.029	0.638	1.03 (1.00; 1.06)	0.043	0.946
Lung	222,571	592	1.00 (0.99; 1.02)	0.604	1.00	1.01 (0.99; 1.02)	0.279	1.00	1.01 (0.99; 1.02)	0.356	1.00
Lymphatic	222,612	233	1.02 (1.00; 1.04)	0.117	1.00	1.02 (1.00; 1.04)	0.073	1.00	1.02 (1.00; 1.04)	0.114	1.00
Melanoma	222,634	38	0.96 (0.91; 1.01)	0.091	1.00	0.96 (0.91; 1.01)	0.105	1.00	0.96 (0.91; 1.01)	0.114	1.00
Multiple Myeloma	222,631	51	1.01 (0.97; 1.06)	0.560	1.00	1.02 (0.98; 1.07)	0.400	1.00	1.02 (0.97; 1.06)	0.479	1.00
Non-Hodgkin	222,629	97	1.01 (0.98; 1.04)	0.603	1.00	1.01 (0.98; 1.04)	0.495	1.00	1.01 (0.98; 1.04)	0.572	1.00
Oesophagus	222,629	76	1.01 (0.97; 1.05)	0.650	1.00	1.01 (0.97; 1.05)	0.584	1.00	1.01 (0.98; 1.05)	0.535	1.00
Oral	222,634	28	1.00 (0.94; 1.06)	0.959	1.00	1.01 (0.95; 1.07)	0.858	1.00	1.01 (0.95; 1.07)	0.832	1.00
Ovary	222,622	246	1.01 (0.99; 1.03)	0.573	1.00	1.01 (0.99; 1.03)	0.458	1.00	1.01 (0.99; 1.03)	0.441	1.00
Pancreas	222,610	256	1.01 (0.99; 1.03)	0.564	1.00	1.01 (0.99; 1.03)	0.542	1.00	1.00 (0.99; 1.03)	0.634	1.00
Stomach	222,628	65	1.01 (0.97; 1.05)	0.544	1.00	1.02 (0.98; 1.06)	0.417	1.00	1.01 (0.97; 1.05)	0.529	1.00
Thyroid	222,632	3	0.89 (0.75; 1.07)	0.218	1.00	0.89 (0.75; 1.06)	0.180	1.00	0.88 (0.74; 1.05)	0.152	1.00
Uterine	222,630	104	1.01 (0.98; 1.04)	0.680	1.00	1.01 (0.98; 1.04)	0.500	1.00	1.00 (0.97; 1.04)	0.773	1.00

Data is presented as hazard ratio (HR) and their 95% confidence interval (95% CI) in men and women, $P_{adjusted}$: P-value adjusted for multiple testing.
Model 1: Adjusted for age, sex ethnicity, deprivation index and comorbidity.
Model 2; Adjusted for model 1 plus smoking, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity and sedentary behaviours.
Model 3: Adjusted for model 2 plus waist circumference.

Supplementary Table S4: Association height (per 5 cm) and breast, cervix, endometrium, ovary and uterine cancer incidence and mortality by menopausal status.

	Overall	**Postmenopausal**	**Premenopausal**	**P interaction**
Breast				
Total/event	221,445/4,283	131,976/2,744	55,743/883	
HR (95% CI)	**1.01 (1.01; 1.02)**	**1.02 (1.01; 1.02)**	**1.02 (1.01; 1.02)**	0.936
Total/deaths	222,616/272	132,751/180	55,956/56	
HR (95% CI)	1.02 (1.00; 1.04)	1.02 (0.99; 1.04)	1.02 (0.99; 1.04)	0.509
Cervix				
Total/event	222,608/50	132,745/34	55,952/13	
HR (95% CI)	0.98 (0.94; 1.02)	0.98 (0.93; 1.03)	0.98 (0.93; 1.03)	0.774
Total/deaths	222,628/10	132,759/6	55,957/3	
HR (95% CI)	0.97 (0.88; 1.07)	0.97 (0.85; 1.10)	0.97 (0.85; 1.10)	0.621
Endometrium				
Total/event	222,486/646	132,638/526	55,944/94	
HR (95% CI)	0.99 (0.98; 1.00)	0.99 (0.98; 1.01)	0.99 (0.98; 1.01)	0.150
Total/deaths	222,628/69	132,758/62	0,001/1	
HR (95% CI)	1.00 (0.96; 1.04)	1.00 (0.96; 1.04)	1.00 (0.96; 1.04)	0.931
Ovary				
Total/event	222,497/515	132,663/380	55,940/78	
HR (95% CI)	1.01 (0.99; 1.02)	1.00 (0.99; 1.02)	1.00 (0.99; 1.02)	0.953
Total/deaths	222,617/246	132,749/197	55,956/21	
HR (95% CI)	1.01 (0.99; 1.03)	1.01 (0.98; 1.03)	1.01 (0.98; 1.03)	0.563
Uterine				
Total/event	222,443/713	132,607/574	55,934/111	
HR (95% CI)	0.99 (0.98; 1.00)	0.99 (0.98; 1.01)	0.99 (0.98; 1.01)	0.249
Total/deaths	222,625/104	132,756/89	55,957/9	
HR (95% CI)	1.00 (0.97; 1.04)	1.01 (0.97; 1.04)	1.01 (0.97; 1.04)	0.801

Data is presented as hazard ratio and their 95% intervals in women

Model: Adjusted for age, sex ethnicity, deprivation index, comorbidity, smoking, hormone replacement, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity, sedentary behaviours and waist circumference. HR: hazard ratio.

Supplementary Table S5: Association height (per 5 cm) and lung cancer incidence and mortality by smoking status.

	Overall	**No smokers**	**Ex-smokers**	**Current smokers**	**P interaction**
Lung Incidence					
Total/event	192,076/1,026	95,266/104	73,286/468	23,524/454	
Men	**1.02 (1.01; 1.02)**	1.01 (0.98; 1.04)	**1.02 (1.00; 1.03)**	**1.02 (1.00; 1.03)**	0.720
Total/event	222,478/881	133,818/180	69,255/380	19,405/321	
Women	1.00 (0.99; 1.01)	1.01 (0.99; 1.03)	1.00 (0.99; 1.02)	1.00 (0.98; 1.02)	0.129
Lung Mortality					
Total/deaths	192,194/790	95,283/68	73,353/368	23,558/354	
Men	**1.01 (1.00; 1.02)**	1.03 (0.99; 1.07)	**1.01 (1.00; 1.03)**	**1.01 (1.00; 1.03)**	0.870
Total/deaths	222,571/592	133,843/90	69,292/270	19,436/232	
Women	1.01 (0.99; 1.02)	1.02 (0.99; 1.06)	1.00 (0.98; 1.02)	1.00 (0.98; 1.02)	0.247

Data is presented as hazard ratio and their 95% intervals in men and women

Model: Adjusted for age, sex ethnicity, deprivation index, comorbidity, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity, sedentary behaviours and waist circumference. HR: Hazard ratio

Supplementary Table S6: Association height (per 5 cm) and liver and stomach cancer incidence and mortality by alcohol risk.

	Overall	**No risk OH**	**Risk OH**	**P interaction**
Liver Incidence				
Total/event	192,253/220	25,139/49	167,114/171	
Men	0.99 (0.97; 1.01)	1.00 (0.96; 1.04)	0.98 (0.96; 1.01)	0.700
Total/event	222,610/156	52,950/59	169,660/97	
Women	1.02 (1.00; 1.05)	1.03 (0.99; 1.07)	1.02 (0.98; 1.05)	0.525
Liver mortality				
Total/deaths	192,272/155	25,141/31	167,131/124	
Men	1.00 (0.97; 1.02)	1.00 (0.95; 1.05)	0.99 (0.97; 1.02)	0.971
Total/deaths	222,621/110	52,952/42	169,669/68	
Women	**1.03 (1.00; 1.06)**	1.04 (0.99; 1.09)	1.03 (0.99; 1.07)	0.553
Stomach incidence				
Total/event	192,216/314	25,131/58	167,085/256	
Men	0.99 (0.97; 1.01)	0.99 (0.96; 1.03)	0.99 (0.97; 1.01)	0.849
Total/event	222,611/120	52,948/40	169,663/80	
Women	1.01 (0.98; 1.04)	1.01 (0.96; 1.06)	1.01 (0.98; 1.05)	0.984
Stomach mortality				
Total/deaths	192,270/131	25,142/33	167,128/98	
Men	1.01 (0.98; 1.04)	1.03 (0.98; 1.08)	1.00 (0.97; 1.03)	0.463
Total/deaths	222,628/65	52,955/22	169,673/43	
Women	1.01 (0.97; 1.05)	1.02 (0.96; 1.09)	1.00 (0.96; 1.05)	0.600

Data is presented as hazard ratio and their 95% intervals in men and women

Model: Adjusted for age, sex ethnicity, deprivation index, comorbidity, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity, sedentary behaviours and waist circumference. OH: alcohol: Alcohol risk unit > once a week.

Supplementary Table S7: Association height (per 5 cm) and 24 cancer sites incidence by group of height ≥ or < 162 cm, for women, ≥ or < 176 cm for men.

Site cancer	Category Height	Total	Event	HR 95% CI	P value	$P_{adjusted}$	$P_{interation}$		Total	Event	HR 95% CI	P value	$P_{adjusted}$	$P_{interation}$	Padj
			Men								Women				
All-cause	<176m, <162w	98,433	8,101	**1.01 (1.00; 1.01)**	**0.003**	0.114	0.731	1.00	102,882	6,550	**1.01 (1.01; 1.02)**	**<0.001**	**<0.001**	0.242	1.00
	≥176m, ≥162w	90,261	6,738	**1.01 (1.00; 1.01)**	**0.013**	0.455			116,191	7,294	**1.01 (1.00; 1.01)**	**0.024**	1.00		
Bladder	<176m, <162w	100,258	484	1.01 (0.99; 1.03)	0.594	1.00	0.643	1.00	104,516	140	0.99 (0.95; 1.03)	0.536	1.00	0.810	1.00
	≥176m, ≥162w	91,798	364	1.01 (0.99; 1.04)	0.407	1.00			118,045	138	0.98 (0.94; 1.02)	0.336	1.00		
Brain	<176m, <162w	100,352	134	1.02 (0.98; 1.06)	0.314	1.00	0.647	1.00	104,539	89	1.02 (0.97; 1.08)	0.389	1.00	0.691	1.00
	≥176m, ≥162w	91,870	126	1.00 (0.96; 1.04)	0.962	1.00			118,056	82	1.00 (0.95; 1.06)	0.922	1.00		
Colorectal	<176m, <162w	100,152	819	1.00 (0.99; 1.02)	0.675	1.00	0.133	1.00	104,431	576	1.00 (0.98; 1.02)	0.747	1.00	0.284	1.00
	≥176m, ≥162w	91,715	684	0.99 (0.97; 1.00)	0.133	1.00			117,937	566	1.02 (1.00; 1.04)	0.051	1.00		
Gallbladder	<176m, <162w	100,379	19	0.98 (0.89; 1.08)	0.695	1.00	0.798	1.00	104,552	22	1.05 (0.95; 1.17)	0.344	1.00	0.838	1.00
	≥176m, ≥162w	91,903	4	1.01 (0.80; 1.28)	0.922	1.00			118,076	22	1.04 (0.94; 1.15)	0.442	1.00		
Kidney	<176m, <162w	100,338	235	1.00 (0.98; 1.04)	0.746	1.00	0.210	1.00	104,534	121	1.01 (0.96; 1.05)	0.762	1.00	0.600	1.00
	≥176m, ≥162w	91,858	201	0.98 (0.94; 1.01)	0.228	1.00			118,049	113	0.99 (0.95; 1.04)	0.679	1.00		
Leukaemia	<176m, <162w	100,351	173	**1.04 (1.01; 1.08)**	**0.018**	0.612	0.613	1.00	104,539	83	1.03 (0.97; 1.08)	0.342	1.00	0.854	1.00
	≥176m, ≥162w	91,876	177	1.03 (0.99; 1.06)	0.139	1.00			118,061	117	1.01 (0.97; 1.06)	0.554	1.00		
Liver	<176m, <162w	100,355	136	0.97 (0.94; 1.00)	0.091	1.00	0.078	1.00	104,542	79	0.99 (0.94; 1.05)	0.784	1.00	**0.030**	**0.660**
	≥176m, ≥162w	91,898	84	1.02 (0.98; 1.08)	0.340	1.00			118,068	77	**1.08 (1.03; 1.13)**	**0.002**	0.09		
Lung	<176m, <162w	100,259	599	**1.03 (1.01; 1.05)**	**0.003**	0.114	0.146	1.00	104,469	475	**1.02 (1.00; 1.05)**	**0.030**	1.00	**0.019**	**0.437**
	≥176m, ≥162w	91,817	427	1.01 (0.98; 1.03)	0.601	1.00			118,009	406	0.98 (0.96; 1.01)	0.173	1.00		
Lymphatic	<176m, <162w	100,261	571	**1.02 (1.00; 1.04)**	**0.045**	1.00	0.100	1.00	104,480	367	**1.03 (1.00; 1.06)**	**0.024**	1.00	0.273	1.00
	≥176m, ≥162w	91,791	521	**1.04 (1.02; 1.06)**	**<0.001**	**<0.001**			117,987	468	1.01 (0.99; 1.03)	0.525	1.00		
Melanoma	<176m, <162w	100,329	249	1.02 (0.99; 1.05)	0.140	1.00	0.648	1.00	104,490	220	1.02 (0.99; 1.06)	0.165	1.00	0.550	1.00
	≥176m, ≥162w	91,842	307	1.01 (0.99; 1.04)	0.295	1.00			118,002	323	1.01 (0.99; 1.04)	0.350	1.00		
Multiple Myeloma	<176m, <162w	100,359	126	1.00 (0.96; 1.04)	0.858	1.00	0.177	1.00	104,543	89	1.02 (0.97; 1.07)	0.404	1.00	0.859	1.00
	≥176m, ≥162w	91,882	102	1.04 (0.99; 1.08)	0.089	1.00			118,059	99	1.01 (0.97; 1.06)	0.562	1.00		
Non-Hodgkin	<176m, <162w	100,319	284	1.03 (1.00; 1.05)	0.074	1.00	0.181	1.00	104,510	187	1.04 (1.00; 1.07)	0.055	1.00	0.183	1.00
	≥176m, ≥162w	91,846	240	**1.05 (1.02; 1.08)**	**<0.001**	**<0.001**			118,025	251	1.00 (0.97; 1.03)	0.997	1.00		
Oesophagus	<176m, <162w	100,317	235	**0.96 (0.93; 0.99)**	**0.005**	0.180	0.647	1.00	104,541	67	1.03 (0.97; 1.09)	0.314	1.00	0.128	1.00
	≥176m, ≥162w	91,873	173	**0.96 (0.92; 1.00)**	**0.028**	0.924			118,061	68	0.96 (0.91; 1.03)	0.256	1.00		
Oral	<176m, <162w	100,339	173	1.01 (0.97; 1.04)	0.761	1.00	0.657	1.00	104,542	89	0.96 (0.92; 1.01)	0.140	1.00	0.061	1.00
	≥176m, ≥162w	91,876	138	1.00 (0.96; 1.04)	0.823	1.00			118,055	75	1.02 (0.97; 1.07)	0.431	1.00		
Pancreas	<176m, <162w	100,352	197	1.01 (0.98; 1.04)	0.588	1.00	0.597	1.00	104,526	156	1.01 (0.98; 1.05)	0.471	1.00	0.454	1.00
	≥176m, ≥162w	91,877	167	1.03 (0.99; 1.06)	0.162	1.00			118,057	143	1.03 (0.99; 1.07)	0.146	1.00		
Stomach	<176m, <162w	100,339	174	0.97 (0.94; 1.00)	0.056	1.00	0.784	1.00	104,542	57	0.98 (0.92; 1.04)	0.410	1.00	0.260	1.00
	≥176m, ≥162w	91,877	140	0.98 (0.94; 1.02)	0.386	1.00			118,069	63	1.03 (0.98; 1.09)	0.272	1.00		
Thyroid	<176m, <162w	100,373	18	1.00 (0.90; 1.12)	0.928	1.00	0.644	1.00	104,536	43	0.97 (0.91; 1.04)	0.387	1.00	0.223	1.00
	≥176m, ≥162w	91,903	25	0.96 (0.87; 1.06)	0.402	1.00			118,062	70	1.02 (0.97; 1.08)	0.470	1.00		
Prostate /Breast	<176m, <162w	99,976	2,014	1.00 (0.99; 1.02)	0.343	1.00	0.858	1.00	104,015	1,884	**1.02 (1.00; 1.03)**	**0.008**	0.352	0.327	1.00
Breast	≥176m, ≥162w	91,553	1,552	1.01 (0.99; 1.02)	0.293	1.00			117,435	2,399	1.01 (1.00; 1.02)	0.070	1.00		
Testis/Cervix	<176m, <162w	100,378	19	1.08 (0.96; 1.22)	0.191	1.00	0.077	1.00	104,544	26	1.03 (0.93; 1.13)	0.584	1.00	0.120	1.00
	≥176m, ≥162w	91,897	37	0.96 (0.88; 1.04)	0.292	1.00			118,069	24	0.91 (0.81; 1.01)	0.089	1.00		

Endometrium	<176m, <162w	--	--	--	--		--		104,484	354	1.00 (0.98; 1.03)	0.918	1.00	0.718	1.00
	≥176m, ≥162w	--	--	--	--		--		118,007	292	1.00 (0.97; 1.03)	0.926	1.00		
Ovary	<176m, <162w	--	--	--	--		--		104,500	251	1.01 (0.98; 1.04)	0.395	1.00	0.710	1.00
	≥176m, ≥162w	--	--	--	--		--		118,002	264	1.00 (0.97; 1.03)	0.943	1.00		
Uterine	<176m, <162w	--	--	--	--		--		104,457	380	1.00 (0.97; 1.02)	0.845	1.00	0.796	1.00
	≥176m, ≥162w	--	--	--	--		--		117,991	333	0.99 (0.97; 1.02)	0.679	1.00		

Data is presented as hazard ratio and their 95% intervals in women. Model: Adjusted for age, sex ethnicity, deprivation index, comorbidity, smoking, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity, sedentary behaviours and waist circumference. HR: hazard ratio. No data available (--). Padj: P-value adjusted for multiple testing

Supplementary Table S8: Association between height and cancer incidence and mortality by IGF-1 concentration levels in men

		INCIDENCE				**MORTALITY**			
Site cancer	**IGF-1 level**	**Total/event**	**HR 95% CI**	**P value**	$P_{adjusted}$	**Total/Death**	**HR 95% CI**	**P value**	$P_{adjusted}$
All-cause	Low	94,400 /7,364	1.01 (1.00; 1.01)	**<0.001**	**<0.001**	96,001 /1,887	1.01 (1.00; 1.01)	0.132	1.00
	High	94,294 /7,475	1.01 (1.00; 1.01)	**<0.001**	**<0.001**	95,880 /2,099	1.01 (1.00; 1.01)	0.051	1.00
Bladder	Low	96,093 /410	1.01 (0.99; 1.02)	0.303	1.00	96,198 /74	1.00 (0.96; 1.03)	0.939	1.00
	High	95,963 /438	1.00 (0.99; 1.01)	0.949	1.00	96,086 /65	1.02 (0.98; 1.05)	0.387	1.00
Brain	Low	96,161 /144	1.02 (0.99; 1.05)	0.127	1.00	96,180 /125	1.02 (0.99; 1.05)	0.162	1.00
	High	96,061 /116	1.00 (0.97; 1.03)	0.961	1.00	96,074 /106	0.99 (0.96; 1.02)	0.531	1.00
Colorectal	Low	95,979 /746	1.01 (0.99; 1.02)	0.339	1.00	96,182 /214	0.99 (0.97; 1.01)	0.520	1.00
	High	95,888 /757	0.99 (0.98; 1.00)	0.203	1.00	96,072 /203	1.01 (0.99; 1.03)	0.238	1.00
Gallbladder	Low	96,196 /8	0.92 (0.82; 1.02)	0.108	1.00	96,197 /5	0.96 (0.84; 1.10)	0.525	1.00
	High	96,086 /15	0.96 (0.89; 1.04)	0.284	1.00	96,087 /9	0.90 (0.82; 0.99)	0.035	1.00
Kidney	Low	96,147 /229	1.01 (0.99; 1.03)	0.263	1.00	96,190 /81	1.01 (0.98; 1.05)	0.431	1.00
	High	96,049 /207	0.99 (0.97; 1.01)	0.308	1.00	96,083 /72	0.98 (0.95; 1.01)	0.247	1.00
Leukaemia	Low	96,170 /164	1.02 (1.00; 1.04)	0.085	1.00	96,193 /74	1.00 (0.97; 1.04)	0.990	1.00
	High	96,057 /186	1.04 (1.02; 1.06)	**<0.001**	**<0.001**	96,082 /86	1.04 (1.01; 1.08)	0.011	0.429
Liver	Low	96,187 /48	0.98 (0.94; 1.02)	0.284	1.00	96,192 /34	0.97 (0.92; 1.02)	0.199	1.00
	High	96,066 /172	1.00 (0.97; 1.02)	0.681	1.00	96,080 /121	1.01 (0.98; 1.04)	0.519	1.00
Lung	Low	96,100 /419	1.01 (1.00; 1.03)	0.056	1.00	96,147 /315	1.01 (0.99; 1.02)	0.385	1.00
	High	95,976 /607	1.02 (1.00; 1.03)	0.006	0.204	96,047 /475	1.02 (1.00; 1.03)	0.013	0.494
Lymphatic	Low	96,093 /530	1.02 (1.00; 1.03)	0.008	0.264	96,183 /185	1.01 (0.99; 1.03)	0.522	1.00
	High	95,959 /562	1.03 (1.01; 1.04)	**<0.001**	**<0.001**	96,067 /195	1.03 (1.01; 1.05)	0.010	0.400
Melanoma	Low	96,141 /304	1.02 (1.00; 1.04)	0.020	0.640	96,198 /33	1.03 (0.98; 1.09)	0.260	1.00
	High	96,030 /252	1.03 (1.01; 1.05)	**<0.001**	**<0.001**	96,085 /31	1.00 (0.95; 1.05)	0.978	1.00
Multiple Myeloma	Low	96,172 /117	1.01 (0.98; 1.04)	0.620	1.00	96,194 /28	1.00 (0.94; 1.06)	0.895	1.00
	High	96,069 /111	1.01 (0.99; 1.04)	0.308	1.00	96,088 /26	1.06 (1.00; 1.12)	0.040	1.00
Non-Hodgkin	Low	96,147 /251	1.03 (1.01; 1.05)	0.003	0.105	96,192 /76	1.03 (0.99; 1.06)	0.104	1.00
	High	96,018 /273	1.02 (1.00; 1.04)	0.051	1.00	96,079 /81	0.99 (0.96; 1.03)	0.680	1.00
Oesophagus	Low	96,148 /195	0.98 (0.96; 1.00)	0.049	1.00	96,187 /131	0.99 (0.96; 1.02)	0.429	1.00
	High	96,042 /213	0.98 (0.96; 1.00)	0.086	1.00	96,076 /131	0.97 (0.94; 0.99)	0.014	0.518
Oral	Low	96,161 /121	1.01 (0.99; 1.04)	0.317	1.00	96,197 /28	1.02 (0.96; 1.08)	0.557	1.00
	High	96,054 /190	0.99 (0.97; 1.02)	0.632	1.00	96,088 /45	1.01 (0.97; 1.06)	0.557	1.00
Pancreas	Low	96,169 /197	1.01 (0.99; 1.03)	0.248	1.00	96,176 /168	1.02 (0.99; 1.04)	0.171	1.00
	High	96,060 /167	1.01 (0.99; 1.03)	0.340	1.00	96,070 /138	1.00 (0.98; 1.03)	0.924	1.00
Prostate	Low	95,798 /1,896	1.00 (0.99; 1.00)	0.572	1.00	96,188 /165	1.00 (0.97; 1.02)	0.851	1.00

	High	95,731 /1,670	1.01 (1.00; 1.01)	0.052	1.00	96,085 /177	1.02 (1.00; 1.04)	0.087	1.00
Stomach	Low	96,164 /144	0.97 (0.95; 1.00)	0.049	1.00	96,189 /65	1.01 (0.97; 1.04)	0.781	1.00
	High	96,052 /170	1.00 (0.98; 1.03)	0.724	1.00	96,081 /66	1.01 (0.98; 1.05)	0.511	1.00
Testis	Low	96,191 /27	1.04 (0.98; 1.10)	0.204	1.00	0,001 /1	1.00 (1.00; 1.00)	1.000	1.00
	High	96,084 /29	1.03 (0.98; 1.09)	0.238	1.00	0,001 /1	1.00 (1.00; 1.00)	1.000	1.00
Thyroid	Low	96,190 /28	1.02 (0.97; 1.08)	0.440	1.00	96,198 /2	0.96 (0.77; 1.20)	0.733	1.00
	High	96,086 /15	0.99 (0.91; 1.06)	0.716	1.00	96,090 /3	0.97 (0.82; 1.15)	0.741	1.00

Data is presented as hazard ratio and their 95% intervals in men and women

Model: Adjusted for age, sex ethnicity, deprivation index, comorbidity, smoking, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity, sedentary behaviours and waist circumference.IGF-1: Insulin-like growth factor. HR: Hazard Ratio, CI: confidence interval. IGF-1: Low (Mean: 15.7, SD: 2.9), Middle (Mean: 21.1, SD: 1.9), High (Mean: 27.3, SD: 4.2). Padj: P-value adjusted for multiple testing

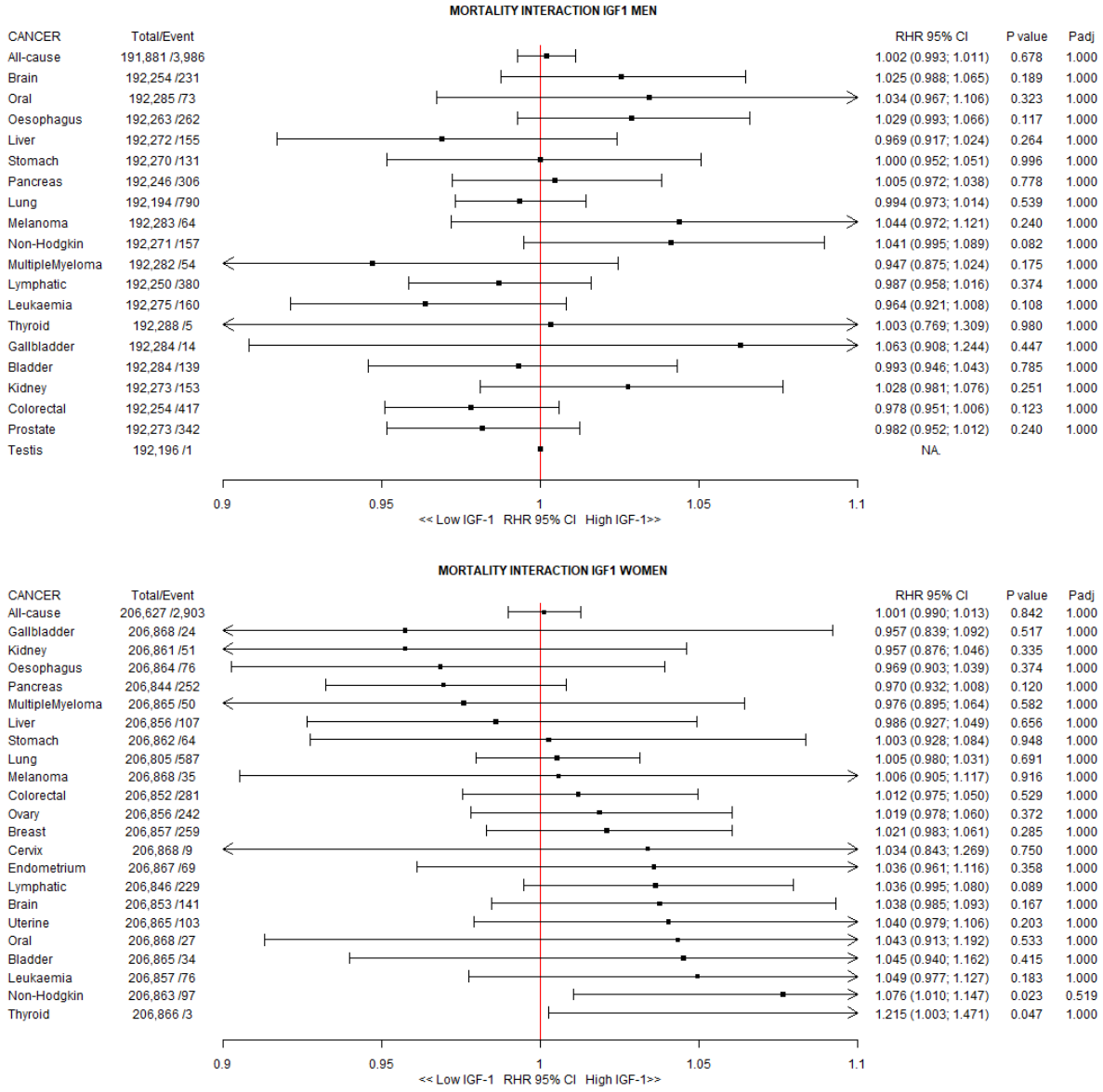
Supplementary Table S9: Association between height and cancer incidence and mortality by IGF-1 concentration levels in women.

		INCIDENCE				MORTALITY			
Site cancer	**IGF-1 level**	**Total/event**	**HR 95% CI**	**P value**	$P_{adjusted}$	**Total/Death**	**HR 95% CI**	**P value**	$P_{adjusted}$
All-cause	Low	94,563 /6,422	1.01 (1.01; 1.02)	**<0.001**	**<0.001**	96,109 /1,352	1.01 (1.00; 1.02)	0.021	0.945
	High	108,875 /6,819	1.01 (1.01; 1.01)	**<0.001**	**<0.001**	110,518 /1,551	1.01 (1.00; 1.02)	0.035	1.00
Bladder	Low	96,206 /131	1.01 (0.98; 1.04)	0.632	1.00	96,237 /15	1.03 (0.95; 1.11)	0.529	1.00
	High	110,590 /140	0.99 (0.97; 1.02)	0.636	1.00	110,628 /19	0.99 (0.92; 1.07)	0.852	1.00
Brain	Low	96,211 /91	1.02 (0.99; 1.06)	0.176	1.00	96,227 /79	1.01 (0.98; 1.05)	0.515	1.00
	High	110,619 /74	0.97 (0.93; 1.00)	0.077	1.00	110,626 /62	0.98 (0.94; 1.02)	0.358	1.00
Breast	Low	95,682 /2,034	1.01 (1.01; 1.02)	**<0.001**	**<0.001**	96,232 /129	1.02 (1.00; 1.05)	0.084	1.00
	High	110,074 /1,957	1.01 (1.01; 1.02)	**<0.001**	**<0.001**	110,625 /130	1.01 (0.98; 1.04)	0.553	1.00
Cervix	Low	96,229 /18	0.98 (0.91; 1.06)	0.676	1.00	96,232 /0	1.00 (1.00; 1.00)	1.000	1.00
	High	110,621 /30	0.98 (0.92; 1.04)	0.434	1.00	110,630 /5	0.95 (0.83; 1.10)	0.501	1.00
Colorectal	Low	96,105 /554	1.00 (0.98; 1.01)	0.681	1.00	96,229 /142	1.02 (0.99; 1.05)	0.111	1.00
	High	110,501 /540	1.01 (1.00; 1.03)	0.057	1.00	110,623 /139	1.00 (0.97; 1.03)	0.999	1.00
Endometrium	Low	96,173 /281	1.00 (0.98; 1.02)	0.849	1.00	96,237 /33	1.02 (0.96; 1.08)	0.486	1.00
	High	110,552 /344	0.98 (0.96; 0.99)	0.009	0.342	110,630 /36	0.98 (0.93; 1.04)	0.546	1.00
Gallbladder	Low	96,236 /16	1.02 (0.94; 1.10)	0.635	1.00	96,237 /9	0.99 (0.89; 1.10)	0.854	1.00
	High	110,626 /28	1.03 (0.97; 1.09)	0.340	1.00	110,631 /15	1.04 (0.96; 1.13)	0.366	1.00
Kidney	Low	96,218 /97	1.00 (0.97; 1.03)	0.881	1.00	96,235 /30	0.96 (0.91; 1.02)	0.179	1.00
	High	110,599 /133	1.00 (0.97; 1.02)	0.779	1.00	110,626 /21	1.01 (0.94; 1.08)	0.804	1.00
Leukaemia	Low	96,219 /98	1.04 (1.01; 1.08)	0.013	0.481	96,231 /36	1.06 (1.00; 1.11)	0.047	1.00
	High	110,615 /96	1.03 (0.99; 1.06)	0.124	1.00	110,626 /40	1.01 (0.96; 1.06)	0.634	1.00
Liver	Low	96,229 /56	1.01 (0.97; 1.05)	0.722	1.00	96,233 /38	1.02 (0.97; 1.08)	0.402	1.00
	High	110,616 /96	1.03 (1.00; 1.07)	0.051	1.00	110,623 /69	1.04 (1.00; 1.08)	0.055	1.00
Lung	Low	96,165 /415	1.01 (0.99; 1.02)	0.355	1.00	96,202 /271	1.01 (0.99; 1.03)	0.467	1.00
	High	110,548 /454	1.00 (0.98; 1.01)	0.973	1.00	110,603 /316	1.01 (0.99; 1.02)	0.582	1.00
Lymphatic	Low	96,154 /379	1.03 (1.02; 1.05)	<0.001	<0.001	96,225 /105	1.04 (1.00; 1.07)	0.029	1.00
	High	110,552 /432	1.02 (1.01; 1.04)	0.005	0.195	110,621 /124	1.00 (0.98; 1.03)	0.790	1.00
Melanoma	Low	96,171 /249	1.03 (1.01; 1.05)	0.004	0.160	96,237 /15	0.96 (0.89; 1.05)	0.375	1.00
	High	110,566 /260	1.02 (1.00; 1.04)	0.039	1.00	110,631 /20	0.96 (0.90; 1.04)	0.310	1.00
Multiple Myeloma	Low	96,220 /92	1.02 (0.99; 1.06)	0.168	1.00	96,236 /26	1.00 (0.94; 1.06)	0.918	1.00
	High	110,617 /88	1.02 (0.98; 1.05)	0.334	1.00	110,629 /24	1.04 (0.98; 1.11)	0.211	1.00
Non-Hodgkin	Low	96,191 /188	1.04 (1.01; 1.06)	0.002	0.082	96,235 /42	1.06 (1.01; 1.11)	0.029	1.00
	High	110,581 /239	1.02 (1.00; 1.05)	0.022	0.748	110,628 /55	0.98 (0.94; 1.02)	0.278	1.00
Oesophagus	Low	96,222 /64	0.99 (0.95; 1.03)	0.522	1.00	96,235 /38	0.99 (0.94; 1.04)	0.752	1.00

	High	110,616 /68	1.04 (1.00; 1.08)	0.057	1.00	110,629 /38	1.03 (0.98; 1.09)	0.236	1.00
Oral	Low	96,221 /67	0.98 (0.95; 1.02)	0.448	1.00	96,237 /7	1.03 (0.91; 1.16)	0.686	1.00
	High	110,613 /92	0.98 (0.95; 1.02)	0.329	1.00	110,631 /20	1.00 (0.93; 1.07)	0.965	1.00
Ovary	Low	96,185 /222	1.03 (1.00; 1.05)	0.018	0.630	96,231 /103	1.02 (0.99; 1.06)	0.157	1.00
	High	110,554 /273	0.99 (0.97; 1.01)	0.460	1.00	110,625 /139	1.00 (0.97; 1.03)	0.886	1.00
Pancreas	Low	96,215 /140	0.99 (0.97; 1.02)	0.600	1.00	96,225 /123	0.99 (0.97; 1.02)	0.733	1.00
	High	110,603 /154	1.03 (1.00; 1.06)	0.031	1.00	110,619 /129	1.02 (0.99; 1.04)	0.291	1.00
Stomach	Low	96,224 /55	0.99 (0.95; 1.04)	0.707	1.00	96,234 /27	1.02 (0.96; 1.08)	0.554	1.00
	High	110,622 /62	1.03 (0.99; 1.07)	0.177	1.00	110,628 /37	1.01 (0.96; 1.06)	0.735	1.00
Thyroid	Low	96,215 /52	1.02 (0.98; 1.07)	0.276	1.00	96,236 /0	NA.		
	High	110,617 /52	1.03 (0.99; 1.08)	0.172	1.00	110,630 /3	0.87 (0.72; 1.06)	0.165	1.00
Uterine	Low	96,156 /302	1.00 (0.98; 1.02)	0.919	1.00	96,237 /51	1.03 (0.98; 1.08)	0.208	1.00
	High	110,529 /388	0.98 (0.96; 1.00)	0.014	0.504	110,628 /52	0.98 (0.94; 1.03)	0.461	1.00

Data is presented as hazard ratio and their 95% intervals in men and women

Model: Adjusted for age, sex ethnicity, deprivation index, comorbidity, smoking, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity, sedentary behaviours and waist circumference.IGF-1: Insulin-like growth factor. HR: Hazard Ratio, CI: confidence interval. IGF-1: Low (Mean: 15.7, SD: 2.9), Middle (Mean: 21.1, SD: 1.9), High (Mean: 27.3, SD: 4.2). Padj: P-value adjusted for multiple testing



Supplementary Figure S4. Ratio of HR of low to high IGF-1 level for the association of height with mortality of 24 cancer sites men and women.

Data presented as ratio of hazard ratio (interaction term of IGF-1 level and height) and their 95% CI per 5-cm increment in height. Models were adjusted for age, ethnicity, deprivation index, comorbidity, smoking, alcohol consumption, fruit & vegetable, processed meat intake, oily fish, sleep, physical activity, sedentary behaviours and waist circumference. Padj: P-value adjusted for multiple testing