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# Height and pancreatic cancer risk: a systematic review and meta-analysis of cohort studies

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**Abstract**

**Background:** Greater height has been associated with increased risk of several cancers, but epidemiological data on height and pancreatic cancer are inconclusive. We conducted a systematic review and meta-analysis of prospective studies to clarify these results.

**Methods:** PubMed and several other databases were searched up to September 2011. Prospective studies that reported relative risk (RR) estimates and 95% confidence intervals (CIs) associated with height and pancreatic cancer were included. Summary relative risks were estimated by use of a random effects model.

**Results:** We identified ten cohort studies that were included in the meta-analysis. The summary RR for high vs. low height was 1.27 (95% CI: 1.12-1.45, $I^2$=33%) and in the dose-response analysis the summary RR per 5 cm increase in height was 1.09 (95% CI: 1.05-1.15, $I^2$=61%). The results were similar among men and women, summary RR=1.07 (95% CI: 1.01-1.14, $I^2$=52%) and summary RR=1.09 (95% CI: 1.01-1.18, $I^2$=59%), respectively. There was indication of small study bias with Egger's test, p=0.05. The summary estimate was attenuated when we included results from two pooled analyses together with these studies, summary RR = 1.04 (95% CI: 1.01-1.07, $I^2$=44%, $p_{heterogeneity}$=0.08) and Egger's test was no longer significant, p=0.17.

**Conclusions**: This meta-analysis of cohort studies provides support that greater adult attained height is associated with increased risk of pancreatic cancer. Although the strength of the association may have been overestimated due to publication bias, the positive association persisted in several sensitivity analyses taking this into account.

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# Introduction

Pancreatic cancer is the 9th most common cause of cancer with 277 000 new cases diagnosed in 2008 worldwide, accounting for about 2.2% of all cancer cases (1). There are few early symptoms of the disease and it is usually diagnosed in the later stages. Because of this, survival among pancreatic cancer patients is very low, on average only 6 months after the diagnosis (2). Established risk factors include tobacco smoking, which explains about 20-25% of pancreatic cancer cases (3, 4), family history of pancreatic cancer (5), pancreatitis (6), diabetes (relative risk, RR=1.8) (7) and body fatness (RR=1.10 per 5 kg/$m^2$) (8).

Tall people are at increased risk of several cancers (9, 10), but the evidence relating height to pancreatic cancer risk is not convincing (9). Both genetic and environmental factors determines adult attained height, which is partly a surrogate marker for *in utero* and childhood conditions (11). Adult height is related to birth weight, rate of growth, and age of puberty and periods of peak growth, such as in infancy and adolescence, are particularly important in determining adult height (12). Undernutrition and infectious diseases are the most important non-genetic factors affecting growth and adult body height, and as the prevalence of these conditions is reduced, an increase in height is observed (11).

The World Cancer Research Fund/American Institute for Cancer Research report from 2007 stated that greater height probably was associated with increased risk of pancreatic cancer (9), however, studies published subsequent to this report have reported inconsistent results. The large European Prospective Investigation into Nutrition and Cancer reported a 74% increase in pancreatic cancer risk comparing those with the highest with the lowest height (13). However, other large studies (10, 14-17) and three pooled analyses (18-20) did not find a significant association between greater height and pancreatic cancer risk. To clarify these findings we conducted a systematic review and dose-response meta-analysis of

prospective cohort studies of adult height and pancreatic cancer risk. In particular we wanted to clarify the dose-response relationship and explore potential heterogeneity by conducting subgroup and meta-regression analyses.

## Methods

### Data sources and searches

The literature search and data extraction up to December 2005 was conducted by several reviewers at University of Leeds. Initially several databases were searched including Pubmed, Embase, CAB Abstracts, ISI Web of Science, BIOSIS, LILACS, Cochrane library, CINAHL, AMED, National Research Register, and In Process Medline. Because all the relevant studies were identified through searches in PubMed a change in the protocol was made and only PubMed was used for the updated searches from January 2006 to September 2011. A predefined protocol was followed for the review (http://www.dietandcancerreport.org/downloads/SLR_Manual.pdf) and includes details of the search terms. Standard criteria for conducting and reporting meta-analyses were followed (21). We also searched the reference lists of all the studies that were included in our analysis to identify any further studies.

### Study selection

To be included, the study had to have a prospective cohort, case-cohort or nested case-control study design and to investigate the association between physical activity and pancreatic cancer risk. Estimates of the relative risk (hazard ratio, risk ratio) had to be

available with the 95% confidence intervals in the publication. For the dose-response analysis, a quantitative measure of height had to be provided. We identified 18 possibly relevant publications in the search (10, 13-17, 22-33). Two publications that only provided mean height among cases and controls were excluded (27, 30), two duplicate publications were excluded (29, 31) and one publication which did not provide any risk estimates was excluded (28). Each study was only included once in the main analysis or in the subgroup analyses, but for some studies overlapping publications provided results which were not available in the publication used for the main analysis, and these were used for some of the subgroup analyses. One of the remaining publications was only included in the subgroup analysis by gender (26) because a superseding publication (which was included in the overall analysis) only reported results for men and women combined (15) and two other publications (32, 33) were only included in the subgroup analysis of pancreatic cancer mortality as a publication from the same study with a larger number of cases was included in the overall analysis (15).

Data extraction and Quality Assessment

The following data were extracted from each study: The first author's last name, publication year, country where the study was conducted, the study name, follow-up period, sample size, gender, age, number of cases, height assessment method (self-reported vs. measured), comparison of high vs. low height in cm, RRs and 95% CIs for the highest vs. the lowest level of intake and variables adjusted for in the analysis. The search and data extraction up to December 2005 was conducted by JEC, DSMC, VB and several other reviewers at the University of Leeds. These data were checked for accuracy by DA. The

search and data extraction from January 2006 to September 2011 was conducted by DA and was checked for accuracy by TN.

Data Synthesis and Analysis

We used random effects models to calculate summary RRs and 95% CIs for the highest vs. the lowest height and for the dose-response analyses (34). The average of the natural logarithm of the RRs was estimated and the RR from each study was weighted by the inverse of its variance. A two-tailed $p<0.05$ was considered statistically significant.

For the dose-response analyses we used the method by Greenland and Longnecker (35) to compute study-specific slopes (linear trends) and 95% CIs from the natural logs of the RRs and CIs across categories of height. The method requires that the distribution of cases and person-years or non-cases and the RRs with the variance estimates for at least three quantitative exposure categories are known. We estimated the distribution of cases or person-years in studies that did not report these, but reported the total number of cases/person-years, for example, the total number of person-years was divided by 5 when data were analyzed by quintiles in order to derive the number of person-years in each quintile. The Chene and Thompson method was used to calculate the mean level of height in each category (36). The dose-response results in the forest plots are presented for a 5 cm increment in height. We examined a potential non-linear dose-response relationship by using fractional polynomial models (37). The best fitting second order fractional polynomial regression model was determined, defined as the one with the lowest deviance. A likelihood ratio test was used to assess the difference between the non-linear and linear models to test for nonlinearity (38).

Heterogeneity between studies was assessed by the Q test and $I^2$ (a measure of the proportion of total variation in study estimates that is due to heterogeneity) (39). Subgroup

and meta-regression analyses by sex, duration of follow-up, number of cases, geographic location and adjustment for confounding factors such as alcohol, smoking, diabetes, body mass index, physical activity energy intake were conducted to investigate potential sources of heterogeneity. Small study effects, such as publication bias, was assessed by inspection of the funnel plots and with Egger's test (40) and with Begg's test (41), and the results were considered to indicate small study effects when $p<0.10$. We conducted sensitivity analyses excluding one study at a time to clarify whether the results were simply due to one large study or a study with an extreme result. In addition, results from three pooled analyses were included together with the identified studies in a sensitivity analysis (18-20).

# Results

We identified 10 cohort studies (13 publications) that were included in the analysis of height and pancreatic cancer risk (10, 13-17, 22-26, 32, 33) (Table 1, Figure 1). One of the publications were only included in subgroup analyses by sex (26) and two were only included in the subgroup analysis of mortality (32, 33). One publication reported results from two cohort studies (24). Seven studies were from Europe, two from North-America and one from South Korea (Table 1).

## Height

### *High vs. low analysis*

Nine cohort studies (eight publications) (13-17, 23-25) were included in the high vs. low analysis of height and pancreatic cancer risk and included 5273 cases among 2635802

participants. The summary RR for all studies was 1.27 (95% CI: 1.11-1.48), with low heterogeneity, $I^2$=33% and $p_{heterogeneity}$=0.15 (Figure 2).

*Dose-response analysis*

Nine cohort studies (eight publications) (10, 13-16, 22, 24, 25) were included in the dose-response analysis and included 5914 cases among 2602498 participants. The summary RR per 5 cm increase in height was 1.09 (95% CI: 1.05-1.15), with high heterogeneity, $I^2$=61% and $p_{heterogeneity}$=0.009 (Figure 3). The summary RR ranged from 1.08 (95% CI: 1.04-1.13) when excluding the Nurses' Health Study to 1.11 (95% CI: 1.05-1.17) when excluding the Million Women's Study. There was some indication of small study effects with Egger's test, p=0.05, but not with Begg's test, p=0.35. There was no evidence for a nonlinear association between height and pancreatic cancer risk, $p_{nonlinearity}$=0.21 (Figure 4).

*Subgroup, meta-regression and sensitivity analyses*

In subgroup analyses, the results were consistent when stratified by gender and geographic location, but there was some indication of heterogeneity when stratified by number of cases ($p_{heterogeneity}$=0.03) and adjustment for diabetes ($p_{heterogeneity}$=0.02). There was a weaker association among studies with a larger number of cases than among studies with a low number of cases, but the association was stronger among studies that adjusted for diabetes, than for studies without such adjustment (Table 2). Excluding one study of mortality (25) did not affect the results, summary RR= 1.10 (95% CI: 1.05-1.16, $I^2$=65%, $p_{heterogeneity}$=0.006) (Table 2). Restricting the analysis to four studies of mortality (17, 25, 32, 33) resulted in a summary RR of 1.04 (95% CI: 1.00-1.07, $I^2$=0%, $p_{heterogeneity}$=0.84) (Table 2).

We also conducted additional sensitivity analyses including data from the Pooling Project of Prospective Studies (835340 participants and 2135 cases) (18) in the analysis (RR per 5 cm= 1.02, 95% CI: 0.97-1.06 for men and 1.00, 95% CI: 0.95-1.06) for women), excluding the three cohorts (Health Professional's Follow-up Study, Nurses's Health Study, and Netherlands Cohort Study) in our analysis that were included in the pooled analysis. The summary RR was 1.04 (95% CI: 1.01-1.08, $I^2$=55%, $p_{heterogeneity}$=0.04) per 5 cm increase in height and 1.16 (95% CI: 1.06-1.26, $I^2$=6%, $p_{heterogeneity}$=0.38) in the high vs. low analysis (Supplementary Figure 1). When we included the results from the Asian Pacific Cohort Studies Collaboration (506648 participants and 294 deaths) (20) in our analysis (HR=1.08, 95% CI: 0.94-1.24 for men and HR=0.99, 95% CI: 0.82-1.21 for women per 6 cm increase in height), the summary RR was 1.08 (95% CI: 1.04-1.13, $I^2$=55%, $p_{heterogeneity}$=0.01) per 5 cm increase in height. When we included both these pooled analyses together with our analyses and excluding the overlapping studies the summary RR was 1.04 (95% CI: 1.01-1.07, $I^2$=43%, $p_{heterogeneity}$=0.08) and Egger's test was no longer significant, p=0.18 (Supplementary figure 2). In an additional sensitivity analysis we included the results from the Pancreatic Cancer Cohort Consortium (2170 cases and 2209 controls) (19) in the high vs. low analysis (OR = 1.08, 95% CI: 0.83-1.41 for men and 0.95, 95% CI: 0.74-1.21 for women) and excluding the overlapping studies the summary RR for high vs. low height was 1.10 (95% CI: 1.00-1.20, $I^2$=0%, $p_{heterogeneity}$=0.88) (Supplementary Figure 3).

# Discussion

We found a weak positive association between height and pancreatic cancer risk, which was present both among men and women in stratified analyses.

Our meta-analysis may have several limitations which must be taken into consideration. The possibility of confounding from other risk factors cannot be ruled out. Although, the results persisted in subgroup analyses of studies that adjusted for the most important confounding factors such as smoking, diabetes and BMI, fewer studies had adjusted for other potential confounding factors. There was evidence of small study effects in our analysis and if this is due to publication bias it may have led to exaggerated risk estimates. Our results are in contrast to those of three pooled analyses (18-20), which found no significant association between height and pancreatic cancer risk, but included more than twice as many cases and more than three times as many participants as the two largest of these (18, 19). Although some of the studies included in our analysis overlapped with some of the pooled analyses (13, 14, 16, 24), several cohort studies (10, 15, 22, 23, 25) not included in the pooled analyses may have driven the overall result towards an increased risk in our analysis. However, a number of the studies included in the pooling projects have not yet published on height and pancreatic cancer individually. In several sensitivity analyses we added the pooled results of the Pooling Project of Prospective Studies (18), the Asian Pacific Cohort Studies Collaboration (20) and the Pancreatic Cancer Cohort Consortium (19) to our analyses, and although the results were attenuated there was still a significant positive association. This suggests that the summary estimate from our primary analysis may have been overestimated, but may not entirely be due to publication bias. Publication bias may have occurred because several of the individual studies contributing to the pooled analyses may have had moderate sample sizes and possibly insufficient statistical power to detect an association with a relatively uncommon cancer such as pancreatic cancer. In addition, it may not have been a priority in more modest sized cohorts to investigate a non-modifiable risk factor for pancreatic cancer.

Measurement errors in the assessment of height may have influenced the results. Several studies have reported high correlations between measured and self-reported height (42-44). Although in our analyses studies using self-reported height reported higher estimates than studies using measured height, there was no evidence of heterogeneity between these subgroups, suggesting that this may have been due to chance variation.

Although increased height is an established risk factor for colorectal and breast cancer and a possible risk factor for several other cancers (9, 10) the specific mechanism(s) that may explain an association between greater height and pancreatic cancer risk is not clear. It is also possible that common mechanisms may underlie the association between height and several cancers including pancreatic cancer. Adult height reaches its maximum between age 20 and 30 years and both childhood and adolescent dietary factors and infections are thought to be of importance (45, 46). Particularly elevated levels of insulin-like growth factor-1 (IGF-1) may play an important role in determining growth and may also influence cancer risk. Higher IGF-1 levels in childhood is associated with childhood growth (47). Insulin-like growth factors may contribute to cancer risk by stimulating proliferation, adhesion, and cell migration and by inhibiting apoptosis (48). However, greater concentrations of circulating IGF-1 in adulthood has not been significantly associated with pancreatic cancer risk in epidemiological studies (30, 49-51), but if the relevant time period of exposure is in childhood or adolescence this could explain the lack of association reported in these studies. At last, taller people have a greater number of cells and thus a greater probability of mutations leading to malignancy.

Our meta-analysis also has several strengths. Because we based our analyses on prospective studies we have effectively avoided recall and selection bias. The large sample size and large number of cases provided statistical power to detect moderate associations. In addition, we conducted more detailed subgroup and sensitivity analyses than what has been

done previously and we assessed the dose-response relationship using both linear and nonlinear models. In sensitivity analyses, we included the results of pooled analyses to increase the number of cohort studies contributing information. We have therefore obtained a more precise estimate than in the primary analyses. However, it has to be noted that including pooled results does not allow to properly assess heterogeneity. Nevertheless, the one pooled analysis that reported on heterogeneity found no evidence of heterogeneity across studies so this should be less of a concern (18).

In conclusion, our results indicate that greater height is associated with increased risk of pancreatic cancer. Although the strength of the association may have been overestimated due to publication bias, the positive association persisted in several sensitivity analyses taking this into account.

## Contributors

V.J. Burley, J.E. Cade, D.S.M. Chan, D.C Greenwood and the systematic literature review team at the University of Leeds conducted the search, data selection and data extraction up to December 2005. RV was responsible for developing and managing the database for the Continuous Update Project. T. Norat wrote the protocol for the review, and is the PI of and coordinates the Continuous Update Project at Imperial College. D. Aune did the updated literature search and wrote the first draft of the original manuscript. D. Aune, A.R. Vieira, and D. A. Navarro Rosenblatt did the data extraction and D. Aune and A.R. Vieira did the study selection, and statistical analyses. DC Greenwood was expert statistical advisor and contributed towards the statistical analyses. All authors contributed to the revision of the manuscript.

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The sponsor of this study had no role in the decisions about the design and conduct of the study, collection, management, analysis or interpretation of the data or the preparation, review or approval of the manuscript.

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Table 1: Prospective studies of height and pancreatic cancer risk

| Author, publication year, country/ region | Study name | Follow-up period | Study size, gender, age, number of cases | Assessment of height | Exposure | Level | RR (95% CI) | Adjustment for confounders |
|---|---|---|---|---|---|---|---|---|
| Green J et al, 2011, United Kingdom | The Million Women Study | 1996-2001 – 2008, 11.7 million person-years | 1297124 women, age: 2044 cases | Self-reported | Height | Per 10 cm increase | 1.05 (0.95-1.17) | Age, region, SES, smoking, alcohol intake, BMI, strenuous exercise, age at menarche, parity, age at 1st birth |
| Stevens RJ et al, 2009, United Kingdom | The Million Women Study | 1996/2001-2006/2007, 7.2 years follow-up | 1290000 women, age 50-64 years: 1338 cases 1710 deaths | Self-reported | Height, incidence<br>Height, mortality | ≥170 vs. <155 cm<br>≥170 vs. <155 cm | 1.11 (0.95-1.27)<br>1.09 (0.95-1.25) | Age, region, SES, BMI |
| Meinhold CL et al, 2009, Finland | ATBC Cancer Prevention Study | 1985/1988 – 2004, 19.4 years follow-up | 27035 smoking men, age 50-69 years: 305 cases | Measured | Height | 182 vs. 167 cm | 1.23 (0.87-1.75) | Age, BMI, cigarettes per day, years of smoking, total energy, DM |
| Sung J et al, 2009, South Korea | Korea Medical Insurance Corporation Study | 1994 – 2003, 8.7 years follow-up | 449214 men and 339575 women, age 40-64 years: 920/334 cases | Measured | Height, men<br><br>Height, women | >171 vs. ≤151 cm<br>Per 5 cm<br>>158 vs. ≤151 cm<br>Per 5 cm | 0.98 (0.81-1.19)<br>0.99 (0.93-1.06)<br>1.12 (0.80-1.57)<br>1.03 (0.92-1.14) | Age, BMI, cigarette smoking, alcohol, regular exercise, monthly salary, occupation, area of residence |
| Song YM et al, 2008, South Korea | Korea Medical Insurance Corporation Study | 1993/1994 – 2004, 9.86 years follow-up | 344519 women, age 40-64 years: 239 deaths | Measured | Height | ≥161 cm vs. <149 cm | 1.22 (0.71-2.09)<br>0.99 (0.87-1.13) | Age, SBP, serum cholesterol, fasting blood glucose, BMI, cigarette smoking, alcohol, regular exercise, monthly salary, occupation, area of residence |
| Berrington de Gonzalez A et al, 2008, South Korea | Korea Medical Insurance Corporation Study | 1992/1995-2005, 12 years follow-up | 631172 men and women, age ≥45 years: 2194 cases | Measured | Height | ≥171/≥158 vs. <162/<148 cm | 1.09 (0.94-1.25) | Age, sex, smoking, fasting serum glucose levels |
| Verhage BA et al, 2007, Netherlands | Netherlands Cohort Study | 1986-1999, 13.3 years follow-up | 4774 men and women, age 55-69 years: 446 cases | Self-reported | Height, men<br><br>Height, women | 188 vs. 166.1 cm<br>Per cm<br>177 vs. 155.7 cm<br>Per cm | 0.99 (0.56-1.75)<br>1.01 (0.99-1.03)<br>1.32 (0.67-2.60)<br>1.02 (1.00-1.05) | Age, smoking, number of cigarettes per day, number of years smoked, DM, history of hypertension |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Berrington de Gonzalez AB et al, 2006, Europe (EPIC) | European Prospective Investigation into Nutrition and Cancer | 1991/2000-2004, 6.5 years follow-up | 438405 men and women, age 19-84 years: 324 cases | Measured and self-reported | Height | ≥180/≥167 vs. <170/<158 cm (m/w)<br>Per 10 cm | 1.74 (1.20-2.52)<br>1.37 (1.15-1.64) | Age, sex, country, smoking, diabetes |
| Batty GD et al, 2006, United Kingdom | The Whitehall Study | 1967/1970 – 2002, ~30 years follow-up | 17353 men, age 40-64 years: 150 deaths | Measured | Height | ≥181 vs. <171 cm<br>Per 5 cm | 1.26 (0.71-2.22)<br>1.02 (0.90-1.15) | Age, employment grade, physical activity, smoking habit, marital status, BMI, triceps skinfold thickness, SBP, cholesterol, IGT, DM, disease at entry |
| Song YM et al, 2003, South Korea | Korea Medical Insurance Corporation Study | 1992 – 1998, ~6 years follow-up | 386627 men, age 40-64 years: 276 deaths | Measured | Height | ≥175 vs. ≤162 cm<br>Per 5 cm | 1.09 (0.65-1.84)<br>1.07 (0.95-1.20) | Age, DBP, glucose, cholesterol, BMI, alcohol, smoking, exercise |
| Michaud DS et al, 2001, USA | Nurses' Health Study | 1976-1996, 20 years follow-up | 117041 women, age 30-55 years: 210 cases | Self-reported | Height | >167.6 vs. <157.5 cm | 1.77 (1.15-2.72) | Age, BMI at baseline, pack-years of smoking, DM, cholecystectomy |
| Michaud DS et al, 2001, USA | Health Professionals Follow-up Study | 1986-1998, 12 years follow-up | 46648 men, age 40-75 years: 140 cases | Self-reported | Height | ≥185.4 vs. ≤172.7 cm | 1.88 (1.14-3.11) | Age, BMI at baseline, pack-years of smoking, DM, cholecystectomy |
| Lund Nilsen TI et al, 2001, Norway | Nord Trondelag Health Survey | 1984-1986 – 1996, 12 years follow-up | 31000 men and 32374 women, age ≥30 years:166 cases | Measured | Height, men<br>Height, women | >176 vs. ≤176 cm<br>>162 vs. ≤162 cm | 1.09 (0.70-1.71)<br>1.36 (0.81-2.29) | Age |
| Tulinius H et al, 1997, Iceland | The Reykjavik Study | 1968-1995, 4-27 years follow-up | 11580 women and 11366 men, age years: 36/65 cases | Measured | Height, men<br>Height, women | Per cm<br>Per cm | 1.035 (0.994-1.078)<br>1.055 (0.993-1.120) | Age |

BMI=Body Mass Index, DBP = diastolic blood pressure, DM = diabetes mellitus, FH=Family history, IGT=impaired glucose tolerance, SBT=systolic blood pressure, SES = socioeconomic status

Table 2: Subgroup analyses of height and pancreatic cancer, dose-response analysis

| | **Height** | | | | |
|---|---|---|---|---|---|
| | *n* | RR (95% CI) | $I^2$ (%) | $P_h$[1] | $P_h$[2] |
| All studies | 9 | 1.09 (1.05-1.15) | 60.9 | 0.009 | |
| Sex | | | | | |
| Men | 6 | 1.07 (1.01-1.14) | 52.1 | 0.06 | 0.76/ 0.75* |
| Women | 5 | 1.09 (1.01-1.18) | 59.0 | 0.05 | |
| Men and women | 2 | 1.09 (0.97-1.23) | 83.6 | 0.01 | |
| Outcometype | | | | | |
| Incidence | 8 | 1.10 (1.05-1.16) | 64.7 | 0.006 | 0.15 |
| Mortality | 4 | 1.04 (1.00-1.07) | 0 | 0.84 | |
| Measured or self-reported height | | | | | |
| Self-reported | 4 | 1.08 (1.04-1.13) | 71.3 | 0.02 | 0.94 |
| Measured | 4 | 1.04 (1.01-1.08) | 20.6 | 0.29 | |
| Self-reported & measured | 1 | 1.17 (1.07-1.28) | | | |
| Duration of follow-up | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| <10 yrs follow-up | | 1 | 1.17 (1.07-1.28) | | | 0.32 |
| ≥10 yrs follow-up | | 8 | 1.08 (1.04-1.13) | 56.9 | 0.02 | |
| Geographic location | | | | | | |
| Europe | | 6 | 1.09 (1.03-1.16) | 59.8 | 0.03 | 0.69 |
| America | | 2 | 1.17 (1.08-1.27) | 0 | 0.38 | |
| Asia | | 1 | 1.03 (0.99-1.08) | | | |
| Number of cases | | | | | | |
| Cases <250 | | 4 | 1.14 (1.05-1.23) | 39.5 | 0.18 | 0.03 |
| Cases 250-<500 | | 3 | 1.13 (1.06-1.19) | 27.5 | 0.25 | |
| Cases ≥500 | | 2 | 1.03 (1.00-1.06) | 0 | 0.79 | |
| Adjustment for potential confounders | | | | | | |
| Alcohol | Yes | 1 | 1.02 (0.97-1.08) | | | 0.24 |
| | No | 8 | 1.11 (1.05-1.17) | 58.6 | 0.02 | |
| Smoking | Yes | 8 | 1.09 (1.04-1.14) | 61.1 | 0.01 | 0.29 |
| | No | 1 | 1.22 (1.03-1.45) | | | |
| Diabetes | Yes | 6 | 1.12 (1.07-1.18) | 26.9 | 0.23 | 0.02 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | No | 3 | 1.05 (0.99-1.10) | 49.3 | 0.14 | |
| Body mass index | Yes | 5 | 1.08 (1.01-1.14) | 52.5 | 0.08 | 0.46 |
| | No | 4 | 1.12 (1.04-1.22) | 73.8 | 0.01 | |
| Physical activity | Yes | 2 | 1.02 (0.98-1.07) | 0 | 0.95 | 0.13 |
| | No | 7 | 1.12 (1.06-1.18) | 62.2 | 0.01 | |
| Energy intake | Yes | 1 | 1.05 (0.95-1.16) | | | 0.58 |
| | No | 8 | 1.10 (1.05-1.16) | 65.6 | 0.005 | |

*n* denotes the number of studies, [1]P for heterogeneity within each subgroup, [2] P for heterogeneity between subgroups with meta-regression analysis.

*P for heterogeneity between men and women

Figure 1. Flow-chart of study selection

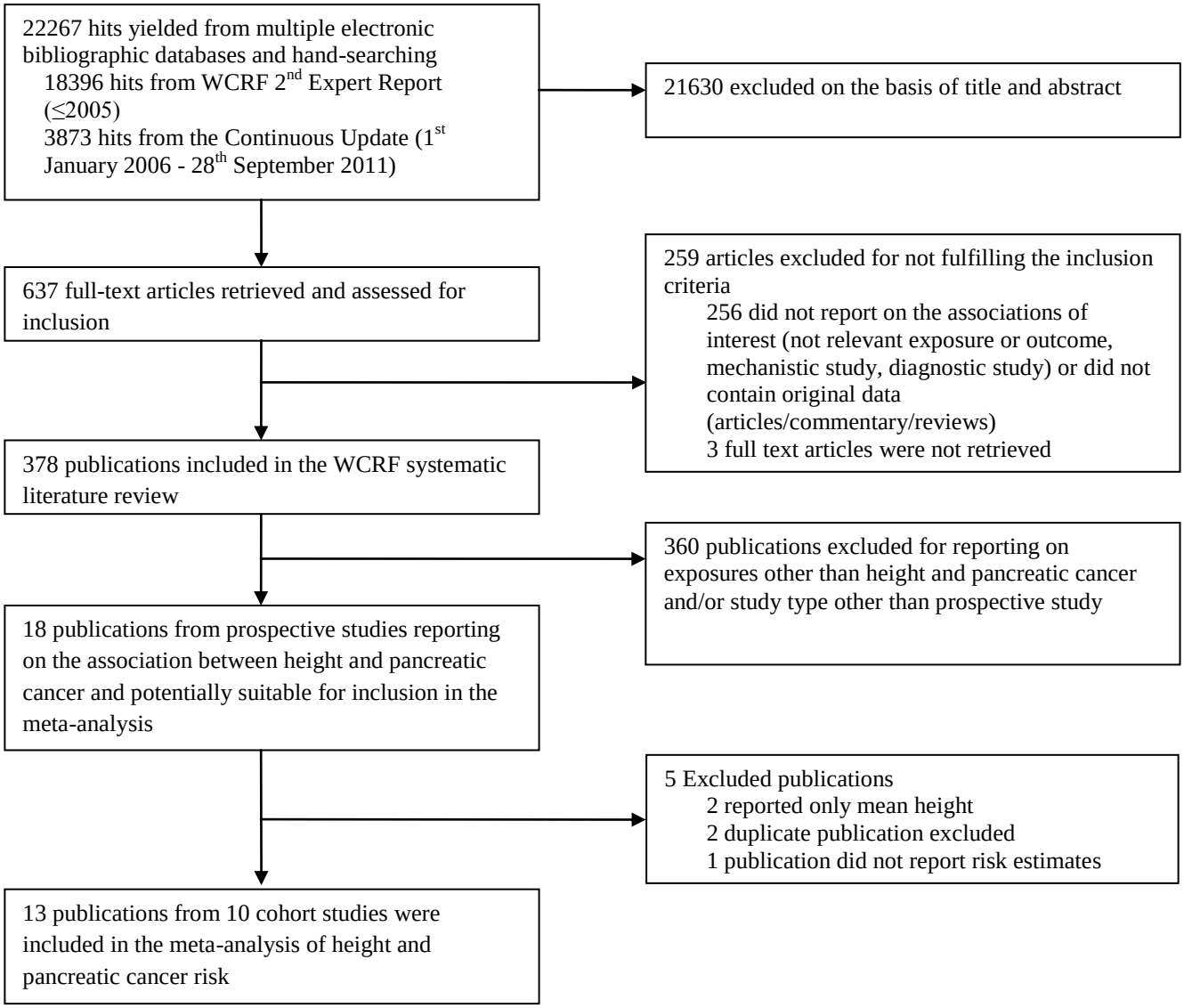


Figure 2. Height and pancreatic cancer, high vs. low analysis

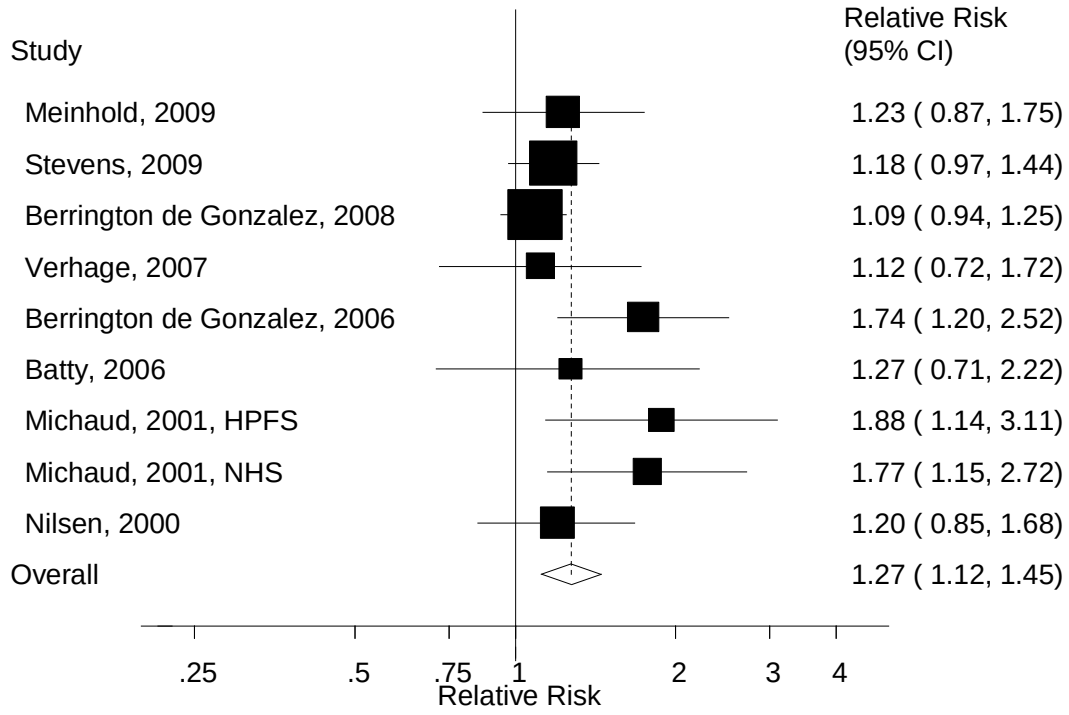



Figure 3. Height and pancreatic cancer, per 5 cm

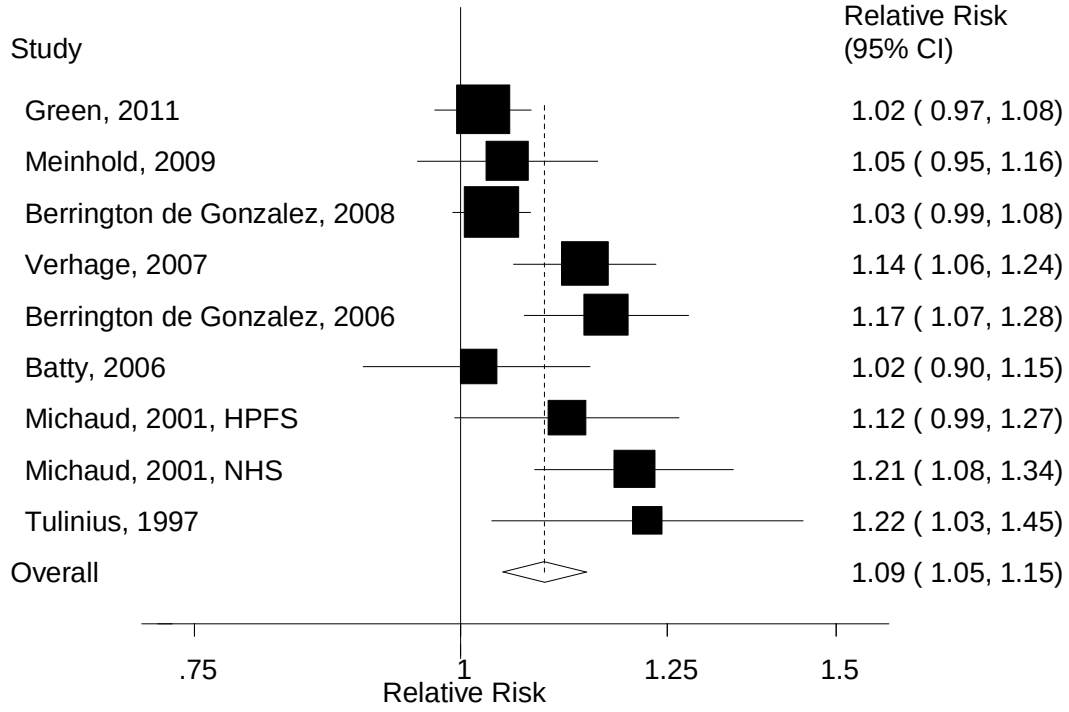
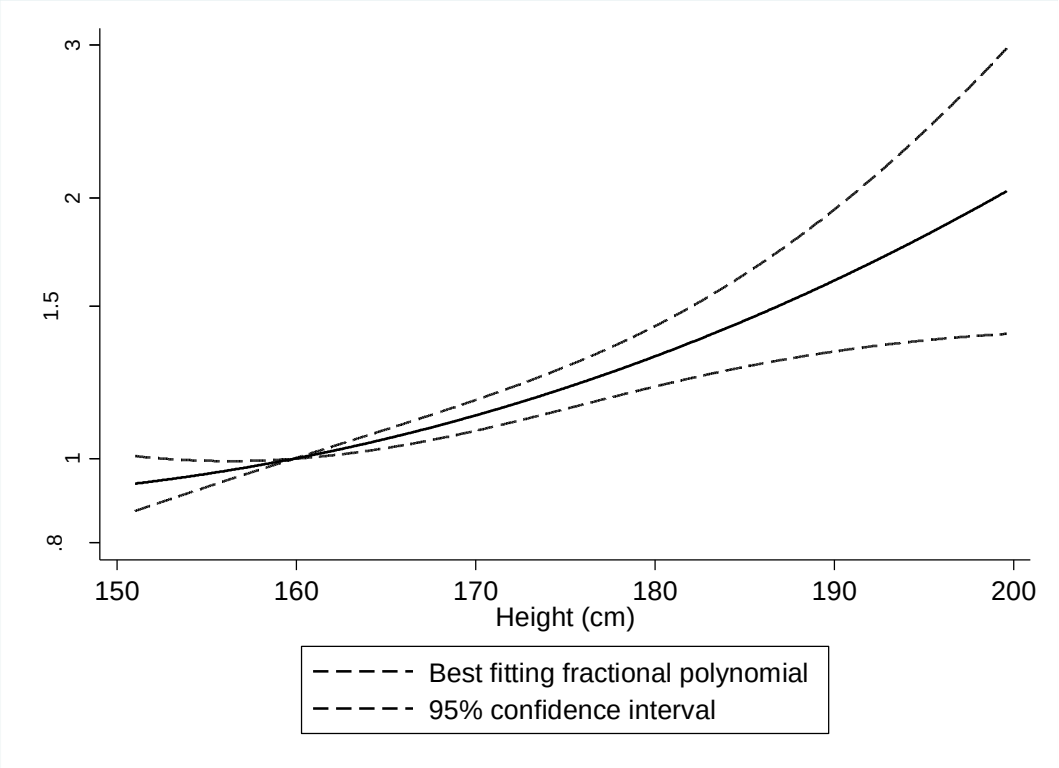
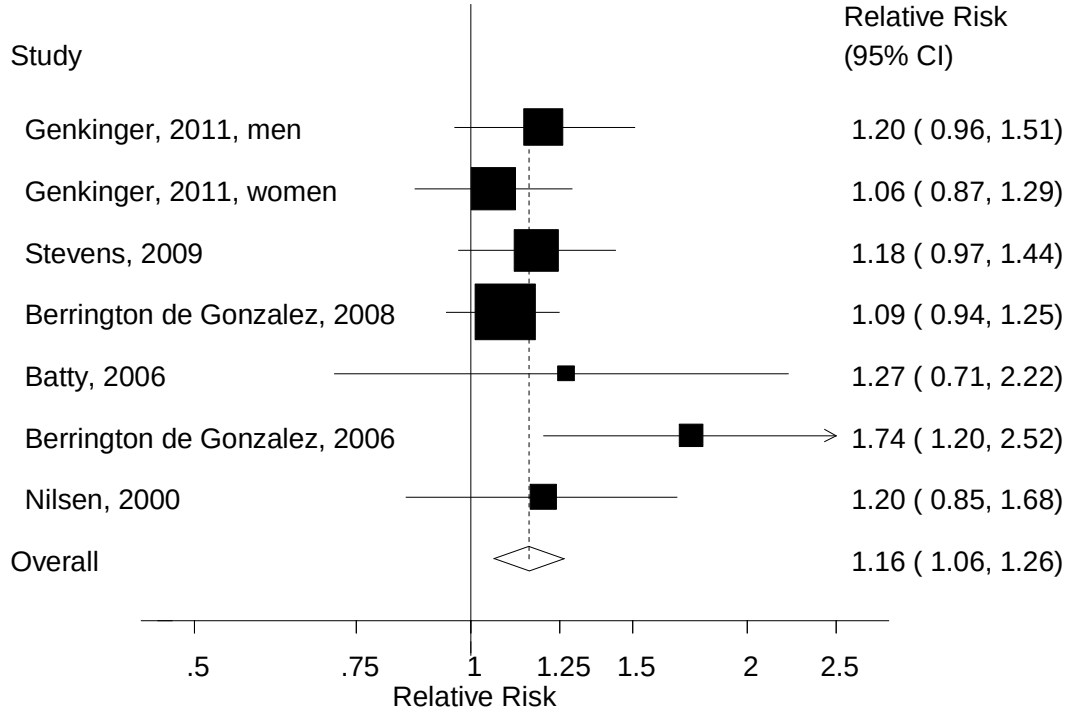


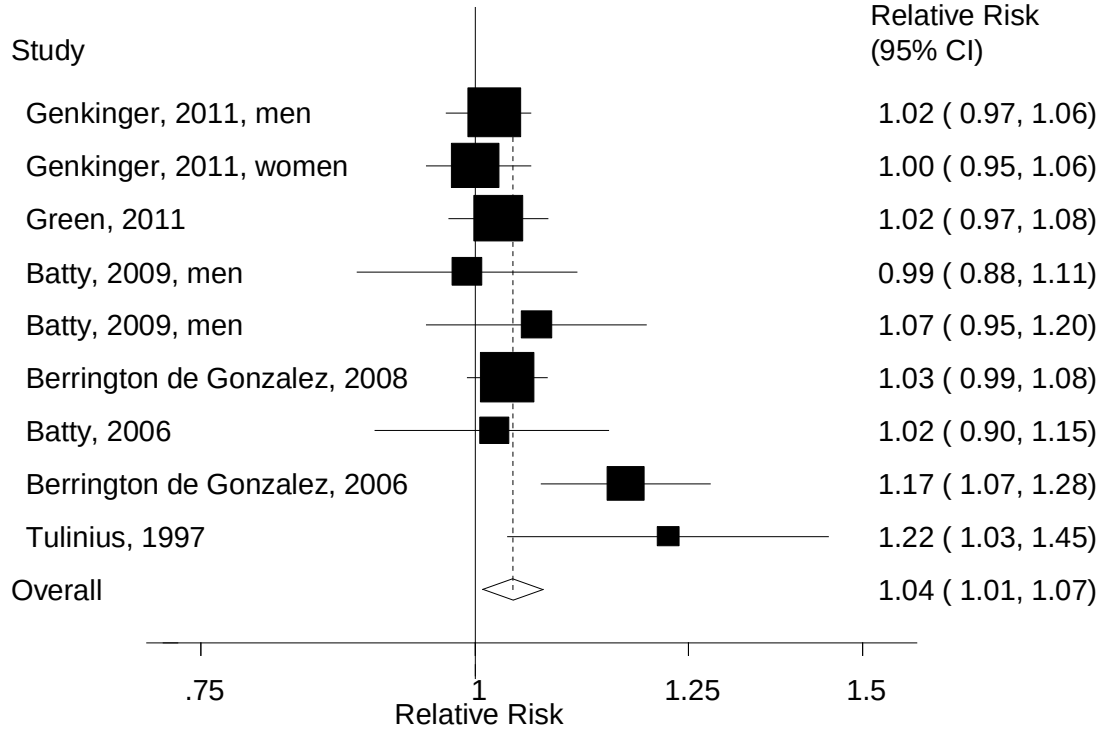
Figure 4: Height and pancreatic cancer, nonlinear dose-response



Supplementary figure 1: Height and pancreatic cancer risk, including the Pooling Project of Prospective Studies (Genkinger, 2011), high vs. low analysis




Supplementary figure 2: Height and pancreatic cancer risk, including Pooling Project of Prospective Studies (Genkinger, 2011) and the Asia Pacific Cohort Studies Collaboration (Batty, 2009), per 5 cm



Supplementary figure 3: Height and pancreatic cancer risk, including PANSCAN (Arslan, 2009), high vs. low analysis