Associations between adult height and type 2 diabetes mellitus: a systematic review and meta-analysis of observational studies

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ABSTRACT

Background Although short adult height is generally associated with increased risks of type 2 diabetes mellitus (T2DM), there are large inconsistencies across studies. The aims of this study were to describe and quantify currently available evidence on the association between adult height and T2DM, to examine whether the reported associations differ by sex, and to examine the shapes of the height and T2DM associations.

Methods Relevant literature was identified using PubMed (1966–May 2018), EMBASE (1947–May 2018) and Google Scholar (May 2018). We identified cross-sectional and cohort studies with original publications on human subjects, which were included in a random-effects meta-analysis.

Results From 15 971 identified sources, 25 studies met the inclusion criteria for the systematic review (N=401 562 individuals). From these 25 studies, 16 (9 cross-sectional studies and 7 cohort studies) were included in the meta-analysis (n=261 496 individuals). The overall random-effects meta-analysis indicated an inverse association between adult height and T2DM (effect estimate=0.88, 95% CI 0.81 to 0.95). No sex differences in the associations between adult height and T2DM were found (effect estimate for men: 0.86, 95% CI 0.75 to 0.99; effect estimate for women: 0.90; 95% CI 0.80 to 1.01; p value for sex interaction=0.80). Due to lack of data, results on the shape of the association between height and T2DM were inconclusive.

Conclusions Shorter height is associated with an increased risk of T2DM and the association does not significantly differ by sex. The currently available data are insufficient to support conclusions regarding the shape of the association between height and T2DM.

Trial registration number CRD42017062446.

INTRODUCTION

Globally, the prevalence of type 2 diabetes mellitus (T2DM) in adults has doubled since 1980, with 422 million adults suffering from diabetes in 2014.[1] Despite the complex aetiology of T2DM, obesity is one of the strongest risk factors.[1] Although height is generally non-modifiable, it has emerged as a potential risk factor for T2DM; thus, increasing awareness of its potential effects may contribute to the formulation of more accurate risk prediction models and may allow individuals to change their other behaviours to help reduce the risk of T2DM.

Height is mainly determined by genetics, but factors such as nutrition, childhood disease burden, socioeconomic conditions and geographical location, among others, may also affect individuals' attained height.[2 3] Height matters for health; it is related to mortality and a range of diseases such as cancers (generally positive associations) and cardiovascular diseases (generally inverse associations).[4] The potential association between height and the risk of T2DM, however, is not clear as most studies have investigated body mass index (BMI) instead of height, and results from studies on height are inconsistent.[5–20] Additionally, little is known about whether or not the association between height and T2DM differs by sex.[7 13 15 18] This is important as there are differences in the incidence rates and severity of T2DM between men and women.[21] Further, it is reported that men with T2DM suffer more microvascular complications, although higher morbidity and mortality related to cardiovascular diseases are reported in women.[22] When it comes to the shape of association between adult height and T2DM, more studies reported that there is an inverse non-linear shape in men[7 12 16] compared with women,[8] and no sign of non-linearity was found in one study.[18]

A systematic review and meta-analysis was conducted in 2012 on the association between hip circumference, height and the risk of T2DM, and it identified nine studies of height and T2DM.[23] However, the review used combined estimates for men and women in sex-specific analyses and did not report on the shape of the height–T2DM association. Therefore, the aims of the present study were to explicitly examine potential sex differences in the associations and the shape of the association, and to update and expand on the previous systematic review and meta-analysis[23] by including additional 6 years of new research in this area.

METHODS

Registration

This systematic review was registered with PROSPERO on 10 April 2017.

Information sources and search strategy

The protocol of the systematic review was designed using the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2015,[24] and the review and meta-analysis was reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[25] Further, it was supplemented by sections of the Meta-Analysis of Observational

Studies in Epidemiology guidelines.[26] No restrictions were placed on publication date, language or setting.

The electronic databases of PubMed (1966–May 2018), EMBASE (1947–May 2018) and Google Scholar (up to May 2018) were used to search and identify relevant literature. The literature search was supplemented by checking reference lists. Grey literature sources refer to science that is produced by governments, academia, non-governmental organisations, business and industry, but which is not controlled by commercial publishers. These sources were also searched to include all available studies in the field, using the databases of Cumulative Index to Nursing and Allied Health Literature, WorldCat and OpenGrey. We used free text and the medical subject heading terms for PubMed and EMBASE. Electronic searches in databases were conducted in March and April 2017 and updated in May 2018, and specific search strings were developed with guidance from an information specialist. The search logs and search strings are provided in online supplementary table 1.

Selection criteria and data extraction

Studies were eligible for inclusion in our review and meta-analysis when the following criteria were met: (1) the study was conducted on human subjects, that is, healthy adult humans of 18 years or older, of either sex from any country; (2) the study used a cross-sectional or cohort (observational) design; and (3) the study investigated the association between adult height and T2DM (any sort of diagnosis including diagnoses based on haemoglobin A1c, oral glucose tolerance test, fasting glucose, self-report of T2DM or use of glucose-lowering drugs). Studies were excluded from the present review and meta-analysis if they were (1) dual publications (n=2; figure 1), in which case the most recent study reporting on the population was included (2) on animals, (3) on type 1 diabetes or gestational diabetes, and (4) trials of any sort (randomised or non-randomised). Additionally, for inclusion into the meta-analysis, the results had to be reported as an effect estimate (relative risk [RR], OR or HR) and include 95% CIs for the height and T2DM association.

Data from all included studies were extracted using a prespecified data extraction form. The form included information on year of publication, year of study and type of study, and population and settings, participants' characteristics, information on exposure and outcomes including exposure/outcome measuring/reporting, and quality assessment of the included studies using the Risk of Bias Assessment tool for Non-randomised Studies (RoBANS) (RoBANS consists of six domains) and measures of association used. The study was judged as having high risk of bias (RoB) in overall RoBANS if it had at least two domains with the high RoB category and low RoB if it had four or more domains with the low RoB category. Information on testing for non-linearity was also included in the data extraction form. A data extraction on a random sample of the primary studies (n=2) and results (n=2) was cross-checked by SHR.

Data synthesis and statistical analysis

The statistical analysis was conducted in Stata V.14.1 (www.stata.com). ORs, HRs and RRs were used in the overall meta-analysis and referred to as effect estimates. If available, height was used as a continuous variable in the analyses. Otherwise the estimates reported for the tallest categories of height compared with the shortest categories of height were used in the meta-analysis. In studies where estimates for the lowest category of height were reported, they were converted to the highest category by using the reciprocal of the estimates. The studies were categorised into three groups depending on how the estimates for men and women were reported (men only, women only, and men and women combined). T2DM was categorised into 'only T2DM' or 'mostly T2DM' depending on the study's definition of diabetes. The 'only T2DM' category included studies in which all cases of diabetes were ascertained as T2DM. Otherwise, cases were considered as 'mostly T2DM'.

Forest plots were generated based on fitting random-effects meta-analysis models. The tau-squared test was used to evaluate the between-study variance.[27] Random-effects models were used in this study as this model type allows for variation of true effect sizes over studies.[28] Heterogeneity was investigated using the I-squared statistic.[29] The Q test, or the test of χ^2 heterogeneity for meta-analyses, was also calculated. Meta-regression and subgroup analyses were conducted to identify the sources of heterogeneity. A priori subgroup analyses investigating heterogeneity included sex; categorisation of T2DM ('only T2DM' and 'mostly T2DM'); measures of association (RR, OR, HR); study design (cross-sectional, cohort studies); categorisation of height, as we suspected stronger associations when the tallest groups were compared with the shortest groups than when height was used as a continuous variable; and adjustments for BMI and socioeconomic status (SES), depending on data availability. Funnel plots were produced to assess potential publication bias.

RESULTS

Studies and characteristics

The initial electronic search and checking of reference lists identified 15 968 studies and 3 studies, respectively. Exclusions were made for studies identified in duplicate through the different databases (n=5615) and for studies that did not fulfil the inclusion criteria (n=10 322) (figure 1). From the 34 studies read in full text and examined in detail, 25 studies[5–20 30–38] met the inclusion criteria and were included in the systematic review (online supplementary data material). Of these, the 16 studies[5–20] which reported ratio-based measures of associations and 95% CIs were entered into the meta-analysis.

The number of individuals in the 25 studies that met the inclusion criteria for the systematic review ranged from 30 to 129 085, with baseline ages from 20 to 95 years. The follow-up period in the cohort studies ranged from 5.5 to 12 years. Five studies included in the review were conducted in the USA,[6 9 10 19 31] four in the UK,[11 12 30 38] three in Iran,[13 18 20] one in Israel,[16] four in Asia,[14 17 34 35] one in Australia,[37] one in Africa[33] and the remaining six in other European countries.[5 7 8 15 32 36] Two cross-sectional studies that were included in the review had only abstracts available.[35 36] Two studies included in the review included only women,[11 32] and two of the cohort studies included only men.[5 16] Two studies reported the ethnicity of participants.[8 9] Study quality was assessed using RoBANS, and only four of the included studies in the review were classified as having a low risk of bias in all 'RoB' domains.[5 16 19 20] Most of the studies were judged as having unclear or high risk of bias in one or more 'RoB' domains. Information on the study characteristics including RoBANS can be found in tables 1 and 2.

Systematic review

The results from the studies included in this systematic review of 25 observational studies[5–20 30–38] varied widely. Most of the studies (n=17) reported an overall inverse association between adult height and T2DM.[5 6 10–16 20 30 32–36 38] The findings were reported as correlations in 3 studies,[30 32 35] linear regression (beta)-coefficients in 2 studies[36 38] and ratio-based effect

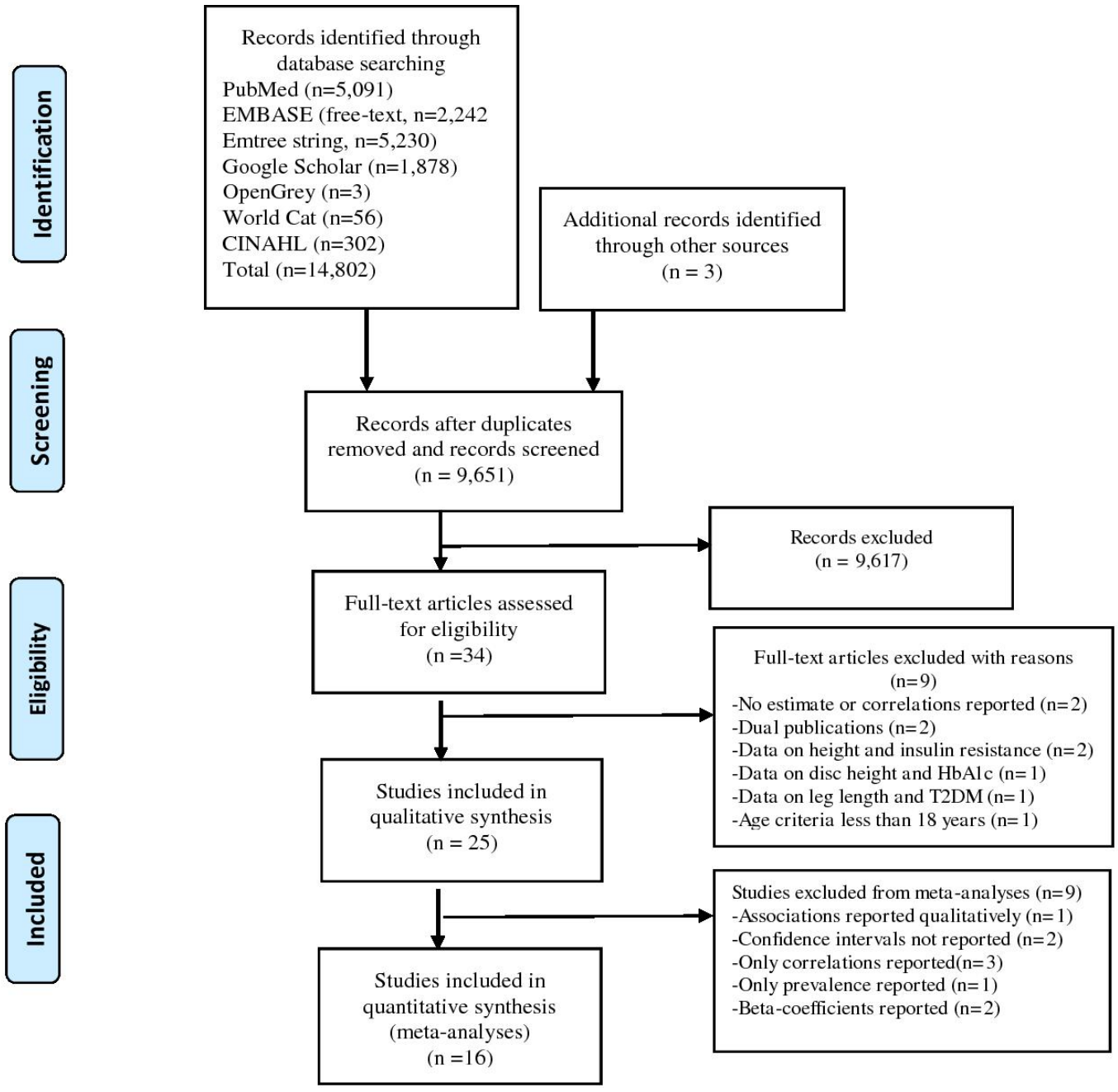

Figure 1 Flow diagram of the study selection process. CINAHL, Cumulative Index to Nursing and Allied Health Literature; HbA1c, haemoglobin A1c; T2DM, type 2 diabetes mellitus.

estimates (ORs, HRs or RRs) in 16 studies.[5–20] Two studies reported estimates without 95% CI,[33 34] one study reported the associations qualitatively,[31] and one study reported the prevalence of impaired glucose tolerance and diabetes combined for the tallest men and women[37] (tables 1 and 2). Out of 16 studies that reported ratio-based effect estimates, 9 reported them separately by sex.[7–10 12 13 15 17 18]

Meta-analysis of adult height and risk of T2DM

The overall random-effects meta-analysis used information from 16 studies, which included a total of 261 496 individuals and 7410 cases of T2DM. Based on 25 effect estimates from these studies (sex-specific when available), the meta-analysis showed that there was an inverse and statistically significant association between height and T2DM (effect estimate=0.88, 95% CI 0.81 to 0.95) (figure 2). Sex-specific analyses are presented in the following paragraph. This result suggested that the shorter the height the higher the risk of T2DM. The Q test had a $p<0.001$, indicating significant heterogeneity across the estimated associations, which was further supported by the high value of 72.1% for the I-squared statistic.

Sex-specific meta-analysis results

The meta-analysis including only studies that reported sex-specific estimates (11 effect estimates in men and 10 in women) indicated that there were inverse associations between height and T2DM; the effect estimates were 0.86 (95% CI 0.75 to 0.99) for men and 0.90 (95% CI 0.80 to 1.01) for women (online supplementary figure 1). In a meta-regression, there was not a significant interaction with sex ($p=0.80$).

Table 1 Descriptive characteristics of included cross-sectional studies

Author and year of publication	Sex and participants (n)	Age range (years)	Country	Exposure (units)	Outcome	Diabetes cases (n)	Summary of results	Adjustments	Risk of bias assessment (RoBANS)
Brown *et al*, 1991[30]	M: 145 F: 201	40–64	England	Height (cm)	Glucose tolerance	12	Correlation between 120 min plasma glucose and height: M: r=−0.23 (95% CI −0.38 to −0.07), p<0.007 F: r=−0.24, (95% CI −0.37 to 0.11), p<0.006	Age and BMI.	Low
Williams *et al*, 1995[38]	M: 502 F: 654	40–65	UK	Height (m)	Glucose intolerance	51	Adjusted standardised beta coefficient= −0.12, p<0.01	Age, waist to hip ratio and BMI.	Low
Han *et al*, 1998[15]	M: 5887 F: 7018	20–59	The Netherlands	Height in tertiles (cm)	T2DM	M: 93 F: 66	Third vs first tertile: M: OR=0.23 (95% CI 0.09 to 0.79) F: OR=0.62 (95% CI 0.31 to 1.22)	Age, cigarette smoking, alcohol intake, physical activity and education.	Low
Olatunbosun and Bella, 2000[33]	M: 581 F: 417	NR	Nigeria	Height (cm)	Glucose intolerance	NR	M+F combined: OR=0.01, (95% CI NR)	NR.	High
Pan *et al*, 2001[34]	M: 3044 F: 3588	>20	Taiwan	Height (cm)	Diabetes	M: 72 F: 94	M: OR=0.61 F: OR=0.68 (95% CI NR)	Age, BMI, height, waist, waist to hip ratio, subscapular skinfold.	High
Lawlor *et al*, 2002[11]	F: 4286	60–79	UK	Height (cm)	T2DM	F: 375	F: OR=0.91 (95% CI 0.8 to 1.03)	BP, DBP, HDL, LDL, logged triglycerides, weight, waist to hip ratio, smoking, adult and childhood social class.	Low
Martín *et al*, 2002[32] (article in Spanish)	F: 30	35–55	Spain	Height (NR)	Glucose	NR	Correlation between glucose levels and height, r=−0.395, p<0.05	NR.	Unclear
Asao *et al*, 2006[19]	M: 2831 F: 3113	40–74	USA	Height (cm)	T2DM	M: 396 F: 436	M+F combined: OR=1.10 (95% CI 0.94 to 1.29)	Age, parental history of diabetes, physical activity, education, income, smoking, age at menarche and per cent body fat.	Low
Janghorbani and Amini, 2008[13]	M: 614 F: 1754	30–60	Iran	Height (cm), categories	2hPG	M: 78 F: 165	M: OR=0.81 (95% CI 0.39 to 1.68) F: OR=0.97 (95% CI 0.59 to 1.58)	Age.	Low
Sicree *et al*, 2008[37]	Total: 11 247	25–95	Australia	Height (cm)	Glucose intolerance	NR	Age-adjusted prevalence (IGT+diabetes) for the tallest: M: 5.0% (3.1%–8.1%) F: 10.4% (7.6%–14.2%)	Age, height, BMI and waist to hip ratio.	Low
Rathmann *et al*, 2008[36] (only letter available)	M: 697 F: 656	55–74	Germany	Height (cm)	FPG and 2hPG	NR	Beta coefficients: M: B=−0.03, p value: 0.009 F: B=−0.03, p value: 0.056	Age, BMI, height, FFM and FPG.	Unclear
Liu *et al*, 2009[10]	M: 3128 F: 3060	20–85	USA	Height (1 SD)	T2DM	NR	M: OR=0.91 (95% CI 0.75 to 1.1) F: OR=0.99 (95% CI 0.82 to 1.21)	Age, race, smoking status, family income and waist circumference.	Low
Ranasinghe *et al*[35] (only abstract)	Total: 4477	>18	Sri Lanka	Height (cm)	Diabetes	NR	Correlation between height and diabetes: r=−0.069, p<0.001	NR.	Unclear
Smits *et al*, 2012[6]	M: 349 F: 309	37.4–68.1	USA	Height (cm)	T2DM	145	M+F combined: OR=0.72 (95% CI 0.44 to 1.17)	Age, sex, weight, intra-abdominal fat area, family history and smoking.	Low
Hoque *et al*, 2014[14]	M: 3734 F: 3831	>35	Bangladesh	Height (m), categories	Diabetes	NR	M+F combined: OR=0.82 (95% CI 0.69 to 0.98)	Education level, wealth index, place of residence, division and BMI.	Unclear

BMI, body mass index; BP, blood pressure; DBP, diastolic blood pressure;F, female; FFM, fat free mass; FPG, fasting plasma glucose; HDL, high-density lipoprotein; IGT, impaired glucose tolerance; LDL, low-density lipoprotein; M, male; NR, not reported;RoBANS, Risk of Bias Assessment tool for Non-randomised Studies; T2DM, type 2 diabetes mellitus; 2hPG, 2-hour plasma glucose.

Table 2 Descriptive characteristics of cohort studies

Author and year of publication	Sex and participants (n)	Age range (years)	Country	Exposure (units)	Outcome	Diabetes cases (n)	Duration of follow-up (years)	Summary of results	Adjustments	Risk of bias assessment (RoBANS)
Colditz *et al*, 1990[31]	F: 113 861	30–55	USA	Height (unit NR)	Diabetes	873	8	Estimates not reported.	None.	Unclear
Njølstad *et al*, 1998[8]	M: 6098 F: 5556	35–52 at baseline	Norway	Height (5 cm)	Diabetes	M: 87 F: 75	12	M: RR=1.15 (95% CI 0.97 to 1.35) F: RR=0.71 (95% CI 0.58 to 0.87)	Ethnicity, age, BMI, SBP and DBP, cholesterol, HDL, triglycerides, glucose, smoking, hypertension treatment and physical activity.	Low
Kumari *et al*, 2004[12]	M: 5807 F: 2579	35–55	England	Height categories (unit NR)	T2DM	M: 242 F: 119	10.5	M: OR=0.65 (95% CI 0.50 to 0.90) F: OR=0.82 (95% CI 0.50 to 1.40)	Age, length of follow-up, employment grade, ethnic group, family history of diabetes, height, blood pressure, ECG abnormalities, BMI, physical activity and smoking.	Low
Schulze *et al*, 2006[7]	M: 9711 F: 15 402	M: 40–65 F: 35–65	Germany	Height in quintiles (cm)	T2DM	M: 492 F: 357	7	M: RR=0.71 (95% CI 0.53 to 0.95) F: RR=1.10 (95% CI 0.78 to 1.55)	Age, education, occupational activity, sport activity, biking, smoking and alcohol intake.	Low
Lorenzo *et al*, 2009[9]	M: 730 F: 1000	25–64	USA	Height (1 SD)	Incidence of diabetes	M: 76 F: 118	7.4	M: OR=1.14 (95% CI 0.85 to 1.51) F: OR=0.88 (95% CI 0.70 to 1.11)	Age and ethnicity.	High
Bozorgmanesh *et al*, 2011[18]	M: 1589 F: 2132	>20	Iran	Height (cm)	Incident diabetes	M: 85 F: 139	6	M: HR=1.02 (95% CI 0.69 to 1.50) F: HR=0.71 (95% CI 0.52 to 0.96)	Age, waist circumference, family history of diabetes, SBP, weight, triglycerides/HDL ratio.	Low
Conway *et al*, 2012[17]	M: 57 635 F: 71 450	M: 40–74 F: 40–70	China	Height (m)	Diabetes	M: 831 F: 538	M: 3.6 F: 7.3	M: HR=1 (95% CI 0.90 to 1.11) F: HR=1.05 (95% CI 0.99 to 1.11)	Birth cohort, education and income, BMI at baseline, smoking before age 20, BMI at age 20, BMI at baseline, and team sports during adolescence.	Low
Janghorbani and Amini, 2012[20]	M: 254 F: 838	42.8	Iran	Height (cm), categories	T2DM	M: 18 F: 84	5.5	M and F HR=0.54 (95% CI 0.31 to 0.93)	Age, gender and WC.	Low
Furer *et al*, 2015[16]	M: 32 055	31.0±5.6	Israel	Height (cm), categories	Incident diabetes	M: 702	6.3±4.3	M: HR=0.50 (95% CI 0.29 to 0.80)	Age, birth year, BMI, FPG, HDL-C, triglycerides, white cell count, physical activity, smoking, MSQ score, breakfast consumption, family history of diabetes, country of origin, intelligence score, SES and education.	Low
Vangipurapu *et al*, 2017[5]	M: 8746	57.2±7.1	Finland	Height (cm)	T2DM	M: 693	8.2	M: HR=0.81 (95% CI 0.75 to 0.87)	Age, waist, physical activity, smoking, alcohol, family history of diabetes, follow-up time, LDL cholesterol and drug treatment for hypertension, Matsuda Insulin Sensitivity Index, the Disposition Index, 2hPG at baseline, CVD, presence or absence of T2DM.	Low

BMI, body mass index;CVD, cardiovascular disease; DBP, diastolic blood pressure; F, female; FPG, fasting plasma glucose; HDL, high-density lipoprotein;HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein; M, male; MSQ, Mini Sleep Questionnaire; NR, not reported;RoBANS, Risk of Bias Assessment tool for Non-randomised Studies; SBP, systolic blood pressure; SES, socioeconomic status; T2DM, type 2 diabetes mellitus; WC, waist circumference; 2hPG, 2-hour plasma glucose.

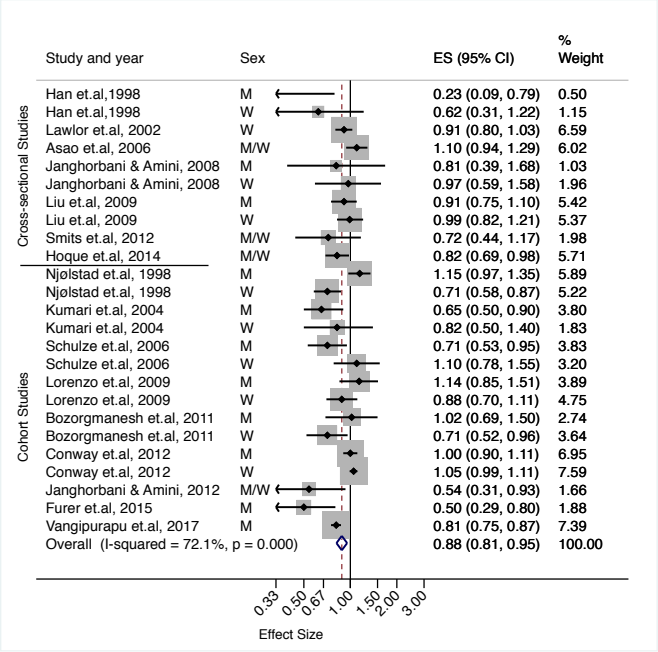

Figure 2 Forest plot of the associations between adult height and type 2 diabetes mellitus in the included studies. M indicates men, W indicates women, and M/W indicates men and women. ES denotes effect size. Studies are primarily arranged by their design—cross-sectional studies followed by cohort studies—and second by year of publication.

Shape of the height and T2DM associations

Three studies conducted in men reported an inverse non-linear shape between height and T2DM[7 12 16] compared with one study in women.[8] In one study, restricted cubic splines were used to assess the potential non-linearity of the association of height with incident diabetes in both men and women,[18] and the authors reported no deviations from linearity for both sexes. In another study, the relationship between the median height of each category of height and incidence rate of diabetes was fitted with linear and quadratic models.[16] This study found that the quadratic model explained the association better than the linear model, with a significant increase for those shorter than 170 cm and comparable risks for those taller than 175 cm, indicating an inverse non-linear shape of the association. Based on these limited data, we were unable to conduct a meta-analysis investigating this question, and the evidence remains insufficient to draw clear conclusions about the shape of the association.

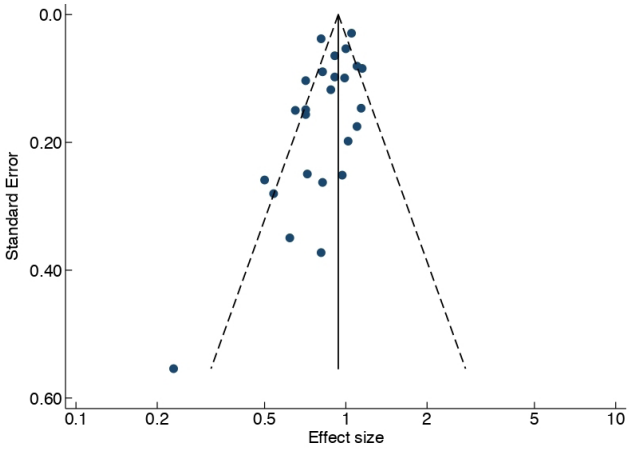

Figure 3 Funnel plot of effect estimates of the association between height and type 2 diabetes mellitus from 16 studies. The solid vertical line represents the summary estimate of the effect, and the dotted lines represent 95% confidence limits around the summary effect.

Subgroup analyses

The meta-analysis summarising 15 individual effect estimates (from 10 studies)[5–7 9–12 15 19 20] that assessed 'only T2DM' showed an inverse and statistically significant association between height and T2DM in adulthood (online supplementary figure 2). The association between height and 'mostly T2DM'[8 13 14 16–18] was of similar strength (online supplementary figure 2), which was confirmed in a meta-regression analysis (p=0.69).

The association between height and T2DM based on studies reporting the effect estimates as ORs (n=9)[6 9–15 19] was inverse and statistically significant, and this was not different from studies reporting the effect estimates as RRs (n=3)[7 8 20] or HRs (n=4)[5 16–18] (p=0.85) (online supplementary figure 3). Correspondingly, the association did not differ in cross-sectional and cohort studies (p=0.80) (online supplementary figure 4).

Continuous height was inversely associated with T2DM (n=10)[5–11 17–19] (online supplementary figure 5). The associations seemed to be stronger between categorical height and T2DM (online supplementary figure 5). The meta-regression showed a significant interaction with categorisation of height (p=0.02). We could not conduct meta-regression based on the adjustment of BMI and SES due to lack of studies reporting the results with and without adjustment for these factors (n=1).[14]

Publication bias

The overall meta-analysis (16 studies, 25 effect estimates) showed limited evidence of publication bias (figure 3). Nonetheless, as the meta-analysis test for heterogeneity showed that there was a high degree of heterogeneity among the included studies, and given the limited number of estimates, the results of the funnel plots should be interpreted cautiously.

DISCUSSION

The systematic review of the association between height and T2DM indicated that the associations were inverse. This finding is supported by results from our meta-analysis that included 16 observational studies and showed an inverse and statistically significant association between adult height and T2DM. In our meta-analysis, no evidence was found supporting that there are sex differences in the associations. Due to lack of available data, we were unable to conduct an analysis investigating the shape of the height and T2DM associations. Future studies should take potential confounding factors into account and investigate the shape of the height and T2DM association.

A previous meta-analysis conducted in 2012 included nine studies that assessed the relationship between adult height and T2DM.[23] In addition to those nine studies, we added seven more studies in our meta-analysis, and overall the findings are similar. In the 2012 meta-analysis, the summary RR was 0.85 (95% CI 0.76 to 0.96; p_{het}=0.001), which is similar to our finding. Sex-specific analyses from the current systematic review and meta-analysis showed that there were significant associations for men and borderline significant associations for women. The previous meta-analysis found a significant

association for women only, but did not test for sex differences.[23] Nevertheless, from the sex-specific results presented in the forest plot of the previous meta-analysis, it appears that the effect estimates are similar for both sexes.

Although height is seemingly associated with T2DM, it is likely an indicator of risk that likely reflects both biological and environmental factors.[16] Biological links, although plausible, remain speculative. A potential biological pathway linking height and T2DM could be the fetal programming of metabolism,[39 40] as high insulin-like growth factor 1 (IGF-1), a major determinant of fetal and childhood growth, also predicts reduced risks of adult diabetes.[41 42] Leg length, an indicator of long bone growth in childhood, appears to be more important than trunk length in the associations with T2DM.[11] Additionally, adult height is positively and significantly associated with beta-cell function and insulin sensitivity,[5] and inversely correlated with liver fat content,[43] conditions that are involved in the pathogenesis of T2DM. Both height[3] and T2DM[44] are influenced by genetic factors, and these could also be potential confounders of the association observed in our meta-analysis. We could not explore this, however, as only few studies included in this review and meta-analysis adjusted for factors such as having a family history of diabetes[5 6 12 16 18 19] or ethnicity.[8 9 12] Further, it is also possible that other potentially confounding factors could explain the associations between height and T2DM. For example, child and adult SES are positively associated with height[3 45 46] and negatively associated with T2DM.[47] Components of SES were adjusted for in only eight of the studies[5 7 11 12 14–17] included in this meta-analysis. In the one study[16] that adjusted for SES, however, the association between adult height and diabetes remained. Due to the low number of studies incorporating this information, we were unable to examine the potential effects of these factors.

Height and BMI are correlated, and given the strong positive relationship between BMI and diabetes,[31] BMI may be a potential confounder of the height and T2DM association. Among 16 studies included in the meta-analysis, 5 studies[8 12 14 16 17] adjusted for BMI and 2[6 18] adjusted for factors similar to BMI, such as weight or waist circumference. In general, these studies showed inverse associations between height and T2DM after adjustment for BMI. Overall, however, there was insufficient information available for conducting subgroup analyses based on adjustments for BMI.

The major strengths of this study were the use of broad search terms and preplanned subgroup analyses. Seven studies included in this review were cross-sectional studies and the remaining were cohort studies, which may be limited by selection, information bias and/or confounding.[14] The relatively heterogeneous set of contributing studies was one of the main drawbacks of our meta-analysis. Similarly, due to differences in the factors adjusted for in these studies, we were unable to perform detailed subanalyses to investigate the effects of relevant potentially confounding variables. Nonetheless, we were able to conduct the overall analyses and examine the sex differences explicitly.

What is already known on this subject

- Short stature in adulthood may indicate an increased risk for type 2 diabetes.
- Whether these associations differed between men and women and whether there were thresholds at which the risks changed were not clear.

What this study adds

- Short adult stature is associated with an increased risk of type 2 diabetes.
- The associations did not differ between men and women.
- Further studies are needed regarding potential threshold effects as conclusions regarding the shape of the associations could not be made due to lack of data.

Contributors LGB and JLB conceived the study. SS and SHR conducted the literature search and quality assessment independently. Data from all included studies were extracted by SS and researcher SHR extracted data on a random sample of the primary studies. LHA assisted in the meta-analysis. All authors were involved in the data interpretation. SS drafted the manuscript. All authors critically revised the manuscript for important intellectual content and gave final approval of the version to be submitted.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The meta-analysis was conducted on anonymous data. The project was approved by the Danish Data Protection Agency. The project does not involve personal examinations that require permission from the Regional Ethics Committee.

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