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REVIEW ARTICLE

Systematic review and meta-analysis of age at menarche and risk of type 2 diabetes

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Abstract The relation of early menarche with type 2 diabetes mellitus (T2DM) remains inconsistent across studies. The objective of this systematic review and meta-analysis of published population-based observational studies was to assess the association between age at menarche and T2DM risk. We searched online data bases through December 2013 and examined the reference lists of pertinent articles. Summary relative risks (RRs) with 95 % confidence intervals (CIs) were calculated with a random-effects model. A total of 14 effect estimates from 10 eligible studies (three cross-sectional and seven cohort studies) included 315,428 participants and 22,085 cases of T2DM. Compared with the highest or middle category, women in the lowest category of age at menarche had higher risk of T2DM [summary RR (95 % CI) 1.22 (1.17, 1.28)]. These results were consistent between studies that conducted in the United States and in Europe. The association between age at menarche and T2DM was slightly stronger for cohort than for cross-sectional studies. These findings strongly support an association between younger age at menarche and increased risk of T2DM. Age at menarche may help identify women with increased risk of developing T2DM.

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Introduction

The association between early menarche and type 2 diabetes mellitus (T2DM) is important public health problem because average age at menarche, the age at onset of first menstruation in girls, is declining [1, 2], coincidental with the trend of increasing prevalence of obesity and T2DM [3, 4]. Age at menarche represents a distinct event in puberty, is usually well recalled into adulthood, and therefore is a convenient noninvasive measure of pubertal timing [5, 6]. Although several observational studies have investigated the association between age at menarche and risk of T2DM [7–10] and its risk markers [10–16], the role of age at menarche as a risk factor for T2DM remains unsettled: Reported associations have been inverse [8, 9, 17–19] or null [7, 10, 17, 20]. It is well established that obesity is strongly associated with increased risk of T2DM [21, 22], factor that inversely related to age at menarche too [23–25]. The interpretation of these findings, however, has been hampered by the low frequency of occurrence of both early menarche and T2DM in the same individual, which results in the lack of statistical power to adequately analyze this association in many studies, and confounding by obesity.

Whether early menarche increases risk of T2DM independently is an important question because there is a possibility of early intervention.

We conducted a systematic review and meta-analysis of cross-sectional and cohort studies to summarize the epidemiologic evidence on the association between age at menarche and T2DM and to identify possible sources of

heterogeneity between studies. We also aimed to evaluate whether the associations varied by study design, geographic area, and follow-up duration. This approach can strengthen the statistical power and generalizability of our findings, and thus help resolve inconsistencies from seemingly divergent individual study estimates.

Materials and methods

The present systematic review was done in accordance with the Metaanalysis of Observational Studies in Epidemiology (MOOSE) guidelines for reviews of observational studies [26].

Search strategy

We searched online databases (Pub Med, ISI, EMbase, Google Scholar, and Cochrane Collaboration) through December 2013 using terms "menarche" and "menstruation" combined with "diabetes mellitus", "diabetes", "glucose", or "insulin", limited to studies in humans. We also reviewed reference lists of the identified publications for additional pertinent studies. No language restrictions were imposed.

Eligibility criteria

Published studies were included in the meta-analysis if they met the following criteria: (1) peer-reviewed original article, (2) cohort, case–control, or cross-sectional study, and (3) adult women population. Studies were excluded if they did not provide data that allowed us to calculate standard errors for effect estimates and if the estimates were not adjusted for BMI.

Figure 1 shows a flow diagram describing the study selection process. The initial search by key words yields 276 reports, of which 256 were excluded due to not eligible study design or irrelevant to the original research question.

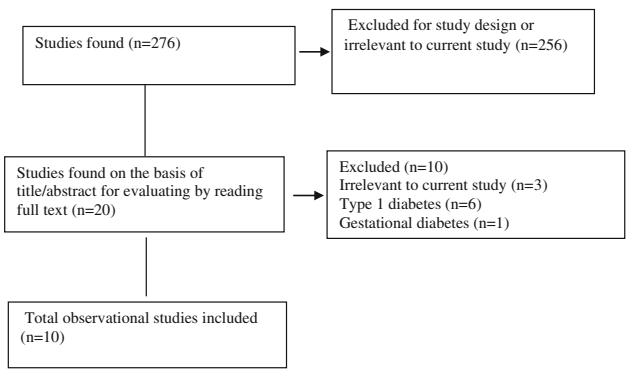

Fig. 1 Flow diagram of study selection process

Additional 10 studies were excluded because the disease of interest was either type 1 or gestational diabetes, or found irrelevant to the original research question. The 10 epidemiological studies considered for inclusion in this meta-analysis were three cross-sectional and seven cohort studies on the association between age at menarche and the prevalence or incidence of T2DM [7–10, 17–20, 27, 28].

Data extraction

We extracted data on publication (the first author's last name, year of publication, and country of population studied), study design, number of exposed and unexposed subjects, follow-up period (for cohort studies), age, risk estimates with their corresponding confidence intervals (CIs), and variables controlled for in the multivariable model. From each study, we extracted the risk estimates that reflected the greatest degree of control for potential confounders. Information on study design, participant characteristics, measurement of diabetes, adjustment for potential confounders, and estimates of associations was extracted independently by two reviewers (MJ and EH). Discrepancies were resolved by discussion. For studies [8, 10, 18–20, 28] that compared the highest and lowest categories of age at menarche or entered it as continuous variables, we converted the results to compare the lowest and highest categories or each 1 year early in menarche with the reciprocal of the odds ratio or rate ratio. Age at menarche was defined as age at the first menstrual period and was ascertained by self-reported recall questionnaire or personal interview.

Statistical analysis

The lowest category of age at menarche was compared with highest or middle category. Three measures of association were used for the meta-analysis: odds ratio (cross-sectional studies), incidence rate ratio and hazard ratio (HR) (cohort studies). For simplicity, we refer to relative risk (RR) for all three types of measures of association. Because the frequency at which diabetes occur is relatively low, the odds ratio in cross-sectional studies and rate ratios and HR in cohort studies yield similar estimates of RR [29].

We produced forest plots to assess the multivariate-adjusted RR and corresponding 95 % CI visually across studies. We used the logarithm of the RR with its standard error for the meta-analysis. Summary RR estimates with their corresponding 95 % CIs were derived by the method of DerSimonian and Laird [30] with use of a random-effects model, which incorporates between-study variability. The method of DerSimonian and Laird is the simplest and most commonly used method for fitting random-effects

models in meta-analyses. Statistical heterogeneity of the RR between studies was evaluated with Cochran's Q test and quantified with the I^2 statistic [31] ($I^2 = 0$ % indicates no observed heterogeneity, $I^2 \geq 50$ % indicated substantial heterogeneity [32]).

To assess sources of heterogeneity, we conducted a meta-regression analysis with region (USA, Europe or China), study design, and duration of follow-up in cohort studies as independent variables and the logRR as the dependent variables and subgroup analyses. Sensitivity analysis was done by successively removing a particular study or group of studies (if any) which had the highest impact on the heterogeneity test. Publication bias was assessed by visual inspection of funnel plots [33]. In these funnel plots; the RR's were displayed against the inverse of the square of the standard error (a measure of the precision of the studies). Formal statistical assessment of funnel plot asymmetry was done with Egger's regression asymmetry test [34]. The reported P values are from the intercept in the regression analysis, which provides a measure of asymmetry. In addition, Begg's adjusted rank correlation test and the trim-and-fill method were used [33, 35]. Statistical analyses were carried out with Comprehensive Metaanalysis Software version 2.0 (Englewood, NJ Bio-Stat). P values <0.05 were considered statistically significant. All statistical tests were two-sided.

Results

Study characteristics

A total of 14 effect estimates from 10 independent studies with 315,428 participants and 22,085 cases of T2DM from

Table 1 Cross-sectional studies of age at menarche and risk of type 2 diabetes mellitus (T2DM) that satisfied eligibility criteria for inclusion in the systematic review and meta-analysis

Source, country	Age at menarche (year) (% or mean (SD)	Age (year)	Study population and no. of participants	No. of T2DM and measurement method	OR (95 % CI)	Controlled variables
Saquib et al. [10], USA	<12 year = 14.5 % 12–15 year = 78.9 % ≥16 year = 6.6 %	50–92	Rancho Bernardo Study: 997 postmenopausal women	125 physician diagnosed or use of anti-diabetic medication or blood glucose test (OGTT)	≥16 year = referent <12 year = 2.27 (0.62, 9.09)[a]	Age, BMI, no. of pregnancies, physical activity, smoking, current estrogen use, family history of diabetes
Stockl et al. [19], Germany	13.5 (1.6)	32–81	Cooperative Health Research in the Region of Augsburg, South Germany : 1503 women	140 self-reported glucose-lowering medications and blood glucose test (OGTT)	1.19 (1.02, 1.37)[a] per year early age at menarche	Year of birth, BMI, BMI at age 25, physical activity, education, marital status, smoking, alcohol consumption, menopausal status.
Dreyfus et al. [17], USA	White: 12.9 (1.6) African American: 12.9 (1.7)	45–65	Atherosclerosis Risk in Communities study: White women: 5,504 African American women: 1997	White: 482 self-reported physician diagnosed and blood glucose test (fasting glucose ≥ 126 mg/dl, non-fasting glucose > 200 mg/dl) African American: 508 self-reported physician diagnosed and blood glucose test (fasting glucose ≥ 126 mg/dl, non-fasting glucose > 200 mg/dl).	White: 13 year = referent 8–11 year = 1.41 (1.05, 1.89) African American: 13 year = referent 8–11 year = 0.94 (0.68, 1.30)	Age, center, family history of diabetes, smoking, use of oral contraceptives, education, BMI, BMI at age 25, height, waist circumference
Qiu et al. [20], China	16 (0.5)	37–92	Population-based cross-sectional study in Fujian, China: 3,304 post menopausal women	738 physician diagnosed or use of antidiabetic medication or blood glucose test (OGTT)	16 year = referent 9–14 year = 1.11 (0.83, 1.52)[a]	Age, physical activity, parity, smoking, alcohol consumption, family history of DM, BMI, waist circumference.

OR odds ratio, *CI* confidence interval, *T2DM* type 2 diabetes mellitus, *OGTT* oral glucose tolerance test

[a] We converted the results to compare the lowest and highest categories with the reciprocal of the odds ratio

Table 2 Cohort studies of age at menarche and diabetes mellitus (DM) risk that satisfied eligibility criteria for inclusion in the systematic review and meta-analysis

Source, country	Average follow-up period (year)	Age at enrollment (year)	Mean (SD) age at menarche (year)	Study population	No. of T2DM and measurement method	RR (95 % CI)	Controlled variables
Cooper et al. [7], USA	Unknown	63–81	12.4 (1.7)	The Menstruation and reproductive history study: 668 white, college-educated women Comparison group: unknown	49 self-reported physician diagnosed	1.1 (0.9, 1.3) per year early age at menarche	Age, BMI at age 30
Lakshman et al. [8], UK	8	40–75	13.0 (1.6)	The Norfolk cohort of the European Prospective Investigation into cancer and Nutrition: 13,308 women. Comparison group: 2,208 (17 %) women in highest quintile of age at menarche	734 self-reported physician diagnosed, diabetes drug use, general practice and local hospital diabetes registers, hospital admission data, Office for National Statistics mortality data	Highest quintile (15–18 year) = referent Lowest quintile (8–11 year) = 1.52 (1.18, 1.96)[a]	Age, BMI, reproductive factors, smoking, occupational social class, education, physical activity, family history of diabetes
He et al. [9], USA	NHS I: 26 NHS II: 14	NHS I: 34–59 NHS II: 26–46	NHS I: unknown NHS II: unknown	The Nurses' Health study (NHS) I and II: 201,962 NHS I: 101,415 NHS II: 100,547 Comparison group: NHS I: 31,439 (31.1 %) women with age at menarche 13 year NHS II: 26,995 (27.6 %) women with age at menarche 13 year	NHS I: 7,963 NHS II: 2,739 Self-reported and confirmed by means of supplementary questionnaire and medical records review.	NHS I: 13 Year = referent ≤11 Year = 1.18 (1.10, 1.27) NHS II: 13 Year = referent ≤11 Year = 1.40 (1.24, 1.57)	Age, parity, race/ethnicity family history of diabetes, lifestyle and reproductive factors, childhood characteristics, BMI at age 18

Table 2 continued

Source, country	Average follow-up period (year)	Age at enrollment (year)	Mean (SD) age at menarche (year)	Study population	No. of T2DM and measurement method	RR (95 % CI)	Controlled variables
Conway et al. [28], China	7.3	40–70	14.8 (0.1)	The Shanghai Women's Health Study: 69,385 women. Comparison group: 13,877 women in highest quintile of age at menarche	1,831 self-reported physician diagnosis based on fasting glucose, OGTT and use of hypoglycemic agent	Highest quintile (17–26 year) = referent Lowest quintile (8–13 year) = 1.13 (0.95, 1.33)[a]	Birth cohort, education, income, BMI at age 20, BMI at baseline, physical activity during adolescence
Pierce [18], UK	53	53	13.2 (1.8)	The Medical Research Council National Survey of Health and Development: 1,632 women Comparison group: unknown	26 Physician diagnosed	1.16 (0.85, 1.59) per year early age at menarche[a]	BMI
Dreyfus et al. [17], USA	7.1	White: 54.0 African American: 53.3	White: 12.9 (1.6) African American: 12.9 (1.7)	The Atherosclerosis Risk in Communities study : 7,501 White: 5,504 African American: 1,997 Comparison group: White: 125 women with age at menarche 13 year African American: 671 women with age at menarche 13 year	White: 433 self-reported physician diagnosed and blood glucose test (fasting glucose ≥126 mg/dl, non-fasting glucose >200 mg/dl) African American: 322 self-reported physician diagnosed and blood glucose test (fasting glucose ≥126 mg/dl, non-fasting glucose >200 mg/dl)	White: 13 year = referent 8–11 year = 1.22 (0.92, 1.63) African American: 13 year = referent 8–11 year = 1.11 (0.80, 1.56)	Age, center, family history of diabetes, smoking, use of oral contraceptives, education, BMI, height, waist circumference

Table 2 continued

Source, country	Average follow-up period (year)	Age at enrollment (year)	Mean (SD) age at menarche (year)	Study population	No. of T2DM and measurement method	RR (95 % CI)	Controlled variables
Elks et al. [27], 8 European countries	9.4	52.4	13.1 (1.7)	The European Prospective Investigation into cancer and Nutrition: 15,168 women Comparison group: 2,396 (25 %) women in middle quintile of age at menarche	5,995 self-reported (physician diagnosed history of diabetes or diabetes drug use) and confirmed by means of medical records review or through local and national diabetes and pharmaceutical registers	Middle quintile (13 year) = referent Lowest quintile (8–11 year) = 1.42 (1.18, 1.71)	Age, center, smoking, physical activity, alcohol intake, education, age at first full-term pregnancy, parity, menopausal status, use of oral contraceptive pill, use of hormone replacement therapy, BMI, waist circumference

RR relative risk, *CI* confidence interval; *T2DM* type 2 diabetes mellitus

[a] We converted the results to compare the lowest and highest categories with the reciprocal of the RR

twelve countries met the predefined inclusion criteria. Of these 10 studies, three were cross-sectional studies that used odds ratio as the effect estimate [10, 19, 20] (Table 1), six were cohort studies that used incidence rate ratios as the measure of RR [7–9, 17, 18, 28] and one was a nested case-cohort study that used HR as the measure of RR [27] (Table 2). One study [17] analyzed both baseline data (cross-sectional) and follow-up data (cohort). Five studies were conducted in the United States [7, 9, 10, 17, 27], three in Europe [8, 18, 19], and two in China [20, 28]. One of European studies conducted in 26 research centers across eight European countries [27]. In the primary meta-analysis of age at menarche and T2DM, we included 14 effect estimates from four cross-sectional studies [10, 17, 19, 27] and the seven cohort studies [7–9, 17, 18, 20, 28]. Tables 1 and 2 show that the most common covariates considered by the studies were BMI, physical activity, smoking, and reproductive factors. We performed meta-analysis for maximally adjusted estimates where available.

Age at menarche and type 2 diabetes

Individual study results and the overall summary results for the 14 effect estimates from four cross-sectional and seven cohort studies of age at menarche and T2DM are shown in Fig. 2. Six of these 14 effect estimates found a statistically significant inverse association between age at menarche and T2DM. The prevalence study of one of the cohort studies [17] reported a significant positive association between age at menarche and T2DM [RR 1.41 (95 % CI 1.05, 1.89). The range of individual RRs was 0.94–2.27 and the summary RR (95 % CI) for all 14 effect estimates from 10 studies was 1.22 (1.17, 1.28)]. Heterogeneity among studies was not found ($I^2 = 30.4$ %; $P_{\text{heterogeneity}} = 0.134$).

When age at menarche was treated as continuous variables for three studies, there was also a significant relationship between early age at menarche and T2DM (summary RR (95 % CI) 1.15 (1.04, 1.29) per year early age at menarche).

We also conducted subgroup meta-analyses by study design, geographic area, number of T2DM cases, and duration of follow-up (Table 3). The association between age at menarche and T2DM was somewhat stronger in cohort studies than in cross-sectional studies, although differences were not statistically significant. Results were consistent for studies conducted in Europe and in the United States. The summary RR for two studies conducted in China was not statistically significant (RR 1.13; 95 % CI 0.97, 1.30). The summary estimate was similar [summary RR (95 % CI) 1.23 (1.16, 1.31)] for the two cohorts with ≥10 years of follow-up and for the four cohorts with follow-up duration <10 years [1.27 (1.15, 1.41)], there was heterogeneity among two studies with ≥10 years of

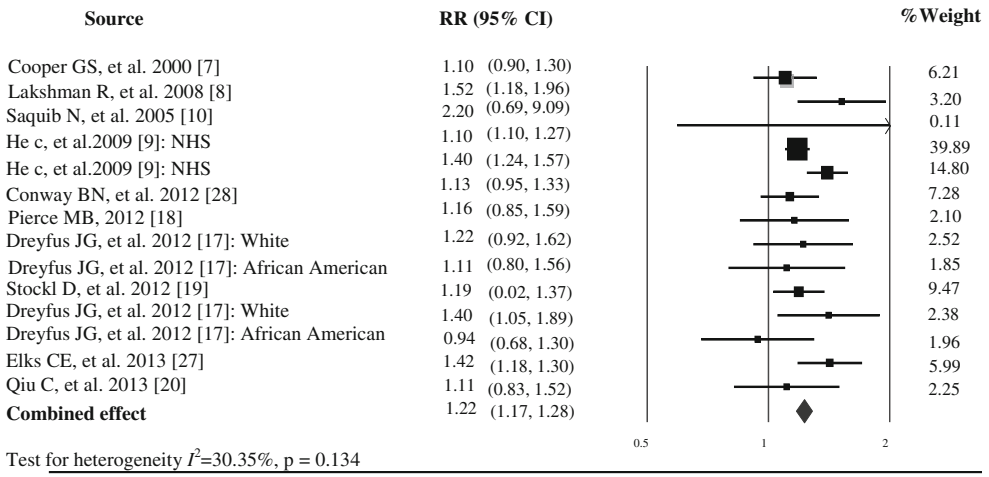

Fig. 2 Forest plot of the association between age at menarche and type 2 diabetes risk in cross-sectional and cohort studies. *RR* relative risk, *CI* confidence interval, *square* study-specific RR estimate, *horizontal line* 95 % CI, *diamond* summary RR estimate and its corresponding 95 % CI. All statistical tests were two-sided. Statistical heterogeneity between studies was assessed with the I^2 test. Weights are from random-effects analysis

Table 3 Summary relative risk (RR) estimates [95 % confidence intervals (CIs)] for cross-sectional and cohort studies of the association between age at menarche and type 2 diabetes by study design, geographic area, and duration of follow-up

Subgroup	No. of studies	Summary RR (95 % CI)	Between studies		Between subgroups	
			Q	$P_{\text{heterogeneity}}$	Q	$P_{\text{heterogeneity}}$
Study design						
Cross-sectional	4	1.18 (1.05, 1.32)	4.382	0.357	0.481	0.488
Cohort studies	7	1.23 (1.17, 1.29)	13.815	0.087		
Geographic area						
United States	5	1.22 (1.15, 1.28)	11.832	0.106	2.608	0.271
Europe	4	1.30 (1.17, 1.43)	4.216	0.239		
China	2	1.13 (0.97, 1.30)	0.010	0.919		
Follow-up duration						
<10 years	4	1.27 (1.15, 1.41)	5.869	0.209	0.285	0.593
≥10 years	2	1.23 (1.16, 1.31)	6.035	0.049		
Diabetes cases						
< 100 cases	2	1.11 (0.95,1.30)	0.083	0.774	1.463	0.226
≥ 100 cases	8	1.23 (1.18,1.29)	17.120	0.104		

follow-up ($P_{\text{heterogeneity}} = 0.049$). Finally, the summary RR for two studies with <100 T2DM cases was not statistically significant [summary RR (95 % CI) 1.11 (0.95, 1.30)].

The heterogeneity tests showed no significant differences between individual studies. As expected, the summary RR and statistical significance from fixed-effect models were similar to those derived from random-effects models.

Publication bias

There was no funnel plot asymmetry for the association between age at menarche and T2DM risk (data not shown). P values for Begg's adjusted rank correlation test and Egger's regression asymmetry test were 0.91 and 0.38, respectively, indicating a low probability of publication bias. No missing studies were identified with the trim-and-fill method.

Discussion

Findings from this meta-analysis indicate that early menarche was associated with significantly higher risk of T2DM. The results were consistent for studies carried out in the United States and in Europe. The association was

observed in both cross-sectional and cohort studies. When age at menarche was treated as continuous variables, the association remained similar. To the best of our knowledge, this is the first systematic review and meta-analysis to assess the effect of early menarche on T2DM risk. Despite differences in the age groups, study designs, statistical power, measurement methods, definitions of T2DM, obesity, and early menarche, the studies we included showed inconsistent association between early menarche and T2DM. For example, one cross-sectional study linked early menarche to T2DM [19] but two other such studies found no consistent association [10, 20]. In the cross-sectional study of Cooperative Health Research in the Region of Augsburg of 1,503 German women, the association between early menarche and higher T2DM risk remained significant after adjustment for BMI [19]. Some cohort studies have linked age at menarche to T2DM [8, 9, 17, 27], but another cohort study found no consistent association [28]. Data from Nurses' Health study (NHS) I and II [9], prospective EPIC-Norfolk cohort studies [8], Atherosclerosis Risk in Communities (ARIC) study [17], and the InterAct nested case-cohort study [27] collectively showed age at menarche is inversely associated with T2DM. The EPIC-Norfolk study suggests that age at menarche and its association with T2DM are completely mediated by adult obesity [8]. The NHS I showed an increase risk of T2DM in women with early menarche, with a stronger effect in younger than older women, and this effect seems to be mediated through excessive adult obesity. Evidence of associations among younger and middle-aged women in NHS II could not be fully explained by increased adult BMI, suggesting a risk pathway between age at menarche and T2DM beyond excessive obesity [9]. In the ARIC cohort [17], early age at menarche was associated with increased risk of T2DM among white women, but not among African-American women. The association was stronger for prevalent diabetes at baseline than for incidence diabetes during 9 years of follow-up. Adulthood obesity partially attenuated the association between early menarche and prevalent diabetes and completely attenuated the association with incident diabetes. Pierce et al. [18] that followed women from birth to age 53 years found that age at menarche was associated with T2DM before, but not after adjustment for BMI. Data from Shanghai Women's Health Study [28] found no association between early menarche and T2DM after further adjustment for baseline BMI. The large nested case-cohort study of InterAct [27] showed early menarche conferred a 42 % increase in the risk of developing T2DM independently of adult BMI. It seems that studies reported an association tended to be large and included both postmenopausal and premenopausal women [8, 9, 17, 19], while those that did not find an association included only postmenopausal women and might have been under powered [7, 10, 18, 20].

Published studies on the association between age at menarche and T2DM are currently limited and have very different characteristics and interpretations, so our analysis must be interpreted in the context of the limitations in the available data. Four of the effect estimates (28.6 %) were based on cross-sectional studies. The prevalence analysis is subject to a number of biases to which the incidence analysis was less susceptible. Two of the studies did not distinguish between type 1 and type 2 DM [7, 8]. Type 1 DM has been associated with delayed menarche [36], so any effect of including women with type 1 diabetes would have attenuated the association between earlier menarche and T2DM. In addition, because T2DM is an underdiagnosed disease, some degree of misclassification of exposure to T2DM is likely to have occurred. Such non-differential misclassification would tend to weaken the true relationship between age at menarche and T2DM. Women in all studies could have had difficulty with recall of age at menarche. The age at menarche has been assessed many years later; therefore, misclassification may have occurred. One study shows that women's recall of menstrual history is quite reliable [37]. In one longitudinal study, approximately 84 % of women, mean age 50 years, were able to recall their age at menarche to within 1 year of the actual date [5, 37]. There is no reason to believe that women with T2DM recalled age at menarche any differently to those without diabetes and such bias would be unlikely in this systematic review and meta-analysis. Because of the observational nature of included studies, the possibility of residual confounding due to unmeasured or imperfectly measured confounders cannot rule out. Lack of power is another restriction of included studies. As in any meta-analysis, the possibility of publication bias is of concern. However, the results obtained from funnel plot analysis and formal statistical tests did not provide evidence for such bias.

Nearly all published studies included in this meta-analysis were conducted in whites, except one [17] and little information is available on the relationship between age at menarche and T2DM in minority populations. In this meta-analysis, we were unable to conduct separate analyses by ethnicity.

Obesity is a risk factor in both age at menarche and T2DM. Thus, the observed increased risk of T2DM associated with a history of early menarche may reflect residual confounding by this risk factor. However, an inverse association between age at menarche and T2DM risk remained when we limited the meta-analysis to studies that controlled for body mass index.

The mechanisms whereby early menarche increase T2DM risk is not entirely clear. The putative mechanisms

as discussed in earlier studies include hormone exposure and/or change in glucose metabolism that track into adulthood and have been shown to be a factor in T2DM pathogenesis [9, 38]. Early menarche is associated with higher estrogen levels and decreased serum sex hormone-binding globulin levels that persist in adulthood [9, 37]. Increasing evidence suggests that endogenous sex hormones play important roles in the pathogenesis of T2DM [38, 39]. Another possible cause of the increased risk of T2DM in women with early menarche is higher socio-economic status of the parent's generation compared with earlier generation, leading to more rapid childhood growth and obesity in offspring, which in turn lead to earlier menarche and greater obesity and then insulin resistance and eventually T2DM [17]. The association between early menarche and T2DM may exist because early menarche may be a marker of higher prepubertal BMI, with prolonged effects of increased obesity being the main risk factor for T2DM. Another possible cause of the increased risk of T2DM in women with early menarche is genetic factors [27]. Animal studies showed that over express Lin28 exhibit both later pubertal maturation and increased glucose uptake [40] and provide a possible mechanistic link between early menarche and T2DM risk.

In conclusion, the results from this meta-analysis strongly support an inverse association between age at menarche and increased risk of T2DM. With a worldwide decreasing age at menarche, the contribution of early menarche to incidence of T2DM may increase. These findings emphasize the need for obesity prevention strategies in girls with early menarche.

Conflict of interest Mohsen Janghorbani, Marjan Mansourian and Elham Hosseini declare they have no conflict of interest.

Human and Animal Rights This article does not contain any studies with human or animal subjects performed by the any of the authors.

References

1. Euling SY, Herman-Giddens ME, Lee PA, Lee PA, Selevan SG, Juul A et al (2008) Examination of US puberty-timing data from 1940 to 1994 for secular trends: panel findings. Pediatrics 121(Suppl 3):S172–S191
2. Harris MA, Prior JC, Koehoorn M (2008) Age at menarche in the Canadian population: secular trends and relationship to adulthood BMI. J Adolesc Health 43:548–554
3. Hu FB (2003) Overweight and obesity in women: health risks and consequences. J Women Health 12:163–172
4. Colagiuri S, Borch-Johnsen K, Glümer C, Vistisen D (2005) There really is an epidemic of type 2 diabetes. Diabetologia 48:1459–1463
5. Coleman L, Coleman J (2002) The measurement of puberty: a review. J Adolesc 25:535–550
6. Must A, Phillips SM, Naumova EN, Blum M, Harris S, Dawson-Hughes B et al (2002) Recall of early menstrual history and menarcheal body size: after 30 years, how well do women remember? Am J Epidemiol 155:672–679
7. Cooper GS, Ephross SA, Sandler DP (2000) Menstrual patterns and risk of adult-onset diabetes mellitus. J Clin Epidemiol 53:1170–1173
8. Lakshman R, Forouhi N, Luben R, Bingham S, Khaw K, Wareham N et al (2008) Association between age at menarche and risk of diabetes in adults: results from the EPIC-Norfolk cohort study. Diabetologia 51:781–786
9. He C, Zhang C, Hunter DJ, Hankinson SE, Louis GMB et al (2010) Age at menarche and risk of type 2 diabetes: results from 2 large prospective cohort studies. Am J Epidemiol 171:334–344
10. Saquib N, Kritz-Silverstein D, Barrett-Connor E (2005) Age at menarche, abnormal glucose tolerance and type 2 diabetes mellitus: the Rancho Bernardo Study. Climacteric 8:76–82
11. Frontini MG, Srinivasan SR, Berenson GS (2003) Longitudinal changes in risk variables underlying metabolic syndrome X from childhood to young adulthood in female subjects with a history of early menarche: the Bogalusa Heart Study. Int J Obes Relat Metab Disord 27:1398–1404
12. Heys M, Schooling CM, Jiang C, Cowling BJ, Lao X, Zhang W, Cheng KK et al (2007) Age of menarche and the metabolic syndrome in China. Epidemiology 18:740–746
13. Remsberg KE, Demerath EW, Schubert CM, Chumlea WC, Sun SS, Siervogel RM (2005) Early menarche and the development of cardiovascular disease risk factors in adolescent girls: the Fels Longitudinal Study. J Clin Endocrinol Metab 90:2718–2724
14. Feng Y, Hong X, Wilker E, Li Z, Zhang W, Jin D et al (2008) Effects of age at menarche, reproductive years, and menopause on metabolic risk factors for cardiovascular diseases. Atherosclerosis 196:590–597
15. Kivimäki M, Lawlor DA, Smith GD, Elovainio M, Jokela M, Keltikangas-Järvinen L et al (2008) Association of age at menarche with cardiovascular risk factors, vascular structure, and function in adulthood: the Cardiovascular Risk in Young Finns study. Am J Clin Nutr 87:1876–1882
16. Chen L, Zhang C, Yeung E, Ye A, Mumford SL, Wactawski-Wende J, Schisterman EF (2011) Age at menarche and metabolic markers for type 2 diabetes in premenopausal women: the BioCycle Study. J Clin Endocrinol Metab 96:E1007–E1012
17. Dreyfus JG, Lutsey PL, Huxley R, Pankow JS, Selvin E, Fernández-Rhodes L et al (2012) Age at menarche and risk of type 2 diabetes among African–American and white women in the Atherosclerosis Risk in Communities (ARIC) study. Diabetologia 55:2371–2380
18. Pierce MB, Kuh D, Hardy R (2012) The role of BMI across the life course in the relationship between age at menarche and diabetes, in a British Birth Cohort. Diabet Med 29:600–603
19. Stockl D, Doring A, Peters A, Thorand B, Heier M, Huth C et al (2012) Age at menarche is associated with prediabetes and diabetes in women (aged 32–81 years) from the general population: the KORA F4 Study. Diabetologia 55:681–688
20. Qiu C, Chen H, Wen J, Zhu P, Lin F, Huang B et al (2013) Associations between age at menarche and menopause with cardiovascular disease, diabetes, and osteoporosis in Chinese women. J Clin Endocrinol Metab 98:1612–1621
21. Vazquez G, Duval S, Jacobs DR Jr, Silventoinen K (2007) Comparison of body mass index, waist circumference, and waist/hip ratio in predicting incident diabetes: a meta-analysis. Epidemiol Rev 29:115–128
22. Janghorbani M, Amini M (2010) Comparison of body mass index with abdominal obesity indicators and waist-to-stature ratio for prediction of type 2 diabetes: the Isfahan Diabetes Prevention Study. Obes Res Clin Pract 4:e25–e32
23. Himes JH, Obarzanek E, Baranowski T, Wilson DM, Rochon J, McClanahan BS (2004) Early sexual maturation, body

composition, and obesity in African–American girls. Obes Res 12(Suppl):64S–72S
24. Demerath EW, Li J, Sun SS, Chumlea WC, Remsberg KE, Czerwinski SA et al (2004) Fifty-year trends in serial body mass index during adolescence in girls: the Fels Longitudinal Study. Am J Clin Nutr 80:441–446
25. Adair LS, Gordon-Larsen P (2001) Maturational timing and overweight prevalence in US adolescent girls. Am J Public Health 91:642–644
26. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D et al (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 283:2008–2012
27. Elks CE, Ong KK, Scott RA, van der Schouw YT, Brand JS, Wark PA et al (2013) Age at menarche and type 2 diabetes risk: the EPIC-InterAct study. Diabetes Care 36:3526–3534
28. Conway BN, Shu XO, Zhang X, Xiang YB, Cai H, Li H, Yang G et al (2012) Age at menarche, the leg length to sitting height ratio, and risk of diabetes in middle-aged and elderly Chinese men and women. PLoS ONE 7:e30625
29. Greenland S (1987) Quantitative methods in the review of epidemiologic literature. Epidemiol Rev 9:1–30
30. DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. Control Clin Trials 7:177–188
31. Higgins JP, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21:1539–1558
32. Higgins JP, Green S, eds (2011) Cochrane handbook for systematic reviews of interventions. Version 5.1.0. The Cochran Collaboration 2011. www.cochrane-handbook.org
33. Egger M, Smith GD, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. Br Med J 315:629–634
34. Egger M, Smith GD, Altman DG (2001) Systematic reviews in health care: meta-analysis in context. BMJ Publishing Group, London
35. Sutton AJ, Duval SJ, Tweedie RL, Abrams KR, Jones DR (2000) Empirical assessment of effect of publication bias on meta-analyses. Br Med J 320:1574–1577
36. Strotmeyer ES, Steenkiste AR, Foley TP Jr, Berga SL, Dorman JS (2003) Menstrual cycle differences between women with type 1 diabetes and women without diabetes. Diabetes Care 26: 1016–1021
37. Casey VA, Dwyer JT, Coleman KA, Krall EA, Gardner J, Valadian I (1991) Accuracy of recall by middle-aged participants in a longitudinal study of their body size and indices of maturation earlier in life. Ann Hum Biol 18:155–166
38. Ding EL, Song Y, Malik VS, Liu S (2006) Sex differences of endogenous sex hormones and risk of type 2 diabetes: a systematic review and meta-analysis. JAMA 295:1288–1299
39. Vikan T, Schirmer H, Njølstad I, Svartberg J (2010) Low testosterone and sex hormone-binding globulin levels and high estradiol levels are independent predictors of type 2 diabetes in men. Eur J Endocrinol 162:747–754
40. Zhu H, Shyh-Chang N, Segrè AV et al (2011) The Lin28/let-7 axis regulates glucose metabolism. Cell 147:81–94