BULISZAK, Agnieszka, BABCZYŃSKA, Monika, MARCJASZ, Piotr, BIOŁY, Anna, DRYJA, Patryk, BOCZAR, Agata, CHODKOWSKA, Ewa and BIELAS, Kinga. The Impact of Puberty Timing on Future Metabolic and Hormonal Disorder Risk. Quality in Sport. 2025;42:60439. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.42.60439
https://apcz.umk.pl/QS/article/view/60439

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).
The authors declare that there is no conflict of interest regarding the publication of this paper.
Received: 20.04.2025. Revised: 30.04.2025. Accepted: 01.06.2025. Published: 03.06.2025.

THE IMPACT OF PUBERTY TIMING ON FUTURE METABOLIC AND HORMONAL DISORDER RISK

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ABSTRACT:
Introduction and Objectives:

Puberty is occurring earlier across populations, raising concerns about long-term health effects. Early onset—marked by younger age at menarche in girls or early voice change in boys—has been linked to adverse metabolic outcomes, including type 2 diabetes mellitus (T2DM) [1]. This review explores how pubertal timing influences the risk of metabolic and hormonal disorders, focusing on T2DM.

Brief Literature Review:

Earlier puberty correlates with higher risks of obesity, insulin resistance, and T2DM [1]. Each one-year delay in menarche reduces T2DM risk by ~9%, independent of adult adiposity [2]. Girls with menarche ≤11 years and boys with early voice breaking show elevated T2DM odds [2]. Early puberty is also associated with higher adult BMI, gestational diabetes, and PCOS [1,13]. Mechanisms include childhood obesity, insulin resistance during puberty, and hormonal shifts [14]. Some effects persist beyond body weight influences [5,6].

Conclusions:

Early puberty is a marker—and possibly a mediator—of increased T2DM and hormonal disorder risk [1,2]. Pubertal timing may independently impact long-term health. Identifying at-risk youth could support early interventions. Further research should explore causal pathways and prevention strategies.

Keywords: puberty timing, menarche, type 2 diabetes, metabolic risk, insulin resistance, polycystic ovary syndrome, gestational diabetes

1. Introduction:

The timing of puberty – the transition from childhood to sexual maturity – varies widely among individuals and has shifted markedly over time [1]. Normal pubertal onset occurs between ~8–13 years in girls and 9–14 years in boys [1]. Over the past century, many populations have experienced a **secular trend toward earlier puberty**, as evidenced by declining ages at breast development and menarche in girls and earlier genital maturation in boys [1]. For example, a meta-analysis found that the average age at breast development in girls worldwide fell by about three months per decade from 1977 to 2013 [1]. In the United States, the mean age of menarche declined from ~13.3 years in the early 20th century to around 12.5 years in recent decades [1], with similar downward trends observed in countries across Asia, Europe, and Africa [1,9]. This acceleration of pubertal timing is commonly attributed to improved nutrition and **rising childhood obesity rates**, as well as

other factors like **endocrine-disrupting chemical exposures** and general health improvements [9]. These shifts in puberty timing have prompted concern because **puberty is a pivotal developmental window** that can have lasting effects on physiology. In particular, an **earlier onset of puberty** has been hypothesized to increase risks for various health problems later in life, including metabolic and hormonal disorders [1,9]. Epidemiologic studies have noted correlations between earlier pubertal maturation – such as a younger age at menarche in females or early voice breaking in males – and adverse outcomes like adult obesity, type 2 diabetes, cardiovascular disease, and even hormone-related cancers [1,9].

Type 2 diabetes (T2DM), a metabolic disorder characterized by insulin resistance and hyperglycemia, is a particularly significant outcome to consider given its high and growing global prevalence. If puberty timing influences T2DM risk, it could partly explain individual and population differences in diabetes incidence and might open new angles for early-life prevention strategies. Despite mounting evidence of an association between pubertal timing and later health, important **research gaps** remain. Many early studies were limited by small sample sizes or inadequate control for confounders (such as body mass index) [3]. Only in the last two decades have large prospective cohort studies and meta-analyses rigorously examined the link between puberty timing and adult diseases like diabetes [1,2] . Furthermore, most research has focused on **female puberty (age at menarche)** as an easily measurable marker, whereas analogous data on male pubertal timing have been scarcer. This leaves questions about whether the puberty–diabetes relationship is sex-specific or similar in boys (for whom markers like age at peak height velocity or voice change can be used). The **biological mechanisms** underlying any observed association are also not fully understood: Is early puberty directly contributing to metabolic dysfunction, or is it merely a **marker of underlying factors** (genetic, nutritional, or developmental) that drive both earlier maturation and diabetes risk? Lastly, it is unclear whether modifying pubertal timing is feasible or would confer health benefits – for instance, would preventing excessive weight gain in childhood (and thereby possibly delaying puberty) reduce future diabetes incidence? These uncertainties form the basis for our inquiry.

In this context, the objective of this paper is to **critically review and synthesize the evidence** on how the timing of puberty impacts the subsequent risk of metabolic and hormonal disorders, with a particular focus on type 2 diabetes. We aim to highlight consistent findings, discuss potential mechanisms linking puberty timing with metabolic health, and identify gaps for future research. Understanding this connection is important both scientifically – for insight into the developmental origins of metabolic diseases – and clinically, as it could help identify high-risk individuals early in life and inform preventive strategies.

2. Literature Review: Puberty Timing and Later Metabolic/Hormonal Disorders

2.1. Early Puberty and Metabolic Risk Factors

A wide range of studies has examined the health trajectories of individuals who mature earlier versus later. **Early puberty (precocious or toward the lower end of the normal age range)** has been consistently associated with a less favorable metabolic profile in adolescence and adulthood [1]. One of the most immediate links is with **adiposity**: children who enter puberty early tend to have a higher body mass index (BMI) and fat mass in later adolescence and adulthood [1]. A comprehensive 2024 review noted that early-developing children are more likely to become obese adults [1]. This is partly intuitive, since higher childhood adiposity can both accelerate pubertal onset and track into adult obesity. However, even after accounting for body weight, early pubertal timing itself appears to confer additional metabolic risks beyond obesity alone [2,5].

One important metabolic change during normal puberty is a transient decrease in insulin sensitivity. Healthy puberty is accompanied by a ~25–50% decline in insulin sensitivity (a physiologic “insulin resistance” of puberty), which typically resolves by the end of pubertal development [15]. In early-maturing children, this pubertal insulin resistance occurs at a younger age – often on a background of pre-existing high BMI or genetic predisposition – and may persist or exacerbate longer-term. Research shows that **hyperinsulinemia and insulin resistance are present in many youth with early or rapidly progressing puberty**. For instance, **girls with idiopathic premature adrenarche/pubarche** (appearance of pubic hair before age 8, a sign of early adrenal maturation) show elevated insulin levels during oral glucose tolerance tests and increased central adiposity

throughout puberty [14] These girls are comparatively insulin resistant despite often having a normal BMI, suggesting a unique metabolic derangement accompanying early hormonal maturation [14]. Such findings hint that early pubertal timing can disrupt normal metabolic homeostasis during a critical developmental window.

Beyond insulin, other hormonal changes in early puberty may predispose to metabolic problems. Early puberty entails prolonged exposure to **growth and sex hormones** during adolescence, which can affect body composition and organ development. Higher levels of estrogen (in girls) or testosterone (in boys) at younger ages might influence how muscle and fat are distributed. There is evidence that early-maturing girls have higher leptin levels and altered adipokine profiles, which could promote further fat gain and insulin resistance [14]. Additionally, growth hormone and IGF-1 (insulin-like growth factor-1) surge during puberty; in girls with early pubarche, IGF-1 levels are elevated, potentially compounding insulin secretion and ovarian androgen production [14]. Thus, the **endocrine milieu of early puberty** – characterized by relative hyperinsulinemia, increased IGF-1, and sex steroid changes – may set the stage for metabolic syndrome features.

2.2. Pubertal Timing and Type 2 Diabetes Risk

Type 2 diabetes (T2DM) is a central focus of research on puberty timing due to its strong links with obesity and insulin dynamics. A wealth of epidemiological data now supports a robust association between **earlier puberty and a higher risk of T2DM** in adulthood [1]. This relationship has been observed in diverse populations and appears to hold for both women and men.

In women, age at menarche (AAM) has been the primary measure of pubertal timing. Large cohort studies have consistently found that a younger **age at menarche is associated with a greater likelihood of developing T2DM** later on. One landmark analysis pooled data from two large U.S. cohorts (Nurses' Health Study I and II, >200,000 women) and reported a clear gradient of diabetes risk by menarche age [3]. Women who had menarche at age 11 or younger had about a 18–40% higher risk of T2DM compared to those who menstruated at age 13 (the reference category), even after adjusting for factors like childhood body shape and BMI at age 18 [3]. Conversely, those with later menarche (age 14 or 15) showed a trend toward lower diabetes risk (relative risk ~0.9, though not all estimates reached statistical significance) [3]. Importantly, in that study the association was strongest among younger adults and attenuated somewhat after accounting for adult BMI gain [3], suggesting part of the effect is mediated by obesity attained in the interim.

Another pivotal study is the **EPIC-InterAct project**, a large European prospective investigation across 8 countries. EPIC confirmed that **earlier menarche correlates with a higher incidence of type 2 diabetes**: women in the earliest menarche quintile (menarche at 8–11 years) had about a 70% higher risk of developing diabetes than those in the mid-range (menarche at 13 years) [4]. Each additional year of delayed menarche was associated with a modest reduction in adult BMI and significantly lower diabetes rates [4]. These findings align with numerous other cohorts in Europe, Asia, and the Americas linking early menarche to diabetes [1]. In a Korean study, for example, the prevalence of T2DM was higher among women with menarche before 12 years than in those after 14 [1]. A meta-analysis by Cheng et al. (2020) pooled 28 studies (over 1.2 million women) to quantify this relationship [2]. It concluded that **for each one-year increase in age at menarche, the relative risk of developing T2DM (or impaired glucose tolerance) dropped by approximately 9%** (RR 0.91 per year later) [2]. Conversely, women at the extreme of early menarche had significantly elevated risk – those with menarche in early puberty had roughly 1.4 times higher odds of T2DM than those with later puberty [2]. Notably, even after adjusting for adult adiposity, the association, though weakened, remained statistically significant: about a 3% risk reduction per year later menarche (pooled RR ~0.97 per year) persisted independent of BMI [2]. This suggests that **puberty timing itself has an influence on diabetes risk that is not entirely explained by body fatness** in adulthood. From a population standpoint, the meta-analysis estimated that in a contemporary Western population, around 5–13% of T2DM cases in women could be attributable to early menarche, depending on whether adiposity is accounted for [2]. **In men**, analogous investigations have been more recent but show parallel trends. Because boys lack a single clear pubertal event like menarche, studies use proxies such as self-reported age at voice breaking or physician-recorded age at peak height velocity (PHV). The **UK Biobank** study (over 500,000 UK adults) collected age at voice breaking in men and first menstruation in women, and found that **early-developing men were at increased risk for diabetes to a similar degree as early-maturing women** [5]. Men who reported voice breaking at a younger age (in the earliest 20% of the cohort, roughly before age 13–14) had ~25% higher odds of later-life T2DM compared to average-timing peers, even after adjusting for obesity and socioeconomic factors [1]. Another analysis from the Biobank illustrated a

U-shaped pattern: both the earliest and latest 20% for puberty timing carried higher disease risks than the middle, with **early puberty conferring about a 50% increase in relative risk for T2DM in both sexes** [5]. A focused longitudinal study in Sweden of 30,000 men using age at PHV (a precise pubertal marker) strengthens this evidence [6]. Men who hit their growth spurt fastest and earliest (around ages 9–13, indicating very early puberty) had **twice the risk of developing type 2 diabetes by mid-adulthood** compared to those who matured late (PHV at 15–18 years) [6]. This two-fold risk persisted even after controlling for BMI at age 8 (pre-puberty) and at age 20 [6], implying that early pubertal timing in males has a significant independent association with the onset. Moreover, the excess risk was most pronounced for relatively **early-onset T2DM** (diagnosed before the age of 57 in that study) [6]. Men with early puberty not only developed diabetes more frequently but also tended to develop it at younger ages, and they were more likely to require insulin treatment, reflecting greater disease severity [6]. This Swedish cohort concluded that about **15% of T2DM cases in men** could be theoretically prevented if those men had not undergone puberty so early [6].

Taken together, the epidemiological literature robustly indicates that **earlier pubertal timing elevates the risk of type 2 diabetes in later life** for both women and men. Later-than-average puberty, conversely, tends to be protective (with some nuances, as extremely late puberty might carry other health trade-offs, discussed below). The association has been replicated in numerous populations across North America, Europe, and Asia [1], making it a consistent finding. It is also **dose-dependent** to an extent – the farther from the population norm puberty occurs, the greater the deviation in risk. For instance, females in the bottom 5th percentile for menarche age have substantially higher diabetes risk than those in the middle, whereas a more modest increase is seen for those in the 20th percentile. Notably, these relationships often hold even after adjusting for **adult BMI**, **childhood BMI**, and other factors, though adjustments typically attenuate the strength of the association [2,3]. This suggests that shared factors (like adiposity) explain some, but not all, of the link between puberty timing and diabetes. We will explore these factors and mechanisms in the discussion.

2.3. Other Metabolic and Hormonal Outcomes Associated with Puberty Timing

While type 2 diabetes is a key outcome of interest, **puberty timing has been linked to a broader spectrum of metabolic and endocrine disorders**. Early menarche or precocious puberty can be viewed as a signal of an "adverse metabolic trajectory" beginning in childhood [6], which may manifest in several ways:

- **Obesity and Metabolic Syndrome:** As noted, early-puberty individuals often have higher adult BMI and adiposity [1]. They are more likely to meet criteria for metabolic syndrome (clustering of abdominal obesity, impaired glucose tolerance, hypertension, and dyslipidemia) in adulthood [1]. Some studies have found early menarche is associated with higher triglycerides and blood pressure and lower HDL cholesterol later in life [1,5], although these links are largely mediated by concurrent obesity. Early puberty may also contribute to **fat distribution changes** – for example, women with early menarche tend to have a higher waist-to-hip ratio (more central fat) as adults, compounding cardiovascular risk.

- **Cardiovascular Disease (CVD):** Given the ties to metabolic risk factors, it is not surprising that early puberty has been associated with elevated cardiovascular disease risk. Large cohort studies in women report that those with menarche before ~12 years have higher rates of coronary heart disease and stroke in later adulthood
  [1]. In the Million Women Study in the UK, for instance, women with menarche at age 10 had about 1.2-fold higher risk of heart disease and stroke compared to those at 13 years [1]. Early puberty in both sexes also correlates with higher odds of hypertension and impaired vascular function as adults [1,5]. These outcomes are interrelated with diabetes; early puberty's impact on CVD is partly via promoting diabetes and metabolic syndrome, but there may be independent pathways (e.g. hormonal effects on vascular development).

- **Gestational Diabetes and Reproductive Health:** In women, early menarche has been identified as a risk factor for **gestational diabetes mellitus (GDM)**, a form of glucose intolerance first recognized in pregnancy. A 2018 meta-analysis found that women who had menarche earlier had significantly higher odds of GDM compared to those with later menarche [1]. In fact, the association between early menarche and GDM risk appears dose-dependent, mirroring the pattern seen with type 2 diabetes [1]. This suggests a common biological link – possibly insulin resistance or ovarian function – tying early

reproductive maturation to glucose metabolism in pregnancy. Additionally, early menarche is associated with a higher likelihood of irregular menstrual cycles and anovulation in adolescence, which can presage conditions like polycystic ovary syndrome.

- **Polycystic Ovary Syndrome (PCOS):** PCOS is a hormonal disorder characterized by hyperandrogenism, ovarian dysfunction, and often insulin resistance. While full PCOS typically declares after puberty, there is evidence that **early pubertal events can increase PCOS risk**. Girls with **central precocious puberty** (onset of pubertal development before age 8 in girls) seem to have a higher prevalence of PCOS in later adolescence. One study found that among girls treated for idiopathic precocious puberty, **12% were diagnosed with PCOS by their mid-teens**, which was ~2.5 times the rate seen in age-matched peers [13]. Moreover, long-term follow-ups of girls with a history of premature pubarche (often an early sign of androgen excess) show they frequently develop PCOS features (such as irregular menses and hyperandrogenemia) after puberty [26]. The mechanistic link likely involves **insulin resistance driving excess ovarian androgen production**. Early pubertal insulin resistance and compensatory hyperinsulinemia can stimulate the ovaries and adrenal glands, promoting androgen excess and follicular arrest – hallmarks of PCOS [14,26]. Thus, **early puberty can be both a consequence and a contributor to the insulin–androgen cycle** that underpins PCOS. Conversely, later puberty (and menarche) might be protective against PCOS. Notably, many **daughters of women with PCOS** have early adrenarche or menarche, suggesting familial or genetic factors that simultaneously influence puberty timing and PCOS risk [14].

- **Other Endocrine Outcomes:** Early puberty has also been linked in some studies to a higher risk of hormone-sensitive cancers (like breast cancer, due to longer lifetime estrogen exposure) [9] and perhaps thyroid disorders (though data are limited). On the other hand, **very late puberty** or hypogonadism can carry risks such as reduced bone density (due to delayed estrogen/testosterone effects on bone accrual) and, as UK Biobank data indicated, possibly increased asthma and, in women, some CVD risk [5]. These outcomes, however, lie beyond the primary metabolic focus of this review.

In summary, the literature establishes puberty timing – particularly when it is on the early end of the spectrum – as a significant correlate of future metabolic and hormonal health. Early puberty is associated not only with higher risks of **type 2 diabetes** but also with **obesity, dyslipidemia, hypertension, gestational diabetes, and PCOS**, forming a constellation of interrelated outcomes. Many of these relationships show a gradient effect (earlier = higher risk) and persist to varying degrees even after controlling for confounders like BMI. This consistent pattern across studies lends credibility to the idea that puberty timing itself may play a role in **"programming" long-term metabolic risk**. The next section will discuss plausible biological mechanisms for this link and consider whether – and how – pubertal timing might be targeted or leveraged in interventions to reduce metabolic disease burden.

3. Discussion

The evidence reviewed above indicates a clear epidemiological link between puberty timing and later risk of metabolic and hormonal disorders. The **associations are strongest for early puberty**, which appears to set an individual on a trajectory of increased risk for obesity, insulin resistance, type 2 diabetes, and related conditions. A central question is: **Does early puberty cause these outcomes, or is it simply a marker of other factors that cause them?** The answer is likely a combination of both – with **shared underlying causes** (like genetics and early-life environment) and **direct causal influences** of pubertal processes on the body's metabolism. Here we discuss key mechanisms and considerations:

- **Shared Early-Life Determinants (Confounding and Mediation):** Children who experience earlier puberty often have pre-existing characteristics that predispose them to metabolic disorders. **Excess childhood adiposity** is a prime example. Higher BMI in childhood is a well-established accelerator of pubertal onset, especially in girls . The global rise in childhood obesity is thought to be a major driver of the secular trend toward younger puberties . At the same time, childhood obesity frequently tracks into adult obesity and directly increases diabetes risk. Thus, obesity is a confounding factor that links early puberty and diabetes. Indeed, many studies find that adjusting for BMI (in childhood or adulthood) attenuates the puberty–diabetes association [2,3]. In the Nurses' Health Study analysis, the relative risk of early menarche for T2DM dropped substantially when adult BMI gain was accounted for [2]. Similarly, Mendelian randomization analyses (using genetic variants as instruments for puberty timing)

suggest that once one controls for early-life adiposity, the direct effect of puberty timing on most cardiometabolic traits is modest . This implies that **much of the link is mediated by body weight and related factors established in childhood**. Other shared determinants include **socioeconomic status** (low-income conditions may lead to both faster maturation and higher disease risk due to diet and stress) and **nutrition in early life** (overnutrition or certain nutritional imbalances can advance puberty and program metabolism). However, even after accounting for known confounders, **residual associations persist**, which points to independent effects of pubertal processes. For example, the Cheng et al. meta-analysis found a continued 15% higher diabetes risk for early-menarche women versus later, even after BMI adjustment [2]. The Swedish boys' study saw a two-fold risk in early maturers remain after adjusting for childhood BMI [6]. And notably, UK Biobank analyses found that even **normal-weight individuals** who matured very early still had elevated risks of diabetes and heart disease [5]. Lead investigators of that study remarked that prior assumptions attributing the link solely to obesity were too simplistic, and that puberty timing itself, independent of weight, "carries these risks" [5]. This hints that **early puberty is part of an underlying phenotype** (potentially determined by genetics or developmental programming) that predisposes individuals to metabolic disease beyond just fat mass.

- **Hormonal and Developmental Effects of Early Puberty (Causal Pathways):** Puberty is a time of extensive hormonal change, and **timing might matter** because it alters the duration or sequence of exposure to key hormones during development. An early onset of puberty means a child's body transitions to an insulin-resistant, high-sex-hormone state sooner, at a time when other organ systems (like muscle, pancreas, and brain) are still maturing. The **pancreatic β-cells** may be forced to adapt earlier to increased insulin demand, potentially leading to β-cell stress or dysfunction over a longer period [1]. Likewise, **insulin resistance and impaired glucose tolerance** can appear transiently in early pubertal adolescents [1]; if puberty comes early and is superimposed on pre-existing insulin resistance (from obesity or genetics), it might accelerate the progression to chronic hyperglycemia. The review by Sun et al. noted that underlying mechanisms for the puberty–diabetes link likely involve such **glucose metabolism disturbances during adolescence, including impaired glucose tolerance and β-cell strain** [1]. Another pathway is through **organ growth and fat distribution**. Puberty usually leads to an increase in lean body mass (especially in boys) and a redistribution of fat (with girls gaining more fat relative to boys). If puberty occurs early, the hormonal triggers for fat deposition (e.g., estrogen's effect of increasing subcutaneous fat) kick in sooner, potentially resulting in a higher total fat mass by adulthood. Early estrogen exposure might also limit height growth (by causing earlier epiphyseal closure of growth plates), leading to shorter adult stature – and shorter stature has itself been linked to a higher T2DM risk, possibly due to fewer lean tissues like muscle and liver relative to weight. In boys, early androgens could lead to earlier muscle mass accrual, but if not matched with a healthy lifestyle, could also mean earlier cessation of growth and perhaps less muscle gained overall. The long-term impact of pubertal timing on **body composition** is complex: some data suggest earlier puberty yields slightly increased adult BMI and central fat even independent of childhood weight [1], which contributes to diabetes risk. Moreover, puberty timing might influence **behavioral and psychosocial factors** that indirectly affect metabolic health. For example, early-maturing girls may experience psychosocial stress, depression, or engage in earlier substance use and sexual activity [1]. Some studies indicate early menarche is linked to higher rates of adolescent depression and risk-taking behaviors. These factors could translate into poorer health habits (less exercise, unhealthful diet, etc.), thereby elevating obesity and diabetes risk. While harder to quantify, such **lifestyle and psychological mediators** are also part of the picture linking early puberty to adult health.
- **Genetic Pleiotropy:** Genetics play a significant role in pubertal timing – twin studies estimate ~50–80% of variation in age at menarche is genetically determined. It turns out that some genetic loci associated with earlier pubertal timing are also associated with higher BMI and increased risk of diabetes. For instance, variants in the **LIN28B gene** are linked to earlier puberty and have been associated with altered glucose metabolism. Genome-wide association studies (GWAS) have identified hundreds of genes related to menarche timing; many overlap with pathways for metabolism and adipose tissue function. This raises the possibility of **pleiotropy**: the same genetic factors that program an individual to develop earlier might also predispose them to insulin resistance or obesity. Mendelian randomization using genetic scores for puberty timing gives conflicting results – some analyses found that genetically earlier puberty leads to higher metabolic risk markers , while others suggest the effect is small after accounting for BMI . Nevertheless, genetics likely accounts for some of the correlation. It also means puberty timing could serve as a **marker for inherent metabolic risk** – e.g., a girl with very early menarche may carry a genetic load that also puts her at risk for diabetes, even if the early

menarche itself is not directly causing the diabetes. Disentangling genetic correlation from causation is an active area of research.

- **Sex Differences:** Interestingly, while early puberty impacts both sexes, there may be **differences in sensitivity and outcomes between girls and boys**. The health impact of early puberty has generally been found to be more pronounced in girls [1]. This could be because menarche is a more extreme landmark (with associated physiological changes like menstruation and cyclic estrogen exposure) and because girls tend to accumulate more fat during puberty than boys. Also, conditions like PCOS and gestational diabetes uniquely affect females. Boys with early puberty do show higher diabetes and CVD risk, but some studies suggest the gradient is a bit steeper in females. Additionally, late puberty might have opposite effects in men vs women for certain outcomes – e.g., UK data showed late-maturing men had *lower* heart disease risk, whereas late-maturing women had *higher* heart disease risk [5]. The reasons are unclear but might relate to hormonal differences (testosterone vs estrogen timing) or societal factors. Nonetheless, for type 2 diabetes, both genders seem to be adversely affected by earlier maturation. Future research should continue to explore these sex-specific nuances, as they might inform tailored interventions (for instance, monitoring early-maturing girls for PCOS and early-maturing boys for early-onset diabetes signs).
- **Public Health and Clinical Implications:** Recognizing early puberty as a risk factor for metabolic disease has practical implications. First, **pubertal timing is an easily observable trait** that could help flag at-risk youth. Pediatricians and endocrinologists monitor pubertal development; those who enter puberty remarkably early (e.g. in the lowest decile of age) could be counseled about potential long-term health considerations. It does *not* mean every early-developing child will develop diabetes – most will not – but it adds to their risk profile. Encouraging a healthy lifestyle (diet and exercise) is especially vital in such individuals to counteract the metabolic tendencies. For example, a girl with menarche at age 10 who is already overweight might merit more aggressive obesity prevention efforts to mitigate her elevated risk of future T2DM [7]. There is also interest in whether treating **precocious puberty** (with medications like GnRH analogues to delay progression) has any long-term metabolic benefit. Some evidence suggests that normalizing the timing of puberty in girls with central precocious puberty can improve their adult height and perhaps reduce the risk of ovarian cysts, but effects on diabetes or obesity rates remain uncertain and understudied. This could be a valuable area of follow-up research: do women who underwent therapy for precocious puberty have a lower metabolic disorders than similar women who went through early puberty untreated? The answer could inform treatment decisions. From a population perspective, the connection between puberty timing and diabetes underscores the importance of **childhood obesity prevention**. Preventing excessive weight gain in childhood might delay puberty (keeping it in a healthier age range) and simultaneously reduce metabolic disease risk – a double benefit. However, as the Biobank authors cautioned, **altering puberty timing is not straightforward,** and "avoidance or treatment of abnormal puberty timing will not invariably have widespread benefit" on its own [5]. It should rather be seen as one piece of the risk puzzle.
- **Future Research Directions:** Despite significant advances, some key questions remain. We need a better understanding of the **biological mechanisms** – for instance, how exactly do early estrogen or androgen exposure affect pancreatic development or muscle insulin signaling? Animal models could help clarify if inducing early puberty in rodents leads to diabetes-like changes later, thus establishing causality. Additionally, research should delve deeper into the **role of endocrine disruptors and other environmental factors**. If chemicals or stressors that shift puberty earlier are also diabetogenic, reducing such exposures could be protective. Large, long-term follow-ups are needed to see if the recent trend toward earlier puberty will indeed translate into higher rates of young-onset T2DM in the coming generations. Another gap is **male puberty timing**. Studies like Ohlsson et al. (2020) have started to address this, but we lack as rich a literature for boys as for girls. Routine data on age at voice breaking or peak height velocity could be collected in more cohorts. Moreover, **interventional studies or natural experiments** would be highly informative. For example, does slowing puberty in extremely early-developing kids (via medical therapy) alter their metabolic outcomes? Or conversely, do conditions that delay puberty (like undernutrition or intensive athletic training in adolescence) lower diabetes rates (bearing in mind that such delays can have other downsides)? Answering such questions would strengthen the causal inference.

Finally, investigating **gene-environment interactions** could illuminate why some early-maturing individuals escape metabolic disease while others do not. Perhaps certain genotypes confer resilience or vulnerability to the metabolic strain of early puberty. Understanding this could refine risk stratification – e.g., identifying which early-puberty children are at *especially* high risk and might benefit from prophylactic

interventions such as metformin (which has been trialed in adolescents with risk factors to improve insulin sensitivity).

4. Conclusion

Puberty timing is emerging as an important factor in lifelong health, and the evidence is particularly compelling for its impact on metabolic and endocrine disorders like type 2 diabetes. An abundance of studies indicates that **earlier pubertal onset is associated with higher risks of obesity, insulin resistance, and diabetes in adulthood** [1]. Girls who reach menarche early and boys who mature early consistently show a greater propensity for T2DM later on, even when controlling for many other variables. Although part of this link is explained by shared influences (like childhood weight), a body of research suggests that **puberty timing per se plays a role** in shaping an individual's metabolic trajectory [2]. Early puberty can be viewed as a marker of an "at-risk" metabolic phenotype, one that warrants attention and possibly early lifestyle intervention. From a public health standpoint, ongoing trends toward earlier puberty worldwide could contribute to a rising burden of diabetes and metabolic syndrome, making this topic highly relevant. Conversely, **later puberty (within a normal range) appears to be metabolically protective**, aligning with lower rates of diabetes and better cardiovascular profiles in those individuals [2].In addition to diabetes, puberty timing has been linked to other hormonal disorders: early puberty in girls is tied to higher odds of **gestational diabetes** [1] and **PCOS** [13], conditions that have significant health implications for reproductive-age women. These connections reinforce the concept that the tempo of sexual maturation can influence the endocrine system in enduring ways.

Clinicians should be aware of these patterns. Pediatricians observing **precocious or early-normal puberty** might consider counseling families on healthy lifestyles and monitoring cardiometabolic indicators as the child grows. For adult practitioners, a patient's history of very early puberty could be a clue prompting vigilant screening for diabetes or dyslipidemia at younger ages. Importantly, early puberty is **not destiny** – it is a risk factor, not a guarantee of disease. Many individuals with early menarche or voice change never develop metabolic problems, especially if they maintain healthy behaviors. Thus, puberty timing should be integrated into a multifactorial risk assessment.

For future research, several directions are key. Longitudinal studies that follow children from pre-puberty into adulthood can help disentangle causality and identify critical periods for intervention. Further exploration of the **biological mechanisms** linking the brain's pubertal timing signals with peripheral metabolism will deepen our understanding – for example, the role of hypothalamic neurons that regulate both puberty (GnRH release) and energy balance. Genetic studies, including polygenic risk scores for puberty timing and diabetes, could clarify shared pathways. And intervention trials (even small-scale or mechanistic ones) could test whether modifying pubertal timing or addressing its hormonal consequences (such as using insulin-sensitizing agents during puberty) can improve outcomes.

In conclusion, accumulating evidence demonstrates that **the timing of puberty has a measurable impact on the risk of future metabolic and hormonal disorders**. Early pubertal timing, in particular, acts as a red flag for heightened diabetes risk and related metabolic derangements, whereas later timing tends to be protective. This insight bridges pediatrics and chronic disease epidemiology, illustrating how events in early life can shape health decades later. It underscores the importance of a life-course approach to disease prevention – one that might one day incorporate pubertal development as a factor in stratifying risk and tailoring early interventions. By addressing underlying causes like childhood obesity and by closely monitoring those who mature fastest, we may reduce the burden of diabetes and improve metabolic health in the population. Continued research at the intersection of developmental endocrinology and metabolic disease will be crucial to translate these findings into effective prevention and treatment strategies for future generations.

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All authors have read and agreed with the published version of the manuscript.

FUNDING STATEMENT
This research received no external funding.

INSTITUTIONAL REVIEW BOARD STATEMENT
Not applicable.

INFORMED CONSENT STATEMENT
Not applicable.

DATA AVAILABILITY STATEMENT
Not applicable

ACKNOWLEDGEMENTS
Not Applicable.

CONFLICT OF INTEREST
The author declares no conflict of interest.

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