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Review

The association between adverse childhood experiences (ACEs) and gestational diabetes mellitus (GDM): A systematic review and *meta*-analysis

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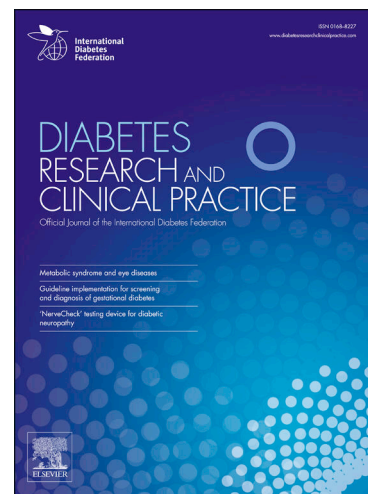
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The Association Between Adverse Childhood Experiences (ACEs) and Gestational Diabetes Mellitus (GDM): A Systematic Review and Meta-analysis

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Abstract

Gestational diabetes mellitus (GDM) has consequences for maternal and offspring health. Adverse childhood experiences (ACEs) contribute to GDM risk, but findings have been inconsistent. We synthesised evidence using a systematic review and meta-analysis of observational studies on ACEs before age 18 and GDM, including dose-response effects. Nine databases were searched from inception to 30 May 2025 based on a PROSPERO-registered protocol (CRD420251035754). Studies without extractable estimates or assessing diabetes not restricted to gestational onset were excluded. Two reviewers independently screened studies, extracted data, and assessed risk of bias using ROBINS-E. Random-effects models pooled adjusted odds ratios (aORs), with dose-response analyses using the Greenland-Longnecker method. Thirteen studies met eligibility criteria, 11 contributed to meta-analysis ($n = 326,797$). ACE exposure was associated with higher odds of GDM (aOR 1.15, 95% CI 1.12–1.18; $I^2 = 0\%$). A cumulative dose-response effect was observed, with each additional ACE increasing GDM odds (aOR 1.13, 95% CI 1.08–1.19). This study extends prior work by incorporating dose-response modelling, updated pooled estimates from recent cohorts, a pregnancy-focused risk window, and consideration of mediating and moderating pathways. Overall, ACEs are associated with increased risk of GDM, supporting a life-course approach to maternity care.

Keywords: adverse childhood experiences; gestational diabetes mellitus; early-life adversity; childhood trauma; pregnancy outcomes

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1. Introduction

Gestational diabetes mellitus (GDM), defined as glucose intolerance first identified during pregnancy,[1] affects 14% of pregnancies worldwide.[2, 3] Its prevalence has increased over the past two decades,[4] driven by demographic shifts, widening inequities, and improved detection.[5,6] Previously thought to fully resolved after birth, it is now clearly recognised that GDM is an independent risk factor for type 2 diabetes mellitus (T2DM) and cardiometabolic disease in women.[7,8] Furthermore, it is also associated with adverse metabolic and neuro-behavioural outcomes in the offspring.[9-11] Pregnancy has therefore been described as a physiological stress test that can reveal underlying metabolic susceptibility.[9]

Psychosocial determinants are increasingly recognised as important contributors to metabolic health alongside traditional biomedical factors.[12] Adverse Childhood Experiences (ACEs), such as abuse, neglect, or household dysfunction before age 18,[13] are a common form of early-life stress. Globally, most adults report at least one ACE,[14–16] with higher prevalence among socioeconomically disadvantaged groups and those facing structural adversity.[17–19] Increases in reported ACEs may reflect both greater awareness and widening social inequities.[20,21]

ACEs are associated with long-term alterations in stress-responsive systems,[22–24] including dysregulation of the hypothalamic–pituitary–adrenal axis (HPA) and low-grade inflammation,[25–28] which overlap with biological pathways implicated in insulin resistance and GDM.[4] Evidence suggests that early-life adversity may shape cardiometabolic risk across the life course,[29–31] while pregnancy represents a physiological context in which these vulnerabilities may be amplified. The extent to which these processes influence GDM remains incompletely understood.

Empirical findings on the association between ACEs and GDM have been inconsistent. Some studies report increased risk among women exposed to childhood adversity,[32] while others show attenuated or null associations after adjustment for key confounders.[33] Existing reviews have examined ACEs in relation to broader perinatal or cardiometabolic outcomes, limiting detailed exploration of GDM-specific pathways.[13,34] In parallel, evidence from systematic reviews on ACEs and T2DM demonstrates a long-term metabolic dysregulation across the life-course,[3] while GDM is a known risk factor for subsequent T2DM.[7] Taken together, these findings suggest a potential continuum linking ACEs, GDM, and later-life metabolic disease. However, a focused synthesis quantifying the ACEs-GDM association and examining dose-response relationship remains limited. This study addresses this gap by isolating GDM as a primary outcome and integrating a life-course perspective.

This study aimed to systematically review and meta-analyse evidence on the association between maternal ACEs exposure and GDM, quantify dose–response relationships, and summarise psychosocial and physiological factors reported across studies that may shape this association.

2. Methods

2.1 Data sources

This systematic review and meta-analysis followed PRISMA 2020 guidelines and was registered with PROSPERO (CRD420251035754). Methodological considerations were guided by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines. The protocol is available online (<https://www.crd.york.ac.uk/PROSPERO/view/CRD420251035754>).

We searched nine databases from inception to 30th May 2025 (MEDLINE, Embase, PsycINFO, CINAHL, Scopus, Web of Science, Psychiatry Online, Global Health, and MIDIRS) using terms related to ACEs, trauma, early-life stress, and GDM. Equivalent search strategies were adapted for each database (Table S1). Additional studies were identified through reference list screening. Grey literature was explored via WorldCat and the Conference Proceedings Citation Index.

Eligible studies were peer-reviewed quantitative observational designs (cohort or cross-sectional) that examined ACEs before age 18 and reported GDM diagnosis. Studies had to present an effect estimate (OR, relative risk [RR], or hazard ratio), or sufficient data to calculate one. Exclusion criteria were qualitative studies, conference abstracts without full data, non-English reports, and studies examining diabetes not restricted to gestational onset. Inclusion decisions and reasons for exclusion are detailed in the PRISMA flow diagram (Figure 1).

Two reviewers (SNF and MB) independently screened titles, abstracts, and full texts in Covidence, resolving disagreements through discussion or consultation with a third reviewer (SB).

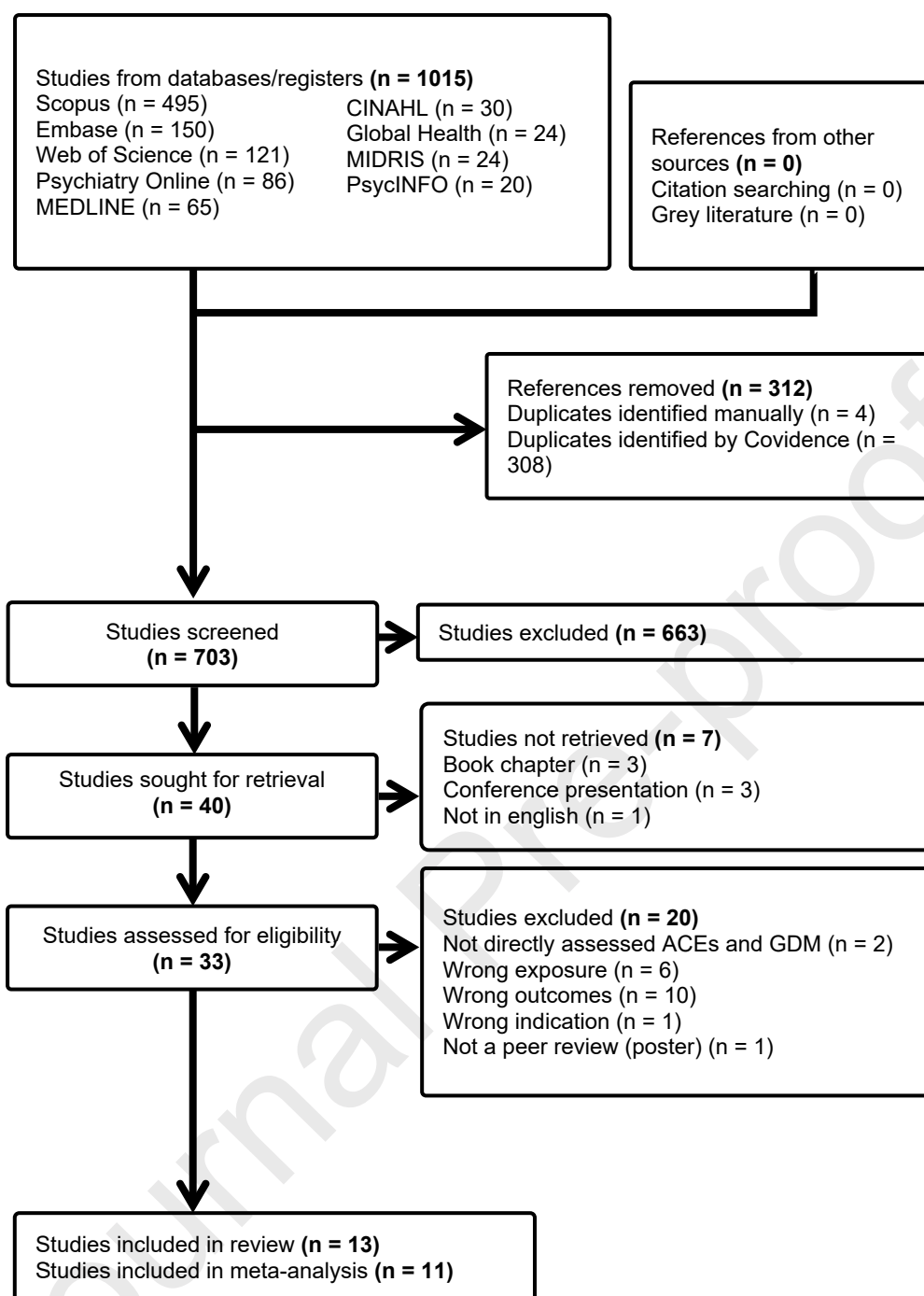


Figure 1. PRISMA diagram illustrating the study selection process

2.2 Data extraction and risk-of-bias assessment

Data extraction was conducted by one reviewer using a standardised form and independently verified by a second reviewer. Extracted variables included study design, sample characteristics, ACE assessment, GDM diagnostic criteria, covariate adjustment, and effect estimates. When multiple estimates were available, most adjusted estimates were used. Studies were included if sufficient information was provided in the main text or supplementary materials to facilitate calculation, including raw counts to reconstruct 2×2 tables. Duplicate data from overlapping cohorts were

resolved by retaining the study with the largest or most complete dataset. Where information was unclear or missing, corresponding authors were contacted; studies with unresolved gaps were retained qualitatively but excluded from quantitative pooling.

Risk of bias was assessed independently by two reviewers using the ROBINS-E tool,[35] across domains of confounding, exposure classification, participant selection, missing data, outcome measurement, and selective reporting. Ratings reflected the highest-risk domain. Disagreements were resolved by consensus.

2.3 Data analysis

The primary outcome was the association between any ACE exposure (≥ 1 ACE vs none) and GDM, expressed as pooled aORs. Secondary outcomes included high vs low exposure and dose-response effects per additional ACE. Study-specific cut-offs were harmonised by classifying low ACE exposure as 0–1 ACEs and high exposure as ≥ 2 or ≥ 3 ACEs, depending on each study's categorisation. Because the included studies used different ACE measurement tools and reporting formats (e.g., dichotomous any vs none, categorical low vs high, or continuous score), studies were grouped into three comparable analytical subsets (Figure 2).

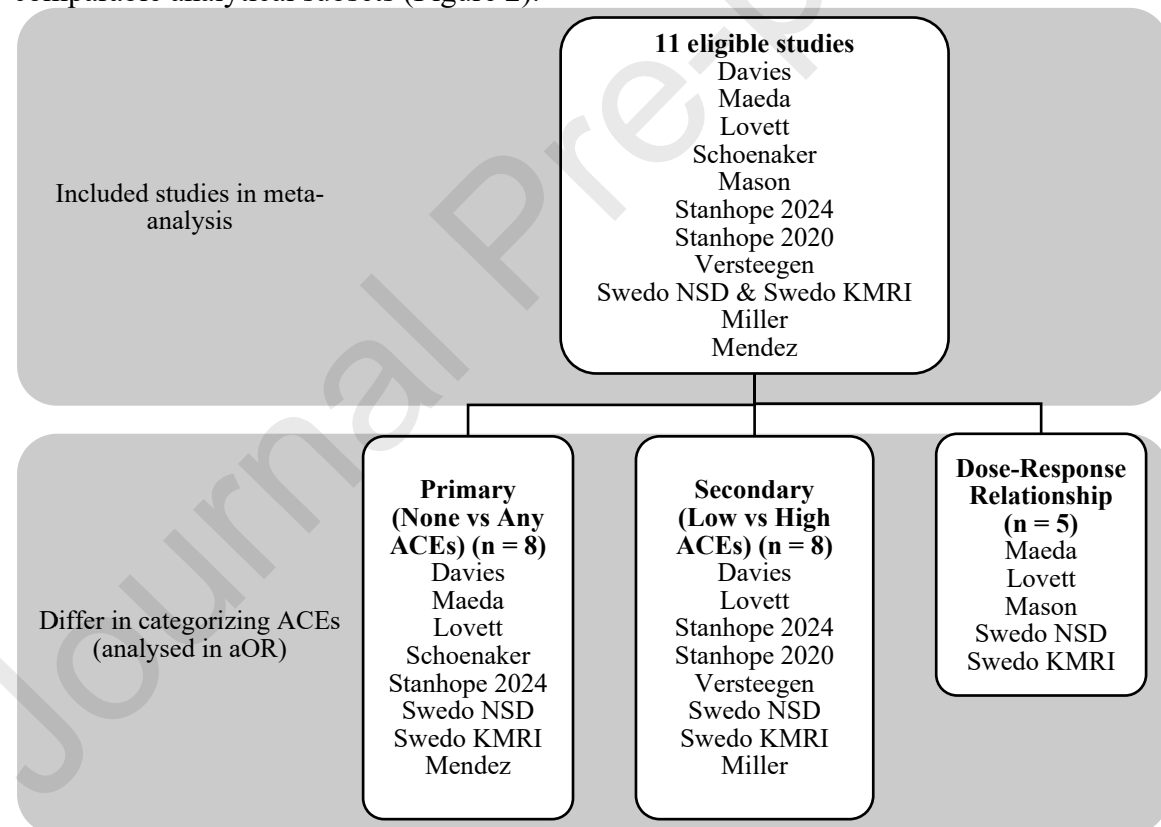


Figure 2. Flow diagram of included studies for the primary, secondary, and dose-response meta-analyses.

Effect estimates from 11 studies,[32,33,41-46,48,49,51] were eligible for inclusion in the meta-analysis, as shown in the appendix (Table S3 and S4). One study by Swedo et al.[48] reported findings for two distinct populations: North and South Dakota (NSD) and Kansas, Michigan, and Rhode Island (KMRI), which were treated as separate estimates.

Random-effects meta-analysis was conducted in R (version 4.0.2) with the metafor package.[36] Dose-response analysis applied the Greenland and Longnecker method via dosresmeta.[37] Heterogeneity was quantified with I^2 and Cochran's Q.[38]

Prespecified subgroup analyses examined study design (prospective vs retrospective), country income level (high-income (HIC) vs low- and middle-income country (LMIC)), and risk-of-bias category (low, medium, high). However, because all included studies were conducted in HIC settings, the prespecified subgroup analysis by country income level could not be performed. We instead examined population risk profile: general vs at-risk population (e.g., low-income clinics, mental health referrals, or adversity-exposed groups) as this better reflected variation across studies.

A narrative synthesis was conducted to summarise potential psychosocial and biological moderators and mediators. Sensitivity analyses omitted one study at a time ("leave-one-out"). Publication bias was assessed using funnel plots and Egger's regression.[39] Evidence certainty was evaluated using GRADE.[40]


3. Results



3.1 Study characteristics



The search identified 1015 records, of which 13 studies met inclusion criteria. Eleven studies were included in the meta-analysis, comprising 326,797 participants (Figure 1). Studies were published between 2016 and 2025, and most were conducted in high-income countries (HICs), primarily the USA ($n = 8$). [33,43,45,46,48-51] Study characteristics are summarised Table 1.


ACEs were most commonly assessed using the CDC–Kaiser ACE-10 questionnaire ($n = 5$),[33,46,49-51] although several studies used the culturally-modified version,[32,42,47] or different instruments. Risk of bias was generally moderate, mainly reflecting retrospective ACE reporting and sampling limitations (Supplementary Table S2).



Table 1. Study Characteristics

Authors	Country	Participants N = 335,293	Study Design	Study Overviews	Adjustment	ACEs tools	Overall Outcomes	Meta-Analysis	Overall risk of bias
<i>Davies et al. 2024.⁴¹</i>	Denmark	208,207	Pro-spective cohort	<p>Ethnicity: predominantly European origin,</p> <p>SES: high income and education level</p> <p>Parity: Nulliparous,</p> <p>Mean maternal age: 27.1 (low adversity) vs 24.1 (high adversity)</p> <p>ACEs prevalence: 52%</p> <p>GDM prevalence: 2.6%</p>	Maternal age, SGA, parental education, birth year	Administrative records, maternal questionnaires, and child reports from DANLIFE to construct domains of adversity.	Any adversity (vs. low) associated with higher GDM risk, but increasing adversity does not show a linear or graded increase in risk beyond a certain point.	Included	


<i>Maeda et al. 2024.</i> ⁴²	Japan	5,444	Cross-sectional	<p>Ethnicity: Japanese</p> <p>SES: high income and education level</p> <p>Mean maternal age: ~32 years old</p> <p>ACEs prevalence: 6.9%</p> <p>GDM prevalence: 5.8%</p>	Parity, maternal age at delivery, maternal pre-pregnancy BMI, household income, maternal academic backgrounds, smoking status, gestational weight gain	ACE-J	The highest GDM risk was in the 1 ACE group, showing possibility of buffer effects (e.g. support from welfare system).	Included	
<i>Lovett et al. 2024.</i> ⁴³	US	34,879	Prospective cohort	<p>Ethnicity: predominantly NHW</p> <p>SES: College or associate degree (34%), middle income (41%), never smoke (58%)</p> <p>Parity: 2nd (46%)</p> <p>Median age: 40-50s</p>	Age at baseline, race and ethnicity, childhood SES	Brief Betrayal Trauma Survey (BBTS)	22% increase in the risk for GDM was observed among women with a history of any trauma in early life. The high trauma class had nearly double the risk of GDM compared to the low trauma group; moderate was second.	Included	


				ACEs prevalence: 67%					
				GDM prevalence: 4.1%					
<i>Schoenaker et al. 2019.</i> ³²	Australia	6,317	Pro-spective cohort	Ethnicity: predominantly Australian born (White) SES: highly educated Parity: nulliparous 88.7% Mean maternal age: ~28 years ACEs prevalence: 45.3% GDM prevalence: 8%	Family history of diabetes, age at menarche, PCOS, preconception BMI, diet quality, parity, maternal age, and antenatal depression.	Modified CDC–Kaiser ACE-10 into Custom 9-item questionnaire (covering common ACE domains)	The association between ACEs and a greater GDM risk was confined to pregnancies where the mother had symptoms of depression before conceiving; a dose-response pattern was also observed in this group.	Included	
<i>Mason et al. 2016.</i> ⁴⁴	UK	45,500	Pro-spective cohort	Ethnicity: predominantly NHW Mean maternal age: 28 years	Demographics (maternal age, birth year, race), SES (parental education, occupation, home ownership), and health history (parental diabetes,	Revised Conflict Tactic Scales; sexual abuse screening	A statistically significant link emerged between a history of childhood physical and sexual abuse and an increased GDM risk. This risk was greatest for women exposed to	Included	




				<p>SES: mean over 12 years of education</p> <p>Parity: mean 2.3</p> <p>Physical abuse: 53%</p> <p>Sexual abuse: 32.7%</p> <p>GDM prevalence: 5%</p>	child's body size at age 5).		both severe physical and forced sexual abuse, and a graded, dose-response relationship was also observed for physical abuse.		
<i>Stanhope et al. 2024.</i> ⁴⁵	US	1,033	Pro-spective cohort	<p>Ethnicity: white (53.8%) and black (46.2%)</p> <p>SES: predominantly 12-15 years of school, and unmarried (73.1%)</p> <p>Parity: predominantly nulliparous</p> <p>ACEs prevalence: 2.6%</p>	Parental education level, race, maternal age during pregnancy, and parity.	Childhood Family Environment Scale (CFE)	A statistically significant link emerged between higher childhood abuse scores and an increased likelihood of GDM, with the odds of GDM rising by 30% for every point increase on the abuse subscale.	Included	

GDM prevalence: 13.1%									
<i>Stanhope et al. 2020.</i> ⁴⁶	US	2319	Cross-sectional	<p>Ethnicity: Hispanic / Latina women</p> <p>SES: predominantly greater than high school graduates, and never smokes (72.6%)</p> <p>Parity: mean 2.9</p> <p>Mean maternal age: 46.9 years</p> <p>ACEs prevalence: 77.4%</p> <p>GDM prevalence: 9.2%</p>	Childhood SES, including education, race, age at US arrival, and migration status.	CDC-Kaiser ACE-10	No significant association between ACEs and GDM was identified	Included	
<i>Versteegen et al. 2021.</i> ³³	US	266	Pro-spective cohort	<p>Ethnicity: NHW (52.4%)</p> <p>SES: predominantly low-income (16%), post-high school</p>	Age, BMI	CDC-Kaiser ACE-10	No significant relationship between ACEs and GDM both for continuous and categorical ACEs.	Included	

				graduates (62%), and unmarried (62.4%)					
				ACEs prevalence: 70.6%					
				GDM prevalence: 8.3%					
<i>Imanishi et al. 2025.</i> ⁴⁷	Japan	5693	Retro-spective cohort	Ethnicity: Japanese	-	ACE-J	No association between ACEs and GDM nor linear or graded increase of GDM risk with greater ACEs exposure.	Excluded from meta-analysis. Reason: double data possibility with Maeda et al.	●
				SES: predominantly high income					
				Parity: nulliparous					
				Mean maternal age: 32 years					
				ACEs prevalence: 37.8%					
				GDM prevalence: 5.6%					
<i>Swedo et al. 2023.</i> ⁴⁸	US	14510	Cross-sectional	Ethnicity: predominantly NHW	Age, race / ethnicity, marital status, parity,	8 items Behavioral Risk Factor	There is a significant association between ACEs and GDM	Included	●

			<p>SES: high school or higher</p> <p>Maternal age: predominantly 25-34 years</p> <p>Parity: predominantly multiparous</p> <p>ACEs prevalence: 51.3%</p> <p>GDM prevalence NSD: 10.3%</p> <p>GDM prevalence KMRI: 9%</p>	education, and insurance status.	Surveillance System (BRFSS)	especially at higher exposure.			
<i>Miller et al. 2021.</i> ⁴⁹	US	1274	Cross-sectional	<p>Ethnicity: White (58.8%)</p> <p>SES: no data</p> <p>Mean maternal age: 32-33 years</p> <p>Parity: predominantly nulliparous</p>	Maternal age, insurance, marital status, tobacco use, chronic medical conditions, and obesity.	CDC-Kaiser ACE-10	No statistically significant association between ACEs and GDM, while GDM prevalence appeared higher in group with higher ACEs exposure (7.4% vs 6.7%), the trend was weak and insignificant.	Included	

							ACEs prevalence: 93%		
							GDM prevalence: 6.8%		
<i>Jasthi et al. 2023.</i> ⁵⁰	US	192	Retro-spective cohort	<p>Ethnicity: black (91.7%)</p> <p>SES: high school or higher graduate (75.6%), low-income women referred to a specialist in mental health case management to elevated psychosocial risk</p> <p>Mean maternal age: 25.5 years</p> <p>Parity: mean 3.2</p> <p>ACEs prevalence: 47.4%</p> <p>GDM prevalence: 7.3%</p>	-	CDC-Kaiser ACE-10	No significant association was found between ACEs and GDM. While there was a slight, non-significant increase in GDM cases at higher levels of ACE exposure, the magnitude of this difference was minor	<p>Excluded from meta-analysis.</p> <p>Reason: not enough data, the number of GDM cases is too low.</p>	

<i>Mendez et al. 2024</i> ⁵¹	US	1163	Pro-spective cohort	<p>Ethnicity: 45% African American, 35% White, 16% Hispanic</p> <p>ACEs prevalence: 48%</p> <p>GDM prevalence: 5.9%</p>	Age, education, Medicaid status at delivery, marital status, race, employment status, tobacco use during pregnancy, BMI, parity, and care group.	CDC-Kaiser ACE-10	No significant association for the general exposure to ACEs, however those with both childhood abuse and high work stress had nearly 4 times the odds of developing GDM.	Included		
									Low risk	
									Moderate risk	
									High risk	

SES: Socioeconomic status, SGA: Small for gestational age, BMI: body mass index, DANLIFE: the DANish Life-course Cohort, ACE-J: Culturally adapted version of the CDC-Kaiser ACE-10 questionnaire; NHW: Non-hispanic white, PCOS: Poly-cystic ovarian syndrome

3.2 Meta-analysis results

In the primary analysis (eight studies),[32,41-43,45,48,51] exposure to any ACE was associated with increased odds of GDM (pooled aOR 1.15, 95% CI 1.12–1.18; $I^2 = 0\%$; Figure 3a). In the secondary analysis (eight studies),[33,41,43,45,46,48,49] high ACE exposure was associated with higher odds of GDM compared with low exposure (pooled aOR 1.29, 95% CI 1.08–1.53; $I^2 = 46.9\%$; Figure 3b).

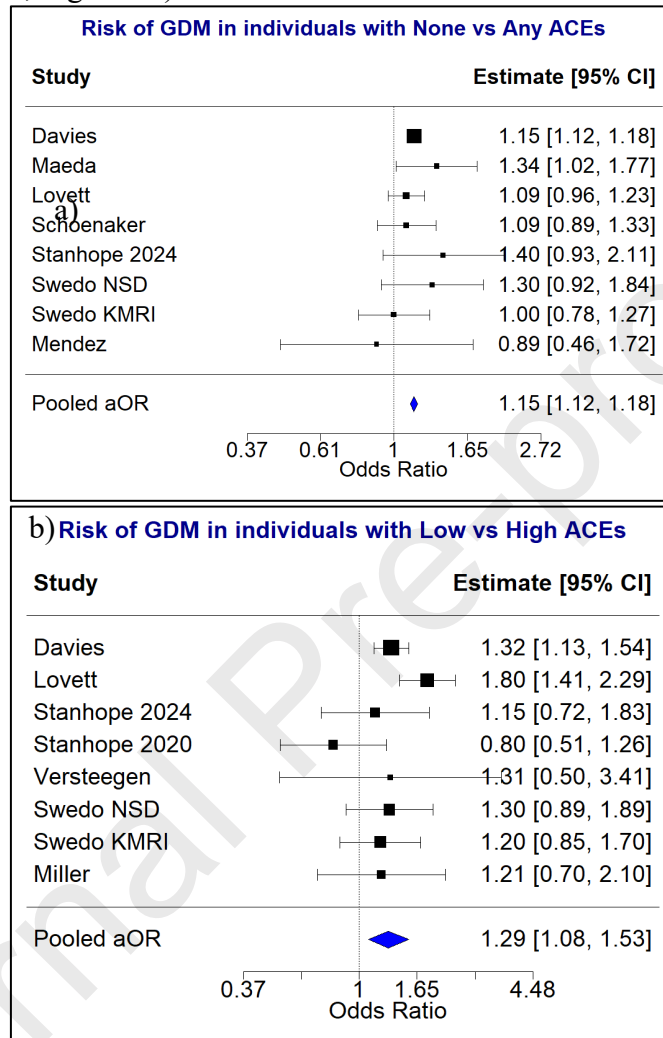


Figure 3. Risk of GDM in individuals with:
a) No ACE vs Any ACEs and a) Low ACEs vs High ACEs

Dose–response modelling, based on five studies,[42–44,48] demonstrated a cumulative association, with increasing odds of GDM per additional ACE (pooled aOR 1.13, 95% CI 1.08–1.19; $I^2 = 25.6\%$; Figure 4). Effect estimates were consistent in direction across studies, although confidence intervals varied according to study size and exposure categorisation.

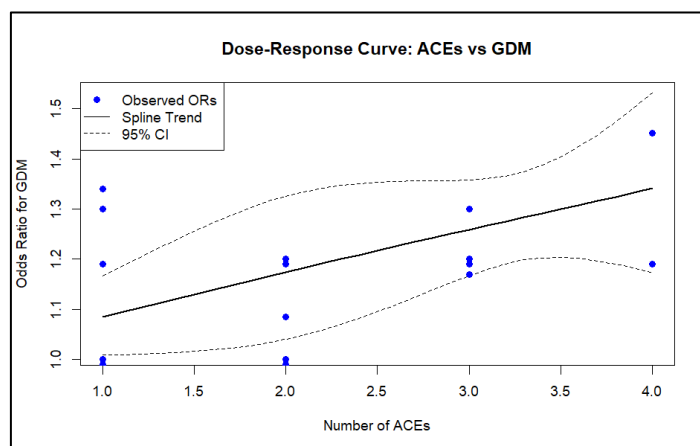


Figure 4. Dose-Response Relationship of ACEs and GDM

3.3 Heterogeneity, sensitivity, and certainty of evidence

Subgroup analyses for the primary outcome showed no statistically significant differences by study design (prospective vs retrospective), population risk profile (general vs at-risk populations), or risk-of-bias category (all $p > 0.05$; Supplementary Table S5). For the secondary analysis, moderate heterogeneity was observed, with studies rated as having some concerns contributing most to between-study variability.

Sensitivity analyses indicated that pooled estimates were robust to exclusion of individual studies (Supplementary Figures S1 and S3). No small-study effects were detected (Egger $p > 0.10$; Supplementary Figures S2 and S4). Overall certainty of evidence for the primary and secondary analyses was rated as moderate using GRADE criteria (Supplementary Table S7).

4. Discussion

4.1 Main findings

This systematic review of 13 studies (11 meta-analysed) provides evidence for a significant, dose-dependent association between maternal ACEs and GDM. Exposure to any ACE increased GDM odds by 15%, with risk rising cumulatively for each additional ACE. These findings support a cumulative-risk model consistent with allostatic load theory,[53] in which chronic stress exerts physiological strain revealed during the metabolic challenge of pregnancy.[54]

The associations were consistent across analytical approaches and remained robust in sensitivity analyses, despite heterogeneity in study design and exposure assessment. The absence of detectable small-study effects suggests that the pooled estimates are unlikely to be driven by selective publication. While effect sizes were modest, their consistency across large population-based cohorts underscores their public health relevance, particularly given the high global prevalence of both ACE exposure and GDM.[2-4,14-16]

The pooled estimates are broadly consistent with previous reviews of ACEs and adverse pregnancy outcomes, which reported increased risk of metabolic-related complications with

similar effect sizes.[14, 34] However, these reviews treated GDM as part of composite outcomes, limiting interpretation of GDM-specific pathways. By isolating GDM as the primary outcome, this study provides more precise evidence of a dose–response relationship, supporting a cumulative biological embedding mechanism.

These findings also align with evidence linking ACEs to T2DM,[7] where early-life adversity is associated with long-term metabolic dysregulation. Pregnancy may represent a clinical context in which this vulnerability becomes apparent, with GDM as an early expression of underlying risk.

GDM is a well-established risk factor for subsequent T2DM, and offspring of affected pregnancies are also at increased metabolic risk. Together, these findings suggest a potential intergenerational pathway linking ACE exposure, maternal metabolic dysregulation, and long-term risk in both mother and child, positioning ACEs as an upstream determinant of metabolic disease.

This study contributes by isolating GDM from broader pregnancy outcomes, demonstrating a dose–response relationship, and integrating a life-course perspective linking childhood adversity, pregnancy, and later metabolic disease.

4.2 Possible mechanisms

The association between ACEs and GDM likely reflects convergent neuroendocrine, inflammatory, metabolic, and placental pathways originating early in development. ACEs have been linked to long-term dysregulation of the HPA axis, including altered cortisol awakening responses and blunted reactivity that persist into adulthood and re-emerge during pregnancy.[55] These endocrine changes contribute to chronic inflammation, reduced glucocorticoid sensitivity, and impaired insulin signalling.[56]

Psychosocial factors may also influence risk expression (Supplementary Table S6). Associations were stronger among women with preconception depression or high work stress,[32,51] whereas race/ethnicity and childhood social support did not consistently modify estimates.[45,46,51] The non-linear associations observed in some groups may reflect protective cultural or social environments.[6,42,47] Adiposity appeared to have a modifying rather than mediating role; adversity-exposed women had elevated GDM risk even after adjustment for BMI, suggesting that physiological embedding of stress may contribute independently of fat mass while still influencing visceral adiposity and metabolic flexibility.[32,44,45]

Placental pathways may also contribute to risk. Maternal adversity has been associated with reduced placental 11 β -hydroxysteroid dehydrogenase type 2 activity and altered cortisol transport, which may affect maternal metabolic adaptation and fetal glucocorticoid exposure.[57]

The cumulative dose–response pattern observed across studies is consistent with models of stress accumulation rather than single-exposure effects.[53] This pattern suggests that repeated or clustered adversities may progressively erode metabolic resilience, lowering the threshold at which pregnancy-related insulin resistance manifests as GDM.[54] Such cumulative processes may operate through both biological embedding and behavioural adaptation,

whereby early adversity shapes long-term stress responsivity, health behaviours, and access to protective resources.[12] Pregnancy may therefore act as a critical inflection point at which these latent vulnerabilities become clinically apparent.[9]

4.3 Strength and limitations

Several limitations should be considered when interpreting these findings. Most included studies relied on cross-sectional or retrospective ACE reporting, limiting causal inference and introducing potential recall bias.[59] ACE definitions, severity, and timing were inconsistently measured across studies, and adjustment for key confounders, such as pre-pregnancy BMI, socioeconomic position, and maternal mental health, varied.[60] The predominance of evidence from HIC restricts generalisability to LMIC where adversity patterns and metabolic risk structures may differ.[61,62]

Heterogeneity in exposure definition and outcome assessment represents a key challenge in synthesising observational evidence in this field. However, the directionally consistent associations observed across studies using different ACE instruments and GDM criteria suggest that the relationship is not artefactual. The use of adjusted estimates mitigates concerns regarding residual confounding, although unmeasured factors such as lifetime stress or intergenerational adversity may still influence results. These considerations support cautious interpretation while reinforcing the need for more harmonised measurement.

Despite these limitations, this review has notable strengths, including a comprehensive search across nine databases, dual-reviewer screening and extraction, structured risk-of-bias assessment using ROBINS-E, and dose–response meta-analytic modelling. Together, these methodological features strengthen confidence in the robustness of the findings.

4.4 Implications for research and practices

These findings support viewing GDM as a manifestation of cumulative life-course adversity. Trauma-informed approaches in maternity services may therefore be essential. Best-practice recommendations emphasise sensitive enquiry about past adversity, clear communication, continuity of care, psychological safety, and staff training to avoid re-traumatisation.[63] Such approaches are relevant given the heightened psychological and metabolic vulnerability among women with ACE histories.[64]

Within diabetes research and clinical practice, these findings support broader recognition of psychosocial history as a relevant component of metabolic risk stratification in pregnancy. While ACE screening is not intended as a diagnostic tool, incorporating trauma-informed principles into routine antenatal care may enhance engagement, reduce stress-related barriers to care, and improve uptake of preventive interventions among women at elevated risk. Such approaches complement, rather than replace, established biomedical risk assessment and may be particularly relevant in settings serving socially disadvantaged populations where both ACE exposure and GDM prevalence are high.

The results also identify a population at increased risk for GDM for whom targeted preventive and management strategies may be beneficial.[5,12] This includes tailored metabolic and psychological support during pregnancy and postpartum, when the risk of developing type 2 diabetes is substantially increased.[3,65] At a population level, the findings reinforce the

importance of framing GDM prevention as an intergenerational challenge.[66] Preventing childhood adversity should therefore be considered a long-term public health strategy to reduce chronic disease burden across generations.[67]

Intervention need not be limited to early childhood. Because ACEs may increase GDM risk through physiological and behavioural pathways, the preconception period represents a critical secondary window for intervention.[68] However, women face substantial barriers to engaging in preconception care, including limited information, time constraints, affordability, and inconsistent primary-care support, although peer support may help mitigate these challenges.[69] For women with known adversity histories, preconception care may need to extend beyond routine supplementation to include targeted metabolic screening, psychological support, and interventions aimed at normalising stress physiology and inflammation, consistent with upstream life-course strategies.[5,55-58] Later-life supports, including trauma-focused therapies, social support programmes, and workplace stress management, may also help buffer the long-term physiological imprint of adversity and reduce cumulative metabolic strain.[64]

Together, these implications align with evidence linking ACEs to multiple pregnancy outcomes, suggesting shared biopsychosocial pathways. Unlike broader reviews,[14,34] this synthesis clarifies the metabolic sequelae of ACE exposure and highlights opportunities to interrupt the trajectory from early adversity to GDM and later cardiometabolic disease.[70]

4.5 Future Research

Future research should prioritise large, prospective peri-conceptual cohorts to strengthen causal inference, reduce recall bias, and test biopsychosocial pathways linking ACEs to GDM. Incorporating placental epigenetic analyses may clarify biological transmission.[64] Standardised ACE and GDM measures and improved capture of adversity timing would enhance comparability.[1,5,60,71] Developmental neuroscience highlights adolescence as a sensitive window in which stress may shape later metabolic trajectories,[72,73] underscoring the importance of longitudinal designs. Embedding HPA-axis and inflammatory biomarkers into future cohorts will further advance mechanistic understanding.[55-57] Research in diverse populations, particularly in LMIC, remains essential to understand how adversity interacts with structural inequities, nutritional transitions and sociocultural buffering.[6,21,61]

4. Conclusion

Maternal exposure to ACEs is associated with increased risk of GDM in a dose-dependent manner. Although limitations in the available evidence preclude causal inference, the consistency of findings across studies supports the relevance of early-life adversity to metabolic vulnerability during pregnancy. These results reinforce a life-course perspective on GDM, in which psychosocial exposures contribute alongside established biomedical risk factors. Integrating trauma-informed principles into maternity care and strengthening prevention of childhood adversity may therefore represent important, complementary strategies for improving maternal and offspring metabolic health.

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Declaration of interests

We declare no competing interests.

Data sharing

The protocol for this review is publicly available on PROSPERO (CRD420251035754). Data extracted from included studies and the R scripts used for statistical analyses are available from the corresponding author upon reasonable request. Summary data used in the meta-analyses are provided in the Supplementary Materials.

References

- [1] Nakshine VS, Jogdand SD. A Comprehensive Review of Gestational Diabetes Mellitus: Impacts on Maternal Health, Fetal Development, Childhood Outcomes, and Long-Term Treatment Strategies. *Cureus*. 2023 Oct 23;15(10):e47500. doi: 10.7759/cureus.47500. PMID: 38021940; PMCID: PMC10663705.
- [2] Wang H, Li N, Chivese T, Werfalli M, Sun H, Yuen L, et al. IDF Diabetes Atlas Committee Hyperglycaemia in Pregnancy Special Interest Group. IDF Diabetes Atlas: Estimation of Global and Regional Gestational Diabetes Mellitus Prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's Criteria. *Diabetes Res Clin Pract*. 2022 Jan;183:109050. doi: 10.1016/j.diabres.2021.109050. Epub 2021 Dec 6. PMID: 34883186.
- [3] Huang H, Yan P, Shan Z. Adverse childhood experiences and risk of type 2 diabetes: A systematic review and meta-analysis. *Metabolism - Clinical and Experimental*, 2015; 64, 1408-1411. doi: 10.1016/j.metabol.2015.08.019.
- [4] Kapur A, Hod M. Maternal health and non-communicable disease prevention: An investment case for the post COVID-19 world and need for better health economic data. *Int J Gynaecol Obstet*. 2020 Aug;150(2):151-158. doi: 10.1002/ijgo.13198. Epub 2020 Jun 2. PMID: 32401348; PMCID: PMC9087486.

- [5] Sweeting A, Wong J, Murphy HR, Ross GP. A Clinical Update on Gestational Diabetes Mellitus. *Endocr Rev.* 2022 Sep 26;43(5):763-793. doi: 10.1210/endrev/bnac003. PMID: 35041752; PMCID: PMC9512153.
- [6] Daneshmand SS, Stortz S, Morrisey R, Faksh A. Bridging Gaps and Understanding Disparities in Gestational Diabetes Mellitus to Improve Perinatal Outcomes. *Diabetes Spectr.* 2019 Nov;32(4):317-323. doi: 10.2337/ds19-0013. PMID: 31798289; PMCID: PMC6858080.
- [7] Vounzoulaki E, Khunti K, Abner SC, Tan BK, Davies MJ, Gillies CL. Progression to type 2 diabetes in women with a known history of gestational diabetes: systematic review and meta-analysis. *BMJ* 2020;369:m1361. doi: 10.1136/bmj.m1361.
- [8] Xie W, Wang Y, Xiao S, Qiu L, Yu Y, et al. Association of gestational diabetes mellitus with overall and type specific cardiovascular and cerebrovascular diseases: systematic review and meta-analysis. *BMJ.* 2022 Sep 21;378:e070244. doi: 10.1136/bmj-2022-070244. PMID: 36130740; PMCID: PMC9490552.
- [9] Thornton JM, Shah NM, Lillycrop KA, Cui W, Johnson MR, et al. Multigenerational diabetes mellitus. *Front Endocrinol (Lausanne).* 2024 Jan 15;14:1245899. doi: 10.3389/fendo.2023.1245899. PMID: 38288471; PMCID: PMC10822950.
- [10] Rowland J, Wilson CA. The association between gestational diabetes and ASD and ADHD: a systematic review and meta-analysis. *Sci Rep.* 2021 Mar 4;11(1):5136. doi: 10.1038/s41598-021-84573-3. PMID: 33664319; PMCID: PMC7933135.
- [11] Wilson CA, Santorelli G, Howard LM, Ismail K, Reynolds RM, et al. Child educational progress in Born in Bradford pregnancies affected by gestational diabetes and also exposed to maternal common mental disorders. *Sci Rep.* 2023 Oct 21;13(1):17991. doi: 10.1038/s41598-023-44619-0. PMID: 37865701; PMCID: PMC10590408.
- [12] Wicklow B, Retnakaran R. Gestational Diabetes Mellitus and Its Implications across the Life Span. *Diabetes Metab J.* 2023 May;47(3):333-344. doi: 10.4093/dmj.2022.0348. Epub 2023 Feb 8. PMID: 36750271; PMCID: PMC10244196.
- [13] Nelson CA, Scott RD, Bhutta ZA, Harris NB, Danese A, Samara M. Adversity in childhood is linked to mental and physical health throughout life. *BMJ.* 2020 Oct 28;371:m3048. doi: 10.1136/bmj.m3048. PMID: 33115717; PMCID: PMC7592151.
- [14] Mamun A, Biswas T, Scott J, Sly PD, McIntyre HD, et al. Adverse childhood experiences, the risk of pregnancy complications and adverse pregnancy outcomes: a systematic review and meta-analysis. *BMJ Open.* 2023 Aug 3;13(8):e063826. doi: 10.1136/bmjopen-2022-063826. PMID: 37536966; PMCID: PMC10401231.
- [15] Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. *Am J Prev Med.* 1998 May;14(4):245-58. doi: 10.1016/s0749-3797(98)00017-8. PMID: 9635069.
- [16] Asmussen K, Fischer F, Drayton E, McBride T. Adverse childhood experiences: what we know, what we don't know, and what should happen next. 2020. London: Early Intervention Foundation; 2020.
- [17] Moog NK, Buss C, Entringer S, Shahbaba B, Gillen DL, Hobel CJ, et al. Maternal Exposure to Childhood Trauma Is Associated During Pregnancy With Placental-Fetal Stress Physiology. *Biol Psychiatry.* 2016 May 15;79(10):831-839. doi: 10.1016/j.biopsych.2015.08.032. Epub 2015 Sep 3. PMID: 26444076; PMCID: PMC4777678.
- [18] Gaston SA, Riley NM, Parks CG, Woo JMP, Sandler DP, Jackson CL. Racial/Ethnic Differences in Associations Between Traumatic Childhood Experiences and Both Metabolic Syndrome Prevalence and Type 2 Diabetes Risk Among a Cohort of U.S.

- Women. *Diabetes Care*. 2023 Feb 1;46(2):341-350. doi: 10.2337/dc22-1486. PMID: 36525647; PMCID: PMC9887611.
- [19] Walsh D, McCartney G, Smith M, et al. Relationship between childhood socioeconomic position and adverse childhood experiences (ACEs): a systematic review. *J Epidemiol Community Health* 2019;73:1087-1093. doi: 10.1136/jech-2019-212738.
- [20] Finkelhor D. Trends in Adverse Childhood Experiences (ACEs) in the United States. *Child Abuse Negl*. 2020 Oct;108:104641. doi: 10.1016/j.chiabu.2020.104641. Epub 2020 Jul 30. PMID: 32739600.
- [21] Mersky JP, Choi C, Plummer Lee CT, Janczewski CE. Disparities in adverse childhood experiences by race/ethnicity, gender, and economic status: Intersectional analysis of a nationally representative sample. *Child Abuse Negl*. 2021 Jul;117:105066. doi: 10.1016/j.chiabu.2021.105066. Epub 2021 Apr 9. PMID: 33845239.
- [22] Zhang Y, Yin Y, Zhang X, Ye J, Zhang J. Association of adverse childhood experiences with diabetes: A systematic review and meta-analysis. *J Diabetes Complications*. 2022 Oct;36(10):108289. doi: 10.1016/j.jdiacomp.2022.108289. Epub 2022 Aug 31. PMID: 36067703.
- [23] Gluckman PD, Hanson MA. Living with the past: evolution, development, and patterns of disease. *Science*. 2004 Sep 17;305(5691):1733-6. doi: 10.1126/science.1095292. PMID: 15375258.
- [24] Woods-Jaeger BA, Cho B, Sexton CC, Slagel L, Goggin K. Promoting Resilience: Breaking the Intergenerational Cycle of Adverse Childhood Experiences. *Health Educ Behav*. 2018 Oct;45(5):772-780. doi: 10.1177/1090198117752785. Epub 2018 Feb 12. PMID: 29433342.
- [25] Howell KH, Miller-Graff LE, Martinez-Torteya C, Napier TR, Carney JR. Charting a Course towards Resilience Following Adverse Childhood Experiences: Addressing Intergenerational Trauma via Strengths-Based Intervention. *Children (Basel)*. 2021 Sep 24;8(10):844. doi: 10.3390/children8100844. PMID: 34682109; PMCID: PMC8534646.
- [26] Steine IM, LeWinn KZ, Lisha N, Tylavsky F, Smith R, Bowman M, et al. Maternal exposure to childhood traumatic events, but not multi-domain psychosocial stressors, predict placental corticotrophin releasing hormone across pregnancy. *Soc Sci Med*. 2020 Dec;266:113461. doi: 10.1016/j.soescimed.2020.113461. Epub 2020 Oct 17. PMID: 33126094; PMCID: PMC9380779.
- [27] Horsch A, Seon Kang J, Vial Y, Ehlert U, Borghini A, Marques-Vidal P, et al. Stress exposure and psychological stress responses are related to glucose concentrations during pregnancy. *Br J Health Psychol*. 2016 Sep;21(3):712-29. doi: 10.1111/bjhp.12197. Epub 2016 May 12. PMID: 27169679.
- [28] Miller NE, Lacey RE. Childhood adversity and cardiometabolic biomarkers in mid-adulthood in the 1958 British birth cohort. *SSM Popul Health*. 2022 Oct 4;19:101260. doi: 10.1016/j.ssmph.2022.101260. PMID: 36238817; PMCID: PMC9550530.
- [29] Suglia SF, Koenen KC, Boynton-Jarrett R, Chan PS, Clark CJ, Danese A, et al. Childhood and Adolescent Adversity and Cardiometabolic Outcomes: A Scientific Statement From the American Heart Association. *Circulation*. 2018 Jan 30;137(5):e15-e28. doi: 10.1161/CIR.0000000000000536. Epub 2017 Dec 18. PMID: 29254928; PMCID: PMC7792566.
- [30] Demers CH, Hankin BL, Hennessey EMP, Haase MH, Bagonis MM, Kim SH, et al. Maternal adverse childhood experiences and infant subcortical brain volume. *Neurobiol Stress*. 2022 Sep 23;21:100487. doi: 10.1016/j.ynstr.2022.100487. PMID: 36532374; PMCID: PMC9755027.
- [31] Bowers K, Ding L, Gregory S, Yolton K, Ji H, Meyer J, et al. Maternal distress and hair cortisol in pregnancy among women with elevated adverse childhood experiences.

- Psychoneuroendocrinology. 2018 Sep;95:145-148. doi: 10.1016/j.psyneuen.2018.05.024. Epub 2018 May 18. PMID: 29859342.
- [32] Schoenaker DAJM, Callaway LK, Mishra GD. The Role of Childhood Adversity in the Development of Gestational Diabetes. *Am J Prev Med.* 2019 Sep;57(3):302-310. doi: 10.1016/j.amepre.2019.04.028. Epub 2019 Jul 25. PMID: 31353162.
- [33] Versteegen M, Bozlak CT, Larkin H, Appleton AA. Maternal depression, adverse childhood experiences, and social support in relation to gestational diabetes risk: results from the Albany Infant and Mother Study (AIMS). *BMC Pregnancy Childbirth.* 2021 Apr 27;21(1):335. doi: 10.1186/s12884-021-03814-5. PMID: 33906618; PMCID: PMC8077784.
- [34] Kern A, Houry B, Frederickson A, Langevin R. The associations between childhood maltreatment and pregnancy complications: A systematic review and meta-analysis. *J Psychosom Res.* 2022 Sep;160:110985. doi: 10.1016/j.jpsychores.2022.110985. Epub 2022 Jul 2. PMID: 35816769.
- [35] Higgins JPT, Morgan RL, Rooney AA, Taylor KW, Thayer KA, Silva RA, et al. A tool to assess risk of bias in non-randomized follow-up studies of exposure effects (ROBINS-E). *Environ Int.* 2024 Apr;186:108602. doi: 10.1016/j.envint.2024.108602. Epub 2024 Mar 24. PMID: 38555664; PMCID: PMC11098530.
- [36] Deeks JJ, Higgins JP, Altman DG, McKenzie JE, Veroniki AA (editors). Chapter 10: Chapter 10: Analysing data and undertaking meta-analyses [last updated November 2024]. In: Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.5. Cochrane, 2024. Available from [cochrane.org/handbook](https://www.cochrane.org/handbook).
- [37] Crippa A, Discacciati A, Bottai M, Spiegelman D, Orsini N. One-stage dose-response meta-analysis for aggregated data. *Stat Methods Med Res.* 2019 May;28(5):1579-1596. doi: 10.1177/0962280218773122. Epub 2018 May 9. PMID: 29742975.
- [38] Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ.* 2003 Sep 6;327(7414):557-60. doi: 10.1136/bmj.327.7414.557. PMID: 12958120; PMCID: PMC192859.
- [39] Cressey, Daniel. (2017). Tool for detecting publication bias goes under spotlight. *Nature.* 10.1038/nature.2017.21728.
- [40] Neumann I, Schünemann H (Editors). *The GRADE Book* version 1.0 (updated September 2024). The GRADE Working Group. Available from: <https://book.gradepro.org>
- [41] Davies M, van Houten CS, Bengtsson J, Elsenburg LK, Kragelund Nielsen K, Andersen GS, et al. Childhood adversity and the risk of gestational diabetes: a population-based cohort study of nulliparous pregnant women. *Diabet Med.* 2024 Jan;41(1):e15242. doi: 10.1111/dme.15242. Epub 2023 Oct 31. PMID: 37845190.
- [42] Maeda Y, Tabuchi T, Fujiwara T. Association between adverse childhood experiences and pregnancy morbidities: A nationwide online-based cross-sectional study. *J Obstet Gynaecol Res.* 2024 Dec;50(12):2231-2238. doi: 10.1111/jog.16124. Epub 2024 Oct 16. PMID: 39414244.
- [43] Lovett SM, Woo JMP, O'Brien KM, Parker SE, Sandler DP. Association of Early-life Trauma With Gestational Diabetes and Hypertensive Disorders of Pregnancy. *Epidemiology.* 2025 Mar 1;36(2):149-159. doi: 10.1097/EDE.0000000000001817. Epub 2024 Dec 31. PMID: 39739403; PMCID: PMC12380080.
- [44] Mason SM, Tobias DK, Clark CJ, Zhang C, Hu FB, Rich-Edwards JW. Abuse in Childhood or Adolescence and Gestational Diabetes: A Retrospective Cohort Study. *Am J Prev Med.* 2016 Apr;50(4):436-444. doi: 10.1016/j.amepre.2015.08.033. Epub 2015 Nov 4. PMID: 26547539; PMCID: PMC4801767.

- [45] Stanhope KK, Gunderson EP, Suglia SF, Boulet SL, Jamieson DJ, Kiefe CI, et al. Understanding the role of childhood nurture, abuse, and stability on gestational diabetes in the Coronary Artery Risk Development in Young Adults study (CARDIA). *Ann Epidemiol.* 2024 Mar;91:30-36. doi: 10.1016/j.annepidem.2024.01.007. Epub 2024 Jan 23. PMID: 38266664; PMCID: PMC10922764.
- [46] Stanhope KK, Cammack AL, Perreira KM, Fernández-Rhodes L, Cordero C, Gallo LC, et al. Adverse childhood experiences and lifetime adverse maternal outcomes (gestational diabetes and hypertensive disorders of pregnancy) in the Hispanic Community Health Study/Study of Latinos. *Ann Epidemiol.* 2020 Oct;50:1-6. doi: 10.1016/j.annepidem.2020.08.004. Epub 2020 Aug 11. PMID: 32791197; PMCID: PMC7991739.
- [47] Imanishi Y, Wada I, Tabuchi T. The Association between Perinatal Complications and Adverse Childhood Experiences: Findings from a Nationwide Online Survey. *Am J Perinatol.* 2025 Jul;42(9):1168-1178. doi: 10.1055/a-2464-3665. Epub 2024 Dec 13. PMID: 39672194.
- [48] Swedo EA, D'Angelo DV, Fasula AM, Clayton HB, Ports KA. Associations of Adverse Childhood Experiences With Pregnancy and Infant Health. *Am J Prev Med.* 2023 Apr;64(4):512-524. doi: 10.1016/j.amepre.2022.10.017. Epub 2023 Jan 23. PMID: 36697281; PMCID: PMC10033436.
- [49] Miller ES, Fleming O, Ekpe EE, Grobman WA, Heard-Garris N. Association Between Adverse Childhood Experiences and Adverse Pregnancy Outcomes. *Obstet Gynecol.* 2021 Nov 1;138(5):770-776. doi: 10.1097/AOG.0000000000004570. PMID: 34619717; PMCID: PMC8542582.
- [50] Jasthi DL, Lappen JR, Garber S, Kennedy S, McCarther N, Nagle-Yang S, et al. Associations between adverse childhood experiences and obstetrical outcomes in a predominantly Black-identifying and low-income pregnant population. *Am J Obstet Gynecol MFM.* 2023 Jul;5(7):101008. doi: 10.1016/j.ajogmf.2023.101008. Epub 2023 May 6. PMID: 37156467.
- [51] Mendez L, Li J, Hsieh CT, Zhang L, Britt J, Crockett A, et al. Examining childhood and adulthood stressors as risk factors for gestational diabetes mellitus in working pregnant individuals: A prospective cohort study. *Prev Med.* 2024 Dec;189:108163. doi: 10.1016/j.yjpm.2024.108163. Epub 2024 Nov 4. PMID: 39505116.
- [52] Madigan S, Deneault AA, Racine N, Park J, Thiemann R, Zhu J, et al. Adverse childhood experiences: a meta-analysis of prevalence and moderators among half a million adults in 206 studies. *World Psychiatry.* 2023 Oct;22(3):463-471. doi: 10.1002/wps.21122. PMID: 37713544; PMCID: PMC10503911.
- [53] Danese A, McEwen BS. Adverse childhood experiences, allostasis, allostatic load, and age-related disease. *Physiol Behav.* 2012 Apr 12;106(1):29-39. doi: 10.1016/j.physbeh.2011.08.019. Epub 2011 Aug 25. PMID: 21888923.
- [54] Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield C, Perry BD, et al. The enduring effects of abuse and related adverse experiences in childhood. A convergence of evidence from neurobiology and epidemiology. *Eur Arch Psychiatry Clin Neurosci.* 2006 Apr;256(3):174-86. doi: 10.1007/s00406-005-0624-4. Epub 2005 Nov 29. PMID: 16311898; PMCID: PMC3232061.
- [55] Epstein CM, Houfek JF, Rice MJ, Weiss SJ. Integrative review of early life adversity and cortisol regulation in pregnancy. *JOGNN.* 2021;50(3):242-55. doi: 10.1016/j.jogn.2020.12.006.

- [56] Panisch LS, Murphy HR, Wu Q, Brunner JL, Duberstein ZT, Arnold MS, et al. Adverse childhood experiences predict diurnal cortisol throughout gestation. *Psychosom Med.* 2023;85(6):507–16. doi: 10.1097/PSY.0000000000001218.
- [57] George J, Muzik M, Townsel C. Placental cortisol dysregulation in mothers with experiences of childhood adversity: Potential mechanisms and clinical implications. *J Clin Med.* 2024;13(7):2020. doi: 10.3390/jcm13072020.
- [58] Fleming TP, Sun C, Denisenko O, Caetano L, Aljahdali A, Gould JM, et al. Environmental exposures around conception: developmental pathways leading to lifetime disease risk. *Int J Environ Res Public Health.* 2021;18(17):79380. doi: 10.3390/ijerph18179380.
- [59] Naicker SN, Norris SA, Mabaso M, Richter LM. An analysis of retrospective and repeat prospective reports of adverse childhood experiences from the South African Birth to Twenty Plus cohort. *PLoS One.* 2017 Jul 26;12(7):e0181522. doi: 10.1371/journal.pone.0181522. PMID: 28746343; PMCID: PMC5528894.
- [60] Holden GW, Gower T, Chmielewski M. Methodological considerations in ACEs research. In: *Adverse Childhood Experiences: Using Evidence to Advance Research, Practice, Policy, and Prevention.* Elsevier; 2019. p. 161–82. doi: 10.1016/B978-0-12-816065-7.00009-4.
- [61] Kaminer D, Bravo AJ, Mezquita L, Pilatti A, Bravo AJ, Conway CC, et al. Adverse childhood experiences and adulthood mental health: a cross-cultural examination among university students in seven countries. *Curr Psychol.* 2023 Jul 1;42(21):18370–81. doi: 10.1007/s12144-022-02978-3
- [62] Kragelund Nielsen K, Damm P, Bygbjerg IC, Kapur A. Barriers and facilitators for implementing programmes and services to address hyperglycaemia in pregnancy in low- and middle-income countries: A systematic review. *Diabetes Res Clin Pract.* 2018 Nov;145:102-118. doi: 10.1016/j.diabres.2018.04.009. Epub 2018 Apr 21. PMID: 29684614.
- [63] Benton MR, Wittkowski A, Edge D, Reid HE, Quigley T, Sheikh Z, et al. Best practice recommendations for the integration of trauma-informed approaches in maternal mental health care within the context of perinatal trauma and loss: A systematic review of current guidance. *Midwifery.* 2024;131:103949. doi: 10.1016/j.midw.2024.103949.
- [64] Velazquez MA, Fleming TP, Watkins AJ. Periconceptional environment and the developmental origins of disease. *J Endocrinol.* 2019;242(1):T33–T49. doi: 10.1530/JOE-18-0676.
- [65] Adam S, McIntyre HD, Tsoi KY, Kapur A, Ma RC, Dias S, et al. Pregnancy as an opportunity to prevent type 2 diabetes mellitus: FIGO Best Practice Advice. *Int J Gynaecol Obstet.* 2023 Jan;160 Suppl 1(Suppl 1):56-67. doi: 10.1002/ijgo.14537. PMID: 36635082; PMCID: PMC10107137.
- [66] Wexler DJ, Powe CE, Barbour LA, Buchanan T, Coustan DR, Corcoy R, et al. Research Gaps in Gestational Diabetes Mellitus: Executive Summary of a National Institute of Diabetes and Digestive and Kidney Diseases Workshop. *Obstet Gynecol.* 2018 Aug;132(2):496-505. doi: 10.1097/AOG.0000000000002726. Erratum in: *Obstet Gynecol.* 2018 Oct;132(4):1068. doi: 10.1097/AOG.0000000000002908. PMID: 29995731; PMCID: PMC6124493.
- [67] Di Lemma L.C.G., Davies A.R., Ford K., Hughes K., Homolova L., Gray B and Richardson G. (2019). *Responding to Adverse Childhood Experiences: An evidence review of interventions to prevent and address adversity across the life course.* Public Health Wales, Cardiff and Bangor University, Wrexham, ISBN 978-1-78986-035-1.
- [68] Steel A, Strommer S, Adams J, Schoenaker D. Preconception health policy, health promotion, and health services to achieve health in current and future generations: a

- narrative review. *BMC Pregnancy Childbirth*. 2025;25(1):1–10. doi: 10.1186/s12884-025-07176-0.
- [69] Benton MR, Tape N, Deussen AR, Turnbull D, Dodd JM. Barriers to and facilitators for addressing overweight and obesity before conception: A qualitative study. *Women Birth*. 2021;34(5):e493–e497. doi: 10.1016/j.wombi.2020.09.02534.
- [70] Osei-Safo EK, McIntosh J, Onwuka S, Torkel S, McGowan M, Cocotis K, et al. What Is My Risk? A Mixed-Methods Systematic Review of Risk Perception for Cardiometabolic Pregnancy Complications and Future Cardiometabolic Disease Development. *Obes Rev*. 2025 Nov;26(11):e13967. doi: 10.1111/obr.13967. Epub 2025 Jul 9. PMID: 40635374; PMCID: PMC12531758.
- [71] Raymond C, Marin MF, Wolosianski V, Journault AA, Longpré C, Leclaire S, Cernik R, Juster RP, Lupien SJ. Early childhood adversity and HPA axis activity in adulthood: The importance of considering minimal age at exposure. *Psychoneuroendocrinology*. 2021;124:105042. doi: 10.1016/j.psyneuen.2020.105042.
- [72] Schalbetter SM, Von Arx AS, Cruz-Ochoa N, Dawson K, Ivanov A, Mueller FS, Lin H-Y, Amport R, Mildenerger W, Mattei D, Beule D, Földy C, Greter M, Notter T, Meyer U. Adolescence is a sensitive period for prefrontal microglia to act on cognitive development. *Sci Adv*. 2022;8:100355. doi: 10.1126/sciadv.100355.
- [73] Pollmann A, Fritz J, Barker E, Fuhrmann D. Networks of adversity in childhood and adolescence and their relationship to adult mental health. *Res Child Adolesc Psychopathol*. 2023;51(12):1769–84. doi: 10.1007/s10802-022-00976-4.

Supplementary Material

Table S1. Full search terms for one database.

OVID (Embase)
Adverse childhood experience*
(child* adj3 abuse*).mp.
(child* adj3 adversit*).mp.
(child* adj3 trauma*).mp.
(child* adj3 maltreatment).mp.
(child* adj3 violence*).mp.
(child* adj3 hardship*).mp.
(child* adj3 suffer*).mp.
(child* adj3 stress*).mp.
adverse child* event*.mp.
(child* adj3 neglect*).mp.
(early-life adj3 trauma*).mp.
(early-life adj3 stress*).mp.
early abuse* experience*.mp.
(adolescen* adj3 trauma*).mp.
(adolescen* adj3 stress*).mp.
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
exp gestational diabetes/
GDM.mp.
(gestational adj3 diabetes).mp.
18 or 19 or 20
17 and 21

Table S2. ROBINS-E

References	I	II	III	IV	V	VI	VII	Overall risk of bias	Main issues
<i>Davies 2024.</i> ⁴¹									-
<i>Maeda 2024.</i> ⁴²									Cross-sectional and online form prone to selection bias
<i>Lovett 2024.</i> ⁴³									Retrospective ACEs assessment may introduced recall bias
<i>Schoenaker 2019.</i> ³²									Differential recall of ACEs—potentially influenced by current mental health state
<i>Mason 2016.</i> ⁴⁴									Retrospective ACEs assessment may introduced recall bias
<i>Stanhope 2024.</i> ⁴⁵									Non-standard exposure and



























































<i>Stanhope 2020.</i> ⁴⁶									attrition may bias results Selection and measurement issues from unmeasured confounders and retrospective ACE reporting
<i>Versteegen 2021.</i> ³³									Web-based design may exclude vulnerable groups; retrospective reporting adds bias risk
<i>Imanishi 2025.</i> ⁴⁷									Small, selective sampling and retrospective exposure limit conclusions.
<i>Swedo 2023.</i> ⁴⁸									Measurement variability and self-report warrant caution
<i>Miller 2021.</i> ⁴⁹									Clinical sample and retrospective data raise bias risk despite rigorous analysis
<i>Jasthi 2023.</i> ⁵⁰									Limited adjustments and high-risk sampling reduce generalisability
<i>Mendez 2024.</i> ⁵¹									A focus on employed women may limit applicability.
Domain I: confounding; Domain II: exposure measurement; Domain III: participant selection; Domain IV: post-exposure interventions; Domain V: missing data, Domain VI: outcome measurement, and Domain VII: selection of reported results.									
		Low risk		Moderate risk		High risk			

Table S3. Effect estimates for ACEs exposure in relation to GDM

		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
None vs Any ACEs	Davies	1.29 (1.22, 1.36)	1.15 (1.1, 1.6)
	Maeda	1.08 (0.85, 1.35)	1.34 (1.02, 1.77)

	Lovett	1.23 (1.11, 1.37)	1.09 (1.00, 1.28)
	Schoenaker	1.18 (1.00, 1.40)	1.09 (0.89, 1.33)
	Mason	1.16 (1.10, 1.23)	-
	Stanhope 2024	-	1.40 (0.94, 2.14)
	Stanhope 2020	-	-
	Versteegen	-	-
	Swedo NSD	1.22 (0.96, 1.57)	1.3 (0.9, 1.8)
	Swedo KMRI	1.00 (0.88, 1.14)	1.00 (0.8, 1.3)
	Miller	-	-
	Mendez	0.96 (0.52, 1.75)	0.89 (0.46, 1.71)
Low vs High ACEs	Davies	1.06 (0.91, 1.23)	1.32 (1.13, 1.53)
	Maeda	0.98 (0.62, 1.55)	-
	Lovett	1.97 (1.48, 2.61)	1.80 (1.46, 2.37)
	Schoenaker	1.64 (1.24, 2.19)	-
	Mason	1.31 (1.20, 1.43)	-
	Stanhope 2024	-	1.15 (0.72, 1.86)
	Stanhope 2020	-	0.8 (0.51, 1.27)
	Versteegen	-	1.31 (0.5, 3.39)
	Swedo NSD	1.22 (0.97, 1.54)	1.3 (0.9, 1.9)

Swedo KMRI	1.00 (0.81, 1.21)	1.2 (0.8, 1.6)
Miller	1.04 (0.61, 1.75)	1.21 (0.7, 2.11)
Mendez	0.96 (0.52, 1.75)	0.89 (0.46, 1.71)

Table S4. Odds ratio for Dose-Response Analysis

Study	ACEs Frequency				
	0	1	2	3	≥4
Maeda	ref	1.34 (1.02, 1.77)	0.97 (0.66, 1.43)	1.19 (0.72, 1.95)	0.81 (0.49, 1.33)
Lovett	ref	1.19 (1.09, 1.37)	1.19 (0.94, 1.46)	1.8 (1.46, 2.37)	1.19 (0.94, 1.46)
Schoenaker	ref	-	0.99 (0.67, 1.48)	1.73 (1.02, 3.01)	1.76 (1.04, 2.99)
Mason physical	ref	-	1.08 (0.95, 1.23)	1.17 (1.04, 1.30)	1.45 (1.22, 1.72)
Swedo NSD	ref	1.3 (0.9, 1.8)	1.2 (0.8, 1.8)	1.3 (0.90, 1.9)	-
Swedo KMRI	ref	1 (0.8, 1.3)	1 (0.7, 1.4)	1.2 (0.8, 1.6)	-

Table S5. Subgroup analysis

Subgroup Characteristic	No. of studies (k)	Pooled (95% CI)	aOR	p-value for Subgroup differences	Heterogeneity each group	within
Primary Analysis ($I^2 = 0\%$, $\tau^2 = 0$, $p = 0.65$)						
Study Design		$p = 0.86$				
Longitudinal	5	1.15 [1.12, 1.18]			$I^2 = 28.1\%$, $\tau^2 = 0.01$, $p = 0.24$	

Cross-sectional	3	1.17 1.41]	[0.92,	$I^2 = 0\%$, $\omega^2 = 0$, $p = 0.68$
Population Type		$p = 0.57$		
General	3	1.15 1.18]	[1.12,	$I^2 = 0\%$, $\omega^2 = 0$, $p = 0.50$
At-Risk	5	1.11 1.25]	[0.97,	$I^2 = 0\%$, $\omega^2 = 0$, $p = 0.49$
ROBINS-E		$p = 0.68$		
Low	1	1.15 1.18]*	[1.12,	-
Some	5	1.10 1.21]	[0.99,	$I^2 = 0\%$, $\omega^2 = 0$, $p = 0.49$
High	2	1.13 1.33]	[0.92,	$I^2 = 0\%$, $\omega^2 = 0$, $p = 0.34$

Secondary Analysis ($I^2 = 40\%$, $\omega^2 = 0.0436$, $p = 0.11$)

Study Design		$p = 0.80$		
Longitudinal	3	1.30 1.49]	[1.11,	$I^2 = 0\%$, $\omega^2 = 0$, $p = 0.85$
Cross-sectional	5	1.25 1.60]	[0.91,	$I^2 = 63.8\%$, $\omega^2 = 0.09$, $p = 0.02$
Population Type		$p = 0.12$		
General	3	1.15 1.18]	[1.12,	$I^2 = 52.8\%$, $\omega^2 = 0.04$, $p = 0.12$
At-Risk	5	1.11 1.25]	[0.97,	$I^2 = 0\%$, $\omega^2 = 0.01$, $p = 0.49$
ROBINS-E		$p = 0.07$		

Low	1	1.32	[1.12, 1.52]*	-
Some	4	1.42	[1.08, 1.76]	$I^2 = 26.5\%$, $\omega^2 = 0.04$, $p = 0.25$
High	3	0.96	[0.67, 1.48]	$I^2 = 0\%$, $\omega^2 = 0$, $p = 0.45$

Table S6. Synthesis of Formally Tested and Hypothesised Factors Moderating the ACEs-GDM Relationship

Domain	Specific Factor	Key Finding	Evidence Type	Supporting Study
Physiological & Behavioural Factors	Adiposity / BMI	The association was not explained by overweight status or pre-pregnancy weight	Formally Tested (via subgroup analysis)	Mason
		No evidence of mediation, but there was an effect modification among women with high waist circumference (≥ 88 cm).	Formally Tested (via mediation analysis)	Stanhope 2024
		Preconception BMI explained only 4.9% of and diet quality just 3.8% of the effect.	Formally tested via mediation analysis	Schoenaker
	Mediating Network Nodes	Network models identified factors like household mental illness, smoking, and BMI as key nodes linking ACEs to GDM.	Hypothesised (via Network Model)	Mesner
Psychosocial Factors	Preconception Depression	ACEs-GDM link was only present in women with these symptoms; absent in those without.	Formally Tested (Effect moderation and mediation)	Schoenaker
		Proposed this mechanism, but could not examine this due to the lack of data.	Hypothesised	Mason, Stanhope 2020

	Maternal Work Stress	High work stress combined with childhood abuse significantly increased GDM odds.	Formally Tested (Effect moderation)	Mendez
	Coping Style (John Henryism)	No significant difference in effect was found between active (high-effort) vs. passive coping.	Formally tested via regression analysis	Stanhope 2024
	Childhood Social Support	No significant moderation by social support was found.	Formally tested (Effect moderation)	Lovett
	Prenatal support	Socioeconomic status and prenatal care were suggested as potential indirect influences on the ACEs-GDM link.	Hypothesised	Swedo
Sociodemographic Factors	Race / Ethnicity	No significant difference in the ACEs-GDM association was found between the racial/ethnic groups examined.	Formally Tested via regression analysis	Mendez
		No significant interaction found between black vs white group.	Formally tested via regression analysis	Stanhope 2024
		Potential buffering by cultural values like familismo and healthcare access in Hispanic/Latina women.	Hypothesised	Stanhope 2020
	Resilience & Cultural buffering	Non-linear trends and null findings in Japanese populations suggest unmeasured resilience or cultural factors may be protective.	Hypothesised	Maeda, Imanishi
	Maternal Age	Younger maternal age was hypothesized as a potential protective mediator that could offset risk from ACEs.	Hypothesised	Davies

Table S7. GRADE Assessment

GRADE Domain	Assessment	Impact on Evidence Quality
Primary Analysis		
Risk of Bias	Most studies rated as moderate risk due to retrospective self-reporting of ACEs and residual confounding.	Downgrade to Moderate
Consistency	Low heterogeneity ($I^2 = 0\%$).	No Change
Precision	Narrow confidence interval for aOR (1.15, 95% CI [1.12, 1.18]).	No Change
Indirectness	Studies are directly applicable to the review's target population (pregnant women with GDM and ACE exposure).	No Downgrade
Publication Bias	No evidence of publication bias reported or tested.	No Downgrade
Secondary Analysis		
Risk of Bias	Most studies rated as moderate risk due to retrospective self-reporting of ACEs and residual confounding.	Downgrade to Moderate
Consistency	Low heterogeneity ($I^2 = 46.9\%$).	No Change
Precision	Narrow confidence interval for aOR (1.29, 95% CI [1.08, 1.53]).	No Change
Indirectness	Studies are directly applicable to the review's target population (pregnant women with GDM and ACE exposure).	No Downgrade
Publication Bias	No evidence of publication bias reported or tested.	No Downgrade

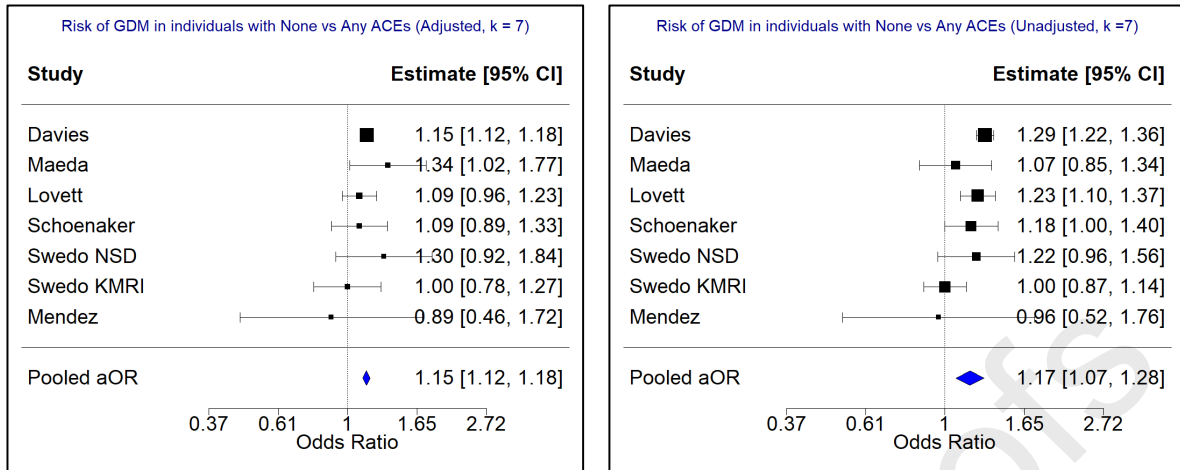


Figure S1. Sensitivity analysis for None vs Any ACEs

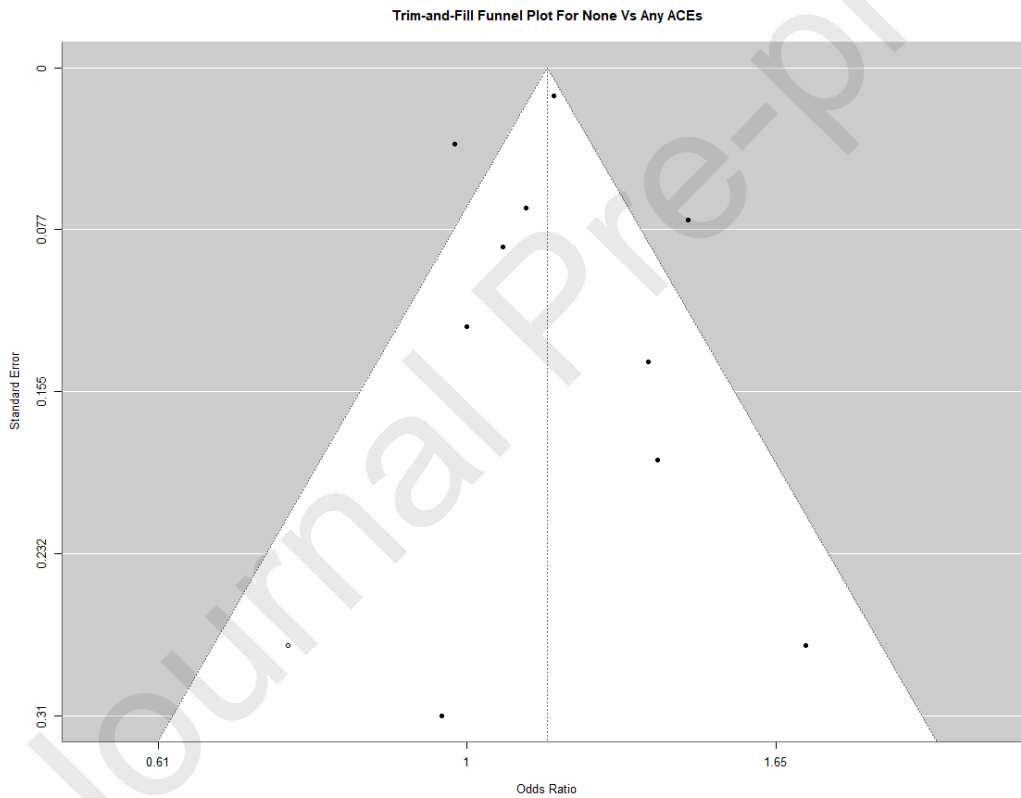


Figure S2. Trim-and-Fill Funnel Plot For No ACE vs Any ACEs

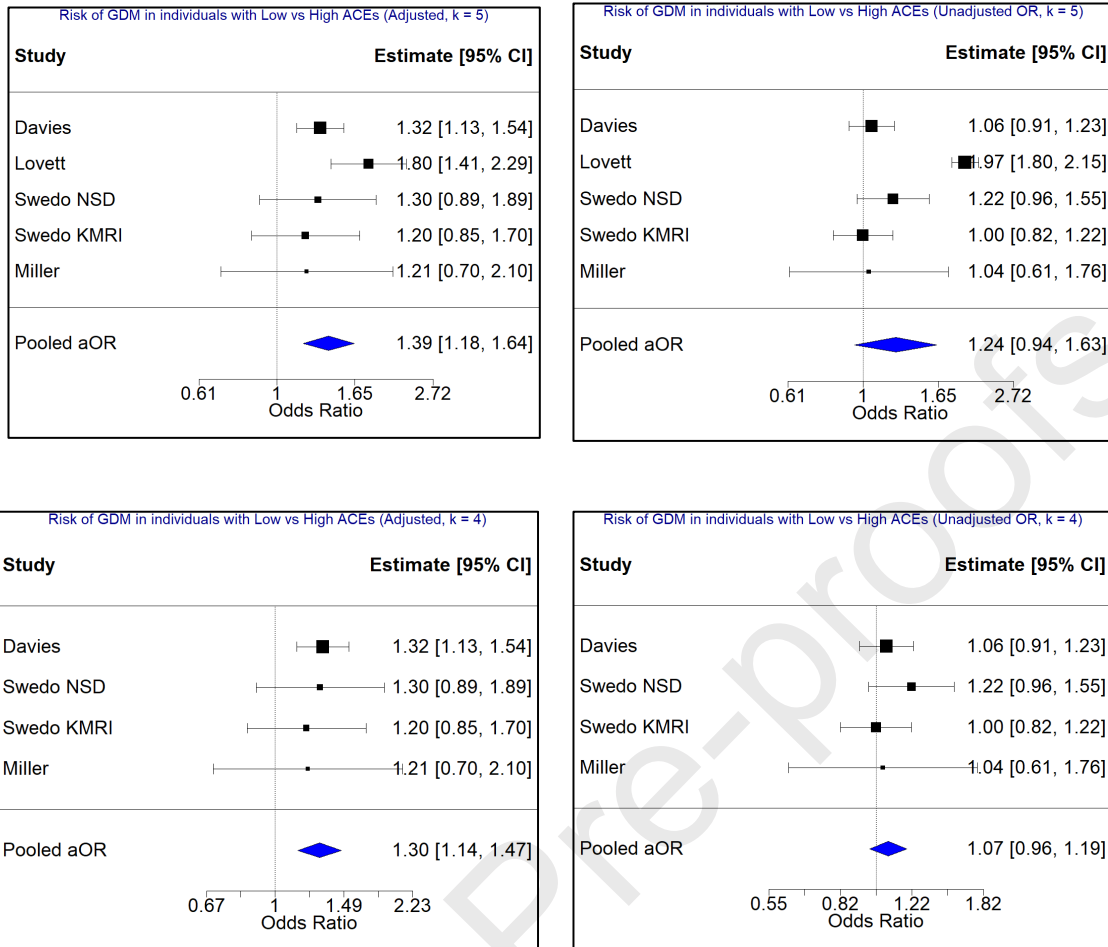


Figure S3. Sensitivity analysis for Low vs High ACEs

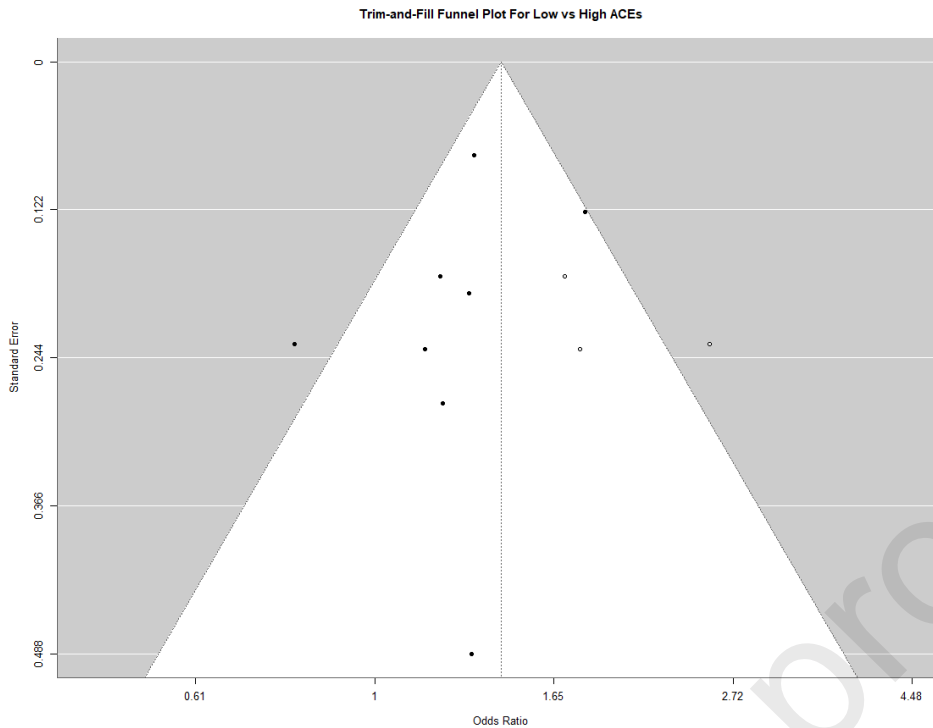


Figure S4. Trim-and-Fill Funnel Plot for Low vs High ACEs

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Figure 4. Dose-Response Relationship of ACEs and GDM

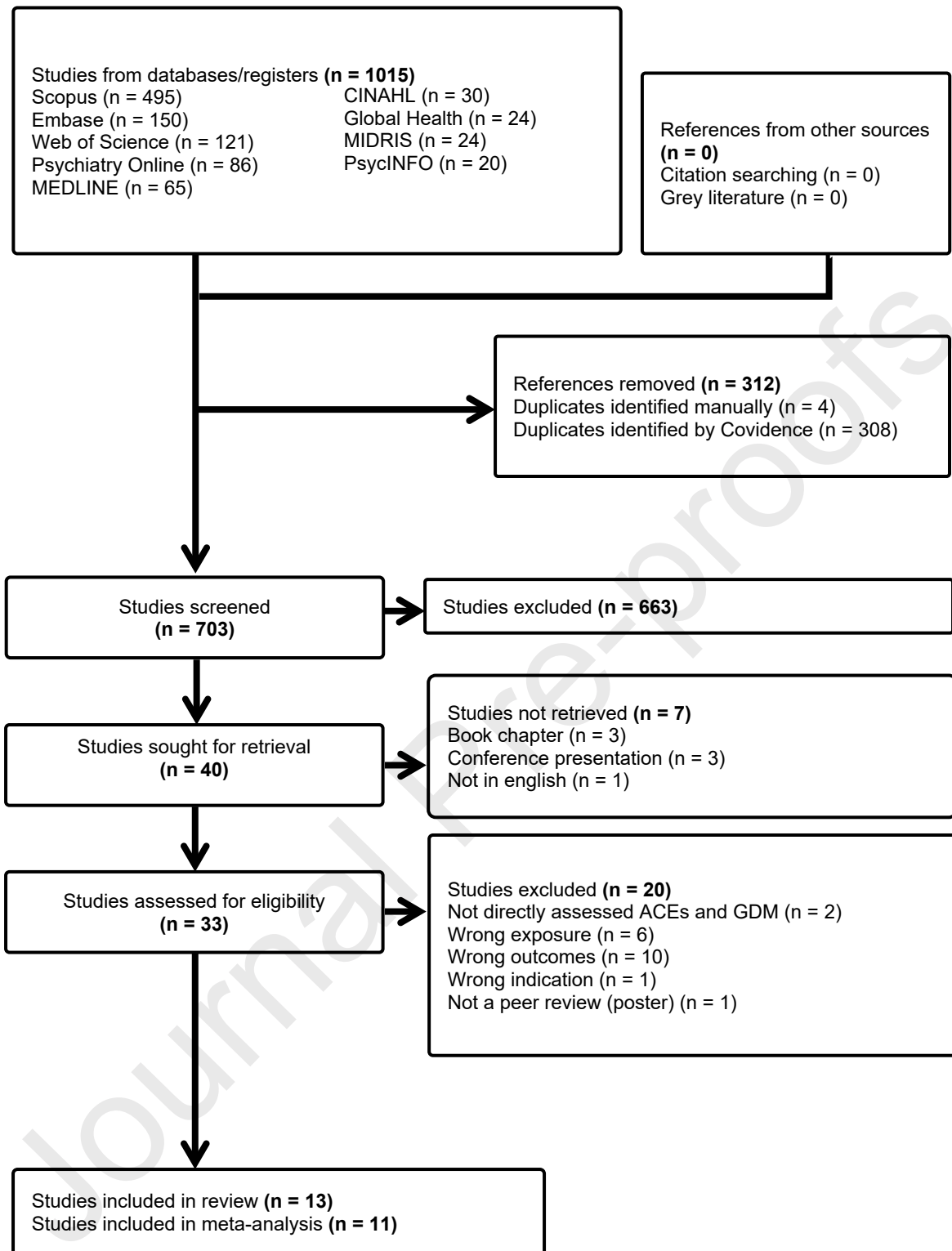


Figure 1. PRISMA diagram illustrating the study selection process

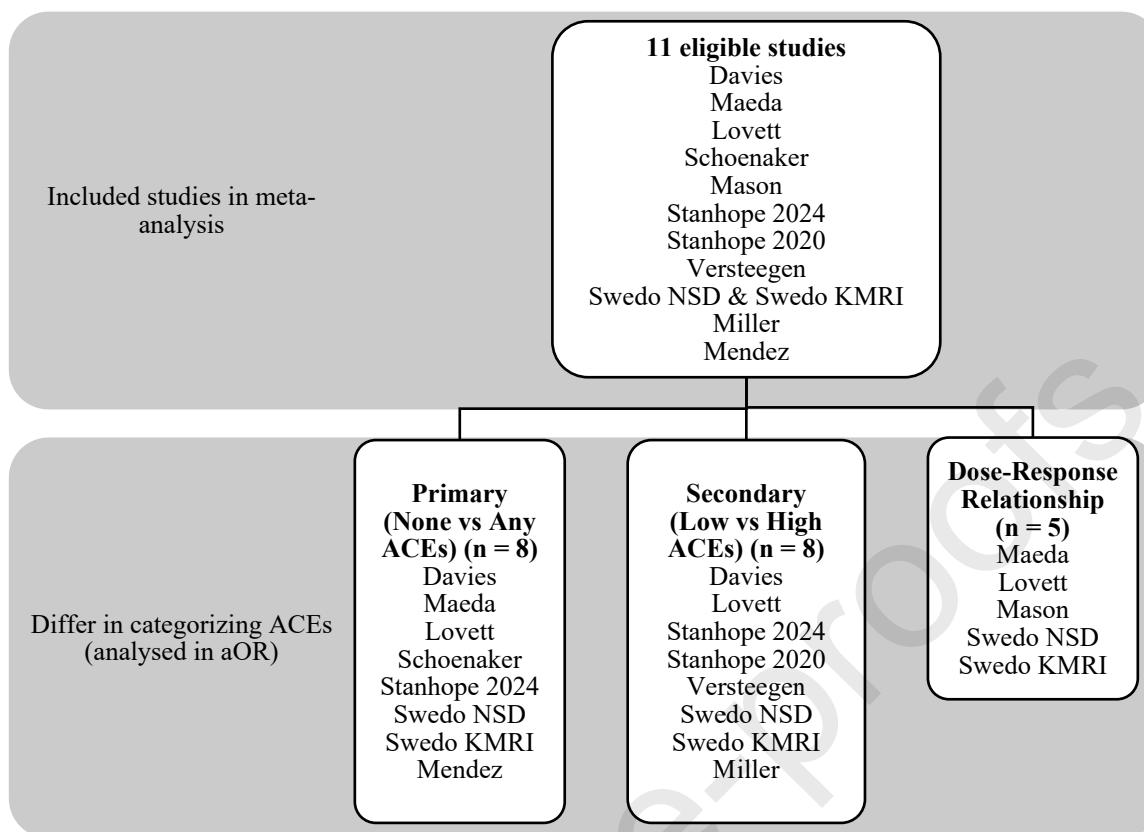


Figure 2. Flow diagram of included studies for the primary, secondary, and dose-response meta-analyses.

Effect estimates from 11 studies,^{32,33,41-46,48,49,51} were eligible for inclusion in the meta-analysis, as shown in the appendix (Table S3 and S4). One study by Swedo et al.⁴⁸ reported findings for two distinct populations: North and South Dakota (NSD) and Kansas, Michigan, and Rhode Island (KMRI), which were treated as separate estimates.

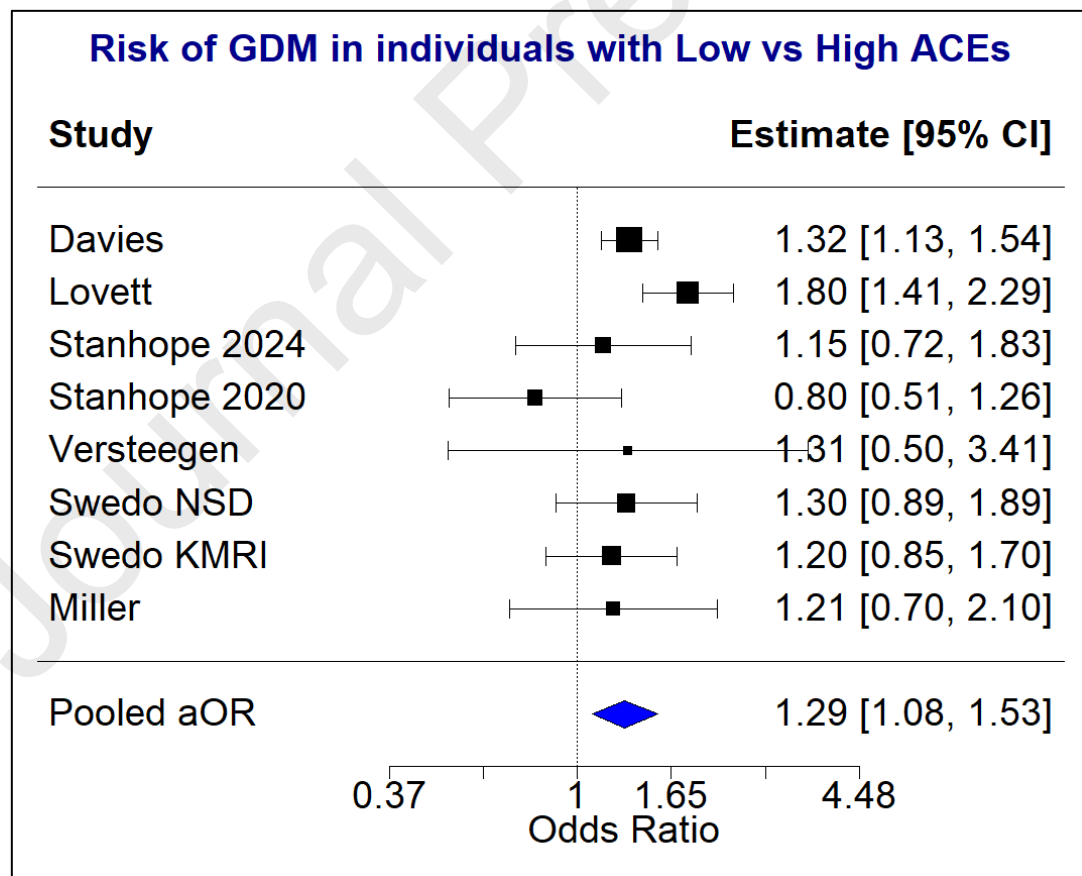


Figure 3. Risk of GDM in individuals with No ACE vs Any ACEs and Low ACEs vs High ACEs

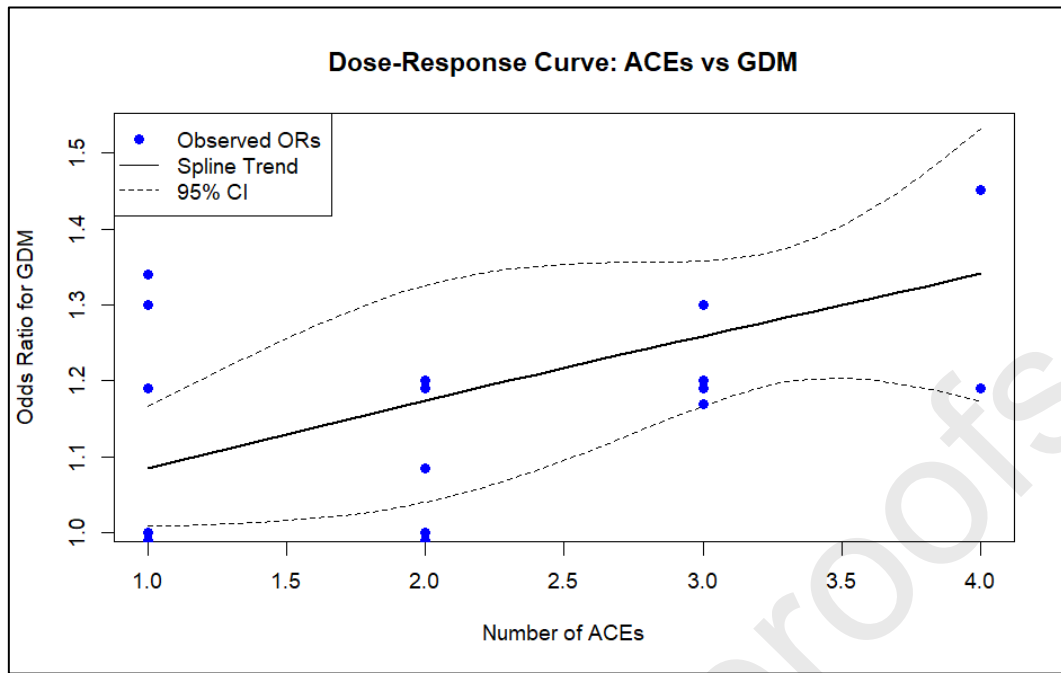






Figure 4. Dose-Response Relationship of ACEs and GDM


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Table 1. Study Characteristics



Table 1. Study Characteristics



Authors	Country	Participants N =	Study Design	Study Overview	Adjustment	ACEs tools	Overall Outcomes	Meta-Analysis	Overall risk of bias
<i>Davies et al. 2024.⁴¹</i>	Denmark	208,207	Prospective cohort	<p>Ethnicity: Maternally predominantly European origin,</p> <p>SES: high income and education level</p> <p>Parity: Nulliparous,</p> <p>Mean maternal age: 27.1 (low adversity) vs 24.1 (high adversity)</p> <p>ACEs prevalence: 52%</p> <p>GDM prevalence: 2.6%</p>	Maternal age, SGA, parental education, birth year	Administrative records, maternal questionnaires, and child reports from DANLIFE to construct domains of adversity.	Any adversity (vs. low) associated with higher GDM risk, but increasing adversity does not show a linear or graded increase in risk beyond a certain point.	Included	
<i>Maeda et al. 2024.⁴²</i>	Japan	5,444	Cross-sectional	<p>Ethnicity: Japanese</p> <p>SES: high income and education level</p> <p>Mean maternal</p>	Parity, maternal age at delivery, maternal pre-pregnancy BMI, household income, maternal	ACE-J	The highest GDM risk was in the 1 ACE group, showing possibility of buffer	Included	


				age: ~32 years old ACEs prevalence: 6.9% GDM prevalence: 5.8%	academic backgrounds, smoking status, gestational weight gain	effects (e.g. support from welfare system).		
<i>Lovett et al. 2024.</i> ⁴³	US	34,879	Prospective cohort	Ethnicity: predominantly NHW SES: College or associate degree (34%), middle income (41%), never smoke (58%) Parity: 2 nd (46%) Median age: 40-50s ACEs prevalence: 67% GDM prevalence: 4.1%	Age at baseline, race and ethnicity, childhood SES	Brief Betrayal Trauma Survey (BBTS)	22% increase in the risk for GDM was observed among women with a history of any trauma in early life. The high trauma class had nearly double the risk of GDM compared to the low trauma group; moderate was second.	Included 
<i>Schoenaker et al. 2019.</i> ³²	Australia	6,317	Prospective cohort	Ethnicity: predominantly Australian born (White) SES: highly educated	Family history of diabetes, age at menarche, PCOS, pre-conception BMI, diet quality, parity,	Modified CDC-Kaiser ACE-10 into Custom 9-item questionnaire (covering common	The association between ACEs and a greater GDM risk was confined to	Included 





				<p>Parity: nulliparous 88.7%</p> <p>Mean maternal age: ~28 years</p> <p>ACEs prevalence: 45.3%</p> <p>GDM prevalence: 8%</p>	maternal age, and antenatal depression	ACE domains)	pregnancies where the mother had symptoms of depression before conceiving; a dose-response pattern was also observed in this group.	
<i>Mason et al. 2016.</i> ⁴⁴	UK	45,500	Prospective cohort	<p>Ethnicity: predominantly NHW</p> <p>Mean maternal age: 28 years</p> <p>SES: mean over 12 years of education</p> <p>Parity: mean 2.3</p> <p>Physical abuse: 53%</p> <p>Sexual abuse: 32.7%</p> <p>GDM prevalence: 5%</p>	Demographics (maternal age, birth year, race), SES (parental education, occupation, home ownership), and health history (parental diabetes, child's body size at age 5).	Revised Conflict Tactic Scales; sexual abuse screening	A statistically significant link emerged between a history of childhood physical and sexual abuse and an increased GDM risk. This risk was greatest for women exposed to both severe physical and forced sexual abuse, and a graded, dose-response relationship was also observed for	Included 

							physical abuse.		
<i>Stanhope et al. 2024.</i> ⁴⁵	US	1,033	Prospective cohort	<p>Ethnicity: white (53.8%) and black (46.2%)</p> <p>SES: predominantly 12-15 years of school, and unmarried (73.1%)</p> <p>Parity: predominantly nulliparous</p> <p>ACEs prevalence: 2.6%</p> <p>GDM prevalence: 13.1%</p>	Parental education level, race, maternal age during pregnancy, and parity.	Childhood Family Environment Scale (CFE)	A statistically significant link emerged between higher childhood abuse scores and an increased likelihood of GDM, with the odds of GDM rising by 30% for every point increase on the abuse subscale.	Included	
<i>Stanhope et al. 2020.</i> ⁴⁶	US	2319	Cross-sectional	<p>Ethnicity: Hispanic / Latina women</p> <p>SES: predominantly greater than high school graduates, and never smokes (72.6%)</p> <p>Parity: mean 2.9</p> <p>Mean maternal</p>	Childhood SES, including education, race, age at US arrival, and migration status.	CDC-Kaiser ACE-10	No significant association between ACEs and GDM was identified	Included	

				age: 46.9 years					
				ACEs prevalence: 77.4%					
				GDM prevalence: 9.2%					
<i>Versteegen et al. 2021.</i> ³³	US	266	Prospective cohort	Ethnicity: NHW (52.4%) SES: predominantly low-income (16%), post-high school graduates (62%), and unmarried (62.4%)	Age, BMI	CDC–Kaiser ACE-10	No significant relationship between ACEs and GDM both for continuous and categorical ACEs.	Included	
				ACEs prevalence: 70.6%					
				GDM prevalence: 8.3%					
<i>Imanishi et al. 2025.</i> ⁴⁷	Japan	5693	Retrospective cohort	Ethnicity: Japanese SES: predominantly high income Parity: nulliparous Mean maternal age: 32 years	-	ACE-J	No association between ACEs and GDM nor linear or graded increase of GDM risk with greater ACEs	Excluded from meta-analysis. Reason: double data possibility with Maeda et al.	

							exposure	
				ACEs prevalence: 37.8%			.	
				GDM prevalence: 5.6%			.	
<i>Swedo et al. 2023.</i> ⁴⁸	US	14510	Cross-sectional	Ethnicity: predominantly NHW SES: high school or higher Maternal age: predominantly 25-34 years Parity: predominantly multiparous ACEs prevalence: 51.3% GDM prevalence NSD: 10.3% GDM prevalence KMRI: 9%	Age, race / ethnicity, marital status, parity, education, and insurance status.	8 items Behavioral Risk Factor Surveillance System (BRFSS)	There is a significant association between ACEs and GDM especially at higher exposure	Included 
<i>Miller et al. 2021.</i> ⁴⁹	US	1274	Cross-sectional	Ethnicity: White (58.8%) SES: no data Mean maternal	Maternal age, insurance, marital status, tobacco use, chronic medical conditions	CDC–Kaiser ACE-10	No statistically significant association between ACEs and GDM,	Included 

				<p>age: 32-33 years</p> <p>Parity: predominantly nulliparous</p> <p>ACEs prevalence: 93%</p> <p>GDM prevalence: 6.8%</p>	, and obesity.	<p>while GDM prevalence appeared higher in group with higher ACEs exposure (7.4% vs 6.7%), the trend was weak and insignificant.</p>		
<i>Jasthi et al. 2023.</i> ⁵⁰	US	192	Retrospective cohort	<p>Ethnicity: - black (91.7%)</p> <p>SES: high school or higher graduate (75.6%), low-income women referred to a specialist in mental health case management to elevated psychosocial risk</p> <p>Mean maternal age: 25.5 years</p> <p>Parity: mean 3.2</p> <p>ACEs prevalence: 47.4%</p>	CDC–Kaiser ACE-10	<p>No significant association was found between ACEs and GDM. While there was a slight, non-significant increase in GDM cases at higher levels of ACE exposure, the magnitude of this difference was minor</p>	<p>Excluded from meta-analysis.</p> <p>Reason: not enough data, the number of GDM cases is too low.</p>	

GDM prevalence: 7.3%								
<i>Mendez et al. 2024.⁵¹</i>	US	1163	Prospective cohort	Ethnicity: 45% African American, 35% White, 16% Hispanic ACEs prevalence: 48% GDM prevalence: 5.9%	Age, education, Medicaid status at delivery, marital status, race, employment status, tobacco use during pregnancy, BMI, parity, and care group.	CDC–Kaiser ACE-10	No significant association for the general exposure to ACEs, however those with both childhood abuse and high work stress had nearly 4 times the odds of developing GDM.	Included 
<div style="text-align: right;"> Low risk    Moderate risk High risk </div>								

SES: Socioeconomic status, SGA: Small for gestational age, BMI: body mass index, DANLIFE: the DANish Life-course Cohort, ACE-J: Culturally adapted version of the CDC-Kaiser ACE-10 questionnaire; NHW: Non-hispanic white, PCOS: Poly-cystic ovarian syndrome

Highlights

- Adverse childhood experience is associated with a higher risk of gestational diabetes.

- A dose–response relationship links increasing adversity to gestational diabetes risk.
- Evidence is synthesised from 13 studies including over 320,000 pregnancies.
- Retrospective adversity assessment contributes to a moderate risk of bias.
- Findings support life-course and trauma-informed approaches in maternity care.

Abstract

Gestational diabetes mellitus (GDM) has consequences for maternal and offspring health. Adverse childhood experiences (ACEs) contribute to GDM risk, but findings have been inconsistent. We synthesised evidence using a systematic review and meta-analysis of observational studies on ACEs before age 18 and GDM, including dose–response effects. Nine databases were searched from inception to 30 May 2025 based on a PROSPERO-registered protocol (CRD420251035754). Studies without extractable estimates or assessing diabetes not restricted to gestational onset were excluded. Two reviewers independently screened studies, extracted data, and assessed risk of bias using ROBINS-E. Random-effects models pooled adjusted odds ratios (aORs), with dose–response analyses using the Greenland–Longnecker method. Thirteen studies met eligibility criteria, 11 contributed to meta-analysis ($n = 326,797$). ACE exposure was associated with higher odds of GDM (aOR 1.15, 95% CI 1.12–1.18; $I^2 = 0\%$). A cumulative dose–response effect was observed, with each additional ACE increasing GDM odds (aOR 1.13, 95% CI 1.08–1.19). This study extends prior work by incorporating dose-response modelling, updated pooled estimates from recent cohorts, a pregnancy-focused risk window, and consideration of mediating and moderating pathways. Overall, ACEs are associated with increased risk of GDM, supporting a life-course approach to maternity care.